Società Chimica Italiana

XXIV Congresso Nazionale della Società Chimica Italiana

Lecce 11-16 settembre 2011

International Year of CHEMISTRY 2011

ATTI DEL CONGRESSO

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Cari Colleghi,
c'è chi fa risalire la nascita della Chimica come scienza moderna al settembre del 1860 quando a Karlsruhe, nel corso del primo Congresso Internazionale di Chimica, Stanislao Cannizzaro presenta una teoria che, sulla base delle ipotesi di Amedeo Avogadro, permette di costruire la prima scala dei pesi atomici degli elementi.
Ad oltre 150 anni da quell'evento che idealmente unisce sin dalle origini, dal Piemonte alla Sicilia, la Chimica Italiana, nell'Anno Internazionale della Chimica, siamo lieti di invitare a Lecce il XXIV Congresso della Società Chimica Italiana.

I Comitati Scientifico ed Organizzatore

Amedeo Avogadro Torino 1776 – Torino 1856

Stanislao Cannizzaro Palermo 1826 – Roma 1910

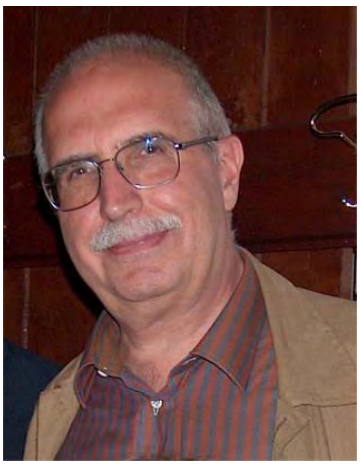
Le Medaglie della S.C.I.

Medaglia d'oro "Raffaele Piria"

PROFESSOR OTTORINO DE LUCCHI
Università Ca' Foscari - Venezia

"PER IL SUO CONTRIBUTO ALLO SVILUPPO DELLA CHIMICA ORGANICA, IN PARTICOLARE PER LA SINTESI DI STRUTTURE CHIRALI AD ALTA SIMMETRIA ED IL LORO IMPIEGO COME RECETTORI MOLECOLARI"

Medaglia d’oro “Stanislao Cannizzaro”



PROFESSOR SALVATORE COLUCCIA

Università degli Studi di Torino

“DISTINTOSI PARTICOLARMENTE NELLO STUDIO DELLA SUPERFICIE DI MATERIALI AD ELEVATA DISPERSIONE, CONTRIBUENDO IN MODO FONDAMENTALE ALLA COMPRENSIONE DEI PROCESSI INTERFASALI CHE SI MANIFESTANO NEI PROCESSI CATALITICI, DI FOTOCATALISI E NELLA SENSORISTICA. IL PROFESSOR COLUCCIA HA ANCHE MIRABILMENTE CONTRIBUITO A PROBLEMATICHE AMBIENTALI, QUALI L’ABBATTIMENTO DI INQUINANTI E ALLO STUDIO DELLA TOSSICITA’ DI POLVERI. LA SUA ATTIVITA' HA CONTRIBUITO IN MODO SOSTANZIALE ALLA CRESCITA DELL’IMMAGINE DELLA CHIMICA ITALIANA A LIVELLO INTERNAZIONALE”

Medaglia d’oro “Emanuele Paternò”

PROFESSOR ELIO SANTACESARIA

Università degli Studi di Napoli “Federico II”

“SCIENZIATO DI LEVATURA MONDIALE NELLO STUDIO ED IMPLEMENTAZIONE DI PROCESSI CHIMICI ECO-SOSTENIBILI, PARTICOLARMENTE NEI CAMPI DELLA PRODUZIONE DEI TENSIOATTIVI NON IONICI, DELL’ACQUA OSSIGENATA E PIU’ RECENTEMENTE DELLA PRODUZIONE DI BIODIESEL, IL PROFESSOR SANTACESARIA SI E’ SEMPRE CARATTERIZZATO PER IL SUO STRETTO RAPPORTO CON NUMEROSE AZIENDE CHIMICHE ITALIANE PER LE QUALI HA SVILUPPATO NUOVI PROCESSI O NE HA MIGLIORATO LE TECNOLOGIE. MAESTRO DI CHIMICA INDUSTRIALE PER I SUOI STUDENTI E COLLABORATORI, HA CONTINUAMENTE SVOLTO UN’INTENSA E RILEVANTE OPERA NELLA SOCIETÀ CHIMICA ITALIANA, NON SOLO NEI CAMPI SCIENTIFICI A LUI PIU’ VICINI MA ANCHE IN ALTRI, QUALI AD ESEMPIO IL BANDO DELLE ARMI CHIMICHE, IN CUI HA POTUTO FAR RISALTARE I PROPRI VALORI ETICI”

Medaglia d’oro “Giulio Natta”

PROFESSOR GIULIANO LONGONI

Università di Bologna

“PER L'AUTOREVOLEZZA, L'ORIGINALITA', L'AMPIEZZA DI VEDUTE CON CUI DA MOLTO TEMPO GUIDA A LIVELLO INTERNAZIONALE LA RICERCA CHIMICA NEL SETTORE DEI CLUSTER METALLICI MOLECOLARI. IL PROFESSOR LONGONI HA MOSTRATO DI POSSEDERE SIA LA CAPACITA' DI RACCOGLIERE CON SUCCESSO L'EREDITA' PIONIERISTICA DEL COMPIANTO PROFESSOR PAOLO CHINI, CHE LE RISORSE NECESSARIE PER FAR PROGREDIRE LA RICERCA SUI CLUSTER METALLICI MOLECOLARI VERSO APPLICAZIONI NUOVE E DI FRONTIERA NEI SETTORI DELLE SCIENZE NANOTECNOLOGICHE E DELLA CATALISI, ONORANDO COSI' CON LE SUE RICERCHE L'INTERA CHIMICA ITALIANA ED ACCRESCENDONE IL PRESTIGIO NEL MONDO”

Medaglia d'oro "Amedeo Avogadro"

PROFESSOR ENRICO RIZZARELLI

Università di Catania

"PER IL PRESTIGIOSO LAVORO SCIENTIFICO CHE LO VEDE SCIENZIATO DI INDISCUSSA FAMA INTERNAZIONALE NELL'AMBITO DEI PROCESSI DI RICONOSCIMENTO MOLECOLARE ASSISTITI DA IONI METALLICI E NELLO STUDIO DELLE MALATTIE DERIVANTI DA MISFOLDING PROTEICO. COME SCIENZIATO E ORGANIZZATORE DI VARI ASPETTI DELLA RICERCA UNIVERSITARIA HA ONORATO LA COMUNITÀ CHIMICA, ITALIANA ED INTERNAZIONALE, ED HA APERTO NUOVE STRADE PER LO SVILUPPO DELLE SCIENZE CHIMICHE IN AMBITI INNOVATIVI E FORTEMENTE INTERDISCIPLINARI"

Medaglia d’oro “Domenico Marotta”

PROFESSOR FRANCESCO DE ANGELIS

Università degli Studi dell’Aquila

“PER I MERITI ACQUISITI NELLA ORGANIZZAZIONE DI ATTIVITÀ IN CAMPO CHIMICO E NELLA DIFFUSIONE DELLA CULTURA CHIMICA, OLTRE CHE LA PARTICOLARE ATTENZIONE RIVOLTA ALLA DIDATTICA ED ALLE ISTANZE PROVENIENTI DAL MONDO DELL'ISTRUZIONE. IN PARTICOLARE IL PROFESSOR DE ANGELIS HA SVOLTO UNA STRAORDINARIA ATTIVITÀ NELL'AMBITO DELLA SOCIETÀ CHIMICA ITALIANA, CULMINATA CON LA CARICA DI PRESIDENTE NEL TRIENNIO 2005-2007, PORTANDO PARTICOLARE ATTENZIONE ALLO SVILUPPO DELLE NUOVE ATTIVITÀ EDITORIALI IN COLLEGAMENTO CON LE SOCIETÀ CHIMCHE EUROPEE E ALL'ATTIVAZIONE DI IMPORTANTI CONVENZIONI QUALI QUELLE CON ECTNA, FEDERCHIMICA, AIDIC, CONSIGLIO NAZIONALE DEI CHIMICI E WWF ITALIA”

Medaglia d'oro "Enzo Tiezzi"

PROFESSOR DEMETRIO PITEA

Università degli Studi di Milano - Bicocca

"PER IL SUO CONTRIBUTO ALLA COMPRENSIONE E ALLA RISOLUZIONE DI PROBLEMATICHE AMBIENTALI, ATTRAVERSO LO SVILUPPO E L'APPLICAZIONE DI UN APPROCCIO CHIMICO INTERDISCIPLINARE, ALL'INTERNO DI UNA VISIONE SISTEMICA E COMPLESSA DEL RAPPORTO UOMO-NATURA. IL PROFESSOR DEMETRIO PITEA SI È PARTICOLARMENTE DISTINTO PER GLI STUDI RIGUARDANTI LA VALUTAZIONE E LA MITIGAZIONE DELL'IMPATTO SULL'AMBIENTE DI PRODOTTI E PROCESSI IN UN'OTTICA DI SVILUPPO SOSTENIBILE, DEDICANDOSI ALL'OTTIMIZZAZIONE DELLA GESTIONE DEL CICLO DEI RIFIUTI, STUDIANDO I MECCANISMI DI FORMAZIONE E DISTRUZIONE DI MICROINQUINANTI ORGANOCLORURATI IN PROCESSI TERMICI E SVILUPPANDO L'APPLICAZIONE DI NUOVI INDICATORI DI SOSTENIBILITÀ"

Programma comune

PC-01 TiO_2 Photocatalysis and Related Surface Phenomena

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The field of photocatalysis can be traced back more than 80 years to early observations of the chalking of titania-based paints and to studies of the darkening of metal oxides in contact with organic compounds in sunlight. During the past 20 years, it has become an extremely well researched field due to practical interest in air and water remediation, self-cleaning surfaces, and self-sterilizing surfaces. During the same period, there has also been a strong effort to use photocatalysis for light-assisted production of hydrogen. The fundamental aspects of photocatalysis on the most studied photocatalyst, titania (TiO2), are still being actively researched and have recently become quite well understood. The mechanisms by which certain types of organic compounds are decomposed completely to carbon dioxide and water have been delineated. However, certain aspects, such as the photo-induced wetting phenomenon, remain controversial, with some groups maintaining that the effect is a simple one in which organic contaminants are decomposed, while other groups maintain that there are additional effects in which the intrinsic surface properties are modified by light. During the past several years, powerful tools such as surface spectroscopic techniques and scanning probe techniques performed on single crystals in ultrahigh vacuum, and ultrafast pulsed laser spectroscopic techniques have been brought to bear on these problems, and new insights have become possible. Quantum chemical calculations have also provided new insights. New materials have recently been developed based on TiO2, and the sensitivity to visible light has improved. The new information available is staggering, but we hope to offer an overview of some of the recent highlights, as well as to review some of the origins and indicate some possible new directions.

In this lecture, I will follow the history of TiO2 photocatalysis, outline the contribution of photocatalysis to a comfortable and safe urban environment, and highlight some important points related to the future development of photocatalysis, including the problem of utilizing visible light and the standardization of photocatalytic systems. I will also introduce our Photocatalysis Museum, which is attached to the Kanagawa Academy of Science and Technology. In addition, I will present some of our recent studies on novel photocatalyst materials and novel applications of photocatalysis.

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PC-02 Nutraceuticals and Functional Foods: Their Chemistry and Role in Health Promotion

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Nutraceuticals and functional food ingredients are important in rendering physiological benefits and reducing the risk of a myriad of degenerative disorders. Therefore, their intended use is for prevention rather than treatment. While nutraceuticals are used in the medicinal form, functional foods resemble commonly used traditional foods. In this connection, there are two classes of compounds that have received increasing attention in recent years. These include antioxidants, represented mainly by phenolic and polyphenolic compounds, and omega-3 oils. Phenolic compounds are secondary metabolites of phenylalanine and tyrosine, and are widely distributed in plants. The health benefits of antioxidants, including phenolic compounds, are rendered by their ability to neutralize free radicals, among others, for relieving oxidative stress and associated disorders. Meanwhile, omega-3 fatty acids, mainly those from the liver of lean fish such as cod and halibut, the body of fatty fish such as salmon, mackerel and herring or blubber of marine mammals such as whales and seals as well as algal sources, are appreciated for their cardioprotective role and anti-inflammatory function. The presentation will provide a cursory account of the chemistry and health promotion and disease risk reduction of these bioactives. It will also provide examples of unexpected results when bioactive compounds are conjugated together, such as green tea catechins with omega-3 fatty acids where the resultant esters played a multifunctional role in disease risk reduction.

PC-03 The importance of secoiridoid derivatives in food chemistry

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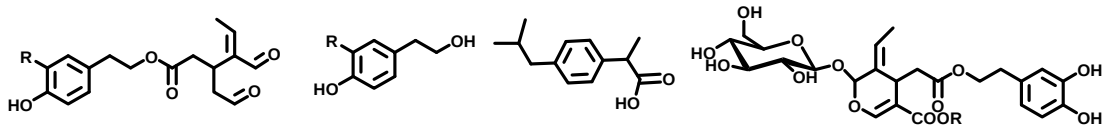
Oleuropein and its derivatives are secoBiophenols present in considerable amounts in olive leaves, drupes and virgin olive oils, which are responsible for its peculiar bitter taste and its stability.[1] Recent findings demonstrate that olive vegetation water (OVW) is active like a natural anti-inflammatory drug. Moreover, (-) oleocantal, a fenolic aglycone of olive oil responsible for throat irritation, inhibit the cyclooxygenase enzymes in the prostaglandin-biosynthesis pathway with the same potency and profile of ibuprofen.[2]
The easy access to the oleopentadial,[3] High-Throughput Assayed the UHPLC-ESI-MS/MS and Isotope Dilution Methods,[4] has allowed us also to investigate the the anti-inflammatory effect of oleopentanedial in a cell model we developed to mimic inflammatory injury of endothelium. Another a set of hydroxytyrosol conjugates with fatty acids at different molecular weights was synthesized under mild conditions. The topical delivery features of these new set of antioxidant molecules was evaluated as a function of their permeation profiles through the human stratum corneum and viable epidermis (SCE) membranes.[5]



1. R= OH; Oleopentanedial
2. R= H; Oleocanthal

3. R= OH; Hydroxytyrosol
4. R= H; Tyrosol

(+) Ibuprofen

5. R= Me; Oleuropeine
6. R= H; Demethyloleuropeine

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A. Procopio, C. Celia, M. Nardi, M. Oliverio, D. Paolino, G. Sindona *Journal of Natural Products*, **2011**, submitted

PC-04 Traceability of extra virgin olive oil by tandem mass spectrometry and spectroscopic analyses

Enzo Perri,[a] Laura Del Coco,[b,c] Gianluigi Cesari,[d] Innocenzo Muzzalupo,[a] Cinzia Benincasa,[a] Vito Simeone,[d] Giovanni Sindona,[e] Francesco P. Schena,[b] Francesco P. Fanizzi. [b, c]

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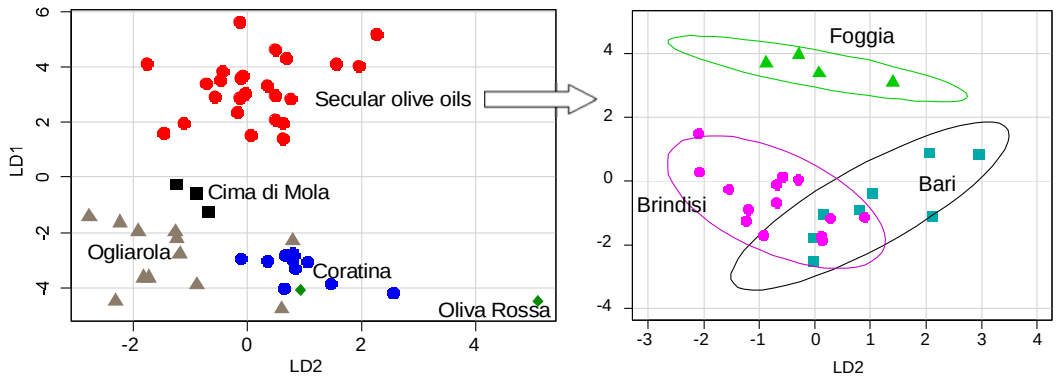
Recently, the European directives need that the origin of extra virgin olive oils should be clearly stated in the label. Particularly, PDO production is usually confined in a well-determined area and any fraudulent addition of foodstuff produced outside the defined area may alter the quality of the product. The discrimination between olive oils coming from different country, regions and/or area can be afforded by multivariate analysis of analytical data from extra virgin olive oils.

Analytical methods based on ICP-MS and high field NMR spectroscopy allows rapid determination of trace metals and ^{1}H resonances, respectively. Quantitative ^{1}H NMR data and ICP-MS data are very suitable to chemometrical analysis.

In general, the determination of metals and trace elements by ICP/MS in olive oil is important because of both the metabolic role of metals, for toxicological reasons and for olive oil traceability [1]. Rapid determination of 18 elements present in olive oil by ICP/MS, allowed, by means of linear discriminant analysis (LDA), the classification of unknown samples after checking possible differentiation of samples of known origin [1].

Apulia region is, traditionally, the most important area for olive oil production in Italy. Nevertheless the wide olive germplasm collection is not completely identified and a number of valuable cultivars are not enrolled yet in the Register of olive cultivation. About 10% of the genetic patrimony is constituted, in particular, of the secular and monumental olive trees. Characterization of extra virgin olive oils obtained from secular olive trees is a key factor to increase the value for this specific production. On the other hand this economic issue is very important to preserve the unique landscape offered by the ancient olive groves of the Apulia region in south east Italy. In this work, a first level investigation was carried out to study the variability and the relatedness inside a sample of secular trees and in comparison with known autochthonous cultivars. Multivariate analysis of ^{1}H NMR data for microextracted apulian extra virgin olive oils has been successfully used beside other spectroscopic techniques to characterize and differentiate secular from single cultivar genetically certified samples [2]. Moreover, olive oils obtained from secular olive trees could be easily differentiated not only from oils produced outside Italy but also according to their geographical origin within the different districts of the Apulia region.



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PC-05 Combined efforts of Apulian institutions, research centers and companies to setup new strategies for valorization of food products: the role of Chemistry

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In the foodstuff market, development of valorization strategies of food products represents an “ever green” issue that companies must face. In this framework, chemistry has always helped to preserve the trust between producers and consumers. Continuous efforts to develop powerful analytical methods resulted in excellent levels of quality control in terms of food safety. In fact, before commercialization, producers are obliged to follow strict protocols with the aim to certify, for instance, the absence (or the presence within the allowed limits) of dangerous residues from phytosanitary products. However, quality control in terms of merchandising is still based on declarations of typicality and geographical origin of the food products by producers, without the support of analytical methods. This makes difficult the valorization of food products, especially when producers apply for getting valuable valorization tools such as PDO (Protected Designation of Origin), PGI (Protected Geographical Indication) or TSG (Traditional Speciality Guaranteed) appellations.
Metabonomics aims to measure the global, dynamic metabolic response of the living systems to biological stimuli and represents the appropriate tool to certify quality, typicality and geographical origin of food products. Unfortunately, metabonomics is not yet recognized as a tool for official certifications, mainly because of lack of dialogue between institutions, research centers and companies.
In this communication, some projects launched by SAMER (Special Company of the Chamber of Commerce of Bari) that are aimed to valorize Apulian food products (wine, olive oil and table grapes) will be presented. In particular, two points will be highlighted: 1) the results of cooperation between SAMER, DIAC – Polytechnic of Bari, Innovative Solutions (Spin Off at Polytechnic of Bari) and other partners; 2) the role of Chemistry in the valorization of Apulian table grapes.

PC-06 Cultura chimica, scuole, cittadinanza scientifica

Pietro Greco

Viviamo nell'era della conoscenza ed emerge una nuova domanda di diritti diffusi chiamati diritti di cittadinanza scientifica, il cui presupposto è una diffusa cultura scientifica. La scuola è uno dei luoghi privilegiati per la diffusione di questa cultura.

Della cultura scientifica di base necessaria nell'era della conoscenza è parte imprescindibile la cultura chimica. Luoghi critici di diffusione della cultura chimica sono la scuola e i mass media.

La scuola non sempre riesce a trasmettere le nozioni e i concetti chimici di base che tutti devono possedere; la specifica identità culturale della chimica; il ruolo della chimica nello spazio delle scienze. Anche sui mezzi di comunicazione di massa l'immagine della chimica continua a essere distorta.

I chimici devono impegnarsi in maniera più sistematica per la diffusione di una solida cultura chimica nell'ambito della costruzione di una matura cittadinanza scientifica.

PC-07 Dynamic Covalent Capture: Dynamic Chemistry for Biomolecular Recognition and Catalysis

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Catalyst development is a challenging task, caused by the subtle effects that determine whether a catalyst is efficient or not. The chance of success is enhanced by using methodology that relies to a smaller extent on rational design.[1] The use of dynamic or reversible chemistry for the construction of catalysts is an attractive option as it allows for self-assembly and self-selection processes by the target.[2] Synthesis is restricted to the building blocks after which diversity is simply generated upon mixing.
Our initial challenge was to develop methodology that allows small differences in binding energy to be detected accurately. Recently, we have started to use a dynamic covalent capture approach in which intramolecular interactions affect the thermodynamic landscape of a dynamic combinatorial chemistry.[3] Because relying on the occurrence of intramolecular interactions, the dynamic covalent capture approach has a high sensitivity and is able to detect weak interactions that would go unnoticed otherwise. We have shown that this allows for the self-selection of functional groups able to assist intramolecularly in the cleavage of a neighbouring carboxylic ester.[4]
Currently, we are increasing the complexity of the system by assembling catalytic units on the surface of monolayer protected Au nanoparticles (Au MPCs).[5,6] It will be shown that the assembly of small peptides on the surface of a Au MPC causes a strong increase in catalytic activity.

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PC-08 MOSAIC: Patterning the surface of monolayer-protected nanoparticles to obtain intelligent nanodevices

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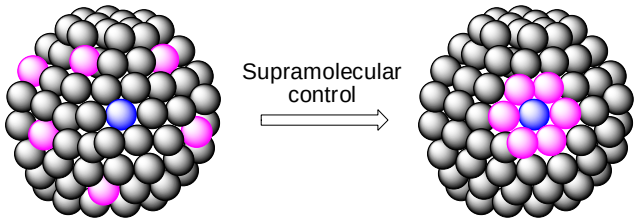

The concept of "molecular machines" has become common even in the everyday language to describe the ultimate achievements expec-ted from chemical research. The term has gained a much broader significance than the original one and includes any molecular or nanoscopic entity capable to perform the highly sophisticated functions typical of macroscopic devices, ranging from controlled dislocation to transformation, delivery and information processing.

While chemical science is still striving in the search for such molecular machinery, real and perfectly working molecular machines have been developed millions of years ago by Nature. When the main characters at play in biological systems, such as proteins, nucleic acids, and membranes, are examined in detail, one striking feature that emerges is their intrinsic functional simplicity, since only a few building block are used to build complex structures. Apparently, what matters is not chemical complexity but the ability of precisely control the spatial arrangement and organization of simple building blocks.

Functional nanoparticles, where a metal nanocluster is stabilized by a monolayer of organic molecules, offer unmatched opportunity to build complex structures with simple building blocks and relatively simple manipulations. The main goal of the Mosaic project is to gain the ability to hierarchically control the self-assembling of metal nanoparticles coating monolayers and take advantage from such ability to obtain complex function from the materials realized. This objective will require to reach a complete understanding of the structure and dynamic of nanoparticles coating monolayers developing new tools for their investigation. Then, we plan to learn how to use supramolecular interactions to control the monolayer organization and to gain, in this way, the ability to program functional groups patterns on the surface of the particles. In this way, it will possible to achieve a degree of organization comparable to that of biologic systems, such as enzymes or membranes. This organization of functional groups will be then used to obtain highly sophisticated function by these nanosystems, such as recognition, sensing, catalysis and transport.

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PC-09 Electronic Structure of Chemical and Biochemical Systems: Multiscale Approach with Electron Correlation

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The currently available computational methods have often serious limitations to treat systems where electron correlation plays an important role. Many issues concerning the electronic structure of radicals, photoreceptors and near-half-filled transition metals (Cr,Mo,Fe,Ni) are of paramount relevance in basic and applied research in Chemistry and Biochemistry, but still out of the capabilities of standard and conventional tools such as Density Functional Theory (DFT). On the other hand, the application of more computationally demanding post-Hartree-Fock methods are currently limited to few atoms. The objective of the European Research Council project MultiscaleChemBio (Grant n° 240624) is to overcome these limitations and to develop and apply an innovative and unconventional computer simulation technique to unravel the electronic properties of strongly correlated chemical and biochemical systems. The methodology is based on a multiscale approach based on Quantum Monte Carlo (QMC), DFT and Molecular Mechanics. In term of scaling of the computer time as a function of the system size N, the proposed approach has a better behaviour than others standard quantum chemistry methods of equivalent level (~ N4 vs ~ N7). The multiscale technique is under development and it will be used to address challenging open problems in the chemistry and biochemistry of radical compounds, photoreceptors, transition metal catalysis and enzymatic activity. One important part of the applications will be devoted to the study of the molecular mechanisms regulating natural and artificial photosynthesis.

PC-10 New functionalized nanoparticles as MRI and molecular imaging contrast agents: chemical, physical and relaxation properties.

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In this presentation, I will talk about the project "*Caratterizzazione chimico fisica di nuovi agenti di contrasto per risonanza magnetica di imaging (MRI) a 7 Tesla*", granted by L'Oreal Italia-Unesco in 2010. In particular, the focus is on functionalized iron oxide nanoparticles, deeply investigated in the last years for their high potentialities for biomedical applications, both diagnostic and therapeutic ones [1,2]. The efficiency of these nanoparticles as MRI contrast agents and in particular their effect on the 1H relaxation rates, R (s-1), of water molecules is related to a complex interplay [3] among different features, such as magnetic-core size, monodispersivity, type of coating, concentration in water, magnetic field strength and cluster formation [4].

Acknowledgments:
I wish to thank Prof. Carlo Alberto Veracini for helpful discussions; Sara Dolci, Dr. Vincenzo Ierardi, Dr. Mario Cifelli, Prof. Guido Pampaloni, Dr. Anton Gradišek and Prof. Žvonko Jagličič are acknowledged for their collaboration. I thank **L'Oreal Italia-Unesco "Donne per la Scienza" grant 2010**.

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PC-11 ‘Vincenzo Caglioti’ Prize and Computational Chemistry

A. Pedone

The computational simulation of matter at the atomic level is now an essential tool for contemporary science. Atomic modeling techniques are used routinely in the study of proteins and pharmaceuticals and in the conformational analysis of organic molecules. Computational methodologies have, however, an equally important role in the study of inorganic and hybrid materials.
My research activity, which started in 2005, is focused on the calculation of chemical-physical properties of complex systems such as silica-based glasses, biomaterials and dye-doped silica nanoparticles.
In this communication, a brief discussion on the potentialities reached by computational chemistry to the study of real systems will be offered by taking some examples from my previous works which allowed me to win the prestigious prized released by the ‘Accademia Nazionale dei Lincei’.
The final aim is to demonstrate that computational chemistry is now an essential tool to guide and support experimental studies and succeed in ambitious Italian and European research projects.

PC-12 Molecular/Hybrid Micro-Nanotechnologies for Photonic Applications

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Despite the growing interest in organic and hybrid materials based on colloidal nanocrystals, related to their excellent properties in terms of colour tuning, flexibility and low cost of fabrication, the persisting limit for their full exploitation in advanced devices stands in the lack of well established lithographic and device fabrication techniques suitable for this class of materials. Conventional lithographic technologies, such as photolithography and electron beam lithography, are not in fact compatible with soft and soluble molecular materials and standard deposition techniques are not suitable for novel hybrid nanocomposites. This prevents the possibility to realize complex devices and nanostructures able to increase device performances. Thus, a step forward for organic/hybrid opto-electronics necessarily passes through the development of a suitable technology for high resolution patterning and material deposition. In this talk novel approaches for the fabrication of advanced organic and hybrid photonic devices , such as lasers, light emitting diodes, emitting fibers and solar cells will be presented.

PC-13 Application of Semiconductor Nanomaterials in Solar Energy Conversion Processes

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The contribution will focus on the use of semiconductor nanomaterials for direct conversion of solar energy to electricity in Dye Sensitized Solar Cells (DSSCs) as well as in photoinduced water splitting processes.
DSSCs are among the most promising solar energy conversion devices of new generation, since they may couple ease of fabrication, low cost and offer the possibility of building integration in photovoltaic windows and facades. Although in their earliest configuration these systems are close to commercialization, fundamental studies are still required for developing new molecules and materials with more desirable properties. Some recent advances made in the effort of improving DSSCs efficiencies by finding alternative materials are presented.
In the field of hydrogen production, it has recently been found that potentiostatic anodization of metallic tungsten in a suitable solvent provides an effective mean for producing a highly efficient nanostructured WO_3 layer for photoassisted electrolysis. Under 0.3 W/cm^2 solar irradiation, plateau photocurrents in the order of 10 mA/cm^2 are reproducibly observed in acidic medium.
Recent advances in the field of photoelectrochemical (PEC) cells applied to water and H_2S splitting are also discussed.

PC-14 Con le Nanotecnologie copiamo la Natura: Biomimetismo e Geomimetismo.
"La Natura, il supremo architetto da cui imparare a costruire i materiali del domani"

N. Roveri

Chiamiamo "materiali biogenici", i materiali prodotti dai sistemi biologici, ovvero i materiali di cui sono costituiti gli esseri viventi che popolano il nostro pianeta, siano essi vertebrati o invertebrati, esseri umani o unicellulari. I materiali biogenici sono costituiti da un limitato numero di molecole e composti chimici che la Natura utilizza per ottenere materiali con proprietà e funzionalità molto diverse tra loro. I materiali biogenici presentano un elevato grado di sofisticazione strutturale, miniaturizzazione, organizzazione gerarchica, efficienza , resistenza alla fatica, capacità autoriparative ed adattabilità ai cambiamenti dell' intorno. Tutte proprietà che i materiali biogenici hanno acquisito attraverso specifici meccanismi di formazione selezionati dall' evoluzione che possono essere ottenute solo molto parzialmente nei materiali che noi prepariamo con gli attuali processi di sintesi. Per questa ragione la Natura è una importante scuola e fonte di ispirazione per chi si occupa di scienza dei materiali e il biomimetismo rappresenta una guida importante per la progettazione e la sintesi di materiali innovativi e tecnologici.
Mimando la Natura noi possiamo progettare e sintetizzare nuovi materiali sia inorganici che macromolecolari che vengono definiti "intelligenti" perché sono reattivi con i tessuti biologici e stimolano specifiche reazioni cellulari. Il biomimetismo dei materiali sintetici può essere portato avanti a vari livelli: composizione chimica, struttura, morfologia, area e reattività superficiale, aggregazione delle unità nanometriche fino a livello macroscopico cercando di mimare il più possibile i materiali biogenici. La chimica oggi grazie alle nanotecnologie e alle biotecnologie può spingere il biomimetismo fino a mimare le condizioni dei processi biochimici naturali utilizzando processi sintetici in base acquosa senza l' utilizzo di solventi organici, utilizzando soluzioni diluite e condizioni sintetiche a bassa pressione e temperatura. La chimica biomimetica non perturba l' ambiente e riesce a produrre materiali sintetici che le cellule scambiano per biogenici e come tali li accettano e li utilizzano.
Il biomimetismo si accompagna al geomimetismo il quale mima i materiali naturali di origine geologica quando questi presentano delle proprietà chimiche e strutturali che li rendono interessanti per specifiche applicazioni. L'esempio, io credo, più eclatante è quello delle fibre minerali di amianto che hanno rappresentato, rappresentano e continueranno a rappresentare uno dei pericoli più terrificanti per la salute umana. L'utilizzo delle fibre di amianto nel preparare manufatti industriali ha rappresentato un tragico errore del passato , ma la sintesi geomimetica di fibre di amianto sta rappresentando una prospettiva tecnologica del futuro. Infatti fibre che mimano per composizione, struttura e morfologia le fibre di amianto possono essere sintetizzate in laboratorio senza la presenza di certi ioni metallici che rendevano tossiche e cancerogene le fibre minerali. Non solo queste fibre sintetiche di amianto geomimetico non risultano tossiche e pericolose per la salute umana , ma rappresentano un innovativo materiale nanostrutturato a morfologia tubolare che potrà in futuro essere utilizzato per innovative applicazioni tecnologiche come nella realizzazione di nuovi pannelli fotovoltaici e pile per un più efficiente utilizzo dell' energia solare.

PC-15 Multiscale Simulations of Membrane Proteins

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Membrane proteins account for 25% of genes. They perform a number of key functions in cells, including transport and signalling across membranes. Advances in structural biology will reveal ca. 2500 structures for membrane proteins by 2020. However, experimental structures of isolated membrane proteins do not reveal their interactions with lipid bilayers or with other proteins in membranes. Multiscale MD simulations, by combining coarse-grained and atomistic resolution [1], allow us to probe the interactions of membrane proteins with their lipid bilayer environment. I will discuss the use of such simulations to probe protein/lipid and protein/protein interactions in membranes. I will illustrate this discussion with examples of recent studies of such interactions, including recognition of cell membranes by lipid binding PH domains [2], and signalling across cell membranes by integrins [3].

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PC-16 Ingegneria inversa delle idrogenasi: il contributo degli studi QM e QM/MM.

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Con il nome di ingegneria inversa vengono convenzionalmente indicati quei processi che permettono di rivelare i principi alla base del funzionamento di un dispositivo, mediante l'analisi della sua struttura, della sua funzione e del suo modo di operare. Dal punto di vista operativo, l'ingegneria inversa solitamente prevede l'analisi delle componenti di un dispositivo, al fine di progettare un dispositivo caratterizzato da analoghe funzioni.
Anche se il termina ingegneria inversa si applica generalmente allo studio di dispositivi progettati dall'uomo, la sua logica e le sue operazioni sono altrettanto efficaci nello studio di dispositivi molecolari (quali ad esempio gli enzimi) che sono stati plasmati e ottimizzati in milioni di anni di selezione naturale.
In particolare, l'ingegneria inversa applicata agli enzimi prevede generalmente i seguenti passaggi: a) identificazione della funzione dell'enzima, b) caratterizzazione strutturale, c) caratterizzazione del modo in cui opera il dispositivo molecolare (cioè descrizione del meccanismo catalitico), d) valutazione del ruolo di specifiche componenti dell'enzima sul modo di operare, e) progettazione di dispositivi molecolari originali utilizzando i principi acquisiti studiando il dispositivo originale.
Le idrogenasi sono enzimi che catalizzano la trasformazione di protoni ed elettroni in idrogeno molecolare, e rappresentano un esempio particolarmente interessante di dispositivi molecolari di origine naturale su cui si possono applicare i metodi dell'ingegneria inversa [1-3]. In particolare, tra i vari strumenti a disposizione del chimico, i metodi quantomeccanici si sono rivelati particolarmente efficaci in tutti gli stadi del processo di ingegneria inversa delle idrogenasi. In questo contributo verranno presentati recenti risultati riguardanti le proprietà elettroniche e strutturali di [FeFe] idrogenasi in differenti stati redox e di protonazione, e verrà discussa la loro rilevanza nella progettazione razionale di nuovi catalizzatori sintetici [4-7].

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PC-17 Probing the link between target affinity, ADMET and physicochemical properties: use of the "drug efficiency index" in modern drug discovery

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One of the key goals of drug discovery is to develop new medicines with low therapeutic dose to reduce drug burden and so to limit the attrition for direct organ toxicity. In order to achieve this, a common strategy is to maximize the target affinity under the assumption that only highly potent compounds have greater potential to translate into successful, low-dose therapeutics. This has led to the development of screening cascades with in vitro potency embedded as an early filter. However, this approach is beginning to be questioned, given the bias in structural properties that it can introduce early in lead generation and optimization. This bias is due to the often diametrically opposed relationship between physicochemical parameters associated with high in vitro potency and those associated with desirable absorption, distribution, metabolism, excretion and toxicity (ADMET) characteristics.

This lecture emphasizes the need to link early on in the process structural and biological design considering mathematically relevant equations for the prediction of drug efficacy. The drug efficiency index (DEI) is introduced as a single parameter directly connected to therapeutic dose with the potential to help lead optimization towards the selection of superior clinical candidates.

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PC-18 The Future of Fossils

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The today total primary energy supply is 112300 Mtoe[1]; the fossil fuels cover a little more than 80% of the total. The request of energy is expected to growth substantially in the next two decades. The percentage may range from 35% to 20% depending of the scenario adopted: the highest connects with the Reference Scenario, where the business continues as usual, and the lowest connects with the Alternative Policy Scenario (known as 450_Policy Scenario) where governments are adopting energy policies favouring a low carbon economy to reduce the GHG concentration in the atmosphere. Even in the latter scenario, however, the fossil fuels will cover about 70% of the energy mix in the year 2030.
Today the proved reserves of oil, gas and carbon amounts respectively to 1191 billion of barrels[2], 193,117 billion cubic meters[2] and over 847 billion tonnes[3]. This means that the life index, i.e. how many years a resource is expected to last of the current rates of production, are respectively 40 years for oil, 60 for gas and 118 for coal.
Earth hides more fossil fuels, often referred to as "unconventional" for oil and gas, that can easily double the amount of fossil energy available per source. Even more some of them are already tapping the world energy scenario: the shale gas is today booming particularly in the USA, allowing them to export gas while until a few years ago they were net importers.
Coal reserves to production ratio instead has been falling in the past years, probably because the use has grown quite rapidly (pushed by the large use of India and China as a very cheap primary source) and because a lack of incentives to promote the discovery of new reserves. The general conviction is that new discoveries are possible and the potential of developing countries are partially unknown.
.
The presentation discusses how the fossil fuels can constitute the back bone of the world energy system in the transition toward a carbon free energy

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PC-19 Recent developments on CO_2 capture process

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The aim of this contribution is to provide an overview of the state of the art on the CO_2 capture technologies with a mention on Enel CCS project.
CCS (Carbon Capture and Storage) technologies are seen as an important option for the climate change strategy in order to control the CO_2 emissions. Post-combustion CO_2 capture with amines technology is considered the most mature technology for medium term industrial application because i)experience on CO2 capture (up to 300 TPD) by means of chemical absorption processes had been developed for CO2 separation in Oil and Gas and chemical industry; ii) amine-base processes have been already tested at pilot.
One of the main research issues in the field of amine based solvent is finding the optimal solvent components: sterically hindered amines, ionic liquids, amino acids.
Moreover several alternative approach are under investigation: solid sorbent, membranes, enzyme based solvents, etc.

PC-20 Towards a CO_2-H_2 economy?

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The urgent need for strategies to develop new methodologies which allow to move towards a cleaner energy system has prompted actions from national and international governments and industries, and a number of high-profile collaborative programs have been established (Intergovernmental Panel on Climate Change, United Nations Framework Commission on Climate Change, and Global Climate Change Initiative). The first step to change our energy system seem to be the reduction of CO_2 emission which requires new technologies able to reduce the CO_2 emission.
Besides the well established CCS (Carbon Capture and Storage) technology a CCU (Carbon Capture and Utilisation) approach may play a major role: Carbon dioxide may represent an interesting raw material for developing innovative synthetic methodologies less intensive in carbon and energy. It can be used as building block for the synthesis of other C1 molecules, such as formic acid and methanol, and molecular and polymeric chemicals or source of carbon for fuels.
Concurrently, much attention is paid to the production and use of dihydrogen which rises concerns for its storage and transportation.
Then, why not to merge the two issues above and implement an operative solution for the conversion of large volumes of CO_2 by its hydrogenation into liquid fuels or methane?
Two possible approaches will be discussed: (i) the preliminary production of dihydrogen from renewable sources and water; (ii) the direct reduction of CO_2 in water.
The actual barriers to a large scale exploitation will be highlighted.

PC-21 The Central Role of Catalysis in Next Generation Biorefineries

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The development and implementation of biorefinery processes is of the upmost importance to meet the vision towards a sustainable economy based on bio-resources. In this context, catalysis, either enzymatic, heterogeneous or homogeneous is playing a major role like this is already the case in a 'conventional' refinery based on the treatment and the conversion of petro-resources. Nevertheless, contrary to petro-resources of which the nature and composition variations are 'relatively' limited, under the term 'bio-resource' or 'biomass' are gathered compounds of very different natures, namely cellulose, hemicellulose, oils, lignin and so on… Thus, a complete set of specific technologies must be developed in order to convert each fraction as smartly as possible. This implies, among others, the elaboration of a lot of processes based on catalysis. These latter constitute core technologies that will be implemented in the so-called 'biorefineries'. Within this frame, we are coordinating the elaboration and the development of the EuroBioRef concept 'EUROpean multilevel integrated BIOREFinery design for sustainable biomass processing', as a 'large-scale' European project. EuroBioRef is a new highly integrated, diversified and sustainable concept, which involves all the biomass sector stakeholders. The potential of all the fractions issued from the various types of biomass is used to yield a value-added as high as possible in a sustainable and economical way. The overall efficiency of this approach will be a vast improvement to the existing situation and considers options such as: Production and use of a high diversity of sustainable biomass adapted for European regions / Production and use of high specific energy bio-aviation fuels (42 MJ/kg) / Production of multiple products (chemicals, polymers, materials) in a flexible and optimized way that takes advantage of the differences in biomass components and intermediates / Improvement of the cost efficiency by as much as 30 per cent through improved reaction and separation effectiveness, reduced capital investments, improved plant and feedstock flexibility and reduction of production time and logistics / Reduction by 30 per cent of the required energy / Zero waste production and reduction of feedstock consumption. The EuroBioRef novel concept will be presented, in which the central and key role of catalysis will be discussed.

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PC-22 Perspectives in Chemistry: From Supramolecular Chemistry towards Adaptive Chemistry

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Supramolecular chemistry is actively exploring systems undergoing *self-organization*, i.e. systems capable of spontaneously generating well-defined functional supramolecular architectures by self-assembly from their components, on the basis of the *molecular information* stored in the covalent framework of the components and read out at the supramolecular level through specific non-covalent interactional algorithms, thus behaving as *programmed chemical systems*.

The design of molecular information controlled, "programmed" and functional self-organizing systems provides an original approach to nanoscience and nanotechnology. The spontaneous but controlled generation of well-defined, functional molecular and supramolecular architectures of nanometric size through self-organization represents a means of performing programmed *engineering* and *processing* of *functional nanostructures*. It offers a very powerful alternative to nanofabrication and to nanomanipulation for the development of nanotechnology.

Supramolecular chemistry is intrinsically a *dynamic chemistry* in view of the lability of the interactions connecting the molecular components of a supramolecular entity and the resulting ability of supramolecular species to exchange their components. The same holds for molecular chemistry when the molecular entity contains covalent bonds that may form and break reversibility, so as to allow a continuous change in constitution by reorganization and exchange of building blocks. These features define a *Constitutional Dynamic Chemistry* (CDC) on both the molecular and supramolecular levels.

CDC introduces a paradigm shift with respect to constitutionally static chemistry. The latter relies on design for the generation of a target entity, whereas CDC takes advantage of dynamic diversity to allow variation and selection. The implementation of selection in chemistry introduces a fundamental change in outlook. Whereas *self-organization by design* strives to achieve full control over the output molecular or supramolecular entity by explicit programming, *self-organization with selection* operates on dynamic constitutional diversity in response to either internal or external factors to achieve *adaptation*.

Applications of this approach in biological systems as well as in materials science will be described.

The merging of the features: - information and programmability, - dynamics and structural diversity, -constitution and selection, points towards the emergence of *adaptive* and *evolutive chemistry*.

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PC-23 Exploring the Protein Universe with Physical Chemistry Tools

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Structural biology is a highly attractive area for applications of methods of physical chemistry. For example, my research team is specialized in the use of nuclear magnetic resonance (NMR) spectroscopy for studies of proteins and other biological macromolecules. Thereby, NMR studies in classical "structural biology" are focused on proteins of well-known biological or biomedical interest, with examples from my laboratory in the areas of oxygen transport, immune suppression, differentiation in higher organisms, and transmissible encephalopathies such as mad cow disease. In today's post-genomic era, with the availability of the complete DNA sequences of a wide range of organisms, we are additionally faced with new opportunities and challenges in "structural genomics". The focus is then on gene products with unknown structures, unknown functions, and minimal similarity to previously studied proteins, in order to increase coverage of the protein sequence universe with three-dimensional structures. My team participates in projects of the Protein Structure Initiative (PSI:Biology, www.jcsg.org/prod/newscripts/sg-centers.cgi) and the NIH Roadmap for Medical Research (http://commonfund.nih.gov/aboutroadmap.aspx) which use another method of physical chemistry, structure determination by X-ray crystallography, as the principal technique. This presentation describes our strategies for use of solution NMR spectroscopy with soluble and membrane proteins in these crystallography-centered environments Our approaches should ensure an exciting role for NMR in the longer-term challenge leading from the expanding protein structure universe to new insights into protein functions and chemical biology, by generating data on protein structure, conformational equilibria, dynamics and intermolecular interactions in solution.

Indice Degli Autori

Chimica dell'Ambiente e dei Beni Culturali

ABC-OR-01 Development and evaluation of new paint cross-section preparation procedures

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A polychrome sample is generally characterized by a multilayer (10-100 µm each) structure where both organic and inorganic compounds are present. The characterisation and spatial location of these substances is of the outmost importance both for technical studies and the evaluation of the state of conservation of the painting under examination. The characterization of the chemical composition of painting materials may be considerably limited by the way in which cross sections are prepared for analysis. In particular, when paint samples are embedded into synthetic resins (epoxy, polyester, acrylic) the characterisation of the organic components is hard to be achieved unambiguously. Furthermore, the cross section surface morphology can affect the analytical performances of FTIR microscopy applications when spectra are collected in both total reflection and ATR mode. Recently [1] KBr has been proposed as an alternative embedding system to avoid pollution from embedding resins. However, the proposed procedure has some drawbacks concerning the fact that KBr is highly hygroscopic and fragile. Moreover, the dry polishing technique adopted may result in the contamination of paint layers with materials belonging to other layers as well as the retention of KBr particles. The polishing procedure, when carried out not automatically, relies on the skill of the operator who plays a crucial role in obtaining flat and regular cross sections. In order to overcome such limitations NaCl is proposed as alternative embedding system. The obtained cross sections resulted to be harder and less hygroscopic. Moreover, KBr procedure has been improved in order to obtain more reproducible cross section. To this purpose KBr cross sections were further embedded in a resin support. The obtained block was then polished using a hand lap which allowed to better control the applied pressure.

Argon Ion Milling was also tested as an alternative polishing system to prevent intra layers and KBr pollution.

Standard and real samples were embedded following the above mentioned procedures and the preparation methods evaluated by confocal microscopy, SEM-EDX and FTIR microscopy in both total reflection and ATR mode.

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ABC-OR-02 Application of scanning electrochemical microscopy as alternative immunochemical imaging technique for the detection of proteins in paint cross-sections

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The identification and localization of organic substances in paint complex stratigraphies plays a crucial role in studies on painting techniques and conservation of artworks. Immunological methods represent a valid approach for the detection of proteins in artistic samples thanks to the high specificity of antigen-antibody reactions, which would allow to distinguish between different proteins and to determine their biological source. Different detection procedures relying on specific labels can be applied for the recognition of immunocomplexes. Among them, chemiluminescence (CL) imaging already showed high performances in terms of spatial resolution and sensitivity, allowing the localization of proteins in paint cross-sections [1].

The present research has been focused on the development of an alternative detection approach for the immunolocalization of proteins (i.e., ovalbumin) in paint cross-sections based on Scanning ElectroChemical Microscopy (SECM) [2]. The immunochemical analysis has been performed directly on the paint cross-section using an anti-ovalbumin primary antibody and a secondary antibody labelled with horseradish peroxidase (HRP). The addition of a proper mediator has allowed the localization of the target protein by SECM through the detection of the products of the HRP-catalyzed oxidation reaction. Preliminary promising results have been obtained on cross-sections of samples from standard paint's mock ups.

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ABC-OR-03 Raman and luminescence spectroscopy of the "purple of the poor": the ancient colorant orcein

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Orcein is a natural dye widely used since ancient times for dyeing textiles but also for decorating miniatures and manuscripts. Known as the "purple of the poor", orcein was used in place of the more expensive Tyrian purple. Unlike the latter, orcein has a low lightfastness and in ancient works it is often faded. From a chemical point of view, orcein is a complex mixture of different colored compounds, they all share a common structure resulting from phenoxazone and a number of different substituents which are the various chromophores. In the present work, UV-Vis fluorescence combined with micro-Raman spectroscopy allowed for the non destructive identification of orcein in a fragment from the 9th century Bible de Théodulphe. Raman spectroscopy has been applied also for studying a parchment fragment sampled from a 16th century map of Auvergne. In both cases, subtracted shifted Raman spectroscopy (SSRS) has been exploited for removing the strong fluorescence background. Overall results have been confirmed by LC/MS Q-TOF analysis.

The electronic and vibrational characterization highlighted some interesting spectral differences with respect to a fresh orcein standard sample. Taking into account the poor lightfastness of the purple colorant, the same investigation has been carried out on artificially aged orcein, by exposure to visible light, reproducing the spectral modification observed on the ancient fragments.

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ABC-OR-04 Provenance and technological features of monochrome faiences recovered in Pompeii

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This study was carried out within the framework of a wider research project aimed at acquiring knowledge on technological processes, raw materials and decay phenomena of Roman finds (pottery, glass and mosaic)[1,2]. The research focuses on blue faiences recovered in Pompeii, most of whose remind the iconography, the decoration and the appearance typical of Egyptian faience[3,4]. The investigation was aimed at defining the compositional and structural features, to figure out provenance on the basis of their technological characteristics. Different complementary analytical techniques were used: SEM to investigate the morphological aspects of the samples and in particular the interfaces, μ-Raman Spectroscopy and XRPD to identify crystalline phases, and LA-ICP-MS to assess the elemental composition . Statistical data treatment of the elemental concentrations of bodies and glazes allowed to classify the objects into groups and to verify the previously established archaeological hypothesis suggesting an Egyptian provenance for faience of Pompeii. Also, analyses have permitted to identify raw materials, technology and to reconstruct the glazing method.

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ABC-OR-05 FTIR and Micro-Raman characterization of ancient paper materials

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The archive and library assets are an important part of the national cultural heritage. In order to identify appropriate methods of preservation and restoration of such property, it is important to understand the current chemical-physical state of the artifact and how it can be influenced by the microstructure of the fibers that compose it. Since the nature of the aggregates forming the paper semi-crystalline polymers, the degree of crystallinity and orientation of the fibers have a significant influence on its mechanical properties. The native cellulose is mainly crystalline, with only a few amorphous areas, however, many physical and chemical reactions can lead to the increase of amorphous areas and to the susceptibility of a biological attack, as well as a greater fragility of the paper [1, 2].

Figure 1. Ancient Book.

Spectroscopy is one of the most powerful tools for the characterization of paper materials and the identification of the degradation products. This work describes the application of FTIR and Micro-Raman spectroscopy to the characterization of paper of high historical and artistic interest.

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ABC-OR-06 In-situ Laser-Induced Breakdown Spectroscopy (LIBS) and X-Ray Fluorescence (XRF) Analysis of Roman Silver Denarii

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This communication presents the results of a study performed on a large collection of silver roman republican denarii, encompassing about two centuries of history. The joint use of LIBS and XRF spectroscopy allowed for an accurate determination of the coins' elemental composition; the measurements, performed mostly in situ at the 'Monetiere' in Florence, revealed a striking correlation of the 'quality' of the silver alloy with some crucial contemporary events. This finding was used for classifying a group of denarii whose dating was otherwise impossible.

The comparison with other contemporary denarii allowed also to controvert a recent theory [1,2] on the origin of the so called 'serrated' denarii (denarii showing notched chisel marks on the edge of the coin).

Fig. 1 – One of the serrated denarii analyzed (Gens Papia, Crawford 384/1)

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[2] G.M. Ingo, E. Angelini, T. De Caro, G.Bultrini, *Appl. Phys. A*, 79, **2004**, 171.

ABC-OR-07 Characterisation of synthetic varnishes and paint materials by analytical methods based on pyrolysis and mass spectrometry

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The wide use of synthetic polymers in art and in restoration makes mandatory the assessment of their stability and degradation pathways, and the development and evaluation of adequate analytical methods for their characterization.

This knowledge is extremely relevant for the selection of preventive conservation conditions as to reduce frequency and invasivity of restoration work.
In the context of the PAR-FAS Regione Toscana COPAC Project - *Preventive Conservation of Contemporary Art* (2011-2013) we applied two analytical methods based on pyrolysis and mass spectroscopy, namely direct exposure mass spectroscopy (DE-MS) and pyrolysis coupled with gas chromatography/ mass spectrometry (Py-GC/MS), to characterize a series of synthetic resins used as paint binders, varnishes and consolidants, before and after natural ageing (1-12 months): acrylic resins (Paraloid B67 and Acril 33), alkyd resins (Ferrario and Griffin, Windsor &Newton alkyd paint), an hydrocarbon resin (Regalrez 1094), an aldehyde resin (Laropal A81), and a polyethyl-oxazoline (Aquazol 500).

Characteristic pyrolytic profiles and mass spectra of significant pyrolysis markers were collected for each of the investigated materials. Principal component analysis was performed on the DE-MS spectra, proving this approach a useful tool for a fast and efficient comparison of the results obtained on raw materials, reference varnish layers and samples collected from works of art.
The proposed analytical methods do not require previous treatment of the sample, and, due to their high sensitivity, only a small sample amount in the microgram is recquired. This makes them particularly attracting for applications to works of art, to characterise new materials, and analyse samples of unknown composition.

Case studies relative to artworks from Keith Haring (Mural painting *Tuttomondo*, Pisa), Anselm Kiefer (*Die Grosse Fracht*, Biblioteca Comunale San Giorgio di Pistoia) and Fernando Melani (*Bandiera* and *Teatrino*, Museo Casa-Studio Melani, Pistoia) are discussed.

ABC-OR-08 "Sustainability" in conservation and restoration of the cultural heritage: considerations about the criteria in protecting and consolidating the architectural surfaces

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In the field of Cultural Heritage the propose introduction of "sustainable" technologies is becoming increasingly important, although it is not completely clear what is the meaning of "sustainability". This is often defined in terms of energy saving, but also a revival of traditional techniques and materials which are compatible with the artifact and, again, in terms of valorisation of the artifact itself [1, 2]. It is obvious that it is not possible to talk about sustainability in the context of Cultural Heritage without considering environmental sustainability, and vice versa. The system itself requires an complex evaluation: the use of materials and technologies which respect the human health and the environment; the revision of the criteria of efficiency of the conservation treatments; a larger attention to maintenance and monitoring of the artifact; the possible use of non-invasive techniques [3]; the evaluation of the impact linked the use and the tourism; the creation of databases accessible to the operator and the institutions responsible for safeguarding of the cultural heritage [4] , etc. This paper aims to analyze several different aspects associated to the definition of "sustainability" in the conservation and restoration of Cultural Heritage; in particular it takes into consideration the technological aspects linked to materials and methods currently used in the protection and consolidation of stone materials. The research wishes to propose a "numerical parameter of efficiency" defined by standard methods (as like UNI-Normal tests) but also in terms of environmental impact of the treatment in relation to the support, the safeguards of the operator, the expected duration of the treatment and the consequent maintenance operations.

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ABC-OR-09 Synthesis and characterization of wood-silica gel nanocomposites anchoring copper complexes active against biotic decay

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Interpenetration of wood samples of pine sapwood (*Pinus sylvestris* L.) with hybrid inorganic-organic silica xerogels bearing amine functions able to coordinate copper(II) cations has been successfully carried out. These materials have been prepared by sol-gel processing TEOS/APTES mixtures inside the wood. Solid state ^{29}Si NMR data provide evidence that the interpenetrated xerogel material has the same degree of condensation of the corresponding xerogel formed outside the wood. Copper(II) is effectively vehiculated inside the wood by coordination linkages with two ammine functions well evidenced by ESR measurements.

SEM/EDX investigations show that the chlorine/copper atomic ratio inside the wood is lower than that of the starting salt $CuCl_2$, suggesting an exchange reaction with silanol groups with the formation of Si-O-Cu linkages and HCl. This reaction could be promoted by the excess of amine functions with formation of ammonium chloride species which remain onto the surface of the wood and in the mother solution owing to a higher degree of condensation. The obtained wood treatments have shown high preservation performance against brown-rot fungi and subterranean termites, due to both the presence of copper and of the amino-functionalized xerogel [1]. The environmental impact of these preservatives also results lower than that of the commonly used copper formulations. This is due to the TEOS/APTES xerogel capability to reduce the amount of released Cu owing to an adequate fixation to wood, as demonstrated by 10-days lasting leaching tests.

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ABC-OR-10 A copper-containing metalloenzyme in tandem with a PQQ-dependent glucose dehydrogenase for monitoring phenolic compounds

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Recently we and others proposed an innovative method to make redox proteins suitable for sensing applications. The scheme builds on the translation of the binding event occurring at the enzyme cofactor binding-site into a change in the emission of a fluorescent probe covalently attached to the protein through a Förster Resonance Energy Transfer (FRET) mechanism. This principle has been advanced in the past few years for a number of applications based on oxygen detection by fluorescently labeled Type-3 copper proteins.[1-4] In the present contribution, the basic idea builds on the use of two enzymes that are coupled through a common substrate/product pair, *i.e.*, the product of the enzymatic activity of enzyme **1** is identical to the substrate of enzyme **2** and vice versa.[5] Co-substrates of the two enzymes are oxygen and glucose, respectively. In the presence of excess of oxygen and glucose, minute amounts of the common substrate/product are enough to ensure a continued cyclic reaction: instead of one turn-over by one enzyme a, in principle, indefinite number of turn-overs can be realized once a single molecule of the substrate/product pair is detected. The result is a large amplification in detection. The enzyme pair in our case consists of the copper-containing metalloenzyme tyrosinase (Ty) and the pyrroloquinoline quinone (PQQ)-dependent glucose dehydrogenase (GDH).[5] Ty converts mono- and di-phenols into quinones under consumption of oxygen, while GDH converts quinones back into the corresponding di-phenols under consumption of glucose. The challenge is to monitor the enzymatic consumption of oxygen as a function of the concentration of a mono- or di-phenolic compound. Recently Streffer et al reported the use of the Ty/GDH substrate-recycling couple as a sensor for phenolic compounds by monitoring the oxygen consumption with a Clark electrode.[6] Despite its numerous merits, the Clark cell is bulky and can be compromised by electrical interference.

The advantage in the present case is that we monitor the enzymatic consumption of oxygen by observing the fluorescence of a label that is covalently attached to the Ty.

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ABC-OR-11 Assessment of an ozone-based hygiene system for household dishwasher

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This work evaluates the oxidizing effect and antibacterial properties of ozone, related to the bacterial contamination control in the washing tub of the dishwasher. This concern is due to the fact that a dishwasher is not always operated immediately after its loading, which indeed may be partial load. Thus implying a time gap (some days) between loading and the start of the washing cycle in the appliance.
There is a difference of time in the loading and washing cycles. This is due to the energy saving and optimizing water consumption habits of the customer [1]. This induces a microbial degrading effect on the dishes due to the food residue leading to a smell inside the dishwasher.
Tests were performed on two identical dishwashers, of which one was equipped with an external device, generating ozone and pumping it into the washing tub of appliances [2], whilst the other one served as control. The system was configured with a suitable duty on/off cycle, aiming to reach less than 0.3 ppm ozone peak levels in the compartment and less than 0.1 ppm average. The two dishwashers were loaded in the same way with dishes spread with standard soiling agent that contains standard bacterial strains. A first step consisted of testing 3 standard soiling agent [3], each contaminated with an array of 3 bacterial strains, selected amongst 7 different strains based on trophic and metabolic characteristics. Every 24 hours, the soil were sampled from the dishes and analysed, to determine the variation of each strain's contamination. The two strains showing the most resistance towards ozone (*Pseudomonas aeruginosa* and *Listeria monocytogenes*) were selected for further analysis, consisting of two implanted non-standard soiling agents, showing the same traits as in the first step. A highly significant static bacteria effect was observed both for all the tested strains and for the types of soiling agents .With levels of bacterial contamination ranging 8% to 300% more in the control dishwasher than in the ozone dishwasher; the 2 strains showed different sensitivity to ozone action, with the substrate playing a probable role in affecting the sensitivity itself.

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ABC-OR-12 Polybrominated diphenyl ethers (PBDEs) in the atmosphere surrounding two WWTPs in Tuscany (Italy)

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Polybrominated diphenyl ethers (PBDEs) constitute an important group of brominated flame retardants that have been extensively produced and used in numerous everyday products. The market demand for PBDEs has been dominated by three major industrial formulations (penta, octa, deca-BDE mixtures), which are mixtures of tetra- to deca-congeners at various proportions[1,2]. The penta and octa formulations were banned in Europe in 2004, deca-BDE was also prohibited by July 2008. PBDEs enter the waste water treatment plants (WWTPs) from a variety of sources including urban and agricultural run-off, domestic wastewater, industrial point discharges, etc. and can be released to the atmosphere by volatilization and aerosol formation generated by bursting bubbles produced by the diffused aeration systems that provide oxygen to the microbial flora in the activated sludge processes. Thus, wastewater treatment processes are often overlooked as responsible for the emission of PM10 and associated pollutants. In this study, we collected PM10 samples in the inner and surrounding area (downwind and upwind) of two waste water treatment plants (WWTPs) in Tuscany (Italy), between 2004 and 2006, in order to determine the atmospheric occurrence and distribution of PBDEs and investigate WWTPs as source of these pollutants to the atmosphere.

PBDEs concentrations were compared to those found in samples taken simultaneously at reference sites that were not influenced by the WWTPs. Particulate and gas-phase samples were also collected to evaluate not only the gas-particle partitioning of PBDE, which is fundamental for assessing their fate and human exposure, but also to evidence temporal variations. Moreover, the risk of potential adverse health risks was calculated using the mean measured concentrations.

[1] van Esch, 1997
[2] UNEP; 2005

ABC-OR-13 Talitrid amphipods as biomonitors of PCBs and PBDEs contamination of supralittoral of sandy shores

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Coastal areas are characterized by a great input of environmental contaminants that can reach these zones by land based sources (including wastes from industrial, urban and agriculture activities, aquaculture, tourism), from sea based sources (oil spills, oil exploration and production) as well as atmospheric depositions. The contaminants of main concern include persistent organic pollutants (POPs), oils, fertilizers, heavy metals and pathogens[1]. Talitrid amphipods constitute one of the main animal components (in terms of biomass) of sandy beaches representing, moreover, a key species in the food web of these ecosystems[2]. In the last two decades, many species of sandhoppers and beachfleas have been successfully employed as biomonitor of trace metals contamination. In fact, studies carried out along European sandy shores have shown the ability of one of the most common Mediterranean sandhopper species (*Talitrus saltator*) to accumulate many trace heavy metals [3]. To date, no studies have been reported about POPs contamination of supralittoral of sandy shores and their presence in talitrid amphipods. In this study we analysed *T. saltator* collected from different coastal areas of Tuscany (Italy) looking for PBDEs and PCBs in order to verify if this species could represent a suitable biomonitor of POPs contamination of supralittoral of sandy shores. 20 PCBs and 9 PBDEs were identified in both sand and amphipods samples and their concentration in *T. saltator* was, for most part of PCBs and PBDEs congeners. Furthermore, results showed significant differences in bioaccumulation between amphipods form different localities. Therefore *T. saltator* could represent a promising biomonitor of PCBs and PBDEs contamination of the supralittoral band of sandy shores.

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[3] Ugolini et al., 2005

ABC-OR-14 Humic substances dissolved and particulate in the system pack ice-superficial water in the Gerlache Inlet (Antarctica)

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Antarctic environment is a good "laboratory" to study natural processes in the environment because anthropogenic sources are absent. In particular, humification processes and the influence of algal bloom on marine humic compounds (HS) can be studied without the interference of alloctonous humic compounds because the input of terrigenous humic material is negligible. Nevertheless, because of the particular climate conditions, it is not possible to neglect the presence of pack-ice and their possible influence on the presence of humic compounds in water. In water humic compounds are present both as dissolved and particulate material and play an important role in the fate and transport of metal ions and organic pollutants. In particular, pollutants can be scavenged from water to sediments [1]or transported from sea to air from sea-salt aerosol, deriving from sea-surface microlayer, the interface between the ocean and the atmosphere. We have studied time to time humic substances present in superficial sea water both particulate (PHS) and dissolved (DHS) evaluating the influence of primary production on humic compounds (HS) concentration. Humic material recovered from Antarctic samples consists only of fulvic acids both dissolved (DFA) and particulate (PFA). All data confirm that PFA are younger than DFA and richer of nitrogen containing groups, even if aromatization and condensation processes are not in an advanced stage. The primary production increases the amount of particulate matter with a consequent decrease of the PFA percentage. In a successive time begins the humification process, but at the same time it is in progress the sedimentation process owing to particulate matter shifts along water mass into deep layers. Consequently in superficial water the PFA concentration depends both from the primary productivity and from the sedimentation rate, whereas when pack ice is present the PFA concentration depends both from the ice melting and from the sedimentation rate. DFA are only slightly influenced from primary productivity.

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ABC-OR-15 Principles and application of Industrial Ecology for a sustainability of the waste management system

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The principles of Industrial Ecology are inspired by the integration of green chemistry and green engineering. Some key ideas can be defined: - system analysis, i.e. a wide vision of interrelations among human activities and environment; - flows and transformation of matter and energy; - multidisciplinary approach; - analogy with natural systems; - closed cycles vs. open cycles.
Some basic elements are:
Ecodesign: an approach to the design of products and services in which environmental issues are considered from the beginning of an industrial supply chain: reduce materials, energy consumption, toxic substances; and increase recyclability, use of renewable resources, product durability.
Life Cycle Thinking: to see products and processes from a life cycle standpoint.
Flow Analysis: to map and quantify used and discharged materials by a user network (companies, industrial districts, regions, supply chains...)
Industrial Symbiosis: based on the idea of exchange, where the wastes of a company are inputs for other producers.
Green Policy: actions and directives aimed at promoting environmental sustainability (Environmental certification, Extended Product Responsibility, Product to Services...)

The sustainability in waste management sector is strongly affected by these innovative concepts. In order to create a European recycling society, within 2020 Member States are called to achieve targets of 50% for household waste and 70% for construction & demolition wastes. The Ecodesign approach could highly influence the production of sustainable, reusable and recyclable goods.

From a technical-scientific perspective, an integrated waste management system must be followed by the application of different tools: monitoring of waste flows, their composition and physic-chemical features, implementation of best treatment and disposal techniques. Furthermore, validation approaches must be applied, as LCA, Risk Analysis, and integrated environmental monitoring system.

The final scope is to reach a definition of a practical waste management system for each area, in relation to specific territorial features.

ABC-OR-16 A new (OPIE + OPEE) device for simazine and atrazine analysis in olive oil

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To complete the research begun last year, several tests were carried out concerning the possibility of fabricating immunosensors working in organic solvents mixture (OPIE) and aimed at developing new immunosensors for the analysis of triazinic pesticides present in hydrophobic matrices such as olive oil.

Initially, an immunosensor for atrazine was tested in which a hydrogen peroxide electrode was used as transducer and peroxidase enzyme as marker. The competitive process took place in the chloroform-hexane (50% V/V) mixture while the subsequent enzymatic measurement was performed in an aqueous buffer solution. A linear response of between about 50 nM and 5.0 μM was obtained versus atrazine, in presence of olive oil. Subsequently, attempts were also made to use a Clark electrode as transducer and to perform not only the competition but also the final enzymatic measure in organic solvent, such as for the OPEEs. The latter enzymatic measurement was therefore carried out in several different organic solvents, such as decane, hexane, chloroform and chloroform-hexane mixture. The best analytical results were obtained using decane as solvent and tert-butylhydroperoxide as substrate of the enzymatic reaction. As far as measurements of K_{aff} using the Langmuir curves are concerned, the latter value was found to be equal to about 10^6 M^{-1} in all tests performed in the presence of the oil phase and about 10^7 M^{-1} in the absence of the oil phase. These values show that even when the antibody reaction occurs in organic solvent, antibody complex formation takes place more than satisfactorily and allows an immunological method to be developed properly. Selectivity of new immunosensor was found to be similar to the same device studied in previous work, but operating in aqueous medium. It was pointed out that when using the same antibody as that used also in the present research, the only interferents are practically simazine and to some extent terbuthylazine and buthylazine desethyl. Also the response to non triazinic pesticides was tested. For this type of pesticide (organophosphorus and carbamates) the response was found to be extremely low, although non negligible. In the case of simazine it was found that the calibration sensitivity is 40-50% lower than that of triazine although the linearity range and the LOD are of the same order. It is thus possible to analyse also this pesticide, which is also the one most frequently found in olive oil samples. The observed data showed that in practice traces of triazinic pesticide, probably simazine, were found only in two out of the four extravirgin olive oil samples tested. Lastly, recovery tests carried out on extravirgin olive oil spiked with atrazine always yielded recoveries in the vicinity of 100%.

ABC-OR-17 Study of the stability and reactivity of sulfur compounds against copper in dielectric insulating fluids: definition of a corrosiveness ranking

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Failure events in large power electrical apparata for energy generation, transmission and distribution are of extreme interest, since they can cause either socio-economical (interruptions of power energy supply, civil black-out, lose of production in industrial plants) or environmental (explosion, fire, pouring of dangerous compounds) consequences. In the last years, several failure events have been ascribed to the presence of sulfur based compounds inside the insulating liquids used for the impregnation of power transformers. While some sulfur compounds show antioxidant properties (such as thiophenes and their derivatives), others may induce corrosion phenomena against Cu of the windings' conductors.
The aim of this work is the study of the stability and the reactivity of classes of compounds (aliphatic and aromatic mercaptans, sulfides, disulfides, thiophens) which could be present in the insulating liquids of transformers in service, as a result of poor refining, back-blending or addiction. To fulfill this task, nine compounds representative of the above mentioned classes have been selected: dodecylmercaptan, hexadecylmercaptan, benzylmercaptan, butyldisulfide dibenzylsulfide, phenylvinylsulfur, phenyldisulfide, dibenzyldisulfide, dibenzothiophene. Their stability has been firstly investigated as a function of temperature (80-200 °C) and of ageing time (36-288 h) with or without oxygen, to simulate the natural ageing of either hermetically sealed or free breathing type transformers. Subsequently, their reactivity against Cu has been investigated, by repeating the experiments in the presence of Cu strips. The amount of each sulfur compound was quantified by a GC-AED (atomic emission detection) method, optimized for the purpose. Several on-sites investigations on failed transformers revealed that the formation of Cu_xS_y on the Cu conductor surface and onto the adjacent insulating paper tapes was involved in the failure mechanism. To investigate the corrosiveness of different sulfur compound families, the conversion of 22 sulfur compounds to Cu_xS_y was studied as a function of temperature in the presence of Cu. The total sulfur amount was determined by nephelometry after the oxidation of sulfide species to sulfate. The data obtained allowed us to define a corrosiveness ranking for the families of compounds tested, which was proven to vary with temperature. In particular, for T between 80-120 °C, mercaptans are the most corrosive compounds, while for T between 150-180 °C, the highest corrosiveness properties are exhibited by disulfides.

ABC-OR-18 An organo-zeolite for environmental applications

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A novel organo-zeolite material for water purification from organic pollutants has been developed and characterized. A sample of a phillipsite/chabazite-rich tuff (PCT) coming from a quarry near Naples, with grain size ranging between of 0.5 and 1.0 mm, has been initially full enriched in calcium ion. Afterword, the Ca-PCT sample was eluted with a solution of humic acids (HA) in a chromatography column (HA solution concentration = 100 mg L-1, pH = 7.4, flow rate = 1.0 mL h-1). HA are natural organic polymers containing aromatic blocks and are produced by the biological decomposition of organic matter from plants and other organisms. HA is the main component of the organic matter of surface water and of the soils. They are soluble in water at neutral and basic pH, moreover, they are able to adsorb hydrophobic compounds in their core within their molecules. In previous studies [1] we have shown that the phillipsite-chabazite-containing tuffs are able to bind HA and that the binding ability was markedly enhanced when the zeolitic material was enriched with divalent cations, especially Ca2+. In line with this result, the elution on Ca-PCT of HA solution produced an organo-zeolite adduct with a content of approximately 3000 mg of HA for kilogram of tuff. The solubility of the adsorbed HA was markedly decreased by treatment with a 10 % glutaraldehyde solution followed by heating at 330 °C for 1.5 h and the composite material so obtained was tested for adsorption of organic compounds. The figure reports an adsorption test carried out eluting a column of HA-Ca-zeolite adduct or zeolite alone eluted with a phenol solution, 220 mg L-1. The comparison between the breakthrough curves for the organo-zeolite combination and for the zeolite alone highlights the excellent adsorbing properties of this inexpensive, easy to prepare and environmentally-friendly novel material.

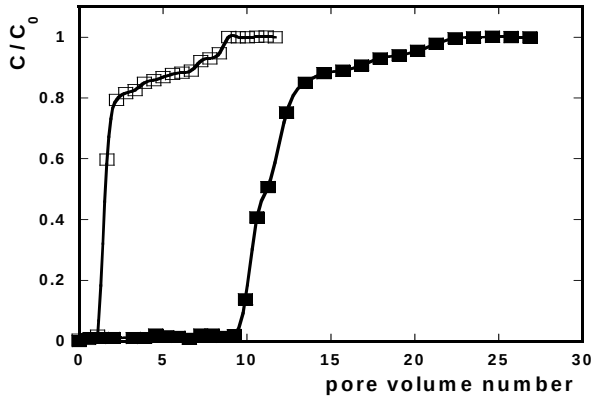

Figure: Breakthrough curves for the adsorption of phenol on the (■) immobilized HA on zeolitic tuff and on (□) zeolitic tuff alone.

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ABC-OR-19 Adsorption of pharmaceuticals from water by zeolites

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A large amount of pharmacologically active substances are used yearly to treat human and animal illnesses, in farming and aquaculture. These substances can be excreted unmetabolized or as active metabolites; they can escape degradation in sewage treatment plants and can be detected in sewage, surface, ground, and drinking waters. Improper disposal of expired medications also contributes to this contamination. Atenolol (β-blocker) and hydrochlorothiazide (diuretic) have been detected in several sampling sites along rivers Po and Lambro: these two drugs are poorly metabolized in humans, and are therefore mainly excreted as parent compounds (90-95%) [1].

Many drugs don't exhibit an acute toxicity but have a significant cumulative effect on the metabolism of non-target organisms and ecosystem as a whole, showing specific pharmacological and physiological functions [2].
Zeolites are microporous aluminosilicate minerals which combine a well-defined crystalline structure, including regular void spaces (pores and cavities), with well-defined functional groups generated by the controlled substitution of elements into silicate or aluminumphosphate lattices. These materials can be used as alternative sorbent materials for several classes of contaminants such as hydrocarbons, MTBE and also pharmaceuticals.

In this study, the retention of atenolol, ketoprofen and hydrochlorothiazide on three types of zeolite Beta is investigated. The zeolites differ from each other in hydrophobicity degree (different Si/Al ratios). To accomplish this task, the adsorption properties are characterized by adsorption isotherm determination; the influence of both ionic strength and pH on the adsorption properties are single out. Since the knowledge of the mechanisms governing zeolite/pharmaceuticals interaction can be helpful for the potential use of these minerals in wastewater remediation, structural and thermogravimetric measurements are carried out to investigate the role of the zeolite structure on the drug retention. The results demonstrate that Beta zeolite show fast adsorption kinetics and good removal properties for the studied drugs.

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ABC-OR-20 A methodological approach for the development of a guideline for odour emissions and odour impact evaluation

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In the perspective of the improvement of life quality and citizens wellness, odour pollution is becoming a more and more relevant topic. In fact, among the variables that could influence the citizens sense of a healthy environment, odour emissions play an important role, as they deeply affect the human life quality and psycho-physical wellness [1]. The increasing attention of the population to olfactory nuisance and the proximity of industrial plants to residential areas have generated the need of evaluating odour impact and regulating odour monitoring and control. Odour emission monitoring and its regulation are characterized by a great complexity due principally to the strict association of odour pollution to human perception. In order to establish a proper management and policy for odour emissions, different approaches have been developed [2] but they do not adequately satisfy the requests of monitoring and control expressed by the population directly exposed.

In this work, a proposal of a methodological approach for an odour guideline is presented with the purpose of defining acceptability and monitoring criteria for odour emission produced by industrial activities. According to the principle of pollutant prevention and reduction, commonly adopted by environmental legislations, the present methodology suggests a coupling between a predictive approach, based on dispersion models, and a systematic approach to carry out the monitoring and the control through reliable methodologies [3]. The novelty of the proposal is represented by the introduction of a buffer zone, individuated by means of dispersion models, in which prescriptive limits have to be fulfilled and verified by standard measurement methodologies. In addition, the odour guideline recommends to perform a process control for particularly impactful plants, realized through continuous monitoring systems.

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ABC-OR-21 Testing different treatment strategies for the treatment of municipal landfill leachate

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Municipal landfill leachates, resulting from the percolation of water through solid waste, represent an environmental issue due to their toxic potential [1]. Their treatment should include advanced oxidation processes (AOPs) after a biological step.

The treatment of a medium-age landfill leachate was investigated by employing several set-ups including a sequencing batch biofilter granular reactor (SBBGR) step [2], with or without ozone enhancement, followed or not by a polishing stage with solar photo-Fenton (SphF). Objectives of the investigation were to compare different treatment strategies in order to achieve the lowest operating cost and to reduce the toxicity of the final effluent, evaluated by three different tests (respirometry, *Vibrio fischeri* and *Lepidium sativum* phytotoxicity). These objectives were addressed for two different target COD values, namely 160 and 500 mg/L, to be met in the final effluent for disposing of to water bodies and to sewers, respectively, requested by Italian environmental regulation. The different treatment strategies have demonstrated to be technically suitable for achieving the requested COD (160 or 500 mg/L) and initial toxicity reduction (using three different bioassays) goals. For the COD target of 500 mg/L, the two investigated treatment set-ups showed to have comparable operating cost (3.2 €/$m^3_{inf.}$).

Instead, when the target COD is 160 mg/L, the combination SBBGR+SphF is economically more convenient (4.1 €/$m^3_{inf.}$) being the operating cost of the other two investigated treatment set-ups (SBBGR/O_3 and SBBGR/O_3+SphF) 5.7 and 4.8 €/$m^3_{inf.}$, respectively. As for toxicity reduction, for both the COD target of 500 and 160 mg/L, the SBBGR/O_3 set-up gave better results than other treatment options.

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ABC-OR-22 Atmospheric pollutants deposition flow close to a municipal solid waste incinerator: 5 years-monitoring results.

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In Italy, Municipal Solid Waste (MSW) treatment represents an issue of persistent concern. Even though more stringent emission limits for incinerators have been established (2000/76/CE directive), and the implementation of *best available techniques* should ensure low environmental impact, local contribution of pollutants in atmospheric flux depositions could be not negligible. Among these, persistent organic pollutants (POPs), such as polychlorinated dibenzo-p-dioxins/furans (PCDD/Fs) or polychlorinated biphenyl (PCBs), and heavy metals (HM) generate the greatest alarm.

The aim of this study is to estimate the relative contribution of a MSW incinerator to the pollutants burden in the surrounding area. To do that, organic (PCDD/Fs, PCBs, PAHs) and inorganic (Cd, Cr, Cu, Ni, Pb, Mn, Zn and As) pollutants have been determined in different samples of atmospheric depositions and soil.

The plant is located in a sub area, not far from a tourist town (Riccione), an important Italian highway (A14), and the Adriatic coast. It was opened in 1976; it increased its capacity to 127.000 tons/year in 1992. The plant was revamped in 2008 and for this reason, it shut down its activity for about six months and it operated at reduced capacity for the following six months.

Monitoring network was drawn on the basis of the dispersion map of incinerator stack emissions, calculated by the atmospheric dispersion model *Calpuff*. Sampling sites (5) were located in zones affected by different incinerator emissions fallouts.

From 2006 to 2010, bulk atmospheric deposition samples were collected monthly for heavy metal analysis and at intervals of about 6 months for organic pollutants analysis, whereas soil samples were collected once a year.

Results show that the studied area is subject to low contamination, as far as these compounds are concerned. Deposition flows show neither higher pollutants burden at sites most affected by emission plant fallouts, nor differences in deposition flux during the plant switch off. Furthermore, soil contamination seems to be more influenced by the nearby urban area emissions, than those from incinerator.

In conclusion, study area is apparently characterized by a homogeneous and widespread contamination that cannot be ascribed to the only incinerator emissions.

ABC-OR-23 Biogenic Volatile Organic Compounds from trees in the province of Trieste (NE-Italy)

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Within the Province of Trieste, anthropogenic emissions of Volatile Organic Compounds (VOCs) from trafic, steelwork and a crude oil tankfarm have previously attracted attention for toxicology and odour nuisance assessment. Vegetation contributes to VOC emissions budget, and atmospheric oxidation of these Biogenic VOCs contributes to new particle formation and atmospheric organic aerosol mass [1].

A study was started for the evaluation of BVOCs emission from major tree species spread over the Province, and deciduous *Quercus ilex* and *Quercus pubescens,* as well as evergreen *Pinus niger* were considered. Experiments allowed to identify α-Pinene, β-Pinene, Camfene e R-Limonene, β-fellandrene and δ-3-carene, among other compounds.

BVOCs emission rates were determined by dynamic branch enclosure with active samplers, at different times. Experimental data are aimed also at supporting validation of computational models, as Model of Emissions of Gases and Aerosols from Nature (MEGAN) [2], or Biogenic Emission Model (BEM) [3], that can be used for PM and ozone impact management.

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ABC-OR-24 Particle-Phase Polycyclic Aromatic Hydrocarbons in the Venice area: The relative importance of local emissions and Transboundary Movements of Air Masses. Preliminary Results

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In the atmosphere, the high m.wt. Polycyclic Aromatic Hydrocarbons (PAHs) are mainly present in the particulate phase and many of them are recognized having carcinogenic effects. The concentrations of 11 particle-bound PAHs were measured in the Venice-Mestre atmosphere. In this area, the air quality is affected by local anthropogenic emissions [1,2], but a strong influence of regional-scale transport of pollutants was recently detected as well[3].

A sampling campaign of fine particulate matter ($PM_{2.5}$) has been extended for one year in three sites selected to be representative of different emissive scenarios: urban background, industrial fall-out and semi-rural coastal site. PAH contents were determined using GC/MS after solvent extraction and liquid–solid chromatography clean-up. In addition to the identification of the most probable emission sources using common approaches, the main goal of this study was to test a procedure to assess the relative importance of local air circulation and regional-scale transports on PAHs levels. A first factor-cluster analysis [3] was performed to highlight the impact of local sources evaluating the relationship between variations of PAH levels as a function of wind speed and direction. Results revealed a strong influence of locally generated processes and atmospheric circulation on PAHs levels. In particular, the absence of significant advective transport episodes resulted in severe pollution events due to the accumulation of local anthropogenic emissions.

The variations in PAH levels were also related to backward air mass trajectories to trace the history of air masses and the potential impact of regional-scale transports. Results evidenced that the levels of PAHs increased when air masses came from Eastern Europe and spent most of their time over the Po Valley. Conversely, pollutant levels had dropped when the origin of trajectories was North and Northwestern Europe.

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ABC-OR-25 Harmful algae in the Venice Lagoon and in the Po River Delta (northern Adriatic Sea, Italy)

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An integrated approach for the structural identification and quantification of algal toxins, in Northern Adriatic Sea, specifically in the Po river delta and in the Venice lagoon, by applying a combination of analytical techniques such as optical and scanning microscopy (OM, SEM), and Liquid Chromatography coupled with High Resolution Time of Flight Mass Spectrometry (HPLC-HR-TOF-MS), is presented. The proposed approach has been preliminary applied to the investigation of harmful algae occurrence and distribution in the above mentioned coastal areas.

The performed sampling sessions showed that potentially harmful algae such as *Dinophysis caudata*, *D. mitra* and *D. sacculus* were present during summer period in most of areas directly influenced by seawater, such as the Venice port entrances and the Po river delta, but not in the inner Venice lagoon parts.

Nevertheless, quantitative observations demonstrated that their abundance were always significantly below the conventional limit (~200 cells/L) for which poisoning events could occur [1]. The presence of Pectenotoxin2 (PTX2) in phytoplankton cells extract was anyway confirmed by HPLC-HR-TOF-MS at Venice lagoon port entrance, so indicating the potential release of toxins in detectable amounts even at such low cell concentration levels [2, 3].

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ABC-OR-26 Importance of the particulate matter ionic fraction in the planning of data centres for the prevention of corrosion

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The planning and construction of Data Centre with Direct Free Cooling by using outdoor air as direct fluid of heat transfer inside the computers, consents to obtain a fuel saving in the conditioning phase, which translates less environmental impact; however, the legislation (ASHRAE 2009) [1] requires monitoring of air quality, with particular reference to concentrations of particulate matter and its hygroscopic properties, in order to prevent corrosion phenomena in the computers. The study focused on the planning of the ENI Green Data Center located in Sannazzaro dé Burgondi, in the middle of the Po Valley at the same named refinery and tubogas station with combined cycle ENI 1 GW. Two measurement campaigns were conducted (during winter and summer) at the Sannazzaro de Burgondi site near EniPower. $PM_{2.5}$, PM_1 e $PM_{0.4}$ samples (FAI-Hydra dual channel) were collected in conjunction with measurements of its number concentration and dry and humidity size distribution through the use of an OPC-Tandem (OPC GRIMM 1.107 *"Environcheck"*) and with measurements of the mainly meteorological parameters. The particulate matter samples were analyzed using ionic chromatography (Dionex ICS-90 e ICS-2000) in order to determinate the inorganic ionic fraction (Na^+, K^+, Ca^{++}, Mg^{++} NH_4^+, F^-, Cl^-, NO_3-, $SO_4^{=}$) and the organic one (mono and di-carboxylic acids). The PM ionic fraction analysis allowed the determination of its deliquescence using the application of a thermodynamic model of phase partition: the Extended *AIM* Aerosol Thermodynamics Model [2] (http://www.aim.env.uea.ac.uk/aim/aim.php). The deliquescence point was on average 60% greater than RH%, both through simulation modelling and experimental measurements (Tandem-OPC), thus favouring the presence of dehydrated aerosol in the thermodynamic operating conditions of the data centre (298.15 K, 10-60% RH%), condition that prevents the onset of corrosion related to the deliquescence of the particulate matter.

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ABC-OR-27 Airborne Particulate Matter in Apulia Region: features and critical episodes

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Airborne particulate matter (PM) is a complex mixture of particles which show substantial differences in size, chemical properties and thus in the toxicological and carcinogenic effects they cause. Several epidemiological studies, in fact, suggested the relevant role of PM concentration in contributing to a range of health effects [1]. Based on these implications on public health, many countries have developed plans to suggest effective control strategies which involve the identification of PM sources, the understanding of PM transport, mixing and transformation processes and the identification of the main factors influencing PM concentrations.

In this work, the results obtained by applying an integrated approach in PM monitoring campaigns are shown. The integrated prototype denominated 'SIMPA' consists of a Swam dual-channel sampler, an OPC Monitor, a sonic anemometer and a PBL Mixing monitor. The high time resolution of data and many information produced by the prototype allowed to identify the contribution that one source gives to the particulate matter concentrations respect to the bottom of the surrounding environment, and to identify optically particle size range of particles involved in the localized emission sources. The data collected in different sites in Apulia Region have allowed to identify different 'indicators' for the characterization of PM sources. PM2.5/PM10 ratio, daily mean values of natural radiation, particle numerical concentrations for the most significant optical diameters were considered. These informations, the chemical characterization of filters, the weather data and the information obtained by aerosol models such as HYSPLIT and DREAM, have allowed to evaluate the contribution of local anthropogenic sources, long-range transport from East Europe and African dust outbreaks. Finally, the obtained results were confirmed by applying Principal Component Analysis (PCA) to the numerical particle concentration dataset. It allowed to identify samples characterized by coarse mode of aerosol particles (natural events) and the accumulation one (anthropogenic events).

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This work was supported by the Strategic Project PS_122 founded by Apulia Region.

ABC-OR-28 Characterization of PM10 of three different site by analyzing individual particles

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SEM/EDS was applied to study the chemical and morphological parameters of PM particles. Considering both the parameters, the study and evaluation of the effects of many processes can be adequately done, i.e. the absorption of volatile molecules present in atmosphere, chemical reactivity and not least the origin of the particles. In particular, in literature some studies have been concerned to relate the composition and morphology of particulate highlighting the special relationship with atmospherical conditions.

In this work the PM10 samples, collected by a low volume sequential sampling on polycarbonate membranes, belong to three sites characterized by different boundary conditions: a yard site, an urban site and a rural site. In this work a protocol for the morphochemical characterization of single particles has been developed. Morpho-chemical characterisation of particles was performed by ESEM - EDS microanalysis: 20 chemical parameters (C, O, Na, Mg, Al, Si, P, Cd, Cl, K, Ca, Sn, Ti, Cr, Mn, Fe, Co, Ni, Cu, Zn) were determined and 7 morphological parameters (area, aspect ratio, roundness, fractal dimension, box width, box height, perimeter) were measured by Image Pro Analyzer 6.3. A set of 1340 particles from three sites has provided three sets of structured data in a poly-dimensional matrix (27 variables x 1340 particles).

Results revealed the presence of different clusters of particles, differentiated on the bases of chemical composition and morphological parameters (aluminosilicates; calcium particles; biological particles; soot; cenosphere; sodium chloride; sulphates; metallic particles; iron spherical particles).

ABC-OR-29 Interactions between cinnabar (HgS) and proteinaceous binders in paint-layers studied by Thermoanalytical (TGA) , Spectroscopic (FTIR) and Chromatografic techniques (SEC)

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Paints layers are generally made up of one or more pigments, which are a fine powder of inorganic coloured minerals, and a fluid binder, which enables the pigment to be dispersed, and to adhere to the support.

Historically, binding media were natural products from plants or animals, including protein-based materials such as egg, casein or animal glue, vegetable gums, drying oils, and natural waxes. These could be used alone or in mixtures, determining the different painting techniques. Egg proteins have commonly been used as binders, in the “tempera” painting technique. The organic paints constituents, and thus proteins as well, undergo to phisico-chemical modifications which are referred to as "ageing", leading to the formation of new functional groups and intermolecular and intramolecular bonds. This work aims caracterizing the interactions between ovalbumin and casein and the pigment cinnabar (HgS) in paint layers and how these evolve with time. The degradation of proteinaceous materials was also investigated.

The research was carried out on a set of paint replicas on glass slides freshly prepared, which were analysed fresh and after artificial light ageing. Multiple physical-chemical techniques were used, including Thermogravimetric Analysis (TGA), Fourier Transform Infrared Spectroscopy (FTIR) and size exclusion chromatography coupled to UV and cold vapour generation atomic fluorescence spectrometry (SEC-UV-CVG-AFS). TGA, FTIR and conventional SEC have been widely used in the field of cultural heritage showing that these techniques are of primary importance for the comprehension of structural changes of binders during aging in the presence or not of other organic and inorganic materials [1]. SEC coupled to CVG-AFS detector is instead a novel approach for the comprehension of the protein-mercury interactions [2].

TGA and SEC allowed us to highlight the occurrence of interactions between proteins and pigment, and permitted to partially investigate into their nature and evolution with ageing. In particular we found that cinnabar forms stable complexes

with both albumin and casein. Moreover the most part of mercury resulted to be associated with albumin monomer in not aged samples and with the high MW fraction in aged samples. On the other hand, in casein samples, cinnabar is complexed only with the high MW species both in not aged and aged paint replicas.

FTIR proved to be useful for chemically characterise the modifications undergone by the proteinaceous binders alone and in the presence of pigment, as an effect of light ageing. In particular FTIR spectra of aged samples showed data consistent with oxidation and hydrolisis of the proteins.

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ABC-PO-01 Use of the macroalgae of Orbetello lagoon for biofuels production

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The Orbetello lagoon is an important site for fish farming activities and in recent years there has been an excessive macroalgal growth that caused serious problems to the entire ecosystem. Two actions have been undertaken to reduce the ecological impact: the installation of pumps in order to increase water exchanges between the sea and the lagoon, and the harvesting of macroalgal biomass. This last activity is executed every year from May to November by boats collecting approximately 40 t per day of two dominant species: *Gracilariopsis longissima* and *Chaetomorpha linum*. Also *Ulva sp.* was present and collected for analyses. Until now the algae are transported and confined in a landfill, with very high annual cost. We analysed the potential production of oil from the 3 species considered as waste.

The aim of this work is to evaluate the lipid composition of macroalgae from Orbetello Lagoon (southern Tuscany, Italy) in order to produce biodiesel
Lipid extraction was carried out according both to Bligh and Dyer method and using a Dionex ASE200 (Accelerated Solvent Extractor). The total lipid content was determined by microgravimetry and the fatty acids by GC-FID and GC-MS after acid transesterification.

No statistical differences were found between the two extraction methods, lipid concentrations were higher in *G. longissima* than in *C. linum* and *Ulva sp.*

Fatty acids compositions were similar in the three species with C16:0 as dominant compounds. Generally, lipid contents and profiles of Orbetello Lagoon's macroalgae were comparable with those reported in the literature for the same species. The macroalgal fatty acids corresponded to those normally constituting the biodiesel.

The results demonstrate that by improving the oil extraction methodology, macroalgae could be considered a good residual biomass for biofuel production.

ABC-PO-02 Colloidal AgNP for LSPR based glucose-sensor

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Gold and silver nanoparticles have been widely used during the past years in various technical and biomedical applications [1, 2].
In particular, the resonance optical properties of nanometer sized particles have been employed to design biochips and biosensors used as analytical tools.

The dependence of the resonance condition on the local dielectric environment enables a simple form of molecular sensing in which analyte binding to the nanoparticles surface causes a shift in the spectral extinction peak [3].

Furthermore, nanoparticles have a highly localized LSPR sensing volume which eliminates the need to trap the interacting molecules of interest in a polymer matrix to enhance the signal, as is often done in SPR measurements. In this work, silver nanoparticles in ethanol have been synthesized by using poly(vinyl alcohol) as capping agent. The obtained nanoparticles have been analyzed by transmission electron microscopy methods in order to optimize the synthesis method to obtain monodisperse particles, in particular, the poly(vinyl alcohol) concentration has been calibrated in order to avoid particles agglomeration. Then the optical properties of the silver nanoparticles in solution have been analyzed and a progressive shift of LSPR caused by the adding of increasing quantities of glucose has been observed. High Resolution Electron Microscopy (HREM) shows the presence of superstructures onto the silver nanoparticles surface imputable to glucose.

The LSPR nanosensor developed in this study is expected to demonstrate a wide range of biomedical and environmental applications [4]. Its simplicity and low cost will make it accessible to the public, which could revolutionize medical diagnostics and medical economics. While the commercially available SPR biosensor has some of these capabilities, a nanoparticle based sensor could improve both medical diagnostics and biomedical research by easily diagnosing large numbers of biomolecules quickly.

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ABC-PO-03 Microstructural investigations of archaeological pottery from site of Mersin-Yumuktepe (Turkey)

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The great potential of synergy between archeology and scientific disciplines for the study of artifacts of historical and artistic interest is undeniable. The primary purpose of a scientific approach to archaeological objects is their conservation, preservation and study of knowledge and technologies in place for their production. Such information are essential to assess the cultural and technological aspects of past societies.

In particular, the use of scientific techniques allows to study the chemical composition of products, obtaining important information on identity and origin of raw materials. In addition, these data can help assess the commercial trade or exchange of artifacts between cultural groups, the technological capabilities and development, working conditions and living conditions, social customs and the differentiation features of the products on the destinations.

n present work, this multidisciplinary approach was applied to study some bricks that are part of the remains of the walls of some buildings found in site of Mersin-Yumuktepe, on the Southern coast of Anatolia, and from two different historical contexts: Neolithic and Chalcolithic.

For this purpose, we have used a scanning electron microscope, equipped with X-ray microanalysis system energy dispersive (SEM-EDX), and an X-ray diffractometer (XRD) in order to assess the morphology, the majority elements (Si, Ca, Al), the minority elements (Fe, Mg, K, S, Ti, P, Na, Cr) and the crystallographic phases. Moreover, it was possible to determine possible crystallographic changes and to reconstruct the evolution after any thermal annealing.

The experimental results obtained from these bricks, were compared with other pottery samples found previously in the same site, by using PCA (Principal Component Analysis), in order to highlight the presence of possible common sources of supply of raw materials for manufacture of different use.

ABC-PO-04 Study of the *patinas* on the Medieval bronze door of the cathedral of Troia (Foggia, Apulia)

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In Europe there are about thirty specimens of Medieval bronze doors, all made in the early years of the eleventh century and the mid-thirteenth century.
Many of these ports are located in Southern Italy and five can be observed in Apulia. In particular, a door (dated 1076) is the sanctuary of St. Michael the Archangel at Monte Sant'Angelo, a door (made in the eleventh century) is at Mausoleum of Boemondo d'Altavilla in Canosa, a door (made during the main phase of construction of the cathedral, completed by 1186) is at Cathedral of Trani. This door, recently restored, is now kept inside the temple.

The remaining two bronze doors can be seen at the Cathedral of Troia and they are both the work of Oderisio of Benevento: the main door was commissioned by bishop Guglielmo II in 1119 and the secondary door, located in the southern side of the Cathedral, is dated 1127. In 1127 in the city of Troy was celebrated a council convened by pope Onorio II and the secondary door is made of carved panels, enclosed by simple frames with inscriptions that sing the praises of the bishop Guglielmo II.

In this paper, we have reported the experimental results of non-destructive analysis performed on the *patinas* of the second door of the Cathedral of Troia.

In order to carry out this archaeometric study, we have used a portable apparatus of Energy Dispersive X-Ray Fluorescence (EDXRF).

ABC-PO-05 Study of XIX-XX century pigmented filler of tombstone inscriptions of the Monumental Cemetery *Villetta* of Parma

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The *Villetta* of Parma is the urban cemetery dating back to the beginning of XIX century at the time of Maria Luigia of Austria government. Designed as a city with orthogonal streets and chapels, it is rich in memorial monuments of great value for Parma history. The inscriptions show ancient prayers, signatures, dedications that reflect a singular approach to the commemoration ofthe dead person no longer in use. The materials used for making inscriptions have not been widely studied yet: their knowledge is important to understand ancient recipes and to identify suitable conservation treatments. This work is focused on the study of pigmented pastes filling carved inscriptions preserved both along the Portico and inside the Galleries of the monumental cemetery. They show heterogeneous conservation conditions up to the loss of legibility. The Raman spectroscopy analyses resulted the main useful technique to characterize these particular pastes and their alteration products; the obtained results were confirmed by micro-FTIR spectroscopy (ATR) and elemental analysis coupled with the scanning electron microscope. Black pastes, based on Carbon and Calcite, grey pastes, Carbon and Barium Sulfate, and red one of Hematite were found on white marble tombs; gildings on gypsum-based preparation layer and more recently yellow paste made of lead chromates were used on slate and other dark stones.

Organic material, ranging from paraffin waxes to proteins and lipidic substances, were also identified. Most of the originally black inscriptions have changed to green due to the formation of copper compounds such as Atacamite/Paratamite, antlerite, copper oxalates (Moolite) [1] copper and zinc metal soaps. The gilding layers have detached leaving out the gypsum-made preparations. The stratigraphy of many pastes allowed to recognize the subsequently added materials: paraffin waxes, modern painting layers made of Rutile and lead chromates. The conservation planning in the monumental area of *Villetta* in Parma has been defined thanks to the collected data.

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ABC-PO-06 Pd-Nanoparticles catalyzed one-pot sequential Heck and Suzuki couplings of bromo-chloroarenes in ionic liquids and water

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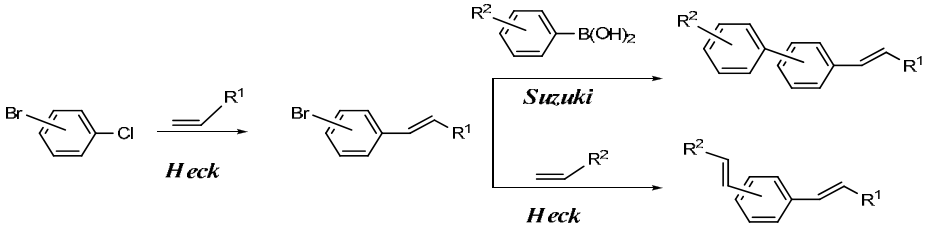
The Pd-catalysed cross-coupling strategy has gained considerable attention as a straightforward method for the synthesis of highly conjugated systems such as polyenes, aryl polyenes, and polyaryls, that are a common structural motif in many products.[1] In pursuit of this objective, several authors has been attracted by the potentiality of the sequential multiple couplings strategy involving the well-known Heck, Suzuki, Stille, etc. reactions, because these processes are usually high-yielding, stereoselective and tolerant towards a wide array of functional groups.

However, in many cases this approach can suffer from some disadvantages often requiring two different catalysts or the isolation of the intermediate product. One very attractive variant can be the one-pot double coupling of commercially available dihaloarenes, performing the consecutive coupling in the same reaction flask and in the presence of a single metal catalyst. There are only a handful of reports of such reactions on polyhaloaromatics, and in most of them the more reactive iodo/bromoarenes are usually preferred as substrates, while the cheaper and challenging bromo/chloroarenes are unexploited, with few exception,[2] due to the hard activation of the C-Cl bond.



As a result of our recent success with simple chloroarenes, [3] we report here that Pd nanoparticles generated in green reaction media (viz. ionic liquids and water) can catalyze the one-pot sequential Heck and Suzuki coupling reactions of bromo-chloroaryls to afford unsymmetrically substituted arenes in good yields.

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ABC-PO-07 Metal concentrations in Mediterranean blue mussels and evaluation of the mussels quality and possible risks of high human consumption

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Urban and industrial activities introduce large amounts of pollutants into the marine environment, causing significant and permanent disturbances in marine systems and, consequently, environmental and ecological degradation. This phenomenon is especially significant in the coastal zones that are the main sinks of almost all anthropogenic discharges of pollutants. In marine environment the persistent inorganic elements (e.g. metals) and organic contaminants (e.g. POPs and PCBs) are global issue, since continuous exposure of marine organisms to their low levels may result in bioaccumulation, and subsequent transfer to man through the food web. Although trace metals are normal constituents of the marine environment, and some of them are essential to marine organisms, all metals are toxic above some threshold level. Mussels have proven to be useful for biomonitoring chemical contamination and, therefore, have been used for indicating levels of trace metal concentrations, in the marine environment. Moreover, mollusks are study organisms for their inclusion in the human diet.

The aim of this work was to determine the concentration of metals in the mussels (*M. galloprovincialis*) collected at 8 sites from Apulia coast, to investigate contamination level and public health risks associated with consuming mussels harvested from these areas. Moreover the goal of this study was also to estimate the weekly intake and compare it with the provisional tolerable weekly intake (PTWI) recommended by JECFA [1]. Metal concentrations were similar to those detected in other Italian coastal zones, and indicate that the seafood under investigation poses no hazard to human health because metal content is within the permissible range established for safe consumption by humans.

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ABC-PO-08 Zinc oxide (ZnO) oil pigment: chemical aspect of delaminating processes after drying

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Zinc oxide (ZnO) is a pigment today well commonly present in the oil paintings both alone and in mixture with titanium dioxide and lead carbonate. Although the use of this pigment is over all the world very common nevertheless some of its characteristics seem to represent a risk to the painted surface. In the literature, it is often reported that "Paints containing zinc oxide exhibit severe delaminating problems after drying" so much that fragility of the painted layer by this pigment results.

This phenomenon occurring expecially when the pigment is applied alone and brings to its loss. The reaction, probably of radicalic origin, has not yet been understood: the most supported hypothesis is that hydroxide and superoxide radicals start the reaction able to go on through the interaction among humidity, atmospheric oxygen and UV light, so producing the degradation of the oil binders.

The development of the reactions seems to largely depend on purity degree and particle dimensions. Particularly, as reported by Morgan [1-3] the particles of smaller dimensions seem to promote the formation of the "crequalure". To assist this hypothesis, different commercial ZnO products (alone, not mixed with other products) were used as preparing layer on which another pigment layer was spread.

The pigments were examined both for their organic components and for inorganic ones in order to point out similarities and differences of composition and of behaviour in presence of other pigments.

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ABC-PO-09 Distribution of metals and PCB in deep-sea sediments of the Mediterranean Sea

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The Mediterranean Sea has been recognized as a marine region of special concern from the environmental point of view due to its particular hydrographical characteristics. It is a semi-enclosed basin with a negative water budget, where evaporation exceeds precipitation plus river runoff, which is compensated by a water inflow from the Atlantic Ocean through the Strait of Gibraltar. This feature has significant implications for the accumulation of contaminants from point and diffuse land based sources [1]. Most of the research on Mediterranean bottom sediments was performed in coastal areas [2-3], but data on metals and PCB in Mediterranean deep-sea cores is still lacking.

This study represents a systematic research performed on metals and PCBs determination in deep-sea cores sediments. The vertical profiles of metals in sediment were investigated in detail to elucidate the temporal behavior of metals. Sediment samples were collected with a box corer from ten sites during an oceanographic sampling campaign aboard the Italian research vessel Urania in July 2006 in the Eastern and Western basins of the Mediterranean.

As regards metal and PCB levels recorded in this study generally fall in the range of the lowest values available in the literature. Metal concentrations in sediment profiles were not uniform. In most cores the concentrations decreased from the surface and were within the range of values of the earth's crust.

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ABC-PO-10 Hydroxide nanoparticles for deacidification and concomitant inhibition of iron-gall ink corrosion of paper

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Historically valuable paper objects are rapidly deteriorating and their long-term conservation requires a full understanding of the chemical degradation mechanisms to conceive appropriate methodologies for conservation. The main cellulose degradation pathways are the acid hydrolysis of glycosidic bonds and oxidation. Low pH values can lead to cellulose depolymerization even at room temperature [1]. Ancient manuscripts were usually executed by using iron-gall-inks. These were obtained by reaction of iron (II) sulfate (i.e. *vitriol*, as reported in old recipes) with tannins extracted from gall-nuts, to give a pyrogallate complex of iron (III) and sulfuric acid [2]. However, acid-catalyzed hydrolysis of cellulose is not the only paper degradation pathway due to the presence of iron-gall ink. In fact, transition metal ions usually catalyze cellulose oxidation through a free radical mechanism, which produces hydrogen peroxide *in situ* [3].

This paper reports an investigation on the use of magnesium hydroxide nanoparticles dispersed in alcohols to inhibit two different and synergistic degradation processes usually affecting historically valuable manuscripts and common paper documents. We show that the preservation of paper from acid hydrolysis and oxidative ink corrosion can be achieved by stabilizing the final pH of deacidified paper around 6.5-7.5. PH control may allow to reduce the catalytic action of metals and minimize radical production. The inhibiting action of magnesium hydroxide nanoparticles are compared to magnesium oxide particles present in one of the best mass deacidification method (Bookkeeper) [4].

Note: This work has been partly supported by the project *TemArt*; *Programma Operativo Regionale - Regione Toscana*, co-financed by *Fondo Europeo di Sviluppo Regionale* (*POR CreO FESR 2007-2013*).

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ABC-PO-11 Application of multivariate statistical methods for the classification of the Apulian region ground waters.

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Multivariate statistical techniques such as Discriminant Function Analysis, Cluster Analysis, Principal Component Analysis, Absolute Principal Component Score and Neural Networks have been applied to data set formed by 895 samples and 15 parameters divided among four provinces of Apulia region (Bari, Lecce, Foggia, Taranto). The data set used has been obtained in the frame of the project "Expansion of regional agro-meteorological network" (2004-2007) funded by Apulia Region. Within the project 473 wells were monitored in order to assess, monitor and manage of regional groundwater quality.

Principal Component Analysis and Absolute Principal Component Analysis allowed to identify, for each province, the sites diverging from the mean cluster; while Discriminant Function Analysis pointed out the effective division among waters quality of different provinces.

Province	1	2	3	4	Total	correct %
1	181,6686	21,5539	11,29014	9,237385	223,75	81,19%
2	16,35096	172,1154	18,93269	16,35096	223,75	76,92%
3	2,712121	2,712121	174,9318	43,39394	223,75	78,18%
4	15,98214	15,09425	49,72222	142,9514	223,75	63,89%
Total	216,7138	211,4757	254,8769	211,9337	895	75,05%

Tab.1 Confusion matrix on dataset considered: 1 denotes Foggia Province, 2 Bari, 3 Lecce and 4 Taranto Province.

In Table 1 the confusion matrix obtained through leave one out cross validation method is shown. Results show a correct percentage of classification equal to 75%.

Variables whit high discriminatory power among groups, individuated by Wilks' lambda, are shown in table 2; they are: Ca^{2+}, NO_3^-, Na^+, Cl^-, Electrical Conductivity. In the further investigations a neural network model will be applied in order to improve the correct classification.

Var	Wilks	Partial Wilks
pH	0.377256	0.648061
Elect Cond	**0.252416**	0.968579
Ca^{++}	**0.251305**	0.972862
Mg^{++}	0.311180	0.785672
K^+	0.268803	0.909532
Cl^-	**0.257734**	0.948595
NO_3^-	**0.251545**	0.971934
SO_4^{2-}	0.270020	0.905434
HCO_3^-	0.289341	0.844971

Tab. 2 Variables selected by Wilks' lambda

ABC-PO-12 Nanoparticles for the Consolidation of Lecce Stone

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Nanotechnology provides new concepts and materials for the conservation of cultural heritage items. In particular, innovative products based on nanometric particles of different compounds have been proposed in recent years for the conservation of stone materials. In the present study the consolidation effectiveness of some inorganic nanoparticles dispersions (silica, calcium hydroxide and strontium hydroxide) are evaluated and compared to that exhibited by tetraethoxysilane.

$Ca(OH)_2$ and $Sr(OH)_2$ nanoparticles [1, 2] have been prepared and characterized by transmission electron microscopy (TEM), dynamic light scattering (DLS), fourier transform infrared spectroscopy (FTIR) and micro raman spectroscopy. The dispersions stability of both $Ca(OH)_2$ and $Sr(OH)_2$ nanoparticles in water as well as in propan-2-ol has also been determined by UV-vis spectrophotometry. Moreover, the process of the nanolime carbonatation has been examined using FTIR and micro raman spectroscopy.

Aqueous dispersions of the considered nanoparticles have been applied to standard specimens of Lecce Stone, a highly porous biocalcarenite. Other specimens of the same stone have been treated by tetraethoxysilane (white spirit solution), used as a reference.

The effects of treatment on the stone surface have been studied by water capillary absorption and permeability to water vapour tests as well as by colorimetric measurements and optical microscopy observations. Distribution of the applied product into the stone has been examined by porosimetry measurements and SEM-EDX experiments.

The resistance to salt crystallization of the treated specimens has been evaluated by performing the dry weight loss (DWL) test. [3]

All the results obtained after treatment by the considered nanoparticles and tetraethoxysilane will be compared each other and discussed.

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ABC-PO-13 Carbonaceous nanoparticle molecular inception from radical addition and van der Waals coagulation of polycyclic aromatic hydrocarbon systems. A theoretical study.

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Carbon nanoparticles, [1] generated during combustion at relatively low [O_2] or under pyrolysis conditions, can be seen both as soot precursors and as primary pollutants in themselves. Soot particle inception, with transition of relatively low-mass molecular systems from the gaseous phase to a solid nature through coagulation/condensation, is believed to take place via chemical reactions as well as van der Waals (vdW) interactions involving polycyclic aromatic hydrocarbons (PAHs) or derivatives[2]. Here, radical addition between open and closed shell molecular PAH-like systems is examined by density functional theory, and different σ bond formations are compared with the previously discussed stacking of the aromatic components[3]. Energetic and entropic effects are examined. At higher T, formation of aliphatic bridges (hence reticulation) appears to be of the utmost importance to link PAH-like moieties, with a preference for more extended arrangements (due to entropic effects). More packed structures, promoted by vdW interactions (an energetic effect), may be favored by lower T. Thus, when the gas in the flame cools down, reticulation could be followed by inter- or intramolecular stacking. These distinct processes can take place within different T ranges, but are not mutually exclusive: in particular, σ bond formation helps subsequent stacking, since crystallites would be more easily produced at lower T by stacking of already bound elements. Therefore, the mechanistic picture offered by the calculations bears out a structural model for carbonaceous particle growth in which an initial more amorphous core, generated at higher T through successive radical attacks and σ bond formations (hence reticulation involving growing adducts), can subsequently become enclosed in an external shell which grows at a lower-T regime and presents more ordered zones[4]. It cannot be excluded that limited transitions from amorphous zones to more ordered zones could take place within internal regions of the particle, provided the local texture of these regions were sufficiently sparse to allow "extended to packed arrangement" rotations in the adducts.

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ABC-PO-14 Preliminary studies of paint samples by ToF-SIMS technique

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In this work we present preliminary results obtained by Time of Flight-Secondary Ion Mass Spectrometry (ToF-SIMS) of paint cross sections collected from different parts of a Sienese painting. The aim of this study is to identify both the pigments and the binders present in the painting cross sections and their distribution within the different pictorial layers in order to define the state of conservation of the painting and the pictorial technique used by the artist. The presence of proteinaceous binders (rabbit glue and/or casein) suggests the use of tempera technique. Cholesterol is not detected, so we can exclude the use of the egg binder. The preparatory layer is composed by gypsum and proteinaceous binders, i.e. rabbit glue and/or casein. Cinnabar and white lead are also identified.

The ToF-SIMS results will be discussed and compared with those obtained by means of other well established techniques in painting studies, such as Scanning Electron Microscopy-Energy Dispersive x-ray Spectroscopy (SEM-EDS), Fourier Transform Infra Red (FTIR) spectroscopy and Gas Chromatography-Mass Spectrometry (GC-MS).

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ABC-PO-15 The Roman wall paintings at Pompeii: archaeometrical investigation of preparatory drawings (*sinopie*) and pigments.

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The archaeological site of Pompeii is a unique heritage of architecture, sculpture, paintings and mosaics. The wall decorations that adorn the *domus* and *villae*, constitute the most extraordinary aspect of the site, not only for the variety of styles but also for the refined pictorial technique used. The definition of the chemical nature of the pigments and binders used in Pompeii, results in an abundance of information on the origin, on the workshop production, on the technical knowledge of workers and lines of communication and marketing of painting shops that operated on the site. There are several studies that were conducted to learn about materials and production techniques used at that time [1] and different hypotheses have been advanced such as the use of encaustic, fresco, tempera or more elaborate methods [2] [3]. These hypotheses were tested on more than fifty samples taken from the wall paintings of seven different buildings of the famous archaeological site. In particular, this study concerned two major research areas, such as identification of the materials used for the fabrication of preparatory drawings (*sinopie*) and reconstruction of the palette and painting techniques used and, to this aim, a multi analytical approach, comprising optical, chromatographic and spectroscopic methods, was used. In the present communication the relevant results will be reported.

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ABC-PO-16 A reconstruction of the living space in a community of Early Bronze Age in Sicily: results of a multidisciplinary study.

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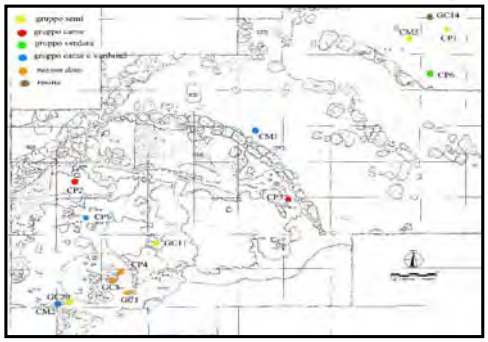
The main aim of this paper is to trace the use and the organization of space in a prehistoric human groups. The purpose, therefore, is to reconstruct the living space of this community, as produced by the interaction between the physical space and the actions and activities which took place within it. Both archaeological and chemical analyses seemed appropriate to carry out the study aimed at understanding the actual use of the vessels and linking the vessel function with the use of space finding as well. In the past, in fact, certain activities could take place outdoors or in specific areas inside the hut. The aim was to trace the connection among the type of food consumed, the shape of the used vessel, the sort of activity and space in which it took place. The case study is the Sicilian Early Bronze Age (2200-1450 b.C.) hill site of Santa Febronia. The village of Santa Febronia was discovered in 1995 [1]. At the top of the hill the remains of a hut of 4.80 m in diameter were found; the hut was destroyed by a fire; a large quantity of artefacts in their original functional position has been found. The study consisted in two steps. The objects distribution, mainly pottery, respect to the space and the structure has permitted to distinguish the storage areas from the ones destined to preparation and consumption of food. The chemical residue analysis in search of absorbed lipid and protein [2] has been used to identify the connection between the food processed and the space. The study revealed the multifunctionality of both space and pottery and confirmed the distinction of storage areas from the others. Moreover, it permitted to distinguish an area probably dedicated to storage of water.



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ABC-PO-17 Application of HPLC-HR-TOF-MS to the Analysis of Natural Pigments and Dyes in Cultural Heritage Artefacts

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The identification of complex mixtures such as lakes applied to paintings is an analytical challenge in cultural heritage studies because of many factors, such as the matrix intrinsic chemical complexity, the availability of very small fragments of pictorial film and the low thickness of the organic pigments layer usually employed for the realization of glazes and shading effects.

In this work we present the application of High Liquid Chromatography coupled with High Resolution Time of Flight Mass Spectrometry (HPLC-HR-ToF-MS) to the characterization of organic pigments traditionally employed by artists from antiquity to the first decades of XX century. The main goal is the development of an innovative approach to be used for routine analysis of natural substances present in cultural heritage artworks.

Only the combination of efficient chromatographic separation procedures coupled with the high mass resolution of the employed spectrometer allows to obtain the selectivity and sensitivity required for such characterization activity.

The planned approach involves three steps: 1) the extraction and preparation of lakes starting from natural (seeds, leaves, roots, berries, bark, flowers, insects, etc.) raw materials prepared according to selected original traditional recipes found in ancient treatises, such as the *Bolognese Manuscript*, the *De Arte Illuminandi*, and the *Il libro dell'arte of Cennino Cennini*; 2) the development of specific HPLC-MS methods for the analysis of the above mentioned pigments, also after artificial aging processes; 3) the validation of the developed methods by application to real samples collected from paintings of various ages and origins.

Concurrently, a detailed characterization of lakes by spectroscopic tecniques (e.g. FTIR, UV-Visible Spectrophotometry) will be carried out resulting in the creation of a complete reference spectra database.
Here we present the state of the art and the obtained results so far obtained.

ABC-PO-18 Extracts from Karité nuts reveal an ambivalent resource against termite pests

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Termites (Isoptera) are among the worse insect pests for wooden structures and their presence may represent a serious threat for cultural heritage, especially in those areas where climate and environmental conditions are favourable to these insects.The Old Continent is increasingly jeopardized by the obnoxious assaults of these insects, due to the high density of housing, to the haphazard urbanization and globalization, to the novel ecological patterns in use in the bio-masonry and to the antique remnant of mansions and sacred architecture.
Presently, sustainable management of termite pests includes the use of preventative measures (eg. application of repellents/antifeedants) and the use of baits with slow-acting termiticides.

The nuts of *Butyrospermum parkii* (Sapotaceae), tree native to West-Central Africa, are used to produce shea (karité) butter, welcome in the manufacture of cosmetics and food stuff. Aborigens believe that the residue from shea-butter extraction is capable to protect their houses from termites, which are extremely abundant in these regions (1). To verify if these popular beliefs have scientific basis, experiments were performed with European subterranean and drywood termites, respectively *Reticulitermes lucifugus* (Rhinotermitidae) and *Kalotermes flavicollis* (Kalotermitidae). Therefore an hydroglyceric extract of shea nut shells (the only pericarp) and an acqueous extract of shea cake (obtained from de-husked ground kernels, and thus phase oil-free) were used in short-term choice-tests and in long-term force-feeding trials, in order to assess the feeding deterrence or stimulation.. The results show that for both termite species shea cake extract is a feeding deterrent, thus confirming its potential as a wood preservative. However, most interestingly, the extract from shea nut shells elicited a very strong feeding stimulant effect, which looks extremely promising to increase the attractiveness - and therefore efficiency- of the baits.

Further analytical investigations (to determine the total rate of terpenoids and polyphenols) on both extracts are in progress in order to identify the active components responsible for the observed effects.

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ABC-PO-19 Changes in Sediment Heavy Metals Contamination and Bathymetry in The Lagoon of Venice over the Last Two decades

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The Lagoon of Venice is a transitional ecosystem, on the Northwestern coast of the Adriatic Sea, covering a 550 km^2 wide area, whose depth is shallower than 2 m for its 75%. It is connected to the sea through three inlets which regularly exchange water and sediments during the tidal cycles. Over the past millennium, the Lagoon has been modeled by both natural and human factors. Man activities, which included some engineering works, commercial shipping, dredging of channels, severe and in many cases illegal clam harvesting, have strongly modified the natural structure of channels, salt-marshes and bottom. Moreover, the central lagoon area has been affected by an heavy pollution from the industrial zone of Porto Marghera, atmospheric fall-out of pollutants and drainage of contaminants from the mainland.

This study has examined the trend of sediment heavy metals pollution in the central part of the Lagoon over the last 25 years (1987–2010) in relation to the changes in bathymetry. Five sediment sampling campaigns were carried out in 1987, 1993, 1998, 2003 and 2010 and the levels of some heavy metals (Cr, Mn, Co, Ni, Cu, Zn, Cd and Pb) were analyzed with ICP-OES after microwave acid digestion [1]. A number of articles have monitored the pollution extent of the lagoon and the deposition/erosion processes and pointed out some changes in the existing legislation, which imposed stricter limits to waste discharges [2,3] . Variations in bathymetry were calculated from the data of two campaigns (1970s and 2000s) carried out by the Servizio Informativo del Magistrato alle Acque di Venezia [2]. Bathymetry variations evidenced moderate erosion in the largest part of the lagoon with the exception of some border sectors where a moderate sediment accumulation was recorded. Chemical results showed a progressive evident decrease in contamination from 1987 to 2010 for all the analyzed elements.

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ABC-PO-20 Analysis of perchlorate in Italian drinking waters

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Perchlorate (ClO_4^-) is used as an oxidant in rocket fuel, missiles, flares and fireworks [1] and is persistent in the environment due to its high solubility in aqueous media. It has been detected in matrices associated with human exposures, including drinking water and food [2]. Exposure to perchlorate is of concern, due to the compound's ability to reduce the uptake of iodide by the thyroid gland and, subsequently, the production of the thyroid hormones thyroxin (T4) and triiodothyronine (T3) [3]. In 1998 perchlorate was added to the U.S.EPA Contaminant Candidate List and many states adopted their own drinking water standards to limit its health impact [4]. The analysis of perchlorate is usually performed by ion chromatography with conductivity detection [5]. Since detection by conductivity is not specific to perchlorate but responds to any species with sufficient specific conductivity, the IC method does not provide absolute evidence for the presence of perchlorate. To improve the specificity of detection, EPA method 331.0 used ion chromatography electrospray ionization tandem mass spectrometry (IC-ESI-MS/MS) for the determination of perchlorate ion in drinking water with a detection limit of 0.022 µg/L [6].

Prior to our study, there was no documentation of the occurrence of perchlorate in Italian waters. In this study, concentrations of perchlorate were determined in sixty two drinking water samples collected from different Italian regions. A rapid, accurate and sensitive reversed-phase LC-ESI-MS/MS method was used for the determination of trace level perchlorate. Pre-treatment of samples using silver and barium cartridges (Dionex) was used to remove chloride and sulphate anions. Perchlorate was detected in more than 70% of the analysed samples with concentration ranging from 5 to 74.8 ng/L. The lowest level detected belongs to water samples from Calabria, whereas the highest concentration belongs to Basilicata region.

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ABC-PO-21 Adsorption and Competitive Adsorption of organic compound mixtures on zeolites

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Groundwater pollution by organic compound mixtures is an actual problem because of their noxious effects on human health and ecosystem. Volatile aromatics, toluene, chlorinate compounds, dichloroethane, and oxygenates, (tert butyl methyl ether MTBE), have been received worldwide attention due to theirs widespread contamination of surface water [1].
The conventional process of polluted water treatment was found to be obviously insufficient with the improvement of water quality demands; thus it is needed to develop more efficient, economic and convenient water treatment technology.

Considerable attention have been paid to adsorption technologies as efficient and versatile methods for water treatment.
Zeolites are a class of molecular sieves that have a well-defined micropore dimensions and composition in a rigid crystal lattice. These materials are stable at high temperature and have good adsorption capacity [2].

In this work, adsorptions of dichloroethane, MTBE and toluene on different hydrophobic zeolites, faujasite (FAU) and MFI (ZSM5) were studied. Both adsorption equilibrium and the adsorption kinetics of organic compounds in water solution were investigated. The experiments were carried out for single-component as well as mixtures of the compounds in order to investigate adsorption competition. The interactions between zeolite and organic compounds were furthermore investigated by thermogravimetric and structural analysis.

Favourable adsorption kinetics along with effective adsorption of organic compounds into zeolite pores make this environmentally-friendly material a tool with interesting applications for the removal of organic contaminants from wastewater [3].

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ABC-PO-22 Atmospheric corrosion of quaternary bronzes: 1-year field exposure to an urban marine environment

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This work is part of a long-term project, aimed at investigating the correlation between environmental parameters and corrosion of different alloys, used for artistic purposes, in an urban marine atmosphere.

Since June 2010, a metal/environment monitoring station is active in the sea-town of Rimini, where specimens of the quaternary bronze G85-5-5-5 and weathering steel are exposed in sheltered and unsheltered conditions.

Weight variations, colour changes and patina evolution are periodically monitored. As far as the specimens exposed in unsheltered condition, the release of the alloying metals is monthly evaluated by analysing the leaching rain, collected through racks suitably designed. At the same time, microclimatic parameters (temperature, relative humidity, wind direction and intensity, solar radiation) and concentration of main pollutants (NO_x, O_3, PM_{10}) are daily recorded; bulk depositions are monthly collected and analysed for main soluble ions and trace metals. Data from specimens and environmental monitoring are compared and correlated.

Results obtained for the quaternary bronze during one year of exposure are presented.

ABC-PO-23 Evaluation of the ultrafine particle concentration at different sites of the Veneto Region

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Particulate matter has been recognized as one of the most important air pollutants, and recently the health and environmental implications associated with atmospheric nanoparticles have prompted considerable research activities [1]. In the framework of the RESMIA project, founded by the Regione del Veneto, an intensive monitoring campaign of the ultrafine fraction of the aerosol is in progress; the aim of the study is to evaluate the spatial and temporal variability of the ultrafine particle distribution at seven sites of the Veneto Region where the impact of the human activities is different, by considering both the particle number and the mass concentration.

Some preliminary results show that the median number particle concentration (> 4 nm) at the background site is about 3 times lower than the particle concentration found at the traffic site; however at both stations a clear circadian variability appears, as shown in figure 1 and previously reported in literature [2].

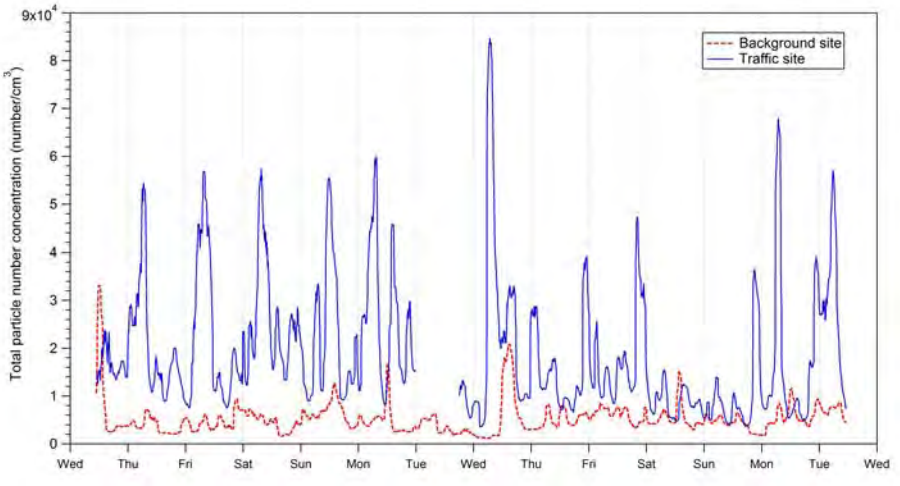

Figure 1. Temporal (smoothed) trends of number particle concentration at background and urban sites.

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ABC-PO-24 Extraction of BTEX from diffusive samplers

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The use of CS_2 in the extraction of volatile organic compounds (VOCs), when sampled in the atmospheric ambient by means of active or passive devices filled with activated charcoal, is by far a standardized procedure. However, due to the highly hazardous nature of CS_2 a challenge to the research community has been to find alternative non-toxic solvents or mixture, or at least with a lower level of toxicity. Few years ago Bertoni et al. proposed a comparative study were dichloromethane, a less dangerous and unpleasant solvent, was used in comparison to carbon disulphide. Their results highlighted that CH_2Cl_2 is useful in the extraction of aromatics molecules but the recovery factor was lower than that of CS_2 , in most cases in the order of 60%. In this study we report the results obtained by different extraction pathways using several solvents, selected among the most common solvents usually present in a chemical laboratory, for their low boiling point and high TLV-TWA value. Each solvent was used following the standard procedure by immersing the exposed charcoal for 60 min, followed by gaschromatografic analysis. Moreover, in each case, as an alternative procedure the use of a mini Soxhlet extractor was introduced which allows several extraction cycles, depending upon the extraction time. The Soxhlet apparatus was appositely realized for the treatment of extremely low volume of solvent. As it is shown in Figure1, the entire amount of BTEX adsorbed by charcoal was recovered after only few cycles of extraction by using dichloromethane as a solvent.

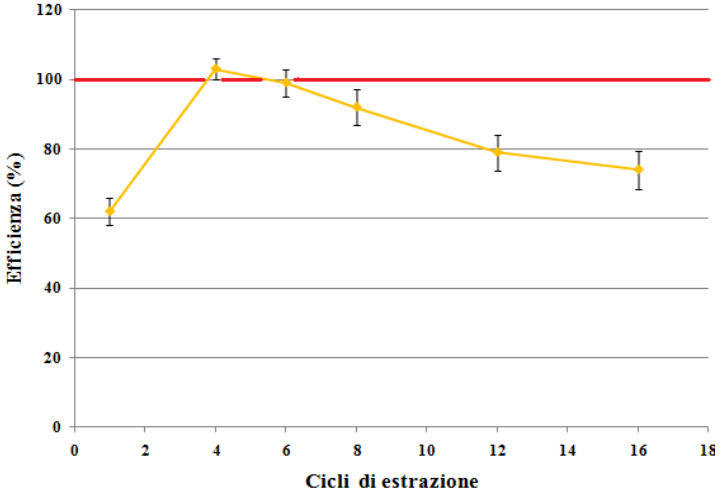

Figure 1. Extraction of BTEX from activated charcoal by CH_2Cl_2 in Soxhlet apparatus. The red line refers to 100% recovery performed by the usual CS_2 extraction procedure.

ABC-PO-25 Thermodynamics-based orientors for holistic interpretation of ecosystem services.

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Ecosystems can be viewed as thermodynamic systems, open to energy and matter, that self-organize towards higher complexity and organization of matter, create order, and self-maintain far from thermodynamic equilibrium [1]. Ecosystems also produce goods and services that are beneficial for human society and economy.

In order to detect ecosystem properties and dynamics in this context, some relationships can be acknowledged among the input supporting them, work capacity and useful output. These relationships can be represented by thermodynamics-based orientors e.g. emergy and eco-exergy, and the concept of ecosystem services. In particular, the ratio of eco-exergy to emergy flow is an indicator of efficiency in transforming the basic solar energy available into the structure of an ecosystem [2]; the ratio of eco-exergy to ecosystem services represents the annual work capacity increase of an ecosystem as a measure of all the possible services it can offer (not only the services that anthropic systems actually utilize), and can be compared with the actual flow of services utilized [3]; the ratio of the value of the ecosystem services to the emergy flow that supports the system can be considered as a measure of the ability of the ecosystem to use inputs and provide services [4].

A 3D diagram is introduced to present the inflows of resources, measured in terms of solar emergy, on the x axis, the work capacity embodied in the system biota, expressed in terms of eco-exergy, on the y axis, and the useful services for humans, valuable in economic terms, on the z axis. This multi-dimensional holistic approach makes clear that inputs are used up, directly or indirectly, to produce services in output and/or to develop the system, and enables to have an indication of changes in ecosystem dynamics, structure, services. Within this framework, a thermodynamic/socio-ecological evolutionary time path is proposed: from young system, to climax-stage system, to socio-ecological integrated system.

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ABC-PO-26 Biomonitoring of trace metals and organic compounds along the Apulian Coasts (Southern Italy) using *Mytilus galloprovincialis*.

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The present work reports the final results from a biota monitoring program, during the years 2008-2009. This project is mainly targeted toward the monitoring of the coastal water quality, using mussels as bioindicators, and the identification of contamination spatial trends. Mussels were sampled in 26 stations located along the marine coastal and transitional waters of the Apulian region, including both south-western Adriatic and Ionian areas. The analyzed contaminants were: heavy metals, chlorinated pesticides, chlorinated solvents, organophosphate pesticides, polychlorinated biphenyls, polybrominated diphenyl ethers (PBDEs), alkylphenols, polycyclic aromatic hydrocarbons and organotin compounds. Results were also compared with the National and International Regulations. Concerning metals, the maximum concentration of mercury (0.8 mg/kg d.w.) was found at the mouth of Saccione River (Station MC1A), in the Adriatic Sea, while Pb and Cd levels where found to be maximum in stations MC5A – Capoiale Mouth (3.3 mg/kg d.w) and AT7 - Varano Lake (2.5 mg/kg d.w.) respectively. For these three metals, no mollusks collected in any station exceeded the legal limits set by EU Regulation n. 1881/2006 (0.5 mg/kg w.w. for Hg, 1.5 mg/kg w.w. for Pb and 1.0 mg/kg w.w. for Cd). Concentrations of total PAHs (Σ PAHs) ranged from not detectable to 287.4 μg/kg d.w. (VM71A – mouth of Galeso River, Mar Piccolo of Taranto). Also in the station VM70A, Mar Grande (Ionian Sea) was observed high concentration of total PAHs (205.7 μg/kg d.w.). It is worth to mention that in the station VM71A, naphthalene represents about 73% of the total PAH concentrations. No stations exceeded the EU limit (EU Regulation 1881/2006) of 10.0 μg/kg w.w. for benzo[a]pyrene in bivalve mollusks. This compound represents a "contamination target" for carcinogen PAH pollution. The sum of PCB congeners ranged from not detectable to 383.8 μg/kg d.w. near the mouth of Galeso River (station VM71A), Mar Piccolo of Taranto, Ionian Sea.

Concerning chlorinated pesticides, only 4,4' DDE was found with the maximum concentration in the Mar Piccolo (second inlet) and near the mouth of Ofanto River (26.9 and 18.7 μg kg^{-1} d.w. respectively).

In these situations, frequent controls are needed in order to safeguard marine ecosystem and human health due to the consumption of seafood.

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ABC-PO-27 A preliminary study on the influences of paper components on the degradation of cellulose

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Archival holdings are strongly subjected to degradation due to the materials they are made and, to be able to intervene effectively, the knowledge of the causes and mechanisms behind the processes of degradation of cellulose in these artefacts is required. [1,2] In addition, the interventions have to be differentiated according to the specific "pathologies" of each item.

Paper is a complex system made up of several components interacting each other, such as cellulose, sizing, inks, coatings, and so on. Most of the articles on paper degradation currently reported in the literature refer to the simple degradation of cellulose, which clearly represents its main component, but certainly not the only one. The aim of the study presented in this communication is the study of the interactions between the different components of the paper and how these interactions influence the mechanisms and the rate of polymer degradation.

Among all considered variables, particular attention will be given to iron gall ink for the importance played as a writing material from the middle ages until the 20th century. Its relevance in paper conservation is also related to the so-called phenomenon of *corrosion* that can be observed in many ancient documents. *Corrosion* occurs with noticeable paper degradation and can even results in perforations or losses of material. [3]

The project involves the development and the optimization of different methods of artificial aging in order to balance the main degradation mechanisms of paper, hydrolysis and oxidation. [4] Data obtained from simulated samples will be compared with those from original documents to evaluate the effectiveness of the methodologies applied in simulating aging.

Both ancient and modern papers are considered and compared in the present work, to verify if the changes in the historical manufacture have introduced or replaced components affecting the rate of degradation of the artefacts.

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[2] P. Calvini, A. Gorassini, A. L. Merlani, *Cellulose*, 15, 2008, 193-203.
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ABC-PO-28 Protection of Lecce Stone by fluorinated polymers

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Lecce Stone represents a very challenging substrate to protect, due to its characteristics, most of all its porosity and pore size distribution.

Different products have been proposed as suitable to protect this substrate, acting as efficient hydrophobic barrier, thus preventing condensed water uptake by capillary absorption, which represents one of the main causes of degradation of the material.

In the present work some commercially available fluorinated polymers (i.e. a fluoroelastomer [1], a fluorinated polyurethane [2] and a perfluoropolyether derivative) have been applied as hydrophobic agents to Lecce Stone. They have been used as received and after proper modifications (for instance a chemical cross-linking or an addition of little amount of filler).

As the performance of a treatment may depend not only on the applied product and on the stone characteristics, but also on the procedures used for its application [3], different treatment procedures were considered.

The effectiveness of each treatments was evaluated by water capillary absorption and water vapour permeability tests as well as by color variation and contact angle measurements.

Different instrumental techniques such as micro ATR-FTIR and SEM-EDS were also used for surface and cross-section characterization of the stone specimens, in order to investigate the distribution of the protective materials after the treatment.

This work has shown that fluorinated polymers may be considered effective protecting agents for Lecce Stone, but their performance can be strongly affected by treatment procedures. For instance the considered fluoroelastomer afford a satisfactory protection from water when the formation of a film on the stone surface is allowed, while the effectiveness of the perfluoropolyether derivative is not affected by the application method.

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Chimica Analitica

ANA-KN-01 Functionalized carbon nanostructures and metal nanoparticles: from effective charge propagation to enhancement of electrocatalytic, photoelectrocatalytic and bioelectrocatalytic properties

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Of particular interest to the preparation of advanced materials is synthesis and characterization of carbon nanostructures (e.g. nanotubes) and noble metal nanoparticles, their stabilization (e.g. through self-assembly), as well as organization into two-dimensional arrays and controlled fabrication (e.g. through the sequential attraction) into three-dimensional network films. They can form nanosized materials with well-defined composition, structure and thickness. The interfaces can be also highly functionalized, and they can exhibit specific catalytic or unique electronic, charge storage, optical and sensing properties. We explore here the ability of inorganic structures to stabilize and derivatize metal and carbon nanostructures. Among inorganic systems, polyoxometallates of molybdenum and tungsten are attractive since they can not only adsorb irreversibly on solid surfaces but also exhibit reversible stepwise multielectron transfer reactions. The concept of the layer-by-layer formation of hybrid (organic-inorganic) assemblies composed of anionic polyoxometallate-protected carbon nanotubes (or metal nanoparticles) and ultra-thin films of positively charged conducting polymers (e.g. such as polyaniline or PEDOT) will be described and discussed here. The resulting novel composite materials have been fabricated as thin or moderately thick (μm level) films on electrode surfaces. As evidenced from STM and scanning electron microscopy, their morphology is still granular but the structure is fairly dense. Further, they are characterized by fast dynamics of charge propagation. Obviously, this research is of importance to the construction of effectively operating charge storage devices (capacitors), charge mediators (e.g. in bioelectrochemistry), molecular electronic systems and electrocatalysis. In the latter case, polyoxometallates can also be applied to stabilize and link Pt-Ru, Pt-Sn and various alloyed Pt-based nanoparticles. It is apparent from diagnostic cyclic voltammetric, rotating disk voltammetric and chronoamperometric measurements that such systems exhibit attractive properties towards electroreduction of oxygen or oxidation of alcohols (ethanol, methanol). Here, it is possible that addition of polytungstate or molybdate clusters to ruthenium or tin hydroxo species at the catalytic interface results in activating effect on dispersed platinum particles. An alternate explanation may involve a possibility of electronic effects and/or different morphologies of the catalytic films in the presence and absence of polyoxometallate.

ANA-KN-02 Comprehensive Chromatography (GCxGC, LCxLC) coupled to Mass Spectrometry for the Analysis of Complex Matrices

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Comprehensive two-dimensional GC (GCxGC)[1,2], up to now the most used comprehensive chromatographic technique, presents the advantages of an enhanced resolving power, the chromatogram-formation of chemically-similar compound patterns, of great help in identifying “unknowns”, and enhanced sensitivity through solute band re-concentration. Its main limitations are that retention mechanisms are more or less dependent on solute vapour pressures, and that only volatile, thermally-stable components can be analysed. These limitations can be overcome by using comprehensive two-dimensional LC (LCxLC) [3,4], a technique which is undergoing a very wide diffusion due to its great potential. The number of LC modes with distinct separation mechanisms is greater, and hence the number of possible orthogonal combinations is higher. The present contribution is focused on the use of comprehensive chromatographic methods applied to the analysis of complex mixtures with emphasis to the coupling of these techniques with Mass Spectrometry detection such as the one reported in Figure 1 for the Comprehesive LCxLC separation of intact triacylglycerols.

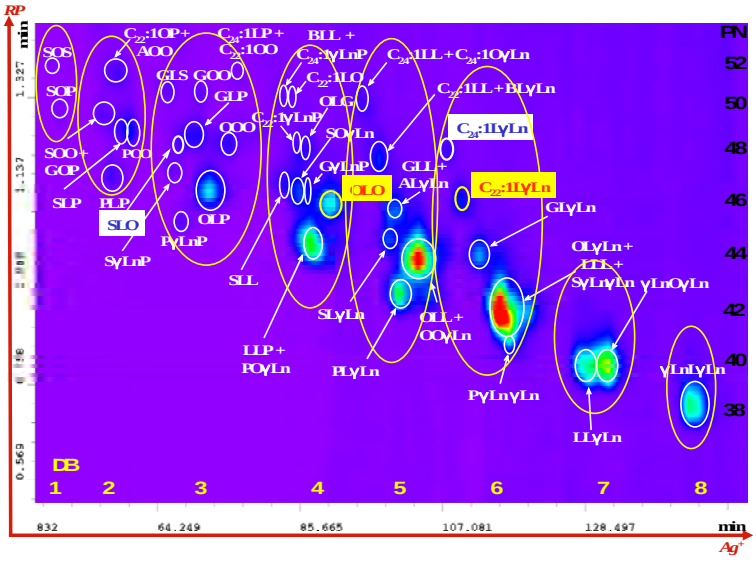

Figure 1

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ANA-OR-01 Detection Of Benzo[a]Pyrene Oxidation Products Via Electrochemical DNA Biosensors

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The toxic effect of polycyclic aromatic hydrocarbons (PAHs) occurs via their activation to more reactive species, usually oxidized species, via metabolic pathways. Benzo[a]pyrene is generally considered as one of the more toxic PAHs. In the present study we report the use of DNA biosensors based on screen printed electrodes for the indirect detection of the oxidized form of Benzo[a]pyrene. Benzo(a)pyrene-r-7,t-8-dihydrodiol-t-9,10-epoxide (DE-BAP) and Benzo[a]pyrene oxidized using a protocol standardized in our lab were the target molecules. Two different approaches have been tested: the use of genomic DNA sensors and the use of hybridization DNA sensors. In the former approach a different electrochemical signal was evidenced for benzo[a]pyrene vs. benzo[a]pyrene oxidized products.
The use of oligonucleotides consisted in the design of an electrochemical biosensor able to generate an electrochemical response for a particular sequence of DNA upon hybridisation. The same sequence, after formation of adducts with oxidized benzo(a)pyrene, was supposed to give a decreased signal with respect to the native.
Different DNA probes have been designed, immobilized via thiol-gold on gold screen-printed electrodes and gold nanoparticles. Amplification of the signal has been obtained using a biotinylated complementary probe in conjunction with a streptavidin-alkaline phosphatase conjugate.
An interesting correlation exists between DE-BAP concentration and the inhibition of the hybridization reaction for 24-mer oligonucleotides immobilised onto screen printed gold electrodes. Experiments on oligonucleotides immobilised on gold nanoparticles are in progress. The approach reported appears very promising for the realisation of DNA sensors able to assess the potential toxicity of PAHs and other genotoxic molecules.

ANA-OR-02 Proteins integrated into organic field effect transistor as electronic biosensors

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To satisfy the demand for smart analytical systems a great interest has been focused on the development of novel biosensors and several devices have been proposed. However, miniaturization, signal amplification and label-free detection are still open issues. Organic Field Effect Transistors (OFETs) appear as a new class of sensors able to overcome some of the presently available biosensors drawbacks. They have already demonstrated the ability to electronically detect numerous analytes in vapour systems [1] and even to detect chiral compounds at unprecedented low concentrations [2]. OFET sensors allows for simple and low-cost fabrication techniques, miniaturization, multi-parametric responses, signal and response amplification as well as label-free detection. Proteins such as antibodies, receptors or enzymes, can be exploited as highly performing recognition elements in OFET sensing devices. In this presentation an overview of the Bio-FET sensors (not necessarly organic based) field will be presented showing the advancements of the last years. Besides, the integration of biological recognition elements such as antibodies or other proteins to confer specificity will be discussed. Focus will be on the coupling of the FET device transduction mechanism and the biological recognition system. Recent achievements obtained with organic semiconductor FET biosensors realized through the full integration in the electronic device of the biological recognition elements will be also presented [3, 4]. The coupling of the OFET device and the biological recognition system is actuated by assembling supra-molecular structures in which biomolecules, such as membranes and proteins become an integral part of the OFET active material. Specific reactions (i.e receptor/analyte binding) are then used for analyte detection. To perform the bio-sensing measurements, the solution containing the analyte is deposited on the organic semiconductor, or through a proper microfluidic system. Preliminary results show that such bio-electronic devices can be very selective reaching detection limit (LOD) in the low ppt range. In addition, such sensors allow for label-free detection.

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ANA-OR-03 Graphene-based modified electrodes for the determination of strong oxidants

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Graphene-based systems constitute a novel, potentially powerful family of materials. At present they are extensively investigated for a number of different applications, such as energy storage and conversion and catalysis. In addition they appear to be promising materials for the modification of electrode surfaces, aiming at the amperometric determination of a number of different species.

In the present contribution, a graphene-based material have been employed for the modification of Au electrodes. Soluble oxidised graphene have been prepared through graphite exfoliation. Then graphene oxide "aggregates" have been anchored on Au electrode by means of thiol molecules. Finally, the aggregates have been electrochemically reduced. Atomic force microscopy and surface-enhanced Raman spectroscopy have been employed to confirm the deposition of the aggregates while electrochemical tests have demonstrated the stability of the grafting.

The modified electrodes have been succefully employed for the determination of strong oxidising species in aqueous solution, such as hydrogen peroxide. The determination of these species is crucial in order to achieve a reliable process control in a large number of industrial sectors. Different detection systems have been developed so far, the spectrophotometric methods being most popular. At the moment, methods that are reliable, selective and simple at the same time are still absent. In this frame, the development of amperometric sensors for oxidising species represents a significant innovation: similar systems are easy to use, cheap and potentially portable. They can also be employed for online measurements, as well as detectors in chromatographic systems.

Au, Pt, Hg and carbon-based electrodes have shown to constitute interesting sensing probes for these species. However, these materials lack of selectivity, being unsuitable to distinguish among the different oxidising species present in the samples at the same time. In addition, the presence of interfering species, such as oxygen, prevents from application to real matrices.

In the case of hydrogen peroxide, graphene modified electrodes exhibit promising performance with respect to the conventional electrode materials previously reported. In particular, a significant shift of the reduction potential towards less negative values has been observed, indicating the activation of electrocatalytic charge transfer processes. Oxygen presence does not interfere with the hydrogen peroxide electrochemical response.

ANA-OR-04 Gold Nanostructures for Affinity Biosensing Applications

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Recent advances on nanotechnology have led to discovery of many nanoscale materials (whose size is between 1 and 100 nm), because they present properties that are significantly different respect to bulk materials due to their dimensions (i.e.: large fraction of surface atoms, large surface energy, spatial confinement and reduced imperfections[1]).

In particular, gold-based nanomaterials (i.e.: gold nanoparticles, gold nanorods, etc.), that show unique optical, electronical, catalytical properties combined with easy functionalization with biomolecules and low toxicity, have been extensively used in biological field. In particular the combination of nanomaterials with bio-assays offer the possibility to design optimal sensing devices able to facilitate disease diagnosis (molecular diagnostics) as well as therapy optimisation (theranostic).

The goal of this work was to design a gold-based nanomaterial sandwich assay for the detection of different tumor markers (such as carbohydrate antigen CA 125, human epidermal growth factor HER2, prostate-specific antigen PSA etc), exploiting the easy functionalization of gold nanostructures with a specific antibody anti-marker.

Each phases of sandwich assay have been studied and optimized in order to increase the sensitivity and the reproducibility. For this purpose optical and electrochemical techniques were used.

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ANA-OR-05 Functionalization of Graphene Nanoribbons in Ionic Liquids: Myoglobine based biosensors and Prussian Blue modified chemical sensors.

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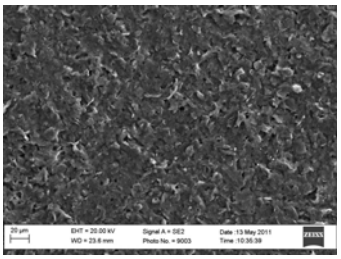
Following early attempts for producing graphene by mechanical exfoliation of highly oriented pyrolitic graphite (HOPG), many research groups are seeking high-throughput processing routes. In this paper, we propose an ILs-assisted electrochemical exfoliation of graphite electrode to obtain stable and homogeneous nano-emulsions of graphene nanoribbons and to perform electrochemical synthesis of graphene nanomaterials. Ionic liquids are salts containing organic cations, whose melting point is below 100 °C, most importantly, ILs have surface tensions very close to the surface energy of graphite, which is a solvent key prerequisite for direct exfoliation of graphite. In addition, the basic structural attribute of ILs (their ionicity), appears to be a unique feature for stabilization of exfoliated graphene via Coulombic interactions. Such advantages over most solvents make ILs the ideal systems for graphene synthesis. In the present study, a characterization of the new graphene based nanomaterials has been carried out under a topographic (by SEM/EDX) and structural (by FT-IR, UV-Visible and XPS) point of view. Subsequently, the [BMIM$^+$][Cl$^-$] (1-butyl-3-methylimidazolium chloride) and the [Bupy$^+$][Cl$^-$] (1-butylpyridinium chloride), were used to disperse the oxidized graphene nanoribbons, prepared as described in our previous paper [1], where the Myoglobine (Myb) protein has been successfully immobilized by physisorption interaction [2]. This biosensor, is very useful to detect NO_2^-,an environmental pollutant, and H_2O_2, an electroactive probe and substrate, with an improved Signal/Noise ratio, sensitivity and Limit of detection (L.O.D.), thanks to the extraordinary electronic properties of graphene nanoribbons and their higher surface area as compared with the conventional electrode materials. Moreover, the H_2O_2 electro-analytical detection could be improved, by using the one-step-electro-synthesis of the Prussian Blue (an electrochemical mediator-PB), directly electro-deposited on the SPE surface (Screen Printed Electrodes; ϕ=3mm) previously modified with the [Bupy$^+$][Cl$^-$] and BMIM$^+$[Cl$^-$] /graphene nanoribbon dispersions. Finally, the H_2O_2 and NO_2^- electrochemical measurements were performed working in a new drop detection mode.



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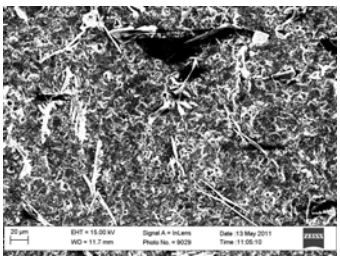

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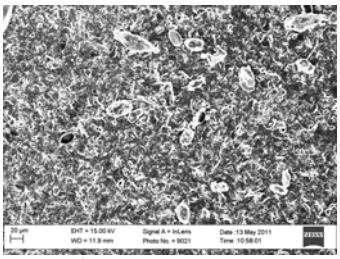

(c)

Figure 1. SEM micrographs of (**a**): the bare SPEs, (**b**): the[Bupy$^+$][C]/graphene nanoribbons modified SPEs; and finally (**c**): the [BMIM$^+$][Cl$^-$]/graphene nanoribbons modified SPEs.

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ANA-OR-06 Rapid and efficient size exclusion sample treatment for the LC-MS/MS multi allergen detection in food by targeted proteomic

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Hidden allergens in foods represent a major health problem in the food safety issue. In particular, tree nuts are considered among the major food allergens and their presence in foods could be intentional or could occur accidentally *via* cross-contamination at any stage of food production. Legislation in several countries, especially in the USA and EU, was put in place to increase food safety [1]. Analytical methods for qualitative and quantitative determinations of food allergens including immunochemical and mass spectrometric-based methods have been recently reviewed by Kirsch et al. [2]. In this context, our research group successfully proposed analytical methods using liquid chromatography-electrospray ionization-tandem mass spectrometry by selecting univocal biomarker peptides of digested proteins for reliable allergen quantification in foods [3-5]. In this work, fast shot-gun selected reaction monitoring methods were developed for the reliable and efficient detection of Ana o 2 (cashewnut), Cor a 9 (hazelnut), Pru 1 (almond), Jug r 4 (walnut) and Ara h3/4 (peanut) allergens in complex matrices as dark chocolate, biscuits and cereals. A rapid size-exclusion solid phase extraction-based procedure was devised enabling allergen detection in the 0.1-1.3 mg nut/kg range for biscuits and 4-11 mg nut/kg range for dark chocolate. Precision in terms of intra-day repeatability and intermediate precision was always lower than 19% (RSD). Linearity was demonstrated up to about three orders of magnitude for each matrix. Assay recovery was in the 84(±6)-106(±4) % and 98(±5)-108(±6) % range for biscuits and dark chocolate, respectively. Finally, the method was successfully applied for the investigation of hidden nut traces in commercially available foodstuff of different brands aiming to ascertain possible discrepancies between food content and labels.

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ANA-OR-07 Differential label free quantitative analysis of protein corona adsorbed onto different non-viral gene delivery systems

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One of the most important requirements for gene therapy is the development of safe and efficient gene delivery systems. In the last two decades non-viral vectors have attracted a growing interest. The cationic liposomes (CLs) have been extensively studied as non-viral vectors since the first lipofection was reported in 1987 [1]. One of the most common non-viral gene delivery vectors is DNA-cationic lipid complex (lipoplex). Medical administration of these gene delivery vectors is frequently made by parenteral injection. Therefore, upon exposure to biological media, these are immediately covered by plasma proteins forming a rich “protein corona” [2]. Indeed, the binding of plasma proteins to nanoparticles, is a critical step in determining their fate in vivo.

A shotgun proteomics approach was used to characterize and compare the plasma proteins constituting the protein corona adsorbed onto CLs, CL-DNA complexes (lipoplexes) and lipid/polycation/DNA (LPD) complexes surface after contact with plasma. The nanoparticle-protein complex was separated from plasma by centrifugation, then the proteins were digested, and the resulting tryptic peptides were analyzed by nano-high performance liquid chromatography coupled to a high resolution Orbitrap mass spectrometer. This is the first study that characterizes the "protein corona" of CLs, lipoplexes and LPD complexes with this approach. We found that these nanoparticles bind different plasma protein categories with important biological functions, e.g. lipoproteins, immunoglobulins, acute-phase proteins, proteins playing an essential role in protein synthesis, proteins strongly related to cellular activity and proteins involved in complement pathways and coagulation. After identification, the proteins present in at least two different nanoparticle corona were quantified by means of the statistical software Sieve.

These results could help in designing gene delivery systems able to bind selectively certain proteins rather than others, and to drive their biodistribution *in vivo* for obtaining more efficient and effective gene therapy.

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ANA-OR-08 Synthesis and Analytical Characterization of Composite Nanomaterials for NO_x Sensors

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The control of pollutants emission from internal combustion engines is a worldwide issue, in the automotive field. The roadmap for the reduction of vehicle emission limits is driving the academic and industrial interest towards the development of innovative systems integrating novel detection elements and fast feedback circuits and actuators. Based on a tighter control over emissions, and starting from 2014, Euro 6 standards are expected to improve the environmental compatibility of a new generation of vehicles in Europe. This scenario calls for a significant improvement of the sensors technologies for the detection of the main pollutants related to the automotive field, including nitrogen oxides (NO_x).
In this work, we report on the synthesis and analytical characterization of hybrid nanocomposites containing gold nanoparticles (Au-NPs) and metal oxide nanostructures (MO-NPs, such as zirconium oxide, indium oxide, oxide mixtures, etc.). These species are promising for real-time detection of low levels of NO_x species, owing to their low cost, high sensitivity and availability under a variety of stoichiometric and mixing ratios, showing different gas sensing characteristics [1-2]. Different MO-NPs and mixed MO-NP systems were prepared using a simple but efficient sol-gel method. Subsequently, the nano-oxides were electrodecorated by Au-NPs. Since Au nanophases exhibit pronounced selectivity toward NO_x gases [3], the resulting hybrid nanocomposites are expected to improve the nanomaterial sensing performance. All the nanomaterials were characterized using FTIR, XPS, XRD, TEM, and SEM techniques. Experimental evidences support further application of these NPs as active elements in novel NO_x sensors.

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ANA-OR-09 Surface Plasmon Resonance imaging: improving analytical performances for DNA sensing applications

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In Surface Plasmon Resonance imaging (SPRi) based sensing, NPs can act as signal enhancers [1,2,3] or they can be used for nanostructured surfaces. An improvement in sensitivity is reported when nanoparticles (NPs) are exploited for functionalizing the interacting surface [1,2,4] using NPs on gold electrodes coupled to piezoelectric sensing (QCM) [3]. Sharpening the performances of a sensor is a prominent objective in developing innovative biosensors for clinical applications. SPRi technique proved to be a suitable asset for developing versatile DNA affinity biosensors. Probe-target interactions can be monitored in real time and simultaneously recorded as a sensorgram (intensity of reflected light % vs time) or real time image of the interacting surface. A differential image of the functionalized biochip renders the changes on the interacting surface in a color scale monitoring interactions in real-time.

The possibility of multi-analyte detection using an array format is very attractive [4]. In particular, current research is focused on very sensitive molecule detection i.e. target sequences analysis directly in genomic DNA.[2]
With the final aim to improve analytical performances of SPRi-based sensing, a nanostructure-modified surface's was developed and the sensing behavior studied. As model system polymorphism detection in the gene of the opioid receptor was applied. The detection of this polymorphism is used for theranostic approaches, i.e. for a tailored pain treatment.

Different probes, selected computationally, were immobilized on the surface via thiol chemistry and hybridization reaction recorded. The system analytical performances are evaluated.

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ANA-OR-10 Development and characterization of electrosynthesized polypyrrole on microstructured silicon prepared by electrochemical micromachining

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Polypyrrole (PPY) is an electroactive conducting polymer widely used in various research and commercial fields from coating technology to sensor applications [1-4]. In particular, the electrochemical synthesis represents an effective way of easily interfacing PPY with an electrode surface allowing the deposition of films with controlled thickness even on complex geometry surfaces [5]. Recently, research has been devoted to the miniaturization of electrosynthesized PPY-based devices [6, 7] with the aim to construct complex micrometer- and nanometer-scale systems offering advantages in view of their larger surface area and, in turn, of the higher rate of interface processes. A polymeric thin film having both high conductivity and fine structure at the micro- or nanoscale is a suitable material particularly as sensing element in the fabrication of sensor devices [6, 7]. Various methods for preparing micro- and nanostructured PPY films have been proposed, which are generally based on template-assisted synthesis [7] exploiting carbon nanotubes [8], porous alumina templates [9], and porous silicon [10]. A drawback of this method is that dimension and morphology of the PPY structures is limited by the template architecture. Moreover, in some cases, PPY electrosynthesis requires a preliminary modification of the template surface to make it conductive [9]. Finally, each polymerization step needs a single-use template that is removed after film deposition, typically by chemical etching.

The present work describes a novel approach for the development of microstructured PPY films. The proposed approach is based on PPY electrosynthesis on microstructured silicon substrates prepared by electrochemical micromachining [11,12]. Electrochemical micromachining is a low-cost high-flexible technique allowing for silicon microstructuring at the microscale [13]. The great flexibility of silicon micromachining techniques for the fabrication of three-dimensional microstructured systems is here conjugated, for the first time, with conducting polymers technologies, thus leading to the development of novel PPY films with three-dimensional features that can be selected on the basis of specific applications. Experimental conditions for PPY electrosynthesis on silicon substrates have been firstly selected and different thickness films have been prepared. The influence of silicon microstructure has been tested by performing

PPY electrosynthesis, under the same experimental conditions, on flat substrates and on silicon substrates integrating regular array of square-like pores with pitch of 8 μm, size (s) of 5 μm and depth (d) of 5 μm, 10 μm and 50 μm. Interestingly, Scanning Electron Microscopy (SEM) analysis revealed that a three-dimensional polymer structure perfectly replicating the silicon microstructure is achieved on micromachined substrates. An isotropic PPY growth, i.e. same growth rate both in the horizontal and vertical direction, occurs independently from the aspect-ratio (HR = d/s) of the microstructure (HR from 1 to 10). The resulting PPY layer uniformly covers the microstructured silicon surface with constant thickness. Evaluation of the film thickness by SEM analysis also allowed the correlation with the circulated charge during PPY electrosynthesis to be established. Chemical analysis on microstructured PPY films has been also performed by X-Ray Photoelectron Spectroscopy (XPS). Preliminary tests aiming to verify the sensing properties of the developed microstructured systems will be presented.

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ANA-OR-11 Peptide Modified Gold Nanoparticles E-Nose For Food Analysis

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During food production the addition of aromatic compounds or the release of them during the technological steps has to be monitored for the assessment of the quality of the final product. The final aroma is the result of the entire process [1].
The complexity of the aromatic patterns released by food it is also dependent of the composition of the matrix and can be monitored using "electronic noses" [2].
In this study we added new functionalities to piezoelectric sensors by modification with gold nanoparticles (GNPs) bearing short peptide moieties.
GNPs has been synthesized using the $NaBH_4$ method that yields GNPs in alkaline solution. GNP are unstable due to their high surface energy and need to be stabilized against aggregation by suitable surface modifications. Some functional groups such as cyano (-CN), mercapto (-SH) and amino ($-NH_2$) are known to have an high affinity for gold [3]. The addition in homogeneous solution of compounds as cystein (CYS), glutathione (GSH), γ-glutammylcystein (γ-GLU-CYS) and cysteinylglycine (CYS-GLY) resulted in the formations of modified GNPs. Closely related aminocids were selected to assess potential relationships between structure and sensor behavior. The synthesized GNPs have been characterized using TEM, VIS spectroscopy and electrochemistry.
Modified sensors have been obtained by casting GNPs on 20 MHz quartz crystal microbalances.
The modified piezoelectric sensors have been characterized in the e-nose with different kinds of solvent to understand the interaction ability of each kind of sensors. Acqueous model solutions of aromas as isopentyl acetate, cis-3-hexen-1-ol, terpinen-4-ol, 2,3-pentandione, 2,3-butandione, hexanal and etylpyrazine were tested.
Headspace analysis of different samples of extravirgin olive oils were also tested and the data compared with GC and sensory analysis.
The data demonstrates that this approach is useful to improve the performance of QCM based e-noses. Particularly, for acqueous solutions the discrimination ability obtained by a simple Principal Component Analysis appears similar to the well known porphyrin–based QCMs for acqueous samples. Improved ability to

discriminate vs. porphyrin based e-nose was observed for extra-virgin olive oil samples; in this case the peptide based e-nose was able to clearly distinguish defected samples.

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ANA-OR-12 Rationalization of the behaviour of a bi-label oxygen optical sensor

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The determination of oxygen concentration is important in many areas of industry, medicine and the environment. Oxygen optical sensors are more and more attractive than conventional amperometric devices, because, in general, they have a faster response time, they do not consume oxygen and are less easily poisonable. Sensor operation is based on the quenching of luminescence in the presence of oxygen. We rationalized the behaviour of an oxygen optical sensor made of two luminophores simultaneously embedded in polymeric matrices[1]. Theoretical findings were confirmed by experiments. Platinum(II) 5,10,15,20-tetraphenyl-21H,23H-porphyrin (PtTPP), Palladium(II) 5,10,15,20-tetrakis(pentafluorophenyl)-21H,23H-porphyrin (PdFTPP), Ruthenium (II) (4,7-diphenyl-l,l0-phenanthroline)$_3$ (octylsulfate)$_2$ (Ru(dpp)OS) were used as luminophores and embedded either in polyvinylchloride or in polysulfone matrices. Their different life-times allowed preparing sensing membranes having optimized precision in the required concentration interval by proportioning the luminophores relative amounts. We demonstrated that, in the experimental conditions adopted, the two luminophores behave as if they were independent, giving to the sensing layer enlarged working range with respect to the most sensitive membrane and improved precision with respect to the less sensitive membrane, as shown in Figure 1. A working curve may indicate the most suitable membrane composition. The choice of a bi-label sensor may be justified when it is necessary to detect oxygen in a chosen concentration interval with the best precision possible.

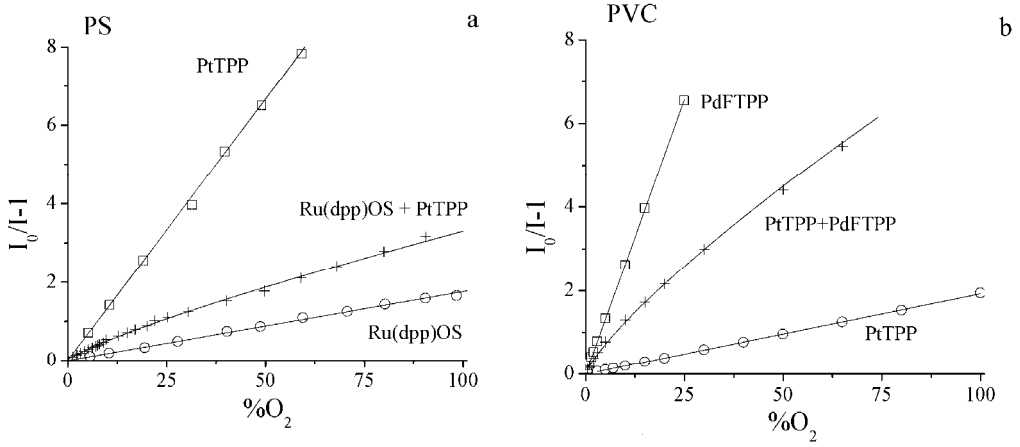

Figure 1.Stern-Volmer calibrations for single and bi-label systems in PS (a) and PVC (b) matrices

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ANA-OR-13 Identification and Localization of Proteins in Painting Cross-Sections by Chemiluminescent Immunochemical Microscope Imaging

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The characterization of the complex, multilayer, and multimaterial structure of a painting is fundamental for studying painting techniques and for authentication purposes. Among the various paintings' materials, organic ones (e.g., proteins, oils, waxes, gums, and resins) are the most difficult to characterize and their identification, localization and mapping in a painting structure still represents an analytical challenge. Imaging techniques relying on immunological reactions represent a promising approach to protein localization thanks to the high avidity and specificity of antibodies, which allow sensitive detection and (unlike other techniques such as Micro Fourier-Transform Infrared Spectroscopy) discrimination between different proteins. We have developed chemiluminescent (CL) immunochemical microscope imaging techniques for the identification and localization of ovalbumin and casein, commonly present in binding media or varnishes [1]. The immunological detection was performed by means of specific primary antibodies revealed by enzyme-labelled secondary antibodies and suitable enzyme CL substrates. The combination of CL imaging detection with optical microscopy permitted to localize the target proteins in micro cross-sections (1-2 mm^2) of standard and real aged painting samples with high sensitivity, low signal background and spatial resolution of the order of micrometers (i.e., within the single painting layers). Localization of bovine collagen has been also performed and multiplexed assays for the simultaneous detection of two different proteins have been developed by employing secondary antibodies labelled with enzymes detectable with different CL substrates. In perspective, these protein binders could be detected in the same cross-section by a triple multiplexed CL assay.

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ANA-OR-14 Identification of viable pathogenic bacteria by an olfactory mos-based sensor array coupled with field-flow fractionation

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Every year, almost 80 million cases of food borne illness occur in United States and 1.5 millions in Italy, among these 30% are caused by bacteria and their connected toxic products [1].
Conventional microbiological methods for the identification of food borne pathogenic bacteria are labor-intensive and time-consuming. Recently, immuno- or nucleic acid-based bioassay allowed significant reduction in the analysis time [2]. Nevertheless, their response does not provide information about viability and even dead bacteria are recognized. An approach based on bacteria metabolomics, which greatly differ among species, could be more reliable. Matrix-assisted laser desorption ionization mass spectrometry (MALDI-MS) methods have been described, but due to high cost of instrumentation are not suitable for screening purposes [3]. The metabolomic approach can also be pursued employing electronic olfactory system (EOS), which can detect and classify volatile components, thus enabling rapid bacteria detection. However, EOS are not selective enough to identify bacteria when present in a complex mixture and a preliminary separation is required. Field-flow fractionation (FFF) are separative techniques suitable for the non invasive fractionation of bacteria. This work presents the use of an FFF system coupled with an EOS (EOS 835, SACMI, Imola, Italy) equipped with six metal oxide semiconductor sensors (MOS) for the analysis of volatile metabolites produced by pathogenic bacteria. The sensor technology yields a distinct response signature for each vapour regardless of its complexity, resulting in a "smell fingerprint" which can be used for sample identification by chemometric data analysis. To set up the method, *E. coli* O157:H7 and *Yersinia enterocolitica* were used as model samples. Upon training the EOS with suspensions of each bacteria species (2,4 X 10^9CFU/mL), cells mixtures with different bacteria proportions (1:4; 1:1; 4:1) were injected in an FFF system (final concentration 4,8 X 10^9CFU/mL). Fractions corresponding to the retention time typical for the two bacteria species were collected, grown in 1 mL Luria Bertani (LB) broth for 2h at 37°C, and then analyzed with the olfactory system. The data recorded for each sample were averaged and subjected to chemometric analysis using PARVUS software [4]. The selection of 10 variables allowed clearly discriminating by PCA the *Y.*

enterocolitica and *E. coli* samples when present in different relative proportion, and the LDA analysis allowed obtaining a correct classification and prediction ability of respectively 90 and 91 %. The analysis of collected fractions from the different mixtures confirmed that after fractionation, the olfactory system was able to distinguish and identify the different fractions. The inter-assay variability is low but a fully highly standardized procedure is required and this is achieved also with the use off the FFF system. This method could be applied for food safety applications, as well as to biological samples for diagnostic purposes and an on-line FFF coupling with EOS is in progress.

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ANA-OR-15 Study of the Vitamin K Cyclic Metabolism in absence and presence of coumarin anticoagulants by Liquid Chromatography- Linear Ion Trap Mass Spectrometry.

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In mammalians the only known function of vitamin K is that of γ-glutamylcarboxylase cofactor [1,2], enzyme catalyzing the posttranslational carboxylation of the so-called vitamin K-depending proteins [3]. Well-known for the activation of the coagulation proteins, vitamin K has also been shown to be required by extra-hepatic proteins involved in bone metabolism, vascular calcification, and apoptosis. This vitamin is characterized by a cyclic metabolism: it is its stable quinonic form to be absorbed and transported in blood, but it is the hydroquinone one to act as enzymatic cofactor and to be transformed into vitamin K 2,3-epoxide. The latter is then recycled to quinone and hydroquinone in successive reactions catalyzed by vitamin K reductases, dithiol-depending enzymes inhibited by coumarin drugs. A second NAD(P)H-dependent quinone reductase is relatively insensitive to these anticoagulants and operates at high concentrations of vitamin K.

Probably because of its efficient recycle system, very low levels of vitamin K circulate in plasma. Moreover, its Recommended Daily Allowance has currently been set at 1 μg/kg/day [1]; this value is surely suitable for its hepatic function, but an extra demand might be required for guaranteeing the bone and vessel health, especially in subjects under anticoagulant therapy [4]. For these reasons, an accurate determination of the vitamin K and its metabolites is a real analytical challenge. This work was just addressed to overcome the above-mentioned difficulties making use of an advanced analytical technique such as liquid chromatography-linear ion trap mass spectrometry. After its development and validation, the method was applied for refining the status of phylloquinone (vitamin K1) and for defining that of vitamin K1 2,3-epoxide in a significant cohort of healthy subjects and of patients under anticoagulant therapy. An accumulation of both forms was verified in individuals taking long-term coumarin drugs.

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ANA-OR-16 Determination of some phytohormones in Zea Mays under chemical and physical stress.

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As reaction to stress condition, plants can modify the amount of produced hormones. In this work we have considered the alteration of main phytohormones concentration in corn plants (Zea Mays) exposed to different types of stress. Some plants were exposed to water stress, other were fed with herbicide solutions (Flufenacet or Metolachlor) commonly used in corn cultivation.

The investigated hormones were *Indole-3-acetic acid* (IAA), *abscisic acid* (ABA) and *gibberellic acid* (GA3). The study of these hormones is particularly important because of their great physiological involvement in plants.

Hormones determination was done by HPLC-UV/ fluorescence and GC-MS; two different internal standards were used: ascorbic acid and naproxene. For HPLC-UV/fluorescence separation, a gradient procedure was adopted using acidified water (pH= 3) with phosphoric acid and acetonitrile. In fluorescence analysis, only IAA can be observed because it is the only hormone with fluorescence properties; as naproxene shows similar fluorescence properties, it has been chosen as internal standard. GC-MS analysis needs a preliminary stady about compounds derivatization with N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) or with Trimethylsilyldiazomethane (TMSHN2).

Hormones extraction procedure from a so complex matrix was done with an aqueous solution of methanol 80% followed by a clean up on SPE column.

Compared with plants grown without stress, plant exposed to water stress shows an increase of ten times in IAA concentration; opposite trend is shown by ABA whose concentration decreases considerably. The same type of plant has a quite different behaviour when exposed to chemical stress. Plants fed with Metolachlor or Flufenacet show, in fact, a decrease of all hormones'concentration.

These results demonstrate that the same plant can react in different way depending on the different type of stress to which they are subjected.

ANA-OR-17 Correlation between salivary concentration of oral anticoagulants and anticoagulant effect in thrombotic patients.

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Oral anticoagulants are essential and not replaceable in a large number of long-lasting clinical conditions which require an accurate control of the coagulation of blood, such as thrombotic diseases and vascular pathologies. Oral anticoagulants have such a narrow therapeutic index that small changes in plasma concentration may have serious consequences: bleeding if the dose is a little too high, or thrombosis if it is a little too low.
The large number of factors that may interact with the therapy (diet, comorbidities, other drugs, etc.) significantly increases the risk of being outside the optimal value, and consequently entails constantly monitoring the patient by means of continuous and frequent blood analysis, even for long periods of time. The dose is adjusted from time to time according to the anticoagulant effect, as evaluated by measuring in a blood sample the prothrombin time expressed as International Normalized Ratio (INR).
Clearly new alternative methods to blood tests are needed that would be less invasive, simple to use, implementable in low cost devices, and, if possible, allowing self-monitoring.
In this work, an analytical method is described for the determination of an oral anticoagulant (warfarin) in oral fluid samples by HPLC with a spectrofluorimetric detector. The correlation between the salivary warfarin concentration and INR values highlighted the key role played by the salivary pH.

ANA-OR-18 A multi-enzyme biosensor for detection of cyanobacterial hepatotoxins based on PP2A inhibition

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Microcystins and nodularin are natural toxins produced by cyanobacteria such as *Microcystis*, *Oscillatoria*, *Anabaena* and *Nodularia*, which grow worldwide in fresh and brackish waters. They are potent hepatotoxic cyclic peptides that exert the cytotoxic effects by inhibiting the catalytic subunits of serine/threonine protein phosphatase-1 and 2A (PP1 and PP2A), which play essential roles in the reversible phosphorylation and dephosphorylation of proteins and are implicated in a large number of cellular events. Cyanobacteria and their toxins, especially microcystins, are recently a drinking water public health issue with a provisional drinking water guideline of 1 µg/L for microcystin-LR, published by World Health Organization. Rapid and reliable analytical methods capable of determining microcystins in water at concentrations ≤ of 1 µg/L are therefore required. A promising approach in measuring microcystins and nodularin is based on their inhibitory effect of PP2A and PP1 enzymes. The degree of inhibition of these enzymes can therefore be used as a measure of toxin concentration.

In this work, we propose a bi-enzyme electrochemical probe to monitor the inhibition of the enzyme PP2A by microcystin-LR and nodularin. This enzyme has a significant activity towards glycogen phosphorylase *a* (PHOS*a*), which in turn catalyses the conversion of glycogen to glucose-1-phosphate (G-1-P). The proposed system involves a preliminary phase of off–line enzymatic incubations (microcystins/PP2A, PP2A/PHOS*a*, PHOS*a*/glycogen+phosphate) followed by the electrochemical detection of H_2O_2 which is the final product of two sequential reactions catalyzed by glucose oxidase (GOD) and alkaline phosphatase (AP), co-immobilized on a H_2O_2 Pt probe inserted into a FIA system.

The total analysis time includes 50 min for the off–line enzymatic incubations and 3 min for the biosensor response.

The system calibration shows a working range of 0.5-1.3 ppb and 5-24 ppb for nodularin and microcystin-LR, respectively. These values, referred to toxin concentrations in the final assay solution, correspond to 5-13 ppb for nodularin and 50-240 ppb for microcystin-LR in water samples. For this reason, in order to assess the maximum level recommended for microcystin-LR, water samples have to be concentrated prior to the analysis. Preliminary results obtained analyzing *Planktothrix rubescens*-contaminated water samples, with a preconcentration step (using SPE Carbograph 4) will be presented. Experiments to improve the sensitivity of the method, to allow the direct analysis of water samples, are in progress.

ANA-OR-19 Total suspended solids (TSS) and polycyclic aromatic hydrocarbons (PAHs) removal from industrial/civil wastewater: a comparison between different wastewater treatments

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In this work two wastewater treatment lines (Line 1 and Line 2) treating both industrial and domestic sewages from the west urban area of Prato and differing one from the other for the secondary settlement system, were comparatively investigated for one year. Both the treatment lines were based on conventional denitrification/nitrification systems followed in Line 1 by secondary settlement and clariflocculation tanks and in Line 2 by a membrane biological reactor. The removal of particulate material was statistically more efficient in Line 2 than in Line 1 ($P<0.01$), being mean removal percentages equal to 98.2±2.5 and 83.1±9.6, respectively. This result highlighted the very good performances of MBR for TSS removal, in agreement with literature data [1] that described a removal efficiency very close to 100% for this system and therefore much higher than the one determined for chemical clariflocculation. In any case, effluents from both the treatment lines showed TSS concentrations much lower than the legal Italian limit for discharge in surface water (35 mg l^{-1}; D.Lgs 152/2006); moreover, TSS concentrations from Line 2 were also lower than the Italian limit for wastewater reuse (10 mg l^{-1}; D.M. 185/2003), while effluent concentrations from Line 1 were often higher than this limit. PAHs with 2-3 aromatic rings were found in all the inlet wastewater samples and showed the highest concentrations, ranging from tens to hundreds of ng l^{-1}; conversely, PAHs with four to six rings were present in a smaller number of samples and at lower concentrations (from few ng l^{-1} to tens of ng l^{-1}), with the only exception of pyrene, which averaged 108 ng l^{-1}. Naphthalene represented more than 40% of total PAHs probably because of its use in the industrial production of dyes and moth repellent, both utilized in textile industry [2], whereas the priority hazardous, PAHs according to the 2455/2001/EC, represented approximately 10% of the whole PAH content. Overall PAH removal was 84±12 and 82±18 for Line 1 and Line 2, respectively, evidencing that, under the experimental conditions adopted, the two treatment lines achieved comparable performances. Removal in the particulate phase was generally higher than that in the water phase, especially for Line 2 which showed an overall PAH removal of 94% in particulate phase versus 70% in the water phase, while, for Line 1, more

similar removal percentages were observed (88 and 80% in particulate and water phases, respectively). These findings were in accordance with the results obtained for TSS. Removal percentage found for each PAH in the water phase was linearly correlated with the corresponding log K_H values, either in Line 1 (R^2=0.73; P<0.01) or in Line 2 (R^2=0.53; P<0.01), indicating that stripping phenomena play an important role in PAH removal from the water phase, especially when the more volatile compounds are considered. Mean concentrations of the six priority hazardous PAHs in outlet samples evidenced values within the environmental quality standard (EQS) of D.Lgs. 152/2006 for the sum of these compounds (0.2 µg l^{-1}) in surface waters, while the sum of Benzo(g,h,i)perylene and Indeno(1,2,3-c,d)pyrene was higher than the 2455/2001/EC EQS for inland surface waters. Benzo(a)pyrene was found to be present in 50-60% of the outlet samples, at concentrations approximately included between 10 and 30 ng l^{-1}.

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ANA-OR-20 Electrochemical Bioassay for miRNA detection

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MicroRNAs (miRNAs) are naturally occurring small RNAs (approximately 22 nucleotides in length) that act as regulators of protein translation.
Because many diseases are caused by the misregulated activity of proteins, microRNAs have been implicated in a number of diseases including a broad range of cancers, heart disease, immunological and neurological diseases. Consequently, microRNAs are intensely studied as candidates for diagnostic and prognostic biomarkers. The analysis of the intracellular levels of miRNAs is challenging, however, because their short lengths, low abundances, and high levels of sequence similarity present obstacles in the use of conventional analytical methods. Currently, miRNAs are predominantly detected with Northern blot, PCR, or microarray analysis. These detection technologies are expensive and time-consuming and require well-trained scientists.

In this paper, an innovative electrochemical method based on paramagnetic beads and enzyme amplification for multiplexing miRNA detection was reported.
Magnetic beads allow easy separation and washing steps in a biosensing experimental set-up, whereas, between the different transduction principles, electrochemistry is considered one of the most appealing in term of cost, ease of use, possibility of in situ multiplexing analysis (point of care testing). The proposed method is based on biotinylated DNA CPs immobilized on streptavidn coated paramagnetic beads. Total RNA is extracted from the sample, biotinylated, and then hybridized with the beads. The beads were then incubated with streptavidin alkaline phosphatase and exposed to α-naphtyl- phosphate. The product of the enzymatic reaction was electrochemically monitored. The assay was finally tested onto a compact microfluidic platform which allows multiplexed analysis of 8 different samples.

ANA-OR-21 Analytical device based on lens-less bio-chemiluminescence imaging as a companion diagnostics tool for personalized medicine

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Companion diagnostics are assays intended to assist physicians in making treatment decisions for their patients, by elucidating the efficacy and/or safety of a specific drug for a targeted patient group. With this respect, multiplexed Point-Of-Care Testing (POCT) devices, suitable to perform the analysis directly where the sample is obtained, are requested in order to perform rapid and accurate disease progression monitoring along with drug levels assessment.

This work describes the development of POCT devices exploiting "contact" lens-less imaging detection, in which the bio-chemiluminescence (BL-CL) analytical signal is produced directly on the surface of a CCD light sensor. This configuration provides high light collection efficiency and has been exploited in different bioanalytical assay formats [1,2]. A CL microfluidics-based device was developed for performing panel tests, including enzyme activity assays, immunoassays and nucleic acid hybridization assays, which were performed simultaneously to obtain a complete panel assay. Adequate LODs were obtained for a panel of model analytes, such as alkaline phosphatase (10 IU/L), proteins analyzed by immunoassay (3.5 fmol/L of HRP), and nucleic acids (0.05 μmol/L of amplified Parvovirus B19 target DNA). A biodevice based on BL whole-cell biosensors was developed for multiplexed detection of compounds with hormone-like activity. Cells, which were genetically engineered to express the BL reporter protein luciferase upon interaction with analytes able to activate a specific receptor, were immobilized in a modified clear bottom black 384-well microplate to obtain a BL cell array. A LOD of 0.5 nM of testosterone was obtained with immobilized yeast cell-based biosensor for androgen detection.

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ANA-OR-22 Stacking Interactions in Oligonucleotides by Differential Pulse Voltammetry and Spectroelectrochemistry Measurements

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Oxidative DNA damage is a consequence of cellular metabolism, with a propensity for increased levels following exposure to UV and ionizing radiation, and toxic insults. One electron oxidation of DNA generates a radical cation, an electron hole, which is able to migrate along the strand and to irreversibly react leading to strand breaks and nucleobase modifications, with loss or corruption of genetic information, possibly resulting in cellular aging or disease.

Differential pulse voltammetry and spectroelectrochemistry proved to be very effective techniques to investigate the oxidation properties of isolated nucleosides and nucleotides in solution. [1-3] Here we present the results concerning the extension of our previous works to oligonucleotides, systems which are better biomimetic DNA models than single nucleosides, allowing molecular processes of free radical reactions to be examined in a less complex environment than DNA, but respectful of its biological characteristics. Short sequences (hexamers), which possess coiled conformations in water solution, have been considered. The higher order structures of the oligonucleotides have been studied by one- and two-dimensional NMR spectroscopy, circular dichroism, and molecular mechanics. Differential pulse voltammetry and spectroelectrochemistry have allowed to characterize the distribution of low lying energy states of one electron oxidized oligonucleotides, giving access to a series of important information about the chemico-physical effects which controls the long range charge transfer in DNA and determines the sites where oxidative DNA damages occur.

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ANA-OR-23 Characterization of the Fat-soluble Vitamin and Carotenoid Profile of Green and Golden Kiwi by HPLC-DAD-Tandem MS Hyphenation

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Fat-soluble vitamins are essential micronutrients involved in important biological functions and classified into four groups: vitamin A, vitamin D, vitamin E, and vitamin K [1]. Each group is characterized by an heterogeneity of forms about whose natural distribution little is known. In fact, the conventional analytical methods are often addressed to determine one single form, i.e. the most stable and/or widespread one. The reasons of this choice are basically economic, but also due to a series of analytical difficulties: 1) subtle chemical differences between vitamers belonging to the same vitamin group; 2) unavailability of standards; 3) low and different endogenous levels in complex food matrices; 4) occurrence of bound forms.

The main purpose of this work was to characterize the fat-soluble vitamin and carotenoid fraction of kiwifruits belonging to the genuses *Actinidia deliciosa* (green kiwi whose Italy is the world leader producer) and *Actinidia chinensis* (golden kiwi, launched on the worldwide market under the trade name Zespri Gold in 2000). A novel analytical approach, based on LC-DAD-APCI-MS/MS hyphenation, was developed in order to perform both the quantitative analysis of ten target micronutrients (lutein, zeaxanthin, β-carotene, β-cryptoxanthin, α-tocopherol, δ-tocopherol, γ-tocopherol, ergocalciferol, phylloquinone, menaquinone-4) and the screening analysis of other pigments whose standards are commercially unavailable. MSPD was used as a mild technique for the extraction/clean-up procedure, with recoveries of all compounds exceeding 60%. Non aqueous reversed phase (NARP) chromatography on a C30 column was used for the analytes separation. The combined DAD-MS chromatographic detection proved itself as a potent tool for obtaining a comprehensive profile of fat-soluble vitamers and carotenoids occurring in the analyzed fruits. The unexpected presence of menaquinone-4 (K2 vitamer) and the detection of geometric isomers, which were not artefacts of the applied extraction procedure, were only some of the achieved results.

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ANA-OR-24 Determination of collagen by pyrolysis/GC-MS. Evaluation of the degree of conservation of archeological bones from Vicenne (Italy) by comparison with XRD, TGA and FTIR analysis

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Human bones and teeth are frequently recovered at archaeological sites. Their state of preservation may depend on the mode and the burial environment. The content of collagen and the degree of crystallinity of carbonate hydroxyapatite (HA) are among the indicators adopted to evaluate the conservation status of bones. Analytical pyrolysis (Py) [1] together with X-ray powder diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) and thermogravimetric analysis (TGA), were used at this scope. In this work, a new quantitative procedure in Py was employed to characterise residual proteins in five bone samples from the medieval necropolis of Vicenne-Campochiaro (Molise, Italy)[2].
The yields of cyclic dipeptides (2,5-diketopiperazines, DKPs) evolved form the pyrolysis of the samples, including the cyclo(proline-hydoxyproline) as distinctive marker of collagen, were determined by GC-MS with and without silylation. The detection of DKPs enabled the identification of collagen in all the analysed samples, in accordance to the FTIR spectra showing the characteristic amide peak. The presence of organic matter along with that of carbonatic phases was confirmed and estimated by TGA. XRD data showed that the samples mainly contained HA having different degrees of crystallinity; small amounts of quartz and calcite were also detected in some samples. The quantitative experimental data were combined to provide a relative estimate of the degree of conservation of the bone samples. The bones of an adult young female (t.139) and an aged male (t.165) resulted to be the worst and best preserved, respectively. The tombs were located in the same area where the acidity of the soil has damaged nearly all the skeletons. The skeleton from t.165 was almost complete, whereas the one from t.139 was lacking in many bones. Therefore biological (age-at-death, sex) and ritual (care, depth) factors as well as specific conditions of each burial could be involved in the observed different preservation state.

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ANA-OR-25 An Alternative Method for Microcystins Analysis in Aerosol Samples.

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Cyanobacteria are a small group of photosynthetic planktonic bacteria, which produce a large group of potent hepatotoxins called microcystins (MCs). Waterborne toxins can be found in the aerosol phase due to bubble-bursting processes. It has been demonstrated that some respiratory symptoms can be associated with exposure to high levels of cyanobacteria during recreational activities.

While biological assay or physicochemical approaches can reveal the presence of MCs, but not identify which specific toxins are present, chromatographic methods can separate them allowing individual identification.

The aim of this study was to obtain a sensitive method for the determination of trace concentrations of individual cyanotoxins in aerosol samples, using an Agilent 1100 series HPLC system (Agilent, Waldbronn, Germany) coupled to an API 4000 triple quadrupole mass spectrometer (Applied Biosystems/MDS SCIEX, Toronto, Ontario, Canada).

During method development improved electrospray ionization was found in negative ion mode for the MCs. For this reason, in contrast with others authors, we have developed a chromatographic separation using alkaline conditions, thus achieving good resolution, improved electrospray ionization and therefore better sensitivity.

A sensitive analytical method has been obtained for measuring trace concentrations of MC family of cyanotoxins and nodularin in aerosol samples, allowing a simultaneous detection of six MCs (MC-LA, -LY, -YR, -LR, -LW, -LF, and NOD) in a single 27 min chromatographic analysis.

The limit of detection for all the toxins were determined to be between 2 fg/μL (-LA and -LF) and 178 fg/μL (NOD), values that are similar or lower than those reported in the literature. In this work the internal standard method has been used for calibration and the analytical procedure was validated by evaluating the accuracy, precision and recovery .

The method was applied to seven aerosol samples from the Venice Lagoon. In these samples, trace concentrations of MC-LA ranged between 90 fg m^{-3} and 706 fg m^{-3}, MC-LF between n.d. - 369 fg m^{-3} and MC-LW between n.d. - 262 fg m^{-3}. More research needs to be conducted in order to investigate the origin of these compounds in the Venetian atmosphere.

ANA-OR-26 Assessment of the direct exposure of honeybees to particulate matter containing neonicotinoid insecticides during the corn sowing and its relevance to the colony loss phenomena.

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The last decade was characterized by rapid disappearances of honeybees' colonies failing to return to the hives. The phenomenon, called Colony Collapse Disorder (CCD), represents a worldwide crisis with consequences both in plants pollination and crops productivity. Although on the causes of CCD several hypothesis have been advanced (parasitic mites, viruses, insecticides etc.), none of them was clearly supported or refused by experimental results. Colonies losses have been reported in Italy concurrent with the sowing of corn seeds coated with neonicotinoid insecticides using pneumatic drilling machines [1]. During the sowing operations, the seeds are sucked into the pneumatic drilling machine causing the erosion of the seed coating and the fragments are then expelled through a waste pipe. In a first hypothesis, bees uptake neonicotinoids through the nectar and pollen of the contaminated vegetation at field margins. However, the insecticides content on the surrounding vegetation was shown to be not sufficient to cause acute toxicity in foraging bees [2]. In this connection, novel routes of exposure and intoxication of honeybees to neonicotinoids have been proposed [3].
In the present study the direct exposure of bees to particulate matter emitted by the drilling machine during the corn sowing has been quantified. Numerous experiments were conducted in open field and accurate analytical procedures were optimized to determine both the effective emission capability of the drilling machine and the consequent uptake of the insecticide by the bees flying over the field. Test were performed using new types of seed coating, proposed in 2009 and 2010, and three different types of pneumatic drilling machines. The results of the experiments confirm the hypothesis of the relationship between the extended honeybees losses and the sowing of corn seeds coated with neonicotinoid insecticides.

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ANA-OR-27 Application of high temperature liquid chromatography coupled to inductively coupled plasma mass spectrometry for speciation analysis of environmental samples

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The determination of arsenic is of great environmental interest because it derives from both natural and anthropogenic sources and its toxicity and bioavailability are strongly dependent on its chemical form. The inorganic compounds (e.g. arsenite, arsenate) have been found to be very toxic, while the organic compounds can be either toxic (e.g. methylarsonic and dimethylarsinic acid) or non-toxic (e.g. arsenobetaine and arsenocholine). Furthermore, arsenosugars can occur at relatively high concentrations in organisms used as human food. Hence, it can be easily understood that speciation studies are necessary for toxicological and environmental considerations, while the determination of total arsenic is insufficient for this purpose.
The hyphenation of high performance liquid chromatography (HPLC) to inductively coupled plasma mass spectrometry (ICP-MS) is a technique of choice for speciation analysis. In recent years, high temperature liquid chromatography [1] (HTLC) has emerged as a new chromatographic technique where the mobile phase is heated up to get important advantages, such as faster separations and better resolution; moreover, organic solvents can be replaced by pure water as the mobile phase, thus making HTLC cheaper, simpler, more environmental friendly and suitable to ICP-MS than conventional HPLC.
In this work we developed new analytical methods based on HTLC-ICP-MS for arsenic-speciation analysis of environmental samples. Work temperatures higher than 100 °C allowed to obtain good separations without the need to use salts or organic solvents as the mobile phase. This method was finally applied to biological samples such as Antarctic crustaceans and molluscs.

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ANA-OR-28 Preparati per la medicina ayurvedica. Contenuto di metalli essenziali e di elementi potenzialmente tossici

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La medicina ayurvedica ha avuto origine in India migliaia di anni fa; è tuttora ampiamente utilizzata nel Paese di origine e sta diventando sempre più diffusa nei Paesi occidentali. In letteratura sono riportati numerosi casi di intossicazione dovuti alla presenza, in alcuni preparati ayurvedici, di elevate concentrazioni di elementi quali arsenico, piombo e mercurio, che possono essere introdotti volutamente in ciascuna formulazione, seguendo i dettami della tradizione, oppure possono derivare dai trattamenti di preparazione [1].

Per questo motivo è stato determinato il contenuto di elementi (Al, As, Ca, Cd, Cr, Cu, Fe, Hg, K, Mg, Mn, Na, Pb, Si and Zn) in quindici preparati per la medicina ayurvedica acquistati in India. Gli analiti sono stati scelti tenendo conto del loro ruolo di elementi essenziali e/o tossici ad elevate concentrazioni. Sono state prese in considerazione quattro famiglie di prodotti denominate Bashma, Guggulu, Parpati, Pishti. Le analisi sono state effettuate con la spettroscopia atomica di emissione o di assorbimento, a seconda dei livelli di concentrazione in gioco, previa mineralizzazione dei campioni in forno a microonde [2]. I risultati sperimentali sono stati elaborati con tecniche chemiometriche di pattern recognition, allo scopo di rilevare similitudini e differenze tra i campioni e correlazioni tra le variabili.

Sono stati calcolati i quantitativi di ciascun elemento ingeriti seguendo la posologia riportata per ciascun preparato. Tali quantitativi sono stati confrontati con valori di riferimento, quali le concentrazioni limite tollerabili dall'organismo stabilite da organismi internazionali. Si è osservato che le concentrazioni di Hg in quasi tutti i campioni e quelle di As, Cd, Cr e Pb in alcuni casi sono superiori ai limiti di accettabilità. I risultati di questa indagine confermano i rischi associati al consumo di prodotti estranei ai circuiti di controllo regolamentati dalla Comunità Europea, soprattutto se utilizzati senza il controllo di un personale competente.

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ANA-OR-29 X-ray photoelectron spectroscopy and X-ray excited Auger electron spectroscopy of alkali metal sulphates

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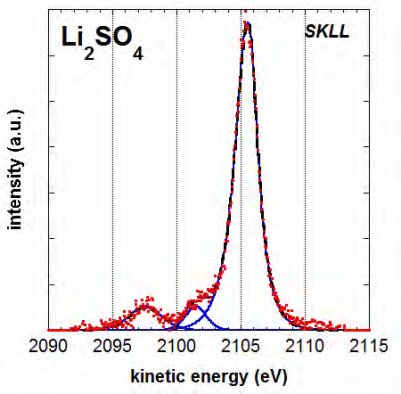
The dissolution of sulphide minerals results in acid-mine drainage with possible release of toxic elements. The surface reaction is controlled by a sulphur-containing thin film in intermediate oxidation states [1-4]; their assignment is still controversial. XPS and XAES are powerful techniques for directly probing the chemical state of the elements, but their application to these minerals has been hampered by difficulties in interpreting the small shifts in S2p binding energies in the region of 164-165 eV and in the curve fitting of the SKLL spectra. So far the sulphur Auger parameter $\alpha'=KE_{Auger}+BE_{photoelectron}$[5] was calculated considering the kinetic energy of the maximum of SKLL peak [2-4]. Here the results of the peak-fitting of the sulphur SKLL signal of alkali metal sulphates are provided. The example in the figure shows the presence of three components that can be identified as follows: the most intense, ^1D, is due to the $KL_{2,3}L_{2,3}$ transition that corresponds to the $2s^22p^4$ final configuration. The second one at lowest kinetic energies, ^1S, is due to the other possible transition, KL_1L_1, that corresponds to the $2s^02p^6$ final configuration; the third signal, between ^1D and ^1S lines, is probably an excitation line due to a satellite. This component is present in all SKLL sulphate spectra. An increase in SKLL KE was observed with increasing metal atomic number (from 2105.1 eV for Li_2SO_4 to 2107.5 eV for Cs_2SO_4) together with a decrease of S2p binding energy. The Auger parameter is fairly constant and the difference of S2p and SKLL energy values are interpreted as differences in Madelung potentials.



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ANA-OR-30 Determination of YLOID, Zr and Hf in seawater by ICP-MS technique: method validation and evaluation of measurement uncertainty

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In the last years many researches were focused on behaviour and naturally abundances of Y, La, Lanthanoids (YLOID), Zr and Hf in marine systems increasing the attention to their capability to trace geochemical processes occurring along the water column, ocean circulations and at the solid-liquid interface [1-2]. In contrast YLOID and Zr-Hf behaviour can have a geochemical significance only if their contents in seawater is analysed according to a robust, reliable and comparable chemical analytical approach. Therefore the ability of an analytical protocol to obtain reproducible values is paramount. Unfortunately, the analysis of these metals in natural waters is often complicated by their ultra low concentrations (0.5–100 pmol/L), the high matrix concentration and a wide range of severe spectral interferences (*e.g.*, Ba^{2+}, seawater salts).

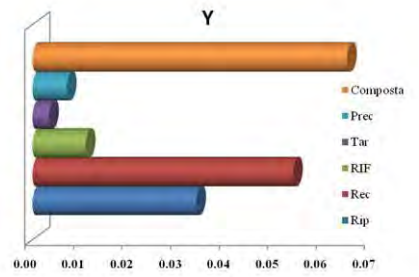

Fig. 1

To perform simultaneous ultra-trace YLOID, Zr and Hf analyses in seawater, we developed a preconcentration method based on coprecipitation with $Fe(OH)_3$ and determination by ICP-MS. In this study the metals behaviour was quantitatively investigated during coprecipitation and estimation of composed uncertainty associated to measurements was evaluated with a rigorous metrological approach based on method validation and quality data control. These goals were achieved using spiked natural seawater samples where YLOID, Zr and Hf had concentrations as occurring in natural seawater, (20 pg/mL).

Under these conditions the metals were quantitatively recovered from seawater with good precision (2–5%), apart for La (10%). Composed measurement uncertainty was expressed in terms of precision, recovery, reference materials and instrumental calibration uncertainty (Fig.1). The obtained results were critically discussed on the basis of the different contributions and confirm the quadrupole ICP-MS technique as highly sensitive to determine very low YLOID, Zr and Hf concentrations.

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ANA-OR-31 Development and analytical characterization of a novel *in situ* antibiotic delivery system to prevent titanium implant-related infections

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Orthopedic infections often represent one of the major causes of implant failure [1]. In this context, an efficient approach is based on local antimicrobial prophylaxis generally performed by coating titanium implant surfaces with active thin films able to release antibiotic [2]. In this work, a novel Ciprofloxacin (CIP) loaded chitosan nanoparticles (CSNPs) coating onto titanium surface has been developed and characterized.
The model antibiotic CIP is active against Gram-positive and Gram-negative bacteria in vitro and it also shows high stability and efficiency [3]. On the other hand, NPs based on the cationic polysaccharide chitosan are biocompatible and their ability to load and deliver hydrophilic molecules such as CIP is well documented [4, 5].
CSNPs loading CIP were prepared according to a modified ionic gelation method [4]. Afterwards, CIP loaded CSNPS were set by casting onto titanium sheets. The determination of particle size and polydispersity index of CIP loaded CSNPs were determined using a Zetasizer NanoZS. X-ray Photoelectron Spectroscopy (XPS) analysis was performed on pure materials and on CIP loaded CSNPs system in order to provide information about the drug surface location on the coating.
Drug release profile from the investigated coatings, tested in physiological solution by HPLC, showed that, since the first hours of incubation, the CIP amount released over time is higher than the minimum inhibitory concentration (MIC) values of the most common pathogens causing orthopaedic implant infections. A study on the antibacterial activity of these nanoparticles-based coatings was performed on *S. aureus* and *P. aeruginosa* cultures, demonstrating the total inhibition growth of both bacteria.

Coatings biocompatibility was also assessed by MTT test and SEM morphological analysis using MG63 ostoblast-like cells highlighting a good cell viability. Thus, the novel antibiotic delivery system investigated represents a promising coating that could act as potential *in situ* drug carrier.

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ANA-OR-32 Looking at the liquid surface-vacuum interface by X-ray photoelectron spectroscopy

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The strength or the weakness of an electrolyte in organic solvents is interesting both from the technological and the scientific point of view, e.g. in high-energy battery production and the elucidation of organic reactions mechanisms, respectively. In this work the behavior of tetraethyl-ammonium bromide (TEABr) in polyethylene glycol (PEG) 200 by means of conductimetric measurements and angle resolved X-ray photoelectron spectroscopy (ARXPS) has been investigated to verify if they are strong or weak electrolytes and to characterize the spatial distribution of the ions at the vacuum-solution interface.

Comparing our conductimetric data with Onsager's equation shows that solutions of TEABr in PEG 200 exhibit the typical behavior of strong electrolytes. The specific conductivity has also been measured for saline solutions in water and in ethylene glycol and a good agreement between the data of this work and those of the literature was found.

The XP-spectra of the 5wt% of TEABr in PEG 200 were taken on the liquid deposited as drop on gold. All peak positions appear to remain unchanged with respect to those of pure PEG and TEABr. ARXPS has shown that both anions and cations are repelled from a vacuum-solution interface. The thickness of the ion-depletion layer is found to be approximately 8 Å.

ANA-OR-33 Solvation effects on the supramolecular conformation adopted by an elastin-like polypeptide, polyValGlyGlyValGly. An investigation on interfacial properties by combined surface techniques.

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Previous work on elastin-like polypeptides (ELPs), made of hydrophobic amino acids, such as valine, glycine and leucine, has shown that helical fibres easily form in aqueous media [1,2] while globules and 'string of bead' structures were observed to form in deposits from methyl alcohol [3]. The supramolecular organization seems governed by local interfacial interactions and, thus, considerations of the interface properties, in the given environment, are important.

We have here focussed our attention on polyValGlyGlyValGly, chemically synthesized and characterized in our laboratories [1-3]. This polypeptide, the most inclined in forming long helical fibres in water [4], see Figure, was dissolved in solvents having different protic and polar characters (H_2O, MeOH, DMSO, EG). Based on past experience, we have then examined the deposits, evaporated onto silicon substrates, using AFM and XPS analyses to combine the images of the obtained supramolecular structures with their surface composition.

The manner in which the preferred organization of polyValGlyGlyValGly are obtained, in dependence of the environment, is discussed also in the light of the possible biological role of this polypeptide, as a support for tissue regeneration and engineering applications.

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ANA-OR-34 Reaction chromatography: design and characterization of new stationary phases for flow-chemistry applications

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Organocatalysis uses small organic enantiopure molecules, usually derived from the natural world (proline, amino acids, alkaloids of the cinchona family, etc.). These molecules do not require controlled reaction conditions such as anhydrous or purified solvents or an inert atmosphere. Compared to metallocatalysis, organocatalysis has the advantage that product contamination is avoided since metals are not used. On the other hand, organocatalysts are characterized by lower catalytic efficiencies than metallocatalysts. For this reason, they are employed in higher loading, generally in the range 5-20% which has to be compared with 0.01-1% usually employed for metal based catalysts.
The immobilization of reagents or catalysts on insoluble solid supports (such as silica gel) enables the synthetic processes to occur in heterogeneous phase, a situation that shows clear advantages compared to homogeneous systems. In fact, the simple isolation of the catalyst and its potential recycling make the solid-supported catalyst processes particularly attractive in many fields of fine chemicals (included that of asymmetric synthesis of chiral enantiopure products). Heterogeneous catalysis performances are strictly depending on both the nature of support and the type of surface immobilization of catalytically active fragments. The support should ensure high thermal, chemical and mechanical stability together with high surface area, thus enabling rapid mass transfer for reagents, products and catalysts. In this work, we describe the preparation and the chromatographic characterization of new materials prepared by covalently binding proline and proline-like organocatalysts to silica gel. These materials can be used in chromatography as chiral stationary phases or in chromatographic-like applications as supports to perform chemical reaction in flow-mode.
In particular, the slow aldol reaction of cyclohexanone with p-nitro benzaldehyde has been selected as model reactions to study the activity and stability of these materials under continuous-flow conditions.

ANA-OR-35 Effect of temperature on packing and performance of nano-LC columns.

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Over the years, much effort has been addressed to increase the speed of analysis and the efficiency in HPLC. Nano-LC columns allow to work with minute sample size and small volumetric flow-rates, therefore, they show an increase of sensitivity due to a reduced sample dilution. Concentration-sensitive detectors, such as electrospray mass spectrometry, can take advantage of this increase when high sensitivity is required.

In this work, we evaluated the effect of temperature on the packing procedure of nano-LC columns (75 µm i.d.) and on their performance.

Different slurries of packing material were prepared using different solvent mixtures, and the stability of the suspension was evaluated at different temperatures. At high temperature (70° C) the slurry sedimentation is slow and the suspension looks stable for, at least, 30 minutes. As a consequence, at high temperature it was possible to easily pack long and more efficient columns (50 cm and longer). Long (40-50 cm) and short (15-20 cm) columns were packed at room temperature and at 70° C, using three different slurries. For long columns, a lab-made end-frit was syntherized directly in the fused silica capillary tubing. The empty tubing was packed with C18 Pinnacle II stationary phase (Restek, Bellefonte, PA, USA). For short columns, used Integrafrit fused silica capillary tubing was used and packed with Poroshell 120 SB-C18 stationary phase (courtesy of Agilent Technologies, Santa Clara, CA, USA). Long columns were tested at 70°C to reduce the mobile phase viscosity; short columns were tested at room temperature. The performance of the columns was evaluated through the calculation of the following parameters: capacity factor, k; asymmetry factor, As; number of theoretical plates, N; Van Deemter with reduced parameters plot [1]. A test mixture containing uracil (t0), benzene, naphthalene, and biphenyl (Restek, Bellefonte, PA, USA) was used to evaluate the chromatographic parameters.

The columns packed at a high temperature show a better efficiency, in terms of theoretical plates, that those packed at room temperature, depending on the slurry composition, with both stationary phases. The asymmetry factor is worse for the Poroshell packed columns, with all three slurries, compared to C18 Pinnacle II. The unsatisfactory As values can indicate that the Poroshell stationary phase deteriorates at 70°C.

ANA-OR-36 Retinoids in Raw Milk from Different Animal Species: a Complete Analytical Strategy Based on LC-MS/MS Hyphenation

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Milk is an almost complete single food containing significant amounts of essential nutrients; its whey is a good source of water-soluble vitamins, while its lipid fraction is an important delivery medium of fat-soluble vitamins, especially vitamin A [1]. Vitamin A-active compounds occur in milk mainly as retinoids and to a lesser extent as carotenoid precursors (provitamins A).

Very little is known about the quali-quantitative profile of retinoids in bovine milk as well as in that of other ruminant species. Only one study [2], describes the HPLC-UV analysis of retinyl esters in cow, goat and human milk. The main analytical difficulties are related to the unavailability of standards, their cost and the complexity in development chromatographic separation; in fact, vitamin A vitamers are characterized by subtle differences in chemical structures so a highly efficient and selective chromatographic system is needed for achieving their resolution.

A reliable analytical approach, based on high performance liquid chromatography coupled to tandem mass spectrometry (HPLC-MS/MS), allowed us to establish the real occurrence and distribution of several retinoids in raw cow, sheep, goat and water buffalo milk samples. Direct liquid extraction with solvents was performed for isolating retinoids while alkaline hydrolysis enabled the total retinol determination; yields exceeding 68% were obtained for all analytes. Chromatographic separation was carried out using two tandem systems of reversed-phase columns (C18/C18 and C18/C30) in order to achieve total separation of the vitamin A vitamers. The chromatograph was coupled on-line with a triple quadrupole mass spectrometer, and the MS detection was accomplished by means of positive atmospheric pressure chemical ionization (APCI), operating in the Selected Reaction Monitoring (SRM) mode.

According to our results, and in the light of the FAO/WHO recommendations [3], the consumption of milk may supply a significant portion of the daily intake of vitamin A, proving to be an important food, ***especially for infants and children.*** Buffalo milk, in particular, has a high level of retinyl linolenate, that represents an additional nutritional value, since omega-3 fatty acids are essential for the proper functioning of the organism.

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ANA-OR-37 Ionic liquids as novel coatings for solid-phase microextraction

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Ionic liquids (ILs) are molten salts made of cations and anions having a melting point below 100 °C [1]. Beside the intrinsic non-molecular nature of ILs giving them unique solvent properties, the major advantage is their extremely low vapor pressure. Some properties, such as thermal stability and miscibility, mainly depend on the anion, whereas others, such as viscosity, surface tension and density, depend on the length of the alkyl chain in the cation. By a proper combination of anions and cations, different ILs having desired chemico-physical properties can be obtained. In a research program aimed at devising novel SPME coatings for forensic applications [2], the aim of this study was the development of novel IL fibers for solid-phase microextraction (SPME) of drugs of abuse. Four polymeric ILs (Fig. 1) were synthesized and used for the environmental monitoring of drugs of abuse with the aim of detecting both consumption and their illicit import.

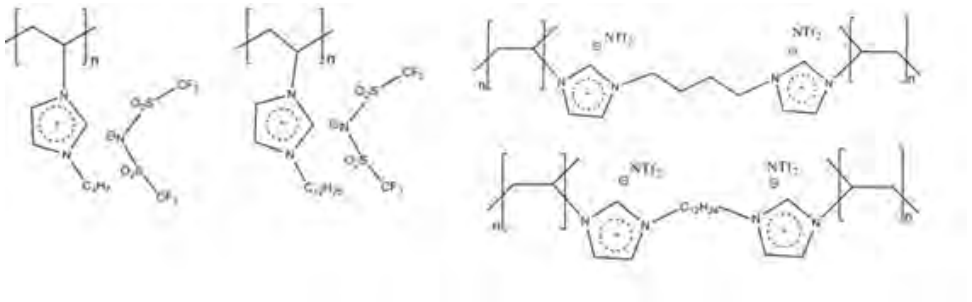

Figure 1

The SPME fibers were characterized in terms of coating thickness, thermal stability, bleeding and pH stability obtaining extraction capabilities higher than those obtained using commercial devices.
Method validation proved the reliability of the developed SPME-GC-MS method for the environmental detection of drugs of abuse at trace levels. Finally, the method was applied to the analysis of seized drapery showing the presence of ketamine at high concentration levels.

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ANA-OR-38 Pressurized solvent extraction for the determination of illicit drugs in hair by HPLC-MS/MS

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Plasma and urine are the most commonly used matrices for illicit drug testing, but since 1979 there has been an increasing interest in the development of analytical methods in alternative matrices such as hair [1]. Hair has the advantage of a substantially longer detection window (months to years) which enables retrospective investigation of chronic consumption. In addition, hair is a durable and stable matrix difficult to adulteration in which toxic substances are pre-concentrated and remain for a long time without significant alterations; furthermore the sampling is not invasive [2]. Indeed hair analysis of illicit drugs has recently been codified in the Italian legislation as a monitoring tool in the field of workplace safety [3]. The critical step is certainly the extraction phase, usually performed by solid liquid extraction for multiclass methods; the main drawback is the long contact time (from 16 to 20 hours) between hair and solvent necessary to have good recoveries. Times are greatly reduced if the extraction is assisted by ultrasonic or increased temperature.

Pressurized Liquid Extraction (PLE) was applied to significantly reduce extraction time since there are no PLE applications in this field. So a method based on HPLC-ESI-MS/MS has been developed and validated for multiresidual determination of illicit drugs from hair: amphetamine, methamphetamine, mescaline, MDA, MDMA, MDEA, cocaine, benzoylecgonine, nor-cocaine, ketamine, phencyclidine, diacetylmorphine, morphine, 6-monoacetylmorphine, codeine. PLE led to reduce the analysis time and automate the extraction process, taking into account sample washing to remove external contamination and the clean-up of the extracts. Satisfactory extraction rates have been obtained using water as extracting and 10 minutes as extraction time.

[1] M. Wada et al., *Anal.Bioanal.Chem.*, 397, **2010**, 1039.
[2] F. Pragst et al., *Clin.Chim.Acta*, 370, **2006**,17.
[3] Accordo Stato/Regioni 18.09.**2008** (G.U. n. 236 del 08.10.08)

ANA-OR-39 Optimization of the Separation of Biomolecules by Capillary Electrophoresis and High Performance Liquid Chromatography: Effects of the Liquid Phase Composition

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This communication discusses the results of our recent studies carried out to shed light on theoretical and practical aspects of capillary electrophoresis (CE) and high performance liquid chromatography (HPLC), which are widely employed analytical techniques for the separation and identification of biomolecules in natural complex matrices [1]. We examine the influence of the composition of the liquid phase (i.e. the electrolyte solution (BGE) in CE and the mobile phase in HPLC) on the electrophoretic and chromatographic behaviour of several classes of biological compounds, which are typically analysed by CE or/and by HPLC, either with UV-Vis or mass spectrometry (MS) detection. In addition, we discuss the successful employment of CE to investigate the occurrence of interactions between the analytes and the components of the solutions used as the mobile phases in HPLC.

The research has been carried out investigating mobile phases and BGEs of composition requested to control the protonic equilibrium in solution and to modulate the selective separation of peptides, proteins and other biomolecules either by CE or by HPLC. Variations of the mobile phase composition in a wide range of ionic strength determine significant differences in the chromatographic behaviour of peptides and proteins on size exclusion and ion-exchange silica based HPLC columns, which have been related to the capability of the investigated analytes to establish electrostatic and hydrophobic interactions with the above columns. The interactions of peptides and proteins with the acidic components of the mobile phases employed for their separation by reversed phase HPLC have been confirmed by CE and their effects on the chromatographic behaviour of these analytes are discussed. Also examined is the use of buffering agents capable to controlling the protonic equilibrium in a wide pH range and the use of additives incorporated into the BGE to suppress the untoward interactions of basic proteins with the inner surface of the bare fused-silica capillary employed in CE [2-3].

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[2]S. Bachmann, R. Vallant, R. Bakry, C.W. Huck, D. Corradini, G.K. Bonn, Electrophoresis 31, **2010**, 618-629.

ANA-OR-40 Thermodynamics of a Supramolecular Host in Water: Deconvoluting the External and Internal Guest Binding

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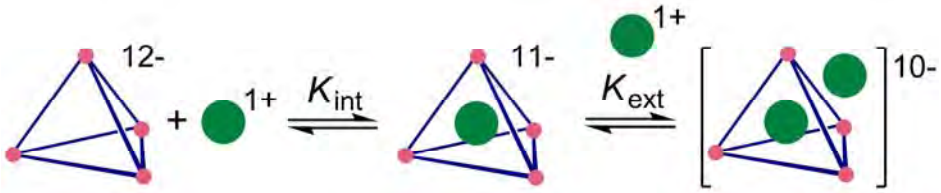
The supramolecular assembly $[Ga_4L_6]^{12-}$ (L = 1,5-bis(2,3-dihydroxybenzamido)naphthalene) has been reported to act as a chiral, nanoscale flask suitable to mediate the reactivity of encapsulated reactive guests and to carry out enzyme-like chemical transformations [1]. The highly anionic exterior surface of the assembly imparts solubility in water and other polar solvents and affinity for the external ion-association of cationic molecules [2]. The driving forces for the external and internal guest binding are very different thus complicating the determination of the thermodynamic parameters. We have used a combination of NMR, UV-vis and isothermal titration calorimetry to definitively separate multiple guest binding to the interior and exterior of the supramolecular host and to determine the corresponding $\Delta G°$, $\Delta H°$ and $\Delta S°$ values [3]. Data obtained by each independent technique measure different components of the host-guest equilibria and only when analyzed together and simultaneously a complete picture of the solution thermodynamics emerges. Striking differences between the internal and external binding of ammonium guests are found as a consequence of the high charge and hydrophilic outer space of the host contrasted by its hydrophobic inner space.



[1] M. D. Pluth, R. G. Bergman and K. N. Raymond, *Acc. Chem. Res.*, *42*, **2009**, 1650.
[2] M. D. Pluth, D. W. Johnson, G. S. Szigethy, A. V. Davis, S. J. Teat, A. G. Oliver, R. G. Bergman and K. N. Raymond, *Inorg. Chem.*, *48*, **2009**, 111.
[3] C. Sgarlata, J. S. Mugridge, M. D. Pluth, B. E. F. Tiedemann, V. Zito, G. Arena and K. N. Raymond, *J. Am. Chem. Soc.*, *132*, **2010**, 1005.

ANA-OR-41 Lanthanides(III) compounds with quercetin

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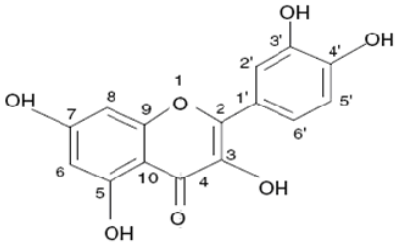
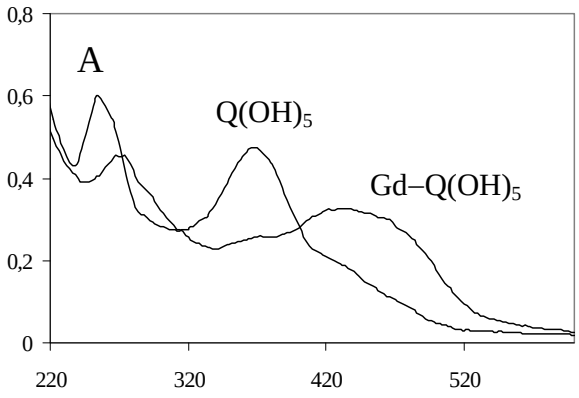


Quercetin (3, 3', 4', 5, 7 – pentahydroxyflavone), $Q(OH)_5$, belongs to the group of flavonoids, a class of polyphenols, found in high concentrations in a wide variety of plants. Flavonoids have been associated with prevention of heart disease and cancer. Quercetin is the most abundant of the flavonoid molecules and exhibits strong antioxidant properties and inhibitory effects on several enzymes. These properties are ascribable to their abilities to act as chelators to metal ions. Recent studies have, in fact, highlighted the possibility of using quercetin as a binder to reduce the toxicity of many metals[1].

quercetin = $Q(OH)_5$



The complexation of lanthanoids(III) with quercetin has been evidenced by spectroscopic and potentiometric techniques. The system Gd(III)–quercetin has particular relevance in medical imaging. In patients with diabetes and kidney dysfunction, the Gd^{3+} is not well tolerated[2]. However, the administration of complexed gadolinium will reduce their toxicity.

The aim of this work is the study, at 25°C and 0.5 mol/dm^3 NaCl by potentiometric (glass electrode) and spectrophotometric titrations, of the complex formation between quercetin and H^+ as well as between Gd^{3+} ion and quercetin in H_2O–C_2H_5OH 5%(w/w) solutions. The presence of ethanol has been necessary to increase the quercetin solubility due to its low solubility in water (4×10^{-6} mol/dm^3).
The data were processed by numeric methods (HYPERQUAD2008) and the results are explained by the equilibria and constants.

Equilibria	EMF data log$K \pm 3\sigma$	SPECT data log$K \pm 3\sigma$
$Q(OH)_5 \rightleftharpoons Q(OH)_4O^- + H^+$	–5.6 ± 0.1	–5.46 ± 0.05
$Q(OH)_5 \rightleftharpoons Q(OH)_3O_2^{2-} + 2H^+$	–13.2 ± 0.2	–12.93 ± 0.08
$Q(OH)_5 \rightleftharpoons Q(OH)_2O_3^{3-} + 3H^+$	–21.2 ± 0.2	–21.0 ± 0.1
$Gd^{3+} + Q(OH)_5 \rightleftharpoons GdQ(OH)_3O_2^+ + 2H^+$	–2.5 ± 0.1	–2.48 ± 0.05

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[2] RY. Kwong et al., *Circulation*, 2008,118,1011–1020.

ANA-OR-42 Constants of slight soluble acids. Determination by Coulometry

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The flowing of constant direct current allows planning a coulometric method to determine solubility and acidity constants of slight soluble acids. Coulometry and electromotive force measurements are applied to obtain such parameters for eight bile acids in solutions without formation of micellar aggregates. This method can be applied to little soluble acids without complicated elaboration of the experimental data.

This communication is applying it to cholic (HCol, (3α,7α,12α-trihydroxycholanic), glycocholic (HGC), deoxycholic (HDC, 3α,12α-dihydroxycholanic), glycodeoxycholic (HGDC), chenodeoxycholic (HCDC, 3α-7α dihydroxycholanic), ursodeoxycholic (HUDC, 3α,7β-dihydroxycholanic) lythocholic (HLC, 3α-hydroxycholanic) and dehydrocholic (HDHC, 3α,7α,12α-trihyketholanic) acids.

Solubility and acid constants are determined at 25°C and in constant ionic medium 1.00, 0.50 and 0.15 mol dm^{-3} NaCl. The values determined in 0.15 mol dm^{-3} NaCl are directly applicable (in physiologic conditions). Also the others have thermodynamic values. The method of the ionic medium [1], minimizing the variation of the reagent activity coefficients in spite of the change of their concentration, allows to substitute activities with concentrations.

To determinate solubility, *s*, an excess of each acid is added to an aqueous solution of the selected ionic medium stirring until equilibrium was reached. The saturated solutions are filtered (Solutions S') and potentiometrically titrated by means of the following galvanic cell: R.E. /Solution S' / G.E. (I)

The titration of solution S' is carried out coulometrically. The equivalence point was appreciated applying a modification to the method proposed by Gran [2].

The equilibrium: $HA \Leftrightarrow H^+ + A^-$, is defined by the constant: $k = c_H\, c_A / c_{HA}$ (1).

The free concentration c_{HA} in equilibrium with the corresponding solid is constant (i.e. HA solubility, *s*). Eq. (1) can be written: $c_{HA}\, k = K' = c_H\, c_A$ (2), where K' is constant. Electromotive force (e.m.f.) measurements of the galvanic cell:

R.E. /solution S/ G.E., (II) provides c_H.

The solution was gradually alkalinised generating constant current by coulometry. The e.m.f. measurement and the electricity quantity allow to calculate K'of eq. (2) for each addition of current. Combining K' values with solubility, *s*, acid constants k for each HA are calculated.

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ANA-OR-43 Analytical performances of bioluminescence cell-based portable biosensors for on-site multiplex applications.

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Genetically engineered cells such as bacteria, yeasts, or mammalian cells able to produce a specific bioluminescent (BL) analytical signal in response to a target analyte represent a potent analytical tools for environmental toxicity, medical, and food analysis, being characterized by potential low cost and high content screening and multiplex applications [1].
Nevertheless some important issues such as portability and reliability related to the use of “live” cells have still to be addressed to make these biosensing devices true analytical biosensors giving precise and accurate quantitative information. Indeed, their main pitfall is the high variability of the BL signal produced by the engineered cell, in fact the emitted light changes according to the metabolic state of the cell. To solve this problem we introduced in the cell a vitality internal BL control to correct the analytical signal [2].
In the same cell, we introduced two firefly luciferases mutants requiring the same luciferin substrate emitting at different wavelengths, green and red, which are spectrally resolved. The expression of one was analyte specific and the other, constitutively expressed, was used as a cell viability internal control.
Cells were then immobilized in a polymeric matrix composed of an aqueous mixture of agarose, PVP and collagen ensuring their long term viability .
A device was constructed with the cell array in contact, through a fiber optical taper, with an imaging light sensor, a portable charge-coupled device (CCD) camera able to localize and quantify the luminescent signal. Lensless light detection, in which the signal is produced on (or very close to) the detection surface, allows to achieve much higher optical efficiency than that of conventional camera-based imaging systems. The performance of the biosensor was also compared with conventional benchtop instrumentation in terms of LOD and dynamic range, confirming its suitability for low-cost multiplex bioluminescence on-site applications.
Different biosensors were developed. The first detects androgenic compounds using yeast cells carrying a green-emitting P. pyralis luciferase regulated by the human androgen receptor and a red mutant of the same species as internal vitality control. The second biosensor detects two classes of compounds (androgens and estrogens) using yeast strains engineered to express green-or red-emitting mutant firefly luciferases in response to androgens or estrogens, respectively. The third biosensor detects lactose analogue isopropyl β-d-1-thiogalactopyranoside using two E. coli strains. One strain exploits the lac operon as recognition element for the

expression of P. pyralis luciferase. The other strain serves as a vitality control expressing Gaussia princeps luciferase, which requires a different luciferin substrate. A biosensors for heavy metals detection in environmental samples has been developed. The immobilized cells were stable for up to 1 month. The analytes could be detected at nanomolar levels with good precision and accuracy when the specific signal was corrected using the internal vitality control. This portable device can be used for on-site multiplexed bioassays for different compound classes and in combination with other chemilumunescent based device to set up companion diagnostics for personalized medicine [3].

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ANA-OR-44 Use of polyamidoamine dendrimers anchored on nanogold for development of amperometric immunosensors based on non-competitive and competitive ELISA.

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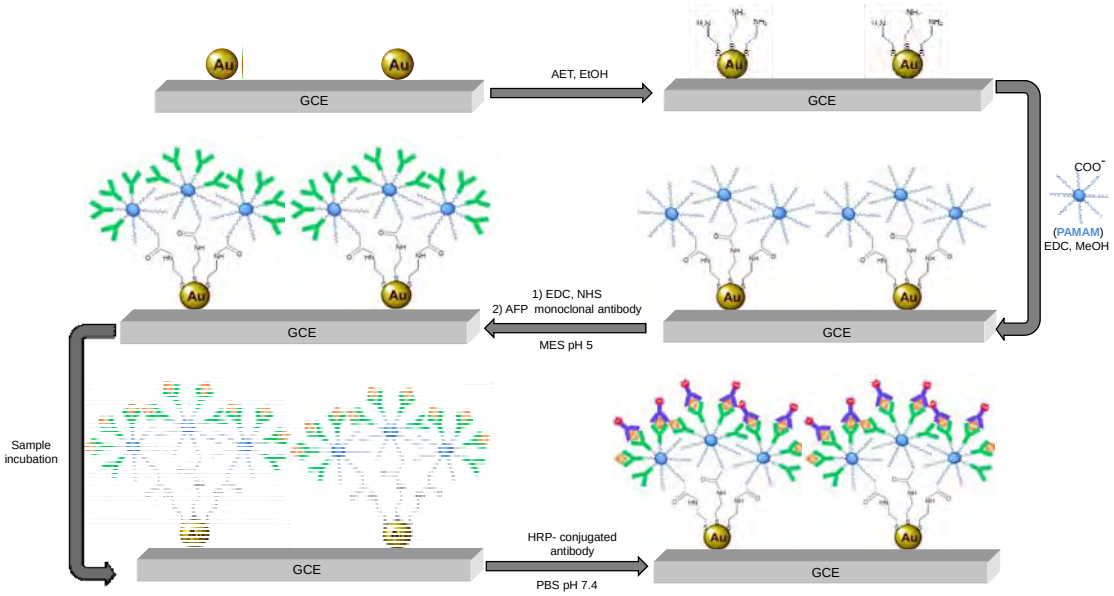
New amperometric immunosensors based on nanobiocomposite substrate and with response enhanced by polyamidoaminic (PAMAM) dendrimers were developed and characterized. The nanostructurated substrate obtained by electrochemical deposition of 100 nm-sized gold nanoparticles on glassy carbon electrodes (GCE) was functionalized by deposition of a self assembled monolayer of 2-aminoethanethiol (AET), used as linker for the subsequent immobilization of polyamidoaminic dendrimers (PAMAM G.1.5). This immobilization procedure was suited for the covalent linking of capture antibodies for direct non-competitive assays aimed to determination of proteins of biological interest, such as alpha-fetoprotein[1**].**



The same methodology was also investigated for the linking of haptens in order to develop competitive immunosensors for determination of small molecules of forensic or environmental interest. Studies focused on the application of PAMAM dendrimers for realization of piezoelectric immunosensors were also undertaken.

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ANA-OR-45 DNA BASED MOLECULAR SWITCHES FOR THE DETECTION OF ANTIBODIES

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Here we report the development of a versatile DNA-based switch which enables the single-step quantitative detection of antibodies through direct optical or electrochemical outputs triggered by binding-induced structural changes. We did so by designing a DNA-based nanoswitch that is triggered by binding to two distinct sites on a single target macromolecule. By coupling this bidentate nanoswitch to optical and electrochemical outputs, we achieve the rapid (seconds/minutes), quantitative detection of sub-nanomolar concentrations of Ab raised against many antigens (*e.g.*, small molecules, peptides etc) even in highly complex samples, such as whole blood. Antibody beacons could be easily implemented in inexpensive, easy to use, electronic hand-held devices, suggesting that they may be particularly well suited for point-of-care applications. Given these attributes, we believe that Ab-beacons will enable important advances in diagnostic and Point-of-Care applications.

ANA-PO-01 Elettrodeposizione "On-Line" di Ossidi di Cobalto (III, IV) in Condizioni Alcaline per la Determinazione Amperometrica di Idrazine.

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Alcuni ossidi del Co(III,IV) presentano importanti attività di elettrocatalisi verso l'ossidazione di molecole organiche o la formazione/evoluzione di O_2 in condizioni neutre e/o alcaline [1,2]. L'utilizzo di sensori amperometrici a base di ossidi metallici, particolarmente in condizione di flusso (FIA, HPLC) e di elettrolisi massive prolungate, porta ad una graduale erosione della superficie elettrodica con conseguente decadimento dell'attività elettrocatalitica del sensore stesso. Un modo per affrontare questa problematica, ovvero preservare una adeguata attività catalitica, consiste nell' introdurre in continuo nel sistema di analisi, ovvero in condizioni "on-line", uno specifico mediatore redox atto ad esplicare la desiderata attività catalitica. Così la superficie elettrodica, sottoposta ad una inevitabile erosione meccanica (o di passivazione chimica) può essere rigenerata attraverso un processo di continua elettrodeposizione di nuove unità catalitiche.

La presente comunicazione riguarda una ipotesi di modificazione superficiale di elettrodi tradizionali di carbone vetroso con ossidi di Co(III, IV) in condizioni alcaline (0.1 M – 1 M NaOH), tramite l'applicazione di potenziali anodici (i.e., 0.2 V – 0.6 V vs. SCE). In tali condizioni amperometriche, il mediatore Co(III, IV), come è noto dalla letteratura, esplica la sua massima attività catalitica verso l'ossidazione di alcune importanti classi di molecole organiche [3-5] e pertanto la definizione di una procedura di elettrodeposizione di un film di Co (III,IV) in condizioni anodiche ed a pH alcalini, rappresenta un passaggio importante nella progettazione di sistemi amperometrici di analisi robusti e riproducibili. Pertanto sarà studiato un sensore amperometrico per l'analisi dell'idrazina e suoi derivati utilizzando un elettrodo di grafite e soluzioni alcaline contenenti Co-gluconato (CoL_2^{2-}) come specie modificante "on-line" dello stesso.

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ANA-PO-02 Copper nanoparticles/poly-3-methylthiophene: preparation, characterization and application in glucose sensing in a flow injection system

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The use of nanoparticles in electroanalysis is a continually expanding area of research as shown by the wealth of available research papers about the synthesis, characterization and application of nanoparticles [1]. This is due to the unique properties of nanostructured materials (e.g. enhanced mass transport, high surface area, improved signal-to-noise ratio) making their use very advantageous in many electroanalytical techniques. The advances of nanotechnology have opened up interesting research opportunities on nanocomposite fabricated not only with different nanostructured materials, but also with various conducting polymers [2]. Such composite materials have an advantage to possess properties of the individual ones with a synergistic effect [2]. In particular, the design of composite materials consisting of a mixture of organic and inorganic phases in the nanometer range has flourished in the last few years. Different strategies for fabrication of nanocomposites have been reported in literature, among which the entrapment of metal nanoparticles in conducting polymers [see: e.g. 3-5] revealed to be a simple and effective approach producing nanostructured materials with remarkable catalytic properties [6-8].

In the present work a simple non-enzymatic sensor for glucose detection has been fabricated being based on a hybrid film of electrosynthesized poly-3-methylthiophene modified by copper nanoparticles (P-3MT/CuNPs). The deposition of copper was achieved by applying a potential pulse program [9] both on Pt and on screen-printed electrodes (SPEs). The microscopic characterization of the film was performed by scanning electron microscopy/energy dispersive X-ray analysis (SEM) and showed a correlation between the pulse width and the amount and size of the deposited particles. The nanocomposite P-3MT/CuNPs was analyzed also by X-ray photoelectron spectroscopy (XPS). The electrocatalytic properties of P-3MT/CuNPs towards glucose oxidation were investigated and the composite film deposited on SPEs was used for glucose detection in a flow-injection analysis system. The effect of the applied potential as well as of the flow rate of carrier stream was evaluated: under the selected experimental conditions, the sensor revealed a satisfactory response in terms of detection limit, linear range and repeatability.

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ANA-PO-03 Study of the deposition of amine terminal groups on Au surfaces for the development of amperometric genosensors

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The development of efficient enzyme biosensors, immunosensors, and genosensors is attracting the interest of scientific community, due to the need of fast responses in such an important field as that of human health. With this respect, electrochemical biosensors can also satisfy the increasing demand of low cost and easy-to-use devices.

The stable anchoring of recognition elements on the electrode surface has been generally achieved by functionalising the bio-molecule with thiol terminal groups, thanks to their high affinity with Au substrates. In the present communication we show the capability of amino terminal groups to stably interact with Au surfaces. To this aim, the deposition of hexylamine on flat Au surfaces has been studied through spectroscopic and electrochemical investigations. In particular, photoemission, X-ray absorption and vibrational spectroscopies allowed us to clarify the mechanism of the amine interaction with Au substrates, which constitutes quite a debated aspect. The stability of the adsorbed molecules on the surface and the reproducibility of the surface functionalisation have been checked through the deposition of amino derivatives bearing a ferrocene electroactive moiety.

These investigations have been exploited in the development of amperometric genosensors based on peptide nucleic acids (PNA) as recognition elements: PNA molecules functionalised with a lysine terminal group have been deposited on Au substrates and the occurrence of DNA hybridisation has been detected electrochemically. Finally, the advantages of the use of Au nanostructured surfaces, replacing the most widely used smooth ones, have been ascertained and discussed.

ANA-PO-04 Dielectric properties of lipid layers integrated in OTFT

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Recent advancements in the electronic devices based on organic materials have opened up novel applications of Organic Thin Film Transistors (OTFT) based biosensors such as, chemical sensing and label free detection [1]. The use of cell-membrane mimics such as liposome and lipid bilayers has recently attracted great attention in the OTFT sensors and several immobilization methods on a solid substrates have been reported [2-3]. Supported membranes show an intrinsically low bioactivity, making them interesting as an interface between the non-biological material on the surface of OTFT and biologically active fluids. The dielectric properties of such supported membranes are critical for the electrical performance of OTFT based sensors, because majority of the biomaterials possess insulating properties [4].
Investigation of the dielectric properties of supported lipid bilayer membrane (sBLM) has been done using impedance spectroscopy in two steps. In the first one, sBLM has been characterized directly on a metal support and in the second an organic semiconductor was used to improve the quality of the supported lipid bilayer. The sBLMs structure in the two systems is explained in terms of equivalent circuits composed of resistors and capacitors. Information on the presence of lipid bilayer inhomogeneities are gathered from the electrical parameters determined by fitting the frequency-dependent impedance of the equivalent circuits to the measured data. Furthermore, X-ray photoelectron spectroscopy was employed for the characterization of the active layers, in terms of surfaces and interfaces quality, e.g surface elemental composition etc.

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ANA-PO-05 Reliability testing in OFET Biosensors

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A lot of efforts have been invested in more recent years to improve the specificity and selectivity for the detection of chemical and biological species. A lot of analytical well established methods have been used in the past for the detection of chemical and biological analytes, such as mass-spectrometry, enzyme linked immunosorbent (ELISA) assays, gas and liquid chromatograph. These methods although high throughput and reliable, require extensive sample treatment involving incubation steps or amplifications.

The advantage of using Organic Field Effect Transistors as transducing tools for biosensor applications, resides in the chance of avoiding, or at least minimizing the sample pre-treating, fabrication costs, and to open up new perspectives in the development of portable and disposable device for a large area of applications.

Recently OFET biosensors have shown, in fact, the potential to offer [1] very high performance level while organic electronics allow to fabricate sensing circuits, also in an array configuration [2], on flexible, paper substrates by low cost printing procedures. The coupling of the OFET device and the biological recognition element can be actuated by assembling supramolecular structures embedding biomolecules, and depositing them directly over the OFET active layer.

A comparison of different deposition procedures based on the use of phospholipids bilayers will be presented, providing also morphological and structural investigations. Preliminary reliability data for this novel bio-OFET will be also presented.

The incorporation of biomaterials into an organic based electronic device has the potential for unique applications in medicine and point-of-care diagnostics. Future efforts will need to be focused on the development of new hybrid biomaterials integrated into electronic devices capable of being processed on flexible substrates.

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ANA-PO-06 Spectroscopic characterization of Te-based micro- and nanostructured materials for sensing applications

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Micro- and nanomaterials have emerged as advanced tools in several research and technology applications because of the possibility of tuning material properties reducing their size [1]. Especially nanoparticles with an anisotropic morphology (e.g. tubes and wires) are advantageous because they possess a high surface area and multiple contacts (borders, inner and/or outer surfaces) that in principle can be functionalized in several ways [1]. In particular, Tellurium microtubes have been successfully proposed in gas and liquid sensors [2, 3]. Recently, Te(IV) oxide nanowires (NWs) have been synthesized by thermal evaporation of Te(0) in an oxygen atmosphere [4] and their direct growth onto Pt substrates to develop novel electrochemical sensors is proposed in the present contribution. In particular, the intimate contact between NWs and Pt and their potential modification upon electrochemical treatments have not been addressed. Such issue regarding surfaces and interfaces TeO_2 NWs/Pt may be of particular relevance in terms of sensing applications. Moreover, only few studies have addressed such topic (mainly on elemental Te [5] and tellurides [6]) by X-ray Photoelectron Spectroscopy (XPS). In this communication we report preliminary results on XPS study in relation to electrochemical and X-Ray Diffraction (XRD) analyses on TeO_2 NWs grown on Pt electrodes. A comparison with results on Te(0) microtubes will be also presented.

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ANA-PO-07 INNOVATIVE ELECTRODES TO CONTROL TRACE METAL IONIZATION USED TO TREAT PATHOGENS IN WATER DISTRIBUTION SYSTEMS

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The control of hazardous pathogens in water distribution systems, is a priority for health authorities world wide. An estimated 8,000 to 18,000 people get Legionnaires' disease in the United States each year. Hospitals, hotels, old people's homes, prisons and ships are high risk environments due to the nature of the water distribution system. Treatment is essential, and one of the most effective methods is copper-silver ionization. The positively charged copper and silver ions thus released, form electrostatic bonds with negatively charged sites on bacterial cell walls; this leads to cell lysis and cell death. Importantly, some authors have demonstrated that these ions are able to penetrate the biofilms in which other bacteria, algae, protozoans, and fungi cohabit with Legionella species in water pipes. The amount of copper and silver must remain within a certain range for efficiency, and at the same time remain well below the WHO and other guidelines. High oral intake of copper and silver can result in liver failure and argyria (blue-bluish grey discoloration of the skin) for copper and silver respectively. Recommended values for copper are between 0.3 and 0.5 mg l^{-1} and, for silver, between 0.03 and 0.05 mg l^{-1}.
The specific aim of this work was to study the electrochemical behaviour of screen-printed graphite electrodes in the determination of silver and copper, with the final purpose of development and construction of mercury-free electrodes to be used in the determination of silver and copper concentrations in water samples by anodic stripping voltammetry.
Particular attention was focused on the chemistry of complex formation in solution optimizing pH and reagents concentration to obtain the better reproducibility, dynamic range and selectivity.

ANA-PO-08 A proteomics approach to study as DNA affects the composition of lipoplex protein corona

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The in vivo organ distribution of intravenously administered drug carriers strongly depends on plasma proteins adsorbed onto their surface, furthermore, a precise knowledge of the structure and morphology of drug carriers is relevant to understand their role as gene delivery [1]. In the present study, we investigated and compared the binding of human plasma proteins onto CLs and onto their relative DNA lipoplexes. A shotgun proteomics approach based on high performance liquid chromatography coupled to high resolution mass spectrometry was employed for an efficient identification of proteins adsorbed onto liposome and lipoplex surface. The distinct pattern of proteins adsorbed helps to better understand the DNA compaction process. The experimental evidence leads us to hypothesize that negatively charged DNA is adsorbed onto lipoplex surface and can interact with basic plasma proteins, in agreement with the existence of cluster-like aggregates made of multilamellar DNA/lipid domains coexisting with other multilamellar lipoplexes or, alternatively, with DNA-coated vesicles. Proteomics experiments showed that the lipoplex corona is rich of biologically relevant proteins such as fibronectin, histones and complement proteins. Our results provide novel insights to understand how lipoplexes activate the immune system and why they are rapidly cleared from the blood stream. The differences in the protein adsorption data detected in the presented experiments could be the basis for the establishment of a correlation between protein adsorption pattern and in vivo fate of intravenously administered nanoparticles and will require some consideration in the future.

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ANA-PO-09 An analytical strategy for studying proteins differentially adsorbed onto surface of three liposome formulations

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The knowledge about the interaction between plasma proteins and nanocarriers employed for in vivo delivery is fundamental to understand their biodistribution [1]. Protein adsorption onto nanoparticle surface (protein corona) is strongly affected by vector surface characteristics. In general, the primary interaction is thought to be electrostatic, thus surface charge of carrier is supposed to play a central role in protein adsorption. Because protein corona composition can be critical in modifying the interactive surface that is recognized by cells, characterizing its formation onto lipid particles may serve as a fundamental predictive model for the in vivo efficiency of a lipidic vector.

In the present work, protein coronas adsorbed onto three differently charged cationic liposome formulations were compared by a shotgun proteomic approach based on nano-liquid chromatography coupled to high resolution mass spectrometry. About 130 proteins were identified in each corona, with only small differences between the different cationic liposome formulations. In particular, surface charge did not show to drive a preferential protein absorption. Therefore, to better understand the interactions between the single liposome formulation and plasma proteins, a label free quantitative analysis was performed by the aid of the software Scaffold. The results allowed to point out the differences not found out from the simple qualitative analysis.

This study could be useful for the future controlled design of colloidal drug carriers and possibly in the controlled creation of biocompatible surfaces of other devices that come into contact with proteins into body fluids.

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ANA-PO-10 Near infrared spectroscopy and class modelling techniques for the verification of authenticity of Taggiasca table olives

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The Mediterranean coastal areas are characterised by a mild, warm climate – an ideal habitat for growing of *Olea europaea* L. tree. *Taggiasca* is a typical Ligurian olive cultivar, whose cultivation is very important for the local economy and the preservation of the regional landscape. A part of *Taggiasca* crop is used to prepare table olives, which can be easily adulterated with olives having similar morphological features but a lower commercial value. The potential of near-infrared (NIR) spectroscopy and multivariate analysis to characterise the *Taggiasca* olives has been evaluated in the present study.

A considerable number of samples of table olive of *Taggiasca* cultivar and of cultivars *Leccino* and *Coquillo* were collected and analysed. The traceability and representativeness of sampling was assured.

Olives were washed with water, dried and stoned, then the pulp was ground and submitted to spectroscopic analysis in the reflectance mode. The measurements were replicated in two different laboratories and with two different spectrophotometers: a FT-NIR Buchi based on a polarisation interferometer (NIRFlex N-500) and a FT-NIR Thermo Scientific (AntarisII FT-NIR Analyzer). This allowed to evaluate the reproducibility of the method proposed. Principal component analysis (PCA) was applied to visualise the multivariate data distribution. Then, two class modelling techniques (soft independent modelling of class analogy - SIMCA, unequal class models - UNEQ) were tested to characterise *Taggiasca* olives.

For both of the laboratories, the PCA score plots showed a satisfactory distinction between the three cultivars. This result was confirmed by the supervised techniques (SIMCA and UNEQ), which allowed to build efficient class-models for the verification of authenticity of olives.

The present study demonstrated the potential of NIR spectroscopy coupled with multivariate analysis as a rapid and low-cost tool to characterise olives.

ANA-PO-11 Multivariate methods for experimental-data analysis applied to identification of bacteria by means of Py/GC-MS

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There is the need to identify bacteria by means of reliable but rapid analytical methodologies: the already assessed current analytical methodologies require laborious preparative steps; moreover, they are often very expensive. In order to solve these problems, a more rapid and less expensive analytical technique based on Py/GC-MS has been here developed.

Analytical pyrolysis (Py) allows the characterization of a material by controlled thermal chemical degradation in inert atmosphere; degradation products are characteristic of the original sample and can be characterized using a GC-MS system [1]. When Py/GC-MS is applied to bacteria, trivial visual examination of *pyrograms* easily allows discrimination between different *genera* of bacteria. But to obtain discrimination in terms of *species* chemometric data analysis is necessary.

Among chemometric methods for *data exploration*, *Principal Components Analysis* (*PCA*) is extensively used in Analytical Chemistry. As for *classification procedures*, Soft Independent Modeling of Class Analogy (SIMCA) is particularly suitable for analytical problems, since it works even when the number of samples is very low with respect to the number of variables characterizing samples.

The purpose of the present work was to develop a rapid Py/GC-MS methodology for the analysis and identification of bacteria in terms of *genus* and *species*. Methylated fatty acids (FAMEs) were chosen as biomarkers of bacteria in the pyrolysates. *In situ* Thermal Hydrolysis and Methylation (THM) was applied. Pyrographic peak areas, and relevant normalized or relative values, were chosen as variables for chemometric data processing by PCA and SIMCA.

Satisfactory results were obtained in classifying bacteria in terms of *genus* and *species*.

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ANA-PO-12 Experimental design optimization of a solid-phase microextraction coupled with gas chromatography-tandem mass spectrometry methods for the determination of carbamate pesticides in water

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Carbamate pesticides are a wide family of pesticides whose structures ($R_1OCONR_2R_3$) are derived from carbamic acid by the introduction of different substituent [1]. They are class of synthetic organic pesticides annually used on a large scale worldwide as insecticides, herbicides, fungicides, nematocides, acaricides and molluscicides. Most of the carbamates have high melting points and low vapor pressure and are often present in aqueous environments because of their high solubility in water [2]. This class of pesticides are toxicity to the central nervous system and they are suspected carcinogens and mutagens. The European Union has set a maximum admissible concentration of 0.5 µg/L for the sum of all pesticides and 0.1 µg/L for an individual compound in drinking water [3]. Due to their thermal instability their analytical determination is usually carried out by HPLC techiques [4]. The purpose of this work was the development of an solid-phase microextraction coupled with gas chromatography-tandem mass spectrometry (SPME-GC-MS/MS) analytical method, for the determination of six carbamate pesticides in water (aldicarb, propoxure, carbofuran, carbaryl, methiocarb and pirimicarb). Experimental design was used in order to select the optimal SPME and gas chromatographic experimental conditions which allow the controlling of thermal degradation of analytes and their successful extraction avoiding on-fiber memory effects. Carbamates quantification was carried out using two internal standards (carbaryl-d7 and trimethacarb). Triple quadrupole tandem mass spectrometry was applied to decrease the limit of detection (LOD) and the limit of quantification (LOQ) for the analytes using multiple reaction monitoring mode (MRM). The method developed shows accuracy and precision levels between 70-108 % and LOQ values between 0.06-2.9 ng/L.

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ANA-PO-13 FAST ANALYSIS OF SOME PHENOLICS BY HPLC-DAD AND CHEMOMETRIC RESOLUTION TECHNIQUES

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In recent years, the prevention of cardiovascular diseases and cancer has been intensively focused on the beneficial effects of olive oil and, in particular, of its phenolic pool. These species are powerful inhibitors of the formation of atherosclerotic plaques and reactive oxygen species, cause of "fat-related" cancers.
It seems clear that the phenolic composition represents a specific index of nutritional quality of the product and how important it is to develop rapid, economic and simple analytical methods for its determination in olive oils.
To this end, since chemometrics allows the mathematical a posteriori resolution of overlapping peaks, it is possibile to operate with experimental conditions even leading to a not perfect chromatographic separation, with a corresponding saving of money and time and reduction in the amount of solvents used. Accordingly, in this communication, the possibility of operating a rapid HPLC-DAD analysis of a wide range of polyphenols, using a fast gradient involving two solvents only ($MeOH/H_2O$) and chemometric multivariate and multiway techniques, will be discussed. In particular, two approaches were tested for the resolution of peak clusters: the use of Multivariate Curve Resolution (MCR [1]) after unfolding of the experimental data cube and the application of PARAFAC2 [2] directly on the three way array. The results obtained by both methods have been validated by comparison with a complete chromatographic resolution of the co-eluted peaks. In particular, it was shown that both chemometric approaches led to good results but MCR performed better on the investigated data set. A possible explanation of this outcome could be found in the fact that, as the spectral profiles of the analytes are very similar, further constraints are needed to separate the contribution of the individual components, for instance unimodality of the peaks, and these constraints can't be applied in PARAFAC2 due to algorithmic reasons.

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ANA-PO-14 Spectrophotometric and DFT characterization of uranyl carboxylate complexes in aqueous solution

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This investigation is an advance in the understanding of uranyl chemistry in water solution. Our previous works [1-3] were addressed to the speciation of uranyl with carboxylic acids by potentiometry and UV-visible absorption spectrophotometry. In this session we propose an enhancement on structural description of complexes by means of a deep analysis of spectrophotometric absorption data and by means of DFT (Density Functional Theory) characterization. The spectrophotometric study of metal - ligand systems can provide information about the structure of complexes, especially if it is supported by theoretical data. Moreover, the recent literature confirms that the theoretical DFT approach provides complementary information and validates the structural and solution chemical information [4]. We report the investigation on coordination compounds of uranyl ion with citric and oxydiacetic (diglycolic) acids in aqueous solution. The different binary systems were previously studied [2, 3] by potentiometric and spectroscopic techniques at t = 25 °C and I = 0.1 mol dm^{-3}. A speciation model was proposed for both metal/ligand systems from potentiometric data. Moreover, the joint elaboration of potentiometric and spectroscopic data obtained on the uranyl - ligand containing solutions allowed us to calculate the individual spectra of the complex species. With the carboxylate ligands we have found that the co-ordination environment produces an increase in the molar absorptivity values and a light bathochromic shift in the position of ε_{max} [1-3]. The bathochromic shift is higher for citric acid [3] and we observed a remarkable raise of the relative intensity of the vibronic bands which appear at λ>440 nm for uranyl-oxydiacetate complexes.

Uranyl - carboxylate species assumed from potentiometric speciation, have been checked by means of a computational modelization. Differing coordination geometries have been explored, both in gas phase and in solution (assuming the polarizable continuum model). The different protonation constants of uranyl - citrate complexes have been analyzed and electronic and vibronic spectra computed with time - dependent density functional method. Results are compared with experimental spectra.

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ANA-PO-15 Sequestering ability of S-donor ligands towards metal and organometal cations

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Sulfur containing compounds play a key role in protecting biological systems against oxidative injury and heavy metal intoxication. The ability of many of these compounds to penetrate cellular membranes has made them useful chelating agents in the treatment of metal poisoning (*chelating therapy*). The use of a ligand as chelating agent requires the knowledge of both coordination models and formation constants of complexes with the metal ions to compare the strength and the characteristic of the species. Therefore, the study of the solution chemistry of metal ions in the presence of sulfur containing ligands can provide useful information regarding the nature and magnitude of the complexes so formed and represents an essential first step in the development of models to predict the metal transport and fate. In turn, this information can be used to evaluate methods of removing undesirable compounds from biological systems.

For these reasons, we planned a study on the solution chemistry of different metal (Hg^{2+}, Zn^{2+} and Pb^{2+}) and organometal (CH_3Hg^+, $(CH_3)_2Sn^{2+}$ and $(CH_3)_3Sn^+$) cations in the presence of sulfur containing ligands. In particular, a natural occurring detoxificant (glutathione, *gsh*) and some pharmaceutical chelating agents [2-mercaptopropanoic acid (*tla*), 3-mercaptopropanoic acid (*mpa*), 2-mercaptosuccinic acid (*tma*), penicillamine (*pen*) and L-cysteine (*cys*)] were selected as case studies. The thermodynamic parameters were determined by potentiometry (ISE-H^+), ^{1}H-NMR and titration calorimetry, at different ionic strength ($0.1 \leq I \leq 1$ mol·L^{-1}) and temperature ($15 \leq t \leq 45$°C). For all systems, the results showed the formation of mononuclear ML and MLH and binuclear ML_2 species, and, in some cases, the formation of other protonated MLH_2, ML_2H, ML_2H_2 and mixed hydrolytic ML(OH) species. As expected, the higher stability was found for species of Hg^{2+} and CH_3Hg^+, owing to the strong affinity between a typical soft metal, such as Hg(II), and a ligand with soft donor atoms, such as S.

Formation constants and speciation profile for each metal-S donor ligand systems, were useful to quantitatively define the sequestering ability of sulfur containing ligands towards methylmercury(II) ion. Sequestering ability of ligands towards metal cations was quantitatively evaluated by determining an empirical parameter ($pL_{0.5}$) that numerically represents the ligand concentration [-log (total ligand concentration)] necessary to sequester the 0.5 of metal ion fraction. The $pL_{0.5}$ values were evaluated for all systems, in different conditions of temperature and ionic strength.

ANA-PO-16 Influence of mixed $metal_1$ – $metal_2$ – ligand and metal – $ligand_1$ – $ligand_2$ species on the speciation of multicomponent aqueous solutions

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Natural waters and biological fluids, as well as wastewaters, can be considered, from a chemico-physical point of view, as multielectrolyte aqueous solutions in which a wide number of cations and ligands (including water / OH^-) are simultaneously present in different concentration ranges and ratios. This variability determines the formation of several complex species in solution, of different stability. Moreover, it is important to take into account that the most of these cations and ligands forms many polymeric species, also at low concentration. As a result, the formation of hetero-cationic or hetero-ligand mixed species is frequent in the conditions of these multicomponent aqueous solutions. Unfortunately, these mixed species are very often neglected in the formulation of various speciation models, though it has been demonstrated that they strongly affect the reliability of these models, especially in relation to the fact that the formation of mixed species is often thermodynamically favored with respect to parent ones. For all these reasons, since some years our group undertook various studies in this direction, in order to evaluate the formation and the stability of several mixed $metal_1$ – $metal_2$ – ligand and metal – $ligand_1$ – $ligand_2$ species in aqueous solution. In this contribution, some results of these investigations are reported.

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ANA-PO-17 Comparison of accelerated nonisothermal DSC and long-term isothermal measurements to evaluating kinetic data and predictive model for isothermal degradation time in two commercial acetylsalicylic acid-based tablet formulations

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Differential scanning calorimetry was used as a rapid screening technique to study the stability of acetylsalicylic acid (ASA), pure or contained in two commercially available pharmaceutical formulations, where ASA is present at a high nominal concentration, along with some of the most commonly used excipients (starch, cellulose, saccharin).

The stability study was focused on the kinetic analysis of the thermal decomposition of ASA, which occurs in pure ASA as well in the two pharmaceutical formulations (PF1 and PF2) using two well–known multi–heating model–free kinetic methods: Kissinger and Ozawa–Flynn–Wall. The knowledge of the Arrhenius parameters related to this process (activation energy E_a, pre–exponential factor A, kinetic constant k) enable to calculate the half–life time values (extrapolated at 25 °C), calculated at fixed percentages of product degraded for pure ASA as well for both dosage forms considered. Finally, the results of long–term isothermal measurements, consistent with short–term non–isothermal (accelerating) ones, provided a reasonable predictive model to calculate the isothermal degradation times, thus demonstrating the reliability of extrapolated half–life time values obtained in this study.

Half–life values for degradation of pure ASA was found to be higher than those of ASA contained in PF1 and PF2, thus demonstrating that the presence of these excipients (even though their content in the dosage forms tested is very low in both cases) has a non negligible destabilizing effect.. Very reasonable degradation time values were obtained from accelerated stability experiments from pure ASA, PF1 and PF2, whose reliability was confirmed by long–time experiments, carried out at constant temperature (70 °C) for different time values.

ANA-PO-18 Identification and quantification of berberine and its main metabolites in human plasma by HPLC-ES-MS/MS

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Berberine is an isoquinoline alkaloid of the protoberberine type, usually found in the roots, stems, rhizomes and bark of plants such as *Berberis*, *Hydrastis*, *Coptis*, etc. Recently, clinical trials have shown its usefulness in the treatment of hypercholesterolemia. Indeed, administration of berberine determines a decrease of the levels of total cholesterol, LDL-cholesterol and triglycerides levels by a dual mechanism of action: inhibition of the synthesis of triglycerides and up-regulation of the activity on the low-density-lipoprotein receptor (LDLR).
The extensive use of the therapeutic agents called "nutraceuticals", which do not require a conventional drug approval trial in term of pharmacokinetics, metabolism and safety, evidenced the need to monitor their blood levels to avoid undesiderable side effects (i.e., ipertension in the case of berberine). At present, only a few chromatographic methods are sufficiently sensitive for the determination of berberine and its metabolites in human plasma. In the present study berberine, its major metabolites (including berberrubine and demethyleneberberine synthetized in our laboratory) and their glucuronide conjugates were quantified in human plasma by high performance liquid chromatography/tandem mass spectrometry with electrospray ionization (HPLC-ES-MS/MS).

The chromatographic separation was performed at a flow rate of 0.3 mL/min using a Luna C18 column at a temperature of 40°C, and with a mobile phase constituted by a gradient of 10 mM formic acid (pH = 4.00):acetonitrile. The analysis time was 15 min. Detection was performed by Multiple Reaction Monitoring (MRM) operating in the positive ionization mode, by monitoring the transitions at m/z 336→320 (berberine), m/z 322→307 (berberrubine), m/z 322→307 (thalifendine), m/z 324→280 (demethyleneberberine), m/z 338→323 (jatrorrhizine), and m/z 414→220 (IS noscapine). The method was validated according to current guidelines (Guidance for Industry: Bioanalytical Method Validation, FDA, 2001) and applied to pharmacokinetic studies aimed at increasing the bioavailability of berberine after chronic oral administration. The developed method fulfil all the standard requirements of precision and accuracy with a LOQ of 0.5 ng/mL and is therefore appropriate for the quantification of berberine plasma levels after chronic feeding of berberine at a daily dose of 500 mg.

ANA-PO-19 A new methodology for the analysis of bile acid profile in human serum based on an ultrafiltration clean-up step and LC-MS/MS analysis.

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Bile acids (BAs), the major end products of cholesterol catabolism, are useful biomarkers for the diagnosis of many diseases. The pathologies related with bile acids are generally expressed in the first years of life and may lead to serious liver injury. Usually the balance between bile acid synthesis, secretion and re-absorption is tightly regulated: elevated concentrations of bile acids in peripheral circulation are evidence of disorders; similarly, low concentrations may suggest inborn errors of bile acid metabolism [1]. Measurement of total bile acids, as often performed in routine analysis, is only of limited value whereas the analysis of BAs profile in body fluids is an important tool to establish the therapy (pharmacological or surgical) [2].

Here we present a sensitive and rapid method for the analysis of the main 15 bile acids in human serum by liquid chromatography-tandem mass spectrometry. The chromatographic separation is performed using a core-shell column which provides a good separation, particularly useful because of the small structural differences of the analytes. All isomeric BAs of interest were resolved from each other in less than 10 min. Serum sample pretreatment only requires an ultrafiltration step with centrifugal filter devices. This simple procedure on the one hand allows a minimal consumption of serum sample (about 100 µl) and on the other hand is simple, rapid and easily applicable in a routine analysis getting anyhow a satisfying clean up. The calibration curves were linear for all the BAs over a range of 0.005–5 ppm. The extraction recoveries for all the analytes were greater than 80%. Intra-day and inter-day coefficients of variation were all below 15%. The method proposed has been validated according to FDA guidelines for bioanalytical methods and has been applied for the serum analysis of pediatric patients.

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ANA-PO-20 GLUCOSE OXIDASE IMMOBILIZED IN POLYVINYL ALCOHOL FILM FOR ANTIBACTERIAL SYSTEMS

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The development of new devices based on biocide surfaces has been an intangible objective for many decades. Nowadays scientists need to carry out materials with a surface that has a very broad spectrum of biocidal activity, that can be used repeatedly and that kills via a mechanism which will not result in the emergence of resistant strains [1].
In this work a novel antibacterial system based on immobilization of Glucose oxidase enzyme (GOx) in a poly(vinyl alcol) (PVA) film is presented. PVA represents an ideal enzyme immobilization material because the abundance of hydroxyl groups provides a microenvironment similar to the enzyme's natural environment [2]. It has been in fact widely used because of its inherent good biocompatibility and desirable physical properties, such as elastic nature and good film-forming property [3]. The GOx-PVA composite material has been extensively characterized by UV-vis and X-ray photoelectron (XPS) spectroscopy, to verify the preservation of the enzyme structural integrity and of the enzymatic activity in PVA membrane. Moreover, XPS characterization, revealed a homogeneous film whose structure is not altered under operative conditions.
The antibacterial lysozyme-like activity of GOx-PVA was evaluated by a standard assay on Petri dishes employing *Micrococcus luteus* cell walls. GOx-PVA showed a lysozyme-like activity with a maximum at pH 6.0 and I=0.175. Lysozyme represents the best characterized enzyme involved in the defence against bacteria. This enzyme dissolves certain bacteria by cleaving the B1-4 bonds between N-acetylglucosamine and N- acetylmuramic acid of bacterial cell walls. Thus the findings from this study have implications for future investigations related to employment of GOx-PVA as a compound of pharmaceutical and technological interest.

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ANA-PO-21 Skin penetration of gold nanoparticles: a new analytical approach using the synchrotron radiation computed microtomography

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The potential for AuNPs to penetrate the skin lies at the centre of the debate concerning the safety for their use and, on the other hand, the possibility of biomedical applications [1]. In a recent study a high concentration of Au in the skin was found after a 24 hour exposure to 12 nm AuNPs suspension in an in vitro test with the Franz diffusion cell method [2].

The present work aims to identify the distribution of gold into the skin using synchrotron radiation computed micro-tomography (μ-CT). Human skin samples were exposed to a 5 nm-AuNP suspension for 24h, fixed in formaldehyde and analysed at the SYRMEP beamline, Sincrotrone Elettra (Trieste, Italy) at an energy of 14.8 keV (proposal n° 20095290) and at the ID17 beamline of ESRF (Grenoble, France) at an energy of 80.7 keV (proposal n° MD-529).

After the tomographic reconstruction, areas of high absorption were identified in the skin samples exposed to AuNPs. These areas have the size and shape of the hair follicles (Fig. 1) and the result seems to confirm the hypothesis that the hair follicles should be the main route of the nanoparticle skin penetration process.

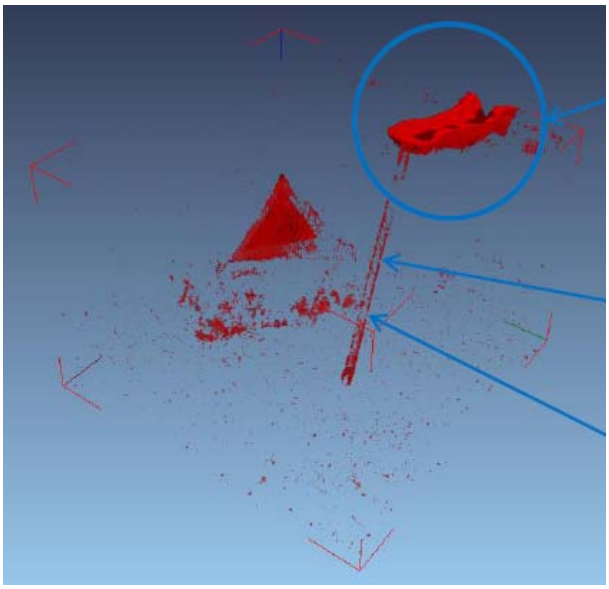

Fig. 1: A rendered 3D volume of the acquired μ-CT slices: a threshold was applied in order to distinguish between skin tissue and high absorbing AuNPs. The arrows and the circle indicate the hair follicles.

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ANA-PO-22 Simultaneous determination of meropenem, ciprofloxacin, and ofloxacin in human plasma using RP-HPLC-DAD: method development, validation and optimization of various experimental parameters

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Infections by multidrug-resistant (MDR) *Pseudomonas aeruginosa* are a serious threat in the nosocomial environment often associated with considerable mortality. The type of management for such infections is a matter of debate. Often a combination of one β-lactam agent with an aminoglycoside or fluoroquinolone is suggested as the empirical treatment of choice, but the true effectiveness of that combination is doubtful. Meropenem is a semi-synthetic antibiotic that exhibits significant activity against important aerobic and anaerobic pathogens. Its chemical structure is shown in figure 1A.

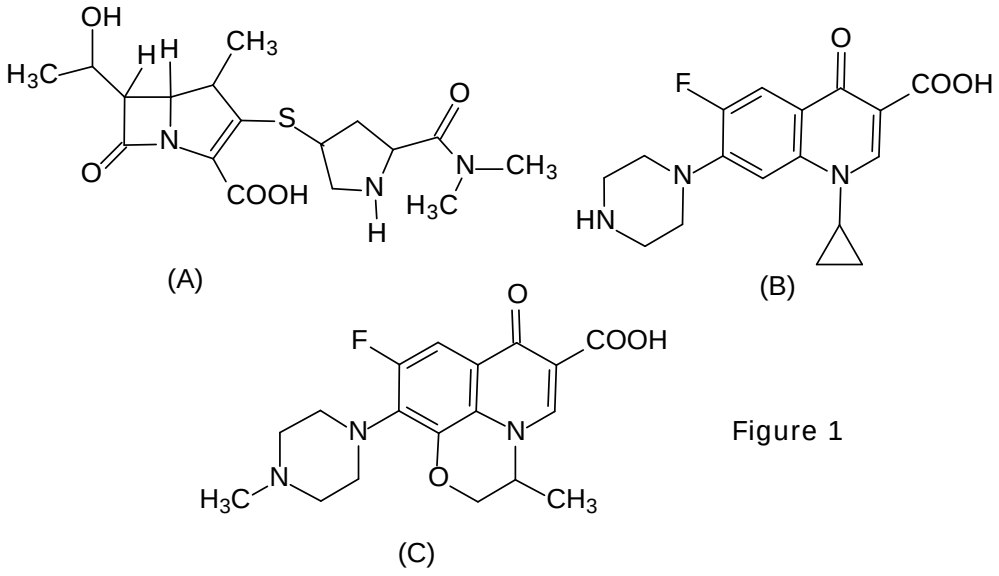

Figure 1

Meropenem is resistant to hydrolysis by bacterial β-lactamases. Ciprofloxacin (figure 1B), is the most potent quinolone against Gram-negative bacteria. Ofloxacin (figure 1C), is effective in treating a variety of acute and chronic infections. The target of the highly selective action of these fluoroquinolones is bacterial DNA-gyrase, a type of topoisomerase II.

A HPLC method with DAD detection was developed optimized and validated for the simultaneous quantification of meropenem, ciprofloxacin and ofloxacin in human plasma. The best resolution was achieved with a

Zorbax Extend (150 x 4.6 mm I.D., 5 μm) column using a gradient mobile phase. Solid-phase extraction were used for sample preparation. Effect of different experimental parameters and various particulate columns on the analysis of these analytes was evaluated.

ANA-PO-23 PAHs determination in rain water: optimization of a HPLC/fluorescence modified method and its application for an environmental monitoring

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The Italian regulations, actually in use, provides for the *benzo(a)pirene* determination in atmosphere as unic indicator of the PAHs quantities in air. In fact the actual reference method, indicated by the D. Lgs. Agoust 13th 2010, n. 155 (actuation of the European Directive 2008/50/CE) refers to the law UNI EN 15549/2008, which indicates only the sampling and measurement of the PAHs in air. This methodolgy seems very poor, because of the variable ratios values among the different PAHs present in the urban atmosphere particulate.

The HPLC/fluorescence method here outlined could become a useful and reliable alternative to be proposed for a new and better regulation to the European Community. The method makes use of an HPLC instrumentation (Shimadzu LC-10 ATVP) equipped with a fluorimeter (Shimadzu RF-10AXL), and different chromatographic columns and pre-columns have been tested to optimize the results to obtain the best separation and the minimum time of analysis. To be noticed the particular clean-up method [1,2] used, which allows very concentrated samples to be injected into the HPLC system. By means of the proposed method the determination of 16 PAHs in rainwater samples [3], collected in different sampling stations of the Rome district, are in progress and they will performed over at least 1 year period of time. The PAHs content in raiwater seems a good information regarding the PAHs pollution in the urban atmosphere, even if the season time, the weather and also temperatures must be taken into account for each sample. The proposed method could be a useful method not only with respect to the humid depositions, but also to resolve the poorness of the *benzo(a)pirene* single determination as it is recommended by the European Directives.

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ANA-PO-24 Simultaneous determination of salicylates and benzoic acid in food by SPME-LC-UV-DAD

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Salicylate, acetylsalicylic acid (aspirin) and their derivatives (salicylates) are used as fungicidal and antimicrobial agents in pharmaceuticals preparations (external use) as well as in the treatment of inflammatory processes as antipyretic and analgesic drugs (internal use).
Salicylates have been also used in beverages and foods for preservation, but it has been forbidden since the sixties in several countries due to its toxicity [1].
These chemicals occur also naturally in many plants, including many fruits vegetables, and herbs. Salicylates in plants act as a natural immune hormone and preservative, protecting the plants against diseases, insects, fungi, and harmful bacteria.
Salicylates are generally regarded as safe for adults, even if high enough doses are harmful to everyone. However, most people can handle average amounts of salicylate in food, products and medications without any adverse affects on their health. Unfortunately, there is a small percent of the population for which even a small dose of salicylates can be a problem. Some adults and children may develop symptoms and health problems from salicylates which are dose-related. This is called ‘Salicylate Sensitivity’ or ‘Salicylate Intolerance’.
Individuals that are sensitive to salicylates may suffer with urticaria, angiooedema, rhinitis, bronchial asthma and recurrent nasal polyps [2]. The chronic nature of some of these clinical presentations, without other obvious cause, may suggest an underlying etiology related to dietary salicylates. A low salicylate diet may be of clinical benefit to such affected individuals. This cannot be established however, until the salicylate content of different food and drinks is known. Data on the salicylate content of foods are scarce and contradictory. Our aim was to develop an accurate analytical method to measure the salicylates content of selected food commodities.
Existing papers on this topic have been essentially based on chromatographic techniques, after purification of the analytes by means of complicate isolation procedures. A good alternative could be represented by the use of solid-phase microextraction (SPME), a solventless technique initially coupled to GC and later interfaced also to LC [3].
Thus, in the present work, a solid-phase microextraction (SPME)–LC–UV-DAD method for the simultaneous determination of salicylates and benzoic acid in food samples was developed for the first time using a

polydimethylsiloxane/divinylbenzene (PDMS/DVB) coated fiber. The procedure required very simple sample pretreatments, isocratic elution, and provided highly selective extractions. The applicability of the method was demonstrated on different food products, i.e. kiwis, blueberries, lemons, mandarins, oranges, broad beans, and commercial fruit juices.

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ANA-PO-25 Characterizing parameters of Chocolate.

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The protein nitrogen and the metallic components were evaluated to characterize chocolate. Ten marks with a percentage of cocoa generally in the range 70 – 100% were analyzed. Only one was 50%. In one case the declared origin of cocoa was Venezuela. The protein nitrogen was determined by applying the Kjeldhal procedure. The percentage of the product (i.e. % of cocoa) per protein nitrogen was in the range 0.7 – 1.2, except, as expected, for the sample with 50%. In this case the percentage was 0.33.

As some cations are toxic and others can have nutritional or toxic effect depending on their concentration, total arsenic, cadmium(II), lead(II), copper(II), zinc(II) and total selenium were determined. To eliminate the organic components, weighed samples of chocolate of different firms were ignited at 900°C to obtain ashes at constant weight. The range of the percentages of ashes was within 1.4 and 3.7%. Ashes were dissolved in HCl and the content of the above cations was determined by means of Atomic Adsorption (AA) spectrometry. Cadmium(II), copper(II) and lead(II) were determined in flame acetylene – air (or in furnace on the basis of the concentration), whereas total arsenic, total selenium and mercury(II) were determined by using the hydride kit and treating the samples with sodium bore hydride and 10% HCl.

Concerning the cation concentration, it was observed that cadmium(II) and lead(II) are present at level less than 1 ppm (mg/kg) and then their analysis had to be carried out by using the graphite furnace. The concentration of zinc(II) and copper(II) was more than 5 ppm, often it reached 30 ppm. Zinc(II) was often double than copper(II). Copper was in the range 6 – 18 ppm, whereas zinc (II) was in the range 15 – 30 ppm.

Cations analyzed by the hydride kit were present in very different amounts, but in the range of ppb (μg/kg) quantities. Mercury is present generally at about 1 ppb, except for one sample where was about 4 ppb. Higher values can be observed for arsenic present in the range within 7 – 31 ppb. The selenium concentration showed a large variability, because it was present within 3 and 50 ppb. Only one sample contains 100 ppb of selenium. It means that a range of about 100 ppb is covered.

By taking in account that the cocoa percentage are different for the analyzed samples, the found quantities of arsenic can be considered near. However, such quantities are higher than the generally accepted value, about 0,2 ppb.

The values relative to selenium are acceptable, even advantageous for the alimentary diet. Only one sample containing 100 ppb of selenium can be dangerous. It seems interesting to observe that the same chocolate sample with 100 ppb of selenium, contains high quantities also of the other cations, so that it can be considered the worst sample.

ANA-PO-26 Formulation and characterization of new packaging material incorporating chitosan nanoparticles-vitamin E and C for food shelf life improvement

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One of the principal causes of food quality deterioration is the oxidation of unsaturated lipids initiated by free radicals. When lipids are exposed to environmental factors such as air, light and temperature, oxidation reactions start to produce undesirable flavours, rancid odours, discoloration and other forms of spoilage. During oxidation, a series of volatile and non-volatile compounds are originated, altering sensory proprieties, causing rancid flavors and decreasing the nutritional quality and safety, which may play a role in the development of some diseases [1]; in addition lipid oxidation could cause a consumer rejection of the food product.
The rate of autoxidation depends on temperature, pH, the degree of unsaturation of the fatty acids and the number of unsaturated fatty acids in the triacylglycerol or phospholipid molecule, as well as on the availability of oxygen and transition metal ions. The other major cause of food spoilage during storage is the bacterial contamination arising from several sources, such as the animal itself, the external environment and its handling.
Packaging is important to preserve the quality and safety of fruits, vegetables and processed foods for assured shelf life extension. The new generation of edible coatings is especially designed to allow the incorporation and/or controlled release of antioxidants, vitamins, nutraceuticals, and natural antimicrobials [2-4].
Among packaging material, chitosan has been well-known for its excellent film-forming property, antimicrobial activity, and unique coagulating ability with metal and other lipid and protein complexes. It seems to be due to the presence of high density of amino groups and hydroxyl groups in the chitosan polymer structure. Its high binding ability and antimicrobial properties are both beneficial in developing new applications of this natural polymer in food preservation. Herein, we aimed at the formulation of chitosan-cyclodextrin nanoparticles (NPs) obtained by the ionic gelation process in order to load vitamin E and C selected as powerful antioxidant agents. In fact, vitamin E is important in the prevention of lipid peroxidation, whereas vitamin C reacts effectively with superoxide and hydroxyl radicals. Vitamins C and E and vitamin precursors (e.g. carotenoids) should reduce the rate

of initiation or prevent the propagation of free radicals as notable non-enzymatic antioxidants.
The NPs will be characterized in terms of light scattering, zeta-potential, vitamins content and by X-Ray Photoelectron Spectroscopy (XPS) measurements. Afterwards, the NPs loading vitamin C and E will be dispersed on polymeric films that are usually found as food packaging materials.

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ANA-PO-27 Phenolic content and radical scavenging ability of wild fruits of *Rubus* species and related jam and seeds from Calabria

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Small berries are rich sources of bioactive compounds such as flavonoids, phenolic acids and vitamin C, which are known to display potential health-promoting effects [1]. Blackberry is an edible fruit produced by several species of the *Rubus* genus of the *Rosaceae* family. In this study, we have determined the chemical composition, the phenolic content, and the antioxidant activity of Southern Italy blackberries (*Rubus ulmifolius* Schott) growing wild in Calabria. In particular, the studies were extended to two anatomically distinct parts of fruit, the pulp and the seeds and a derived product such as jam. The fruits were picked randomly from different parts of wild bushes on mountain slopes at an altitude of 1000 m above sea level (C.da Pallone, Cosenza). The freeze-dried fruits were crushed in a mortar and were sieved using a 60 mesh screen to achieve the separation of seeds from the pulp. One part of the pulp was directly analyzed, while another part was cooked to make jam. Total lipids were extracted from ground seeds (5 g) with hexane at 90°C for 2 h (22% yield w/w). The fatty acid composition was then determined by GLC after a direct transesterification procedure [2] carried out in methanol-benzene with acetyl chloride. The most represented fatty acids were linoleic and linolenic acids (89,6%). The methanolic extract of defatted seed flour showed a strong radical scavenging activity determined using DPPH test (97%). On the other hand, the antioxidant activity of two phenolic fractions extracted from the pulp (ethyl acetate extract containing phenolic acids and flavonol glicosides, and acidic methanol extract containing anthocyanins) was lower than that of seeds (70% and 69% respectively). The processing of the berries into jam, prepared by cooking 50 g of pulp with 25 g of sugar and 1,25 g of pectins for 3 min, led to a significant loss of radical scavenging activity (50 %). HPLC-UV/vis and HPLC-ESI analyses were used to determine anthocyanin and phenolic composition. The results indicated that cyanidin-3-glucoside was the major anthocyanin in the pulp while the most abundant non-anthocyanin phenolic was epicatechin. The main phenolic compound detected in the metanolic extract of the seeds was free ellagic acid.

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ANA-PO-28 Determination of very low levels of 5-(hydroxymethyl)-2-furaldehyde (HMF) in natural honey: comparison between the HPLC technique and the spectrophotometric White method.

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HMF (5-hydroxymethyl)-2-furaldehyde is a molecule of interest both as a marker of quality deterioration, caused by excessive heating or inadequate storage conditions, and for its cancerogenic effects. The European Union [1] established that its concentration in honey (except baker's honey and in products from regions with tropical climate) should not exceed 40 mg kg^{-1}. The International Honey Commission [2] reports three official methods for the analysis of HMF in honey, two spectrophotometric methods, determinations after White [3] and after Winkler [4], and an HPLC method [5], however the Winkler method has been abandoned because of the toxicity of the reagents used.

In this work we have compared the official methods still in use (the White method and the HPLC method) for the determination of HMF in unifloral honeys (acacia, chestnut, coriander, linder, sunflower) and honeydews with very low HMF contents (< 4 mg kg^{-1}), i.e. the most critical determinations, in terms of concentration results of samples and precision of the method.

For concentrations in the range 1-4 mg kg^{-1} the HMF values obtained with the two methods are comparable both for unifloral and honeydew samples. For samples with HMF content < 1 mg kg^{-1}, generally results significantly in excess were obtained with the spectrophotometric method in comparison to the HPLC method. In particular, 20-30% higher for samples with HMF content in the range 0.5-1 mg kg^{-1}, ~70% higher for samples with HMF content < 0.5 mg kg^{-1}. As regards precision, the HPLC method (±3.3% as RSD) is better than the White method (±6.4%) for unifloral honey samples, except for the chestnut honey and for honeydew samples, where precision is comparable for the two methods, about ±10% and ±7-9%, respectively.

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ANA-PO-29 Sorption and Photodegradation Studies of Marbofloxacin and Enrofloxacin on Clays

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Marbofloxacin (MAR) and Enrofloxacin (ENR) are two largely employed veterinary Fluoroquinolones (FQs) in the South Lombardy plain. Their occurrence and fate have been already investigated in natural waters [1] and agricultural soils [2,3], where they can be accumulated up to mg kg^{-1} levels as a result of manuring [4]. Their strong adsorption makes them persistent pollutants. This study focused on adsorption and interaction of FQs on three different clay minerals, montmorillonite, kaolinite and sepiolite. Adsorption/desorption behavior depends on pH of the medium, and only in the case of montmorillonite, both MAR and ENR cause an expansion of the spacing between layers (from XRD analysis). As clay percentage plays a significant role in the FQs soil adsorption, an influence on their photodegradation rate is expected too. Photodegradation experiments are ongoing on clays spiked with each antibiotic (mg kg^{-1}). Results will be compared to those obtained from typical agricultural soil collected near Pavia [2].

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ANA-PO-30 Development and validation of a GC/ECD method for analysis of PCBs in milk

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PCBs are synthetic organic compounds characterized by their toxicity and persistence in the environment, and for this reason in 2001 PCBs were banned by the Stockholm Convention on Persistent Organic Pollutants. PCBs can be transported long distances, and have been found in places which are far from where they were manufactured or used. They have been detected in all indoor and outdoor environmental media (surface and ground water, soil and food).Since these compounds exhibit a high affinity for lipophilic matrices, they can also accumulate in milk of animals, which eat PCB-contaminated feed.The aim of the present work was the development and validation of a method based on a simple cleanup procedure and a GC/ECD determination of 6 PCB-NDL (28,52,101,153,138,180) in milk samples. Several purification procedures involving sulphuric acid treatment and different solid phases extraction, [1] were tested in order to minimize interferences and to achieve high recovery values. Performance parameters, such as precision, specificity, ruggedness, linear range, LOD, LOQ, for the method validation were determined by the GC/ECD analysis of standard solutions and spiked samples in the range 0,5-4 ng g^{-1} containing 10 μg L^{-1} PCB 209 as the internal standard. The GC experimental conditions were optimized to allow an improvement of the time and the chromatographic resolution. Calibration curves of the investigated PCBs were obtained by using three replicate injections of the standard solution at five calibration levels, from 1 to 40 μg L^{-1} Calibration curves were linear over the whole range of concentrations tested for all congeners, as indicated by the very good values of the determination coefficients ($r^2 \geq 0.99$). LODs and LOQs were in the range 0.03-0.09 and 0.10-0.27 μg L^{-1}, respectively. The only use of Bond Elut PCB [2] gave short cleanup times, less viscous solutions, with few interferent compounds and clean extracts with good recoveries (71-111%) and CV% (3,3-18,0%), lower than reference value (23%) derived from Thompson's equation. [3]

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ANA-PO-31 Optimization and validation of a multi-matrix confirmatory method for the determination of Nicarbazin by HPLC-Diode Array Detection

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Nicarbazin is an authorised feed coccidiostat that is used for chickens for fattening. The actual feed production technologies cause unavoidable cross-contamination in feed for non-target animal species with possible repercussions on public health (1). Recently two European Union rules (Directive 2009/8/EC L 40/19 of 11.02.2009 and Regulation 2009/124/EC L 40/7 of 11.02.2009) have been issued, in which the nicarbazin maximum levels in non-target feed and foodstuffs of animal origin were reported. The development of a suitable method for official controls is necessary to reach these Maximum Residue Limits (MRL) for nicarbazin in feed and animal derived food.

In this work a sensitive, accurate and fast multi-matrix confirmatory method was optimized and validated for quantitative determination of nicarbazin in egg, liver, muscle and feed matrices. The method is based on high performance liquid chromatography and diode-array detection. The sample preparation requires a rapid extraction with acetonitrile and a purification step by *n*-hexane. A sensitive detection was obtained by using an absorbance wavelength of 350 nm and an exploration wavelength range 200-420 nm. Under optimized experimental conditions, nicarbazin separation was obtained in less than 20 minutes, using a C18 column eluted with a mixture of acetonitrile/water 50/50 (v/v) at a flow rate of 1.0 mL min^{-1}. The excellent analytical parameters (see table) of accuracy, detection and quantification limits and measurement uncertainty (%) were evaluated by following a validation procedure indicated in the European guidelines of Regulation 882/2004/EC (2) and Decision 657/2002/EC (3).

Sample	Repeatability RSD (n=6)	Reproducibility RSD (n=18)	Recovery % (n=18)	LOD (µg kg^{-1})	LOQ (µg kg^{-1})	Measurement uncertainty (%)
Eggs	3.4	4.0	75.2	8.6	26.2	11.1
Liver	1.2	4.0	80.0	8.6	26.2	11.1
Muscle	1.3	2.4	87.0	4.1	12.3	6.9
Feeds	3.3	3.7	74.4	3.7	11.2	6.6

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ANA-PO-32 The potentialities of capillary electrophoresis for the characterisation of wheat germplasm. A case study.

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In response to market demand, the interest toward old landraces of wheat, legume etc. surviving *on-farm* in marginal areas of Italy is constantly increasing. The survival of this germplasm is related to its characterisation and discrimination from modern varieties. Methods based on morphological plant traits or on DNA-based analyses are expensive and time demanding. Conversely, biochemical analyses are cheap and require short time. Gliadins, one of the most abundant storage protein of the caryopsis, is a very useful tool in the discrimination and characterisation of cereal accessions. Capillary electrophoresis (CE) allows automated and fast electrophoretic analysis of gliadins [1]. Presently, the literature on Italian landraces belonging to Oriental wheat (*T. turanicum* Jakubz.) is scarce. This study was undertaken to investigate by CE, the genetic similarity between some Oriental wheat samples gathered from Italian farmers and the accession QK-77, registered as Kamut®.

Nine samples acquired from farmers, seed trade companies and USDA gene-bank (PI278350, collected in Italy) were analysed. They were designated with different names such as 'Saragolla', 'Kamut', 'Farro lungo', 'Grano del faraone' and durum wheat. Kamut® was included as a reference. Gliadins were extracted from single caryopsis, 10 seeds per sample were analysed. CE analyses were carried out as previously described [2]. The samples were cultivated in an experimental field located at Urbisaglia (MC) to record the main morphological plant traits.

A very low intra-population variation of gliadin profiles was observed. The comparison of gliadin profiles among samples evidenced a very high similarity of profiles with the exception of 'Saragolla di Abbateggio'. Plant morphological traits agreed with electrophoretic analyses. These findings suggest that in Italy there are wheat landraces genetically very similar to Kamut®, though they are indicated with different vernacular names. It can be inferred that these landraces were originated by the same pool of seeds. The efficacy of CE as a fast and cheap method for the study of genetic relationships among wheat germplasm has been evidenced by the agreement of morphological and electrophoretic data.

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ANA-PO-33 Recent temporal variations of trace metal contents in wine.

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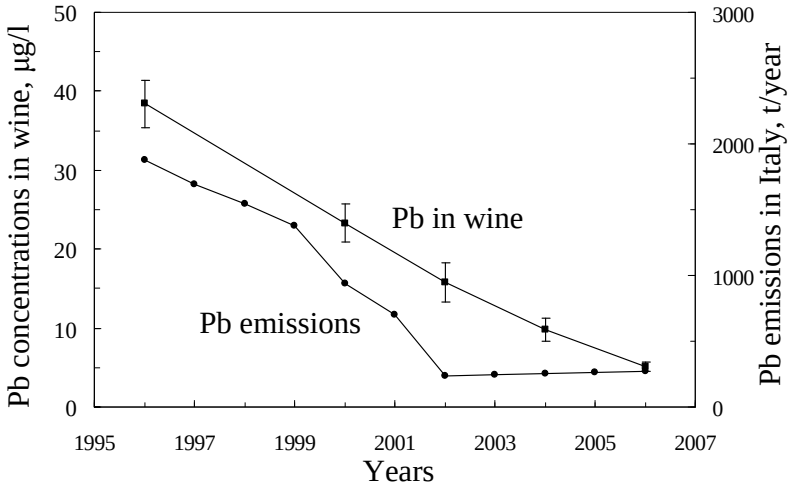
In a previous work, voltammetric stripping determination of Cd, Pb and Cu in wine (after UV digestion) was set up by us using the square-wave technique (SWASV) for the first time [1,2]. A thin mercury film electrode was used, applying the following parameters: E_{dep} = –950 mV (Cd), –750 mV (Pb, Cu) *vs*. Ag/AgCl, 3 M KCl; SW scan from –950 mV (Cd), –750 mV (Pb, Cu) to + 30 mV; E_{SW} = 20 mV; f = 100 Hz; ΔE_{step} = 8 mV, t_{step} = 100 ms, t_{wait} = 60 ms, t_{meas} = 3 ms.



In this work, a study of the recent temporal trends of the three metal concentrations was carried out, also to evaluate the potential relationship between the Pb content in wine and the removal of the metal from gasoline (which has been operative in Italy since 2002). The white wine *Podium* (a 100% *Verdicchio* wine) was used. This wine keeps well and samples of vintages between 1996 and 2006 were available. The results show that the Pb content in wine decreased from 38.4 µg/L in 1996 to 5.1 µg/L in 2006, a reduction of ~80%. This can be related to the recent phasing out of Pb from gasoline in Italy, which led to a similar decreasing trend of Pb emissions in the atmosphere (see Figure). Note that the current legal limit for Pb is 200 µg/L [3] (OIV limit 150 µg/L [4]), a considerably higher value than those measured here. By contrast, Cd and Cu do not show significant variations in the same period, with average measured values of: Cd ~0.3 µg/L (OIV limit 10 µg/L [4]) and Cu 50 µg/L (legal and OIV limits 1000 µg/L [4,5]).

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ANA-PO-34 UV-A and Visible Photolytic and Photocatalytic Degradation of Aqueous Fluoroquinolones: Reaction Kinetics and Byproducts

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Fluoroquinolones (FQs) are antibacterial agents employed in human and veterinary medicines, especially in animal breeding, and they have been widely detected in environmental waters [1], indicating their ineffective removal by conventional wastewater treatment plants [2].
Photodegradation is actually a significant removal pathway in water systems [3,4]. In this study we investigated the photolytic and titanium dioxide (TiO_2) photocatalytic degradation using UV-A, visible and natural solar light, in ultrapure and river water. Different FQs have been examined, i.e. Ciprofloxacin, Danofloxacin, Levofloxacin, Enrofloxacin, Marbofloxacin and Moxifloxacin, the last ones belonging to the most recent generation. Experiments were carried out at environment-significant concentration (20-50 $\mu g\ L^{-1}$) and at mg L^{-1} levels, and samples have been analyzed by HPLC-UV and FD. First order kinetics were observed both under direct photolysis and with TiO_2. Degradation rates were faster by heterogeneous photocatalysis for all of the drugs, except for Ciprofloxacin. Byproducts from both photocatalysis and photolysis were identified by HPLC-ESI-MS and the chemical paths compared.

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ANA-PO-35 Determination of YLOID in soil and grapevine systems (Vitis vinifera L.) by ICP-MS technique: a hopeful proxy for the geographical characterization of food products?

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Chemical behavior of YLOID (Y and Lanthanoid) into soil was extensively studied both to evaluate geochemical process. Metal cations can be immobilized onto particle surface of soil due to the formation of stable complexes with organic matter. If environmental conditions change metals can be mobilized and therefore to became bioavailable [1].

In recent years identification of the geographical origin of food has acquired very importance because consumers are more and more interested in knowing the provenance of the food purchased and/or eaten [2]. Then the knowledge of a relationship between the chemistry of the substrates and the food could be an important tool for the quality guarantee of traditional food products.

The uptake of YLOID and their distribution in grapevine system were studied under controlled conditions following the plants growth.

The experimental system consisted of a set of 30 plants, divided into two groups: blank and YLOID. The first group (blank) was used as control, the other was polluted in an unique step with a YLOID concentration of $2.5 \cdot 10^{-3}$ mmol for Kg of substrate (peat and gravel).

Three replicates for each group and for each phenological stage were sampled. To study the metal distribution, the main part of plants: roots, stem, woody and herbaceous shoot and apex were analysed.

The obtained results were critically discussed on the basis of the different amount presents in all parts of plants.

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ANA-PO-36 Detection of fraudulent addition of barley to coffee powder by means of NIR spectroscopy and multivariate regression

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Coffee characterisation by means of instrumental fingerprints has gained increasing attention as a tool for controlling and avoiding adulterations [1]. The objective of the present study was to verify the feasibility of detecting fraudulent additions of barley to coffee, by means of NIR spectroscopy and multivariate calibration methods. In order to generalise the results, nine different types of grain coffees, including both *arabica* and *robusta* species as well as mixtures, with different roasting degrees, and four different barleys were collected. Beans were grounded and the powders were mixed at 10 different levels, between 2 and 20% (w/w) of barley. Since all the possible combinations of coffee and barley samples at each level would have required 360 mixtures, D-optimal design was applied to select 100 and 30 representative mixtures as calibration and test sets, respectively. NIR spectra of the powder samples were recorded in the reflection mode, in the range 4,000-10,000 cm^{-1} with a 4 cm^{-1} resolution, by an FT near-infrared spectrophotometer based on a polarization interferometer (Buchi NIRFlex N-500). Spectra of the nine pure coffee samples were also added to the calibration set.

Partial least squares (PLS) regression and kernel orthogonal partial least square (KOPLS) techniques [2] were used to build the predictive models. The number of latent variable, orthogonal components and kernel band width were optimised within cross validation cycles. The optimised models were validated by prediction of barley concentration for the samples of the test set. In addition, eleven different mixtures of two different coffee and barley samples (not included in the training samples) were evaluated as an external test set. The root mean square error (RMSE) of the PLS model for the calibration, test and external test sets were 1.2, 1.4 and 1.04, respectively. The corresponding RMSE values of the KOPLS models were 0.63, 0.83 and 0.97. The method presented can be considered as a rapid and reliable tool for detecting the adulteration of coffee by addiction of barley.

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ANA-PO-37 LA-ICP-MS analysis of otoliths: a new prospecting tool of marine metal pollution.

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Trace elements in otoliths may provide information on dispersal history of marine fishes. We propose the use of the fish otoliths as biomarkers of marine pollution. The longitudinal section of otoliths of fish shows, indeed, daily growth rings whose elemental composition reflects the composition of the waters where the fish has been.

Interest in analytical mass spectrometry associated with laser ablation for sample introduction has increased markedly during the past few years. Laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) appears to be the only analytical approach for nearly non-destructive determination of a large number of elements with very low detection limits, permitting the characterization of the distribution of trace elements in geological, archaeological and environmental materials. Moreover, laser ablation can be performed with beam diameters ranging from few microns to hundredths microns, allowing both space resolved and 'bulk analysis'.

Space resolved capabilities of LA-ICP-MS have been employed to study the concentrations of trace elements in otoliths to obtain information about the origin of fish and rebuild their migratory flows [1,2]. However otolith matrix can incorporate trace elements from its environment [3] and the findings of elements having environmental concerns in these structure is the signal that fish has experienced polluted waters. As a result LA-ICP-MS provides precise positional information with the potential for chronological studies of otoliths and the history of the environment that the fish have lived in.

In this work the development and the optimization of LA-ICP-MS method and the relevant application will be shown.

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ANA-PO-38 An innovative derivatisation GC/MS procedure for the identification of proteins in the Paint Microsample

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The complex chemical composition of paint layers in artworks may be related to many factors: the technique followed by the artist, the effect of aging and the environment, and the effect of past conservation practices [1]. The chemical characterization of materials used in the creation and restoration of a painting is extremely useful for surveying historical events and for gaining a better knowledge of the artistic heritage.
For determining proteinaceous materials it is necessary a multistep chemical pretreatment of the samples based on the ammonia extraction of proteins and polysaccharide materials, in order to separate them from lipid and resinous materials [2]. The proteinaceous fraction is analysed by GC-MS after hydrolysis and derivatisation of the free amino acids. A new derivatisation GC/MS procedure for the identification of proteins in the same microsample from painted works of art has been optimized. The amino acid fraction is derivatized using as solvent anhydrous dimethylformamide (DMF) instead of pyridine. More polar solvent such as pyridine is used more often because they tend to facilitate the reaction. Pyridine is an excellent solvent for TMS reactions. Although some regard pyridine as a silylation catalyst, there are many instances in which silylation reactions actually are slower in pyridine than other solvents. In addition, pyridine also may have other undesirable effects such as the promotion of secondary products and other chromatographic anomalies. DMF is used extensively, especially for large molecules. Using DMF we can limit the formation of by-products and improve the resolution of hydrophilic amino acids such as proline and hydroxyproline. The method was tested on reference materials for the identification of proteinaceous binders (egg, collagen, casein) on the basis of the quantitative determination of the amino acid profile.

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ANA-PO-39 A study on the curing and ageing of alkyd paints layers

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The range of modern oil-based paint media nowadays used by artists has expanded far beyond the traditional drying oils. Alkyd paints were introduced in the 1940s as alternative for traditional drying oils, and they became immediately widespread given their ability to dry fast. Chemically, alkyds are oil-modified polyesters manufactured from polyols (tipically glycerol or pentaerythritol), polybasic acids (phtalic anhydride, phtalic acid and its isomers) and a source of fatty acids, usually a vegetable oil.

In the context of the PAR-FAS Regione Toscana COPAC Project (Preventive Conservation of Contemporary Art , 2011-2013) we investigated the chemical transformations occurring in alkyd paint layers during curing and ageing by a multi-analytical approach entailing: direct exposure-mass spectrometry (DE-MS), gas chromatography /mass spectroscopy (GC/MS), analytical pyrolysis coupled with gas chromatography /mass spectroscopy (Py-GC/MS), Differential Scanning Calorimetry (DSC) and thermogravimetric analysis (TGA). Aim of the research was to achieve a complete characterization of the paints, to study autoxidation during curing and ageing, and to investigate the effect of the pigment.

Two kinds of alkyd paints were studied: Ferrario and Griffin, Windsor & Newton, containing both inert and metallic pigments. The paints were used to prepare reference layers that were naturally and artificially aged. Preparation of some of the paint layers was in collaboration with the IFAC CNR group (Florence).

In particular, GC/MS analysis after hydrolysis and silylation permitted to identify the fatty acid profile and the aromatic fraction of the paint, and to study molecular changes associated to curing and ageing as oxidation of double bonds.

TGA permitted to investigate the thermal stability and the thermo-oxidative behavior of alkyd paints. In particular it allowed us to achieve information on the interactions taking place between inorganic and organic species within the paint film, to investigate the occurrence of cross-linking, oxidation and hydrolysis phenomena in alkyd paints during ageing .

DSC has been used to study the oxidative polymerisation of alkyd coatings and to quantify the peroxides formed during oxidative drying. Peroxidation of fatty acid chains is the primary step in oxidative process and can used to control their drying extent.

The results permitted to highlight the differences in the formulation of the two kinds of alkyd products, and to model the main reactions occurring during the curing of the alkyd paint films investigated.

ANA-PO-40 Analysis of perfluorinated acids by online SPE-LC/MS/MS

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Perfluorinated alkyl sulfonic acids (PFSAs) and perfluorinated carboxylic acids (PFCAs) are two classes of compounds widely used for industrial and household applications. They are presents in hydrorepellant coatings, stain repellents, fire-fighting foams, paints, cleaning products (especially for metal surfaces and carpets) etc. Because their resistance to degradation in the environment and their bioaccumulation properties, PFSAs and PfCAs are considered emerging pollutants and potential endocrine disrupters. During the last decades PFSAs and PFCAs spread in any compartment of the environment and nowadays can be considered ubiquitary. Due to the concern over possible effect on human health, in 2009, Stockholm Convention on Persistent Organic Pollutants suggested to impose restrictions to the use perfluorooctane sulfonic acid (PFOS) [1] and, US-EPA [2] intends to propose actions in 2012. In order to carefully evaluate the risks arising from their presence efficient analytical procedures are required. The aim of the study was to evaluate the feasibility of improving the performances of conventional reversed phase using graphic materials. The use of porous graphitic carbon (PGC) as stationary phase relevantly increase breakthrough volumes generating reproducible chromatographic conditions compatible with robust and sensitive ESI detection. Under described conditions LOD are ranged. In this study, the advantages of using online SPE was also deeply investigated. The method significantly improves previous methodology in terms of organic solvent use reduction, shorter analysis time, reduced sample manipulation and risks of contaminations. Moreover, online methods can be easily automatised.

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ANA-PO-41 Magnetic solid-phase extraction based on diphenyl functionalization of Fe_3O_4 magnetic nanoparticles for the determination of polycyclic aromatic hydrocarbons in urine samples

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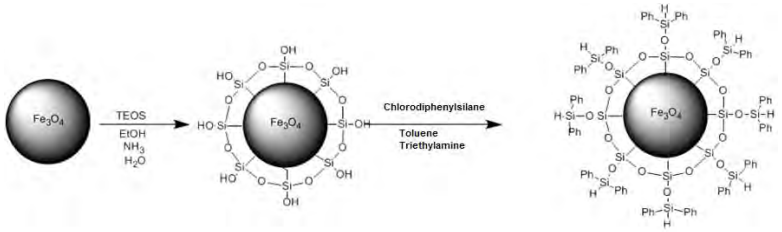
Superparamagnetic Fe_3O_4 diphenyl nanoparticles (Scheme 1) were prepared according to a solvothermal procedure and characterized by X-ray diffraction, infrared spectroscopy and transmission electron microscopy.



Scheme 1

The magnetic phases present in the nanoparticles samples were analyzed by thermomagnetic analysis and the magnetic properties of the samples were studied by vibrating sample magnetometry. The resulting nanoparticles having an average diameter of 200 nm and characterized by a Ms value of 20 emu/g were then used as solid-phase extraction sorbents to extract polycyclic aromatic hydrocarbons from urine samples. Method validation proved the feasibility of the developed beads for the quantitation of the investigated compounds by gas chromatography-mass spectrometry at trace levels, limits of quantitation being in the ng/l range [1]. CV was always lower than 15%, which points to a good precision of the method. Finally, the superior extraction performance of the synthesized nanoparticles with respect to commercially available beads was proved.

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ANA-PO-42 HPLC/MS^2 to detect and analyse TATP and HMTD in swabs.

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Peroxide-based explosives such as triacetone triperoxide (TATP) and hexamethylene triperoxide diamine (HMTD) are not difficult to synthesize and synthesis can be performed starting from readily available basic chemicals: this led to increasing use of TATP and HMTD by terrorists [1]. Whenever there is the need of collecting traces of explosives, both post blast and post transfer, surface sampling plays a critical role, especially because only reasonably small objects can be sent to a laboratory to be analyzed. Traces can also be searched on hands of suspect, where they can disappear faster than from objects.

In this work TATP and HMTD were synthesized and spiked solutions or aliquots of a few milligrams of explosive compounds were then spread on different surfaces (e.g. floors, tables) or used in handling tests. Three different swabbing systems were used: dry paper swabs, cotton swabs wetted with propan-2-ol and a commercial swab, pre-wetted with propan-2-ol and water (7:3). A simple solvent extraction procedure from swab was developed with quantitative recoveries. Paper and commercial swabs were used also to sample a metal plate, where a small charge of about 4 g of TATP was detonated. Both ESI and APCI ion sources were exploited for better ionization and fragmentation condition of analytes. All the three swabbing systems gave some positive results. The developed method was validated and showed its suitability to be used in real cases, allowing TATP detection in several simulations. Confirmation by HPLC/MS^2 was essential to give proper forensic identification of analytes and low limits of detection were reached.

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ANA-PO-43 Application of 3 µm Particle-Based Amylose-Derived Chiral Stationary Phases for the Enantioseparation and Absolute Configuration Determination of Potential Histone Deacetylase Inhibitors

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Enantioselective analysis covers a significant area of analytical chemistry and it has been gaining a growing interest within a wide variety of fields dealing with drugs, flavours, fragrances, natural products and so on. The importance of this topic in view of both basic research and industrial application has given a strong impulse to the design of new and efficient chiral stationary phases (CSPs) to be used in HPLC. Currently more than 100 CSPs for HPLC are available on the market. Among them the benzoates and arylcarbamates of cellulose and amylose have been successfully employed to resolve a broad range of chiral compounds on analytical and preparative scale. Only recently (2008) amylose-derived CSPs based upon 3 µm silica (Chiralpak IA-3 and Chiralpak AD-3) were developed for applications with organic and aqueous mobile phases.

The chiral selector of both CSPs is the same, the tris(3,5-dimethylphenylcarbamate) of amylose, but it is physically coated in the case of Chiralpak AD-3 and immobilised in the Chiralpak IA-3. In this work, we report on the difference in versatility and performance of the two 3 µm particle-based CSPs towards four racemic cinnamyl 2-aminoanilides (Figure 1), endowed with HDAC inhibitory activity. The 3 µm CSPs were explored to determine if they could provide a rapid resolution of enantiomers in analytical conditions in presence of alcoholic eluents such as pure 2-propanol. The second part of work was devoted to the optimization of the mg-scale enantioseparations using an analytical 100 x 4.6 mm i.d. column. Finally, the isolated enantiomers were submitted to chiroptical analysis and their absolute configuration was established by a combined strategy based on chemical correlation/circular dichroism methods.

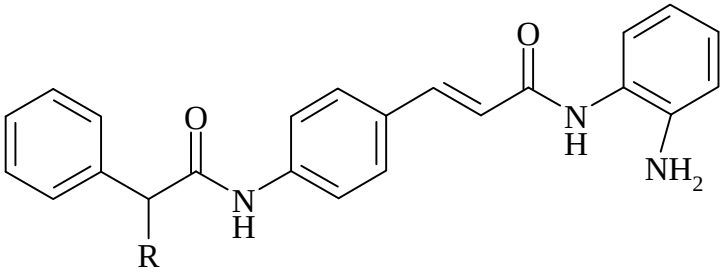

Figure 1.

ANA-PO-44 Extending the applicability of pressurized hot water extraction to compounds exhibiting limited water solubility by pH control: Curcumin from the Turmeric rhizome

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Pressurized hot water extraction (PHWE; also known as subcritical water extraction, SWE) is commonly considered to be an environmentally-friendly extraction technique that could potentially replace traditional methods that use organic solvents [1]. Unfortunately, the applicability of this technique is often limited by the very low water solubility of the target compounds, even at high temperatures [2].

In this paper, the scope for broadening the applicability of PHWE by adjusting the pH of the water used in the extraction is demonstrated in the extraction of Curcumin (which exhibit very limited water solubility) from untreated turmeric (*Curcuma longa*, L.) rhizomes. Although poor extraction yields were obtained even at high temperatures when using degassed water or neutral phosphate buffer as the extraction medium, yields exceeding those obtained by Soxhlet extraction were achieved using acidic pH buffers. Optimized conditions for the extraction of Curcumin from turmeric by PHWE were identified, and the influence of the temperature, pH, and buffer concentration on the extraction yield were investigated in detail by means of a series of designed experiments. The relationships between these variables were subjected to statistical analysis using response surface methodology.

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ANA-PO-45 Capillary electrophoresis of *Escherichia coli*: a first attempt

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In the last few years, capillary electrophoresis have been used to characterize and separate microorganisms on the bases of their electrophoretic mobility [1]. Indeed microorganisms have an external structure, the "cell wall", with a characteristic molecular composition which distinguishes microbial species and strains from each other (yeasts, bacteria, viruses). More importantly, the cell wall contains several ionizable groups that in particular conditions give rice to a superficial charge causing them to migrate with a typical migration time under an applied electric field [2,3]. Our previous works on backer's yeast [4] have demonstrated that the characteristic electropherogram of this species shows two peaks ascribed to neutral and negative charged cells. Relevant microscopic studies have further pointed out that the electrophoretic profile also reflects the dimensional distribution of cells in the analyzed sample.
In the following work, our interest has been focused on the electrophoretic behavior of *Escherichia coli*, a microorganism of significant interest for its role in several infectious diseases and its importance in biotechnological industries. As a first attempt, it was necessary to optimize the electrophoretic conditions for the identification and efficient separation of this microorganism by capillary electrophoresis; accordingly, the effects of the running buffer, pH, the separation voltage and the microbial aggregation on the electrophoretic profile of *Escherichia coli* were studied. Once typical electropherogram of that bacteria was identified, a sample containing *Saccharomyces cerevisiae* and *Escherichia coli* was analyzed using capillary electrophoresis and the experimental results have demonstrated the power of the technique in detecting the bacterial contamination of fungal sample.
Thus capillary electrophoresis is able to replace traditional method of microbial identification because it permits rapid, easy and highly sensitive microbial analysis and diagnoses at low costs on several biological samples.

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ANA-PO-46 Characterization of non-volatile polyphenol compounds in coniferae by liquid chromatography-mass spectrometry

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Vascular plants synthesize a large number of diverse biochemical compounds with specialized functions. It has been estimated that up to 200,000 different metabolites occur in the plant kingdom, and each species may contain its own chemotypic expression pattern [1]. Secondary metabolites are present in all higher plants, usually in a high structural diversity. As a rule, a single group of phytochemicals dominates within a given taxon. Plant phenolics are one of the most important groups of secondary metabolites in plants and approximately 8000 of them are known. From a structural point of view, phenolic compounds include a wide range of substances: simple phenols, phenolic acids, phenylpropanoids, coumarins, quinones, flavonoids, tannins, and other miscellaneous phenols [2].

A liquid chromatography/electrospray ionization mass spectrometry (LC/ESI-MS) method employing a time-of-flight (TOF) analyzer with LockSpray source for continuous accurate mass measurements was developed for evaluation of phenolic content in some coniferae, i.e. pine (*Pinus Pinea*), cypress (*Cupressus sempervirens* L.) and thuja (*Thuja* L.).

Matrix Solid Phase Dispersion (MSPD) using C18 as dispersing material and methanol as eluent was applied to extract the analytes from matrices. The fragmentation patterns of phenolic compounds were obtained using both positive and negative ion mode, and accurate mass data were used for identification of compounds. In all the three plant extracts, various phenolic compounds were identified, most of them belonging to flavonoid group. Cypressus extract showed the richest chromatographic profile compared to pine and thuja extracts.

Recovery and quantitative estimation were performed by using biochanin A (not present as endogenous compound in the extracts) as internal standard and other selected analytes as references of the various compound typologies (aglycones, monoglycosilated, and diglycosilated).

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ANA-PO-47 Single column Ag^+-HPLC analysis of CLA isomers

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It is known that conjugated linoleic acid (CLA) isomers possess many important biological properties, including anticarcinogenic, antidiabetogenic and antiadipogenic effects [1]. The most CLA found in human tissues is from dietary origin (meat and dairy products), because endogenous synthesis is very limited [2]. Therefore many nutritional complements containing CLA, as free fatty acids, alkyl ester or triacylglycerol mixtures, are now available. Since CLA biological effects are isomer-specific, it is very important to have reliable and precise techniques for identification and quantification of CLA isomers in food and nutritional supplements. A combination of high resolution gas chromatography and multi-column silver-ion high performance liquid chromatography (Ag^+-HPLC) was found to be necessary to resolve all CLA isomers [3].

In this research a CLA standard mixture, containing four *c,t*/*t,c* positional isomers (*c,t*-11,13, *t,c*-10,12, *c,t*-9,11 and *t,c*-8,10), was derivatized using different length chain alcohols; the obtained compounds were analyzed by Ag^+-HPLC coupled with UV detection system, set at 232 nm. The analytical technique was optimized by using a single Ag^+ column to separate different alkyl esters of CLA isomers. The use of a single column allowed to obtain the separation of CLA isomers in less time and with lower cost with respect to multi-column Ag^+-HPLC. Good reproducibility of CLA isomer retention times was obtained using daily prepared mobile phase and a column oven. The separation degree of the four CLA isomers increased with the alkyl chain length. The best resolutions were observed for hexyl ester derivatives.

The optimized analytical technique could represent a useful tool to evaluate the quali- and quantitative profile of CLA isomers in nutritional supplements so to provide accurate information for the consumers.

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ANA-PO-48 Fluorinated stationary phases for alternative selectivity. Separation of compounds of biological and biomedical relevance

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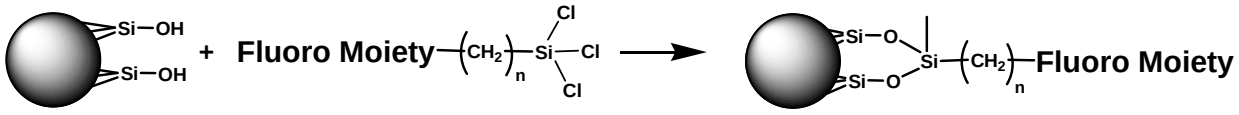
In recent years, growing interest has been posed in the use of fluorinated stationary phases (FSPs) in liquid chromatography, because of their orthogonality respect to traditional alkyl phases. In fact fluorinated phases are characterized by alternative retention mechanisms, in particular show more polar interactions compared to traditional alkyl phases, offering a different selectivity [1-3].

We prepared new FSPs, containing polyfluorinated aryl or alkyl fragments bound to silica with different particle sizes (1.7-5.0 micron) and pore size of 100 or 300 Å. In order to improve the stationary phase chemical stability, the matrix synthesis is based on the employment of functional silanes, where the polyfluorinated fragment is located far from silicon atom by an non-fluorinated alkyl spacer according to the following scheme:



These new phases, packed in columns of different geometries (spanning from standard to nano-) were compared to conventional alkyl-bonded phases (C18, C8, phenyl-) analyzing the loading density and the nature of the stationary phases in terms of hydrophobicity, selectivity for neutral (CH_2 selectivity) and polar solutes.

Moreover, the new FSPs have been employed for the HPLC-MS analysis of halogenated compounds and also for the separation of biological and biomedical relevant peptides whose selective retention could be influenced by the stationary phase fluorination.

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ANA-PO-49 Purification of bistrifluorosulfonimide (NTf_2) based Ionic Liquids for electrochemical and photochemical purposes

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Ionic liquids (ILs) are peculiar compounds with several smart properties, they are liquid at room temperature, with high thermal and chemical stabilities and they can be synthesized in several different combinations to modulate their properties in view of their use. [1]
Their synthesis is normally easy and fast, but the products often contain great amounts of water and other impurities that could impart to them a yellowish color and poor electrochemical properties.[2]
In the present work a purification protocol was developed that can lead to suitable ILs to be used as supporting electrolytes for electrochemical applications and/or as solvents for photochemical reactions.
Water immiscible ILs are preliminary investigated namely $[Py_{1,4}]^+[NTf_2]^-$, $[Py_{1,102}]^+[NTf_2]^-$, $[bmim]^+[NTf_2]^-$.The purification protocol of the IL involves a washing step with water in a liquid/liquid extractor, treatment with activated carbon and C-18 resin disk, and a drying step by using alumina or calcium hydride.
The effect of each purification step was evaluated by fluorescence spectroscopy, UV-Vis, NMR, IR, GC-MS and cyclic voltammetry.
It was shown that the purification leads to an improvement of the electrochemical stability and to a better reversibility of the redox probe ferrocene.
A well-known photochemical reaction, viz the addition of a photogenerated phenyl cation onto benzene [3], was performed in unpurified and purified $[Py_{1,102}]^+[NTf_2]^-$, showing the effectiveness of the purification protocol and the chemoselectivity imparted to the reaction by the IL itself.

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ANA-PO-50 An efficient and reliable DoE optimized SPME-GC-MS/MS method for determination of hydrazine in drinking water

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Hydrazine is a genotoxic and neurotoxic compound, classified as probable human carcinogen by the U.S Environmental Protection Agency. Hydrazine drinking water contamination can originate from military and industrial wastes, wastewater treatment plant (WWTP) effluents, and possible formation in drinking water disinfection [1]. Various papers describes hydrazine determination by gas chromatography by different extraction and derivatization techniques [2],[3]. The purpose of this work was the development of a method for the determination of hydrazine in drinking water by solid-phase microextraction coupled with gas chromatography-tandem mass spectrometry (SPME-GC-MS/MS). Derivatization reaction was carried out using chloroformates in accordance with the procedure proposed by Hušek [4]. Derivatization parameters are investigated by the multivariate approach of "Experimental Design" in order to find the best experimental condition that lead to formation of the di-derivatizated compound only. For this purpose are tested three different alkyl chloroformate (ethyl, propyl and isobutyl). The performances of five fibers (both in DI and HS mode) and three chloroformates were surveyed by mean of a 5×3 multi-factor categorical design. From this study the fiber and the chloroformate that gave best results were selected for experimental design optimization in order to improve the extraction process. The variables affecting thermodynamic aspects of SPME such as desorbtion temperature and NaCl concentration will be optimized by a central composite design (CCD). Sample extraction time and agitation, which are variables that affecting kinetic aspect, will be optimized by the univariate method.

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ANA-PO-51 Electrochemical Properties and Analytical Application of Bio-Nano-Electrodes

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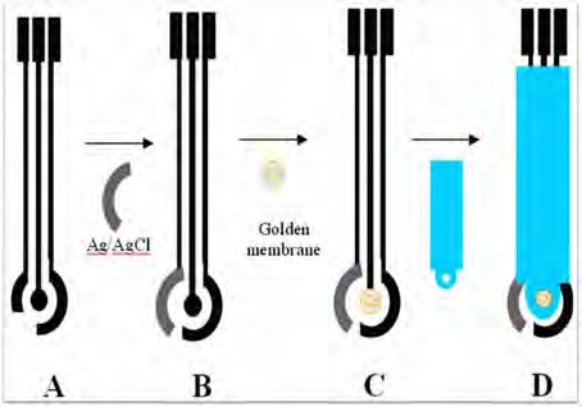
Gold electrodes are mainly used because of their window of working potential and the possibility to easily functionalize their surface by self assembled monolayers (SAMs) or electrochemically deposited multilayers (EDM) through thio- or amino-coordinate derivatives [1]. By using nanoporous membranes as templates for Nano Electrode Ensembles (NEE), it is possible to obtain an assembly of gold ultra-microelectrodes confined in areas to a few mm^2 , which can be either used such as or as platform for further immobilization of biomolecules [2]. Gold NEE were synthesized within porous polycarbonate membranes and coupled with a screen printed substrate to give a disposable and versatile electrochemical system for biosensing and bio analytical applications. Scanning Electron (SEM) and Scanning Probe Microscopy (SPM) techniques have been used to characterize the gold nanostructures morphology. Efficiency and sensitivity of the electrodes so obtained were tested using glucose-oxidase immobilized on the nanosized surface. Electrodes responses to hydrogen peroxide and glucose were collected and compared to other glucose-oxidase macro-electrodes [3]. Different enzymes were immobilized on the nano-sensor surface and different immobilization techniques have also been taken into account. Novel nanowire depositions (using Ni, Pt, Ag) in template nanosystems have been recently experimented for several bioanalytical applications, e.g. in detection of phenolic compounds, choline and biogenic amines.

Figure 1- Schematic sequence of NEE preparation on screen printed substrate (SPS):
A) carbon graphite tracks and contact pads obtained by screen printing; B) Ag/AgCl paste deposition (reference electrode); C) placement of the NEE based membrane on the working electrode; D) dielectric paste deposition



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Indice degli Autori

Didattica Chimica

DID-OR-01 Didattica universitaria, ricerca didattica e formazione degli insegnanti

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La trasformazione della didattica universitaria è un tema di particolare attualità perché riguarda tutte quelle attività educative che si rivolgono ad insegnanti sia nella prima formazione che nella formazione continua. Il modo di trasmissione delle conoscenze e delle abilità che sarà utilizzato per trasmetterle a coloro che già insegnano o che si preparano a diventare insegnanti è cruciale rispetto al loro futuro svolgimento del ruolo educativo.
Una didattica fondata sulla passività dell'allievo e sulla accumulazione-ripetizione delle conoscenze trasmesse, che non ammette mai l'acquisizione delle procedure necessarie a produrre e controllare conoscenze non può far altro che riprodurre se stessa nel passare dall'università alla scuola.
Analogamente, nel momento in cui si chiede agli insegnanti di aiutare gli allievi a costruirsi progressivamente competenze per comprendere, valutare, produrre conoscenze in modo autonomo, è indispensabile che la formazione degli insegnanti sia congruente a questo nuovo e diverso modello ed è pertanto decisivo il contributo che può venire dalla ricerca didattica.
La didattica universitaria è chiamata in causa direttamente in un discorso di rifondazione dei criteri e dei curricoli per la formazione iniziale degli insegnanti. Nelle lauree magistrali per l'insegnamento di nuova istituzione sono previsti sia corsi di didattica disciplinare che richiedono competenze specifiche sia corsi disciplinari. Questi ultimi dovrebbero poter essere condotti connotandoli opportunamente in modo che siano riconoscibili le parti più significative e quelle che possono creare ostacoli cognitivi agli allievi.
La Divisione di Didattica ha costituito una commissione di studio che si propone di collaborare con i colleghi coinvolti nella preparazione dell'offerta didattica delle nuove lauree per l'insegnamento e del tirocinio formativo attivo (TFA) transitorio allo scopo di favorire una riflessione sui contenuti e sui metodi degli insegnamenti previsti e di realizzare un coordinamento tra le diverse sedi.

DID-OR-02 CLIL (Content and Language Integrated Learning) per un apprendimento "learner-centred" della chimica: *Part I*. Un esempio

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Sebbene sia nato nell'ambito educativo delle lingue straniere, la metodologia CLIL (Content and Language Integrated Learning) si sta rivelando molto di più della somma delle sue parti, molto di più di quanto si potrebbe prevedere dal contributo dei singoli aspetti in cui essa è articolata [1]. Difatti, gli studenti devono comprendere il contenuto disciplinare attraverso una lingua straniera per la quale dispongono di risorse linguistiche limitate. Il docente che prende atto di questo è naturalmente portato a riconsiderare il tipo di "linguaggio di istruzione" adoperato da lui stesso e/o dal materiale di cui si avvale: gli studenti comprendono questo linguaggio in input? Questo è un approccio *language-aware*. Come riportato nella Special Section di *Science* dal titolo "*Science, Language and Literacy*" [2], anche se sembra ovvio che il docente debba essere cosciente del fatto che il linguaggio di istruzione debba essere comprensibile, in realtà non è sempre così. Spesso, più che trovare i concetti incomprensibili, gli studenti trovano incomprensibile il linguaggio con cui sono presentati i concetti. Per il suo approccio language-aware, il CLIL offre una metodologia pragmatica per rendere più comprensibile il linguaggio della scienza. Ma non è soltanto questo. Un insegnante che diventa più language-aware, è portato automaticamente a rivedere anche come è strutturato il suo contenuto disciplinare, ovvero se esso è presentato "in aliquote masticabili e quindi digeribili" dagli studenti. L'insegnante allora diventa anche *content-aware*.

Il workshop dimostrerà come il CLIL sia in grado di trasformare un esperimento abbastanza usuale in un nuovo modo di apprendere la chimica che è altamente language-aware e content-aware quindi, *learner-centred*.

[1] Y.L.T. Ting, *English Language Teaching Journal,* 65, **2011**, 314.
[2] *Science*, April 23, **2010,** pp. 448-466.

DID-OR-03 CLIL (Content and Language Integrated Learning) per un apprendimento "learner centred" della chimica: *Part II*. Analisi. Il ruolo della SCI

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Nell'ottica di un'impostazione didattica fondata *sull'apprendimento anziché sull'insegnamento*, il docente si deve impegnare a ricercare percorsi e progettare strumenti attraverso i quali l'allievo possa creare sempre più autonomamente il proprio sapere, tramite processi di scoperta, invenzione e costruzione di concetti. Dall'attività del workshop proposto, dovrebbe emergere come in ambiente CLIL si dia ampio spazio a tali metodologie costruttiviste: in esse i docenti si impegnano a realizzare situazioni che permettano agli allievi di riconoscere ed utilizzare le proprie abilità nel fornire soluzioni personali, metterle al confronto con i propri pari, verificarle e migliorarle, trasformandole via via in vere e proprie competenze. In questo senso le pratiche CLIL, se fatte bene, consentono agli studenti di ottenere un *valore aggiunto* nel loro saper essere, nel capire e nell'agire con una certa autonomia, in un contesto anche non familiare e in una dimensione più ampia.

Nata per l'allestimento di *moduli didattici*, l'attività CLIL è andata via via crescendo e sviluppandosi, assumendo nel tempo ruoli ed importanza per l'allestimento di una vere e proprie *sequenze di apprendimento*, con connotazioni di flessibilità ed applicabilità anche in diversi contesti scolastici. Tutto questo coerentemente ai suggerimenti di tipo pedagogico didattico che hanno assunto una certa unitarietà di intenti all'interno della Comunità Europea nell'ultimo quinquennio[1] Da numerose testimonianze di chi pratica CLIL provenienti da tutta Europa, sembra che l'educazione scientifica sia particolarmente avvantaggiata dalla pratica di tali metodologie. Vi è dunque un reale potenziale nell'*usare il CLIL anche in chimica*, ed è molto diverso e *molto di più che non usare la lingua straniera per insegnare la chimica.*

Pensando alle più recenti occasioni in cui i docenti di Chimica provenienti da diverse parti del paese hanno avuto modo di confrontarsi all'interno dei dibattiti organizzati dalla DDSCI ed a quanto i docenti fossero coinvolti nei nuovi aspetti della programmazione per competenze ed al nuovo ordinamento dei cicli scolastici

1 **Decisione del Parlamento Europeo e del Consiglio del 12 dicembre 2006** (periodo 2007-2013, programma "Europa per i cittadini" mirante a promuovere la cittadinanza europea attiva); R**accomandazione del Parlamento Europeo e del Consiglio del 18 dicembre 2006 (**competenze chiave per l'apprendimento permanente); T**rattato di Lisbona**, firmato a Lisbona il 13 dicembre 2007.

nel nostro Paese[2], nell'ottica soprattutto di dover praticare una disciplina scientifica interamente attraverso una lingua straniera, si può ben sperare che la nostra Associazione abbia da essere interessata al CLIL , e che anzi possa fornire più di un ausilio per la divulgazione delle sue pratiche grazie alla possibilità di attuare aggiornamenti, collegamenti di esperienze, ulteriori occasioni di confronto.

2 D.P.R. n. 87, n. 88, n. 89 del 15 marzo 2010. Regolamento recante revisione dell'assetto ordinamentale, organizzativo e didattico degli istituti professionali, degli istituti tecnici, dei licei

DID-OR-04 Teaching and learning of the concept of chemical equilibrium

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Educational research in chemistry has identified the most common learning difficulties and alternative conceptions concerning the concept of chemical equilibrium. These studies show that students have difficulty in predicting the evolution of a system from an initial state or from an equilibrium state, or also that students believe that the forward and reverse reactions alternate and exist as distinctly separate events when equilibrium is attained, or even believe chemical equilibrium as a static state [1]. These students misunderstandings and learning difficulties require the design and testing of educational sequences that allow for meaningful learning of the concept of dynamic chemical equilibrium. Many authors report that a concept is learned significantly when the teaching takes into account of the questions that scientists have set themselves during their research. In such a way issues, contexts of meaning and empirical referents on which the concept of dynamic equilibrium is structured, can be clarified [2]. Moreover, education should be thought of as producing change in a student's conceptions rather than simply accumulating new information within the student's memory [3].

The design of the teaching sequence, which is the subject of this communication, started from the historical and epistemological evolution of the concept of dynamic chemical equilibrium, by taking into account the alternative conceptions and learning difficulties of the students and with the aim to put both the student and the topic to learn within the process of learning and hence to focus on the the dialectical relationship between "the logic of scientific knowledge" and "logic of the student" [4]. The teaching sequence, which was divided into six sections (1. Incomplete chemical transformations, 2. Reverse chemical transformations, 3. Systems in dynamic chemical equilibrium, 4. Evolution of systems I: from a state of non-equilibrium to a state of equilibrium, 5. The equilibrium constant, 6. Evolution of systems II: from a state of equilibrium to another equilibrium state), is based on theoretical questions and practical problems that should allow students to compare and contrast each other ideas and to learn in an active way the concept of dynamic chemical equilibrium. The teaching sequence has been successfully tested in a fourth class of Liceo Scientifico Tecnologico (progetto Brocca) during the school year 2010/2011.

[1] (a) A. C. Banerjee, Misconceptions of students and teachers in chemical equilibrium, Int. J. Sci. Educ., 13, 1991, 487-494. (b) K. Ganaras, A. Dumon, C. Larcher, Conceptual integration of chemical equilibrium by prospective physical sciences teachers, Chem. Educ. Res. Pract., 9, 2008, 240–249.
[2] (a) J. Quìlez, From chemical forces to chemical rates: a historical/philosophical foundation for the teaching of chemical equilibrium, Science & Education, 18, 2009, 1203-1251. (b) F. Marchetti, R. Pettinari, C. Pettinari, A. Cingolani, C. Di Nicola, Sviluppo storico del concetto di equilibrio chimico, CnS, XXXI, 1, 2009, 18-29.
[3] A. Giordan, Les nouveaux modèles pour apprendre: dépasser le construttivisme?, Perspectives, 25, 1995, 109-127.
[4] (a) E. Roletto, La scuola dell'apprendimento, Erickson, 2005, Trento. (b) D. Antiseri, Didattica delle scienze, Armando Editore, 2000, Roma.

DID-OR-05 Considerazioni generali sulle strutture per la formazione iniziale degli insegnanti

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In tutti i Paesi europei ci si è mossi, negli ultimi decenni, per una progressiva "universitarizzazione" della formazione degli insegnanti: non più *Teachers colleges* in una ottica prevalentemente addestrativa, ma scientificità: scientificità, peraltro, riferita alle Scienze dell'educazione oltre che alle discipline di insegnamento. Al tempo stesso, si sono rilevati i rischi di una accademizzazione della formazione: da ciò l'accento sulla *partnership* università-scuola.
L'impostazione dell'ultimo Regolamento ministeriale è fortemente dissonante rispetto a queste tendenze relativamente a due aspetti essenziali: la sostituzione di una logica "di Facoltà" (ora, di Dipartimento?) in luogo di una "di Ateneo", e la restrizione dei rapporti università-scuola al solo anno di Tirocinio Formativo Assistito.
Occorre che gli Atenei come tali (e non solo i volenterosi docenti impegnati nella ricerca didattica) si facciano carico di questa problematica. In caso contrario, la prospettiva di una sostanziale esclusione dell'università dai processi di formazione (in servizio, oltre che iniziale) degli insegnanti è molto concreto.

DID-OR-06 Le nuove lauree magistrali per l'insegnamento: il ruolo degli insegnanti in servizio e la DD-SCI

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Nelle strutture formative che hanno preceduto l'introduzione delle Lauree Magistrali per la formazione degli insegnanti di scuola secondaria (le Scuole di Specializzazione all'insegnamento secondario) gli insegnanti di scuola media e di scuola secondaria superiore hanno dato un contributo fondamentale. Questo contributo non si è limitato ai ruoli che venivano loro assegnati dalla normativa (azione di tutoraggio e azione di accoglienza nella classi nel tirocinio diretto). In molte sedi universitarie, infatti, per fruire più compiutamente delle competenze acquisite "in servizio", sono stati affidati loro i corsi di didattica e di laboratorio di didattica.

Facendo riferimento, per esempio, all'abilitazione per la classe di insegnamento 13/A presso la SSIS di Genova, ciascun insegnamento di didattica attivato (di Chimica Generale, di Chimica Analitica, di Chimica Fisica, di Chimica Organica) è stato affidato a due docenti, un universitario e un insegnante di scuola secondaria superiore esperto. Ciò ha consentito di evitare che questi insegnamenti riproducessero quelli dei tradizionali corsi di laurea, favorendo una continua riflessione sui concetti trattati e permettendo ai docenti universitari di acquisire competenze aggiuntive.

La Divisione di Didattica conta tra i suoi soci insegnanti, numerosi docenti "esperti in formazione" che, anche in collaborazione con il MIUR (Piano ISS-Insegnare Scienze Sperimentali, Piano Nazionale Lauree Scientifiche (PLS), Formazione Neoassunti), hanno attivato e coordinato gruppi di ricerca didattica. Ciò ha favorito una continua riflessione critica nei confronti del loro ruolo professionale e sociale e ha consentito loro di acquisire la capacità di integrare gli apprendimenti disciplinari con competenze metodologico-didattico, di acquisire rigore nel perseguire gli obiettivi, di accrescere la consapevolezza che l'insegnamento è una ricerca.

Poiché la qualità dell'educazione dipende in primo luogo dalle caratteristiche dell'insegnante, questi docenti rappresentano una risorsa indispensabile nei nuovi percorsi per la formazione iniziale degli insegnanti, il loro ruolo sarà argomento della riflessione.

DID-OR-07 IL DISASTRO DI BHOPAL: ANALISI DEL CONTESTO E DELLE CAUSE E COMUNICAZIONE DI EMERGENZA NELLA STAMPA QUOTIDIANA ITALIANA

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L'incidente di Bhopal è stato oggetto di studi approfonditi su riviste di notevole spessore scientifico[3,4], nelle quali si trovano dettagli imprescindibili per l'analisi dei molti aspetti ancora controversi di carattere tecnico, ambientale, economico, sociale, legislativo e giurisprudenziale. L'approfondimento a livello pluri-disciplinare, ha il fine di comprendere tempi, cause ed effetti del disastro che ancora insistono su tutta l'area coinvolta. Nella definizione di uno scenario soddisfacente risulta necessaria la consultazione critica di alcune qualificate risorse presenti in Internet, quali i siti di Greenpeace, della Union Carbide5 e, per gli aspetti più generali, quelli dell'Enviromental Protection Agency (EPA) e del National Institute for Occupational Safety and Health (NIOSH)6.
Un secondo filone di ricerca è quello dell'informazione da parte della grande stampa nazionale. Esso è rivolto allo studio dei modi e dei tempi della comunicazione nei quotidiani: *La Stampa*, *La Stampa Sera* e *La Repubblica*, nella divulgazione di una situazione di grave emergenza.
Sotto questo secondo profilo si deve segnalare che, nonostante l'immane tragedia, il caso di Bhopal ebbe un effetto sull'opinione pubblica italiana quantitativamente limitato e a livello cronologico l'informazione fu di brevissimo momento, con una durata approssimativa di circa un mese. Ciò può essere spiegato da un effetto "distanza", assolutamente determinante, non soltanto dal punto di vista geografico. In realtà una percezione molto ridotta (ad esempio rispetto a quanto accaduto a Seveso), fu determinata più in profondità dalle grandi differenze sociali, religiose, culturali delle popolazioni coinvolte e, in una certa parte, da informazioni almeno inizialmente troppo frammentarie.
In sostanza si tratta degli effetti più rimarchevoli prodotti dai fenomeni peculiari di un'economia già globalizzata, caratterizzata da una decisa delocalizzazione

1 L. Rosnati, "Ambiente Considerazioni sul disastro di Bhopal", La Chimica e l'Industria 1985, **67**, 338; "Dalle altre riviste. Chimica Organica. Sintesi di isocianati senza impiego di fosgene"; S.Notargiovanni, "Chimica e Ambiente: Resoconto convegno FILCEA-CGIL 21/02/1986", La Chimica e l'Industria 1986, **68**, N.4, 45; M. Cerri, C. Tribuno, "Problematiche associate al controllo e ispezione degli impianti chimici", La Chimica e l'Industria 1986, **68**, N.5, 60; "Dall'industria chimica. Il colosso rigenerato. Union Carbide", 1986, **68**, N.6, 18.

2 K.S. Jayaraman, "Pesticide plant leak wreaks disaster in India", *Nature*, 1984, **312**, 581; K.S. Jayaraman, "Bhopal disaster: Technical inquiry under way", *Nature*, 1985, **313**, 89; Stephen Budiansky, "Bhopal aftermath: Legal complications mount", *Nature*, 1985, **314**, 663; Anna Lubinska, "EEC plans risk management", *Nature*, 1985, **316**, 570; David L. Sills, "Hazards beyond number", *Nature*, 1985, **317**, 117; K. S. Jayaraman, "Bhopal disaster: India blames Union Carbide", 1986, **319**, 7.

3 http://www.greenpeace.it/bhopal/bhopal.php; http://www.bhopal.com/

4 http://www.epa.gov/; http://www.cdc.gov/niosh/

industriale in paesi subalterni e meno sviluppati, nei quali i margini di controllo ambientale e sociale risultano spesso quasi assenti.
Per ricomporre il difficile mosaico della comunicazione dei quotidiani saranno esaminati gli aspetti quantitativi inerenti numero e collocazione degli articoli e la loro evoluzione nel tempo, procedendo successivamente all'analisi critica qualitativa delle informazioni fornite ai lettori, ponendo come parametri di riferimento quanto venne pubblicato nelle riviste specialistiche.
La complessità e la multidisciplinarità dello studio, al di là delle difficoltà intrinseche, può rappresentare una risorsa di notevole valenza didattica, in grado di consentire la progettazione di uno stimolante percorso di ricerca da realizzare in un corso di scuola secondaria superiore.
In tale ipotesi, sarebbe una valida prospettiva quella di proporre uno sviluppo aperto per filoni tematici da interconnettere sotto la guida dei differenti docenti. I vari spezzoni realizzati con una serie di presentazioni multimediali e articoli monografici nella fase finale dovrebbero essere raccordati in un ipertesto. Esso potrebbe infine essere inserito nel sito della scuola e costituire un qualificante progetto complessivo.

DID-OR-08 Insegnare/Apprendere chimica nella scuola secondaria di I grado: una proposta di conoscenze e competenze di un laureato nella classe LM/95

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Anche se l'insegnamento della chimica, come disciplina separata, non esiste nella Scuola secondaria di I grado, molti contenuti chimici sono particolarmente funzionali allo sviluppo di abilità trasversali e, se opportunamente presi in considerazione nell'attività didattica, favoriscono la formazione di una mentalità scientifica nei ragazzi fino al 15° anno di età.
Considerata la difficoltà dei giovani di apprendere contemporaneamente gli aspetti macroscopico, microscopico e simbolico propri della disciplina chimica [1] si propone un elenco di argomenti/concetti che si ritiene possa rappresentare il bagaglio di conoscenze della disciplina al termine della Scuola secondaria di I grado e che, secondo noi, permette ad insegnanti ed allievi di affrontare e discutere fenomeni osservandoli anche con gli occhiali del chimico.
Anche se non sono affrontati problemi specifici di trasposizione didattica si propone un esempio semplice di lavoro trans disciplinare che dai concetti di massa conduca alla gestione del concetto di densità come rapporto e alla sua misura.
Infine si propongono dieci argomenti, spunti per altrettanti percorsi didattici e una sequenza logica di concetti che, partendo dalla descrizione della materia e dei modi in cui si può presentare, si propone di riflettere sulle sue molteplici trasformazioni (focalizzando, in particolare, l'attenzione sui cambiamenti di stato di aggregazione, sui processi di dissoluzione, fino alle trasformazioni di sostanze in altre sostanze)

[1] Alex H.Johnstone, *Chemistry Education: Research And Practice In Europe*, **2000**, Vol. 1, No. 1, 9

DID-OR-09 DIDATTICA LABORATORIALE: costruire conoscenze per sviluppare abilità nell'ottica delle competenze

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PREMESSA

Sviluppare maggiori competenze scientifiche negli studenti è una delle priorità che il nostro Paese,
assieme agli altri della UE, ha assunto con le decisioni di Lisbona 2000. Lo sviluppo culturale dei ragazzi
pone prioritariamente l'accento su conoscenze, competenze, atteggiamenti, disponibilità,
motivazioni, che noi insegnanti "mediatori" dovremmo essere in grado di mobilitare e quindi di
tradurre in pratiche efficaci.
L'esperienza pluriennale di docente TUTOR in percorsi di Formazione Scientifica in ricerca- azione (Progetto SET - Scienza e Tecnologia; PIANO ISS - Insegnare Scienze Sperimentali; e Formazione Nazionale PON E2) rivolti a docenti della scuola primaria, della sec. di 1°grado e biennio della sec. di 2°grado, ha maturato, in contesti formativi e costruttivi," processi" che portano al bisogno di rafforzare ed implementare le iniziative di sperimentazione con l'applicazione del modello disciplinare ISS e Formazione Nazionale, nella pratica curriculare.

I PERCORSI FORMATIVI

La **progettazione condivisa**, le esperienze e la metariflessione sui percorsi e processi attivati, rafforzano l'insegnamento delle scienze integrate nella pratica curriculare: come si legano le esperienze, quale la scansione verticale dei tempi e dei concetti, nello specifico nel nucleo tematico "TRASFORMAZIONI"
Costruire il **modello particellare della materia, in una dimensione ludica e creativa,** porta sicuramente al successo in un ambito disciplinare di non facile comprensione : dall'esperimento –protocollo chiuso, a volte banalizzato come "ricetta", **ad un processo di ricerca-scoperta** mediante **investigazioni:il laboratorio come "spazio mentale",** ogni fase dell'esperimento è sottoposta ad analisi critica; cio'aumenta l'interesse ed il rendimento dei ragazzi , stimola la motivazione di noi docenti.
Puntare sugli apprendimenti per processi e costruire competenze:

- Conoscenza dei materiali e delle loro proprietà, durante e dopo le trasformazioni fisiche e chimiche; applicare quanto appreso a contesti e problemi reali, riguardanti la conservazione ambientale , la qualità dell'aria e dell'acqua.
- Correlare le trasformazioni fisiche e chimiche dei materiali alla natura delle particelle costituenti. Come riconoscere che i materiali sono formati da particelle microscopiche separate da spazi vuoti. e comprendere che le

particelle microscopiche, che compongono solidi, liquidi e gas, hanno massa e sono in costante moto.

- Caratterizzare il comportamento acido/basico ed il comportamento degli indicatori ricavati da sostanze molto comuni: fagioli neri, radicchio, fiori rossi e di laboratorio es. il BTB

Porre domande, investigare e interpretare le evidenze raccolte: **metodologia dell'investigazione, come modo di pensare e come modo di lavorare.** Per ciascuna investigazione, si attivano opportuni spazi di riflessione. "Cercate di ripensare mentalmente a quanto si è investigato": attenzione a quanto si sta facendo con le proprie mani e con la propria mente, memorizzare le abilità manipolative e le strategie risolutive, immaginare cosa accade a livello atomico – molecolare per avviare alla comprensione dei concetti collegati all'esperimento, riflettere sulle possibili applicazioni di quanto appreso durante l'investigazione.

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(Autori abstracts Convegni YORK- UK e PISA : S. D'Oronzo, M.A. Guarnieri, M.R. Tancredi).

DID-OR-10 Alcune riflessioni relative all'insegnamento di Didattica della Chimica

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La didattica di una certa disciplina analizza la complessa problematica che entra in gioco considerando l'insegnamento di quella disciplina in relazione al suo apprendimento. L'aspetto centrale di questo studio consiste pertanto nell'esaminare i contenuti inerenti la disciplina non per se stessi ma in relazione a colui o a coloro che debbono apprenderli, per verificare se sono adatti a quegli specifici interlocutori. Occorre stabilire quali sono i requisiti che i contenuti richiedono per essere appresi in maniera significativa e verificare se questi requisiti sono posseduti da chi deve apprenderli. In questa riflessione entra in gioco anche il livello a cui i contenuti vengono trasferiti e la loro significatività in termini formativi per gli allievi.
Poiché un insegnante non è solo un didatta disciplinare ma un educatore e non si può ragionevolmente pensare che il suo ruolo sia semplicemente quello di trasferire contenuti, il suo compito è molto più ampio e complesso, soprattutto nella scuola dell'obbligo dove, prima di tutto, la riflessione riguarderà il valore formativo dei contenuti da proporre agli alunni. L'insegnante dovrà poi convincersi che il suo atteggiamento nei confronti dell'insegnamento e dell'apprendimento, il suo modo di lavorare e di far lavorare influenza in maniera rilevante gli atteggiamenti dei suoi alunni.
Per favorire un atteggiamento riflessivo dell'insegnante, in modo che acquisisca "l'abitudine" a porsi come un vero e proprio ricercatore, sempre attento all'andamento dei processi che innesca e porta avanti con gli studenti, è importante fare riferimento a contesti concreti, stimolandolo alla messa a punto di percorsi didattici e ad una loro attenta analisi critica e lavorare in modo che il futuro insegnante impari a cogliere gli ostacoli cognitivi presenti nei contenuti che propone e quelli linguistici connessi alla descrizione e interpretazione di ciò che gli alunni sono indotti ad osservare. L'insegnante dovrà perciò anche acquisire la consapevolezza di poter contribuire all'educazione linguistica dei propri alunni facendoli lavorare in maniera sistematica attraverso lo scritto.
In quest'ottica, il ruolo del laboratorio riveste particolare importanza nei processi di insegnamento-apprendimento di ambito chimico

DID-OR-11 Lauree Magistrali per l'Insegnamento: nuove prospettive per la Chimica e per i Chimici

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L'istituzione delle nuove Lauree Magistrali per l'insegnamento non solo pone i Chimici di fronte a nuovi impegni didattici e opportunità, ma, più sostanzialmente, cambia il ruolo della Chimica e il suo inserimento culturale in ambiti anche trasversali alla Chimica stessa.
Pur nella incompletezza delle direttive ministeriali (mancano ancora i riferimenti curriculari per buona parte delle Lauree Magistrali per le classi di concorso della scuola secondaria di secondo grado), pure si intravedono notevoli cambiamenti nell'inquadramento culturale delle diverse discipline.
Nelle competenze richieste agli studenti e nella articolazione dei curricula si coglie finalmente un'ispirazione unitaria dell'insegnamento delle scienze, che restituisce alla chimica un ruolo importante nella formazione scientifica generale degli studenti e degli insegnanti di vario ordine e grado.
Valgano per tutti, gli esempi delle nuove lauree magistrali per l'insegnamento di Matematica e Scienze (LM95) e di Tecnologie (LM96) per il primo ciclo della scuola secondaria (ma anche i futuri docenti della primaria dovranno avere conoscenza di elementi di chimica organica e inorganica). I nuovi laureati LM95 dovranno avere tra le competenze elencate, una solida preparazione di base nelle discipline chimiche, unita ad una buona padronanza della pratica di laboratorio. Questo si traduce in almeno 6 CFU di Chimica nel curriculum LM, uniti ai 6 CFU chimici necessari per l'accesso alla LM (in nessun corso di laurea triennale in Matematica attualmente si insegna Chimica e l'accesso alla LM è per legge senza debiti formativi).
Per la LM96, anche qui non solo si richiede una solida preparazione di base nelle discipline chimiche, ma anche di saper relazionare sviluppo tecnologico e impatto ambientale. Significativamente, tutti i raggruppamenti disciplinari chimici sono riconosciuti per l'accesso alla LM.
Tutto questo mette la Chimica e i Chimici in movimento e richiederà l'acquisizione e la messa a punto di nuove metodiche di insegnamento, anche in ambiti tradizionalmente poco permeabili alle tematiche chimiche.

DID-OR-12 Le competenze scientifiche e l'orientamento degli studenti nel passaggio dal primo al secondo ciclo.

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I cambiamenti in atto nella Scuola– in particolar modo i Regolamenti di riordino dell'Istruzione secondaria superiore – e il divario ancora particolarmente ampio tra i risultati degli apprendimenti in scienze degli studenti italiani nelle rilevazioni internazionali evidenziano l'esigenza di un attento ripensamento metodologico della mediazione didattica e di una rinnovata attenzione alle attività per l'orientamento scolastico degli studenti soprattutto nel passaggio dal primo al secondo ciclo (1, 2).

Un orientamento che, nella quotidianità scolastica, assume significati molteplici avendo come "obiettivo prioritario" la maturazione dello studente " in termini di autonomia e responsabilità ai fini dell'acquisizione delle competenze chiave per l'esercizio della cittadinanza attiva" e che può risultare efficace solo "a partire da una collaborazione rafforzata tra scuole del primo e del secondo ciclo...(2)".

Ciò richiede interventi non occasionali e nuovi modelli di collaborazione interscolastica dinamicamente inseriti nei diversi contesti e rispondenti ai bisogni specifici (3) secondo "logiche di rete" incentrate sulla dimensione di raccordo verticale tra primo e secondo ciclo di istruzione.

Inoltre, per sostenere l'orientamento degli studenti alle discipline scientifiche, occorre fare riferimento ad un'impostazione metodologica volta a favorire le scelte autonome degli alunni.

Occorre indirizzare le scelte metodologiche avvalendosi dele logiche della "didattica orientativa" per favorire lo sviluppo della capacità del soggetto di rapportarsi con "successo" ai diversi contesti.

La presentazione orale riguarderà l'illustrazione degli aspetti descritti con esempi concreti di intervento.

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4) Linee guida sull'orientamento (C.M. n.43 del 2009)

*** dall'a.s. 2008-09 è docente comandata per l'autonomia scolastica presso la Direzione Generale dell'USR Puglia**

DID-OR-13 EP*Magazine: una risorsa educativa*?

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EP*Magazine* (European Pupils *Magazine*) è una rivista educativo-scientifica quadrimestrale pubblicata da nove anni in Europa da un gruppo di scuole secondarie superiori e Università del Vecchio Continente. Al momento, la Redazione è formata da Romeni, Turchi, Greci, Italiani, Bulgari. Le collaborazioni e le contribuzioni - aperte senza limiti - provengono anche da diversi altri Paesi europei.

Uno dei principali *target* della Rivista è la **creazione di una banca dati di Storia della Scienza e della Tecnologia** scritta da studenti per altri studenti, allo scopo di motivare - così - gli universitari e i liceali europei a imparare e sviluppare le **tecniche della ricerca compilativa** e a **scrivere i risultati** in maniera essenziale e personale, ma corretta.

Un altro obiettivo educativo è quello di ***Orientare e educare gli studenti europei attraverso la Storia della Scienza e della Tecnologia***, di cui la ***Chimica costituisce uno dei maggiori capisaldi***, e spingerli a imparare ed utilizzare al meglio (in maniera sempre più *professionale* e *professionalizzante*) le nuove **tecnologie informatiche** utili per il loro futuro professionale: dai **sistemi di comunicazione** e video comunicazione ai **software per l'editoria scientifica,** ai sistemi per **scoprire il plagio**, al significato dei **referee**, per arrivare alla **preparazione di comunicazioni scientifiche in lingua inglese** e alla loro esposizione nei convegni scientifici in un diretto e continuo **confronto con docenti e altri pari**.

Per questo ultimo obiettivo il gruppo **EP*Magazine*** normalmente organizza due Convegni internazionali ogni anno.

In **conclusione**, si propone ai docenti di **Chimica** di incoraggiare e responsabilizzare i propri studenti a:

1. produrre materiale scientifico divulgativo di **Storia della Chimica** da pubblicare sulla Rivista come risultato di personali ricerche;
2. organizzare un piccolo gruppo redazionale per produrre materialmente il periodico;
3. partecipare ai convegni europei di **EP*Magazine***;
4. utilizzare la banca dati della Rivista sia per scopi didattici, che ricreativi.

Negli ultimi incontri, il Comitato di Redazione ha già preso in seria considerazione la possibilità di aggiungere una Sezione speciale dedicata alla **Storia della Chimica**, così come quella già esistente di Tecnologia per le Energie Rinnovabili, proposta dai due politecnici rumeni del Comitato di Redazione.

DID-PO-01 Rappresentazione di modelli microscopici in diversi livelli di istruzione

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Le caratteristiche di un materiale, percepibili tramite i sensi, sono il risultato macroscopico della somma delle proprietà microscopiche del materiale stesso. È importante, perciò, sapere come appaia la materia a livello atomico o molecolare. Questa operazione è tutt'altro che semplice poiché presenta differenti ostacoli cognitivi che si protraggono durante i diversi livelli dell'istruzione. Nelle scuole secondarie inferiori, gli studenti non sono ancora pienamente capaci di utilizzare il POF – Pensiero Operativo Formale. Le idee, giuste o sbagliate che siano, permettono agli studenti di ottenere un corretto equilibrio tra assimilazione e approssimazione. Essi possono comprendere gli effetti di alcuni fenomeni, effettuare attività di misurazione, proporre operazioni mentali volte alla modellizzazione della realtà non percepibile. Questo processo evolve fino al pieno possesso delle facoltà astrattive e logico-deduttive. Ciò rende possibile la modificazione delle rappresentazioni mentali in base all'analisi delle proprietà della realtà percepita.
Erronee conoscenze pregresse, acquisite durante il percorso formativo, possono generare misconcezioni che, "cristallizzando", potrebbero compromettere il futuro apprendimento: l'identificazione delle loro diverse tipologie consentirebbe un efficace intervento preventivo.
Questo lavoro intende valutare l'evoluzione dell'apprendimento riguardo la *modellizzazione microscopica della materia* nell'ambito della scuola secondaria e dell'università. A circa 250 studenti è stato chiesto di rappresentare, entro appositi riquadri, come appare una sostanza a livello microscopico nei tre stati fisici della materia: solido, liquido e gassoso. Il test è anonimo ed il tempo a disposizione per rispondere è stato di trenta minuti. Obiettivo della ricerca è rilevare l'eventuale presenza d'ostacoli cognitivi e definirne la loro tipologia nelle differenti fasi dello sviluppo degli studenti. Dalle prime analisi si evidenzia la presenza di misconcezioni in ognuno dei tre livelli considerati; è in atto lo studio delle tipologie d'errore e delle conseguenti proposte didattiche d'intervento.

DID-PO-02 PLS laboratories: a bridge between training and job

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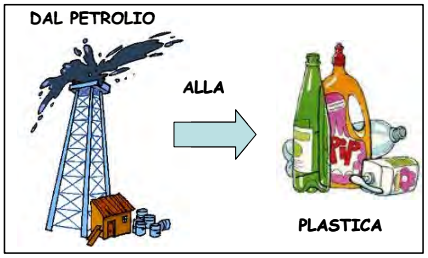
The Scientific Degrees Plan (PLS)-Liguria Region-Chemistry Section, addressed to students of the last year of high schools, aimed to show them some different jobs that call for the degree in chemistry and to guide them in carrying out relevant laboratory activities. For this purpose, important Ligurian Companies (Porto Petroli SpA and Fratelli Parodi Srl), the Forensic Department of Genoa and the Aquarium of Genoa joined the Department of Chemistry and Industrial Chemistry in order to organize suitable 'packages' consisting in seminars, visits under the guide of experts and relevant laboratory activities.

Package 1: a collaboration with Porto Petroli SpA



Porto Petroli is an important company, located in Genoa, dedicated to collect petroleum from ships and to address it to refineries. Students visited the harbor under the guide of the person responsible for security, followed a lesson about petroleum and plastic, its most important derivative, and finally carried out laboratory activities about synthesis of plastics and properties of special materials as expanded polymers and super-absorbent polymers.

Package 2: a collaboration with Aquarium of Genoa

Aquarium of Genoa offered a tour of the part that is usually not allowed to visitors in order to show students the specific work involving chemists and biologists. Then, laboratory activities allowed students to face topical problems such as acidification of seawater due to CO_2 emissions and to analyze and purify seawater samples with modern methodologies.

[1] Package 3: a collaboration with the Forensic Department of Genoa

Chemists of the Forensic Department told their work during a successful seminar in the Aula Magna of the Department of Chemistry and Industrial Chemistry. The laboratory that followed the seminar allowed students to test some of the most famous methodologies of forensic chemistry and, ve ry important, to correct wrong information coming from mass media (i.e. popular movies).

Package 4: a collaboration with Fratelli Parodi Srl

The company, expert in the production of several products, showed its production implants and described its activities, in particular the extraction and refining of vegetable oils for cosmetic and pharmaceutical sectors. The laboratory activities were carried out at the Department of Chemistry and Industrial Chemistry and students become enthusiastic by producing cosmetics like soap and hand creams.

DID-PO-03 Un esempio di approccio laboratoriale alla chimica in un contesto di scuola secondaria di 1° grado: "I segreti del sale"

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La ricerca didattica, che rientra nel macrotema delle "trasformazioni" è stata pensata come curricolo trasversale, per generare un raccordo significativo con i diversi argomenti proposti in due classi 2^{e} di scuola s. di 1° grado, in parallelo, allo scopo di aiutare gli alunni/e a superare la difficoltà di approccio alla Chimica. L'esperienza, progettata in modo condiviso, ha permesso a noi docenti una riflessione sulle scelte metodologico didattiche e sulla validità del processo. La ricerca presenta un duplice "contesto di senso", [1] uno legato al curricolo e l'altro al territorio (presenza in Puglia delle Saline di Margherita di Savoia). La finalità è quella di abituare gli alunni/e all'osservazione e descrizione di fenomeni naturali, a formularne spiegazioni scientifiche condivise, stimolando in loro la modellizzazione di concetti e processi.

Gli alunni/e hanno imparato a distinguere le trasformazioni chimiche da quelle fisiche, [2] a riconoscere una nomenclatura essenziale ed hanno compreso alcune tecniche implicate nel processo di estrazione del sale dalle Saline. [1] La metodologia è quella laboratoriale, che, partendo da un braistorming, ha reso le attività significative per gli alunni/e, in quanto progettate insieme e vissute come opportunità per rispondere a curiosità ed interessi endogeni alle classi. Ciò ha consentito agli alunni/e di effettuare una ricerca a maglie larghe, che li ha condotti a diverse scoperte quale quella dell'adattamento dei viventi ad ambienti estremi, dell'utilità dei sali per la salute dell'uomo, del legame del sale con le realtà socio – economiche, storico – geografiche e antropologiche. [3] Si è fatto ricorso ad una sperimentazione scientifica semplice e facilmente riproducibile dagli alunni/e, di reperimento d' informazioni sul web, di apprendimento in contesti non formali (visita guidata alle Saline). [3] Le diverse attività ed esperienze hanno utilizzato gli organizzatori cognitivi sistema, complessità, trasformazione, puntando a far acquisire i concetti di miscugli omogenei ed eterogenei, [4] composti e reazioni, energia, adattamento dei viventi. La valutazione dell'intero processo e delle competenze acquisite si è servita di diari di bordo e relazioni, rilevazione di comportamenti osservabili in laboratorio e durante le visite guidate, di un test semistrutturato.

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DID-PO-04 Un Museo di Storia Naturale, un paese nato con la Chimica e le nuove sfide culturali

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Il Museo di Storia Naturale del Comune di Rosignano Marittimo (LI) nasce quasi per gioco nel 1966 quando, nei locali della Biblioteca Comunale, in Piazza Risorgimento a Rosignano Solvay, vennero esposte le collezioni degli insetti raccolti dai ragazzi delle scuole durante un soggiorno alla colonia montana di Gavinana (PT).[1]
Il Museo, tenuto in piedi da un'associazioni di volontari appassionati di scienze, naturalisti, ricercatori ed educatori, con l'appoggio finanziario del Comune di Rosignano Marittimo, ha sempre avuto una missione educativa, grazie al rapporto diretto con le scuole primarie e secondarie del territorio comunale.
Da alcuni anni, all'organizzazione di laboratori per bambini e di una mostra annuale dedicata a diversi aspetti delle scienze naturali, si sono aggiunte altre attività, come cicli di conferenze e presentazioni di libri, che stanno spostando sia il target sia la missione del Museo. Inoltre, la presenza sul territorio di una grande industria chimica, lo Stabilimento Solvay, e le conseguenti problematiche ambientali ed economiche ad essa connesse, hanno spesso influito sulla scelta delle tematiche delle varie attività.
Per tutto l'arco del 2011, Anno Internazionale della Chimica, il museo ha organizzato conferenze, mostre e incontri dedicati alla Storia della Chimica, al rapporto tra Chimica e Società e all'Immagine della Chimica con una positiva partecipazione della cittadinanza.
In questa presentazione intendiamo analizzare il ruolo del museo scientifico nel particolare contesto di Rosignano Solvay. Sulla base delle esperienze degli ultimi anni, che verranno brevemente descritte, vorremmo contribuire a rispondere ad alcuni quesiti che riguardano il ruolo del museo scientifico nella nascita di una nuova cultura scientifica e di una maggiore consapevolezza della cittadinanza su questioni che riguardano il rapporto tra la Chimica e la Società.

[1] V. Domenici, A. Lenzi, *La Chimica nella Scuola*, Vol. II, aprile-maggio 2011, p. 88-91.

DID-PO-05 Electrolysis, Internet and CLIL

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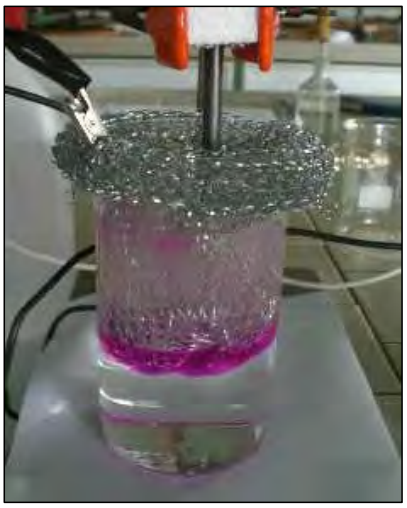
Electrochemical phenomenon are usually presented to the students since the primary school with examples taken from everyday life. Despite this early familiarity with redox reactions, most young people are in trouble when they're asked to apply theoretical principles of electrochemistry to concrete situations.
The aim of this work is to improve the observation ability and deductive reasoning skills of the pupils of a third secondary school.
This teaching proposal consists of a series of experiments of electrolysis in aqueous solution[7] by which the students internalize the concept of standard potential[8] and are able to make use of it to predict which reaction will occur among the possible ones.
The pupil is led to solve problems more and more complex up to introduce the concept of overvoltage[9].
The inquire-based learning approach is adopted and the effectiveness of the teaching unit is enhanced by the choice of CLIL (Content and Language Integrated Learning).



This project starts with the vision and the listening of a video from You Tube[10] concerning water electrolysis.
Most pupils believe that the Internet is a truth worthy source of information and that everything appears in the web is true.
By the first activity the students discover that the video is manipulated because it shows events which don't occur really[11].
The connection of electrochemistry with industrial technologies is another aspect of this teaching sequence. This section is a simulation of chloralkali[12]

7 Duranti "Problemi di sovratensione nell'elettrolisi di alcune soluzioni saline" CnS- La Chimica nella Scuola, 2006, **28**, 115
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10 http://www.youtube.com/watch?v=OTEX38bQ-2w "Hydrogen and oxygen from water"
11 Duranti: "Why does this happen?", Science on Stage Festival 16 - 19 April 2011, Copenhagen Denmark, Festival project catalogue, 80
12 http://www.minerva.unito.it/chimica&industria/dizionario/Supplementi01/Cloro.htm

industrial process that yields a solution of NaOH at 10% . As the electrolytic process proceeds the so called side reactions begin to take place with the consequence of lowering the pH of the solution. This phenomenon is simulated by a simple and low-cost apparatus which allows the pupils to observe the acidification of the solution by the change of colour of the phenolphthalein from.
Another side reaction is the consumption of the graphite electrode, a well known industrial problem.

DID-PO-06 Chem Quiz

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Since 2004, the Faculty of Science of University of Rome "Tor Vergata" organizes "Scienza Orienta", an one week event, dedicated to the guidance of High School students attending the last year. During this week, the Faculty organizes many lectures and teaching conferences proposed by each department of the Science Faculty. The target of this event is to attract young students to the field of science. In occasion of "The International Year of Chemistry -2011" the Chemistry Department of "Tor Vergata" University, in collaboration with L.U.D.I.S srl, has decided to test new strategies for science divulgation in order to maximize the involvement of people taking part to the 2011 edition of "ScienzaOrienta" (February 7-11 2011).
Two classrooms of different schools, took part in a real quiz challenging for the victory through chemistry experiments and scientific questions. The same high school students performed the experiments helped by the question masters (PhD Student graduated in chemistry). Every question has been discussed and explained alternating "ludic" moments to more didactic phases.
This scientific show lasted 75 minutes and has been performed inside the University.
Acids and basis, heat and temperature, combustion reactions, were some of the themes discussed during this quiz.
At the end of this event the winner classroom received a science divulgation book.

This event was funded by Ministero dell'Istruzione , dell'Università e della Ricerca; ex art.4 legge 6/2000.

DID-PO-07 Proposta di un percorso laboratoriale trasversale sulla chimica degli alimenti.

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L'alimentazione è un bisogno essenziale, fornisce al nostro corpo l'energia e i "mattoni" essenziali per la nostra sopravvivenza. L'alimentazione è però anche una componente importante della nostra cultura, del nostro modo di socializzare ed un fattore determinante della nostra salute fisica e psichica. Mangiare bene ci fa sentire meglio e ci fa vivere in modo migliore.

Ognuno di noi ha le proprie abitudini alimentari e segue una sua dieta ogni giorno. Le attuali conoscenze scientifiche evidenziano che non è l'alimentazione in se a far male, ma sono gli errori dietetici che possiamo compiere a determinare l'insorgenza di numerose patologie. Purtroppo conosciamo tutti i danni prodotti dalla celebrazione del culto del "magro è bello": anoressia, bulimia e diete prive di senso che generano disfunzioni e malattie.

Nonostante l'ampia varietà degli alimenti di cui disponiamo e delle tante maniere per realizzare una dieta sana ed equilibrata, moltissimi sono gli errori nutrizionali presenti nella dieta dei più, alcuni dovuti al "palato", altri dovuti alla mancanza di conoscenza. Spesso mangiamo cose che ci fanno male senza saperlo perché non sappiamo esattamente cosa stiamo mangiando.

Riguardo al palato c'è poco da fare, già gli antichi romani dicevano "*De gustibus non disputandum est"*. Per quanto riguarda la conoscenza invece possiamo fare tanto ed in questo la chimica può e deve dare un contributo importante.

In questo contributo presentiamo un percorso laboratoriale che è stato sviluppato e realizzato in maniera diversa per gli studenti degli ultimi anni della scuola primaria e della scuola secondaria di I e II grado con la finalità di sviluppare conoscenze in ambito alimentare. Tutto il percorso è stato progettato e realizzato in modo tale da sviluppare la capacità degli studenti di avere cura del proprio corpo, effettuando scelte adeguate di comportamenti e di abitudini alimentari, e di porsi in maniera critica verso i messaggi mediatici grazie ad una buona conoscenza di base degli alimenti.

In aggiunta a tali finalità, peculiari del percorso svolto sull'alimentazione, si è anche cercato di promuovere lo sviluppo di capacità operative, progettuali e manuali in contesti di esperienza-conoscenza per un approccio scientifico ai fenomeni.

DID-PO-08 A PLS experiment: the cis-trans isomerization of methyl orange revealed

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The time evolution of chemical processes is rarely presented to students of the secondary schools, despite the importance of kinetics to determine most of the real behavior of chemical systems. Here we propose a simple flash-photolysis experiment that can be realized with home-made equipment. A standard spectrophotometer was modified to insert into the sample compartment a photographic flash, oriented perpendicularly to the measuring beam.
An alkaline solution of methyl orange, showing an approximate absorption A≈1 at λ=460 nm, is repeatedly excited by the intense white light pulse of the flash. At room temperature only the trans conformer of methyl orange is significantly populated. The flash causes almost instantaneously a significant population of cis conformers, leading to a sudden decrease of the absorption of the methyl orange solution at 460nm, as the molar extinction coefficient of the cis form at this wavelength is significantly lower than that of the trans conformer. After that, the cis form slowly returns to the trans conformer. The cis→trans transition is completed in a few seconds (each kinetic run lasts 12 seconds in our procedure, taking a point every 0.1 seconds), following a simple first order kinetics.
The measurements of the cis→trans transition rate constants at different temperatures (between 25°C and 55°C) allowed for the determination of the activation energy of the cis→trans transition (E_a=60 kJ·mol^{-1}), averaged on the results of different groups of students.

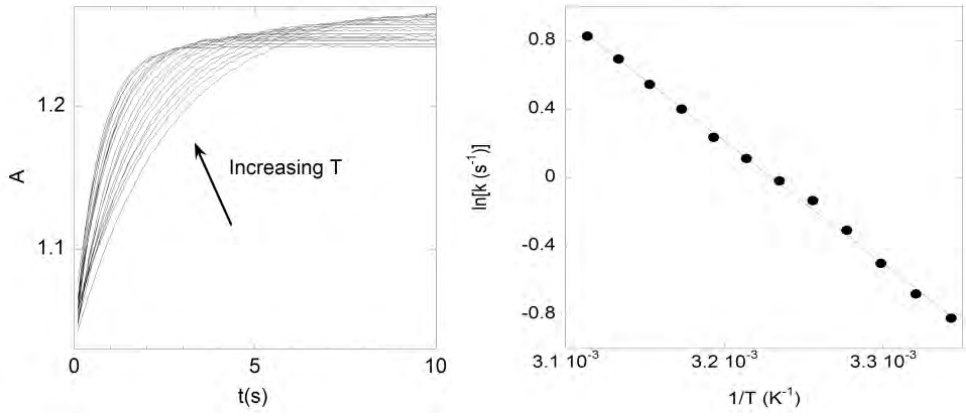

Figure 1. Arrhenius plot of the rate constants obtained from the experimental curves reported in the left panel.

DID-PO-09 La Materia si trasforma

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Dopo aver seguito il corso di formazione docenti PON E2 – Educazione Scientifica, ho sperimentato, in classe con i miei alunni, il percorso didattico riguardante le Trasformazioni della materia.
Partendo dal presupposto che la scienza è soprattutto un metodo di scoperta, attraverso le varie esperienze ho stimolato i ragazzi a cercare una risposta a interrogativi concreti, mediante l'osservazione e la discussione di fenomeni naturali. Tutto ciò ha portato ad una conoscenza delle proprietà fisiche della materia, delle trasformazioni che possono subire in natura le diverse sostanze e alla scoperta quindi che i materiali non sono continui, ma formati da particelle microscopiche.
Le sperimentazioni sono state condotte nella mia classe prima, facendo lavorare i ragazzi in gruppo e assegnando ad ogni alunno compiti e responsabilità diverse a seconda della situazione problematica presa in esame.
L'osservazione di un'immagine del ciclo dell'acqua in natura ha rappresentato l'organizzatore cognitivo, legato ad un contesto di senso, che ha portato a simulare il ciclo dell'acqua in laboratorio mediante la costruzione di un modello: un microambiente costruito utilizzando un barattolo di vetro con chiusura ermetica.
In una seconda fase i ragazzi hanno verificato, quali sono le temperature alle quali l'acqua si trasforma e cambia il suo stato fisico. Utilizzando del ghiaccio, un becher, un termometro, una piastra riscaldante, i ragazzi hanno misurato le diverse temperature dell'acqua nei vari passaggi di stato raccogliendo i dati in una tabella e costruendo infine un grafico su carta millimetrata.
In seguito sono stati verificati quali sono i fattori che influenzano l'evaporazione dell'acqua in natura: mettendo la stessa quantità di acqua in quattro contenitori (due bicchieri uguali e due piatti uguali) e ponendo poi un bicchiere ed un piatto all'aria aperta e gli altri due contenitori all'interno dell'aula, gli alunni hanno scoperto che l'evaporazione dipende dalla temperatura e dalla superficie evaporante.
L'osservazione che il ghiaccio galleggia sull'acqua ha portato i ragazzi alla scoperta della densità, prima determinando quella dell'acqua allo stato liquido e del ghiaccio, poi quella di altre sostanze quali l'olio e l'alcol e quindi ad identificare materiali sconosciuti partendo dal calcolo della loro densità e consultando in seguito la Tavola Periodica degli elementi.
Infine, la costruzione di modelli macroscopici di materiali ha portato a rafforzare il concetto che la materia non è continua, ma è formata da particelle microscopiche.
Utilizzando la didattica laboratoriale e il metodo della ricerca-azione, gli alunni hanno costruito conoscenze e si sono resi attivi protagonisti delle esperienze che hanno vissuto. Tutto ciò è stato, infine, documentato mediante un diario di bordo.
Riferimenti bibliografici: G. Valitutti, M. Falasca.

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Elettrochimica

ELE-KN-01 Lithium Batteries: a look into the future

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Li-ion batteries today exceed at least by a factor of 2.5 any competing technology thanks to the high value of energy density, i.e. 150 $Whkg^{-1}$ and 650 Whl^{-1}. Due to their unique features, these batteries are the power sources of choice for the portable electronic market (including popular products such as cellular phones, lap-top computers, mp3s, etc) and are aggressively entering in the power tool equipment market and, in particular, in the emerging sustainable vehicle market. However, the present Li-ion batteries, although commercial realities, are not yet at such a technological level to meet the power requirements of efficient hybrid or electric vehicles. Reduction in cost, enhancement in safety and rate, and, especially improvement in energy density, are mandatory requirements. In this presentation, after a brief introduction on the basic characteristics of lithium-ion cells, the research currently in progress in our laboratory for upgrading their performance, are reviewed and discussed. It will be shown that the safety issue may be addressed by replacing the current, flammable liquid organic carbonate electrolyte solutions with more reliable polymer membranes, e.g., based on chemically stable polymer matrices and/or on not flammable ionic liquids. The cost of the battery may be reduced by moving from the common, expensive cathode and current collector materials to more affordable alternatives. The rate capability is strictly depending upon the morphology of the electrodes, as in fact demonstrated by few examples here illustrated. Finally, jumps in energy density may be achieved by totally renewing the battery chemistry. The most significant examples are provided by the lithium-sulfur and the lithium-air systems. Few preliminary results obtained on these “superbatteries” will be also presented.

Bruno Scrosati is Senior Professor at the University of Rome La Sapienza. He has been Visiting Professor at the University of Minnesota and at University of Pennsylvania, in the US. He received the title of Doctor in Science “honoris causa”,from the University of St. Andrews in Scotland and from the Chalmers University in Sweden. He was awarded by the Research Award from the Battery Division of the Electrochemical Society, by the XVI Edition of the Italgas Prize and by the “Volta” Medal of the European Section of the Electrochemical Society. He is European Editor of the “Journal of Power Sources” and member of the Editorial Boards of various international journals. Professor Scrosati is author of more than 450 scientific publications; 30 books and chapters in books and 18 patents. His H-factor is 43.

ELE-KN-02 Advanced Electrocatalysts for Intermediate Temperature PEM Fuel Cells

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Pt-alloy electrocatalysts have been investigated for operation in a polymer electrolyte membrane (PEM) fuel cell up to a temperature of 130 °C and at pressures up to 3 bar abs. [1, 2]. The aim was to evaluate their performance and resistance to degradation. Nanosized Pt and PtCo catalysts with crystallite size of about 3 nm were prepared by using a colloidal route. A suitable degree of alloying and a face-centered cubic (fcc) structure were obtained for the PtCo catalysts by using a carbothermal reduction. The surface properties were investigated by X-ray photoelectron spectroscopy (XPS) and low-energy ion scattering spectroscopy (LE-ISS, $3He^+$ at 1kV) [2]. The formation of a Pt skin layer on the surface of the alloy electro-catalyst was obtained by using a pre-leaching procedure. Furthermore, the amount of Pt-oxides on outermost atomic layers was much smaller in the PtCo than in the Pt catalyst. These characteristics appeared to influence catalysts' performance and degradation. Accelerated tests (electrochemical cycling) at 110 °C and low R.H. showed good stability for the PtCo alloy. Furthermore, better performance was obtained at intermediate temperatures for the pre-leached PtCo as compared to the Pt cathode catalyst.

Acknowledegement
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Surface Properties of Pt and PtCo Electrocatalysts and Their Influence on the Performance and Degradation of High-Temperature Polymer Electrolyte Fuel Cells,
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ELE-KN-03 Dissociative Electron Transfer to Organic Halides: From Theory to Applications.

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The electrochemical reductive cleavage of carbon-halogen bonds in organic compounds has been the object of intense interest and investigation for many years, both from mechanistic and synthetic viewpoints. An important issue of the reduction process is whether the reductive cleavage occurs in a single step, breaking of the bond being concerted with the electron transfer, or in two steps with the transient formation of a radical anion.

The electroreduction of various organic halides, representative of both stepwise and concerted mechanisms, has been comparatively analysed at GC and at some potential electrocatalytic cathodes, namely Ag, Cu, Pd, Ag-Pd and Cu-Pd. All these materials are good electrocatalysts and, among them, Ag, either bulk or nanoparticles, is one of the best. So far, various factors such as the type of the halogen atom, the molecular structure of RX, the surface morphology of the electrode and adsorption/desorption behavior of the halide ions have been identified to play an important role in the electrocatalytic reduction. Furthermore, the existence of a strong linkage between catalysis and mechanism of dissociative ET has been shown for the reduction of a series of chlorides in aprotic solvents.

The reduction of organic halides and, in particular, the extraordinary catalytic properties of silver have been applied in several electrosynthetic processes. In particular, the electrosynthesis of fine chemicals and pharmaceutical products by electrocarboxylation of the corresponding chlorides at Ag has been successfully achieved and, in some cases, also a first scale up has been developed with very encouraging results.

More recently, the mechanism of catalytic reduction of activated alkyl halides has attracted much attention, in relation to atom transfer radical polymerization (ATRP), which is a powerful method of living radical polymerization (LRP) that can be applied to a wide range of monomers for the synthesis of polymeric materials with pre-determined molecular weights, low polydispersities and desired molecular architectures The mechanism of reductive cleavage of model alkyl halides used as initiators in LRP, has been investigated in acetonitrile using both experimental and computational methods. Both theoretical and experimental investigations have revealed that DET to these alkyl halides proceeds exclusively via concerted rather than stepwise manner, giving useful information on the mechanism of LRP and the possibility of optimizing the polymerization processes.

ELE-KN-04 Carbon Molecular Nanosystems Investigated by Electrochemical Tools

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Over the last two decades, we have assisted to the subsequent rise on the stage of the new molecular materials of the three different low dimensional carbon nanomaterials, from 0D fullerenes to 1D nanotubes and, more recently, 2D graphene. Their unique structural, optical and redox properties are showing an increasing potential for a wide range of applications, energy conversion devices, in-vivo and in-vitro biosensing and catalysis [1], and electrochemistry has always played a special role in the investigation of their electronic properties, as either individual entities [2] or functionally integrated in molecular or macroscopic devices [3].

Herein we shall report examples of our recent studies on the fundamental redox properties of pristine and chemically-modified carbon nanosystems, investigated by either bulk or scanning probe techniques and on their exploitation in electrochemical biosensing and energy conversion devices (Figure 1).

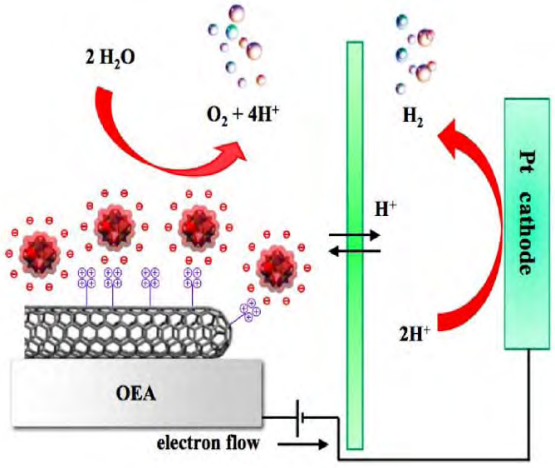

Figure 1

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ELE-KN-05 Electrochemistry in wastewater and soil remediation

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The progress of the research in electrocatalysis and electrode material science since the middle of last century, has led to a substantial decrease of the environmental impact in important fields of industrial electrochemistry like chlor alkali and aqueous electrometallurgy.

As far as anode materials are concerned, the introduction of oxide-modified titanium devices, originally proposed for chlorine production in the second half of the ‘60ies, found further important applications for oxygen-evolving anodes.

Research on this topic has led, in turn to processes related with pollution abatement in wastewaters. In fact, stable oxygen-evolving anodes are currently used in electrochemical processes of abatement of heavy metals by cathodic deposition, of consolidated commercial interest. More recently, specific types of anode materials have been tested for the so called electrochemical incineration of organic pollutants. This type of application, which would be of great interest for the abatement of bio-refractory substrates, and more, generally, for the minimization of chemical reactants involved in the decontamination process, has been the subject of a number of fundamental papers, although the level of commercially interesting technology has not been reached yet. In this communication, the main features, pros and cons, of different types of electrochemical incineration will be discussed, together with results of possible practical interest.

One more potential application of electrochemistry in environmental remediation is represented by soil decontamination. The so called electrokinetic soil remediation substantially consists of an electrochemically sustained solvent transport through a saturated soil matrix which causes transfer of neutral and charged contaminants through the soil. Together with solvent transport, also electromigration of ionic components of soil solution also takes place and may favor the yield of the overall decontamination. Electrokinetic soil remediation has been discussed first by R. Lagemann in late 80ies, and then in early 90ies by Y.B. Acar and A.N. Alshawabkeh. Much experimental results have been accumulated, essentially on model-polluted-soils, essentially caolinite and a few other clay components and data on real soil samples are rare. In this frame, inevitably, also the evidence for commercial installations is practically missing, even considering pilot-plant scale. Yet, the future of soil reclamation more and more imposes the *in.situ* or at least *on-site* technologies and this makes the electrokinetic approach a promising one, provided the level of knowledge on the performance under real conditions are mdae available.

On these aspects some basic elements of knowledge will be dealt with in the communication, together with some original experimental results.

ELE-OR-01 Electrodeposited iridium oxide as studied by tip/substrate steady state voltammetry

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Iridium oxide is well known for its wide field of applications that range from electrocatalysis to electroanalysis, from electrochromism to neural stimulation.
In this work, the properties of electrodeposited iridium oxide films (EIROFs) have been studied by scanning electrochemical microscopy (SECM) in the feedback mode by means of the so-called tip/substrate (T/S) voltammetry under steady state conditions.
This SECM mode was intensively used in the past for the study of conducting polymers, as in reference [1].
The main purpose is the study of the reversible solid state-redox transitions that occur over iridium oxide in the potential range around 0.4 -1.4 V (RHE) and that are at the basis of all its applications. The transitions are observed and studied by combining (i) the use of suitable reversible redox couples and (ii) the effect of selecting different solution pHs for "shifting" the potential of the redox transitions themselves. In fact, the latter are pH dependent as evident from the common equation:

$$IrO_x(OH)_y + \delta H^+_{(solution)} + \delta e^-_{(oxide)} = IrO_{x-\delta}(OH)_{y+\delta} \qquad (1)$$

Moreover, being EIROFs highly hydrated films, protons are free to move in the whole electrode mass. In particular conditions, the transition includes a conversion semiconductor/conductor (like in the Ir(III)/Ir(IV) transition), that has a remarkable effect on the feedback current. The possible individuation of electrogenerated iridium species of different valencies via their reaction with one form of the redox couple, by analogy with a recent publication [2] on oxidized Pt, is also discussed.

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Acknowledgements: The financial contributions of PRIN 2008 – "Pt-free electrocatalysts for direct alcohol fuel cells." 2008N7CYL5 and PUR-Università degli Studi di Milano (2009 – 2010) funds are gratefully acknowledged.

ELE-OR-02 Electroanalytical determination of benzidine by differential pulse voltammetry on different electrodes.

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Benzidine is a solid organic compound which evaporates slowly, especially from water and soil. It was used in the synthesis of azo-dyes widely employed in textile, printing, leather, paper making, drug and food companies around the world. However, in 1973 benzidine was identified as a carcinogenic agent for human urinary bladder because its oxidation by human enzymes can permit its binding with DNA. For these reasons, it belongs to the list of the Priority Pollutants [1-2]. Although benzidine production and use was forbidden in many countries since 1970s, benzidine based azo-dyes are still used in many research laboratories and industries, and its detection and determination is a primarily concern.
Various methods for detection of benzidine are proposed in the literature, such as colorimetric, spectroscopic, electrochemical [3] and chromatographic ones. In particular, liquid, high performance liquid and gas chromatography are the most used techniques, frequently associated with mass spectrometry.
Electroanalytical techniques and particularly those based on pulsed voltammetry, which are suitable for trace analysis, constitute an interesting alternative in terms of very high sensitivity, low response time, small dimensions and low costs.
In this presentation a new method for quantitative detection of benzidine based on differential pulse voltammetry on Glassy Carbon (GC) and Platinum wire bare electrodes is proposed. The use of carbon-based or platinum-based screen printed electrodes (SPE) is also investigated.

[1] Environmental Protection Agency of United States (US EPA)
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ELE-OR-03 ELECTROKINETIC REMEDIATION OF SOILS CONTAMINATED BY MERCURY

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The electrokinetic approach, for the extraction of metal ions from dispersed solid matrixes, has received extensive description in the scientific literature of the last twenty years. The application of electric fields of suitable intensity, through saturated portions of soils, can determine the displacement of charged species. In principle, this effect has two components: one is the electromigration, the other is the component due to the electroosmotic drag of the spatial ionic charge facing the charged surface of soil particles.
In the case of electromigration, the electric field has essentially the role of "driving force" for the movement of ionic species through the water impregnating the dispersed solids and the soil in particular. The effect remains even if the solid matrix is finely divided.
The application of this technology, when aimed to the removal of mercury present in metallic form, requires its prior dissolution, which can be facilitated by adding appropriate chemicals. Designing an intervention requires a preliminary speciation of the contaminant in the soil, as well as the execution of electrochemical tests at a laboratory scale.
The analysis of soil with speciation of the pollutant was carried out following the approach proposed by Boszke et al. *"Mercury mobility and bioavailability in soil from contaminated area"*, Environmental Geology (2008) 55: 1075-1087. The soil analysis was repeated after the electrochemical laboratory test, for an assessment of the amount of removed Hg. In addition, results obtained with this method were compared with those acquired using the alternative EPA 3200 procedure for speciation.
The electrochemical laboratory test was performed on approximately 400 kg of soil, and for a period of about three months. After treatment, the soil analysis showed a significant reduction of total Hg (approximately 60% of the total).
Basing on these results, an intervention in the field is being planned: estimation of time required to achieve the objective of remediation has been based on the removal of mobile and mobilizable forms of Hg.

ELE-OR-04 Electrochemical capabilities in both photoreduction and detection of toxic Cr(VI) pollutant

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Chromium is widely used in several industrial processes such as metal plating, leather tanning, paint making and others [1,2]. Due to its acute toxicity, carcinogenic action and high mobility in water, Cr(VI) is in the list of priority pollutants of most countries. In aquatic environments, chromium is present mostly as hexavalent Cr(VI) and trivalent Cr(III). Cr(III) is less noxious and usually immobile through precipitation or adsorption onto solid phase. Therefore, the rapid and accurate monitoring of both chromium species and the efficient reduction of Cr(VI) to Cr(III) in contaminated waters are highly desirable.
Specifically, Cr(VI) ions in water can be completely photoreduced to Cr(III) at the surface of UV-excited TiO_2 photocatalysts [3]. The transfer of photocatalytic results from slurry to immobilized particles on substrates is a general concern, primarily due to the elimination of filtration steps. Thus, the first part of this presentation is focused on the electrophoretic deposition (EPD) of TiO_2 as an alternative procedure to deposit the oxide in dense layers, avoiding slurry filtration steps [4]. The second part of the presentation will be devoted to the study of the photocatalytic performances of titania layers by comparing traditional polarographic techniques with a new environmentally friendly electroanalytical approach based on the use of bismuth screen printed electrodes [5].

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ELE-OR-05 Electrodeposition of metal nanoparticles on commercially available Digital Versatile Disk (DVD) for sensing and catalysis.

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The success and the spreading of a technology strongly relies on the possibility of employing economical and widely available row materials, and easy production methods. In this work, we have exploited the possibility to use the metallic surface of a commercial Digital Versatile Disc (DVD) as an electrodic support for the fabrication of optical and electrodic devices to be employed in sensing and in catalysis. Nowadays, with the advent of the new storing devises, DVDs represent nothing else than a technological waste. On the other hand, they are also a real silver/gold mine in the form of smooth reflecting films, usually prepared by sputtering over a polycarbonate nanostructured support. In fact, DVDs have a surface layer made of Ag or an Ag alloy, which in this work has been used as a support for the electrodeposition of nanoparticles (NPs) of Ag or Cu. The electrodeposition has been carried out in a galvanostatic or potential-controlled pulsed deposition mode, evaluating important parameters, such as current density, applied potential and the chemical environment, which influence the nucleation and the growth of the metal NPs. The modified substrates have been characterized by cyclic voltammetry in aqueous and organic electrolytes in order to evaluate the stability of the metal NPs. Furthermore, the electroreduction of molecular probes, such as benzyl chloride, has been investigated to check whether nanostructuring and surface morphology affect the electrocatalytic activities of these metals.

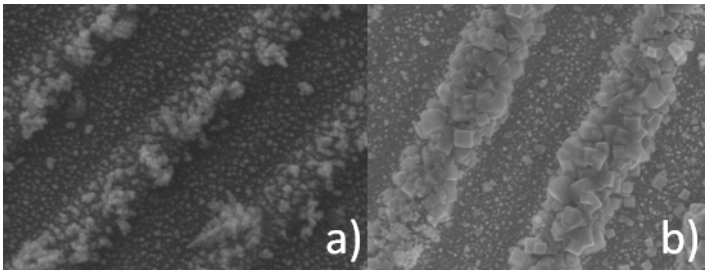

Figure 1.

AFM and SEM characterizations of the functionalized supports reveal that the deposited NPs preferentially pack over the groves of the DVD grating (Fig. 1 a and b). Furthermore, microRaman experiments have pointed out that DVD derived SERS substrates are very good candidates for the development of convenient and disposable sensing platforms [1]; in fact, the substrates show really interesting SERS properties and Enhancement Factors, which are clearly affected by the shape and distribution of the NPs.

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ELE-OR-06 Pyrrolidinium imide - based composite gel electrolytes for Li batteries

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Blends of PVdF and ionic liquids (ILs) are interesting for application as electrolytes in plastic Li batteries. They combine the advantages of the gel polymer electrolytes (GPEs) swollen by conventional organic liquid electrolytes with the nonflammability, and high thermal and electrochemical stability of ILs.

In this work we report on some PVdF-HFP composite membranes swollen with a solution of LiTFSI in ether-functionalized pyrrolidinium-imide ionic liquid ($PYRA_{12O1}TFSI$). The liquid electrolyte was tested both as pure system (Li-IL) and mixed with proper amounts of EC/DEC as co-solvents in order to find an optimal composition with an enhanced ionic conductivity and preserved thermal stability. The membranes were filled in with silica nanoparticles of different microstructures. The ionic conductivity and the electrochemical properties of the gel electrolytes were studied in terms of the nature of the filler.

Each membrane was thoroughly characterised from the physico-chemical and electrochemical points of view. Particular attention was devoted to the investigation of the Li/gel compatibility by taking into account several key-factors, like the filler morphology and IL amount in the liquid electrolyte.
Battery tests, performed at room temperature on the conventional solid state cell Li/composite gel polymer/$LiFePO_4$, are also presented.

ELE-OR-07 New electrocatalyst for Li/Air cathode batteries: MnO_2 *via* hydrothermal method

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Since the first announcement in 1996 by Abraham, Li/air batteries have attracted the attention because of their high specific capacity (up to 1800mAh·g^{-1}), thanks to the positive pole reaction based on the reduction of O_2, that can be directly provided by the air without the necessity to upload the chemical reagent in the battery. At the same time, secondary Li/air cells suffer serious limitations under recharging conditions, because the "combustion" products, Li_2O_2 and/or Li_2O, can clog the carbon-based cathode pores, thus reducing the performance and lifetime of the batteries. It is well accepted that their complete removal during the charge cycle is hard to accomplish without an appropriate catalyst. The use of electrolytic MnO_2 has been proved to be rather effective, but the overall performance of the modified cathode material is still inadequate to guarantee the expected long life cycles to the new Li/air batteries.
In this context we present a new composite material based on ordered mesoporous carbon cathode modified with MnO_2 electrocatalytic nanopowders prepared by an hydrothermal method, based on the oxidation of Mn^{2+} by ammonium peroxodisulphate. The syntheses were carried out for 24 h at different temperatures (60, 90, and 120 °C) also in the presence of dopant species. The results are discussed in term of cyclic voltammetry experiments performed by hosting the new composite powders in cavity microelectrodes, and in term of laboratory Li/Air battery life cycles.

The financial contributions of PRIN 2008 – "*Development of the Li/air cell for automotive applications.*" 2008PF9TWZ, CARIPLO 2010 – 2010-0506 and PUR-Università degli Studi di Milano (2009 – 2010) funds are gratefully acknowledged

ELE-OR-08 Electrochemical behavior of Na_xCoO_2 prepared by hydrothermal reaction

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The cheaper and much higher natural abundance of sodium than lithium have renewed interest in compounds of the former as electrode materials for rechargeable batteries in the last years.
In the present contribute we report about the electrochemical behavior of Na_xCoO_2. The material was obtained by, cheap and easy to scale up, two steps preparation route: a solvothermal reaction, to produce cobalt oxide with controlled and nanometric morphology, followed by a solid state reaction with Na precursors. In particular, the phase prepared using NaOH as precursor shows the X-ray spectrum corresponding to $Na_{0.71}CoO_2$, according to the 30-1182 JCPDS card. SEM and TEM images point out a sub-micrometric morphology with well defined crystalline particles.
Electrodes were fabricated by standard battery technique on 304 stainless steel foils. Preliminary electrochemical characterizations were carried out in a three electrode flooded cell using 1.0 M Na_2SO_4 aqueous solution and a large $Na_{0.44}MnO_2$ intercalation compound counterelectrode. The CV trace (Figure 1) shows two electrochemical process taking place at potential ranges of 0.2-0.4 and 0.65-0.75 V vs. SCE, respectively. The electrode was cycled in the potential range 0.20-0.78 V vs. SCE at very low current density (2 $\mu A/cm^2$). The discharge specific capacity was about 26 mAh/g at the first cycle decreasing to 20 mAh/g after 20 cycles. The electrochemical properties will be also measured in organic electrolyte, in order to explore larger potential windows, and presented.

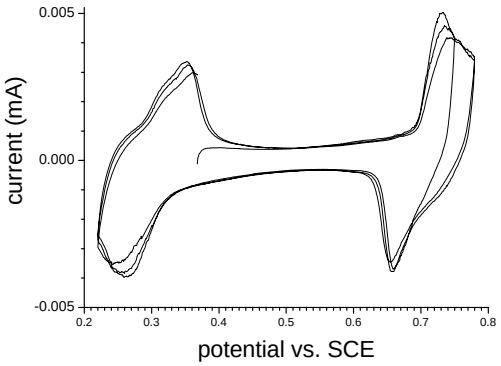

Figure 1. CV profile of Na_xCoO_2 in Na_2SO_4 water solution (scan rate 0.05 mV/s).

ELE-OR-09 New technologic Substrates for Energy devices by Electrodeposition

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The global environmental concerns and the escalating demand for energy, coupled with a steady progress in renewable energy technologies, are opening up new opportunities for the utilization of renewable energy resources. Electrodeposition is extensively used to deposit metals and metallic alloys at the industrial level, with a wide range of applications from large area surface treatments to most advanced electronic industries. Electrodeposition of semiconducting materials represents a new challenge, not only from the academic but also from the economic point of view, since this method presents interesting characteristics for large area, low cost and generally low temperature and soft processing of materials. The Electrochemical Atomic Layer Epitaxy (ECALE) method was used to obtain binary compound semiconductors such as Cu_xS and Sn_xS_y on Ag(111). The amount of the elements deposited in the first layers of the compound was determined by the oxidative stripping of cations, followed by the reductive stripping of anions. This study reviews the state of art of the literature on the knowledge about these binary and pseudo ternary system, and it sets up perspectives for photovoltaic applications. Chalcogenide based materials are of considerable interest as promising semiconductor for electro-optic devices, thermoelectric devices and optical recording media.
Selective Electrodesorption Based Atomic Layer Deposition (SEBALD) was used to prepare new bimetallic electrodes for fuel cells. This new method of Electrodeposition, recently pointed out in Florence on the base of ECALE method, allows to deposit under morphological and compositional control those metals that cannot be deposited at underpotential.

ELE-OR-10 Dye sensitised solar cells with nickel oxide photocathodes prepared via microwave plasma sintering

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NiO electrodes for cathodic dye-sensitised solar cells (DSSCs) can be obtained by sintering the spray deposited NiO nanoparticulate layers through a newly developed treatment that involves microwave plasma technique (PAMW).[1] This technique proved to be versatile in controlling the morphology of NiO coatings and the adhesion of these to the electrically conductive transparent substrates. NiO coatings have been tested in cathodic DSSCs with Erythrosin B,[2] P1[3] and Fast Green[4] sensitisers. The largest overall efficiencies of the DSSCs with a single photoactive NiO cathode were obtained with P1-sensitised samples. The incident photon-to-current conversion efficiency (IPCE) reached values as high as 30% for NiO electrodes with a highly mesoporous morphology. The photogenerated charge carriers in the PAMW-NiO DSSCs displayed relatively long lifetimes (in the order of 1 s) under open circuit conditions. The transport times of the charge carriers in the DSSCs were independent on the incident light intensity under short-circuit conditions.

1. (a) McConnell, M.L.; Dowling, D.P.; Pope, C.; Donnelly, K.; Ryder, A.G.; O'Connor, G.M. *Diamond Rel. Mater.* **2002**, *11*, 1036-1040; (b) Awais, M.; Rahman, M.; MacElroy, J.M.D.; Dini, D.; Vos, J.G.; Dowling, D.P. *Surf. Coat. Techn.* **2011**, *in press*, corrected proof.
2. (a) He, J.; Lindström, H.; Hagfeldt, A.; Lindquist, S.E. *Sol. En. Mat. Sol. Cells* **2000**, *62*, 265-273; (b) Awais, M.; Rahman, M.; MacElroy, J.M.D.; Dini, D.; Vos, J.G.; Dowling, D.P. *Surf. Coat. Techn.* **2011**, *in press*, corrected proof.
3. Li, L.; Gibson, E.A.; Qin, P.; Boschloo, G.; Gorlov, M.; Hagfeldt, A.; Sun, L. *Adv. Mater.* **2010**, *22*, 1759-1762.
4. Perera, V.P.S.; Pitigala, P.K.D.D.P.; Senevirathne, M.K.I.; Tennakone, K. *Sol. En. Mat. Sol. Cells* **2005**, *85*, 91-98.

ELE-OR-11 Electrochemical Deposition of Cu and Ni Nanowires Directly on Electrode Surface

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Electrochemical deposition is a popular method for the preparation of conductive nanowires or nanotubes in suitable templates, like alumina and polymeric track etched membranes. The procedure normally includes coating of one side of the membrane with a noble metal or alloy to provide the conductive substrate. We propose an alternative approach based on a specific cell assembly: the membrane, laid over a commercial sponge soaked with electrolyte, is pressed against the disk working electrode, placed face down, by raising the cell containing the counter electrode (two-electrode operation). In this way, a deposit of metal nanowires may be directly obtained on the electrode substrate of identical or different material.

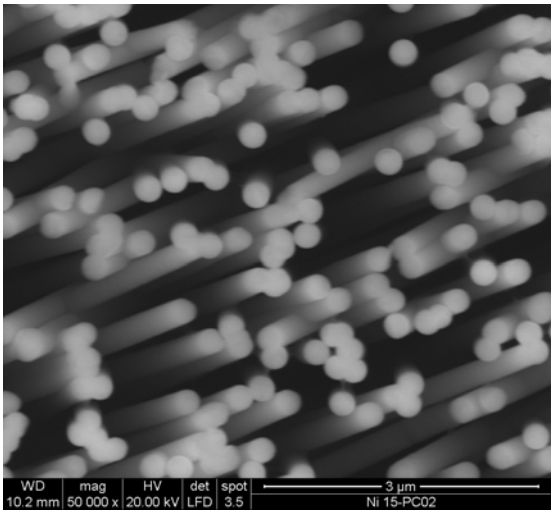

Figure 1. SEM image of Ni nanowires deposited in a Whatman membrane with pores of 200 nm nominal diameter.

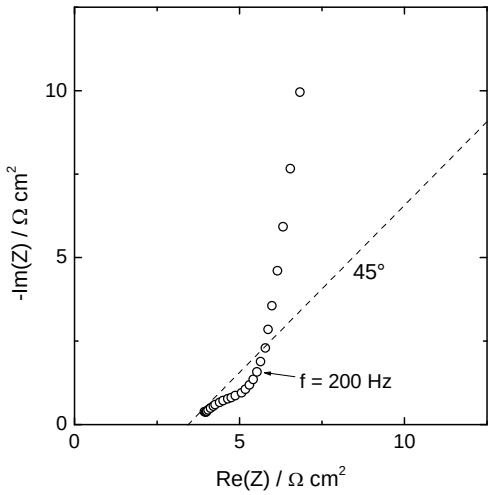

Figure 2. Impedance plot of a Ni disk with Ni nanowires of 200 nm diameter (0.1 M NaOH, E = 0.1 V vs Hg/HgO).

Figure 1 shows the morphology of Ni wires and Figure 2 the impedance data of the electrode, from which we could estimate a roughness factor f_r = 23±2. Electron backscatter diffraction (EBSD) shows that the head of wires with diameter of 200 nm or lower is almost always monocrystalline for Cu and frequently also for Ni.

Acknowledgments. Financial support of the Regione Veneto to the 12 months stay of A. Gambirasi at IENI-CNR (Asse "Capitale Umano", DGR 2215/2009) is gratefully acknowledged.

ELE-OR-12 Microstructure and transport properties of thin film electrolytes for Solid Oxide Fuel Cells

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Alternative energy production is one of the major problems for future sustainable development. Solid oxide fuel cells (SOFCs) are a promising technology for this aim, but their mass development is hindered by high costs and stability issues related to their high operation temperature (1000°C). Significant research efforts are thus being devoted to decreasing the SOFC operation temperature in the intermediate range (below 700°C, IT).
Aim of our research is to push the limit of SOFC operation temperature to the lowest possible value, developing highly performing nanostructured materials and innovative device architectures to eventually fabricate miniaturized SOCFs operating at 450-700°C.
Proton and anion conducting electrolytes, characterized by high conductivity at IT, were developed in thin film form to reduce their ohmic resistance.
One of the main factors impairing the electrolyte conductivity is the presence of blocking grain boundaries. The strategies adopted in our laboratory to solve this problem are the fabrication of monocrystalline or highly textured [1] films using pulsed laser deposition (PLD) and the modification of the grain boundary nature using nanostructured materials prepared by wet-chemistry methods to control the sintering procedures.
Pulsed laser deposition (PLD) is particularly promising amongst the different film deposition techniques because of its ability in reproducing complex target compositions onto the film.
Highly-textured, epitaxially oriented $La_{0.8}Sr_{0.2}Ga_{0.8}Mg_{0.2}O_3$ (LSGM) and $BaZr_{0.8}Y_{0.2}O_3$ (BZY) films were grown by pulsed laser deposition on different substrate (e.g. MgO, NGO, LAO). The study of the microstructure/transport properties correlation was the main aim of the present work. In both cases films with good crystalline quality were obtained.
BZY films grown on (100)-oriented MgO substrates showed the largest proton conductivity ever reported for BZY samples (0.11 S/cm at 500°C).The excellent crystalline quality of BZY films allowed for the first time the experimental measurement of the large BZY bulk conductivity above 300°C, expected in the absence of blocking grain boundaries.[2]

Our results demonstrated that optimizing the control of the crystallographic quality by reducing the mismatch between the substrate and the deposited film is a key issue to achieve electrolyte thin films with optimized electrical performances.

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ELE-OR-13 Preparation and characterization of Pt/IrO_2 electrocatalysts for unitized regenerative fuel cell (URFC) applications

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Hydrogen energy storage systems coupled to renewable power sources are being proposed as a means to increase energy independence, improve domestic economies, and reduce greenhouse gas emissions from stationary and mobile fossil-fueled sources. New technologies for production and utilization of hydrogen as energy carrier are electrolysers and fuel cells, respectively. Both processes may alternatively occur in the same device based on a proton exchange membrane (PEM). This device is called unitized regenerative fuel cell (URFC). Compared with conventional secondary batteries, URFCs advantages rely on high energy density, long-term energy storage, durability and environmental protection. Whereas in comparison to the separate fuel cell and electrolyzer based systems, URFCs are significantly more compact and they allow considerable system simplification. Moreover, URFC devices are characterized by rapid start up, they can operate efficiently at low temperature without the need of cumbersome power consuming auxiliaries and can provide stable operation even in the presence of a large number of start up/ shut down cycles. However, URFC electrodes are not the simple linear combination of electrodes used in fuel cells with those used in electrolysis cells. One of the main technical breakthroughs for URFCs is the development of efficient bi-functional electrocatalysts for the oxygen reaction.

In this work, nanosized Pt/IrO_2 electrocatalysts are synthesized by decorating Pt nanoparticles onto the surface of a nanophase IrO_2 support using an ultrasonic polyol method. The synthesis procedure allows deposition of metallic Pt nanoparticles on Ir-oxide without causing any occurrence of metallic Ir which is significantly less active for oxygen evolution than the corresponding oxide. The nanosized Pt/IrO_2 (50:50 wt.%) is sprayed onto a Nafion 115 membrane and used as bi-functional oxygen electrode, whereas 30 wt.% Pt/C is used as bi-functional hydrogen electrode in the URFC. Electrochemical activity of the membrane-electrode assembly (MEA) is investigated in a single cell at room temperature and atmospheric pressure both under electrolysis and fuel cell mode to assess the perspectives of the URFC to operate as energy storage device in conjunction with renewable power sources.

ELE-OR-14 Nafion influence on Oxygen Reduction Reaction catalyzed by Pt-free materials.

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Fuel cells for low temperature applications are the subject of intensive research because they may offer a reduction of primary fossil fuel consumption and greenhouse gas emission. However, one most problematic aspect arises from the kinetic slowness of the oxygen reaction. For this reason, electrode materials are, at present, based on platinum nano-dispersed onto carbon. Nevertheless, the natural scarcity and cost of platinum justify the search for alternate, non-precious materials, even though less catalytically performing. Their utilization may introduce unexpected or unpredictable electrocatalytic behaviour, because of the unknown interactions between these new materials and Nafion. In fact, in fuel cells Nafion is used as both the electrode separator and as an ion-conducting binder of the catalyst layer affecting platinum activity and fuel cell performance [1]. Catalytic sites of platinum and platinum-free catalysts obviously have different nature, thus implying possibly different interaction mechanisms with the Nafion binder, to affect catalytic activity.

In this work, we present some results about the oxygen reaction reduction (ORR) on a Pt/C commercial catalyst and on lab-synthesized platinum-free catalysts in acid, that were obtained by varying the electrode preparation method and the added Nafion quantity. In a first method a Nafion suspension was deposited onto a catalytic layer previously dried onto the Rotating Disk Electrode (RDE) graphitic tip, in a second one Nafion was directly added to catalyst suspensions, before the RDE tip deposition.

Voltammetric results show that the catalytic layer thickness and the relative Nafion quantity affect the experimental I/E curve morphology and the presence of a well defined limiting current regime. Optimized experimental conditions (relative quantity of Nafion to carbon quantity) to obtain good results were determined differing for Pt/C and Pt-free catalysts.

[1] M. Watanabe, H. Igarashi, and K. Yosioka *Electrochimica Acta, 40,* **1995**, 329.

ELE-OR-15 Fuel flexibility: a key challenge for SOFC technology

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A major worldwide challenge is the development of cleaner and sustainable sources of energy aimed at reducing the environmental threat of global warming and overcoming the finite nature of fossil fuel reserves. Promising energy conversion and storage technologies, including fuel cells and lithium batteries, are being developed to solve these problems. The performance of such energy systems depends crucially on the properties of their component materials; therefore, it is primarily through the development of innovative materials with improved functional properties and more affordable costs that the pressing need for environmentally-friendly technologies could find a solution. The choice of Solid Oxide Fuel Cells (SOFCs) compared to other fuel cell technologies has the great potential of the fuel flexibility especially those widely available and/or characterized by low cost [1]. Like most fuel cells, SOFCs will operate better on hydrogen than on conventional fuels whereas the direct feed of coal-based fuels directly in a SOFC in the presence of a state-of-the-art anode would result in carbon deposition and rapid as well as irreversible cell degradation [2]. Typically, air or steam have to be introduced with fuel into the anode with systematic control to prevent coking [3]; therefore, the introduction of an anode materials resistant towards coke formation under non humidified conditions would improve the commercialization path for applications ranging from small and medium distributed generation systems (0.5 - 50 kWel) to uninterrupted power supply (UPS), auxiliary power units for vehicles and mobile generators for civilian as well as military applications.

This paper concerned the investigation of an innovative electrocatalyst as anode material for the direct oxidation of various kinds of fuel in SOFCs and the main purpose of this work was the investigation of the effect of the use of hydrogen, syngas, methanol, ethanol, glycerol, and propane on the cell performance.

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ELE-OR-16 Preparation and Characterization of Electrocatalysts by Spontaneous Deposition of Noble Metals (Pd, Pt) on Ni Foam

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Pd and Pt were deposited by metal displacement reactions, using a commercial Ni foam as a supporting frame. The modified foam samples were characterized by electrochemical techniques and SEM-EDX, to assess the noble metals loading, their distribution on the Ni foam and their electrochemically active surface areas.

Figure 1.

Cyclic voltammograms recorded with Pd-modified Ni foam electrodes (volume 0.0425 cm^3) in 1 M KOH for different spontaneous depositions times. The reduction peak at ca.-0.28 V, ascribed to the reduction of Pd oxides, was used to quantify the Pd surface area.

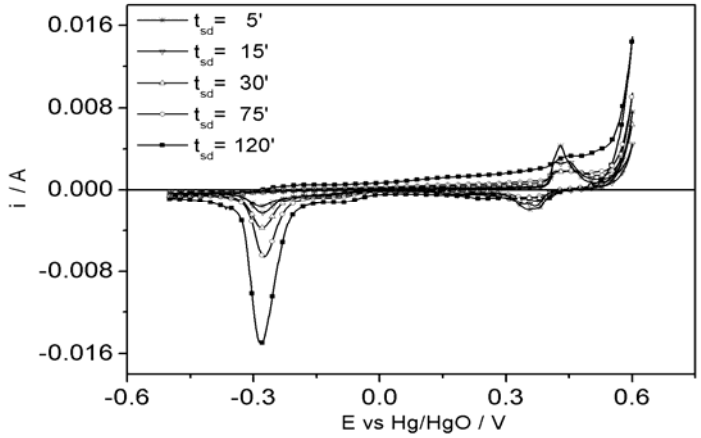
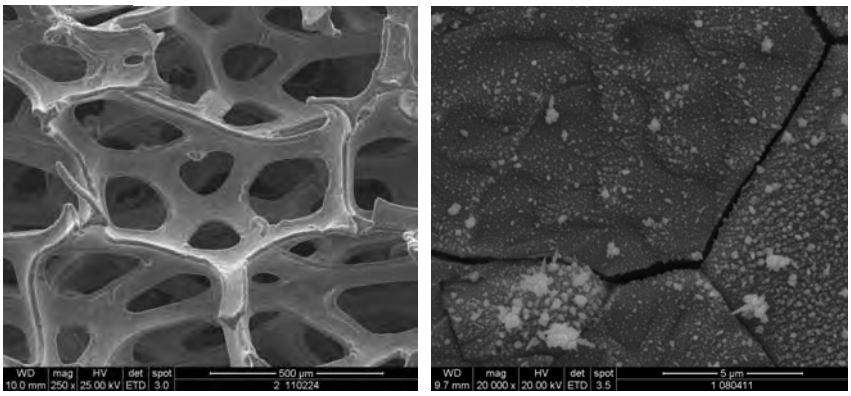


Figure 2.

SEM images of the commercial Ni foam (left) cell and of Pd deposits obtained by immersion of the foam in 0.005 M $PdCl_2$, for 60 min (right).



Different morphologies, from nano- to micro-scale clusters were obtained by varying deposition parameters (concentration of $PdCl_2$ solution and deposition duration). The Pd-modified electrodes were tested in the oxidation of alcohols. In the case of methanol, the peak current per unit Pd mass exceeded 600 A g^{-1}.

Acknowledgments. The authors acknowledge the financial support of the Italian Ministry for Economic Development (MSE) – MSE-CNR Agreement on National Electrical System.

ELE-OR-17 Oxidation of Methanol, Ethanol, Ethylene Glycol and Glycerol at Pd-modified Ni Foam Electrodes

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Electrodes prepared by spontaneous deposition of Pd onto Ni foams were investigated as anodes for the oxidation of various alcohols and polyols (methanol, ethanol, ethylene glycol and glycerol) in alkaline media. Figure 1 shows the voltammograms obtained in 1 M KOH + 0.5 M alcohol solutions, with electrodes with a 2.4 mg cm^{-3} Pd loading per unit foam volume, corresponding to a 8 to 9 μg cm^{-2} Pd loading per unit true surface area of the Ni foam. The current, expressed in A g^{-1}, is normalized with respect to the Pd mass.

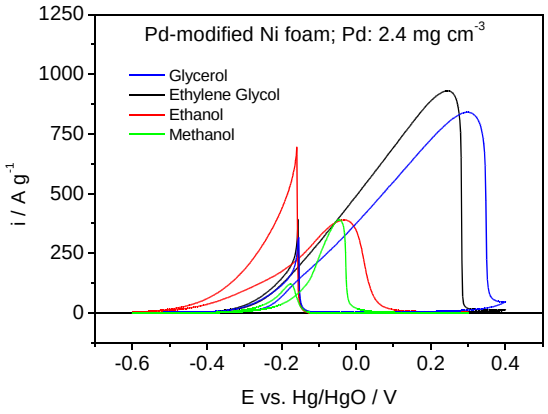

Figure 1
Cyclic voltammograms recorded with Pd-modified Ni foam electrodes in 1.0 M KOH + 0.50 M alcohol.

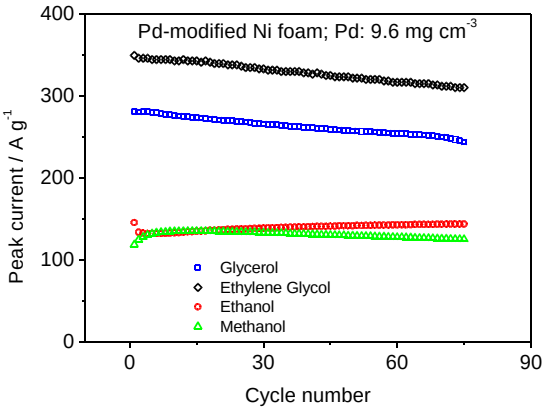

Figure 2
Stability test of Pd-modified Ni foam electrodes.

The Pd-modified Ni foam electrodes are very active in the oxidation of all alcohols and polyols. The peak current per unit Pd mass increases upon decreasing Pd loading. For ethylene glycol, oxidation currents higher than 2000 A g^{-1} are obtained with Pd loading lower that 1 mg cm^{-3}. Figure 2 shows that the performance of Pd-modified Ni foam electrodes is stable upon repetitive cycling.

Acknowledgments. The authors acknowledge the financial support of the Italian Ministry for Economic Development (MSE) – MSE-CNR Agreement on National Electrical System.

ELE-OR-18 Tuning of the optical and dielectric properties of anodic film on sputtered deposited Ta-Nb alloys.

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Anodic oxides on tantalum and niobium have been studied in the last decades for their possible application in electrolytic capacitors industry owing to their large values of dielectric permittivity (ε_{Nb2O5} = 53 - 57 and ε_{Ta2O5} = 27 - 31). More recently, Ta_2O_5 or mixed tantalum oxides (containing d-metal cation, for instance Ti or Nb), have been proposed as possible candidates to be used as gate dielectric in integrated circuits. Mixed tantalum-niobium oxides appear very promising dielectrics for electrolytic capacitors or integrated circuit, owing to the expected higher values of dielectric permittivity with respect to pure Ta_2O_5, provided that an improving in thermal stability and leakage current with respect to niobium oxide are obtained.

In this frame we have started an extensive investigation on the characterization of anodic oxides grown on magnetron sputtered Ta-Nb alloys covering all the range of composition. More specifically, in this work we want to discuss the influence of the anodizing bath composition on the solid state properties of anodic films grown on these alloys. Thus, anodic layers were grown at several formation voltages in electrolytes with different composition in order to study the effect of possible incorporation into the oxide of species coming from the solution.

The grown films were characterized by photocurrent spectroscopy in order to derive information on their optical band gap as well as on the zero photocurrent potential of the mixed oxide/electrolyte interfaces. Differential admittance and electrochemical impedance measurements were also carried out for some selected composition (including pure Ta_2O_5 and Nb_2O_5) to get information on their electronic properties.

ELE-OR-19 Electrocatalytic Activation of Alkyl Halides at Copper Electrodes

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The electrochemical activation of carbon-halogen bonds is a widely investigated subject because of its importance in synthetic and environmental applications, especially the abatement of polychlorinated volatile organic compounds (VOCs). Reduction of alkyl halides suffers from a very high activation free energy owing to the concerted nature of bond rupture and electron transfer. The process requires electrocatalysis and a few metals such as Ag, Cu, Pd and their alloys [1] are known to possess good electrocatalytic properties, which in some cases have been exploited in different applications [2].

Although, from an economic point of view, Cu is more appealing than Ag or Pd, its use as a cathode for RX reduction has been less examined. Herein we report the results of a study on the feasibility of preparative-scale electrolyses of alkyl halides at Cu cathodes. As model compounds we selected some VOCs of environmental interest, namely CCl_4, $CHCl_3$, CH_3CHCl_2 and CH_3CCl_3.

The process was investigated in DMF + 0.1 M $(C_3H_7)_4NBF_4$, both in the absence and presence of proton donors. All electrolyses resulted in a complete dehalogenation of the starting substrate as well as its intermediates. No electrode fouling was observed during electrolysis, but both the charge consumption and product distribution were found to be strongly dependent on the proton availability of the reaction medium (Fig. 1).

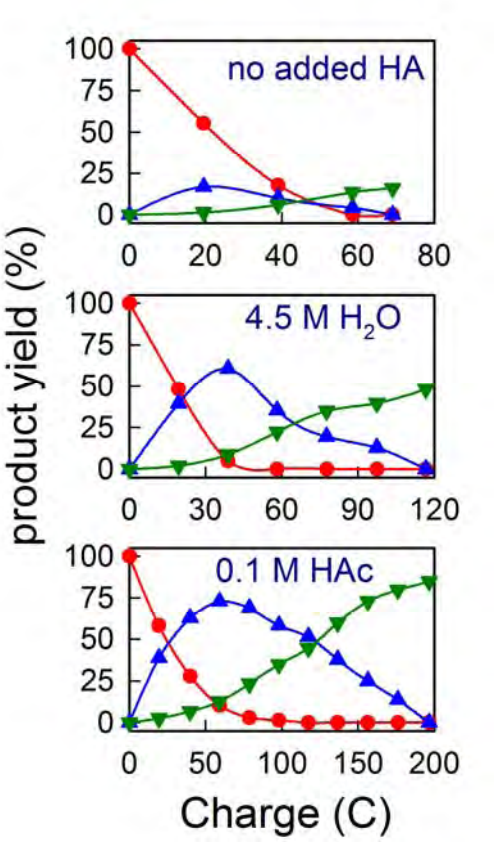

Fig. 1. Electrolysis of 0.01 M $CHCl_3$ (●) in DMF at Cu; products: CH_2Cl_2 (▲),CH_4 (▼).

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ELE-OR-20 Mechanism and Kinetics of Activation of Alkyl Halides by Cu(I) Complexes Used as Catalysts in Atom Transfer Radical Polymerization

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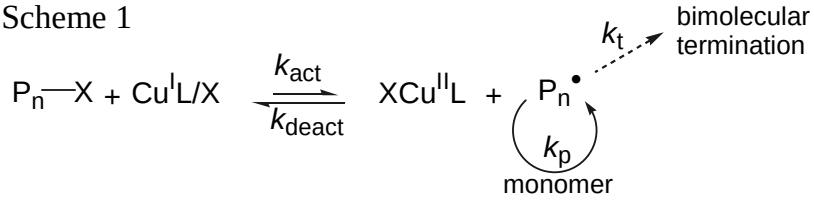
Atom transfer radical polymerization (ATRP) is one of the most used methods of controlled/living radical polymerization for the synthesis of a vast range of well-defined, low-polydispersity polymeric materials [1]. The process is initiated by a reversible reaction between a transition metal complex (mainly Cu(I) with an amine ligand, $Cu^{I}L^{+}$) and an activated alkyl halide to produce the propagating radical (Scheme 1).

Scheme 1



The initiation reaction is considered to involve a transfer of a halogen atom from the alkyl halide to the metal center. A fundamental question which, however, has not been adequately addressed is on the nature of the active Cu(I) species, since the metal ion exists under ATRP conditions as a multiplicity of species [2]. A second important issue on the activation reaction regards determination of the activation rate constants. Several methods, mainly limited to the study of slow reactions, have previously been proposed to measure k_{act} [3].

Herein, we first examine the mechanism of the activation reaction with the aim of unambiguously identifying the active Cu(I) species. We investigated the kinetics of activation of RX by $Cu^{I}L^{+}$ (L = Me_6TREN) in CH_3CN both in the absence and presence of X^{-}. It is found that although the system $Cu^{I}/L/X^{-}$ is mainly composed of $Cu^{I}L^{+}$, $XCu^{I}L$ and $Cu^{I}X_2^{-}$, only $Cu^{I}L^{+}$ is an active catalyst reacting with RX. Next, we describe electrochemical methods for the determination of k_{act} both for slow and fast reactions and apply them for the measurement of k_{act} for a variety of activated alkyl halides and Cu(I) complexes.

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ELE-OR-21 Enhanced structural order of Self-Assembled Monolayers of aromatic thiols in contact with aqueous solution.

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Owing to their ease of preparation and their versatility, Self-Assembled Monolayers (SAMs) are still today the most popular way to finely tailor the surface of noble and coinage metal to every need [1]. Even if they are essentially stable and highly ordered systems, their employment is still conditioned by their limited durability and by the presence of defects in the layer. For several years SAMs have been studied as corrosion inhibitors for copper and its alloys. The direct relationship between the layer thickness and its protective properties [2] drove the investigation, until now, toward long-chain alkylic thiols, whereas very few studies were carried out on the aromatic thiols [3]. In the present work we used different techniques to study the adsorption on polycrystalline copper of one aromatic thiols, Benzenethiol (BT), and one alkylic thiol, 1-Undecanethiol (1-UT), comparing their protective properties and their stability up to a week in an aggressive environment such as H_2SO_4 0.5 M. Both Electrochemical Impedance Spectroscopy (EIS) and linear polarization highlighted different trends for aged 1-UT and BT. In fact, although freshly prepared 1-UT showed the best performance, as expected from its thickness, it degraded very rapidly. On the contrary BT SAMs showed a noticeable increase of the protective properties during the first hours of exposure to the electrolyte; this led to a superior performance of BT over any 1-UT sample. Raman spectroscopy suggested that this behaviour is related to an enhancement of the structural order of the aromatic layer, whereas XP spectroscopy allowed us to reveal that the bond with the substrate is very much stabler for BT than 1-UT. Finally Dynamic Contact Angle (DCA) experiments showed a surprisingly increase in the BT hydrophilic character, leading us to suppose a direct role of the water molecules in the BT structural reorganization. This hypothesis was supported observing that the same thiols adsorbed on a polycrystalline gold surface and aged in ultrapure water showed a very similar behaviour, as verified by EIS and Cyclic Voltammetry in the presence of a reversible redox couple such $[Fe(CN)_6]^{3-/4-}$. The pinholes analysis carried out by the EIS data revealed for BT an increase in the average distance between the defects, which is coherent with a reduction of the number of collapsed sites and thus with an improvement of the three-dimensional structural order.

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ELE-OR-22 "Genetically modified" spider-like oligothiophenes: electron properties and electropolymerization

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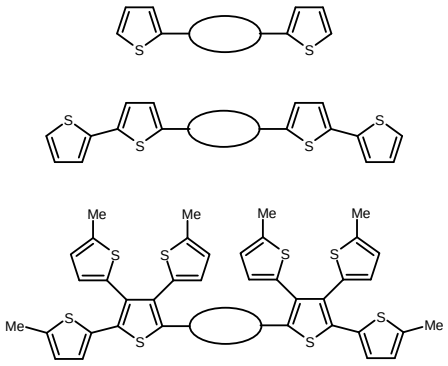
Multithiophene-based semiconductors are a virtually boundless class of molecular functional materials with very promising potential applications in a variety of fields, like electronics, energetics, sensoristics. Starting from our previous exhaustive work on "spider-like" branched oligothiophenes, affording a reliable rationalization of the relationships between structure and electronic properties[1,2], we have recently developed many structure modifications with respect to the original all-thiophene systems, aiming to achieve finer and wider modulation of both the HOMO and LUMO levels. In particular, the "core" of our oligothiophene systems has been modified by inserting appropriate building blocks of different electron richness, asymmetrically affecting both the LUMO and HOMO energy levels and localization along the main conjugated backbone, thus achieving one more freedom degree in tuning the electron properties of the molecule.



A wide series of "genetically-modified" spider-like oligothiophenes and their electrodeposited conducting polymers have been investigated by CV and EIS, focusing on the effect of core modification at constant thiophene side chains, and on the effect of increasing length and/or branching in the thiophene side chains at constant modified core. The core modification appears to be much more effective on the HOMO and LUMO energy levels and positions, while effective conjugation in the thiophene side chains is more determining on the oligomerization ability. The exhaustiveness of our investigation affords interpretative and predictive criteria which could usefully exploited in target-oriented molecular design.

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ELE-OR-23 Self-limited growth of Ag nano-rods into AAO nanopores

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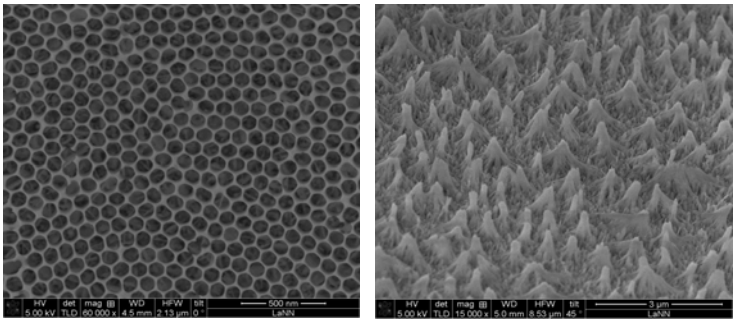
The anodization process of aluminum to give Anodic Alumina Oxide (AAO) described by Fukuda[1] is an effective way to prepare a regular and reproducible nano-patterned substrate on large areas. An extraordinarily large number of papers has been published on this subject and many of them focus on the growth of metal nano-rods inside the AAO pores. The formation of ordered arrays of metals nano-rods (e.g. Au, Ag or Cu) can find application in many fields, from (electro)-catalysis to Surface Enhanced Raman Scattering (SERS). Despite the relatively easy way in which AAO is prepared, there is a serious drawback in the use of DC electrodeposition for the filling of the pores because of the barrier layer which forms at the base of the AAO pores and at the interface with the Al metal substrate. In this contribution we describe an optimized preparation of the AAO substrates (see SEM on Fig. below, left), and we exploit an alternative approach to deposit the nano-rods by AC electrodeposition. The characterization of the final samples has been carried out by Angle Resolved X-ray Photoelectron Spectroscopy (ARXPS) and Scanning Electron Microscopy (SEM) measurements. It was possible to observe by ARXPS a somehow unexpected “shadowing” effect due to the incomplete filling of the pores by the metal nano-rods. It was observed that the metal nano-rods growth is self-limited and not-depending on the amount of current which flows in the electrochemical cell, producing an unfilled gap at the top of the pores whose average depth is measured simply by varying the detection angle with respect to the sample surface. A simple etching procedure in NaOH solutions allows to partially dissolve the AAO matrix so that the upper part of the Ag nano-rods protrudes outside the AAO matrix and its XPS signature start to loose the angle-dependence. Bunches of nano-rods eventually form (see Fig. below, right), with their tips in contact.



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ELE-OR-24 Electronic Properties of Corannulene Species and their Electrochemically Generated Graphene-like Structures.

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Corannulene is a bowl-shaped aromatic hydrocarbon recalling the fullerene surface and it is particularly intriguing to develop new materials, for its unique redox and luminescent properties. It is known to undergo several reduction processes and an oxidation which has been scarsely investigated, so far, being a completely irreversible process that brings about the rapid fouling and passivation of the electrode surface [1]. As for the reduction processes only the anion and dianion of corannulene have been electrochemically reported, while its tetraanion cluster was prepared with alkali-metal in THF [2].
We have reinvestigated the redox properties of this species over a large range of experimental conditions, by using "*traditional*" solvents for electrochemistry or "*unconventional*" ones (i.e., liquid NH_3 and liquid SO_2). This allowed us to observe, for the first time, the reversible electrochemical generation of up to the triply reduced corannulene [3]. On the oxidation side, the adoption of suitable ultra-dry solvents and electrolytes with very high oxidation resistance and low nucleophilicity allowed to explore the reactivity of the electrogenerated corannulene carbocations.
In this communication the interesting redox, spectroelectrochemical and luminescence properties of a class of corannulene species, together with the structure of their electrochemically generated films, will be discussed. Also the highly efficient blue electrochemiluminescence (ECL) of corannulene [4] compounds and the obtained polymeric films will be reported.

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ELE-OR-25 Thiophene/Ferrocene Systems as Possible Catalyst in the Cathodic Oxygen Reduction Reaction.

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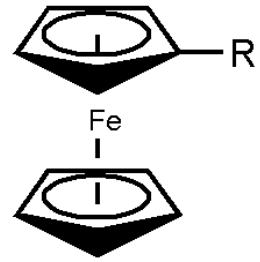
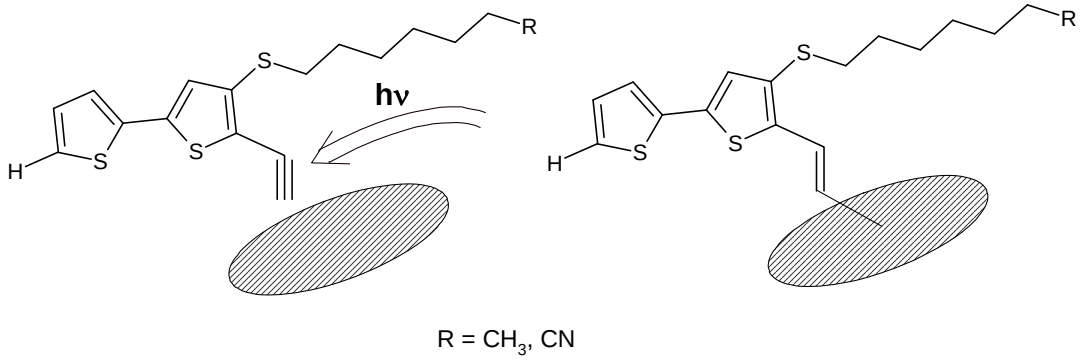
Various experimental strategies are exploited to graft Glassy Carbon and Si(111) surfaces. The Ferrocene redox couple on the Si(111) surface: photochemical grafting, surface chemical reaction using a Pt catalyst, post functionalization Si(111) surface previously modified with undecanoic acid. In figure 1 consider the substituent as being R = –H (FC), $–CH_2–OH$ (MFC), $–CH=CH_2$ (VFC). Cyclic voltammetry and electrochemical impedance spectroscopy are used to characterize the grafting process and the surface state. In particular, the dynamics of the electron transfer is assessed as a function of different Si(111) - molecular spacer - ferrocene systems. In addition bithiophene compounds are synthesized bearing suitable groups, which allow the grafting on the electrode surface. As shown in figure 2. In this case the chemisorption is achieved by UV triggered grafting of an alkyne moiety *via* a double bond formation (*figure 2*).





$R = CH_3$, CN

Fig. 2: The BT grafted to the silica surface

The organic film was characterized with various techniques, such as Cyclic Voltammetry, MALDI-TOF, XPS. The presence of the double bond allows to extend the conjugation (and thus the conductivity) of the OT chain to the electrode (transducer). The possibility to functionalize the thiophenes (at present the substitution of ferrocenes on the beta position is pursued) with different moieties the lateral chain makes these system very versatile and easily customizable.

ELE-OR-26 Electrochemical and theoretical studies for a better insight of the features of doped TiO_2 nanoparticles

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Doping titania by both metals[1] and non-metals[2] has attracted considerable attention due to a red-shift of the light absorption edge. A lively debate on the causes that provoke the shift of the absorption onset has arisen and grown. The main point of discussion concerns the eventual narrowing of the semiconductor band gap as a consequence of the doping or the creation of intra gap states. Also, the chemical nature and the location in the solid of the guest species responsible for visible light activity is still controversial.[3]
In this work, we report on TiO_2 samples obtained by a sol-gel synthesis using different dopant species.
From the electrochemical point of view the shift of the flat-band potentials (E_{fb}) of semiconductors plays an important role deciding photocatalytic as well as photoelectrochemical properties of thin oxide films and powders in general.
In particular, impedance spectroscopy has been applied to determine the value of the flat-band potential[4] of TiO_2 thin film electrodes prepared on conducting glass substrates and photovoltage measurements[3] in slurry to assess the Quasi Fermi level.
Theoretical ab initio Density Functional Theory (DFT) calculations[3] were performed to evaluate the Fermi Energy location at the band-gap and the presence of intra-gap states for doped samples. By the conjunction of the theoretical DOS calculations and the electrochemical measurements a deeper insight of the properties of doped titania semiconductors was achieved.

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ELE-OR-27 Development of new PBI membranes for high-temperature polymer fuel cells

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The current research on polymer electrolytes for fuel cells is focused on the optimization of a membrane working at about 120°C and low humidity levels (<30%), which are the real operative conditions in case of automotive applications [1]. Among the wide variety of tested polymer systems, PBI-based membranes, doped with phosphoric acid, are considered to be the best alternative to Nafion, due to their high conductivity even with no or low humidification and other promising electrochemical performances.

After a brief introduction on the problems of the membranes for HT-PEMFCs, I will report on the experimental strategies followed in our laboratory in order to design better systems. First of all, new polymeric architectures, based on polybenzimida-zole, have been synthesized with an increased number of basic sites, differently interspaced along the polymer backbone [2]. Subsequently, composite membranes were prepared by dispersing in the previously prepared matrices micro- and nanosized fillers, which differ for morphology, microstructure and chemical nature [3, 4].
Finally, new monomers including oxygen and other chemical moieties have been synthesized, and the consequent polymer have been prepared and tested [5]. In all cases, in situ-electrochemical tests and impedance spectroscopy were performed to evaluate the MEA performances.

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ELE-OR-28 Exhaustive depletion of recalcitrant chromium fraction by electrocoagulation in a continuous flow pilot plant.

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Nowadays there is a great concern about the increasing release of heavy metals into environment, since these substances can have harmful effects on many form of life. In this frame, Cr release represents a menace to natural life and public health for its mutagenic and carcinogenic properties. Wastewaters containing Cr are discharged into the aquatic environment from various industries like those of metal finishing, electroplating, pigments, tannery and chemical manufacturing. In particular, the leather industry which uses Cr for the tanning of animal skins and hides, produces a large amount of wastewater containing Cr concentrations much higher than those allowed for the more stringent environment requirements.

Conventional treatments generally assure quite satisfactory Cr removal; the rising problems are the requirements of expensive equipments and monitoring systems, the use of additional chemicals that cause a secondary pollution, high energy consumption and large production of toxic sludge which require disposal. Electrochemical processes have been proved to be competitive methods allowing high removal efficiency without requiring supplementary addition of chemicals and reduced volume of sludge produced. Electrocoagulation and electroprecipitation, in particular, seem to be promising technologies when wastewater with high Cr concentrations are considered. The limit for these processes is represented by the presence, in wastewater, of stable Cr complexes with the organic substances. Recent studies [1] have shown that recalcitrant Cr abatement may be improved by using an ozonization pre-treatment followed by an electrocoagulation with Fe electrodes.

In order to evaluate the possibility to develop this process on industrial scale, electrocoagulation treatment was investigated using a specifically designed pilot plant. Working conditions were first defined by experiments done on laboratory apparatus. Then tests were carried out in the pilot plant which operates in batch recirculation mode until selected working conditions are reached and then as a continuous flow system, in steady-state conditions. Mathematical models to represent the behaviour of the whole system in the different operating mode were developed. Comparison of experimental data against simulation results of the whole system operating in batch recirculation mode validated the proposed model.

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ELE-OR-29 Template electrosynthesis of nanostructures for water electrolysis

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About 95% of the hydrogen used today comes from natural gas or light hydrocarbons reforming and coal gasification, the remainder being high-purity hydrogen produced by water electrolysis. In order to realize benefits of a hydrogen economy, this must be produced cleanly, efficiently and affordably from renewable resources, preferentially available close to the end-users. The goal is a sustainable cycle of hydrogen production and use: in the first stage of the cycle, hydrogen is produced from renewable sources then used to power a fuel cell [1]. This cycle produces no pollution and no greenhouse gases.
In this context, development of low size electrolysers producing high-purity hydrogen with high efficiency and low cost is of great importance. Electrode materials play a fundamental role in influencing electrolyser performances; consequently, in the last years considerable efforts have been put for obtaining highly efficient and inexpensive catalysts. To reach both goals, we have developed nanostructured electrodes, with very large active area, constituted by PdCo alloys (cathode) and RuO_2 (anode) [2], to be potentially used in PEMEL electrolyzers. In fact, PdCo alloy is a valid alternative to Pt for hydrogen evolution, whilst ruthenium oxide is one of the most active catalysts for oxygen evolution. In this work, both these materials were electrodeposited using two different types of support: carbon paper, in order to fabricate a porous nanostructured film, and anodic alumina membrane, in order to obtain regular arrays of nanostructures.

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ELE-OR-30 Electrochemical treatment of organic pollutants in macro and micro reactors

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Electrochemical processes are considered among the more promising for the treatment of waste waters contaminated by bio-refractory or toxic organic pollutants. These methods are environmental friendly, involve very mild operative conditions (ambient temperature and atmospheric pressure), limited operative costs and can oxidize toxic organic compounds effectively. However, electrochemical processes present some important disadvantages when performed in conventional reactors such as: 1) To achieve reasonable cell voltages when the medium has not an adequate conductivity, one needs adding to the system a supporting electrolyte. 2) Low current efficiencies are usually achieved in direct oxidation processes when a high abatement of the organic pollutants is required, mostly due to the fact that mass transfer rates towards electrodes are extremely reduced at low pollutant concentrations.
It has been recently shown that the utilization of microfluidic electrochemical reactors (e.g. cells with a distance between the cathode and the anode of tens or hundreds of micrometers) can contribute to minimize these problems. Thus, very small distances between electrodes lead from one side to a drastic reduction of the ohmic resistances, thus allowing electrochemical incineration of organic pollutants without supporting electrolyte, and on the other side to the intensification of mass transport of the pollutants towards electrodes surfaces. Furthermore micro devices may simplify the scale-up procedure, since this only requires a simple parallelization of many small units and allow a fast screening of the effect of operative parameters. We have recently studied the electrochemical abatement of some organic pollutants such as 1,1,2,2-tetrachloroethane and Acid Orange 7 in both conventional and micro reactors. A critical evaluation of the effect of the micro reactor on the performances of the process has been, in particular, carried out.

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ELE-OR-31 Carbon dioxide as C_1 source in ionic liquids: role of electrogenerated $O_2^{\cdot -}$ as activating agent.

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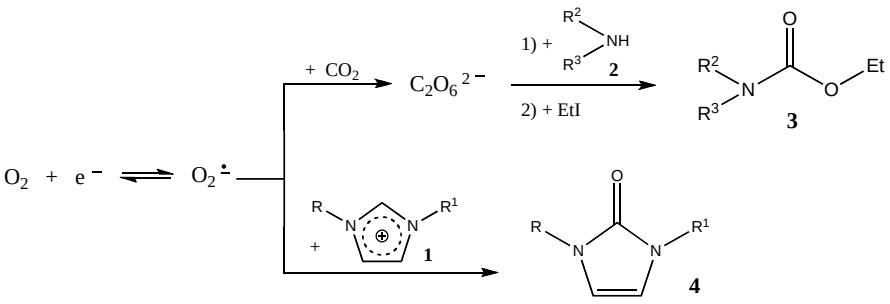
The set up of ecofriendly methodologies of synthesis (a significant target in modern organic chemistry) requires, *inter alia*, the removal of any toxic and/or hazardous reagent and solvent. Many authors have suggested the utilization of room temperature ionic liquids (RTILs) as green solvents (due to their negligible vapour pressure, chemical and thermal stability, etc.) [1] and of CO_2 as harmless and cheap renewable carbon source [2], in particular in the synthesis of carbamates, in place of toxic and harmful classic reactives (phosgene and its derivatives) [3].

In the past, the electrochemical activation of CO_2 for the syntheses of carbamates from amines has been carried out by us via: a) direct cathodic reduction of carbon dioxide in CO_2-saturated CH_3CN solutions or CO_2-saturated RTILs solutions of amines; b) selective cathodic reduction of O_2 to superoxide ion $O_2^{\cdot -}$ in O_2/CO_2-saturated CH_3CN solutions of amines. Recently, we have studied the possibility to extend this last methodology to O_2/CO_2-saturated ionic liquids **1** solutions containing amines **2** (Scheme) [4]. The activation of CO_2 has been carried out at -1.4 V (*vs* Ag), less negative than the reduction potential of CO_2 (-2.4 V, *vs* Ag) and in the absence of volatile and toxic organic solvents, supporting electrolytes and any catalyst (according to the growing demand of ecofriendly methodologies). The complex reactivity of $O_2^{\cdot -}$ has been analyzed: its reaction with CO_2 (yielding the carboxylating agent $C_2O_6^{2-}$) instead of RTIL (yielding 2-imidazolones **4**) is selective enough and carbamates **3** have been isolated in valuable current yields.



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ELE-OR-32 The microbiocidal electrolyzed activated solution (EAS) protects plants against pathogens and stimulates plant defenses.

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The fight against plant pathogens is of primary importance in agriculture, to ensure that quail/quantitative features of fruits and vegetables fit the market requirements. Synthetic products like pesticides and agrochemicals can protect plants against pathogens but they can be toxic or environmental unfriendly; therefore, the use of less toxic and less persistent products is highly encouraged.

It is known that the electrolysis of water enriched in salts can produce highly reactive oxidative species, which are characterized by a short life span and a potent antimicrobial activity, even at low doses.

In the last few years, our group has developed the system for the production of an electrolytically activated solution (EAS) and has been studying the beneficial microbiocidal effect of EAS on plants affected by different pathogens.

Investigations have been also focused on the effects of EAS on plant cells at the molecular level, to ascertain possible prompting of plant defences against pathogens. Through a RealTime PCR approach, we found that this solution is able to stimulate endogenous defences by a rapid and strong activation of several pathogen-related genes, when sprayed on tobacco and apple plants.

Repeated treatments with EAS amplify the gene induction pattern without showing phytotoxicity or stress effects. In addition, dedicated GC-MS analyses have shown that salicylic acid, one of the plant hormones involved in pathogen-resistance, is only partially involved in this phenomenon. These results show for the first time that EAS can be easily produced and used for the protection of crops against pathogens, with little impact on the environment and low costs. This solution is not simply microbiocidal but it also acts as signal molecule for the plant cells to synthesize defense proteins.

ELE-OR-33 Electroreduction of benzyl chloride on silver-based electrode materials in acetonitrile media: the role of water and of Ag surface

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The remarkable electrocatalytic activity of silver is well documented in the literature [1] and recently, the combination of electrochemical, spectroscopic and theoretical studies [2], using benzyl chloride (BzCl) as model organic compound, has demonstrated that the reduction pathway implies the formation sequence of silver-substrate/product adducts, starting from a weakly adsorbed benzyl chloride-Ag specie, followed by the strongly adsorbed benzyl radical-Ag and benzyl anion-Ag species. The last ultimately desorbing to give the final reaction products.
In this context the present contribution discusses the effect on the voltammetric signal of the presence of small amounts of water in the acetonitrile used as solvent. The source of proton from water may affect the normal reaction pathway and change the electrode activity. This provokes significant variations in electrode currents and potentials even at very low water content, thus providing an internal diagnostic signal for the quality of the solvent. This has immediate application to the comparison between electrode materials (e.g., massive silver, silver nanocubes and Ag-nanocubes supported on carbon) prepared by different procedures, and allows to evidence the effects of the morphology and size of silver particles on their electroactivity.

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[2] Yi-Fan Huang, De-Yin Wu, An Wang, Bin Ren, Sandra Rondinini, Zhong-Qun Tian, and Christian Amatore "Bridging the Gap between Electrochemical and Organometallic Activation: Benzyl Chloride Reduction at Silver Cathodes", J. Amer. Chem. Soc. 2010, *132*, 17199-17210; DOI: 10.1021/ja106049c

ELE-OR-34 Synthesis and characterization of materials for electrochemistry

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In this thesis work, materials that can find application in lithium ion batteries have been explored. In particular, cathode materials and electrolytes have been studied.
Concerning cathode materials, the interest have been focused on the highly studied, both in academic research and in commercial industry, $LiFePO_4$ compound, but also on NASICON type materials such as $LiTi_2(PO_4)_3$ and $Li_3V_2(PO_4)_3$. An extensive study has been carried out on $LiFePO_4$ in order to optimise its properties in view of its final application in cells. Therefore, an accurate investigation on different synthesis procedures has been carried out over the entire doctoral period. The development of a hydrothermal synthesis has allowed to obtain samples with a high level of purity and therefore suitable for the use in lithium ion batteries. Then, studies on the relationships between transport properties and microstructure of the synthesised olivine have been carried out. Our findings contribute to shed further light on the complex relationships among chemistry, morphology and electrochemical properties of the technologically relevant $LiFePO_4$ compound [1].
Many efforts were also devoted during the doctoral period to the study of electrolytes. In particular ionic liquids, being a very promising ionic transport media for liquid electrolytes, have received much attention in this thesis work. New pyrrolidinium-based and piperidinium-based ionic liquids with ether functionalities have been deeply characterized. Encouraging results have driven the work to the use of these ionic liquids in the preparation of gel polymer electrolytes and films based on the PVdF-HFP copolymer, on the thermoplastic polyurethane TPU and on PEO. The use of silica fillers in the case of PVdF-HFP and TPU based GPEs has allowed to obtain membrane with good mechanical properties and also good electrochemical features. In particular the PVdF-HFP membranes showed very good cycling performances [2].

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ELE-OR-35 Glucose electrooxidation

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The electrooxidation of glucose has attracted a lot of interest due to its application in blood glucose sensors and biological fuel cells. Glucose sensors optimization is highly necessary to improve the treatment of Diabetes Mellitus while biological fuel cells have been studied in order to explore new, renewable energy sources alternative to fossil fuels. During my PhD I worked on both *abiotical* and *microbial* electro-catalyzed glucose electrooxidation; the former (at gold electrodes) applied to glucose sensing and glucose-gluconate fuel cells, the latter for the development of microbial fuel cells (MFCs).
The complex oxidation of glucose at the surface of gold electrodes was studied in detail by cyclic voltammetry. An oxidative current peak occurs during the cathodic sweep showing a highly linear dependence on glucose concentration. Its application in blood glucose sensing has been hindered by the presence of inhibitors: chlorides are the most problematic because of their high concentration in the blood and the difficulty inherent in trying to separate them from glucose. In order to overcome this problem, on the basis of mechanistic studies, a four-step, three electrode (silver gauze, gold pin and platinum counter electrode) technique was exploited.
After optimizing fuel composition and operating conditions in order to selectively oxidize glucose to gluconate we developed a new anode material for glucose-gluconate direct oxidation fuel cells by electrodepositing gold nanoparticles on a "conductive textile" realized by conformally coating polyester textile substrates with single walled carbon nanotubes. The electrochemical characterization showed higher current densities with respect to the previously reported materials.
MFCs are devices that convert chemical energy into electrical energy by the catalytic activity of microorganisms. A novel carbon nanotube-cotton composite material with high conductivity and high porosity was proposed to be used as anode. The randomly intertwined CNT-cotton fibers create a 3D active space for biofilm growth while the incompact macroporous structure allows efficient mass transfer for microbial metabolism inside the anode. Compared to commercial carbon cloth anode, the CNT-cotton achieves 64% higher power density and 75% higher energy recovery efficiency in MFCs.

ELE-OR-36 Development and characterization of catalysts for electrolytic hydrogen production and chlor – alkali electrolysis cells

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The industrial production of chlorine is today essentially achieved through sodium chloride electrolysis, with only a minor quantity coming from hydrochloric acid electrolysis. The main problem of all these processes is the high electric energy consumption which usually represents a substantial part of the total production cost.

This activity was addressed to the investigation of the oxygen reduction at gas-diffusion electrodes as well as to the surface and morphology analysis of the electrocatalysts. Specific attention was focused on deactivation phenomena involving this type of GDE configuration. The catalysts used in this study were based on a mixture of micronized silver particles and PTFE binder. In this study, fresh gas diffusion electrodes were compared with electrodes tested at different times in a chlor-alkali cell. Electrode stability was investigated by life-time tests. The surface of the gas diffusion electrodes was analyzed for both fresh and used cathodes by scanning electron microscopy and X-ray photoelectron spectroscopy. The bulk of gas diffusion electrodes was investigated by X-ray diffraction and thermogravimetric analysis.

Water electrolysis is one of the few processes where hydrogen can be produced from renewable energy sources such as photovoltaic or wind energy without evolution of CO_2. In particular, an SPE electrolyser is considered as a promising methodology for producing hydrogen as an alternative to the conventional alkaline water electrolysis. This work was mainly addressed to a) the synthesis and characterisation of IrO_2 and RuO_2 anodes; b) conducting Ti-suboxides support based on a high surface area.

a) Nanosized IrO_2 and RuO_2 catalysts were prepared by using a colloidal process at 100°C; the resulting hydroxides were then calcined at various temperatures. The attention was focused on the effect of thermal treatments on the crystallographic structure and particle size of these catalysts and how these properties may influence the performance of oxygen evolution electrode. Electrochemical characterizations were carried out by polarization curves, impedance spectroscopy and chrono-amperometric measurements.

b) A novel chemical route for the preparation of titanium suboxides (Ti_nO_{2n-1}) with Magneli phase was developed. The relevant characteristics of the materials were evaluated under operating conditions, in a solid polymer electrolyte (SPE) electrolyser, and compared to those of the commercial Ebonex®. The same IrO_2 active phase was used in both systems as electrocatalyst.

ELE-OR-37 Electrodeposition of Metal-Oxide-Metal nanowire heterostructures for ReRAM applications

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As larger capacity is required to modern semiconductor non-volatile memories, technical and physical limits arise, which the conventional scaling down of the photolithographic technology will hardly overcome. One of the most promising approaches for future high-density mass storage is represented by the Resistive switching Random Access non-volatile Memories (ReRAM). The functioning of such memories is based on the switching between high and low conductive states under applied electrical pulses. In particular, nanoscaled Metal/Oxide/Metal (MOM) heterostructures are currently investigated as possible building blocks for memory devices beyond the 16 nm technology node [1]. Whereas the resistive switching behavior of MOM thin films has been widley investigated, a better characterization and understanding of switching phenomena at the nanoscale is still required.

In the present study, the electrochemical synthesis and resistive switching characterization of MOM heterojunctions nanowires (NWs) are addressed. MOM NW array were fabricated by electrodeposition of either Ni or Au/Ni/Au multilayers into Anodic Aluminum Oxide (AAO) templates (pore diameter og 60 nm), followed by mechanical polishing of the AAO template and thermal oxidation.

The electrodeposition of Ni and Au was carried out from sulphate-based and cyanide-based electrolytes, respectively. Mechanical polishing of the resulting AAO templates was performed in order to expose the NWs from the AAO template surface, favoring thermal oxidation and allowing the electrical characterization of the NW array. Thermal treatment were carried out at 400 °C in oxygen atmosphere for times ranging from 3 to 30 minutes. Structure and morphology of the heterojunction NWs embedded into the AAO matrix were characterized by Scanning Electron Microscopy (SEM), High Resolution Transmission Electron Microscopy (HR-TEM), X-Ray Diffraction (XRD) and Atomic Force Microscopy (AFM). The resistive switching properties of the MOM heterojunction nanowires arrays were studied by current-voltage measurements.

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ELE-OR-38 The PVD approach for the preparation of Ir-Sn dioxide thin films*

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The request for electrodes exhibiting satisfactory catalytic activity and high stability, under particular conditions of potential and current density, has stimulated the synthesis of new materials with improved performances. Among them, devices based on RuO_2 and IrO_2 found wide application in the field of DSAs (dimensionally stable anodes) for their ability to associate a good electrocatalytic activity to a high resistance to corrosion. Often, a greater stability leads to a decrease of catalytic activity, but it is possible to find a compromise by using mixtures of oxides. Besides the conductive and electroactive oxide (typically noble metal oxides, such as IrO_2, RuO_2, PtO_x and RhO_x), other oxides are added to the mixture (these are oxides of so-called "valve" metals, like TiO_2, SnO_2, Ta_2O_5, Nb_2O_5 and ZrO_2), which have the dual purpose of increasing the corrosion resistance of the electrode, and to dilute the primary oxide as to minimize the device production costs.
For the preparation of film electrodes, a physical vapor deposition (PVD) technique has been used: in particular, the attention was focused on the reactive sputtering. This method ensures a better homogeneity of the film, in terms of thickness and roughness, compared to conventional pyrolytic techniques used for electrodes preparation.
The synthesis of thin-film-electrodes was carried out at room temperature, and their characterization was attained through electrochemical as well as surface tests; then, further information was obtained studying the catalytic properties of films towards the chlorine evolution reaction.

** Premio di Laurea 2011 "Photoanalytical".*

ELE-OR-39 Electrochemical Immunosensors and Peptide Self-Assembled Monolayers for Cancer Biomarker Protein Detection

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This Thesis concerns the development of a very efficient immunosensor electrochemical device for detecting cancer biomarker proteins, and possible ways to improve its efficiency by modifying parts of the system that are relevant to improve stability and electron transfer through the modified electrode surface (see Figure 1). [1]
We focused our attention on Nanog detection. Nanog is a protein that may be involved in carcinogenesis of cervix and progression of cervical carcinoma. Nowadays, the researchers still do not know the detection limit of this biomarker and the difference of concentration between healthy individuals and patients with cancer. Therefore, we aimed at making an electrochemical sensor capable of displaying very high-sensitivity immunoarrays and low detection limit. Sensors were prepared and, particularly, several conditions to make Nanog-based electrodes were essayed. Eventually, we could optimize the conditions and obtain a nice calibration plot. Most of the initial work was carried out using the sample handling technology, but then we integrated the system into a microfluidic device, the goal being to automate the method as much as possible.
To improve the efficiency, we are about to further optimize the immunosensor by changing some elements of the transducer, particularly by using a SAM formed by peptides allowing very fast ET and by increasing the active superficial area thanks to nanostructured gold electrodes as an alternative to a bed of gold nanoparticles.
We carried out an investigation of related issues by using SAMs formed with thiolated α–aminoisobutyric acid (Aib) peptides of different lengths. The effect of the orientation of the peptide dipole moment was studied by attaching the thiolated moiety to either the nitrogen or carbon terminus.
The stability and conformational properties of such SAMs were assessed by an extensive IRRAS investigation, in comparison with the IR absorption spectroscopy of the free peptides. This study showed that, in these SAMs, most of the Aib peptides form 3_{10}-helices, and pack tightly, the surface coverage depending on both the peptide length and orientation.
The results nicely supported what recently found concerning the chemical and electrochemical stability of these SAMs as well as the efficiency of ET through them. Main outcome of this study is that we now know which peptides should

provide the best transducer substrate supporting the actual Nanog-sensor architecture.

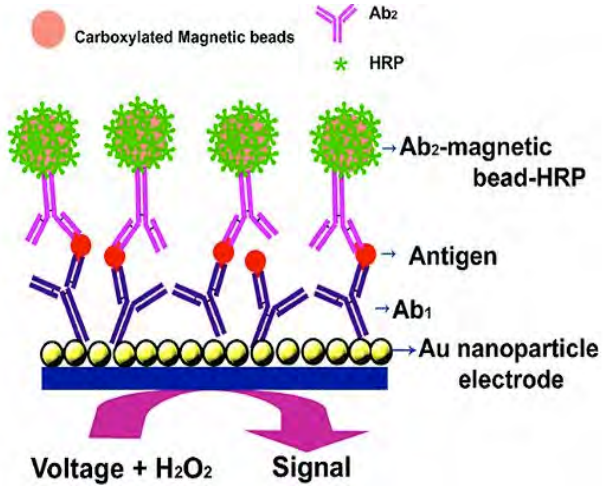

Figure 1. Scheme of the gold nanoparticles immunosensor.
The detection step involves immersing the sensor into buffer containing mediator, applying voltage, and injecting H_2O_2.

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ELE-PO-01 The electrocatalytic cleavage of carbon-halide bonds on Ag and Au in protic solvents

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In the last years we have showed in detail how the electrocatalytic cleavage of carbon-halide bonds is modulated by (a) the stepwise or concerted nature of the DET mechanism, (as a function of the electrode surface, of the nature of the halogen atom, and of the molecular structure of RX) and (b) the double layer structure (as a function of the nature and bulkiness of the supporting electrolyte ions). To both complete and support our interpretative scheme we are now concentrating on the solvent role.

Comparing aprotic with protic organic solvents after appropriate intersolvental normalization, interesting peculiarities emerge concerning protic media. Solvent proticity deeply affects both the reaction mechanism (on both non-catalytic and catalytic electrode surfaces) and the extent of the catalytic effects. We will discuss these items on the basis of a complete investigation carried out with a carefully controlled experimental protocol on two chloride and bromide couples, one aromatic and one aliphatic (representative of stepwise and concerted mechanism, respectively), in eight solvents, four of them aprotic and four protic, on the non-catalytic GC electrode and the catalytic Ag and Au ones. The results will be also discussed in the frame of our recently developed interpretative scheme of the carbon-halide cleavage mechanism.

ELE-PO-02 Controlled Aqueous Atom Transfer Radical Polymerization Under Electrochemical Generation of the Active Catalyst

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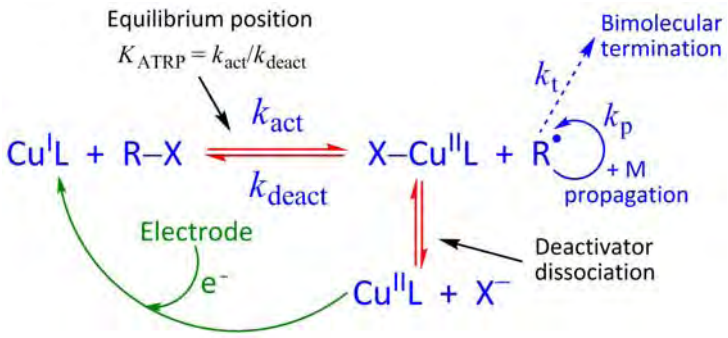
Controlled Radical Polymerizations (CRPs) in aqueous medium are very attractive from an economic and environmental point of view; besides the production of water soluble polymers, aqueous media are largely employed in the polymerization of non polar monomers through emulsion or miniemulsion techniques [1,2]. Moreover, the effectiveness of CRPs in aqueous saline buffers is a pre-requisite for the preparation of polymer-biomolecule conjugates under biological conditions [3]. Atom Transfer Radical Polymerization (ATRP) is nowadays the most used method in the field of the CRPs; despite its importance, well controlled aqueous ATRP remains a challenge, achieving only a limited success in the literature. The main drawbacks stem from a relatively high equilibrium constant K_{ATRP} and the instability of $X–Cu^{II}L$, resulting in a fast and uncontrolled polymerization. Recently, the first example of electrochemically mediated ATRP has been introduced as a technique allowing an unprecedented modulation of the rate of polymerization through the variation of the external applied potential, E_{app} [4]. In this communication, we report the successful controlled polymerization of poly(ethylene glycol) methyl ether methacrylate (PEOMA) in water under electrochemical reduction of the catalyst precursor $Cu^{II}L$ (L = TPMA, tris 2-pyridylmethylamine). Herein, we demonstrate that the magnitude of E_{app} not only acts as an electrochemical switch of the polymerization, but also as a tuner of the degree of control obtained in the final polymer.



Mechanism of electrochemical aqueous ATRP

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ELE-PO-03 BETA ALUMINA SOLID ELECTROLYTE FOR ZEBRA BATTERY

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Recently, there has been growing interest in sodium beta alumina battery technology as electrochemical energy storage systems for renewable storage. This technology is based on a solid Na^+-conducting electrolyte that separates a liquid sodium anode and a cathode containing sulphur (sodium/sulphur batteries) or metal chloride (ZEBRA batteries). The issues that hamper a widespread commercialization of this type of technology are related to the materials and manufacturing methods that affect cost, safety and performance. Beta alumina solid electrolyte (BASE) is the most widely used electrolyte in these systems because of its high Na^+ ionic conduction. β"-Al_2O_3 is the preferred phase for these applications since it exhibits a high sodium ionic conductivity (usually 0.2-0.4 S cm^{-1} at 300°C) [1]. It has been reported that the synthesis of this material by solid state reaction method starting from α-Al_2O_3 precursor yielded both β'- and β"-Al_2O_3 phases [1]. In order to identify the precursor composition suitable to achieve the highest β"-phase content, in this work the synthesis of Mg^{2+}- and Li^+-doped BASE ($Na_{1.67}Mg_{0.67}Al_{10.33}O_{17}$ and $Na_{1.67}Li_{0.33}Al_{10.67}O_{17}$ respectively) was carried out starting from different Al_2O_3 precursors such as α-Al_2O_3, γ-Al_2O_3, Boehmite (AlOOH) and Bayerite ($Al(OH)_3$) with Na_2CO_3; $MgCO_3$ or $LiCO_3$ were added as dopant. The effect of the experimental conditions on phase purity and microstructure of sintered specimens was inspected by XRD and SEM analyses. The sintering of Mg^{2+}- and Li^+-doped BASE samples were carried out by conventional heating technique. Moreover, a microwave-assisted heating process was investigated to obtain high heating rates, short holding time and attainment of the desired phase with improved homogeneity and microstructure at a significantly reduced cost. In light of the promising preliminary results, further studies with a single mode applicator are in progress, in order to evaluate the microwave absorption of these electrolyte materials and to improve the heating homogeneity, with the final aim of scaling up the process for the device development.

[1] Journal of Power Sources 195 (2010) 2431–2442

ELE-PO-04 Substrates for Energy devices

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The global environmental concerns and the escalating demand for energy, coupled with a steady progress in renewable energy technologies, are opening up new opportunities for the utilization of renewable energy resources. In this context Direct Alcohol Fuel Cells (DAFCs) represent a promising energy conversion device for mobile and stationary applications. Among the key issues to be addressed for their technological exploitation, the alcohol cross-over represents a limiting factor since the alcohol can be directly oxidized on the cathode and short-circuit the cell. In parallel, the recent improvement of anion membranes makes the development of alkaline DAFCs competitive with the acid ones.
In this work we present the preparation (electrodeposition and sol-gel) and characterization of Pt free metal and metal oxides as possible cathode and anode materials in alkaline DAFCs.
More specifically, the electrodeposition protocols include the Selective Electrodesorption Based Atomic Layer Deposition (SEBALD) used to prepare new bimetallic electrodes for fuel cells. This new method of Electrodeposition, recently pointed out in Florence on the basis of ECALE method, allows to deposit under morphological and compositional control those metals that cannot be deposited at underpotential. In parallel, low-temperature sol-gel synthetic process are adopted to produce tailored nanostructured mixed oxide disperse phase electrocatalysts, to be used as cathode material in membrane-electrode-assemblies (MEA).

Acknowledgements: The financial contributions of PRIN 2008 – "*Pt-free electrocatalysts for direct alcohol fuel cells.*" 2008N7CYL5 .

ELE-PO-05 Dissociative Electron transfer to Activated Alkyl Halide Initiators Relevant to Living Radical Polymerization.

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The mechanism of reductive cleavage of model alkyl halides (methyl 2-bromoisobutyrate, methyl 2-bromopropionate and 1-bromo-1-chloroethane), used as initiators in living radical polymerization (LRP), has been investigated in acetonitrile using both experimental and computational methods. Both theoretical and experimental investigations have revealed that dissociative electron transfer to these alkyl halides proceeds exclusively via concerted rather than stepwise manner. The reductive cleavage of all three alkyl halides requires a substantial activation barrier stemming mainly from the breaking C-X bond.

The activation step during single electron transfer LRP (SET-LRP) was originally proposed to proceed via formation and decomposition of $RX^{\bullet-}$ through an outer sphere electron transfer (OSET) process. These radical anion intermediates were proposed to decompose via heterolytic rather than homolytic C–X bond dissociation.

Here it is clearly shown that injection of one electron into RX produces only a weakly associated charge induced donor acceptor type radical anion complex without any significant covalent σ type bond character between carbon-centered radical and associated anion leaving group. Therefore, neither homolytic nor heterolytic bond dissociation applies to the reductive cleavage of C-X in these alkyl halides inasmuch as a true radical anion does not form in the process. In addition, the whole mechanism of SET-LRP has to be revisited.

The comparison of the experimental activation free energies with theoretically computed values shows a close agreement between theory and experiment. The agreement with experimental data, which fit very well the sticky model, is a relevant support for the appropriateness of this simplified model, which considers only the ion-dipole interactions.

ELE-PO-06 Pt free metal and metal oxides electrocatalysts for the Oxygen Reduction Reaction in alkaline DAFC

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Direct alcohol fuel cells (DAFCs) represent a promising energy conversion device for mobile and stationary applications. In comparison with H_2-based fuel cells, the alcohol cross-over may represent a limiting factor for their technological success since the alcohol can permeate the polymeric electrolyte and be directly oxidized at the cathode. This short-circuit implies not only an energy loss but may also result in the poisoning of the ORR electrocatalyst by CO and other products of alcohol oxidation.
In parallel the recent improvement of anion membranes, that allow for alkaline operating conditions with predictable advantages in terms of energy yield, makes the development of alkaline DAFCs competitive with the acid ones.
In this work we studied metal (Ag/C) synthetized by the wet method and metal oxides synthetized by the sol-gel technique (IrO_2-SnO_2), as possible cathode materials in alkaline DAFCs. The investigation is carried out using potentiodynamic techniques and the Rotating Ring Disk Electrode (RRDE) as support. The electrocatalytic powders are glued to the support with thin layer of Tokuyama anion exchange membrane. The influence of alcohol cross-over on the oxygen reduction reaction (ORR) kinetics was also considered.
The use of RRDE allow to obtain important information about the reaction mechanism since it is possible quantify *inter alia* the amount of hydrogen peroxide produced in a broad range of potentials.
A comparison study of different electrode materials in term of kinetic current, amount of hydrogen peroxide produced and the potential of the beginning the ORR was carried out. A interesting dependence of morphology and size of the Ag nanoparticles and of the iridium content (15-100%mol) on the ORR activity is observed.
The influence of the alcohol cross-over on the oxygen reduction reaction (ORR) kinetic is also presented and discussed.

Acknowledgements: The financial contributions of PRIN 2008 – *"Pt-free electrocatalysts for direct alcohol fuel cells."* 2008N7CYL5 and PUR-Università degli Studi di Milano (2009 – 2010) funds are gratefully acknowledged.

ELE-PO-07 Spontaneous Deposition of Palladium onto Fecralloy®. Characterization of Pd-modified Fecralloy® Foam Electrodes

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Fecralloy® is a ternary alloy that typically contains 65-70 At% Fe, ca. 20 At% Cr and 10-15 At% Al. Owing to its very high stability at high temperature it is often used as supporting material for hydrocarbon oxidation catalysts, both in devices for low-temperature catalytic combustion and for pollutants abatement.
We report on the spontaneous deposition of Pd on either Fecralloy® sheets or Fecralloy® foams with variable grade, defined by the number of pores per linear inch (ppi), by simple immersion of the Fecralloy® samples in acid $PdCl_2$ solutions, and on the characterization of the resulting materials by electrochemical and microscopic techniques. Although the final aim of this work is the preparation of catalysts for the gas-phase oxidation of biofuels, the Pd-modified Fecralloy® foam electrodes were preliminarily tested as anodes for the anodic oxidation of alcohols in alkaline media. Figure 1 shows cyclic voltammograms recorded with Pd-modified Fecralloy® foam electrodes in KOH and KOH+methanol solutions, for 3 different foam grades corresponding to different electrochemically active areas per unit foam volume.

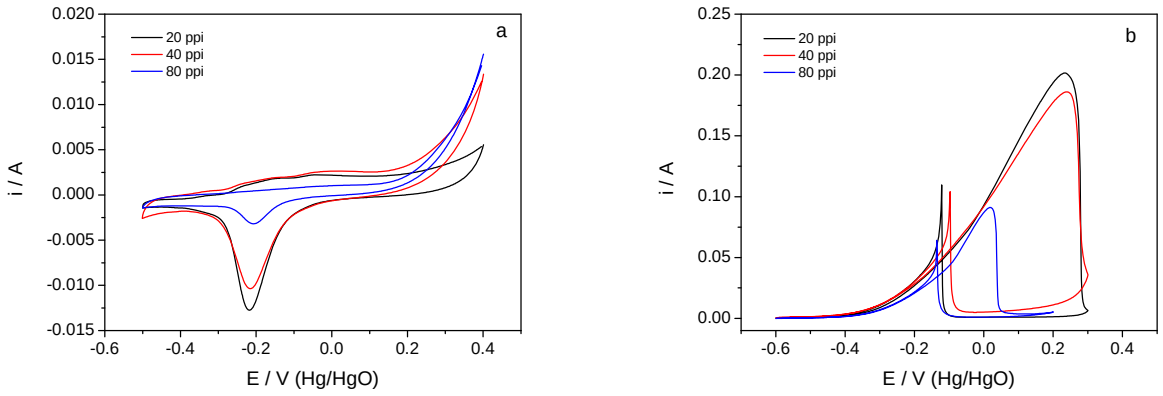

Figure 1. Voltammetric responses of Pd-modified Fecralloy® foam electrodes in 1 M KOH (a) and 1 M KOH + 0.5 M methanol (b). Electrode volume: 0.3 cm^3.

Acknowledgments. The authors acknowledge the financial support of the Italian Ministry for Economic Development (MSE) – MSE-CNR Agreement on National Electrical System.

ELE-PO-08 Synthesis of $LiFePO_4$/C cathode materials for Li secondary battery

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Recently, $LiFePO_4$ has received a lot of attention, owing to its potential use as a cathode material in the next-generation lithium-ion batteries [1]. It features several interesting properties, such high specific capacity (170 $mAhg^{-1}$), high thermal stability and excellent electrochemical performance, and is low cost and not toxic. However the compound is an electric insulator at r.t. (10^{-9} Scm^{-1}) and it shows low Li^+ ionic mobility. In order to improve the physical properties of the material many studies have been focused on finding means to reduce these mentioned drawbacks. Several methods of synthesis of $LiFePO_4$ are known in the literature the most used ones being the solid state reaction and carbon-thermal reduction. The latter favors the formation of $LiFePO_4$/C composite, which shows a measurable electrical conductivity. Here we report on an original synthetic route to prepare $LiFePO_4$/C composites [2,3]. The idea behind it was to provide a precursor source containing iron, phosphorus and carbon, and, for this purpose, an appropriate hybrid organic-inorganic iron(II)-phenyl phosphonate, $[Fe(C_6H_5PO_3)(H_2O)]$ has been chosen. This compound is stable to the air and, when mixed with Li_2CO_3, under heat treatment provides sub-micrometric carbon coated $LiFePO_4$/C composites. The thermal decomposition was carried out in a furnace by varying the experimental conditions, *i.e.* different heating temperatures, calcination times and inert gases in order to investigate the influence of the latter on the final product. The samples were characterized by elemental analysis, TG/DTA, X-ray powder diffraction analysis (XRPD), FT-IR spectroscopy. The morphology of the final products was investigated by means of scanning electron microscopy (SEM). The dependence of particle size and the role of impurities on the electrochemical behavior of the cathode material will be presented and discussed.

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ELE-PO-09 Novel acidic hydrogel electrolytes based on PVA and PVA blends

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Polymeric gels are attracting growing attention as "intelligent materials" because of their peculiar performances. They are materials with a network structure and can swell considerably in aqueous medium without dissolution [1].

In recent years, use of solid or gel electrolyte in batteries and other electrochemical devices has been considered especially for improving reliability, safety, flexibility and processability [2].

Research for materials with high ionic conductivity, large transport number, good electrochemical stability and mechanical strength is a very important part of the effort for synthesizing new solid polymeric electrolytes (SPEs) for different applications.

Due to its unique structure, chemical properties of polyvinyl alcohol (PVA) can be tailored either adjusting the hydrolysis degree or blending PVA with other polymers. PVA is a biocompatible and nontoxic polymer and exhibits minimal cell adhesion and protein absorption; in addition it has good chemical stability and can be easily gelled by a crosslinking agent.

We synthesized an acidic polymer hydrogel electrolyte using a methan sulfonic acid aqueous solution, PVA and glutaraldehyde solutions.

The polymer hydrogel viscosity was controlled adjusting the glutaraldehyde concentration, used as crosslinking agent: the relationship between its concentration and hydrogel viscosity was determined. For the use as gelled electrolyte in nanostructured electrochemical cells, the best compromise between viscosity and electrical conductivity was found, leading to performances close to those of the methan sulfonic acid solution.

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ELE-PO-10 Effect of Different Carbon Electrode Materials on the Specific Capacity of Non-aqueous Li-O_2 Cells in Various Electrolytes.

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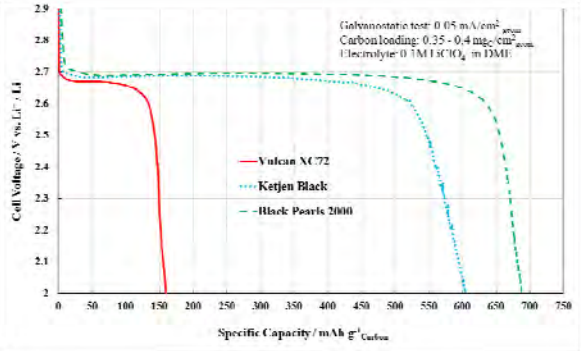
The demand for higher energy density power sources for future sustainable transportation has triggered the development of new Li-battery chemistry concepts. Since for current Li-ion batteries the positive electrode limits the specific energy of the battery, its improvement in capacity can lead to a remarkable increase of energy density in the whole battery, even more than improving its working voltage to ≈5 V vs. Li pursued in high-voltage cathode concepts [1]. Mankind use of the Oxygen Reduction Reaction (ORR) at the positive electrode in the so-called Li-Air battery could lead to a three-fold increase in specific energy for fully packaged batteries compared to state-of-the-art Li-ion batteries [2].

Some crucial factors for the optimization of the positive electrode are the specific surface area of the carbon material, affecting specific capacity and rate capability, and the binder/carbon ratio, which affects electrode porosity, oxygen diffusivity, and resistivity. On the other hand, the stability of the electrolyte in presence of the ORR intermediates like the superoxide ion-radical [3] and the stabilization of such intermediates with the solvent [4] are other very important factors to be taken into account.



In this contribution we examine the effect of different carbons as positive electrode materials on the specific capacity and cyclability of the test cells (Figure 1) in various organic solvents as electrolyte media.

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ELE-PO-11 Environmentally friendly corrosion inhibitor of the copper in 0.5 M sulphuric acid solution.

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Copper corrosion inhibition by gramine [3-(dimethylaminomethyl)indole] in the 0.5 M sulphuric acid solutions was studied in the temperature range 25-55 °C using electrochemical impedance spectroscopy techniques (EIS).

Gramine was dissolved at various concentrations (from $5 \cdot 10^{-4}$ to $7.5 \cdot 10^{-3}$) in 0.5 M sulphuric acid. The surface preparation of the specimens was carried out using silicon carbide paper up to grade 1200.

EIS measurements were performed after dipping the working electrode into the 0.5 M sulphuric acid solutions with or without inhibitor at E_{corr} with an a.c. voltage amplitude of 5mV. The frequency range was swept between 100 kHz and 10 mHz with 10 point for hertz decade.

The presence of gramine led to changes of the impedance plots in both shape and size. The plots of Nyquist exhibited that some impedance spectra consisted of one capacitive loop at the higher frequencies which was attributed to a faradaic process involving a charge transfer resistance in parallel with double-layer capacitance element [1]. The size of the capacitive arc increased by increasing the concentration of gramine. This indicated that gramine increased the charge transfer resistance and then it had an inhibiting effect on copper corrosion in 0.5 M sulphuric acid solutions. Inhibition efficiencies results showed that the gramine inhibited the copper corrosion in the temperature range 25-55 °C reaching the maximum value of 86% at 55 °C.

Impedance spectra also showed a depression of Nyquist-plot semicircles that can be related to the surface heterogeneity due the microscopic roughness of the electrode surface and inhibitor adsorption [2]. Moreover at the lower frequencies in both the uninhibited solutions and inhibited ones by lower inhibitor concentrations, the Warburg impedance appeared. In the copper corrosion in oxygenated sulphuric acid solutions at E_{corr} the anodic reaction is copper dissolution and cathodic reaction is oxygen reduction being the hydrogen discharge current density negligible as compared to oxygen reduction current density. Then the Warburg impedance could be attributed to oxygen transport from the bulk solution to the copper surface [3].

The adsorption behaviour of gramine followed Temkin's isotherm. The values of the standard free energy of adsorption of the gramine at 25 °C, 35 °C, 45 °C and 55°C were calculed.

A structural model of the interface copper/0.5 M H_2SO_4 was proposed.

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ELE-PO-12 Modulating Interfacial Interaction in the Electron Transfer Process of an Immobilized Cupredoxin

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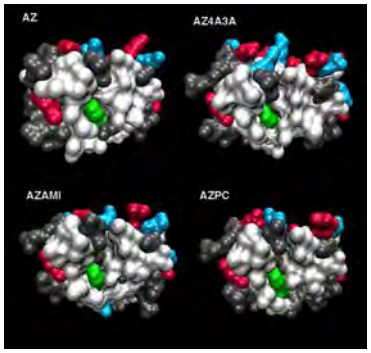
The hydrophobic patch involved in the electron transfer (ET) reaction of *Pseudomonas aeruginosa* azurin (AZ) was modified by mutating the C-terminal copper-binding loop. These proteins were non-covalently adsorbed onto gold electrodes modified with alkanethiol self-assembled monolayers (SAMs). In this way, a series of constructs were obtained which feature protein-SAM interactions of variable strength due to alterations in the area of azurin's hydrophobic patch. The distance-dependence of the ET kinetics for these adsorbed chimeric cupredoxins, measured through cyclic voltammetry using alkanethiols SAMs of variable chain length, indicate that the activation barrier for short range ET is dominated by the dynamics of molecular rearrangements accompanying ET at the protein-SAM interface. Contributions from internal protein dynamics and solvent molecules, but not protein reorientation, appear to be involved. This work provides direct experimental evidence for this mechanism which was proposed previously for azurin and also for electrostatically and covalently immobilized cytochrome *c*. This mechanism may therefore be utilized for short-distance ET irrespective of the type of metal center, the surface electrostatic potential and the nature of the protein-SAM interaction. The high electric field generated at the SAM-solution interface under these conditions would mimic those at the membrane-solution interfaces, where most ET proteins operate, therefore this mechanism is of relevance for physiological redox chains.



ELE-PO-13 RECLAMATION OF SOILS CONTAMINATED BY CHLORINATED ORGANICS: RESULTS FROM ELECTROOXIDATION TESTS

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The *in situ chemical oxidation* (ISCO) is a technology that requires injecting an oxidant into the ground, in order to treat organic pollutants (present in the soil matrix, or possibly in the groundwater).
A specific oxidant is chosen evaluating laboratory tests where the reactivity between the organic pollutants (targets) and the oxidant is assessed; concerning the area to be remediated, pre-treatment investigations are generally limited to the determination of pollutants distribution into the site, the characterization of the latter being realized through geological, topographical and hydrodynamic studies. Both an appropriate distribution of the oxidant in the subsurface, which must cover the entire impacted area, and the total amount of oxidant to be used are essential factors, deciding of the effectiveness of the approach to the field. In the traditional application scheme, the recourse to ISCO is usually limited to soils having medium to high permeability, and where the chemical oxidant demand is limited. Typically, the ISCO technology is applied to fields of prevalently sandy or gravelly character; however, if the matrix is characterized by a chemical oxidant demand much greater than that of polluting targets, the ISCO remediation does not appear to be feasible. The possibility of assisting the ISCO technology using an electrokinetic treatment, aiming at mobilizing the oxidant in soils with low permeability, through phenomena such as electromigration and electroosmotic flow, will be discussed. Besides, laboratory tests have shown that the application of an electric field can lead to a reduction of the aforementioned chemical oxidation demand of the soil, as well as of the concentration of halogenated pollutants (a phenomenon merely mentioned in the literature, and to whom the name of "*in situ electro oxidation*", ISEO, was given).
To deal with soils having a high chemical oxidation demand, a preliminary ISEO treatment may then allow the subsequent application of ISCO.

ELE-PO-14 Reverse electro dialysis processes. Selection of redox processes and electrodes.

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The extraction of the "osmotic energy" from two salt solutions showing a large difference in salt concentration is called salinity gradient power (SGP) 1-15. The potential energy available is very high; the osmotic energy in 1 m^3 of seawater is 0.75 kWh, equal to lifting a mass of 1000 kg to a height of 270 m. For exploiting this energy: (a) pressure retarded osmosis and (b) reverse electrodialysis, have been suggested. A proper selection of redox processes and electrodes is necessary to perform successfully the reverse electrodialysis process. The appropriate redox couples and electrode materials should be characterized by high chemical and electrochemical stability, fast electrochemical reaction of the redox couple, no poisoning of electrodes and membranes, low cost and absence or minimization of waste water treatment requirements.
A large number of redox processes and electrodes has been recently studied in our laboratories by electroanalytical investigations, electrolyses in divided and undivided cells and experiments performed in small stacks in order to select proper electrode processes for a reverse electrodialyis process.

ELE-PO-15 Electrochemical deposition of different semiconductors for application in solar cells.

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Among the latest generation solar cells, those based on copper, indium, gallium and selenium (CIGS) compounds are very interesting, because they show many advantages including high efficiency of energy conversion and excellent long-term reliability [1-2]. Recently, using a CIGS thin-film [3] the world highest photovoltaic energy conversion efficiency among flexible solar cell (15.9 %) was achieved. Interest towards flexible thin-film solar cells is due to their possible installation on curved surfaces and/or structurally weak supports, but also to their possible use as a power source for mobile devices.
Goal of this work is to show the fabrication of flexible thin-film CIGS/ZnS solar cells using a very simple method, which can be extended easily to large areas. In particular, thin films were obtained on a flexible substrate (PET/ITO) by potentiostatic deposition from aqueous baths. Different deposition parameters (bath composition and temperature, deposition time) were tested in order to obtain deposits with stoichiometric composition.
Films characterization was performed using several techniques (EDS, SEM, RAMAN, XRD) giving information on both chemical composition and structure. Preliminary results on the photoelectrochemical behavior of ZnS thin films will be also presented and discussed.

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ELE-PO-16 Performance of a DEFC for PtxSny/C catalysts prepared with formic acid

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There is presently a great interest on Direct Alcohol Fuel Cells, particularly on the Direct Ethanol Fuel Cell (DEFC), because it is a renewable and low toxic fuel. Pure platinum is not the most efficient anode catalyst for DEFC, because its surface is rapidly poisoned by strongly adsorbed species coming from the dissociative adsorption of ethanol. Thus, addition of a second metal has been proposed to alleviate this problem. In this sense, tin has demonstrated to be the most effective one. However, the performance and efficient to ethanol oxidation of PtSn catalyst highly depends on its composition and structural characteristics (degree of alloying and oxide content). In this sense, this work intends to elucidate the effect of the composition of different PtSn/C catalysts prepared by reduction with formic acid, using different reducing agent (formic acid) concentration. Four different Pt:Sn ratios were studied, 9:1, 3:1, and 1:1 on 60% metal on carbon catalyst, using three different formic acid concentrations (0,5, 1 and 2 M). EDX, XRD, TEM and XPS were used for physico-chemical characterisation. Electrochemical performance was studied on an actual fuel cell setup. Studies indicate that the modification of Pt by tin1gives very interesting results leading to the oxidation of ethanol at lower potentials than on pure platinum. The presence of Sn oxides on the catalyst surface can supply surface oxygen-containing species for the oxidative removal of CO and CH_3CO species adsorbed on adjacent Pt active sites, enhancing in this way the ethanol electro-oxidation activity at low potentials.
Best electrochemical performance and efficiency was achieved for the composition PtSn/C prepared with 0,5 M formic acid, achieving a power peak of approximately 45 mW/cm^2 at 90°C and 2 relative bars in the cathode. Reasons for this arise from the small particle size achieved, and the existence of an optimum ratio degree of Sn alloyed/oxide amounts, as XRD and XPS results confirmed. Lower Sn amounts did not favour the cell performance, because of the diminution of the synergic tin effect.

An excess of Sn decrease the cell performance for two reasons: (i) probably excessive amount/formation of SnO_2 semi-conductive species, and (ii) poorer platinum distribution in the catalyst in order to perform the ethanol dehydrogenation. Formic acid concentrations mostly affect the particle size, with an increase the higher is the amount of reducing agent in the synthesis medium.

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Chimica Farmaceutica

FAR-PL-01 Orthosteric and Allosteric Ligands Selectively Acting at Cholinergic Receptor Subtypes

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The presentation will focus on the results recently achieved by our research group in the design, synthesis and pharmacological evaluation of selective ligands which target cholinergic receptor subtypes, belonging to both the nicotinic (nAChR) and the muscarinic (mAChR) acetylcholine receptor families.

A set of spirocyclic derivatives will be illustrated, in which the simultaneous presence of the quinuclidinyl and Δ^2-isoxazolinyl moieties, coupled with suitable stereoelectronic features of the substituent at position 3 of the spirocyclic ring, engendered a selective agonist profile at the homomeric neuronal α7 nAChRs [1]. The most promising compound in the series has been further investigated in preclinical studies and in *in vivo* models of CNS disorders and neuropathic pain. A group of novel hybrid peptides structurally related to natural α-conotoxins MII and PIA will be also presented, which behave as competitive antagonists able to discriminate α6β2* and α3β2* nAChR subtypes [2].

The five mAChR subtypes bind their physiological transmitter in the highly conserved orthosteric site within the transmembrane domains of the receptors. Orthosteric muscarinic agonists have negligible binding selectivity and poor signaling specificity. A less conserved allosteric site has been also characterized at the extracellular entrance of the binding pocket of mAChRs. To gain subtype-selective M_2 receptor activation, we designed a group of putative bitopic compounds, i. e. hybrid derivatives fusing highly potent, unselective oxotremorine-like orthosteric activators with M_2-selective bis(ammonio)alkane-type allosteric fragments. The new ligands interacted simultaneously with both recognition areas of the receptor protein, thus allowing the exploitation of favorable features of the orthosteric and the allosteric site by a single ligand molecule. The orthosteric interaction provided high affinity binding and activation of M_2 mAChRs. The allosteric interaction yielded receptor subtype-selectivity and, in addition, could modulate efficacy and activate pathway-specific intracellular signaling [3].

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FAR-PL-02 Modulation of Hydrolysis of Fatty Acid Ethanolamides: Rational Drug Design for Novel Therapeutic Opportunities

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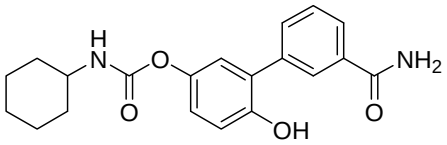
Fatty acid ethanolamides (FAEs) are a class of bioactive lipids, the effects and metabolism of which can be modulated by new compounds with potential application in different therapeutic areas, e.g. the treatment of pain and inflammation. Two relevant members of this family are anandamide, an endocannabinoid, and palmitoylethanolamide (PEA), endowed with anti-inflammatory activity. Selective control of their levels may be achieved through the design of new compounds, either affecting FAE metabolism at different levels or having tissue-selective distribution.



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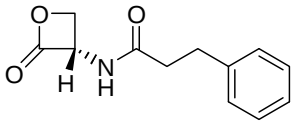

(*S*)-OOPP

This lecture will focus on the development of carbamate-based inhibitors of Fatty acid amide hydrolase (FAAH), and of the first potent and selective inhibitors of N-acylethanolamine-hydrolyzing acid amidase (NAAA). Starting from the well-known FAAH inhibitor URB597, through the study of its inhibition mechanism by molecular modelling [1] and of structure-reactivity relationships we developed *p*-hydroxy derivatives with improved *in vivo* properties. This class includes URB937, a peripherally-restricted FAAH inhibitor with remarkable analgesic activity [2].
NAAA is a lysosomal enzyme which preferentially hydrolyzes PEA. Homology-based models, supported by mutagenesis studies, helped the discovery of a new class of NAAA inhibitors, including the stereoselective compound (*S*)-OOPP [3]. This compound showed remarkable anti-inflammatory activity and allowed a better characterization of the role of NAAA activity in inflammation.

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FAR-PL-03 Advances in the Characterization of New Challenging GPCRs

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Purinergic receptors are classified in P2X, a ligand-gated ion channel family, activated by ATP and ADP, and P1 and P2Y, two G protein-coupled receptor (GPCR) families, activated by adenosine and purine/pyrimidine nucleotides, respectively. They are widely distributed in the body and involved in several cellular functions, most of them still poorly understood, although in recent years a number of clinical applications of purinergic receptor ligands have been proposed and few compounds are already on the market or in clinical trials.
Purinoceptor families include also purinergic-like receptors, which need to be better characterized and, between them, the recently deorphanized GPR17 seems to be dually activated by uracil nucleotides and cysteinyl-leukotrienes. GPR17 was found to be highly expressed in organs typically undergoing ischemic damage, thus representing a potential target for new therapeutic approaches to acute and chronic neurodegenerative diseases.
Characterization of this receptor has been performed on transfected 1321N1 cells by using [^{35}S]GTPγS binding assay. Known and newly synthesized nucleotides were screened and proved to behave as ligands for this receptor with a wide range of activity. Moreover, an innovative and non-radioactive functional cAMP assay was validated, which showed a strong correlation with the data obtained with [^{35}S]GTPγS binding assay and confirmed that GPR17 is coupled with a Gαi [1].
Furthermore, specific binding sites for [^{3}H]-guanosine, which are not recognized by other purinergic receptor ligands, were detected on membrane preparations from rat brain. These findings supported the hypothesis of the existence of a specific GPCR for guanosine that could account for the actions played by this naturally occurring purine nucleoside. An innovative assay was optimized for the characterization at rat brain membranes of the putative guanosine binding site by using a series of known and novel guanosine derivatives, prepared by modifying the purine and the sugar moiety of guanosine. Results of these experiments proved that guanosine, 6-thioguanosine, and their derivatives activate a new GPCR, which is different from the well characterized adenosine receptors [2].

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FAR-PL-04 Multidisciplinary and Multitarget Approaches in the Search for Novel Drugs in the Treatment of Neurodegenerative Diseases

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Research in medicinal chemistry has recently shifted towards the design of multitarget/multipotent agents that, interfering with different biological pathways critical for either the onset or the progression of a given disease, may have higher therapeutic benefits compared to single-target–selective drugs [1,2]. Multitarget ligands would be simpler to develop in a clinical setting and present lower risks of drug-drug interactions compared to multicomponent drugs and drug combinations. On the other hand, the design and optimization of multiple ligands exhibiting high and, more importantly, well-balanced affinities at selected targets, is quite a daunting task.

Within this challenging scenario, we developed new multitarget ligands which act as reversible, dual MAO-B and acetylcholinesterase (AChE) inhibitors [3,4] or as ChE inhibitors and beta-amyloid (Aβ) anti-aggregating agents [5], with the potential for treating Alzheimer's disease (AD) [6].

In a parallel research, we have been working along the amyloid hypothesis of AD that has led to a deeper understanding of the pathology of AD and has provided insight into the design of novel potential drugs [7]. According to this hypothesis, the increase of Aβ production and aggregation into low-molecular weight oligomers, fibrils and, ultimately, amyloid plaques are the leading cause of AD. The reduction of both Aβ formation (with β- and γ-secretase modulators) [8] and aggregation and the increase of Aβ clearance (with active and passive immunization) [9] are promising therapeutic strategies for AD. Pursuant to the development of a fast spectrofluorimetric method for the kinetic analysis of Aβ aggregation [10], a screening of medium-sized molecular libraries was carried out and several classes of novel anti-aggregating agents, including two anticancer drugs, have been discovered.[11,12] The optimization of the most interesting molecules afforded compounds capable of blocking Aβ-fibril formation at a sub-micromolar concentration. Spectroscopic, analytical and biophysical methods have been used to elucidate the inhibition mechanism of Aβ aggregation. Among them, capillary electrophoresis proved particularly efficient to detect the oligomeric species targeted by the compounds blocking Aβ fibril formation.[12] Finally, molecular dynamics simulations on carefully conceived model systems have shed light on Aβ fibril formation and on how small molecules may hinder the early phase of Aβ aggregation.[13]

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FAR-KN-01 Furthering the Understand of Polypharmacology in Nuclear Receptor Superfamily.

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Recent years have seen an increasing awareness that drugs often bind to more than one molecular target, exhibiting polypharmacology [1]. Although this aspect has commonly been considered as undesirable promiscuity being responsible for unwanted side effects, in many cases it is a key component to the therapeutic efficacy of drugs [2]. The knowledge on polypharmacology can therefore aid the explanation of why some drugs work better than expected, or why other drugs have diverse side effects, albeit acting on the same target.
Polypharmacology is the result of poor ligand specificity that combines with protein promiscuity [3]. Accordingly, in order to further the understand of polypharmacology, both ligand-based and protein-based computational techniques are being developed that provide predictions of proteins to which ligands are likely to bind [4].
In this communication, we investigate aspects of polypharmacology in the superfamily of human nuclear receptors (NRs). Human NRs comprise 48 members of ligand-dependent transcription factors that offer important druggable targets for therapeutic interventions in multiple disease areas [5]. Many NRs are promiscuous with respect to the wide range of ligands that act as modulators, and many NR modulators are not specific with respect to the number of NRs they bind.
The construction of a target-centric chemical space [6, 7] and the application of integrative approaches are discussed as instrumental in charting key components and interactions of NR binding sites, with the aim of aiding the rationalization and optimization of selectivity and/or multi-target profile of selected NR ligands.

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FAR-KN-02 Optimization and simplification of pyrazolo-triazolo-pyrimidine nucleus for searching new adenosine receptor antagonists

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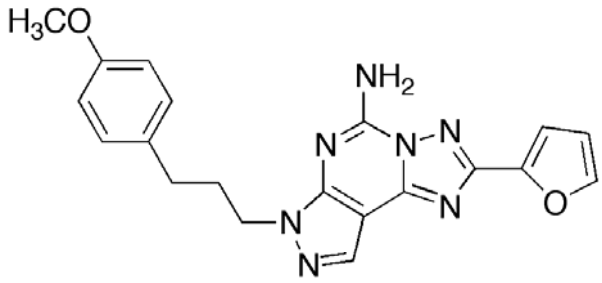
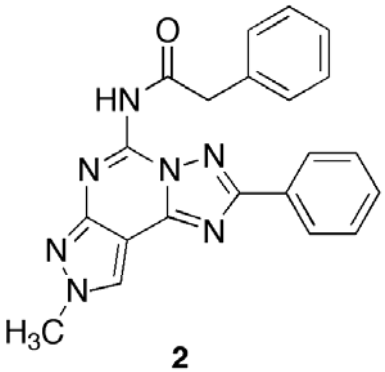
Blokade of adenosine receptors (ARs) is largely responsible for the broad variety of effects in several organ systems permitting to consider that regulation of ARs has substantial therapeutic potential. In antagonists field several classes of heterocyclic derivatives have been reported as ARs antagonists with high levels of both affinity and selectivity. In particular our group in the last years deeply investigated the nucleus of triazolo-pyrazolo-pyrimidine as ARs antagonists. Modulating the substitution at the N5, N7 and N8 positions potent and selective A_{2A} (**1**) and A_3 (**2**) ARs antagonists have been synthesized.[1] Nevertheless this class of compounds, such as other tricyclic structures, showed several problems such as poor water solubility and most importantly tangled synthetic preparation.

On these bases we focused our attention versus the optimization and a simplifications of this nucleus in order to avoid the problems related to this structure. All the obtained results will be summarized. [2,3]



SCH 442416, **1**
hA_1 = 1,111 nM
hA_{2A} = 0.048 nM
hA_{2B} = >10,000
hA_3 = >10,000



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hA_1 = 562 nM
hA_{2A} = 778 nM
hA_{2B} = >10,000
hA_3 = 0.108 nM

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FAR-KN-03 Immobilized enzymes as Efficient tools in drug discovery

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Immobilised enzyme reactors (IMERs) have proven to be a useful and economic alternative to conventional in-solution methods, when increased reliability, automation and fast data output are required. In particular, considering the high cost and difficulty in over-expression, isolation and purification of recombinant enzymes, this analytical technique represents an extremely useful approach to preserve the activity when a small amount of enzyme is available. In the IMER format, enzymes are ready to be reused and can be coupled to chromatographic systems and appropriate detectors (UV-Vis, MS, FL). This coupling generally increases automation, reproducibility and analyses accuracy and reduces sample handling and operator time consumption.

In the field of drug discovery, IMERs can be reliably applied to different phases of the drug discovery pathway, i.e., to rapidly screen for potential drugs candidates (lead selection), to characterize the mode of action at specific targets and perform SAR studies (lead optimization), and to determine ADMET parameters (early ADMET studies). In fact, in a second stage following the screening step, selected hits need to be further characterized in terms of mechanism of action and kinetic parameters.

In this talk, a few IMERs applications will be presented, useful in all the steps of drug discovery and development. At this regard, acetyl-, butyryl-cholinesterase and BACE-1 (beta secretase) immobilized reactors were validated for the screening and determination of the mechanism of action and inhibitory constants of new leads for the treatment of Alzheimer's disease in a highly reliable and automated mode. Remarkably, besides representing valid tools to screen new reversible inhibitors, immobilized reactors were also used to characterize pseudo-irreversible inhibitors.

In drug development stage, the monolithic disk-shaped mini-columns (2 mm x 6 mm I.D.) containing immobilized 2D6 and 3A4 isoforms of cytochrome P450 were developed as tools for phase I drug metabolism studies, for the early estimates of the drug metabolism, toxicity and possible drug-drug interactions.

FAR-KN-04 From the central benzodiazepine receptor to the adenosine receptors exploiting the 3-diketoindole moiety.

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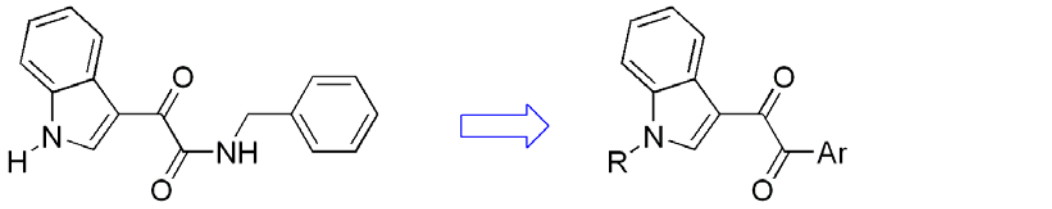
The first non-xantinic antagonists at the adenosine receptors (ARs) were reverse agonists at the benzodiazepine receptor (BzR) showing SNC stimulating properties [1].

Some time ago our research group disclosed 3-aryl[1,2,4]triazino[4,3-*a*]benzimidazol-4-(10*H*)-ones as A_1 AR antagonists designed by modifying analogous compounds binding to the BzR [2].

Following a similar approach, we have more recently investigated indol-3-ylglyoxylyamides as potential AR antagonists starting from previously reported chemically analogous BzR ligands. As a reference compound we selected the high affinity indol-3-ylglioxylylbenzylamide (**1**) which was modified taking into account pharmacophore-based and modelling studies (Fig. 1) [2].

In this lecture, the design, synthesis and biological activity of a number of new compounds featuring the 3-diketoindole moiety will be presented.



1

R = $CH_2C_6H_5$, $CH_2CH_2C_6H_5$
Ar = C_6H_5, 2-furyl, 2-thienyl, ...

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FAR-KN-05 Design and in vivo evaluation of PET radiotracers for imaging P-gp expression

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ABC transporters, in particular P-gp, BCRP, and MRPs are highly expressed in various physiological barriers such as blood-brain barrier, blood-testis barrier, blood-tumor barrier [1]. They modulate the accumulation of various drugs by active efflux transport. It has been demonstrated that changes in ABC transporter expression and function are involved in various neurodegenerative pathologies such as Alzheimer's and Parkinson's disease as well as epilepsy [2]. Moreover, the overexpression of these transporters in tumour cells causes Multidrug Resistance. PET radiotracers allow a noninvasive in vivo imaging of transporter function and expression. Recently several probes have been developed but their unfavorable pharmacodynamic and pharmacokinetic properties limited the in vivo investigation [3]. The design of new imaging probes to visualize efflux transporters is complicated by the overlapping substrate recognition pattern of different ABC transporter types. Three probes for PET analysis displaying favorable preclinical studies will be presented:
- **[11C]MC266**, a P-gp substrate, to image the pump activity;
- **[11C]MC18**, a P-gp inhibitor, to detect the pump expression;
- **[11C]MC113**, a P-gp substrate, to identify chemosensitive and chemoresistant tumors [4]

[1] W. Löscher, H. Potschka, *Prog. Neurobiol. 76*, **2005,** 22.
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FAR-KN-06 Design, synthesis and biological evaluation of potent and selective non-hydroxamic matrix metalloproteinases inhibitors

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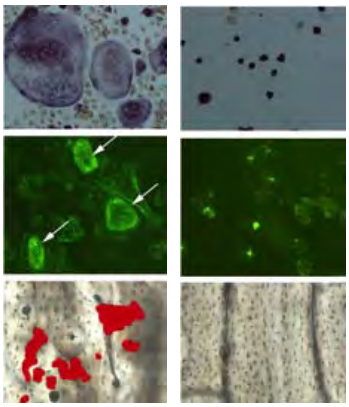
In the last 20 years, a great variety of synthetic, low molecular weight MMP inhibitors (MMPIs) have been synthesized and tested, and some of them entered phase III clinical trials as anticancer drugs, although none has reached clinical utility. A general structure for an effective MMP inhibitor includes a zinc-binding group (ZBG) capable to bind the catalytic zinc (II) ion of these proteinases, at least one functional group that provides crucial H-bonding interactions with the enzyme backbone and one or more side chains giving rise to effective van der Waals interactions with the enzyme subsites.



The hydroxamic acid group is by far the most commonly used ZBG in inhibitor design and has generally been found to be the most effective. Hydroxamate binds the catalytic zinc (II) ion in a bidentate fashion, blocking substrate access to the active site and rendering the metal incapable of peptide hydrolysis. The failure of hydroxamic acid-based MMPIs in vivo may stem from poor pharmacokinetics (low oral bioavailability and short half-life), from the ability to bind other metal ions, and from the lack of specificity due to very strong binding to the catalytic zinc ion. As a consequence, it has been pointed out that the design of selective inhibitors should involve weaker ZBGs to effectively modulate affinity by variation of substituents on the molecule scaffold.
With a single coordinate bond to the metal center, inhibitors with monodentate ZBGs (such as carboxylic acids or phosphonic acids) are generally weaker inhibitors. We have been studying non-hydroxamic MMPIs for a long time, with a particular attention towards phosphonic derivatives.[1-3]
In this lecture, the design, synthesis, structure-activity relationship and in vitro pharmacological evaluation of new phosphonic MMPIs will be presented.

[1] G. Pochetti, E. Gavuzzo, C. Campestre, M. Agamennone, P. Tortorella, V. Consalvi, C. Gallina, O. Hiller, H. Tschesche, P. A. Tucker, F. Mazza, *J Med Chem 49*(3), **2006**, 923.
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FAR-KN-07 4-Phenyl-2-propionamidotetralin derivatives: useful ligands to define the stereochemical requirements for MT_2-selective melatonin receptor antagonists

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Understanding the therapeutic potential of melatonin (*N*-acetyl-5-methoxytryptamine, MLT) has become an interesting topic in medicinal chemistry research, and MT_1 and MT_2 receptors are emerging as possible therapeutic targets for sleep disorders and depression. Three therapeutic agents (Circadin®, Rozerem®, and Valdoxan®) are already in use, and other compounds are currently under study for the treatment of sleep disturbances or depression.[1] Consistent information is available for non-selective MT_1/MT_2 ligands, and several molecular models, both ligand- and receptor-based, have been proposed to rationalize their SARs.[2] On the contrary, only limited data on MT_1 or MT_2 subtype-selective compounds are available up to now, and a clear definition of the structural requirements for subtype selectivity is still lacking. During the present decade, SAR investigations on melatonin receptor ligands were therefore aimed at both the discovery of new chemical classes and the definition of structural requirements for subtype selectivity.

Conformational restriction of bioactive molecules is a valuable tool for investigating the topographical and chemical features of small-molecule ligands. For instance, the β-aminotetralin skeleton has been successfully used as a rigid template for the synthesis of non-indolic melatonin-like agents, and several other substances possessing important biological activities. 4-Phenyl-2-propionamidotetralin (4-P-PDOT) [3] is a prototypical MT_2-selective ligand employed in pharmacological tests to discriminate the role of MT_1 and MT_2 receptors in MLT mediated effects. Despite its pharmacological application, the SARs for its derivatives have been poorly explored.

In this lecture the design, synthesis [4] and pharmacological characterization of 4-phenyl-2-amidotetralin derivatives will be described, focusing on their SAR, active conformation and configuration. A convenient protocol providing access to all four 4-P-PDOT enantiomers (ee >99%), and the determination of their absolute configuration will also be described. Binding data

on each single stereoisomer, conformational analysis and pharmacophore-based superpositions led to a new chiral pharmacophore model which can be applied to both melatonin receptor agonists and MT_2-selective antagonists. Validation of this pharmacophore model has been achieved synthesizing conformationally constrained tetrahydronaphthalene derivatives.

Superposition of (*2S,4S*)- and (*2R,4S*)-4-P-PDOT

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FAR-KN-08 Antimicrobial PhotoDynamic Therapy: a new tool for the treatment of localized infections

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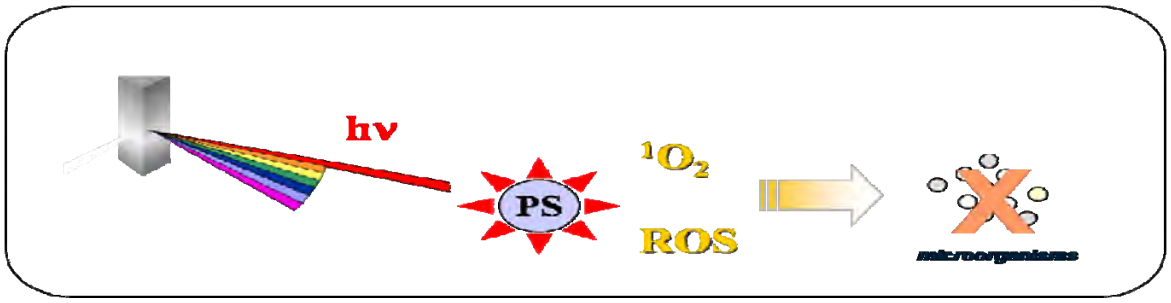
The pandemic diffusion of new microbial infections, as well as the onset of resistance toward antibiotic treatment of many pathogens, urge the development of new antimicrobial therapies as an alternative to the use of classical drugs.[1]

In this area, and particularly for the treatment of localized infectious diseases, the use PhotoDynamic Therapy (PDT) could represent a new appealing strategy to combact pathogens, help the wounds healing, reduce the risk of systemic infections and limit the spread of resistance.[2]

Molteni Therapeutics (MT) is involved since many years in the synthesis, analytical characterization and pharmaco-biological testing of new photosensitizers belonging to several classes of derivatives (Zinc and Silicon phthalocyanines [3], as well as porphyrins [4]), with the aim to discover new PDT agents and to elucidate the structure-activity relationships of these active compounds.

Up to now, very good results in the photoinactivation of yeasts and bacteria have been obtained with many of the synthesized compounds. In particular, the use of Zn(II)-phthalocyanines bearing quaternary ammonium groups has been extensively studied, starting from Discovery to Development for a restricted number of selected molecules. RLP068, the lead compound of MT pipeline, is currently being evaluated in a Phase IIa Clinical Trial.

In this presentation a brief introduction on PDT principles and an overview of the work done by MT on photosensitizers, spanning from synthetic and analytical data to *in vitro* and *in vivo* biological results, will be given.



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FAR-OR-01 Drugs of abuse analysis: are Dried Blood Spots suitable for "on street" controls?

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Driving under the influence (DUI) of psychotropic substances, such as drugs of abuse (DoA) and/or alcohol, is one of the leading causes of traffic collisions. Furthermore, car accidents are the first cause of death (and of acquired disability) for young people under the age of 35. As a consequence, roadside controls are routinely performed by law enforcement agencies as part of prevention/dissuasion policies. Within this framework, the correct and timely sampling of a significant biological matrix, followed by a reliable qualitative/quantitative analysis, is the cornerstone of a fair assessment of the DUI state. For alcohol intake, the use of breathalizers has reached a satisfactory level of reliability and speed. However, assessing the actual state of drug intoxication is much more complicated. It is important to have at disposal fast and reliable analytical methods, able to provide good results for the identification and the quantitation of the most important DoA.

The Laboratory of Pharmaco-Toxicological Analysis develops advanced methods for the analysis of DoA in different biological fluids and tissues, in particular in an innovative matrix: Dried Blood Spots (DBS) [1]. DBS are obtained from blood drops collected on filter paper from a simple finger prick; the technique represents a very attractive and feasible alternative to the traditional blood sampling. It is especially useful “on street”, because is minimally invasive and allows sample collection, transport and storage, granting good stability without requiring refrigeration nor other pre-treatments. A few original analytical methods are for the analysis of different DoA in human DBS, for the purpose of reliable “on street” drug testing.The methods are based on LC-ESI-MS/MS (triple quadrupole) and samples are directly injected into the system, after a very fast solvent extraction. The results obtained until now on cocaine, cannabinoids and their main metabolites are promising, in terms of extraction yields, sensitivity and selectivity. Assays are in progress in order to fully validate the methods.

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FAR-OR-02 Selective serotonergic 5-HT$_7$ receptor agonists as a new therapeutic venue for treatment of cognitive disorders: focus on Fragile X syndrome.

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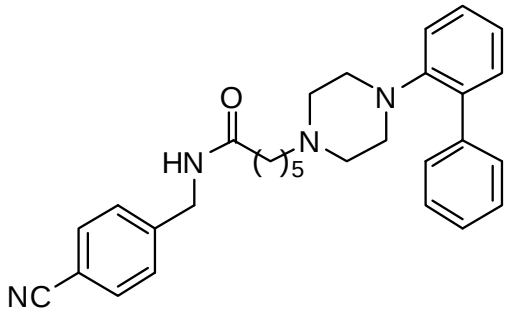
Serotonin (5-HT) affects the excitability of hippocampal neurons and hippocampal-dependent cognitive functions. We have recently shown that 5-HT$_7$ receptor activation modulates glutamate AMPA receptor-mediated basal transmission [1] and metabotropic glutamate receptor-induced long-term depression (mGluR-LTD) in the CA3-CA1 synapse of mouse hippocampus. Activation of 5-HT$_7$ receptors is able to reverse mGluR-LTD also in the Fmr1 knockout (KO) mice model of Fragile X syndrome (FXS) [2], the most common form of hereditary intellectual disability, in which hippocampal mGluR-LTD is abnormally enhanced [3], suggesting that a pharmacological treatment selectively targeting 5-HT$_7$ receptors might be considered in the therapy of FXS.

LP-211, a selective 5-HT$_7$ receptor agonist [4], is able to modulate AMPA-mediated synaptic currents and to reverse mGluR-LTD in the CA3-CA1 hippocampal synapse similarly to 8-OH-DPAT, the standard 5-HT$_7$ non selective agonist.



LP-211

5-HT$_7$ K_i: 0.58 nM; 5-HT$_{1A}$ K_i: 188 nM

On the basis of these results, we have undertaken a new project for the identification of new selective 5-HT$_7$ receptor agonists endowed with pharmacodynamic and pharmakocinetic properties suitable for in vivo use. This will allow to clarify the therapeutic potential of 5-HT$_7$ receptor agonists in the pharmacological treatment of cognitive disorders.

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FAR-OR-03 The Medicinal Chemist's Toolbox: Versatile Approaches for the Rapid Identification of Promising Biologically Active Hits

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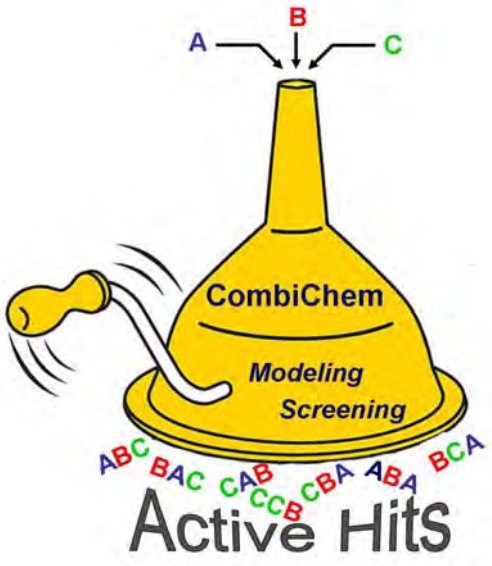
In the last few years, the synergistic relationship between organic chemistry, molecular modeling and biology has played a growing role in the identification of new potential drug candidates. A key contribution to this successful multidisciplinary approach has been given by modern instruments/techniques which have significantly accelerated the drug-discovery process. Despite molecular modeling approaches have significantly speed-up the identification of potential hits from large libraries of compounds, synthetic chemistry still play a key role in producing new chemical entities both for the discovery and optimization phase.



Within the medicinal chemist's "toolbox", high-speed chemical techniques have become an important device for the rapid identification of new biologically active compounds. Parallel synthesis, microwave assisted techniques, click-chemistry and multicomponent reactions represent nowadays commonly used techniques for rapid identification of novel hit compounds and for the hit-to-lead optimization of promising inhibitors. An overview on the application of these modern techniques to the synthesis of different heterocyclic scaffold with antiviral, antitumor and antitubercular activities will be given [1].

[1] a) M. Radi, et al. *J.Comb.Chem.*, *7*, **2005**, 117. b) D. Castagnolo, et al. *Tetrahedron-Asymmetry*, *18*, **2007**, 1345. c) M. Radi, et al. *Bioorg. Med. Chem. Lett.*, *18*, **2008**, 1207. d) M. Radi, et al. *Tetrahedron Lett.*, *49*, **2008**, 4464. e) M. Radi, et al. *Nucleosides, Nucleotides & Nucleic Acids*, *28*, **2009**, 504. f) M. Radi, et al. *Tetrahedron Lett.*, *50*, **2009**, 6572.

FAR-OR-04 Synthesis and biological screening of new chiral α-aryloxy-alkanoic acids as PPARs agonists.

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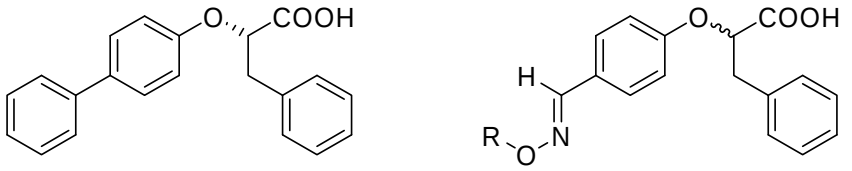
Peroxisome proliferator-activated receptors (PPARs) are ligand-activated transcription factors that govern lipid and glucose homeostasis, therefore they play a central role in cardiovascular disease, obesity and diabetes. Recently, novel PPAR ligands have been identified that are claimed as potentially superior therapeutic agents for human metabolic disorders. These include dual PPARα/γ agonists and PPARγ partial agonists or selective modulators (SPPARγMs) with concomitant hypolipidemic and hypoglycaemic activity and fewer adverse effects than currently available agonists.[1,2] Here, we present the synthesis and the preliminary biological evaluation on the PPARα/γ isoforms of some new (oxy)iminomethyl analogs obtained by the bioisosteric substitution of the distal phenyl ring of the novel lead compound LT175, recently synthesized and tested in our laboratories (Figure 1).[3–5]



LT175 **R =** H, alkyl chain, alkylaryl chain

Figure 1

Different substituents on the hydroxyl group of the (oxy)iminomethyl moiety have been introduced and the preparation of the eutomers of the most active derivatives has been achieved. Docking experiments were performed to provide a molecular explanation for their different activity. The preliminary biological results revealed some interesting compounds with mixed PPARα/γ agonist activity which can be further explored to assess their pharmacological properties in *in vitro* and *in vivo* studies.

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[5] Montanari R. et al. *J. Med. Chem*. **2008**, 51, 7768.

FAR-OR-05 Avicholic Acid: A Primary Bile Acid from Birds on the Route to Potent and Selective TGR5 Ligands

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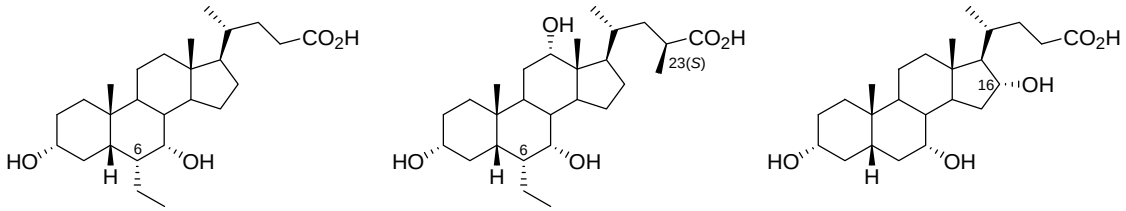
Bile acid (BA) activated receptors are widely recognized as relevant targets for drug discovery efforts. The key members of this family, namely FXR and TGR5, are implicated in a number of liver and metabolic diseases such as cholestasis, non-alcoholic steatohepatitis (NASH), obesity and type II diabetes.[1] In this framework, we have developed a small library of BA derivatives which was instrumental to defined the SAR of BAs as FXR/TGR5 agonists and to disclose selective and potent ligands for both receptors (Figure 1).[2] As a continuation of our efforts aimed at finding novel potent and selective chemical tools to probe the functions of BA related receptors in different tissues, we have been engaged in the further chemical elaborations of the BA scaffold. Our attention, in particular, was attracted by the peculiar structure of avicholic acid, a natural BA isolated from avian species (Shoebill stork and herons) and characterized by a hydroxy group at the C16α-position (Figure 1). Polar groups at this position were indeed suggested by our QSAR model as favoring the activity to the TGR5 receptor.[3] Starting from this observation, we report the synthesis, the biological and PK appraisals, and structure activity relationships of novel avicholic acid derivatives as TGR5 ligands.



Obeticholic Acid (INT-747)
FXR Agonist, Phase II/III Clinical Trials

S-EMCA (INT-777)
TGR5 Agonist, Preclinical Trials

Avicholic Acid

Figure 1. Bile acid derivatives as potent and selective FXR/TGR5 ligands.

[1] Thomas, C.; Pellicciari, R.; Pruzanski, M.; Auwerx, J.; Schoonjans, K. *Nat. Rev. Drug Discov.* **2008**, *7*, 678. [2] a) Pellicciari, R.; Fiorucci, S.; Camaioni, E.; Clerici, C.; Costantino, G. *et al. J. Med. Chem.* **2002**, *45*, 3569. b) Pellicciari, R.; Gioiello, A.; Macchiarulo, A.; Thomas, C.; Rosatelli, E.; Natalini, B.; Sardella, R.; Pruzanski, M.; Roda, A. *et al. J. Med. Chem.* **2009**, *52*, 7958. [3] Macchiarulo, A.; Gioiello, A.; Thomas, C.; Massarotti, A.; Nuti, R.; Rosatelli, E.; Sabbatini, P.; Schoonjans, K.; Auwerx, J.; Pellicciari, R. *J. Chem. Inf. Model.* **2008**, *48*, 1792.

FAR-OR-06 Acrylamido derivatives inhibitors of the mitochondrial permeability transition pore (mPTP)

Daniele Fancelli[1,5], Raffaella Amici[1,5], Gilles Pain[1,3], Manuela Villa[1], Agnese Abate[2,5], Anna Cappa[2,5], Marco Ballarini[1], Eva Milanesi[1], Alessandra Saccani[1], Cristina Contursi[1], Mariangela Storto[1], Paolo Bernardi[6], Saverio Minucci[4], Mario Varasi[2,5], Simon Plyte[1].
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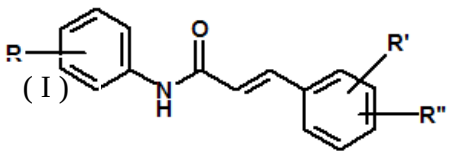
Mitochondria play a central role in the control of both necrotic and apoptotic cell death. A key mitochondrial mechanism promoting cell death is the opening of the permeability transition pore (mPTP), a high conductance channel of the inner mitochondrial membrane. The role of mitochondria-mediated cell death in the aetiology of many diseases is well established and inhibitors of PTP are regarded as potential therapeutic agents, particularly for the prevention and/or treatment of diseases and conditions characterized by ischemia/reperfusion, oxidative or degenerative tissue damage.

In this report we describe the synthesis, structure−activity relationships (SAR) for inhibition of mPTP opening induced by Calcium overload, and preliminary biological characterization of acrylamido derivatives (I), a novel series of potent inhibitors of mPTP.



(I)

(E)-3-(4-Fluoro-3-hydroxy-phenyl)-N-naphthalen-1-yl-acrylamide, one of the most interesting compounds in this series, was effective in an *in vivo* Rabbit model of heart ischemia/reperfusion injury.

FAR-OR-07 Microfluidics for radio-tracers labeling

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One of the most interesting technological novelties in the field of radiochemistry is the use of microfluidic devices to perform efficient, rapid, cost effective reactions in a user-friendly environment. Microreactors have considerable advantages in radiochemistry where short-life positron-emitters are used to produce radiotracers for molecular imaging with positron emission tomography (PET) [1-3].

A lots of advantages may be expected from this technology, such as the use of smaller amounts of radioactive precursors for saving precious materials, the possibility to work in safer conditions, to accurately control the reaction parameters and to use cheap, interchangeable, disposable and quality-assured radiochemistry processors[4].

This work provides an overview of materials and microfluidic networks suitable for radiochemistry at microscale. Several micro devices are realized to perform on-chip reactions and separations. Preliminary results demonstrate the effectiveness of the proposed microfluidic platforms for radiopharmaceutical applications.

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FAR-OR-08 Design of Novel Dual and Selective Allosteric Inhibitors Acting on C5a/CXCR1: Lead Likeness Strategy of a Series of Innovative Aryltrifluoromethanesulfonates Reparixin Analogues

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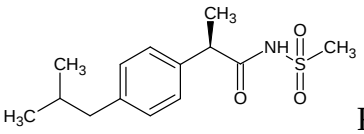
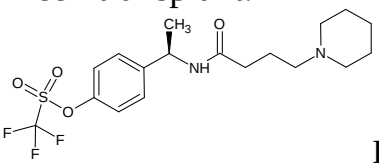
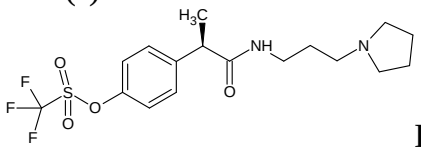
Among the chemokine family, CXCL8 and CXCL1 play a key role in the activation and recruitment of neutrophils at the site of inflammation. CXCL8 binds two membrane receptors, CXCR1 and CXCR2, whereas CXCL1 is a selective agonist for CXCR2[1-2]. A novel class of small molecular weight allosteric CXCR1 inhibitors was previously identified in our laboratories and reparixin (**I**)[3-4], the first drug candidate, is currently under clinical investigation in Pancreatic islet -cell transplant.



Reparixin (**I**)



DF2593(**II**)



DF2297 (**III**)

Starting from the derived binding model, a rational design program has been undertaken with the aim to identify novel potent inhibitors with comparable inhibitory efficacy for both CXCR1/C5aR.

The replacement of the isobutyl group with the trifluoromethanesulfonyl (triflate) group, led to a significant potency increase on C5a strongly enhanced the affinity at CXCR1 and C5a. The sulfonate spacer was confirmed as optimal from a spatial point of view for the correct orientation in the hydrophobic pocket of the receptors and by a retro-inversion of the amide bond was able to obtain a selective C5aR inhibitors. Among these, the C5aR selective inhibitor DF2593A**(II)** and the dual CXCR1/C5aR inhibitor DF2297A **(III)** were selected as promising candidates for *in vitro* and *in vivo* pharmacological characterization. Both DF2593A and DF2297A potently inhibited C5a-induced human (IC_{50} of 5×10^{-9}M and 8×10^{-9}M, respectively) and murine (IC_{50} of 1×10^{-9}M and 8×10^{-9}M, respectively) PMN migration.

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FAR-OR-09 3-Substituted-1,5-Diaryl-2-Alkylpyrroles Nitroesters, Highly Selective COX-2 Inhibitors and Nitric Oxide Donors

Angela Di Capua,[a*] Salvatore Valenti,[a] Andrea Cappelli,[a] Lidia Sautebin,[b] Carla Ghelardini,[c] Vincenzo Calderone,[d] Paola Patrignani,[e] Antonio Giordani[f], Mariangela Biava,[g] and Maurizio Anzini.[a]

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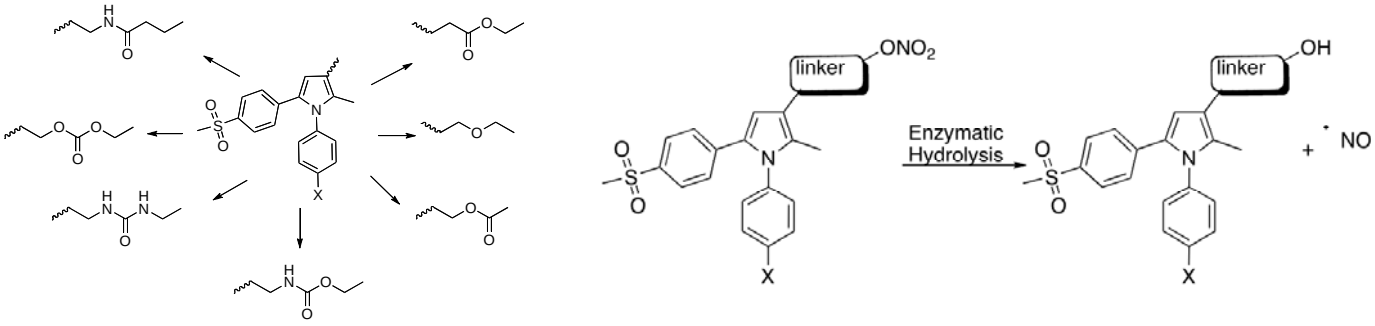
A new generation of selective cyclooxygenase-2 (COX-2) inhibitors (coxibs) was developed to circumvent the major side effects of cyclooxygenase-1 (COX-1) and COX-2 inhibitors (stomach ulceration and nephrotoxicity).
A series of previously patented 1,5-Diarylpyrrol-3-acetic esters and 1,5-Diarylpyrrole-3-alkoxyethyl ethers proved to be potent and selective COX-2 inhibitors in *in vitro* cell culture assay.[ref] The potential anti-inflammatory and antinociceptive activities of these compounds were evaluated *in vivo*, where they showed a very good activity against both carrageenan-induced hyperalgesia and edema in the rat paw test. [1,2,3]
These classes of compounds (International Patent: PCT/EP2006/065011 and WO 2008/014821 A1) were at the basis of the development of new compounds, the COX-2 inhibiting nitric oxide (NO) donors (CINODs).
CINODs are a new class of anti-inflammatory and analgesic drugs that may minimize gastrointestinal toxicity compared with standard non-steroidal anti-inflammatory drugs (NSAIDs) along with reduced cardiovascular risks associated with the Coxibs (celecoxib, valdecoxib, etc.) by virtue of their nitric oxide donation.
This project was based on the synthesis of NO-donor's compounds characterized by modifications of the side chain at position 3 of 1,5 diarylpirrole derivatives in which the 1,5-diarylpyrrole scaffold is linked to a nitric oxide moiety. In particular, the aim of the project is the extended functionalization of position 3 by means of "linkers" with different stereo-electronics properties in order to obtain "hybrid molecules" that after releasing NO are able to show elevated selective COX-2 activity *in vitro* along with elevated anti-inflammatory and anti-nociceptive activity in *in vivo* animal models.[4]



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FAR-OR-10 Synthesis and SAR of New Pyrazolo[4,3-h] quinazoline -3-carboxamide Derivatives as Potent and Selective MPS1 Kinase Inhibitors

Marina Caldarelli,[a] Mauro Angiolini,[a] Dario Ballinari,[a] Jay Aaron Bertrand,[a] Riccardo Colombo,[a] Teresa Disingrini,[a] Daniele Donati,[a] Maria Laura Giorgini,[a] Marco Guanci,[a] Jürgen Moll,[a] Stefano Nuvoloni,[a] Helena Posteri,[a] Francesca Quartieri,[a] Marco Silvagni,[a] Francesco Sola.[a]

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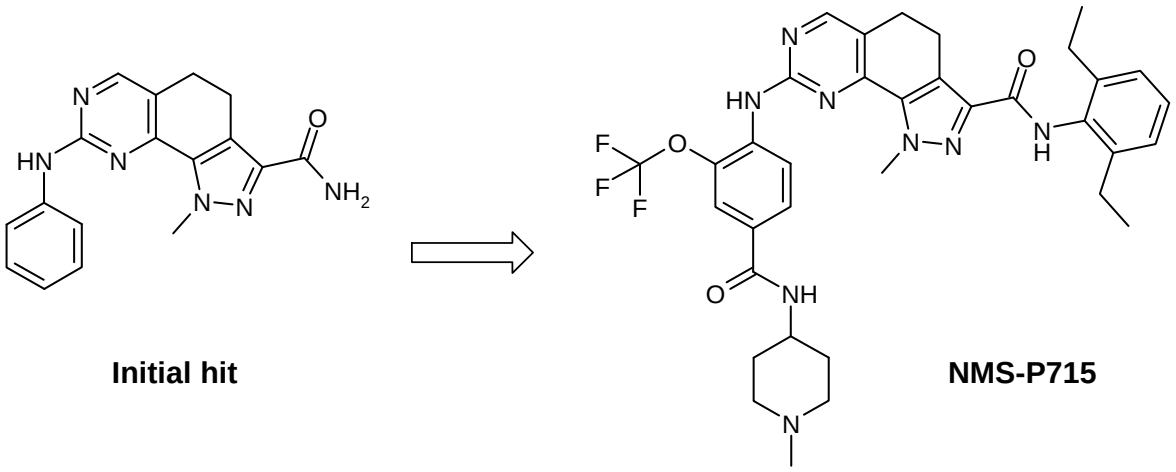
MPS1 (Monopolar Spindle-1 kinase), also known as TTK, plays critical roles in the proper execution of mitosis, is frequently over-expressed in human tumors, and is required for tumour cell proliferation. Selective inhibitors of this target may provide an innovative therapy for the treatment of tumors and spindle assembly checkpoint inhibition could be a way to selectively target aneuploid tumor proliferation.

In this poster we report the synthesis and SAR of a series of novel pyrazolo-quinazolines as potent and selective MPS1 inhibitors. We describe the optimization of the initial hit, identified by screening the internal library collection, into an orally available, potent and selective MPS1 inhibitor (NMS-P715).



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FAR-OR-11 The Click Chemistry Approach in the Discovery of Potent and Selective PI3K Inhibitors

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Click chemistry has recently made an outstanding contribution to medicinal chemistry research [1]. This term, coined by K. B. Sharpless, refers to a new synthetic approach which exploits nearly perfect reactions. Among them, the copper-catalyzed Huisgen cycloaddition between azides and alkynes plays a prominent role.

Over the past few years, we have exploited this reaction in the discovery of resveratrol [2] and estrogenic analogues [3], HDAC inhibitors [4], and, lately, PI3K inhibitors. Phosphatidylinositol-3-kinases (PI3Ks), a class of lipid kinases, are an emerging target in antitumoral therapy as they play a major role in proliferation and survival in a wide variety of human cancers [5].

Our approach in the discovery of potent and selective PI3 kinase inhibitors involved the functionalisation of TGX-155, a micromolar PI3 kinase inhibitor, in the 8-position with differently substituted triazole rings (Figure 1).

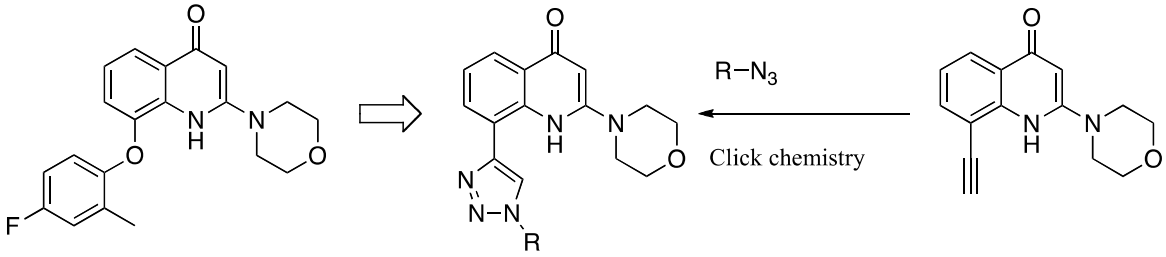

Figure 1: TGX-155

Three lead compounds have been identified, which display inhibitor activity at the nanomolar level, having a clear selectivity against α and δ isoforms [6]. In this communication, design, synthesis, and biological evaluation of this promising class of PI3K inhibitors will be illustrated.

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FAR-OR-12 Synthesis and Biological Characterization of 4-Spirochromane Analogues as New HDAC Inhibitors

Florian Thaler,[a,b] Agnese Abate,[c,b] Andrea Colombo,[d] Giacomo Carenzi,[c,b] Roberto Boggio,[a] Giulio Dondio,[d] Stefania Gagliardi,[d] Saverio Minucci,[e,f] Mario Varasi[c,b] Ciro Mercurio[c]

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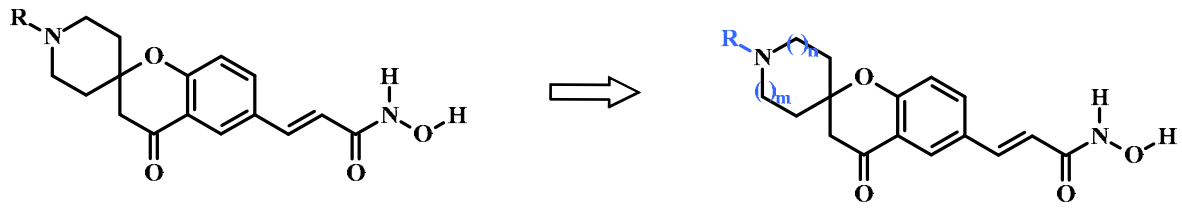
Reversible post-translational modifications of histones such as acetylation/deacetylation play an important role in chromatin structure and control of gene expression. The histone acetylation status is regulated by two enzyme families: histone acetyltransferases (HATs) and histone deacetylases (HDACs)[1]. HDACs have emerged as an attractive target for the development of new anticancer agents, and several compounds are currently in clinical studies for solid and hematological tumor therapy[2]. Two inhibitors, vorinostat (SAHA) and romidepsin (FK228), have been recently approved by the FDA for the treatment of cutaneous T-cell lymphoma. Despite these recent successes, there remains significant interest in identifying new HDAC inhibitors with a superior pharmacokinetic profile, improved efficacy, and good tolerability[3].

With the objective to find new HDAC inhibitors we had synthesized a series of spiro[chromane-2,4'-piperidine]hydroxamic acid derivatives[4] by combining privileged structures with minimal structures able to inhibit histone deacetylase enzymes[5]. Herein, we wish to describe the identification of 4-oxospirochromane-*N*-hydroxyacrylamides, leading to highly potent compounds in biochemical and antiproliferation assays as well as with a good *in vitro* ADME profile.



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FAR-OR-13 Mannich bases as novel irreversible Epidermal Growth Factor Receptor inhibitors

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Second generation, irreversible inhibitors of Epidermal Growth Factor Receptor (EGFR) are characterized by a recognition scaffold, resembling those of clinically-employed reversible inhibitors, and by a cysteine-reactive warhead, able to covalently interact with a conserved cysteine residue in the kinase domain of the ErbB family members (C797 in EGFR) [1]. Cysteine-trapping groups reported in literature so far (acrylamides, β-chloroacetamides) are endowed with high intrinsic reactivity. This could cause rapid metabolic deactivation of the inhibitor or, at worst, enhanced *in vivo* toxicity, due to the aspecific reactivity towards off-target thiol-containing nucleophiles.
We have recently started systematic exploration on the role and reactivity of warheads for irreversible EGFR inhibition, introducing different cysteine-trapping groups on the 4-anilinoquinazoline scaffold [2]. In the present work, our attention is focused on a new set of inhibitors, in which a β-aminocarbonyl group (Mannich base) is linked to different scaffolds through an amide bond. These derivatives proved to be as efficient as the irreversible acrylamide derivative PD168393 in inhibiting EGFR-TK activity in different cell lines. For both acrylamide and Mannich-base derivatives, inhibition persisted for 8 hours after the wash-out of the compound from cell medium. However, their *in vitro* reactivity profile markedly diverged, with Mannich bases being stable in the presence of low MW thiols (GSH, cysteine, cysteamine), compared to the highly reactive acrylamide. A combined approach, employing: i. fluorimetric analysis of inhibitors incubated with cell-free EGFR, ii. quantification by HPLC-MS of inhibitors and their metabolites in A549 cell lines and in cell lysates, showed that Mannich bases can act as prodrugs, partially releasing acrylamide in the cellular environment.

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FAR-OR-14 Exploring the interaction capacities of TRPM8 channel by docking analyses and MD simulations

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The transient receptor potential (TRP) superfamily is a large group of ion channels that has received increased attention in recent years. TRPM8, on which this study is focused, belongs to the subfamily of thermo-TRP channels which are triggered by diverse chemical and physical stimuli and whose precise activation mechanism is still unknown. Specifically, TRPM8 is activated by cold temperature, ligands such as menthol and icilin (a synthetic derivative), positive membrane potential and the endogenous signaling lipid, PIP2. Therefore, TRPM8 could find therapeutic applications in several pathological conditions, including neurogenic inflammation, neuropathic pain, overactive bladder and prostate cancer. [1] An homology model of the TRPM8 tetramer was recently generated using a fragmental strategy by some of us. [2] Beside the global architecture of the TRPM8 channel, such a model revealed the key residues involved in ligand recognition and suggested that the agonist binding is able to induce a cascade of conformational shifts which globally may orchestrate the channel opening (at least partially). Such a mechanism was then confirmed by classic all-atoms MD simulations which evidenced how agonists are able to trigger such structural changes whereas agonists block the channel in its starting conformations. Considering the rather nonspecific nature of TRPM8 binding site and the resulting difficulty of predicting ligand bioactivity by docking calculations, adaptive biasing force (ABF) MD simulations [3] were exploited to derive the free energies involved in TRPM8 activation and the obtained energy values are in line with the activity of a representative set of TRPM8 ligands. These results emphasize that suitably targeted MD runs can be fast enough to be systematically applied to predict the bioactivity of rather large ligand datasets.

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FAR-OR-15 Discovery of new positive allosteric modulators of $GABA_B$ receptor

Claudia Mugnaini,[a] Valentina Pedani,[a] Serena Paquini,[a] Simone Brogi,[a] Andrea Tafi,[a] Mauro A.M. Carai,[b] Giancarlo Colombo,[b] Carla Lobina,[b] Federico Corelli[a]

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GABA is the main inhibiting neurotransmitter in the CNS. It modulates the neuronal activity by mediating its action *via* GABAA, GABAB and GABAC receptors The $GABA_B$ receptor belongs to the family 3 of the G-protein coupled receptors and it is an heterodimer made of two similar but distinct subunits. Although drugs activating the $GABA_B$ receptor were found to have a number of possible therapeutic actions, these were limited because of tolerance and undesired side effects which include sedation, myorelaxing activity and hypothermia.[1]

Allosteric modulators are molecules that bind to a site on a receptor which is topographically distinct from the orthosteric-binding pocket. They have little or no intrinsic agonistic activity of their own but induce conformational changes in the receptor protein, which affect its interaction with the endogenous neurotransmitter. Thus, positive allosteric modulators (PAMs) of $GABA_B$ receptor appear as a better alternative to $GABA_B$ agonists, allowing the specific enhancement of receptor activity when and where needed, and as such, are less prone to tolerance in contrast to the pure agonists (such as baclofen) that constantly activate the receptor in any region where it is expressed. These compounds are valuable anxiolytics and effectively reduce craving for drugs of abuse such as alcohol, nicotine and cocaine.[2] Four companies have invested substantial resources into the search of PAMs of $GABA_B$ receptors (Novartis, Roche, AstraZeneca and Addex) with significant differences in the target indications. These medicinal chemistry efforts have enlarged the number of scaffolds, which lead to potent compounds and thus expanded our knowledge on structure-activity relationships significantly. Nevertheless, substantial efforts are still needed in order to optimize drugs for a given indication to get all the ADMET parameters right as well, such as metabolic stability, brain penetration for the CNS indications (or no brain penetration for the peripheral indications), sufficient water solubility, no alerts in Ames and genotoxicity tests, and several other parameters.

Our research in the area started from a structure-based computational approach which allowed, through a virtual screening, the identification of a number of possible PAMs of $GABA_B$ receptor. Among those selected, one molecule gave interesting results both *in vitro* and *in vivo* studies.

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FAR-OR-16 New Purine Derivatives as $P2X_3$ Receptor Antagonists

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Among the ligand gated ionotropic P2X receptors activated by ATP, the $P2X_3$ subtype plays an important role in neuropathic and chronic pain pathways [1]. Hence, ligands blocking this receptor could be useful for the treatment of chronic pain conditions and migraine [1]. Recently, a number of purine acyclic-nucleotides have been synthesized and proved to behave as partial agonists of $P2X_3$ receptors [2]. Furthermore, since non-nucleotide benzylic diamino-pyrimidine derivatives were reported to block $P2X_3$ receptors with high potency [3], a new series of purine derivatives bearing a substituted benzyl chain in 9-position (Figure 1) was designed and synthesized in the search for new $P2X_3$ antagonists.

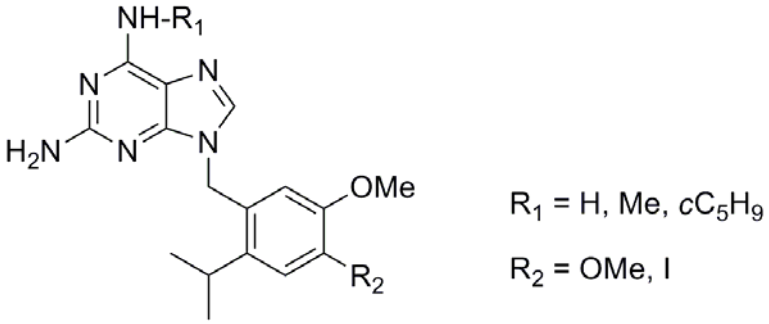

Figure 1.

The compounds were evaluated on recombinant murine and human $P2X_3$ receptors using patch clamp technique. Furthermore, an assay on native $P2X_3$ receptors expressed by trigeminal ganglion sensory neurons in culture has been performed. The new compounds resulted to behave as $P2X_3$ receptor antagonists with IC_{50} in the low micromolar range.

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FAR-OR-17 A novel human recombinant antibody (dAb) against a synthetic glycopeptide cross-reacts with human auto-antibodies, biomarkers of multiple sclerosis

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We have previously described a synthetic glycopeptide, termed CSF114(Glc), able to detect specific auto-antibodies in sera of patient affected by Multiple Sclerosis (MS), an inflammatory, demyelinating disease of the central nervous system [1]. The pathogenesis of MS involves an autoimmune mechanism against myelin auto-antigens, even if the target antigens remain elusive. Accordingly, we focused our attention on both the characterization of the antigenic properties of CSF114(Glc) and the identification of the native auto-antigen(s) recognized by anti-CSF114(Glc) auto-antibodies.

In this context, we have recently used the glycopeptide CSF114(Glc), coated on magnetic beads, to select by phage display specific human domain antibodies (dAb) from a domain antibodies library [2]. Purified dAbs (15 kDa) were characterized by Biacore for binding specificity to CSF114(Glc) versus unglycosylated CSF114, showing a good specificity and affinity.

Subsequent Biacore experiments demonstrated that these recombinant dAbs cross-react with anti-CSF114(Glc) auto-antibodies isolated from MS patients' sera by immuno-affinity chromatography. Accordingly, the new recombinant dAb may be used for the characterization of the native auto-antigens in human tissues or as a positive control in an in vitro diagnostic assay based on CSF114(Glc).

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FAR-OR-18 Exploring the space of histidine containing dipeptides in search of novel efficient RCS sequestering agents

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Experimental evidence confirmed that reactive carbonyl species (RCS) are involved in the pathogenesis of several human diseases including diabetes related disorders and distress metabolic syndrome. Hence RCS, beside to be considered biomarkers of oxidative damage, can be also seen as potential targets for the development of bioactive compounds acting as detoxifying agents of RCS (carbonyl quenching compounds). We found that the endogenous dipeptide carnosine (β-alanyl-L-histidine) is a selective and potent RCS sequestering agent, even though its clinical application is limited due to the rapid hydrolysis in blood by a specific dipeptidase (carnosinase). With a view to finding stable and effective agents, several carnosine derivatives were recently proposed in literature and some of these compounds proved promising in vivo in suitable animal models. Despite the mentioned variety of carnosine analogues, the chemical space of the proteinogenic histidine containing dipeptides was never exhaustively investigated.
On these grounds, the study is focused on the synthesis, physicochemical profiling, in silico analysis and biological evaluation of a set of diastereoisomeric pairs of histidine containing dipeptides suitably chosen to cover a large part of the accessible chemical space. In detail, the examined peptides were designed as diastereoisomeric pairs in order to delve the configurational effects on the activity which could shed additional light on the quenching mechanism. Finally, some relevant physicochemical properties (namely pKi, log P and log $D^{7.4}$) were experimentally determined to clarify the main factors governing the quenching activity and their relationships with in silico determined descriptors were also investigated.

FAR-OR-19 Recombinant Albumin as Chiral Selector in Enantioselective HPLC

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Human serum albumin (HSA) has been successfully used as chiral selector in enantioselective HPLC. These HSA-based columns usually present the problem of a significant variation of the chromatographic performances depending not only on the immobilization procedure, but also on the origin of the anchored protein from different sera. This makes difficult the application of developed and validated HPLC methods. Recombinant human albumin, rHA (RECOMBUMIN®, Novozymes Biopharma UK Limited) can overcome the problem, because of the high homogeneity of the structure and binding properties of the protein samples.
RECOMBUMIN®, produced from Novozymes' *Saccaromyces cerevisiae* was purified and defatted before use. The protein was then characterized for its conformation and its binding properties by circular dichroism (CD). In particular the analysis of the CD at high energy showed substantially the same secondary structure for the recombinant albumin with respect to the serum albumin. In addition the binding of selected markers for the most important binding sites (i.e. phenylbutazone for site I, diazepam for site II, and bilirubin for site III) was proved to be stereoselective. A sample of RECOMBUMIN® was then anchored *in situ* to an epoxy silica matrix of a HPLC column. The anchoring method was validated by checking the binding parameters of known ligands on the immobilized protein. The RECOMBUMIN® -based column was efficiently used for the enantioselective analysis of a variety of chiral drugs and amino acid derivatives. As an example enantiomeric resolution was obtained for *rac*-warfarin (α = 2.1), *rac*-lorazepam hemisuccinate (α = 5.3), N-benzoyl-DL-leucine (α=2.8), using 1-propanol/phosphate buffer (pH 7.5) 15/85, 0.6 ml/min flow rate. The obtained values of enantioselectivity are comparable or higher with respect to those obtained with the corresponding HSA-based columns, under the same experimental conditions. The rHA based column has also a great potential for its use as affinity support for characterizing the binding of new active compounds in terms of K_D and location of primary binding site.

FAR-PO-01 One-pot transformation of anthranilic acids to fluorazone derivatives, valuable intermediates for the synthesis of anticancer agents

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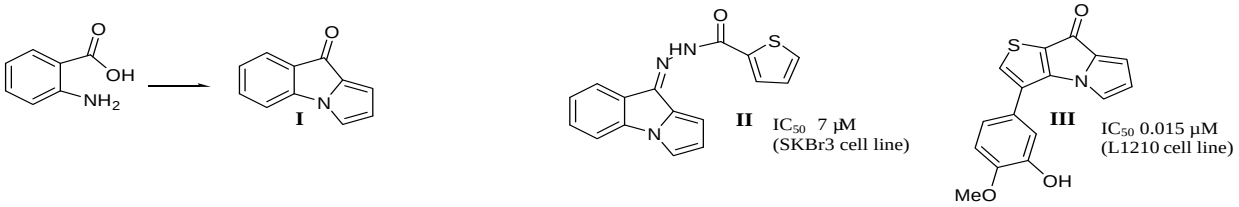
Fluorazone (9*H*-pyrrolo[1,2-*a*]indol-9-one) **I** and its analogs represent valuable intermediates in the synthesis of biologically active compounds. They have been extensively studied in relation to a variety of activities showed by many of their functionalized derivatives. In particular, we found that some *N*'-heteroacyl-hydrazone derivatives (es. cpd **II)** possess noticeable cytotoxic activity against a colon cancer cell line [1], while thienopyrrolizinone **III**, belonging to the *tripentones* family, has been shown to act as a microtubule polymerization inhibitor [2].



A number of synthetic strategies have been therefore developed for the preparation of (un)substituted-fluorazones and analogs. Amongst the known synthetic methods, the most appealing appear those starting from *ortho*-(1*H*-pyrrol-1-yl)aryl and heteroaryl carboxylic acids, in turn obtained by pyrrolation of *ortho*-aminoaryl (anthranilic) and *ortho*-aminoheteroaryl carboxylic acids, respectively [3]. We herein investigated the possibility of directly converting anthranilic acids into fluorazones, through a sequential one-pot pyrrole formation/cyclization, by using DMTHF and 4-chloropyridine hydrochloride as the acid catalyst. This allows the preparation of fluorazone based derivatives from *ortho*-aminoaryl and heteroaryl carboxylic acids in generally good yield and after a simple work-up, avoiding any intermediate manipulation. A further advantage of the procedure lies in the easy availability of the starting aminoacids, most of which are commercial reagents.

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FAR-PO-02 A3 Adenosine Receptor: homology modeling and 3D-QSAR studies

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Adenosine receptors (AR) belong to the superfamily of G-protein-coupled receptors (GPCRs). They are divided into four subtypes (A1, A2A, A2B, and A3) [1], and can be distinguished on the basis of their distinct molecular structures, distinct tissues distribution, and selectivity for adenosine analogs [2,3]. The hA3R, the most recently identified adenosine receptor, is involved in a variety of intracellular signaling pathways and physiological functions [4]. Expression of A3R was reported to be elevated in cancerous tissues [5], and A3 antagonists have been proposed for therapeutic treatments of cancer. The recent literature availability of crystal structure of hA2A adenosine receptor (PDB code: 3EML) provided us a new template for A3R homology modeling. The validation of the obtained structure model was performed by inspecting the Ramachandran plot (Fig. 1). The modeled protein was optimized using nanosecond scale molecular dynamics simulation. One hundred twenty two active and selective compounds were docked into the obtained model using Induced Fit Docking [6] and used as training set to generate pharmacophore models by means PHASE [7]. Energy-optimized pharmacophore mapping was performed; to each pharmacophore feature site was assigned an energetic value as the sum of the GLIDE XP contributions of the atoms included in the site. This pharmacophore model addresses the prevalent features to be used for the search of new inhibitors. Therefore it was employed as template to screen the ZINC database in the attempt to find new potent and selective human A3R antagonists.

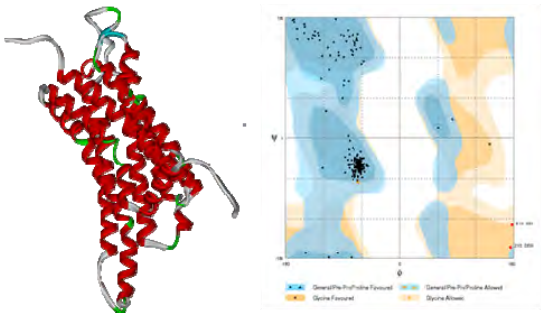

Figure 1

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FAR-PO-03 Selective inhibition of iNOS by benzyl- and dibenzyl derivatives of N-(3-aminobenzyl)acetamidine on cellular line H2C9

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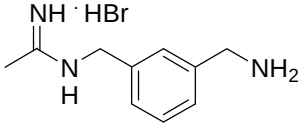
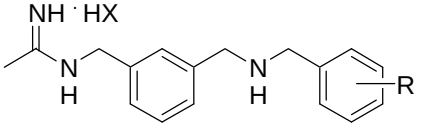
Nitric oxide (NO) is an important mediator involved in the regulation of many physiological and pathological processes.[1] The formation of NO is catalyzed by the enzyme nitric oxide synthase (NOS) via the NADPH- and O2-dependent oxidation of L-arginine. Three distinct isoforms of NOS have been identified: the constitutive endothelial (eNOS) and neuronal (nNOS), and the inducible (iNOS). The overproduction of NO by iNOS may have detrimental consequences, and seems to be involved in the pathophysiology of several human diseases, such as asthma, arthritis, multiple sclerosis, colitis, psoriasis, neurodegenerative diseases, tumor development, transplant rejection or septic shock. In the last years, considerable effort has been directed toward the selective inhibition of iNOS as a strategy for the prevention of excessive NO production, while maintaining the basal formation of NO from constitutive NOS that is required for normal physiological function. Selective inhibition of iNOS would be a useful therapy for inflammatory diseases.[2]
Recently we have reported the synthesis of acetamidines **2** and **3,** differing from known inhibitor W1400 (**1**) by the amino substitution at the 3-aminomethyl group with one or two benzylic groups. We have evaluated their iNOS inhibitory effect in vitro by an enzymatic assay. Here we will report the biological evaluation of the same molecules on H9C2 cells, spontaneously immortalized ventricular myoblasts from the rat embryo.



1 (W1400)



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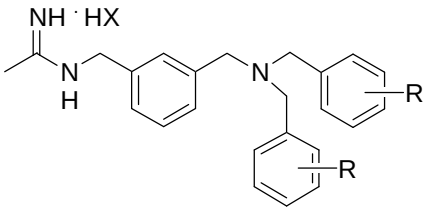

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FAR-PO-04 Follicle Stimulating Hormone: evaluation of glycan content by liquid chromatography-mass spectrometry

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Follicle Stimulating Hormone (FSH) is a glycoprotein, member of the gonadotropins family, which also includes luteinizing hormone (LH), chorionic gonadotropin (CG) and thyroid stimulating hormone (TSH). FSH is secreted from the pituitary gland and regulates reproduction in mammals. In females, FSH targets a receptor (FSHR) expressed only on granulosa cells, and induces the maturation of ovarian follicles. In males, FSH stimulates Sertoli cell proliferation in testes and supports spermatogenesis [1]. FSH and the other members of the gonadotropin family have closely related structures, composed of two non covalently linked α- and β-subunits. Both subunits are glycosylated. The glycosylation state plays a key role in determining and modulating biological functions *in vivo*; therefore, glycoproteins intended for pharmaceutical use in humans need to be carefully characterized, both in terms of their amino acid sequence and oligosaccharide structure. As a consequence, it is essential to develop methodologies for a fast and accurate monitoring of gonadotropin glycosylation.

Due to their extensive structural heterogeneity, the elucidation of glycosylation patterns in glycoproteins, such as the FSH, remains one of the most challenging problems in the proteomic analysis of post-translational modifications. The glycosylation state is usually studied after decomposition of the intact proteins to the proteolytic peptide level [2], or after glycan release by hydrazinolysis [3]. These approaches are often laborious, and give no information on the whole protein [4]. Here we report the oligosaccharide profile of commercial FSH preparations, as obtained by intact molecular mass analysis and bioinformatic tools. The results obtained by RP-HPLC/IT-TOF mass spectrometry show a predominance of highly sialylated, highly branched glycans in human urinary FSH if compared to the recombinant FSH expressed in rodent cell lines.

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FAR-PO-05 The Libra Project: An Italian chemical library for drug discovery

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The aim of the LIBRA project is to collect small organic molecules, produced within scientific institutions in Italy, and distribute them in a format suitable for biochemical screening. The idea of building such a collection arose out of the observation that the Italian organic and medicinal chemistry communities annually produce a wealth of interesting novel small molecules. Often, these molecules undergo just one or very few tests, whereas with an appropriate organization and logistics up to 100 different biochemical or phenotype tests might be feasible with only 3-5 mg of a typical compound (MW < 500). One of the objectives of LIBRA is to offer new opportunities of screening, thus encouraging public-public and public-private collaborations.
The Drug Discovery and Development unit of the Italian Institute of Technology decided to share part of its storage facility in favor of this initiative and to develop a procedure comprising several automated steps for the preparation of solutions, physico-chemical characterization, storage, cherry-picking and distribution on microplates of the LIBRA's chemical collection. Details of the whole process will be illustrated, including methods and validation on the first experimental sets. Specifically: storage as DMSO solutions (10 mM), frozen and under nitrogen, will follow a well-established practice of modern screening centers; distribution (the smallest quantities compatible with screening needs) will occur in 96-well microplates with appropriate liquid handling work stations.
The collection will be limited to molecules with published or patented structure, in order to limit intellectual property issues, but is a must of LIBRA to protect the interest of the provider while keeping the collection appealing for the screening needs of all users. The construction of a web site to advertise and display the available molecular structures is part of the project, such as to offer a "One Stop Showcase" for biochemists and pharmacologists with specific screening initiatives ready to start. A highly requested option, delivery of selected portions of the collection (cherry picking), will be possible.

FAR-PO-06 NEW PYRROLE-BASED SELECTIVE COX-2 INHIBITING NITRIC OXIDE DONORS: SYNTHESIS, *IN VITRO* AND *IN VIVO* EVALUATION

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[b]Rottapharm S.p.A., via Valosa di Sopra 7, I-20052 Monza; [c] Università di Napoli "Federico II", Via D. Montesano 49, I-80131 Napoli; [d]Università di Firenze, Viale G. Pieraccini 6, I-50139 Firenze ;[e]Università di Pisa, Via Bonanno 6, 56126 Pisa; [f]Università di Chieti "G. D'Annunzio" e CeSI, Via dei Vestini 31, I-66013 Chieti; [g]Dipartimento Farmaco Chimico Tecnologico, Università degli Studi di Siena, Polo scientifico. Miniato, Via A. Moro, snc, I-53100 Siena.

The development of *COX-inhibiting nitric oxide donors* (CINODs) has been driven by the pursuit for the search of novel analgesic/anti-inflammatory agents devoid of adverse side effects, especially those related to *traditional* Non Steroidal Anti-inflammatory Drugs (*t*-NSAIDs)[1]. Starting from new diarylpyrrole-based selective COX-2 inhibitors previously individuated by some of us [2,3] and taking into account all the structural features that were responsible for COX-2 inhibition and selectivity, we planned the synthesis of novel COX-2 selective CINODs, in which the nitric oxide (*NO*) release aims at cutting down the side effects displayed by COX-2-like structures [4]. Thus, for improving the biological profile of these class of compounds, we synthesized new derivatives introducing a nitrated amidic side chain. All compounds were evaluated to assess their inhibition towards both COX-1 and COX-2 through a cell-based assay, *NO*-dependent vasorelaxing effect and *in vivo* analgesic and anti-inflammatory profiles.

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FAR-PO-07 GN8 Fluorescent Analogues as Chemical Probes for Prion Diseases

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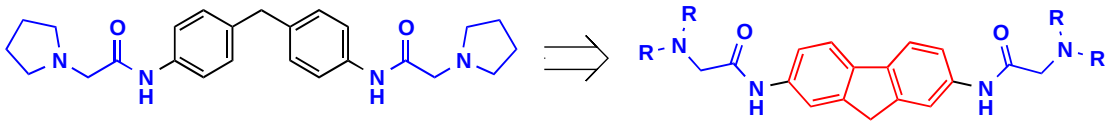
Prion diseases, or transmissible spongiform encephalopathies (TSEs) are a family of invariably fatal neurodegenerative disorders for which no effective curative therapy currently exists. A common feature of TSEs is the deposition of insoluble aggregates of disease-associated prion protein (PrP^{Sc}), the post-translationally refolded and partially protease-resistant isoform of normal cellular prion protein (PrP^{C}). These observed deposits of PrP^{Sc} are thought to be the cause of neuronal cell death in TSEs, a process that leads to the spongiform degeneration of brain tissue [1].
A potential therapeutic approach for inhibiting the accumulation of PrP^{Sc} is to stabilize PrP^{C} through the direct binding of a small organic molecules to make $PrP^{C} \rightarrow PrP^{Sc}$ conversion less energetically favourable. Recently, GN8 (see Scheme), an antiprion compound that specifically binds PrP^{C}, has been discovered. Interestingly, GN8 was found to inhibit PrP^{Sc} production in vitro on a mouse neuronal cell culture infected with TSE and to prolong the survival time of prion-infected mice [2].
From our computational study dedicated to analyze GN8-PrP^{C} interactions and from structure-activity relationship studies [3,4], we argued to modify the diphenylmethane core of GN8. By the introduction of an additional bond linking the two phenyl rings, we ended up with the fluorene derivative **1** (see Scheme). The fluorescent property of fluorene ring offers a unique opportunity to obtain chemical

probes which may elucidate the mechanism of action of GN8 derivatives in vitro and in vivo.
Herein, we report the synthesis of a small library of fluorene-based analogues of GN8 and the evaluation of their antiprion activity in TSE infected cells.



GN8 1

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FAR-PO-08 New selective PDE4D inhibitors devoid of sedative effects in mice

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Strategies designed to enhance cerebral cAMP by phosphodiesterases inhibition have been proposed as symptomatic treatments to counteract cognitive deficits. We have recently reported a series of new 3-cyclopentyloxy-4-methoxybenzaldehyde derivatives endowed with selective inhibitory activity toward the long-form PDE4D3 [1]. In a recent pharmacological study **GEBR-7b**, the most active of them, increased hippocampal cAMP and did not influence Aβ levels; furthermore, in the object recognition test it improved spatial as well as object memory performance, at doses that did not cause emesis-like behaviour in rodents [2]. Therefore, our results further support the hypothesis that specific PDE4D isoforms play a critical role in the mediation of memory processes, as recently reported by other researchers [3-4]. It is well known that rolipram, a PDE4 inhibitor lacking in isoforms selectivity, combines pro-cognitive properties with undesirable sedative effects, decreasing both locomotion and rearing in rodents [5]. Recently, Li et al. observed no changes in locomotor activity between PDE4D knock out and wild type mice, suggesting that PDE4D inhibition couldn't induce sedation [4]. With the aim to develop PDE4 inhibitors endowed with a better tolerability, we synthesized a new series of analogues of previous compounds and evaluated "in vitro" their inhibitory activity on different PDE4 isoforms as well as their ability to affect spontaneous locomotor activity. Some of them (compounds **4a**, **5b**, **7b**, selective toward PDE4D isoforms and compounds **6b** and **9b**, inactive toward all PDE4 isoforms), when studied in open field test in mice, did not affect locomotor activity at doses comparable with those of rolipram able to decrease locomotor activity and prolong immobility time. Compound **11**, having a non-selective rolipram-like enzymatic profile, caused a similar even if not significant reduction in spontaneous motor activity.

In conclusion, these findings further support the idea that selective PDE4D inhibition may represent an innovative cognitive-enhancing pharmacological strategy lacking side-effects such as emesis and sedation.

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FAR-PO-09 Synthesis and Enzymatic Evaluation of NAD Mimics as Nicotinamide Adenine Dinucleotide Kinase (NADK) Inhibitors

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NAD kinase (NADK) is a key enzyme that regulates supply of NADP in the cell. At this time no other pathway of NADP biosynthesis has been found in prokaryotic or eukaryotic cells. Human NAD kinase catalyzes a magnesium-dependent phosphorylation of the 2'-hydroxyl group of the adenosine ribose moiety of NAD using ATP as phosphoryl donor to give NADP. Bacterial enzymes can use inorganic polyphosphates as phosphoryl donors in addition to ATP. Significant differences between the human and the mycobacterium enzyme were found that might allow for construction of inhibitors with selectivity against these proteins. Therefore, *M. tubercolosis* NADK has became an appealing new target for the development of potential drugs against multi-drug resistant (MDR) and extensively drug resistant (XDR) tubercolosis (TB).

Recently, we have reported that dinucleoside disulfide NAD mimics, such as diadenosine disulfide (DTA), were found to be moderate inhibitors of *M. tubercolosis* and human NADKs. A restriction of the conformation of adenine moiety to *syn* by substitution with a bulky bromine atom at the C8 of one or two adenine rings of DTA, furnished the most potent inhibitors of both human and mycobacterium NADK reported so far. On the contrary, fixing the sugar conformation in the "North" or "South" conformation by introduction of a methyl group at the 2'- or 3'-position of the ribose ring was detrimental for NADK inhibitory activity [1].

To further investigate the structural features of the ribose moiety, herein we report the synthesis and the NADK inhibitory activity of 2'-deoxy-, 3'-deoxy-, and 2',3'-dideoxy-DTA. The results of this study will be presented.

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FAR-PO-10 Dual-Acting Drugs: Antioxidant Activity of Voltage-Gated Sodium Channel Blocking Agents Coupled To A Pyrroline Moiety.

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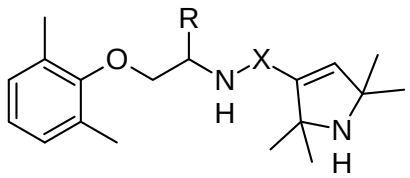
The oxidative stress plays an important role in the pathogenesis of many diseases such as cardiovascular and neurodegenerative disorders, accounting for the great interest in the identification and development of better and more effective antioxidants. Mexiletine (Mex), a well-known voltage-gated sodium channel blocker, can also act as an antioxidant by inhibiting hydroxyl radical-mediated lipid peroxidation in brain membranes.[1] Mex has also been reported to protect the neuronal tissues against diabetic oxidative and ischemia-reperfusion damages.[2] Moreover, a pyrroline derivative of Mex (R=CH_3, X=CH_2) has been demonstrated to be capable of providing marked protection against ischemia-reperfusion myocardial injury.[3] In the last ten years we have prepared several Mex analogues, most of which act more potently than Mex in blocking skeletal muscle voltage-gated sodium channels.[4] Thus, looking for a synergism between sodium channel blocking activity and antioxidant properties, we have coupled our most potent and selective compounds with a pyrroline moiety in order to obtain potential dual-acting drugs.



X = CO, CH_2

R = CH_3, *i*Pr, *t*Bu, Ph, Bn

Results obtained on skeletal muscle voltage-gated sodium channels for the pyrroline derivative of Mex (R=CH_3, X=CO) and its isopropyl analogue (R=*i*Pr, X=CO) revealed that both compounds show improved potency compared to Mex as use-dependent sodium channel blockers. Herein we report on the activity of pyrroline derivatives as scavengers of hydroxyl radicals.

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FAR-PO-11 Monitoring the effect of antagonist on P53-MDM2 interaction with NMR spectroscopy. Recent results.

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The tremendous challenge of inhibiting therapeutically important protein-protein interactions has created the opportunity to extend traditional medicinal chemistry to a new class of targets and to explore nontraditional strategies. Holak and co. have recently described a two-dimensional ^{15}N-HSQC based NMR assay for studying the effect of antagonists on protein-protein interactions [1]. The method, named AIDA (for antagonist induced dissociation assay), provides information on whether an antagonist of a protein-protein interaction is strong enough to dissociate the complex and whether its action is through denaturation, precipitation, or release of a protein in its functional folded state. AIDA requires the use of a large protein fragment (larger than 30 kDa) to bind to a small reporter protein (less than 20 kDa). In appropriate conditions (flexible residues), 1D proton NMR spectra may suffice for monitoring the states of proteins in complexes upon treatment with ligands. Because of the highly flexible nature of the N-terminal domain of p53, p53-MDM2 complex is suitable for 1D proton NMR application. In particular, the NHε side chains of W23 and W53 produce sharp lines in the free p53 1D proton spectrum. On formation of the complex with MDM2, W23 signal disappears, since W23, together with the p53 residues 17-26, comprises the primary binding site for MDM2. Hence it is possible to determine the activity of potential p53-MDM2 antagonists acquiring the ^{1}H NMR spectrum of the protein complex. We have recently applied this method to a series of spiro(oxindole-3,3'-thiazolidine) derivatives thus discriminating the compounds able to block the p53-MDM2 interaction [2]. The method is now applied to new series of peptide and small molecule compounds to screen their p53-MDM2 antagonist properties.

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FAR-PO-12 Targeting the FXR Nuclear Receptor through a Virtual Screening Approach

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Farnesoid X Receptor (FXR) belongs to a family of nuclear receptors that are ligand-inducible transcription factors. FXR is highly expressed in the liver and intestine and is activated by bile acids, such as chenodeoxycholic acid (CDCA) and cholic acid (CA), and their corresponding conjugates at physiological concentrations. FXR functions as a bile acid sensor in enterohepatic tissues, regulating several target genes associated with bile acid synthesis and transport [1]. Activation of FXR by bile acids or synthetic agonists results in transcriptional repression of cholesterol 7α-hydroxylase (CYP7A1), the rate-limiting enzyme in the bile acid biosynthesis pathway, induction of the small heterodimer partner (SHP), a transcriptional repressor found in the liver and intestine, an induction of genes encoding for some bile acid transport proteins, such as intestinal bile acid-binding protein (IBABP) [2] and bile salt export pump (BSEP) [3]. Furthermore, bile acid-mediated FXR activation is recently recognized as a major underlying pathway for energy homeostasis and glucose as well as lipid metabolism.

FXR has also been suggested to counteract pro-inflammatory and pro-atherogenic responses in cardiovascular diseases.

All these evidences make FXR a promising potential target for the treatment of a variety of metabolic disorders, including hyperlipidemia, cholelithiasis, cholestasis, and diabetes mellitus.

Over the past few years, many efforts have been dedicated to the search of highly potent steroidal- and nonsteroidal FXR modulators. With the aim of discovering novel classes of nonsteroidal FXR ligands, we initiated a virtual screening protocol based on the information retrieved by the crystal structures of FXR in complex with agonists. A multistep approach using ligand and structure-based techniques will be presented.

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FAR-PO-13 Recent Advances in the Development of New Human Monoamine Oxidase Inhibitors: (Hetero)arylidene-(4-substituted-thiazol-2-yl)hydrazines

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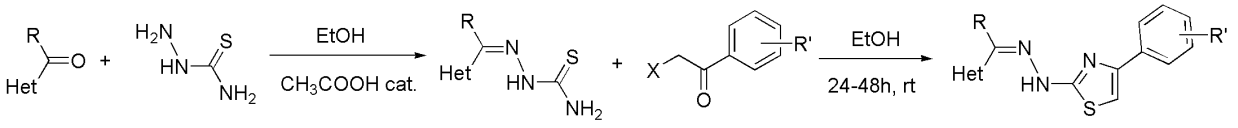
Monoamine oxidases are flavoenzymes which exist in two isoforms: MAO-A and MAO-B. They catalyze the oxidative deamination of endogenous and exogenous monoamines, and are involved in the pathogenesis of mental disorders, particularly depression (hMAO-A), and neurodegenerative diseases such as Parkinson's and Alzheimer's (hMAO-B).

In previous studies conducted by our research group, several 1-(4-substituted-thiazol-2-yl)-2-(alkyl/cycloalkyl/aryl)hydrazines have been studied as potent and selective hMAO inhibitors.[1-4] A large number of new (hetero)arylidene-(4-substituted-thiazol-2-yl)hydrazine derivatives were synthesized in high yields (Scheme 1) and tested for their in vitro ability of inhibiting hMAOs. All compounds showed weak or absent inhibitory activity against hMAO-A, while they were able to inhibit hMAO-B at micromolar or nanomolar concentration. The anti-hMAO activity and selectivity are associated with the presence of small heterocyclic moieties on the hydrazonic nitrogen and electron withdrawing substituents at the *para* position of the phenyl ring, in particular fluorine, which is oriented towards the FAD coenzyme.



Scheme 1 : Synthesis of (hetero)arylidene-(4-substituted-thiazol-2-yl)hydrazine derivatives

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FAR-PO-14 Synthesis and antiplasmodial activity of new heteroaryl derivatives of 7-chloro-4-aminoquinoline

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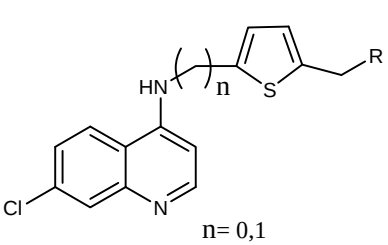
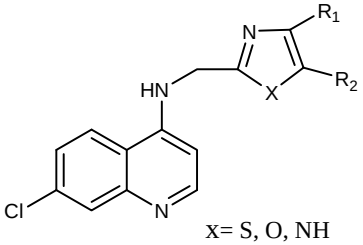
Presently, the most promising and successful strategy in fighting malaria is the artemisinin-based combination therapy (ACT). Recent reports of ACT treatment failure in southeast Asia and the potential emergence of artemisinin resistance indicate that the search of new drugs or new combinations is still highly necessary. In order to develop new classes of antimalarial agents, we recently demonstrated that the replacement of the phenolic ring of amodiaquine and tebuquine with a pyrrole nucleus, still linked to the quinoline moiety through the usual NH, is associated with a good activity against both chloroquine sensitive (CQ-S) and chloroquine-resistant (CQ-R) strains of *P. falciparum* [1-2].
With the aim to investigate the effect of other different heterocyclic rings linked to the 4-aminoquinoline nucleus on the antimalarial activity, a set of 7-chloro-N-(heteroaryl)-methyl-4-aminoquinoline and 7-chloro-N-(heteroaryl)-4-aminoquinoline was synthesized and tested. All compounds exhibited from moderate to high antiplasmodial activities, and the most potent molecules inhibited the growth of both CQ-S and CQ-R strains of *P. falciparum* with IC_{50}<30 nM. The activity was strongly influenced both by the presence of a methylenic group, as a spacer between the 4-aminoquinoline and the heterocyclic ring, and by the presence of a basic head. Moreover, preliminary data indicate that the new compounds exhibit low toxicity against a human endothelial cell line (HMEC-1). All these results confirm that the presence of an heteroaryl moiety in the side chain of 7-chloro-4-aminoquinoline is useful for the design and development of new powerful antimalarial agents.



n= 0,1



x= S, O, NH

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FAR-PO-15 Synthesis and Pharmacological Evaluation of *meta*-Hydroxymexiletine, a Polar Metabolite of Mexiletine

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Mexiletine, 1-(2,6-dimethylphenoxy)-2-propanamine (Mex, Fig. 1), a class IB antiarrhythmic drug, represents the standard therapy for myotonic patients because of its ability to use-dependently block hNav1.4 skeletal muscle voltage gated sodium channel [1]. In Italy it has been withdrawn because of CNS and cardiac toxicity.

We recently reported the first synthesis of *meta*-hydroxymexiletine (MHM, Fig. 1), a minor metabolite of Mex, more polar than the parent compound, and thus probably endowed with less side effects than Mex. MHM had been already isolated and partially characterized, in 1991, from urine of rats [2] but it had never been synthesized.

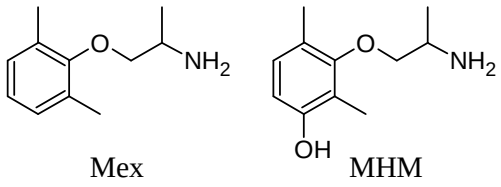

Figure 1. Structures of Mex and MHM

A new synthetic route to both racemic and homochiral MHM will be presented. Moreover, results from pharmacological tests run on MHM will be reported. In particular, unlike other Mex metabolites (*para*-hydroxymexiletine and hydroxymethylmexiletine) [3–5], which were significantly less active than Mex, MHM does retain skeletal muscle sodium channel blocking activity being even more potent than Mex.

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FAR-PO-16 Novel 8-aroylamino-2-phenylimidazo[1,2-a]pyrazines as human A_3 adenosine receptor antagonists.

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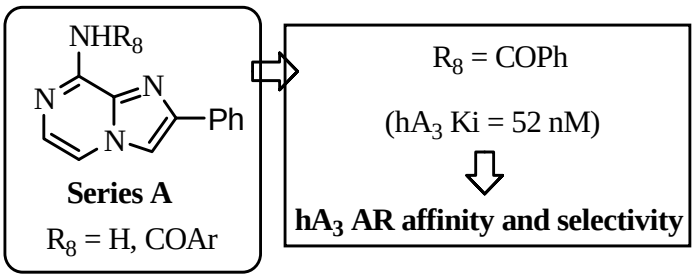
Adenosine is an endogenous purine nucleoside that modulates many physiological processes by interacting with four G-protein coupled receptors termed A_1, A_{2A}, A_{2B}, and A_3. There is concrete evidence that adenosine receptors (ARs) could be promising therapeutic targets in a wide range of pathological conditions [1]. Recently, the involvement of A_3 ARs in neuroprotection has been proposed [2], thus suggesting the investigation of A_3 antagonists as neuroprotective in stroke [3]. This promising therapeutic application has produced a growing interest for this research field. In fact, also in our laboratory, much effort has been directed toward the study of human (h) A_3 AR antagonists belonging to different classes of heteroaromatic systems. The present research project takes its place into this scenario. Structural simplification of our previously reported tricyclic AR antagonists [3-5], has led to the design of some suitably substituted 2-phenylpyrazolo[1,2-a]pyrazines (**Series A**) as hA_3 AR antagonists. Preliminary results are encouraging. In fact, thought the 8-amino-2-phenyl-imidazo[1,2-a]pyrazine was inactive at all four ARs, introduction of a benzoyl substituent on the 8-amino group moved the affinity towards the hA_3 AR. To improve hA_3 affinity and selectivity, the synthesis of some new 8-acylamino derivatives of **Series A** are in progress. Molecular docking studies will be performed to interpret the observed affinities of the new AR antagonists.



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FAR-PO-17 BIOACTIVE LIPIDS METABOLITES IN *AMANITA VIROSA* AS THROMBIN INHIBITORS

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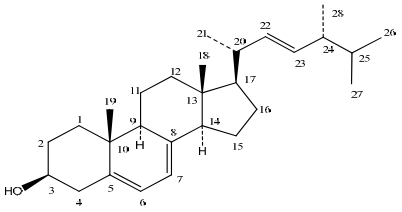
Amanita fungi are the main lethal toadstool among the 1000 poisonous mushrooms known in the world. Thrombin is the key serine proteinase of the coagulation cascade and therefore a suitable target for inhibition of blood coagulation. An extract of *Amanita virosa* considerably inhibited thrombin (48%) and showed no inhibitory activity on trypsin. On the basis of inhibition selectivity between thrombin and trypsin and potency of thrombin inhibition, *Amanita virosa* constituted a good starting material for isolation of further compounds that are active against thrombin.

In a preliminary study, 95 selected mushroom species have been screened in order to find novel specific non-peptidic thrombin inhibitors. The extract of *Amanita virosa* considerably inhibited thrombin (48% at concentration of 120 µg/mL).[1]



A bioassay oriented fractionation of the extract of *Amanita virosa* has led to the isolation of active compounds. On the basis of spectroscopic data, chemical reactions and GC-MS analysis, complex mixtures of triglycerides, monoacylglycerols, free fatty acids and ergosterol have been isolated and identified.

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FAR-PO-18 NO-Donor Cyanines As Potential Anti-Alzheimer Drugs

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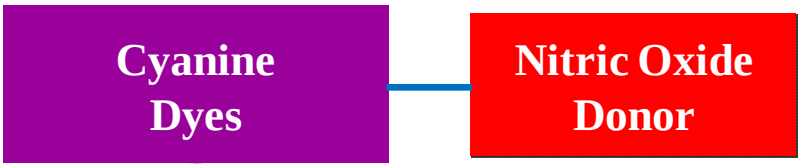
A first report of what was later named "Alzheimer's disease" (AD) was made by Alois Alzheimer in 1907, where he described a 51-year old women with rapid memory degeneration. Although the disease was once considered rare, it is now established as the leading cause of dementia which involve more than 20 millions of persons in the world with enormous social and affective costs [1]. Despite major research efforts AD is still not curable. The difficulty for developing satisfactory therapy of AD lies in the complex pathophysiology of disease which involves numerous pathways. These include deficiency in cholinergic neurotransmission, defective β-amyloid protein metabolism, accumulation of aggregated τ-proteins within neuronal cell, abnormalities of glutamatergic, adrenergic, serotonergic and dopaminergic neurotransmission, and involvement of inflammatory, oxidative and hormonal pathway [2, 3]. Although the exact aetiology of AD is still unclear an increasing amount of experimental data suggests that AD is a cerebral microvascular disorder with neurodegenerative consequences. Microvascular disorders occurring in advanced ageing or in the presence of increased oxidative stress are consequent to the endothelial dysfunction, namely reduced endothelial cell capacity to produce nitric oxide (NO) [4].

Due to the multy-pathogenesis of AD, and considering the statement that there is a link between endothelial dysfunction and AD, we designed new multitarget drugs, potentially useful in modifying the development and the progress of the disease (figure 1). The products were obtained by combining a carbocyanine dye substructure, endowed with inhibitory properties of β- and τ-protein aggregation, as well as antioxidant activity [5], with NO-donor moieties. Synthesis, inhibitory properties of β-amyloid protein aggregation and vasodilator properties, due to activation of cGMP-dependent protein kinase (PKG) pathway of these products are reported and discussed.



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FAR-PO-19 3-Hydroxy-1H-quinazoline-2,4-dione derivatives as new antagonists at ionotropic glutamate receptors: molecular modeling and pharmacological studies

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Glutamate (Glu) plays pivotal roles in regulating many physiological processes by activation of metabotrobic and ionotropic receptors (iGluRs), these latter being classified as NMDA, AMPA and Kainate (KA) receptors. Excessive glutamatergic transmission is involved in several neurological disorders, including hypoxia/ischemia brain damage and epilepsy, thus the blockade of iGluRs could be employed for the treatment of these pathologies [1].

In our laboratory, some research has been devoted to the study of iGluR antagonists such as the 3-hydroxyquinazoline-2,4-dione derivatives of series **1**, in which the 7-chloro substituent was combined with various groups at position 6 (R_6). Structure-affinity relationship (SAR) studies showed that the nature of R_6 was critical for the selectivity toward the different iGluRs (Figure 1) [2,3]. Recently, we planned the synthesis of new 6-substituted 3-hydroxyquinazoline-2,4-diones (series **2**) bearing a 7-trifluoromethyl residue, since this group was thought to increase AMPA and KA receptor selectivity. Preliminary binding results showed that the new compounds possess increased AMPA receptor affinity and selectivity, with respect to the previously reported 7-chloro derivatives. Selected compounds exhibited good protective effect in an in vitro rat model of cerebral ischemia. To interpret the observed SAR, molecular modeling studies are in progress by docking compounds to models of the target receptors.

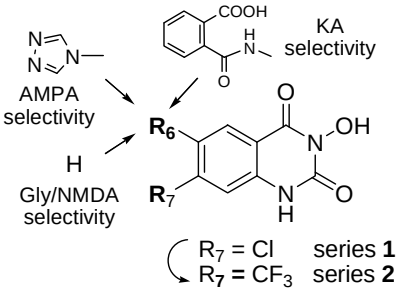

Figure 1

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FAR-PO-20 Indolylarylsulfones as HIV-1 Non-Nucleoside Reverse Transcriptase Inhibitors. New Cyclic Substituents at the Indole-2-carboxamide.

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New indolylarylsulfone (IAS) [1,2] derivatives bearing cyclic substituents at the indole-2-carboxamide linked through a methylene/ethylene spacer are potent inhibitors of the HIV-1 WT replication with inhibitory concentrations in the low nanomolar range.

We report the results of docking and molecular dynamics experiments on this family of compounds. Analysis of the proposed binding pose into the WT and mutated RTs for the highly active compounds 5-chloro-3-((3,5-dimethylphenyl)sulfonyl)-*N*-(pyrroldin-1-yl)-1*H*-indole-2-carboxamide (**1**), it is possible to highlight a series of crucial interactions: (i) a H-bond between the indole NH and Lys101; (ii) the 3,5-dimethylphenyl moiety forms hydrophobic interactions in an aromatic cleft formed by Tyr181, Tyr188, and Trp229; (iii) a H-bond between the nitrogen atom of the heterocycle and the Glu138:B.

The model proposed is in good agreement with the biological results: **1** EC_{50} 3.3 nM; IC_{50wt} 12nM; $IC_{50L100I}$ 26nM, $IC_{50K103N}$ 93nM

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FAR-PO-21 Synthesis and Carbonic Anhydrase Inhibitory Activity of New 2-Aminochromenone Derivatives

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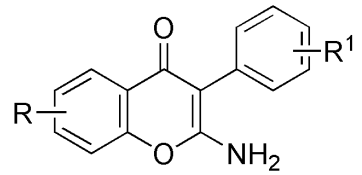
Carbonic anhydrase (EC 4.2.1.1, CA) is a family of metalloenzymes that catalyze the conversion of CO_2 to HCO_3^- and H^+, being involved in many physiologic processes [1]. CA isoforms are found in a variety of tissues where they participate in several important biological processes such as acid–base balance homeostasy, respiration, carbon dioxide and ion transport, bone resorption, ureagenesis, gluconeogenesis, lipogenesis, electrolyte secretion, and tumorigenesis among others [2]. Among the various natural antioxidants, phenolic compounds are reported to be active, quenching oxygen-derived free radicals by donating hydrogen atom or an electron to the free radical. Resveratrol, catechin, silymarin, and curcumin are natural compounds which are potent drugs, and dobutamine is a cardiac drug used after operations. Resveratrol (trans 3,4,5-trihydroxystilbene) is one such polyphenolic compound; it is found in red wine and is reported to have a variety of beneficial health effects, including protection against cardiovascular diseases [3]. We are now interested in evaluating of a new series of 2-aminochromenone derivatives **1** strictly related to the above-mentioned natural phenols in order to study their inhibitory activity towards CA isoforms.



1

Here, we reported synthetic route to this family of compounds, and preliminary results of biological in vitro assays on carbonic anhydrase, using the esterase activity of hCA I and II, with 4-nitrophenyl acetate as substrate.

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FAR-PO-22 Synthesis and Antimicrobial Activity of of new-substituted-4*H*-1,4-benzothiazines

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Bacterial resistance to antibiotics has become an increasingly serious problem in recent years. Drug-resistant pathogens have evolved the MRSA and the VRSA phenotype. Unfortunately, bacterial resistance has also emerged against newer agents such as linezolid and daptomycin shortly after their use in clinic[1] . Therefore the development of new and different antimicrobial drugs is very important goal and most of the research program efforts in this field are directed towards the design of new agents.

It is well documented that benzothiazine template is generally recognized as a privileged structure in medicinal chemistry to investigate both potentially anticancer[2] and antibacterial molecules[3]. Looking at the importance of benzothiazine nucleus, in the recent past, we reported several examples of benzothiazine derivatives bearing substituents on the heterocyclic ring able to exhibit both antibacterial and antifungal activity (Figure 1).

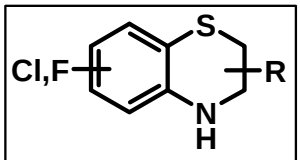
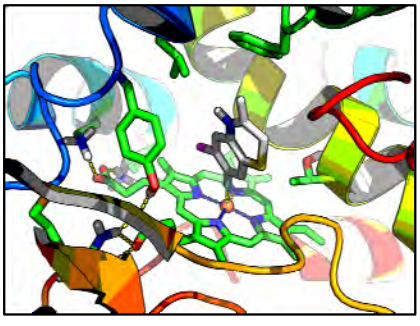


Figure 1

Here in, in continuation to extend our research on the synthesis and biological behaviour of *4H*-1,4-benzothiazine analogues as potential drugs for antimicrobial management, we have been interested in the preparation and in SAR studies of new compounds containing modified benzothiazines.

In order to enhance selectivity and potency, the MIC (Minimal Inhibitory Concentration) of the benzothiazine derivative, recorded on different Gram positive, Gram negative and Fungi strains belonging to American Type Colture Collection (ATCC) was reported. Docking studies carried out on the most active compound suggested a plausible binding mode for this class of antimicrobial agents.



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FAR-PO-23 Synthesis and pharmacological evaluation of Spiroxatrine derivatives as potential ligands for NOP receptor

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Nociceptin or orphanin FQ neuropeptide (N/OFQ) was identified in 1995 as the endogenous ligand for the NOP receptor, formerly known as ORL-1, a fourth member of the classical μ, δ and κ opioid receptors family [1]. N/OFQ-NOP system is found in central and peripheral nervous tissue, where it plays a key role in the nociception modulation, among other biological phenomena. Therefore, NOP receptor may provide a target for novel therapeutics against acute cancer pain [2]. On the basis of the confirmed affinity towards NOP receptor of the α_2 adrenergic and 5-HT_{1A} partial agonist spiroxatrine (K_i= 127 nM) [3], we focused our attention on the design, synthesis and characterization of novel NOP receptor ligands with a spiropiperidine core. At first, we studied the replacement of 1,4-benzodioxanyl moiety of spiroxatrine with 2-phenyl-, 2,2-diphenyl-1,3-dioxolanyl and 1,4-spirodioxolanyl moiety, as in derivatives **1-3** (**Fig.1**). These compounds were evaluated in Chinese Hamster Ovary cells co-expressing the human recombinant NOP receptor and the C-terminally modified $G\alpha_{qi5}$ protein (CHO_{hNOP} cells). The bioassays showed that derivative **3** behaves as weak NOP receptor agonists (**pEC_{50} 6.29**), with potencies ~1000 fold lower than N/OFQ (**pEC_{50} 9.39**). From the most promising lead candidate **3**, we synthesized a series of 1,4-spirodioxolan-1,3,8-triazaspirodecanones (derivatives **4-13**, **Fig.1**). Biological assay results showed that the most interesting compounds of this series are **6** and **7**, with pEC_{50} values comparable to that of spiroxatrine (**pEC_{50} 5.81**, **6.33** and **6.10** respectively), but still ~1000 fold lower than N/OFQ.

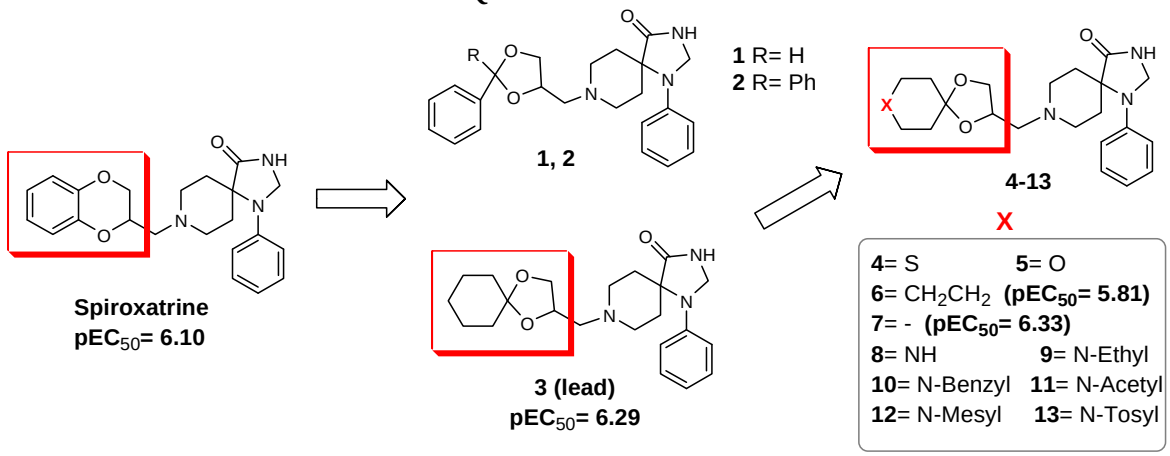

Figure 1

The key reaction to obtain derivatives **1-13** is the nucleophilic substitution between 1-phenyl-1,3,8-triaza-spiro[4,5]decan-4-one and the toluensulfonate- or 2-chloromethyl-intermediates resulting from the appropriate ketone or aldehyde, in the presence of Na_2CO_3 and dimethylformamide as solvent [4].

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FAR-PO-24 Synthesis, antiproliferative activity, and mechanism of action of new benzamido derivatives

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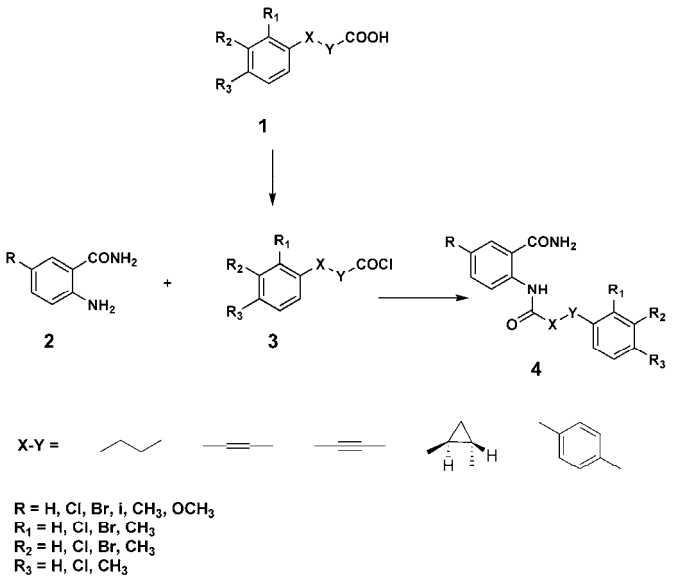
The cinnamoyl anthranilamides represent a class of biological active substances of great importance in medicinal chemistry [1,2]. Moreover, despite their wide range of biological activities, a review of the literature revealed that no anticancer activity is described for this kind of substances. Starting from the 2-cinnamamido-5-iodobenzamide, resulted able to inhibit the leukemic cell line K-562 proliferation with a percent of inhibition of 74% at 10μM concentration [3], we undertake the following structural modifications on cinnamamidobenzamide skeleton: the introduction of various substituents both on the benzamido and the cinnamamido moieties, the substitution of olefinic bond with the ethane, ethyne, cyclopropane and phenyl groups as reported in the scheme.



Compounds **4,** bearing an ethylene bond, caused growth inhibition against many tumor cell lines at low micromolar and submicromolar concentrations against every tumor cell line investigated The best activity was obtained when the 5 position of the benzamido moiety was substituted with an iodine moiety. COMPARE analysis, effects on tubulin polymerization and cell cycle distribution (G2-M phase block), including induction of apoptosis, indicate that these new antiproliferative compounds act as antitubulin agents [3]. Preliminary biological data on 2-(3-phenylpropiolamido)benzamides **4**, bearing an ethyne bond, showed a different mechanism of action considering that they caused a G0-G1 block of the cell cycle on K526 cell line.

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FAR-PO-25 Rationalization of the Efficacy at the Human A_3 Adenosine Receptor of 2- and N^6-Substituted Adenosine and NECA Derivatives

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A_3 adenosine receptor (A_3AR) subtype is highly expressed in lungs, liver, and immune cells, and at lower densities in heart and brain and it is involved in a variety of key physiological processes such as release of inflammatory mediators and inhibition of tumor necrosis factor-α production. Agonists of this receptor have been recently analysed for pharmaceutical development based on their anti-inflammatory, anticancer, and cardioprotective effects [1,2]. On this basis, the design and synthesis of potent and selective A_3AR agonists could be helpful to provide tools for further characterization and evaluation of the physio-pathological role of this receptor and for the development of new drugs.
Some years ago, we have reported the synthesis and binding affinity of a number of adenosine (Ado) derivatives bearing in 2-position (ar)-alkynyl chains, endowed with good affinity and different degrees of selectivity for the human A_3AR [3]. The replacement in these compounds of the hydroxymethyl group in 4'-position of the sugar moiety with an ethylcarboxamido function or the introduction in N^6-position of small alkyl groups enhanced A_3AR affinity and selectivity, leading to compounds with A_3AR K_i values at low nanomolar level.
These molecules were tested for their ability to inhibit forskolin-stimulated adenylyl cyclase activity. Results showed that all the 5'-*N*-ethylcarboxamidoAdo (NECA) derivatives behave as full agonists of A_3AR, while the 4'-unmodified Ado derivatives present a partial agonist profile at the same receptor. The N^6-substituents do not change the partial agonist activity observed for Ado derivatives unsubstituted at N^6-position.
Molecular modeling analyses, carried out by using the recently solved A_{2A}AR crystal structure as template for homology modeling studies, helped to get a rationalization of the different pharmacological profile of the presented molecules at the human A_3AR.

[1] G. Cristalli, R. Volpini, *Curr. Top. Med. Chem., 3,* **2003**, 355.
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FAR-PO-26 Benzothiopyranoindole and Pyridothiopyranoindole-based antiproliferative agents: Synthesis, Cytotoxicity and Topoisomerases Inhibition Properties.

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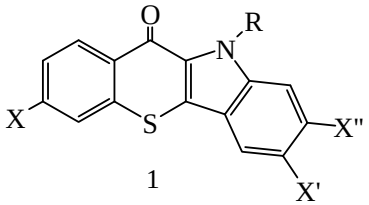
DNA topoisomerases (Topo I and Topo II) are essential enzymes that regulate the topological state of DNA during cellular processes such as replication, transcription, recombination, and chromatin remodelling, by catalyzing the relaxation of superhelical DNA through cycles of cleavage and religation. Under normal conditions, the covalent Topo I or II cleaved DNA intermediates are constitutively transient and, since the DNA relegation step is much faster than the cleavage one, they are tolerated by the cell. On the contrary, conditions that significantly alter the physiological concentration or lifetime of these breaks are responsible for DNA alterations that play a crucial role in inhibiting cell cycle progression. In this connection, the ability to interfere with the enzymes or generate enzyme-mediated damages is an effective strategy for cancer therapy; therefore DNA Topos (I and II) proved to be the excellent targets of clinically significant classes of anti-cancer drugs, forming the basis of widely used chemotherapy combinations. As a part of our extensive studies in this field [1,2], we describe the new series of Benzothiopyranoindoles **1** and Pyridothiopyranoindoles **2,** which were functionalized with basic side chains on the indole nitrogen atom.



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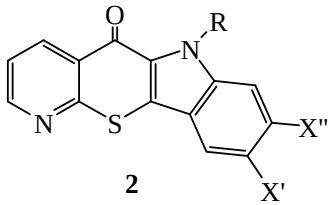

2

The novel derivatives, evaluated *in vitro* for their antiproliferative activity on human tumour cell lines (HeLa, A-431 and MSTO-211H), showed a significant ability to inhibit cell growth with IC_{50} values in the low micromolar range. Linear dichroism measurements showed that the compounds behave as DNA-intercalating agents. Moreover, relaxation assays evidenced a dose-dependent inhibition of Topo I and/or II activity.

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[2] L. Dalla Via, S. Marciani Magno, O. Gia, A. M. Marini, F. Da Settimo, S. Salerno, C. La Motta, F. Simorini, S. Taliani, A. Lavecchia, C. Di Giovanni, G. Brancato, V. Barone, E. Novellino, *J. Med. Chem.*, 2009, *52*, 5429.

FAR-PO-27 Refinement of the Translocator Protein Pharmacophore/Receptor Model via Structure-activity Relationships of Novel *N,N*-Dialkylindolylglyoxylamides

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The Translocator Protein (18 kDa) (TSPO), is widely expressed in glial cells and in peripheral tissues, and is involved in a variety of biological processes (steroidogenesis, cell growth and differentiation, apoptosis induction...) [1,2] TSPO basal expression is alterated in several disorders, including a variety of tumours, neuropathologies and neuroinflammation, anxiety and mood disorders. [1,2]
In last years, we have described potent and selective TSPO ligands, the *N,N*-dialkyl-(2-phenylindol-3-yl)glyoxylamides **I**, [3,4] which allowed the development of newfluorescent or radio-labeled probes targeting this protein [5-7]. In this study, we reported a novel series of indolglyoxylamides, designed to investigate the binding role of the lipophilic pocket L1 of the hypothesized pharmacophore/receptor model.[1,2] Specifically, compounds featuring a bulky biphenyl **II** or 2-napthyl **III** group, phenyl with hydrophilic substituents **IV**, and fur-2-yl or thien-3-yl rings **V** at the 2-position of the indole nucleus, were synthesized and biologically evaluated.

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FAR-PO-28 Lead optimization studies, synthesis and biological evaluation of new isonipecotamide-based orally active thrombin inhibitors

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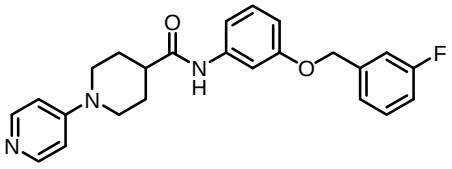
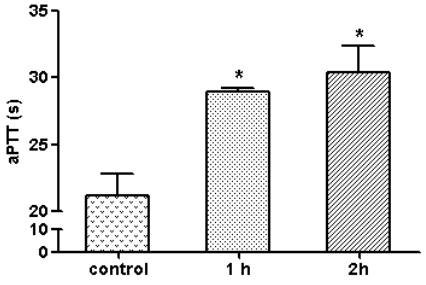
Current anticoagulant therapy of venous thromboembolism (VTE) is based on parenterally administered heparins and orally administered vitamin K antagonists (e.g., warfarin), but narrow therapeutic window and side effects, such as bleeding, diet and genetic makeup influence, are associated with their use [1]. Recently, key serine proteases of the blood coagulation cascade, such as thrombin (thr) and factor Xa (fXa), have emerged as promising targets for anticoagulants, and indeed several direct inhibitors of thr (e.g., argatroban, dabigatran) and fXa (e.g., rivaroxaban, apixaban) have been introduced in therapy or in advanced clinical trials [2,3].
Some years ago we investigated the isonipecotanilide scaffold for new thr/fXa inhibitors [4]. Further optimization studies led us to develop new benzyloxy derivatives of *N*-(phenyl)-1-(pyridin-4-yl)piperidine-4-carboxamide, one of them (i.e., the 3-F analog, see below) showing low nanomolar K_i (thr) value, high selectivity against other serine proteases and good anticoagulant activity as measured by the activated partial thromboplastin time (aPTT) test.



K_i (thr) = 6 nM
K_i (fXa)= 5640 nM
$aPTT_2$ (*in vitro*) = 6.60 μM



Ex vivo aPTT prolongation in mice at 1 h and 2 h after oral administration (100 mg/kg dose).

Physicochemical profiles of the newly synthesized compounds were assessed and their potential oral bioavailability estimated, by measuring effective permeability coefficients using PAMPA (Parallel Artificial Membrane Permeability Assay).

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de Candia, M.; Liantonio, F.; Altomare, C. et al. *J Med. Chem.* **2009**, *52*, 1018-1028.

FAR-PO-29 Novel Bifunctional Compounds Targeting Nicotine and Dopamine Receptor Subtypes: Synthesis and Pharmacological Investigation

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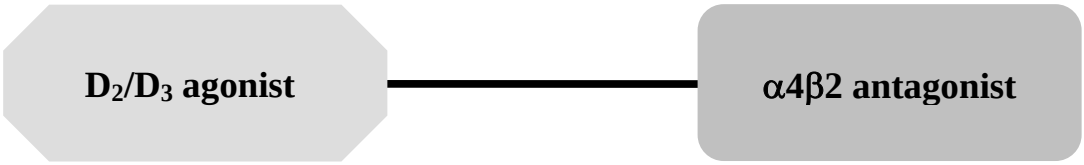
Future therapies for diseases associated with altered dopaminergic signaling, including Parkinson's disease, schizophrenia and drug addiction or drug dependence, may be substantially built on the existence of intramembrane receptor-receptor interactions within receptor mosaics where it is believed that the D_2 receptor may operate as the "hub receptor" [1]. In particular, it has been proposed that striatal dopaminergic neurotransmission could be under the control of receptor heteromers containing D_2 autoreceptors and non-α7 nicotinic acetylcholine heteroreceptors [2].

In an attempt to investigate the biochemical and functional interactions between dopaminergic autoreceptors and nAChRs containing the β2 subunit, we designed and prepared a group of potential bifunctional derivatives incorporating a D_2/D_3 *agonist* moiety and a nicotinic $\alpha4\beta2$ *antagonist* fragment, linked by polymethylene spacers of different length.



The new compounds have been biologically characterized for their affinity/specificity/functional profile at the target nACh and D_2 receptor subtypes. The synthesis of the designed derivatives and the results of their pharmacological investigation will be presented and discussed.

[1] K.Fuxe, D.Marcellino, A.Rivera, Z.Diaz-Cabiale, M.Filip, B.Gago, D.C.S.Roberts, U.Langel, S.Genedani, L.Ferraro, A.de la Calle, J.Narvaez, S.Tanganelli, A.Woods, L.F.Agnati, *Brain Res.Rev.*, *58*, **2008**, 415-452.

[2] D.Quarta, F.Ciruela, K.Patkar, J.Borycz, M.Solinas, C.Lluis, R.Franco, R.A.Wise, S.R.Goldberg, B.T.Hope, A.Woods, S.Ferré, *Neuropsychopharmacol.*, *32*, **2007**, 35-42.

FAR-PO-30 Targeting protein-protein interaction: novel thiophene-pyridine based alpha helix mimetics.

Marcella De Giorgi,[1,2] A.S. Voisin-Chiret, [1] J. Sopková-de Oliveira Santos, [1] M. Muraglia, [2] F. Corbo, [2] C. Franchini, [2] S. Rault[1]

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Protein-protein interactions (PPIs) are attractive targets because they control numerous cellular processes. Consequently their misregulation can result in numerous disease states.[1] In particular, in oncology, among these PPIs, several approaches have been developed to target Bcl-2 family proteins and numerous strategies of non-peptidic small molecules, structurally and functionally alpha helix mimetics have been presented in the literature.[2]

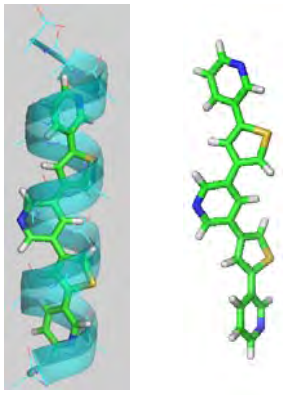

Figure 1

The research program of our laboratory consists the design and synthesis of small to medium sized oligo(het)aryl scaffolds based on a new methodology using iterative Suzuki cross-coupling reactions named Garlanding concept.[3] In particular, this work is focused on the change of the nature of (het)aromatic units with the aim to obtain new less hydrophobic thienyl pyridyl scaffolds (Figure 1). Further, in the case of the peculiar interaction of Bcl-X_L and the BH_3 domain the length and the size of these oligopyridines were guided by our molecular modeling studies on bi-, ter- and quater-pyridines in according with Hamilton's work.

Synthetic aspects, molecular modeling studies and preliminary biological evaluation will be reported in the poster presentation.

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FAR-PO-31 3-Chloroethyl-pyrrolo[2,1-d][1,2,3,5]tetrazines: synthesis and antitumor activity

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diana@unipa.it

Temozolomide is a 3-methyl-imidazotetrazine currently in the market with trade name Temodal® and is used in the treatment of melanoma, mycosis fungoides, and brain tumors [1-4]. Temozolomide itself is a prodrug, spontaneously hydrolyzing at physiologic pH into MTIC (3-methyl-(triazen-1-yl)imidazole-4-carboxamide) and a methyldiazonium ion. This latter acts as a DNA methylating agent mainly at the N7 position of guanine [5-7]. We synthesized pyrrolo[2,1-*d*][1,2,3,5]tetrazinones that hold the deaza skeleton of temozolomide. Surprisingly the 3-methyl derivatives were the least active whereas the 3-aryl compounds had remarkable antineoplastic activity having GI_{50} values from the low micromolar-nanomolar range. Pyrrolotetrazinones showed a mechanism of action different from that observed by temozolomide. Infact they inhibit microtubule polymerization, induce G2/M arrest of cell cycle and cause apoptosis through the mitochondrial pathway. Considering the previous results we synthesised new 3-chloroethyl-pyrrolotetrazinones to verify whether the mode of action would resemble to that of temozolomide or to that of the deaza-analogues. Cytotoxicity was evaluated 72 h after incubation with compounds in several human cell lines. Generally compounds were cytotoxic in Jurkat cells, whereas one of them presents an antiproliferative activity in all cell lines with GI_{50} 20-0.6 μM. Moreover, since the resistance onset is one of the main problems for classical anticancer drugs, the cytotoxicity of this latter compound was also studied in a P-glycoprotein over-expressing cell line and its antiproliferative effect was maintained. We also performed cell cycle analysis to investigate the kind of cellular death (necrosis or apoptosis) and it resulted that compounds induced cell death by apoptosis. However, no clear block in some specific phase was detected. Other studies were also carried out to check the involvement of mitochondria in the apoptotic process after JC-1 cell staining. Other experiments to identify their mechanism of action are now in the pipeline; in particular since temozolomide is a DNA alkylator, DNA will be considered as the possible target for these new compounds.

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FAR-PO-32 Synthesis, Biological Evaluation, and Pharmacokinetic Profile of 1,5-Diarylpyrrole-3-Propoxyethyl Ethers as Selective Cyclooxygenase-2 Inhibitors Endowed with Anti-inflammatory and Antinociceptive Activity

Angela Di Capua,[a*] Michele Rovini,[a] Giulia Ferretti,[a] Andrea Cappelli,[a] Lidia Sautebin,[b] Carla Ghelardini,[c] Paola Patrignani,[d] Antonio Giordani,[e] Mariangela Biava,[f] and Maurizio Anzini.[a]

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A new generation of selective cyclooxygenase-2 (COX-2) inhibitors (coxibs) was developed to circumvent the major side effects of cyclooxygenase-1 (COX-1) and COX-2 inhibitors (stomach ulceration and nephrotoxicity).[1]Structural features of known selective cyclooxygenase-2 inhibitors and of COX isozymes led our research group to synthesize the novel class of 1,5-diarylpyrrole derivatives.A series of previously patented 1,5-diarylpyrrol-3-acetic esters and 1,5-diarylpyrrole-3-alkoxyethyl ethers proved to be potent and selective COX-2 inhibitors in *in vitro* cell culture assay.[1,2] The potential anti-inflammatory and antinociceptive activities of these compounds were evaluated *in vivo*, where they showed a very good activity against both carrageenan-induced hyperalgesia and edema in the rat paw test. In particular, compounds **1** and **2** appear to be equipotent with rofecoxib. In the Human Whole Blood (HWB) test, compound **2** demonstrated to be as selective as valdecoxib. The potential anti-inflammatory and antinociceptive activities of compounds **1** and **2** were evaluated *in vivo*, where they showed a very good activity against both carrageenan induced hyperalgesia and carrageenan induced oedema in the rat paw, with a complete remission 1 hour after the administration.[2,3] Compound **2** was then selected for a preliminary pharmacokinetic analysis in male Sprague−Dawley rats. Unfortunately, plasma levels of this compound showed a low oral bioavailability, probably due to a rapid first-pass metabolism (Fig. 1). So a new series of fluorinated derivatives, **4** and **5**, was synthetized in order to obtain an improved parmacokinetic profile: substitution of the 4'-H by the fluorine atom can profoundly change the conformational preferences of a small molecule because of size and stereoelectronic effects[4] along with the possibility for 4'-F to exert an advantageous metabolic obstruction.

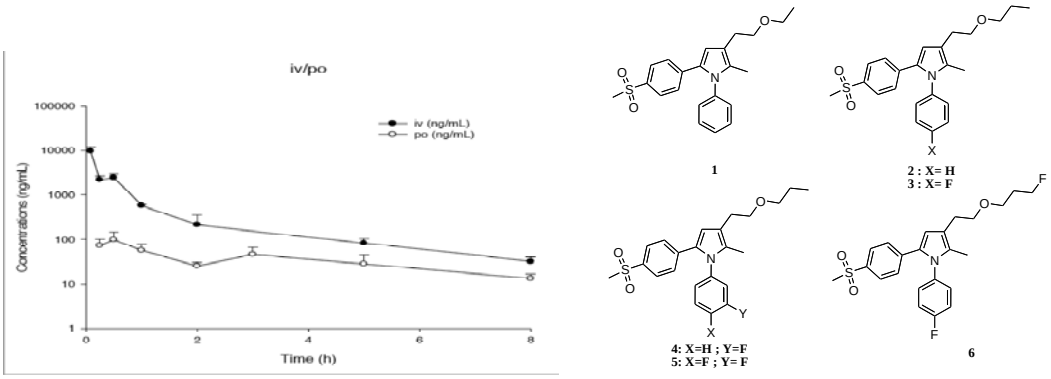

Figure-1: *Profilo della Concentrazione Plasmatica del 2 dopo singola smministrazione orale (10 mg/Kg) e intravenosa (10mg/Kg) in ratti maschi "Sprague-Dawley".*

Compounds **3** and **6** were also synthesized and evaluated as candidate ligands for Positron Emission Tomography (PET) to characterize their pharmacokinetic and distribution properties.

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FAR-PO-33 Elucidating the selective binding behaviour of a series of COXs inhibitors

Francesco Saverio Di Leva,[a] Jagdish Suresh Patel,[a] Vittorio Limongelli,[b,c] Davide Branduardi,[d] Luciana Marinelli,[b] Ettore Novellino,[b] Michele Parrinello,[c] and Andrea Cavalli[a,e]

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Nonsteroidal antinflammatory drugs (NSAIDs) inhibit the cyclooxygenase enzymes (COXs), and are widely used for the treatment of inflammation, pain, and cancers. A selective inhibition of the COX-2 isoform is desirable, as this is overexpressed during inflammatory events.[1] Therefore, many efforts have been directed towards the development of COX-2 selective inhibitors. Unfortunately, most of these inhibitors have been found to be highly cardiotoxic, as they produce a strong prostacyclin/thromboxane imbalance.[2] Therefore, a deep understanding of the molecular bases of COXs selective inhibition is of great demand. Recently, we have successfully used metadynamics[1] to study the binding behavior of a highly potent COX-2 selective inhibitor, SC-558, in both COX-1 and COX-2 isoforms.[2] Following the line traced in our previous work, we have here extended the metadynamics studies on a series of potent COXs inhibitors endowed with different selectivity profiles. Our results provide useful computational tools to design small organic molecules with fine-tuned COX-1/COX-2 potency and selectivity. Furthermore, these results can be of paramount importance in the design of less toxic novel anti-inflammatory drug candidates.

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FAR-PO-34 5-Alkylamino-pyrazolo[4,3-*e*]1,2,4-triazolo[1,5-*c*]pyrimidines. Influence of the Substituent on the Affinity at the Adenosine Receptor Subtypes.

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It is well known that adenosine interacts with G-protein coupled receptors that were classified in four receptors subtypes: A_1, A_{2A}, A_{2B} and A_3 adenosine receptors (AR). Adenosine receptor antagonists have several potential therapeutic applications. In particular, A_1 antagonists are diuretic. Because antagonism towards A_{2A} AR gave neuroprotection, antagonists for this receptor subtype are useful in neurodegenerative diseases, in particular for the treatment of Parkinson's disease. A_{2B} AR antagonists could be used in asthma and diabetes, while A_3 antagonism is useful in glaucoma, moreover, due to the fact that A_3AR is widely expressed in some cancer cells, A_3AR antagonists could be used for tumoral diagnosis.[1]

It was demonstrated by several studies that pyrazolo-triazolo-pyrimidine (PTP) core is a good template to obtain potent and selective adenosine receptor antagonists.[2] Until now all the PTP derivatives substituted at the 5 position bear phenylureidic or phenylacetamidic moieties, with a very poor variability.[3] So we have synthesized a novel class of 5-alkylamino-pyrazolo[4,3-*e*]1,2,4-triazolo[1,5-*c*]pyrimidines. This kind of substitution allows the introduction of several different amines, such as alkyl, cycloalkyl and benzyl amines, but also disubstituted-amines and hydroxylamines, which enabling the investigation of both the volume and nature of the receptor binding cavity.

Good results were obtained towards the A_3 adenosine receptor subtype, in particular when a 5-bulky substituent, such as a benzhydrylamine, was present (K_ihA_3=0.83 nM). Moreover a stereoselectivity by the binding pocket was observed for the derivatives substituted with a 1-phenyl-ethylamine, where the S isomer was 12-fold more potent than the R isomer at the A_3 AR.

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FAR-PO-35 Synthesis and Evaluation of Platelet Aggregation Inhibitory Activity of Some 3-Phenyl-pyrroloquinazolinones

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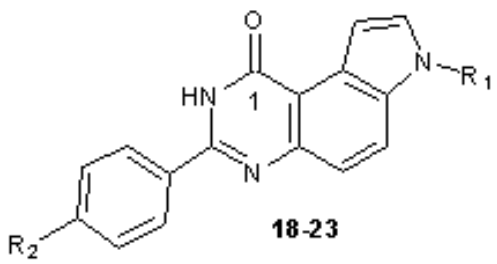
Continuing our research on synthesis and study of biologically active compounds, a series of 3-phenyl-pyrrolo[3,2-*f*]quinazolin-1-one derivatives was synthesized starting from 5-amino-indoles via a condensation with *N*-ethoxycarbonylthiobezamides and next thermal cyclisation. . The newly synthesized compounds showed the absence of cytotoxic activity on human cell lines in vitro up to 50-100 µM concentrations. On the basis of their structural analogy with anti-thrombin pyrroloquinazolines reported in Literature [1-4], some of them were chosen to evaluate their inhibitory effect on platelet activation and aggregation**.** The most active compound **18** inhibited collagen- and thrombin-induced platelet aggregation in concentration dependent manner causing a complete inhibition at a concentration of about 4 µM. Other experiments, performed with compound **18**, addressed to study the action-mechanism of these pyrroloquinazolinones, suggest that they act at least at two sites: one preceding the agonist-induced increase of cytosolic [Ca^{2+}], deriving from the endoplasmic reticulum, and protein-kinase activation, and one following these events in the platelet activation cascade leading to aggregation. Synthesis of new compounds **18-23** (Fig. 1) and results from a preliminary biological activity evaluation will be reported.



18-23

compound	R_1	R_2
18	H	H
19	C_2H_5	H
20	C_3H_7	H
21	CH_2-cyclopropyl	H
22	C_2H_5	OCH_3
23 (1-tione)	C_3H_7	H

Figure 1. Structures of phenyl-pyrroloquinazolinones synthesized and screened for their platelet aggregation inhibitory activity.

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FAR-PO-36 NO-Donor Carnosine Derivatives As Potential Neuroprotective Agents

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Ageing affects many cellular processes which favor chronic neurodegenerative diseases, among them Alzheimer's disease (AD). AD is a complex pathology which involves more than 20 million individuals in the world.[1] AD is characterized by memory loss and other cognitive deficiencies, by the progressive dissolution of the personality as well as of the intellectual capacities. AD is accompanied by damages to brain capillaries, impairment of cholinergic transmission in both the hippocampus and the cerebral cortex as well as by extracellular accumulation of β-amyloid (Aβ) plaques and intracellular tau protein aggregates in different area of the brain. In addition, it has been shown that oxidative stress, related to an abnormal production of reactive oxygen species (ROS) and nitrogen species (RNS) and/or depletion of the antioxidant defences, is an important early event in AD.[2] An increasing amount of experimental data suggests that AD is a cerebral microvascular disorder with neurodegenerative consequences, rather than the opposite. Microvascular disorders occurring in advanced ageing or in the presence of increased oxidative stress are consequent to the endothelial dysfunction, namely to a reduced capacity of the endothelial cells to produce nitric oxide (NO).[3] On this basis we designed new "multifunctional" molecules potentially useful in modifying the development and the progress of AD. These products were obtained by combining the structure of L-carnosine, a natural dipeptide endowed with a complex and multifactorial antioxidant action, with nitrooxy NO-donor moieties. These two pharmacophores were joined through an amide bond which, in a previous work, allowed us to obtain compounds stable in human serum, overcoming the major drawback of carnosine, while preserving its beneficial properties.[4] Synthesis, serum stability, vasodilating properties, antioxidant activity, ability to scavenge reactive carbonyl species (RCS) as well as copper (II) chelating properties of the obtained models are reported.

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FAR-PO-37 *Eremurus persicus* Boiss: ethnobotanical relevance, analytical fingerprint and preliminary biological results of root extracts

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Recently, the drug discovery process has been frequently focused on the screening of plant extracts commonly used in traditional medicines as source of novel therapeutic agents. In this context, the object of the present study was to evaluate the folk claims of *Eremurus persicus*. Genus *Eremurus* (*Asphodelaceae*), with its 45 species, is distributed over large area in Central Asia [1]. *Eremurus persicus* (Jaub. & Spach) Boiss is a medicinal plant of Kurdistan; its root extracts are used by native people as folk remedies for managing wounds, inflammatory and skin diseases. Basing on our previous experience [2] several extracts were prepared by varying either the solvent mixture or the extraction procedure. All prepared extracts were tested *in vitro* to evaluate anti-tyrosinase and free radical scavenging properties, since these are relevant bioactivities related to skin disorders and inflammation [3]. The ethanolic extract obtained from maceration of plant material pre-treated with petroleum ether gave rise to the most interesting antiradical and antityrosinase effect, therefore it has been selected as the *hit* extract. The phytochemical fingerprint of the *hit* extract was investigated by HPLC-UV-PAD coupled by either CD or MS detector and herein presented together with the preliminary biological results reached till now.

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FAR-PO-38 New diazabicyclononane derivatives as potential antimalarial agents

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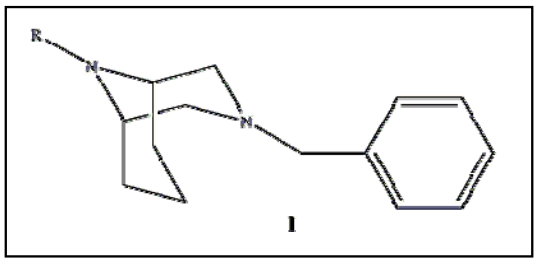
Malaria is a global health problem and a major cause of morbidity and mortality worldwide, especially in SubSahara Africa. The extensive and often suboptimal use of common antimalarial drugs led to the rapid spread of drug resistant strains of *Plasmodium falciparum*, the cause of the most severe form of the disease. To overcome resistance, new antimalarial agents with innovative structure are necessary.

Due to the consolidated experience of our research group on the synthesis of diazabicyclo compounds [1] and the evidence that some diaryl substituted azabicyclo nonanes show antimalarial activity [2], we designed and synthesized a series of novel 3,9-diaza-bicyclo[3.3.1] nonane derivatives (**I**), as new scaffolds for potential antimalarial agents. The compounds present a benzyl group at position 3, and different substituents of variable dimension, lipophilicity and electronic features at position 9. Synthesis, molecular modeling studies and *in vitro* activity against both chloroquine sensitive or resistant strains of *P. falciparum* strains will be presented.



I

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FAR-PO-39 A comparison between the photobiological properties of tetracyclic angelicin derivatives.

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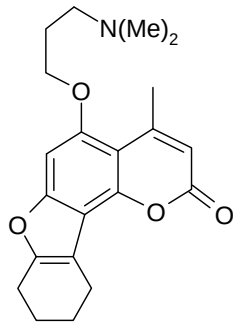
The psoralen tricyclic moiety constitutes the basic chromophore from which the drugs employed in the PUVA therapy (psoralen plus UVA light) were developed. Nevertheless, this treatment presents some drawbacks, both short-term (erythema, hyperpigmentation) and long-term (premalignant keratoses, skin cancers)[1-2].
Within the attempt to obtain promising new photochemotherapeutic drugs, two strategies were developed: fusing the furan ring to the coumarin moiety in [2,3-*h*] or [2,3-*f*] to obtain angular furocoumarin, angelicins or allopsoralens, respectively. A further interesting approach led to tetracyclic derivatives, characterized by the condensation of a fourth nucleus to the tricyclic furocoumarin chromophore and by a protonable side chain to increase the solubility in aqueous media [3-4].
In this connection we prepared and studied a structure characterized by the condensation of a cyclohexenylic ring at the 4′,5′-double bond of the angelicin nucleus and a dimethylaminopropoxy side chain inserted in position 5 (**1**). The photoantiproliferative activity on human tumor cell lines along with the interaction with DNA was studied both in the dark and after UVA irradiation in comparison with the analogue benzoderivative (**2**) [3].



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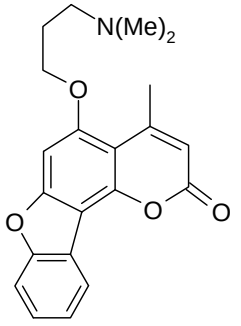

2

The isolation and characterization of the furan side photoadduct with the pyrimidine base thymine is also reported. Finally, the ability to interact with topoisomerase II in the dark was investigated.

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FAR-PO-40 Analysis of Structurally-Solved Matrix Metalloproteinases via Chaotic Map Clustering of Electrostatic Similarity

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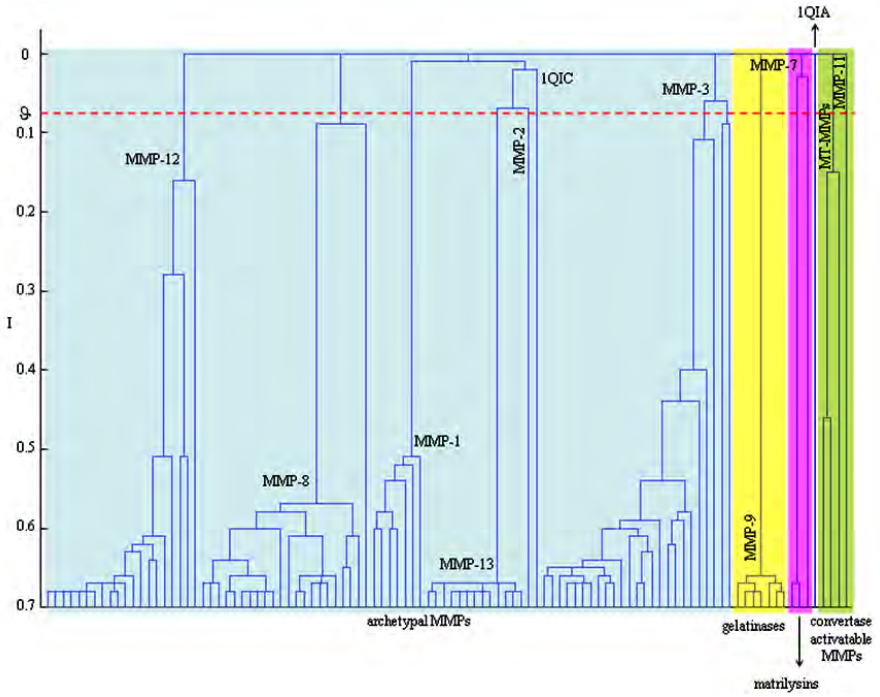
Matrix Metalloproteinases (MMPs) represent a family of proteolytic enzymes involved in a variety of important physiological and pathological processes. [1] In the present study, 104 structurally-solved MMPs were examined to gain insights into the structural features governing molecular recognition and underlying distinct biological activities. Protein electrostatic similarity was, for the first time, analyzed through the Chaotic Map Clustering (CMC), an algorithm successfully used in other fields of applied sciences. [2] The investigation was conducted on the entire MMP structures as well as on the protein binding sites. Interestingly, CMC provided a reliable and comprehensive representation of the structural and functional relationships existing among MMPs enlarging and complementing the current knowledge in the field. [3]
Based on the variation of the electrostatic potentials, CMC was successful in analysing MMP target family landscape and their different subsites. The first investigation resulted a rational figure interpreting both the domain organization as well as the substrate specificity classifications. The second enabled to discriminate the diverse MMP classes related to the high specificity of the S_1' pocket, to detect both the occurrence of punctual mutation of ionisable residues and different side chain conformation accounting for likely induced fit phenomena. In addition, CMC was successful even for standard pairwise analyses of protein sequences. Finally, the CMC algorithm was used to properly explain the complementarity existing between the ligand molecular shapes and the accessible MMP void volumes. [4]



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FAR-PO-41 Allyphenyline Analogues Potentially Useful in the Management of Chronic Pain and Opioid Addiction.

Eleonora Diamanti,[a] Fabio Del Bello,[a] Mario Giannella,[a] Valerio Mammoli,[a] Alessandro Piergentili,[a] Wilma Quaglia,[a] Antonio Carrieri,[b] Giuseppe Carbonara,[b] Giuseppe Fracchiolla,[b] and Maria Pigini.[a]

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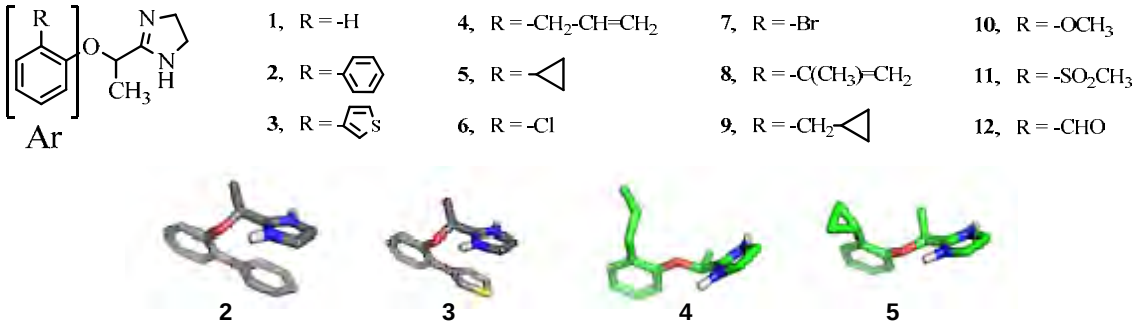
We have previously demonstrated that α_2-adrenergic (α_2-AR) molecules, related to the non-subtype selective antagonist **1**, displayed different activity at α_{2A}-, α_{2B}- and α_{2C}-AR subtypes, depending on the peculiar nature of the ortho substituent in the Ar ring. For example, phenyl and thienyl groups converted **1** into the efficacious agonists **2** (biphenyline) and **3**, respectively, activating α_{2A}- and α_{2C}-subtypes. Allyl or cyclopropyl groups of lower steric bulk turned the biological profile of the antagonist **1** only at α_{2C}-subtype: **4** (allyphenyline) and **5** were potent α_{2C}-agonists, whereas efficiently antagonized α_{2A}-AR. From in vivo study **4** significantly enhanced morphine analgesia (due to α_{2C}-AR agonism), was devoid of sedative side effects (due to α_{2A}-AR antagonism) as well as prevented and contrasted morphine tolerance and dependence at very low dose (0.05 mg/Kg) [1]. Encouraged by these results, we prepared and studied compounds **6-12** inspired by **4**. They were characterized by ortho substituents of moderate steric bulk and positive or negative σ and π contributions in all the combinations. A molecular modeling study performed on **2-12** highlighted that the desired α_{2C}-agonism/α_{2A}-antagonism combination was displayed by ligands having favoured *extended* conformation (i.e. **4** and **5**). In contrast, the activation of both α_{2A}- and α_{2C}-subtypes was produced by ligands endowed with favoured *folded* conformation (i.e. **2** and **3**).



This work was supported by the Monte dei Paschi di Siena Foundation Award.

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FAR-PO-42 Design, synthesis and biological evaluation of peptidomimetic boronic acids targeting 20S proteasome

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The ubiquitin-proteasome pathway is the major proteolytic system of all eukaryotic cells and plays a very important role in the degradation of many proteins critical for cell division, growth activation, signaling and transcription. A deregulation of this system could lead to an anarchic cell proliferation and to a tumor development [1]. For these reasons, ubiquitin/proteasome inhibition has become a new and significant strategy for the drug development in cancer treatment.

Within the present work, the strategy targeting proteasome has been delineated with the aim of developing efficacious antitumor agents. This approach was based on the design of conformationally constrained peptidomimetics by reducing the peptidic character of the tripeptide boronate Z-Leu-Leu-Leu-$B(OH)_2$ (MG262, K_i=18 pM, Figure 1), reversible inhibitor of the chymotrypsin-like activity of the 20S proteasome. This strategy has been accomplished by bioisosteric replacement of the P_3 Leu residue with a 2-pyridone nucleus [2]. This structural modification could ensure stability towards degradation by enzymes, enhancement of oral bioavailability, reduction of conformational freedom of peptides, improvement of the selectivity towards the target enzyme.

Further modifications of new conformationally constrained peptidomimetics involved the P_2 site according to the features of the dipeptide boronate bortezomib (Velcade®, Figure 1), the first proteasome inhibitor approved by FDA for the treatment of haematological malignancies such as multiple myeloma and mantle cell lymphoma. In this context we introduced bulky substituents at the P2 site (i.e. Phe residue, Figure 1), whereas the P1 site was kept constant because of its importance for substrate specificity. Additional changes involving the N-terminal protective group have been realized in order to improve the binding properties of the new inhibitors (Figure 1).

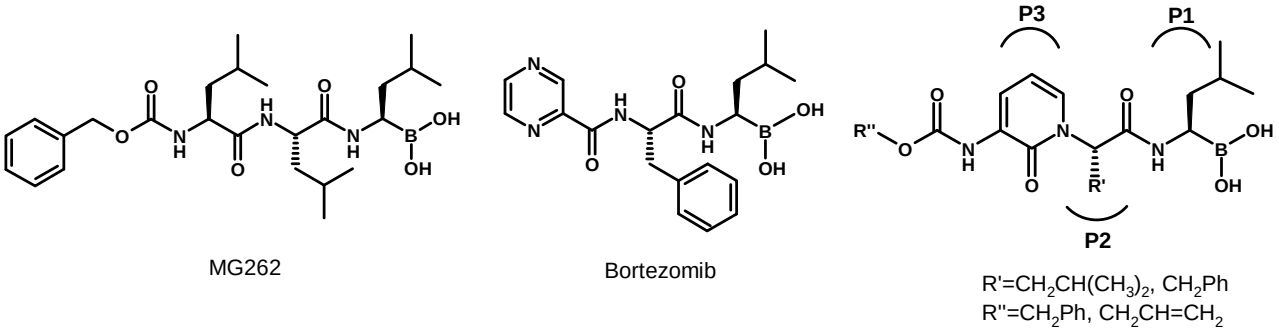

Figure 1

The synthesized peptidomimetic boronates are currently under screening to evaluate their inhibitory properties against the *chimotripsyn-like, trypsin-like* and *peptidyl-glutamyl peptide hydrolase* proteasome activities. Selectivity towards the target enzyme will be also evaluated by testing them against bovine pancreatic α-chymotrypsin. The results of such investigation will be presented and discussed.

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FAR-PO-43 Praziquantel analogues containing NO-donor furoxans and related furazans as agents active against *Schistosoma mansoni*.

Francesca Vottero,[a] Stefano Guglielmo,[a] Roberta Fruttero,[a] Alberto Gasco,[a] Daniela Cortese,[a,b] Latasha Day,[b] Valerie Kommer,[b] and David L. Williams.[b]

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Today around 200 million people worldwide are parasitized by several species of *Schistosoma* and in particular *S. mansoni*, and more than 200 000 people die every year from this neglected disease. Praziquantel (PZQ) is the only drug currently administered. The mechanism of action of this drug has not been elucidated; however, inhibition of calcium channels and inhibition of adenosine uptake have been suggested to be involved in PZQ activity. Since PZQ-resistant worms have been identified, the development of new anti-schistosomiasis drugs is urgently needed [1].

Recently, several furoxans (1,2,5-oxadiazole 2-oxides) have been shown to be endowed with good activity against *S. mansoni*. The proposed mechanism of action consists in the inhibition of thioredoxin glutathione reductase (TGR), an essential enzyme for parasite redox balance, through nitrosylation of cysteine and/or selenocysteine residues of the protein. This reaction takes place as a consequence of the interaction of the compounds with the enzyme and subsequent NO release [2].

On this basis we decided to conjugate PZQ and furoxan pharmacophores in a single molecule in order to obtain dual drugs exploiting antischistosomal properties through two different mechanisms of action. Through slight modifications of an inexpensive and straightforward synthesis [3], six novel PZQ derivatives were prepared, three of them bearing furoxan moieties with the remainder bearing the corresponding furazan (1,2,5-oxadiazole) moieties and devoid of NO-donor properties.

All the compounds have been subjected to structural and pharmacological characterization for their activity against adult *ex vivo* worms and their capability to inhibit TGR activity. Moreover *in vivo* studies are in progress in order to evaluate whether the compounds are able to decrease worm burdens in infected mice.

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FAR-PO-44 Bioactive natural daucane sesquiterpenes: antiproliferative and proapoptotic activity against human tumor cell lines.

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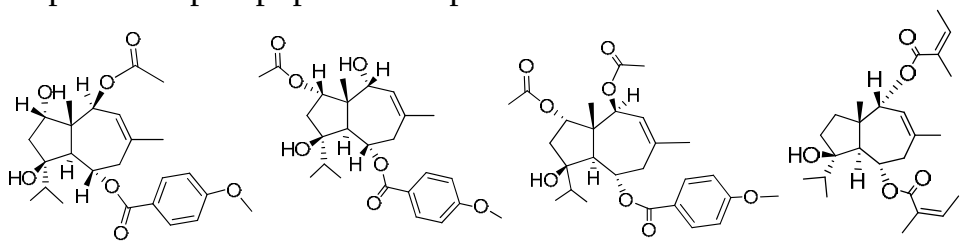
In our ongoing researches of cytotoxic natural compounds[1,2], we isolated sixteen daucane esters (**1 16**) from plants of the genera *Ferula* and *Ferulago*, in which two of the daucane derivatives (**3** and **4**) are new natural compounds. The daucane derivatives can be considered as attractive compounds especially as potential antiproliferative and anticancer compounds [3,4].

The cytotoxic activity of the isolated compounds was evaluated against a panel of seven human tumor cell lines. Fourteen of the daucane derivatives showed antiproliferative activity at least against one of the human tumor cell lines tested, four compounds (**5, 8, 11** and **16**) were active against all the tested cell lines. Preliminary structure activity relationships suggests that the most active compounds in the daucane series present the *trans* fusion of the penta- and hepta-atomic cycles, and lipophylic ester groups linked to position 6. Isomeric derivatives such as **8** and **9** or **3**, **4** and **5** exhibited significant differences in their IC_{50} supporting that the β orientation for the ester group in the position 2 enhances the cytotoxic activity. Furthermore, the pro-apoptotic effect of the most active compounds (**8** and **11)** evaluated in Jurkat cell line showed that these compounds are able to induce apoptosis in a time and concentration-dependent manner.

Our findings suggest the potential role of daucane derivatives as models for the development of proapoptotic compounds.



3 **4** **8** **11**

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FAR-PO-45 MONITORING AND TOXICOLOGICAL EVALUATION OF ANTIHISTAMINIC DRUGS IN SURFACE WATERS

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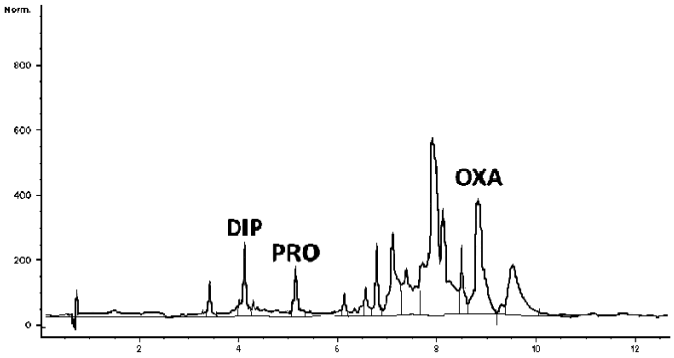
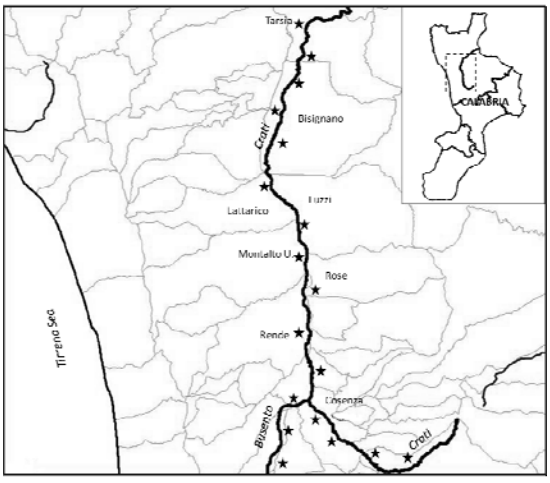
A HPLC method for the simultaneous determination of three widely used antihistaminic drugs, diphenhydramine (DIP), oxatomide (OXA) and promethazine (PRO), in surface waters and a toxicological assay using the bioluminescent bacterium *Vibrio fischeri* were developed. The analytical procedure was extended to the by-products from PRO photodegradation. The method involved pre-concentration and clean-up by SPE and HPLC analysis with diode array detection.



HPLC chromatogram from analysis of a surface water sample spiked with DIP, OXA and PRO at a concentration of 10, 20 and 10 μg/L, respectively.

Validation of the method was performed on synthetic mixtures and surface water samples spiked with the drugs, showing mean recoveries ranging from 93 and 107%, with RSD below 5.5%. Limits of detection in surface waters, calculated on 1.0 L of sampled waters, were in the range 0.6 – 0.8 μg/L.

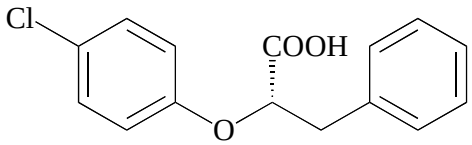
The *Vibrio fischeri* test demonstrated toxicity due to PRO at a concentration of just 3.94 μg/mL while the other antihistamines showed no significant toxicity until to 50.0 μg/mL. However, toxicity of drug mixtures was greater than the sum of the values from single component samples. The presence of the studied drugs was monitored in two rivers in Calabria (Italy), collected along a period of seven months. DIP and OXA were not detected in any samples. On the contrary, PRO was found in two samples taken in July at a concentration of 1.98 and 2.31 μg/L, both significantly below the values causing toxicity.



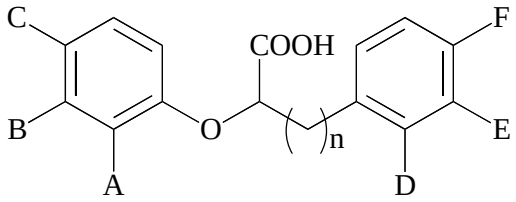
FAR-PO-46 Synthesis and biological evaluation of new fluorinated analogues with PPARα and PPARγ agonist activity.

Antonio Laghezza, Luca Piemontese, Giuseppe Fracchiolla, Mariagiovanna Parente, Giuseppe Carbonara, Antonio Lavecchia, Paolo Tortorella, Fulvio Loiodice.
Dipartimento Farmaco Chimico dell'Università degli Studi di Bari "Aldo Moro", Via E. Orabona 4, 70125, Bari, Italy. *(e-mail: a.laghezza@farmchim.uniba.it)*

Peroxisome proliferator-activated receptors (PPARs) are members of the nuclear receptor superfamily of ligand-activated transcription factors.[1] The combination therapy with drugs acting on both PPARα and PPARγ isotypes may have synergistic and wider therapeutic effects improving both glucose and lipid metabolism and could be a new strategy in the treatment of metabolic syndrome. [1–4] In the recent past we have synthesized and reported the effects on human PPARα and PPARγ of chiral clofibric acid analogues, identifying MS39 as a lead compound.[2–4] With the aim to investigate the possibility to fine-tune the activity of this ligand, a new series of its analogs were synthesized in which fluorine atom or trifluoromethyl group were introduced on the aromatic rings in place of chlorine or as additional substituents (Figure 1). Fluoro or trifluoromethyl substituents generally have a profound effect on the physical and/or biological properties of the target molecule. Their introduction, in fact, beyond improving metabolic stability by blocking metabolically labile sites, can modulate physicochemical properties, such as lipophilicity or acidity, change molecular conformation, and increase binding affinity by exploiting specific interactions of F with the target protein.[5]



MS39



A-F= H, Cl, F, CF_3; n= 0, 1

Figure 1

The biological activity on PPAR isoforms of all new synthesized derivatives was evaluated by the transactivation assay, a powerful and widely used assay whose good correlation with in vivo activity is generally accepted. [2–4]

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FAR-PO-47 Design, synthesis and biological profile of new piperidin-4-carboxamide derivatives as effective σ_1-ligands.

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Sigma (σ) receptors are involved in several functions such as modulation and biosynthesis of several neurotransmitters, motor control, cell growth and proliferation[1]. Several classes of structurally unrelated compounds interact with σ receptors, but only few σ ligands are gifted with affinity and selectivity against a specific receptor subtypes.

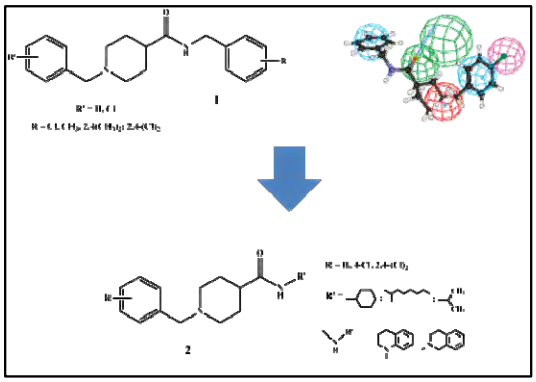

Figure 2

The interest in σ ligands stems from the possibility to develop clinical agents for the treatment of several CNS diseases, for neuroprotection, tumour treatment and diagnosis[2]. Therefore σ_1 receptor ligands could be involved in treatment for schizophrenia, depression, lack of memorization skill, difficulty of learning and increase of analgesic action.

Recently, we developed a 3D pharmacophore model for σ_1 receptor (**Figure1**) [3], that we exploited to design a series of piperidin-4-carboxamide derivatives **1**. All molecules are provided with good affinity and, above all, high selectivity.

With the aim to increase the skill of these compounds to bind σ_1 receptor, we synthesized a new series of piperidin-4-carboxamide derivatives **2**. Maintaining the main scaffold, we changed the N-benzyl portion of the amide groups with an aliphatic or arylaliphatic moiety in order to evaluate the effect on σ binding. All the synthesized compounds have been tested to estimate their affinity and selectivity toward σ_1 receptor. Despite the work is in progress, the achieved results seem positive since the new derivatives showed a good affinity against σ_1 receptors in the range of 1.98-350 nM and they gifted with a fairly good selectivity toward σ_1 receptor.

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FAR-PO-48 Identification of Chemically Diverse Cdc25 Phosphatase Inhibitors by Receptor-based Virtual Screening

Antonio Lavecchia,[a] Carmen Di Giovanni,[a] Vincenza Elena Rea,[b] Nunzia Montuori,[b] Mariorosario Masullo,[c] Emmanuele De Vendittis,[c] and Ettore Novellino[a]

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The cell division cycle 25 (Cdc25) family of proteins are highly conserved dual specificity phosphatases that regulate cyclin-dependent kinases, the main gatekeepers of the eukaryotic cell division cycle. The three isoforms of Cdc25, including Cdc25A, Cdc25B and Cdc25C, appear to act on different cyclin-dependent kinase/cyclin complexes at different stages of the cell cycle. Overexpression of Cdc25A and/or Cdc25B, but not Cdc25C, has been detected in numerous cancers and is often correlated with a poor clinical prognosis; Thus, the inhibition of these phosphatases may represent a promising therapeutic approach in oncology [1-2]. So, a computer-aided drug design protocol involving virtual screening was performed on Cdc25B crystal structure (Figure 1) [3] in order to identify novel classes of inhibitors. In vitro experiments carried out on a selected list of 30 molecules led to the discovery of 4 compounds able to inhibit Cdc25A and B activity at low micromolar concentrations and to the significant inhibition of the MCF-7 breast cancer cell proliferation. All selected compounds also affected MCF-7 cell cycle progression. Furthermore, kinetics studies were realised on the phosphatase activity catalysed by Cdc25B in the presence of the above-mentioned compounds, in order to establish type and power of inhibition.

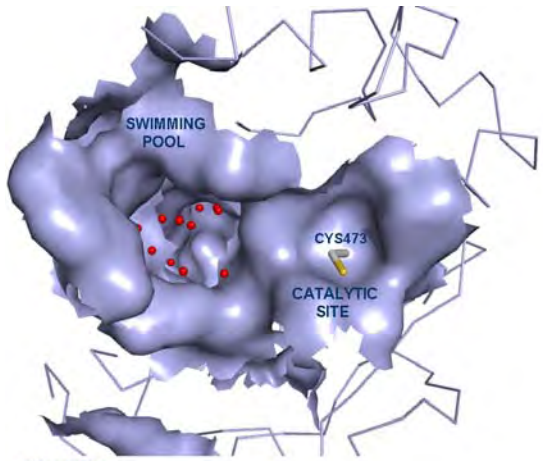

FIGURE 1

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FAR-PO-49 Label-free, Reagentless, Straightforward Capillary Electrophoretic Method to Individuate Potent Calmodulin Ligands

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In the last decade, drug repositioning (drug repurposing or indication switch) strategies have become more and more attracting as useful ways for drug discovery [1–5], and promiscuous ligands let envisage the way toward a new generation of efficacious drugs [6].

Calmodulin (CaM) ligands are a chemically heterogeneous class of biologically active compounds, many of which behave as anthypertensive and antianginous, neuroleptic, anxiolytic, antidepressant, antiarrhythmic, antiestrogen, and antineoplastic agents. Several CaM ligands display polypharmacology. Thus, this class of compounds might be mined to detect leads for repositioning: both new and clinically established CaM ligands might prove useful in some of the above mentioned therapeutic areas.

Here we propose a label-free, reagentless, straightforward affinity capillary electrophoretic (ACE) method to screen compounds as CaM ligands. Apparent dissociation constants between bovine brain CaM and various small ligands were found in good agreement with those reported in the literature. The method was successfully used to demonstrate that lubeluzole—a well-known neuroprotective agent—is a high-affinity CaM ligand.

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FAR-PO-50 Pyrazole[3,4-*e*][1,4]thiazepin-7-one Derivatives as a Novel Class of Farnesoid X Receptor (FXR) Agonists

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[a] Dipartimento di Chimica e Tecnologia del Farmaco, Universita' degli Studi di Perugia, Via del Liceo 1, 06123 Perugia, Italy; [b] Intercept Pharmaceuticals Italia Srl, Via Togliatti, 06073 Corciano, Perugia, Italy.
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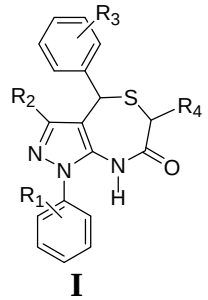
The farnesoid X receptor (FXR) is a nuclear hormone receptor expressed in the liver, kidney and intestine that is activated by bile acids, such as chenodeoxycholic acid (CDCA) and cholic acid (CA). Upon activation, FXR binds to DNA as a heterodimer with the retinoid X receptor (RXR), thus regulating the expression of various genes and proteins involved in bile acid and cholesterol homeostasis (CYP7A1, SHP, IBABP, BSEP, and ApoA-I), triglyceride synthesis, and lipogenesis (SREBP-1c, and ApoC-III). Furthermore, bile acids-mediated FXR activation has been recently recognized as a major pathway for energy homeostasis and glucose metabolism. All these evidences make FXR a promising potential target for the treatment of a variety of metabolic disorders, including hyperlipidemia, cholelithiasis, cholestasis, and diabetes mellitus.[1] Over the past few years, many efforts have been dedicated by our group to the search of highly potent steroidal FXR modulators by rational structural modification of CDCA. Following this approach, we discovered in 2002, the highly potent and orally bioavailable FXR full agonist, 6α-ethylchenodeoxycholic acid (6ECDCA, INT-747),[2] that has positively completed phase II clinical trials for primary biliary cirrhosis and type 2 diabetes. More recently starting from a virtual screening protocol we were successful in the identification of a novel class of non- steroidal FXR agonists, structurally characterized by 4,8-dihydro-1*H*-pyrazole[3,4-e][1,4]thiazepin-7-one scaffold (**I**). The synthesis and the preliminary structure-activity relationships of this class of non-steroidal FXR agonists will be presented.



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FAR-PO-51 Driving into the topological versatility of 29mer TBA

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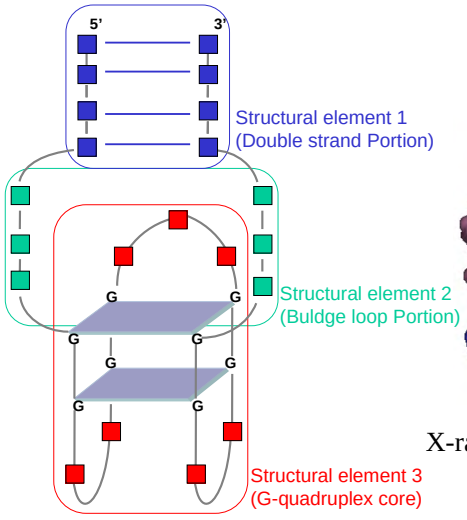
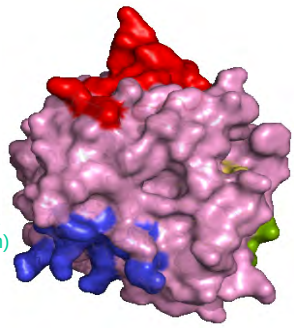
An emerging class of macromolecules acting on thrombin is represented by oligonucleotide aptamers, short DNA/RNA sequences which recognize a target with an high specificity and affinity. A peculiar feature of these molecules is their structural flexibility which allows them to assume distinct foldings depending upon their sequence and/or environment.

Leading examples are represented by the Thrombin Binding Aptamers (TBAs), which comprise a 15-mer DNA (15fTBA) selected by its high affinity for the exosite I (fibrinogen binding site) and a 29-mer DNA (29hTBA) selective for the exosite II (heparin binding exosite) of the coagulation factor.

The 29hTBA structure consists in a 15-mer quadruplex core with the two 5' and 3' portions that can partially pair producing a mixed quadruplex/duplex dual structure. The structured core shares a close similarity with the 15fTBA; the major loop sequence (GCA that replaces TGT) and a single T-A nucleotide mutation in one minor loop are sufficient to drive the sequence to a distinct epitope.[1] Considering the complexity of the TBAs' topology some questions raised. Which structural motif the sequences adopt? How are they involved in defining the thermodynamic stability and/or the thrombin affinity?





X-ray structure human thrombin (pdb code: 1HUT))

Here, we studied and compared a series of DNA sequences derived by rational modifications of 29hTBA sequence, selected to dissect the role of the different structural elements in these processes.[2]
Early results suggest that the bulge domain largely impairs the thermal stability and modulates the folding kinetic of the G-quadruplex core.

Similarly, the length of the double strand portion, does not seem to influence protein binding affinity although it plays a significant role in defining the folded DNA thermal stability.
Finally we designed and characterized an ExositeI/Exosite II DNA binder that merges 15fTBA structural elements in the 29hTBA general structure.
Our work is aimed to define the minimal structural motifs required to preserve the target affinity, to finally translate them to not-oligonucleotide molecules (e.g. PNA) characterized by better drug-like properties.

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FAR-PO-52 Synthesis and antiproliferatve activity of Naphtalenyl substituted 1,2-dihydropyrazol-5-one and related fused tetrazinone

F. Mingoia,[a] R. Muriana,[b] M. Fazzari,[b] A. Alfio,[b] C. Di Sano,[c] A. Martorana,[b] A. M. Almerico,[b] A. Lauria[b]

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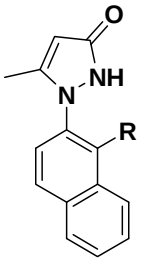
In recent years, besides the main field of nonsteroidal anti-inflammatory agents, the interest towards pyrazolone derivatives has been renewed because of their wide biological and pharmacological applications [1]. Currently, particular attention is focused on such a class of compounds due to the affinity with sigma receptor and their relationship with cancer [2].To these purposes we planned to design, synthesize and evaluate the antiproliferative activity (MTS assays) of a new series of 3-methyl-2-(1-R-naphthalen-2-yl)-1,2-dihydropyrazol-3-one derivatives **1** against HeLa, MCF-7, LAN-5, Caco2 in order to explore their anticancer potential. Additionally, further elaboration of the amino derivative **1** led to the tetracycle **2**, possessing a reactive tetrazinone core which conferred valuable antiproliferative activity as previously reported [3]. Synthesis and biological results will be presented.

1a; R = H
1b; R= Cl
1c; R= NO_2
1d; R= NH_2
1e; R= N_3



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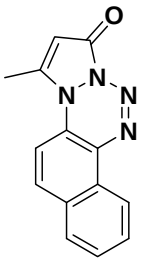

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FAR-PO-53 Identification of Putative Guanosine Receptor in Rat Brain

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G protein coupled receptors (GPCRs), recognizing adenosine and purine and pyrimidine nucleotides as extracellular messengers, have been characterized and classified as purinergic P1 and P2 receptors, respectively. However, some experimental data suggest that other nucleosides as guanosine, inosine and hypoxanthine can also act as signalling molecules via the activation of specific membrane receptors [1]. In particular, extracellular guanosine seems to possess many trophic effects, including promotion, division, and growth of astrocytes and other neuron-like cells. Binding studies, performed on rat brain membranes using [^{3}H]guanosine, have shown that the compound interacts with binding sites, which are distinct from the well-characterized ATP and adenosine receptors. Furthermore, guanosine itself and 6-thioguanosine are equally effective in displacing [^{3}H]guanosine from rat brain membranes [2]. Hence, potent and selective agonists and antagonists are highly needed for the characterization of the physiopathological profile of the new putative guanosine receptor. Starting from these observations and aimed at developing a new assay that allows to evaluate the potency of ligands at the putative guanosine receptor, Eu-GTP assay was performed in rat brain. This technique, using the principle of the [^{35}S]GTPγS binding assay, replaces the radioactive material with Eu-GTP and exploits the unique fluorescence properties of Europium lanthanide chelate. New molecules, prepared by modifying the purine and sugar moieties of guanosine at the 6- and 5'-positions, were tested using Eu-GTP assay. Results showed that the new compounds are able to activate the putative guanosine receptor more than guanosine itself. On the other hand, this functional assay seems to demonstrate that a GPCR activated by guanosine is present in rat brain [3].

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FAR-PO-54 3-[2-(4-aryl-1,3-thiazol-2-yl)hydrazin-1-ylidene]-1H-indol-2-ones as new potential dual inhibitors of polimerase and ribonuclease HIV-1 RT associated function

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RT is an essential enzyme for viral replication which has two associated catalytic functions: a DNA or RNA dependent polymerase activity and a ribonuclease H (RNase H) activity.[1-2]
The two catalytic sites are distinc but inter-dependent and mutations in the polymerase domain affect the RNase H activity, and *vice versa*. Furthermore, both RT associated activites are essential for virus replication. Thus, both enzyme functions are attractive targets for drug development.
Aiming to identify new scaffolds capable to combine inhibitory activity on both enzymatic functions, some of us performed a combined shape-, 2D-fingerprint-, and pharmacophore-based virtual screening and identified a 3-substituted-2-indolinone derivative as a promising dual inhibitor of both RT functions.[3]
2-indolinone derivatives are of biological interest and their biological properties have been recently investigated.[4-6] However their activity on HIV-1 RT has never been investigated. Prompted by the virtual screening results we have synthesised a series of 3-[2-(4-aryl-1,3-thiazol-2-yl)hydrazin-1-ylidene]-1H-indol-2-ones and evaluate their biological activity as potential dual inhibitors of the Human Immunodeficiency virus-1 (HIV-1) Reverse Transcriptase (RT). Furthermore we have investigated on the site of interaction on the HIV-1 RT.
In this presentation we wish to report on our first approach dedicated to the synthesis and the biological behaviour investigation of new rationally designed RNase H and RDDP dual inhibitors.

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FAR-PO-55 NEW CARBAZOLE SCAFFOLDS AS SIRT INHIBITORS

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The class III family of histone deacetylases also called sirtuins (Sirt1-7), is characterized by a conserved 270 amino acid catalytic core domain and requires NAD^+ as cofactor[1] to catalyze the removal of acetyl groups from acetyl-lysine residues on protein substrates (i.e.FOXO1,4, NF-kB, p53, p73, p300, tubulin etc.) including histones (H1,3,4). Sirt1-7 also possess mono-ADP-ribosyl transferase activity and have pathophysiological relevance in many diseases such as cancer, obesity, muscle differentiation, inflammation and neurodegeneration.

Sirt1 inhibition causes hyperacetilation of p53, a major tumor suppressor, and activates this protein through the use of nongenotoxic compounds which may result in new therapeutically useful tools in cancer therapy[2]. Furthermore, the inhibition of NAD^+ consumption by sirtuin inhibitors can increase its availability for cellular metabolic function.

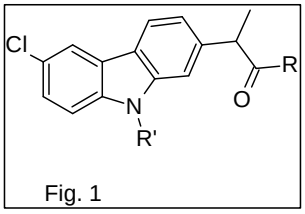

Fig. 1

The observation that EX-527, the most potent Sirt1 inhibitor, and carprofen (an anti-inflamatory drug) presented a good overlay in the carbazole core, suggested us to design a carpofen amide derivatives (Fig.1), to be evaluated as SIRT inhibitors. All the derivatives are active against Sirt1 using a fluorimetric assay. In particular one of them (STP16) is a powerful inhibitor of Sirt1 showing an IC_{50} of 7,95µM.

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FAR-PO-56 Cystamine-tacrine dimer: a new multi-target-directed ligand as potential therapeutic agent for Alzheimer's disease treatment

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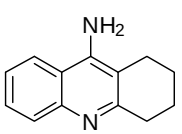
Alzheimer's disease (AD) is the most common cause of dementia, clinically characterized by loss of memory and progressive deficits in different cognitive domains due to a pronounced degradation of the cholinergic system and alteration in other neurotransmitter systems such as the glutamatergic and serotoninergic ones. From a neuropathological point of view, the hallmarks of AD are represented by senile plaques, which are insoluble deposits of amyloid-beta (βA) protein, and neurofibrillary tangles (NFT) composed of hyperphosphorylated tau protein. These pathological lesions have been considered to be the causative features of AD, giving rise to several theories about AD pathogenesis mainly including the cholinergic hypothesis, the amyloid cascade hypothesis, oxidative stress and free radicals formation. Actually the AD therapy is mainly bolstered on acetylcholinesterase inhibitors (AChEIs) able to increase the acetylcholine (ACh) levels in the cholinergic synapses but their clinical effectiveness is still under debate. A more appropriate approach to face the multifactorial nature of AD may be represented by the development of Multi-Target Directed Ligands (MTDLs) which is based on the assumption that a single compound may simultaneously modulate different targets involved in the neurodegenerative AD cascade [1]. The structure of tacrine (**1**) [2], one of the most known AChEIs, and, in particular, its dimer bis(7)tacrine (**2**) [3], have been widely used as scaffolds to design novel MTDLs against AD. **2** exhibited a 1000 times higher AChE inhibition, a double interaction with active and peripheral sites of AChE and a better pharmacological profile consisting on the inhibition of the AChE-induced Aβ aggregation through its peripheral site, and neuroprotective effects due to the interaction with beta-secretase enzyme, NMDA and $GABA_A$ receptors.

Thus, in the search of new rationally designed MTDLs against AD, we replaced the heptamethylene linker of bis(7)tacrine with the structure of cystamine, leading to cystamine-tacrine dimer characterized by a disulfide bridge. We focused our attention on



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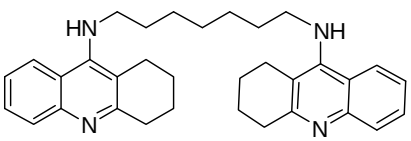

2

cystamine for its biological activities as antioxidant, cyto- and neuroprotective agent [4].
In this study we demonstrated that the cystamine-tacrine dimer, in comparison to bis(7)tacrine, is endowed with a lower toxicity, it is able to inhibit AChE, BChE, self and AChE induced Aβ aggregation in the same range of the reference compound and to protect the neuroblastoma SH-SY5Y cell line against H_2O_2-induced damage by activating the extracellular signal-regulated kinase 1 and 2 (ERK1/2) and Akt/protein kinase B (PKB) pathways.

(This research was supported by grants from MIUR, Rome (PRIN), and University of Bologna (RFO))

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FAR-PO-57 BENZOTRIAZOLE UREAS AS TUNABLE SELECTIVE MAGL AND FAAH INHIBITORS

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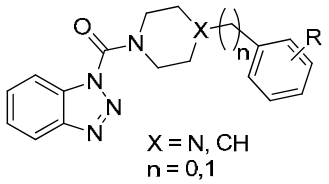
The two most studied endocannabinoids, 2-arachidonoylglycerol (2-AG) and *N*-arachidonoylethanolamine (anandamide, AEA), are principally degraded by two enzymes from the serine hydrolase superfamily: monoacylglycerol lipase (MAGL) and fatty acid amide hydrolase (FAAH), respectively. Inhibitors of these enzymes can constitute important pharmacological tools to explore the endocannabinoid system and could also be developed as a new promising class of analgesic drugs.[1] Considering that MAGL and FAAH are both inhibited by carbamates bearing a *N*-piperidine/piperazine group,[2,3] we synthesized a series of compounds by using the benzotriazole moiety as the leaving group and by substituting the carbamic functional group for an urea.

The compounds were tested on recombinant human MAGL and FAAH and, on the basis of the pharmacological evaluation, we found that these derivatives can be tuned for MAGL- or FAAH-selectivity as well as for dual MAGL-FAAH inhibition by attachment of appropriate groups on the piperazine ring nitrogen. As general trend, we observed that the phenyl piperazyl moiety is better for the FAAH inhibition, while the benzyl piperazyl ureas are more potent MAGL inhibitors.



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FAR-PO-58 NOVEL POTENT AND SELECTIVE FAAH REVERSIBLE INHIBITORS

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Endocannabinoids are a class of signalling lipids such as N-arachidonoyl ethanolamine (anandamide, AEA) and 2-arachidonoyl glycerol (2-AG), which activate cannabinoid receptors CB_1 and CB_2 to modulate a range of effects including pain, inflammation, appetite, motility, sleep, and thermoregulation, cognitive and emotional states. AEA and related bioactive fatty acid amides are inactivated by the membrane-bound serine hydrolase fatty acid amide hydrolase (FAAH). The development of FAAH inhibitors represents an elegant alternative to CB receptor agonists. Accordingly, inactivation of FAAH may have beneficial effects on pain and anxiety without the side effects (hypomotility, hypothermia, and catalepsy). To preserve this lack of “cannabinoid side effects”, the inhibitors should not interfere with CB_1 receptor, which is involved in most of the unwanted effects of exogenous cannabinoids.

With the aim to discover new scaffolds for selective FAAH inhibition we identified a series of potent and selective FAAH inhibitors characterized by a phenyl-1-pyrrole structure bearing differently functionalized lateral chains to improve hydrophylic and pharmacokinetic properties. Some representative hits proved to be extremely potent and selective FAAH inhibitors, reversibly binding the enzyme.[1]

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FAR-PO-59 The effect of the Cu(II) salt anion in a ligand exchange system operating with a chiral mobile phase

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With the use of a chiral ligand-exchange chromatography (CLEC) system operating with the O-benzyl-(*S*)-serine [(*S*)-OBS] [1,2] as the chiral mobile phase (CMP) additive to the eluent, the effect of the copper(II) anion type was evaluated on the thermodynamic parameters, retention (k) and separation (α) factors, by rationally changing the following experimental chromatographic conditions: column temperature, absolute configuration of the chiral selector, and salt concentration. The CLEC-CMP analysis was carried out on ten amino acidic racemates and with nine cupric salts. While the group of analytes comprised both aliphatic (leucine, isoleucine, nor-leucine, proline, valine, nor-valine, and α-methyl-valine) and aromatic (1-aminoindan-1,5-dicarboxylic acid, phenylglycine, and tyrosine) species, representative organic (formate, methanesulphonate, and trifluoroacetate) and inorganic (bromide, chloride, fluoride, nitrate, perchlorate, and sulphate) Cu(II) salts were selected as the metal source into the eluent. This route of investigation was pursued with the aim of identifying analogies among the employed Cu(II) salts, by observing the profile of variation of the selected chromatographic parameters, upon a change of the above experimental conditions. All the data were collected and analyzed through a statistical approach (PCA and k-means clustering) that revealed the presence of two behavioural classes of cupric salts, sharing the same variation profile for k and α values. Interestingly, this clustering can be explained in terms of ESP (Electrostatic Surface Potential) balance values, obtained by an *ab initio* calculation operated on the cupric salts.

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FAR-PO-60 DESIGN, SYNTHESIS, BIOLOGICAL ACTIVITY AND SAR OF DUAL FAAH – COX INHIBITORS

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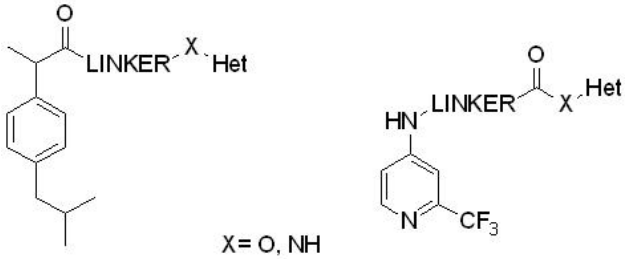
Fatty acid amide hydrolase (FAAH) is a serine hydrolase that catalyzes the deactivating hydrolysis of the fatty acid ethanolamide family of signaling lipids, which includes endogenous ligands for cannabinoid receptors such as anandamide (AEA). Endogenous FAAH substrates such as AEA serve key regulatory functions in the body and have been implicated in a variety of pathological conditions including pain, inflammation, sleep disorders, anxiety, depression, and vascular hypertension, thus there has been an increasing interest in the development of inhibitors of this enzyme. Furthermore the contribution of endocannabinoid system to Nonsteroidal anti-inflammatory drugs (NSAIDs) action has been demonstrated [1], although inhibition of prostaglandin production by cyclooxygenase (COX) is NSAIDs primary mechanism of action. Acidic NSAIDs like ibuprofen, inhibit the activity of FAAH and this effect is particularly noticeable at low pH, such as is seen in inflamed tissue. It is has been reported that COX-2 is capable of utilising AEA as a substrate to produce prostaglandin E2 ethanolamide and that the other main endocannabinoid, 2-arachidonoylglycerol (2-AG) is also a substrate for COX-2. FAAH and COX inhibitors produce synergistic effects upon visceral nociception [2], this is of considerable potential importance, given the gastrointestinal and cardiovascular problems associated with NSAID use. One of the difficulties, however, associated with polypharmacy is patient compliance and the potential for pharmacokinetic interactions between the drugs used. For this reason, there has been increased interest in the design of compounds with effects upon several targets. The findings led us to design and synthesis of new series of FAAH – COX dual inhibitors based on NSAID templates.



In this communication we report synthetic pathways, FAAH, MGL and COX inhibition results and SAR studies on the new inhibitor series.

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FAR-PO-61 Isoxazole and pyrazole core in COX-1 inhibitors

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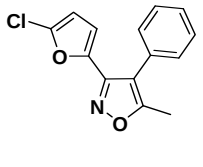
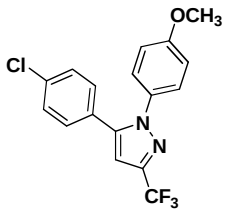
COX-1 isoenzyme has been recently reconsidered as therapeutic target, due to its crucial role exerted in a variety of pathological conditions, such as atherosclerosis, endothelial dysfunction, neuroinflammation, pain processing, pre-term labor and some type of cancers.
Hence, highly selective COX-1 inhibitors might be particularly relevant for the treatment of several diseases [1]. 3-(5-Chlorofuran-2-yl)-5-methyl-4-phenylisoxazole, **P6**, a highly selective COX-1 inhibitor, recently uncovered by us[2], has been chosen as "lead compound" for structure-activity relationship studies [3].They assessed that the presence of the P6-furanyl group is crucial for COX-1 inhibitory potency and selectivity, as it is important the substituent size (bromine, chlorine or methyl group) on that furanyl.
In addition, the replacement of a methyl by CF_3-group at isoxazole C_5 and the introduction of a substituent on the phenyl bonded to the isoxazole C_4 still provide selective COX-1 inhibitors.
Among the diarylheterocycle class of COX-1 inhibitors, the most studied COX-1 inhibitor is the **SC-560** that has a pyrazole as a core ring instead of an isoxazole [4]. Thus, to identify the **P6** and **SC-560** common (if any) structural and/or electronic determinants responsible of the selective COX-1 inhibition, a series of new pyrazole analogues of **P6** have been prepared by substituting the P6-isoxazole core ring with a pyrazole.



P6

COX-1 IC_{50} = 39 μM
COX-2 IC_{50} >100 μM



SC-560

COX-1 IC_{50} = 0.16 μM
COX-2 IC_{50} > 100 μM

The results of this investigation will be presented.

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FAR-PO-62 Reactivity of platinum- based drugs toward selected proteins

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Anticancer platinum drugs represent one of the most successful groups of compounds clinically used. Their biological mechanism of action is referred to platination of nuclear DNA, preferentially at guanine sites: the formation of stable DNA adducts is recognized as a DNA damage event and can ultimately drive to the apoptotic cell death.

From the discovery of their anticancer properties, research has been largely focused on the description of the DNA adduct formation by Pt drugs [1]. Although it was proposed that Pt-protein adducts could play an important role in modulating pharmacokinetics, resistance mechanisms, drug activity and side effects during this anticancer treatment, poor attention has been dedicated to characterize the interaction of platinum compounds with selected proteins [2].

In order to investigate the nature of metallodrug-protein interaction, we monitored the reactivity of different platinum compounds, included the *trans* planar platinum ammines [3] with model proteins such as bovine α-lactalbumin and hen egg lysozyme. The reactions were performed for 24 hours at 37 °C using different protein-Pt compound molar ratios. The reaction mixtures, containing the putative protein-Pt adducts, were resolved by SDS-PAGE gel electrophoresis and identified by electrospray ionization mass spectrometry technique (ESI-MS), a powerful technique to investigate metallodrugs-proteins interactions [4].

Our results clearly confirmed the formation of the metallodrug-protein adducts. In particular, we observed that the tested Pt compounds specifically react with each selected model protein according to different kinetics. Additionally, the structural features of Pt drugs have been shown to play a crucial role in promoting the reactivity and the selectivity toward tested proteic substrates.

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FAR-PO-63 1-Aryl-5-(1*H*-pyrrol-1-yl)-1*H*-pyrazole-3-carboxamide: an effective scaffold for the design of either CB_1 or CB_2 receptor ligands

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The endocannabinoid system is involved in pain, immunosuppression, vascular disease, appetite management and locomotor disorders [1]. The CB_1 inverse agonist Rimonabant (**1**), launched for the treatment of overweight, obesity and associated cardiovascular and metabolic disorders, was withdrawn because of psychiatric adverse events. There is a need of effective drugs to treat obesity because of the: (i) rapid increase of overweight people in the developed countries, and (ii) restricted therapeutic potential displayed by the FDA approved drugs sibutramine and orlistat [2].

New 1-aryl-5-(1*H*-pyrrol-1-yl)-1*H*-pyrazole-3-carboxamides were synthesized as CB receptor ligands. Compound **11** (CB_1 K_i = 2.3 nM, CB_1 SI = 163.6) showed CB_1 receptor affinity and selectivity superior to Rimonabant and AM251. Acute administration of 2 mg/kg **11** resulted in preferentially reduced intake of sucrose rather than intake of regular food in rats. On the other hand, compound **23** (CB_2 K_i = 0.51 nM, CB_2 SI = 30.0) showed signficant affinity and selectivity for the CB_2 receptor. The results presented here show that the 1-aryl-5-(1*H*-pyrrol-1-yl)-1*H*-pyrazole-3-carboxamide may serve as an effective scaffold for the design of either CB_1 or CB_2 receptor ligands.

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FAR-PO-64 Capillary electrophoresis coupled to laser induced fluorescence detection for the analysis of penicillamine in a non-conventional matrix

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Penicillamine (DL-2-amino-3-mercapto-3-methyl-butanoic acid) is a chelating agent derived from the hydrolysis of penicillin, lacking any antibiotic properties. The therapeutic form is D-penicillamine, while L-penicillamine is toxic. This drug is used in the treatment of severe active rheumatoid arthritis and acts by reducing the number of T-lymphocytes, inhibiting macrophage function and preventing collagen from cross-linking. It is also used as a chelating agent in Wilson's disease (a rare genetic disorder of copper metabolism), in cystinuria and in the treatment of heavy metal poisoning [1].

Adverse effects are frequent and may include: membranous glomerulonephritis, antibody-mediated myasthenic syndrome, drug-induced systemic lupus erythematosus, toxic myopathies and elastosis perforans serpiginosa. This last one may persist even after the therapy withdrawal [2].

Thus, to evaluate toxic effects in clinical cases we are developing a method based on capillary electrophoresis coupled to laser induced fluorescence detection (CE-LIF) in specific biological matrices such as epithelium.

The analysis is carried out in a fused silica capillary, using a carbonate buffer as the background electrolyte. Satisfactory sensitivity was obtained by exciting the molecule at 488 nm after a derivatisation step with 5-(iodoacetamido)fluorescein (IAF). Preliminary results are promising and the validation of the method is in progress. At the same time, we are developing another technique based on reversed phase liquid chromatography with amperometric detection to analyse penicillamine in epithelium samples.

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FAR-PO-65 Influence of ring size on the cognition-enhancing activity of DM235 and MN19, two potent nootropic drugs

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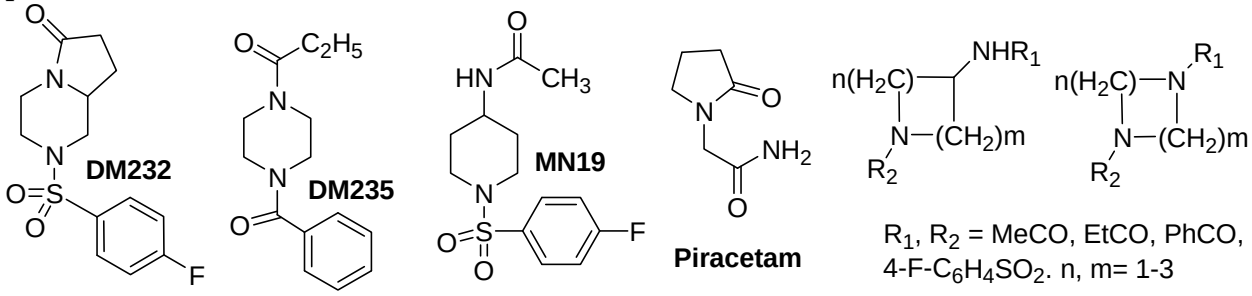
Piracetam is a nootropic compound which has been studied for more than four decades; this compound and some of its analogues are in use in several countries as drugs to control cognition impairment, to afford neuroprotection after stroke and to treat epilepsy [1]. We have previously reported about the cognition-enhancing properties of DM232 (unifiram), DM235 (sunifiram) and MN19 (Sapunifiram) in rodents [2]. DM232 shares some structural similarity with piracetam (the 2-oxopirrolidine ring) but Unifiram, as well as its analogues DM235 and MN19, are 3-4 orders of magnitude more potent than piracetam. These compounds are well tolerated in rodents, but their development has been impaired because their mechanism of action has not been clarified. In order to find substances with improved potency, and possibly to understand the mechanism of action of this class of compounds, we have prepared new derivatives of the lead compounds DM235 and MN19. In a previous paper we reported that the enlargement of the piperazine ring of DM235 into a diazepane moiety gave derivatives displaying good antiamnesic and procognitive activity, with a potency similar to the parent compound [3]. As a continuation of this research, we have synthesized a series of analogues of MN19 where the piperidine ring has been contracted or enlarged into an azetidine, pirrolidine, azepane or azocane moiety. In addition, the piperazine ring of DM235 has been further expanded into a diazocane cycle. These compounds have been tested for their cognition-modulating activity in the mouse passive-avoidance test. Structure-activity relationships will be discussed in this presentation.



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FAR-PO-66 New perspectives in neurodegenerative diseases: chiral resolution and configurational assignment of novel PKC alpha ligands

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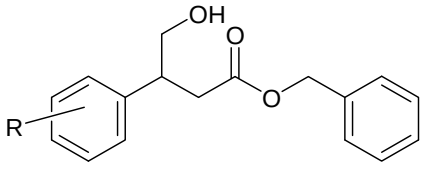
The Embryonic Lethal Abnormal Vision (ELAV) proteins, in response to intra- and extra-cellular signals, preferentially interact with ARE (*Adenine and Uracile-Rich Elements*) sequences present in the 3'-untranslated region of a subset of mRNAs, increasing their cytoplasmatic stability and translation speed, and thus gene expression. The ELAV-mRNA cascade is involved in many physiological and pathological contexts [1-2]. Evidence in the literature indicates that the ARE-dependent mRNA decay can be affected by the Protein Kinase C (PKC) pathway. Particularly, the involvement of PKC α isozyme in ELAV protein activation has been recently demonstrated by us [3].

In our recent research we focused on PKC alpha ligands as positive modulators of ELAV-mRNA cascade. A small compounds library was designed taking into account the known PKC alpha ligands and the synthetic feasibility. For all the synthesized compounds the ability to compete with phorbol ester for the C1 domain of recombinant human PKC α has been determined [4].

In this communication, we report on the analytical and preparative chiral chromatographic resolution of the most interesting compounds **1** and **2**. The configurational assignment was then performed comparing the circular dichroism (CD) spectra of the pure enantiomers of **1** and **2** with (R)-Baclofen HCl spectrum. To gain an additional direct proof for the configuration assignment, the HPLC/PAD/CD analysis was also carried out using Chirobiotic T.



1: R= 4-benzyloxy

2: R= 3-benzyloxy

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FAR-PO-67 Structure-Activity Relationships studies of GRK2 inhibitors Peptides

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G protein-coupled receptor kinase 2 (GRK2) regulates cell signaling by promoting agonist-specific desensitization of several metabolism-related GPCRs, including the β-adrenergic receptors, endothelin, and glucose-dependent insulinotropic polypeptides. Interestingly, GRK2 expression and function has been shown to be altered in several pathological conditions. Thus, the upregulation of GRK2 and corresponding desensitization of these metabolism-related GPCRs seem play an important role in the onset or progression of diseases such as heart failure, myocardial ischemia, hypertension and Type 2 diabetes. In these diseases, understanding of the molecular mechanisms leading to altered GRK2 levels, as well as the identification of GRK2 inhibitors is a very active field of research.
In this communication we report the preliminary results obtained with a small libraries of short analogues of peptides KRX_{107} and KRX_{124} derived from HJ loop of GRK2/3 [1]. **1** and **2** show a positive effect on glucose metabolism in animal models of Type 2 diabetes, increasing insuline sensitivity and improving glucose homeostasis and emerge as a valuable starting point for the development of a novel class of GRK2 inhibitors.

1	KRX_{107}	G L L R r H S
2	KRX_{124}	G L L R r H S I

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FAR-PO-68 Design, synthesis and biological evaluation of new 4 -thiazolidinone derivatives as STAT3 inhibitors

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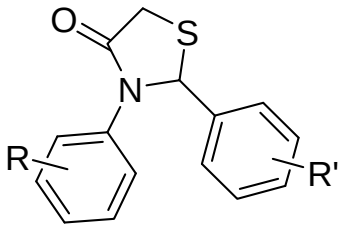
Signal Transducer and Activator of Transcription 3 (STAT3) belongs to the STAT family of proteins, which are both signal transducers and transcription factors. Constitutively-active Stat 3 induces oncogenic processes, such as dysregulated growth, survival, angiogenesis, and immune modulation, and thereby contributes to malignant transformation and progression [1]. Thus, Stat 3 is an attractive molecular target for the development of novel cancer therapeutics.
A recent study has shown that new4-thiazolidinones compounds bearing cumarin moiety inhibit STAT 3 pathway. 4-Thiazolidinone ring system is a core structure in various synthetic compounds displaying broad spectrum of biological activities, including an anticancer and antiproliferative effect[2].
So in this context, drawing inspiration from literature data, we present the synthesis of new thiazolidinone derivatives and their biological evaluation.



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FAR-PO-69 EXPLORING β-BEND STRUCTURES IN THE NEUROPEPTIDE S SEQUENCE

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Neuropeptide S (NPS) was identified as the endogenous ligand of an orphan receptor now referred to as NPSR. NPS injected supraspinally in rodents has been shown to modulate arousal, sleep-wakefulness cycle, anxiety-related behaviours and feeding. To identify novel NPSR ligands, structure-activity relationship studies were performed on the NPS sequence. In the context of such studies [D-Xaa^5]NPS analogues were recognized as the first NPSR antagonists, among these molecules [^{t}Bu-D-Gly^5]NPS was the most potent (pK_B 7.06) [1].

The presence of Asn^4-Gly^5 in the N-terminal region hints at the possibility for this domain to assume, in its bioactive conformation, a regular turn centered on Asn^4-Gly^5, in fact these residues are found with high frequency in position i+1 and i+2 respectively of many natural turns of globular proteins [2].

Thus, we designated NPS analogues in which Asn^4 or Asn^4-Gly^5 was substituted in turn with Pro/D-Pro or $^\delta$Orn in order to stabilize I, II or II' beta turns centered in this position.

The NPSR agonist and antagonist properties of these NPS analogues were investigated by measuring the intracellular calcium levels in response to NPS in cells expressing the recombinant murine receptor.

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FAR-PO-70 NEW PROMISING SCAFFOLDS FOR THE INHIBITION OF MONOAMINE OXIDASE B

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Monoamine oxidase (MAO) (EC 1.4.3.4) are a family of enzymes responsible for the deactivation of active monoamines such as epinephrine, norepinephrine, dopamine, and serotonin [1]. MAO exist as 2 isoenzymes, A and B, with different affinities for various amines as substrates. The activity of monoamine oxidase helps to maintain neuron firing rates throughout the body within homeostatic limits. Because of the vital role that MAO play in the inactivation of neurotransmitters, MAO dysfunction is thought to be responsible for a number of psychiatric and neurological disorders, and, as a result, MAO inhibitors (MAOi) are studied for the treatment of several psychiatric and neurological disorders. Part of the biochemical activity of monoamine oxidase generates hydroxyl radicals, very toxic members of the oxygen free radical group, that may be involved in neurodegenerative disorders such as Parkinson's disease. Therefore, MAO-B inhibitors are coadjutant in the treatment of Parkinson's diseases [2]. MAO-A inhibitors are used as antidepressant and anxiolytic drugs. Furthermore, the activity of MAO-B is enhanced by aging and in Alzheimer's diseases patients [3].
Aiming at the identification of new leads for the selective inhibition of the B isoform of MAO, we have recently reported on the design, the synthesis, and the biological properties of a wide selection of differently substituted heterocyclic nuclei [4]. In this work we wish to present further studies on MAO inhibitors, particularly focusing on the structural modifications leading to an increase of MAO-B activity and selectivity. Thus the synthesis, the biological properties and the SARs of different series of 3-acetyl-2,5-diaryl-2,3-dihydro-1,3,4-oxadiazoles and 3,5-diaryl-4,5-dihydroisoxazoles will be reported. Moreover the influence of stereochemistry on the activity and the selectivity towards the different enzymatic isoforms will be discussed.

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FAR-PO-71 HPLC/ELSD analysis of conjugated bile acids: a way to assist flow chemistry processes

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The employment of flow chemistry [1] in the process optimization of the *N*-acyl amidation of natural and unnatural bile acids (BAs), has required the connection with an *in-line* analysis and validation method for the determination of the reaction yields as well as of purity grade of the synthesized glyco- and tauro-conjugated derivatives. In this framework, an unique HPLC method was successfully established and validated for chenodeoxycholic (CDCA), cholic (CA), deoxycholic (DCA), and ursodeoxycholic (UDCA) acids, as well as the corresponding glyco- and tauro-conjugated forms. Because of the shared absence of relevant chromophoric moieties in the sample structure, an Evaporative Light Scattering Detector (ELSD) [2] was profitably utilized for the analysis of such steroidal species. For each of the investigated compounds, all the runs were contemporarily carried out on the free and the two relative conjugated variants. The different ELSD response of the free and the corresponding conjugated BAs, imposed to build-up separate calibration curves. In all the cases, very good precision and accuracy (evaluated both in the short and long period) along with appreciably low LOD and LOQ values turned out.

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FAR-PO-72 Benzoxadiazole Derivatives: Atypical Inhibitors of Aldose Reductase

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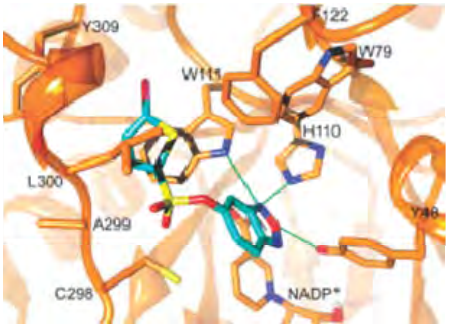
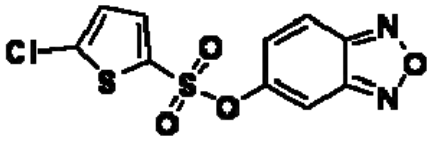
Aldose Reductase (ALR2) is the first enzyme of the polyol pathway and catalyzes the NADPH-dependent reduction of glucose to sorbitol. Under hyperglycaemic conditions the activity of aldose reductase becomes important, triggering to the backlog of sorbitol. The resulting elevated concentration of this sugar increases cellular osmolarity and initiates a cascade of events resulting in the development of long term diabetic complications. ALR2 is also a key regulator of ROS signals induced by growth factors such as FGF, and PDGF, and cytokines such as TNF-α. Therefore, it is clearly involved in additional pathologies such as inflammation and cancer. ALR2 is an excellent therapeutic target, and its inhibition represents a useful therapeutic tool in the treatment of different pathologies. [1, 2]
The last class of Aldose Reductase Inhibitors (ARI) synthesized and tested in our laboratory is represented by a series of variously substituted benzoxadiazole derivatives, emerged from a virtual screening study whose lead compound is illustrated below. [3]
In this communication synthesis and biological properties will be discussed.





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FAR-PO-73 Novel Pyrazolopyrimidine Derivatives as Therapeutic Agents for the Treatment of Medullary Thyroid Carcinoma

S. Sartini,[1] M. Morelli,[1] A. Patti,[1] F. Simorini,[1] S. Taliani,[1] S. Salerno,[1] A. M. Marini,[1] S. Cosconati,[2] V. La Pietra,[2] L. Marinelli,[2] A. Fioravanti,[3] T. Di Desidero,[3] G. Bocci,[3] S. M. Ferrari,[3] P. Fallahi,[3] A. Antonelli,[3] C. La Motta,[1] F. Da Settimo,[1] and E. Novellino.[2]

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Medullary thyroid carcinoma (MTC) is a malignant endocrine tumour originating from parafollicular calcitonin-producing C cells. Mainly sporadic, it may be also present in an inherited form, accounting for up to 8% of thyroid cancers. At present, the treatment of choice for both forms of MTC relies in their complete surgical resection. However, disease can persist or recur, with local and distant metastases which are often fatal. The limited effectiveness of conventional cytotoxic agents in thyroid carcinomas suggests the need of novel therapeutic strategies. Recent advances in the knowledge of pathogenic mechanisms leading to MTC identified receptor tyrosine kinase RET as a new and promising target. 'Gain of function' mutations and rearrangement of RET activate the kinase activity of the receptor, thus providing mitogenic and survival signals to calcitonin-producing C cells. As mutations of RET have been identified in about 98% of inherited MTC cases, at the germ-line level, and in 30% to 50% of the sporadic forms, at the somatic level, this protein represent a sound target for the molecular therapy of most people affected by MTC [1,2]. Different approaches have been considered to repress the kinase function of RET, the most pursued one being the use of small molecules able to compete with the ATP site of the catalytic domain of this receptor. Recently, we described a number of pyrazolo[3,4-*d*]pyrimidine derivatives as effective inhibitors of both RET and VEGFR2 [3,4]. Here we present the synthesis and the functional evaluation of novel compounds of the same series, characterized by suitable substituents in the positions 3 and 6 of the heterocyclic core.

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FAR-PO-74 Antiproliferative activity of *"Lycopersicon esculentum"* leaves (var. Paul Robenson): preliminary study.

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Among plants, the *Lycopersicon esculentum* (Solanaceae) is the most important for its beneficial effects on health. Several epidemiological studies have shown the benefits of tomato consumption in the cancer and cardiovascular disease prevention.
In traditional medicine, also, the leaves of chopped tomatoes are used as a remedy for insect bites, against diarrhea, dysentery, gonorrhea, anal irritation and eyes infections. These properties could be ascribed to alpha-tomatine, contained only in the green part of the plant, with antibiotic, insecticide, insectifuge, fungicide and antibacterial properties.
This study was aimed to evaluate the cytotoxic activity *in vitro* of *Black Tomato* leaves extracts (var. Paul Robenson) on human embryonic kidney (HEK-293), rat glioma (C6) and human breast cancer cells (MCF-7).
Data obtained by the MTT test, showed that both hydrophilic and chloroform fractions exert a citotoxic activity comparable to that of cis-platinum (used as a reference drug) on C6 cell line. No significant activity was exerted by all three extracts on MCF-7 and HEK-293 cell lines.
Regarding MCF-7, our data was in agreement with a previous study of Friedman et al. who demonstrate that these cells are insensitive to lower concentration of glycoalkaloid contained in tomato and that lower concentration of the extracts cause an initial increase in cell growth. Regarding HEK-293 the inactivity of our extract could be advantageous because these are human cell but not tumor cells.
Further studies needed to explore these preliminary observations that indicate the involvement of the extracts of tomato leaves in the reduction of tumour cell proliferation.

FAR-PO-75 6-Substituted carbazoles: synthesis and biological evaluation

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Most anticancer drugs, both synthetic and natural, interact with DNA or its precursors, causing irreversible damage to DNA and inhibiting the synthesis of new genetic materials [1]. 9*H*-Carbazole is found in coal-tar creosote and exhibits a widespread range of applications. Several 9*H*-carbazole possess various pharmacological activities [2].
The aim of this work was the synthesis and the biological evaluation of a series of different-substituted carbazoles **2,3**. Thus, the conventional methodology for carbazole ring construction was applied using the substituted indole **1** as a starting material [2]. Alkylation of the carbazole NH was gave the N-alkylated derivatives **3** in good yields.
The anti-proliferation activity of the carbazoles prepared was evaluated using MTT methodology. Thus, different concentrations of 0.1-, 1-, and 10 μM of carbazoles **2** and **3** were tested against human breast adenocarcinoma (MCF-7) and human endometrial cancer Ishikawa (ISK) cell lines.
The compounds under testing have reduced significantly the proliferation of both cell lines after 96h (for MCF-7 cells) and 24h (for ISK cells) treatments.
These results indicate that these compounds could be used as a new therapeutic approach for the anti-proliferation treatment of the cancer.

[1] M.K. Roy, et al., *British Journal of Pharmacology 145*, **2005**, 145.
[2] A. Caruso, et al., *Tetrahedron 65*, **2009**, 10400.

FAR-PO-76 Group 4 metallocenes : synthesis, characterization and cytotoxicity activity

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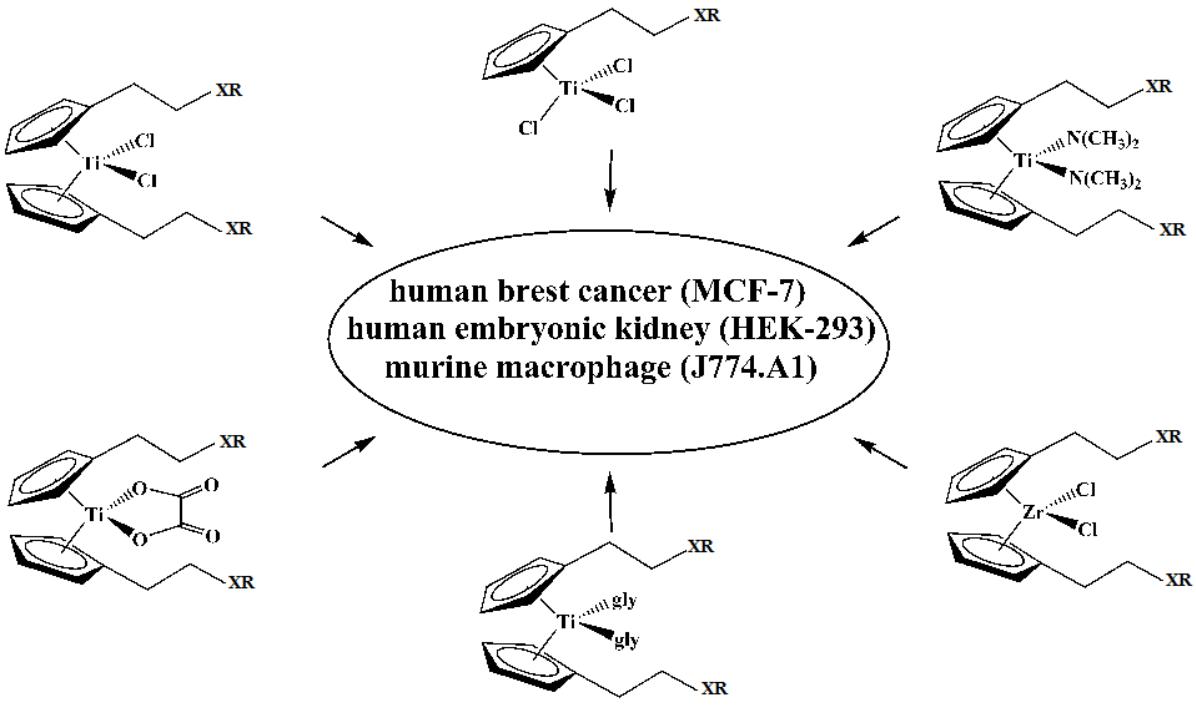
Novel titanocene derivatives and zirconium analogues, having cyclopentadienyl-alcoxyde or sulfoxyde ligands, were synthesized [1,2] and fully characterized by NMR, FT-IR, and elemental analysis. Some of these complexes showed a good cytotoxic activity [3] on human breast cancer (MCF-7) cell lines and on HEK-293. Additionally,a study on the rate of hydrolysis of these compounds showed that the leaving groups significantly affect the rate of hydrolysis of cyclopentadienyl groups too. The different activity of synthesized compounds was tentatively related to the rate of hydrolysis.



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FAR-PO-77 Modulation of thiol homeostasis induced by a novel H_2S-releasing compound

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Recently, the physiological function of hydrogen sulfide (H_2S) has been discovered and a potential therapeutic use of this gas for the treatment of diseases characterized by its altered concentrations has been suggested. A possible approach for a therapeutic administration of H_2S is represented by molecules able to release H_2S in a controlled manner, mimicking what happens physiologically. Dithiolethiones have been found to behave as H_2S donors in physiological conditions.

N-Acetylcysteine (NAC) is under investigation as potential therapeutic agent against several different pathologies characterized by the occurrence of oxidative stress and a decrease in GSH although results deriving from large, multi-center, prospective clinical trials are on most case contradictory and inconclusive. It is possible that the scarce efficacy of NAC is due to its low oral bioavailability (about 8%).

We have recently observed that both dithiolethione containing molecules and the derivative of NAC, N-acetylcysteine ethylester (NACET) are able to significantly reduce circulating and tissue levels of hyperomocysteinemia (hCys), probably via an increase of the thiol to disulfide ratio in extracellular fluids. Mild hCys is considered an independent risk factor for cardiovascular and cerebrovascular disease.

Starting from these observations, we synthesized new dithiolethione–cysteine hybrids (ACS94, ACS96, ACS97) with the assumption that they could have synergic effect in reducing plasma hCys, as well (by tissue glutathione increase) correcting the redox imbalance process present in several diseases.

The effects on thiols pool in different organs and in plasma, after iv or oral administration of NAC (10mg/kg) or equimolar ACS94 to healthy rats and after ip administration of paracetamol (as a model of hepatic toxicity), have been investigated.

The results clearly indicate that ACS94 protects from paracetamol induced hepatic toxicity better than NAC and that ACS94 prevents paracetamol induced thiol depletion in kidney and liver. In addition a more significant decrease of hCys compared to NAC, was observed in some rat target organs and in plasma.

FAR-PO-78 Coumarin as a versatile scaffold to selectively target biologically relevant cytochrome P450 enzymes: aromatase, steroid 11β-hydroxylase and aldosterone synthase

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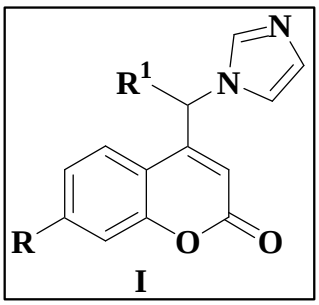
Aromatase (AR, CYP19) is a cytochrome P450 enzyme targeted by drugs, such as exemestane, anastrozole and letrozole, largely used in the therapy of ER^+ (estrogen dependent) breast cancer. Our contribution to the field was given with the design, synthesis, biological evaluation and modeling studies of a series of 4 (or 3)-imidazolylmethyl-7-substituted coumarins as highly potent and selective AR inhibitors.[1]

To evaluate the potential multitarget activity of our compounds of general structure **I** we decided to study their selectivity over other relevant CYPs involved in the biosynthesis of steroids. Representative compounds from our first reports (i.e., from the 7-benzyloxy and 7-aryloxy series) were selected and tested towards CYP11B1 (steroid 11β-hydroxylase) [2] and CYP11B2 (aldosterone synthase), [3] two interesting drug targets for Cushing's syndrome or metabolic disease and for hyperaldosteronism, congestive heart failure and myocardial fibrosis, respectively.



I

Inhibition data indicated that the lead of the benzyloxy series (R = OBn, R^1 = H), was a strong inhibitor of both CYP19 and CYP11B1 (IC_{50} = 0.150 and 0.072 μM, respectively) whereas a lower inhibition was observed for CYP11B2 and more so for CYP17 (IC_{50} = 0.289 μM and 3% at 2.5 μM, respectively).

A similar trend was observed for most of the analyzed benzyloxy-substituted congeners, the most potent and selective CYP11B1 inhibitor being the 3'-trifluoromethoxybenzyloxy derivative which exhibited an IC_{50} value of 5 nM. Preliminary structure-affinity and structure-selectivity relationships will be presented and discussed.

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[3]M. Voets, I. Antes, C. Scherer, U. Muller-Vieira, K. Biemel, C. Barassin, S. Marchais-Oberwinkler, R. W. Hartmann, *J. Med. Chem. 48*, **2005,** 6632.

FAR-PO-79 Quinolizidinyl derivatives of bi- and tricyclic systems as AChE/BChE and beta-amyloid aggregation inhibitors

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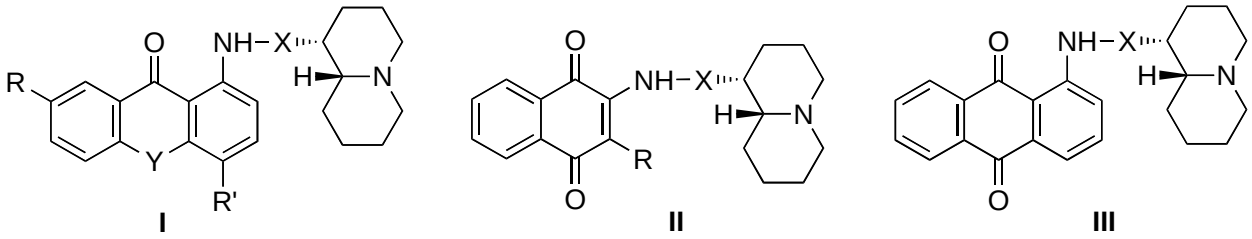
Recently, on the pattern of the potent and selective butyryl cholinesterase inhibitors ethopropazine and Astra 1397, sets of quinolizidinyl derivatives of bi- and mainly tricyclic systems were studied as dual or BChE selective inhibitors. All compounds exhibited activity against both cholinesterases, but inhibition of BChE was generally stronger with submicromolar IC_{50} values for most of them [1]. This study has now been extended to other cyclic structures characterized by the presence of a carbonyl function, as in compounds (**I**) or of a quinone system, as in naphto- (**II**) and anthraquinones (**III**):



These substances were studied for their inhibitory activity on both AChE and BChE. High selectivity against AChE was achieved in compound [**II**: R=Cl; X=$(CH_2)_3$] with IC_{50}=12 nM, while the IC_{50} for BChE was 12 μM. In tricyclic systems, either bearing to structure **I** or **III**, inhibition of BChE was prevailing. Most of these substances were also active in hampering the beta-amyloid aggregation, thus resulting endowed with a promising multitarget behaviour [2,3].

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[3] Pisani, L.; Catto, M.; Leonetti, F.; Nicolotti, O.; Stefanachi, A.; Campagna, F.; Carotti, A. Targeting monoamine oxidases with multipotent ligands: An emerging strategy in the search of new drugs against neurodegenerative diseases. Submitted to Current Medicinal Chemistry.

FAR-PO-80 Nutraceutical properties of red grape juice and its stability after processing for the formulation of food supplements

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[b]Department of Pharmaceutical and Biomedical Sciences, University of Salerno.
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Experimental data have increasingly suggested that cellular oxidative damage induced by reactive oxygen species (ROS) has a relevant pathophysiological role in several types of human diseases, such as atherosclerosis and cancer [1]. Foods, particularly fruits and vegetables, have an important role in maintaining physiological redox equilibrium. These foods supply several antioxidants, such as vitamin C and polyphenolic compounds, to the body. Grapes are rich in phenolic compounds, such as flavonoids and resveratrol, which are mainly found in red grape products [2]. It has been already reported that grape juice compounds can prevent: (i) platelet aggregation, (ii) LDL oxidation and oxidative damage to DNA, (iii) coronary diseases and atherosclerosis [3]. Data on the effects of thermal treatments and subsequent storage on polyphenolics in fruits and vegetables are limited. However, several studies reported that processing may result in significant alterations in antioxidant compounds [4], especially anthocyanins, which may deeply influence antioxidant capacity, color and nutritional quality of food and food products.
The aim of the present study was to evaluate the polyphenolic profile and antioxidant activity of red grape juice before and after freeze-drying. Scientific data on the composition of individual polyphenols in grape juice are scarce.
In this study the sample was compared with the best red wines in the market and then the antioxidant activity of red grape juice was tested by DPPH and FRAP assays and compared with authentic standard. The sample after lyophilization revealed to keep quite unchanged both the polyphenolic composition and the antioxidant capacity when compared with the fresh product.

[1] C. Dani et al., *Food and Chem. Toxicol., 45,* **2007**, 2574-2580.
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[4] T.J. Hager et al., *J. Agric. Food Chem., 56,* **2008**, 689-695.

FAR-PO-81 Multidrug Resistance (MDR) reverting agents: structure-activity relationships of a series of *N*,*N*-bis(arylalkanol)amine aryl esters

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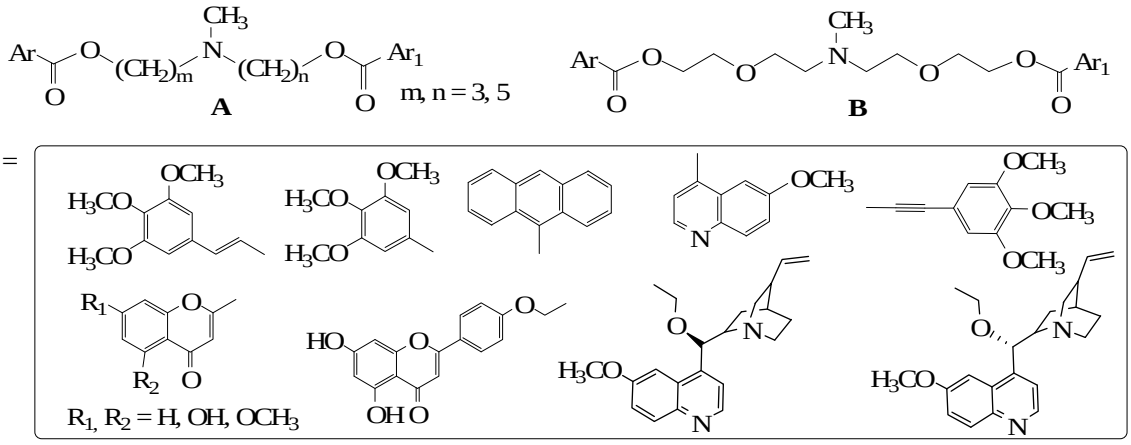
Multidrug resistance (MDR) is one of the main obstacles in cancer therapy; it is due to overexpression of proteins such as ABCB1 (Pgp) and ABCC1 (MRP1) [1] that act as extrusion pumps causing a lower cell concentration of various anticancer drugs that usually are structurally and mechanistically unrelated [2].

Inhibition of the functions of Pgp and related proteins, is considered a suitable approach to circumvent MDR. This is the main reason prompting the design and synthesis of Pgp inhibitors to co-administrate with cytotoxic substrates of Pgp [3].

Recently, we have described a new family of MDR reverters, *N*,*N*-bis(arylalkanol)amine aryl esters, endowed with fairly good potency [4]. Now we report an extension of structure-activity relationships and of pharmacological studies in this series of compounds characterized by the *N*,*N*-bis(arylalkanol)amine scaffold where the aromatic ester portions were suitably modulated.



The new compounds show good potency and efficacy and warrant further studies as MDR modulators.

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[2] L.A. Mitcher, S.P. Pillai, E.J. Gentry, D.M. Shankel, *Med. Res. Rev., 19*,**1999**, 477-496.
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FAR-PO-82 Liposome functionalized by Olygobranched Neurotensin peptides to delivery doxorubicin to tumour cells

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In last years nanoparticles have been generated a strong interest for their potential application as in vivo carriers of active principles [1]. Especially liposome display unique pharmacokinetic properties slowly releasing drugs loaded in the inner aqueous cavity. Recently we have developed supramolecular aggregates decorated by bioactive peptide able to recognize overexpressed receptors on tumour cells membrane [2]. Here we present the synthesis, the structure and the in vitro behaviour of liposomes obtained by co-aggregation of the DOPC phospholipid with a new synthetic amphiphilic molecule, $NT_4Lys(C18)_2$, which contains a lysine scaffold derivatized with a lipophilic moiety and a tetra-branched neurotensin (NT1-13) peptides or a truncated form (NT8–13). The liposome were filled with the cytotoxic drug doxorubicin (Doxo). The synthesis was carried out on solid phase following a Fmoc strategy. The size of liposome was determinated by Dynamic light scattering measurements which indicate a value for the hydrodynamic radius (RH) of 88.3 ± 4.4 nm. The selective internalization and cytotoxicity of liposomes as compared to pure DOPC liposomes, were tested in HT29 human colon adenocarcinoma and TE671 human rhabdomyosarcoma cells, both of which express neurotensin receptors. FACS analysis indicates an increase in fluorescence signal of the NT4-liposomes, in both cell lines and the cytotoxicity is increased four-fold with respect to DOPC. These effects could to be ascribed to the higher rate of internalization for DOPC-$NT4Lys(C18)_2$-Doxo liposomes, due to stronger binding driven by a lower dissociation constant of the NT4-liposomes that bind the membrane onto a specific protein, in contrast to DOPC liposomes, which approach the plasma membrane unselectively.

[1] Torchilin *Nat Rev drug 4*, **2005**, 145.
[2] A. Accardo, et al. *Molecular Biosystems*, *6*, **2010**, 878.

FAR-PO-83 *In vitro and in silico* studies of polycondensed diazine systems as anti-infective agents

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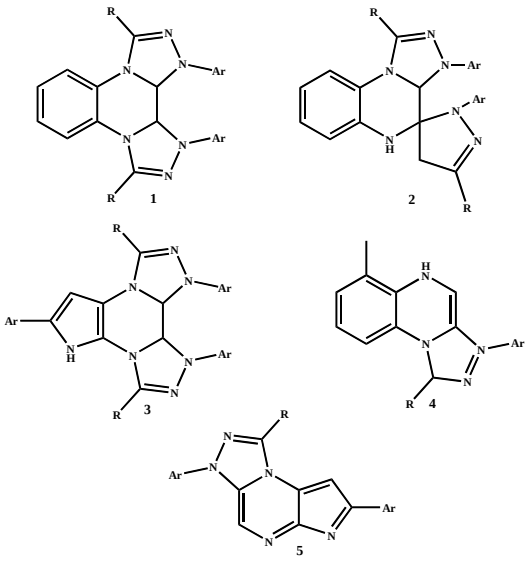
Infective diseases caused by protozoarian agents are still relevant today more than ever. In fact, they represent the first cause of death all over the world with seventeen millions victims every year. The development of drug resistance and the broad diffusion of these pathologies make actual the research of new molecules able to act as selective and effective anti-infective chemotherapics.[1]

Recently several polycondensed diazine derivatives, by means 1,3-dipolar cycloaddition, reactions [2, 3] were synthesized.



A broad selection of these compounds chosen with a wide pattern of substitutions were submitted to biological *in vitro* screening against *Plasmodium falciparum, Leishmania Infantum, Trypanosoma brucei* e *Trypanosoma cruzi*, and they resulted active at micromolar level. In order to identify molecular targets able to explain the mechanism of action of these compounds, we performed Induced Fit Docking/MM-GBSA modeling studies. The obtained results give interesting indications about the probable mechanism of action of the most active compounds.

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FAR-PO-84 Development of an Efficient Continuous Flow Synthesis of Glyco- and Tauro-Conjugated Natural and Semi-Synthetic Bile Acids

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The successful application of flow microreactors in synthetic chemistry has soon attracted a considerable interest for both organic and medicinal chemists. Indeed, moving a reaction from batch to a continuous flow mode turns out to be asset in terms of yield, safety, purity, money, man power, time, scale-up and automation.[1] In the frame of our continuous interest in the development of new synthetic methodologies for the structural modification and functionalization of steroids,[2] we report our ongoing endeavours in the application of flow chemistry for the preparation of bile acid (BA) derivatives. In particular, we describe the results obtained with the employment of a modular flow set-up in the process optimization and experiment design of the *N*-acyl amidation of natural and unnatural BAs. After a microreactor assisted systematic screening of different reaction conditions, including solvent system, base, flow rate and temperature, the connection with an *in-line* purification method allowed us to obtain glyco- and tauro-conjugated BAs in high yield and purity.

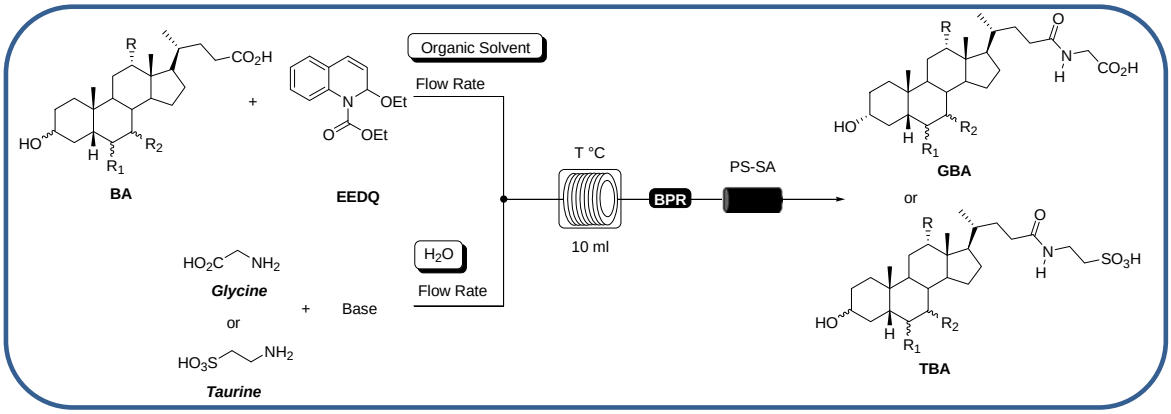

Figure 1. Flow synthesis of conjugated BAs

[1] (a) Microreactors in Organic Synthesis and Catalysis, Ed. T. Wirth, Wiley-VCH: Weinheim, 2008. (b) Ley, S. V.; Baxendale, I. R. *Nat. Rev. Drug Disc.* **2002**, *1*, 573

[2] For recent works see: (a) Gioiello, A.; Sabbatini, P.; Rosatelli, E., Macchiarulo, A.; Pellicciari, R. *Tetrahedron* **2011,** *67*, 1924. (b) Sato, H.; Macchiarulo, A.; Thomas, C.; Gioiello, A.; Une, M.; Hofmann, A. F.; Saladin, R.; Schoonjans, K.; Pellicciari, R.; Auwerx, J. *J. Med. Chem.* **2008,** *51*, 1831. (c) Pellicciari, R.; Costantino, G.; Camaioni, E.; Sadeghpour, B. M.; Entrena, A.; Willson, T. M.; Fiorucci, S.; Clerici, C.; Gioiello, A. *J. Med. Chem.* **2004,** *47*, 4559.

FAR-PO-85 Design, synthesis and biological evaluation of PTPRJ binding Peptides

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[b]Department of Pharmaceutical and Toxicological Chemistry, University of Naples "Federico II".
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PTPRJ (a receptor-type protein tyrosine phosphatase also named DEP-1, HPTPeta, or CD148) is of particular interest for its role in human and experimental tumorigenesis. After its discovery, a consistent body of literature showed the inhibiting effect of the PTPRJ on several players of the mitogenic signal in both normal and cancer cells. In fact, PTPRJ is able to interact and dephosphorylate numerous receptor tyrosine kinases (RTKs) such as PDGFR, HGFR, RET, and EGFR whose aberration or overexpression in cancer cells is responsible of self-sufficiency cell growth. The role of PTPRJ on the inhibition of RTKs was also extended to VEGFR, whose activity is required for the formation of new vessels in tumor progression (angiogenesis).[1] These findings indicate a tumor suppressor activity for PTPRJ and make it an interesting candidate for the generation of novel therapeutic strategies.
In a previous study, we described the isolation and characterization of synthetic PTPRJ binding peptides from a combinatorial phage display library. The cyclic peptides **1** and **2** induced dephosphorylation of PTPRJ targets and moderate cell growth inhibition in HeLa and Huvec tumor cell lines.

1 [Cys-His-His-Asn-Leu-Thr-His-Ala-Cys]-OH
2 [Cys-Leu-His-His-Tyr-His-Gly-Ser-Cys]-OH

In this communication, we present the synthesis, the biological activities and the structure-activity relationships of new analogues of peptides **1** and **2** which we considered as a valuable starting point for the development of a novel class of PTPRJ agonists.

[1] Takamune Takahashi et al., *Blood,* **2006**, Volume 108, Number 4.

FAR-PO-86 Structure-Activity Relationships Studies of CaMKIINtide Analogues

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Ca^{2+} /calmodulin (CaM)-dependent protein kinase is a multifunctional Ser/Thr protein kinase that plays an important role in many cellular function including cell division, differentiation, cardiac contraction and synaptic plasticity [1].
Over the past decade, several CaMKII inhibitors have been reported to study CaMKII function. Most of these compounds showed low potency and absence of highly specific inhibition. In the research of major selectivity the natural CaMKII inhibitor protein, CaM-KIIN, provides a promising alternative, because it potently inhibits CaMKII but not CaMKI, CaMKIV, PKA or PKC. In previous studies COOH-terminal truncations of CaM-KIIN indicated that its inhibitory potency and activities resided largely in a 27 aminoacid residues. This peptide, named CaM-KNtide (KRPPKLGQIGR SKRVVIEDDRIDDVLK) showed a similar IC_{50} value (50 nM) for both the total and the Ca^{2+}-independent CaM-KII activities. As part of our current interest in the study of CaMKII-dependent cell signaling that regulates some many physiological function, we directed our efforts toward the identification of a novel peptide CaMKII inhibitors. Here, we present synthesis, conformational studies and biological evaluation of different CaM-KNtide analogues.

[1]Tsui, J.; Inagaki, M.; Schulman, H. *J Biol Chem.* **2005**, Mar 11, 280(10), 9210-6.
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FAR-PO-87 [1.1.1.]Cryptand: A Bifunctional Kinetic Molecular Device for ^{1}H NMR Automatic Determination of pH-Rate Profile of Drugs

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A bifunctional molecular device is a chemical species able to perform two specific works at a molecular level. [1.1.1]Cryptand [1a] falls into this definition because it is able 1) to change slowly, in an almost linear way,[2] the pH in a reaction medium, working as a molecular titrator, and 2) to measure it, as a molecular pH-meter, making it possible to carry out automatic ^{1}H NMR reaction monitoring for kinetic or thermodynamic investigation, without using physical devices like autoburette and pH-meter. The device performs this role by means of a mechanism [1b] where 1) a fast and reversible protonation followed by a slow, irreversible and highly specific entrapping of the hydrogen ion produce the increase of pH and 2) the partition between unreacted protonated and deprotonated species, in fast equilibrium with each other, produces an averaged CH_2N chemical shift linked to the pH by the Henderson-Hasselbalch equation (Eqn. 1).
This kinetic molecular device (KMD), used before for spectrophotometric automatic titrations,[3a] can be used to carry out unprecedented ^{1}H NMR automatic titrations [3b] for the determination of the pK_a of molecules of pharmaceutical interest. In this contribution it has been used to carry out, for the first time, a variable-pH kinetic experiment where the hydrolysis of aspirin, a classic pH-sensitive reaction, has been followed by ^{1}H NMR while the pH was changing in a controlled way. The kinetic profile obtained has been processed using a mathematical model (Eqn. 2; A = ^{1}H NMR peak area of acetylsalicylic acid) to obtain the entire pH-rate profile of the drug in the range explored.

$$\mathrm{pH} = \mathrm{p}K_\mathrm{a} + \log\frac{\delta - \delta_\mathrm{a}}{\delta_\mathrm{b} - \delta} \qquad (1)$$

$$-\frac{1}{A}\frac{\mathrm{d}A}{\mathrm{d}t} = k_\mathrm{obs}[\mathrm{pH}(t)] \qquad (2)$$

The bifunctionality allows to obtain a variable-pH monitoring without using an added molecular pH-meter. In this way the device system takes only ca. 1 ppm of the entire spectrum and leaves all the rest available for the reaction monitoring.

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FAR-PO-88 The discovery of a carnosine derivative (FL-926-A16) as selective and efficient sequestering agent of cytotoxic carbonyl species: from molecular design to preclinical studies

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Reactive carbonyl species (RCS) are involved in the pathogenesis of several human diseases. Hence RCS, beside to be considered a biomarker of oxidative damage, are also potential targets for the development of bioactive compounds acting as detoxifying agents of RCS (carbonyl quenching compounds) [1]. We found that the natural dipeptide carnosine (β-alanyl-L-histidine) is a selective and potent RCS sequestering agent, even if its clinical application is limited due to the rapid hydrolysis in blood by a specific dipeptidase (carnosinase). Consequently, we developed a drug discovery approach aimed to design, synthesize and evaluate novel CAR peptidomimetics which, beside to maintain or improve the reactivity and selectivity of carnosine towards RCS, are recognized by hPepT1 and hence transported through an active transport but not recognized by carnosinase. The metabolic stability of the synthesized compounds was studied by incubating them with rat plasma and human serum as well as with rat and human liver fractions and reactivity (HNE as substrate) and selectivity (pyridoxal) studied in in vitro models. The pharmacokinetic profile for the most promising derivative (FL-926-A16) was then investigated in rats and its ability to quench HNE and to reduce protein carbonylation and tissue damage was demonstrated in different animal models (*db*/*db* mouse and nApoE null mice).

[1] Aldini G, Orioli M, Rossoni G, Savi F, Braidotti P, Vistoli G, Yeum KJ, Negrisoli G, Carini M., *J Cell Mol Med*, **2010**, Jun 1. [Epub ahead of print].

FAR-PO-89 New Substituted purine nucleotides as potent agonist of the recently deorphanized GPR17

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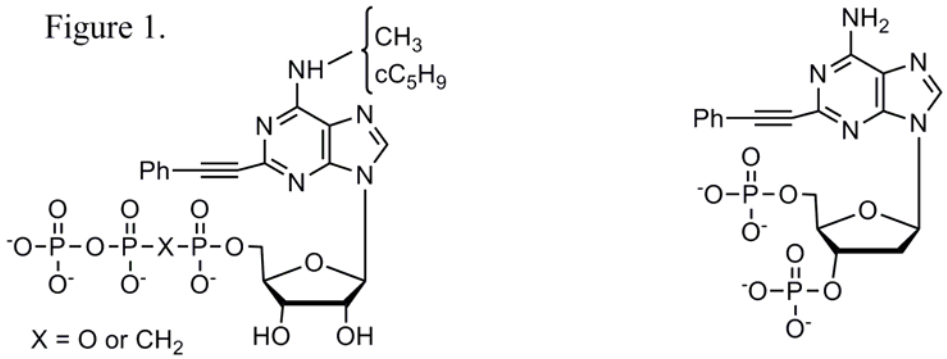
A dualistic G protein coupled receptor named GPR17, which responds to nucleotides and cysteinyl leukotrienes, has been recently deorphanized. GPR17 is believed to represent a novel target for the development of new therapeutic approaches to human stroke and ischemic damage. Biological studies demonstrated that 2-phenylethynylATP behaves as a strong agonist (EC_{50} = 36 pM) of this receptor [1]. On the other hand, N^6-methylATP and some purine nucleotide bisphosphates showed antagonist activity. On these bases, in the search for potent GPR17 ligands, 2-phenylethynylATP derivatives bearing a methyl or a cyclopentyl group in N^6-position, 2-phenylethynyl bisphosphate derivative, and a stable analogue of 2-phenylethynylATP were synthesized (Figure 1). [^{35}S]GTPγS binding assay, performed on transfected 1321N1 cells, showed that the new compounds

Figure 1.



behave as strong agonists of GPR17 with EC_{50} value in the low nanomolar or subnanomolar range, hence they could be efficacious tools for the further characterization of the receptor and to study its role in neurodegeneration processes.

[1] E. Calleri, S. Ceruti, G. Cristalli, C. Martini, C. Temporini, C. Parravicini, R. Volpini, S. Daniele, G. Caccialanza, D. Lecca, C. Lambertucci, M.L. Trincavelli, G. Marucci, I.W. Wainer, G. Ranghino, P. Fantucci, M.P. Abbracchio, G. Massolini, *J. Med. Chem.*, *53*, **2010**, 3489.

FAR-PO-90 Photosensitizing Activity of Pegylated Pheophorbide *a*

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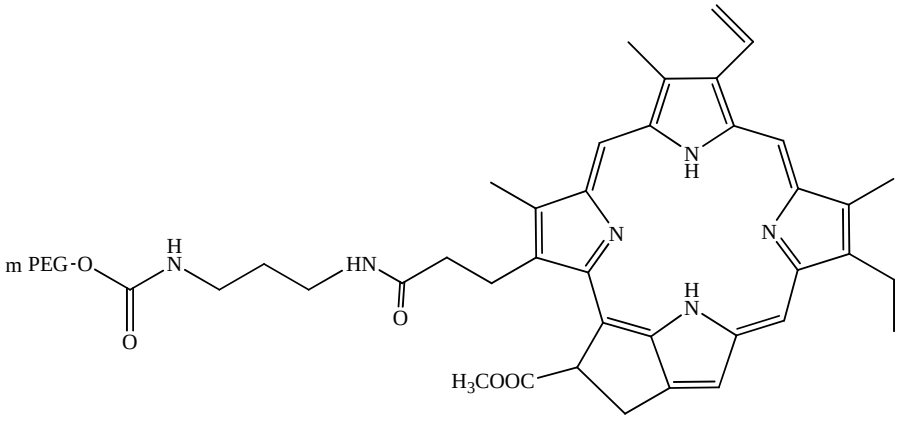
Photodynamic therapy (PDT) is a non-invasive therapeutic modality used in a various number of diseases and cancer. It involves the systemic or topic administration of a photosensitizer, followed by irradiation with light. The activated photosensitizer converts oxygen to singlet oxygen and/or reactive oxygen species (ROS) which lead to cell death and tissue necrosis. One aim of PDT research is the discovery of new photosensitizers possessing minimal dark cytotoxicity, high photodynamic properties, improved pharmacokinetics, preferential retention in diseased instead of healthy tissues, chemical stability and a good cellular uptake [1].
We recently focused our efforts on pheophorbide *a* (Pb*a*), a chlorophyll derivative. *Pba* is characterized by a stronger absorption between 650-700 nm, in the tissue-penetrating wavelength range. For *in vivo* applications the capacity of the photosensitiser to reach in the diseased tissues becomes critical, in particular when a large peritoneal area is interested as occurring in carcinomatosis and sarcomatosis.



To improve the pharmacokinetic and the activity of the photosensitizer we conjugated Pb*a* to polyethylene glycol (PEG).

In vivo the pharmacokinetic analysis performed on living female C57/BL6 mice bearing a subcutaneous melanoma mass, showed that injected mPEG-Pb*a* distributes all over the body, with an higher uptake in the tumor respect to free Pb*a*. Moreover, preliminary data suggest that PEG-Pb*a* in mice bearing B78-H1 amelanotic melanoma reduces the tumor growth after light activation in comparison with Pb*a*.

[1] Josefsen, L.B. and Boyle, R.W., 2008. Photodynamic therapy and the development of metal-based photosensitisers. *Met. Based Drugs,* 276109-276133.

FAR-PO-91 New alkylacetamide derivatives as new sigma ligands.

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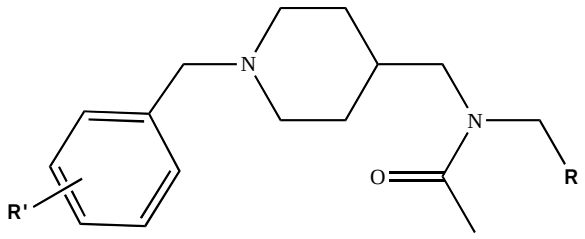
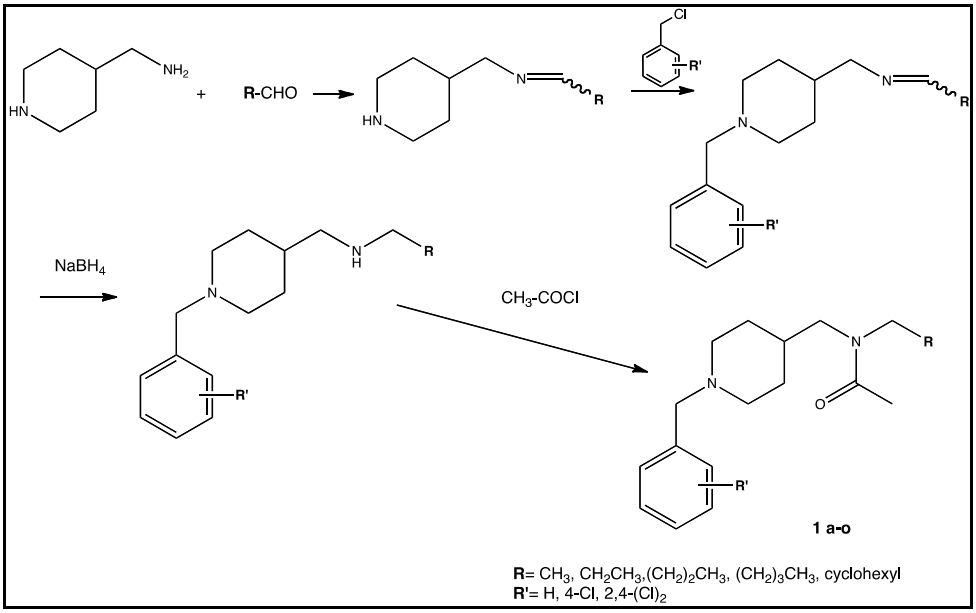
On the basis of some substituted benzylacetamide derivatives previously synthesized by us [1] and gifted with excellent activity toward σ_1 receptor subtype (best σ_1Ki= 0,09 nM), we synthesized a new series (**1 a-o**) of alkylacetamide derivatives in order to establish the influence of an alkyl chain, rather than an aryl moiety, on σ_1 receptor affinity of the corresponding compounds and their selectivity over σ_2 receptor subtype.



1 a-o

R=CH_3, CH_2CH_3,$CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$, cyclohexyl.
R'= H, 2,4-$(Cl)_2$, 4-Cl.

These compounds were synthesized as follow:



The preliminary displacement percentage of the compounds tested over both receptor subtypes showed a remarcable affinity against sigma 1 receptor (average: 78 %) which improves with the lengthening of the alkyl side chain. On the other hand, the results obtained over sigma 2 subtype indicate a constant, moderate affinity throughout all the series (average: 35 %). The K_i values of the entire series will be determined.

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FAR-PO-92 Design, synthesis and molecular modeling studies on peptidomimetic vinyl esters as falcipan-2 inhibitors

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Malaria is currently endemic in 106 countries, with an estimated 225 million clinical cases and nearly 781,000 deaths in 2009 [1]. To date resistance has emerged to all common antimalarial drugs, including recently artemisinins. In this context a new important target for antimalarial drug design is represented by falcipain-2 (FP-2), a hemoglobinase of *P. falciparum* food vacuole [2]. FP-2 is able also orchestrate selective proteolytic events during the release of malaria parasite from human red blood cells, because of its ability to cleavate the cytoskeletal proteins ankyrin and the band 4.1 protein.

In this regard our research group actively worked in the last years on the development of novel peptidomimetic FP-2 inhibitors, containing a 1,4-benzodiazepine (BDZ) scaffold [3] introduced into the dipeptide sequence D-Ser-Gly. Among all the FP-2 inhibitors synthesized, the Michael acceptor vinyl ester **1** [4] (Figure 1) has been shown to be the most potent and selective FP-2 inhibitor. In order to investigate the structure-activity relationship of the lead compound **1**, novel vinyl ester derivatives have been designed (Figure 1) [5], by introducing different substituents on the fused benzene ring or at C-4' of the phenyl substituent on the BDZ scaffold. Additionally the 4-chloro-2-trifluoromethylphenyl group, linked by means of a carbamoyl moiety to the side chain of the P3 site serine, has been replaced with other aromatic rings or with cyclo(alkyl)groups in such a way to investigate the ability of the P3 pocket to accommodate groups of different size. Lately the methyl substituent of the parent inhibitor **1** has been replaced with an ethyl and isobutyl or benzyl group in order to evaluate size and characteristics of the P1' liphophilic pocket. In the present work we now report docking studies in order to explain the different degree of biological activity of synthesized inhibitors as well as their reversible or irreversible inhibition mode of FP-2.

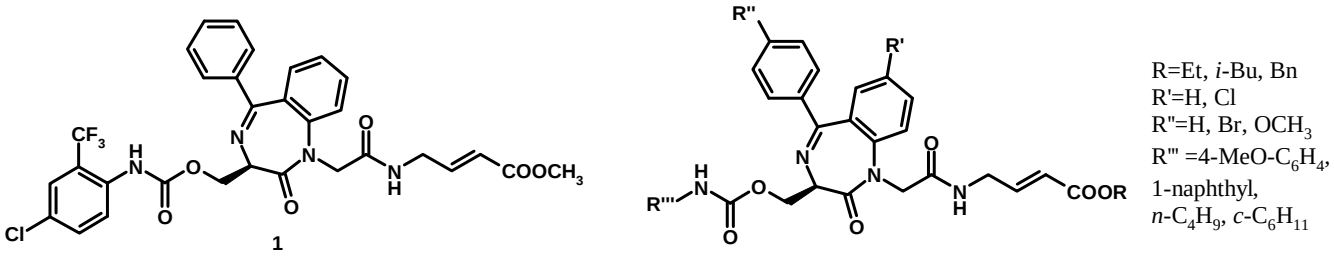

Figure 1

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[3] N. Micale, A. P. Kozikowski, R. Ettari, S. Grasso, M. Zappalà, A. Kumar, M. Hanspal, J.-J. Jeong, A. H. Chishti. *J. Med. Chem., 49*, **2006**, 3064.

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FAR-PO-93 3,4-Isoxazolediamides a Novel Class of Heat Shock Protein 90 Inhibitors

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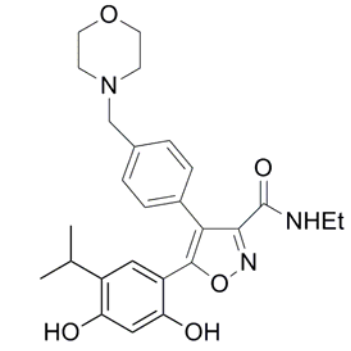
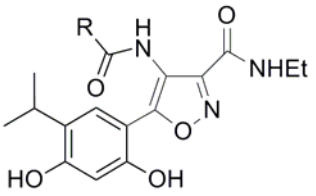
Hsp90 (heat shock protein 90) is a component of a molecular chaperone complex, involved in the folding, maturation and stabilisation of key signalling molecules which control cell proliferation, survival and transformation. It works by a modulation of a set of cancer-associated proteins collectively referred as ‘‘clients’’. Inhibition of Hsp90 causes simultaneous destabilization and eventual degradation of client proteins that result in suppression of tumor growth. This observation led to the idea that Hsp90 is a potential target for a new strategy in human cancer therapy.[1] Recently, investigations on 4,5-diarylisoxazoles generated an important new class of Hsp90 inhibitors, and VER-52296/NVP-AUY922 is currently in Phase II clinical trials.[2]

Here we describe a novel class of Hsp90 inhibitors structurally related to the 3,4-isoxazolediamide scaffold. We have found that compounds possessing a nitrogen atom directly attached to the C-4 heterocycle ring possess in vitro Hsp90 inhibitory properties comparable, and for some aspects better, than the structurally related 4,5-diarylisoxazole derivatives. Remarkable compounds from this series of diamides combine potent binding and cell growth inhibitory activity in both series of alkyl and aryl or heteroaryl amides, with IC_{50} in the low nanomolar level.



VER-52296/NVP-AUY922



R= Aryl, heteroaryl and alkyl

3,4-Isoxazolediamides

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FAR-PO-94 Quantification of artemisinin in *Artemisia annua* Herbal Tea and test *In Vitro* for Anti-Malarial Activity

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A. annua was usually used to prepare a tea and if it contains effective amounts of artemisinin, it might be used today as a self-reliant treatment of malaria [1]. *Artemisia annua* tea has proven itself to be a very effective treatment for malaria in various clinical trials, but to date, his efficacy has not been investigated *in vitro*. Therefore, we have carried out a study for the evaluation of effects of *A. annua* tea on *Plasmodium falciparum* cultures *in vitro*. We also determined the concentration of artemisinin in herbal tea preparation.

The compound was tested against chloroquine-sensitive D10 and chloroquine-resistant W2 strains of *P. falciparum* using the parasite lactate dehydrogenase assay [2]. The quantification of artemisinin in the extract of leaves of *A. annua* was obtained using an ^{1}H NMR method.

The *in vitro* tests conducted in this study confirm the clinical efficacy demonstrated by the tea of *A. annua in vivo* on both chloroquine-sensitive D10 and chloroquine-resistant W2 strains. The concentration of artemisinin in *A. annua* tea is lower with respect to that of pure artemisinin responsible for the same antimalarial activity. The artemisinin present in the tea is probably co-solubilised with other ingredients, some of which may also have antimalarial activity and act synergistically with it. The presence of other active ingredients suggests that *A. annua* is a natural artemisinin combination therapy. These compounds also merit further research, to see whether their presence hinders the development of parasite resistance compared to pure artemisinin [3].

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[2] M.T.Makler, J.M.Ries, J.A.Williams, J.E.Bamcroft, R.C.Piper, B.L.Gibbins, et al, *Am.J.Trop.Med.Hyg., 48(6)*, **1993**, 739-41.
[3] Work supported by Regione Puglia Progetto Strategico PS70.

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Chimica Fisica

FIS-KN-01 Colloidal nanocrystals: Synthesis, properties, assembly

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Fabrication Current efforts and success of nanoscale science and technology are related to the fabrication of functional materials and devices in which the individual units and their spatial arrangement are engineered down to the nanometer level. One promising way of achieving this goal is by assembling of colloidal inorganic nanocrystals as the novel building blocks of matter. This trend has been stimulated by significant advancement in the wet-chemical syntheses of robust and easily processable nanocrystals in a wide range of sizes and shapes. The increase in the degree of structural complexity of solution-grown nanostructures appears to be one of the directions towards which nanoscience will increasingly orient. Recently, several groups have indeed devised innovative syntheses of nanocrystals through which they have been able to group inorganic materials with different properties in the same particle. These approaches are paving the way to the development of nanosized objects able to perform multiple technological tasks.
The talk will highlight the recent advances in the synthesis of colloidal nanocrystals, with emphasis on the strategies developed at IIT (Genova) for the fabrication of colloidal nanocrystals, as well as on their properties and their assembly.

FIS-KN-02 Antibodies and SERS for Targeting and Imaging with Functionalized Gold Nanoparticles

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Gold nanoparticles are biocompatible nanostructures which are under scrutiny for applications in nanomendicine. We synthesized gold nanoparticles by a laser ablation methodology (LASIS) which does not need any stabilizing agent for the colloidal solutions [1]. The free surface of the nanoparticles, with diameters of about 20 nm, is easily functionalized with molecules for the surface enhanced Raman scattering (SERS) [2] and with antibodies.

We obtained nanostructured materials with innovative antibodies for antigens like PSMA and PSCA which allow efficient targeting of prostate cancer cells. Strong SERS signals are registered for targeted cells among others which do not express the recognized antigens. In vivo experiments show that strong SERS signals are observed in cancer tissues. The results show that the gold nanomaterials we obtained are stable also in vivo and allow efficient targeting of prostate cancer cells. Preliminary results with doxorubicine loading the gold nanomaterials for drug delivery will be also reported.

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FIS-KN-03 Time-dependent Modeling of Complex Systems in the Soft Condensed Matter

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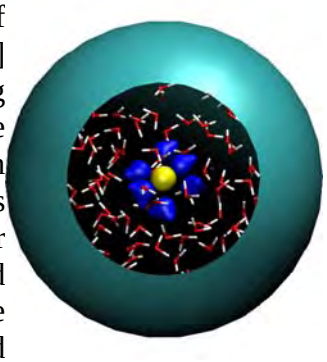

In this presentation, we report on recent developments of the General Liquid Optimized Boundary (GLOB) [1,2] model, an effective computational approach for simulating the time evolution of complex molecular systems in the soft condensed matter at different levels of theory, from purely quantum-mechanics to hybrid QM/MM methods and classical force fields. Moreover, we describe our progress in the modeling of static and time-resolved spectroscopic observables through some illustrative examples [3], ranging from ions in solution to optical and magnetic probes. In this context, a special focus will be put on the description, at molecular level, of the role of the dynamics in the modulation of different spectroscopic parameters.

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FIS-OR-01 Magnetic Nanoparticles and click-chemistry: towards functional nanocomposite materials

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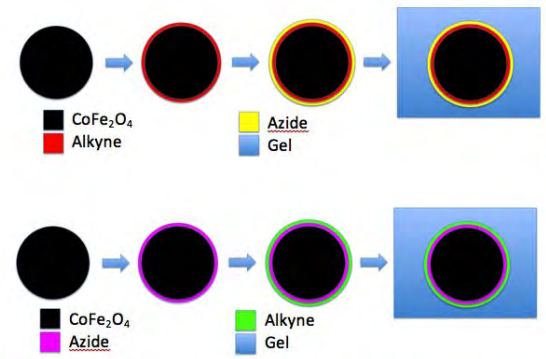

The preparation of nanocomposite materials through the assembly of nanosized building blocks has already been proven as an effective route for the preparation of functional materials.[1,2] In this contribution we describe a versatile approach for the embedding of inorganic nanoparticles within a gel matrix based on click-chemistry.

The nanoparticles, *i.e.* $CoFe_2O_4$ particles with size around 10 nm, are first synthesized via a modified Massart approach.[3] Their surface is then functionalized by reaction with an organic molecule including a carboxylic functionality. Functionalized nanoparticles are then reacted via click-chemistry (Huisgen 1,3-dipolar cycloaddiction between an alkyne and an azide group[4]) to make them polymerizable.

Surface functionalized nanoparticles were finally embedded within the an acrylamide-based hydrogel network through their radical co-polymerization with acrilamide and *N*,*N*′-methylenebisacrylamide.

These results represent an example of the bottom-up approach to the preparation of functional nanocomposites through the surface functionalization *via* Click Chemistry of magnetic nanoparticles.

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FIS-OR-02 NIR-emitting mono- and bimodal PbS NC superlattices

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Recently, increasing attention has been focussed on inorganic nanocrystal (NC) shape- and size-dependent properties, which are crucial for both fundamental studies and their high impact in many technologic fields[1].

Here, we report on the fabrication of superlattices of PbS NCs, characterized by a narrow monomodal size distribution (MSD) or a bimodal size distribution (BSD). In the case of PbS NCs with a MSD, the influence of fundamental parameters, such as NC concentration, dispersing solvent and substrate, on the superlattice formation, was studied.[2] PbS NCs with a BSD were successfully organized in different geometries, as a function of the size ratio of the two PbS NC families. In order to elucidate the spatial arrangement of the NCs and the crystalline structure of the assembly, the fabricated superlattices were investigated by means of structural techniques (small and wide angle XRD and TEM) and theoretical simulations of the XRD patterns.[3] The size-dependent absorption and emission spectroscopic properties of PbS NCs, were intensively investigated. The comparison between the emission features of the PbS NCs in solution and organized in thin film, suggest the occurrence of a FRET energy transfer between the close-packed NCs, only when geometric and energy constrains are fulfilled.

The hierarchical organization of nano-objects has a very high potential for the fabrication of functional “solids”, materials in which collective properties (e.g. electromagnetic properties) mainly arise from the controlled interaction among building blocks, such as metamaterials.

This work has been partially supported by the 7th FP EU funded project METACHEM (Grant CP-FP 228762-2).

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FIS-OR-03 Electron and dielectric properties of TiO_2 nanotubes

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Due to the spatial confinement , oxide nanosheets are characterized by peculiar chemical and physical properties. They grow on appropriate metal substrate or self assembly as nanotubes, nanorods or nanowires. In particular TiO_2 nanotubes have attracted a lot of attentions in the last decade because of their unique chemical and physical properties.[1] One of the most interesting applications is connected to the preparation of dye sensitized solar cells where the one dimensional structures of the tubes are expected to significantly improve the electron transport properties, whereas the high surface area optimize the number of sensitizers anchored to the oxide.[2] The performances of the device however are related to the size, length, thickness and structure of the titania tubes.

Although theoretical calculations can play a major role in providing information on the atomic scale, because of the size of the systems involved, only a handful of computational studies of TiO_2 nanotubes appeared in the literature. In this work TiO_2 nanotubes constructed from anatase TiO_2 layers were investigated with DFT methods and by employing the periodic CRYSTAL09 code.[3] Dependence of electronic and dielectric properties on size and morphology of the tubes has been investigated in the 20-60 Å range.[4]

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FIS-OR-04 Capacitive effects in silicon-supported polyoxometalate-based nanocrystals

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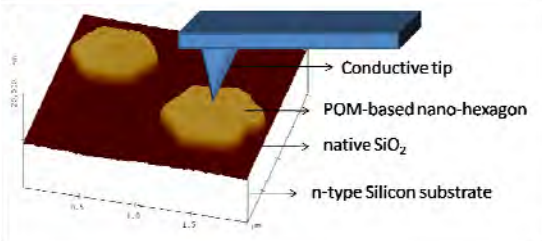
Polyoxometalates (POMs) are complex metal oxide molecules, which have attracted growing interest, due to their wide potential redox, photochemical and catalytic properties. The potentiality for these compounds to be applied in functional devices has shown the need of investigating their assembly and organization in the solid state and on solid substrates. On this respect, we recently showed the possibility to form at solid surfaces a large landscape of supramolecular architectures by employing derivatized POMs under both static and dynamic self-assembly conditions. [1,2] By using Langmuir-Blodgett, here we show that the symmetric C9-alkenes derivatized Mn-Anderson clusters give in combination with dioctadecyldimethylammonium (DMDOA) counter-ions well-defined 2D hexagonal nanostructures at silicon surfaces. Such an organization derives by a nucleation and growth process involving the hopping of DMDOA on top of C9-Mn-Anderson upon barrier compression. We report on the hexagonal nanostructures as effective nanodielectrics, their nanoscale capacitive properties having been measured by scanning capacitance microscopy. Noteworthy, the dielectric properties of these nanoscale structures can be modulated upon the applied bias to the scanning tip. These findings open fascinating perspectives that these novel supramolecular assembly may give in emerging scientific and technological fields including their application as smart materials in plastic and/or hybrid (organic-inorganic) electronics.



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FIS-OR-05 Nanoparticles for Cultural Heritage Conservation: calcium and barium hydroxide nanoparticles for wall paintings consolidation

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Nanotechnology provides new materials with the ideal characteristics for the consolidation and protection of wall paintings. In particular, calcium and barium hydroxide nanoparticles offer a versatile and highly efficient toolset to face the main degradation processes altering wall paintings. Clear example of the efficacy and potentiality of nanotechnology is represented by the rescue, in situ, of Maya wall paintings in the archaeological area in Calakmul (Mexico).
The paint layer is at the interface between the wall and the surrounding environment and it is strongly susceptible to degradation due to the mechanical stresses following salt crystallization.
The effects of this process are usually strongly amplified if any protective coating, possibly applied in previous restoration treatments, is present. Polymers, mainly acrylic and vynil resins, have been widely used to consolidate wall paintings and to confer to the painted layer protection and hydrorepellency [1]. The use of inorganic materials, which are compatible with wall paintings, minimizes the aforementioned risks and prevents from unexpected side effects. Inorganic consolidants are highly chemically stable and preserve the wall painting porosity ensuring long-lasting consolidation effects.
Lime ensures the highest physico-chemical compatibility with the work of art and it should be preferred when degradation results from loss of calcium carbonate [2,3]. The presence of sulfate salts as a contaminant can inhibit the consolidation effects. Innovative formulations based on calcium and barium hydroxide nanoparticles overcome these limitations thank to their synergistic action, which confers to the paintings a stable consolidation.
This contribution reports on the preparation of barium hydroxide nanoparticles, and the formulation of nonaqueous dispersions for their application on wall paintings.

Note: This work has been partly supported by the project *TemArt*; *Programma Operativo Regionale - Regione Toscana*, co-financed by *Fondo Europeo di Sviluppo Regionale* (*POR CreO FESR 2007-2013*).

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FIS-OR-06 Development and Characterization of Nano-Fluids for the Cleaning of Wall Paintings

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Synthetic polymers have been often used in conservation of wall paintings. Polymers are highly harmful for the original material of these artworks [1]. We have proposed the use of alternative methodologies for conservation and formulated innovative cleaning nanostructured systems to remove previously applied polymer films and grime from painted surfaces [2, 3]. In particular, a novel "micellar system", which was named "EAPC", composed of water, SDS, 1-pentanol, propylene carbonate, and ethyl acetate has been recently developed [4, 5]. EAPC was found to be particularly effective in polymer removal. The nanostructure of this system was thoroughly investigate by means of several scattering techniques (QELS, SAXS and SANS) and compared to that one of a xylene-in-water microemulsion. The interaction process that takes place between the nanostructured fluids and a different detergency mechanism from a classical was found. Micellar aggregates act as solvent nano-containers and interact with the polymer film leading to its swelling and the detachment from the surface. After the removal process, the micelles become smaller due to depletion of the organic solvents. These findings represent an important step in opening up new perspectives in the design and formulation of new cleaning systems specifically tailored for intervention on particular conservation issues.

Note: This work has been partly supported by the project *TemArt*; *Programma Operativo Regionale - Regione Toscana*, co-financed by *Fondo Europeo di Sviluppo Regionale* (*POR CreO FESR 2007-2013*).

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FIS-OR-07 Hydrophobic CdSe@ZnS nanocrystals loaded liposomes and their interactions with RC membrane protein

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A versatile and rapid method to encapsulate CdSe@ZnS nanocrystals (NCs) in the lipid bilayer of liposomes has been developed. NC surface has been suitably engineered to improve the hydrophobic interaction between NC capping ligand and the lipid alkyl chain. NC-loaded liposomes of various composition were realized by the Micelles to Vesicles Transition (MVT) method [1]. Several NC-loaded liposomes were prepared as a function of NC capping layer, NC concentration, detergent and lipid mixture composition. The properties and the stability of the system have been characterized from the optical (UV–Vis-NIR and emission spectroscopy) and morphological (RT-TEM, Cryo-TEM and DLS analysis) point of view, in order to investigate the optimal experimental conditions for NC-liposome formation. The experimental conditions were tailored to allow the construction of a vesicular hybrid system containing both CdSe@ZnS NCs and reaction centre (RC) protein of *Rhodobacter sphaeroides* [2]. Absorption spectra suggest that the protein scaffold of RC remained structurally intact in the presence of NCs even after one week. Charge recombination kinetics of RC have confirmed that even at the functional level the protein was not damaged by the NCs.

The obtained results are promising and the proposed method could be extended to any type of hydrophobic nanoparticles (metallic, semiconductor, magnetic), lipids and membrane proteins. On the one hand this technique could extend the study of interactions between nanoparticles and proteins to the important class of integral membrane proteins, on the other hand it can be employed to easily produce a non-specific labeling in reconstituted systems and in natural cell membranes using fusogenic techniques.

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FIS-OR-08 Lattice measurements in metallic nanoparticles by means of HRTEM images.

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In the frame of structural characterization of nanostructures by means of HRTEM (High Resolution Transmission Electron Microscopy) technique, several authors have highlighted the importance of quantifying the errors related to the measurements of lattice spacing. This point is particularly crucial in the case of smaller nanoparticles (<10 nm) in which the effect due to the high surface/volume ratio can give misleading results in the determination of interatomic distances. In this context the method developed by de Ruijter [1] appears a promising approach to achieve the requested sub-pixel resolution in order to quantify properly the atomic distances. To this purpose we implemented a software program to be employed in the study of lattice parameters of nanometer structures. Simulated images of thermodynamic-stable morphology of metal nanoparticles were used as test cases to check for the surface strain effect [2] in the determination of atomic distances. Some experimental HRTEM images of nanoparticles were then analyzed and the lattice parameters consequently determined and compared with those tabulated for the bulk structures (Figure 1).

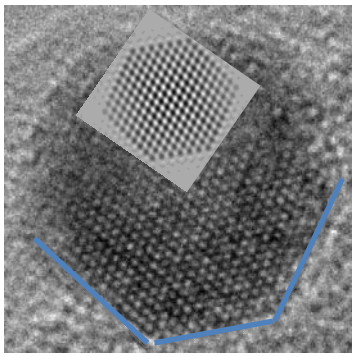

Figure 1: Image simulation of Au cubooctahedral in [101] Zone Axis and experimental HRTEM image of Au nanoparticle.

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FIS-OR-09 Role of base-pairing in the synthesis of nucleolipids obtained through alkylation of Cytidine and Guanosine monophosphates by n-dodecyl-epoxide.

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We recently demonstrated that aqueous colloidal solutions provided suitable environments to investigate the role played by the molecular interaction between complementary nucleobases Adenine-Uracil (A-U) in the synthesis of the respective amphiphilic nucleolipids [1,2,3]. Several types of ribonucleotide mono-phosphates XMP (X=A, U) were hydrophobically modified through a S_N2-type reaction by the water insoluble n-Dodecyl-Epoxide (DE) as alkylating agent, which was dispersed at r.t. in aqueous micellar solutions formulated with the cationic surfactant Cetyl-Trimethyl-Ammonium-Bromide (CTAB). The presence of a charged interface acted as a catalytic locus where both reactants, DE and XMP, were able to meet and react. In the present communication the reaction between DE and CMP/GMP [i.e. nucleotides bearing two further complementary bases (C,G)], present as single reactants or as equimolar mixture, is discussed. In particular, HPLC-ESI-MS using a 3D-ion trap spectrometer as the detector, operated in negative polarity, has been used for a MS and MS/MS characterization of the two nucleotide alkylated by-products. The reaction evolution was monitored at different times and the signals related to the m/z ratios of $[M-H]^-$ ions for nucleolipids of CMP and GMP (i.e. structures derivatized by hydroxyl-dodecyl moieties) were detected in the LC-ESI-MS traces after 40 days. In particular, mono and bi-alkylated species could be observed for both nucleotides, whereas tri-alkylated derivatives were also detected in the case of CMP. Similarly to nucleolipids obtained from AMP and UMP [2], the first alkylation involved either a phosphate OH or one of the nucleophilic sites on the Cytosine or Guanine nucleobases (primary NH_2, OH arising from keto-enolic tautomerization); however, mono-alkylation on the nucleobase was favored in the case of GMP.
Alkylation on both types of sites was obtained for bi-alkylated products, whereas ribose OH groups appeared to be also involved when tri-alkylated CMP were considered. Quantitative estimates, as obtained from extracted ion chromatograms, provided further interesting information, first on single nucleotide systems. Indeed, bi-alkylated species were found to be predominant in the case of GMP, whereas a comparable incidence of tri-alkylated species was observed for CMP. Moreover, the peak areas for residual XMP suggested that alkylation proceeds faster in the case of GMP. The described features were confirmed when the mixed-nucleotide system C+G was investigated, yet a much faster alkylation could be hypothesized for both nucleotides in this case. In fact, no significant signal was detected after 40 days of reaction for residual unreacted CMP and even that related to GMP was quite weak. Moreover, mono-alkylated species were found to be significantly less abundant in mixed systems, compared to single nucleotide ones. Time-resolved zeta-(ζ)-potential measurements performed on the aqueous aggregate dispersions indirectly confirmed the enhanced production of the fraction of the correspondent bi-chained XMP nucleolipids for the system C+G, compared to the germane samples C and G. An involvement of C-G base-pairing might be invoked to explain these original experimental features in terms of molecular recognition effect.

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FIS-OR-10 Self-Assembly of helical peptide foldamers

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Many neurodegenerative diseases have been associated with the early stages of amyloid aggregation, triggered by the formation of small *β*-sheet aggregates that grow to micrometric fibrils through a slow self-assembly process. Experimental evidences indicate that peptide aggregation is mainly driven by hydrophobic interactions, with aromatic residues playing a specific role.

We carried out optical spectroscopy, microscopy with nanometric resolution and computational studies on aggregates formed by Z-Aib$_n$N oligopeptides, with n= 6, 12 and 15. Aib (α-aminoisobutiric acid) is a conformationally-constrained amino acid characterized by the gem-dimethyl substitution on the C^{α} atom. From structural studies in solution and in the crystal state, homo-Aib polypeptides have been shown to populate 3_{10}- or α-helical structures depending on the length of the peptide chain. A naphthyl (N) chromophore was inserted at the C-terminus of the peptide chain to study the influence of aromatic groups on the aggregation properties of the peptides investigated by applying optical spectroscopy techniques. UV-Vis absorption and fluorescence experiments revealed the formation of J- and H-aggregates in water/methanol solutions only for Aib$_{12}$N and Aib$_{15}$N.

Atomic Force Microscopy (AFM) has been employed to analyze the morphology of the aggregates and to establish the mechanical stress resistance of peptide fibrils. To obtain the Young's modulus we used force spectroscopy measurements on for fibrils and the values, 11 ± 1 MPa, 6.7 ± 0.6 MPa, 6.6 ± 0.6 MPa and 15 ± 1 MPa, confirms that a low packing it's a general feature of amyloidal fibrils. The observed variation in the Young's modulus indicates that fibrils produced under identical conditions might exhibit different mechanical properties while the values along the single fibril doesn't vary significantly; same internal packing environments indicate structural homogeneity along the fibril.

Molecular dynamics simulations (MD) revealed the presence of different aggregated species, the morphology of which is determined by the length of the peptide chain and the specific arrangement of aromatic groups.

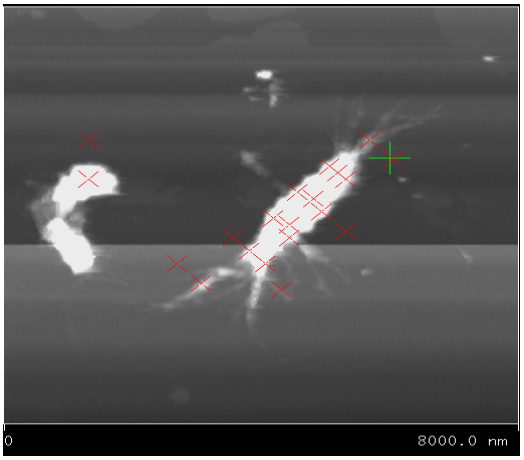

Figura 1 One of the fibrils that were used in force spectroscopy experiments

FIS-OR-11 Peptide-mediated confinement of liposomes in nanopores

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In view of the relevance of nanostructured surfaces for biomedical applications, including sensing, spatially resolved surface-cell interactions, drug delivery, etc.., the idea of confining biofunctional compounds in nanosized structures is gaining more and more interest. Accordingly, in this communication we present a versatile approach to nanostructurate polymeric films, in order to achieve the selective confinement of a multipurpose biological platform, consisting in suitable liposome formulation, driven by an antibacterial peptide anchored within the surface nanostructures.
In particular, in this contribution we demonstrate the use of monodisperse inorganic nanospheres, forming an ordered colloidal crystal on gold surfaces, as a templating system to nanostructurate a poly(methylmethacrylate) (PMMA) ultra-thin film (thickness <30 nm). The nanoparticle array embedded within the PMMA film is then selectively removed giving rise to the formation of hybrid nanopore arrays, having polymeric walls and gold bottom.
Trichogin GA IV, an antimicrobial peptide functionalized at the N-terminus by a thiol-group, was shown to be selectively chemisorbed within the obtained nanopores, due to the interaction of its thiol termination with the nanopore-paving gold . The Trichogin GA IV strong affinity for the liposome structures is then exploited to drive the selective confinement of phospholipid bilayers within the functionalized nanopores. It is found that liposomes are efficiently included within the trichogin-functionalised pores, and that only the liposomes in direct contact with trichogin remain firmly attached within the pores.
The formation of a peptide self-assembled monolayer covalently linked to the gold surface inside the pores, as well as the immobilization of liposome bilayers was demonstrated by using cyclic voltammetry (CV), Atomic Force Microscopy (AFM), Quartz Crystal Microbalance with Dissipation monitoring (QCM-D) and X-ray Photoelectron Spectroscopy (XPS), obtaining information on the peptide/liposome interaction as well as on the best suited conditions of liposome immobilization.

FIS-OR-12 Characterization of vesicles formed by lipopolysaccharides: from the molecular structure to the aggregate architecture

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Lipopolysaccharides (LPSs) are amphiphilic macromolecules indispensable for the growth and the survival of Gram-negative bacteria, one of the most diffuse classes of pathogenic bacteria. [1] LPS are composed of a hydrophilic heteropolysaccharide unit, covalently linked to a lipophilic moiety called lipid A, which is embedded in the outer leaflet and anchors these macromolecules to the lipid membrane. Recent studies have revealed that presumably the physical characteristics of these molecules are correlated to their biological activity. [2-3] Here we present a structural study on the architecture and the conformation assumed by LPSs in the lipid membrane. Particularly, we try to connect their self-aggregation behavior to the molecular structure. The investigation has been performed using an experimental strategy which has been proved to be extremely informative on vesicle aqueous suspension and combines dynamic light scattering (DLS) to estimate vesicle dimension, small angle neutron scattering (SANS) to analyze the aggregate morphology and to estimate the thickness of the lipid bilayer and electron paramagnetic resonance (EPR) to investigate the dynamics of the lipid hydrophobic tail in the bilayer.

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FIS-OR-13 On the common role played by the pre-TM domain of different viral fusion glycoproteins in the infective process.

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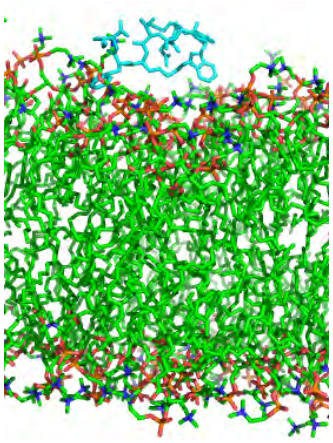
Enveloped viruses require fusion between the viral envelope and the target membrane for entry into the cell. This process is controlled by one or more viral fusion glycoproteins that undergo conformational changes favouring the necessary micro- and mesoscopic lipid re-arrangements. Several membranotropic regions of the fusion proteins cooperate, according to a concerted mechanism, to accomplish the membranes fusion.

We investigated the interaction between peptides deriving from the pre-transmembrane (pre-TM) domain of fusion proteins of different viruses (*i.e.*, HIV, FIV [1], herpes simplex [2] and hepatitis C [3] viruses) and biomimetic lipid bilayers. This comparative study combines experimental results from EPR, Neutron Reflectivity, CD, Fluorescence Spectroscopy and MD simulations.



Despite the little homology between these peptides, the results show that all of them adsorb on the membrane surface with very limited penetration. Lipid packing perturbation due to this interaction propagates along the acyl chains. This originates a marked asymmetry among the bilayer leaflets, definitely favouring a local curvature change. Thus, we suggest that the pre-TM domain role in the viral infection pathway is the destabilization of the target cell membrane, which allows its fusion with the viral envelope.

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FIS-OR-14 On the origin of infrared spectral changes upon protein folding/unfolding

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While the amide I absorption pattern of folded structural elements is rather well understood, the physical origin of the spectroscopic behaviours of unfolded states is much less understood, despite differences in the amide I bands of folded and unfolded states having become a crucial spectral feature to follow protein and peptide folding kinetics in time-resolved and temperature dependent IR spectroscopies. Here, we study by means of a theoretical-computational method, the Perturbed Matrix Method (PMM) [1-3], the IR spectra in the amide I region of two β-hairpin peptides. The main feature of the method is that the IR behavior can be accurately reproduced not only for folded states but also for the very heterogeneous unfolded states, whose IR spectrum is commonly difficult to be computed due to their high conformational flexibility. The computed spectra result to be in good agreement with the experimental ones, thus providing an explanation of the physical origin underlying the differences of the unfolded- and folded-state spectra.

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FIS-OR-15 Bio-membranes integrated into organic thin-film transistors for biophysical studies

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Membrane and proteins integration into an organic thin-film transistor (OTFT) structure will be presented. The proposed architecture allows the direct interfacing between membranes and an OTFT channel retaining both the electronic properties and the biological functionality. Though also enzymes and antibodies have been successfully integrated, the present contribution will focus on the response of phospholipid bilayer (also embedding membrane proteins) integrated into OTFTs.
The response of these OTFT depends on the properties of the integrated biological membrane and thus opens a new way of probing the events involving membranes. The biological membranes are deeply involved in crucial cellular functions such as adhesion, trafficking, recognition, and signalling. Probably the most familiar form of cellular signaling is the synaptic transmission, the central event of the whole nerve transmission. Anaesthetics are drugs and chemicals that strongly hinder the synaptic transmission. We have found that lipid bilayer integrating OTFTs tested against volatile-anesthetics (concentration 1-5%) reveal drug-induced membrane changes [1, 2]. The responses to anesthetics obtained with OTFTs integrating either lipid bilayer or membrane proteins will be discussed and it will be shown how the results of the present study challenges the anesthetic mechanisms model relying on the so far provided evidence that clinically relevant doses (2.4 %) do not alter lipid bilayers overall-structure, significantly.
These examples show how the proposed bio-electronic platform, besides resulting in extremely performing biosensors, can open to insights into phenomena, such as cell-signaling and recognition, involving weak membrane interfacial modifications.

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FIS-OR-16 NANOCLAYS AND BIOPOLYMERS IN AQUEOUS SOLUTION AND IN SOLID STATE. INTERACTIONS AND STRUCTURE

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Over the last years several biopolymers have been investigated because their combination with other compounds may form new composite materials with potential technological applications environmental friendly and available at low cost. In this work, we studied modified cellulose and pectins as biopolymer and nanoclays with different morphologies to prepare nanocomposites materials.

The two clays are: halloysite nanotubes, characterized by a cylindrical-like shape and laponite RD with a disk-like shape. Their affinity towards biopolymeric matrices was studied in both the aqueous and the solid state from the physicochemical view-point in dependence of the composition of both the polymer and the filler.

The nanoclay-biopolymer interactions in water were evidenced by calorimetry (ITC, DSC) and light scattering. Efforts have been devoted in modelling the enthalpy data providing the key thermodynamic properties.

The nanocomposites (prepared by means of the casting method) were imaged by SEM and the different morphologies were correlated to the thermal degradation behaviour, optical transparency, wettability, mechanical properties and dielectric response.

FIS-OR-17 Towards a "surface science model for biology": glycine adsorption on nanohydroxyapatite with well defined surfaces

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Hydroxyapatite (HA), $[Ca_{10}(PO_4)_6(OH)_2]$, the natural major inorganic constituent of bone and teeth in the form of nano-crystals, is usually a system of choice to study protein/biocompatible-surface interactions. The study of these interactions is crucial not only for the development of new biomaterials and to understand biomineralization processes but also for several technological and biomedical applications such as biodevices and drug delivery systems. Nonetheless, despite the great efforts in investigating protein/HA systems, atomistic information on the actual contact occurring at the interface is rather scarce. Suitable to this target is the adoption of a "surface science model" approach, based on the interplay among the preparation of materials with well defined surface features, spectroscopic and accurate quantum mechanical techniques. This approach has been very fruitful to obtain a deep knowledge on surface molecular events relevant for heterogeneous catalysis, hence successfully developing a well-established "surface science model for catalysis". In that respect, it is worth pointing out that for the model to be successful, extended non-defective crystalline faces grown out of a single crystal are usually employed, together with ultra high vacuum conditions. At variance with this approach, here we worked at standard conditions and focused on the possibility to employ nanometric HA particles with well defined surfaces, because in bone tissues, HA is present as nanoparticles embedded in a collagen matrix, to form a highly organized composite material and not as a bulk extended crystal.

These HA nanoparticles were used to investigate the adsorption of non-ionic $HOOC\text{-}CH_2\text{-}NH_2$ glycine (Gly) vapours by means of IR measurements. The adoption of a single aminoacid, as the basic molecular brick of proteins, has allowed to supplement the experimental measurements with modelling techniques (Figure 1) based on first principle quantum mechanical methods which have been successfully adopted in the past by some of us. Details and relevant literature are in ref [1].

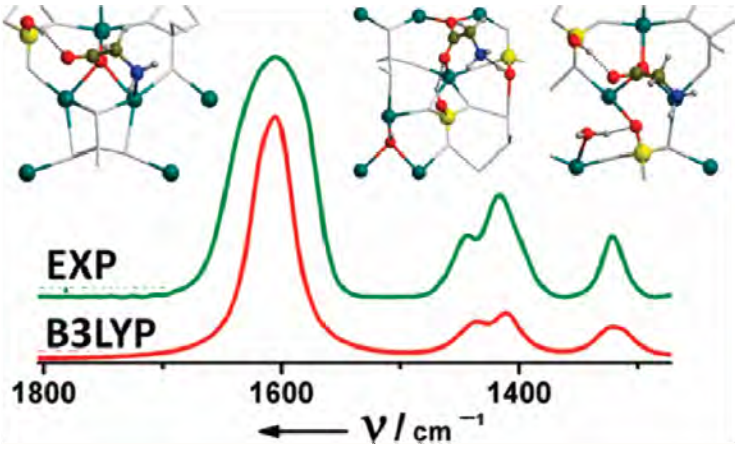

Figure 1.

[1] A. Rimola, Yu. Sakhno, L. Bertinetti, M. Lelli, G. Martra, and P. Ugliengo, *J. Phys. Chem. Lett.*, *2*, **2011**, 1390.

FIS-OR-18 Playing with Peptides: How to Build Supramolecular Peptide Nanostructures by Exploiting Aromatic and Helix-Helix Macrodipole Interactions

E. Gatto[a], A. Porchetta[a], M. Caruso[a], F. Casiero[a], F. Formaggio[b], C. Toniolo[b], M. Scarselli[c], M. De Crescenzi[c], M. Venanzi[a]

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Biomolecules have been extensively investigated as possible components of nanoscaled electronic circuits. In particular, hybrid materials obtained by functionalizing metals with biomolecules have been recently synthesized, paving the way for the fast-growing field of bionanoelectronics.
In this work mono- and bi-component peptide-based self-assembled monolayers (SAMs) have been immobilized on gold surfaces and studied by electrochemical and spectroscopic techniques [1]. The peptides investigated comprised almost exclusively *Cα*-tetrasubstituted *α*-amino acids. These non-coded residues, because of their unique conformational properties, forced the peptide backbone to attain helical conformations, which promote the formation of stable SAMs on gold surfaces.
Blocking experiments performed in ferricyanide solution gave basic information on the stability and packing density of the peptide layers on the electro active surface, while fluorescence experiments performed by using spatially sensitive fluorescent probes, gave information about the possible formation, in the bicomponent SAMs, of raft domains, i.e. segregated single-component regions.
The photocurrent generation properties of these mono- and bi-component peptide-based SAMs were studied by electrochemical and spectroscopic techniques. In fact, all the SAMs investigated were composed of peptides derivatized with chromophores strongly absorbing in the UV region to enhance the efficiency of the photocurrent generation.
The composition of the bi-component SAMs on the surface have been analyzed by a combination of electrochemical and spectroscopic techniques. Interestingly, the surface composition is quite different from the solution stoichiometry used for SAM preparation.

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FIS-OR-19 Resolution of the Redox IR signatures of the Metal Centers of Bovine Cytochrome c Oxidase by Controlled Electrochemistry of Specific Ligated Forms

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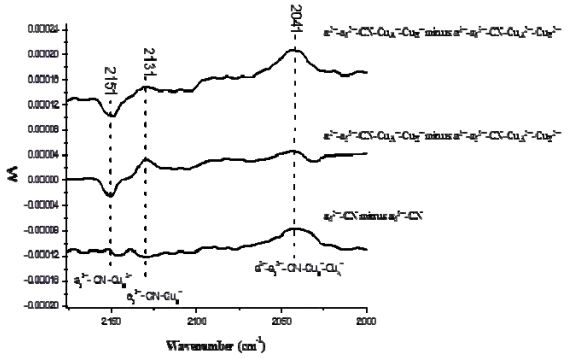
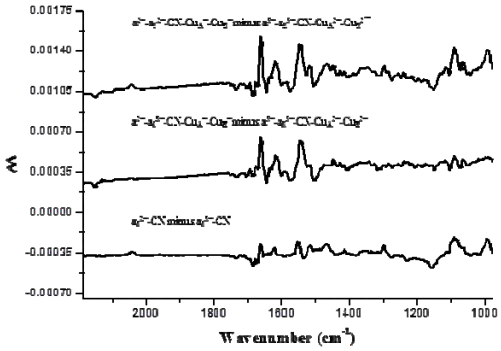
Attenuated Total Reflection (ATR) Fourier transform infrared (FTIR) spectroscopy in the mid-IR range (4000-900 cm^{-1}) is a powerful analytical tool that is increasingly being applied to biological macromolecules, such as proteins. However because of the vast number of IR-active normal modes of a typical protein, interpretation of IR data at the atomic level is usually only feasible when recorded as difference spectra between two defined states in which localized changes are induced. An ATR system has been developed in which electron transfer protein substates can be controlled automatically via a conventional three-electrode potentiostat whilst recording UV/visible changes with a fibre optic reflection probe [1, 2].



Electrochemically-induced ATR-FTIR difference spectroscopy was performed on samples of bovine cytochrome c oxidase (CcO) that had been deposited as thin films on the surface of a silicon microprism. CcO is the terminal enzyme of the mitochondrial and many bacterial respiratory chains. It catalyzes the reduction of molecular oxygen to water and couples energy released to generate a protonmotive force used for ATP synthesis. Four redox active metal centers are present: heme a, Cu_A, heme a_3, Cu_B. Heme a and Cu_A mediate electron transfer from cytochrome c to the heme a_3/Cu_B oxygen reducing binuclear center (BNC). A variety of ligands can also bind to the BNC is specific redox states. For example, CO binds to the reduced binuclear center and raises the redox potentials of both heme a3 and CuB. Cyanide (CN) binds most strongly to oxidized heme a_3 and lowers its midpoint potential .[3-4]



These ligands were used in combination with controlled electrochemistry to separate the IR redox spectra of haem a_3 alone, Cu_B alone and haem a/Cu_A.

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FIS-OR-20 Drug interactions with cation transport ATPases investigated on solid supported membranes

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The solid supported membrane (SSM) represents an experimental model of a lipid bilayer membrane, and is extensively used to investigate charge movements in electrically active membrane transporters [1]. Proteoliposomes or native membranes (vesicles or fragments) incorporating the transport protein can be adsorbed on a SSM and activated by a substrate concentration jump. The substrate jump induces charge displacement within the transport protein, resulting in a current transient which can be detected in the external circuit [1,2]. Therefore, the SSM serves two purposes at once, i.e. offering an adhesive surface to the adsorbed membrane entities and functioning as a transducer of a biosensor system.

BioElectroLab has a wide expertise in the study of charge transfer in cation transport ATPases through the SSM technique [2]. Our attention has recently been focused on the inhibition of ion pumps by molecules of potential pharmacological interest [3] and xenobiotics [4]. Molecules like thapsigargin and cyclopiazonic acid belong to high (nanoM) affinity inhibitors of the Ca-ATPase, whereas curcumin and clotrimazole are medium (microM) affinity inhibitors of both Ca-ATPase and Na,K-ATPase. Moreover, the toxic heavy metal Pb^{2+}, that poses a major public health problem, is able to inhibit Na,K-ATPase activity in the low micromolar range.

By combining biochemical and electrical measurements, we have compared systematically the effects of various compounds demonstrating different degrees of potency and specificity. From our results we may conclude that the inhibition mechanism involves stabilization of intermediate states of the ATPase cycle, whereby progress and completion of the enzymatic cycle are impeded.

The financial support of Ente Cassa di Risparmio di Firenze and M.I.U.R. (PRIN Project) is gratefully acknowledged.

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FIS-OR-21 First-principles modeling of cathode materials for solid oxide fuel cell applications

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The development of efficient cathode materials for solid oxide fuel cells (SOFCs) has been based largely on perovskite-type transition metal oxides ABO_3 (A= La, Sr; B = Cr, Mn, Co, Fe, Ni). The key factors contributing to the usefulness of these materials are: high-temperature stability, the ability to catalyze the oxygen reduction reaction (ORR) at reasonable rates and high enough electronic conductivity. To reduce the SOFC operating temperature and retain good overall performance, significant efforts have been devoted to finding cathode materials that present the characteristics of a mixed ionic electronic conductor (MIEC) [1]. However, a more fundamental understanding of the underlying processes occurring at the cathode surface, within the cathode bulk material, and at the cathode/electrolyte interface, is needed to improve these materials further.

To this aim, we performed a systematic study of $LaMO_3$ (M = Cr, Mn, Fe, and Co) materials based on *ab initio* density functional theory + U (DFT+U) [2]. From the analysis of our results and available experimental data [3], we derived rational design principles that can be easily implemented for new and more effective cathode materials for SOFC applications. Based upon these design principles, we will discuss the role of the presence of alloying elements, at A and B sites, as well as the effects of the element ratio on the following properties: (a) the crystal and electronic structures; (b) the tendency to form oxygen vacancies necessary for bulk oxygen transport and (c) the surface chemistry toward ORR catalysis. In particular, we will present the results for the most exploited SOFC cathode, $La_{1-x}Sr_xMnO_3$ (LSM) [4], and, for comparison, for two promising materials recently proposed for symmetric SOFC applications, namely $La_{0.75}Sr_{0.25}Cr_{0.5}Mn_{0.5}O_{3-\delta}$ (LSCM) [5] and $Sr_2Fe_{1.5}Mo_{0.5}O_{6-\delta}$ (SFMO) [6] materials.

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FIS-OR-22 General-purpose approaches for computational spectroscopy studies of complex molecular systems

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Spectroscopy represents a tool of choice for the characterization of all kinds of molecular systems. Among its many applications, we can cite the determination of the structure, dynamics or the photochemical properties, of utmost importance in the conception of photovoltaic cells, for instance. However, the interpretation of most experimental spectra is difficult due to their inherent complexity caused by the thermal or environmental effects, but also intrinsic properties of the system itself. In this matter, computational spectroscopy has shown to be a valuable tool to help unravel the various contributions to the spectrum, allowing for a better understanding of the underlying phenomena.

Several computational tools, covering a large panel of spectroscopies, in particular those of vibrational and electronic origin, have been developed and coded. However, the most advanced ones are often made available in the form of independent programs, which may be difficult to deploy and use for a non-expert as well as to interact with other programs needed to compute required input data. One of the key challenges, necessary for a broader adoption of advanced theoretical models is the integration in single packages, able to perform the complete task from the determination of the structure to the final output of the spectrum of interest, and simple interfaces to use them.

In this context, we present general-purpose modules for the simulation of the line-shapes for vibrational spectroscopy (e.g. infrared) at the anharmonic level and vibrationally-resolved electronic spectroscopy (one-photon, electronic circular dichroism). The theoretical models used aim at providing a computational support for the realistic IR-UV-vis experimental spectra of complex systems, including their environment, and are less focused on highly accurate predictions for small molecular systems or studies of peculiar features. Various computational strategies exploiting the localized nature of spectroscopic phenomena are available at both levels, allowing to handle larger systems, which may be too cumbersome to treat in their entirety, with limited impact on the accuracy. Those approaches represent a great improvement with respect to the methods still commonly used in such cases (harmonic approximation, vertical electronic transitions) and contribute to the better understanding of experimental spectra of large molecular systems routinely studied nowadays.

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FIS-OR-23 Rotational spectroscopy for astrophysical investigations

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Among the various spectroscopic research fields, the investigation of the phenomena that allow to understand the chemistry of the interstellar medium plays a particularly relevant role. The need of laboratory, experimental as well as computational, investigations in this field is due to the fact that astronomical observations require the knowledge of the spectroscopic parameters involved. For the sake of giving an example, we mention that the recent Herschel, SOFIA and ALMA missions require the accurate knowledge of the transition frequencies in the submillimeter-wave range up to the infrared frequency region for a huge number of molecules, for those of relevance, the so-called "flowers", as well as for the disturbing species, the so-called "weeds". The need of the knowledge of the spectroscopic parameters has then led to the set up of various databases, that are continuously updated and enlarged.
Among the various spectroscopic techniques, thanks to its intrinsic high resolution, rotational spectroscopy is a powerful tool for studying the chemistry and physics of the atmosphere and interstellar medium. In the present contribution, the reseach lines of the LMSB (Laboratory of Millimeter-wave Spectroscopy of Bologna) in the field of astrophysical investigations are prersented. The focus is on the accuracy of the retrieved transition frequencies of neutral as well as ionic species and on line-broadening investigations.

FIS-OR-24 How Does Tacticity Affect the Solution Behaviour of Poly(N-isopropyl acrylamide)? A Molecular Dynamics and Metadynamics Simulation Study

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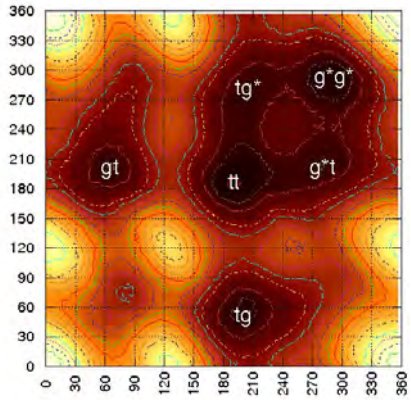

Conformational free energy map of the PNIPAAm syndiotactic dyad in water at 293 K.

The peculiar thermal phase behavior of poly(N-isopropyl acrylamide) (PNIPAAm) in aqueous media caught the attention of physicists and chemists in the last two decades, leading to both elegant chemical physics investigations and smart soft matter devices. The discovery of a new procedure for the stereocontrolled radical polymerization of acrylamides [1] allowed to test the water phase behavior of stereoregular PNIPAAm's, showing a strong influence of the polymer tacticity [2,3]. The purpose of this study is highlight the factors determining the PNIPAAM tacticity-dependent differences of its solution properties, tackling the problem both form a structural and dynamic point of view with a double simulation approach. The conformational free energy behavior as a function of backbone conformation was obtained by metadynamics simulations. The structural characteristics, the intramolecular and water hydrogen bonding and the torsional dynamics were explored by molecular dynamics simulations. The investigation, extended to all stereoisomers of PNIPAAm trimer, representing syndiotactic, isotactic and atactic sequences, showed that the experimentally observed lower hydrophilicity of isotactic poly(N-isopropyl acrylamide), in comparison with the syndiotactic one, is related to a lower conformational entropy. Simulation results were critically compared with available experimental data on solution properties and reactivity of poly(N-isopropyl acrylamide) [4].

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FIS-OR-25 Structural and Dynamic Features of Thermoresponsive Microgels around the Volume Phase Transition Temperature

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Sustained drug delivery requires the use of multi-functional devices with enhanced properties, including responsivity to external stimuli (such as temperature, pH, ionic strength), ability to target specific receptors, enhanced bioadhesion to cells and biocompatibility. Microgels represent one such multifunctional suitable as drug delivery and switchable microdevices. The fabrication of a stable colloidal aqueous suspension of biocompatible microgel spheres is based, for instance, on a poly(vinyl alcohol)/poly(methacrylate-co-*N*-isopropylacrylamide) network [1]. These microgel spheres undergo an entropy driven volume phase transition around physiological temperature, this process being driven by the incorporation of NiPAAm residues in the network. In this study the microgel was loaded with the anti cancer drug, doxorubicin. Upon microgel de-swelling, a marked increase in the amount of doxorubicin released was noted. Sieving and size exclusion effects were studied by laser scanning confocal microscopy with microgel particles exposed to fluorescent probes with different molecular weights (Figure 1). In this contribution we focus on some fundamental issues regarding modifications of the network structure at a nanoscopic level and of the diffusive behavior of water associated with the polymer network around the volume phase transition temperature (VPTT) [2]. Observations carried out at room temperature and at 40 °C (i.e. below and above the VPTT), provided an evaluation of the variation of the average pore size (from 5 nm to 3 nm). The diffusive behaviour of water molecules closely associated to the polymer network around the VPTT was investigated quasi-elastic neutron scattering. Nanostructured changes around VPTT of the microgel particles was probed in direct and reciprocal space, i.e. small angle neutron scattering (SANS) (Figure 2) and scanning transmission X-ray microscopy (STXM), respectively. A transition of the microgel interface from brush-like to smooth surface was evidenced by a power law change from 2 to 4 (Porod's law).

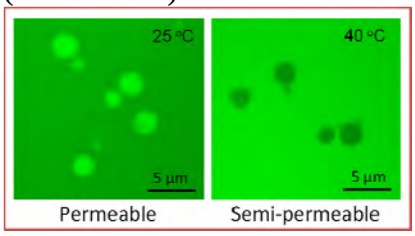

Figure1. Confocal microscopy/size exclusion experiment at 25 and 40°C

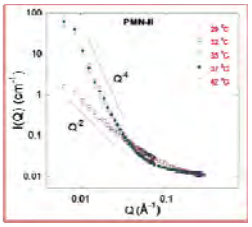

Figure 2. SANS on PMNII microgel around the VPTT

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FIS-OR-26 Tuning the Aerosol-OT surfactant film curvature in water through the 1-butyl-3-methylimidazolium BF_4^-/Br^- ionic liquids

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Through a detailed analysis conducted basically via SAXRD and NMR PGSTE techniques, it is here shown that the curvature of the micellar aggregates originated by the sodium bis(2-ethylhexyl) sulfosuccinate (Aerosol-OT, NaAOT) in water can be severely altered when a polar ionic liquid, namely the 1-butyl-3-methylimidazolium tetrafluoborate (bmimBF_4), is added to the binary system. Although the whole phase diagram is investigated, here the focus is mainly on the isotropic micellar region. Data reveals that the ionic liquid is strongly adsorbed at the interface and that the overall processes can be described as a co-micellization of AOT^- and $bmim^+$ involving roughly two cations for each anion. Concerning the micellar phase, such an adsorbtion induces a huge modification of the interfacial geometry that results in the occurrence of discrete spherical micelles having positive curvature, as evidenced from the self-diffusion experiments.[1] Remarkably, the micellar phase nanostructure can be tuned by the simple substitution of the ionic liquid's counter-ion. Indeed, when bromide instead of tetrafluoroborate is used as the imidazolium counter-ion the nanostructure changes from discrete to bicontinuous.[2] This finding can be accounted for suggesting a decreasing of the NaAOT effective surfactant packing parameter, although the effect in the presence of Br^- is less pronounced. Data modeling shows the same degree of interfacial adsorption for the $bmim^+$ cation in both systems, regardless of the particular counterion used – either BF_4^- or Br^-. Thus, the remarkable differences between the two systems investigated appear to be mainly due to a specific counterion effect. This result highlights once again the ions specificity, which is found ubiquitously in chemistry and biology.

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FIS-OR-27 Inside Complex Sol-Gel Materials: a Detailed Investigation of Organic-Inorganic Hybrid Coatings Through Solid-State NMR

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The sol-gel approach is one of the most convenient way for preparing organic-inorganic nanostructured hybrid materials thanks to the mild chemistry involved and the possibility of obtaining a wide variety of molecular structures and morphologies. The detailed knowledge of the phase and molecular properties of these materials is a very important task, especially for clarifying their complex relationships with preparation conditions and final macroscopic properties. Solid-state NMR (SSNMR) is an extremely powerful technique for the detailed characterization of structural and dynamic properties of complex hybrid materials, on very large spatial (0.1-100 nm) and time (s-ps) scales [1,2]. Here we present an extensive SSNMR study of a set of polyethylene-*b*-poly(ethylene glycol)/poly(4- hydroxystyrene)/silica hybrid coatings, obtained via sol-gel, exhibiting good barrier properties against oxygen diffusion [3]. By exploiting a variety of nuclei available (^{1}H, ^{13}C, ^{29}Si) and a large set of experiments (high-resolution quantitative and selective 1D spectra, 2D Double Quantum and HETCOR spectra), including the most recent technological advances (^{1}H ultra-fast MAS spectra @60 kHz, courtesy of Agilent), we could characterize in detail the chemical structure of the inorganic domains, the phase, dynamic and conformational properties of the organic components, as well as obtain important evidences of the interfacial interactions among the different components. These properties resulted to be strongly dependent on samples composition and showed interesting correlations with the barrier performances.

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FIS-OR-28 LIBS application to the recovery of precious metals from scrap and waste materials

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The LIBS technique was applied to the measure of traces of precious metals in scrap and waste materials, in view of their recovery. Using MODI' (Mobile Dual-Pulse Instrument) several certified samples were analyzed with the purpose of determining the trueness of the method and the detection limits for Gold, Silver, Platinum, Palladium and Rhodium quantitative analysis in copper-based alloys. In this communication, the results of the study are presented and discussed. The possibility of improving the performances of LIBS on this kind of materials through internal standardization, self-absorption correction and calibration-free analysis is also discussed.

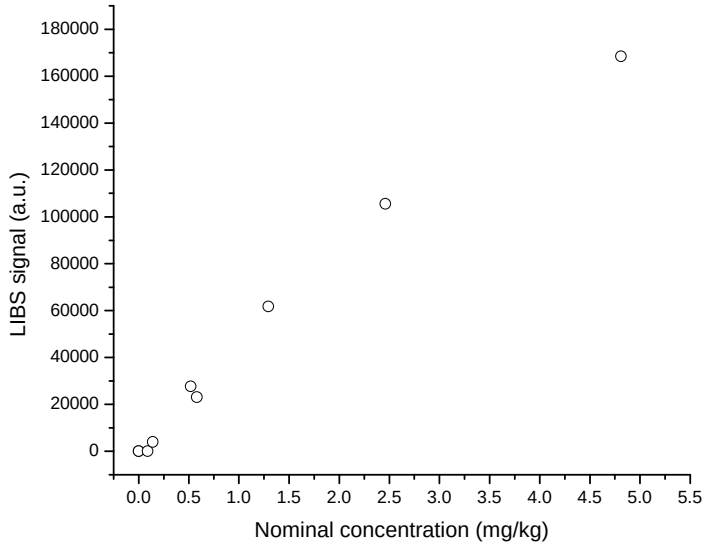

Fig.1 – Calibration curve for Rhodium

FIS-OR-29 Carbon Nanotube Saturable Absorbers For Ultrafast Pulsed Lasers

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Single walled carbon nanotubes (SWCNTs), thanks to their unique physical and chemical properties, have been actively researched to realize efficient non linear components for optical systems, such as passively pulsed lasers [1]. In particular, broad spectral operating wavelength and easy tunability, possibility to realize both transmission- and reflection-type absorbers on a wide variety of substrates, very fast recovery time, low saturation fluence and absence of two-photon absorption are favourable intrinsic properties that make these devices very attractive for passive mode-locking of ultrafast lasers.
A very well known problem concerning the fabrication of SWCNTs films, is their tendency to form clusters, that can cause the interweaving of nanotubes, then showing inferior mode-locking performances. Regarding this, a crucial role is played by the preparation method, in particular the dispersion with ultra-sonication and the successive deposition of the films.

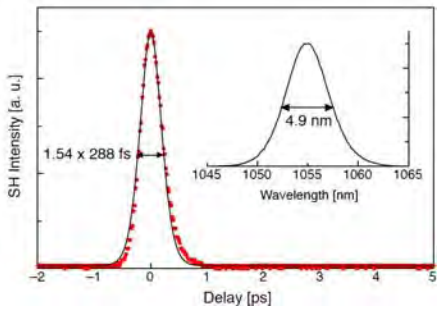

Figure 1

In this work, we present the results of the preparation of a SWCNTs film deposited on a quartz substrate by slow solvent evaporation method. The purified semiconductors nanotubes result well dispersed and homogeneously distributed on the surface of the substrate as verified by Raman spectroscopy and optical response. The film was tested in a Nd:glass based femtosecond laser. 288-fs-long, very stable mode-locked pulse trains at a central output wavelength of 1055 nm were obtained with an average output power of about 20 mW. Both the spectrum and the pulses autocorrelation trace are shown in Figure 1.

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FIS-OR-30 Structural properties of binary poly(ethylene-oxide)/room temperature ionic liquids mixtures: an experimental and computational study.

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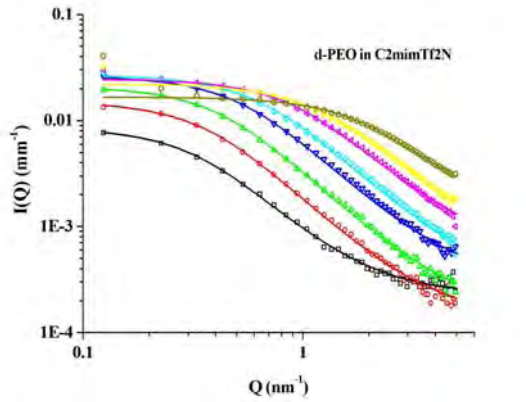
Poly (ethylene oxide) is one of the few polymers that are soluble in room temperature ionic liquids. These mixtures can find several applications such as polymer electrolytes or separation media. A few years ago, we highlighted the good solvent nature of RTILs towards PEO, using SANS technique [1], and Ribeiro simulated the morphology and dynamics of PEO-rich mixtures [2]. Recently the activities of Watanabe's [3], Rogers's [4] and Lodge's [5] groups focused on the phase diagram of PEO-RTIL binary mixtures, detecting the existence of a Lower Critical Solution Temperature for these systems and screening the role of RTIL's chemical details on this complex behavior.



SAXS data from PEO solutions in C2mimTf2N, as a function of polymer concentration.

Here we show recently obtained results from both Small Angle X-ray and Neutron Scattering from PEO-RTILs mixtures at ambient temperature, as a function of polymer concentration, for a variety of RTILs. We screened the role of the RTIL's alkyl chain length, methylation of position 2 in the RTIL imidazolium ring and other chemical details of the RTIL on the morphology of the macromolecule, extracting information as interesting as its average size, the persistence length and chain rigidity.
These results have been complemented with MD simulation study of oligo (ethylene oxide) dissolved in C2mimTf2N and C2C1mimTf2N, in order to explore the role of hydrogen bonding on microscopic organization in such mixtures.

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FIS-OR-31 Microfluidic devices for chemical reactions: fabrication and characterization with computational modeling and fluorescence experiments.

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Recently microfluidic has been proposed for chemical synthesis with the purpose to have a better control on reactions that involve either highly toxic or highly unstable species. This control can be achieved through a programmed mixing of the reagents and a microscopic modulation of other physical parameters (such as: temperature, oxygen content of the solvents etc.).
In particular we have focused our interest on the characterization of controlled mixing of reagents in microfluidic devices through in-silico simulations and fluorescence experiments.
Microfluidic devices in polydimethylsiloxane (PDMS) are realized through replica molding technique of a silicon master. The master itself is realized by means of one- and two-photon induced laser photopolymerization of a commercial photoresist: SU8. With this technique we can build 3D structures with resolution of 1μm in the x-y plane and 8-10 μm on the z axis perpendicular to the x-y plane.
The motion and mixing of fluids in the channels of the microfluidic device is simulated via a Navier-Stokes finite-element approach, coupled to convection-diffusion equations. Time and frequency resolved fluorescence techniques are used to experimentally evaluate parameters such as concentration of chemical species and laminar flow speed. The results of these experiments are compared with the data of the numerical simulations.
Finally we will present our preliminary results on: (i) the investigation of fluorescence quenching of the fluorescein dye in water by controlled mixing with a potassium iodide solution and (ii) tetrakis(4sulphonatophenyl)porphyrin aggregate formation in acidified water.

FIS-OR-32 Charge-assisted hydrogen bonds and weak intermolecular interactions as tools to fabricate complex supramolecular architectures

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Molecular self-assembled crystalline materials are promising in several fields, including gas adsorption, catalysis, selective recognition and modulation of functions of active molecules, although the rational design of synthetic supramolecular architectures based on well-defined structure-directing forces and hydrogen bonding is still a challenge. We present a supramolecular cage assembled through 72 hydrogen bonds which is constructed from two kinds of hexagonal molecular tiles (Figure 1) forming a truncated octahedron, one of the thirteen Archimedean polyhedra[1]. The framework resembles those of sodalite and zeolite A and displays an extraordinary ability to encapsulate a wide range of differently charged species, ranging from transition metal complexes to nanoclusters not observed otherwise. The thermodynamic stability of the octahedral cage is explained by the presence of an extended network of charge-assisted $N\text{-}H^{+}\cdots^{-}O\text{-}S$ hydrogen bonds.
By the exploitation of the same kind of interactions, orientation of polyconjugated guest molecules is obtained in tunable host cavities[2]. Through judicious selection of intermolecular interactions, the framework architectures can be controlled systematically in a manner that enables the regulation of the guest orientation and aggregation. The effects of the distinct packing motifs is manifested as bathochromic shifts in the absorption and emission spectra of the guests. This behavior is supported by ab initio TDDFT calculations that reproduce the bathochromic shifts associated with the effects of guest-guest and guest-host interactions, combined with conformational constraints imposed on the guest molecules by the rigid host framework.

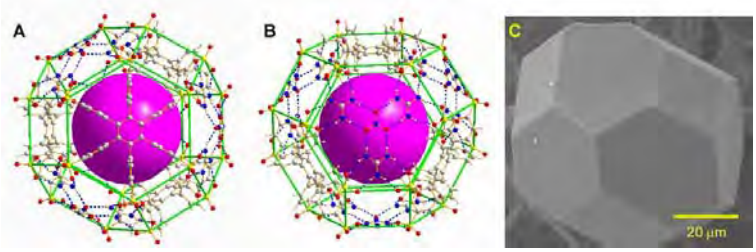

Figure 1. The quasi-truncated octahedron *q*-TO (left) and scanning electron microscopy image of a crystal (right), illustrating the hexagonal and square faces that reflect the symmetry of the *q*-TO.

Interestingly, through CH···π interactions, the molecular recognition of specific blocks of triblock copolymers by a host molecule enables the formation of hierarchical periodic structures [3]. The formation of the supramolecular architectures is followed by *in situ* synchrotron X-ray diffraction while the specific CH···π intermolecular interactions are highlighted by fast-^{1}H MAS NMR and GIAO HF ab initio calculations.

Moreover, weak intermolecular interactions play a key role in modulating the dynamics of molecular rotors in amphidynamic materials. Indeed, the precise engineering of highly-organized porous silica scaffolds supporting organic elements enables the fabrication of fast molecular rotors ($k>10^{8}$ Hz) entirely exposed to the guest molecules which act as regulators [4].

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FIS-OR-33 Protective effect of the mesoporous host towards the photo oxidation of fluorescent guests: a UV-Vis spectroscopy study

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In recent years, mesostructured silica nanoparticles variously functionalized have been studied and tested for a wide range of biological, biomedical and technological applications. In several studies organic or inorganic fluorophores have been hosted in mesostructured materials in order to obtain a new class of hybrids with improved performances in term of brightness, quantum yield, photostability, etc. [1,2]. Fluorescent hybrid organic-inorganic mesoporous nanoparticles can be prepared by physical adsorption or grafting of indocyanine dyes within the channels of MCM-41 nanoparticles. Previous experiments showed that this kind of architecture provides the highest stability and signal intensity upon specific thermal treatments, if compared to the correspondent indocyanine dye in solution and other kinds of nanoparticles [3].

In this contribution the sensitivity of fluorescent hybrid organic-inorganic nanoparticles to the photo oxidation was tested under different experimental conditions and compared to the performances of the correspondent indocyanine dye in solution. Photodegradation experiments were performed under simulated solar illumination and the optical performances of the samples after irradiation were evaluated by UV-Vis absorption and emission spectroscopy, augmented by fluorescence lifetime measurements. The effect of different parameters, such as the absence or the presence of oxygen and TiO_2 and pH, on the photodegradation was investigated.

The results demonstrated a beneficial effect of the silica matrix on the photostability of the embedded indocyanine dyes, showing an increased stability both in presence and in absence of TiO_2 as well as in alkaline conditions. Interestingly, the analysis of the fluorescence lifetimes data allowed us to highlight a selective degradation of the indocyanine molecules located on the external surface of the silica nanoparticles, with respect to the molecules hosted within the pores.

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FIS-OR-34 Autoinhibition of angiogenins: insights from the X-ray structure of RNase 2 from Atlantic salmon

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Recently, the superfamily of animal, extracellular, pyrimidine-specific RNases, often called the RNase A superfamily, has been shown to include not only tetrapod enzymes, but also fish enzymes [1]. In particular, five RNases from zebrafish (*Danio rerio*) [1-3] and two from the Atlantic salmon (*Salmo salar*) [4] have been reported to have a very low RNase activity and to be endowed, like RNase 5 (human angiogenin), with powerful angiogenic activity. We have determined the X-ray structure of two zebrafish RNases [3]. In these proteins, like in human angiogenin, the putative binding subsite B1 of the pyrimidine base is partially obstructed by the side chain of Glu located in the C-terminal segment of the protein, and this structural feature well account for their low catalytic activity.
More recently, the crystal structure of RNase-2 from *Salmo salar* (Ss2) has been also determined. Surprisingly, within an essentially unmodified RNase folding, the enzyme presents an extensive reorganization of the active site region with respect to other pancreatic RNases. In particular, although it has the highest catalytic activity among fish RNases, it presents an active site fully obstructed by a peptide segment at C-terminal region (CTR), and with the two catalytic histidines in direct contact. Thus the enzyme appears to be auto-inhibited in a completely different manner compared to the other angiogenins. Comparison of the structure of Ss2 with those of RNase complexes with substrate analogs suggests that Ss2 could adopt two distinct conformations: a closed form with the CTR blocking the substrate binding cleft (observed in the crystal structure) and an open conformation, where the CTR swings out forming an open cleft with the active site exposed. Overall, these data provide novel structural insights into the mechanism that modulates RNase activity of angiogenins.

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FIS-OR-35 Clusters Fingerprint in Lysozyme Protein Solutions

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The comprehension of the phenomenon of protein clustering is of fundamental importance in various diseases and in new promising routes for drug delivery based on storing high concentrated functioning protein.

Neutron spin echo (NSE) and small angle neutron scattering (SANS) were used to investigate the correlation between structure and short-time dynamics of lysozyme solutions. It was found that, upon increasing protein concentration, the self-diffusion coefficient at the short time limit becomes much smaller than that of the corresponding hard-sphere and charged colloidal suspensions at the same volume fraction. Moreover contrary to literature conclusions, at relatively low concentrations, there is evidence that the system consists mostly of monomers or dimers, while, at high concentrations, large dynamic clusters dominate[1]. From the estimation of the mean square displacement by using short-time and long-time diffusion coefficient measured by NSE and NMR, we find that these clusters are not permanent but have a finite lifetime longer than the time required to diffuse over a distance of a monomer diameter.

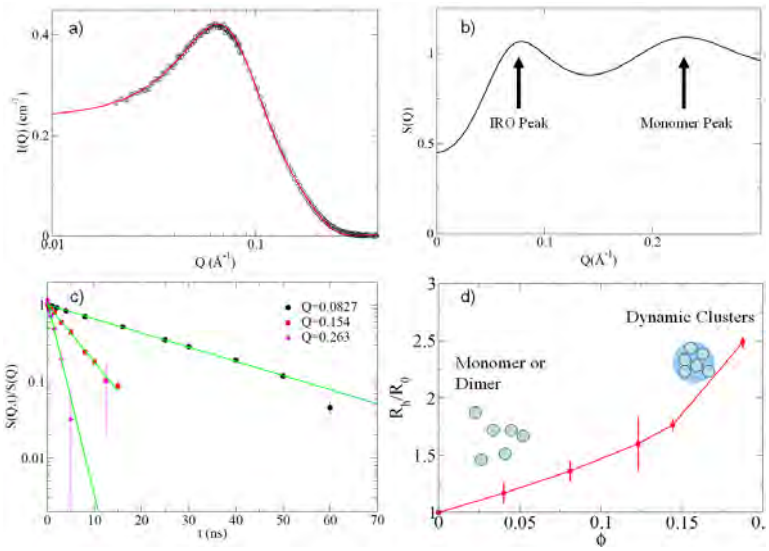

Figure 1. a) Fitting curve (solid line) together with the experimental points of 5 wt% lysozyme solution measured by SANS, **b)** Extracted inter-particle structure factor, S(Q), for the 5 wt% sample, **c)** *S(Q,t)/S(Q) vs t* in the Q

By using statistical mechanics models[2], it is clear that the appearance of a low-Q peak is not a signature of the formation of clusters. Rather, it is due to the formation of an intermediate range order (IRO) structure governed by a short-range attraction and a long-range repulsion.

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FIS-OR-36 Soft X-ray photoelectron-photoabsorption spectroscopy and electronic structure of barbituric and 2-thiobarbituric acid.

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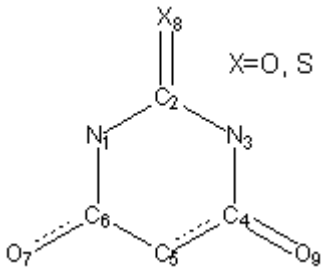
We present a combined experimental and theoretical investigation of the electronic spectra of barbituric acid (BA) and 2-thiobarbituric acid (TBA) molecules in the vapour phase. The valence band photoemission and the core level (O, N, C 1s and S 2p) photoemission and photoabsorption spectra have been measured in the vapour phase using synchrotron light and then assigned with the support of quantum chemical calculations. First the valence band binding energies have been calculated using the Koopman's approximation at the B3LYP/6-311++G** level, then the outer valence behaviour has been better approximated with electron propagator calculations (OVGF and P3 approximations), available in the G09 software package. [1] The core ionized states and core-to-excited states transitions were solved within the Hartree-Fock approximation by explicitly taking into account the core hole, using the GSCF3 code developed by prof. N. Kosugi. [2] The calculations were run for both the tri-keto and the hydroxy-di-keto form, where the enolization of one of the two equivalent keto groups is produced by proton transfer from the methylene group, which is more acidic than the NH groups. In agreement with previous *ab initio* [3, 4] and gas-phase electron diffraction [5] works, only the tri-keto tautomers have been detected.



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FIS-OR-37 Complexes of water with freons: an interim perspective by microwave spectroscopy

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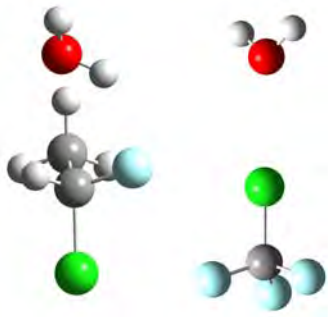
In recent years very importance have been purchased by CFCs. Their impact in atmosphere arises both the role in ozone reduction and greenhouse effect. Because the abundance of atmospheric water, the information of intermolecular interaction between CFCs and water will be helpful in understanding the behavior and impact of CFCs in atmosphere. In fact its internal dynamics contribute to determine the properties of these systems. [1] In freons, all data suggest O-H···Hg (Hg = F, Cl) to be a weak interaction but different behaviors are observed and it is quite difficult to rationalize them. We measured the molecular beam Fourier transform microwave spectra of six isotopologues of the 1:1 adducts of CH_3CHClF with water and five isotopologues of CF_3Cl with water (see the Figure). In the first case [2] the water prefers to form an O-H···F rather than an O-H···Cl hydrogen bond. This is exactly the contrary of what observed in the chlorofluoromethane-water adduct, where a O-H···Cl link was formed.[3] In the second case [4] the interaction between the subunits occurs via C-Cl···O(H_2O) halogen bond. For both complexes, besides the rotational constants, the quadrupole coupling constants of the chlorine atom and structure information have been determined. In addition, information on the internal dynamics has been obtained. Ab initio calculation (MP2 level of electron correlation and 6-311++G** basis set) have been carried out in order to obtain information about the structure and relative stability.



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FIS-OR-38 Detailed Characterization of the Dynamics of Organic Molecules in the Solid State: a Multi-Technique NMR Approach

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The molecular dynamics of a solid drug strongly affects its pharmaceutical properties and other important characteristics, such as solid state reactions and degradations. Moreover, it plays an important role in drug-excipient interactions, in turn significantly affecting the drug release properties.
Solid State Nuclear Magnetic Resonance (SSNMR) is one of the most powerful techniques to investigate molecular dynamics of organic molecules, since it offers several approaches to study motions over a wide range of frequencies [1]. In order to monitor the widest possible range of frequencies and to get the most detailed information about individual motional processes, a variety of techniques must be applied and the results simultaneously analyzed. In our approach we combined: ^{13}C and ^{1}H longitudinal relaxation times (T_1) to investigate fast motional processes, with characteristic frequencies (ν_C) of the order of MHz; ^{13}C and ^{1}H longitudinal relaxation times in rotating frame ($T_{1\rho}$), ^{1}H T_1 dispersion curves, and ^{13}C line shape analysis (both arising from chemical shift anisotropy and MAS spectra) to investigate the intermediate motional regime (ν_C of the order of kHz), while insights about the slow motional regime (ν_C of the order of 1 kHz or less) could be obtained from exchange effects occurring in ^{13}C high-resolution spectra. In particular, this approach was applied to the characterization of the dynamic properties of two forms of ibuprofen, acid (IBU-A) and sodium salt (IBU-S), which, from a preliminary previous work [2], were found to exhibit different dynamic behaviour, in spite of their very similar chemical structure. The combined analysis of all the data allowed the identification and the detailed characterization, in terms of correlation times and activation energies, of all the reorientational and interconformational motions, such as the π-flip of the phenyl rings, the reorientation of methyl groups and aliphatic chains, as well as the π-flip of the dimeric structure formed by the acidic groups in IBU-A [3, 4].

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FIS-OR-39 Proton transfer in homo- and hetero-dimers of carboxylic acids: Precise information from the rotational spectra.

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Tunneling effects have been measured in the pulsed jet Fourier transform microwave spectra of two isotopologues of the benzoic acid-formic acid bi-molecule and of four isotopologues of the dimer of acrylic acid. The dimer of acrylic acid can exist in two forms, depending on the *entgegen* or *zusammen* orientations of the two allyl groups. The latter one (*zusammen*) has a permanent value of the μ_b dipole moment component, which allowed to measure its pulsed jet Fourier transform microwave (MW) spectrum (see Figure 1). From the tunneling splittings originated by the concerted proton transfer of the two carboxylic hydrogens, measured for the various isotopologues of the two bi-molecule, we could size the barrier and the dynamics of the proton transfer.

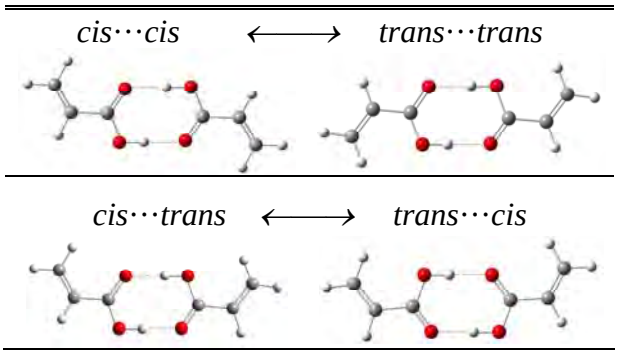

Figure 1. Homo-conformational dimers of AA (s-cis···s-cis, s-trans···s-trans) are non-polar, while hetero-conformational dimers

By applying a suitable flexible model to the experimental tunnelling splittings it has been possible to determine the barrier to the double proton exchange; In addition, from the ratios between the tunnelling splittings measured for the various H/D species, we could estimate the dynamics of the skeletal structural relaxation.

FIS-PO-01 The strange world of polyprotic inorganic acids

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Recent results on polyprotic inorganic acids, $\{Mo_{72}X_{30}(H_2O)_{91}\}\sim 150H_2O$ (X=Fe, Cr, V , see fig.1 right) are presented, with emphasis on water dynamics and self-assemblies properties.

The dynamics of the crystal water in the voids between the well-defined and arrayed nanocages is significantly slower than that of bulk water at the same temperature. Our data show a non-Debye relaxation behavior originating from a distribution of relaxation times, probably related to the different local environments experienced by the water molecules. In the investigated range the temperature dependence of the relaxation time can be described in terms of an Arrhenius law (E_a=47.3 kJ/mol), indicating that the dynamics is triggered by breaking of the bonds connecting the crystal water molecules with the hydrophilic nanocage surfaces. Interestingly, in the case of $\{Mo_{72}Cr_{30}\}$ it was possible to decouple the dynamics of the in-cage water from the total while the presence of V in $\{Mo_{72}V_{30}\}$ allowed the monitoring of the dynamics of the inorganic cage itself.[2]

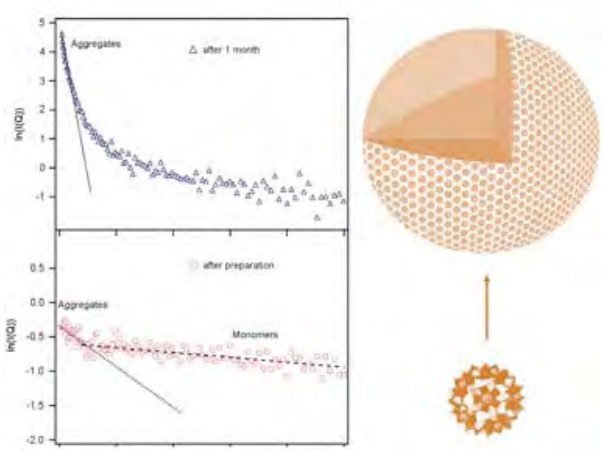

Figure 1. Left) 1-month evolution of the SAXS pattern **Right)** Sketch of the monomer to "blackberry" transition.

Small angle X-ray scattering on freshly prepared aqueous solution evidences the presence of hollow nanostructructures proper of the monomer (2.5 nm in diameter) that coexist with a small amount of oligomers. After 1 month the polyoxomolibdate specie self-assembles in a supramolecular structure with a polydisperse distribution of dimensions spanning from the monomer to a ‘‘blackberry" vesicular structure of about 10-60 nm.[3] The aggregation properties can be tuned by changing the pH, ionic dissolved species and the polarity of the solvent offering unique opportunities for both fundamental studies and practical applications in many different fields.

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FIS-PO-02 Bis-Histidyl coordination in tetrameric hemoglobins: Cold-adapted fish hemoglobins *versus* human hemoglobin

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All tetrameric hemoglobins from the Antarctic fish, included *Trematomus bernacchii*, HbTb, in its ferric state promptly, and distinctively from all the other tetrameric hemoglobins, form a mixture of aquo-met at the α subunits and bis-histidyl adduct (hemichrome) at the β subunits [1,2]. The role of the tertiary and quaternary structure in the hemichrome formation in HbTb is still unknown. Here we report the cloning, expression, purification, spectroscopic and computational characterization of the β-chain of HbTb (Tbβ), along with a novel crystallographic determination of the ferric β-chain of human Hb (β_4-HbA). As β_4-HbA [3,4, Tbβ self assembles to form a β_4 homotetramer, but, differently from β_4-HbA, Tbβ forms quantitatively a reversible bis-histidyl adduct in the ferric state. Indeed, the herein presented crystal structure of the ferric β_4-HbA hosts an aquo-met coordination in all the four independent chains, and not hemichrome. A molecular dynamics study on the isolated β-subunit of HbTb indicates that the ability to form hemichrome is an intrinsic feature of Tbβ chain, probably due to the higher flexibility of this chain with respect to that HbA. Differently from HbTb $\alpha_2\beta_2$ heterotetramer [5,6], Tbβ forms a bis-histidyl adduct also in the ferrous state (hemochrome). On the basis of these experimental, crystallographic and computational results, the effect of the quaternary assembly on the stability of the ferrous and ferric endogenous hexa-coordination is presented.

We acknowledge PNRA and PRIN for financial support

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FIS-PO-03 Insights on the homocoupling reaction of 4-methylamino benzoic acid mediated by *Trametes versicolor* laccase

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Studies on eco-friendly oxidation processes represent an important alternative in the synthetic reactions. The potential benefits of utilizing enzymes in industrial processes arise from their activity under mild conditions of temperature, pH and pressure, compared to inorganic catalysts [1]. Enzyme-catalysed oxidations in the presence of air as co-substrate, such as laccases work, are low cost reactions that use non-toxic reagents in aqueous solutions. These enzymes belong to the multicopper oxidases which are able to catalyze the one-electron oxidation of a wide variety of organic compounds, including mono-, di- and polyphenols, aminophenols, methoxyphenols, aromatic amines with the concomitant four-electron reduction of oxygen to water [2,3]. In recent years the coupling activity of the laccase-precursor system has been widely used in the synthesis of novel compounds and materials [4]. In this work we investigate the synthetic reaction starting from the precursor molecule 4-methylamino benzoic acid catalysed by the *Trametes versicolor* laccase. The study concerns a multidisciplinary research approach, where a variety of spectroscopic measurements (EPR, NMR, UV-Vis) combined with Density Functional Theory (DFT) calculations have been applied to understand the reaction mechanism. The attempt was to synthesize a new azo-dye. The biocatalytic reaction gave as the main final product a polymer containing a secondary amine function with a single N-N bond. This represents a novel example of the homocoupling reaction mediated by laccase [5].

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FIS-PO-04 Dynamics of methane accumulation in the Hearth atmosphere.

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During the last century the methane content of the atmosphere, increased as never occurred in the last 800,000 years. Note that methane is much more effective (25 times) than CO_2 [1]. The increasing concentration of methane in the atmosphere, indeed, could influence the future of the climate by means of non linear positive and dangerous feedback, with the risk of the achievement of a no-return threshold, beyond which the Global Warming (GW) become out of human control. This is made easier promoted by the increasing of the same GW on the dynamics of emission processes from the natural sources (destabilization of hydrates, stimulation of metabolic production by plants and animals, etc.) and by the leaks of gas during the extraction and management activities. The methane concentration in the atmosphere is 780 at the end of 19° Century. At present it achieved 1787 ppbv at 2008 [2]. Conspicuous emissions of methane were recently observed from the Arctic and were attributed to the anaerobic decomposition of organic sediments on the deep of marshes due to the fusion of permafrost [3]**.** Also unexpected methane flows were observed during the 2010 year from the Central and Eastern Siberian Seas [4]**. T**he decomposition of the methane hydrates in this case seems more convincing [5]. The residence times of each Green House gas affect differently the Radiation Forcing (RF) power, then the GW. The methane concentration in the atmosphere is regulated by the dynamical interplay between sources and sinks. The lifetime of CH_4 is mainly limited by the reactions with the (OH) radicals and is estimated 9.6 years. A recent detailed analysis of the contributions to the GW due to the methane emissions from the Arctic has been published [6]. The conclusions are impressive as it is forecast an increase of the RF of 0.6 Wm^{-2} on a Time Horizon of 50 years for the methane increase alone,

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FIS-PO-05 Plant oil bodies as nano/microcarriers to deliver natural polyphenols for anti-cancer therapy

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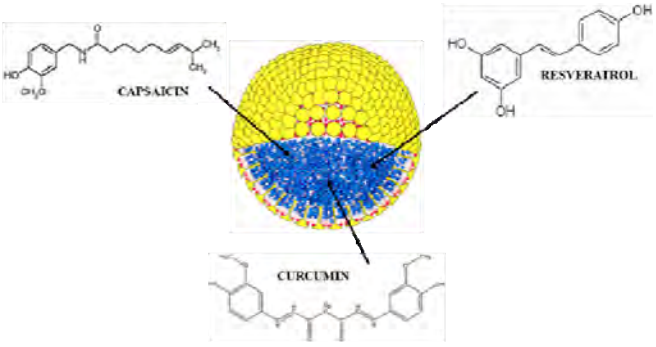
Oil bodies (OBs) are specialized organelles ubiquitously detected in plant oil seeds, that serve as lipid storage compartments. OBs consist of a hydrophobic core of triacylglycerol (TAGs), surrounded by a monolayer of phospholipids (PLs) with some specific embedded proteins, including oleosins and some minor proteins, i.e. caleosin and steroleosin. The diameter of OBs range from 0.5 to 2 μm [1-2]. In order to demonstrate that OBs could have potential applications as micro\nano carriers to deliver hydrophobic drugs, we developed an easy method to reconstitute OBs, of similar shape to the natural ones, starting from their natural constituents and some structural proteins[3].

The aim of this work was to efficiently encapsulate into reconstituted OBs a series of polyphenols, with well-known anti-cancer properties, but with poor intestinal absorption. We first verified the effects of some different polyphenols on the vitality of ovarian cancer cell lines.



This allowed us to identify some natural compounds with promising anti-proliferative/pro-apoptotic activities. Selected polyphenols were then efficiently encapsulated either singly or in pairs into artificial oil bodies and were used to monitor their uptake into the ovarian cancer cell lines.

Our results indicated that OBs could act as novel carriers to deliver hydrophobic bioactive compounds and that the therapeutic effects of encapsulated natural polyphenols are similar or even stronger than those of the free drug.

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FIS-PO-06 Sensitization of nanostructured electrodes with colloidal CdSe nanocrystals towards nanocrystal based solar cells

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In the last years, a growing interest has been addressed to innovative and economic solar cells. Among this class of devices, the most promising are the photoelectrochemical cells, also called sensitized solar cells, whose main part is a photoactive anode which provide to absorb light and transport photogenerated electrons. Such an electrode is made of a conductive and transparent substrate, covered with a thin-film of a wide-gap semiconductor, such as TiO_2 or ZnO, sensitized with a low-gap dye material, such as small molecules, metal-complexes or semiconductor nanocrystals. The use of semiconductor NCs in lieu of widely-used photosensitive dyes can provide an enhancement of the conversion efficiency in solar cells, due to the large NC extinction coefficients, the multiple exciton generation phenomenon[1] and their intrinsic stability.
Here, colloidal CdSe NCs, 5.5 nm in diameter, were used to sensitize two kinds of nanostructured electrodes, made respectively of TiO_2 nanoparticles, deposited by means of a doctor-blade technique, and ZnO nanowires electrochemically grown on ZnO thin-film[2]. CdSe NCs were synthesized as reported by Peng et al.[1], in presence of a mixture of three long-chain capping agents, which allowed an high control on NC size and shape, and make NCs dispersible in organic solvents. Two different strategies were tested for the electrode sensitization, namely the direct absorption and the linker-mediated absorption. In the last method, pristine CdSe capping agents were replaced with cysteine molecules, which are short chain three-functional organic ligand, able to link NCs to the ZnO electrode and allow an effective charge transfer between NCs and oxide. Sensitized electrodes were characterized by means of steady-state absorption and PL spectroscopy, confocal microscopy and scanning electron microscopy (SEM) investigations. A promising electrode sensitization degree has been obtained.

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FIS-PO-07 Characterization of the self-assembly of 8-armed amphiphilic star block copolymers in water by NMR spectroscopy

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Self-assembly of amphiphilic block copolymers in water has been exploited to prepare physically cross-linked hydrogels of interest for biomedical applications. Indeed, at low concentration micellar aggregates form by association of the hydrophobic copolymer blocks, while at high concentration inter-micellar hydrophobic interactions give rise to networks. In recent years 8-armed star block copolymers, having poly(ethylene glicol) (PEG) as the hydrophilic polymer in the inner part, and hydrophobic polyesters, such as poly(lactide) (PLA), poly(ε-caprolactone) (PCL), and poly(trimethylene carbonate) (PTMC), as the outer chains have been extensively investigated, thanks to their ability to yield physically cross-linked hydrogels at much lower concentration compared with linear di- and triblock copolymers. It has been found that the hydrogel mechanical properties and stability to degradation are strongly dependent on the interactions governing self-assembly, in turn influenced by the degree of polymerization, the hydrophobicity, and the stereochemistry of the hydrophobic blocks. Therefore, a molecular-level investigation of the structural and dynamic properties of the polymeric components in water is of fundamental importance for the comprehension of self-assembly for these systems. In this respect, the application of suitable Nuclear Magnetic Resonance (NMR) techniques in solution and in the solid state reveals valuable. In this work representative examples of applications of NMR experiments to the investigation of the self-assembly of 8-armed PEG-PLA and PEG-PTMC copolymers are presented [1-4].

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FIS-PO-08 Factors determining the superior performance of lipid/DNA/protammine nanoparticles over Lipoplexes

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The utility of using a protammine/DNA complex coated by a lipid envelope made of cationic 1,2-dioleoyl-3-trimethylammonium propane (DOTAP) for transfecting CHO (Chinese hamster ovary cells), HEK293 (human embryonic kidney cells), NIH 3T3 (mouse embryonal cells) and A17 (murine cancer cells) cells was examined. The widely used DOTAP/DNA lipoplex was employed as a reference. In all the tested cell lines lipid/protamine/DNA (LPD) nanoparticles were more efficient in transfecting cells than lipoplexes even though the lipid composition of the lipid envelope was the same in both devices. Physical-chemical properties were found to control the ability of nanocarriers to release DNA upon interaction with cellular membranes. LPD complexes easily release their DNA payload, while lipoplexes remain largely intact, and accumulate at the cell nucleus. Collectively, these data explain why LPD nanoparticles do often exhibit superior performances compared to lipoplexes in trasfecting cells and represent a promising class of nanocarriers for gene delivery.

FIS-PO-09 A novel bionanotechnological approach for water filtration

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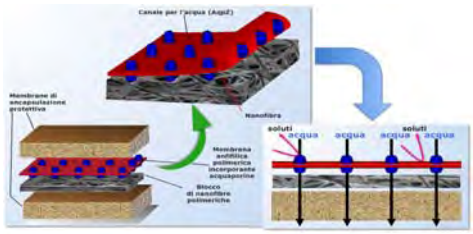
Le acquaporine (AQP) sono canali di natura proteica che mediano il flusso di acqua attraverso le membrane biologiche. Sotto l'azione di gradienti osmotici, ogni singolo poro formato da AQP può trasportare miliardi di molecole di acqua per secondo. Tale straordinaria peculiarità rende le AQP uniche in natura offrendo notevolissime potenzialità di tipo applicativo. Ciò ci ha suggerito la progettazione e realizzazione di membrane biomimetiche incorporanti AQP, con applicazioni basate sulla filtrazione dell'acqua, come la dissalazione dell'acqua a scopi potabili, il trattamento e riciclo di acque reflue, la produzione di acqua ultrapura, la dialisi ed il *drug delivery* e la produzione di energia ecosostenibile da gradienti di salinità.

Il primo stadio della ricerca è stato la preparazione su larga scala di AQP ricombinanti e, successivamente, di membrane artificiali. Quindi, per l'incorporazione funzionale delle AQP in membrane selettive, resistenti ed economiche sono stati progettati, sintetizzati e caratterizzati nuovi copolimeri [ad es., polimetil ossiazolina(block)PDMS (block)polimetil ossiazolina]. Questi copolimeri sono stati trasferiti via tecnica di Langmuir-Blodgett sia attraverso co-deposizione sia attraverso l'utilizzazione diretta di proteoliposomi su supporti solidi con una struttura composta da un substrato in vetro, un film sottile di polimetilmetacrilato (PMMA) sul quale sono depositate nanofibre di PMMA, realizzate per elettrospinning.



FIS-PO-10 Surface features and interfacial behaviour towards proteins of engineered silica nanoparticles

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Silica based/coated nanoparticels (NPs) are an emerging tool in nanobiotechnology. Among the various preparation methods, polymerization in microemulsion of reverse micelles results in spherical NPs highly homogeneous in size, with relevant advantages in behaviour homogeneity in both cell-free and cell tests and applications. Most part of the performances of such NPs in biological media are ruled by their surface/interface features, that have been the subject of this work. The converging use of different methodologies (HR-TEM, Z-potential, Dynamic Light Scattering, FT-IR, BET, TGA) made allowance to establish that NPs (50±2 nm in size; monodispersed in water) exhibit a structured, highly hydroxylated surface, where all silanols are engaged in H-bonding with neighbour –OH. Such a rich hydroxyl layer appeared poorly active towards Bovine Serum Albumin (BSA) adsorption (ca. 50% of the theoretical side-on momolayer), producing a thin, incomplete corona around the silica core. Moreover, by *in situ* FT-IR ATR and UV-Circular Dichroism, it was found that adsorbed BSA underwent severe modifications in terms of both tertiary and secondary structure.

FIS-PO-11 Nanostructured semiconductors in photocatalytic processes for protection of stone materials

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Under UV irradiation TiO_2 exhibits photocatalytic activity leading to the degradation of a wide range of organic pollutants resulting in self-cleaning effect.[1] Owing to their high surface to volume ratio nanostructured TiO_2 catalysts exhibit a photoactivity higher than their bulk counterpart. Moreover, the possibility to tune the band gap and the redox potential as a function of size and shape, is expected to improve the interface charge transfer enhancing their photocatalytic activity.[2]
The application of TiO_2 coatings on stone has been investigated in order to provide surface protection and self-cleaning properties. Several synthetic approaches (namely hot injection, sol-gel and hydrothermal nanophase crystallisation) were used to synthesise colloidal TiO_2 nanocrystal differing in size, shape and surface chemistry. The obtained nanocrystals (NCs) were characterized from optical and morphological point of view and subsequently deposited onto two different kinds of stone (calcarenite and limestone, as example of porous and compact stone, respectively) without any post-deposition thermal curing.
A morphological and physical characterisation was carried out both on coated and uncoated stone, in order to elucidate the TiO_2 NC film distribution, and evaluate possible colour change, water absorption phenomena as well as water vapour permeability of the investigated materials.
The self-cleaning properties of the coated surfaces were evaluated under solar irradiation (radiating source: Solar Light Simulator) using an organic dye as target compound.
The obtained results suggest that the nanocrystalline TiO_2 coating seems good candidate for environmental protection of stone materials.

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FIS-PO-12 Bio-conjugation of Semiconductor Nanocrystals in PEG-Modified Phospholipid Micelles for bio-medical application

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The design of artificial bioconjugated nanocrystals (NCs) remains an attractive and important research area for bio-imaging, bio-labeling, and bio-sensing applications. Recent advance in colloidal synthesis have opened the possibility of producing hydrophobic NCs with very elaborated shapes and with different composition.[1] Despite its success in obtaining an excellent control on size, shape and crystallinity, the colloidal synthetic approach typically produces NCs with hydrophobic surfaces. Therefore, their surface chemistry has to be conveniently manipulated to promote their water solubility and to provide a conjugation moiety for a targeting ligand. In this work, organic capped NCs, namely magnetic or photoactive oxides (Iron Oxide and TiO_2, respectively) and binary asymmetric nanocrystals formed by a spherical γ-Fe_2O_3 magnetic domain epitaxially grown onto a lateral facet of a rodlike anatase TiO_2 (BNCs), have been incorporated into water dispersible block copolymer micelles composed of polyethylene glycol modified phospholipids (PEG lipids).[2] The obtained water soluble NC including PEG lipid micelles have been successfully covalently bound to BSA. Each step has been thoroughly monitored by using optical, structural and electrophoretic techniques. DLS measurements have proved that the obtained NC/micelles and BSA/NC conjugates, with a hydrodynamic diameter smaller than 100 nm, are homogeneously dispersed and sufficiently stable in aqueous solution. The magnetic characteristics of the Iron Oxide NCs and BNCs, before and after incorporation in PEG lipid micelles and subsequently to the bio-conjugation, are mostly retained. The proposed approach to achieve water soluble anisotropic BNCs and their bioconjugates could have a large potential in catalysis and biomedicine, and offers key functional building blocks for biosensor applications.

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FIS-PO-13 Formation of ROS by Photosyntentic Pigment/Cyclodextrin Inclusion Complexes

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Photodynamic therapy (PDT) is a treating modality of malignant tumours and hyperproliferative diseases. It is based on the use of photosensitizer (PS), herein the chlorophyll a, and a light having appropriate wavelength. The interaction of the PS with the light produce ROS, reactive oxygen species, a powerful oxidizing agents that cause critical damage to the tissue.

In order to solubilize in aqueous solution chlorophyll a and to obtain it as monomer, we have used cyclodextrins, carriers which are able to interact with the pigment and form the inclusion complex.

The aim of this work is to examine which type of ROS are formed in the system using specific molecules, named primary acceptor, that react selectively with the reactive species. In fact the changes of the absorption and the emission spectra of this molecules after the illumination of the PS provide information on the specific ROS formation. Uric acid, 9,10-diphenilanthracene and singlet oxygen sensor green have been used as primary acceptors in order to verify the formation of the $^1O_2$. Moreover 2,7-dichlorofluorescin and ferricytochrome c have been used to detect the formation of the hydrogen peroxide and superoxide radical anion that reduces Fe^{3+} of the ferricytchrome to Fe^{2+}, respectively.

FIS-PO-14 Investigation of laser-induced degradation mechanism by micro-Raman spectroscopy and thermal analysis of some pigments and alteration products

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In order to contribute to the improvement of restoration and conservation science of artworks belonging to the Cultural Heritage, this paper allows to investigate the possible degradation induced during micro-Raman analysis owing to the use of laser.

Recently Raman microscopy has been widely developed and applied as a suitable methodology for the identification of pigments, corrosion and alteration products, minerals and other substances in the field of archaeometry and diagnostic analysis.

Anyway, in some cases this technique results micro destructive for some substances or compounds because it can induce thermally phase transitions or decomposition processes. With the aim of evaluate those chemical physical alterations we first identified them through simultaneous thermal analysis (STA) and differential scanning calorimetry (DSC) on standard samples, commercial or prepared *ad hoc* in laboratory, such as copper carbonates, lead oxides [1][2], iron oxides and hydroxides [3][4] and others[5]. Then we tested in which conditions they occur using a micro-Raman spectrometer with a 632.8 nm laser.

Coupling these two techniques it is possible to define the potential applicability of micro-Raman spectroscopy as non destructive method and also avoid ambiguous identifications of compounds.

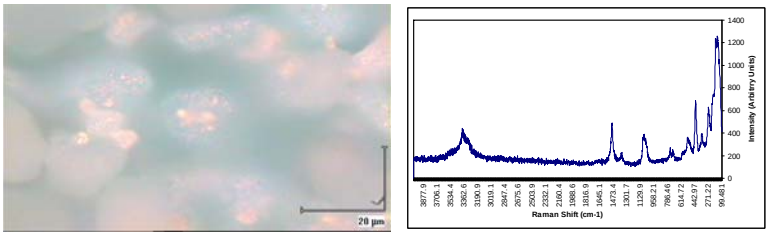

Fig. 2. OM Commercial Malachite 50x (copper carbonate) and micro Raman spectrum at 25% of power.

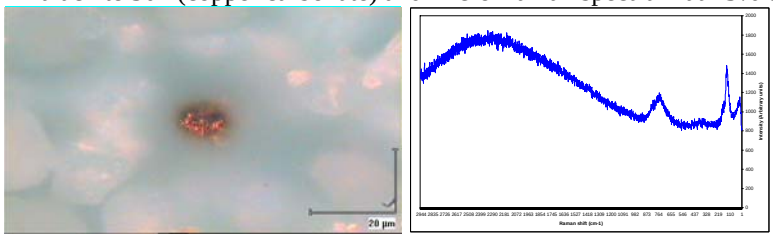

Fig. 3. OM Commercial malachite deterioration after a micro Raman analysis at 50% of power and its spectrum.

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FIS-PO-15 CdSe nanocrystals – conjugated polymers based nanocomposite for photovoltaic applications: effect of surface chemistry on morphological and spectroscopic properties

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Photovoltaic devices based on conjugated organic polymers are promising alternatives to conventional silicon-based technology thanks to their flexibility and low costs. More recently, blend of conjugated polymers and nanocrystals (NCs) of inorganic semiconductors have been investigated for the production of "hybrid solar cells", where NCs, acting as good electron acceptors from polymers, offer high electron mobility or improved spectral coverage, enhancing device efficiency. It is fundamental in the above device to obtain a homogeneous dispersion of NCs in the polymer matrix, to create a high interfacial surface area between the two materials. Self-assembly of rod-coil block copolymer is a potentially elegant path to improve nanosegregation of the blend.
Here we report the preparation and the characterization of nanocomposite materials consisting of semiconducting CdSe NCs and the rod fragment: poly[2,6-(4,4-bis-(2-ethylhexyl)-4H-cyclopenta[2,1-b;3,4-b′]dithiophene)-*alt*-4,7-(2,1,3-benzothiadiazole)] (PCPDTBT). The rod polymer has been obtained via two different policondensation reactions, namely Stille and Suzuki. The best results in terms of molecular weight control have been obtained by using the Suzuki pathway. The CdSe NCs have been synthesized via a colloidal chemistry reaction, by using trioctylphosphine oxide (TOPO) as coordinating agent. Hybrid materials have been obtained by mixing an appropriate amount of Cdse NCs chloroform solution with PCPDTBT solution. Thin films of the nanocomposite have been fabricated by spin coating on silicon or glass. In order to modify the interfacial transfer reactions the pristine TOPO ligand has been replaced with pyridine (Py). The surface chemistry of NCs has been investigated by means of ATR-FTIR spectroscopy. Atomic force microscopy (AFM) images of the nanocomposite films clearly demonstrate that Py-treated NCs provide more homogeneous and well-dispersed polymer composites compared with TOPO–capped CdSe NCs. The optical properties of the composite materials have been investigated by means of UV-visible spectroscopy, steady-state and time-resolved photoluminescence spectroscopy. The next step is then to prepare a nanocomposite material, based on rod-coil di-block copolymer having PCPDTBT as functional block.

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FIS-PO-16 Vibrational analysis of trans N-methyl-acetamide in aqueous solution from ab-initio molecular dynamics

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The knowledge of the proteins secondary structure has in the vibrational spectroscopy a valid instrument, structural motifs can be identified by characteristic changes in position and shape of IR or Raman bands, in particular the amide bands (Amide I, Amide II and Amide III) are often used as structural probes.

The basic theoretical approaches to study vibrational spectroscopy are provided by quantum-mechanics (e.g. perturbative approach of the anharmonic treatment [1]), that allows for sophisticated studies of IR and related properties.

Nowadays, we are able to obtain a complementary solution of the vibrational problem by the ab-initio molecular dynamics [2] [3]. Indeed, through the study of the time evolution of the system and the statistical analysis of molecular dynamics trajectories [2] [3] [4] it is feasible to account for finite temperature effects and for the explicit solute-solvent interactions.

We have performed our study on a molecular compound often used to simulate the backbone of proteins: trans N-methyl-acetamide (NMA) in aqueous solution [5] [6] [7]. By the analysis of the obtained trajectories, we have analyzed NMA in water, and then we have extracted NMA clusters to investigate in an accurate way the interactions of the solute with the environment. We have noticed that clusters with three water molecules are representative of the specific interactions involved in the Amide modes solvatochromic shift.

In this way it is possible to reproduce the characteristic amide mode (Amide I, Amide II, Amide III) and to obtain a detailed knowledge of the factors characterizing IR spectroscopy of NMA and the coupling with the solvent of these peculiar modes of peptides.

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FIS-PO-17 Immobilization of photosynthetic materials onto quartz by a Layer-by-Layer procedure for applications in the detection of herbicides

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In this work, the Layer-by-Layer (LbL) technique was employed to modify quartz substrates with photosynthetic materials (PMs). In particular, the biomaterials were obtained from the thylakoid membranes of spinach leaves. For performing the LbL, poly(ethyleneimine) (PEI) was used as positively charged polyelectrolyte to be alternated to the biocomponents, so obtaining an increasing number of PEI/PM layers. Due to the optical transparency of quartz, it was possible to analyze the optical properties of the photosynthetic materials, naturally rich in pigments, even after their deposition. The bio-modified substrates were characterized by UV-Vis absorbance and/or fluorescence emission techniques, and the morphological aspects were evaluated by Atomic Force Microscopy. The electron transfer efficiencies of the photosynthetic materials before and after the immobilizations were studied by assays in solution. The multilayers obtained were found to be interestingly able to give electron transfer and the optical signals were found to be proportional to the number of deposited layers until a plateau level. The responses of the multilayers were tested in the presence of a target herbicide at different concentrations, evidencing that the electron transfer activity of the immobilized PMs can be used to detect terbutryn at concentrations higher than 10^{-7}M. Such results are very remarkable, since they open up possibilities to employ LbL multilayers based on PMs to produce biomaterials applicable to energy transduction and environmental fields.

FIS-PO-18 On the Cl···N halogen bond: a microwave spectroscopy study of $CF_3Cl\cdots NH_3$ complex

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The CF_3Cl-NH_3 complex was studied by using pulsed jet Fourier transform microwave spectroscopy.[1] The conformer formed via Cl···N halogen bond was observed. MP2/6-311++G (d, p) level calculation suggested four stable conformers. The global minimum has a conformation formed via a Cl···N halogen bond interaction. The structure and relative stability of these conformers are shown in Figure 1.

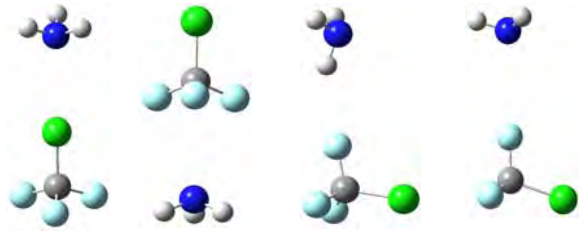

Figure 1. Four stable conformers and their relative energy obtained at MP2/6-311++G (d, p) level calculations.

We investigated first the spectra of the ^{15}N enriched isotopologues, which have simpler spectra respect to those of the ^{14}N isotopologues, because, according to the nuclear spin quantum numbers [$I(^{15}N) = 1/2$, $I(^{14}N) = 1$], is free from quadrupole hyperfine structures. Then, ^{14}N and full deuterated ammonia isotopologues were studied.

Rotational, centrifugal distortion and quadrupole (^{35}Cl, ^{37}Cl, ^{14}N) coupling constants have been precisely obtained. From the experimental rotational constants, the r_0 structure of the complex was evaluated, which gives a 3.083 Å length of the Cl···N halogen bond. The force constant, k_s = 6.3 Nm^{-1} has been obtained, which corresponds to a harmonic stretching frequency of 86 cm^{-1}. The dissociation energy of the complex is 11.0 $kJmol^{-1}$. This value is quite similar to the dissociation energy values of weak hydrogen bonds (O-H···F, O-H···Cl, CH···N).

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FIS-PO-19 Do intermolecular interactions affect the relaxation dynamics of dimers of quadrupolar dyes?

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Fluorescence experiment on dimers of the quadrupolar dye 2,5-Bis[1-(4-N-methylpyridinium)ethen- 2-yl)]-N-methylpyrrole ditriflate (PEPEP) connected by C3 and C6 saturated alkyl chains revealed a striking decrease of fluorescence quantum yield only for the C3 linked dimer.[1]
To shed further light on the origin of such behavior, time resolved fluorescence and transient absorption experiments in the fs and ps time range will be presented.
Time-resolved fluorescence experiments show a marked decrease of the lifetime of the emitting state going from PEPEP monomer to the C3-dimer, confirming the behavior revealed by the FQY experiments. More detailed information on the global decay mechanisms in the PEPEP monomer and dimer can be gained through transient absorption experiments with polarized laser light. Transient absorption spectra recorded with VV polarization for pump and probe beams of PEPEP and its dimer are remarkably similar up to 50 ps, whereas on longer timescales they reflect the same behavior already observed with time-resolved fluorescence experiments.
Preliminary data on anisotropy decay at selected wavelengths seem to confirm the presence of an ultrafast energy transfer process between the two moieties forming the dimer.

We are deeply thankful to Prof. A. Painelli for insightful discussion on the properties of these molecular systems.

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FIS-PO-20 Anti-site defects formation in $LiFePO_4$ cathode material prepared by microwave-assisted hydrothermal synthesis

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Among the cathode materials for lithium-ion batteries, $LiFePO_4$ is indeed the most promising for large-scale applications; its olivine structure presents suitable thermal stability, no toxicity and low cost [1]. Numerous low temperature synthetic routes have been recently used in order to have control on size and shape of $LiFePO_4$ particles and to reach optimized morphologies, promising for the electrochemical applications [2]. In all these cases intrinsic defects are formed and can be removed only after annealing for long time at high temperature. Our study deals with the preparation of crystalline $LiFePO_4$ by an innovative procedure based on the simultaneous application of microwave and hydrothermal processes, in order to overcome the limitations of the hydrothermal method alone, that makes use of low operating temperature, but requires long reaction times and can produce olivine with a non-homogeneous particles dimension and shape. The combined use of spectroscopic and structural techniques allowed a detailed study of the local order of olivine. The results obtained by the Mössbauer spectroscopy, combined with the overall and local structural evidences obtained by the Rietveld refinement and PDF analysis of synchrotron radiation X-Ray diffraction data allowed to characterize the defectivity of $LiFePO_4$. The PDF analysis, applied for the first time to the $LiFePO_4$ structure, shows that the anti-site defect and the symmetry lowering resulted more probable, and Mössbauer spectroscopy confirmed these findings. In particular, a few percent of anti-site defect has been determined and also the presence of a small amount of Fe^{3+} on regular octahedral sites has been revealed.

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FIS-PO-21 Light-controlled nitric oxide delivery from Langmuir-Schafer films

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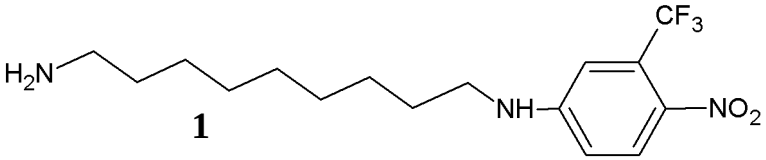
Nitric oxide (NO) plays a crucial role in the bioregulation of a wide range of pathophysio- and physiological processes such as vasodilatation, neurotransmission, hormone secretion, macrophage induced cytotoxicity [1], anticancer process [2]. This multifaceted role of NO has prompt many researchers to develop compounds which can serve to deliver NO. The main problem associated with NO donors is the precise spatiotemporal control of the nitric oxide released. In this context, light seems to be an ideal external on/off trigger to regulate, with a high control, the NO dosage. The compound **1** used in this work is reported in figure and acts as the NO photo-deliverer which can be transferred by means of Langmuir-Schaefer (LS) technique. Due to the presence of the -CF_3 substituent, the nitro group is placed almost perpendicular to aromatic plane, and this twisted conformation is crucial for NO photorelease. As we reported in other works [3], LS method ensures the transfer of an efficient solid film; on the contrary, other deposition techniques, such as spin coating or casting, quench the nitric oxide emission. Silver nanoparticles (AgNPs), used for their well-known antibacterial properties, were dissolved in the aqueous subphase and the interaction among **1** and the hydrosoluble Ag nanoparticles allowed to transfer, by the LS method, a multilayered film of **1**/AgNPs. The increase of NO concentration after an appropriate light stimulus and the transfer of nitric oxide to myoglobin was observed after the illumination of the LS film.



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FIS-PO-22 Effect of the molecular packing on the efficiency of an organic solar cell: a comparison between Langmuir-Blodgett and spin coating photovoltaic devices

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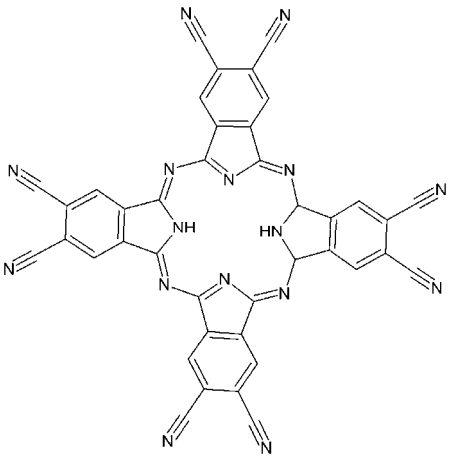
An important parameter that strongly influences the performances of an organic solar cell is the percolation path of the free carriers [1]. A not uniform matrix, as well as a long percolation path, provides traps for the free electrons and holes and, of course, a deterioration of the solar device efficiency. In order to optimize the charge collection, many researchers suggested both the use of highly anisotropic materials, such as nanotubes and quantum wires [2, 3], and very expensive deposition techniques. In this work, Langmuir-Blodgett technique, one of the most elegant and well-suited approaches that allows accurate control of both packing and molecular orientation, was used to deposit a dyad of a functionalized phthalocyanine (Pc) (see figure) and the [6,6]-phenyl-C_{61}-butyric acid methyl ester (PCBM). Absorption spectra in the UV-Visible range carried out at different polarization angles of incident light, showed a high oriented LB film of the co-spread Pc/PCBM dyad. On the contrary, dichroic ratio calculated for the spin-coated film is about 1. The device realized with 10 LB layers of the dyad showed a rapid photoresponse and a J_{sc} of 48 μA cm^{-2} was recorded; spin coated solar cell exhibited a short circuit current of 0.9 μA cm^{-2}. Short circuit current is an important parameter closely linked to the percolation path.



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FIS-PO-23 FTIR studies on paper mache composition of "Madonna delle Alcantarine" statue

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Today's science and technology development has led to many different kinds of approaches in the study of Cultural Heritage. New non-destructive methodologies have been employed for the physical and chemical analysis of several valuable remains. The goal of this work was to lead to a wider knowledge of technical processes used in the production of paper mache statues by baroque artists in Salento. Objects of the investigation were few samples from one of the five little angel heads of the *Madonna delle Alcantarine* composition statue. Each specimen represented a particular paper mache layer. The analysis was carried out using a FTIR Spectrometer in the region of MIR. As it is well-known, IR spectroscopy is a technique sensitive to the presence of chemical functional groups, thus the analysis allowed to identify different kinds of paper[1]. In addition, some comparison permitted to underline the presence of glue made of vegetable between the layers. In particular, we were able to establish that he adhesive material was extracted by wheat bran [2].

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FIS-PO-24 ATR infrared characterisation of the components of a XV century *Responsorium Graduale*

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An ancient religious book, more in detail a *Responsorium Graduale* [1], damaged during the earthquake that upset L'Aquila in April 2009, was examined and restored. During every step of restoring procedure, the specimens were analyzed by means of infrared spectroscopy. All the acquisitions proposed in this work are completely not destructive.

The *Graduale* is constituted by a cover realized in parchment and it was revealed that this cover was tanned with a particular procedure, typical of medieval period. Strings used for giving a more rigid structure to the spine was obtained probably from hemp [2], then they was treated by starch, according to a typical procedure adopted during XV century. Then a wooden axe is used to give rigidity to the book structure.

Another interesting result was obtained comparing the tanning method used for the parchments and the cover of the book with the strings used to bind the book sheets. The binding strings need to be flexible and the infrared analysis clearly shows that the so-called "Chamois" tanning was employed by the ancient craftsmen to obtain this result.

Finally, we compared the adhesive used for realizing the book with the one employed for repairing some inner pages. Infrared analysis showed strong differences between the glues: a cellulosic one [3] was used for "restoring" the book, on the contrary a proteic glue was employed for binding the wooden part with parchment sheets.

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FIS-PO-25 Interaction of azatrux with human telomeric G-quadruplex under molecular crowding conditions: biophysical and molecular modeling studies

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Human telomeric G-quadruplex structures are known to be promising targets for an anticancer therapy [1]. Knowledge of the structures formed by human telomeric G-quadruplexes under physiological conditions is crucial for structure-based drug design of potent and selective small-molecule ligands. It has been reported that human telomeric DNA quadruplexes can be highly polymorphic and can fold into a variety of different conformations [2]. However, there is increasing evidence that crowding solution conditions can significantly stabilize the parallel G-quadruplex topology over others [3]. Since molecular crowding is reflecting the nuclear environment in eukaryotic cells, it is appropriate to study the binding properties of new ligands with the parallel G-quadruplex fold. The present study has employed a combination of spectroscopic, calorimetric and computational methods to explore the binding of the three side-chain triazatruxene derivative, termed azatrux [4], to a human telomeric G-quadruplex, under conditions of molecular crowding. The binding of azatrux to the tetramolecular $[d(TGGGGT)]_4$ parallel quadruplex in the presence and absence of crowding conditions, was also characterized. The selectivity of azatrux for the human telomeric G-quadruplex relative to another biologically relevant G-quadruplex and to duplex DNA was also evaluated. The data indicates that azatrux binds in an end-stacking mode to the parallel G-quadruplex scaffold and shows that azatrux has good selectivity for the human telomeric G-quadruplex over the other investigated DNA structures.

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FIS-PO-26 Reversible binding of metal ions onto bacterial layers revealed by protonation-induced ATR-FTIR difference spectroscopy

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The ability of microorganisms to adhere to abiotic surfaces and the potentialities of attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy have been exploited in order to study protonation and heavy metal binding events onto bacterial surfaces. This work represents the first attempt to apply on bacteria the recently developed method known as perfusion-induced ATR-FTIR difference spectroscopy [1]. Such technique allows measurement of even slight changes in the infrared spectrum of the sample, deposited as a thin layer on an ATR crystal, while an aqueous solution is perfused over its surface. Solutions at different pH have been used for inducing protonation/deprotonation of functional groups lying on the surface of *Rhodobacter sphaeroides* cells, chosen as a model system. The interaction of Ni^{2+} with surface protonable groups of this microorganism has been investigated with a double-difference approach exploiting competition between nickel cations and protons. Protonation-induced difference spectra of simple model compounds have been acquired in order to guide band assignment in bacterial spectra, thus allowing identification of major components involved in proton uptake and metal binding. The data collected reveal that carboxylate moieties on the bacterial surface of *R. sphaeroides* play a role in extracellular biosorption of Ni^{2+}, establishing with this ion relatively weak coordinative bonds.

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FIS-PO-27 Rotational spectrum and dynamics of tetrahydrofuran-krypton

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Due to the higher polarizability of Kr with respect to Ar, a higher dissociation energy interaction is expected for complexes containing Kr. However it is not true for 2,5-dihydrofuran(2,5-DHF)[1-3]. It could be interesting to investigate this comparison in the case of other five-membered heterocyclic molecule, especially with different aromaticity or double bonds.

Tetrahydrofuran (THF), a fully aliphatic member of the furan series, is not a planar molecule like 2,5DHF in the gas phase but exhibits pseudorotation. Here, the rotational spectrum of THF-Kr complex has been investigated by molecular beams Fourier transform microwave spectroscopy. The spectra of normal and ^{86}Kr species showed that the Kr atom is located nearly over the oxygen atom, almost perpendicularly to the COC plane (see Figure 1). Each rotational transition is split into two component lines due to the residual pseudorotational effects of the ring in the complex, according to the observed Coriolis coupling term between the tunnelling states. The splitting between the two vibrational sublevels has been calculated to be 87.462(2) MHz. The dissociation energy, as obtained from centrifugal distortion effects, is 3.73 kJ mol^{-1}, higher than that of its corresponding argon complex[4].

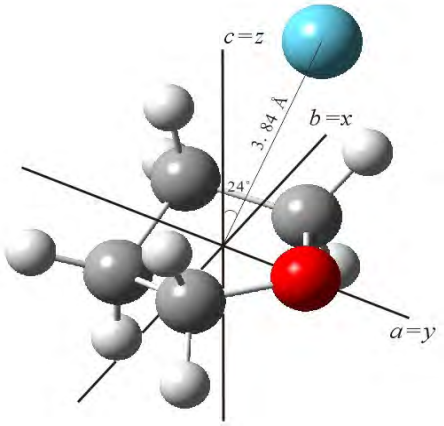

Figure 1. Sketch of THF-Kr in the principle axis system of THF.

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FIS-PO-28 Characterization of the Geographical and Botanical Origin of Italian Cherries by Nuclear Magnetic Resonance and Isotope Ratio Analysis

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In this study, the Isotope Ratio Mass Spectrometry (IRMS) and the Nuclear Magnetic Resonance Spectroscopy (NMR) were used in combination with multivariate statistical techniques for the characterization of Italian cherries of different geographical (Emilia Romagna and Puglia) and varietal (Bigarreau, Ferrovia, Giorgia) origin. In particular, the Discriminant Function Analysis (DFA) was performed on the NMR spectra and isotopic composition data to determine discriminant functions useful in predicting the geographical and variety origin of unknown samples. The statistical analysis conducted on NMR data showed a prediction ability (estimated by the "leave-more-out " procedure) equal to 94.3% for the geographical discrimination identifying malic acid and tyrosine among the most important compounds for this discrimination. The statistical treatment of IRMS data showed a predictive ability of 83.0%. All these results demonstrated the goodness of the models obtained, especially considering that these were constructed from a dataset in which the variability, in addition to their geographical origin, is linked to many other factors such as the degree of ripeness and varietal origin of cherries. In addition, applying DFA to the entire dataset (NMR and IRMS data) very good results were obtained in prediction (98.9%), demonstrating the validity of a synergic approach. Finally, for each of the two growing Italian regions, the NMR and IRMS results have been used for the discrimination of the botanical origin among the three cultivars obtaining a prediction percentage equal to 100.0% and 98.9% for Emilian and Apulian samples, respectively. However, these latter results require further validation using a larger number of samples.

Regione Puglia is gratefully acknowledged for financial support ("Apulian Food Fingerprint" project, n. 68, Reti di Laboratorio Pubblici).

FIS-PO-29 Targeting RGD-recognizing integrins: aggregation behavior of a novel class of amphiphilic RGD integrin binders.

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Receptors that are uniquely expressed or markedly overexpressed in tumors have been the potential targets for cancer therapy and diagnosis. Vascular integrins such as alphaVbeta3 and alphaVbeta5 have become major biological indicators for treating cancer since they are expressed on invasive tumors such as late-stage glioblastomas, breast and prostate tumors, malignant melanomas, ovarian carcinomas, as well as the new-born blood vessels. [1-2] In this domain, low-molecular weight RGD-based integrin antagonists displaying high alphaVbeta3 and alphaVbeta5 binding affinity and selectivity constitute privileged molecules, since they would serve as "tumor targeting navigator systems", while selectively killing angiogenic tumor endothelial cells.

Here we present preliminary results concerning the aggregation behavior of a novel class of amphiphilic integrin binders carrying the RGD peptidic sequence. This class includes molecules capable to be potentially used both for therapeutic and diagnostic purposes. Concerning this latter point of view, Fe/Au based nanoparticles have been synthesized for a potential use for Magnetic Resonance Imaging applications.

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FIS-PO-30 Incorporation of lycopene into lipid vesicles for pharmacological applications

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Lycopene is one of the most powerful carotenoids able to quench singlet oxygen. This high antioxidant activity has received wide attention for possible pharmacological applications. However, being highly hydrophobic, its incorporation in drug delivery systems represents an important issue in order to obtain active and stable preparations.

A natural and solvent-free oleoresin containing lycopene dissolved in a highly unsaturated vegetable oil [1] has been integrated into lipid vesicles in order to obtain liposomial dispersions suitable for pharmaceutical preparations. Size exclusion chromatography has been employed for vesicles preparation using both zwitterionic and negatively charged phospholipids. Elution profiles were followed by visible and infrared spectroscopy revealing the successful incorporation of lycopene into the lipid bilayer. The final preparations for which a complete carotenoid incorporation was achieved contained about 1 mM of phospholipids and 2 μM lycopene. Negatively charged phospholipids proved to effectively prevent the coalescence of liposomes leading to highly stable disperse systems. Finally the antioxidant activity of lipid-embedded lycopene was assessed by following the kinetics of degradation of chlorophyll *a*, a natural hydrophobic pigment, highly sensitive to light and oxygen. A 36% reduction of the degradation kinetic constant was observed when lycopene was present in chlorophyll containing liposomes.

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FIS-PO-31 THERMOGRAVIMETRIC STUDIES OF ARCHAEOLOGICAL WOODS

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Within the cultural heritage field, the wood assumes a relevant importance because of its presence in several art-works. In particular, the waterlogged woods represent a complex matter because they undergo to serious damages if dried being that the loss of water shrinks and deforms the material. Therefore, proper methodologies for their conservation and preservation are required. For a correct conservation process, a deep knowledge of the waterlogged wood state is required, that needs several techniques.
In this report, we will highlight some aspects dealing with archaeological waterlogged woods (*Pinus pinaster* and *Fagus sylvatica L.*) from the ship Chrétienne C, (II century, BC), discovered over the coast of Provence (France) and the sound woods of the same taxa. Thermogravimetry (TGA) has been revealed a proper and suitable technique for this purpose. In particular, TGA enabled us: 1) to define a new protocol to rapidly calculate the Maximum Water Content parameter, which is related to the wood degradation state; 2) to monitor the efficiency of the consolidants as well as to discriminate the consolidants when present in mixtures; and 3) to evaluate the activation energy, which is distinctive parameter for the archaeological woods.

FIS-PO-32 Surface properties of anatase nanocrystals investigated by CO adsorption: a combined experimental and ab initio study

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Titanium dioxide is one of the most important metal oxides because of its applications as white pigment, as important component in solar cells and as photocatalyst [1]. In the last two applications the relevant phenomena are occurring at the surface of anatase nanoparticles, which are generally considered to be more active than rutile ones [2]. Therefore it is relevant for both technological and fundamental motivations to study the structure of the different surfaces terminating the anatase nanocrystals.
In our work we performed periodic DFT calculations of the structure of (101), (100), (001) and (112) anatase faces and of the vibrational properties of CO adsorbed on them at two coverages in order to assign the main features of FTIR spectra of CO adsorbed at 60K on highly dehydroxylated anatase nanocrystals. CO is a weak Lewis and its stretching frequency is related to the electrophilicity of the surface Lewis acid sites: the greater is the electrophilicity of the metal cation, the higher is the blueshift with respect to the value in gas phase [3]. The study of the CO behaviour on different TiO_2 materials can highlight the correlation between surface structure and chemical reactivity.
Our contribution shows that the combination of spectroscopic and computational approaches is of extreme utility for the elucidation of the Lewis acid properties of Ti sites present on the different surfaces and on their influence on the stretching frequencies of adsorbed CO, for the explanation of the coverage dependent effect of dipole-dipole interaction and for the determination of the average nanoparticle morphology. This study highlights that the close comparison of experimental and computational results forms the safest basis for the cross validation of the two approaches [4].

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FIS-PO-33 Protein-protein interactions in the complex ERK2-KIM peptide and identification of putative high affinity mutant KIM peptides: a computational investigation

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MAP kinases have a central role in determining the transduction of a great number of stimuli, such as neurotrasmitters, hormones, cellular stress and cytokines. Any deregulation capable of influencing the normal activity of this pathway can potentially lead to a wide variety of diseases, including Alzheimer's disease, Parkinson's disease, and various types of cancers. The catalytic activity of MAP kinases is mainly regulated by phosphorylation: protein kinases and phosphatases interact with the MAP kinases via a conserved region (KIM), which constitutes a pivotal determinant for the formation of a stable complex.
In the present work, we devised a computational procedure based on molecular dynamics simulations (MD) and free energy perturbation (FEP) in order to select mutant KIM peptides which can putatively bind ERK2 with higher affinity than the wild type.

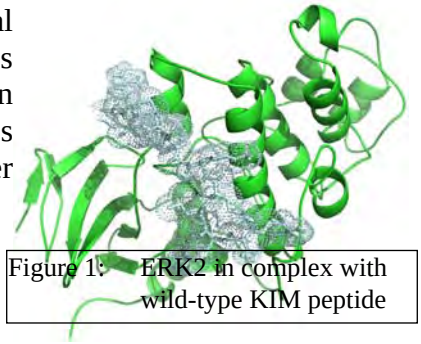

Figure 1: ERK2 in complex with wild-type KIM peptide

Our approach features an initial set of MD simulations of the mutant peptides in complex with ERK2, followed by an analysis of the persistence of the electrostatic and hydrophobic interactions at the complex interface during the simulations. This provided a qualitative insight which led us to the identification of promising mutant peptides to be subsequently energetically evaluated through FEP simulations. These putative high affinity mutant peptides could be used to prevent other interacting protein partners from binding ERK2, therefore modulating its catalytic activity and function during the cell cycle.

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FIS-PO-34 WAVELET ANALYSIS OF MOLECULAR DYNAMICS DATA

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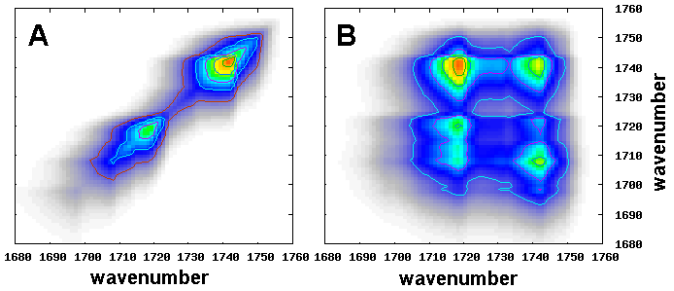
Time resolved IR experiments provide new relevant insights regarding the structure and dynamic behaviour of complex molecular systems. However, to elucidate accurately the spectral features, often new *in silico* experiments are required. Car-Parrinello Molecular Dynamics (CPMD) simulation data contain in principle most of structural and dynamic information revealed by 2D IR experiments. In order to extract this information from the simulations for a straightforward comparison with the experiments, the development of computational tools to analyze CPMD trajectories becomes therefore particularly useful.
The Wavelet Transform (WT) is a mathematical "tool" that performs time-frequency analysis. With WT it is possibile to correlate directly structural and spectoscopic properties, corroborating the usual standard interpretation of experimental spectra.
As case studies, we have tested different WT-based methods on molecular systems whose dynamics is driven by Hydrogen Bonds formation and breaking. The computed vibrational spectra have been calculated from time-resolved bond-lengths and the dynamic effects of the Hydrogen Bonding onto the vibrational modes have been probed with WT. Cases of Chemical Exchange and Inhomogenous Broadening have been elucidated and correlated with the strength and stability of the Hydrogen Bonds.



C=O *stretching region of* Methyl Acetate *in* MeOH*;*
A) *delay time* = 0 ps *;* **B**) *delay time* = 20 ps

Moreover, using the time-localization features of WT, bidimensional frequency correlation plots have been generated (see figure) multiplying frequency spectra obtained at different delay times. When Chemical Exchange occurs due to the Hydrogen Bonding, specific cross peaks appear in the 2D wavelet spectrogram.

FIS-PO-35 Preparation and structural characterization of graphene and vinyl ester/graphene composites.

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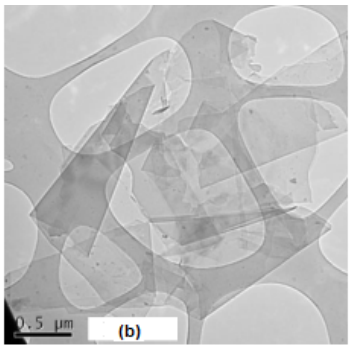
Graphene, one of the allotropes of elemental carbon with a planar monolayer of carbon atoms arranged into a two-dimensional honey-comb lattice, has demonstrated a variety of intriguing properties as new material for future electronic and composite industry [1-2].

The aim of the current research is the preparation and the characterization of graphene and new composite using vinyl-ester resins as matrix.

The preparation of graphene was carried out by thermal treatment of commercial Graphite Intercalation Compounds (GICs) [3]. After the thermal treatment, expanded graphite (also known as worm-like or accordion-like in this phase) was dispersed in a proper solvent and sonicated obtaining Graphite Nano Platelets (GNPs) thick films, having an average thickness of about 200 μm.



TEM micrograph of GNPs flakes.

Structural and morphological characterization of graphene and their composites have been made by means of X-Ray Diffraction, Small Angle X-Ray Scattering, and Electron Microscopy. Results show that, by choosing appropriate conditions (temperature, solvent, sonication time, etc..), the GICs flakes expand their volume producing high quantities few layers graphene sheets.

The electrical investigations show that the measured dc resistance of different thick films decreases as function of the GNP expansion temperature

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FIS-PO-36 Innovative hybrid materials based on colloidal nanocrystals in imidazolium ionic liquids

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In the last decades, Room Temperature Ionic Liquids (RTILs) have attracted the interest of scientific community, and are being considered a novel, promising class of materials for a variety of technological applications.[1] ILs are a class of substances, exclusively composed of ions, typically organic cations and different kinds of anions (i.e. halides, phosphates, imides), which have shown unique physico-chemical properties differing from aqueous ionic solutions and high temperature molten salts. ILs are characterized by a negligible vapor pressure, good thermal and electrochemical stabilities, low flammability, good solvent capabilities for many organic and inorganic compounds.[2] Thanks to these peculiar properties and the enormous potential RTILs offer in fields such as sensors, energy storage and information technologies, such kind of compounds is replacing conventional volatile organic solvents as green solvents in numerous chemical and industrial applications. Moreover, RTILs are also exploited as non-molecular solvents in various synthetic protocols for the preparation of numerous metallic, oxide and semiconductor nanoparticles.[3]

One of the most largely investigated class of ILs, is based on 1-alkyl-3-methyl imidazolium cation. In such imidazolium based ILs, a well defined organization has been found in both the solid and liquid phase.[4] The whole physico-chemical and original structural properties of such a class of materials can be exploited as templating and structure directing agents in the preparation of innovative hybrids and at the same time can convey their intrinsic functionalities, i.e. high ionic conductivity and electroactivity.

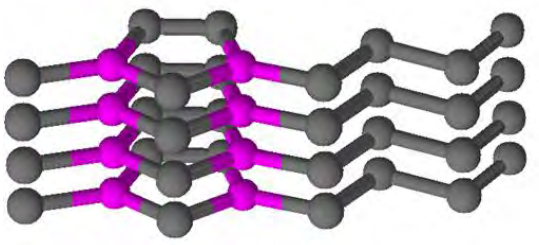

Figure 1. Imidazolium IL structural properties: π-π interactions between cation rings

In the growing field of hybrid materials, the combination of imidazolium based ILs and colloidal nanocrystals (NCs) in a unique nanocomposite is still almost unexplored, although can offer an enormous potential towards the design and the development of original components for advanced electrochemical devices, namely batteries and new generation solar cells. Here, we report on the incorporation of organic capped semiconductor and oxide NCs in different imidazole based ILs. Spectroscopic investigation has been carried out on the various prepared NC-IL composites and the variation of the alkyl chain length as well as the different nature of the inorganic anion on the properties of the prepared composites and the effect of the solvent have been extensively probed. Unexpectedly, time-resolved fluorescence measurements reveal the possible interaction between the different moieties, namely energy transfer or electron transfer, depending on the type of the involved NC. Such a result improves the knowledge on the dynamics involved in the hybrid formation, bringing a potential development in material science towards the fabrication of highly innovative next generation solar cells and electrochemical devices.

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FIS-PO-37 Investigating dynamical systems on a mesoscopic scale with cellular automata

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A well parametrized Molecular Dynamics (MD) simulation can offer a realistic picture of the dynamical (non-reactive) processes in a molecular system. Analogously, molecular Monte Carlo (MC) simulations can provide its static equilibrium properties with quite good accuracy. Even though they are much cheaper than quantum mechanical models, still their level of microscopic detail is pretty high. This making them quite costly, especially if for example one wishes to simulate a rare-event phenomenon, for which really lenghty runs are required in order statistically meaningful data to be collected.

Lattice-gas models (most of them probabilistic) are often referred to when dealing on coarse-graining of molecular simulations. Not only do they represent inalienable tools for the investigation of the very foundations of statistical mechanics, but also their discrete, highly simplified configuration space offers an attractive alternative in the approach to the simulations on the mesoscale. Within the landscape of discrete models, cellular automata (CA) represent one of the most interesting objects at all [1]. Evolving in time as micro-worlds inspired by biological systems, they possess the really attractive feature of *synchronicity* (that the MD technique does possess as well, whereas MC approaches, on-lattice or off-lattice, do not), which makes them well suited to the study of collective dynamical properties, and they are *exact in the evolution*, due to the absence of round-off errors. Problem is, whereas nowadays MD/MC can be (and in fact they are) often used as brutal integrators/samplers to study a variety of systems, CA require to be set up *ad-hoc* for almost any problem one wishes to investigate. We show how progresses are being made by our group in using CA to study problems of adsorption/diffusion in zeolites [2].

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FIS-PO-38 Fabrication and Characterization of Au Nanorod based Layer by Layer Architecture towards Biosensors

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Metal nanoparticles have attracted great research interest in recent years because of their unique optical, electrical, and magnetic properties very appealing for electroanalysis and the construction of electrochemical sensors.[1] A key challenge in molecular bioelectronics is to improve the efficiency of long-range charge transfer. Gold nanoparticles allow the conductive materials to come into a close proximity of the active process and provide bioelectrocatalytic activity that can be utilized in biosensor devices.[2] The direct electron transfer of redox proteins has been realized and applied on various electrodes modified by gold nanoparticles, setting up biosensors based on their electrocatalytic activity.[3]
Layer-by-layer (LbL) assembly can build composite film multilayers containing different molecules or/and metal nanoparticles by simple wet chemistry.[4]
We report on the preparation and characterization of nanostructured film based on Au nanorods (NRs) obtained by using layer-by-layer (LBL) assembling, by exploiting electrostatic interaction among metal nanoparticles and polyelectrolyte. Multilayer films have been fabricated by using LBL assembly of poly(sodium styrenesulfonate) (PSS) and positively charged Au NRs onto polyelectrolyte-modified substrate. The effect of factors like substrate, initial polyelectrolyte anchoring layer, number of layers has been also spectroscopically and morphologically investigated. Finally, hybrid structures, based on Au NR and cytochrome *c*, have been assembled in order to create an effective interface between the red-ox protein and Au NRs deposited onto ITO electrode. The multilayered structures have been investigated by means of UV-vis absorbance spectrum, Atomic Force Microscopy (AFM) and Cyclic Voltammetry, ultimately defining spectroscopic properties, morphology and electrochemical behaviour of the obtained nanostructured architectures

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FIS-PO-39 Crystallographic, kinetic, and spectroscopic study of the first ligninolytic peroxidase presenting a catalytic tyrosine

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Trametes cervina lignin peroxidase (^{LiP}) is a unique enzyme lacking the catalytic tryptophan strictly conserved in all other LiP and versatile peroxidases (more than 30 sequences available to date)[1,2]. Recombinant *T. cervina* LiP and site-directed variants were investigated by crystallographic, kinetic, and spectroscopic techniques. The crystal structure showed three substrate oxidation site candidates involving His-170, Asp-146 and Tyr-181. Steady-state kinetics for oxidation of veratryl alcohol (the typical LiP substrate) by variants at the above three residues revealed a crucial role of Tyr-181 in LiP activity. Detailed spectroscopic and kinetic investigations, including low-temperature EPR, showed that the porphyrin radical in the two-electron activated *T. cervina* LiP is unstable and rapidly receives one electron from Tyr-181, forming a protein radical with a catalytic function. The crystal structure revealed a partially-exposed location of Tyr-181, compatible with its catalytic role, and several neighbor residues probably contributing to catalysis (Fig. 1). This is the first structure-function study of the only ligninolytic peroxidase described to date that has a catalytic tyrosine [3].

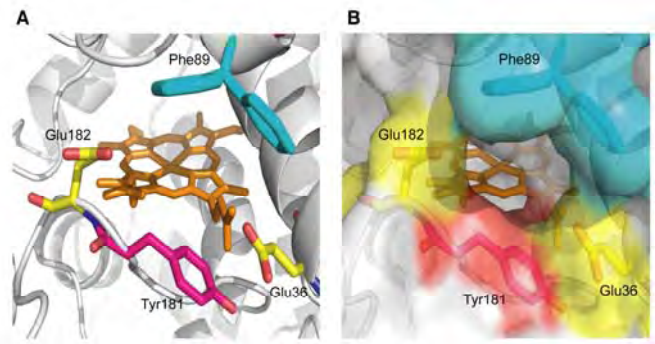

Figure 1

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FIS-PO-40 Nanoparticle-plasma protein interactions: confirmation by nanoLC-MS/MS of existence of hybrid structures in cationic liposome/DNA complexes

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The self-assembling of cationic liposomes (CLs) and DNA can give rise to a variety of nanostructures and morphologies. Multilamellar complexes are made of DNA intercalated between opposing lipid bilayers, while clusters formed by intact vesicles may exist as 'beads-on-a-string' (i.e. CLs attached to a string of DNA). Precise knowledge of the structure and morphology of complexes is relevant in many biological important processes such as gene delivery. Here dynamic light scattering, zeta potential, synchrotron small angle X-ray scattering and one-dimensional polyacrylamide gel electrophoresis were performed to investigate the equilibrium structure, morphology and interactions with plasma proteins of lipoplexes made of the cationic lipid (3β-[N-(N',N'-dimethylaminoethane)-carbamoyl])-cholesterol (DC-Chol), the zwitterionic lipid dioleoylphosphatidylethanolamine (DOPE) and DNA. Results show that DC-Chol–DOPE/DNA complexes are multilamellar systems with DNA protected by cationic lipids. On the other hand, the 'protein corona' associated to lipoplexes after interaction with human plasma was found to be much richer in basic immunoglobulins gamma proteins (Ig-Gs) than that of pure lipid vesicles in the absence of DNA. According to the most recent evidences reported in the literature, this finding would suggest the existence of hybrid structures made of multilamellar complexes either stuck together by DNA or coexisting with DNA-loaded intact vesicles. Because surface properties of lipoplexes may determine their interaction with cells and tissues, these results may be important for predicting biological responses in vivo.

FIS-PO-41 Spontaneous spirals formation in excitable media

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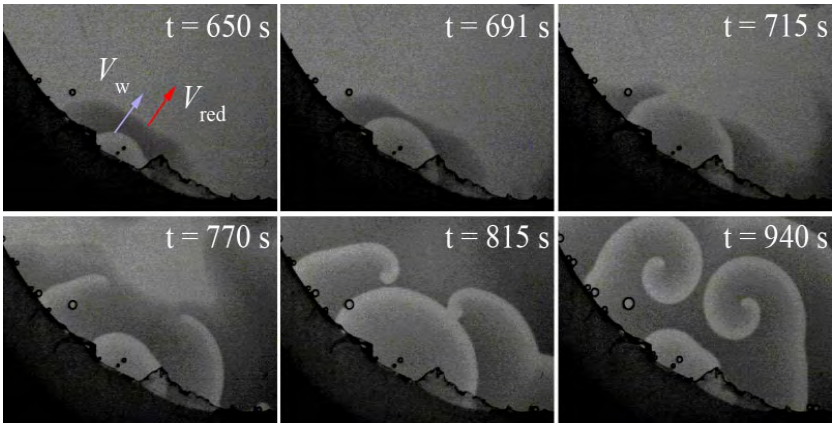

The transition from planar fronts, trigger waves or solitary pulses to spirals in excitable media attracted an increasing interest in the past few decades, mainly because of its relevance for biological and medical applications[1,2]. In this contribute we describe a new and convenient method for spirals generation starting from symmetric wavefronts. By using the micelle-forming zwitterionic surfactant *N*-tetradecyl- *N*,*N*-dimethylamine oxide in a Belousov-Zhabotinsky solution[3,4], it is possible to control to a large extent the domains where spirals can be spontaneously generated. The mechanism responsible for the wavefront break up lies on the interaction of the propagating waves with the unexcitable regions formed by the interaction of the micelles with some of the Belousov-Zhabotinsky key intermediates (see figure).

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FIS-PO-42 Photocatalytic Hydrogen Production from Aqueous Solutions on Noble Metal-Modified and/or Doped TiO_2

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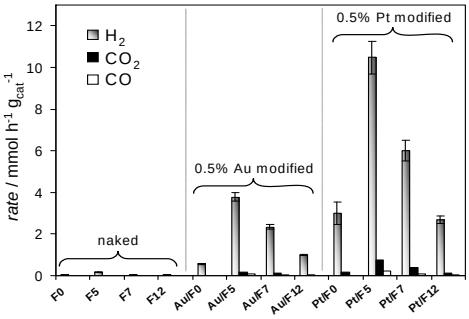
The photocatalytic production of hydrogen from water/methanol solutions was studied on titanium dioxide and on a series of NH_4F-doped TiO_2 photocatalysts prepared by sol-gel synthesis, varying the dopant-loading from 0% up to 12%. The photocatalysts were tested both naked and after deposition of gold and platinum nanoparticles, performed either by the reverse micelles method [1] or by photoreduction of metal precursors. Pt-modified undoped titania with 0-2 wt.% metal loadings was also investigated. The photocatalytic runs were carried out in a recirculation apparatus with the photocatalyst bed continuously fed with methanol/water vapor, employing a xenon lamp as irradiation source. Methanol underwent oxidation up to CO and CO_2; formaldehyde and formic acid were identified as oxidation intermediates [2,3].

For all of the investigated TiO_2 samples, the rate of H_2 production greatly increased upon Au and Pt nanoparticles deposition, because of their ability to enhance the separation of photoproduced electron-hole pairs. In particular Pt was a better co-catalyst than Au, in agreement with their work function values [2]. No significant increase in the H_2 production rate was attained with Pt loadings higher than 0.75% up to 2%.



Doping of TiO_2 enhanced the hydrogen production rate, with an identical bell-shaped trend with increasing the dopant content for the naked, Au- and Pt-modified titania series, with the 5% NH_4F-doped sample always being the best photocatalyst within each series. Thus, the structural properties of bulk doped titania ensure a more effective separation of photoproduced charge carriers. Indeed, doping followed by annealing at 700°C led to the formation of highly crystalline pure anatase [3], which is more photoactive than rutile. In contrast, over-doping led a decrease of the hydrogen production rate, possibly due to an excess of structure defects.

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FIS-PO-43 The first X-Ray structure of a cold-adapted glutathione synthetase

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Glutathione (GSH) is the major antioxidant molecule in most living organisms. Besides its protective role in contrasting oxidative free radical species and in the removal of toxic metals, GSH is involved in redox homeostasis and cell signaling; furthermore, it is essential to maintain cellular proteins in their reduced state and acts as a post-translational regulator of protein function. The synthesis of GSH from its constituent amino acids involves two ATP-requiring enzymatic steps catalyzed by glutamate cysteine ligase (GshA) and glutathione synthetase (GshB), respectively. Its biosynthetic route has been described in details for a variety of organisms; however, nothing is known about this process ***in psychrophilic*** microorganisms. In particular, although various GshBs have been purified and sequenced, none of these enzymes belong to an organism living at low temperatures. Very recently, a recombinant form of GshB from the cold-adapted bacterium *Pseudoalteromonas haloplanktis* (*Ph*GshB) has been purified. The activity of *Ph*GshB was assayed through a direct method, measuring the release of inorganic phosphate from radiolabelled ATP. *Ph*GshB is active at 10°C and its activity significantly increases with temperature, at least up to 30°C; the K_m for ATP ranges between 0.14 and 0.25 mM in the 10 – 30°C interval.
The crystal structure of *Ph*GshB has been determined and refined at 2.3 Å resolution. Structural information is combined with a characterization of the thermal stability of the enzyme performed by circular dichroism and fluorescence measurements. A comparison between our data and those obtained for the closely related GshB from the mesophilic *Escherichia coli* [1-3], sharing 69% identity with *Ph*GshB, is presented in the attempt to understand the mechanisms of cold-adaptation of the psychrophilic enzyme.

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FIS-PO-44 QM/MM characterization of redox-active Trp radicals in LiP and LiP-like systems

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Lignin Peroxidase (LiP) plays a central role in the biodegradation of the plant cell wall constituent lignin and is able to catalyze the oxidation of a variety of high redox potential compounds [1]. Spin-trapping, peptide mapping, site-directed mutagenesis and protein crystallography have been used to demonstrate that a surface oxidation site (Trp 171) in LiP is involved in the electron transfer to the heme cofactor via a long range electron transfer mechanism activated by H_2O_2 (Figure 1A). However, no direct evidence for the formation of the Trp171 radical intermediate has been reported to date. An additional intriguing finding is that Trp171 is stereospecifically hydroxylated at its C -atom as result of an autocatalytic self-oxidation that takes place during the first turnover cycles [1,2].

Recently, site-directed mutagenesis has been used to manipulate the microenvironment of Trp171 site in LiP (E250Q+E168Q, Figure 1B), allowing the detection by EPR spectroscopy of the Trp171 radical species [3]. The same engineering-based approach has been also applied to introduce the catalytic Trp and its acidic environment into Coprinus cinereus Peroxidase (CiP), that has similar protein fold but lacks oxidation activity. A Trp radical in the resulting CiP triple variant (D178W+R257E+R271D, Figure 1C) was identified and characterized by multifrequency EPR spectroscopy (9 and 285 GHz) [3].

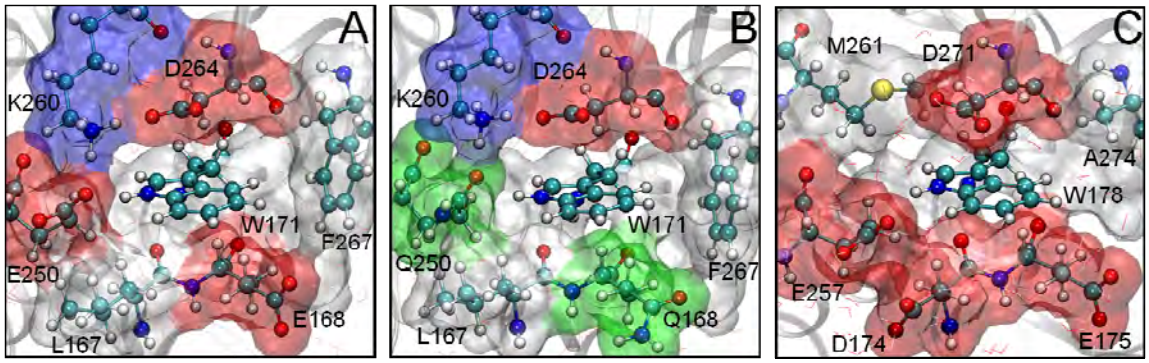

Figure 1

In the light of the newly available EPR experimental data we performed a QM/MM computational study in order to characterize Trp radicals in the protein matrix of these LiP-like systems (Figure 1). In particular, the inclusion in the calculation of all the electrostatic and steric interactions within a QM/MM (DFT/CHARMM) strategy, already applied successfully to the study of Trp and Tyr radical intermediates in a Versatile Peroxidase and in its W164Y mutant [4], allowed a direct comparison between experimental and computed data. Differences in electronic and geometrical structure of Trp radicals among these enzymes are discussed, with the aim of understanding the different behaviour of LiP in comparison to that of LiP and CiP mutants.

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FIS-PO-45 Aggregation properties, inclusion in membrane models and LB film formation of porphyrin scaffolds functionalized by glucosilated steroid units

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New glucosylated steroid modified porphyrins, differing from the number and type of ring substitutions, have been taken in consideration as chiral recognition elements in organized environments (Figure 1). The aggregation properties in solution, the formation of porphyrin films on hydrophilic surfaces and the inclusion in biological membrane models like liposomes or supported lipid bi-layers have been investigated by optical spectroscopy (UV-Vis absorption, steady-state and time-resolved fluorescence spectroscopy, circular dichroism). The aggregation of porphyrin derivatives in DMSO/H_2O (40/60 v/v) gives rise to the broadening of the Soret band and a strong hypochromic shift. Such effects can be ascribed to the formation of J-type supramolecular structures. Circular Dichroism studies revealed the chiral nature of the formed supramolecular species.
Porphyrin multilayers are built up through Langmuir-Blodgett deposition on quartz supports. The behavior of each system at the air/water interface was characterized by recording compression isotherms.
Several experiments were also carried out to investigate the interaction between the synthesized porphyrin derivatives and a membrane model represented by unilamellar 1-palmitoyl,2-oleoyl-sn-glycero-3-phosphocholine (POPC) liposomes. The partition between the aqueous and lipid phase and the inclusion of the above porphyrins in a lipid bilayer have been investigated by fluorescence anisotropy and fluorescence quenching measurements. The results indicate that, while the bi-substituted derivative is most likely located at the outer surface of the liposome, the monosubstituted porphyrin is able to insert the hydrophobic part into the bi-layer, exposing the hydrophilic group to the aqueous solution, out of the vesicle.

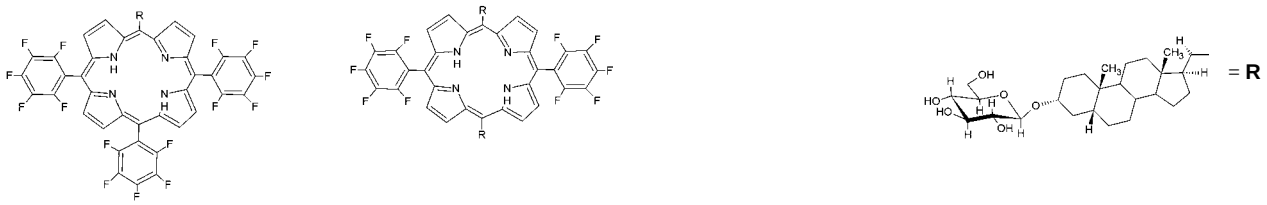

Figure. 1 – Molecular scheme of the functionalized porphyrin investigated

FIS-PO-46 Polyelectrolyte multilayer as a platform for nanocrystal uniform and patterned assembly

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Fabrication of nanoparticle (NP) film allows to transfer onto solid surface the peculiar size dependent properties of nano-sized materials, thus opening access not only to fundamental understanding of new phenomena and characteristics of such nanostructured materials but also to their technological exploitation in devices, such as biochips and sensors.Proper design of substrate and particle surface chemistry defines the driving force directing the assembly of stable particle layer, namely electrostatic interaction, covalent bonding, host guest and, in general supramolecular, interaction.Here the fabrication of uniform and patterned nanocrystal (NC) assemblies was thoroughly investigated. A layer by layer strategy was used to prepare polyelectrolyte functionalized substrates as platform for electrostatically driven NC assembly. Substrate surface charge and morphology were tailored by carefully choosing the suitable deposition condition, substrate treatment as well as post deposition procedures, in order to properly template an effective and uniform NC assembly. In particular water soluble luminescent (CdSe)ZnS and CdS NCs were selected as functional materials, being also a valuable model material for a prompt monitoring of the assembling process. Tuning particle surface chemistry by the implementation of suitable surface engineering, such as ligand- exchange reaction, growth of hydrophilic silica shell and formation of hydrophilic inclusion complex, offered a variety of NPs with specific surface functional groups soluble in aqueous solution and with a good colloidal stability in defined pH-range. The specific interaction between substrate chemistry and NP surface charge was extensively investigated, and found crucial for ultimately direct particle assembly. Finally, particular microcontact printing combined to wet chemistry strategies is demonstrated to be a straightforward approach to fabricate discrete structures where particle positioning is carefully directed and controlled.

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FIS-PO-47 Lipid composition regulates the biomembranes micro-structural properties and modulates the interaction with a peptide deriving from the viral glycoprotein gp36.

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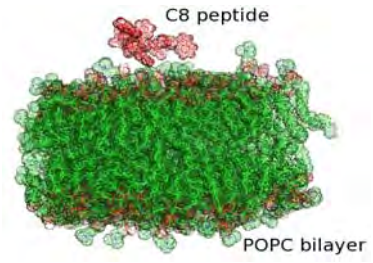
Lipid–protein interactions play a key role in a wide variety of cellular processes. Lipids can affect protein structure and dynamics either via physicochemical characteristics of the membrane, such as elasticity, curvature, surface charge, hydration and the formation of domains, or by specific interactions involving the chemical structure, conformation and dynamics of the lipid head groups and acyl chains. Consequently, much attention has been paid to the lipid composition of biomembranes, which includes a rich diversity of phospholipids, sterols and glycolipids, on influencing several membrane processes.

In this work, we have performed a study on the effect of the cholesterol, at different concentrations (from 0% to 30% wt/wt), and sphingomyelin presence on the micro-structural properties of palmitoyl-oleoyl phosphatidylcholine (POPC) bilayers. The investigation has been carried out by a combined experimental approach, performing Neutron Reflectivity (NR) and Electron Paramagnetic Resonance (EPR) experiments on supported lipid bilayers and liposomes, respectively. We also focusing on the role of lipid composition on the interaction with a peptide (Ac-Trp-Glu-Asp-Trp-Val-Gly-Trp-Ile-NH_2), named C8 and deriving from the membrane-proximal external region (MPER) of the glycoprotein gp36 of Feline Immunodeficiency Virus (FIV).



We observed that C8 peptide adsorbs on the POPC bilayer surface, perturbing the lipid packing and chain motion in the membrane[1, 2]. The addition of cholesterol and sphyngomelin produces significant changes on the POPC bilayer micro-structure, influencing the subsequent interaction with the C8 peptide.

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Indice degli Autori

Chimica Industriale

IND-KN-01 New trends in biodiesel production

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Biodiesel production is increased exponentially in the last decade (2009 world production 16000 Ktons). Biodiesel is a fuel safe, renewable, non-toxic, biodegradable and much less contaminant for the environment than conventional diesel. Moreover, it represents a strategic source of energy especially for the countries that have not oilfields. For these reasons, even if the cost of biodiesel is still greater than diesel from petroleum, many governments sustain this production also considering the forecast of a strong increase of petroleum consumption due to the increasing demand from the underdeveloped countries. An European Directive, for example, impose a 10% volume of biofuels in the transport sector by 2020. The key problems in the production and use of biodiesel are: to reduce the costs of production and to avoid the competition between the production of energy and food. As a matter of fact, many vegetable oils are highly refined edible oils.
The cost of biodiesel is mainly affected by the cost of the feedstock for more than 85%, but also an improvement of the adopted technology can contribute in reducing the costs. Therefore, it is imperative:
1) To employ less expensive feedstock, that is, unrefined or waste oils. These last contain large amount of free fatty acids and the scheme of the process must be modified as a consequence.
2) To use not edible oil coming from alternative sources as, for example, algae or Jathropa Curcas. Jathropa is a plant growing with a high oil productivity in residual dry lands, while, Algae grow in water ponds with an extraordinary productivity. Therefore, all these oil sources are today object of very intensive studies.
3) To improve the actual technology based on the use of homogeneous alkaline catalysts through a better understanding of the reaction mechanism, the development of new biphasic kinetic models and the adoption of techniques of process intensification favouring the reactions occurring at the interphase and the mass transfer operations.
4) To introduce the use of heterogeneous catalysts, simplifying the continuous operation, possibly finding a catalyst promoting in one step both esterification of free fatty acids and transesterification of tri-glycerides. Moreover, the ideal catalyst must be stable to the poisoning and leaching effect.
5) To find new remunerative uses for the by-product glycerol contributing to the reduction of the overall costs.
In this lecture, all the mentioned aspects will be considered in detail by reporting the most relevant results obtained in the last years by both our research group and other researchers operating in the corresponding fields.

IND-KN-02 The role of catalysis in the heavy oil up-grading: past and present

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The unconventional oils will play a much larger role in the growth of fuel supply than is currently recognized. As a matter of fact, whereas the earth's conventional proven world oil reserves are 1.3 trillion barrels (bbl), extra-heavy plus bitumen resources amount to about 4 trillion bbl.

The unconventional oils are characterized by an API gravity lower than 10, high viscosity and an unusual high concentration of poisons such as sulphur, nitrogen, metals, and asphaltenes. For this reason, a key role for the full exploitation of these hydrocarbon resources is played by the downstream processes that are required to upgrade and convert them into valuable products.

To this purpose different technologies has been developed along with the years, all aimed to increase the H/C ratio, both by carbon rejection or hydrogen addition. Thermal processes like visbreaking and coking belong to the former, while the latter include the hydrocracking, with different catalytic reactor technologies: slurry, fixed and ebullated bed.

In the new scenario of oil supply, the hydrocracking processes are required to be well-suited for the conversion and upgrading of a variety of "black oil materials", from conventional vacuum residues up to extra-heavy oils and bitumen, avoiding the production of residual by-products, such as pet-coke or heavy fuel oil.

It is interesting to point out that since the beginning of oil industry, refiners faced the problem of heavy stuff upgrading. The first thermal cracker, realized by Dubbs dated back to 1919. The earliest hydrocracking was introduced later in the 1930s by the American Standard Oil, to produce gasoline and lubricants form heavy petroleum fractions. The process was developed jointly with the German I.G. Farbenindustrie, based on its knowledge for coal liquefaction.

Among the pioneers in this area we can also cite Mario Giacomo Levi at Politecnico of Milan and Giacomo Fauser at Montecatini/ANIC of Novara. The efforts of Levi and Fauser were addressed to find out a valuable route to upgrade the Albanian oil, an asphaltic crude with a very low yield of gasoline (<10%). In Novara research centre, Fauser developed up to the pilot scale an hydrogenation process yielding up to 80% of high quality avio gasoline. This process was than industrially applied at the ANIC refinery of Bari in 1938.

In this communication, a past and present outlook of the main catalytic aspects of the heavy oil upgrading will be discussed.

IND-KN-03 Efficient Palladium(II)-Catalysis. Oxidative Heck Couplings and Addition Reactions

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The aim of the work has been to discover and to study new efficient palladium(II)-catalyzed coupling reactions. Thus, a number of oxidative Heck reactions were developed, in which the aryl-palladium intermediate was formed through transmetallation of an aryl boronic acid, an aryl carboxylic acid or an aryl sulfinic acids to a palladium(II) catalyst.

The first open-vessel, room-temperature palladium(II)-catalyzed oxidative Heck reaction with arylboronic acids, using oxygen from the air as the reoxidant of palladium, was identified. In a further investigation, base-free conditions for the transformation were developed and suitable conditions for microwave-assisted oxidative Heck reactions were established.

A convenient and low-cost palladium(II)-catalyzed method for the synthesis of styrene derivatives, by coupling arylboranes with vinyl acetate, was developed. The reaction mechanism was studied using on-line ESI-MS, which enabled the detection of cationic palladium intermediates in ongoing reactions, and a plausible catalytic cycle was proposed. In an attempt to make the oxidative Heck and the styrene synthesis reactions more attractive from an industrial point of view, conditions for continuous flow synthesis and microwave-assisted flow synthesis were identified. The results were generally good and rapid synthesis of the desired products was obtained.

Finally, novel methods for synthesizing aryl ketones from benzoic acids or aryl sulfinic acids and nitriles, *via* palladium(II)-catalyzed decarboxylation/ desulfination of the aromatic acids, were established. Further, the reaction mechanisms were studied by ESI-MS and plausible catalytic routes were suggested.

IND-KN-04 Catalysis for sustainable chemistry: looking at the future

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Chemical industry has made a considerable effort in recent decades to reduce the impact on the environment, and consumption of raw materials, including energy, but mainly to comply with regulations. The fast evolving world scenario for energy and chemistry, however, has accentuated the need to put innovation at the core of the industrial competiveness instead of the financial aspects. However, it is necessary to rethink the development model of the chemical industry, by introducing new flexible and modular approaches. Catalysis, in combination with microreactor and process intensification, are the core and enabling factors to achieve above objectives and thus realize sustainability through chemistry [1].

However, it is necessary to reconsider catalysis from this perspective. In microreactors, for example, the usual approach by deposition of a thin film on the microchannels walls is not optimal in terms of amount of catalyst and fluidodynamic and safety aspects, particularly for gas-liquid reactions such as the case of the H_2O_2 direct synthesis from H_2/O_2, a good example of key reaction towards the goal of sustainability for chemical production [2,3]. Microchannel reactors offer various advantages to overcome current limits in this reaction, but it is necessary to develop nanofibrous catalysts, because they allow to increase the (i) wall-to-volume ratio for an effective quenching of the radical-type explosive reactions, (ii) surface to volume catalyst ratio and catalyst loading per volume of microreactor, (iii) microturbulence. A further possible extension is the passage from micro- to nano-reactors using the channels of nano-membranes to host the catalyst nanoparticles.

A second challenge that will be discussed regards the need to accelerate the introduction of renewables and to address by catalysis the issue of greenhouse gas emissions [4-6], but putting them in the general perspective of which sustainable energy scenario should be developed, and what are the opportunities and need of catalysis in relation to these scenario. In a short term, energy efficiency and valorization of the less conventional energy sources are the two critical elements. Aspects that will be discussed regard the opportunities for energy efficient processes, and the development of novel routes for using natural gas to produce liquid fuels. In the short-medium term, biomass conversion represents an opportunity, but it is necessary to define which strategies should be adopted. Some aspects of the opportunities and challenges for catalysis for biomass conversion will be presented. Finally, in a long term scenario it is necessary to use the solar energy. This would imply solving the issue of energy storage and transport, and find a sustainable solution to CO_2 emissions. The possible scenario for using solar energy and CO_2 will be commented.

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IND-KN-05 PLASTIC ZEOLITES

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The contribution is devoted to thermoplastic materials whose crystalline phases are able to host low molecular-mass guest molecules.[1] Particularly relevant are polymeric materials including co-crystalline host-guest phases that, by suitable guest extraction procedures (e.g., by carbon dioxide in supercritical conditions), produce nanoporous crystalline phases,[2] which are able to absorb guest molecules also from very dilute solutions. For instance, δ and ε crystalline phases of syndiotactic polystyrene (s-PS) present their nanoporosity organized as isolated cavities and channels, respectively.

It will be also shown that suitable processing conditions can lead to the unprecedented formation of films with three different kinds of planar orientations of the co-crystalline phase.[3] The availability of s-PS films with three different kinds of uniplanar orientation can be, of course, relevant also for practical purposes. For instance, it allows guest orientation control for co-crystalline phases and guest diffusivity (and hence permeability) control for the nanoporous δ and ε phases.[4]

Aerogels including the two nanoporous phases can also be easily obtained by solvent removal by carbon dioxide in supercritical conditions from s-PS physical gels.[5] Guest sorption measurements at low activity have shown that δ-form aerogels present the high sorption capacity characteristic of s-PS δ-form samples (due to the sorption of molecules as isolated guests of the host nanoporous crystalline phase) associated with the high sorption kinetics typical for areogels (due to the high porosity and hence high surface area). Thus, these new materials present a fast sorption kinetics while maintaining a good handiness.[5]

The final part of the presentation will be devoted to possible advanced applications of materials based on co-crystalline and nanoporous crystalline s-PS phases. In particular, applications of nanoporous films for molecular sensor,[6] for sensors of chirality[7] and for active packaging of fruit and vegetable (by removal of ethylene and carbon dioxide)[4] will be presented. Moreover, several possible applications of co-crystalline films will be presented. In particular, advanced optical materials being photoreactive or fluorescent [9] will be reported. Recent studies on dielectric[10] and magnetic[11] properties of co-crystalline materials based on s-PS will be also reported.

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IND-OR-01 CO_2 Capture Technology Applications to the Oil & Gas Industry

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The need to satisfy growing world demand for energy, among the emerging economies in particular, goes hand in hand with the need to tackle the risks to the climate stemming from increased production of CO_2. In the medium-long term, one of the solutions can be represented by CO_2 Capture and Storage (CCS) technology, used to geologically sequester CO_2 generated by fossil fuels, especially from large-point source emitters such as power plants, refineries, cement plants and steel mills. Typically, CCS is defined as the integrated process of gas separation at industrial plants, transportation to storage sites and injection into subsurface formations, either depleted hydrocarbon fields or saline aquifers. Here, attention will be focussed only to the CO_2 Capture step of the CCS technology. The dimensions of the Climate Change issue are such that substantial improvements are to be achieved in the technologies of CO_2 separation, thus representing an intriguing new challenge for industrial chemistry to improve processes very old in their nature. The main activities of *eni* on CO_2 Capture are briefly described in the following.

Since 2001, *eni* has been member of the international CO_2 Capture Project (CCP) consortium (www.co2captureproject.org), together with most of the oil majors. The CCP is a unique collaborative technology development program initiated in 2000 with the aim to advance development of new approaches to capture and store CO_2 and improve efficiencies of existing technologies. The overall objectives are to deliver major cost reductions for carbon capture and demonstrate geological storage is safe, measurable, and verifiable. Phase 3 of the CO_2 Capture Project began in 2009 and is continuing support of R&D work for capture technologies at multiple levels of development, from exploratory research to demonstration. Different scenarios for application have been selected: Steam production for extraction of heavy oils, Natural Gas Combined Cycle for power production, Oil refinery (capture from process heaters, fluid catalytic cracking, hydrogen plants)

New scenarios for cost analyses are being developed and are serving as the basis for comparison of the capture technologies under development. At least two next generation technologies being developed by CCP are planned for demonstration in the Phase 3: a) the regenerator of a large pilot Fluid Catalytic Cracking unit in a Brazilian refinery run by Petrobras is currently being retrofit to oxy-firing with CO_2 recycle; a demonstration test is running in 2011. b) The retrofit to oxy-firing of a commercial Once Through Steam Generator used in tar sands extraction operations in Canada is scheduled for 2012.

In addition, Eni is pursuing the development of other CO_2 capture technologies in a few selected fields and will be briefly mentioned.

IND-OR-02 BIO-ORGANICS FROM BIO-REFUSE AS SOURCE OF CHEMICALS FOR USE IN CHEMISTRY, AGRICULTURE AND ANIMAL HUSBANDRY

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Urban biowastes (UBW) have been proven source of bio-based products for many uses (www.biochemenergy.it). Indeed, soluble bio-organics (SBO) isolated from UBW processed by anaerobic and aerobic digestion have been found to have cost effective performance as auxiliaries for use in chemistry, agriculture and animal husbandry. The potential monetary value of the above SBO is estimated to span from 1 to 70 € kg^{-1} against a processing cost evaluated at 0.10-0.50 € kg^{-1}, depending on the degree of purity required by the intended application. Urban refuse are therefore viewed not as a cost, but as source of revenue. Agriculture and animal biorefuse are likely to contribute organics useful to make a wider range of finished products. A main problem to fully realize these expectations is that SBO however contain 25 % of inorganics which may affect critically the product performance in many applications. This paper reports the most recent results obtained by isolating SBO from different biomass residues and characterizing both inorganics and organics in UBW and SBO in order to understand the partition of the sourcing matter components into soluble and insoluble materials.

IND-OR-03 Hydrogen production by glycerol steam reforming with ruthenium based catalysts, effects of reaction conditions.

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Glycerol is the main byproduct of biodiesel production and it is expected to increase its availability keeping also low prices. Hydrogen production by steam reforming of glycerol/water mixtures was recently reviewed [1] and Ru based systems showed promising performances [1,2].

Catalysts based on Ru nanoparticles supported on Mg(Al)O mixed oxide, derived from hydrotalcite precursor, were tested in the steam reforming of glycerol at different reaction conditions. Namely the effects of reaction temperature and of glycerol concentration in the feed were studied. Particular care was devoted to the study of coke deposition, that is one of the main reasons of catalysts deactivation.

Ru/MG70 catalysts (Ru 0,6% and 1% wt.) were prepared by impregnation using $RuCl_3$ solution on Mg(Al)O mixed oxide, derived from Pural MG70 (Sasol) hydrotalcite-like compound calcined at 900°C. Supported Ru nanoparticles were obtained by calcinations and reduction. Catalytic tests were performed in a fixed-bed quartz reactor, T=450-650°C; feed: 10-40 wt.% glycerol/H_2O mixt. (0.06 ml min^{-1}); He carrier flow = 30 ml min^{-1}; 0.200-0,800 g catalyst (mesh 45-35).

The systems were fully characterized by CO-DRIFTS, TPR, HRTEM, Raman, TGA-DSC, etc.

Working at 550°C catalysts were stable up to 20 hours and reached excellent performances: conversion up to 100%; H_2 yield >95% and CO selectivity less than 5%. Such high stability can be ascribed to the high nanoparticles stability on Mg(Al)O supports and on the high activity in WGS and C gasification reactions that keep a clean and active catalyst surface avoiding excessive coke deposition, so preventing deactivation.

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IND-OR-04 HS- functionalized silica HMS as support for PdAu hydrodesulfurization catalysts

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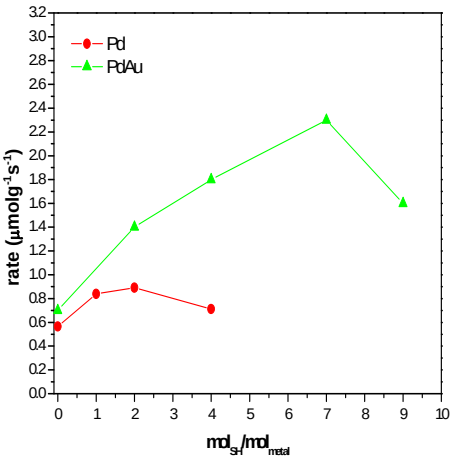
Environmental restrictions regarding the quality of the transportation fuels draw research toward more active and selective catalysts for hydrodesulfurization (HDS)[1]. As alternative to the CoMo or NiMo type of HDS catalysts, noble metal (Pd, Pt, Au) catalysts have been also investigated [2]. Moreover, ordered mesoporous silicas (MCM-41, HMS) have recently attracted much interest in hydrotreating processes due to their high surface area and controlled porosity [1,3].On the basis of a positive effect of the -SH functionalization of silica on the HDS activity of the supported CoMo catalysts [4], the investigation of similarly functionalised mesoporous silica on the hydrodesulfurization activity of the monometallic and bimetallic PdAu catalysts has been here undertaken. To this aim, mesoporous silica HMS was functionalized by suspending calcined silica in dry toluene and adding the appropriate amount of 3-mercaptopropyltrimethoxysilane (MPTMS). The mixture, refluxed for 24 h was recovered by filtration, washed several times with toluene and dried at 120°C overnight. The obtained products, functionalized with different amount of mercaptopropyl groups were labeled as HMS-xSH were x is the mol_{SH}/mol_{metals} ratio. Pd and PdAu catalysts were then prepared by deposition precipitation method using $PdCl_2$ and $HAuCl_4$ as metal precursors and urea as precipitating agent. The metal loading was 1 wt% of Pd in the monometallic Pd and 1 wt%Pd and 1wt% Au in the bimetallic samples. The samples were characterized by XPS and XRD analyses. Catalysts were tested in thiophene hydrodesulfurization (HDS). The reaction was carried out in the vapor phase using a continuous flow microreactor. An amount of 200 mg of catalyst (sieved fraction 210–430 mm), diluted with inert particles of SiC (in a weight ratio of 5:1 with respect to the catalyst) was used for each test. The samples were reduced in situ for 1h in flow of H_2 at 50 ml·min^{-1} and at 400 °C at a rate of 7 °C min^{-1} After purging with nitrogen, the HDS of thiophene was carried out at 340 °C with 5.3 vol. % thiophene in H_2 and WHSV = 7500 h^{-1}.

The reaction products were analyzed by online gas chromatography. The HDS catalytic activities of the monometallic and bimetallic series as a function of mol_{SH}/mol_{metal} ratio are given in Fig. 1. The amount of mercaptopropyl groups anchored on the support had a remarkable effect on the activity of the bimetallic catalysts. A maximum of the beneficial effect was achieved for a molar ratio mol_{SH}/ mol_{metal} = 7, therafter a decrease of the activity was observed. On the contrary a much milder effect was produced on the monometallic Pd catalysts. According to the XPS and XRD analyses, the enhancement of the activity is discussed in terms of an increase of the metal dispersion and on the structural changes of the active phase.



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IND-OR-05 Ceria-promoted Cu-based catalysts for the synthesis of methanol by CO_2 hydrogenation

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The synthesis of methanol from CO_2-rich syngas streams, produced by catalytic partial oxidation instead of energy-intensive reforming processes, would represent a decisive technological breakthrough with a remarkable improvement of the overall processes economics [1]. However, the "poor" performance of traditional methanol catalysts towards CO_2 activation [2] requires the discovery of alternative catalyst formulations [2-4]. This work is aimed at probing the effects of CeO_2 addition on the structure and CO_2-hydrogenation activity of Cu-based catalysts for methanol production. Characterization data revealed that ZnO acts as a structural promoter, while the replacement of zirconia carrier with ceria significantly depresses the extent of surface area of the Cu-ZnO system. Moreover, CO_2-hydrogenation data (Table 1) show that, in the range 453-513K, the activity pattern depends both on catalyst composition and activation atmosphere (pure or diluted hydrogen). In particular, the activation in diluted hydrogen enhances the surface functionality of ceria-promoted Cu-ZnO catalysts, understanding that higher surface methanol yields rely on the dual-site nature of the main reaction path which involves sites at metal/oxide interface.

Table 1. *CO_2 hydrogenation data (P_R, 3.0 MPa; GHSV, 8.8 NL g^{-1} h^{-1}).*

CATALYST	T_R, 453K X_{CO2} - S_{MeOH} (%)		T_R, 473K X_{CO2} - S_{MeOH} (%)		T_R, 493K X_{CO2} - S_{MeOH} (%)		T_R, 513K X_{CO2} - S_{MeOH} (%)	
	pure H_2	*diluted H_2*	*pure H_2*	*diluted H_2*	*pure H_2*	*diluted H_2*	*pure H_2*	*diluted H_2*
ZnCuZr	2.1 – 90	1.7 – 100	4.6 – 75	3.3 – 84	9.5 – 54	6.4 – 68	16.4 – 38	11.8 – 46
CeCuZr	1.1 – 100	1.0 – 99	2.1 – 71	1.9 – 76	4.7 – 58	3.4 – 62	9.4 – 39	6.8 – 42
ZnCuCeZr-1	2.9 – 97	3.2 – 92	5.7 – 88	6.4 – 82	9.9 – 74	11.4 – 65	14.7 – 57	16.9 – 51
ZnCuCeZr-2	1.7 – 100	2.2 – 93	3.6 – 80	4.8 – 86	7.1 – 65	8.6 – 74	11.3 – 46	13.3 – 56
ZnCuCe	0.6 – 100	1.6 – 100	1.8 – 87	3.6 – 89	3.5 – 77	6.0 – 79	6.4 – 62	10.7 – 59

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IND-OR-06 From waste biomass to levulinic acid, its esters and gamma-valerolactone: a high yield catalytic route to valeric biofuels

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The exploitation of waste biomass to produce electricity, biofuels and chemicals can represent a renewable energy source and a safeguard for environment. Recently we have studied some wastes as wood sawdust, paper sludge, exhausted lemon peels, tobacco chops, coffee tofferaction wastes, olive tree pruning, which are economically relevant for our country. A new process for the complete and efficient acid-catalyzed exploitation of the three components (hemicellulose, cellulose and lignin) of the above wastes has been optimized. This process allows us to convert the aqueous biomass slurry to furfural (yield up to 10 wt % with respect to dry biomass) and levulinic acid (4-oxopentanoic acid, LA, yield up to 25 wt % with respect to dry biomass) using a very dilute acid and a temperature of 100-200 °C. When the acid-catalyzed reaction is carried out in ethanol slurry, ethyl levulinate (EL) is obtained (up to 22 wt % yield).
The recovered lignin has been characterized by FT-IR, NMR and DSC: it resulted lignino-similar, with high content of functional groups and low molecular weight. These characteristics make this residue a valuable anti-oxidant and also a promising starting material for the synthesis of polymers.
Aqueous LA or EL were successively hydrogenated to γ-valerolactone (GVL) which is not only a sustainable liquid but also a valuable fuel additive and a precursor for the new platform of "valeric biofuels" which can deliver both gasoline and diesel components that are absolutely compatible with transportation fuels [1]. The bifunctional (acid and hydrogenating) performances of Ru heterogeneous catalysts and the optimization of the reactions conditions have been studied. The optimized catalytic system was recycled in successive runs and resulted completely stable. The inexpensive production of GVL directly from the biomass with an "one pot process" in water was also performed by adopting heterogeneous catalytic systems as well as very mild reaction conditions (only 5 atmospheres of hydrogen and temperatures of 50 °C are involved in the hydrogenation step).

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IND-OR-07 Optimization of the synthesis of 4'-nonafluorobutylacetophenone by metal catalysed cross-coupling reactions

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McLoughlin and Thrower[1,2] discovered the interaction between iodofluoroalkanes and iodofluoroaromatic compounds catalysed by copper in polar aprotic solvents to obtain a fluorinated organic compound having an aromatic group directly linked to a fluorinated alkyl group. This reaction was revisited by Chen and Tamborsky for bromoaromatics[3] and bromoheterocyclic[4] compounds. The results showed that the 4'-bromoacetophenone lead to the highest yield.

In this work, the synthesis of 4'-nonafluorobutylacetophenone (1) by the reaction between perfluorobutyl iodide and 4'-bromoacetophenone in the presence of N,N dimethylformamide (or dimethyl sulfoxide) as the solvent, was carried out with different transition metals as Cu^0, Cu(I), Cu(II), Fe^0, Fe(II), and Fe(III). Investigation on the effects of ligands, solvents, temperature and metal catalyst on the yields was optimized[5], with the purpose to find out the best conditions for the synthesis of the product.

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IND-OR-08 Palladium-catalysis to Dihydrodibenzoazepine Derivatives: Synthesis, Structure and Theoretical Calculations

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In the framework of our research aimed at developing efficient methods for the construction of complex molecules through a series of metal-controlled steps, starting from a pool of simple molecules [1] we have worked out a one-pot process for the synthesis of dihydrodibenzoazepines, an important class of seven-membered heterocycles with pharmacological activity [2].

The process consists of the reaction of one molecule of aryl iodide, one of a bromoaniline and one of norbornene at 105 °C in DMF under the catalytic action of palladium(0)/triarylphosphine. Several steps occur, including the initial oxidative addition of the aryl halide to palladium(0), norbornene insertion, palladacycle formation, new oxidative addition, this time involving bromoaniline, *o*-aminoaryl migration onto the norbornyl site of the palladacycle, azepine ring closure by reaction of the amino group with the palladium-bonded arene carbon [3]. All steps occur chemo- and regio-selectively and are compatible with a variety of substituents. Thus it has been possible to obtain compounds of the type reported in Figure 1 (R^1 = H, alkyl, alkoxy, R^2 = H, alkyl, Cl, carbalkoxy, R^3 = alkyl, Cl, F) in high yields.

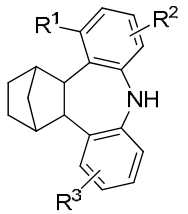

Figure 1

The structure of two members of this class (R^1 = Me, R^2, R^3 = H; R^1 = Me, R^2 = 7-Me, R^3 = H) has been determined by single-crystal X-ray diffraction [4].

Theoretical calculations indicate the critical role played by the chelating amino group in directing the reaction pathway to the seven-membered ring formation [5].

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IND-OR-09 Short Contact Time - Catalytic Partial Oxidation based technologies: recent advance in pilot- and bench-scale testing

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Eni R&D has been active in the field of Short Contact Time – Catalytic Partial Oxidation (SCT-CPO) processes for almost twenty years. The "main stream" activity is oriented to the definition and development of technologies for producing Hydrogen/Synthesis gas. However the SCT-CPO method, for its flexibility and simplicity, can be successfully applied to other fields. Among them, the production of light olefins starting from light hydrocarbons and/or naphtha, has recently re-gained attention thanks to very promising experimental results obtained with catalysts developed together with the Dipartimento di Ingegneria Chimica dell'Università di Napoli [1].

The experimental work devoted to Synthesis Gas production [2] is addressing either the fundamental principles or the technical and economical potential of the technology. Good experimental responses -achieved with peculiar technical solutions- were coupled to favourable techno-economical evaluations and promoted the progressive widening of the field of the investigations. The list of "processable" Hydrocarbons now ranges from Natural Gas (NG) to Liquefied Petroleum Gas (LPG) and Gasoils, including those characterised by high levels of unsaturated and sulphurated molecules and, lately, to other compounds with biological origin.
The defined technological solutions are grouped as follows:

Technology 1: Air Blown SCT-CPO of Gaseous Hydrocarbons and/or Light Compounds with biological origin
Technology 2: Enriched Air/Oxygen Blown SCT-CPO of Gaseous Hydrocarbons and/or Light Compounds with biological origin
Technology 3: Enriched Air/Oxygen Blown SCT-CPO of Liquid Hydrocarbons and/or Compounds with biological origin

Recently, the licence rights on a non-exclusive basis for the commercialisation of SCT-CPO based processes for H_2/Synthesis gas production from light hydrocarbons with production capacity lower than 5,000 Nm^3/h of H_2 or 7,500 Nm^3/h of syngas have been assigned to two external companies. In parallel, the development of a medium-scale demonstrative plant is progressing within the framework of an eni refinery. These activities are addressed to the utilisation of SCT-CPO for matching the variable Hydrogen demand in several contexts of oil refining operation.

This presentation will report on the current status of SCT-CPO based technologies for Synthesis gas and light olefins production with a focus on experimental results obtained, either at pilot- and bench- scale level.

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IND-OR-10 Reforming of the biomass gasification producer gas

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The gasification of lignocellulosic biomass is receiving increasing interest to produce syngas (CO + H_2), which can be further converted to substitute natural gas and via Fischer-Tropsch to liquid fuels [1]. The producer gas obtained by gasification contains CH_4, H_2, CO, CO_2, C_2-C_4, condensable hydrocarbons (tars) and some contaminants such as NH_3, HCl, H_2S and particulate (ash, alkali, soot). In order to generate a suitable syngas for chemical treatment the producer gas must be cleaned and upgraded. After the removal of the particulate by hot gas filtration, reforming or autothermal reforming processes can convert the hydrocarbons and increase the CO and H_2 content, making therefore the gas suitable for the production of biofuels by Fischer-Tropsch. The feasibility of these processes is dependent on the development of reforming catalysts active and stable in presence of the contaminants [2].

Ni- and Rh-based catalysts, commercial-type and obtained from hydrotalcite-type compounds, were studied for the reforming of the producer gas. In a first step, catalysts were tested in a laboratory rig by feeding a simulated producer gas and selected contaminants: model tar compounds (toluene and naphthalene), NH_3 and H_2S. Then, tests were performed under real conditions in a reactor placed downstream an oxygen/steam circulating fluidized bed gasifier. The effect of the biomass fuel composition and reforming temperature on the catalytic performances was studied. High temperatures (950-1050 °C) were required to achieve high hydrocarbon conversions (methane and tar) with Ni-based catalysts; whereas the presence of rhodium in the catalysts allowed to decrease the reaction temperature, even in presence of sulfur. The characterization of the used catalysts evidenced three deactivation mechanisms: sintering, chemical poisoning and fouling by physical deposition of carbon, soot or particulates.

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IND-OR-11 Ni-$CeZrO_2$ catalysts for low temperature steam reforming of methane

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The growing request for the development and diffusion of technologies based on renewable energy sources represents an important challenge for researchers working in catalysis. Steam reforming of methane (MSR) is a well known process for the production of syngas, a valuable feed for important industrial processes and for fuel cells. When the process is coupled to water gas shift reaction, after CO_2 removal hydromethane (a mixture of hydrogen and methane) can be obtained, to power hybrid automotive systems. If the temperature of the process is lowered by employing a proper catalyst, a low green-house impact fuel can be produced in solar powered plants, based on molten salt technology [1].
One of the most promising catalysts for low temperature MSR is based on Ni-Ce-ZrO_2 mixed oxide [2]. The primary difficulty associated with supported Ni catalysts is deactivation, either due to coke formation or to sintering of the metallic and support phases at high temperature [3]. CeO_2 is found to stabilize the catalyst against deactivation due to its redox behaviour and/or better dispersion of the active metal, while the addition of ZrO_2 should improve thermal resistance and the oxygen storage capacity of ceria.
In this work, a one step co-precipitation/digestion method [2] is employed to prepare a series of Ni-Ce-ZrO_2 catalysts with different Ni loading and Ce/Zr ratios. The preparation method has been optimized to obtain nanosized particles with high surface areas (75 – 180 m2/g). Structural and spectroscopic techniques (XRD, TEM, UV-Vis, FTIR) are employed to study the nature of NiO particles and their interaction with the support. The catalytic activity is tested in MSR reaction at 520 °C, varying steam to carbon ratio and spatial velocity, in order to obtain kinetic values for a possible upscale of the process. Comparison of the catalytic performances (conversion and stability) with characterization results is aimed at defining structure/properties relationships.

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IND-OR-12 ION EXCHANGER CATALYST MODIFICATION FOR REACTIONS INVOLVING LIPOPHILIC REAGENTS.

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Sulfonated poly(styrene-co-divinylbenzene) is an effective acid catalysts commonly used in several chemical processes. Conventional materials are fully or almost fully sulfonated. This makes them compatible with polar substances, but implies that lipophilic reagents can be used only when the porosity of the catalyst little (or not at all) depends on swelling or when a polar co-reagent, able to swell the catalyst, is involved and used in large excess. [1] In the latter case the combination of lipohilic and hydrophilic domains within the polymeric framework should give improved catalysts. [2] In this connection, the approaches employed sofar gave materials of limited performance or scope. [3-6] We have prepared new strongly acidic ion exchanger catalysts by partial acylation of common styrene-co-divinylbenzene polymers before sulfonation, [7] with improved catalytic performance in the esterification of stearic acid with MeOH. They are as active as conventional ion exchanger catalysts when the reaction mixture (stearic acid, alcohol, exhausted edible oil) is saturated with MeOH (20% wt), and much more active when the alcohol concentration is lowered to 5 % wt. The swelling behaviour of the acylated and conventional catalysts at relatively high and low MeOH concentrations are very similar and should equally affect them. This suggests that the better performance of the acylated ones is brought about by the presence of lipophilic adsorption domains which assist the activation of the fatty acid inside the catalyst.

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IND-OR-13 Photocatalytic Oxidative Dehydrogenation of Ethylbenzene to Styrene on Sulphated $MoO_x/\gamma\text{-}Al_2O_3$

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Styrene is one of the most important compounds in the chemical industry. It is industrially produced by catalytic dehydrogenation of ethylbenzene on iron-based catalysts. The main problems associated with the dehydrogenation process of ethylbenzene are the thermodynamic limitation, the low conversion rate, the energy demand due to the high endotermicity of the reaction, and the deactivation of catalysts by coke formation. As an alternative way, the oxidative dehydrogenation of ethylbenzene has been proposed. In most cases, the reaction temperature was above 500 °C. For this reason, the use of a photocatalytic process may be beneficial because of its mild reaction conditions that could reduce operating costs and increase selectivity. In this study sulphated $MoO_x/\gamma\text{-}Al_2O_3$ catalysts were used as photocatalysts for the oxidative dehydrogenation of ethylbenzene to styrene in gas phase. The influence of the Mo and sulphate load was investigated. Catalysts, prepared by incipient wet impregnation, were characterized by N_2 adsorption-desorption at -196°C to measure specific surface area, thermogravimetric analysis, Raman and UV-Vis spectroscopy.

A gas-solid heterogeneous photocatalytic reactor at high illumination efficiency [1] was utilized to measure the photoreactivity. It consists of a fluidized bed reactor irradiated by two arrays of UV Leds, emitting at 365 nm, positioned at its external transparent walls. The photoreactor is equipped with an electrical heater immersed within the catalytic bed to control the reaction temperature that was set at 120°C. Catalytic tests were carried out feeding N_2 stream containing an ethylbenzene concentration ranging between 1000 and 6000 ppm, with oxygen/ethylbenzene and water/ethylbenzene ratio equal to 1.5 and 1.6, respectively. The catalyst weight was 14 g diluted with 16 g of $\alpha\text{-}Al_2O_3$ or with 7 g of silica gel. Obtained results showed that it is possible to obtain styrene on MoO_x/Al_2O_3 catalysts with 100% selectivity. The molybdate surface coverage of 50 % gave the maximum photoactivity. An optimum in sulphate loading was found to be 2.4 wt%. The decreasing in catalytic activity at high sulphate load is due to lower accessibility of surface MoO_x species, decorated by sulphates when present in high amount. For all the operating conditions, no deactivation phenomena were detected.

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IND-OR-14 Towards the development of a new reactor technology for the Fischer-Tropsch synthesis

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The adoption of multitubular reactors loaded with washcoated structured catalysts having highly conductive honeycomb supports has been proposed as an alternative to conventional packed-bed reactors in order to approach the ideal plug-flow behaviour while (i) enabling isothermal operation of highly endo and exo-thermic reactions, (ii) facilitating the intraparticle mass-transfer, and (iii) limiting pressure drop.

A systematic study has been carried out in this work to assess the heat transfer characteristics of washcoated conductive structured catalysts for the Fischer-Tropsch synthesis. Following the experimental testing of 27 cpsi aluminum monoliths washcoated with a layer of a representative Co/γ-Al_2O_3 catalyst reported in a previous paper [1], in this work we have simulated the performances of a technical tubular reactor loaded with such catalysts by means a pseudo-continuous, heterogeneous, two-dimensional non-adiabatic numerical model. Lumped CO conversion kinetics, developed for the adopted Co-based FT catalyst, have been adopted. Heat generation by the FTS over the washcoated walls of the monolith channels, heat conduction along the longitudinal and the radial dimensions of the monolith, and heat exchange both with the gas phase flowing in the monolith channels and with the external coolant have been accounted for in the model.

Simulation results indicate that heat conduction in the aluminum support of the catalyst can be exploited to remove effectively the heat generated by the strongly exothermic FT reaction. Flat axial and radial temperature profiles have been found along the catalytic bed, showing the unique ability of the adopted structured catalysts to manage the heat removal issue and to guarantee an excellent temperature control without the need of recycling a fraction of the liquid reaction products. Moreover, due to the high void fraction of the structured support and the laminar flow in the straight washcoated channels, pressure drop has been found negligible at all the investigated process conditions.

These results make highly conductive extruded honeycomb monoliths, washcoated with a Co-based FT catalyst, very promising for the application at the industrial scale, in particular when adopting supports with high cell densities and catalysts with high activity. In fact, the excellent properties of such catalysts could afford new opportunities for intensification of existing processes in externally cooled multitubular fixed-bed reactors, where operation is limited by the onset of severe hot-spots, so that significant amounts of liquid products (at the process conditions) have to be recycled to the reactor to remove the reaction heat. Near-isothermal and isobaric behaviour of tubular FT reactors at high conversions per pass without the need of a liquid cofeed is in fact an interesting perspective.

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IND-OR-15 CATALYTIC LIQUID- AND GAS-PHASE OXIDATIONS FOR THE SYNTHESIS OF INTERMEDIATES AND SPECIALTY CHEMICALS: SOME EXAMPLES OF INDUSTRIAL RELEVANCE

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Nowadays, it is clear that the target of creating a sustainable future for the next generations requires to re-think the industrial application of chemistry. In this context, oxidation reactions play a major role, being the tool for the production of huge quantities of chemical intermediates and specialties.

Actually, in order to implement all these ideas into real projects, the development of more efficient reactions is one primary target. Yield, selectivity and space-time yield are considered the right metrics for evaluating the reaction efficiency[1].

Three reactions that are emblematic of the new approaches used in the chemical industry will be discussed.

The first one is a new process aimed at a more sustainable production of menadione (vitamin K3). The "greener" approach includes the use of hydrogen peroxide in place of chromate (from a stoichiometric oxidation to a catalytic oxidation), and the transformation of 2-methyl-1-naphthol using Nb_2O_5-SiO_2 catalysts prepared with the sol-gel technique. The study of the reaction mechanism was fundamental to get indications about the best operative conditions, and improve the selectivity to menadione [2].

In the second part, I explored the direct oxidation of benzene to phenol with hydrogen peroxide. Titanium silicalite-1 (TS-1) is the catalyst chosen for this reaction. Comparing the reactivity results obtained with some TS-1 samples having different chemical-physical properties, and analyzing in detail the effect of the more important reaction parameters, we could formulate some hypothesis concerning the reaction network and mechanism [3].

Finally, the last part deals with the study of a new process for the valorisation of glycerol by means of transformation of glycerol into acrylic acid, with the intermediate formation of acrolein; the latter can be obtained by dehydration of glycerol, and then can be oxidized into acrylic acid[4].

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IND-OR-16 A New Water Soluble Cationic Pd(II)-Allyl Complex Containing Sulfonate "Click" type Ligand

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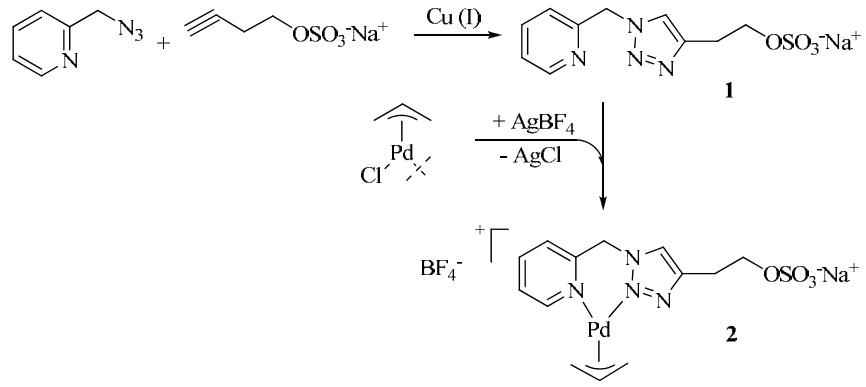
Nowadays, the chemistry that takes place in water receives considerable attention for environmental, economic and safety reasons, and also because it allows for unique reactivities not usually observed in organic solvents [1]. The use of the aqueous medium for metal-mediated synthesis has attracted large interest and there is a increasing demand of water-soluble ligands and metal complexes [2].

An intriguing and efficient method for the synthesis of ligands is the copper catalyzed [3+2] azide-alkyne Huisgen reaction, so called "click chemistry". Recently we have been involved in this topic [3]. We wish to report here the synthesis of a novel water soluble chelating pyridyl-triazole sulfonate ligand **1** and of the water soluble cationic palladium allyl complex **2** (see Scheme 1).



Scheme 1. Synthesis of ligand **1** and of complex **2**.

NMR investigations in D_2O confirm the chelating behaviour of ligand **1** and reveals that **2** is stable up to 90 °C.

Preliminary investigations demonstrate that **2** is an promising catalyst in cross coupling reactions carried out in aqueous media.

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IND-OR-17 Synthesis and self-assembly of biodegradable poly(ε-caprolactone) /poly(ethyleneoxyde) "Y-shaped"copolymer for pharmaceutical applications by click chemistry and R.O.P

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Recently, hydrophobic biodegradable polyesters such as poly(ε–caprolactone) (PCL) and poly(lactide) and their amphiphilic block copolymers with poly(ethyleneoxyde) (PEO) have attracted much attention of pharmaceutical and biomedical applications [1]. These copolymers, due to their excellent biocompatibility and biodegradability, and the remarkable ability to self-assembly in aqueous solution with formation of "core (PCL)-shell(PEO)", micellar structures have been investigated as nanocarriers for controlled and targeted release of various bioactive molecules [2]. These nanocarriers are caracterized by very high thermodynamic stability, small size and biomimetic "stealth" properties provided by the crown of PEO. This allows a high residence time in the bloodstream necessary to the crossing of the blood vessels (extravasation) in tissues with high vascular permeability such as tumors or inflamed tissue (EPR effect). This work was aimed at the synthesis and characterization of copolymers "Y-shaped"wf-assembly in water. Chain-end bifunctional PCL segments were obtained by ROP of ε–caprolactone initiated by bis-azido alcohol. The coupling of the PCL with two PEO segments having a terminal alkyne group was accomplished by 1.3 Huisgen cycloaddition catalyzed by Cu (I).The obtained "Y-shaped" copolymers were characterized by NMR, DSC, DLS WAXS SEC and inherent viscosity measurements, showing high structural regularity and monomodal molecular weight distribution. The critical micelle concentration, CMC, was determined by fluorescence spectroscopy using pyrene as probe.. Different crystalline PCL and PEO phase were evidenced in bulk by DSC and WAXS. Their aggregation in aqueous solution produced micellar structures with hydrodynamic diameter in the 50-200 nm range and very low CMC values. Such systems are good candidate as biomimetic nanocarriers of lipofilic drugs.

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IND-OR-18 Synthesis and Catalytic Applications of Novel Thiolated and Sulfonated Polymers Resulting by Functionalization of Multiblock Syndiotactic Polystyrene-*co*-1,4-*cis*-Polybutadiene.

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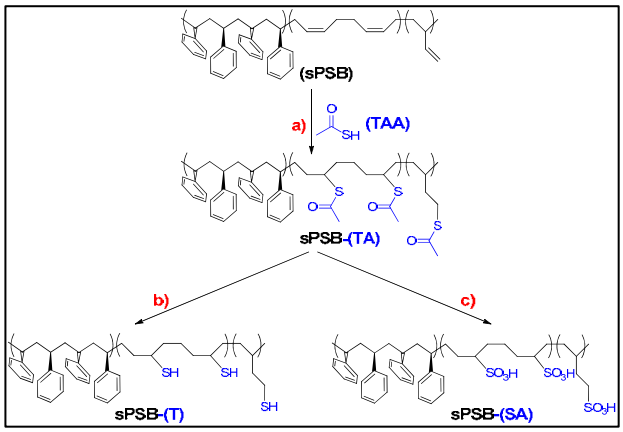
Hydrocarbon polymers carrying side chain functional groups are attractive materials because of their specific chemical reactivity or physico-chemical properties.
Their direct synthesis by copolymerization of suitable monomers is often impracticable because of incompatibility of the transition metal catalysts with the polar monomers; thus post-functionalization is often required to yield these polymer products of interest.
In this work the controlled radical thioacetylation of polybutadiene segments in multiblock copolymers syndiotactic polystyrene-*co*-1,4-*cis*-polybutadiene (sPSB) is described. sPSB are semicrystalline polymers (T_g = 100°C, T_m = 250°C) which exhibit, when shaped as thin film by spin coating, a phase separated morphology, ranging from irregular hard lamellae of sPS in PB to spheres of PB embedded into the sPS phase[1]. The selective functionalization of the PB domains by thioacetylation followed by thioester cleavage lead to thiol functionalized sPSB (sPSB-T). The direct thioester oxidation by *in situ* synthesized performic acid leads to sulfonated sPSB (sPSB-SA) in quantitative yield.
sPSB-SAs with high degree of sulfonation were successful tested as strongly acidic catalysts in esterification reactions.



Scheme 1. Thioacetylation, thiolation and sulfonation of sPSB copolymers.

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IND-OR-19 Dehydrogenation reaction of Ethanol to Ethyl Acetate in one step reaction by using copper chromite based catalysts.

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In the last years the worldwide interest to the use of biomass, as raw materials to obtain energy, is growing as a key technology towards sustainable development. In particular the bio-ethanol is a renewable source available to produce both bio-fuels and commodity chemicals of great interest such as ethylene, acetaldehyde and ethyl acetate. The bio-ethanol based processes have shown great advantages by the environmental and economics viewpoints [1]. In particular the ethyl acetate production by one step ethanol dehydrogenation reaction is a promising alternative process to the classical one that use acetic acid [2]. Therefore our research has been focused on the ethanol dehydrogenation to ethyl acetate in one step reaction using copper based catalysts. In the present paper, we have studied the behaviors of three different commercial catalysts: (i) a $CuO/ZnO/Al_2O_3$ catalyst (BASF-K-310) (ii) a $CuO/CuCr_2O_4$ catalyst (Sud Chemie T-4466) (iii) and a $CuO/Cu/CuCr_2O_4/Al_2O_3/BaCrO_4$ pre-reduced catalyst (BASF Cu-1234-1/16-3F).

The kinetic runs have been performed in a stainless steel tubular packed bed reactor (i.d. 1.8 cm, length 30 cm) by changing the temperature in the range 200-260°C and the pressure from 10 to 30 bars. The best catalytic results, in terms of activity, selectivity and thermal stability, have been obtained with a pre-reduced commercial copper chromite catalyst (BASF Cu-1234) supported on alumina and containing $BaCrO_4$ as promoter. The best results obtained for this catalyst, by operating at 220-240°C, 20 bars and 98 (grams hour/mol) of ethanol contact time, were 65% of conversion with 98-99 % of selectivity to ethyl acetate. One of the advantage of the examined process is the possibility to produce as main co-product pure hydrogen, a promising future energy vector. A depth study of the structural and chemical properties of the catalysts, realized with the common characterization techniques, has been investigated, with the aim to correlate them to their surprising results of activity and selectivity to ethyl acetate. In particular a very interesting study of the surface and structural has been realized using very sophisticated techniques such as the EXAFS, XPS and DRIFT measure. The promising results should be the base for the development of an industrial plant to produce ethyl acetate in a very simple and economic way [3].

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IND-OR-20 Ni based catalyst for Ethanol Steam reforming (ESR)

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ESR seems to be a promising way for the production of H_2 starting from a renewable source, provided that ethanol is produced from bio-mass (bio-ethanol). Verykios et al. studied H_2 production by SR of bioethanol, focusing on Ni as active phase loaded on different supports [1] or on supported noble metals [2]. The key issue was to reduce coke formation and to lower the reaction temperature. Other investigations on low temperature SR were carried out by Llorca et al. [3,4], using Co-based catalysts in microreactors.
In the present work, two different series of Ni-based catalysts were synthesized by Flame-pyrolysis [5] and tested for the low temperature ESR ($\leq 500°C$). TiO_2 and La_2O_3 were chosen as supports and the Ni loading was 5-15 wt% for each set of samples. Activity test were made focused the attention on H_2 productivity, CO/CO_2 ratio and the formation of coke. Comparing the activity of catalysts based on TiO_2 and La_2O_3 we found that the best support was La_2O_3 and that the catalytic performance improved as the content of Ni increased.
Therefore, a $LaNiO_3$ (Ni ca. 36 wt%) catalyst was tested, showing the highest H_2 productivity, with a low CO/CO_2 ratio and above all a very good resistance towards deactivation.
Conversion of ethanol was around 90% at 500°C, with a stable H_2 productivity and selectivity over 24 h-on-stream. The CO/CO_2 ratio was around 0.4 and it was stable for all the duration of the test. Even reducing 4 times the contact time, ethanol conversion was still around 80% after 24 h-on-stream with an increase of H_2 selectivity at the expenses of CH_4 as the conversion decreased.
Future experiments are planned to check the activity of this catalyst under different experimental conditions and to improve the catalytic performance using some metals as doping agent.

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IND-OR-21 TUNGSTEN-VANADIUM MIXED OXIDES FOR THE OXIDEHYDRATION OF GLYCEROL INTO ACRYLIC ACID

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Glycerol is considered one of the Bio-based Building Blocks (B^3) with the greater potential for the implementation of the biorefinery concept into practice.[1] One of the most studied reaction is the transformation of glycerol into acrolein,[2] whereas much less attention has been given to its direct transformation into acrylic acid. The reaction formally includes a first dehydrative step into acrolein, requiring Brønsted-type acidity, and a second selective oxidation step of acrolein into acrylic acid. The approach of a single bifunctional catalyst is aimed at combine several chemical steps into a single catalyzed transformation ("one-pot" and "cascade" reactions).

In the present work we report about an investigation of the properties of a bifunctional W-V-O system (as V-containing WO_x hexagonal bronzes), with the aim of understanding which are the key chemical-physical features needed for the direct transformation of glycerol into acrylic acid. We carried out preliminary experiments aimed at studying the acid-type behavior of WO_3 in the dehydration of glycerol into acrolein; tests were carried feeding also oxygen to reduce considerably the rate of catalyst deactivation due to heavy compounds accumulation on the catalyst surface, finally leading to coke. However, negligible selective oxidation properties were found, because of the absence of V ions. The catalyst was very active in glycerol dehydration, with maximum selectivity to acrolein of 50%, major by-products being heavy compounds and acetaldehyde.

The introduction of V did not increase the activity of the catalyst but the distribution of products changed considerably. Acrylic acid formed with 25% selectivity at 320°C; however, the increase of temperature led to a progressive decline of selectivity to the acid. CO and CO_2 were the major products in the entire range of temperature considered. Experiments made by variation of contact time demonstrated that the only primary products were acrolein and acetaldehyde; the two compounds, however, underwent a consecutive transformation into the secondary products, acrylic acid and acetic acid. The atomic ratio between W and V remarkably affected the catalytic behavior.

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IND-OR-22 Effect of water on NO decomposition over Cu-ZSM5 based catalysts

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The catalytic decomposition of NO into N_2 and O_2 represents the ideal process to remove nitrogen oxides in the presence of oxygen. Cu-exchanged ZSM5 zeolite is the most promising catalyst for this process and, although several limitations hinder practical applications, it was widely investigated to understand its unique behaviour of this zeolite [1,2]. One of the main drawbacks is the presence of water vapour in the feed which causes deactivation generally associated to copper shifting to inactive positions. Rare earth ions addition was reported to be effective to partially prevent catalyst deactivation [3].
In this study the effect of water vapour on the adsorption and decomposition of NO was studied by conducting adsorption, TPD and NO decomposition tests on both pre-reduced Cu-ZSM5 and LaCu-ZSM5 catalysts. The adsorption experiments were carried out at 125°C in the presence or in the absence of H_2O in the NO/He feed mixture. The original catalytic activity towards NO decomposition is totally recovered when water, previously adsorbed at low temperature, is desorbed before starting the reaction at 450°C. This result rules out the hypothesis that water could deactivate the catalyst even at low temperature. Nevertheless, the co-adsorption of water dramatically decreases the amount of adsorbed NO at 125°C under dry conditions. The addition of lanthanum to a Cu-ZSM5 catalyst increased the amount of NO adsorbed in the absence of water and significantly limits the decrease of NO adsorption in the presence of water. TPD experiments carried out after NO adsorption showed that the addition of lanthanum promotes the formation of nitrates which are considered as reaction intermediates in the NO decomposition [4].

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IND-OR-23 Sulfonic Acid Resin: an Useful Support of Palladium for the Direct Synthesis of H_2O_2

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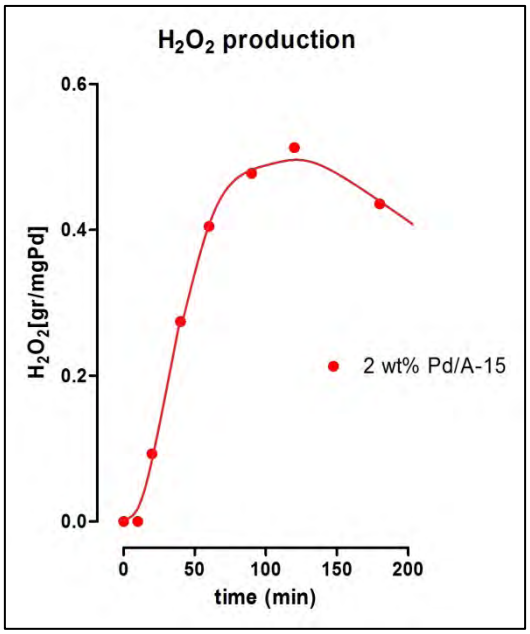
Hydrogen peroxide is a versatile and environmental friendly oxidizing agent. Currently, H_2O_2 is produced on large scale preferentially by the anthraquinone auto-oxidation process which is associated with considerable consumption of energy. The direct synthesis of H_2O_2 from H_2/O_2 could represent a viable alternative.

It's known that one of the most active metals for the synthesis is the Pd and it's important to find the best way to disperse it on a support able to enhance the performance in terms of productivity and selectivity. Acid polymeric resins can be considered a valid support [1] because they don't promote the hydrogen peroxide decomposition. In this work the commercial acid resin Amberlyst 15 was tested for the synthesis of hydrogen peroxide. The catalysts have been prepared by ionic exchange method mixing Amberlyst powder with an aqueos solution of palladium cloride.



The synthesis was carried out in a stainless steal autoclave at room temperature using CO_2 expanded methanol as solvent [2] at 30 bar of total pressure.

The catalytic activity is comparable with the most active catalysts reported in literature and moreover the leaching of palladium in reaction solution is less than 2%.

TEM analysis shows that the distribution of particles is homogenous and the average diameter is almost 15 nm.

The results will be presented in comparison with other catalytic systems of palladium based on oxides and carbon nanotubes.

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IND-OR-24 Effect of the support on Ni catalytic performances in glycerol steam reforming

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In the last years, the use of hydrogen as new energy vector has been widely encouraged, because it is clean and carbon-free [1]. Nevertheless, an effective solution of environmental problems such as the greenhouse effect and the global warming, as well as the decrease of the dependence on fossil fuels, requires the use of renewable sources. In this context glycerol, the main by-product in biodiesel production, has emerged as a promising source of hydrogen, because of its high hydrogen content and renewability, safeness and non toxicity [2].

Several catalysts have been proposed for glycerol steam reforming. In this work we report the catalytic performances of Ni-based catalysts at two different reaction temperatures. Moreover, the effect of the support (*i. e.* TiO_2, SBA-15 and ZrO_2) on the selectivity to hydrogen was studied.

TiO_2 and ZrO_2 were synthesized by a conventional precipitation method [3], whereas SBA-15 was prepared through a template synthesis [4]. Catalysts were prepared by incipient wetness impregnation of the supports with an aqueous solution of the Ni precursor in order to obtain a 10 wt% Ni loading and they were finally calcined. The physico-chemical properties of the catalysts were determined by nitrogen physisorption analysis (BET), temperature programmed reduction (TPR) and high resolution transmission electron microscopy (HR-TEM). The activity tests were carried out in a fixed bed tubular quartz reactor at atmospheric pressure at two different temperatures (500°C and 650°C), after reduction of the samples in H_2 flow for 1 hour at either 500 or 700°C respectively. A water/glycerol solution was fed (10 wt% solution of glycerol in water) at the constant flow rate of 0.06 mL/min. Data were collected up to 20 hours on each sample.

The Ni/TiO_2 sample exhibits negligible activity at 650°C because of the collapse of the support. Concerning Ni/SBA-15, our results indicate the insufficient hydrothermal resistance of the support, which leads to the progressive deactivation of the catalyst. However this support is able to stabilize the active phase in a rather efficient way, thus preventing Ni sintering. Ni/ZrO_2 exhibits the best performances: a stable glycerol conversion of ~72% and a hydrogen yield of ~65% were obtained. This is due to the almost full preservation of the structure of the zirconia support even after 20 h in the SR conditions; moreover, also the dispersion of the Ni active phase remained unchanged.

The different behaviour of the three catalysts can be then ascribed (i) to the chemical, thermal and mechanical resistance of the support in the reaction conditions and (ii) to the intensity of the interactions between the support and the active phase, which affects in particular the stability of the Ni nanoparticles. Our results highlight the importance of the nature of the support, which plays a key role in designing the catalytic performance.

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IND-OR-25 A Photomodulable organometallic catalyst

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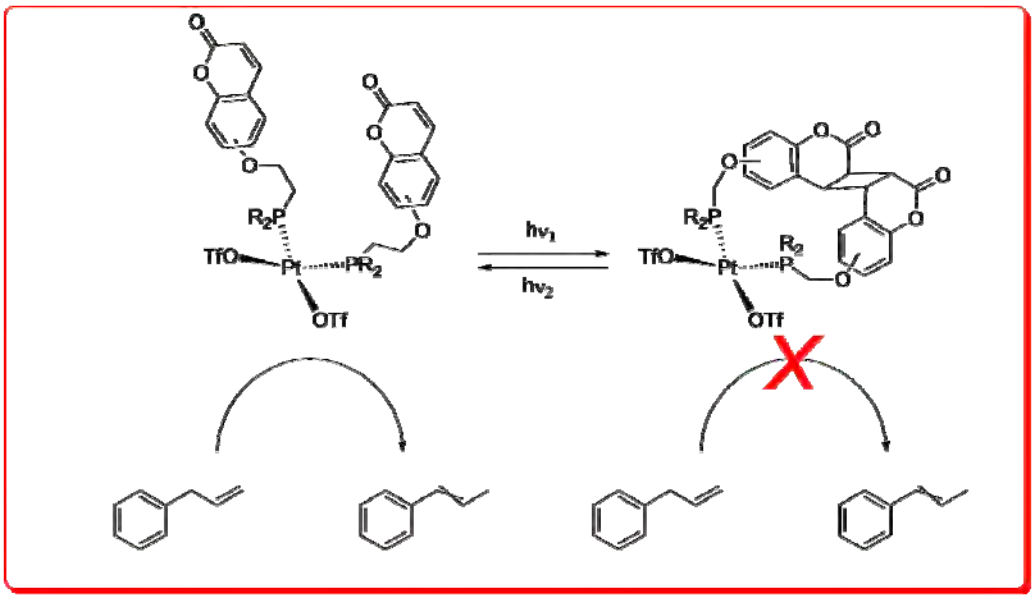
In homogeneous catalysis proper functionalization of a metal center with an appropriate ligand system often represents the most rewarding strategy to achieve the best performance, in terms of activity, selectivity and sometimes recycle. Alternatively the performance of a homogeneous catalyst can be modulated by means of interaction with external stimuli, mimicking what occurs in Nature where the activity of enzymes is triggered on and off as a function of the request of the organism. A possible approach exploits supramolecular interactions (*host-guest*) between the catalytic species and another chemical entity which interact as a second sphere ligand.[1] In this case the restoration of the original activity requires the addition of a third chemical species. A more simple system can be obtained if considering the light as effector in catalysis.[2] The preparation of an organometallic complex bearing a molecular tag that undergoes a photochemical reaction could deliver a new generation of homogeneous catalysts whose activity, selectivity and recycle properties can be tailored by employing an appropriate light source.[3]

In the present contribution are presented the synthesis, the light induced behavior and preliminary results in homogeneous catalysis of a series of new generation soft Lewis acid Pt(II) complexes bearing a coumarinic moiety in the phosphane ligand. Such species undergo reversible 2+2 photo-cycloaddition if irradiated at the proper wavelength changing both their steric and geometrical properties. One of these systems demonstrated a high catalytic activity difference between its light un-reacted and reacted forms in the alkene isomerization reaction.



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IND-OR-26 Screening of Pt-based bimetallic catalysts for the Ethanol Steam Reforming reaction

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The PEM fuel cells fuelled by pure H_2 are the leading candidate for various stationary and mobile applications. In order to ensure a sustainable power supply, ethanol has attracted some attention as a source for H_2 production, with the potential to replace fossil fuels, responsible for environmental problems. The steam reforming of bio-ethanol (BESR) may be considered more attractive since it is renewable, easy to store, safer to handle and transport and is produced from biomass, without net addition of carbon dioxide to the atmosphere. Above all, it is directly usable without water distillation since steam is necessary as a reactant. The involved reaction is strongly endothermic then favoured at high temperature, but to perform BESR reaction directly at low temperatures can favour CO minimization by promoting the CO-WGS reaction. It is important to know that in BESR reaction, the catalyst role is very crucial due to its strong tendency to fast deactivation linked to coke and by-products formation. [1,2,3]

In this work, the performances of CeO_2 supported-bimetallic Pt-Ni and Pt-Co catalysts for low temperature BESR reaction was investigated in a lab-scale plant, in very severe conditions in terms of ethanol concentration and steam to carbon ratio. The feed mixture that simulate the raw bioethanol is properly fed thanks to several optimizations of the feed system. An on line FT-IR multigas analyzer continuously and simultaneously monitors the gas-phase products distribution at the reactor outlet, in order to verify the carbon, hydrogen and oxygen mass balance and the by-products presence.

Preliminary results showed the effect of preparation method on the catalyst performances at different values of main operative parameters such as dilution ratio, temperature, water-to-ethanol molar ratio and GHSV. In terms of catalytic activity and agreement with equilibrium calculations, the Pt-Ni/CeO_2 catalyst prepared through impregnation seems to be promising for the low temperature BESR reaction, yet at low contact time values. Anyway, a deep investigation of deactivation and coke formation tendency together with the evaluation of the kinetic parameters will be crucial to select the best catalyst for the process. Based on preliminar economic evaluation, the process appears economically feasible.

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IND-OR-27 Metal-Binding Polysaccharides: New Bio-Generated Nanostructured Catalysts

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Bio-generated metal-binding polysaccharides may be novel sustainable materials with interesting catalytic properties for many synthetic applications and for supporting environment remediation and with potential application in medicine and as nutraceutical supplement of oligo metals. In this context we are currently investigating the preparation and uses of different metal ions and metal (0) species, such as for example iron, palladium, silver, gold, ruthenium, platinum and nickel, bound to an exopolysaccharide (EPS). These metal-polysaccharides (Me-EPS) are directly produced by a *Klebsiella oxytoca* BAS-10 during fermentation in the presence of suitable metal salts under anaerobic conditions, and/or by a following reductive step with hydrogen. Gel or semi-crystalline metal-binding products may be easily recovered and characterized. An eptameric unit with 4 α-rhamnose, 2 β-glucuronic acids and 1 β-galactose is repeated to form long polysaccharide molecules of several million Dalton; metal species should be located mostly in the proximity of the two glucuronic acids molecules. Very recently, Fe-EPS has been used as fine catalyst in oxidation reactions with 35% H_2O_2 to transform phenol into a mixture of catechol and hydroquinone [1]. At the moment we are studying the catalytic activity of the species Pd-EPS in the aqueous biphasic hydrogenation of some representative compounds as styrene, benzaldehyde and some (E) α,β–unsaturated aldehydes as 2-methyl-3-phenyl-propenal, 3-(1,3-benzodioxol-5-yil)-2-methyl-propenal [2] and 2-methyl-3-[5-(2-isopropyl)-thiophen-2-yil)]-propenal, these two last substrates being precursors of the valuable fragrances Helional® [3, 4] and Lioral® [5], respectively. Preliminary results showed that the catalytic system was very active and selective, working under very mild reaction conditions, and its activity was maintained practically unchanged in some recycle experiments.

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IND-OR-28 Impact of sulphur poisoning during the partial oxidation of methane on Rh-based structured catalysts

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The production of syngas via the catalytic partial oxidation (CPO) of methane is an attractive and feasible alternative to steam reforming reaction in the utilisation of the world's abundant natural gas reserves. [1-2]. Rh-based catalysts have shown the highest activity and selectivity to syngas in the CPO of several hydrocarbons from methane up to diesel [1]. However, the presence of sulphur bearing compounds naturally occurring in the fuel, or added as odorants to pipe-line natural gas (~up to 10 ppm), can have a detrimental effect on the CPO activity.
Accordingly, we set out to investigate the effects of sulphur addition during the CPO of methane at short contact times and self sustained high temperatures over Rh catalysts supported on stabilized aluminas (by La, Si, P) and coated on honeycomb monoliths. Furthermore we studied the enhancement of the sulphur tolerance of Rh-based catalyst by partially substituting Rh with either Pt or Pd, which will be highly economical due to high cost of Rh metal.

The catalysts were fully characterized by BET, SEM-EDS, H_2-TPR, SO_2-TPD and in situ DRIFTS of adsorbed CO, which was used to study changes on the surface state of Rh before and after exposures to sulphur at conditions representative of actual CPO operation.
Results of CPO light-off, steady state and transient operation confirmed that Rh is always the most active and selective element for syngas production from methane in sulphur free conditions, due to its unique ability to catalyze the steam reforming reaction. However, sulphur reversibly inhibits the steam reforming, reducing methane conversion and yields to syngas (mainly H_2), whilst increasing the catalyst operating temperature (Fig.1). Sulphur inhibition occurs by preferential adsorption on smaller, well dispersed Rh crystallites whilst the larger metallic Rh aggregates are mostly unaffected.

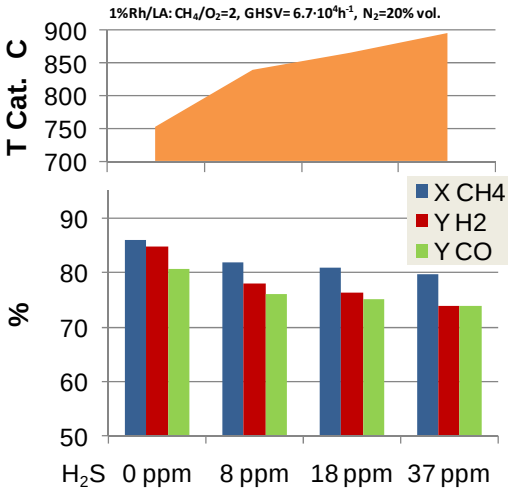

Figure 1.

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IND-OR-29 Biogas dry reforming over bimetallic Ni-Cu/CGO catalysts suitable for SOFCs applications

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Biogas represents an attractive fuel for fuel cells applications. Compared to natural gas, it is considered a renewable source containing a large fraction of CO_2. It could be directly fed into SOFCs under internal reforming conditions to produce H_2-rich fuel for the electrochemical reaction at the anode side [1], but, in presence of a typical biogas composition (CH_4:CO_2=6:4), conventional Ni-based anode materials are deactivated by coke formation [2]. On this account, due to the poor catalytic activity of Cu towards the C-C bond formation, the development of effective and stable bimetallic Ni-Cu catalysts should mitigate the carbon deposition [3].

In this work, several NiCu alloy (70wt.%)/CGO ($Ce_{0.8}Gd_{0.2}O_{1.9}$) (30 wt.%) catalysts have been investigated in terms of activity and stability in dry reforming of a simulated biogas mixture at temperature lower than 800°C. The reaction was carried out in a fixed bed reactor operating at atmospheric pressure. The effects of preparation method, calcination and reduction temperature on the Ni-Cu alloy formation have been probed. Besides catalysts activity, product distribution and coke formation have been also evaluated as a function of fed mixture composition. Irrespective of the preparation route, NiCu/CGO catalysts are active in dry reforming at T_R as low as 650°C. As the temperature increases, CO_2 and CH_4 conversion increases up to ~70% at 800°C (*GHSV, 6000 h^{-1}; CO_2/CH_4=1)*. CO_2/CH_4 ratio strongly affects the conversion rate (Fig. 1); by increasing CO_2 content in biogas, H_2/CO ratio slightly decreases but carbon doesn't form. This is an interesting result which will be adequately discussed.

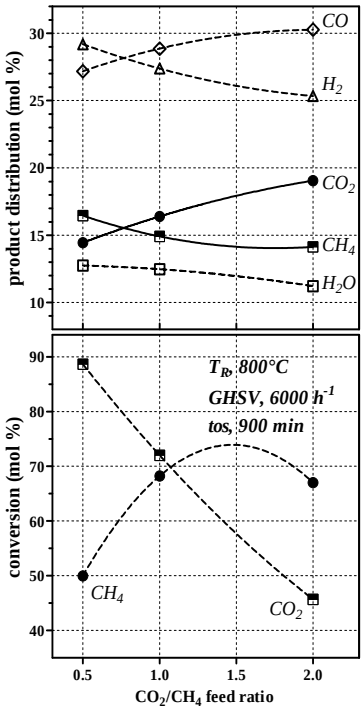

Figure 1.

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IND-OR-30 The reactivity of spinel ferrites in the two-step methanol reforming

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Catalytic steam-reforming (SR) is an option that can be used for the transformation of hydrocarbons and bioalcohols into hydrogen. Because of the fascinating challenge of obtaining an inherent separation of hydrogen from the C-containing products, during last years various alternative approaches to conventional SR + WGS have been investigated. In the so-called chemical-loop approach, the SR reaction is decoupled into two spatially and temporarily separated steps: during the first step a reductant (usually methane) is first contacted with a metal oxide, which oxidizes the former into carbon oxides and water [1]. The reduced metal oxide is then reoxidized with water, to produce hydrogen and restore the original oxidation state and the O^{2-} content of the metal oxide.

We investigated the feasibility of a two-step cycle approach for the catalytic production of hydrogen from methanol and water, using different ferrite-type oxide as the electrons/O^{2-} carrier. Motivation for this research was the development of a process aimed at the production of hydrogen starting from alcohols (in the present case methanol, in perspective bioethanol), and to investigate the structural changes occurring in the spinel mixed oxide during the reduction and oxidation steps.

The study was focused on the characterization of the solid material and the interpretation of the mechanism of the reduction step both from the result of the catalytic tests and from characterization of the used materials (Mossbauer, XRD, XPS). Finally the attention was focused on the reproducibility of the cycle: for this purpose multiple cycles were performed on the different ferrites.

Sperimentally, the fresh spinel was firstly reduced with methanol at different temperatures (first step of the cycle); products were CO, CO_2, CH_4, H_2O, and H_2. The relative amount of each product continuously changed because the reduction grade of the solid material is continuously growing up (from the oxidized fresh material to the completely reduced one). An important aspect of this study is the accumulation of coke, which was formed from the very beginning of the reaction time. The activity and the distribution of products, especially during the initial period of the reaction time, were affected by the morphologic and the chemical features of the spinel.

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IND-OR-31 Catalysts for H_2S abatement from biogas to feed MCFC

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One of the most interesting application of biogas is linked to the energy production by MCFC.

The main problem of biogas application in energy production by fuel cells is due to the presence of the sulphur compounds, usually at level of hundred of ppm, that represents a serious poisoning problem of the cells anode and electrolyte.

For this reasons, it is very important to reduce the H_2S concentrations at values about 1-5 ppm.

In this regard, a very effective and promising solution is represented by the catalytic reaction of the selective partial oxidation of H_2S to sulphur and water performed at very low temperatures (50-250°C), where, any significant thermodynamic limitations are showed. This problem maybe solved if an active and selective catalyst is allowable.

The aim of this work is to prepare and characterize new catalysts, for the selective for the low temperature H_2S oxidation to sulphur.

In a previous work different catalysts[1] (activated carbon, mixed metal oxides) were investigated in the reaction of H_2S oxidation to sulphur. Preliminary results showed that the mixed metal oxide performs better than activated carbon in terms of both catalytic activity and selectivity.

In this work vanadium based catalysts supported on ceria, titania, alumina and copper ferrite was prepared by wet impregnation method. The samples were compared in terms of H_2S and O_2 conversion, SO_2 selectivity and durability in the range of temperature of 50-250°C.

The most interesting catalysts were V_2O_5/CeO_2 and $V_2O_5/CuFe_2O_4$ that showed very high H_2S conversion, higher than 95% and respectively a SO_2 selectivity of 4% and 20%.

On this promising samples a deeper study of catalytic performances were performed by investigating the influence of the O_2/H_2S molar feed ratio, H_2S concentrations, and space velocity, in order to obtain preliminary kinetic data that are fundamental importance to the correct design of a catalytic reactor for the biogas clean-up to feed MCFC.

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IND-OR-32 Propene epoxidation on heterogeneous copper catalysts

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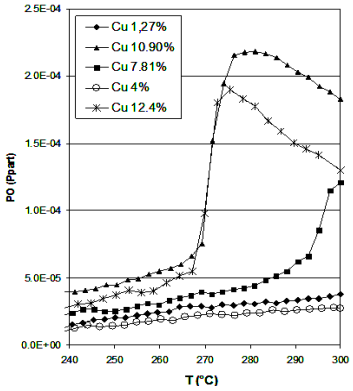
The industrial synthesis of propylene epoxide (PO) is one of the most demanding processes in term of energy requirement. Very high selectivity was observed in the direct epoxidation of propene over Au/TiO_2 and Cu/SiO_2 catalysts and pure Cu (111) facets were found to be very active in epoxidation of styrene [1,2,3]. Here we report our results on the epoxidation of propene on supported Cu catalysts (Cu/SiO_2-Al_2O_3, Cu/SiO_2) prepared by chemisorption-hydrolysis method (CH). The reaction was carried out in fixed-bed reactor with He, C_3H_6 and O_2 and products were analyzed by mass spectroscopy.

In our work we observed a significant activity only on reduced catalysts with high metallic surface area, in contrast with the unreduced ones. This is particularly evident on Cu/SiO_2-Al_2O_3 catalysts (Fig. 1). Only unreducible Cu(I) is formed on for 1-5 wt% of Cu, but to higher loading also a well reducible CuO phase is obtained[4], leading to high catalytic activity. Best activity is showed by reduced Cu/SiO_2: on SiO_2 only reducible Cu is formed as shown by EXAFS-XANES analysis. The FT-IR spectra of CO on reduced Cu/SiO_2 B shows the presence of several bands attributed to a well formed Cu crystallite: the catalyst with high Cu content (15 wt%) exposes in particular (111), unlike 9 wt% Cu catalyst. As a matter of fact 15 wt% Cu/SiO_2 B achieves higher partial pressure of PO. From our results we can say that CH method enables to obtain very small Cu particles also with higher loading compared with other preparation methods, allowing one to increase productivity of the catalysts.



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IND-OR-33 A Biphasic Kinetic Approach to Biodiesel Production

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Biodiesel is normally obtained by transesterification reaction of tri-glycerides (vegetable oils) with methanol in the presence of KOH, NaOH or related alkoxides as catalysts. The reaction is normally performed in stirred tank reactors requiring at least 1-2 hours of reaction time. As the reactants are immiscible the reaction rate, in these types of reactors, is strongly affected by mass transfer limitation. In order to intensify the transesterification process (PI) and to project opportunely a continuous reactor, a detailed study on both kinetics and mass transfer of the reaction still needs to be deepened. Although a lot of studies have been performed about the kinetics of this reaction [1-3], no publication can be found in the literature about a biphasic kinetic approach. Moreover, all the kinetic models developed till now are pseudo-monophasic, i.e., consider the reaction occurring in one phase, catalyzed directly by KOH. In these models, some aspects have been neglected: for example, Aracil et. al [2-3] have experimentally found that by increasing the catalyst concentration, the obtainable methylesters plateau, at long reaction time, strongly changes. This fact can be observed also in the continuous runs performed by using both microreactors and static mixers, where a different maximum in methylesters yield is obtained at different catalyst concentrations. This fact cannot be properly explained simply by imposing the occurrence of a chemical equilibrium. In a recent paper [4], this problem has been theoretically investigated by adopting a via enotales mechanism. In fact, initially the reaction is characterized by the presence of two reacting phases: a polar phase, containing methanol and methoxide anions obtained from KOH by an exchange reaction with OH^- and an apolar phase containing triglycerides and dissolved methanol. Then, methoxide anions promptly react, at the interphase, with triglycerides giving place to methyl ester and diglyceroxide anions [4], that are soluble in the apolar phase and promote the further transesterification steps. As suggested by Dijkstra et al. [4], digliceroxide anions react with triglyceride molecules giving an enolate intermediate and a molecule of diglyceride; then the enolate reacts with methanol dissolved in the apolar phase to give methylester and a new digliceroxide anion. In conclusion the catalyst is transferred from the polar phase to the apolar one. With the same mechanism both the monoglyceroxide anion, glycerol and glyceroxide are formed in successive steps. Glyceroxide is not soluble in the apolar phase and the catalyst return to the polar phase but in a less active form. As a consequence, an increase of the catalyst concentration strongly affects the equilibrium of the anions population and the methylesters yield changes with the amount of used catalyst. For this reason, a more reliable biphasic kinetic model, based on Dijkstra et al. mechanism [4] has been developed in this work with the aim of properly describe both batch and continuous experimental runs, in both static mixers and microreactors. At last, it will be demonstrated that the increase in the interphase area is a crucial aspect in determining the transesterification reaction rate for two reasons: the reaction of CH_3O^- with triglycerides occurring at the interphase and the methanol supply by mass transfer for feeding the reaction occurring in the oil phase. As a matter of fact, by using reactor favouring the local micromixing (microwave assisted reactors, ultrasounds assisted reactors, micromixers, microreactors, static mixers etc.) the activity increases so much that cannot be described with a pseudo-monophasic model.

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IND-OR-34 H_2 production by catalytic dehydrogenation of fuels.

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The study of catalytic dehydrogenation of liquid hydrocarbons is addressing one of the key problems for fuel cell application. The conversion of hydrocarbon mixtures into H_2 can be performed on-site, avoiding the difficulties involved in hydrogen storage; therefore the interest in the application of this technology is getting an increasing interest [1-3].

The dehydrogenation of kerosene surrogate and low sulphur Jet A fuel was investigated for the production of H_2. A complete study on catalytic activity of prepared catalysts has been carried out. The role of acidity has been carried out with the aim of finding a good compromise with dehydrogenation and condensation-polymerization properties of catalysts. Pt/Sn-Al_2O_3 catalysts showed good activity (Figure 1) but a loss of activity with time of stream was evident. Raman and TPO analysis of spent samples confirm that the deactivation was caused by coke deposition. Decreasing catalysts acidity by potassium impregnation leads to small loss of activity but strongly increases catalysts stability. All studied catalysts can be regenerate by thermal treatment.

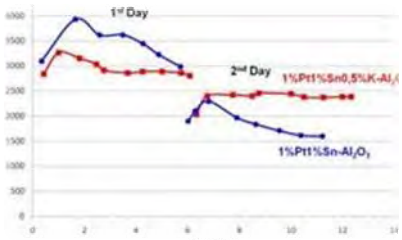

Figure 1: H_2 productivity over 1%Pt-1%Sn/Al_2O_3(■) and K doped 1%Pt-1%Sn/Al_2O_3 (●)

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IND-OR-35 Epoxidation of soybean oil: kinetic study and modeling in continuous reactors.

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Epoxidized vegetal oils are important industrial products nowadays used as plasticizers and stabilizers for polymeric resins, mainly as substitutes of phthalates that have been banned for their toxicity. In our study we have focused on the epoxidation of soybean oil for a detailed investigation on the reaction kinetics in order to acquire sufficient data to develop a suitable mathematical model.
The epoxidation reaction of soybean oil is characterized by an extremely high exothermicity and is a biphasic reaction occurring between the double bonds of soybean oil (oil phase) and an oxidant mixture (acqueous phase) containing hydrogen peroxide, formic acid and a mineral acid like sulphuric or phosphoric acid. These last, act as catalysts for the reaction of formic to performic acid that is the actual epoxidizing agent. Performic acid reacts promptly with double bonds and gives place to the desired product, that is, the epoxidised oil.
The reaction is normally performed industrially by using pulse-fed-batch reactors strategy, according to which the catalyst is initially added to the oil and then only limited amounts of oxidizing mixture are pulsed to the reactor to avoid runaway. The temperature moderately increases and the reaction mixture is cooled by an external or internal heat exchanger until the initial temperature is restored to the desired value. The reactants adding operation is repeated different times and after each addition a more or less prolonged cooling operation is required. This procedure requires many hours of reaction time (5-8 hours) and the conversion from fed-batch to continuous operation represents the key point to increase the productivity of the process. Such shift can be obtained only by acquiring sufficient insight on the reaction kinetics and by developing a reliable physical model able to describe the evolution of all the components involved, considering in particular the secondary reactions that decrease the selectivity.
In an our recent paper we have developed a kinetic model that contains the main physico-chemical peculiarities of the considered reacting system [1]: components partition between the two liquid phases, mass transfer limitation across liquid-liquid interface, heat transfer between the reacting mixture and reactor jacket, different reactivity in epoxidation and oxirane ring opening (degradation).The model has been successfully applied, in a first step, to a set of experimental fed-batch runs performed in controlled isothermal conditions with the scope of evaluating the kinetic parameters at a reference temperature. Subsequently, a group of pulse fed-batch runs with variable temperature has been used to evaluate activation energies and thermal parameters such as the global heat transfer coefficient. The very good agreement between the experimental data and the model prediction has given the confirmation that the model was able to describe the behavior of the fed-batch reactor in different conditions [1].
With the aim to further validate the model, new experiments have been performed in a conventional continuous tubular reactor, filled with glass or stainless steel (AISI 316) spheres. We have found that also for continuous runs the performances of the model are satisfactory.
In conclusion we have now demonstrated that the proposed model and the related kinetic parameters could be useful to design a continuous epoxidation operation in safe conditions and could be the basis for the process intensification in microreactors or static mixer reactors.

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MS-IL-01 Shaping the Beating Heart of Artificial Photosynthesis: Oxygenic Nano-Hybrid Interfaces

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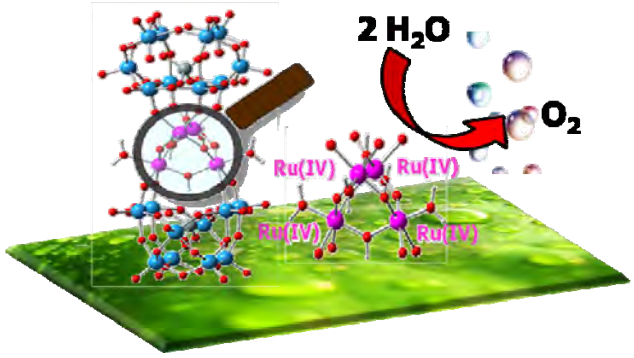
Water oxidation is the crucial stage in the chemical and molecular sequence of photosynthesis, designed by Nature to convert solar light into chemical energy. The artificial "off-leaf" transposition is a major goal of energy research, aiming at the continuous production of hydrogen as solar fuel, through the photo-catalytic splitting of H_2O.[1] Success in this task primarily depends on the interplay of light-activated multi-electron oxidation and reduction routines and on the invention of stable and robust water oxidation catalysts, liberating oxygen with fast rates, high quantum yield, and long-term activity. Indeed, the Achilles' heel of the chloroplast assembled architecture stems from the intrinsic weakness of the functional components chosen by Nature. The artificial perspective should find its roots on more solid materials. The vision here is to transcend the natural wonder, while being inspired by its key guidelines along the design of a functional system/device, with superior operation stability. We will highlight a recently discovered pathway carved within the class of inorganic metal-oxides displaying a unique mimicry of the PSII enzyme.[2] Furthermore, the shaping of their functions at the interface of specifically tailored carbon nano-structures and/or polymeric scaffolds opens a vast scenario for tuning electron/proton transfer mechanisms in term of rates, distance, geometries and communication between donor/acceptor centers.[3]



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MS-IL-02 Supramolecular Ligands in Transition metal catalysis, evolutionary ligand screening and a first approach to catalyst selection

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The interface between supramolecular chemistry and transition metal catalysis has received surprisingly little attention in contrast to the individual disciplines. It provides, however, novel and elegant strategies that lead to new tools for the search of effective catalysts, [1] and as such this has been an important research theme in our laboratories. In this presentation I will focus on supramolecular strategies to make bidentate ligands and compare that to traditional catalyst development. Supramolecular approaches appear ideally suited for the creation of large ligand libraries. The large number of catalyst that become available in this manner, asks for screening strategies and evolutionary approaches. A first academic example of catalyst selection from a mixture will be discussed. In addition, the application of a cofactor strategy will be presented, which is also ideally suited for selection procedures.

Figure 1: New concepts in TM catalysis: Left) a ligand-template approach to porphyrin encapsulated rhodium catalyst. Middle) dinuclear complexes based on METAMORPhos ligand Right) coordination chemistry steered by supramolecular chemistry.

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MS-01 Supramolecural Control on Product and Substrate Selectivity via Encapsulation within a Hydrogen Bonded Self-assembled Hexameric Capsule

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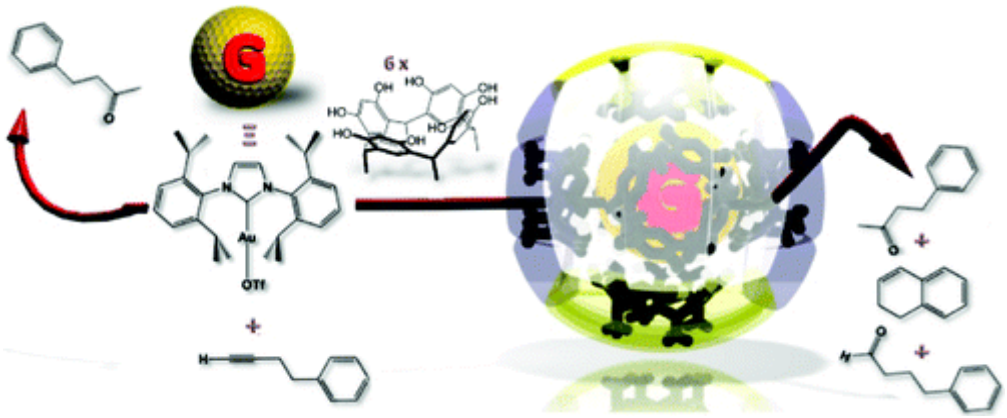
The impressive chemo, regio and stereoselectivity displayed by enzymes are the result of a large number of weak attractive intermolecular interactions as well as repulsive steric requirements operating between the substrate and the catalytic site. In the latter, recognition phenomena allow also the selective picking of the substrate among a series of similar reagents bearing same functional groups but different size. Overall enzymes control both sides of a chemical transformation, while common organometallic catalysis usually puts its effort prevalently on the right side of the catalytic reaction. Hosting of organometallic catalysts within well defined porous supports led to enhancement of enantioselectivitywhile for catalytic systems working under homogeneous conditions, encapsulation within rigid metal-ligand tetrahedral or square bi-pyramidal assemblies allowed rate acceleration and substrate selective reactions for a series of small reagents.
Herein we report about the simple modification of the product and substrate selectivity properties of an organometallic catalyst via encapsulation in a spherical hexameric self-assembled capsule held together by a seam of sixty hydrogen bonds. The steric requirements imparted by the capsule modify product distribution in the alkyne hydration reaction towards uncommon species and, at the same time, steer substrate selectivity in parallel competitive experiments towards the substrate that better fit the residual space available in the cavity.



MS-02 Rhodium-Catalyzed Asymmetric Hydrogenation of Olefins with PhthalaPhos, a New Class of Chiral Supramolecular Ligands

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Nature makes wide use of non-covalent interactions to build its complex supramolecular architectures and to achieve efficient and selective transformations. In recent years, supramolecular approaches to the development of new enantioselective catalysts have gained momentum [1]. Herein we report the design and synthesis of a novel class of chiral monodentate phosphite ligands, named PhthalaPhos [2], which contain a phthalic acid diamide moiety (Figure 1). Such phthalamide group displays both donor and acceptor hydrogen bonding properties that can give rise to supramolecular interactions both between the ligands and with the substrate. The modular nature of the PhthalaPhos ligands allows to tune their properties by simply varying structural elements such as the linker, the BINOL unit and the ancillary amide group (i.e. the amide not connected to the phosphite group), thus allowing a parallel-combinatorial ligand optimization.

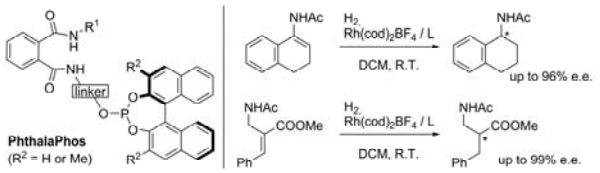

Figure 1

The catalytic properties of the PhthalaPhos library (19 representatives) were tested in the rhodium-catalyzed enantioselective hydrogenation of dehydro aminoesters and *N*-acyl enamides. Excellent results in terms of catalytic activity and stereocontrol were obtained with both benchmark substrates and 'challenging', industrially relevant olefins (Figure 1). Spectroscopic and computational studies, together with control experiments, suggest that the role of the phthalamide group consists in binding and orientating (by hydrogen bonding) the substrate during the catalytic cycle of the hydrogenation process [2b].

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MS-03 Covalent Nano-Clip and Nano-Box Compounds Based on Free Base Porphyrins

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There is an increasing interest in developing smart nanostructures for applications in many different fields, from environmental monitoring to biological, medical and industrial chemistry. For some specific properties (e.g. strong molar absorption, bound metal atoms in pyrrolic cores, extensive aromatic structures, peculiar affinity for neoplastic cells, etc.), porphyrin-derivatives are among the most studied compounds and some applications like chemical and/or biological receptors, artificial sensors for drug determinations, mimesis of biological systems, etc., are already well-defined. Recently, several 3D cyclic oligo-porphyrins with different architectures [e.g. spheres, prisms, regular polyhedra (with a varying number of faces), etc.] have been studied[1]. The properties of these molecules may depend on the size and hydrophobic nature of the cavities inside their 3D structure (for example, suitable to accommodate hydrophobic chemicals).

In the present paper, as the first step in the preparation of water soluble Nano-Clip and Nano-Box compounds, the synthesis and characterization of some novel macromolecular cyclic ethers, constituted by two (Nano-clip, fig. 1) or four (Nano-box, fig. 2) porphyrin units and spaced with methylene bridges, are reported. These compounds, obtained by the reaction between dibromomethane and 5,15-di[p-(9-methoxytriethylenenoxy)phenyl]-10,20-di[p-hydroxyphenyl] porphyrin, have a co-facial (nano-clip) or a four wall-box (nano-box) architecture.

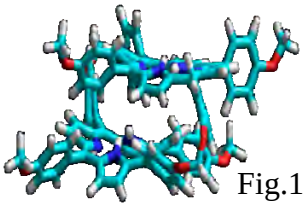
Fig.1

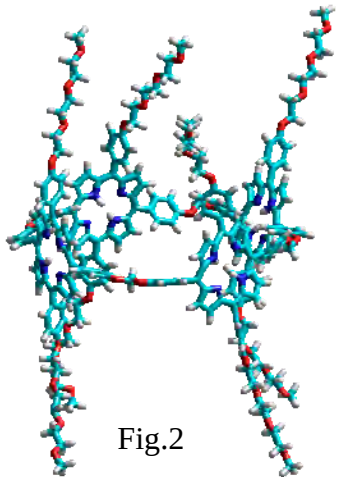
Fig.2

The aim of these syntheses was to obtain molecular systems for the recognition and/or the carriage of bio-molecules. Spectroscopic data of the Nano-clip showed modified Soret and Q-bands, with respect to the monomer and cyclic tetramer, as a probable consequence of a hybrid orbital deformation (HOD) phenomenon involving the two porphyrin π rings forced to a closer co-facial spatial arrangement [2].

A UV-vis titration allowed verification of the easy and reversible protonation of the pyrrolic cores which, by electrostatic repulsion, modifies the spatial distance between the two co-facial porphyrins and, therefore, the cavity size. This reversible modification could be used to change the dimer molecule status from Open to Closed, and facilitate the accommodation or release of suitable chemical species, acting then as a drug carrier.

The tetrameric porphyrin molecule (Nano-box) could also be used as a drug-carrier, forming an inclusion complex with macromolecular drugs, or as a nano-reactor, for the peculiar nano-space conditions inside the box. In this case, ^{1}H-NMR spectroscopic analysis showed a high-field shift of the aromatic and ether protons present in the upper and lower box rims as a specific characteristic of this molecular structure[2]. These compounds differ from previous analogous porphyrinic systems in that their totally covalent structure makes them more versatile potential macromolecular tools.

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MS-04 Novel functionalized PTA ligands, their coordination complexes and use in catalysis

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PTA (1,3,5-triaza-7-phosphaadamantane), the neutral water-soluble and air-stable monodentate phosphine firstly reported by Daigle et al. in 1974 [1], has been used by us and other groups to obtain water-soluble transition metal complexes which have been applied as homogeneous catalysts in aqueous or biphasic systems [2].
The largest part of modifications of PTA has so far involved the P or N atoms, so we focused on the functionalization at one carbon of the upper rim [3]. The optimized derivatization reaction is based on the isolation of the pyrophoric PTA-Li salt, which was then reacted with electrophiles such as aromatic aldehydes and ketones [4]. Thus, new chiral ligands were obtained and used to bind Ir(I) and Ru(II) organometallic moieties. The corresponding complexes were tested as catalysts for hydrogenation reactions under mild conditions. In parallel, modifications of the lower rim of PTA, i.e. alkylations at N atom, were also carried out and the new N-alkylated PTA derivatives so obtained were used as water soluble ligands in biphasic Rh-catalyzed hydroformylations of long-chain olefins in the presence of randomly methylated -cyclodextrins.[5].

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IND-PO-01 Synthesis and Characterization of New Copolyacrylates Containing Porphyrin Units as Pendant Groups and Their Use as Sensors.

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Porphyrins are highly-conjugated organic molecules having useful properties for some functional devices as photodiodes, catalysts, artificial solar energy conversion systems and, particularly, for sensor devices. [1]

Obviously, their use as sensing of specific analytes (as acid vapours or NO_2) requires a direct contact, so that only chromophore units present on sensor surfaces are active. In previous works [2], good results were obtained assembling porphyrin monolayer on a quartz surface, but both materials and synthetic procedure were expensive.

The present work regards the construction of an inexpensive sensor device obtained depositing a thin layer of a MMA/porphyrin copolymer on PMMA plates, with the hope of reducing both the amount of sensitive material and the cost of the support. By reaction between MMA and an acrylic comonomer, obtained by condensation of a porphyrin derivative (having three triethylene glycol mono methyl ether branches and a free-hydroxyl group) and acryloil chloride, copoly-porphyrin-acrylates of different compositions were prepared. Sensor devices were then assembled stratifying very thin layers of these materials on transparent commercial PMMA plates by immersion of these last in very diluted solutions of copolymers.

The efficiency of the devices was tested by exposition to trifluoroacetic and hydrochloric acid vapours or NO_2 gas. Under exposition, as expected, the Soret porphyrin band (at 424 nm) rapidly and totally disappears (substituted, in both cases, by a new band at about 450 nm) to be quickly recovered by treatment of the devices with ammonia or hot air, respectively.

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IND-PO-02 What a chemical industry from biomass?

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The biomass to use to produce chemicals can be of three types: 1) wastes (manly lignocelluloses ones) from agriculture, from forests, form food and papers industries, wastes from municipalities ,from wood transformation , sludges from depuration of water , sewages from animals; 2) food and feeds crops, and in this case we have triglycerides carbohydrates and proteins ;
crops dedicated only to energy and chemistry produced from marginal lands. From biomass we can produce chemicals in several stages: the first one is always a physical extraction of active principles, after having reduced in small dimensions and isolated the single components, leaving unchanged the original structure. Further steps are chemical or biological transformations to produce several products that are called **platform molecules** which are called in petrochemistry building blocks. A further strategy is to arrive to the final product in several steps without separations of intermediates (one pot synthesis) . Some platform molecules are succinic acid, ethanol, fumaric acid, glycerine, butanol, levulinic acid, itaconic acid, glutammic acid, and 3 hydroxipropionic acid. From cellulosic raw materials via gasification or reforming it is possible to obtain syngas. and from syngas is possible through methanol to obtain olefins or paraffins via Fischer Tropsch reaction. With pyrolisis or hydroliquefaction of lignocellulosic materials is possible to obtain aromatics (benzene phenol, toluene and xylens). Triglycerides C12-C18 can be transformed by transesterification with methanol to methyl esters and glycerin and after hydrolyzed to acid and hydrogenated to alcohols. From the single aminoacids isolated from proteins or obtained by fermentation of carbohydrates in presence of ammonia or nitric acid after their isolation and purification with reactions of decarboxilation and deamination is possible to obtain several functionalized molecule . From protein is possible to obtain several intermediates as acrylamide from asparagines, 1,2-etanediamine from serine, ε-caprolactame from l-lisine, styrene from fenilalanine, ethylamine from serine, isobutirraldheyde from valine, isoprene from leucine. By anaerobic fermentation of wastes it is possible to obtain methane and from ethane to create all C1 chemistry .There are four strategies to develop a chemical industry from biomass and from all these strategies the advantages are the reduction of CO_2 emission, the use of rinnovable raw materials , the independence from fossil fuel and further going from the first to the last one there are additional advantages. These strategies are:1) to produce the some building blocks of petrochemistry starting from platform molecules from biomass (ethylene from ethanol etc) 2) to use platform molecules to produce the first building blocks of petrochemistry 3) to use the platform molecules to produce the second or successive intermediate to obtain the some product of petrochemistry 4) to synthesizes new products alternative to the petrochemistry starting from platform molecules or through several steps without separation of intermediates. The advantages of second strategy and third strategy is the simplification of the process to produce the intermediate. Example of first strategy is the production of polyethylene by first dehydratation of ethanol to ethylene. Examples of second strategy is the alkylation of benzene to ethyl benzene with ethanol or the production of phenol from lignin. or synthesis of terephthalic acid starting 5-hydrossimethylfurfurole and glycerin. l'1,2-propandiole can be obtained by hydrogenolysis of the glycerin l'1,3-propandiole can be obtained from glycerin. It is possible to use directly succinct acid for the synthesis of 1,4- butandiole, γ-butyrolactone and tetrahydrofurane, insteas from maleic anhydride from n-butane . The advantages of fourth strategy is the production of bioproducts which can be biodegradable and can us the prefix bio These product are biosolvents, biolubrificants, biopolymers, biofuels, bioadhesives, bionks, biocosmetics, biodetergents and biofarmaceuticals.

IND-PO-03 Reductive mono-alkylation of nitro aryls in one-pot and Suzuki-Miyaura coupling in water: catalysis by polymer-stabilized palladium nanoparticles.

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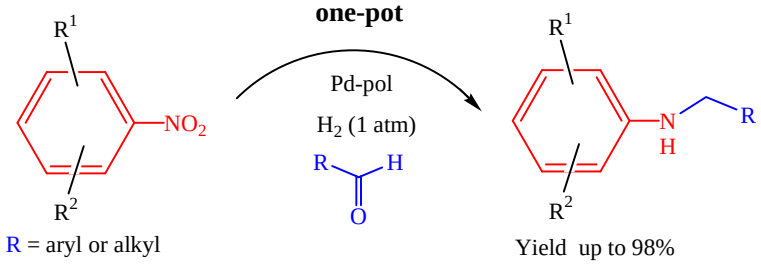
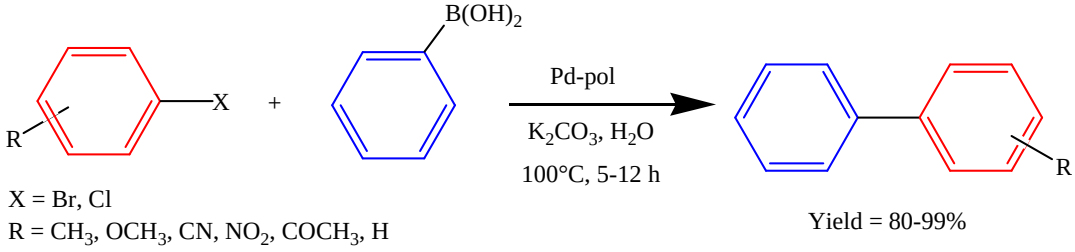
This presentation deals with the use of polymer supported palladium nanoparticles (Pd-pol[1]) in:

i) the direct reductive amination of carbonyl compounds with nitroarenes in the presence of molecular hydrogen as the reductant (scheme 1).



Scheme 1

ii) the Suzuki-Miyaura coupling of aryl bromides and chlorides in water (scheme 2).



Scheme 2

In both the reported reactions, Pd-pol catalyst is recyclable and can be reused without significant loss of catalytic activity for several times.
Chemical and TEM analyses showed that the catalytically active species are supported Pd nanoparticles with a primary particles' size distribution centered around 5 nm formed under reaction conditions.

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IND-PO-04 Surface Properties of a Series of Monodisperse Perfluoroalkylated Polyoxyethylene Glycols

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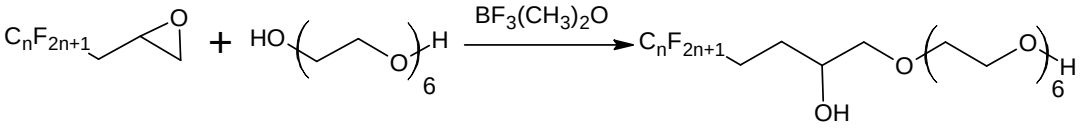
Three monodisperse perfluoroalkylated polyoxyethylene glycols were synthesized by direct addition of a poly(ethylene glycol) having an average molecular weight of 300 (PEG-6) to 2-(perfluoroalkylmethyl) oxiranes having a general formula $C_nF_{2n+1}CH_2CH(O)CH_2$ (n = 4, 6, 8):



Critical micelle concentrations (c.m.c.'s), surface and interface tensions, cloud-point curves, surface-pressure vs. area (π, A) diagrams and micelle hydrodynamic diameters were determined in order to correlate surface properties of surfactant-water systems and the length of the fluorinated chain.

The lengthening of the fluorinated chain was found to induce a strong hydrophobic effect resulting in a abrupt decrease in surface tension, interfacial tension, critical micelle concentration, cloud point and surface area occupied by a surfactant molecule.

Further, the effects of inorganic and organic anions on cloud points and c.m.c.'s of aqueous solution of monodisperse perfluoroalkylated polyoxyethylene glycols were studied. Salt constants k_s were determined for 8 inorganic and 3 organic salts. The magnitude of k_s varied as follows: $P_3O_{10}^{5-}$ > PO_4^{3-} > SO_4^{2-} > Cl^- > Br^- > NO_3^- > I^- > SCN^- for inorganic anions and Ethylenediaminetetraacetic acid tetravalent anion ($EDTA^{4-}$)> 2-hydroxypropane-1,2,3-tricarboxylic acid trivalent anion ($CITRATE^{3-}$) > 1-Hydroxyethylidene-1,1-diphosphonic acid divalent anion ($HEDP^{2-}$) for organic anions.

The salting effect of a specific anion was found to be strongly influenced by the length of the fluorinated tail: the higher the number n of fluorinated carbon atoms, the stronger the salting effect of a specific salt.

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IND-PO-05 Mg/Al Hydrotalcite catalyst for Biodiesel production.

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In the classical biodiesel production technology, the triglycerides (vegetal oils) are transesterified with methanol at 60-80°C, using basic homogeneous catalysts (alkaline metal hydroxides or methoxides), achieving high yields of a mixture of fatty acid methyl esters (FAME). Together with biodiesel, glycerol is also produced (10% by wt of biodiesel). However in this process the use of an homogenous catalyst is a drawback, requiring for product purification, the use of an acid neutralizing agent producing salts which remain dissolved in the glycerol. The obtained crude glycerol have a very lower price than the higher grade product, but to achieve the purity requested by the market, the glycerol distillation is necessary, with a consequent increase of the total energy duty of the process. This problem can be solved using an heterogeneous catalyst as it was demonstrated by the technology Esterfip-H developed by IFP [1]. Despite many catalysts studied in laboratory have shown better performance than the catalyst developed by IFP (zinc aluminates), no other catalyst among the dozens in the literature has been developed up to the construction of an industrial plant.

The principal problem linked with the use of an heterogeneous catalyst, in biodiesel production, is the stability of the catalyst, although in many papers reported by the literature this aspect is often completely neglected [2]. However the only way to reliably establish the stability of a catalyst is to conduct tests in packed bed reactors for long periods [3].

The Mg/Al Hydrotalcites have been proposed as catalysts for biodiesel production in many papers [2] but no one have reported data about the performance of Mg/Al hydrotalcites in a continuous packed bed reactor for a long time working. In this paper, the performances of a commercial Mg/Al hydrotalcite (PURAL® MG 76) have been tested before in an autoclave and then in a continuous packed bed reactor.

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IND-PO-06 Photodegradation of 4-chlorophenol sensitized by waste derived soluble organic substances using experimental design

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Advanced Oxidation Techniques represent an alternative to more traditional water treatments since they are able to promote the degradation of organic substrates, leading to their complete mineralization. These processes are based on the production of highly reactive species (mainly radicals) and are often light assisted. Among the compounds able to photogenerate reactive species, humic and fulvic acids (HS) have been widely studied in order to understand the water auto-purification mechanisms. It is thus in principle possible to propose the use of HS in wastewater photodegradation treatments; however neither waters nor soils can be considered as exploitable source of HS. The organic fraction of urban wastes has been demonstrated to be an interesting source of soluble organic substances (SOS), structurally similar to HS and exhibiting good photosensitizing properties [1].
In the present research the photodegradation of 4-chlorophenol (4-CP), a toxic and hardly biodegradable pollutant, has been studied in the presence of one type of SOS. In order to optimize experimental conditions and to evaluate possible synergistic effects with other photoactive compounds (TiO_2 and H_2O_2) a chemometric approach has been chosen. Two designs of experiments (D-Optimal, DoE) have been planned and the following parameters have been considered: 4-CP concentration (from 10 to 100 mg L^{-1}), SOS concentration (from 0 to 1000 mg L^{-1}), TiO_2 concentration (from 0 to 500 mg L^{-1}) or H_2O_2 concentration (from 0 to 10^{-2} M), cut-off filter for the light source (340 nm, 400 nm and without filter). By mean of the Modde software, 39 experiments were selected for the TiO_2-DoE and 25 experiments for the H_2O_2-DoE. The resulting response surfaces evidenced that, in the presence of TiO_2, a competition for the active photogenerated species seems to take place between 4-CP and SOS, since also SOS can be in turn photodegraded.
On the contrary, a synergistic effect between SOS and H_2O_2 occurs, when the 400 nm cut-off filter is used. After three hours of irradiation 25% of 4-CP abatement was achieved in the presence of 500 mg L^{-1} of SOS, 35 % was achieved in the presence of 5 mM of H_2O_2, whereas 45% of 4-CP abatement was obtained in the presence of both SOS and H_2O_2 at the above mentioned concentrations.
These results encourage the use of chemometric tools and give useful information for a possible scale-up of the process in pilot plants exploiting the solar light as radiation source.

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IND-PO-07 Hydrogen production through $NaBH_4$ hydrolysis over activated carbon supported Ru and Co catalysts

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Nowadays chemical hydrides represent an ideal source of pure hydrogen for fuel cells application. Sodium borohydride ($NaBH_4$) is the preferred hydride due to its high gravimetric and volumetric hydrogen density [1, 2]. The aim of this work was to investigate the $NaBH_4$ hydrolysis ($NaBH_4 + 2H_2O \rightarrow NaBO_2 + 4H_2$) over mono and bimetallic Ru and Co catalysts supported on different activated carbons.

Catalysts were prepared by incipient wet (co)impregnation of the support with aqueous solutions of the precursors ($RuCl_3$, $Ru(NO)(NO_3)_3$, $Co(NO_3)_2$, coded respectively C, NN and N). Three activated carbons, two minerals with surface of area 1059 and 650 $m^2\ g^{-1}$ (coded respectively D and E) and one vegetable from exhausted olive husks (coded H, with 1200 $m^2\ g^{-1}$) were used as support. Catalysts were named MeX(Y)/Z, where Me is the metal, X the precursor, Y the metal charge and Z the support used. Catalytic tests were carried out at atmospheric pressure in isothermal conditions. Catalysts were characterized by TEM, EDX and BET surface area.

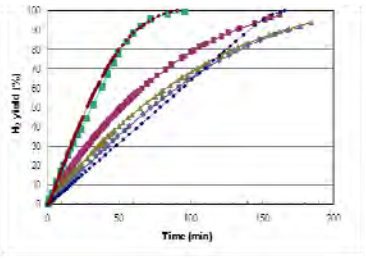

Fig. 1 H_2 yield (T=25°C) over Ru catalysts.
(●)RuNN(2)/H; (■)RuC(2)/D; (■)RuC(2)/E; (▲)RuNN(2)/E; (●)RuNN(2)/D; (♦)RuC(2)/H.

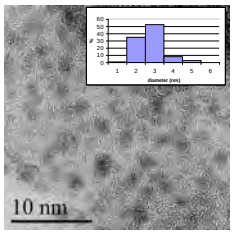

Fig. 2 TEM microphotograph of the most active catalyst, RuNN(2)/H.

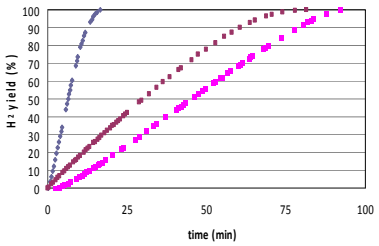

Fig. 3 H_2 yield (T=25°C) over Ru and Co catalysts.
(■)RuNN(0.5)/H;
(■)RuNN(0.5),CoN(10)/H;
(■)CoN(10)/H.

The activity tests of Ru catalysts (Fig. 1), showed that the H_2 yields are in the order: RuN(2)/H≈RuC(2)/D>RuC(2)/E>RuN(2)/E>RuN(2)/D>RuC(2)/H. On the basis of TEM and EDX analyses, it was suggested that this trend is related to the Ru particle size, which depends both on the support and Ru precursor used. The use of an activated carbon from a vegetable source, as the H support, results in bigger Ru particles, probably due to the higher amount of calcium and potassium present on the H support. $RuCl_3$ leads to bigger particles than $Ru(NO)(NO_3)_3$. It was proposed that there is an optimum Ru diameter (2-3 nm, Fig.2) for the hydrolysis reaction. On the most active carbon (H) it was found that Co, even if present at higher amount than Ru (10 wt% vs 0.5 wt%), shows a very low activity (Fig.3). The bimetallic Ru-Co catalysts exhibit a H_2 yield much higher than the sum of the corresponding monometallic Co and Ru samples (Fig. 3). This was attributed to an increase of the Co dispersion caused by the presence of Ru.

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IND-PO-08 $CuFe_2O_4$ catalyzed SiC WFF as MW susceptible catalytic trap for Diesel soot abatement

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The diesel engine emissions control is one of the most important aspects of modern air quality management [1]: the EURO 5/6 standards impose the development of both new engines and more effective exhaust gas after treatment devices. The Wall-Flow Diesel Particulate Filters (DPFs) represent the best technology available to reduce soot emissions under EU standards [2]; they consist of alternately plugged parallel channels, so forcing the exhaust gases through their porous walls, where the PM is collected. When the accumulated PM reaches a certain level, DPF must be regenerated to maintain efficient engine operation; but all the actually used strategies (heating of the exhaust gases or reduction of the soot burning temperature using a fuel borne catalyst) require an extra energy consumption. An appealing technological proposal to perform active DPF regeneration is the combined use of MW energy and of a catalyst for the soot oxidation that is simultaneously MW sensible: so, due to the instantaneous and selective heating process, one can reduce the soot burning temperature and the overall energy employed for the complete regeneration. In this work we studied the MW assisted regeneration of a specifically catalyzed Pirelli Ecotechnology SiC Wall-Flow monolith Filter with 200 cpsi. The selected catalyst is based on the $CuFe_2O_4$, due to its good dielectric properties and oxidation activity [3]. The preliminary results of soot loading and on-line regeneration tests showed that the system realized is able to achieve the complete filter MW assisted regeneration, and monitoring continuously the applied power, to evaluate the overall energy employed in the regeneration phases: in particular the tests showed that using both the MW and the catalysed filter, the energy supplied and the regeneration time are about 50% lower than that necessary for the uncatalysed filter. Further researches are still in progress to study the influence of the operating parameters (i.e. exhaust gas flow rate), in order to find the optimal regeneration conditions allowing further energy saving.

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IND-PO-09 On the regeneration of gold nanoparticles for the selective oxidation of furfural

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Innovative transformations of furfural are highly desired: among these, the synthesis of alkyl furoates can open very interesting perspectives for the use of xyloses, because they can be used either as solvent or extracting agents in many different industrial plants if produced in larger amounts and at low price. Currently we are studying the oxidative esterification of furfural on Au/ZrO_2 samples without the addition of $NaCH_3O$, a base that would make the process less green and more expensive. The goal of the work herein presented is to investigate the stability and the reusability of our best Au/ZrO_2 samples.
Catalysts were prepared by deposition-precipitation (dp) on calcined support. The oxidative esterification of furfural with oxygen and methanol, without $NaCH_3O$ addition, was investigated at 120°C and 12 bar. After the first catalytic run the sample was filtered off, washed with methanol, dried and used again, obtaining very low selectivity in the subsequent runs. As the reason for catalysts deactivation we have excluded gold leaching in the discharged samples. In order to investigate catalyst poisoning, by TPO analyses we have verified on exhausted catalysts the presence of an organic residue. According to TPO profiles, we have decided to heat the catalyst until 450°C in oxygen atmosphere, in order to eliminate organic poisons. The deactivation in this case is reversible and by thermal calcination at a proper temperature it is possible to restore almost fully the initial selectivity. In fact, by pulse-flow CO chemisorptions [1] we have found for the regenerated samples a mol_{CO}/mol_{Au} ratio comparable to the value of the fresh samples, meaning the absence of gold sintering during the catalytic reaction.
FTIR spectroscopy demonstrated that the organic residue can be removed starting from 350°C in O_2. At the same time, CO adsorption reveals that the Au phase is quite stable, even after repeated thermal treatments in O_2 at increasing temperature up to 6 hours.

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IND-PO-10 Catalytic multifuel ATR reformer for distributed H2 production

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Hydrogen fuel cells seem to be the most viable solution to the antithetic problems of pollution reduction and growing energy demand. Distributed production overcomes the difficulties in H2 transport and storage, therefore very compact and flexible plants are required: AutoThermal Reforming (ATR) of hydrocarbons assures self-sustainable operation and high reaction system compactness [1]. Fossil fuels still remain the favorite choice due to the widespread existing delivery pipelines of natural gas and the high energy density of liquid fuels such as gasoline and diesel. Very different characteristics of liquid and gaseous hydrocarbons make it very difficult to realize a multifuel reformer, and to achieve high performances in terms of thermal efficiency and H_2 yield.

A catalytic multifuel autothermal reformer thermally integrated was developed, able to process both methane (as natural gas) and dodecane (as diesel-like hydrocarbon). Great attention was paid to the development of a feed system for liquid fuel. In order to avoid fuel preheating, an alternate high pressure spray system, based on the common-rail technology, was adopted, allowing the formation of micro-droplets that assure a very quick liquid vaporization and an optimal mixing with other reactants, avoiding coke formation and improving hydrogen yield and thermal efficiency. Catalytic region was designed for use structured catalysts such as honeycomb monoliths and foams, according to literature experiences [2, 3]. In order to realize a full self-sustained system, without any external heat sources, great attention was focused to the system thermal integration. An heat exchanger system integrated into the reactor was able to preheat water and air streams by cooling products stream to a temperature consistent with a further water-gas shift stage.

In order to have a very comprehensive process control, temperature and composition was monitored in 6 points of catalytic bed. Preliminary tests showed low start-up times, and a very quick response of the system to the operating conditions changes, with a good hydrocarbon conversion. During whole tests, high thermal efficiency and good fuel conversion was observed.

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IND-PO-11 La/Mn Perovskite catalysts for Biodiesel production.

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Biodiesel (a mixture of Fatty Acid Methyl Esters, FAME) is the second biofuel produced in the world and the first in Europe. Nowadays the major part of biodiesel is produced by transesterification with methanol of refined edible oils such as rapeseed, sunflower, palm, soybean, etc. However, the majority of this raw materials do not fulfill the sustainability criteria indicated by the UE Directive 2009/28/EC, and so they shall not be taken into account for measuring compliance with the requirements of this Directive concerning national targets. Instead, the waste vegetable or animal oils widely fulfill the sustainability criteria and so are more convenient by an ecological point of view. Moreover the use of waste oil is also economically of great interest. Actually more than 85% of the cost of biodiesel obtained from edible vegetable oils is the cost of raw materials.

Biodiesel is produced today by the transesterification of triglycerides of refined/edible type oils using methanol and an alkaline homogeneous catalyst (NaOH, NaOMe): The reaction is normally performed at 60–80 °C. The glycerol and FAME are separated by settling after catalyst neutralization. The crude glycerol and biodiesel obtained are then purified. However, homogeneous alkaline catalysts cannot directly be used with waste oils due to the presence of large amounts of free fatty acids (FFA) [1].

Recently Russubueldt et al [2] found that La_2O_3 leads to an excellent activity for transesterification of refined palm oil. However, the pure oxide shows an insufficient catalytic stability and a partial homogeneous catalysis by the formation of soaps in the reaction with crude palm oil (FFA 5%). Moreover, although La mixed oxides with a perovskite structure are lower active than the pure oxide, they supposed a much better resistance towards free fatty acids.

In this paper we will report the performances of mixed oxide La/Mn with a perovskite structure prepared by flame pyrolysis technique [3] in the transesterification of refined and acid soybean oil.

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IND-PO-12 Chlorohydrins Production by Glycerol Chlorination

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The growing availability of glycerol, obtained as a co-product in biodiesel production, has determined a great interest in the development of new processes using glycerol as feedstock, also with the aim of reducing biodiesel production costs. A promising choice should be the glycerol chlorination reaction, in order to produce chlorohydrins (both mono- and dichlorohydrins). For example, dichlorohydrins can be easily converted into epychlorohydrin, that represents an important intermediate in the production of epoxy resins [1,2]. Moreover, in this process both monochlorohydrins and glycidol can be obtained: these last products could represent a possible intermediate in different industrial syntheses.
The first literature studies and patents on the reaction between glycerol and hydrochloric acid are rather old (about 1940) and are based on the use of aqueous HCI solutions in the presence of acetic acid as catalyst, in a temperature range of 80-100°C. Therefore, these processes have some drawbacks, such as the slow rates for the diluted mixture, the loss of catalyst by evaporation and several difficulties in the separation of the products, as investigated in more recent studies [3-5].
In the present work, the glycerol chlorination reaction has been studied by using a pressurized reactor made in hastelloy, operating in fed-batch conditions by feeding gaseous hydrochloric acid to glycerol in order to maintain the reaction system at a constant pressure. The reactor temperature was kept at 100°C and the total reaction time was of 4 h. Some effects have been investigated, such as the catalyst concentration (2-8 mole %) and reaction pressure (1-8 bar). With the scope to evaluating the mechanistic aspects, in this study different catalysts have been tested, for example, the homologue series of acetic, mono-, di- and trichloroacetic acid, that gave interesting results in terms of selectivity. In particular, acetic acid resulted selective in the production of 1,3-dichlorohydrin, while chloro-substituted acids have produced a mixture of mono- and dichlorohydrins. A decreasing activity has been observed in the order: acetic > monochloro > dichloro > trichloro acetic and a suitable reaction mechanism has been proposed for interpreting the collected results. At last, a reliable kinetic model has been developed for the description of the experimental data collected in the fed-batch reactor, allowing a comparison between different catalysts in terms of kinetic constants.

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IND-PO-13 Gas Phase Photocatalytic Selective Oxidation of Ethanol to Acetaldehyde on $VO_x/TiO_2/SiO_2$ Catalysts

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Aldehydes are important products and intermediates in the field of fine chemicals. A commonly used method for their preparation is the oxidation of alcohols. From an environmental and economic standpoint, the use of heterogeneous photocatalysis is particularly attractive. In this work the gas-solid photocatalytic partial oxidation of ethanol to acetaldehyde on $VO_x/TiO_2/SiO_2$ was studied. The catalysts were prepared by sequential grafting of vanadyl triisopropoxide onto a support of silica coated with TiO_2 by a mono- or multi-step grafting procedure. The obtained samples were characterized by N_2 adsorption-desorption at -196°C, X-ray diffraction, Raman and UV-Vis spectroscopy.

Photocatalytic tests were carried out at 60°C and atmospheric pressure, feeding 30 (stp)L/h He stream containing 0.2 vol. % ethanol, with oxygen/ethanol ratio of 2. The catalyst weight was chosen on the basis of nominal content of TiO_2 and it was equal to 1.2 g. The fluidized bed photoreactor was illuminated by two UVA-LEDs (emitting at 365 nm) modules of 40 pieces each (light intensity: 90mW/cm^2). The outlet gas composition was continuously measured by an on-line quadrupole mass detector and a continuous CO-CO_2 NDIR analyser.

For TiO_2/SiO_2, ethanol conversion passed from 53 to 46% for SiO_2 loaded with a monolayer of TiO_2 ($TiSi_1$) and three layer of TiO_2 ($TiSi_3$), respectively.
The presence of VO_x species anchored on $TiSi_1$ enhanced photocatalytic activity up to 66 %, with acetaldehyde selectivity higher than 99%. On the contrary, vanadium on $TiSi_3$ inhibited photoreactivity decreasing ethanol conversion from 46 to 37%, although acetaldehyde selectivity was higher than 98%.

IND-PO-14 The Baeyer-Villiger oxidation of cyclohexanone to ε-caprolactone with hydrogen peroxide: the role of radicalic reactions

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The Baeyer-Villiger (BV) reaction has aroused great interest as a powerful tool for the preparation of pharmaceuticals (e.g., antibiotics, steroids) and compounds for the fine chemicals and intermediates industry [1]. Within this context, in recent years many efforts have been spent in the study of new catalysts that may allow the selective transformation of cycloalkanones into the corresponding lactones with hydrogen peroxide, the ideal oxidant for developing a cleaner process. In general, it is believed that the electrophilic attack of (activated) hydrogen peroxide generates the Criegee intermediate, which then rearranges into the lactone; the latter may undergo hydrolysis and ring opening to form hydroxyacids.

During our investigation aimed at studying the activity of heterogeneous and easily recyclable catalysts for the BV oxidation of cyclohexanone into ε-caprolactone, we realized that indeed thermally-activated radicalic reactions control the mechanism, and that the lactone may very rapidly react to yield dicarboxylic acids, even when a stoichiometric amount of the oxidant is used [2]. ε-Caprolactone is the primary reaction product, but it is more reactive than cyclohexanone, and quickly undergoes consecutive transformations by means of two different reaction pathways, (a) an hydrolythic pathway to 6-hydroxyhexanoic acid, which also is oxidized to adipic acid, this reaction being however slower than the concurrent ones, and (b) a direct oxidative scission to adipic acid.

The relevant reaction rates are modified when titanium-silicalite-1 (TS-1) is used as catalyst. In this case, in fact, the high concentration of hydroxy radicals within pores accelerates the reaction rates, especially the consecutive formation of adipic acid and of lighter diacids. The proper choice of the solvent, which also may act as a radical scavenger, both without catalyst and with TS-1, is a powerful tool for controlling the rates of the various reactions involved. With either *t*-butanol or dioxane - efficient radical scavengers - all the reaction rates are slowed down, in special mode the consecutive oxidation of the very reactive ε-caprolactone into diacids.

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IND-PO-15 Low molecular phenols: useful starting materials for the production of fine chemicals. Toward the valorisation of active compounds and agro-industrial fractions from vegetal waste.

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In this communication we report our recent results on the preparation of new biologically active compounds from commercially available low molecular phenols by using ecofriendly chemical procedures. As example, flavonoids were converted into new derivatives showing apoptotic activities against tumoral cell lines, antifungal and antioxidant properties [1]; cinnamic acids were converted into the corresponding 4-vinyl phenols, flavoring compounds useful for perfumery, food, and beverage industries [2]; tyrosol into biologically active hydroxytyrosol and its lipophilic derivatives [3].

More recently, our efforts have been turned on the utilization of low molecular phenols which are selectively extracted from agro-industrial wastes by using innovative technologies, in particular, new biophenolic fractions from different waste and tissues of *Olea europaea* L.[4]. Further investigation are in progress to obtain biologically active compounds useful for industrial applications such as food, cosmetic and pharmaceutical fields.

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IND-PO-16 Synthesis and characterization of hydroxylated oligoamides obtained from renewable resources

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Several hydroxylated oligoamides have been synthesized and characterized in order to obtain water soluble compounds with a high affinity for polar materials as wood, paper and natural fibres. The interest for the synthetic procedures is the use of renewable resources as starting compounds. In fact natural compounds or their derivatives, as tartaric acid, *D(+)*-glucaric acid and α,α-trehaluronic acid, have been used as diacids in the polycondensation reactions.

In order to activate the acids, the dimethyl esters have been obtained using modified versions of the procedures reported in literature [1, 2]. The polycondensation reactions between different dimethyl esters and different diamines have been performed in order to obtain oligoamides with different behavior. In fact products with different molecular weight and different hydrophilic/hydrofobic ratio have been obtained using diamines as 1,2-ethylenediamine, 1,6-hexamethylenediamine, 1,12-diaminododecane, 2,2'-(ethylenedioxy)bis(ethylamine), p-xylylenediamine and several polyamines.

Several attempts have been made by changing the reaction parameters (time, temperature, solvent, catalyst). Generally the best conditions for the synthesis have been found using methanol or DMSO as a solvent and triethylamine as a catalyst. All the compounds obtained in this study have been characterized through FT-IR, ^{1}H, ^{13}C NMR spectroscopy and through 2D NMR techniques (gCOSY, gHSQC) .

The oligoamides with low molecular weights have been employed in wood consolidation. Other different applications for example as additives in the commercial formulations of polymers have been studied.

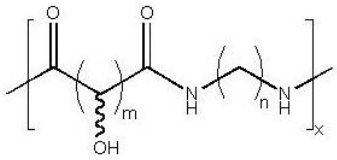

Figure 1

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IND-PO-17 Ethanol Dehydrogenation to Ethyl Acetate: a Kinetic Study

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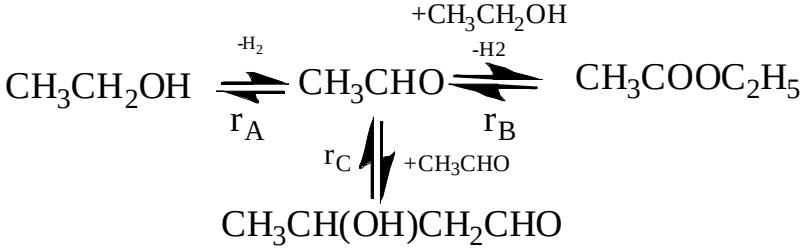
A one step reaction of ethanol dehydrogenation to ethyl acetate, promoted by a copper/copper chromite catalysts, has been studied. The reaction has been performed in a stainless steel fixed bed reactor under pressure (10-30 bar), in a temperature range of 200-260°C and with contact time values, W/F_{EtOH}^{0}, ranging from 30 to 100 $ghmol^{-1}$. In the best operative conditions: T= 220°, P= 20 bars and W/F_{EtOH}^{0}= 100 $ghmol^{-1}$ a conversion of 70% with a selectivity of 98% to ethyl acetate have been obtained. These values are very promising for the industrial development of the process because have never obtained before. Therefore, it is important to study the kinetic behavior of the catalyst that has given the best performances. At this purpose, a depth study of the mechanism and reaction kinetic has been performed. According to the literature, the mechanism of ethanol dehydrogenation to ethyl acetate is not well defined yet, but most authors agree that the first elementary step would be the molecular adsorption of ethanol on the active site to give ethoxide and adsorbed hydrogen [1,2]. The ethoxide species are subsequently dehydrogenated to adsorbed acetaldehyde that can further reacts with an adsorbed ethoxy group to give ethyl acetate. As it was shown [3], the use of optimal operating conditions favor the selectivity to ethyl acetate with respect to acetaldehyde. From the analysis of the reaction products, we have deduced that ethyl acetate is produced in two different steps, as reported in the following scheme:



As reported in the same scheme different by-products can be obtained via aldol condensation as a consequence of the reaction between two acetaldehyde molecules.
A preliminary evaluation of the eventual external and internal mass transport limitations has been made by applying Weisz-Prater and Mears criteria [4], respectively valid for intra-particles diffusion and inter-phase transport. From this analysis we concluded that in our experiments a chemical regime was operative. On the basis of the assumed mechanism, different kinetic models were used for interpreting kinetic data. The obtained results in simulating experimental data have been compared with the aim to individuate the best kinetic model and related parameters.
Moreover, starting from a reliable reaction mechanism, different possible rate-determining steps have been hypothesized, deriving, in each case, the related expressions of the reactions rate laws to be used for describing the collected experimental runs. In alternative also other kinetic models have been considered in the comparison, such as, for example a Langmuir-Hinshelwood-Hougen-Watson model and other different empirical models (power law). The knowledge of the kinetics and the reaction mechanism is of fundamental importance for the scale-up to the industrial process. The best kinetic model has been applied to create a flow-sheet of a continuous industrial plant with ChemCAD 6.2 process simulator.

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IND-PO-18 Experimental and numerical study on methane combustion in a catalytic monolith at elevated pressures

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In view of its capability of burning fuels with high efficiency and at a relatively low temperatures, thus reducing the formation of NO_x and unburned hydrocarbons, catalytic combustion (CC) has been identified as a promising technique for clean and efficient combustion. Despite of this interest, CC suffers from several limitations due to the high cost of materials (catalysts are based on noble metals) and their low thermal resistance (substrates can achieve 1200 °C). These limitations could be partially overcome using low-cost catalysts, such as perovskite oxides that show good activity and high thermal stability [1]. Up to now, CC has been predominantly studied at atmospheric pressure. The extension of these results to higher pressure is not trivial [2]. In this study, combustion of methane in a $LaMnO_3$/La-γAl_2O_3-coated monolithic reactor is studied under conditions relevant to gas turbine applications (temperature up to 800 °C and pressure up to 11 bar). A two-dimensional CFD model is developed to simulate steady and unsteady behaviors of the high-pressure catalytic combustor and its bifurcational features.

In the figure 1, the experimental and numerical bifurcation plots are shown in terms of methane conversion as a function of the combustor pressure. At about P =8 bar, a passage from the non ignited solution to a ignited solution occurs accompanied by a rapid increase in methane conversion (from 15 % to 100 %). The experimental trend is well reproduced by the CFD model which can then be used as a tool for simulating the effect of operating conditions and parameters.

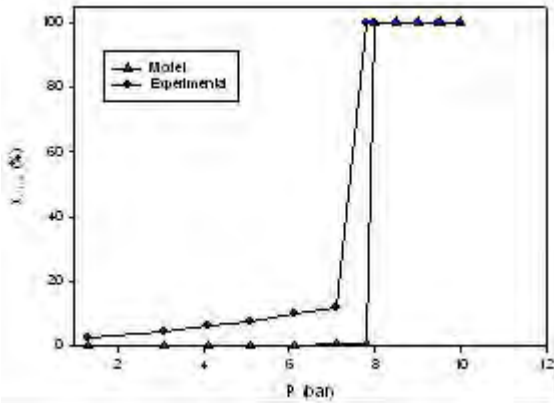

Figure 1.

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IND-PO-19 POLYMER SUPPORTED HETEROGENEOUS CATALYSTS FOR THE FORMATION OF HYDROGEN PEROXIDE FROM THE ELEMENTS

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The formation of hydrogen peroxide from the elements (direct synthesis, DS) has been investigated for years as an alternative to the antraquinone process for the production of low concentrated solutions.[1] Heterogeneous catalysts supported on inorganic solids have been mainly investigated so far.[2] However, organic polymers are suitable candidates as catalytic materials for this reaction in view of the low temperature applied. In particular, strongly acidic ion-exchange resins have been already proposed for this reaction, either as carriers of Pd^{2+} ions [3] or Pd^{0} nanoparticles,[4] but not for bimetallic Pd/Pt catalysts, which are also active in the DS,[5] yet. Commercial ion-exchange resins (Lewatit K2621 and K2629) were ion-exchanged with suitable Pd^{II} and Pt^{II} complexes and subsequently treated with different reducing agents ($H_2C=O$; H_2; aqueous $NaBH_4$) to afford bimetallic Pd/Pt catalysts (1%/0% to 1%/1%, w/w). The catalysts were tested in the DS at 2°C in MeOH, at 3.8 MPa (76% inert gas, 21% O_2, 1% H_2). Preliminary results showed a productivity of 43 $mol(H_2O_2)\cdot h^{-1}\cdot kg_{cat}^{-1}$, with a 0,24 % final concentration of H_2O_2.

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IND-PO-20 Emerging materials for dye sensitized solar cells

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Dye-sensitized solar cells (DSSCs) represent a promising, low cost alternative to silicon photovoltaic devices and are a particular type of photo-electrochemical cell.[1]

Because of low fabrication costs, simple manufacturing process and using no toxic materials, a DSSC is expected to be a large-scale prevalent device and a source of clean renewable energy.

A DSSC consists of a thin mesoporous film (10-15 μm thick) of nanocrystals of a metal oxide, often TiO_2, which is sensitized to visible light with a metallorganic or organic light absorber. The so formed photo-electrode is combined with an electrolyte (based on I^-/I_3^- redox couple) and a counter electrode (covered by a thin catalytically active platinum layer), thus obtaining the photo-electrochemical device.

Daunia's activities on materials development focuse above all on the preparation and optimization of performing, low cost and environmentally friendly materials, whose scale-up process is easy and industrially applicable.

In particular, a screen printing paste based on crystalline anatase nano-rods was developed. NanoTiO_2 for DSSC anode was synthesized by adopting a non-aqueous, solvothermal method, involving the use of a high boiling organic solvent and $Ti(^iPrO)_4$ as precursor.[2] A significant dimensional and morphological control over the resulting TiO_2 nanostructures was obtained and an easily scalable (up to 100 liters) synthetic protocol was developed.

On the other hand, another fundamental component of dye sensitized device is represented by the active redox electrolyte. By using the traditional liquid electrolyte good performances could be reached, but a long-term stability cannot be guaranteed. Therefore, our studies focused on the realization of new quasi-solid polymer gel electrolytes, able to improve cell stability preventing electrolyte leakage. The home-made gel electrolytes have been obtained by adding to the electrolyte solution (molecular solvents containing redox couple) a polyiodide (a methacrylate based polymer containing cationic unities, iodide is the counter ion),[3] that works as gelator for the liquid solution and at the same time enhances a coordination-decoordination of iodide ions mechanism, while ion migration occurs inside liquid phase.

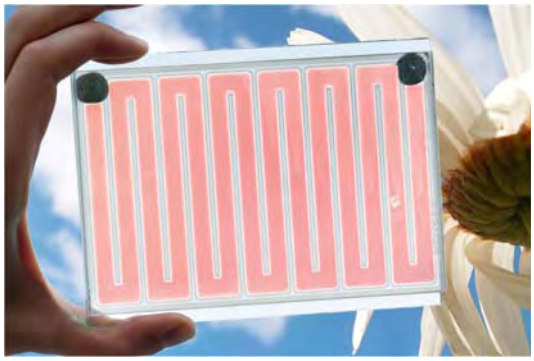

Figure 2. A picture of a DSSC module

Finally, cell long-term stability could be reached thanks to the use of an efficient sealant. It should have the following characteristics: representing a protecting barrier from external agents (such as water, humidity and other impurities), be inert towards electrolyte's chemical aggressivity and resist to photo-degradation and temperature variations. Our studies showed that an inorganic glassy sealant could satisfy the aforementioned requirements.

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IND-PO-21 Synthesis of Titanium Dioxide/PS-b-PEO BCPs Nanocomposites and Inorganic Nanoscopic Materials by Sol–gel Synthesis

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The nano-composites formed by inorganic and polymeric materials have large potential to be the candidates for the next-generation materials owing to their excellent optical, electrical, optoelectronic, mechanical and magnetic properties. We have studied the possibility of obtaining smart hybrid nano-composites combining the techniques of Sol-Gel synthesis for the preparation of inorganic metal oxides and the self-assembly of block copolymers (BCPs) to form periodic nanostructures ordered over large areas. Starting from the hybrid nanocomposites, the possibility to prepare metal oxide nanoparticles of well defined shape and geometry arranged in ordered arrays with periodicities dictated by those of BCP nanostructures [1,2], has also been explored.
The concept of using nanostructured thin films of poly(styrene-*b*-ethyleneoxide) (PS-*b*-PEO) BCP of different morphologies as a "structure guiding host" matrix to drive the selective inclusion of titanium dioxide precursor in the PEO domains, has been exploited. A high molecular mass sample of PS-*b*-PEO with volume fraction of the PEO block of ≈0.20, showing a phase separated nanostructure with cylindrical microdomains of PEO in a PS matrix, and a low molecular mass sample of PS-*b*-PEO with volume fraction of the PEO block of ≈0.50 and characterized by a lamellar morphology, have been employed. The TiO_2 precursor has been selectively included in the hexagonally packed PEO cylinders and in the PEO lamellae of the two PS-*b*-PEO samples. Thin films of these hybrid nanocomposites have been subjected to proper heat treatments to obtain TiO_2 crystals and remove the polymeric matrix.
We show that hybrid nanostructured thin films with high degree of orientational and positional order of PEO cylinders filled with the TiO_2 precursor can be easily obtained. We also show that these hybrid thin films give rise upon heat treatments to TiO_2 nanoparticles of elongated shape, standing up on the surface of the substrate according to a pseudo-hexagonal geometry reminiscent of the hexagonal morphology of the hybrid nanostructure.

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IND-PO-22 RUTHENIUM SUPPORTED ON HYDROPHILIC ALKYLSULFONIC RESINS AS BIFUNCTIONAL CATALYSTS FOR THE HYDROGENOLYSIS OF GLYCEROL TO 1,2-PROPANEDIOL

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The replacement of fossil fuels with renewable energy sources is a challenging goal and in this connection biodiesel could help in reducing the dependence on oil. This fuel is obtained upon transesterification of triglicerides with methanol and glycerol is the main coproduct (10 % w/w). [1] To make the biodiesel production affordable glycerol has to be transformed into valuable products. Its hydrogenolysis to 1,2-propanediol (1,2PD) has been under scrutiny. [2] It entails the dehydratation of glycerol to acetol and its subsequent hydrogenation to 1,2PD; hence it is catalyzed in water either by bifunctional catalysts (e.g. $CuCr_2O_4$) [2] or by a physical mixture of a sulfonic polymeric catalyst (sulfonated polystyrene-divinylbenzene resins) and Ru/C. [3] No bifunctional catalysts based on metals supported on acidic organic resins has been employed yet.

Although the sulfonated polystyrene-divinylbenzene resins are hydrophilic materials, compatible with the aqueous reaction medium often employed for the reaction, in the presence of water their arylsulhonic moieties generally undergo C-S bond cleavage (desulfonation) at T > 120-130 °C. Under this respect, alkylsulfonic resins are much more stable and should withstand the usually higher temperatures employed in the glycerol hydrogenolysis. We report herein on the preparation and catalytic performance of bifunctional catalysts, comprised of ruthenium supported on alkylsulfonic resins. The latter ones are extremely hydrophilic [4] copolymers of N,N-dimethylacrylamide, 2-acrylamido-2-methyl propane sulfonic acid and ethylenedimethacrylate.

This work has been supported by the Italian Ministry of University and Research (PRIN 2008, prot. nr. 2008SXASBC_004)

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IND-PO-23 *Ab-initio* single crystal structure solution of dihydrodibenzoazepines

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X-ray diffraction represents the most direct non-invasive technique to investigate the structure of crystalline material in terms of atom positions in the crystalline cell. The availability of a single crystal of appropriate size and quality is required. X-ray diffraction is based on constructive interference occurring when Bragg's Law ($2d \sin\theta = n\lambda$) is satisfied. Crystal structure solution needs to know the structure factor moduli and their phases. Unfortunately the diffraction experiment provides the moduli and not the phases. Therefore, the phase problem must be solved in order to find the unique set of phases that, combined with moduli, permits to calculate the electron density map from which an approximate structure model is derived. In a final step a reliable model may be carried out by structure refinement.

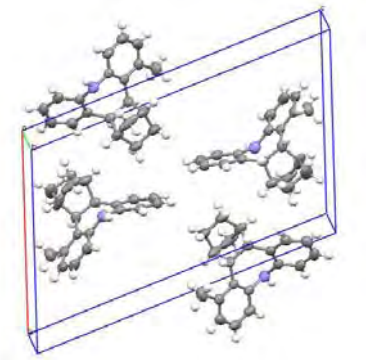

Figure 3. Crystal structure of a dihydrodibenzoazepine molecule.

Direct Methods (DM) are able to estimate the phases and solving *ab-initio* crystal structures. In this work, the structure determination process of two dihydrodibenzoazepines (Figure 1) is performed by means the software Sir2011[1]. This is an automatic program supported by a very user friendly graphic interface. Several new algorithms have been implemented in Sir2011, making the program very efficient: it is able to solve both small/medium-sized structures as well as macromolecules.
Details about synthesis and theoretical calculations of these molecules can be found in a companion paper [2].

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IND-PO-24 Experimental and modelling study of the impact of interphase and intraphase diffusional limitations on the deNOx efficiency of V-based catalyst for NH_3-SCR Diesel exhausts aftertreatment.

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In order to control the emissions of NO_X from Diesel and other lean burn engines, the Selective Catalytic Reduction of NOx by ammonia/urea has been applied in recent years to HD and LD Diesel vehicles with excellent results. In this context, the application of numerical simulations has been found a valuable and important tool to support development and practical applications of SCR sytems. In the present contribution, an evaluation of the impact of mass transport effects on the performances of an extruded SCR monolith catalysts made of V_2O_5-WO_3/TiO_2 is presented, based on both experimental and modelling work.
Intrinsic kinetic data were collected over the catalyst in the form of powder to study the typical SCR reacting systems, covering the effects of temperature and of NO_2/NO_x feed content. These data were used to estimate the rate parameters of the reactions included in a suitable kinetic model. Intrinsic rate equations were afterwards incorporated into a 1D + 1D dynamic mathematical model of SCR monolithic converters which accounts for both gas/solid and intraporous mass-transfer resistances [1]. Simulations were carried out for different feed conditions and temperature variations and then compared to experimental data collected on a 5 cm^3 monolithic catalyst sample. The model predictions were found in good agreement with experimental results: negative deviations for the deNO_x efficiency of the monolith configuration with respect to that of the powdered catalyst were observed at T > 250 -300°C. Comparison between data collected in the kinetic regime over the powdered catalyst and data obtained over the lab scale monolith points out the role of mass transfer in determining the activity of SCR catalytic converters. Numerical simulations by means of the 1D+1D monolith channel model allowed decoupling the effects of intra- and inter-phase mass transfer limitations, emphasizing their impact on the performances of extruded SCR monolith converters: their effect on NO_x conversion was found to be significant, depending on temperature and NO_2/NO_x feed content, in line with recent reports for wash-coated systems [2].

The authors gratefully acknowledge the financial support of Daimler AG, Germany.

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Indice degli Autori

Chimica Inorganica

INO-PL-01 Mechanisms of action and transport of platinum drugs: an update

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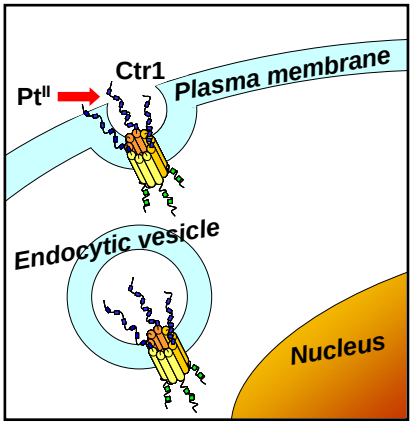
When the antitumor activity of cisplatin was discovered no one would have predicted the existence of specific proteins able to transport platinum across the cell membrane or to specifically recognize DNA modified by this drug. However such proteins do exist and, furthermore, are specific for the platinum substrate considered. [1]

Apart from passive diffusion, a number of carrier-mediated import proteins have been identified, the main players being organic-cation transporters and the copper influx transporter CTR1. Moreover ATPases involved in the removal of excess copper appear to play a role in the excretion/inactivation of platinum drugs. Also the copper chaperone Atox1 has been found to interact with platinum drugs at the same site as copper. Moreover, for longer contact time with platinum, it forms dimers similar to those formed by copper and which have been shown to be able to translocate to the nucleus and act as a transcription factor.



After cisplatin binding to the putative target, double-stranded DNA, a kinked structure is formed that is recognized by certain proteins. Such an interaction has direct consequences on cell viability and eventually leads to cell killing by apoptosis.

In the presentation new insights both in the cellular uptake of the drugs and in the processing of their adducts with DNA will be highlighted.[2,3]

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INO-PL-02 Organometallic Nanoparticles: Growth and Surface Chemistry

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Organometallic nanoparticles are prepared by decomposition in mild conditions of organometallic precursors in solution. The decomposition is preferably achieved under dihydrogen which results in the formation of a clean surface, covered with hydrides and able at performing further chemistry or growth processes. Addition of various ligands may modify both the physical and the chemical properties of the particles as well as the growth process, leading to the formation of particles of defined sizes and shapes, for example nanorods, nanocubes, nanowires of iron and cobalt, nanoarrows or nanocubes of platinum as well as to extended super-lattices of monodisperse nanospheres.

The surface characterization may be achieved by standard techniques of material science as well as by the use of NMR (solid state, solution and gas phase). In this respect, static solid state ^{2}D NMR and MAS ^{13}C NMR are particularly efficient to locate and study the dynamics of surface ligands as well as to study hydrogenation and oxidation reactions. Surface reactivity of these nanoparticles will be presented both for solid / gas reactions such as CO and ethylene hydrogenation revealing some unexpected features such as the facile breaking of a C-C bond and for catalysis in solution, including asymmetric catalysis.

The presentation will detail first the surface reactivity of ruthenium nanoparticles and show in a second step how this knowledge can allow, in the case of iron, the growth nanoparticles of controlled size, shape and physical properties as well as that of iron carbide of tunable size.

INO-PL-03 Low Coordinated Phosphorus Compounds: Fictions, Facts, and Applications

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Rather exactly 50 years ago, H-C≡P - the phosphorus analogue of hydrogen cyanide - with a phosphorus carbon triple bond has been detected as a product in the decomposition of PH_3 in a plasma generated by a rotating arc struck between graphite electrodes. Since then, many unsaturated phosphorus compounds have been prepared by using bulky substituents in order to stabilize these highly reactive species kinetically. We have developed a straight forward access to unsaturated organophosphorus anions which is based on the reductive degradation of elemental phosphorus. Phosphaenolates, R-P=C(OM)R^1 (M = alkaline metal) play a crucial role as intermediates in the synthesis of phosphorus based photoinitiators produced on an industrial scale. A new simple synthesis of Na(O-C≡P) will be discussed which allows the synthesis of a wide range of functionalized organophosphorus derivatives.

INO-PL-04 Transition Metal Reaction Mechanisms via Density Functional Theory

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A focus on making and breaking of chemical bonds is what distinguishes Chemistry from other sciences. Thus, detailed knowledge of the mechanism of a chemical reaction provides a key to the understanding. Transition metals play an important role as catalysts in reactions that span the range from ethylene polymerization to enzymatic reactions.

This lecture will cover the background of modern computational chemistry especially density functional theory and illustrate its use with a number of examples, such as carbon-hydrogen bond activation, ethylene addition to nickel dithiolenes, conversion of azides to metal imidio complexes, alpha elimination on metal clusters, and protonation of diiron complexes related the hydrogenases, and C-X bond forming reactions supported by spin-state changes.

INO-PL-05 Molecular and nanosized catalysts for the conversion of renewables into energy and chemicals

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The simultaneous conversion of alcohols and sugars into energy and chemicals is a target of primary importance for the sustainable development. The realization of such a process provides renewable energy with no CO_2 emission and, at the same time, leads to the production of industrially relevant feedstocks, such as aldehydes, ketones and carboxylic acids. Such a target can be accomplished for a variety of renewable alcohols and carbohydrates, including ethanol, glycerol, ethylene glycol and sugars, by means of two electrochemical devices: *direct fuel cells* and *electrolyzers*. In either case, an aqueous solution of the fuel in the anode compartment is oxidized either on a nanostructured catalyst or on a molecular catalyst that are appropriately designed to promote selectively the partial oxidation of the anolyte with high stability and fast kinetics. When the oxidation process is carried out in a direct alcohol fuel cell (DAFC), the solid electrolyte is an anion-exchange membrane and electrical energy is released, while the alcohol is selectively converted to the corresponding carboxylic acid, isolated as alkali metal carboxylate (Figure 1) [1]. In an electrolyzer, containing an anode electrocatalyst similar to that employable in a DAFC, the electrolyte may be either an anion exchange-membrane or a solution of an alkali metal hydroxide (NaOH or KOH, for example) and the alcohol is converted to the corresponding alkali metal carboxylate, while hydrogen gas is produced at the cathode upon water reduction (Figure 1) [2].

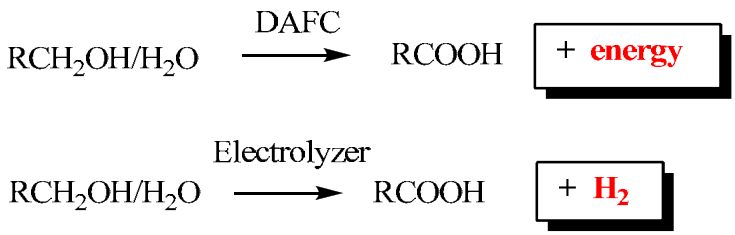

Figure 1.

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INO-PL-06 Photo-activation of TiO_2: insights from theory

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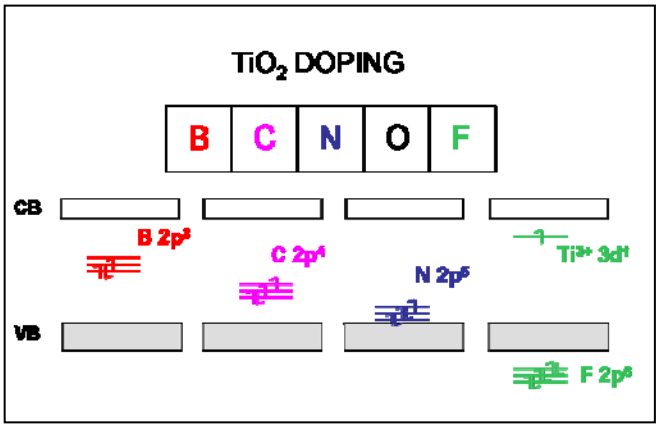
The theoretical approach nowadays has become an essential tool to address fundamental issues regarding inorganic chemistry and material science. Modern computational resources allow the calculation of very large models, thus removing the size limitation problem which in the past has prevented the study of realistic systems.
During the last few years we have applied density functional theory to improve the understanding of titanium dioxide material. TiO_2 is a versatile semiconductor used in several applications ranging from photocatalysis to self-cleaning coatings to solar cells, as a consequence of its ability to harvest solar light and convert it into other forms of energy or chemical reactivity. Most of the investigations are driven by potential applications, however, understanding of the underlying mechanisms is crucial for real progress in these fields.
Most of the times TiO_2 is doped or functionalized in order to lower the threshold energy for band gap electron-hole excitation in the vis-spectrum or to improve the surface photochemistry.[1]
The identification of the species formed and of their specific role is pivotal for improving the material performance. For example, doping with metal (such as Cr, Sb, and Nb)[2] or non-metal atoms (such as B, C, N, and F)[3,4,5] on one side introduces impurity states in the band gap reducing the absorption threshold of the material, on the other it may also cause the formation of oxygen vacancies or of Ti^{3+} species,[6,7] eventually relevant for the electron transport (n-type doping) and for the chemical reactivity at surfaces,[8,9] but also potential recombination centers.



In this lecture we will present an overview on recent findings related to doped, defective and photoexcited TiO_2 of special interest in photocatalysis and photochemistry. We will also show how the correct choice of the method is essential for the accurate description of the various species formed upon doping, functionalization and photoexcitation.

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INO-KN-01 Cell uptake and processing of metalated purines: a new possible path to antitumor and antiviral drugs

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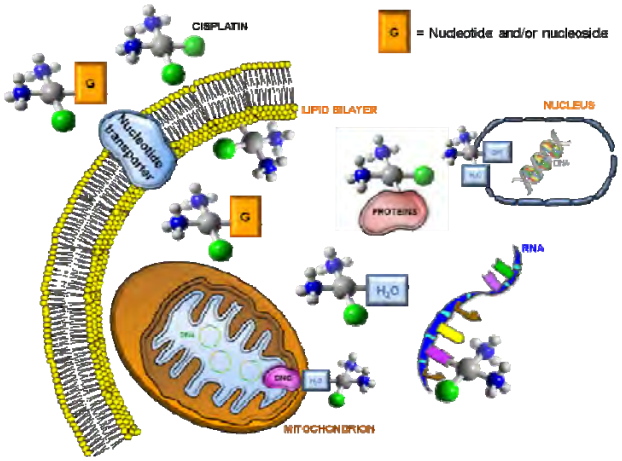
Cisplatin, *cis*-diamminedichloroplatinum(II), is one of the most widely used antitumor drugs in clinical therapy, as a critical component against a broad range of malignancies. Platinum anticancer compounds are known to target DNA where they can bind the *N7* of a purine base. *Cisplatin*, as other bifunctional agents, is also able to bind to adjacent G/A residues, resulting in the cross-link lesions believed to be responsible for the observed antitumor activity [1].

N7-metalated purines, in some cases, seem to be characterized by a relevant antitumor activity [2]. This has led us to hypothesize a *cisplatin* parallel mechanism of action: based on free platinated purines formation, directly in tissues, after drug administration, see Figure. In order to evaluate this possible mechanism as a key path to develop new drugs, we performed a series of experiments [3] focused on platinated nucleobases cell uptake and processing. In particular our researches were focused on the possible insertion of metalated nucleobases into nuclear and/or mitochondrial DNA/RNA synthesis, operated by DNA/RNA polymerases [4]. Model metalated nucleosides/nucleotides with nitrogen carrier ligands have been synthesized, isolated and characterized. For the first time cell uptake and mobility mechanism, related to plasmatic cell and/or mitochondrial membrane crossing, has been studied. The possible development of new drugs based on this new rational base will be discussed.



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INO-KN-02 Chemistry of Ni^{2+} in urease: sensing, trafficking and catalysis

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The biological essentiality of transition metals in enzymatic catalysis, coupled with their limited environmental availability, has driven organisms to evolve mechanisms for selective metal ion sensing and utilization. Changes in metal ions concentration are perceived by metal-dependent transcription factors, proteins that regulate the machineries of competitive metal ion homeostasis and metallo-enzyme activation. The intrinsic toxicity of the majority of metal ions demands a regulated intracellular trafficking, performed by specific chaperones. The Ni^{2+}-dependent urease enzymatic system is a paradigmatic case to study the strategies that cells use to handle an essential and yet toxic metal ion. Recent years have witnessed impressive achievements in the understanding of the biological chemistry of Ni^{2+} in the urease system.

The more recent advances in the comprehension of the specific role of Ni^{2+} in the catalysis and the interplay between Ni^{2+} and other metal ions such as Zn^{2+} and Fe^{2+} in the metal-dependent enzyme activity will be described, with special reference to the work carried out in our laboratory, tightly connected among, and strongly supported by, the partners the framework of CIRMMP (Consorzio Interuniversitario di Risonanze Magnetiche di Metallo-Proteine).

In particular, the structural features of the enzyme bound to inhibitors, substrate analogues and transition state or intermediate analogues have shed light on the catalytic mechanism. Structural and functional information has been correlated to understand the Ni^{2+} sensing effected by NikR, a nickel-dependent transcription factor. The urease activation process, involving insertion of Ni^{2+} into the urease active site, has been dissected and analyzed through the investigation of the molecular properties of the accessory proteins UreD, UreF and UreG. The Ni^{2+} intracellular trafficking has been rationalized through the knowledge of the structural and metal binding properties of the metallo-chaperone UreE. All the while, key general concepts have been revealed and developed, such as the overall ancillary role of Zn^{2+} in nickel metabolism, the intrinsically disordered nature of the GTPase responsible for coupling energy consumption to carbon dioxide requirement for the urease activation process, as well as the role of the accessory proteins regulating this GTPase activity. The overall activity of CIRMMP and its role in the development of this research will be illustrated.

INO-KN-03 A multidisciplinary research under the aegis of the INSTM consortium, exploration of the properties of nanostructured magnetic molecules

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[b] INSTM RU Modena, Dip. Chimica, Università di Modena e Reggio Emilia, Modena, Italy;
[c] INSTM RU Padova, ISTM-CNR, Dip. Chimica, Università di Padova, Padova, Italy;
[d] INSTM RU Siena, Dip. Farmaco Chimico Tecnologico, Università di Siena, Siena, Italy;
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INSTM is a consortium of 45 Italian Universities and groups about 2.000 researchers, post-docs and PhD students working in the area of Chemistry, Materials Science and Technology [1]. It is an original bottom-up aggregation of researchers, with a minimum of bureaucratic structure to efficiently coordinate activities and promote the joint participation of INSTM members to Italian and European projects. INSTM is also active in educational work, technology transfer, and establishing spin-off enterprises.

An example collaborative research coordinated by INSTM is represented by the joint efforts of the Firenze, Modena, Siena and Padova INSTM Research Units to investigate nano-assembling of magnetic molecules and its effects on the molecular properties [2-4]. The team also profited of an external collaboration with a French group through a European Network-of-Excellence project leaded by INSTM. Combining experimental methods like scanning probe microscopy, surface sensitive mass spectrometry and X-ray based spectroscopies with theoretical modelling it has been possible to demonstrate that certain molecules, known to behave as tiny magnets in the bulk phase, maintain their memory effect at the nanoscale, e.g. when assembled into a monolayer film on a metal surface [5,6]. These studies open the way to a strongly motivated research activity focused on the development of single-molecule based devices for spintronics.

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INO-KN-04 Catalysis: a Powerful Tool for Sustainable Chemistry

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There is a strong demand for more sustainable and environmentally benign synthetic methodologies suitable for the synthesis of chemicals and materials which are able to improve or maintain the current quality of life. Moreover an increasing ecological sensibility asks for renewable resources, alternative to fossil fuels, to produce synthons for fine chemicals, or polymers having the potential of biodegradation and/or biocompostation.

The UdRs of CIRCC are mainly active in the following five research lines of interest: *i)* New catalytic processes for industry, environment and energy; *ii)*Biomass for the production of energy and chemicals; *iii)* New environmental benign catalyst for the synthesis of polymeric materials from renewable resources; *iv)*Homogeneous catalysis and biocatalysis; *v)*Reactivity and modelling of organometallics and coordination inorganic compounds.

In this presentation some representative examples related to these topics will be provided. In particular the controlled synthesis of gold nanoparticles (AuNPs) of 4-9nm, incarcerated in a novel semicrystalline nanoporous polymer matrix will be described. This catalyst was successfully tested in the oxidation of primary and secondary alcohols using dioxygen as oxidant under mild conditions. The specific constant rates in the oxidation of (±)-1-phenylethanol to acetophenone and of benzyl alcohol to benzaldehyde are among the highest found for polymer incarcerated AuNPs. Similar values in terms of activity and selectivity were found in the oxidation of primary alcohols as cinnamyl alcohol and 2-thiophenemethanol, and secondary alcohols as indanol and α-tetralol. The catalytic properties were attributed to the formation of the nanoporous ε crystalline form of the polymer matrix that assures easy and selective accessibility of the substrates to the gold catalyst incarcerated in the polymer matrix. A comparison of the catalytic performances between the as synthesized and annealed AuNPs suggests that multiple twinned defective nanoparticle of about 9 nm are the active catalyst in these oxidation reactions. Some features of the reaction mechanism will be also discussed.

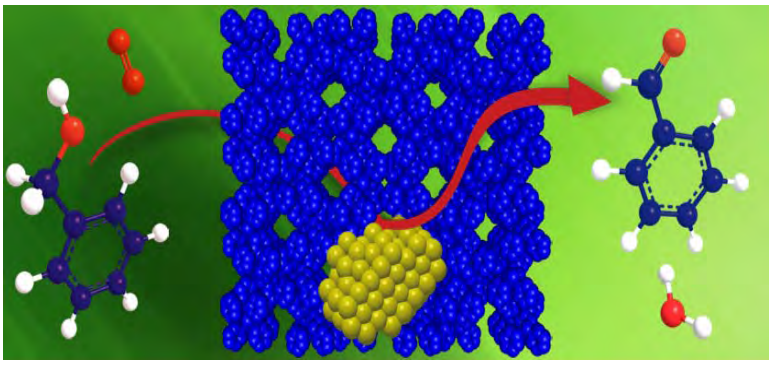

Figura 1. Selective oxidation of benzyl alcohol catalyzed by AuNPs incarcerated in a nanoporous polymer matrix.

INO-KN-05 Correlations between Structures and Chemical Behaviours

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X-ray diffraction, to determine geometries and stereochemical features of molecules, is still a fundamental tool to explore bonding and chemical reactivity. Small geometric differences between compounds and the variable 3D atomic arrangements provide much information on the chemical functionality. The structure-property relationships are based on electronic distributions, so that there are great expectations from the methods based on the electron density topology (QTAIM approach). However, even when they clearly detect bonding between two or more atoms, the underpinnings of the latter, the evolution of the associated chemical effects and their governing parameters may still present obscure points. The topological description of the wavefunctions provides more useful hints on the wider delocalization of the electrons, while perturbation theory concepts help to frame it intuitively. The remixing of the atomic orbitals, which follow a chemical substitution and/or a geometric rearrangement, is in fact rich of chemical information. Accordingly, combined structural and quantum mechanical strategies are often useful, by offering practical suggestions for even practical controls of the chemical behaviors.

An X-ray structure, as a snapshot of a molecule, already frames many chemical features and key aspects. Fortunately, the crystallographers have created, in a half century, a databank such as the Cambridge one, which contains more than a half million of catalogued structures. This should be immediately consulted for the classification of any new species. Moreover, the *horizontal* comparisons between strictly related molecules, with only minor differences, are a key to understand chemistry. Since a long time, our research has inspired to these criteria, which from the structural data address the essence of the bonding and reactivity. Selected cases will be pointed out based on the combination of crystallographic and QM (DFT and qualitative MO analysis) approaches. Our most recent work includes the very rare trigonal bipyramidal Pt_5 clusters, with the electronic stability unexpectedly provided by main group tin atoms [1]. In other cases, the comparative studies have pointed out questionable crystal structures in the databank, even though the X-ray technique is considered as most reliable and almost error-free. Sometimes, atoms of wrong nature have been assigned or the authors have overlooked some essential features [2]. Other examples will be illustrated of key X-ray structures, which have inspired a broader analysis of chemical reactivity or fluxional behaviors, In fact, given that DFT calculations properly mimic the observed compounds, it may be assumed that also the experimentally inaccessible optimized intermediates or transition states have to be regarded with the same confidence. This opens much wider horizons for the evolution of structures and their associated chemical relevance.

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INO-KN-06 Gaseous models of fundamental processes: the crucial role of ionic and neutral intermediates.

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According to a recent recommendation by Hoffmann et al., the thermodynamic and kinetic stability of a species is best described by the extreme concepts of "viable" and "fleeting" molecules [1]. Viable species have half-lives of a day or longer under ambient conditions, whereas fleeting molecules are local minima with barriers that prevent escape from their well. Charged and neutral fleeting species, though very short-lived, are important players in biochemical and atmospheric processes, as energy reservoirs, carriers of isotopic fractionation or intermediates of processes that convert complex starting materials (biomass feedstocks) into useful products [2]. As a consequence, the pivotal question is not "how long a molecule lives" but "the role it plays during its short life, and how strongly it affects other molecules' lives".
Mass-spectrometric approaches to the synthesis of *neutral* reactive intermediates have successfully discovered exotic, elusive species, proving their existence and kinetic persistence as intact, isolated species in the idealized gaseous phase [3]. These laboratory studies, performed under conditions similar to those existing in planetary atmospheres or in microenvironments in the absence of oxygen, pioneer the discover of new molecules in planets and interstellar clouds or help understanding biochemical processes relevant to cell regulation functions or modifications [2].
Useful models for more complex processes are also the ion-molecule reactions that lead to the activation and functionalization of hydrocarbons. Here the very nature of the *charged* intermediate may determine fast and efficient C-H activation steps, necessary to reach the goal of selective functionalization. The study of these gas-phase reactions has allowed the elucidation of the activation step mechanism, unraveling the crucial role played by the radical cationic character developped in intermediates and/or transition states. A significant contribution has been given by reactions that use metal-free electrophiles in the absence of catalyzers, like the radical cations SO_2^+ and $P_4O_{10}^+$ [4]. This has been recently suggested as a new possible route to the conversion of methane to more directly usable compounds [5]. Finally, the synthesis of isotopically specific intermediates proves to be a unique tool to investigate kinetic isotope effects in isotope-exchange reactions, suggesting a two-intermediates model for unconventional heavy-atoms kinetic isotope effects [6].

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INO-KN-07 Metalloprotein models: towards catalytic systems

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The predictive power of protein design methods has dramatically increased over the last years, with the challenge of preparing artificial models whose properties can mimic, enhance, and perhaps improve upon many features found in natural metalloenzymes [1].
To this aim, we designed catalytic artificial metalloproteins from α-helical coiled-coils, called DFs [2] and Mimochromes [3], whose active sites were engineered to reproduce the di-iron-oxo and heme-proteins functionalities, respectively.
Structural features of DFs and natural di-iron proteins, as well as functional elements of Mimochromes and natural horseradish peroxidase, were borrowed to obtain a *de novo* protein class with five-coordinated heme-complex and peroxidase activity, named MPs (Mini-Peroxidases). The basic structure of these models consists in a deuterohemin covalently linked to two *helix-loop-helix* peptide chains (Figure 1). The active site presents: (*i*) an *homo*-Cys/His residue in a single chain that acts as axial ligand to the iron ion,leaving the sixth coordination site able to accommodate exogenous ligands or substrates; (*ii*) an Arg residue in the distal site that should be able to activate hydrogen peroxide to give HRP-like catalytic process. The last analogue MP3 was successfully synthesized and characterized, and its biocatalytic efficiency was evaluated.

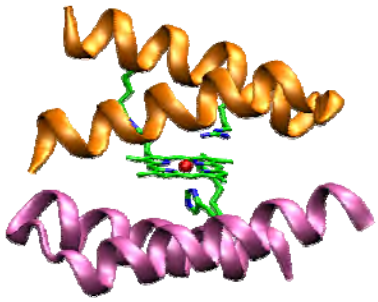

Figure 1

Results on the spectroscopic and structural characterization, together with functional implications, will be discussed.

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INO-OR-01 Metalloprotein mimics by design: strategies and applications

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Metalloproteins take part in a variety of life-sustaining processes and catalyze difficult reactions with efficiency and selectivity that few other natural or artificial molecules can achieve [1]. For this reason, structural and functional studies on metalloproteins have been the focus of many years of research. These studies require a simultaneous and accurate analysis of both the polypeptide chain and the metal cofactor herein embedded. In fact, the plethora of interactions that occur between the metal cofactor and the protein environment mutually affects the properties of each other, thus enhancing, diversifying or tuning their individual functions [2]. Understanding at a molecular level the mechanism by which the protein matrix finely tunes the environment of the metal cofactor is of fundamental importance in both basic and applied science.

Over the years, a large number of low molecular weight chemical catalysts has been developed as metalloenzyme mimics [1,2]. They have been basic in elucidating structure and function of metalloproteins and metalloenzymes; however they often fail in reproducing several features of biocatalysts, such as high turn-over number under mild conditions and high selectivity. Combining the advantages of chemical and biological catalysts would represent a daunting goal for chemists.

Tailoring synthetic models requires the development of sophisticated molecular architectures that distil the quintessential elements responsible for activities. Thus, peptide-based models seem valuable candidates to mimic both the structural features and reactivity of the natural systems. Using a structure-based strategy we have reproduced by design metalloprotein active sites. We centered our attention on iron-containing proteins, and we developed models for heme [3] and diiron-oxo [4] proteins. Our recent results on their structural and functional characterization will be presented. Their usefulness in biomedical and environmental applications, as well in biosensor construction, will be particularly highlighted.

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INO-OR-02 Molecular and Statistical Modeling of Physicochemical and Biological Properties of Antiproliferative Platinum(IV) Complexes

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Since the discovery of the antitumour activity of *cis*-$[PtCl_2(NH_3)_2]$, cisplatin, the search for alternative platinum complexes as antiproliferative agents has been an active area of research. Pt(IV) compounds represent an alternative class of potential prodrugs that are of considerable interest. These species are more inert to ligand substitution reactions than their Pt(II) counterparts, leading to lower systemic toxicity from unwanted side reactions and increasing the likelihood of the drug reaching its cellular target, the DNA. They are believed to be reduced in vivo to the active Pt(II) metabolite in the hypoxic, reducing and acidic tumor milieu. A judicious choice of the six ligands around Pt centre will modify the physicochemical properties of complexes (in particular lipophilicity and reduction potential) and, hence, their biological activity (bioavailability, cellular uptake, activation, and cytotoxicity). The ability to predict relevant physicochemical properties of Pt(IV) complexes directly from their structures would be an important step in rational design of new drugs, allowing potential candidates to be assessed before lengthy synthesis and testing.

We report the results of the quantitative structure-property relationship analysis of a series of Pt(IV) complexes. Molecular properties extracted from theoretical calculations [1] were used to construct models of experimental data such as electrochemical peak potentials (evaluated by cyclic voltammetry) and the octanol–water partition coefficient (evaluated by a RP-HPLC method). Statistically accurate models for both properties were found using combinations of surface areas, orbital energies, dipole moments, and atomic partial charges [2]. Moreover, theoretical and experimental descriptors were used to predict the antiproliferative activity of Pt(IV) complexes, directly from calculated data [3].

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INO-OR-03 What occurs replacing Mn^{2+} with Co^{2+} in Human Arginase I: a theoretical point of view

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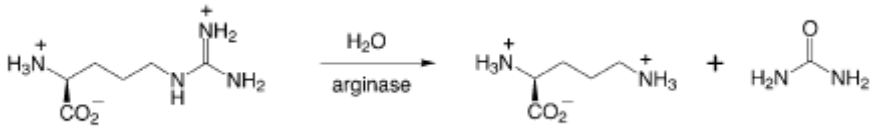
The human Arginase I (hArgI, EC 3.5.3.1) [1-2] is an enzyme containing usually two manganese ions (M_A and M_B) that generates a hydroxide to perform the nucleophilic attack on the guanidinium carbon of L-arginine, following the scheme:



l-ornithine urea

Recently, it has been reported that the incorporation of Co^{2+} in human arginase I (hArgI) shows a greater activity (k_{cat}/K_M) at pH 7.4 (close to the pH of human serum) while the native enzyme works at about 9.5 and has only fractional activity at physiological pH (~7.4). [3]
This behavior induced to consider the Co^{2+} substituted hArgI a promising new candidate for the treatment of L-Arg auxotrophic tumors. In fact, the Co-hArgI exhibits high cytotoxicity against human melanoma and hepatocellular carcinoma cell lines relative to that Mn-hArgI. [3]
With the aim to evaluate the influence of Co ion substitution to the native enzyme, the catalytic mechanism of the di-cobalt arginase has been investigated by using the density functional theory (DFT) employing different exchange-correlation potentials. Results are compared with that relative to the di-manganese native enzyme previously examined [4].

The University of Calabria and MIUR (Grant PRIN 2008F5A3AF_005) are gratefully acknowledged for financial support.

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INO-OR-04 Copper(II) coordination features of human angiogenin protein and related peptide fragments

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Human angiogenin (hAng) is a single-chain blood plasma protein present in physiological conditions, but over-expressed in patients affected by different types of cancers. Interestingly, the binding affinity between Ang and endothelial cells is largely increased in the presence of copper ions. It is well known that copper(II) is a strong angiogenic signal *in vivo*, but the specific molecular mechanism by which it works and the targets of its activity remain unclear. It has been demonstrated that extracellular translocation of the cellular copper occurs during angiogenesis processes, suggesting that the metal coordination by an extracellular protein involved in angiogenesis, such as angiogenin could be part of a signalling process. In this context, the characterization of copper(II) complex species with protein is a valuable aid in a better understanding of potential mutual biological influences. We report the coordination properties of peptide fragments encompassing the hAng N-terminal domain towards Cu^{2+} determined by means of combined potentiometric and spectroscopic techniques. The results obtained show that these fragments have an unusual copper binding ability. At physiological pH, the prevailing complex species formed by hAng(4-17) is [CuLH], in which the metal ion is bound to two imidazole and two deprotonated amide nitrogen atoms disposed in a planar arrangement. These complex species were used to probe the metal binding mode of the whole hAng protein and, at this aim, the recombinant hAng protein was expressed and a preliminary characterization of its copper(II) complexes was performed by means of EPR, CD and UV-vis measurements. The preliminary data indicate that the copper(II) complexes formed by the hAng protein, show a great similarity with those obtained for the N-terminal peptide fragments, suggesting that this domain may be the preferred copper(II) anchoring site in the whole protein. The high affinity for copper ion showed by the protein may give reasons of possible their interactions in vivo, and then of a potential correlation between copper and angiogenin.

INO-OR-05 Adaptive Chirality in Large Random Aggregates of Porphyrins

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Biomolecular structural motifs play a central role in the functioning of biological systems [1], and considerable effort has been focused recently on supramolecular interactions in the search for new probes capable of reporting on specific conformations of nucleic acids and proteins [2].

In the present study, poly-glutamate (PGA) has been chosen as model system to induce chiroptical properties on the aggregating metalloporphyrin trans-bis(N-methylpyridinium-4-yl)diphenylporphirinato copper(II) (t-CuPagg), and their interaction has been investigated through the combined use of UV/vis extinction, circular dichroism (CD), and Resonance Light Scattering (RLS) techniques.

We have previously examined the dependence of the porphyrin/protein interaction on protein concentration, ionic strength and pH, with particular focus on the effect exerted by the pH induced transition between PGA α-helix and random coil conformations [3]. Here, we report on very recent results[4] obtained on the interaction of preformed fractal aggregates of t-CuPagg with the same chiral scaffold. These point to an unprecedented mechanism of chirality induction that does not necessarily require the achiral monomers to self-organize in the presence of a chiral template, suggesting that a local distortion of the mesoscopic structure upon interaction with the asymmetric biopolymer might be sufficient to transfer the chiral information.

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INO-OR-06 Phenoxy-thioether group 3 and aluminium complexes as ε-caprolactone and lactide polymerization catalysts

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The interest in the synthesis of aliphatic polyesters stems mostly from their biodegrability, in relation to the recent concerns with the environments, and their biocompatibility which make them suitable materials for medical and pharmaceutical applications.

The ring opening polymerization (ROP) of cyclic esters via the coordination- nsertion mechanism enables the production of high molecular weight aliphatic polyesters with narrow polydispersities and well defined end groups. Among the wide range of metal compounds explored as catalysts for the ROP of cyclic esters, group 3 metal and aluminium species have been found well suited initiatiors.[1,2] While the former usual show a very high polymerization rate, the aluminium complexes generally lead to a lower activity but a better control over the polymerization process.

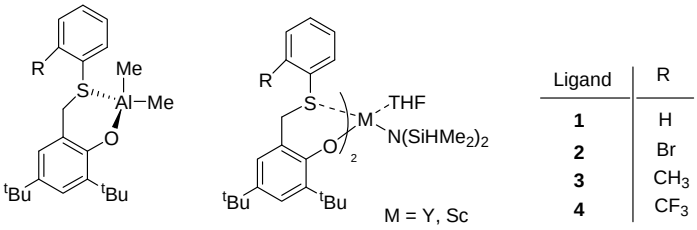

Figure 1

In this contribution we discuss the use of yttrium, scandium and aluminium complexes, bearing monoanionic bidentate phenoxy-thioether ligands, as initiatiors for the ROP of lactones and lactides. Four ligands with different substituents on the aromatic thioether ring have been synthesized and their effect on the catalytic behavior of the related complexes (Figure 1) has been evaluated. Several polymerization experiments, carried out by changing reaction conditions, such as solvent, temperature, etc., showed that, under certain optimized conditions, the ROP of the explored cyclic esters takes place in a living manner. Some caprolactone-lactide copolymerization experiments have been performed as well.

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INO-OR-07 Novel smart bio-materials: bioactive glasses containing metal nano-particles conjugated with molecules of biological interests

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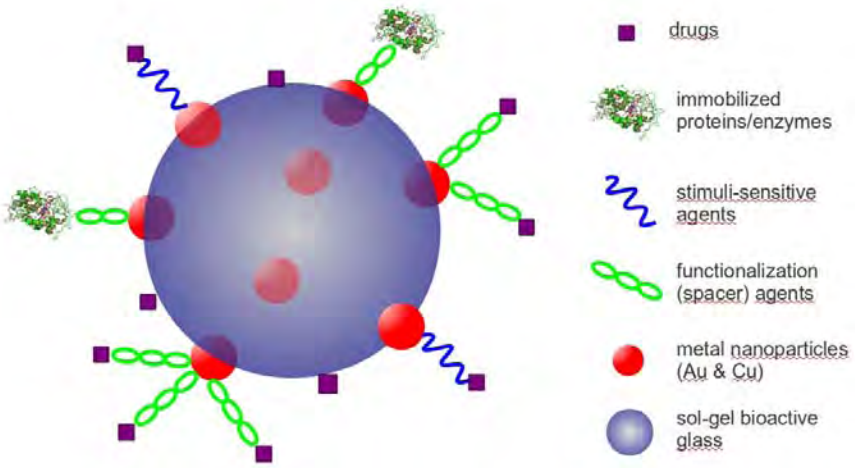
Stimuli-responsive materials (commonly referred to as *smart materials)* hold great promises for social and economic development and are of great relevance in both fundamental research and technological applications. Their design and realization through innovative processes involve complementary expertises, with comparable efforts on both synthetic and analytical sides. Within this work new *smart materials* based on phospho-silicate bioactive sol-gel glasses are been developed. To meet the ever-increasing demands for performing bio-materials, the surface features are been tailored to achieve optimal behaviour in different applications (*drug delivery, enzymes activity, chemo signalling probe, stimuli-sensitive agents*). In particular, the introduction onto the glass surface of metal nanoparticles (Au and Cu NPs) are very useful because the NPs can directly act, for example, as bactericides and imaging agents and can be used to immobilize, *via* a covalent linkage, an enzyme/protein and/or a drug on the glass surface through the formation of self-assembled monolayers (SAMs), in order to obtain a stable bio-conjugate systems. The materials prototyped in this way could be useful as a material bio-implantable into the human body. In this contribution we reported the last results of our works and some prospective in the field of smart bio-materials. [1-4]



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INO-OR-08 Reactivity and cell toxicity of surface modified TiO_2 nanopowders usable as sunscreen agents.

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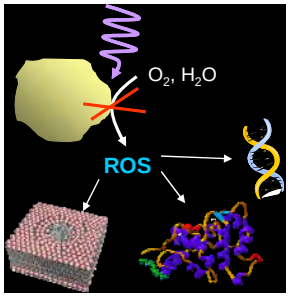
TiO_2 nanopowders are largely employed as UV-filters both in health care products and in polymeric composites. They found also applications in waste water remediation or as antibacterial agents. While in the latter case a good photocatalytic efficiency is needed when TiO_2 are used as UV-filters such activity needs to be suppressed since free radical species generated under sunlight exposure may cause both skin damage [1] and degradation of the organic components of the cosmetic preparations or composite.

In the last years a big effort has been made to increase the photocatalytic activity by the insertion of dopant elements in the structure [2] while a lower number of studies have been focussed on the reduction of the TiO_2 reactivity.



We have recently proposed a new modification of TiO_2 with carbon that reduces the photo-generation of free radical species maintaining unmodified its UV-filtering efficiency [3]. Here we explore a series of new modifications of the surface by using alcohols, carboxylic acids or iron salts. The modified powders have been characterized by TGA, EPR and IR spectroscopy. The oxidative potential of the powders in generating free radical species and the capability to cause damage to lipids, ribose or proteins has been evaluated by means of EPR spectroscopy/spin-trapping technique, UV/Vis spectrophotometry and SDS-page electrophoresis.

We found that the modifications performed largely reduce the oxidative potential of the TiO_2 powders. To investigate whether the observed modifications of photo-activity would affects the toxicological properties of the different TiO_2 powders the cytotoxicity and genotoxicity (oxidative damage) on human keratinocytes have been also evaluated.

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INO-OR-09 Gold and Silver Nanoparticles with Organic and Organometallic Thiols as Capping Agents

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Small metal particles can be used as functional units in innovative optoelectronic devices based on their quantum confined electronic properties. The synthesis and characterization of stabilized gold nanoparticles has been object of extended research studies, due to their enhanced optical properties [1] and cancer therapy applications [2]. Silver nanoparticles have also emerged in biomedicine studies [3]. The colloidal synthesis of organic and organometallic thiols stabilized Au and Ag nanoparticles has been achieved by using a two-phase synthesis. Among others, Pd(II) and Pt(II) containing organometallic thiol complexes [4] have been tested giving rise to nanostructures with controlled dimensions. The synthesis of gold nanoparticles (AuNP) stabilized by the bifunctional organometallic complex containing two Pt(II) centers, i.e. *trans*, *trans*-[$(CH_3COS)(PBu_3)_2Pt$-C≡C-C_6H_4-C_6H_4-C≡C-$Pt(PBu_3)_2(SCOCH_3)$], lead to the formation of dyads based on 4 nm nanoparticles. Water dispersible AuNPs and AgNPs capped by 3-mercapto propane sulfonate have been prepared in well defined and monodispersed structures with diameters in the range 2-4 nm; the dielectric behaviour of these materials has been studied to assess the electrical interfacial properties of metallic nanoparticles in aqueous solution [5].

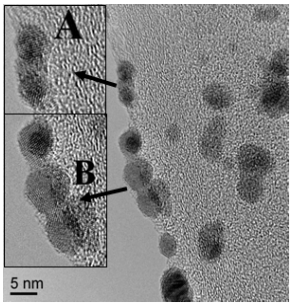

Fig. 1: HR- TEM of Pt(II) bifunctional organometallic thiol AuNP nanoparticles

Acknowledgements. The authors gratefully acknowledge the financial support by MAE-MIUR Progetti di Ricerca Scientifica e Tecnologica Bilaterale 2008-2010, CNPq (Brazil), FAPESP (Brazil) and CNEN (Brazil).

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INO-OR-10 CuO-TiO_2 nanomaterials functionalized with Au nanoparticles: synthesis, characterization and gas sensing performances

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CuO-TiO_2-Au nanocomposites are appealing multi-functional materials for a broad range of applications, ranging from photocatalysis [1], to H_2 generation [2], up to solid state gas sensing. In this work, the above nanosystems were obtained by means of a hybrid vapor phase approach, consisting in: a) the Chemical Vapor Deposition (CVD) of CuO nanomaterials on Al_2O_3, starting from $Cu(hfa)_2$•TMEDA (hfa = 1,1,1,5,5,5-hexafluoro-2,4-pentanedionate; TMEDA = *N,N,N',N'*-tetramethylethylenediamine); b) the CVD over-dispersion of TiO_2 nanoparticles (NPs) from $Ti(dpm)_2(O\text{-}^iPr)_2$ (dpm = 2,2,6,6-tetramethyl-3,5-heptanedionate; O-^{i}Pr = isopropoxide) on the above matrices; c) the functionalization with gold NPs, performed through a mild sputtering process. The adopted strategy enabled to produce nanocomposites nanocomposites with tailored morphology, characterized by an intimate contact between TiO_2, Au and the hosting CuO matrices. Sensing tests for the detection of toxic/flammable gases, both reducing (H_2, CH_3CH_2OH) and oxidizing (O_3), evidenced that the simultaneous presence of TiO_2 and Au appreciably enhanced the overall performances. This effect highlighted the beneficial synergy arising from the high interfacial area *p*-*n* heterojunction between *p*-type CuO and *n*-type TiO_2, the Schottky-type barrier character of the gold-oxide interface, and the catalytic activity of TiO_2 and Au NPs. The high responses and low detection limits at moderate working temperatures are extremely promising for technological applications and evidenced the the importance of engineering oxide nanocomposites in order to design and master their functional performances.

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INO-OR-11 Perylene diimide – POSS dyes as a way to inhibit aggregation caused quenching

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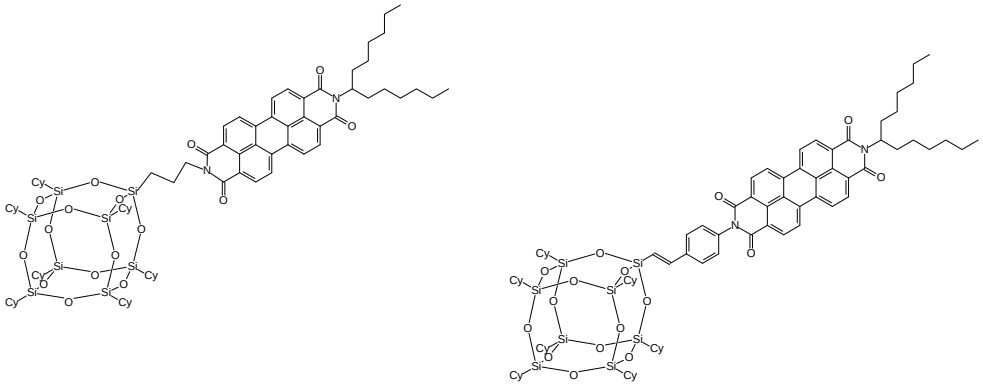
In recent years there has been an extensive research on the development of efficient solid-state emissive organic materials for organic optoelectronic devices, such as light-emitting diodes, organic field-effect transistors, solid-state lasers and fluorescent sensors. However, most organic chromophores are non-luminescent in the solid state, even if they are highly emissive in solution, owing to the quenching caused by intermolecular interactions such as aggregation caused by π–π stacking [1]. This is the case of perylene tetracarboxylic acid diimides (PDI), an important class of industrial pigments, which have been recently investigated for their interesting properties such as near-unity fluorescence quantum yields in solution, high photochemical stability, and strong electron-accepting character, that allow PDIs to be used in many electronic and optical applications [2].

We report on the preparation of PDI derivatives anchored to inorganic scaffolds such as Polyhedral Oligomeric Silsesquioxanes (POSS) with the aim to suppress the quenching which occurs in the solid state due to π–π stacking of this kind of emitting chromophores. The new PDI-POSS compounds here presented show in solution the typical absorption and emission features of the monomeric perylene unit, with a quantum efficiency close to unity, while in the solid state (both as spin-coated films and powders) the fluorescence quantum yield is positively affected by the presence of the POSS cage, with a quantum efficiency about 6 times that of the corresponding perylene tetracarboxylic bisimide in the solid state.



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INO-OR-12 Luminescent Silica Nanoparticles: Extending the Frontiers of Brightness

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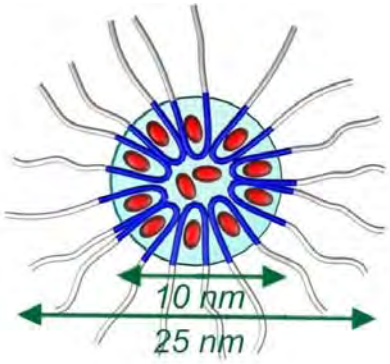
Silica nanoparticles are versatile platforms with many intrinsic features, including a low toxicity. Proper design and derivatization yield particularly stable colloids displaying multiple functions. In particular, a suitable choice of dyes and synthetic strategy yields very bright nanosystems, which can be used for either photoluminescence (PL) or electrochemiluminescence (ECL) sensing, labelling or imaging applications [1,2]. Silica nanoparticles thus offer unique potential in the nanotechnology arena, and further improvement and optimization could substantially increase their applications in fields of high impact, such as medical diagnostics and therapy, environmental and food analysis, and security.

This contribution describes silica-based multi-component nanosystems, tailored for optimization of processes such as directional energy- and electron-transfer, which provide those systems with extremely valuable functions: high light-harvesting capability, signal-to-noise maximization, multiplex output, signal amplification. A particular emphasis will be given to the description of a family of silica-core/PEG-shell nanoparticles, (see scheme 1) that we have recently developed in our laboratories.



Scheme 1: Cartoon of silica-core/PEG-shell nanoparticles as described in refs. 1-3

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INO-OR-13 Tracking thermally-activated transformations in a nanostructured metal/oxide/metal system

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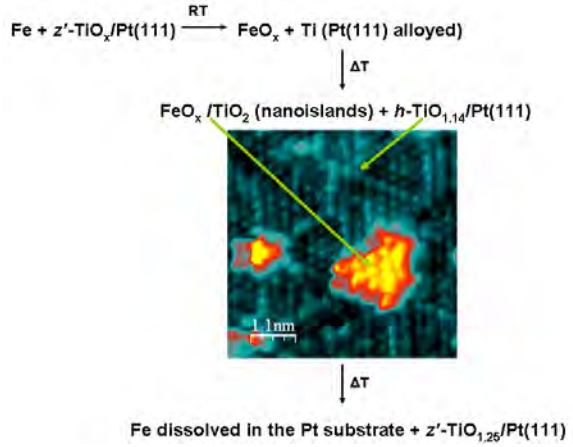
We present evidence of redox processes and structural transformations taking place in a Fe/z'-TiO_x/Pt(111) model catalyst in ultra-high-vacuum, studied by advanced surface science tools (photoemission, scanning tunneling microscopy and thermal programmed desorption) [1]. Competitive solid-state redox processes and chemical/structural transformations of both the Fe and FeO_x nanoparticle (NP) and the oxide ultrathin film take place as a function of temperature (see Figure below), giving rise to several distinctive phases at different temperatures. At RT the Fe and FeO_x NPs are templated by the ordered array of defects (troughs and picoholes) of the z'-TiO_x film, which is further reduced by Fe, partially forming a $PtTi_x$ surface alloy. At higher T (460<T<810 K), the system evolves to an intermediate state formed by a bi-component oxide material, i.e. mixed oxide FeO/TiO_2 nanoislands on a new hexagonal h-TiO_x ultrathin film, whose formation is triggered by the interdiffusion of Fe through the oxide into the Pt substrate. Eventually at higher temperature (>810 K) an almost complete migration of the Fe into the substrate is occurring and the pristine z'-TiO_x film formed again, demonstrating its intrinsic high stability.



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INO-OR-14 Reversibile Tuning of Light Emission Performances of Luminescent Metal-Tetrazolate Complexes

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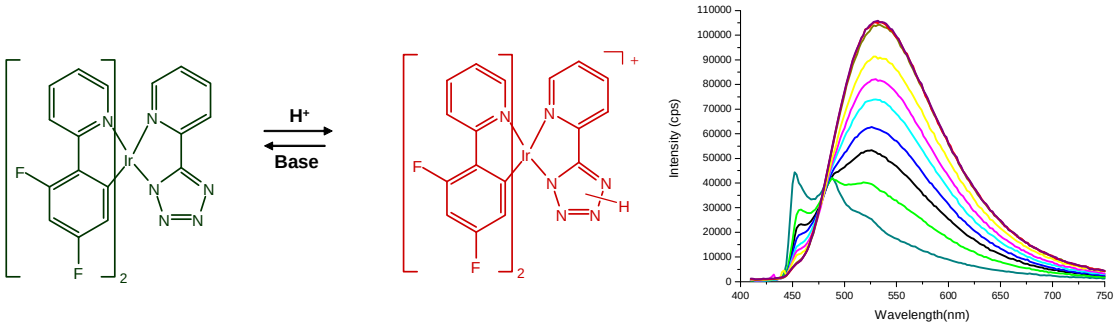
Over the past years, we have deeply explored the coordination chemistry of tetrazolates, $[R\text{-}CN_4]^-$. In particular, these derivatives proved as an excellent class of ligands for a variety of photo- and electroluminescent metal complexes such as Ru(II)-polypyridyls,[1,2], colour tunable Ir(III)-cyclometalates,[3,4] and, as the latest result, intensely emissive tris-carbonyl Re(I)-based compounds. [5] All of these complexes displayed a peculiar reactivity toward electrophilic species, which turns in the chance of performing both permanent and reversible modification of their structural features and, in particular, photophysical properties.



In this latter regard, the effects arising from the addition of CH_3^+ and H^+ to different types of tetrazolate complexes, will be described.

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INO-OR-15 Engineering copper phosphinates and bipyridines: sheets, ladders and (nano)tubes

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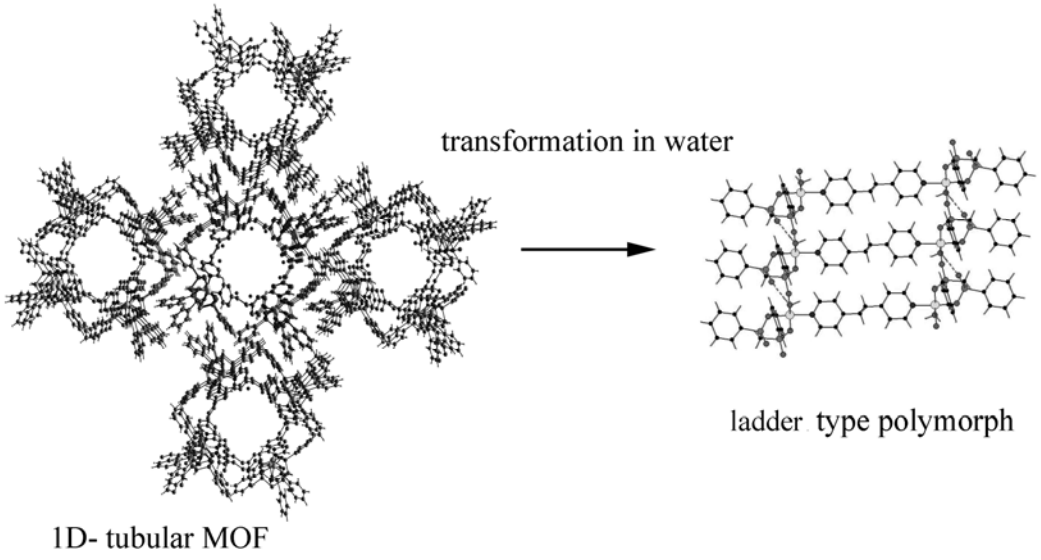
Tubular 1D-MOFs, built of discrete hybrid nanotubes assembled in the crystal packing and held together by Van der Waals interactions can be obtained by reaction of copper soluble salts with *pcp* and two ancillary N- ligands like *bipy* and *bipye* [(pcp = P,P' diphenyl-diphosphinate, bipy = bypiridine, bpye = 1,2-bis(4-pyridyl)ethane)]. The tubes have formula $[[Cu_2(pcp)_2bpye]\cdot 2.5H_2O]_n$,**1** and $[[Cu_2(pcp)_2bipy]\cdot 5H_2O]_n$, **2**. The exfoliation of the tubular MOFs **1** and **2** in organic solvents aided by ultrasonication allow to obtain elongated nanorods of variable size formed by the assembly of few single walled tubular shaped. An alternative synthetic route allows the synthesis of nanorods directly. The tubular 1D-MOFs show good and selective absorption properties towards polar solvents, like water and small alcohols, and gases such as CO_2.While **2** is the only isomer that could be obtain, an interesting spontaneous phase transformation in water of tube **1** leads to the formation of pseudo polymorphic ladder type structure of formula $[Cu_2(pcp)_2bpye(H_2O)_2]_n$ (**1a**) . On the contrary the use of a longer bypridine, namely *bipyp* 1,2-bis(4-pyridyl)propane), leads to a mixture of two different closely packed compounds with formula $[[Cu_2(pcp)_2bipyp(H_2O)]H_2O]_n$ (**3**) and $[[Cu_2(pcp)_2bipyp]\ 2H_2O]_n$ (**4**). Some considerations on how supramolecular forces are involved in the building of the three-dimensional structures in the solid state, will be discuss.



INO-OR-16 Synthesis and characterisation of Cu-Sn-Zn-S photovoltaic materials.

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Photovoltaic devices based on related sulfoselenide compounds show interesting properties, suggesting their possible application in the field of solar cells. In particular the Cu_2ZnSnS_4 (CZTS, kesterite) compound is a promising thin film photovoltaic absorber material and the kinetics of film growth of the Cu-Zn-Sn-S system was investigated by different research groups. Olekseyuk et al. [1] have found that Cu_2ZnSnS_4 melts incongruently at 1253K, crystallizing by peritectic reaction with a composition of the liquid phase far poor in ZnS. As a consequence the crystal growth from the melt, besides the Cu_2ZnSnS_4, results in the presence of impurity phases such as Cu_2SnS_3, ZnS and SnS [2]. The solidification of a CZTS single-phase from the stoichiometric melt might be improved by the presence of a suitable seed or the action of a directional cooling, like in the Czochralski or the Bridgman-Stockbarger techniques [3].
Although many studies have been performed on CZTS thin film, information on the bulk material, such as formation and stability of intermediate phases, extension of the compositional homogeneity range and crystal structures can be very important. Indeed, this has been the subject of recent studies by Muska et al. [4] on monograin powders synthesized via the molten flux technique. During our research, two methods have been used for the synthesis of the Cu_2ZnSnS_4. Single crystals have been produced within sealed quartz ampoules via the Chemical Vapour Transport technique using I_2 as the transporting agent; the effects of temperature gradient and I_2 load on the crystal habit and composition have been considered. Bulk samples have been produced using a solid state reaction method starting from mixed and compressed powders of the elements enclosed in a quartz tube under vacuum for heat treatments. The synthesized samples have been observed using a Scanning Electron Microscope equipped with an Energy Dispersive X-ray Spectrometer. The results obtained will be presented and discussed.

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INO-OR-17 1D and 2D ^{31}P NMR spectroscopy as diagnostic tool to assess chemical exchange around P_4 moieties.

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A surprising "*planetary*" exchange mechanism around the tetraphosphorus cage in complexes $[Ru(H)(P\text{-}P)_2(\eta^1\text{-}P_4)]$, (P-P = $Ph_2PCH_2PPh_2$, dppm, **1**; $Ph_2PC_2H_4PPh_2$, dppe, **2**) was demonstrated by solution NMR experiments and DFT calculations. Further activation of $Ru(dppm)_2$-coordinated P_4 by a Pt(0) carbene-like fragment gave a bimetallic ruthenium/platinum complex showing instead an intriguing "*pendulum-like*" fluxional behaviour in solution[1]. The presence of a ligand with larger bite-angle, *dppe*, seems to be responsible of a new planetary motion involving the $[RuH(dppe)_2]^+$ and $Pt(PPh_3)_2^{2+}$ fragments. Finally, a comparison between the dynamic behavior of **1** and **2** and other η^1-P_4 derivatives such as $[CpM(PPh_3)_2(\eta^1\text{-}P_4)]^+$ (M = Ru, Os) will be shown.[2]

Herein we show that 2D ^{31}P EXSY experiments can be used as qualitative tools to unravel the nature of dynamic processes of transition metal-(η^1-P_4) complexes and their platinum adducts. Rate constants were extracted using DNMR Lineshape analysis of 1D Variable-Temperature $^{31}P\{^1H\}$ NMR spectra.

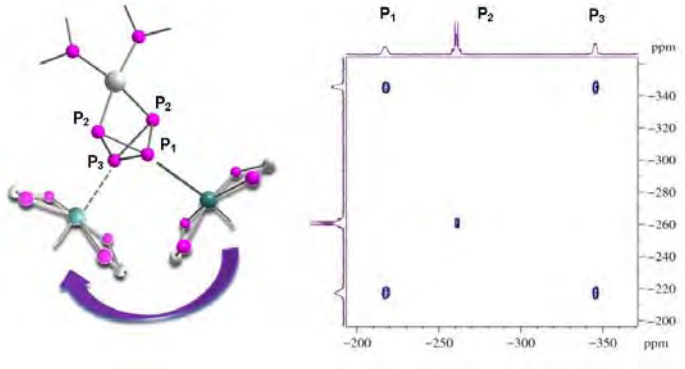

Figura 2. Pendulum motion: ^{31}P EXSY recorded at -25°C, τ_m = 100ms

COST Action CM0802 «PhoSciNet» is kindly acknowledged for support. Thermphos Int. B. V. is thanked for a generous loan of white phosphorus.

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INO-OR-18 Dicationic μ-diborolyl triple-decker complexes [CpCo(μ-1,3-$C_3B_2Me_5$)M(arene)]$^{2+}$ (M = Rh, Ir). Synthesis, Structure, and Electrochemistry

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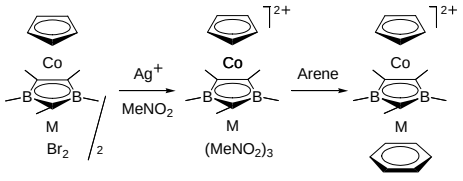
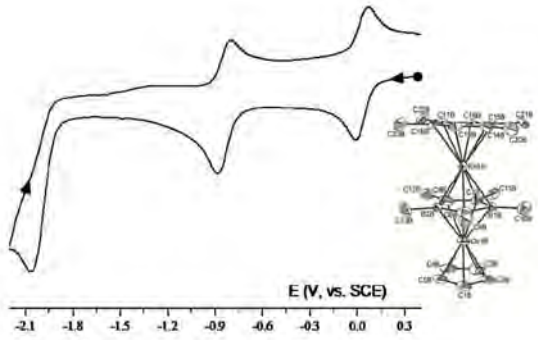


M
1 Rh
2 Ir

M(arene)
5a Rh(C_6H_6)
5b Rh(1,2,4,5-$Me_4C_6H_2$)
5c Rh(C_6Me_6)
6a Ir(C_6H_6)
6b Ir(1,2,4,5-$Me_4C_6H_2$)
6c Ir(C_6Me_6)

Reaction of the bromide complexes [CpCo(μ-$C_3B_2Me_5$)MBr_2]$_2$ (M = Rh, **1**; Ir, **2**) with $AgBF_4$ in acetonitrile solution affords the dicationic tris-(acetonitrile)μ-diborolyl triple-decker complexes [CpCo(μ-1,3-C_3BMe_5)- $M(MeCN)_3]^{2+}$ (Rh, **3**; Ir, **4**).
The labile nitromethane solvates [CpCo(μ-1,3-$C_3B_2Me_5$)$M(MeNO_2)_3]^{2+}$, generated in a similar way, react with benzene and its methyl derivatives affording the arene triple-decker complexes [CpCo(μ-1,3-$C_3B_2Me_5$)M(arene)]$^{2+}$ (M = Rh, **5**; Ir, **6**; arene = C_6H_6 (**a**), 1,2,4,5-$Me_4C_6H_2$ (**b**), C_6Me_6 (**c**)). Crystal structures of **5b**$(BF_4)_2$, **5c**$(BF_4)_2$ and **6b**$(BF_4)_2$ have been determined by X-ray diffraction.
In propylene carbonate solution, complexes **5a-c** and **6a-c** undergo two chemically and electrochemically reversible reductions, followed by further irreversible processes. Representatively, Figure 1 shows the cyclic voltammetric response of



5b. Controlled potential coulometry proved that the first cathodic process involves one electron/molecule.
Methyl substituents play an important role on the location of the redox potentials, in that, as expected, the increase of their number makes the reduction more and more difficult.
Details on structure, electrochemistry and spectroelectrochemistry will be discussed.

INO-OR-19 ACTIVATION OF CARBOPLATIN BY CARBONATE: A THEORETICAL INVESTIGATION

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Carboplatin, cis-diammine(cyclo-butane-1,1-dicarboxylato)-platinum(II), is a second-generation cisplatin analogue with reduced toxicity, widely used in the clinical treatment of cancer and most active against testicular and ovarian tumors.[1] While the cisplatin aquation kinetics is fast enough to allow the drug to react with water and biological components under physiological conditions, the much slower substitution rate of carboplatin likely precludes hydrolysis as a means of activating the drug in vivo, and several suggestions have been made to account for its activity in vivo, focusing on potential ligands for the Pt(II) center present in the blood plasma.[1] Among them, the carbonate ion, which is present in high concentration in the blood plasma, was suggested to play a potential role in the activation of platinum-based anticancer complexes.[2]

We carried out a theoretical study on the thermodynamics and the kinetics of the activation of the anticancer drug carboplatin in carbonate buffer, a process which has been suggested to play an important role in the uptake, antitumor activity and toxicity of this drug. The initial stages of this process have been investigated by considering the bicarbonate ion, the most abundant species at physiological pH, as the attacking species and consist of an initial ring-opening step, involving the displacement of one arm of the chelating ring by the bicarbonate ion, followed by the decarboxylation of the ring-opened species to give the corresponding hydroxo product. The obtained results show that the overall process is essentially thermoneutral with relatively low activation enthalpies for the two considered steps (122.5 and 91.9 kJ mol^{-1}, respectively) suggesting that the reaction with bicarbonate might represent a viable pathway for the activation of carboplatin to give active intermediates which, in the biological environment, may easily further react to give thermodynamically more stable species.

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INO-OR-20 PROTONATION OF A PHOSPHINITO BRIDGED DIPLATINUM(I) COMPLEX CARRIED OUT WITH "CLASSIC" (HBF_4) AND UNUSUAL (HF) BRØNSTED ACIDS

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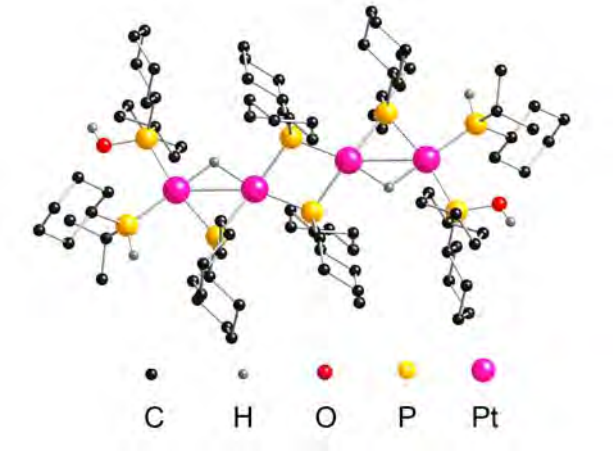
The phosphinito bridge of the complex $[(PHCy_2)Pt^1(\mu\text{-}PCy_2)\{\kappa^2P,O\text{-}\mu\text{-}P(O)Cy_2\}Pt^2(PHCy_2)]$ (*Pt-Pt*)[1] (**1**), differentiates the charge distributions on the two platinum atoms and renders the Pt-O fragment the reaction core of the molecule in reactions with nucleophiles[2] electrophiles,[3] or small molecules such as H_2.4 This presentation deals with the products and the mechanisms of the reaction of complex **1** with Bronsted acids having poorly coordinating anions such as HBF_4 and HF.[5] A comparison will be made between results obtained with HBF_4 and those obtained with HCl and HI. The unexpeted product obtained with diluted HF is depicted below.



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INO-OR-21 Surface Decorated Platinum Carbonyl Clusters

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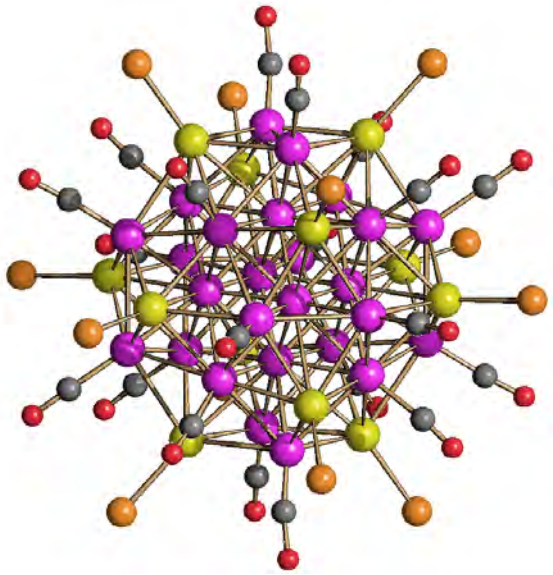
Since the discovery of the so called "platinum carbonyl", $[Pt_{3n}(CO)_{6n}]^{2-}$ (n ~ 10), platinum has played a key role in the development of molecular cluster chemistry.[1] Nonetheless, the number of species completely characterised is rather limited. Aiming at extending this chemistry, we have recently investigated the reactions of platinum Chini clusters, $[Pt_{3n}(CO)_{6n}]^{2-}$ (n = 2-8), with miscellaneous Cd(II) salts and phosphines.[2] This led to the isolation and crystallographic characterisation of new species such as $[Pt_{13}(CO)_{12}\{Cd_5(\mu\text{-}Br)_5Br_2(dmf)_3\}_2]^{2-}$, $[Pt_{19}(CO)_{17}\{Cd_5(\mu\text{-}Br)_5Br_3(Me_2CO)_2\}\{Cd_5(\mu\text{-}Br)_5Br(Me_2CO)_4\}]^{2-}$, $[Pt_{26}(CO)_{20}(CdBr)_{12}]^{8-}$ (Figure) and $[Pt_{22}(CO)_{22}(PPh_3)_6]^{2-}$, which are herein presented.



All these clusters are composed by a Pt-CO core decorated by various Cd(II) or Pt-PR_3 based fragments. These surface decorations may be related to that of Au-Fe-CO clusters, *e.g.* $[Au_{21}Fe_{10}(CO)_{40}]^{5-}$,[3] as well as to the staple motifs stabilizing gold thiolates nanoclusters, *e.g.* Au_{102}(S-p-benzoic)$_{44}$.[4] An oversimplified and unifying approach to interpret the electron counts in all these species is suggested, indicating that molecular metal cluster chemistry may give fundamental contributions to the understanding of some facets of nanochemistry and may provide a reliable guideline to interpret ligand-stabilized metal nanoparticles.

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INO-OR-22 Probing the role of related ring substituents over the electronic structure of ferrocene *via* synchrotron radiation photoabsorption and photoemission

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In the last years, substituted ferrocenes have been investigated as active redox molecules, able to tune the response of a functionalized electrode (especially gold and silicon) on which they are adsorbed, due to their attractive electrochemical characteristics: fast electron-transfer rate, low oxidation potential, and two stable redox states [1]. Ferrocene derivatives present also the advantage of a facile tunability of their redox potential via substitution of one or more H atoms of the cyclopentadyenil (Cp) ring with distinct functional groups. [2,3]

We present the results of an experimental and theoretical investigation on pure ethyl-, vinyl- and ethynylferrocene in the gas phase by means of NEXAFS at the C K-edge, and XPS of the C 1s region, and by DFT calculations.[4] Such a combination probes both the state of charge of the C atoms of the substituent group of the three molecules, and the extent of conjugation of the C-C arm with the Cp ring. A reliable assignment of the characteristic NEXAFS features associated to double and triple C-C bond of the lateral substituents of such closely related molecules may offer the fingerprint of the preservation or loss of the unsaturation in the anchoring arm upon its reaction with a surface, as well as shed light on the reaction mechanism for the surface anchoring on Si with different recipes, which is an actively investigated, yet still open, issue.[5]

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INO-OR-23 Effect of nonsymmetric N-donor ligands in Pd-catalyzed alkene/acrylic ester copolymerization

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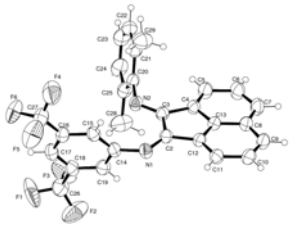
One of the major unsolved problems in the field of polymer chemistry is represented by the synthesis of copolymers of alkenes with polar vinyl monomers [1]. Single-site metal catalyzed polymerization is potentially the most powerful, environmentally-benign method for the controlled synthesis of new polymeric materials. For the target reaction, the most promising catalytic systems are based on late transition metals, in particular palladium. Two major types of catalysts have been reported: Pd complexes based on α-diimines [2]; Pd-phosphino-sulphonate derivatives [3].



We have now studied two new nonsymmetric α-diimine ligands (Ar,Ar'-BIAN) featured by one aryl ring substituted in *ortho* positions with electron-donating groups and the other ring with electron-withdrawing groups on the *meta* positions (Figure). The catalytic behavior of the relevant Pd-complexes $[Pd(CH_3)(Ar,Ar'\text{-}BIAN)(L)][PF_6]$ (L = CH_3CN, dmso) in the alkene/methyl acrylate copolymerization has been studied in comparison with that of the complexes containing the corresponding symmetric α-diimines. The studied alkenes are ethylene and 1-hexene. Alkene/methyl acrylate oligomers are the products of the catalytic reaction.
It was found that the catalysts containing the Ar,Ar'-BIAN ligands show a higher productivity and a higher content of the incorporated polar monomer than the active species with the symmetric α-diimines. The distribution of the polar monomer into the oligomer is also different from that reported in the literature [2].

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INO-OR-24 Nb(V) and Ta(V) Haloanions as Effective Counterions for the Room Temperature Isolation of Salts of Uncommon Organic Cations

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In the framework of our recent studies on the direct interaction of MX_5 (M = Nb, Ta; X = F, Cl, Br) with oxygen compounds, we have been aware that M(V) haloanions possess outstanding capability of stabilizing uncommon organic cations. Reactions involving ketones or polyethers may be accompanied by C–H bond activation, thus the salts $[(MePhCO)_2(\mu\text{-}H)][TaCl_6]$, **1** (Fig. A) [1], and [diglyme(H)][$NbCl_6$], **2** [2], have been isolated in the respective cases. Otherwise the reaction of $NbCl_5$ with $CMe_2(OMe)_2$ proceeds with C–O cleavage and leads to selective formation of the methylated mesityl oxide species $[Me_2C{=}CHC(=OMe)Me][NbCl_5(OMe)]$, **3** (Fig. B) [3]. A series of $[Nb_2F_{11}]$ radical cation salts of monocyclic arenes have been prepared according to unexpected redox reaction including metal reduction [4]. These salts are surprisingly long-lived at room-temperature or above, due to stabilizing cation-anion interactions; the $[C_6H_6]^+$ radical has been identified for the first time by EPR as a *non-transient species* in solution at room temperature. The same redox pathway has been exploited for the straightforward synthesis of thermally stable $[M_2F_{11}]^-$ salts of protonated 1,3-dimethoxybenzene (Fig. C) [5].

A **B** **C**

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INO-OR-25 Metal complexes with dendritic ligands

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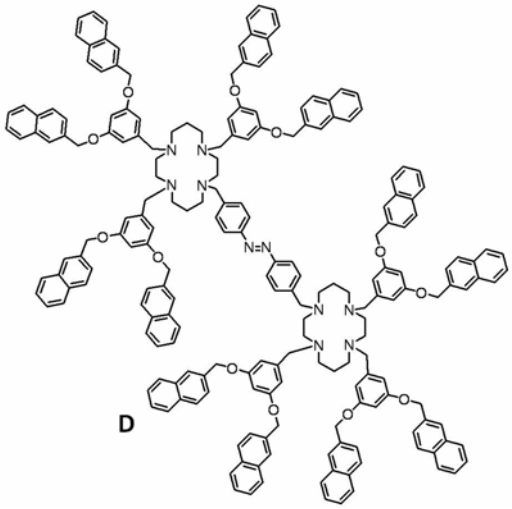
Dendrimers[1] are highly branched tree-like macromolecules with well-defined composition and a high degree of order. They usually consist of a core upon which radially branched layers are covalently attached. By using suitable synthetic strategies it is possible to prepare dendrimers that contain selected functional units in predetermined sites of their structure. Such compounds can often exhibit remarkable chemical, physical and biological properties, with a wide range of potential applications in different fields such as medicine, biology, chemistry, physics, and engineering.

In the last few years, we have investigated several families of dendrimers containing a 1,4,8,11-tetraazacyclotetradecane (cyclam) core, one of the most extensively investigated ligands in coordination chemistry, to build up metal complexes with dendritic ligands.[2] Particularly interesting results have been obtained in the case of dendrimer **D** (see figure). It is constituted by two cyclam units linked by a photoswitchable azobenzene chromophore and 12 naphthalene units at the periphery. In this dendrimer, the distance between the two cyclam units can be modulated by light stimuli thanks to the presence of an azobenzene moiety which can be reversibly switched between trans and cis isomer by light irradiation. Therefore, the trans and cis isomers display different coordination ability toward Zn(II) ion in CH_3CN:CH_2Cl_2 solution. Moreover, upon naphthalene excitation photosensitized azobenzene isomerization takes place.



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INO-OR-26 From covalent to supramolecular wheel-and-axle metallorganic crystalline materials for gas-uptake processes

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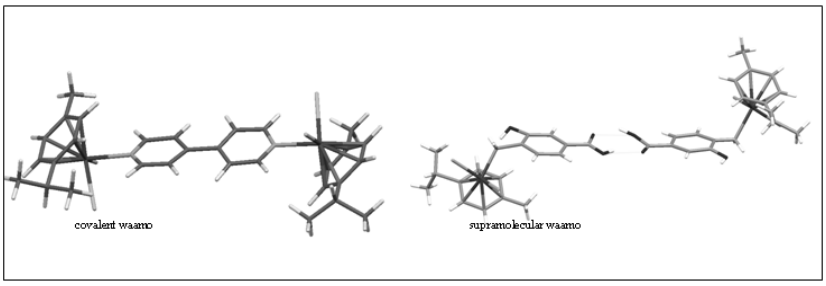
In the last decades much effort has been expended to the development of crystalline materials able of incorporating small molecules into the lattice through weak interactions [1]. These materials appear appealing in different strategic fields such as catalysis, development of chemical sensors as well as gas storage devices. Their inclusion propensities strongly depend on the shape and size of the molecular building blocks chosen for fabricating the crystalline scaffolds. In the last years we have focussed our attention on the development of organometallic complexes with a wheel-and-axle (WAA) morphology, which are constituted by two bulky groups (wheels) connected by a central linear spacer (axle) [2]. In the titled complexes, the wheels are represented by half-sandwich ruthenium(II) units, while the central axle can belong to two different classes: *class I*, covalent axles; *class II*, supramolecular axles. For the construction of WAA compounds belonging to *class I* it is necessary to use divergent rigid bidentate ligands, such as 4,4'-bipiridyl, 4-cyanopyridine, trans-1,2-bis(4-pyridyl)ethylene or 4,4'-bis-(diphenylphosphine)biphenyl, while for WAAs belonging to *class II* the employed ligands must contain organic functions able to give rise to supramolecular linear synthons, such as 4-aminobenzoic acids or the corresponding amides, through the COOH and $C(O)NH_2$ functions.
In this communication an overview of the WAA-metallorganic systems (WAAMO) developed in our laboratory belonging to classes I and II will be shown, together with some case studies of their propensity to capture volatile organic molecules through heterogeneous gas-uptake experiments.



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INO-OR-27 New europium (III) chiral complexes: Spectroscopy and molecular structure in the solid state

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Luminescent lanthanide complexes have interesting photophysical properties mainly due to the spectroscopic features of the metal ion. Although Ln(III) ions have weak absorption intensities, due to the Laporte forbidden nature of the intraconfigurational f-f transitions, this disadvantage can be overcome by indirect sensitization through the absorption bands of the ligand molecules coordinated to the Ln(III) ion using UV light (antenna effect). Concerning the applications in the biomedical field, Eu(III) complexes exhibit some desirable and unusual characteristics when compared with conventional organic fluorophores such as long excited-state lifetime (in the ms-range), large shift between absorbed and emitted wavelength and narrow emission bands both allowing the separation between Ln(III) luminescence and short-lived background fluorescence [1]. Recently, the interest in Ln(III) compounds possessing chiral properties has started to increase due to new chiral sensing/recognition applications [2, 3]. In the present contribution we studied the relationship between the luminescence properties of Eu(III) ion and the solid state molecular structure of the complexes depicted in Fig.1. The results of this study and some preliminary evidences in solution reveal that this new family of Eu(III) complexes are promising candidates for applications in the sensing field as probes in solution of the nitrate anion and of chiral molecules.

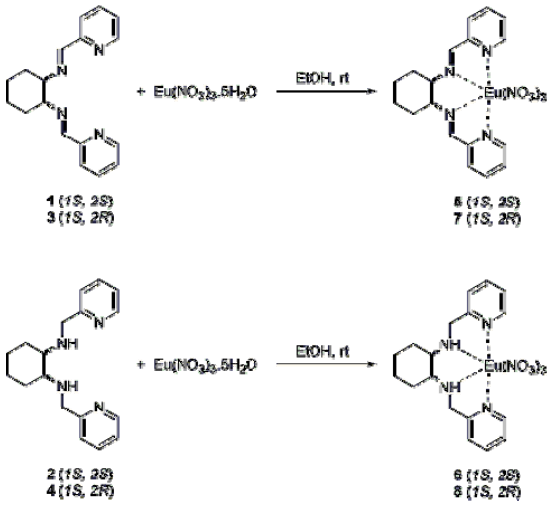

Figure 1

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INO-OR-28 ENANTIOSELECTIVE CYCLOPROPANATION REACTIONS CATALYZED BY CU(I) COMPLEXES OF PYRIDINE CONTAINING MACROCYCLIC CHIRAL LIGANDS (PC-L*) SUPPORTED ON SILICAS.

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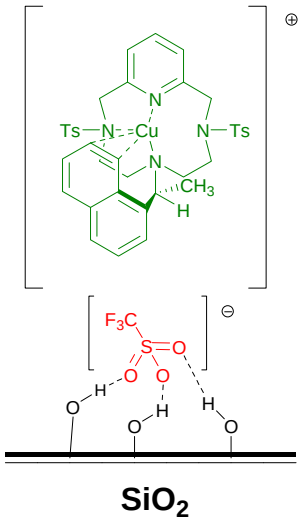
We have reported that copper(I) complexes of the new C_1-symmetric pyridine-based 12 membered tetraaza macrocyclic (**Pc-L***) ligands are competent catalysts in the enantioselective cyclopropanation of olefins employing ethyl diazoacetate (EDA) as carbene precursor in homogeneous phase[1]. Heterogeneous single site catalysts in many cases show superior performances in terms of activity, selectivity and recyclability coupling together the advantages of heterogeneous and homogeneous systems [2]. Aim of the present work has been to heterogeneize the chiral copper(I) complexes on mesoporous silicas and to test them as catalysts in asymmetric synthesis.



Pc-L* Cu(I) complexes were grafted on mesoporous ordered and non-ordered silicas (MCM-41, SBA-15 and Davisil) by the SHB method (Figure).[2] SHB (Supported by Hydrogen Bond) is a simple, very mild, rather strong grafting, procedure applicable to a wide range of metal complexes bearing the SO_3^- moiety as counterion.

Materials obtained were fully characterized for metal content, textural properties, hydrogen bonds between Cu(I) complex and surface silanols by a variety of techniques. Catalysts were tested in enantioselective cyclopropanation reactions of olefins. The results will be presented in terms of chemical yields and stereochemical outcome and compared with those obtained in homogeneous phase. The confinement effects, namely the pore size influence as well as the issue of catalyst separation and recyclability were studied and rationalized.

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INO/OM-KN-01 Metal-coordinated carbenes: reactive species or robust ligands?

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Transition metal carbene complexes have been mainly considered reactive intermediates in several catalytic organic transformations, like for example, the reactions involving the decomposition of diazo compounds (cyclopropanations, C-H insertions, C-C coupling) [1].
However, since the discovery of stable imidazol-2-ylidenes, which were first isolated by Arduengo *et al.* in 1991, much interest has been growing in the chemistry of N-heterocyclic carbenes (NHCs) [2]; in fact, these resulted to be excellent ligands towards transition metal centres both in low and medium-high oxidation state, allowing the synthesis of robust catalysts with negligible carbene dissociation, stable in acidic and oxidative environment.
The dual nature of carbenes can be illustrated by selected examples taken from our recent results involving:
A) reactions of reactive carbene intermediates such as i) insertion of carbenes into C=C, C-H and O-H bonds catalysed by Pt(II) and Rh(II) complexes; ii) reaction of diazo derivatives in presence of olefins to give metathesis and cyclopropanation products catalysed by [RuCl(Cp)(COD)] [3];
B) synthesis of novel di- and tricarbene Pd(II), Pt(II), Cu(I), Ag(I), Au(III) complexes and applications as catalysts in i) Heck reaction, ii) selective hydroarylation of olefins, iii) Ullmann-type arylation [4].
The obtained results show the extraordinary flexibility of the carbene mojety and fully justifies the strong research efforts on this still new and fascinating chemistry.

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INO/OM-KN-02 Stereoselective Gold Catalysis: New Opportunities in Organic Synthesis

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The re-discovery of homogeneous gold(I) catalysis has recently revolutionized the whole organic synthesis scenario, opening up access to unprecedented synthetic manipulations of unfunctionalized unsaturated hydrocarbons under mild and environmental acceptable conditions.[1] At the same time, new opportunities were also created in the "crowded" area of asymmetric catalysis, providing reliable solutions to the preparation of enantiomerically enriched polyfunctionalized molecular architectures in the presence of chiral gold(I) complexes.[2]

In conjunction with our ongoing interests oriented to the catalytic enantioselective decoration of arenes,[3] we have recently reported on the effective gold-mediated direct electrophilic activation of allylic alcohols,[4] in the preparation of functionalized heterocyclic compounds (*i.e. morpholines, indolines, carbazoles*).[5] This consolidated background, along with the use of propargylic alcohols in gold-catalyzed cascade cyclization reactions[6] concur to define new guidelines in organometallic synthesis under noble metal assistance.

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INO/OM-OR-01 Pd/Ln_xO_y (Ln = La, Ce, Pr, Sm, Gd, Dy and Yb): Efficient Precatalysts for a Fast and Green Suzuki-Miyaura Reaction

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In the last two decades, the Pd-catalyzed C-C bond formation has emerged as an outstanding strategy for building more or less complex organic molecules. Of the commonly used reactions, the Suzuki-Miyaura (SM) coupling has been proven to be the most useful and widely applied [1]. Our efforts have been mainly devoted to the development of new Pd-based catalysts that can efficiently promote the SM reaction in mild and green conditions. The focus of interest is: i) use of safe solvents, ii) room temperature catalysis, iii) reusability of the catalytic system.

In recent work from our group, the Pd/CeO_2 system was found to show very good activity for the SM coupling in water/ethanol mixtures at room temperature [2]. We demonstrated that the "heterogeneous" Pd-containing precatalyst acts as "releaser" of "homeopathic" amounts of a catalytically active soluble form of Pd. Furthermore, we succeeded in recycling the Pd/CeO_2 precatalyst at least ten times without a marked decrease of catalytic activity.

The present work is an extension of the study to different Pd/Ln_xO_y catalyst precursors (Ln = La, Pr, Sm, Gd, Dy and Yb). Interestingly, all novel catalytic systems showed an activity much higher than that exhibited by Pd/CeO_2. The reusability of all precatalysts is also good, in particular for Pd/Sm_2O_3.

Current studies are focused on assessing some crucial features of the mechanism of formation of the "true" catalyst. In particular, the higher catalytic activity of Pd/Ln_2O_3 with respect to Pd/CeO_2 seems to be related to the easier release of Pd particles from the surface of the former precatalyst.

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INO/OM-OR-02 New tetracene based materials for organic electronics: organometallic approach to their synthesis.

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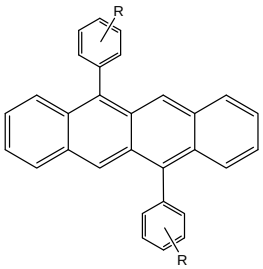
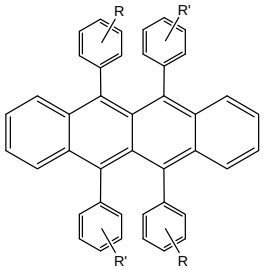
Acene-based organic semiconductors, thanks to their outstanding properties and their good processability, are key molecular materials for the development of organic electronics and derivatives of tetracene represent those where a good compromise between environmental stability and charge transport solid state properties is realised. Among tetracene-based systems, rubrene (5,6,11,12-tetraphenyl-tetracene) showed exceptional high charge carrier mobilities in Organic Field Effect Transistors (OFET) built on single crystals[1] and now represents the state of the art for molecular organic semiconductors.
It is noteworthy that, despite the peculiar and interesting properties of aryl-substituted-tetracenes, few synthetic routes are available (mostly tedious multi steps procedures) and relatively limited examples of molecules belonging to this series are known. This should urge on the organic chemist community to develop synthetic strategies to access to new organic semiconductors belonging to this class with improved transport properties, stability and processability. In principle, these properties (stability against photo-oxidation, solubility and charge carrier mobility) can be optimized by proper chemical modifications both on the tetracene core and on the aryl-substituents and transition metal-catalyzed processes are, from this point of view, particularly appealing both to improve the efficiency and to shorten the synthetic procedures.
Here we present our advances on the synthesis of new diaryl- and tetraaryl tetracenes where Pd-mediated cross-coupling reactions represent the key tools both to access to these systems and to prepare strategic precursors. In particular the synthesis of 1,1,3-triaryl-substituted propargyl alcohols, key intermediate for the synthesis of 5,6,11,12 tetra-aryl-substituted tetracenes (Rubrene-like systems) by copper-free Sonogashira protocol along with their evolution into rubrenes will be described.[2] A new protocol for the preparation of 5,11-diaryl-substituted tetracenes by Suzuki-based cross-coupling reaction from 5,11-di bromo- tetracene in liquid ionic will be also presented.[3] Some properties of the new tetracenes will be discussed.



5,11-diaryl-tetracenes



5,6,1,11,12-tetraaryl-tetracenes

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INO/OM-OR-03 Organometallic Fuel Cell development: the combined effect of molecular architecture with an high surface area carbon support

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The selective and simultaneous conversion of alcohols and sugars into energy and chemicals is a target of primary importance for the sustainable development. Two established types of fuel cells operating in alkaline media can convert the free energy of alcohols ($R\text{-}CH_2\text{-}OH$) into electrical energy and the corresponding carboxylate product: the direct alcohol fuel cell (DAFC), based on feasible metal electrocatalyst for alcohol oxidation [1] and the enzymatic biofuel cell (EBFC) that utilizes oxidation enzymes such as dehydrogenases in conjunction with an electron transfer mediator [2]. From a mechanistic viewpoint, the conversion of ethanol into energy and acetate resembles the process occurring in a biofuel cell where the electrocatalytic system consists of alcohol- and aldehyde-deydrogenases in combination with a hydrogen/electron transfer mediator. Recently, we introduced a third type of fuel cell operating in alkaline media where the anode catalyst is *a molecular metal complex.* We showed that in this device, named "organometallic fuel cell (OMFC)" a molecular rhodium complex is capable of evolving through fast chemical equilibria in the course of the catalytic cycle to form a specific catalyst for alcohol dehydrogenation, a specific catalyst for aldehyde dehydrogenation and a specific catalyst for the H/electron-transfer [3]. From a practical perspective, a molecular metal complex, soluble in different solvents and hence easily dispersible on very small surfaces, but capable of delivering high power densities upon oxidation of alcohols and sugars, paves the way to the further miniaturization of fuel cells for biological applications as well as biosensors. The combination of *well-defined molecular architecture* with a *matching support* (high surface area carbon black types) might allow for the selective oxidation of polyalcohols into valuable chemicals under waste-free conditions which is hardly achievable by traditional methods.

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INO/OM-OR-04 Microwave-Assisted Aminocarbonylation of Ynamides using catalytic $Fe_3(CO)_{12}$ at Low Pressure of Carbon Monoxide

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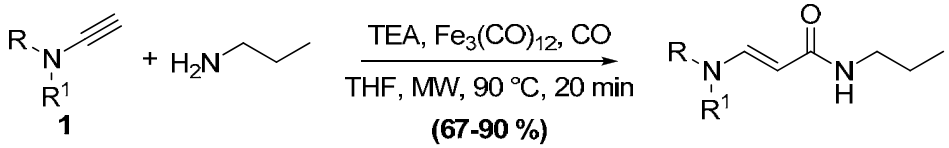
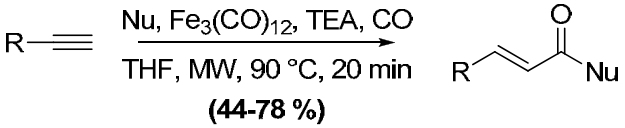
Carbonylation is a wideley applied atom economic reaction providing esters, ketons, carboxylic acids, amides and heterocyclic compounds.[1] Several procedures for the carbonylation of alkene and alkyne derivatives with different catalysts have been investigated but only few reports investigate the use of iron as the catalyst.[2] Iron carbonyl complexes have been increasingly used in organic synthesis in recent years and iron catalysis represents a promising area in the homogeneous catalysis.
Beside our interest on new ecofriendly catalysts for microwave assisted carbonylation reactions using carbon monoxide as a bening source of C, a microwave-assisted procedure for the iron catalyzed carbonylation of ynamides and terminal alkynes was developped.[3]

Starting from ynamides **1** a new class of *E*-acrylamides has been regioselectively synthesized after irradiation with microwaves for only 20 minutes at low pressure of CO (1.3 bar) using $Fe_3(CO)$ and TEA as the catalyst precursors (Scheme 1).



Scheme 1

The same procedure can be easily applied to terminal alkynes giving regioselectively *E*-acryl- and cinnamides. Using alcohols or thiols as nucleophiles *E*-acrylesters and thioesters are obtained in good yields as well (Scheme 2).



Scheme 2

The building blocks obtained by this atomeconomic process are key intermediates in the synthesis of natural products and small bioactive molecules.

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ORG/OM-IL-01 Metal Nanoparticles as Efficient Catalysts in Green Chemistry

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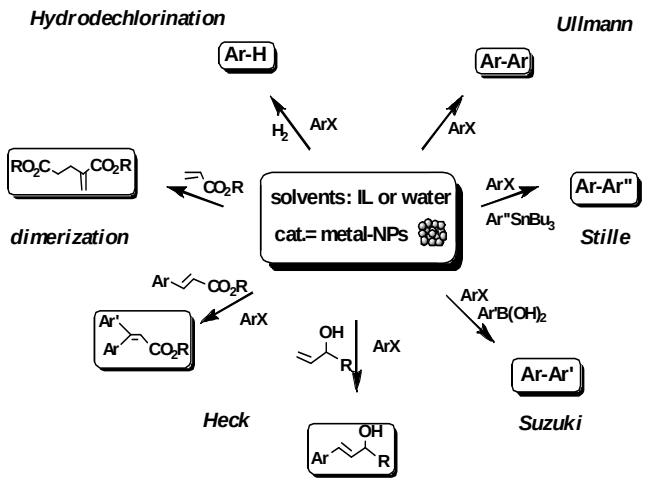
Transition-metal nanoparticles (NPs) are attracting a great deal of attention in almost any scientific and technological field, including catalysis, where nanoscale materials are becoming more prevalent in a wide range of applications such as fuel conversion, pollution abatement and fine chemical production.[1]
An increasing interest is also devoted nowadays to properly exploit the high activity and selectivity of nanocatalysts in order to develop greener and waste-minimized processes. From the Green Chemistry standpoint, new nanocatalysts must be designed to operate under environmentally friendly (for instance phosphine-free) conditions or in neoteric green solvents (e.g. ionic liquids, supercritical fluids, fluorous phases, water and so on).[2]



In this context, during the last decade, we exploited the use of nanostructured metal catalysts based on palladium, copper, and gold, to perform a wide range of C-C bond forming reactions, like for example Heck, Suzuki, Stille, acrylate dimerization, and Ullmann couplings, using tetraalkylammonium ionic liquids and water as green reaction media.[3]

This communication deals with our recent advances in controlling the catalyst performances by choosing appropriately the nature of the ionic liquid or the aqueous medium.

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ORG/OM-IL-02 The Amination of Hydrocarbons Catalysed by Ruthenium Porphyrin Complexes. A Mechanistic Investigation.

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The direct amination of hydrocarbons is a reaction of great synthetic interest due to the biological and pharmaceutical importance of aza-derivatives. We have focused our interest on this class of transformations for ten years using aryl azides as nitrogen sources and metallo porphyrins as catalysts [1]. More recently, we have investigated the catalytic activity of Ru(TPP)CO in C-H bonds aminations and we have isolated and characterised the active bis-imido intermediate $Ru(TPP)(NAr)_2$ (Ar = 3,5-$(CF_3)_2C_6H_3$) (**1**) [2].
To propose a general mechanism for the reaction we have investigated the reactivity of Ru(TPP)CO (**2**) towards several aryl azides, discovering that the nature of the active intermediate strongly depends on the electronic nature of the employed azide. The replacement of 3,5-$(CF_3)_2C_6H_3N_3$ with 4-$CF_3C_6H_4N_3$ in the reaction with Ru(TPP)CO allowed the isolation of the mono-imido complex Ru(TPP)(NAr)CO (Ar = 4-$(CF_3)_2C_6H_4$) (**3**) that showed a good catalytic activity in hydrocarbon aminations. On the other hand, the reaction of Ru(TPP)CO with an aryl azide bearing an electron donating group, 4-^{t}BuC$_6$H$_4$N$_3$, gave a very unstable imido complex (**4**). Complex **4** has been detected by NMR and it rapidly decomposed to the mono-amino compound $Ru(TPP)(NH_2Ar)CO$ (Ar = 4-^{t}BuC$_6$H$_4$) (**5**) that was isolated and characterised.

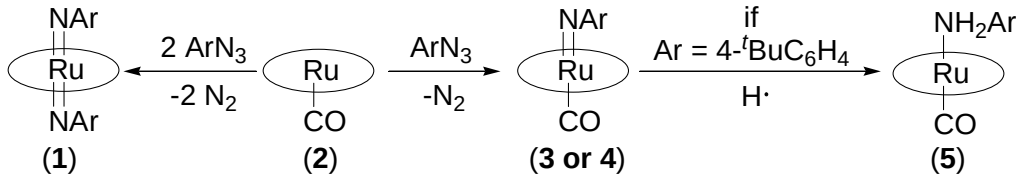

Figure 1

A kinetic study has been also performed to better rationalise the dependence of the reaction mechanism on the nature of the organic azide.

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ORG/OM-OR-01 Cationic Olefin Complexes of Platinum(II): from the Well Established to New Perspectives

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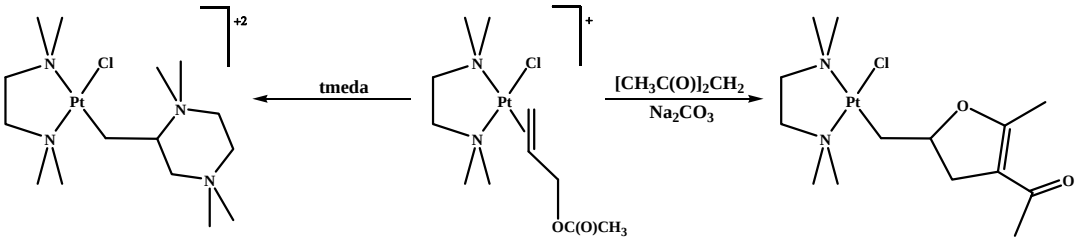
After our first report concerning the complex [PtCl(^{2}-C_2H_4)(N-N)]$^+$, **1**, (N-N = *N*,*N*,*N'*,*N'*-tetramethylethanediamine, tmeda) [1] many properties of this type of species have been clarified.

The obtainment of **1** (the prototype of stable cationic platinum complexes which can contain olefins different from ethene) was a clear experimental proof of the -donating properties of olefins, which could give stable complexes also in the absence of relevant -back-donation from the metal to the unsaturated ligand.

The coordinated olefin is endowed with a good degree of electrophilicity [2] and, in the case of olefins higher than ethene, it can also exhibit Brönsted acidity [3]. Deprotonation can eventually prevail over nucleophilic addition [4].

The dinitrogen ancillary ligand plays an important role in tuning the properties of the complexes; in particular, when tmeda is replaced by an aromatic diimine, the metal becomes more electrophilic and it can compete with the olefin in the reaction with soft nucleophiles [5].

In cationic complexes with allyl acetate, [$PtCl_2$(^{2}-CH_2=$CHCH_2OC(O)CH_3$)(N-N)]$^+$, two reactive sites are present in the coordinated olefin: the allylic carbon and the C=C double bond. Nucleophiles first replace the acetato group and then add to the olefinic bond. In the case of bidentate nucleophiles a heterocycle is built up in the near proximity of the coordination sphere (see Scheme). When the two donor atoms are different, because of the two consecutive reaction steps, only one of the possible isomers is formed.



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ORG/OM-OR-02 Sustainable Oxidations with Tailored Molecular Metal Oxides: Bridging the Gap between Homogeneous and Heterogeneous Catalysis

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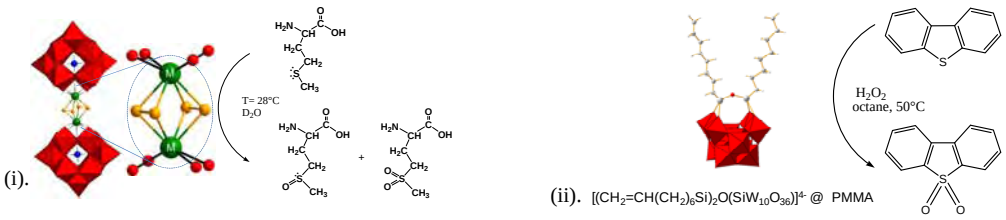
Polyoxometalates (POMs) have been proposed as the homogeneous models of solid metal oxides. Their success of as oxidation catalysts is based on their multi-metallic composition, which is pivotal to access diverse mechanistic pathways and an enhanced stability. The presence of d^0 metals, in particular, can be exploited to activate the non-waste producing oxidant H_2O_2. We present herein two promising strategies to design innovative and sustainable oxidative processes with H_2O_2, involving the use of transition metal substituted POMs (TMSPs) and hybrid organic-inorganic POMs.

(i) The molecular structure of TMSPs, featuring well defined catalytic sites, may be very convenient to study the mechanism and to tune their reactivity. Stable dimeric POM structures containing 4th group transition metals as Zr^{IV} or Hf^{IV}, in particular, form peroxometal-butterflies as active species. They have been used in water to oxidize *L*-methionine (70-99% yields in 20-48 h, at r.t.) and benzyl alcohols (50 min, under MW assisted activation, T_{bulk}=90°C, TOF= 75 h^{-1}) [1].



(ii) Covalent grafting of organic moieties on POMs may implement affinity towards different media, as well as immobilization strategies [2]. POMs functionalized with unsaturated alkyl chains have been used as monomers to prepare methacrylate-based copolymers, by means of radical polymerization. The heterogeneous catalytic material has been used to model a fuel desulfurization process: in octane, dibenzothiophene has been quantitatively converted to the corresponding sulfone in 4h (TOF= 18 h^{-1}).

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ORG/OM-OR-03 Evaluation of counterion and solvent effect in the single insertion of olefin into the Zr-C bond by low-temperature NMR kinetic studies

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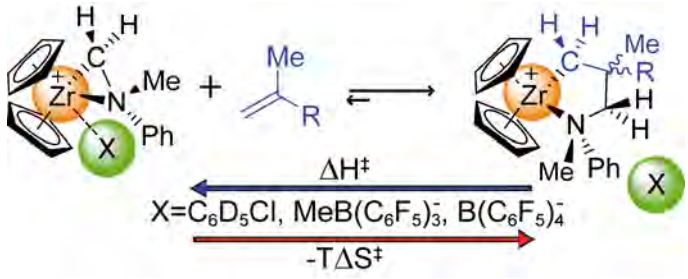
The insertion of olefin into the metal-carbon bond is the elemental step of the Ziegler-Natta catalysis that, in the homogeneous phase, occurs through the initial association of the olefin with the metal cation of the catalytic ion pair. Group IV metallocenium ion pairs polymerize olefins with high rates, but the elevate reactivity of such systems dramatically complicates fundamental kinetic investigations. During our studies on the self-aggregation of zirconocenium ion pairs [1,2], we synthesized some zirconazidirines having ([$Cp_2Zr(\ ^2$-CH_2-$NR_1R_2)$][X] as general formula that show some remarkable requisites to be used as good models for investigating the single insertion of olefin into the Zr-C bond. In particular, they are able to react stoichiometrically with olefins leading to a five-membered azametallacycle, as represented in figure.



With the aim of obtaining thermodynamic activation parameters of the single insertion and determining as they depend on nature of counterion and solvent, low-temperature kinetic NMR studies of the reaction of 2-methyl-1-heptene with [$Cp_2Zr(\ ^2$-CH_2-NMePh)][X] [**1a**:X^- =$MeB(C_6F_5)_3^-$; **1b**:$B(C_6F_5)_4^-$] ion pairs were performed. Results indicate that, in toluene, $H^{\ddagger}$ is higher for $MeB(C_6F_5)_3^-$ than for $B(C_6F_5)_4^-$ ($H^{\ddagger}$=-4.5 kcal mol^{-1}) but the former better compensates the loss of entropy caused by olefin association ($S^{\ddagger}$=-13 cal mol^{-1} K^{-1}). The two ion pairs **1a-b** behave exactly the same in a toluene/chlorobenzene mixture due to the coordination of a chlorobenzene molecule at the zirconium center that pushes the counterion in the second coordination sphere. $H^{\ddagger}$ (ca 11 kcal mol^{-1}) is higher than in toluene ($H^{\ddagger}$=8.5 kcal mol^{-1} and $H^{\ddagger}$=4.0 kcal mol^{-1} for **1a** and **1b**, respectively) while $S^{\ddagger}$ (ca -26 cal mol^{-1} K^{-1}) is similar to that of **1a** in toluene ($S^{\ddagger}$=-32 cal mol^{-1} K^{-1}).

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ORG/OM-OR-04 Synthesis and application of Tetraferrocenylporphyrins as sensitive materials in photoelectrochemical devices

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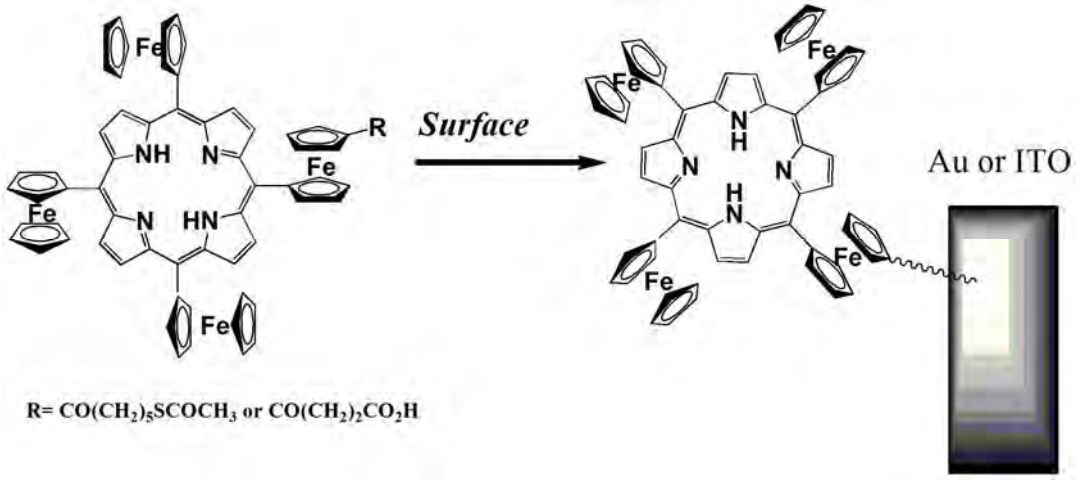
5,10,15,20-tetraferrocenylporphyrins have been object of our interest in different application such as electron transfer reactions [1], mixed-valence states [2], multiredox processes and long-range electronic internal communication [3]. These properties make them suitable for the construction of photochemical devices.
New tetraferrocenylporphyrins containing one functionalized ferrocenyl group were synthetized with the aim to link these molecules on surfaces. A chain with a terminal thioacetate or carboxylic acid was used to obtain functionalized Au or ITO surfaces.



The obtained monolayers were characterized by Uv-vis and electrochemical techniques and used in photoelectrochemical cells. Promising results in terms of photocurrent vs applied potential was obtained and will be discussed in connection with the surface-potential-experimental conditions set.

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INO-PO-01 Structural electronic study via XPS and TEM of sub-nanometric gold particles protected by calixarenes

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Metal nanoparticles (NPs) arise high scientific interest because they display unique properties, relevant in many established or emerging fields as optoelectronics, catalysis and sensing. An attractive property of NPs is their ability to anchor onto the core suitable receptors in a radial 3-D arrangement for the recognition of species [1]. Gold nanoparticles (AuNPs) are the most stable metal NPs, and their production as ligand-covered clusters constitutes a class of emerging hybrid organic-inorganic materials. In particular, thiol-stabilized AuNPs have become a model system in nanomaterials research due to their stability, easy preparation and chemical versatility [2].

A series of differently sized AuNPs stabilized by monodentate, bidentate, tridentate and tetradentate thiolate calix[4,6]arene ligands, prepared by the Brust-Schiffrin two-phase synthesis, were characterized by XPS, in combination with TEM. The experimental data show that the multidentate structure of calixarenes introduces a control element in the preparation, which is crucial to obtain very small (< 1 nm) AuNPs [3]. The core size distribution of the clusters was determined by analyzing TEM images. XPS measurements allow to separate the Au atoms in two subsets, on the basis of their clearly distinct Au 4f binding energy: Central Atoms, at 82.8-83.5 eV, and Surface Atoms bound to S, falling at 1.3 eV from central Au. These values suggest that S ligands attract positive charge on surface leaving a more negative inner atom. The S 2p spectra present a main component due to thiolate-Au bond, compatible with the structural "Staple Motif" reported in the literature [4]. Since very small NPs have a larger percentage of surface atoms, the experimental S/Au and Au-S/$Au_{central}$ ratios are an indirect evaluation of the cluster nuclearity, likely to be assigned to Au_{11} or Au_{13}, both compatible with the observed diameters.

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INO-PO-02 Synthesis, X-ray Crystal Structures and Magnetic Studies of Oligonuclear Manganese(III) and Iron(III) Compounds with 'Strained' Schiff Base Ligands

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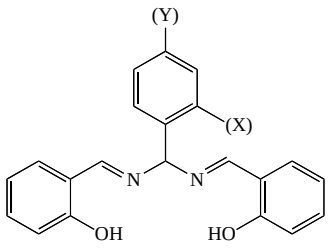
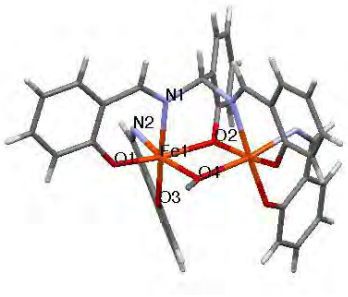
The synthesis and the study of oligonuclear transition metal compounds has been a very active field in the last years, mainly addressed to the comprehension of the spin communication pathways for their potential application as molecular magnets [1].



H_3salmp (X = OH, Y = H)
H_2sal(*o*-X)ben (X = OMe, Cl, NO_2, Y = H)
H_2sal(*p*-Y)ben (X = H, Y = ^{t}Bu, Me, H, F, Cl, CF_3, NO_2)

Few years ago our research group started a systematic approach to this regard using 'strained' tetra- and pentadentate Schiff base ligands (namely the H_2salben and the H_3salmp types, respectively) derived from the condensation of two salicylaldehydes with arylmethandiamines [2]. They possess only one carbon atom between the two donor iminic nitrogen atoms, favouring the formation of di- or oligonuclear complexes.



The reaction between this kind of ligands with manganese(III) and iron(III) yields compounds whose nuclearity ranges from dinuclear to tetranuclear, depending on the reaction solvent, the substituent position on the ligand and the deprotonating base used.
Crystal structures of some derivatives, and the magnetic studies of the most representative cases will be also reported.

[1] E. Tancini, M.J. Rodriguez-Douton, L. Sorace, A.-L. Barra, R. Sessoli and A. Cornia, *Chem. Eur. J.*, *16*, **2010**, 10482–10493.
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INO-PO-03 Xenon-Nitrogen Chemistry: Gas-phase Generation by ITMS and Theoretical Investigation of the Xenon-Difluoronitrenium Ion $F_2N\text{-}Xe^+$

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The xenon-difluoronitrenium cation $F_2N\text{-}Xe^+$, a novel xenon-nitrogen species, is obtained in the gas phase by the nucleophilic displacement of HF from protonated NF_3 by Xe. MP2 and CCSD(T) theoretical calculations reveal that this process is exothermic and exoergic by ca. 3 kcal mol^{-1}. The conceivable alternative formation of the inserted isomer $FN\text{-}XeF^+$ is instead endothermic by as much as 40-60 kcal mol^{-1}, and is not attainable under the employed ion trap mass spectrometric (ITMS) conditions. $F_2N\text{-}Xe^+$ is theoretically characterized as a weak electrostatic complex between NF_2^+ and Xe, with a Xe-N bond distance of 2.4-2.5 Å, and a dissociation enthalpy and free energy into its constituting fragments of 15 and 8 kcal mol^{-1}, respectively. $F_2N\text{-}Xe^+$ is therefore more fragile than the xenon-nitrenium ions $(FO_2S)_2NXe^+$, $F_5SN(H)Xe^+$, and $F_5TeN(H)Xe^+$ observed in the condensed phase as AsF_6^- or $Sb_3F_{16}^-$ salts [1-4]. It is however still stable enough to be observed in the gas phase. Other otherwise elusive xenon-nitrogen species could be obtained under these experimental conditions.

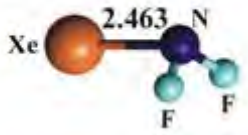

Figure 1. $F_2N\text{-}Xe^+$. The bond distances (Å) are optimized at the MP2/def2-TZVPP level of theory.

[1] D. D. DesMarteau, *J. Am. Chem. Soc.* **1978**, *100*, 10, 6270-6271.
[2] R. Faggiani, D. K. Kennepohl, C. J. L. Lock, G. J. Schrobilgen, *Inorg. Chem.* **1986**, *25*, 5, 563-571.
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INO-PO-04 Synthesis and Properties of Achiral Asymmetric Dinuclear Tris(1-pyrazolyl)methane Complexes of Ru(II).

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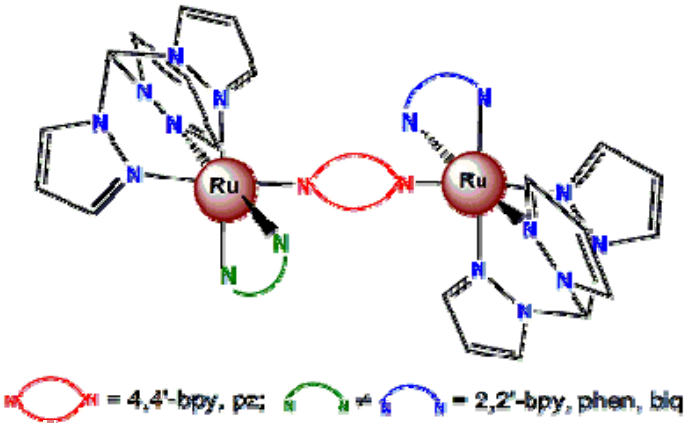
Exploiting the "complexes-as-metals/complexes-as-ligands" synthetic strategy [1] a family of six novel polypyridyl dinuclear species containing two different Ru(tpm)(CL) units [tpm = tris(1-pyrazolyl)methane, CL = 2,2'-bipyridine, 1,10-phenanthroline, 2,2'-biquinoline] bridged either by 4,4'-bipyridine or pyrazine (see the chart) have been prepared as hexafluorophosphate salts.

These compounds re-present the asymmetric analogues of six dinuclear complexes whose synthesis and properties have been recently published [2]. No-tably, owing to the presen-ce of a tripodal ligand, the metal centres are not chiral, thus the samples are not diastereomeric mixtures, a feature that prevents the structural characterization of oligonuclear trischelate complexes [3].



All novel complexes have been thoroughly characterized by elemental analyses and IR spectroscopy, and their ^{1}H NMR spectra completely assigned on the basis of COSY and NOESY experiments.

The photophysical, electrochemical, and spectroelectrochemical properties of the new species will be reported and discussed in terms of their similarities and differences with respect to those observed for their symmetric analogues.

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INO-PO-05 {[Cu_2(*bis*-tren-*ter*-2,5-dimethylfurane)(Cl)]$^{3+}$/[1.1.1]Cryptand}: A Prototype of Composite Kinetic Molecular Device for Slow Anion Releasing

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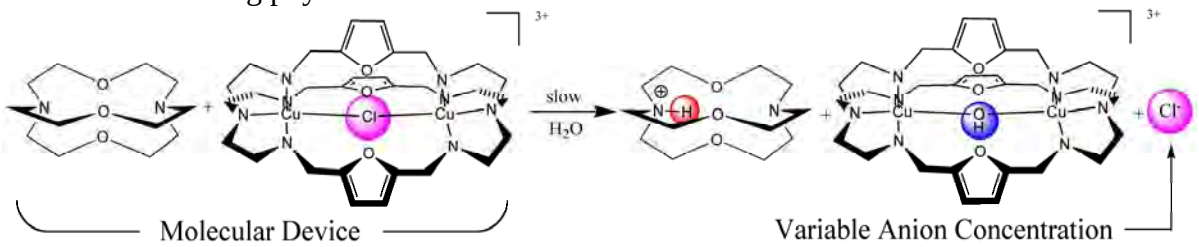
Kinetic molecular devices (KMDs) perform a specific work at a molecular level by using the kinetics of the process in which they are involved. Particularly, variable-parameter kinetic molecular devices (VPa KMDs) are able to change in a controlled way an environmental parameter (pH, *T*, *I*, [Nu], etc.) inside a reaction vessel making it possible to follow automatically parameter-sensitive processes without using external physical devices.[1] Variable-pH and variable-temperature KMDs have been used to carry out, respectively, spectrophotometric and NMR variable-pH kinetic experiments or automatic titrations and variable-temperature kinetic experiments. In some cases *cooperative* composite KMDs have been used, formed by two chemical systems working as a molecular apparatus, able both to change the parameter and to monitor it.[2]

In this contribution a first example of *integrated* composite KMD is proposed where two chemical devices operate together in the same environment, interacting with each other, to perform a work different from those peculiar to the single ones. It is formed by [1.1.1]cryptand,[3] able to change slowly and irreversibly the pH in a linear way,[1] and [Cu_2(*bis*-tren-*ter*-2,5-dimethylfuran)]$^{4+}$, able to capture rapidly and reversibly anions (Cl^-, Br^-, I^-, N_3^-).[4] The two devices, together, act as a variable-anion concentration KMD by releasing slowly and almost linearly with time anions, in this way making it possible to follow automatically anion-sensitive processes without using physical devices.



A mathematical model has been derived to describe the behavior of this complex system and a computer simulation for various anions in various conditions has been carried out. A spectrophotometric method to follow the concentrations of the involved species and the pH has been devised.

An experiment has been carried out in a 1 mm quartz cuvette containing, in water at 25°C, [1.1.1]cryptand 0.1 M, [Cu_2(*bis*-tren-*ter*-2,5-dimethylfuran)]$^{4+}$ 0.003 M and Cl^- 0.003 M. The change in absorbance, processed by the mathematical model, gave, without using external pH and anion sensors, the increasing values of both pH and chloride concentration.

[1] G. Alibrandi, *Angew. Chem., Int. Ed.*, **2008**, *47*, 3026–3028; G. Alibrandi, C. Lo Vecchio, G. Lando, *Angew. Chem., Int. Ed.*, **2009**, *121*, 6450–6452.
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INO-PO-06 (2-Pyrene-1-yl-vinyl)pyridine: a highly transparent chromophore with an unexpected large second-order nonlinear optical response

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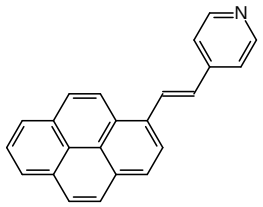
In the field of electrooptic materials, the rational design and synthesis of chromophores endowed with high transparency together with large second order nonlinear optical (NLO) response is a field of intense research activity. Many organic and metallorganic second order NLO chromophores have been designed according to the ''push-pull'' strategy, where electron-donating (D) and electron-withdrawing (A) end groups interact through a delocalized π-electron bridge to generate an intramolecular charge transfer transition [1]. On the other hand, far less attention has been devoted to low dipole moment chromophores, though in some instance they have been shown to possess large hyperpolarizability β [2].

Here we report on the second order NLO properties of (2-pyrene-1-yl-vinyl)pyridine, **1**, a chromophore based on the pyrene moiety which is well studied for its outstanding fluorescence properties (long lifetime and high quantum yield) while its derivatives have never been investigated for their NLO response. Preliminary measurements of the second order NLO properties of **1** in solution by the EFISH technique revealed an unexpectedly high and strongly concentration dependent μβ value, comparable to that of benchmark NLO chromophores. At high concentrations the decrease of the second order NLO response seems to point to the formation of centrosymmetric aggregates, a feature that is supported also by the emissive behaviour of **1**. Interestingly **1** is quite transparent, a relevant property for potential technological applications. These experimental results have been supported by theoretical investigation performed at DFT and Time Dependent DFT level, which has allowed an analysis of the electronic origin of the NLO response.



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[1] T. Verbiest, et al. *J. Mater. Chem. 7*, **1997**, 2175.
[2] J. Gradinaru, A. Forni, et al. *Inorg. Chem. 46*, **2007**, 884.

INO-PO-07 Dynamic behaviour of Pd and Pt tiourea complexes

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Pd^{II} and Pt^{II} thiourea complexes are a crucial topic in inorganic chemistry for the peculiar kinetic and thermodynamic features and for biological properties related to their anti-cancer activity [1-2]. As a matter of this fact, the strong binding ability of these S-donor nucleophiles is currently exploited in chemotherapy to reverse unwanted side effects of Pt-based drugs [3-4]. A typical feature of the S coordinated thiourea is the M-S=C angle (ranging from 106 to 118°) which, in the case of rigid square planar complexes, pushes the thiourea ligand over the coordination plane along a roughly perpendicular plane [5,6]. NMR multinuclear (1H, 13C, 15N and 195Pt) analysis at variable temperature demonstrate that complexes $[M(\widehat{NN})(n\text{-}TU)]Cl_2$ (M= Pd^{II} or Pt^{II} ; $\widehat{NN}$= 2,2'-bipyridil or phenanthroline; n-TU = alkyl substituted thioureas) do show many different conformations in a temperature tunable exchange according to C=N and M-S hindered rotation or S inversion. The $[M(\widehat{NN})(n\text{-butyl-}TU)]Cl_2$ ^{13}C and inverse detected ^{15}N at 225°K show the presence of four conformers. Pulse gradient HMBC-^{15}N detections [7] took great advantage by a large unespected β-C-H long-range coupling (^3J) with nitrogen. An important NMR feature of these complexes (also in view of their biological activity) is the proton donor capability leading to a reversible decrease of the positive charge during the cell membrane-crossing.

[1] G. Marverti, M. Cusumano, A. Ligabue, M. L. Di Pietro, P. A. Vainiglia, A. Ferrari, M. Bergomi, M. S. Moruzzi, C. Frassineti, *J. Inorg. Biochem.*, 102, **2008**, 699.
[2] N. Summa, W. Schiessl, R. Puchta, N. van Eikema Hommes, and R. van Eldik, *Inorg. Chem.*, 45, **2006**, 2948.
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[7] A. Bax, M. F. Summers *J. Am. Chem. Soc.*,108, **1986**, 2093.

INO-PO-08 Nanostructured functional copolymers bioconjugate integrin inhibitors

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Polymeric materials with nanosized structures and self assembly properties have been previously achieved by emulsion polymerization and osmosis based methods[1,2].

Synthesis and properties of bioconjugates based on functionalized polymeric nanoparticles (PNs) and monoclonal anti-Integrin αV CD51 (aI) antibody were now investigated. Polymeric and co-polymeric colloidal nanoparticles with different functionalities, i.e. acid, amine or thiol, namely poly(methylmethacrylate-co-acrylic acid) [P(MMA-co-AA)], poly(methylmethacrylate-co-dimethylpropargylamine) [P(MMA-co-DMPA)], poly(methylmethacrylate-co-allil mercaptane) [P(MMA-co-AM)], were obtained by tailoring emulsion synthesis and fully characterized by means of spectroscopic techniques and scanning electron microscopy (SEM). Bioconjugates (PN/aI) based on P(MMA) or P(MMA-co-AA) were obtained by loading the polymeric nanoparticles with the antibody anti-Integrin with a simple and straightforward immobilization strategy. Qualitative and quantitative loading analyses of bioconjugates were carried out by means of polyacrylamide gel electrophoresis 1D-PAGE, MALDI-TOF and LC/ESI-MS/MS investigations. The biological efficacy of bioconjugates was confirmed by the reduced migration potential of PN/aI-treated human kidney cells (HEK293). The easy immobilization procedure and high immobilization capacity of polymeric nanoparticles together with tuneable chemical functionalities and dimension of the polymeric nanoparticles open applicative perspectives for targeted delivery.

[1] I. Venditti I. Fratoddi, C. Palazzesi, P. Prosposito, M. Casalboni, C. Cametti, C. Battocchio, G. Polzonetti, M. V. Russo, *Journal of Colloids and Interface Science* 348, **2010,** 424
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INO-PO-09 Conjugated Pt-Containing Polymetallaynes for gamma-Radiation Dosimetry

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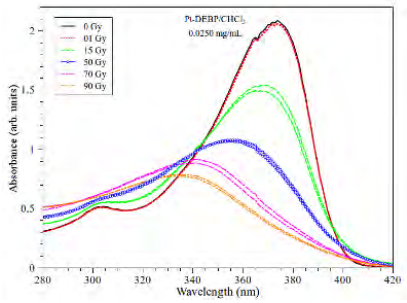
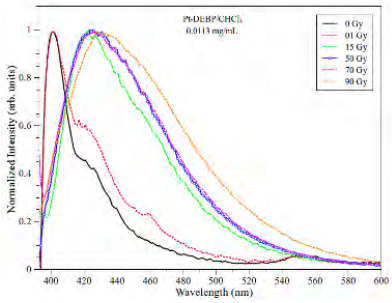
Polymetallaynes show peculiar properties that allow their use in electronic and electro-optical devices sensors and biosensors, electroluminescence and photovoltaic behavior [1]. On the basis of our previous research [2], we report a new application, *i.e.* the gamma rays detection achieved by a Pt containing polymetallayne, Pt-DEBP. This polymer can be used as γ rays dosimeter for doses higher than 15 Gy using the absorption spectra changes. Shifts in the position of the main peak of the absorption spectrum of the solutions had an approximately linear relationship. Changes in the fluorescence spectrum suggest that the system can also be used for doses below 1 Gy (Figure 1, a-b).





a- Optical absorption spectra of Pt-DEBP *b- Emission spectra of Pt-DEBP*

The spectra have been recorded before and after irradiation with γ rays at different radiation doses.

The response of Pt-DEBP to increasing gamma ray exposure has been interpreted as due to the fragmentation of the polymer backbone, likewise the case of already investigated polymers. Theoretical studies have supported our preliminary assessments. In fact, we have fully characterized by TDDFT calculation the absorption spectrum by comparison with a very similar model system.

Acknowledgements. The authors gratefully acknowledge the financial support of this research by MAE-MIUR Progetti di Ricerca Scientifica e Tecnologica Bilaterale 2008-2010, CNPq (Brazil), FAPESP (Brazil) and CNEN (Brazil).

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INO-PO-10 Studies on nickel selenite and related complexes: structural features, magnetic properties and reactivity

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There is a growing interest in the structural chemistry of selenites and tellurites, due to the following properties: (1) the ability to produce solid state structures containing channels and cavities suitable to housing the chalcogen electron lone pair, (2) the ability of the chalcogenite anion to act as a bridge between two transition metal cations, permitting magnetic exchange between paramagnetic centres, (3) the possibility of the chalcogen electron lone pair to give rise to supramolecular interactions.[1]

By reacting $Ni(NO_3)_2$ with Na_2SeO_3 in presence of tetramethylethylenediamine (TMEDA) the heteroleptic dinuclear complex $[Ni(\mu\text{-}SeO_3)(TMEDA)]_2 \cdot 8H_2O$ is obtained. It consists of a dinuclear species in which the two nickel atoms are held together by two bridging selenito anions and 6 water molecules are involved in hydrogen bonds directly with the oxygen atoms of the selenite anions. The two nickel cations exhibit antiferromagnetic coupling with J = -25.7 ± 0.1 cm^{-1}, in good agreement with the DFT calculated value of -27 cm^{-1} for the $[Ni(\mu\text{-}SeO_3)(TMEDA)]_2 \cdot 6H_2O$ species. The coupling between the two metals occurs primarily via the bridging oxygen atom O(1) and also to a minor extent through the O-Se-O bridge, as attested by the spin density distribution.

Regarding the simple selenite salt $NiSeO_3$, it has been reacted with CO with the aim to produce NiSe: the obtained materials have been studied by IR, XRD and XPS.

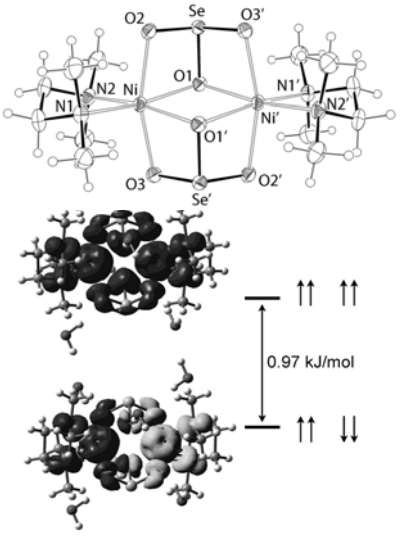

Figure 1. Crystal structure and energy levels of the antiferromagnetic quintet with hydrogen bonded water molecules.

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INO-PO-11 Unexpected Isomerism in "[Pd(2,9-dimethylphenanthroline)X_2" Complexes: Not Always the Same Compound

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Complexes bearing the 2,9-dimethylphenanthroline (neocuproine, Neoc) ligand have attracted a special attention because the steric hindrance caused by the two methyl groups stabilizes unusual coordination geometries and the formation of otherwise unstable adducts. Such feature is also essential to allow high catalytic activity in some reactions. Among these, palladium-catalyzed oxidation reactions are surely worth mentioning. Palladium neocuproine halide complexes have been known for a long time and are often used as the starting material for the synthesis of more complex compounds. Different synthetic approaches have been reported for their preparation, but the products are invariably formulated as Pd(Neoc)X_2 (X = Cl, Br, I). While investigating the reactivity of these complexes, we realized that even apparently minor variations in the synthetic procedure led to products that displayed completely different solubility behaviours despite having the same elemental analysis, always in excellent agreement with that calculated for the expected product. We thus engaged in a more in depth investigation of the identity of these apparently trivial compounds and found that two bonding isomers exist for each of the compounds in the series, one of which had escaped identification for more than 40 years, despite having previously been obtained by many researchers.

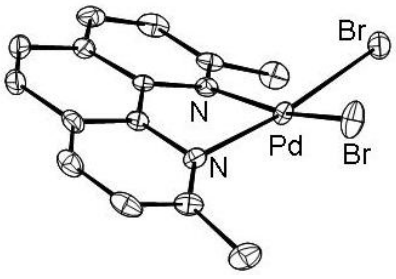

Figure 1. Neutral isomer: Pd(Neoc)Br_2

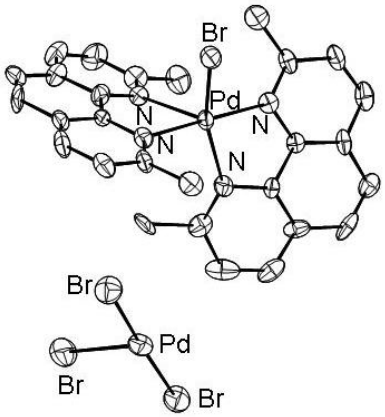

Figure 2. Ionic isomer: $[Pd(Neoc)_2Br]_2[Pd_2Br_6]$ (half of the crystallographic cell shown)

INO-PO-12 Synthesis and advanced characterizations of silver nanoparticles stabilized by organic thiols

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The functionalization of metallic nanoparticles (MNPs) surface with organic molecules allows for tuning the overall properties of particles in order to fit target applications. In this framework, the development of new strategies for the chemical stabilization of MNPs by means of specific ligands has been object of recent research. The chemical stabilization of MNPs by suitable organic ligands, i.e. the so called molecule-capping method, presents several advantages over other preparative methods such as low preparation costs and better NPs size, monodispersity and shape control. Among others, Au and Ag NPs can be functionalized with alkanethiol monolayers that afford high stability to the colloids against aggregation [1,2]. The synthesis and characterization of AgNPs of different sizes stabilized by allyl mercaptane (AM) is presented. The size-control of the AgNPs was achieved by direct control of synthesis parameters and the hybrids were characterized, among others, by means of synchrotron radiation-induced X-ray techniques as X-ray photoelectron spectroscopy (SR-XPS) and Extended Absorption Fine Structure spectroscopy EXAFS. XPS measurements were performed at the C1s, S2p and Ag3d core levels; EXAFS measurements were carried out at the Ag k-edge (25514 eV) and S k-edge (2472 eV). High resolution XPS measurements allowed to assess the anchoring of the thiols onto silver nanoparticles through a stable Ag-S bond. EXAFS measurements at the S k-edge provided further information about the thiols interaction with AgNPs, leading to hypothesize a core-shell system occurrence, with Ag_2S-like and Ag-S-R -like sulphur species, further suggested by SR-XPS S2p data. The EXAFS data collected at the Ag K-edge also provided information about the NPs dimensions and sizes dispersion.

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INO-PO-13 Push-pull Zn^{II}-porphyrin, *meso*-substituted with a benzodithiophene spacer, as promising sensitizer in Dye-sensitized solar cell.

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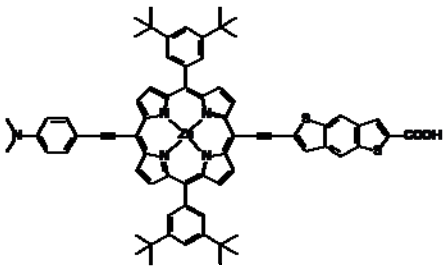
Dye-sensitized solar cells (DSSCs) represent today an interesting class of photovoltaic devices because of their excellent light-to-electricity conversion efficiencies. Many dyes have been investigated and among them the ruthenium sensitizers have shown the best results reaching more than 11% efficiency [1]. It was recently reported the achievement of an 11% efficiency with a push-pull *meso*-substituted Zn^{II}-porphyrin as dye [2].

Here we present the synthesis of a push-pull Zn^{II}-porphyrin with a N,N-dimethylaniline donor group and a carboxy acid acceptor group with a new benzo[1,2-b;4,5-b']dithiophene spacer.



The orthofused aromatic/thiophene system shows a rigid π-conjugated-condensed framework, free from configurational disorder, which leads to unique electronic properties such as conductivity, high field effect mobility and tunable stacking in the solid state relevant for applications such as in LED, FET and organic solar cells [3]. It may play a relevant electronic role in favoring electron transfer along the push-pull system.

Theoretical TD-DFT calculations, electrochemical and photoelectrochemical studies, and a compared investigation of the light-to-electricity conversion efficiency in a dye-sensitized solar cell will be presented.

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INO-PO-14 NEW TERNARY PHASES IN THE La–Ge–Mg SYSTEM

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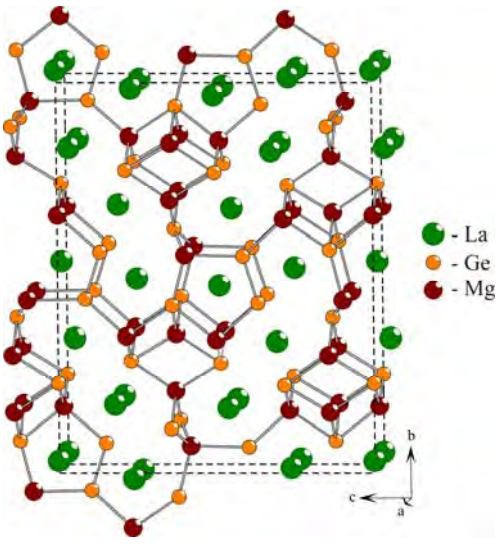
The R–X–Mg systems (R=rare earth metal; X=late transition metal or early post-transition metal) have been intensively studied in the last ten years with respect both to the fundamental and applicative point of view. Their scientific interest is mainly related to the fact that these systems show complex phase diagrams in which many ternary compounds exist, often characterized by peculiar structures, unusual stoichiometries and novel bonding features.

During the investigation of the La–Ge–Mg phase equilibria several ternary phases were detected and analyzed by our research group. The crystal structures of two of them, determined by single crystal X-ray diffraction analysis, are presented in this work: $La_4Ge_6Mg_5$ ($Gd_4Ge_6Zn_5$ str. type, $Cmc2_1$, $oS60$, a=4.5030(7), b=20.085(3), c=16.207(3) Å, Z=4) and $La_4Ge_6Mg_7$ (own structure type, $C2/m$, $mS34$, a=16.878(3), b=4.4702(9), c=12.660(3) Å, β=122.25(3)°, Z=4). Electronic structure calculations were performed applying the COHP formalism [1] within the LMTO method, in order to obtain information on chemical bonding.

Both phases are characterized by Ge–Mg distances close to the covalent radii sum (2.62÷2.84 Å); the bond strenghts of these contacts, expressed as – *i*COHP values, range from 1.22 to 1.96 eV per bond per cell and are the strongest in each structure. This makes it convenient to depict these compounds as formed by a 3D $[Ge–Mg]^{\delta-}$ polyanionic network balanced by electropositive La atoms. Such a network is outlined in the figure for $La_4Ge_6Mg_5$.



The negatively charged framework of typical polar intermetallics is formed by late transition metals and/or early post-transition metal elements close to the Zintl border. The peculiarities of Mg as an admix in the polyanionic network enriches the chemistry of polar intermetallics and allow one to rationalize the exploration of novel phases with desired properties.

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INO-PO-15 HYDROGENATION PROPERTIES OF MG–RICH La-Pd-Mg ALLOYS

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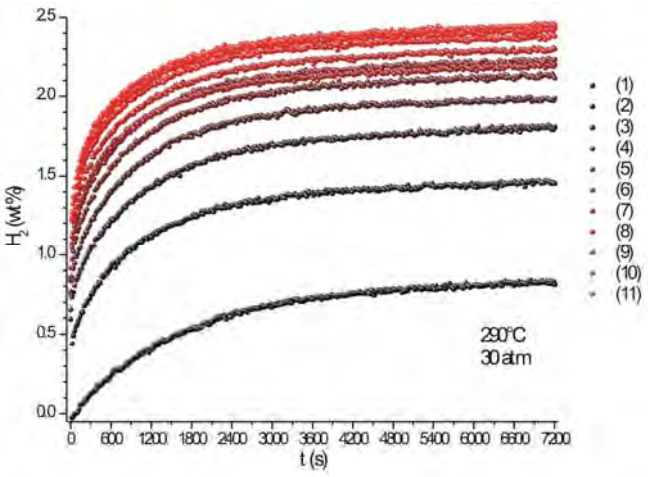
Numerous metals and alloys can absorb hydrogen by forming metal hydrides, some of which are currently being studied as H_2 storage systems in view of an increased use of this energy vector. Mg-based light hydrides are among the most investigated candidates for competitive hydrogen storage with sufficiently high reversible hydrogen capacity for mobile applications. Efforts have been particularly devoted to overcome the main disadvantages of pure Mg, such as the high desorption temperature and the slow kinetics [1]. To this purpose alloying magnesium with transition metals was considered and many binary or ternary systems based on magnesium were studied.

In this work the La-Pd-Mg system was targeted. Some La-Mg phases were already investigated with respect to hydrogenation [2]; on the other hand Pd itself has a great affinity for hydrogen and, similarly to other late transition elements, shows a significant reactivity with Mg and rare earth metals. The La_2Mg_{17} phase was therefore taken as starting composition, and ternary alloys were synthesized where Mg is partially substituted by Pd. Single-phase samples were obtained retaining an hexagonal crystal structure similar to the binary phase, as evidenced by X-ray diffraction analysis. Their hydrogen absorption/desorption behaviour was studied by a Sievert apparatus under different experimental conditions – as an example, the figure shows the increase of hydrogen capacity of a 4 at% alloy during the first 11 cycles – and it will be presented and discussed with respect to hydrogen capacity, desorption conditions, cyclability and structural changes induced in the material.



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INO-PO-16 Computational analysis of I-I bonds in the simplest polyiodides

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In the last decades, halogen bonding has acquired particular relevance for the building up of supramolecular patterns.[1] Heavier halides, especially iodines, are particularly sensitive to residual interactions, which allow formation of compounds of large nuclearities. In fact, anionic I_n^m species with n up 29 and m=-1,-2,-3 have been reported [2], the simplest one being obviously I_3^-. Calculations of the electron density are available, which highlight the points of its accumulation/depletion hence the capabilities of subsequent aggregations [3]. From the MO point of view, it is important to understand the electronic parameters which affect the stereochemistry of the higher nuclearity assemblies and, in particular, the variable strengths of the I-I interactions. The variability of the effects are already observed in the simplest linear systems I_3^- and I_4^{2-}, of which there are numerous crystal structures available. The I-I distances significantly vary depending on the nature of the counterion(s) and the overall packing arrangement. Thus I_3^- has not always the expected $D_{\infty h}$ symmetry but the two distances can become as different as 0.2 Å. Also for I_4^{2-}, which in principle consists of a central I_2 molecule residually interacting with two external I^- anions, it is evident that the three I-I separations depend on the crystal environment with possible loss of the highest symmetry. Here, we present a simple model based on experimental and theoretical data, which highlights how the mixing of the key σ orbitals is affected by a different distribution of the positive charges in various crystals.[4] To determine the latter, the Hirshfeld surface approach has been applied to some selected experimental structures where the differences are most remarkable [5]. Systematic DFT calculations (in vacuum and solvent and) confirm that variously localized positive charges around the polyiodide can significantly affect the geometries of even the smallest I_3^- and I_4^{2-} units. The satisfactory results are interpreted in terms of a simple qualitative MO model, which monitors the σ orbital mixing for different positive charge distributions, hence the variable strength of the I-I bonding. The reciprocal validation between experiment and calculations and the predictability of the trends are the interpretational key to predict the variability of the halogen bonding in the smallest polyiodides and possibly in those of higher nuclearity.

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INO-PO-17 Catalytic membranes for indoor VOCs decomposition

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In indoor environments it is possible to detect different dangerous volatile organic compounds (VOCs). The most common VOCs grow from synthetic or semi-synthetic materials like plastic, wood composites and preservatives, foams insulation, furniture, flooring, paints and other solvents.
One of the most dangerous and common indoor air pollutant is represented by formaldehyde that can be emitted from urea, melamine or phenol formaldehyde resins and from additives used for the wood treatment. The purification from formaldehyde and other VOCs of polluted air with a complete oxidation strategy is the final target of this project.
We are developing and testing a series of polymeric membranes containing catalytic species such as transition metal complexes able to promote the oxidation of VOCs using air's oxygen as oxidant.
Our membranes are obtained as polymer nanofiber webs by electrospinning technique (ES). The complexes choosen in the early step of the research are Cu and Fe complexes able to promote the formation of high reactive oxygen's species [1, 2]. The ES technique allows the dispersion of the metal complexes in the polymer solution before the ES process avoiding any further treatment of the membrane.

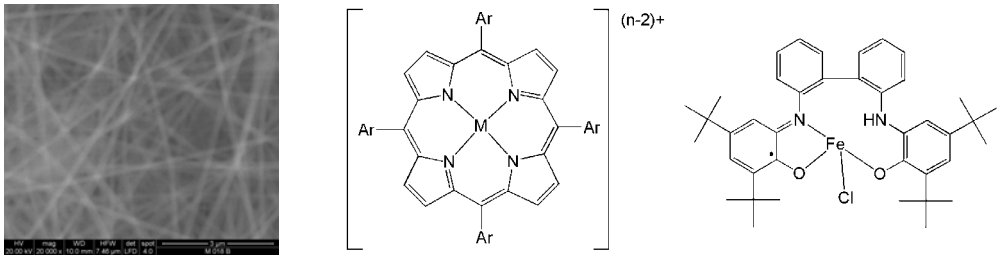

Figure 1. SEM image of a membrane and structure of some dispersed complexes

Aknowledgement. P. S., M. M. and M. R. wish to thank the Università degli studi di Padova (Progetto di Ricerca di Ateneo 2008 - CPDA083825) for the financial support.

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INO-PO-18 Water chemisorption on TiO_2 ultrathin films

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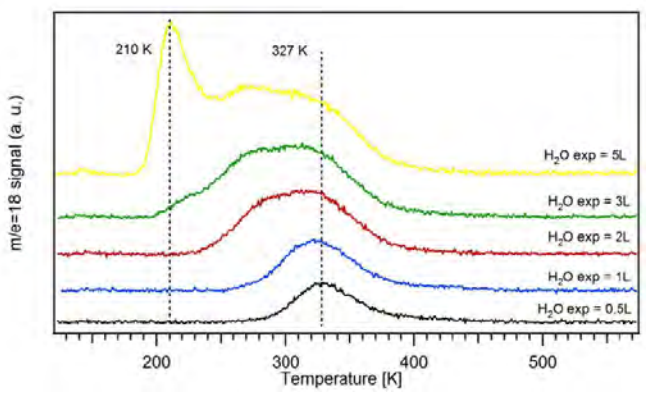
Ordered TiO_2 ultrathin films on Pt(111) surface can be prepared by reactive evaporation of Ti in a high-oxygen background [1]. Two rectangular phases, called *rect*-TiO_2 and *rect'*-TiO_2 can be obtained for Ti coverage up to 2 monolayer equivalent (ML_{eq}) (*rect*), and < 4ML (*rect'*), while for coverage > $4ML_{eq}$ TiO_2 grows forming the rutile TiO_2(100) phase. All the phases were characterized by low energy electron diffraction (LEED), scanning tunneling microscopy (STM) and photoemission measurements. These TiO_2 polymorphs form non-wetting layers on the Pt(111) surface and are characterized by incommensurate unit cells. The *rect*-TiO_2 corresponds to self-standing double layer with lepidocrocite-like structure, the *rect'*-TiO_2 has been assigned to TiO_2(B), while when the oxide thickness exceeds 40 Å the rutile phase appears to be the most stable one. We have then studied water chemisorption on these TiO_2 ultrathin films by Temperature Programmed Desorption (TPD) measurements (see for example Figure reported below). In order to verify the efficiency in the water dissociation process we have performed isotopic labeling experiments: the TiO_2 ultrathin films were grown using $^{18}O_2$ and the TPD measurements were performed by monitoring the peak corresponding to $H_2{}^{18}O$. This method allowed us to distinguish the water signal coming from the scrambling within the ionization chamber of the quadrupole from that actually caused by the water dissociation process on the surface, showing that the different TiO_2 polymorphs have different efficiencies in the dissociation process.



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INO-PO-19 Activity and deactivation pathways of penthamethyl-cyclopentadienyl-iridium molecular catalysts for water oxidation

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The green production of renewable fuels is one of the biggest challenges that scientists are currently facing. To overcome it, a significant contribution could derive from the efficient generation of molecular hydrogen through the catalytic splitting of water, driven by the sunlight. One of the bottlenecks of the entire process is the development of an efficient catalytic system for water oxidation to molecular oxygen.

Several coordination compounds of the transition metals were found to be competent catalysts for water oxidation. Furthermore, it has been recently showed that also organometallic compounds ($[Ir(ppy)_2(OH_2)_2]^+$[1], ppy=2-phenyl-pyridyne; $[IrCp^*L_1L_2(OH_2)]$,[2-6], Cp*= penthamethyl-cyclopentadieny) can be used as robust and fast catalysts for water oxidation.

All these catalysts, used in harsh acidic and oxidative conditions, undergo decomposition and it would be extremely important to evaluate which are the possible deactivation pathways and quantitatively contrast how the decomposition rate depend on the nature of the ancillary ligands.

In this contribution, we report on: (1) the performance of $[IrCp^*(ppy)Cl]Cl$, $[IrCp^*(bzpy)NO_3]$ (bz=benzoyl-pyridine) and $[IrCp^*(H_2O)_3](NO_3)_2$ catalysts in terms of initial activity, long-term activity and TON (TurnOver Number); (2) *in situ* NMR studies aimed at intercepting possible intermediates and decomposition products; (3) DFT calculations on the mechanism of decomposition.

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INO-PO-20 Synthesis, NMR and theoretical study of Au(I) complexes with Nitrogen Heterocyclic Carbenes (NHC)

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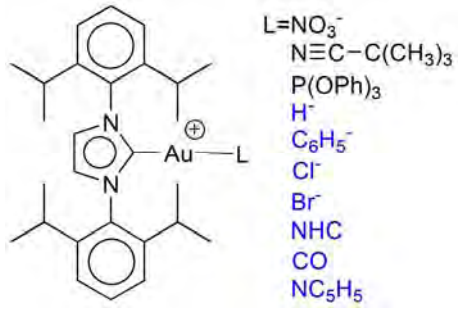
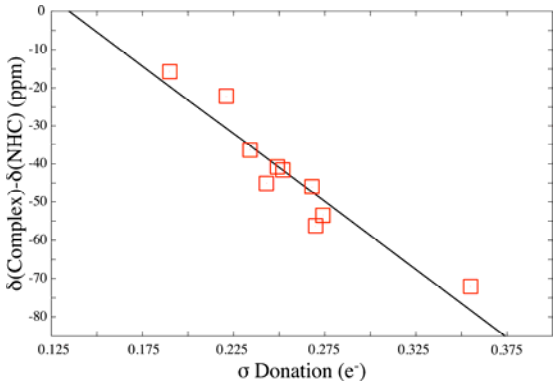
Linear compounds of gold (I) bearing NHCs as ancillary ligands find increasing application in chemistry [1]. Nevertheless, there is still some controversy on the basic aspects of the nature of the gold carbene bond, in particular regarding the relative weight of π-backdonation from the metal to the ligand and σ-donation from the carbene to the metal. Information about the nature of the carbene-gold bond can be obtained by evaluating the ^{13}C chemical shift of the carbenic carbon [2].

In this contribution we report: 1) the synthesis and NMR characterization of neutral and cationic NHC-Au-L compounds (scheme, L in black), 2) the theoretical determination of the chemical shift tensor of the carbenic carbon in a larger set of complexes (scheme, L in black and blue), and 3) the analysis of the charge displacement (CD) separated in terms of σ-donation and π-backdonation [3]. We found: 1) a rather good linear correlation between the chemical shift of the carbenic carbon and the donation component of CD (figure) and 2) that the π-backdonation component must be taken into account in order to correctly describe the gold-carbene bond since its contribution may approach up to 50% of the σ-donation. An analysis of CD and of the chemical shift tensor casts light on these findings.





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INO-PO-21 Novel cyclometallated Ru(II) and Ir(III) complexes as sensitizers for DSSCs

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In the last years research in the field of photovoltaic conversion and materials for solar panel is enormously increased for many fundamental reasons such as reduction of pollution, saving of energy cost and reduction of oil warehouse.
Solar cells based upon the semiconductor technology are at the present commercially available; their main disadvantages are the large energy amount required for the production of semiconductors and the rather high manufacturing cost. The main efforts in this field are therefore devoted to reduction of the costs and to an improvement of the efficiency of the solar cells.
In this framework, an important class of photovoltaic cells named DSSC (Dye-Sensitized Solar Cells) is extremely promising because it is made of low-cost materials and it is easy to produce.
The sensitizer is one of the key components, since it is responsible for the light harvest. It must exhibit excellent light harvesting properties and has to carry anchor groups to guarantee intimate contact with the semiconductor surface.
The pioneering and still one of the best sensitizer used for DSSCs is *cis*-dithiocyanatobis(4,4'-dicarboxylic acid-2,2'-bipyridine)ruthenium(II) (N3).
However, recently cyclometallated Ru(II) complexes appeared as promising candidates for DSSCs, in particular due to their long term stability. [1, 2]
We synthesized and characterised novel cyclometallated Ru(II) and Ir(III) complexes which have been tested in DSSCs.
Details on these studies will be presented.

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INO-PO-22 Functionalized Shvo-Type Catalysts for Mild Upgrading of White Poplar Bio-oil.

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Shvo's diruthenium complex **1** is an active catalyst in a considerable number of homogeneous reactions.[1] Our studies on hydrogenation of bio-oil obtained from pyrolysis of white poplar demonstrated that **1** maintains its performances in spite of the complex chemical nature of the substrate leading to an almost quantitative conversion of the polar double bonds and promoting the hydrolysis of sugar oligomers into monomers.[2]

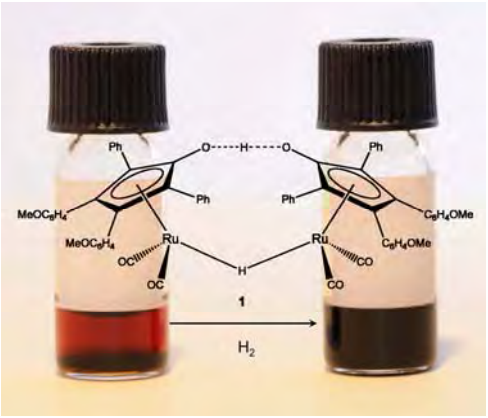

Figure 1**: Hydrogenation of white poplar bio-oil with Shvo catalyst **1

Recovery of the ruthenium catalyst remains the major problem which could be overcome by heterogenization. With the aim of immobilizing type **1** catalyst on insoluble support (*e.g.* silica, resins, hydrotalcites etc.) we investigated the synthesis of new –OH functionalized type **1** hydroxy-cyclopentadienyl-ruthenium-hydride $\{[3,4\text{-}(4\text{-}R\text{-}C_6H_4)_2\text{-}2,5\text{-}Ph_2(\eta^5\text{-}C_4CO)]_2H\}Ru_2(CO)_4(\mu\text{-}H)$ (R= Br, $-C{\equiv}CCR'_2OH$; R' = H, Me, Ph) under both traditional and microwave assisted synthetic routes. Studies on iron analogues and their catalytic activity are also under investigation.

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INO-PO-23 New bis-guanidine Pt(II) complexes: synthesis and biological activity.

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The reactivity of organocyanamides (R_2N-C≡N, with R = alkyl) have been much less explored than that of organonitriles. Recently, the nucleophilic addition of ammonia to Pt(II)-coordinated organocyanamides has been reported to provide the bisguanidine Pt(II) compounds of the type *cis*- and *trans*-[$PtCl_2N(H)=C(NH_2)NR_2\}_2$)] (with R = alkyl) [1].
Our group investigated in the past years the addition reactions of primary ($R'NH_2$) and secondary (R'_2NH) amines to the C≡N triple bond of coordinated nitriles to afford the amidine complexes of the type *cis*- and *trans*-[$PtCl_2\{N(H)=C(NHR')R\}_2$] and *cis*- and *trans*-[$PtCl_2\{N(H)=C(NR'_2)R\}_2$] [2] (with R = alkyl, aryl; R' = alkyl, cycloalkyl). Such derivatives demonstrated to possess a remarkable biological activity (both *in vitro* and *in vivo*) thus constituting a new generation of platinum antitumor drugs [3].
Here we describe the nucleophilic additions of dimethylamine to coordinated dimethylcyanamide to form new Pt(II) complexes (Figure 1) containing guanidine ligands $Me_2NC(NMe_2)$=NH.

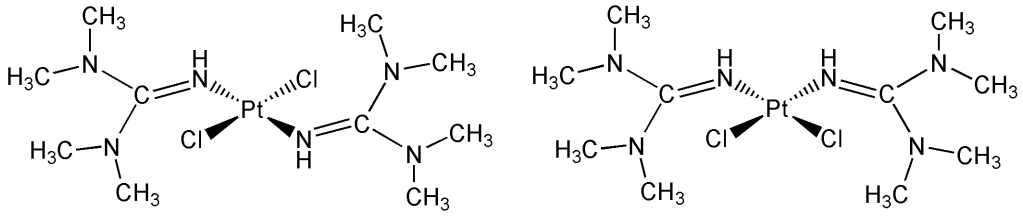

Figure 1. Structure of bis-guanidine Pt(II) complexes.

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INO-PO-24 Controlling quantum dot aggregation by acid/base switching

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Colloidal semiconductor nanocrystals have generated great interest in recent years for both fundamental science and technical applications [1]. Their main characteristic, which made them so popular, is the intense, narrow and size-dependent emission. Nevertheless, the achievement of good spectroscopic properties (high quantum yields, long term photostability) is strictly related to the quality of the material, particularly as far as surface states are concerned [2]. Indeed surface chemistry plays an important role in the manipulation of these materials, and is responsible of the sensitivity of the optical properties of quantum dots to the surrounding environment. In order to use inorganic semiconductor nanocrystals for sensing and biological applications, their response to changes in the environment must be known and understood. On one hand, it is necessary that the material is stable in a range of experimental conditions as wide as possible. On the other hand, the intrinsic sensitivity of the material to a specific analyte can be exploited for sensing applications, without the need of further functionalization of the surface [3].
In our study we focussed our investigation on the effect of acid and base on the properties of CdSe based core and core/shell quantum dots in organic solvent, comparing the same materials originating from different synthesis, materials with different organic ligands, and with different shell thicknesses. The surface of quantum dots is always covered by a shell of organic ligands, that prevent aggregation and passivate the surface of the nanoparticles. The acid competes with the nanocrystals for the ligands, which are Lewis bases, causing their detachment from the surface. As a consequence the nanocrystals aggregate and their luminescence is quenched. The process can be reversed by deprotonation of the ligands with a base.

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INO-PO-25 FROM P_4 TO $H_3P(O)$: UNPRECEDENTED PROCESS FEASIBLE VIA ELECTROCHEMISTRY

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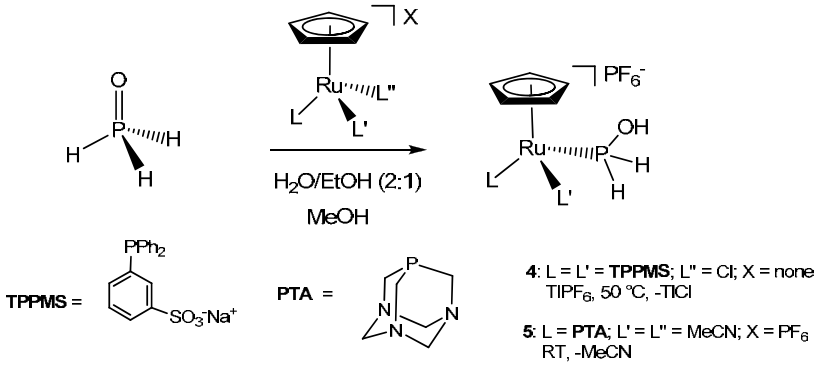
The elusive phosphine oxide has been observed for the first time in 1985 by Hamilton and Murrells,[1] who generated it by reacting O_2 with PH_3 using a discharge-flow system, and later on it was also obtained and trapped as a short-living species in solid argon matrices.[2] Herewith we report the preparation of the first defined compound bearing phosphorus with (-1) oxidation state, namely $H_3P(O)$, by electrochemical means using as starting material a suspension of white phosphorus in water and ethanol. The novel species has been generated through a stepwise process, involving first the reduction of P_4 to PH_3 and consequently its oxidation to phosphine oxide. Following tautomerization to phosphinous acid $H_2P(OH)$, $H_3P(O)$ has been trapped in the coordination sphere of ruthenium(II) moieties forming stable organometallic derivatives as shown in the scheme below.[3]



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COST Action CM0802 "PhoSciNet", NATO(CPB.NR.NRCLG 983375), CNR-RAS bilateral agreement, PRIN 2007 are thanked for funding and Thermphos Int. (Vlissingen, NL) for a generous loan of P_4.

INO-PO-26 Cyclopropanation Reactions Catalyzed by Rhodium Porphyrin Bound to a Merrifield Resin

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The cyclopropyl ring is an important organic function due to the presence of such structure in a number of interesting natural products derivatives with antileukemic activity *in vitro*[1] . Several methods have been discovered in the past for obtaining such ring using copper, rhodium and osmium complexes as efficient catalysts for the synthesis of cyclopropanes from diazocompounds[2].

Synthetic iron, rhodium and osmium porphyrins have been also reported as catalysts for the cyclopropanation reaction of simple olefins by ethyldiazoacetate (EDA)[3]. Comparing with the simple copper catalysts, like CuCl which preferentially affords the *anti* isomers, the porphyrin catalysts give interesting results in reversing the *anti/syn* ratio of the products depending on the nature of the metal. The recycling of the catalyst without any tedious column separation, is an important goal in preparative chemistry because this fact allows to synthesize large amount of the products using small quantity of expensive metal complexes.

In this communication we will show the possibility to use an immobilized metalloporphyrin to catalyze the cyclopropanation of standard olefins with good yields and high *syn/anti* ratios compared with those obtained with normal metal compounds. The catalyst can be reused several time without any loss of activity.

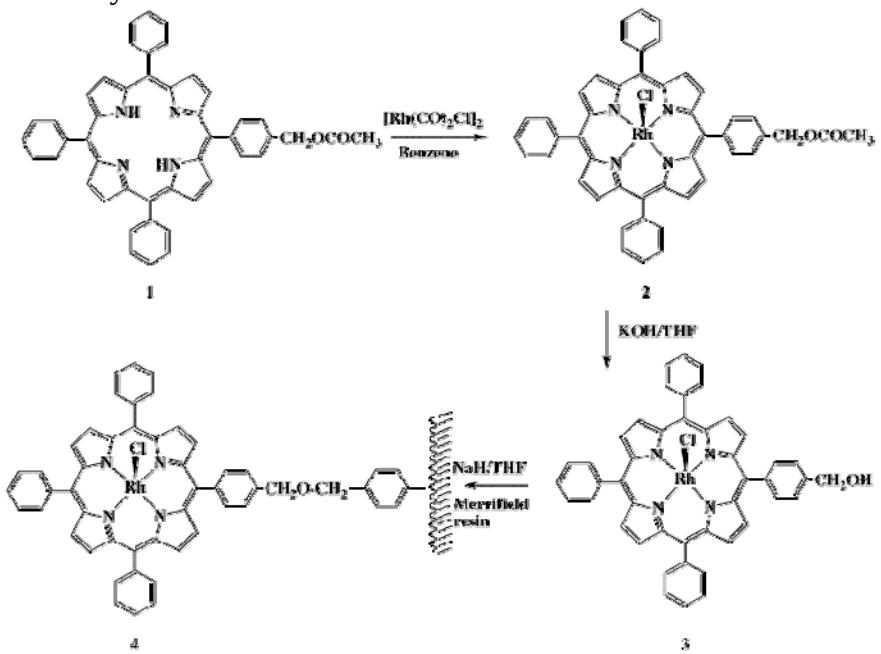

Fig. 1. Synthesis of the catalytic system

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INO-PO-27 New CPs Based on the Trinuclear Triangular SBU $[Cu_3(\mu_3\text{-}OH)(\mu\text{-}pz)_3]^{2+}$ Connected through 4,4'-Bipyridine.

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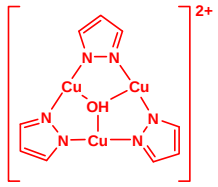
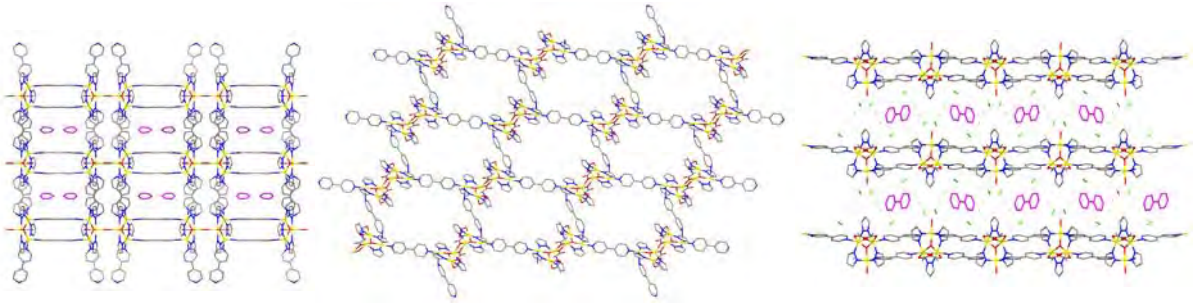
Coordination Polymers (CPs), often obtained by (self)-assembling oligonuclear metal clusters (the so-called Secondary Building Units or SBUs) are the subjects of a large and increasing number of studies due to their interesting properties and promising applications in numerous important fields, as gas storage, molecular recognition, catalysis, etc.[1] An important class of polynucleating ligands, useful to drive the self-assembly of CPs, is represented by donor units containing two 4-pyridyl moieties interconnected by various spacers, which can afford different lengths, linear or non-linear geometries, and conformationally rigid or flexible molecular skeletons.[2]

Recently, we developed a general procedure to obtain trinuclear triangular copper(II) complexes, having the $[Cu_3(\mu_3\text{-}OH)(\mu\text{-}pz)_3]^{2+}$ core,



(pz = pyrazolate) whose charge is balanced by two carboxylate ions.[3]

Continuing our ongoing research on the synthesis of new CPs, we treated $[Cu_3(\mu_3\text{-}OH)(\mu\text{-}pz)_3(CH_3COO)_2(Hpz)(H_2O)]$ with 4,4'-bipyridine, obtaining new CPs, in which the trinuclear core is maintained.



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INO-PO-28 Dinuclear Pt(II)-bisphosphonates complexes: useful precursors of multinuclear or higher oxidation state platinum drugs.

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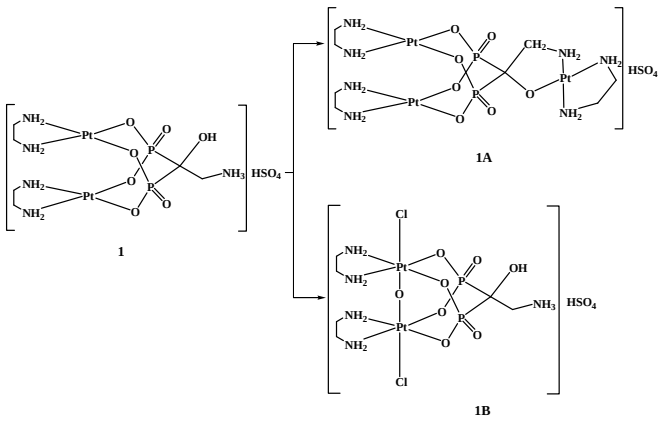
Cisplatin is one of the most successful drugs in cancer chemotherapy. Despite its success, treatment with cisplatin is limited by undesirable side effects[1].
The use of carrier ligands able to promote the specific accumulation of the drug in target organs or cells has been exploited as a strategy to overcome the side effects of cisplatin. In particular, geminal bisphosphonates (BPs), commercial drugs which show affinity for bones and other calcified tissues[2], have been used to promote the specific accumulation of platinum antitumor drugs in the bone with consequent significant improvement of the biological effect and reduction of the systemic toxicity. BPs are also aminable for the synthesis of polynuclear platinum complexes. The interest for the latter type of complexes has greatly increased in recent years thanks to their ability to overcome cisplatin resistance forming Pt-DNA adducts completely different from those of platinum drugs currently in clinical use.[3] Particularly, for mononuclear Pt complexes, has also been exploited their oxidation to Pt(IV) complexes which are much more inert to ligand substitution than their Pt(II) counterparts and are believed to undergo reduction to Pt(II) prior to reaction with DNA.[1]



In this work a dinuclear Pt(II) complex containing a geminal bisphosphonate (**1** in figure) has been used as a building block for the preparation of multinuclear (**1A**) or higher oxidation state (**1B**) platinum drugs.[4] The two new compounds have been fully characterized and their *in vitro* cytotoxicity has been evaluated.

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INO-PO-29 Effect of Si and Ge alloying addition on the electrochemical behaviour of Fe_3Al intermetallic compound

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Among all the intermetallic compounds susceptible to high temperature applications, iron aluminides have been attracting considerable attention for their applications as structural materials, owing to their high strength-density ratio, low row material cost and also good corrosion resistance, due to their ability to form a protective oxide layer. Many studies have been carried out on the oxidation behaviour [1,2] and on the tribological properties [3] of iron aluminides . However, to date, information concerning the corrosion behaviour in aqueous acid solutions of these compounds are scarce.
In this communication the influence of Si and Ge alloying addition on the electrochemical behaviour of Fe_3Al intermetallic compound in H_2SO_4 solution is assessed.
$Fe_{75}Al_{25}$, $Fe_{70}Al_{25}Si_5$ and $Fe_{70}Al_{25}Ge_5$ compounds were prepared by melting the stoichiometric amounts of pure elements in an arc furnace under a bit depression of argon. Light optical microscopy (LOM), scanning electronic microscopy (SEM), electron-probe microanalysis (EPMA) and X-ray powder diffraction (XRPD) were used to investigate the microstructure of samples. The electrochemical behaviour was assessed by means of polarization performed in aerated 0.25 M H_2SO_4 solution at room temperature (25 ± 0.1 °C). Potentiodynamic polarization curves were recorded in the potential range −800 ÷ +2000 mV/SCE (Saturated Calomel Electrode) at a scan rate of 1 mV/s. X-ray photoelectron spectroscopy (XPS) measurements were carried out on the samples surface after the electrochemical tests in order to gain information about the composition of surface layers. Preliminary results show a positive influence of silicon and germanium alloying addition on the passivity of Fe_3Al intermetallic compound.

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INO-PO-30 Acid–Base Interaction between Transition-Metal Hydrides: Dihydrogen Bonding and Dihydrogen Evolution

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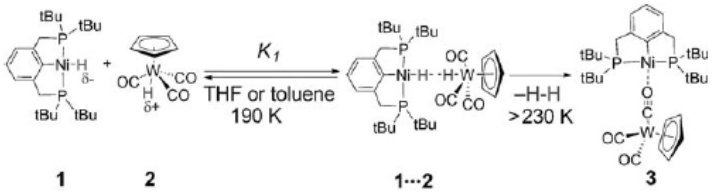
Unconventional hydrogen bonding that involves transition metal complexes has attracted considerable attention and several efforts have been made to rationalize the many conceivable interactions. However, dihydrogen bonding interactions where transition metal hydride complexes serve as both proton acceptor and proton donor in a hydrogen bond have not been described, although dihydrogen evolution was observed when “hydridic” and “acidic” hydride complexes are allowed to react. To further investigate this unconventional acid–base interaction, we report on the reaction of the stable electron-rich nickel(II) pincer hydride [(2,6-$C_6H_3(CH_2PtBu_2)_2$)Ni(H)] (**1**) with the acidic tungsten(II) complex [CpW(H)$(CO)_3$] (**2**).[1] Mixing equimolar amounts of **1** and **2** in carefully degassed THF at 273 K under a nitrogen atmosphere led to a reddish-orange compound, accompanied by H_2 evolution. Replacing **1** with [(2,6-$C_6H_3(CH_2PtBu_2)_2$)Ni(D)] or **2** with [CpW(D)(CO)3] led to HD formation. Single crystal X-ray diffraction analysis revealed that the final product is the bimetallic ion pair [$CpW(CO)_2$(-k,C:k,O-CO)···Ni[(2,6-$C_6H_3(CH_2PtBu_2)_2$)] (**3**).



By monitoring the process by multinuclear VT NMR, relaxation NMR studies and VT IR spectroscopy in the 190–298 K temperature range, strong experimental evidences have been obtained for the formation of a **1···2** adduct in which a NiH···HW unconventional hydrogen bond precedes the H_2 elimination that yields **3**.

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INO-PO-31 Synthesis and Photophysic Properties of new Phosphorescent cyclometallated heteroleptic Iridium(III) phenylpyridinato Complexes

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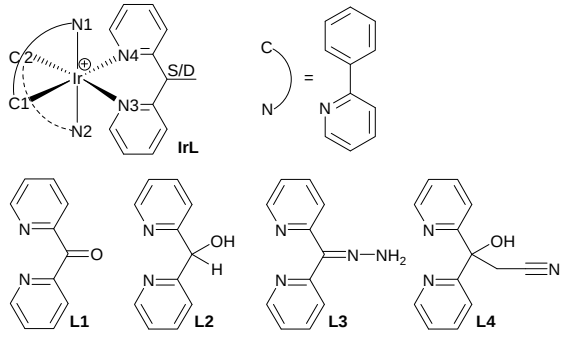
Luminescent iridium(III) complexes received increasing attention for outstanding luminescence properties such as high intensities, lifetimes in the μs time range, and emission wavelengths that can be tuned to cover a full range of visible colors, from blue to red..

However the synthesis of Ir(III) complexes by the preparation of the appropriate organic ligand followed by its reaction with the metal precursor cannot be performed whenever reactive units present in the ligand do not tolerate harsh synthetic conditions. In order to search an effective way of increasing the emission quantum yield at RT we synthesized new phosphorescent cyclometallated heteroleptic iridium(III) phenylpyridinato complexes $[Ir(ppy)_2(L)]^+$ (where ppy = phenylpyridine and L = bipyridine type ligand derived from di-2-pyridylketone) where the usual synthetic procedure of reacting the iridium dimer $[Ir(ppy)_2Cl]_2$ with an appropriate ligand (L) has been substituted by exploiting the reactivity of the carbonyl group of the $[Ir(ppy)_2$(2,2'-dipyridylketone)$]^+$ (**IrL1)** complex. The reduction of the carbonyl group with $NaBH_4$ on **IrL1** affords $[Ir(ppy)_2$(dipyridin-2-ylmethanol)$]^+$ **(IrL2),** whereas $[Ir(ppy)_2$(2,2'-(hydrazonomethylene)-dipyridine)$]^+$ **(IrL3)** and $[Ir(ppy)_2$(3-hydroxy-3,3-di(pyridine-2-yl)propanenitrile)$]^+$ **(IrL4)** have been obtained by nucleophilic addition of hydrazine in methanol and potassium hydroxide in acetonitrile respectively. All the complexes were obtained in reasonable or almost quantitative yield and fully characterized.

It is worth noting that slight modification of the ketone moiety introduces relatively large changes in the photophysical behavior of the iridium complexes. TD-DFT studies were undertaken to rationalize the key role of the ketone group and its modifications to form non-conjugated cyclometallated ligands on the photophysical properties of these closely related iridium (III) complexes.



INO-PO-32 DFT and synchrotron-based X-ray studies of photoactivable complexes

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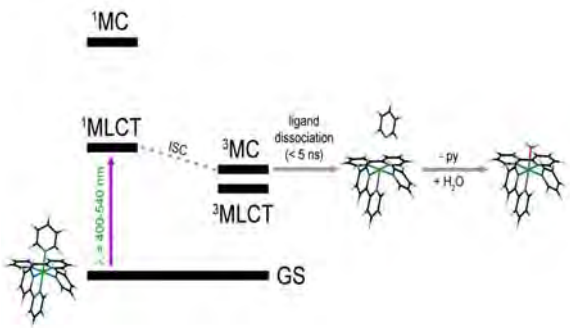
Selective activation of prodrugs can be achieved in cells using photoactivable metal complexes [1]. This class of derivatives offers unique possibilities for new applications in cancer therapy since light activation allows direct control of site, time and dosage of active species in tissues and organs. For example, light irradiation of metal complexes can trigger formation of reactive species and promote selective interaction between metal complexes and target macromolecules (DNA, proteins), which would not take place in the dark.

The study of the ground- and excited-state electronic structure of such derivatives is crucial for understanding the mechanism of action of these molecules and for the development of new anticancer agents with improved photophysical and photochemical properties. Hence, we are exploring the combined use of DFT and TD-DFT with time-resolved X-ray to gain insights into the electronic structure of photoactivable complexes and to capture the time dependence of their excited-state structural evolution.



Here we report a Time-Resolved Wide Angle X-ray Scattering (TR-WAXS) study on photoactive *cis*-$[Ru(bpy)_2(py)_2]Cl_2$. Upon excitation of its metal-to-ligand charge-transfer (^{1}MLCT) band centred at 460 nm, this model compound efficiently releases one pyridine ligand and subsequently coordinates a solvent molecule (H_2O). TR-WAXS allows direct observation of pyridine dissociation from *cis*-$[Ru(bpy)_2(py)_2]Cl_2$ in the 100 ps – 10 ns time-range. The transient structures captured by TR-WAXS were used to complement computational results and to validate DFT-optimized structures [2,3].

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INO-PO-33 Influence of the solvent in carboxylation and/or reduction of axial dihydroxo Pt(IV) complexes with *cis*-1,4-DACH as diamine ligand.

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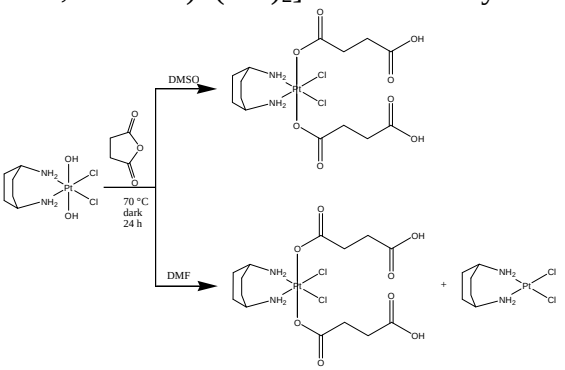
Pt(IV) complexes are seen as potential prodrugs able to be activated to the corresponding active Pt(II) complexes after reduction and loss of the two axial ligands. Pt(IV) complexes are more kinetically inert than the Pt(II) ones and hence can be orally administered. Moreover the presence of two extra ligands in the axial positions allows to tune some very important features such as solubility, lipophilicity and redox potential. Axial disuccinato complexes have an optimal redox potential compared to axial dichlorido complexes (too easily reduced) and axial dihydroxido complexes (too difficult to reduce)[1]. Moreover the presence of two free carboxylic functions allows their conjugation of active molecules which, after their release following the reduction process[2, 3], could improve the pharmaceutical effect. Starting from [$PtCl_2$(*cis*-1,4-DACH)] (DACH= diaminocyclohexane) [4, 5] we performed the synthesis of the axial disuccinato Pt(IV) derivative following a well known synthetic pathway which involves the preparation of the axial dihydroxido Pt(IV) complex and the following carboxylation using succinic anhydride. For cisplatin and other Pt(II) analogs the latter reaction is straightforward if performed in DMF. We have found that starting from *cis, cis, trans*-[$PtCl_2$(*cis*-1,4-DACH) $(OH)_2$] the carboxylation reaction in DMF leads to the desired product but there is also a side reaction leading to the reduced Pt(II) precursor. This behaviour, that is reduction in the absence of a specific reducing agent, is not reported in the literature [6]. Performing the reaction in DMSO we did not observe the formation of the reduced Pt(II) precursor. We have investigated the mechanism of the reduction reaction and the conditions that are crucial for the formation of the reduced species in the absence of specific reducing agents.



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INO-PO-34 Developing new di-iron containing proteins as catalysts for oxidation reactions

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The quantitative and high efficiency detection of several analytes is required in many different areas. Since the basic concept of enzymatic electrode by Clark and Lyons and after successful applications of glucose-oxidase based biosensors in blood glucose measurement [1], a bio-revolution in chemical analysis has been occurring. Recently, interest in organic pollutant biosensing has been growing [2]. In this regard, Toluene Monooxygenase family (TMOs), a four components bacterial multi-component monooxygenase, can be of crucial utility as it is able to hydroxylate a variety of organic compounds, such as halogen alkanes and aromatic derivatives, consuming equivalents of dioxygen or hydrogen peroxide. A cost/time effective alternative to the classic microbial biosensor [2,3] is the adoption of synthetic compounds able to mimic TMO activity, bypassing enzyme purification process and overtaking cell diffusion limits.

Full-organic ligands coordinating two metal centers, which are able to mimic enzyme reactivity [4], and, small peptides, which are able to fold into four-helix bundle motives [5], have been developed in the last decades. An interesting strategy is the synthesis of small peptide chains, with amino acid sequence containing information both for a proper folding and for metal binding. In the last years, several models of a di-metal self-assembling four-helix bundle motif has been obtained by means of *de novo design*, the DF series [5]. Recently, redox activity has been achieved with the di-iron DF3 model [6]. It is able to bind and successfully oxidize phenolic substrates, similar to the natural enzyme alternative oxidase. This result assures the suitability of DF-like scaffolds for engineering new catalytic site through various metals and coordination geometries. Here, we report the design and a preliminary computational study of new DF variants, mimicking TMO active site geometries and second shell interactions.

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INO-PO-35 Design and Preliminary Characterization of New Heme-Protein Models

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Mimochromes are a class of peptide-based heme-protein models, containing two α-helical peptide chains covalently linked to deuteroporphyrin IX [1]. They provide a remarkable opportunity to explore how both catalytic activity and stability of the heme cofactor are regulated by different and specific interactions with the protein matrix, ranging from coordinate and hydrogen bond, to hydrophobic and ionic interactions [2].

Here, we describe two new models, engineered on the Mimochrome IV crystal structure [3]. They are made up of two 17 residue peptides. Unlike the other members of the class, the peptide chains are elongated by 6 residues at the N-termini. This extra peptide segment, modeled in extended conformation, is intended to ensure further protection to the heme, thus increasing stability and specificity. To stabilize the desired protein folding, residues were chosen to give a large number of intra- and inter-chain interactions.

The first model contain two identical peptide chains, with a bis-His heme coordination. Preliminary CD and Uv-vis analysis confirmed the expected conformation and heme coordination. The ability of this symmetrical model to act as an electron-transfer protein is presently under course.

To mimic peroxidase-like activity [4], a second model was developed. The two peptide chains around the heme have different composition: one peptide chain houses the proximal histidine in a mainly hydrophobic environment; the second chain provides a cavity for binding small exogenous compounds and contains key residues for catalysis (Arg and His). The Uv-vis spectra of the un-symmetric model is typical of mono-His coordinated heme. The preliminary structural and functional characterization of these models will be presented.

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INO-PO-36 Electrostatic Interaction between Charged PMMA Core-Shell Nanospheres and Cytotoxic Platinum Complexes

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The drug targeting and delivery approach aims at reducing chemotherapy-related systemic side effects. Passive targeting is based on the use of natural or synthetic macromolecular vectors to exploit the "enhanced permeability and retention" effect (resulting from the low vascularity and abnormal morphology of tumor vasculature) in order to selectively deliver cytotoxic agents to tumor cells.

Previously, we employed positively charged polymethylmetacrylate (PMMA) core-shell nanospheres as vectors for the anionic $[PtCl_3(NH_3)]^-$ complex. The antitumor effect of the resulting adduct was assessed in C57BL/6 mice bearing B16 murine melanoma. When used at the corresponding maximum tolerated doses, the adduct proved to be more effective than cisplatin in inhibiting B16 tumor growth and its in vivo efficacy correlated with Pt-intratumor accumulation.

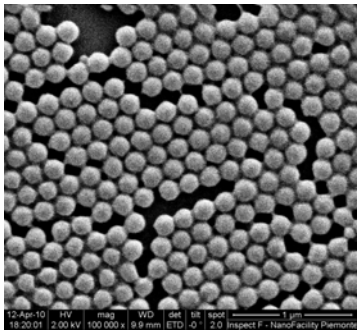

Figure 1.

The interaction between nanospheres and complexes of reversed charge is now studied. For this purpose, two cationic platinum compounds and PMMA core-shell nanoparticles (Fig. 1) bearing anionic ($-SO_3^-$) arms are used to determine whether such particles might serve as drug carriers for positively charged antiproliferative Pt drugs. As expected, the formation constant of the adduct with a dication Pt complex is significantly higher than that of a monocation one. Moreover, the stability of both adducts depends on the ionic strength and surface charge density of competing cations in the medium. The stability of the conjugates and the consequent retention and release of the drug from the nanoparticles will thus depend on both blood and extracellular fluid composition.

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INO-PO-37 Gold Nanoparticles Functionalized with Artificial Metalloenzymes

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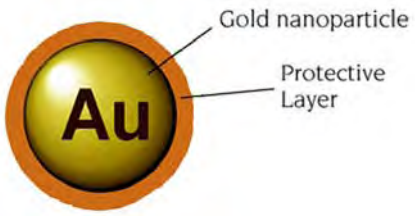
Nanoscience and nanotechnology are growing fields, which are gaining great impact in different areas, ranging from electronics and communication technologies to biomedical engineering. The production of nanomaterials, such as nanoparticles (NPs), is playing a central role. Due to their small dimension (1-100 nm), NPs exhibit properties that are often not observed in the bulk materials. For example, gold nanoparticles (AuNPs), the most stable metal nanoparticles, present unique electronic, magnetic and optical properties, and are experiencing applications in several fields, such as catalysis and biology [1,2,3]. The AuNP properties may be tuned, by controlling two key structural parameters: the size and the chemical nature of stabilizing ligand shell [2]. Therefore, the integration of nanoparticles with biomaterials, which display unique recognition, catalytic, and inhibition properties, may yield novel hybrid nanobiomaterials with synergic properties and functions [4].



In this contest, we are interested in developing biomolecule–nanoparticle hybrid systems, made up of AuNPs conjugated to artificial metalloenzymes [5,6]. In particular, artificial heme-proteins with peroxidase-like activity [7], have been conjugated to AuNPs, with the aim of exploring their potentials in the development of biosensors and immunosensig assays. The synthesis and the spectroscopic and functional characterization of the new nanobiomaterials will be presented.

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INO-PO-38 Ruthenium porphyrin-peptide conjugates: synthesis and characterization

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Early interest in the chemistry of ruthenium porphyrin systems was related to the use of metalloporphyrins as models of the cytochrome P450 and peroxidase enzymes, with respect to the oxidation of organic compounds. The close periodic relationship of iron and ruthenium suggests that ruthenium could represent a useful candidate for replacing the biologically significant iron, in iron-centered reactions. Further, ruthenium displays a rich coordination and redox chemistry, which spans oxidation states from +2 to +7 in the porphyrin ligand environment [1].

Nowadays, studies on ruthenium-porphyrin compounds expand and focus on diverse area of research that acknowledges not only their role as valuable biomimetic models, but also their potential for the development of suitable synthons in coordination and organometallic chemistry [2], building blocks for supra- or super-molecular assemblies [3], materials [4], and sensors [5]. The use of ruthenium-porphyrins in medicinal chemistry [6], as cancer terapeutics and photosensitizer in photodynamic therapy, is also receiving great interest.

In this perspective, our laboratory has developed a series of water-soluble ruthenium porphyrin-peptide conjugates, synthesized through the covalent attachment of peptides to the Ru(II)-deuteroporphyrin. They were designed to accommodate in their interior small ligands, based on the stability of ruthenium-small molecules (O_2, NO) complexes. Therefore, these new ruthenium complexes may represent attractive candidates in the construction of environmental and biomedical sensors.

Here, we report their synthesis and spectroscopic characterization, together with preliminary NO binding analysis.

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INO-PO-39 Synthetic transducers in affinity third generation electrochemical biosensors.

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A biosensor is an analytical device that relies on a biological recognition element, communicating with a signal transducer that provides a measurable response related to the concentration of the analyte. Electrochemical biosensors, which exploit an electron transfer (ET) event at a solid electrode for signal transduction, are the most promising biosensors, in terms of ease of construction, costs, versatility and miniaturization [1]. In particular, third generation biosensors exploit the direct electron transfer occurring between an electrode and a redox-active species immobilized onto it. The biological interaction is transduced into a current signal, thus resulting in an amperometric detection of the analyte [2].

Efficient direct ET reactions have been reported only for a restricted number of redox enzymes [3]; several studies based on heme-proteins adsorbed or immobilized on various electrodes showed that high-molecular weight enzymes are often not suitable for direct electrical communication with the electrode [4]. Our strategy to overcome these limitations is the use of artificial low-molecular weight proteins, designed on rational bases, to own the required activity [5]. We developed a class of covalent heme-peptide conjugate, named Mimochromes, with the aim of understanding the effects of the peptide chain composition and conformation in modulating the heme redox potential [6].

An affinity electrochemical immunosensor was developed using Mimochromes as redox tags for the detection of the binding events. The artificial ET protein, functionalized with a suitable recognition element, was covalently anchored on a gold electrode through self-assembled monolayers. The biosensor was characterized with voltammetric techniques and tested for analyte recognition.

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INO-PO-40 Synthetic metalloproteins for diagnostic applications

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Enzyme-linked immunosorbent assays (ELISA) are commonly used for the detection of analytes in biomedicine, food, and environment control. These tests are based on the formation of immunocomplexes, between an antigen and a specific antibody. The detector system is usually an enzyme (e.g. horseradish peroxidase, HRP), which is covalently bound to the antibodies. Immunocomplexes are quantified by measuring a colorimetric signal, deriving from the enzymatic reaction. The immunological component brings the detection specificity, while the enzyme component gives the analytical sensitivity [1]. The natural protein high dimensions provide quite low enzyme\antibody ratio, thus limiting the analytical sensitivity. The use of artificial, small metalloenzymes would represent an interesting solution, allowing a higher conjugation ratio and a considerable signal amplification. This approach will be crucial for the development of more sensitive immunochemical assays for the detection of very small amounts of analytes.

Herein, Fe^{III}–mimochrome VI is proposed as reporter enzyme for the functionalization of antibodies usable in ELISAs. Fe^{III}–mimochrome VI is a 3.5 kDa synthetic heme-protein model, which displays peroxidase-like activity, with a catalytic efficiency comparable to the native HRP [2,3]. Human polyclonal antibodies (hIgG) have been functionalized with this synthetic enzyme, by the use of cross-linkers. Conjugates with an enzyme/hIgG ratio up to 13 have been prepared. This represents a significant result, when compared to commercial immunoglobulins, which are usually linked to 3 - 4 HRP molecules. The complete characterization of the conjugates is in progress, in order to determine their immunoreactivity, as well as enzyme activity and structural stability.

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INO-PO-41 Which one among the Pt-containing anticancer drugs forms more easily monoadducts with *G* and *A* DNA bases? A comparative study between oxaliplatin, nedaplatin and carboplatin

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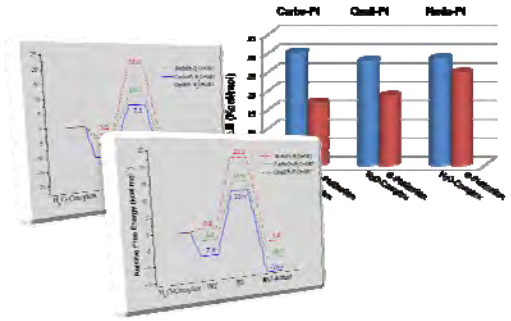
A good understanding of the interaction of platinum anticancer drugs with models of binding sites present in DNA is of fundamental importance to unravel the mode of action of this class of compounds.

In this work, the DNA bases platination processes of second- and third-generation Pt(II) anticancer drugs, have been investigated using Density Functional Theory (DFT) combined with the conductor-like dielectric continuum model (CPCM) approach, in order to describe their binding mechanisms and to obtain detailed data on the reaction energy profiles.

Although there is no doubt that a Pt-N7 bond forms during initial attack, the energetic profiles for the formation of the monofunctional adducts are not known.

Herein, a direct comparison between the rate of formation of CarboPt, NedaPt and OxaliPt adducts with Guanine ***(G)*** and Adenine ***(A)*** DNA bases has been made in order to spotlight possible common or different behaviour.



Together with previous works concerning the hydration mechanisms, [1] the goal of our work is to contribute to the elucidation of the whole mechanism employed by these compounds to reach the biological target.

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INO-PO-42 Investigation of Nanostructured Surface Conjugates with Non-conventional Thermal Analysis Coupled with FTIR and GCMS

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Thermal analysis (TA) is a well-known technique for materials characterization. The recent development of high-sensitive thermal balance has further increased the possibility of expanding thermogravimetric analysis (TGA) to surface features and surface-adsorbed moieties and which could be very promising in the field of the toxicity of mineral dusts. Furthermore, the possibility to analyse furnace gas with sensitive analytical techniques envisaged TA as a powerful tool to investigate complex surface conjugates. The recent in-line coupling of a high-sensitivity TGA with a FT-IR spectrophotometer equipped with a GC-MS dramatically expanded the application areas of the technique.

We report here about some non-conventional application of this innovative system devoted to the unveiling of the complex interactions between the surface of some inorganic nanoparticles and molecular compounds.

TiO_2 nanoparticles impregnated with alcohols or carboxylic acids (ethanol, ethylene glycol and citric acid) were subjected to TA in N_2 or O_2. Coupling thermograms (i.e. the sample weight loss as a function of temperature) with infrared thermograms (i.e. the integrated IR absorbance as a function of temperature) allowed us to discriminate between the weight loss due to water desorption and CO_2 formation subsequent to C-species oxidation. The temperature of desorption/oxidation of each molecular species was discussed in terms of conjugate stability.

The analysis of furnace gas was highly informative in two studies on the stability of pigments obtained by impregnation of sepiolite and palygorskite nanoclays with organic dyes, indigo blue and methyl red respectively. The interaction of the dye with the nanoclays structure was investigated by discriminating the dye desorption temperature from the hydroxyls condensation one. The study [1] indicated the degradation temperature of the pigment within the clay cages and the subsequent enhancement of the dye stability was demonstrated. Insights to the degradation molecular pathways of dyes were obtained.

The high specificity and overall versatility of the TGA-FTIR-GC-MS system in the characterization of complex inorganic conjugates is here showed with some relevant examples.

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INO-PO-43 *trans*-$[Ru(PMe_3)_2(H_2O)_4]^{2+}$ catalyzes H_2 production by selective decomposition of formic acid

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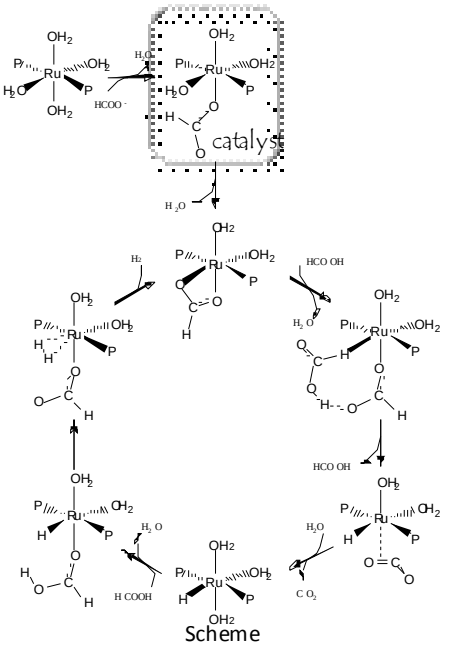
It is known that the reserves of fossil fuels are gradually decreasing and that the CO_2 emissions seem to be responsible for global warming [1]. The replacement of fossil fuels by sustainable energies has become essential for the future. To avoid the negative environmental impact of greenhouse gases, hydrogen has attracted increasing attention as an alternative secondary energy resource. However, the production and transportation of hydrogen in a cost effective, environmentally friendly manner is yet one of the major challenges to the development of the hydrogen economy.

An attractive alternative that can contribute to reduce CO_2 emissions is the use of CO_2 itself as a hydrogen carrier [2]. The combination of CO_2 reduction by H_2 in presence of an appropriate catalyst and selective decomposition of HCOOH to H_2 and CO_2 under mild conditions afford an environmentally benign system. The formation of H_2 by the catalytic decomposition of HCOOH has been the subject of many studies. As shown in a recent work, formic acid (HCOOH) decomposes selectively to afford H_2 and CO_2 in presence of a catalytic amount of a water-soluble, *trans*-$[Ru(tppts)_2(H_2O)_4]^{2+}$, ruthenium aqua complex, in a solution of HCOOH/HCOONa 9:1 [3]. A tentative catalytic cycle has been proposed by the authors on the basis of NMR experiments.



Scheme

We have first investigated, by means of DFT, the mechanism (*Scheme*) proposed by the authors of HCOOH decomposition, catalyzed by *trans*-$[Ru(PMe_3)_2(H_2O)_4]^{2+}$. Next, we have explored other possible pathways that the reaction may follow, guided by computational evidences.

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INO-PO-44 Investigation of the mechanism of reduction of *trans,trans,trans*-[$PtCl_2(CH_3COO)_2${*E*-HN=$C(CH_3)OCH_3$}$_2$].

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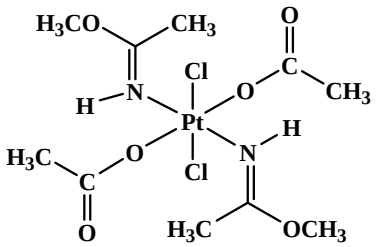
The current search for platinum-based anticancer compounds aims at developing complexes which do not show cross-resistance with respect to the currently used platinum drugs or that can be taken orally.
Concerning the latter aspect, several Pt(IV) compounds have been proposed as antitumour drugs and one of them, satraplatin *cis*-[$PtCl_2(CH_3COO)_2(H_2N$-$C_6H_{11})(NH_3)$], is in phase 3 clinical trial.



***trans,trans,trans*-[$PtCl_2(CH_3COO)_2${E-HN=$C(CH_3)OCH_3$}$_2$]**

However, the reactivity of Pt(IV) complexes towards biologically relevant reducing agents, such as ascorbic acid and gluthatione, is not yet well understood preventing the rational design of new compounds with better pharmacological properties.[1] Among the limited number of investigations so far reported, we whish to mention that of L. I. Elding who studied the ascorbate reduction of JM216 and of its isomers [2] and the investigation of J. D. Ranford who explored the reduction of *cis,trans,cis*-[$PtCl_2(CH_3COO)_2(NH_3)_2$] by methionine and cysteine.[3]
We have extended the investigation to *trans,trans,trans*-[$PtCl_2(CH_3COO)_2${*E*-HN=$C(CH_3)OCH_3$}$_2$] and studied its mechanism of reduction by ascorbic acid, glutathione, and triphenylphosphine using NMR spectroscopy, ESI-MS and electrochemical techniques.

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INO-PO-45 New Coordination Polymers from Cu^{II} Phthalate and Pyrazole

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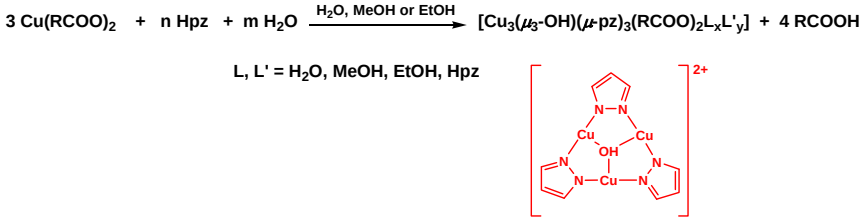
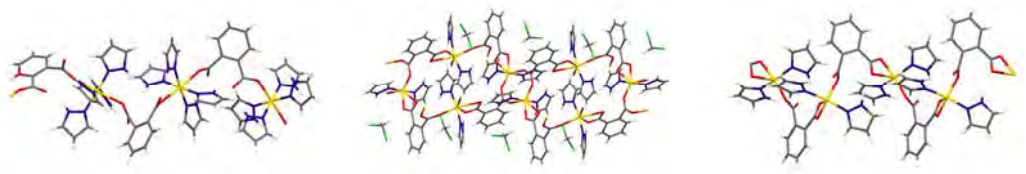
The studies on Coordination Polymers (CPs) [1] continue to produce a great number of publications, due not only to the intriguing "beautiful" structures often found in CPs, but also to their possible applications in different, important fields as catalysis, [2] gas storage, [3] etc.. On the other hand, it is not easy to predict *a priori* the results of the reactions of polytopic ligands with metal ions, to form CPs, avoiding a tedious trial-and-error approach.

In the last years we deeply studied the interaction of Cu^{II} monocarboxylates with pyrazole (Hpz), generating mainly CPs based on the trinuclear triangular Secondary Building Unit $[Cu_3(\mu_3\text{-}OH)(pz)_3]$, [4] (see Scheme).



We are now studying and report here the results obtained in the reactions of Cu^{II} bicarboxylates with Hpz when different synthetic strategies were employed. Particularly, Cu^{II} phthalate was reacted with Hpz in different solvents, obtaining different CPs. The crystal structures of some of them are shown below.



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INO-PO-46 High Throughput Experimentation Studies on $MgCl_2$-Supported Ziegler-Natta Catalysts

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High Throughput Experimentation (HTE) technologies have profoundly innovated the research approach to olefin polymerization catalysts and polymerizations in major chemical companies (e.g., Dow, ExxonMobil, Borealis). In fact, the high complexity of these systems, in which subtle changes of catalyst formulation and/or application protocols may result into dramatic effects in performance, makes them ideal substrates for HTE. The huge potential of HTE for scientific and industrial purposes has been largely demonstrated, both for catalyst and process discovery [1,2].

Since 2006 our laboratory operates powerful HTE platforms for catalyst preparation and screening (*FreeSlate Core Module* and *FreeSlate PPR48,* respectively), housed into high performance glove-boxes and integrated with a large variety of on-line and off-line analytical techniques (es. NMR, ICP-OES, GC, LC, GPC, DSC).

As an example of practical application of these platforms to industrially relevant systems, in this poster we report on studies carried out on modern Ziegler-Natta catalyst systems for the production of isotactic polypropylene. As is well-known, such systems consist of a support ($MgCl_2$), a transition metal precursor (e.g. $TiCl_4$), an activator (e.g. an Al-trialkyl), and one or more electron donor modifiers (e.g. esters, ethers, alkoxysilanes) [3]. Until now, the extreme complexity of these formulations prevented a rational approach, and industrial research has been primarily empirical. In this poster, we demonstrate how a HTE approach can result into a 10x to 100x speed-up of structure/properties correlation studies, which is decisive for the implementation of models for mechanistic interpretations.

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INO-PO-47 Synthesis and Characterisation of Dinuclear N-heterocyclic Dicarbene Gold Complexes in (I-I), (I-III) and (III-III) Oxidation States

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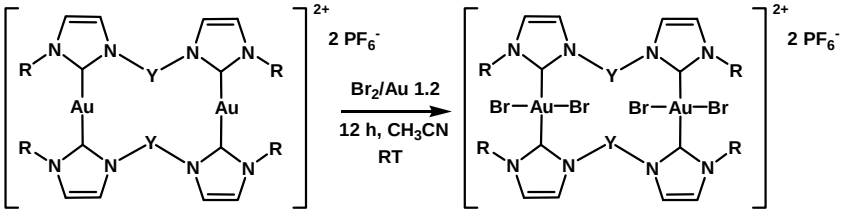
The research activity on the synthesis, characterisation and catalytic applications of N-heterocyclic carbene (NHC) complexes has been extended since few years to gold centers, as a consequence of the increasing interest in the chemistry of this metal [1]. Nevertheless, there are very few examples of gold complexes, bearing in the coordination sphere a dicarbene ligand [2].
In this contribution we report our recent results on the synthesis of novel dinuclear N-heterocyclic dicarbene gold(I) and gold(III) complexes, which are characterised by a dimeric structure with two dicarbene ligands bridging two metal centers.



The stability in solution of the various gold(III) complexes towards reductive elimination of Br_2 as well as towards structural rearrangement mostly depends on the flexibility of the bridging group connecting the two carbene units. Single crystals X-ray analysis indeed shows that this synthetic strategy affords dinuclear and polymeric bis-dicarbene Au(III)-Au(III), dinuclear mono-dicarbene Au(III)-Au(III), and, most notably, dinuclear bis-dicarbene Au(III)-Au(I) mixed valence complexes [3].

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INO-PO-48 Chain-Growth Versus Step-Growth: the Case of the Suzuki–Heck Polymerization between Fluorenyldibromides and Potassium Vinyl Trifluoroborate

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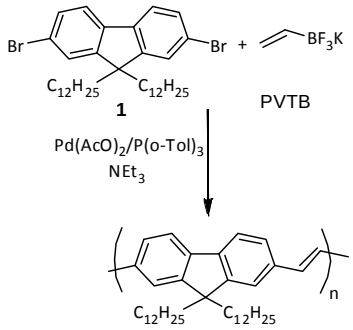
The mechanism of the Pd-catalysed Suzuki-Heck (*SuHe*) polymerization of 2,7-dibromo-9,9-di(*n*-dodecyl)fluorene (**1**) with potassium vinyltrifluoroborate (PVTB) for the synthesis of poly(fluorenylene-vinylene)s (PFVs) has been investigated. It was established that, in a first stage, a palladium catalyzed chain-growth AA/B(C)-type polycondensation occurs, as evidenced by the linear plot of the molecular weights of the forming polymer *vs* conversion. The chain-growth stage takes place until consumption of **1** and envisages the alternate addition of PVTB (by a Suzuki step) and **1** (by a Heck step) to the growing chain. Such alternate addition seems to proceeds via a peculiar catalyst transfer during which the metal is constantly bound to the growing chain and is corroborated by MALDI end group analysis. The second stage takes place by prolonging the reaction time after consumption of **1** and leads to the final polymer, that is formed by step-growth condensation of the fragments generated in the first stage (see Figure 1). With this mechanism operative, the molecular weights of the final PFVs depend on the PVTB/**1** feed ratio. Thus, using a PVTB/**1** molar ratio of 1.1 the final PFV was characterized by a M_n of 39600 Da whereas, using a PVTB/**1** molar ratio of 2.0, the final PFV was characterized by a M_n of 13200 Da.



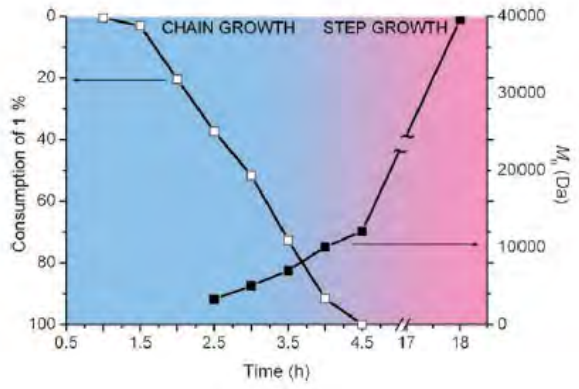


Figure 1. Consumption of **1** and M_n values of the polymer as functions of the reaction time for the *SuHe* polymerisation using a PVTB/**1** molar ratio of 1.1.

INO-PO-49 Functionalization of phosphazene systems with lipoic acid: synthesis, characterization and application.

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Phosphazenes are inorgano-organic materials with the general structure formed of -P=N- units, that may be cyclic or polymeric in nature. These materials showed both high synthetic versatility and good functionalization possibilities. Substituent groups used to prepare new types of cyclophosphazenes are mostly aliphatic and aromatic alcohols or amines commercially available in high quantities and low prices. [1] In our laboratories the synthesis of the 2,2-bis(4-oxazolinophenoxy)-4,4,6,6-bis[spyro(2',2"-dioxy-1',1"-biphenyl)]cyclotriphospha-zene (C-2-OXA) by reacting the corresponding cyclotriphosphazene containing two chlorine atoms, 2,2-dichloro-4,4,6,6-bis[spyro(2',2''-dioxy-1',1''-biphenyl)]cyclotriphosphazene (C-2-Cl), with 4-hydroxyphenyl-2-oxazoline has been previously optimized. [2] Here we describe the synthesis of a new type of cyclotriphosphazene obtained by reaction of C-2-OXA with lipoic acid (Figure 1). The study will be extended to hexa-substituted cyclo-phopshazene and to polymeric systems. Our purpose is to achieve not only a new material for metal coordination and abstraction but also new ligands for stabilization of metal nanoparticles. [3] The use of poly-functionalized ligands offers the advantage to achieve much stronger attachment to the nanoparticle surface to obtain more rigid structures susceptible of further modification.

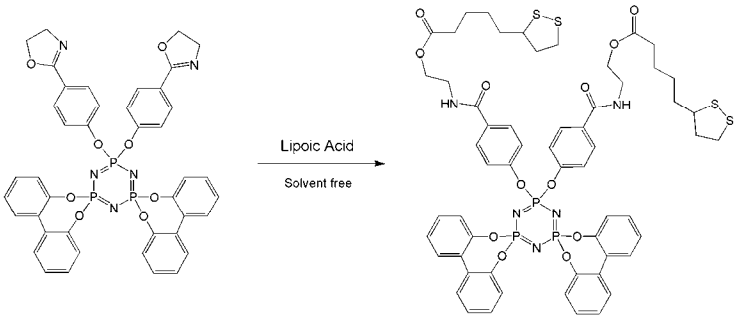

Figure 1. Synthesis of the lipoic acid derivative.

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INO-PO-50 Pt(II) complexes anchored on supramolecular aggregates labelled with Octreotide peptide.

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FDA recognized, more than thirty years ago, cis platinum based compounds for the treatment of a large number of solid tumors; anyway these drugs induce several side effects [1]. Many attempts have been carried out to reduce their toxicity and to prevent in-vivo inactivation. One of the most innovative approaches, is based on the encapsulation of the cytotoxic Pt(II) based drug in liposomes. A liposomal formulation may overcome platinum resistance by delivering a high dose of the drug at the tumor site. Stabilized PEGylated "*stealth*" liposomal formulations of cisplatinum have been developed in last decade [2]. These preparations exhibited an extended circulation time, increased anti-tumor efficacy and reduced toxicity compared to the free drug. In last years we developed peptide containing mixed aggregates able to deliver contrast agents and drugs to tumor cells overexpressing peptide receptors. The objective of present work is to formulate new aggregates able to carry new cytotoxic platinum complexes to cancer cells in a selective way. The new liposomal aggregates are obtained by co-assembling two amphiphilic monomers: a first monomer containing the octreotide bioactive peptide able to recognize somatostatin overexpressed receptors (SSTR2 and SSTR 5) and a hydrophobic tail based on two hydrocarbon chains with eighteen carbon atoms each (figure 1a). The second monomer contains the same lipophilic moiety and a lysine residue bearing on Nα and Nε amino functions an N-ethylglycine platinum complex and a PEG 1500 chain (figure 1b). The aggregates were characterized by dynamic light scattering (DLS) and SANS measurements. Both techniques indicate the presence of liposome.

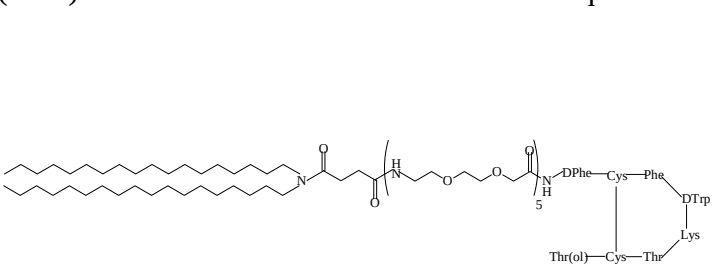

Figure 1a

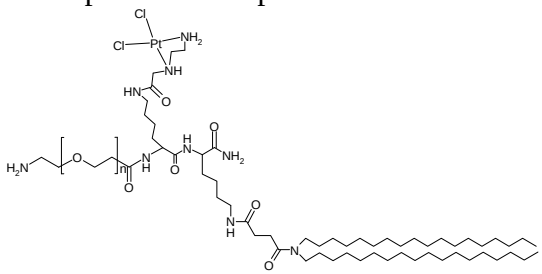

Figure 1b

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INO-PO-51 Mechanistic Study of Molecular Olefin Polymerization Catalysts: an Integrated Conventional and High Throughput Experimentation Approach

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Molecular catalysts for olefin polymerization are generally considered to be more easily amenable to mechanistic studies than heterogeneous ones, due to the well-defined structure of the precursors and a so-called 'single-site' nature [1]. This notwithstanding, discovering or even optimizing a catalyst by design is still a dream, because the number of physical and chemical variables which altogether determine catalytic behavior is simply too high. In fact, an initial phase of trial-and-error is still necessary, particularly in case of complex processes such as copolymerizations. In such a phase, the use of High Throughput Experimentation (HTE) tools and methods can be decisive for success [2].
In the present poster, we will explain how the integration of HTE with classical mechanistic methods can speed up the optimization of a new class of molecular catalysts for the industrial production of ethylene/propylene/diene (EPDM) terpolymers [3] by means of a high temperature solution process. Catalysts suited to this application must fulfill an impressive list of requisites, such as high thermal stability and polymer molecular weight capability, adequate copolymerization statistics, ability to incorporate the diene, etc.
In our laboratory, we operate since 2006 state-of-the-art HTE platforms for catalyst preparation and screening (*FreeSlate Core Module* and *FreeSlate PPR48*, respectively), housed into high performance glove-boxes [4]. Herein we will introduce an experimental HTE protocol for the fast generation of a structure/properties correlation database, that can be used as the starting point for the molecular kinetic modeling. The first conclusions of the mechanistic study of the aforementioned catalysts will be discussed as well.

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INO-PO-52 Which physico-chemical properties may be involved in silica pathogenicity?

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It is well known that occupational exposure to some crystalline silica polymorphs causes health damage. [1] In particular silicosis, the most ancient occupational disease, requires a close attention because of their invalidating consequences for a large number of workers and for a great number of benefits paid by the Italian government agency for the insurance against work-related injuries (INAIL).
In that regard, INAIL (Piedmont division) has funded a Ph. D fellowship in order to evaluate the number of cases of silicosis and lung cancer in Piedmont Region associated to the exposure to crystalline silica; to identify the most hazardous production divisions and to evaluate the physico-chemical properties of the silica dusts involved in the mechanism of pathogenicity. 444 cases of silicosis distributed in the Piedmont Region have been chosen and analyzed in detail. The analysis showed that 43% of the cases occurred in metallurgical activities, 26% to mineral processing, 15% to construction and 10% in other activities. Among all, 24 cases are associated with lung cancer. On the basis of the results obtained different samples selected from the most hazardous productive divisions and their physico-chemical properties wereinvestigated by means of different techniques including crystallinity (XRD), elemental analysis (XRF), micromorphology and particle size (SEM) were carried out for each sample. All samples were also tested for their potential to generate free radicals ($HO^{\bullet}$ and $COO^{\bullet -}$) (EPR/spin trapping) and for their surface charge. All samples contain quartz mixed to other crystalline phases, probably due to the presence of impurities, as shown by elemental analysis. All samples have a morphology and particle size typical of ground quartz and show a remarkable activity in free radical generation. The metallurgic division shows the highest cases of silicosis and their samples are the most reactive in the generation of free radical conferming a possible role of particle-free radical generation in the pathogenicity of crystalline silica. Further cellular studies will be required to support this hypothesis.

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INO-PO-53 Properties in solid and solution and cytoxicity of new thioureas palladium(II) complexes

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A new series of palladium(II) complexes of the type $[Pd(N\text{-}N)(tu)_2]Cl_2$ (N-N = 2,2'-dipyridyle or 1,10-phenanthroline; tu = thiourea, Et_2-tu, *n*-Bu_2-tu, *p*-tolyl-tu, Ph_2-tu) have been synthesized and characterized by elemental analysis and ^1H and ^{13}C NMR. $[Pd(phen)(tu)_2]Cl_2$ and $[Pd(phen)(Et_2\text{-}tu)_2]Cl_2$ have been also characterized in solid by X-ray analysis. This latter has shown that the coordination geometry of Pd(II) is perfectly planar and that distances and bond angles of the cationic fragment are in line with the corresponding structural parameters reported for analogous compounds. For both complexes, one of the two chlorides forms a strong interaction with two hydrogen atoms bound to nitrogen of the thioureas and the metal atom [1].

All the complexes are fairly soluble both in aqueous and in poor polar solvents. Their solutions in water are acidic and pH depends on the nature both of the thiourea and the bidentate ligand. The substances are very inert in solution. In particular, the electronic spectra of all the complexes, at fixed pH, do not vary in time for over a week, while they change with pH. Changes are fast and reversible, unless the pH is raised over about ten. Under these experimental conditions, a brown substance precipitates which in time turns black and becomes almost insoluble in any solvent.

The complexes with 2,2'-dipyridyle interact non-covalently with CT DNA, probably by intercalation [2]. When mixed with DNA, the analogous substrates with 1,10-phenantroline lead instead to precipitation of biopolimer fibres.

The complexes have been tested for in vitro cytotoxicity using cell line pneumocytes A549. Most of the complexes behave as cytotoxic agents comparable or stronger than cisplatin. Complexes with 2-2'-dipyridyle are less active than the analogous substrate with 1,10-phenantroline.

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INO-PO-54 New Phosphido Pincer Yttrium and Zinc Complexes as Efficient Catalysts for Ring Opening Polymerization and Copolymerization of Cyclic Esters

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Aliphatic polyesters, such as poly(lactide), poly(-caprolactone) and their copolymers find a wide range of practical applications, from packaging[1] to more sophisticated biomedical devices.[2] The most convenient route to obtain polyesters with designed macromolecular architecture and controlled properties is the ring opening polymerization (ROP) of heterocyclic monomers initiated by metal complexes. In this context, rare-earth and zinc complexes are catalysts of particular interest because of their low toxicity, low cost, high reactivity and good control.[3-4]

Recently our group explored the use of tridentate phosphido-diphosphine ligands [(o-$C_6H_4PR_2)_2PH$; R = Ph or iPr] for the synthesis of new Groups 3 and 10 metal complexes (Figure 1) and their application as initiators for the ring opening polymerization and copolymerization of lactide and -caprolactone.

The yttrium complexes revealed to be very effective initiators for the ROP of -caprolactone and L-lactide under mild polymerization conditions showing activities among the highest ever reported in literature.[5] Immortal and living reactions were also feasible in presence of alcohol as chain transfer agent.[6] The zinc complexes showed moderate activities towards both monomers but uncommon abilities to copolymerize them to produce copolymers that were shown to possess monomer contents which correlated well with their composition in the monomer feed.

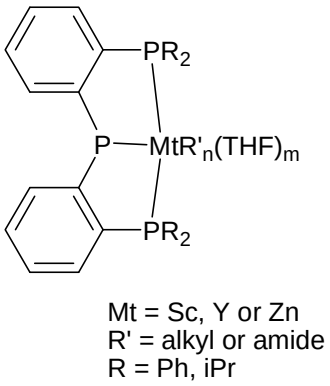

Figure 1

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INO-PO-55 Ruthenium complexes: versatility in supramolecular chemistry

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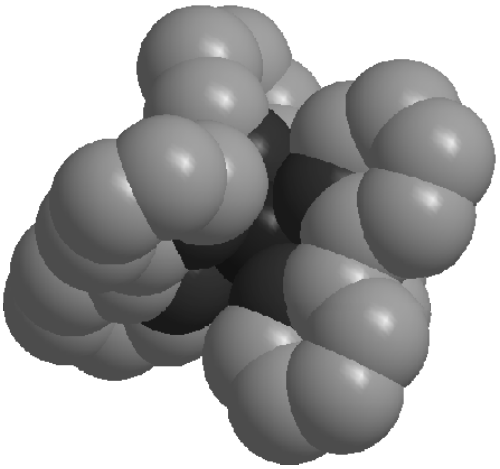
The photochemistry of ruthenium complexes has undergone an impressive growth in the last few decades.[1] Mostly in the last 15 years, Ru(II) polypyridine complexes have also contributed highly to the development of supramolecular photochemistry, and in particular to its aspects related to photoinduced electron and energy transfer processes within multicomponent (supramolecular) assemblies, including luminescent polynuclear metal complexes, light-active dendrimers, artificial light-harvesting antennae, photoinduced charge-separation devices, luminescent sensors, and light-powered molecular machines.



The assembly/disassembly of the luminescent dendritic hosts and the luminescent metal complex $Ru(bpy)(CN)4]^{2-}$,[2] photophysics of Ru^{2+} complexes containing terpyridine ligands appended with terthiophene units[3] and $[Ru(bpy)3]^{2+}$ as a 4-to-2 encoder and 2-to-4 decoder for molecular logic,[4] are three examples studied in our lab that demonstrate the versatility of these "old and well know" complexes in supramolecular chemistry.

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INO-PO-56 New coordination compounds containing nitrogen-rich ligands: synthesis, photophysics and electrochemistry

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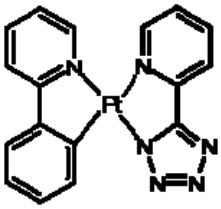
Tetrazolates, $[R\text{-}CN_4]^-$, were reported as excellent ligands for the construction of highly electrochemiluminescent Ru(II)-polypyridyl complexes and intensely emitting Ir(III)-cyclometalates.[1,2,3,4]
In particular, neutral Ir(III)-tetrazolate complexes have been used to fabricate a series of highly efficient OLED-type light emitting devices which displayed tunable emission colour as the consequence of slight modifications of the tetrazolate ligand structure.[5]. These promising results have driven our effort to the preparation of some new neutral Pt(II)- and Re(I)-tetrazolate complexes in order to construct new OLED type devices.

The research activity was also extended to the syntheses of eterobimetallic species; Ir(III)-Ru(II) and Ir(III)-Re(I), in wich the bridging tetrazolate ligand plays a key role in a energy transfer process. In addition, this class of ligands is also employed for the preparation of homo- and heteroleptic Cu(I)-tetrazolate compounds as new luminescent emitters for LEEC type devices.

The synthetic procedure, the photophysical properties together with the opto-electronic performances of all the new tetrazolate-based complexes will be discussed in detail.



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INO-PO-57 A RATIOMETRIC NANOSENSOR BASED ON FLUORESCENCE ANISOTROPY

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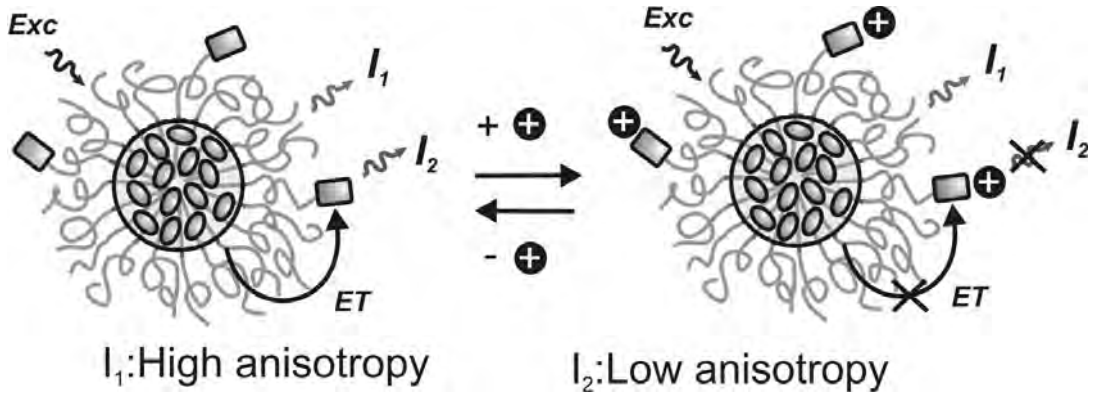
Silica Core-Surfactant shell nanoparticles (SCSS NPs) are versatile and effective platforms for the design of molecular based luminescent materials for energy conversion, imaging and diagnostics, signal processing and sensors.[1] The integration of a simple ON-OFF pH sensor (fluorescein) in SCSS NPs allows to achieve a very sophisticated ratiometric nanosensor (NS) based on dual detection of fluorescence anisotropy. In the NS a silica core, covalently doped with coumarine, behaves as an antenna system which transfers the excitation energy to the fluorescein molecules linked to the external surfactant chains. Energy transfer is not complete and the residual coumarin fluorescence (signal I_1) presents very high anisotropy since the rotational mobility of the molecules in the silica matrix is very low. The anisotropy of the sensitized fluorescence of the fluorescein, on the contrary, is vey low since the ET process causes depolarization (signal I_2). Protonation changes completely the photophysical properties of the fluorescein which, in the protonated form, is no more suitable to behave as an acceptor in the ET process; moreover its quantum yield is strongly reduced. As a consequence, protonation leads to a decrease of the fluorescence of fluorescein an to an increase of the signal of coumarin. In this modality the system hence behaves as a traditional ratiometric fluorescence sensor. As far as fluorescence anisotropy is concerned, its value in the 450-500 nm region (where emission is due only to coumarin: signal I_1) is independent on the pH. In the 500-600 nm region, on the other, hand fluorescence is the combination of I_1 and I_2 and the anisotropy is pH dependent. Fluorescence anisotropy at 480 nm can be hence used as a reference signal and the value at 520 nm analysed to determine the pH. Thanks to the combination of fluorescence anisotropy and multiple detection the NS has several advantages with respect to traditional chemosensors especially as far as elimination of background fluorescence is concerned. Finally the synthetic approach is very versatile and almost any kind of molecular sensor can be integrated in the nanostructure.



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INO-PO-58 Synthesis and characterization of new Ir_4 carbonyl clusters - phosphane ligands complexes.

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The chemistry of $[Ir_4(CO)_{12}]$ and its phosphane substituted products has been widely investigated with particular attention to the substitution kinetics and ligands distribution about the metal cluster.[1]
The neutral tetrairidium cluster and its derivatives are studied as they can find applications in homogeneous or heterogeneous catalysis, particularly in water gas shift and hydrogenation reactions. [2]

We have recently explored the reactivity of $[Ir_4(CO)_{12}]$ and $[Ir_4X(CO)_{11}]^-$ (X=Br, I) towards different types of polyphosphanes. This approach allowed us to aggregate several metal carbonyl clusters in order to get coordination polymers as well as discrete materials. Moreover we are developing a "library" of compounds with a potential catalytic activity.

Syntheses, X-ray structures and characterization of some dimeric mono- or three-substituted Ir_4 phosphane derivatives are here reported (**Fig. 1**).

In some cases, solvothermal approach has been fundamental in order to obtain single crystals, as only microcrystalline powders were available by traditional methods.

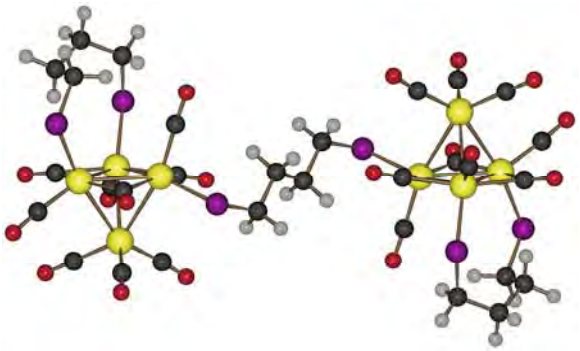

Fig. 1 X-ray structure of $[\{Ir_4(CO)_9(\mu\text{-dppbut})\}_2(dppbut)]$. Phenyls on P atoms are omitted for clarity.

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INO-PO-59 Bifunctional Ethacrynic Acid – Pt Conjugates: *In vitro* Treatment of Malignant Pleural Mesothelioma.

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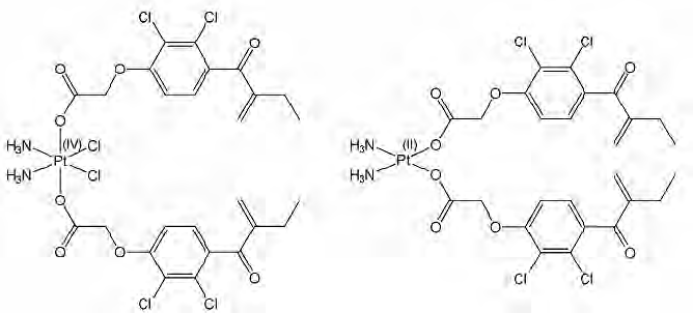
Malignant pleural mesothelioma (MPM) is a rare and aggressive asbestos-related cancer associated with poor prognosis. MPM cells are characterized by strong chemoresistance, often linked to the simultaneous induction of multiple antioxidant enzymes as the family of glutathione-S-transferase (GST).[1] Therefore, GST inhibition could be a adjuvant therapeutic strategy for MPM treated with Pt compounds. Ethacrynic acid (EA), a diuretic in clinical use, has been extensively tested and found to inhibit GST-family.[2]. In the present work, it has been realized the combination of EA and $[Pt(NH_3)_2]$ in a single, bi-functional cisplatin like compound, namely *cis*-[diamminodiethacrynatoplatinum(II)], **1**. Also its analogue Pt (IV)-based complex i.e. *cis*-[diamminodichloridodiethacrynatoplatinum (II)], **2** has been sinthesized. The cytotoxic effects of **1** and **2,** together with the combinations of cisplatin with two equivalent of EA have been tested on mesothelioma cell lines (having both epitelial or sarcomatous phenothype) and on a cisplatin-resistant sub-line. The biological results are reported.



2 **1**

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INO-PO-60 Polymorphism and unusual bonding properties of dimeric Pt^{II}-pyrophosphato coordination complexes

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Isostructural, 'clamshell'-like, neutral dimeric pyrophosphato complexes of general formula {[M(bipy)]$_2$(μ-P_2O_7)} [M= Pd^{II} (**1**) or Pt^{II} (**2**)] were synthesized and studied through single-crystal X-ray diffraction, IR, ^{31}P NMR spectroscopy, and MALDI-Tof mass spectrometry.[1] Both complexes crystallize in the monoclinic chiral space group *Cc* as hexahydrates, **1**·6H_2O (**1a**, yellow crystals) and **2**·6H_2O (**2a**, orange crystals), and exhibit a zig-zag chain-like supramolecular packing arrangement with short and long intra-/inter-molecular metal-metal distances. A second crystalline phase of the Pt species was also isolated, with formula **2**·3.5H_2O (**2b**, deep green crystals), characterized by a dimer-of-dimers (*pseudo*-tetramer) structural sub-motif. Green crystals of **2b** could be irreversibly converted to the orange form **2a** by exposure to air or water, without retention of crystallinity, while a partial, reversible crystal-to-crystal transformation occurred when **2a** was dried *in vacuo* (Figure 1). ^{31}P NMR spectra recorded for both **1** and **2** at various pHs revealed the occurrence of a fluxional protonated/deprotonated system in solution, which was interpreted as being comprised, in the protonated form, of $[HO{=}PO_3]^+$ (P_α) and $O{=}PO_3$ (P_β) pyrophosphate subunits. **1** and **2** exhibited two successive one-electron oxidations, mostly irreversible in nature; however, a dependence upon pH was observed for **1**, with oxidation only occurring in strongly basic conditions. Density functional theory and atoms in molecules analyses showed that a d^8-d^8 interaction is present in **1** and **2**. In both cases, the HOMO is a weakly antibonding dσ* orbital while the LUMO is a ligand-centered orbital. These unusual results suggest d^8-d^8 species can fall into two distinct categories. Category (i) comprises the majority of the known Pt^{II}, Rh^{I} and Ir^{I} dimeric species, in which the LUMO is a weakly metal-metal bonding orbital and the M-M bond order increases of 1 upon excitation. Category (ii) comprises species as all the known Pd^{II} dimers and compounds **1** and **2**, for which the LUMO is a ligand-centered orbital so that, upon excitation, the M-M bond order only increases of 0.5. To the best of our knowledge, **2** is the first example of a Pt^{II} system belonging to category (ii).

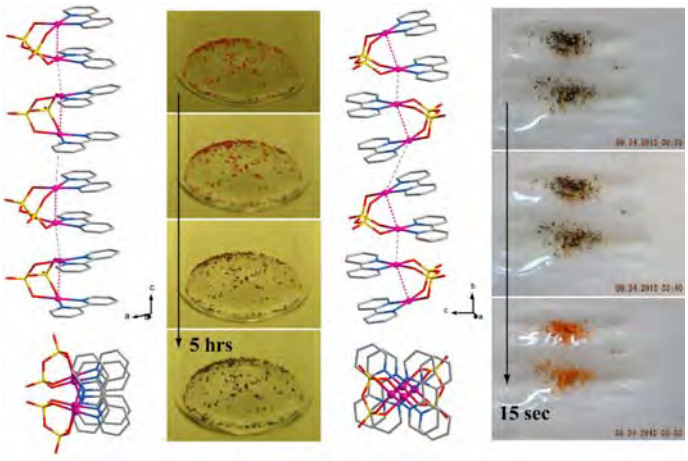

Figure 1.

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INO-PO-61 Ring Closing Metathesis Reactions Promoted by Ru-Catalysts with a *Syn* Substituted N-Heterocyclic Carbene Backbone

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Ruthenium-catalyzed olefin metathesis represents one of the most effective tools for constructing carbon-carbon double bond [1]. The development and improvement of metathesis transformations are essentially dependent on modification of catalyst structure.
Recently, we focused on the preparation of ruthenium complexes bearing *syn* and *anti* methyl substituents on the N-heterocyclic carbene (NHC) backbone and *o*-tolyl groups at the nitrogen atoms of the NHC ring [2]. These catalysts showed high efficiency in Ring Closing Metathesis (RCM) reactions and the *syn* isomers, in particular, revealed among the most active catalysts known in the RCM of hindered olefins up to now.

Herein we report the performances in RCM reactions of catalysts with a *syn* substituted NHC backbone presenting differently encumbered groups both at the *ortho*- position of the N-aryl rings (R in Fig. 1) and on the NHC backbone (R' in Fig. 1). The role of R and R' substituents on the catalytic behavior has been rationalized by investigating the RCM of different sterically hindered olefins with DFT calculations.

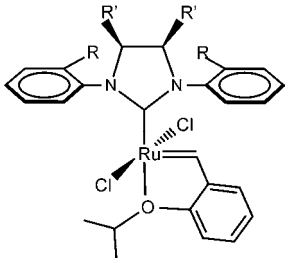

Figure 1.

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INO-PO-62 Copper(II) chiral complexes as components of cholesteric liquid crystals for optical applications

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It is known that chiral compounds mixed with nematic liquid crystals (LC), also commercially available such as TN0623, E7, etc., can generate a chiral liquid crystalline phase, called cholesteric (Ch) [1]. The phase arrangement is characterized by stacked nematic planes whose director gradually rotates on passing from one plane to the other, leading to macroscopic helicalization of the phase. Obviously two possible handednesses are expected, as a consequence of the use of *d* or *l* compounds. When a Ch LC is spread between two parallel surfaces, for example two glass slides, the helix axis spontaneously arranges perpendicularly to the surface of the so formed cell and the mixture generally appears uniformly distributed and optically homogeneous. An incident polychromatic unpolarized radiation can interact with the Ch phase giving rise to interference and reflection of a wavelength band $\Delta\lambda = p\Delta n$ (p=helical pitch, Δn=birefringence), so the mixture could appear colored by using radiation in the visible spectrum. Here we report on the use of copper(II) complexes with optically active (*d* and *l*) bidentate salicylaldiminate ligands, mixed with commercially available nematic LC. The main features of these copper(II) complexes are: the easy and inexpensive synthesis of both the *d* and *l* isomers; the marked thermal, chemical and especially photochemical stability (i.e., resistence to solar radiation); the very high compatibility with the host nematic LC (relevant for possible applications); high solubility in the LC phase also at lower temperatures; strong helicalization properties, that is a low weight percentage of chiral complex can produce a Ch phase with very short helical pitch. As an example, with about 10 wt% of our chiral complex a cholesteric phase with 450 nm helical pitch can be obtained, that is red light is reflected by the layer. The properties and potential applications of these compounds will be presented and discussed.

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INO-PO-63 New material from renewable resourses: Polysilicate-Lignin Composites

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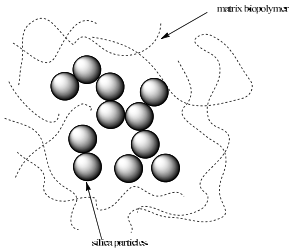
In the last decade Organic-Inorganic porous composite material -in nano or microscale- have been extensively studied since they combine advantages of inorganic materials (e.g. rigidity, thermal stability, inertiness) and the organic-polymeric phase (e.g. ductility and processability).

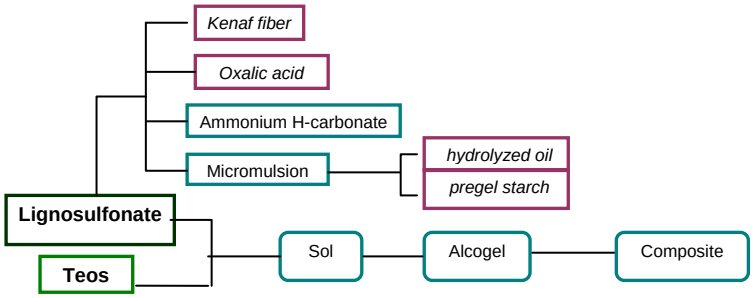
A defining feature of blended polymer composites, is that the dimension of the silica fillers[1] confers a dramatic increase in interfacial area, which may induce intrinsic crosslinking in the bulk. One of the most efficient procedure is colloidal sol-gel processes in the presence of a preformed polymer or monomers with tailored morfologies[2].

Herein we describe the formation of a new ecocompatible insulating material, adopting an hybrid procedure by using the **lignosulfonate,** as it is or subjected to thermal basic treatements (NaOH or NH_3), to provide partial depolymerisation.

The oligomers obtained can be dispersed, upon neutralization, in the **silica** colloidal mixture (TEOS aerogel) and furtherly polymerised in situ by adding a controlled amount of opportune **hydrophobising** additive (starch-oil biopolymer), **pH-moderator and expanding** reactants (NH_4HCO_3 and $H_2C_2O_4$). Ultimately, kenaf fibres (***Hibiscus cannabinus)*** were minced and finely dispersed as reinforcing agent.

Globally, the system is a natural rigid foam mainly composed by blended biopolymer/mesoporous silica. The porous microcomposite material obtained exhibits promising requirements of low density (0.5-0.2 g/cm^3) and low conductivity, adaptable for insulating uses in building application (bored-brick filler or small insulating panel). Preliminary results indicate the feasibility for a crosslinking process of lignin oligomeric chains with silanol and/or siloxane functionalities.





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INO-PO-64 Increasing the Maximum Nuclearity of Homometallic Rhodium Carbonyl Clusters by Interpenetration of Icosahedral Rh Moieties

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High-nuclearity transition-metal carbonyl clusters have always been regarded as chunks of metal lattices in a shell of carbonyl ligands. For instance, the homometallic Rh, Ir, Pt and bimetallic Ni-Pd and Ni-Pt carbonyl clusters systematically display close-packed metal frameworks. [1] In contrast, phosphine-substituted carbonyl clusters of Pd and Ni-Pd, as well as Au thiolate clusters, have a propensity for condensed, fused or interpenetrating centred icosahedral frameworks. [2,3]

We here report the isolation and structural characterization of the new $Rh_{26}(CO)_{29}(CH_3CN)_{11}$ and $[Rh_{33}(CO)_{47}]^{5-}$ clusters (see Figure 1). The latter raises the maximum nuclearity of Rh clusters, viz. $[Rh_{28}N_4(CO)_{41}H_x]^{4-}$. [4] Moreover, they both possess unprecedented frameworks based on interpenetrated Rh-centred icosahedral moieties. [5]

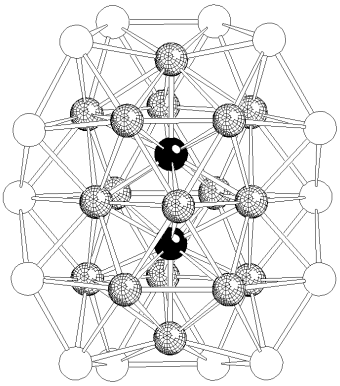

Figure 1. Metal skeleton of $[Rh_{33}(CO)_{47}]^{5-}$

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INO-PO-65 Copper(I) complexes and their application dye sensitized solar cells

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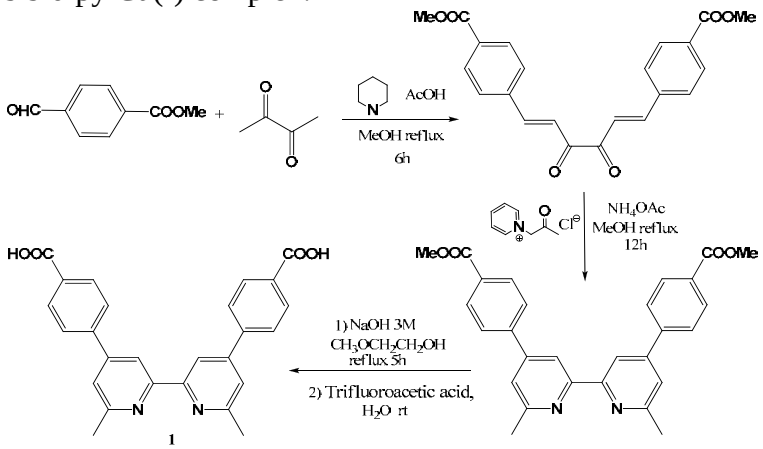
The easy prevision that in the near future the price of the energy derived from fossil fuels could be significantly increased and the well note limits in the applications of silicon-based photovoltaic (PV), get to the conclusion that the development of new, efficient and low-cost PV technologies will be more and more required. Up to day dye sensitized solar cells (DSSCs) represent one of the more attractive technological alternative to silicon-based PV. In this context, the best efficiency for the conversion of solar energy has been realized using a large number of Ru(II) polypyridyl complexes [1], however very good results were also obtained in the presence of metal-free organic dyes [2]. Recently also Cu(I) complexes have been proposed as effective sensitizers in DSSCs [3] even if their efficiency is much lower than that obtained with Ru-based devices, nevertheless copper still remains very interesting in this application because it can offer a considerable opportunity for reduction in cost.

Here we report the synthesis of suitable substituted 2,2'-dipyridil (Scheme 1) together with the corresponding bis-dipy Cu(I) complex.



Scheme 1

Several DSSCs devices have been prepared employing Cu(I) complexes with different protonation degree of the ligand **1**, and the results have been discussed as a function of the variation of the electrolyte.

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INO-PO-66 Reactivity of analogues of Zeise's anion with different ligands *trans* to the η^2-ethene

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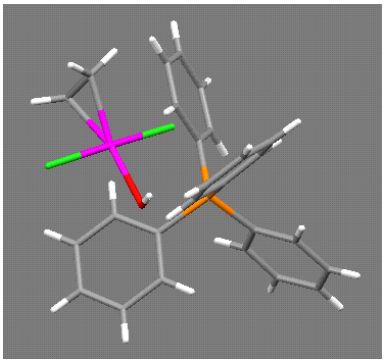
The Zeise's salt, $K[PtCl_3(\eta^2\text{-}C_2H_4)]$, is a paradigmatic example of the olefin to metal bond [1] and still an important starting material for the synthesis of platinum-based organometallic compounds. The great reactivity of Zeise's anion, essentially related to the lability of the chlorido ligand *trans* to the olefin [2], which can be easily substituted by any ligand having a reasonable affinity for platinum.

To get further insights in the reaction of nucleophilic substitution upon changing the ligand *trans* to the η^2-olefin, we tested the reactivity of three monoanionic platinum(II) substrates (Zeise's anion itself, $[PtCl_3(\eta^2\text{-}C_2H_4)]^-$, **1**, *trans*-$[PtCl_2(OH)(\eta^2\text{-}C_2H_4)]^-$, **2**, and *trans*-$[PtCl_2(\eta^1\text{-}CH_2NO_2)(\eta^2\text{-}C_2H_4)]^-$, **3**), towards aromatic imines with different steric requirements (pyridine, 4-methylpyridine, and 2,6-dimethylpyridine). We also performed a *X*-ray crystal structure characterization of the tetraphenylphosphonium salts of **2** (see Figure) and **3**. Our data have highlighted the nature of the Pt-Cl Pt-OH, and Pt-C σ bonds. Cl^- is the only one of the three *trans*-to-olefin ligands which can have a π-acceptor capacity towards the metal. The σ-donor capacity of the ligands can be ranked in the order: $CH_2NO_2^- >> Cl^- > OH^-$. The carbanion has an unexpectedly high weakening effect on the bond between platinum and the *trans*-olefin. As a consequence the olefin is displaced in preference not only by another olefin but also by σ-donors such as pyridines. In the light of the present results, the series ranking the *trans*-effect, which were set up in the 1980's [3], needs to be reconsidered in view of the importance for synthetic chemistry of *trans*-directing ligands.



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INO-PO-67 Reactivity behaviour of a Manganese(V)–Oxo Porphyrin Complex

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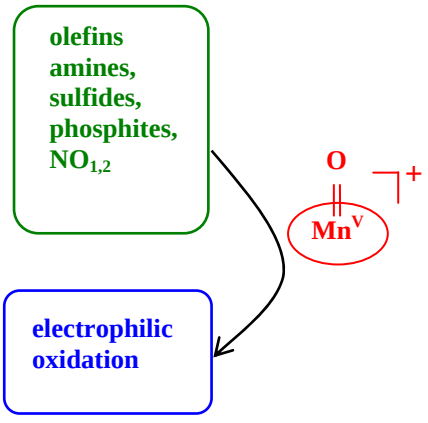
Among biomimetic oxidants developed to disclose the mechanistic routes operative in several metal catalyzed biological and industrial processes, high-valent transition metal-oxo species have been investigated for their function as putative intermediates in mono-oxygenases biochemistry. Although endowed with high reactivity and versatility in various oxidation reactions, manganese(V)–oxo species have eluded detection until recently [1].
Because the nature of these catalysts are strongly affected by several factors, including the pH, the presence and the nature of a trans axial ligand, and the electron promotion energy of the oxidant, gas phase studies may represent a powerful tool to elucidate the complex role of environmental factors as distinct from the intrinsic features of these active species.
We have succeeded in accessing a genuine ligand-free Mn^{V}-oxo porphyrin ion, $[(TPFPP)Mn^{V}O]^{+}$ (TPFPP = 5,10,15,20-tetrakis(pentafluorophenyl)porphinato dianion), **1**, prepared in methanol solution by controlled treatment of $(TPFPP)Mn^{III}Cl$ with iodosylbenzene, gently transferred in the gas phase by electrospray ionization (ESI) and characterized by assay with Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry. The oxidation ability of **1** towards a range of different substrates, including olefins [2], amines, sulfides, phosphites and nitrogen oxides, has been obtained by the direct determination of reaction patterns and thermal rate constants.
The reaction pathways are initiated by electron transfer and yield products reflecting delivery of oxygen and hydrogen atom, besides hydride and electron transfer processes.
Valuable insight into fundamental properties such as the basicity and electron affinity of the ferryl,$(TPFPP)Fe^{IV}O$, versus the manganyl, $(TPFPP)Mn^{IV}O$, unit have been also gathered, which can help to elucidate and generalize reaction mechanisms in bioinorganic oxidations.



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INO-PO-68 Interactions of Cisplatin with Adenine and Guanine Nucleobases: a Spectroscopic-Mass Spectrometric study

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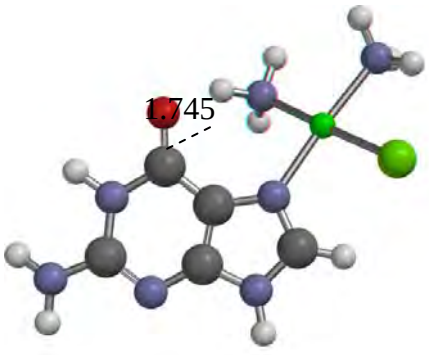
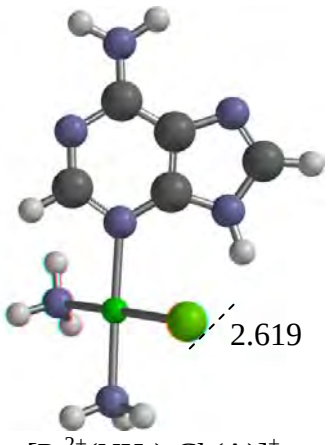
It is the aim of the present contribution to provide an accurate characterization of [cis-$Pt^{2+}(NH_3)_2Cl^-$(G)]$^+$ and [cis-[$Pt^{2+}(NH_3)_2Cl^-$(A)]$^+$, model of the monofunctional adduct between cisplatin and the nucleobases of DNA, using IR spectroscopy of ions directly performed in the cell of a mass spectrometrer. Whereas conventional absorption spectroscopy of gaseous ions is not feasible due to the typically low number density of the sample species, the IR features of a gaseous ion may be disclosed in the IR Multiphoton Dissociation (IRMPD) spectrum reporting the resonance enhanced photofragmentation process following multiple photon absorption in correspondence with the IR active modes of the sampled species. To this end a spectroscopic methodology is applied, based on the coupling of the radiation output of an IR free electron laser (FEL) at the CLIO (Centre Laser Infrarouge d'Orsay) European facility with a Paul-type ion trap mass spectrometer, exploiting the potential emerging from the combination of mass spectrometry with an IR FEL radiation source. The ions of interest have been formed in solution, transferred in gas phase by an ESI source, stored in an ion trap and submitted to IRMPD spectroscopy.
Quantum chemical calculations at B3LYP/6-311G(d,p) level of theory, using the LANL2DZ pseudo-potential basis set for Pt, yield the optimized geometries and IR spectra for the conceivable isomers of cis-[$Pt^{2+}(NH_3)_2Cl^-$(G)]$^+$ and cis-[$Pt^{2+}(NH_3)_2Cl^-$(A)]$^+$, whereby the cisplatin residue is attached to the N7, N1 and N3 positions of the guanine or adenine base.
Both the computational results and the IR characterization point to a covalent structure for the cis-[$Pt^{2+}(NH_3)_2Cl^-$(G)]$^+$ where Pt is bound to the N7 atom of guanine while in the cis-[$Pt^{2+}(NH_3)_2Cl^-$(A)]$^+$ complex Pt is bound to the N3 position of adenine.
To complete the study, measurements of CID (collision induced dissociation) breakdown curves for the selected ions have allowed to determine the apparent binding energy of the Pt complex with the nucleobases showing that the binding energy between Pt and G is greater than that between Pt and A.



[$Pt^{2+}(NH_3)_2Cl^-$(G)]$^+$



[$Pt^{2+}(NH_3)_2Cl^-$(A)]$^+$

INO-PO-69 New High-Nuclearity Ni-Pd Carbonyl Clusters: $[HNi_{30}Pd_5(CO)_{41}]^{5-}$ and $[Ni_{66}Pd_{10}(CO)_{69}]^{6-}$

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A re-investigation of the reaction of $[Ni_6(CO)_{12}]^{2-}$ with $[Pd(MeCN)_4]^{2+}$ in THF affords the new $[H_{6-n}Ni_{30}Pd_5(CO)_{41}]^{n-}$ (n=2-4) and $[Ni_{66}Pd_{10}(CO)_{69}]^{6-}$ clusters, whose metal frames are reported in Figures 1 and 2. The latter represents the highest-nuclearity homoleptic metal carbonyl anion so far reported and structurally characterized. The metal frame of the $[HNi_{30}Pd_5(CO)_{41}]^{5-}$ cluster is identical to that of the previously reported $[Cu_{5-x}Ni_{30+x}(CO)_{40}]^{5-}$ (x = 0,2) [1].

Previously known examples of Ni-Pd homoleptic carbonyl anions were species such as $[Ni_{16}Pd_{16}(CO)_{40}]^{4-}$, $[Ni_{26}Pd_{20}(CO)_{54}]^{6-}$ [2] and $[Ni_{36}Pd_8(CO)_{48}]$6- [3] which were obtained by reaction of $[Ni_6(CO)_{12}]^{2-}$ and $PdCl_2$ or $[PdCl_4]^{2-}$.

The reaction pathway that occurs in solution between Ni and Pd is proved to be rather complex: by changing even one of the boundary conditions (reagents, solvent, reactant molar ratios, temperature, reaction time) the nature of the products may be profoundly influenced.

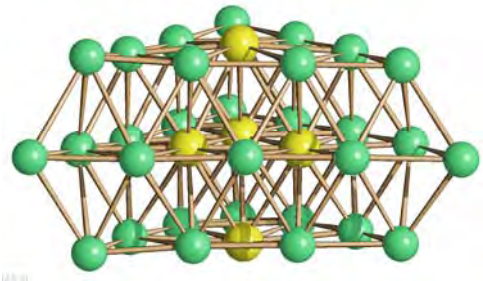

Figure 1
Metal frame of the $[HNi_{30}Pd_5(CO)_{41}]^{5-}$

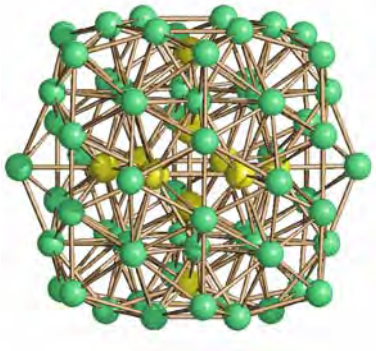

Figure 2
Metal frame of the $[Ni_{66}Pd_{10}(CO)_{69}]^{6-}$

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INO-PO-70 Vibrational behavior , microstructure and morphology of Zinc Ferrite obtained with differing fuels

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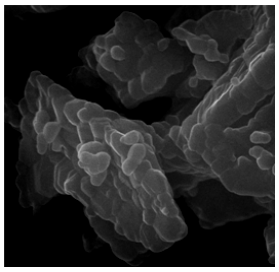
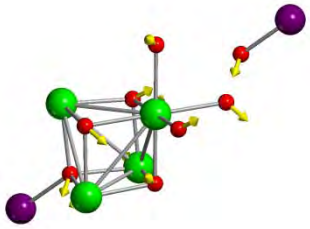
Zinc Ferrite (ZF) is an important oxidic material due to its versatile magnetic and electric properties, that finds wide applications in the field of gas sensors, contrast agents, magnetic materials, photocatalist, etc. A synthetic procedure which permits a fine control of purity and crystallinity of nanoparticles is sol-gel autocombustion method. Many fuels have been explored and their influence on the structure and properties of the spinel-type material has been studied.
In this communication we report the vibrational results of ZF samples obtained by sol-gel autocombustion method using the following fuel agents: citric acid, tartaric acid, urea, glycine, white egg, glucose. Infrared (in the MIR and FIR region) and Raman spectra of samples have been recorded and a complete assignment has been proposed, with particular attention to the spectral behaviour of the simultaneous presence of normal and inverse spinel structures. A fine evaluation of the effect of differing occupation of the A and B sites of the spinel towards vibrational pattern has been explored by means of a computational modelling in the crystalline state and with a normal coordinate analysis of the crystal structure. A microstructure and morphology comparative study was performed by means of SEM analysis.



SEM picture of ZF obtained with citric acid



A vibrational mode of octahedral B site of ZF

Acknowledgements : The authors T.Slatineanu and V.Nica thank for the financial support from the European Social Fund in Romania, under the responsibility of the Managing Authority for the Sectoral Operational Programme for Human Resources Development 2007-2013 [grant POSDRU/88/1.5/S/47646] and [grant POSDRU/89/1.5/S/49944], respectively.

INO-PO-71 A Report on the Potentialities of Tetrakis(thiadiazole)porphyrazines as Photosensitizers: Singlet Oxygen Production and Liposomal Incorporation

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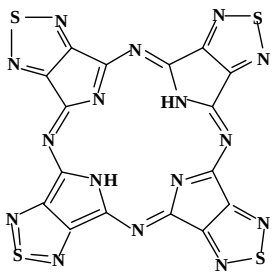
The work on the series of tetrakis(thiadiazole)porphyrazines of general formula [TTDPzM] with M = $2H^{I}$ (see Figure), $Mg^{II}(H_2O)$, Zn^{II}, Cu^{II}, Cd^{II}, $Al^{III}X$, $Ga^{III}X$ and X = OH, Cl, prepared and deeply studied by our group in terms of molecular and electronic structure and physicochemical behaviour, was fairly recently summarized [1]. Moreover, the redox properties of the species [TTDPzM] (M = $2H^{I}$, $Mg^{II}(H_2O)$, Cu^{II}, Zn^{II}) indicated that stepwise reversible or quasi-reversible one-electron reductions lead to the formation of the corresponding $[TTDPzM]^{n-}$ (n = 1÷4) and a detailed DFT/TDDFT theoretical investigation allowed clarification of the electronic structure of all the neutral [2a] and singly one-electron reduced species [2b]. The electrochemical data prove that the all series of compounds behave as highly electron-deficient macrocycles when comparison is made with the behaviour of the related phthalocyanine analogs.



Porphyrins, as well as their azaanalogs phthalocyanines and porphyrazines, are presently intensively investigated as photosensitizers for the generation of singlet oxygen, $^1O_2$, the highly cytotoxic agent in Photodynamic Therapy (PDT). This research field has become in recent years one of the most actively studied by our group [3]. The present contribution will report on the photosensiting properties for the generation of $^1O_2$ of the above series of [TTDPzM] compounds in dimethylformamide solution. Data, showing high photoactivity, will be presented in comparison with similar results for related phthalocyanine and porphyrazine macrocycles. The experimental work, involving partly innovative aspects, has been extended to test the possibility of incorporating the very active Zn^{II} complex into liposome vesicles. The aim is to overcome the insolubility in aqueous media of all these materials with the target of possible clinical applications.

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INO-PO-72 General Properties and Photoactivity of Porphyrazine Macrocycles with Different Degree of π-Electron Delocalization

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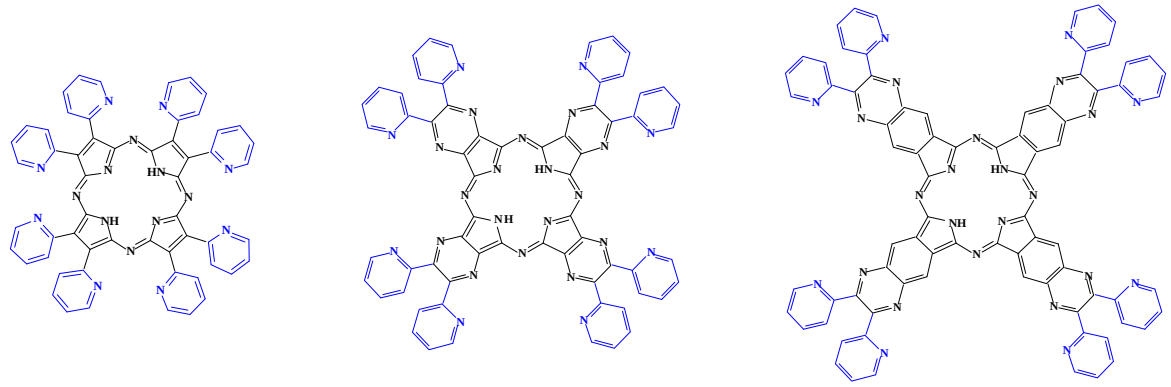
Work in our group was directed to the synthesis and characterization of novel classes of porphyrazine compounds; among them, the pyrazinoporphyrazine macrocycles having formula [Py_8TPyzPzM] with M = $2H^I$ (Figure 1B) and bivalent first transition series and non transition series metal ions were deeply investigated. The presence of external electron-withdrawing dipyridinopyrazine fragments strongly influences the electronic structure of the compounds which behave as electron-deficient macrocycles.



A: [Py_8PzH_2] B: [$Py_8TPyzPzH_2$] C: [$Py_8QuinPzH_2$]

Figure 1

A parallel investigation has recently been started on two novel classes of octapyridinated porphyrazines of formulae [Py_8PzM] (Figure 1A: M = $2H^I$) and [Py_8QuinPzM] (Figure 1C: M = $2H^I$). The compounds [$Py_8PzMg(H_2O)$] and [Py_8QuinPzM] (M = $Mg^{II}(H_2O)$, Zn^{II}, Pd^{II}) have been prepared and their properties studied in the solid state and in solution. UV-visible spectra provide information as to the influence of the different degree of π-electron delocalization in the different types of macrocycles. Two aspects of interest presently under investigation are: a) the ability of the new compounds to act as photosensitizers for the generation of singlet oxygen, $^1O_2$, the cytotoxic agent active in photodynamic therapy (PDT); b) the skill of these macrocycles to generate multimetallic systems by exocyclic metal coordination, already evidenced for the macrocycles of Figure 1B [3, 5].

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INO-PO-73 Coupling of alkynes and bridging ligands in diiron complexes: new route for the formation of functionalized ferrocenes

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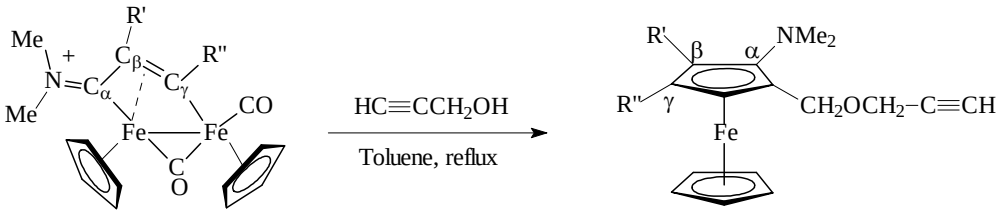
The coupling between small unsaturated molecules and bridging organic ligands in dinuclear complexes provides valuable pathways to the formation of C-C bonds. In particular, the assembling of alkynes with bridging aminocarbyne diiron complexes leads to the formation of μ-vinyliminium ligands, [1] which can be further functionalized, affording variously functionalized C_3 organic frames. [2] Recently we have reported on the possibility of involving the bridging C_3 ligands in cycloaddition reactions with alkynes, with the formation of variously functionalized ferrocenes and cyclohexadienyloxo complexes. [3]
Herein we report on the reactivity of μ-vinyliminium complexes towards propargyl alcohol.



The overall result of the reaction is the one-pot synthesis of a propargyl ether-functionalized ferrocene, in that one molecule of propargyl alcohol is involved in the [3+2] cycloaddition with the C_3 bridging ligand, while another molecule gives rise to the $–OCH_2C{\equiv}CH$ group, with loss of one molecule of water.

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INO-PO-74 Metal-Mediated Multi-Chromophore Assemblies: A Structural Overview

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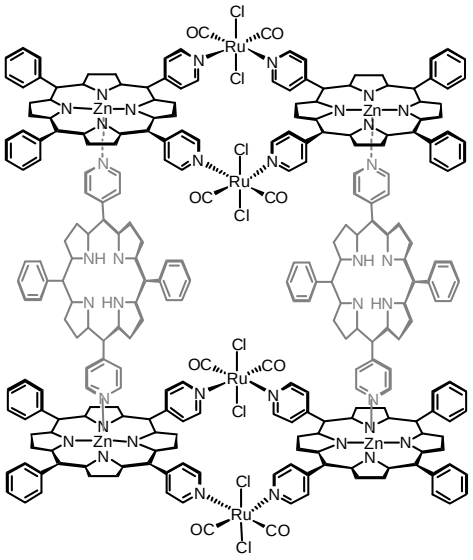
Porphyrins play a major role as active chromophores in artificial systems mimicking the natural photoinduced processes. The formation of coordination bonds between peripheral donor sites on the porphyrins and external metal fragments has proved to be an efficient alternative to covalent synthesis for the construction of multi-porphyrin assemblies, whose complexity and beauty gradually approach those of the multichromophore systems found in Nature.

In a modular approach, relatively simple metal-mediated porphyrin adducts, such as the zinc-porphyrin metallacycle, owing to their thermodynamic and kinetic stability, can be exploited as building blocks in the construction of higher order architectures. We reported that axial ligation of two of these metallacycles by two *trans* bispyridyl porphyrins (4'-*trans*DPyP) led to the formation of molecular box (Figure), both in solution and in the solid state [1, 2].



With the aim to synthesize molecular boxes with different dimensions and photophysical properties, the reactivity of the zinc-porphyrin metallacycle towards a series of other photoactive ditopic nitrogen ligands (such as perylenes) was investigated both in solution and in the solid state [1-3]. The photophysical properties of these novel assemblies have also been investigated [3, 4], but will not be discussed here. Examples in which the X-ray structural determination was essential to establish the real composition and geometry of these multi-chromophore assemblies are highlighted.

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INO-PO-75 Band Gap Engineering in TiO_2 by bulk and surface doping with p-block elements. A reliable perspective for visible light absorption.

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One of the limits for the applications of TiO_2 in photocatalytic systems for abatment of pollutants or in performing up-hill reactions such as hydrogen production by water photosplitting, is the wide band gap (3.2 eV) of this semiconducting oxide which imply the use of UV photons for the promotion of valence band electrons in the conduction band. The modification of the electronic structure of the solid in order to allow the use of visible light in its applications has therefore a paramount importance and two generations of chemically modified titanium dioxide nanomaterials are now available The first generation is that of TiO_2 containing transition metal ions and the second one is that based on doping by non metallic elements. The elements mainly employed in the doping are N, C, S, B and F. An intense debate has grown in the literature, aiming to identify the nature of the doping centers and the reason of the photoactivity in the visible of the doped solids. Some elements of confusion, however, are still present often caused by interpretations based on unreliable hypotheses or on weak experimental grounds.
Our group has attempted, since 2005, to contribute in understanding the role of non metal centres in TiO_2 bulk and at its surface. We have been focused, in particular, on those centers playing some role in visible light absorption[1-4]. This has been done trying to identify well defined centers and to distinguish them from byproducts of preparation reactions having often no role in interaction with light photons.
In this contribution the features of systems based on N doped, F doped, N-F and N-B co-doped TiO_2, prepared in our lab, will be discussed in the aim of elucidating the nature of the photoactive species, the chemical pathway for their formation and the electronic structure of the doped materials. Various experimental tools were employed for this purpose and the most persuasive results were obtained by coupling EPR spectroscopy with state-of-the-art theoretical calculations performed by the group of G. Pacchioni (University of Milano Bicocca).

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INO-PO-76 Catalysis by Group IV Amido-Pyridinate Complexes for the Efficient and Selective Olefin Upgrading; Beware of Metal Precursors!

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Much current interest in organometallic chemistry is linked to the academic and industrial quest for novel types of efficient and selective olefin oligomerization and polymerization catalysts. An improvement of their catalytic performance implies a precise control of the metal coordination sphere, commonly accomplished by a fine tuning of the steric and electronic properties of the ancillary ligands. Nitrogen donor ligands (imines, amides) have proven to be versatile components of bi- and polydentate ligands for the preparation of transition[1] and rare-earth[2] metal complexes in polymerization catalysis.

A recent work by our group on amino-pyridinate ligands in combination with Group IV transition metal precursors [$M^{IV}(NMe_2)_4$ and/or $M^{IV}(Bn)_4$; M = Zr, Hf] has shown a non-innocent role of the precursor species ultimately unveiling unexpected reactivity paths.[3]

Selected Zr^{IV}-amidopyridinate complexes from the same series have revealed outstanding polymerization activities in the production of poly(1-henene). An in-depth study on the nature of the catalytically active species, in combination with the characteristics of the polymers produced (molecular weights, tacticity and regioerror distribution in the polymer microstructure) have demonstrated a close dependence of the nature of the active species from the catalyst aging-time.[4] In the light of the well established efficiency of the Zr^{IV} and Hf^{IV} complexes for the production of specialty polyolefins[5], the result presented in this study provide a useful reference to gain further insight into the wealth chemistry of the nitrogen based early transition metal complexes.

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INO-PO-77 Novel Coinage Metal-NHCs Complexes Derived from Triazoles, Imidazoles and Related Chelating Systems.

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Coinage metal-NHCs are widely studied for their intriguing structural properties and numerous applications [1]. Ag(I)-NHCs are the most studied among coinage metal-NHCs due to their easy preparation via the Ag_2O route and because they are sources of other metal-NHCs through transmetallation. In addition, their different properties in bonding, structure and potential applications in medicine, nanomaterials, liquid crystals, and organic catalysis also contribute to the attraction of Ag(I)-NHCs. Recently we have explored the synthesis of pincer scorpionate type carbene ligands such as the bis(4-benzyl-1,2,4-triazol-4-ium-1-yl)dihydroborate, $\{[H_2B(BnTzH)_2]Br\}$, and related carbene-silver(I) and gold(I) complexes $\{Ag_2[H_2B(BnTz)_2]_2\}$ and $\{Au_2[H_2B(BnTz)_2]_2\}$ [2]. We have also studied trimetallic carbene complexes of general formula $\{Ag_3[HB(RIm)_3]_2\}Br$ (R = Bn, Mes and ^{t}Bu), which were successfully employed in the synthesis of related gold(I) complexes by transmetallation; the silver complexes also proved to be active catalysts in the Sonogashira reaction [3]. Analogous trinuclear copper(I) complexes with triscarbene ligands have been synthesized and proved to be efficient catalysts of Ullmann-type reactions as well as of the Sonogashira reaction. Moreover we have also reported the synthesis of hydrophilic bimetallic complexes of general formula $\{Na_2[H_2C(Tz^R)_2]_2Ag_2\}$ and $\{Na_2[H_2C(Im^R)_2]_2Ag_2\}$ (R = $PrSO_3$ or EtCOO) [4] by treatment, in degassed water solution, of the triazolium or imidazolium species with Ag_2O. As an extension of this research field, we have developed the chemistry of some new water soluble zwitterionic mono-NHC ligands, where imidazolium rings have two alkylsulfonate or alkylcarboxylate side arms. Here we present the synthesis and characterization of these novel hydrophilic carbene ligand precursors $\{HIm^{1R,3R}\}$ (R = $PrSO_3$ or CH_2COOEt) and the related silver(I) carbene complexes of general formula $\{(Im^{1R,3R})AgCl\}$. Gold(I) and copper(I) complexes have been prepared by transmetallation reactions.

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INO-PO-78 Ruthenium(II/III) Complexes of S-donor Ligands: Synthesis, Characterisation and *in vitro* Cytotoxic Activity toward Non-Small Cell Lung Cancer.

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In recent years ruthenium complexes have attracted much attention as promising antitumor and antimetastatic agents with potential uses as an alternative to cisplatin. To date, two ruthenium-based drugs, NAMI-A and KP1019, have reached human clinical testing. These complexes show low systemic toxicity, non cross-resistance and a different mechanism of action compared to platinum containing compounds.[1,2]

During the last decade, our research group has been designing a number of metal–dithiocarbamato complexes (*e.g.* Pt(II), Pd(II), Au(I), Au(III), Ru(III), Zn(II), Cu(II)) that have been tested, at least preliminarily, for their *in vitro* cytotoxic activity toward a panel of human tumor cell lines.[3] Among all, gold(III) complexes have shown outstanding *in vitro* and *in vivo* antitumour properties and reduced or no systemic and renal toxicity, compared to the reference drug.[4,5]

Here we present the syntheses of different Ru(II) and Ru(III) dithiocarbamato complexes: the diamagnetic neutral monomer $[Ru^{II}L_2(dmso)_2]$, the paramagnetic neutral $[Ru^{III}L_3]$ monomer, the antiferromagnetically coupled ionic α-$[Ru^{III}{}_2L_5]Cl$ and β-$[Ru^{III}{}_2L_5]Cl$ dinuclear species, where L = dimethyl- (DMDT) and pyrrolidine- (PDT) dithiocarbamate. All the obtained complexes were fully characterized by elemental analyses, NMR, FT-IR and UV-visible spectroscopies, and in some cases by X-ray analysis. The preliminary *in vitro* cytotoxicity assays on human tumor cells (H1975 non-small cell lung cancer (NSCLC) line) have shown significant antitumor activity of both the monomer and dinuclear Ru(III) complexes.

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INO-PO-79 Palladium nanoparticles synthesized by lignin: an efficient catalyst for C-C cross-coupling reactions

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Metal nanoparticles in water represent useful catalysts because they can operate in environmentally benign conditions. Also their catalytic efficiency is often higher since their high surface to volume ratio [1].

In the present contribution we report both the green synthesis of Pd nanoparticles using a renewable and abundant feedstock like lignin and their use as catalysts in C – C cross coupling reactions (Suzuki [2], Heck [3], Stille [4], Negishi [5]).

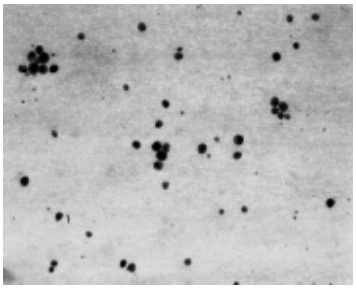

Figure 1: TEM immage of lignin stabilised Pd nanoparticles

G-Ph-I + **Ph-B(OH)$_2$** ⟶ **G-Ph-Ph**

Substrate	% Product yields
G = -H	80
G = -OH	100
G = -NH$_2$	80
G = -COOH	70

Experimental conditions: 0.5 mmol of aryl halide, 0.75 mmol of boronic acid, 1.75 mol of base (K_2CO_3), 5 mL of H_2O, 0.2 mL of nanoparticles solution (5.6 mM is the initial conc. of Pd^{II}), 12 hours of react. time and 80 °C of temp.

Two commercial lignins are able to reduce Pd^{II} in water solution forming stabilised Pd nanoparticles of about 19 nm (by TEM analysis) with a a face-centred cubic metal crystal structure (by XRD analysis). We show the results of Suzuki coupling while we will report in the communication of the congress the results about the Heck, Negishi and Stille reactions, all carried out in water under mild condition. No care to exclude air was necessary.

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Indice degli Autori

Chimica Organica

ORG-KN-01 A study of the intramolecular interactions of pyridine, thiophene, and furan with standard and perfluorinated aromatic systems in some [3,3]metapara-cyclophanes

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A series of [3,3]meta(heterocyclo)paracyclophanes containing pyridine, thiophene, and furan residues have been synthesized as model compounds for a study of the non-bonding interactions between aromatic and heteroaromatic systems. In these derivatives the heterocyclic rings have been connected through two CH_2SCH_2 bridges to the para positons of a standard benzene ring or of its tetrafluorosubstituted analog. These compounds show enough conformational flexibility to allow the easy flip of the heteroaromatic ring over the benzene platform, a motion that makes the two rings adopt parallel stacked, parallel offset, and hedge-to-face relative dispositions. However they also are rigid enough to feature energy barriers to the interconversion process sufficiently high to be experimentally determined.

The study of the static and dynamic behavior of these model systems has been carried out by a combination of variable temperature NMR and X-ray spectroscopy, and computational methods. It was discovered that the interaction between the heterocyclic and the aromatic rings strongly depends on steric factors and can only partially be rationalized on the basis of polar factors (the polar/π effect).

ORG-KN-02 Dye-Sensitized and Polymeric Bulk Heterojunction Solar Cells: New Generation Organic and Hybrid Materials and Devices

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The Sun is by far the most abundant and cheap source of energy to keep pace with the growing energy demand. Thus, capture of sunlight has attracted an increasing interest in the scientific community. New generation thin film organic and hybrid photovoltaic (PV) technologies - dye-sensitized (DSC) and polymeric bulk heterojunction solar cells (OPV) - own a great potential in terms of low cost-performance trade-off, future development, and scale up to market.
Here we review our activity over the past few years on new generation PV materials and devices. We will describe organic (multibranched polar dyes) and organometallic (polypyridine and cyclometallated complexes) DSC sensitizers, highlighting superior optical and photovoltaic properties,[1] and polymeric electrolytes for quasi-solid-state devices.[2] We have investigated a new family of heteroarylene-vinylene donor-acceptor low-bandgap semiconducting polymers, reaching optimal photophysical and electronic properties closely matching optimized materials-design rules for OPV.[3] Finally, we will present our activity in the fabrication of organic and hybrid PV devices in the recently established research center MIB-Solar, in close interaction with industry.[4]

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ORG-KN-03 Why not the real thing? Generating high-energy intermediates by photochemical means.

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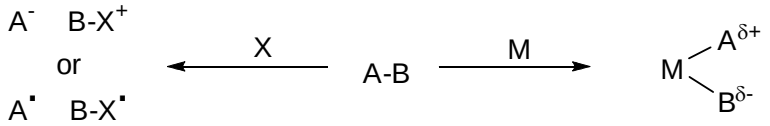
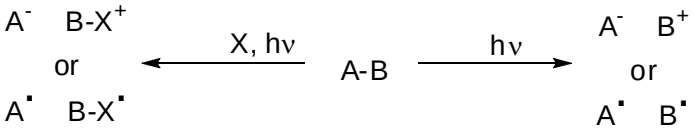
The key to most synthetic methods is the generation of a high energy intermediate, typically by homo/heterocleavage of a bond or its weakening, as is the case for the oxidative addition to metal ions.



This either introduces some limitation in the choice of the reagents and in the reaction conditions, or leads to a complexed or in some way stabilized intermediate. As an example, homolytic cleavage is limited to weak bonds, e.g. C-I bonds, and in the ensuing radical reaction a chain carrier is required. Likewise, a metal-complexed fragment may have some cationic character but is very far from a free cation.

In contrast, photochemical excitation or interaction with an excited catalyst via a non-chain process (stoichiometric in photons, although the catalyst is not consumed) exploits the large amount of energy of excited states for arriving at 'the real thing', e.g. free radicals or free ions. And this occurs under unparalleled mild and extremely versatile condtions.



In recent years we have explored two families of such reactions, involving respectively the heterolytic fragmentation of phenyl halides and esters and hydrogen transfer from aliphatic derivatives.

Some examples of the selective synthetic processes obtained and their rationalization based on kinetic data will be presented in order to define the scope and the peculiarity of the method that realizes the 'green' potential of photochemistry in synthesis.

ORG-KN-04 Nitro Compounds and One-Pot Processes: Useful Combination in Organic Synthesis

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The formation of new carbon-carbon and carbon-heteroatom bonds is the core of organic synthesis, and in this sense, the development of new methodologies, is an essential branch of this science. At the same time, particularly in the last years, there is a diffuse and general request to study new processes that are not only focused on the efficiency of the reaction, but also on their environmental impact. This aspect was rationalized with the "Twelve Principles of Green Chemistry", which are the generally accepted guideline to develop the new eco-sustainable processes [1].

In this context, the one-pot reactions well fit with the green chemistry principles. In fact, a reactant is subjected to successive chemical reactions in just one reactor, avoiding the tedious and expensive work-up and purification of the intermediates, thus saving resources and time [2].

Nitro compounds, thanks to their chemical reactivity, such as the possibility to generate stabilized carbanions under mild reaction conditions, the opportunity to convert the nitro group into other functionalities, or exploit its behavior as a leaving group, have been involved with success, as building blocks in a variety of one-pot processes. In particular we focused our attention to the synthesis of important homo-, heterocycles and other valuable fine chemicals [3].

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ORG-KN-05 Predicting NMR spectra of natural substances by DFT calculations as a tool for structure determination

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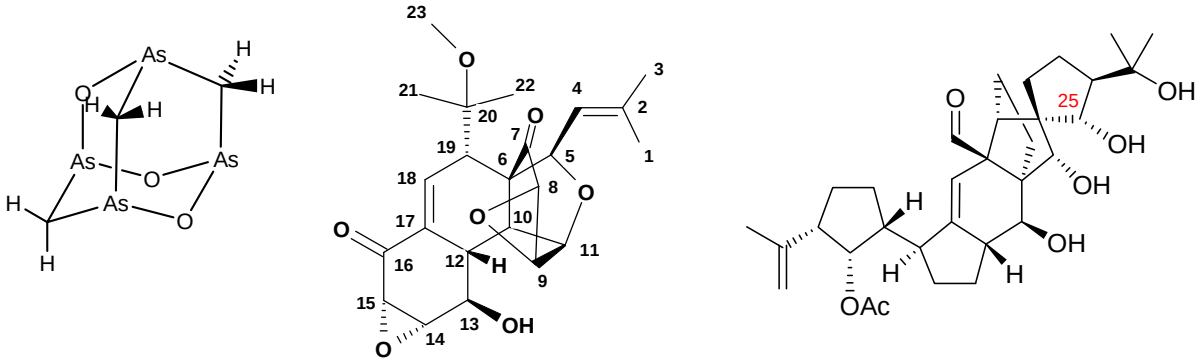
Natural sources supply a fascinating variety of molecules having intricate structures and unusual functionalities. NMR spectroscopy has become a staple methodology for the determination of such complex molecules; however, despite steady technical advancements, this information may not lead to an unambiguous molecular structure. As a result, it is not unusual to see "structure revisions" where a proposed molecular structure is challenged in view of more compelling arguments (often, total synthesis).[1] The conclusive proof of structure is commonly accepted to be the match between the NMR spectrum of the unknown species and of a species deriving from total synthesis (quite often, not a trivial task).

On the other hand, if the NMR spectrum of a molecule whose structure is certain were available, one could work on the problem backwards – from molecular structure to NMR spectrum rather than vice versa as is normally done, which requires *a priori* knowledge of the chemical shifts and coupling constants for all spins of interest.

Density-functional theory (DFT) methods have enabled such computations with great accuracy. Thus, the scope and application of DFT calculations will be presented in several case histories concerning natural substances,[2] including arsenicin A,[3] hexacyclinol [4] and vannusal B.[5]



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ORG-KN-06 L’eccellenza italiana nella produzione dei principi attivi farmaceutici

P. Allegrini

ORG-KN-07 TWENTY FIVE YEARS OF EXPERIENCE AND SUCCESS IN CHIRAL SEPARATION SCIENCE.

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Chiral molecules are currently at the forefront of strategies for the development of safer, more effective, drugs.
The enantiomers of chiral drugs show significant differences in their activity, pharmacokinetics, pharmacodynamics and potential adverse reactions. This in turn has led stereoselective chromatographic separations becoming an important technique in this area, so several Enantioselective HPLC methods (EHPLC) have been successfully developed in recent years.
Analytical techniques relying on chiral stationary phases (CSPs) are preferred as they offer specific advantages over indirect methods.
An overview is presented of the experimental results obtained by our group in the design, realization and applications of HPLC enantioselective stationary phases based on surface linked selectors.
Recent developments in this area relate to the preparation and applications of very small-particle (sub-2 μm) enantioselective packing materials incorporating the well known Welk-O1 selector (Ultra Fast-*subminute*-EUHPLC).
In addition to chiral phases with a "brush-type" architecture incorporating small to medium-sized selectors, chiral polymeric materials are extensively employed for the preparation of chiral stationary phases for HPLC applications.
A new type of HPLC chiral stationary phases has been realized by the covalent attachment of chiral polymers to mesoporous silica particles. The "*grafting-from approach"*, in which the polymerization process starts from the silica surface, was used to produce a thin, densely packed and ordered layer of chiral polymeric chains (Poly-Brush-DACH-ACR, P-CAP). [1]
A further class of innovative CSPs, incorporating highly preorganized, receptor-like, chiral macrocyclic selectors, was prepared by our group. These silica-bound selectors show unprecedented enantioselection for small peptidic compounds. These materials are well suited for the study of molecular recognition mechanism at receptorial level and featuring extreme enantioselectivity value.
Finally several successful applications of DHPLC in the study of stereodynamic process (enantiomerization, diastereomerization etc.) will be shown.

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ORG-KN-08 Sugars in Biomedicine: ideas, results and perspectives

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The structural feature of sugars: diversity, polyfunctionality and structural rigidity, make this class of compounds a unique instrument for nature and synthetic chemists. It is now well established that most biomolecular recognition phenomena involve carbohydrates, and disfunction of such processes often leads to relevant pathologies such as cancer.
Glycochemistry is therefore a field of wide interest in biomedicine and a big effort must be performed by chemists to explore new opportunities [1]. Beside the idea to generate agonists or antagonists of glycidic structures involved in pathological processes, sugars can be used as scaffolds to generate libraries of potential drugs, exploiting the diversity and structural rigidity, or can be incorporated in more complex bioactive structure in order to modulate the pharmacokinetic properties .
Furthermore, conjugation of sugars to materials and nanoparticles can provide them properties of impressive biomedidical interest.
Examples of the exploitation of sugars in biomedicine, such as the finding of a dansyl-C-glucoside preventing septic shock [2], the decoration of nanoparticles with glycofused polycyclic compounds for Alzheimer's disease therapy, the generation of glyco-decorated smart biomaterials for tissue engineering [3,4], will be presented end the future perspectives will be discussed.

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ORG-KN-09 A Few Good Reasons to Love the Chemistry of Natural Products

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Mother Nature still provides organic chemists with a multitude of attractive challenges stimulating different research activities related to the basic and applied sciences of natural products. In this talk the author shall give a brief account of his multidecennial scientific activity in the field. This comprises: the isolation and characterization of new compounds i) from plants collected in extra European countries (Ecuador, Cameroon, Kurdistan) ii) from Italian Basidiomycetes and iii) from insects; iv) the determination of the different biological properties of isolated compounds and their role in the chemical defence system of the producing organisms; v) the functional and structural modification of various active products; vi) the stereoselective total synthesis of monoterpenoids, iridoids, sesquiterpenes, triterpenes, alkaloids, prostaglandins, isoprostanoids, fragrance components. These synthetic activities enabled us to clarify some aspects of the relationship between structure and odour properties of important perfume components, as well as to determine the biological significance of metabolites formed by ROS oxidation of PUFAs occurring in plant tissues and human neuronal membranes. These compounds thus emerged as biomarkers and possible mediators of the so called "oxidative stress", to which severe human diseases are linked. From a stricter chemical point of view, new synthetic methods, based in the chemistry of Si, Pd, B, Re, and Au derivatives, as well as new examples and applications of the Meyer-Schuster rearrangement, and stereoselective biomimetic cyclization and Diels-Alder reactions, have been developed in these studies.

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ORG-KN-10 Mass Spectrometry and the Attractive World of Secondary Metabolism

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The chemistry of natural organic compounds has always elicited the interest of the researcher, and in the XIX century it was the necessary early base for the establishment of organic chemistry as a separate discipline. Nowadays many of the remarkable advances in this area rely upon specialized spectroscopic techniques which, besides being a sophisticated but relatively easy way for structure elucidation, also allow a deep insight into the most intriguing aspects of the metabolic processes. One of these is advanced mass spectrometry, in its more recently developed configurations like Electrospray Ionization (ESI) and Matrix Assisted Laser Desorption Ionization (MALDI). At the same time, also, very sensitive and selective extraction techniques like Solid-Phase Micro-Extraction (SPME), coupled with the long established GC-MS, are successfully exploited for the study of tiny quantities of secondary metabolites, like those present in tissue fragments and secreting glands of living, small organisms.

Some cases, which have engaged our research group as part of a long lasting interest in this field, will be addressed in the course of the lecture. One Dufour gland producing trial and sexual pheromones, directly resected from one ant [1], or also one leaf fragment from artemisinin-rich (antimalarian drug) *Artemisia annua* cultivars [2], once submitted to SPME-GC-MS released their volatile components giving information on their nature and activity, eventually. The study by ESI-MS of a new microperoxidase from an aquatic microorganism gave information on its oxido-reductive role [3]. Finally an ESI-MS and MALDI-MS approach to *in vitro* produced lignins [4] and melanins [5] were of paramount importance for further understanding the biosynthetic pathways involved in the production of these complex natural biopolymers.

[1] A. Di Tullio, F. De Angelis, S. Reale, D. A Grasso, C. Castracani, R. Visicchio, A. Mori, F. Le Moli *Rapid Comm. Mass Spectrom., 17,* **2003**, 2071-2074.
[2] S. Reale, P. Fasciani, L. Pace, F. De Angelis, G. Marcozzi *Rapid Comm. Mass Spectrom.,* **2011,** accepted for publication
[3] A. Di Tullio, L. Caputi, F. Malatesta, S.Reale, F. De Angelis *J. Mass Spectrom., 40,* **2005**, 325-330.
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ORG-OR-01 Oxazolidin-2-one Based Foldamers for the Formation of Supramolecular Materials

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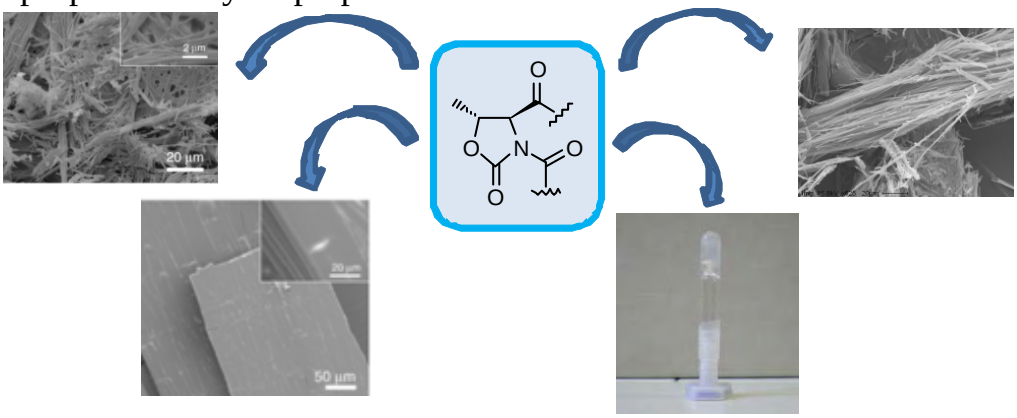
Foldamers are artificial molecules able to get organized in well defined secondary structures, such as helixes, β-sheets and turns. The essential requirement for an oligomer to be included in the foldamer family is to possess a well defined, repetitive secondary structure, imparted by conformational restrictions of the monomeric unit. These compounds may be composed of any kind of subunits, but most of them contain unusual amino acids and/or aromatic units.

We have recently studied the synthesis, the conformational analysis and the application as supramolecular materials of foldamers containing the 4-carboxy oxazolidin-2-one unit or related molecules, where an imido-type function is obtained by coupling the nitrogen of the heterocycle with the carboxylic acid moiety of the next unit. The imide group is characterized by a nitrogen atom connected to an endocyclic and an exocyclic carbonyl which tend to adopt always the *trans* conformation. As a consequence of this locally constrained disposition effect, these imide-type oligomers are forced to fold in ordered conformations, such as PPII helixes, β-band ribbon spirals, β-sheets and β- or γ-turns and a wide variety of unusual secondary structures are obtained from hybrid foldamers.

In the solid state, some of these compounds form supramolecular materials, such as fibers, layers and gels, that may be used for several applications. The synthetic approach is highly tunable with endless variations, so, simply by changing the design and the synthesis of the foldamer, a supramolecular material with the required properties may be prepared "on demand".



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[3] G. Angelici, G. Falini, H.-J. Hofmann, D. Huster, M. Monari, and C. Tomasini, *Chem. Eur. J*., **2009**, *15*, 8037.

[4] C. Tomasini, G. Angelici, and N. Castellucci, *Eur. J. Org. Chem.*, **2011**, in press.

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ORG-OR-02 Ionic Self Assembly in the Design of Fluorinated Ionic Liquid Crystals (ILCs).

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Ionic liquid crystals are a class of compounds containing anions and cations, that combine the properties of liquid crystals and ionic liquids[1].
In the conventional design of ionic liquid crystalline compounds, an ionic core is connected with mesogenic groups *via* chemical covalent bonding . Alternatively, in ionic compounds, strong electrostatic interactions between cation and anion can be used to build up liquid crystalline order at supramolecular level. This general approach, called ionic self-assembly (ISA), allows one to create ionic phases and mesophases with highly organized supramolecular order [2].
In this context, a new series of fluorinated ionic liquids (ILs) and ionic liquid crystals (ILCs) was obtained starting from perfluoro-alkylated carboxylic acids and 1,2,4-oxadiazolyl-pyridine units (Figure 1). Their thermotropic properties were investigated by combined differential scanning calorimetry and polarized optical microscopy.

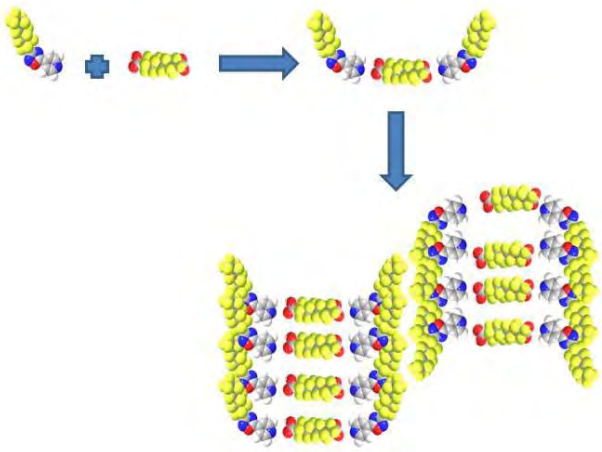

Figure 1.

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ORG-OR-03 Halogen Bonding: A new strategy for pharmaceutical co-crystals

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A large amount of pharmacologically interesting molecules has severe difficulties to become proper drugs because of their bad characteristics in terms of water solubility and/or industrial processability. This derives from both the intrinsic properties of the molecule (logP) and the characteristics of its crystal form (shape, moisture sensitivity, etc.). From the early 90's [1] the co-crystallization of an API (Active Pharmaceutical Ingredient) with an appropriate partner (called CCF - Co-Crystal Former) has represented an original way to overcome in many cases the undesired characteristics of the API itself.

Halogen bonding (XB) [2] is a non-covalent interaction that has proven to be very robust in the creation of several supramolecular architectures [3] and in principle can be successfully used in the design of API co-crystals. Many market drugs contain halogenated APIs (*i.e.* Figure 1), and the halogenated moieties can be exploited for the formation of halogen bonds with CCFs presenting lone-pair possessing residues. In this contribution we will present the first use of halogen bonding in the formation of co-crystals involving halogenated APIs.

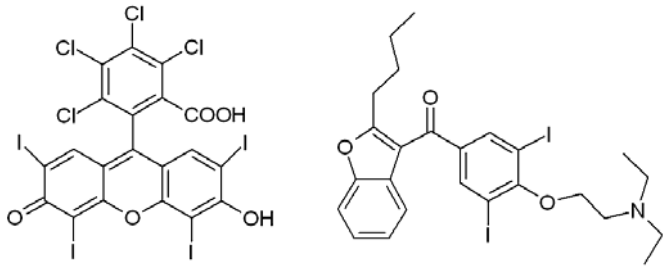

Figure 1: two examples of halogenated API: Rose bengal (left) and Amiodarone (right)

[1] J.A.Zerkowski, C.T.Seto, G.M.Whitesides., *J. Am. Chem. Soc*., **1992**, *114*, 5473.

[2] An IUPAC Task Group set up to examine the definition of halogen bonding has not yet reported, so that given here should be taken as temporary (see www.iupac.org/web/ins/2009-032-1-100 and www.halogenbonding.eu).

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ORG-OR-04 Targeting Medically Relevant Lectins with Multivalent Glycocalixarenes

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The involvement of carbohydrate-protein recognition processes in numerous pathological events make them an attractive target for the development of new therapeutic strategies. The efficiency of glycosides or mimics in the inhibition of lectin activity strongly depends not only on their proper structural features, but also on their exposition. A multivalent presentation can significantly improve their potency, as in fact often occurs at the biological level, and then help in obtaining new potential biologically active compounds.

For these reasons, since some years we are developing glycoclusters based on calixarenes functionalized with different carbohydrate units depending on the target lectin [1-3]. In particular we focused our attention and efforts towards medically relevant proteins such as plant toxins [2], bacterial lectins [1], human galectins [2,3]. Calixarenes of different sizes, conformational properties, valency and functionalized *via* chemical or chemo-enzymatic procedures with galactose, lactose, LacNAc units or oligosaccharides and mimics have shown their high efficiency and selectivity in the inhibition of different types of lectins.

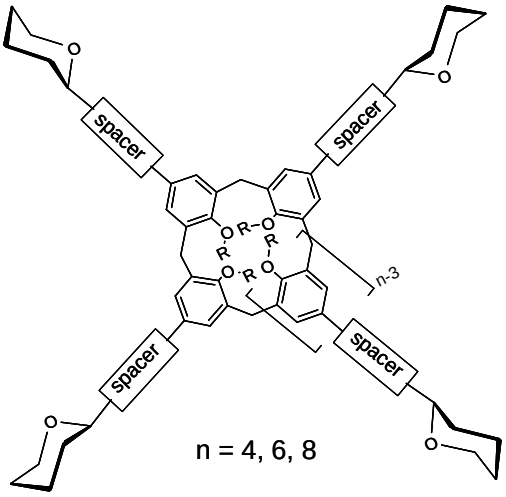

Figure. A general structure of glycocalix[n]arenes.

[1] D. Arosio, M. Fontanella, L. Baldini, L. Mauri, A. Bernardi, A. Casnati, F. Sansone, and R. Ungaro, *J. Am. Chem. Soc.*, *127*, **2005**, 3660.
[2] S. André, F. Sansone, H. Kaltner, A. Casnati, J. Kopitz, H.-J. Gabius, and R. Ungaro, *ChemBiochem*, *9*, **2008**, 1649.
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ORG-OR-05 Getting around counterion effects in the complexation of charged species

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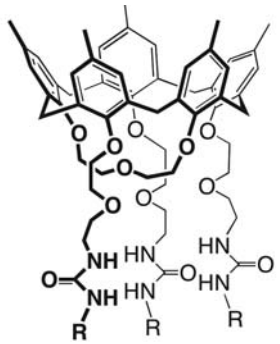
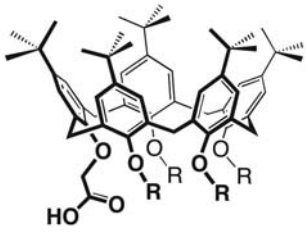
It is commonly accepted that binding of ionic species to neutral receptors is significantly affected by the nature of the counterion of the target charged guest. In low-polarity non-solvating media, saline substrates may tightly associate to form contact ion pairs. As a result, the efficiency is hampered by the reluctance of the target ion to dissociate from its counterion [1].

A first strategy to circumvent this drawback relies on the use of heteroditopic receptors. Calix[5]arene-crown-3 derivatives **1a**,**b**, endowed at their lower rim with alkyl- or arylureido pendant groups, are capable of recognizing (aryl)alkylammonium halides as receptor-separated ion pairs by binding the ammonium cation within the calixarene cavity and the halide anion within the cleft formed by the three urea groups [2].



1a R = *n*-Butyl;
1b R = 1-Naphthyl

An alternative approach takes advantage of ionizable calix[5]arenes (**2a**,**b**) that can selectively transfer protons to 'silent' (di)amines, turning them into active substrates devoid of competitive counterions. This recognition event ultimately yields internally ion-paired *endo*-cavity complexes that effectively harness ion pairing as a stabilizing interaction.



2a R = $(CH_2)_3CH(CH_3)_2$
2b R = $CH_2CO_2C(CH_3)_3$

[1] G. Cafeo, G. Gattuso, F.H. Kohnke, A. Notti, S. Occhipinti, S. Pappalardo, and M.F. Parisi, *Angew. Chem. Int. Ed.*, *41*, **2002**, 2122.

[2] C. Capici, R. De Zorzi, C. Gargiulli, G. Gattuso, S. Geremia, A. Notti, S. Pappalardo, M.F. Parisi, and F. Puntoriero, *Tetrahedron*, *66*, **2010**, 4987. G. Gattuso, C. Gargiulli, C. Liotta, A. Notti, M. F. Parisi, I. Pisagatti, and S. Pappalardo, *J. Org. Chem.*, *74*, **2009**, 4350.

ORG-OR-06 New hydroxyl protecting groups removable under SET conditions

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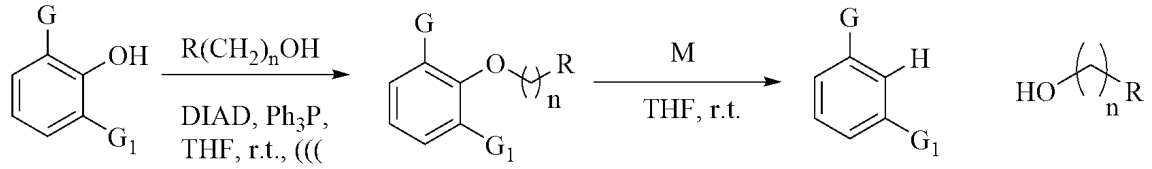
The protection of hydroxyl groups plays a central role in many multistep reactions, and there is a need to develop new and efficient protective groups, which can be selectively removed under mild reaction conditions.[1] In this contest, we have studied the protection of several functionalized and non functionalized alcohols, as *m*-terphenyl, *o*-biphenyl and 2,6-dimethoxyphenyl alkyl ethers. Their syntheses were performed under ultrasound stimulated Mitsunobu reaction,[2] as reported in the Scheme. We next investigated the reductive cleavage of these ethers under SET conditions and we obtained regioselective deprotection in the presence of a slight excess of Na or K metal in THF at room temperature.



G = G_1 = Ph
G = G_1 = OCH_3
G = Ph; G_1 = H

Finally we studied the protection/deprotection of chiral secondary alcohols, fucusing at first our attention on the stereochemistry of *m*-terphenyl and *o*-biphenyl ethers. The preliminary results are very interesting indeed the Mitsunobu protection as *m*-terphenyl ethers proceeds with retention of configuration, while the etherification as *o*-biphenyl ethers proceeds with prevalent inversion.

[1] (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, **2007.** (b) Kocienski, P. *Protecting Groups*; Georg Thieme Verlag: Stuttgart, **2003.**
[2] Lepore, S. D.; He, Y. *J. Org. Chem*. **2003**, 68, 8261-8263.

ORG-OR-07 3,4-Bis(4-ethynylphenyl)-2,5-diphenylcyclopenta-2,4-dienone based organogels: the importance of a hydroxydimethyl group

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Spontaneous self-assembly of low molecular weight molecules is a powerful tool that allows complex supramolecular structures to be built. This strategy can be successfully applied to the creation of soft materials of technological interest, and of potential application of organic materials in optoelectronics.[1]
During our studies on the synthesis of propargyl functionalized cyclopentadienones as Shvo catalysts[2] ligands, we incidentally observed the formation of an organogel from derivative **1**, which then proved to be able to gel both aromatic and polar solvents by cooling hot solutions. The process is reversible and the gel formation is accelerated by ultrasounds.
The presence of two methyl groups on the propargyl substituent proved to be essential for the gel formation, in fact when they are changed in hydrogen or phenyl groups the gelating ability of the compound vanishes.
The gels are transparent and dark red, and form fiber-like structures. VT-NMR studies furnished interesting informations on the role of the solvent on the gel formation.

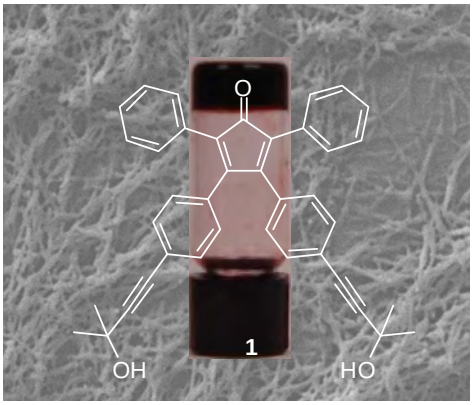

Figure 1: Compound **1** and the SEM image of the corresponding toluene xerogel

[1] a) J. W. Steed, J. L. Atwood, Supramolecular Chemistry; John Wiley & Sons, 2009; b) M. Suzuki, K. Hanabusa, *Chem. Soc. Rev*. **2009**, *38*, 967 and references.
[2] a) B. L. Conley, M. K. Pennington-Boggio, E. Boz and T. J. Williams *Chem. Rev.*, **2010**, *110*, 2294. b) L. Busetto, D. Fabbri, R. Mazzoni, M. Salmi, C. Torri, V. Zanotti, *Fuel*, **2011**, *90*, 1197.
[3] L. Sambri, R. Mazzoni, A. Baschieri, *submitted manuscript*.

ORG-OR-08 Design, Synthesis and Characterization of novel amphiphilic Guanosine-based Nucleolipids

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Hybrid molecules formed by a lipid core covalently linked to a nucleoside, called nucleolipids, occur in eukaryotic and prokaryotic cells and display a variety of biological activities. In order to associate the pharmacological potential of nucleosides with the aggregation properties of vesicle-forming lipids, several nucleolipids have been synthesized.[1] A number of amphiphilic nucleolipids incorporating adenosine, cytosine or uridine have been described; on the contrary, very few guanosine-based nucleolipids are known and almost completely unexplored are their potential applications. Still, lipophilic guanosines play a special role in supramolecular chemistry, being able to generate peculiar architectures in organic solvents based on stacked G-tetrads, stabilized by metal ions, or, in the absence of cations, bidimensional assemblies called G-ribbons.[2-5]

We here describe the design, synthesis, biophysical and biological characterization of a library of novel sugar-modified guanosine derivatives. Decoration with fatty acid chains and diverse hydrophilic groups provided different amphiphilic guanosine analogs, here named **G1**-**G7**. CD studies, ion transport experiments through phospholipids bilayers and *in vitro* screening of their antiproliferative activity showed these amphiphiles as very interesting compounds, with distinctive properties, finely tunable as a function of the ribose substituents.[6]

[1] A.Gissot, M.Camplo, M.W.Grinstaff, and P.Berthélémy, *Org. Biomol. Chem.*, *6*, **2008**, 1324-1333 and literature cited therein.
[2] S.Lena, S.Masiero, S.Pieraccini, and G.P.Spada, *Chem. Eur. J., 15*, **2009**, 7792-7806.
[3] J.T.Davis, and G.P.Spada, *Chem. Soc. Rev.*, *36*, **2007**, 296-313.
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ORG-OR-09 Steric and Electronic Effects on the Configurational Stability of Phosphorus Centred Three - Bladed Propellers

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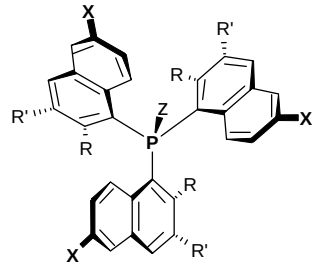
A series of tris-aryl phosphanes and phosphane-oxides structurally designed for existing as *residual* enantiomers or diastereoisomers, bearing substituents differing in size and electronic properties on the aryl rings, have been synthesized and characterized (Figure 1). Their electronic properties have been evaluated through theoretical calculations and experimentally on the basis of their electrochemical oxidative potential determined by voltammetry. The configurational stability of *residual* phosphanes, evaluated by dynamic ^{1}H- and ^{31}P-NMR analysis and by dynamic enantioselective HPLC was found rather modest (stereomerization barriers of about 17 kcal m^{-1}), much lower than those shown by the corresponding phosphane-oxides which have been always obtained in an enantiopure state. Their helix reversal barriers could be inferred by off-column kinetics monitored by HPLC (about 28 kcal m^{-1}) on enantiopure antipodes. In accordance with calculations, an unexpectedly low barrier for phosphorous pyramidal inversion was invoked as responsible for the scarce configurational stability of the *residual* tris-arylphosphanes. A strategy for inhibit phosphorous inversion was based on the production of a frame of hydrogen bonds amongst the blades located inside the conical space of the propeller.



Z = O, lone pair X = H, OEt, NO_2, Br, SO_3H
R = OEt, OH, R' = H
R-R' = O-CH_2-CH_2-O, (*S*,*S*)-O-CHMe-CHMe-O, -$OCMe_2O$

Figure 1.

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[2] T.Benincori, A.Marchesi, P.R.Mussini, T.Pilati, A.Ponti, S.Rizzo, F. Sannicolò, *Chem. Eur. J.*, *15*, **2009**, 86; *Chem. Eur. J.* **2009**, *15*, 94.

ORG-OR-10 Condensed Oxaziridines: Synthesis of Polyhetero-bicyclo and Azodioxy-Carbonyl Compounds

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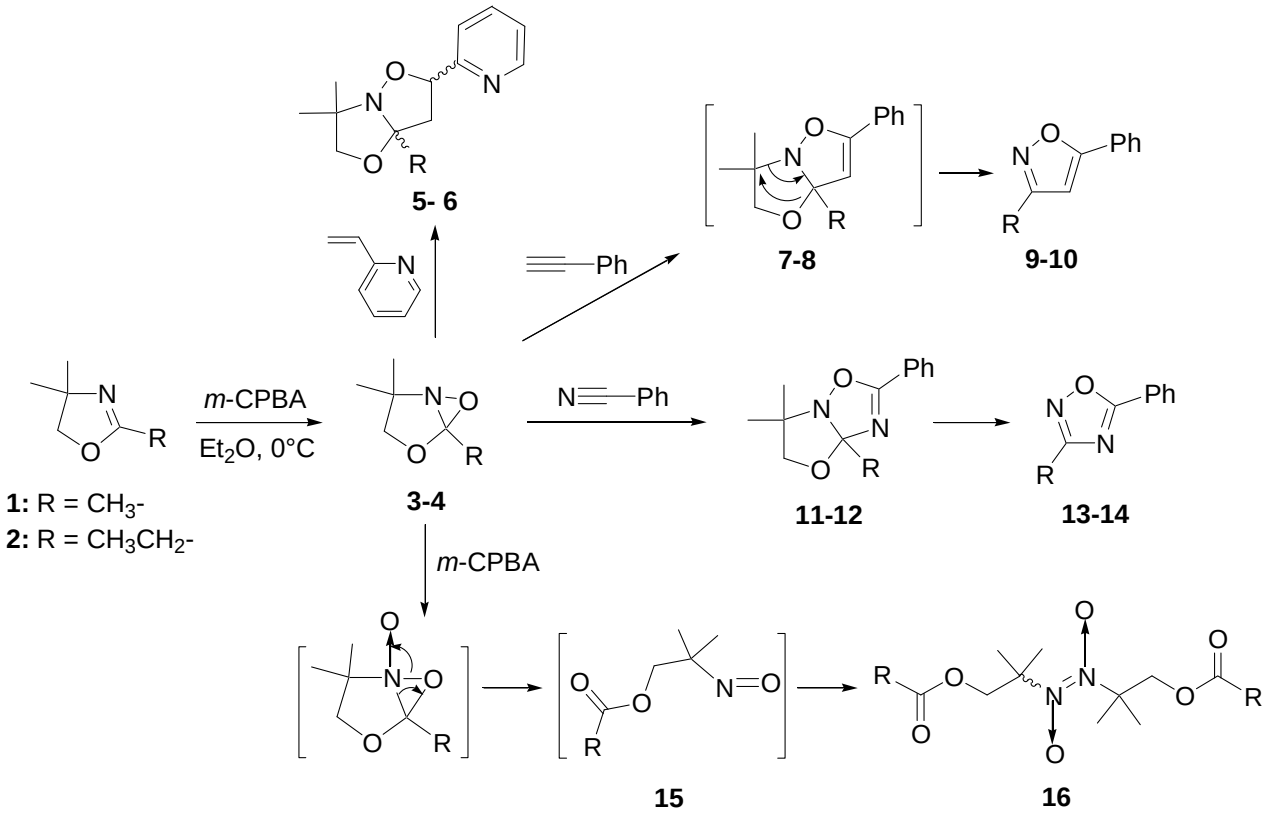
Oxaziridines, very special three-membered heterocycles, are a group of compounds of unusually high reactivity. They are often the scaffold of more complex biologically active molecules, which have been shown to possess antitumor and mutagenic activities [1, 2].
In this contribution we report the synthesis of oxaziridines condensed with heterocycles such as oxazolines, and their reactivity with alkenes, alkynes and nitriles. In addition, in the presence of 3-chloroperbenzoic acid (*m*-CPBA), the condensed oxaziridines are further oxygenated to generate *C*-nitroso (**15**) and subsequently azodioxy-carbonyl compounds (**16**).



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ORG-OR-11 Alkynyl routes to 5,6-dihydroxyindole-based oligomers and functionalized π-extended scaffolds

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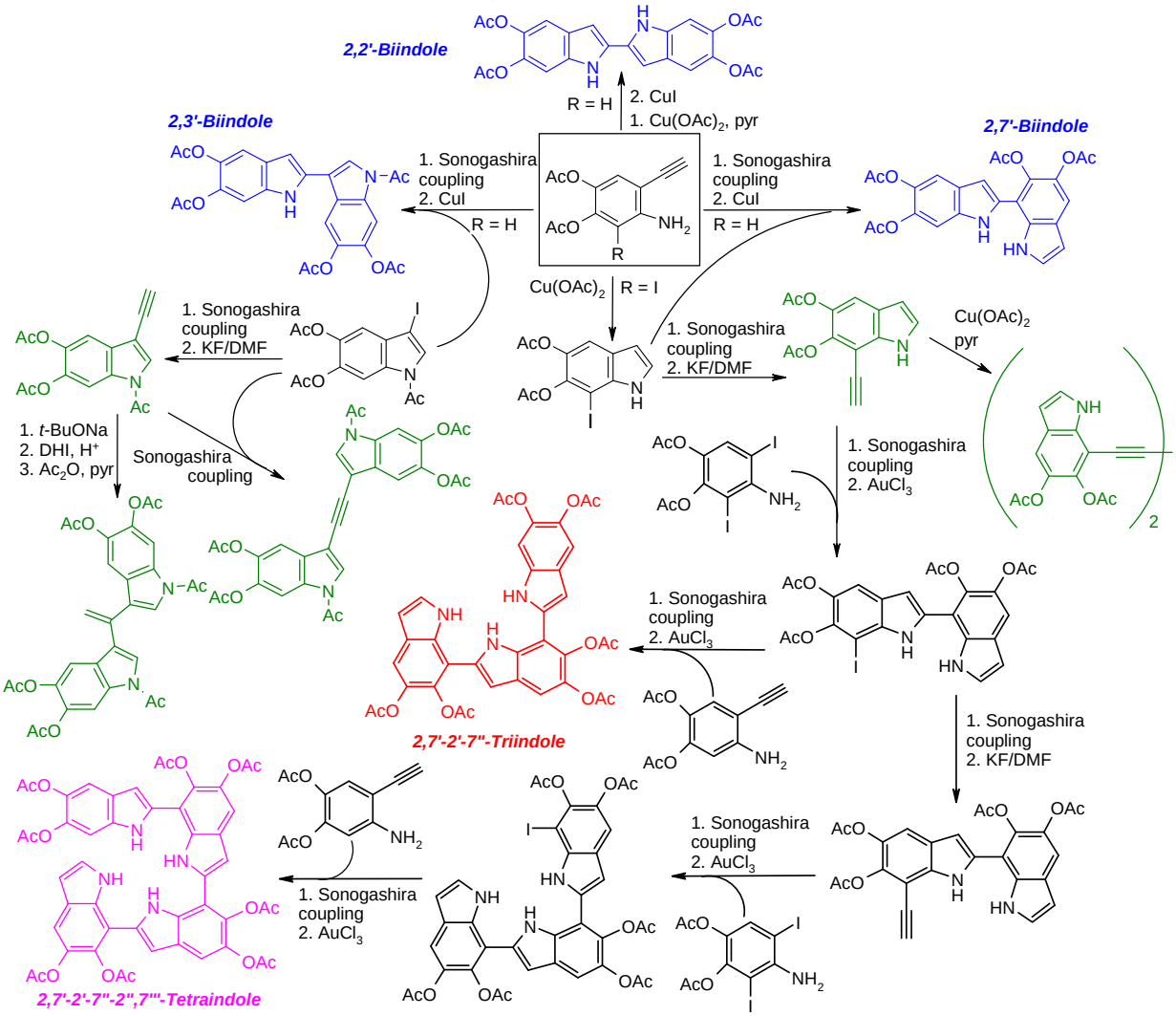
The prospects of developing improved models of eumelanin biopolymers and/or novel bioinspired functional materials/scaffolds for application in organoelectronics have incited increasing efforts toward the rational design and synthesis of 5,6-dihydroxyindole (DHI)-based π-electron systems with tailored structural and electronic properties.[1-3] A valuable entry to this goal has derived from the exploitation of alkynyl chemistry for the assembly of novel oligomers[4,5] and the realization of π-extended systems.[6]



[1] M. d'Ischia, A. Napolitano, A Pezzella, P. Meredith and T. Sarna, *Angew. Chem. Int. Ed.*, **2009**, *48*, 3914-3921. [2] A. Pezzella, A. Iadonisi, S. Valerio, L. Panzella, A. Napolitano, M. Adinolfi and M. d'Ischia, *J. Am. Chem. Soc.*, **2009**, *131*, 15270-15275. [3] J. P. Bothma, J. de Boor, U. Divakar, P. E. Schwenn, P. Meredith, *Adv. Mat.*, **2008**, *20*, 3539-42. [4] L. Capelli, P. Manini, A. Pezzella, A. Napolitano and M. d'Ischia, *J. Org. Chem.*, **2009**, *74*, 7191-7194. [5] L. Capelli, P. Manini, A. Pezzella, and M. d'Ischia, *Org. Biomol. Chem.* **2010**, *8*, 4243-4245. [6] L. Capelli, O. Crescenzi, P. Manini, A. Pezzella, V. Barone, and M. d'Ischia, *J. Org. Chem.* **2011**, ASAP.

ORG-OR-12 Novel Organic Dyes for Photovoltaic Applications

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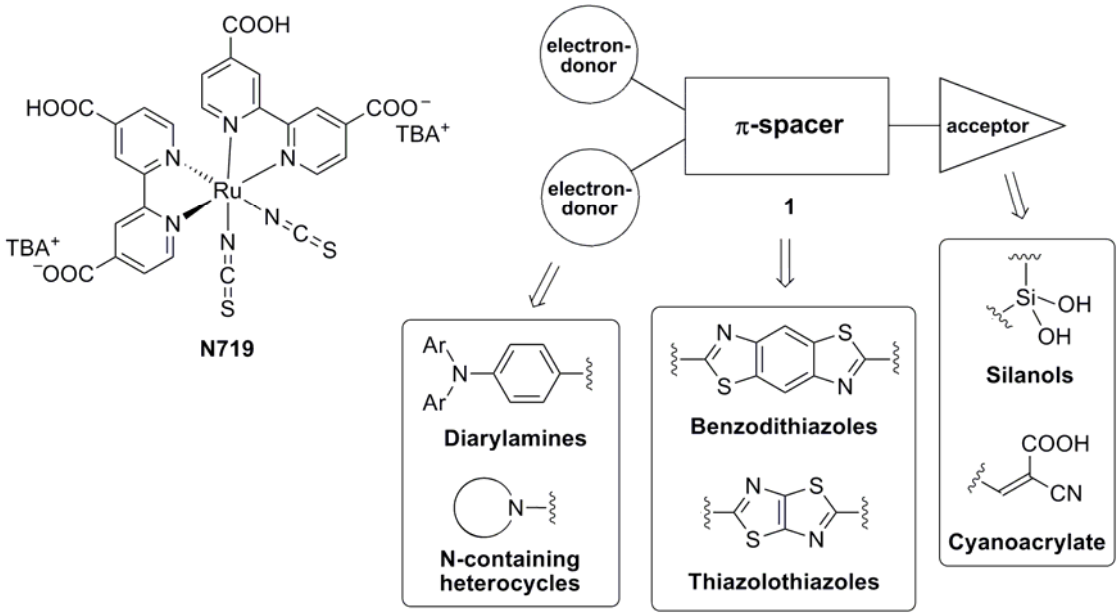
Dye-sensitized solar cells (DSC) recently attracted much attention as promising devices for the conversion of sunlight in electric power.[1] Such cells employ dyes, which act as photosensitizers, together with a suitable inorganic semiconductor, such as TiO_2. Historically, the first class of photosensitizers employed in DSC was represented by transition metal complexes, such as the Ru-bipyridyl complex **N719**.[2] More recently, purely organic sensitizers, not containing any metal atom, have emerged as a cheap and efficient alternative.[3] Such substances are often based on a "donor-π-acceptor" architecture, featuring electron-donating and electron-accepting groups separated by a conjugated spacer.

Here, we will present some of the dyes recently prepared in our laboratories, whose general structure (**1**) is shown in the figure.



The synthesis of these compounds will be described together with the results of preliminary experiments conducted on test cells containing the novel sensitizers.

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ORG-OR-13 Switching between supramolecular assemblies of guanosine derivatives triggered by external stimuli

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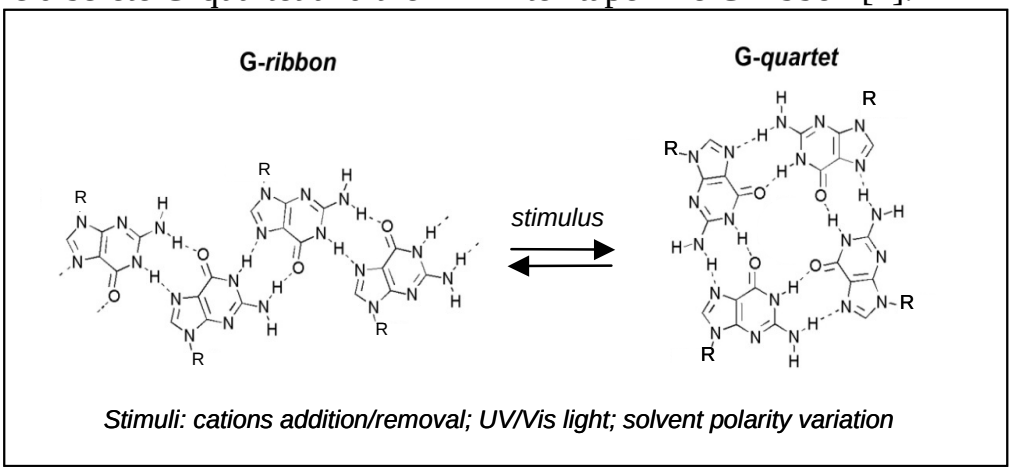
Depending on the experimental conditions, lipophilic guanosines (LipoG's) can undergo different self-assembly pathways based on different H-bonded motifs, e.g. the cyclic discrete G-quartet and the "infinite" tape-like G-ribbon [1].



The switching between different supramolecular motifs have been obtained by a variety of external stimuli. A first example is represented by chemical stimuli: addition of an alkali metal ion stabilizes the G-quartet while its removal shifts the equilibrium toward the G-ribbon [2].
A second type of stimuli is represented by light: the photocontrolled self-assembly of a modified guanosine nucleobase with a photoactive unit at C8 is obtained [3] selecting the appropriate wavelength. Finally, a lipoG armed with a terthiophene unit undergoes a pronounced variation of its supramolecular organisation by changing the polarity of the solvent [4]: in chloroform the derivative assembles via H-bonding in a Guanosine directed structure, while in the more polar (and H-bond competing) acetonitrile different aggregates are observed, where the terthiophene chains are π-π stacked in a helicoidal arrangement.

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ORG-OR-14 Multinuclear Magnetic Resonance Spectroscopy in the Structural Investigation of Reactive Intermediates Useful in Stereoselective Synthesis

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A challenging aspect in the modern synthetic chemistry, also aimed at shedding light on the reaction mechanisms, concerns the structural characterization of those "reactive intermediates" formed in planned stereoselective synthesis. At the same time, crucial parameters such as reaction time, temperature and concentration need to be faithfully checked and taken into consideration in order to improve the yields and reduce the formation of side-products. Such structural characterization and optimization can be carried out employing in a synergistic and complementary way modern spectroscopic and spectrometric techniques.
In this context, the Multinuclear and Multidimensional Magnetic Resonance Spectroscopy (MMRS) hold the potential to fulfill the gap in knowledge on the structure and dynamics in solution of special reactive intermediates such as polar organometallic derivatives, thought as "fleeting species".

In this lecture will be showed as the MMRS has been used to get insight on the structure in solution of some heterosubstituted organolithium derivatives and to get information about the dynamics at molecular level. [1]

The results coming from this investigation have found application in the development of stereoselective synthetic processes useful for the preparation of new molecular scaffolds and architectures even in highly enantioenriched form [2].

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[2] a) R. Luisi, V. Capriati, S. Florio, P. Di Cunto, B. Musio *Tetrahedron* **2005**, *61*, 3251. b) V. Capriati, S. Florio, R. Luisi, B. Musio *Org. Lett.* **2005**, *17*, 3749. c) R. Luisi, V. Capriati, S. Florio, B. Musio, *Org. Lett.* **2007**, *9*, 7, 1263. d) B. Musio, G. J. Clarkson, M. Shipman, S. Florio, R. Luisi, *Org. Lett.*, **2009**, *11*, 2, 325. e) M. Dammacco, L. Degennaro, S. Florio, R. Luisi, B. Musio, A. Altomare *J. Org. Chem.* **2009**, *74*, 6319. f) R. Luisi, S. Florio *Chem. Rev*. **2010**, *110*, 9, 5128. g) M. C. De Ceglie, B. Musio, F. Affortunato, A. Moliterni, A. Altomare, S. Florio, R. Luisi *Chem, Eur. J.* **2010**, *17*, 1, 286.

ORG-OR-15 Multifunctional Peptide Nucleic Acids (PNA) for Alteration of Gene Expression by MicroRNA targeting

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Peptide nucleic acids (PNA), and their modification (Figure 1A) are extensively used for targeting mRNA in the antisense approach for the down-regulation of the expression of target genes.[1] Micro-RNA (miR) are regulatory short (19-23 bp) dsRNA which modulate gene expression of highly relevant biological functions such as differentiation, cell cycle and apoptosis, through mRNA degradation. Inhibition of miR activity by specific molecules (anti-miR, figure 1B) has been shown to be of great interest in drug development [2].

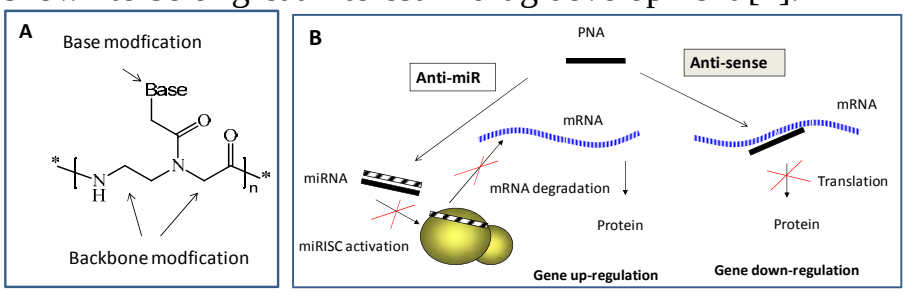

Figure 1.

In the present communication we describe the synthesis of anti-miR PNA either conjugated with a carrier peptide or bearing modified residues along the chain, PNA of high affinity and high specificity for miR210 and miR 221, involved in erythroid differentiation and tumor progression respectively were obtained. Modified PNA showed improved biovailability and effectively entered into tumor cells and exerted anti-miR acivity [2], leading to up-regulation of genes. New strategies for the elaboration of PNA structure during the solid phase synthesis either at the backbone or at the nucleobase level, thus introducing new functionalities for RNA binding or catalysis will also be described.

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ORG-OR-16 Selective Oxidation of Natural Target Molecules using Methyl(trifluoromethyl)dioxirane

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ICCOM-CNR, Dipartimento di Chimica, Università degli Studi Aldo Moro di Bari, Via Amendola 173, 70126 Bari, Italy
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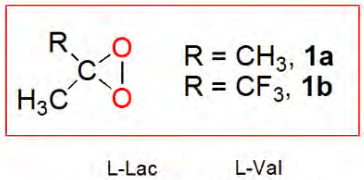
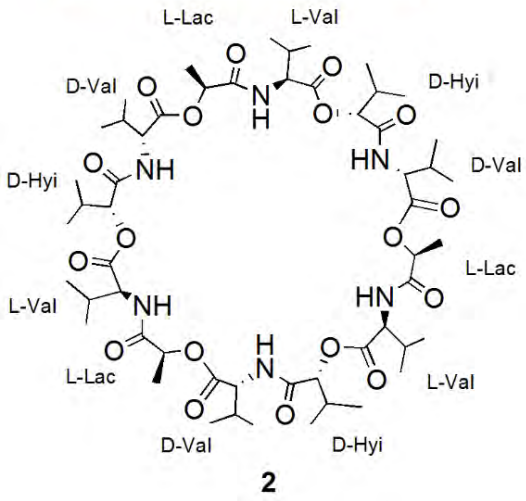
Over the past two decades, the dimethyldioxirane (DDO) (**1a**) and its trifluoro analog **1b** (TFDO) have fruitfully been employed to accomplish the selective oxyfunctionalization of natural targets such as steroids, vitamine D_3 derivatives, terpenes, as well as amino acids. Besides the extremely mild reaction conditions, dioxiranes **1** offer a number of advantages over other classical oxidation reagents, because their high reactivity is often accompanied by an outstanding selectivity.[1,2]





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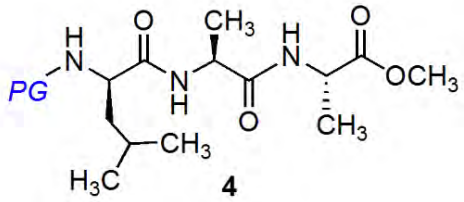

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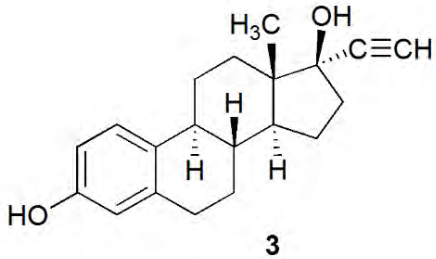

3

We now report on our current investigations in the selective oxidation of target molecules, such as valinomycin (**2**)**,** the steroid **3**, and some model peptides (**4**).

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ORG-OR-17 Water Soluble Functionalized Polymers as New ^{19}F MRI agents

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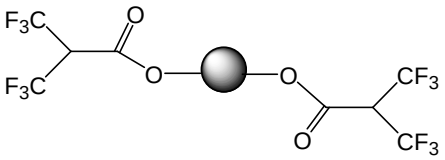
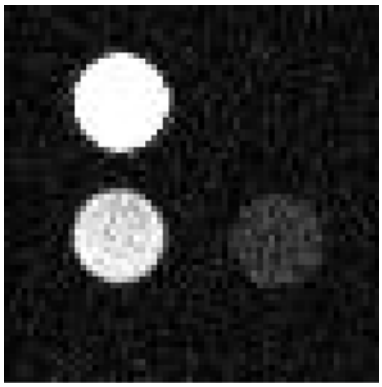
In "multifunctional nanomedicine" the research has been focused towards the development of novel devices that integrate diagnostic and therapeutic functions within the same platform.[1] Multifunctional nanomedicine holds considerable promise as the next generation of medicine, for example in cancer therapy, allowing for the molecular diagnosis of cancer phenotypes, customized therapy to exploit unique cancer targets, and simultaneous treatment and monitoring of therapeutic efficacy.

Our project would like to explore the development of **polymeric materials bearing a fluorinated residue suitable for ^{19}F MRI and that may further implemented with other functions,** a diagnostic or, in the future, even a therapeutic one. Because of the lack of any ^{19}F background in the body, observed signals originating from injected ^{19}F containing agent exhibited an excellent degree of specifity and merging of recorded ^{19}F images on ^{1}H images enables an exact anatomic localization of fluorinated substances as "hot spots". [2]

In a preliminary approach a commercially available polymer was employed as carrier of the fluorinated residue. Polyethylene glycol (PEG) has many positive features: it's a very cheap, atoxic, biocompatible, water soluble polymer that can be easily functionalized by well described standard experimental procedure.[3] The simple condensation of polyethylen glycol with the 2-(trifluoromethyl)-3,3,3-trifluoro-propanoic acid allowed to isolate a new material, bearing an fluorinated moiety. Two different PEGs were employed, having MW of 2000 Dalton and 400 Dalton, to afford two novel polymers, of **2310 Dalton** and **760 Dalton**, respectively, both showing a single ^{19}F signal at NMR in deuterated chloroform and D_2O; both compounds are indeed soluble in water. However when experiments of *in vitro* MR imaging were conducted only with the sample of **760 MW** it was possible to obtain a clear imaging, pointing at the importance of the fluorine content of the carrier. Different images have been obtained for three different concentration to test the sensitivity of the imaging agent (see figure on the right).





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ORG-OR-18 Protein-carbohydrate interactions at host pathogen interface

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The interactions between proteins and carbohydrates are involved in important biological processes such as recognition of antigenic carbohydrates on the bacterial cell surface by antibodies or initiation of inflammatory response. Understanding of molecular recognition events in protein-carbohydrate systems is pivotal for the elucidation, at molecular level, of the events involved at the heart of biological phenomena and drug discovery process. Nuclear Magnetic Resonance (NMR) spectroscopy is a powerful method for studying protein-ligand interactions in solution. Two techniques, Saturation Transfer Difference (STD) NMR and transferred NOE [1], together provide a picture of ligand binding to a receptor. In this communication, preliminary studies on different systems of protein-carbohydrate interactions at host-pathogen interface will be reported.
By this approach we analyzed the interaction between peptidoglycan (PGN) fragments of bacterial cell wall, named muropeptides, and an eukaryotic-like Ser/Thr membrane kinase, characteristic of Gram positive bacteria. This protein contains an extracellular domain, named PASTA, capable of binding the muropeptides of PGN DAP(*meso*-diaminopimelic acid)-type released into extracellular milieu during bacterial growth [2]. The recognition PASTA-peptidoglycan is the trigger of the germination of dormant bacterial spores because it represents a signal of favorable environmental conditions.
In order to fully describe, at molecular level, this system of interaction we performed NMR experiments on the extracellular domain of kinases from two different Gram positive bacteria, *Bacillus subtilis* and *Staphilococcus aureus*, using as ligands monomeric and dimeric muropeptides deriving from the PGN DAP-type.

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ORG-OR-19 Synthesis and Properties of Cyclic Hexapeptoids

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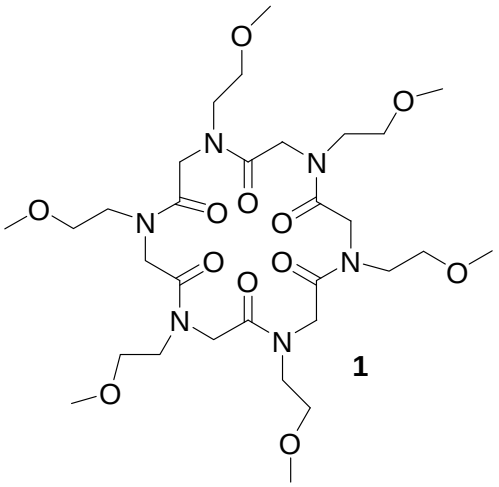
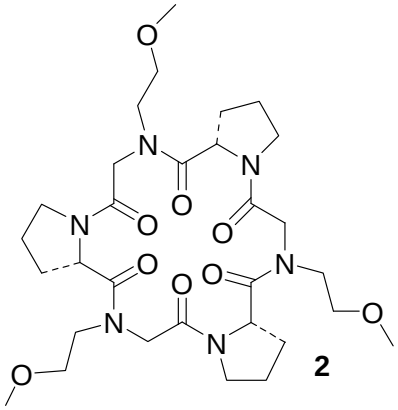
Peptoids, bioinspired peptidomimetics, show unique structural and physical properties. [1] The conformational ordering of their achiral polyimide backbone is dictated by stereoelectronic effects caused by *N*- (and C-) substitution and/or by cyclization. [2]
In this communication the synthesis, X-ray crystallographic investigations and complexation properties of *N*-metoxyethyl cyclic peptoids (*e.g* **1** and **2**) will be reported.





The elaboration of the linear peptoid precursors was accomplished via an expeditious mixed 'monomer', and 'submonomer' approach on solid phase. The oligomerization of the units was performed on a 2-chlorotrityl resin. Once the construction of the linear oligomers was completed, they were cleaved from the resin, and a head-to-tail macrocyclizations of the linear *N*-substituted oligoglycines proceeded smoothly giving, under high dilution conditions, the desired macrocycles. [3]
In particular for both compounds sodium complex were analyzed by X-ray crystallography, they both have all-*trans* backbone configuration, but the solid state assembly is rather different, **1** gives rise to a 1D coordination polymer, **2** to a discrete molecular complex**.**

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ORG-OR-20 Chemical Proteomics, a Powerful Tool in the Analysis of Perthamide C Cellular Effects

Luigi Margarucci, Maria Chiara Monti, Annalisa Vilasi, Alessandra Tosco, Raffaele Riccio, Stefano Fiorucci, Angela Zampella, Agostino Casapullo

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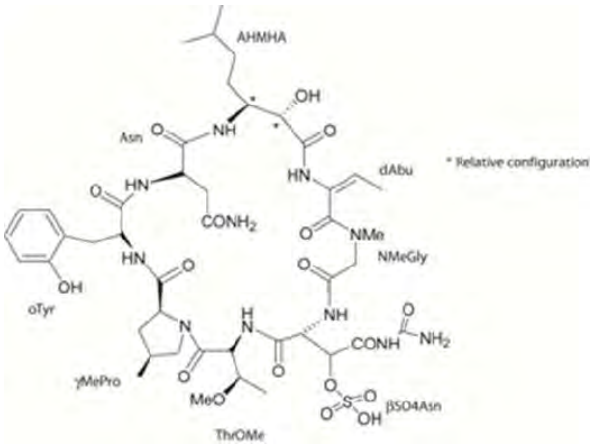
The identification of the biological effects of natural products is becoming crucial to better understand the molecular mechanism of ligand-protein interactions. This is also an essential information to assist the rational development of novel drugs with greater selectivity and/or potency. Here, we describe the application of mass spectrometry-based chemical proteomics to the analysis of perthamide C effects on a cell proteome. Perthamide C is a novel cyclic octapeptide isolated from the polar extract of *Theonella swinhoei*, a marine sponge source of bioactive peptides with interesting biological activities.[1] The combination of mass spectrometry with affinity purification and 1D/2D gel electrophoresis opened the way to a comprehensive picture of perthamide C-induced proteome changes. These results allowed us to speculate on an anti-apoptotic effect of the marine metabolite, mediated through its involvement in several cellular pathways, as finally confirmed by *in vitro* and *in cell* assays.



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ORG-OR-21 Smart Biomaterials for biotechnologies

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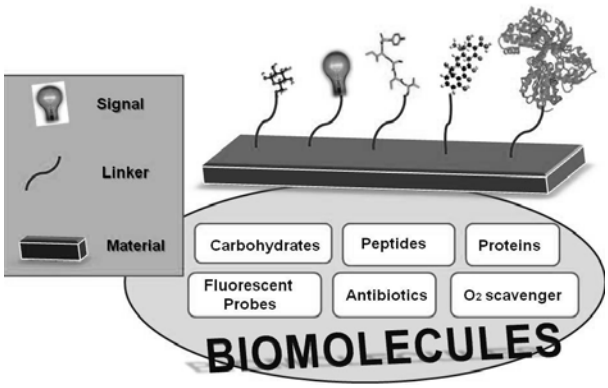
Decoration of nanostructured materials is relevant in a wide variety of applications, including novel tissue engineered scaffolds and devices, site specific drug delivery systems, non-viral gene carriers, biosensor and screening systems, and clinical bio-analytical diagnostics and therapeutics [1]. Through the modification of material surfaces one can control and tailor their properties in a predictable manner, and impart them with biological properties and chemical functionalities to better suit their applications. We wish to report our recent investigations on materials decoration with novel chemical approaches [2-5]. These approaches have been tested taking into accounts different key-points:

a) Chemical nature of the material: organic of natural origin (collagen), polymeric (PP and PCL), inorganic (hydroxyapatite);

b) Chemistry applied to the decoration step: plasma functionalisation, diazo-transfer, silanisation, direct linkage to material functional groups, Huisgen-cycloaddition;

c) Molecules for the (bio)decoration: the different functional groups introduced on material surface are used for the covalent immobilization of small organic molecules.



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Acknowledgments. We gratefully acknowledge Fondazione Cariplo-projects 2010-0378 and 2008/3175, MIUR-project FIRB RBPO68JL9, for financial support.

ORG-OR-22 Diversity-oriented synthesis and chemical genetics to address lead identification in drug discovery

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Chemical genetics is a powerful approach for selecting small molecules possessing the ability to induce a biological phenotype or to interact with a particular gene product, and it is an emerging tool for lead generation in drug discovery. Accordingly, there is a need for robust and versatile synthetic processes capable to generate complex and diverse molecular collections, and Diversity-Oriented Synthesis (DOS) of small molecules is the concept of choice to give access to new chemotypes bearing high structural diversity. Moreover, biological evaluation using cell growth as a phenotypic screening on *Saccharomyces cerevisiae* deletant strains is a powerful tool to identify new chemotypes as hit compounds in the discovery of new antifungal and anticancer agents, and also in the dissection of their mode of action.

Our efforts in this field are focused on the generation of diversity-oriented molecular probes of peptidomimetic nature, and on the evaluation of their ability to induce phenotypic effects with functional implications on a panel of strains of the budding yeast *Saccharomyces cerevisiae* [1]. Recently, we succeeded in generating morpholine-based scaffolds from amino acid and sugar derivatives in a diversity-oriented fashion, and in the successful application of a library of these molecules on a panel of *Saccharomyces cerevisiae* strains, which provided the identification of new chemotypes involved in mitochondria metabolism and respiration [2].

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Acknowledgements: financial support from Fondazione Roma and CINMPIS.

ORG-OR-23 A melanin-inspired system promoting aerial polymerization of catecholamines and deposition of nanosized coatings encasing the redox active core: new opportunities for preparation of functional biomaterials.

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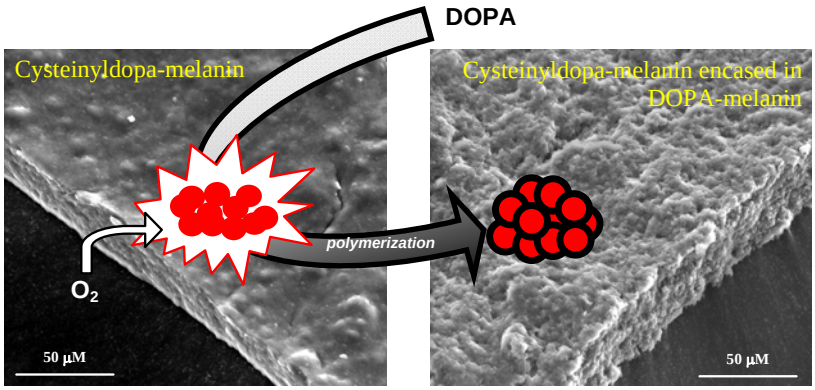
In recent years the opportunity of translating current knowledge of the properties and mechanisms of formation of phenol biopolymers to the design and implementation of innovative functional materials has increasingly been appreciated. Of particular interest are the polymers inspired to eumelanins, the pigments responsible for dark hues of human hair and skin, the pheomelanins typical of the red hair phenotypes, and the black polymers produced by oxidation of dopamine and related catecholamines, the main component of the neuromelanin of substantia nigra of human brain.[1] Melanin precursors, such as DOPA, dopamine and norepinephrine have been used for the preparation of bioactive materials, multifunctional coatings and adhesive films that stick to organic and inorganic surfaces, e.g. silica, dimethyldiethoxysilane emulsions, nanotubes, and even cellular surfaces, for preparation of nanostructures and neuroactive biomaterials.[2] In most of these surface modification processes, however, catecholamine polymerization and coating is induced through a slow autooxidation process subject to substrate and oxygen availability as main determinants of coat thickness. [3]



Herein, we disclose an unprecedented biomimetic chemical system promoting aerial catecholamine polymerization and leading to novel core-shell materials. The new system is built upon the discovery that finely suspended melanin obtained from 5-*S*-cysteinyldopa (CD), a synthetic model for pheomelanins, markedly accelerates the oxygen-dependent polymerization of DOPA and other catecholamines at pH 7.4 leading to deposition of black eumelanin-like polymer

encapsulating the CD-melanin active core. SEM analysis indicated a close similarity of the morphology of the resulting pigment with that of a pure DOPA-melanin sample suggesting encasing of the CD-melanin component into the DOPA-melanin coating. Chemical degradation experiments indicated that, while most of the CD-melanin was readily solubilized and released from the filter by alkaline washings, no CD-melanin was detected in the washings of the DOPA melanin-coated sample, confirming the presence of an insoluble DOPA-washing steps. The oxidative polymerization process is likely mediated by key benzothiazine units through a redox interaction mechanism occurring on the surface of the finely suspended pro-oxidant polymer. These results broaden the field of application of melanin inspired biopolymers indicating methodologies for improving and accelerating coating formation. The presence of cysteine in the CD pigment precursor may allow to use protein residues as an anchor for DOPA to create an encapsulation and functionalization of cell surface with covalently bonded, artificial shells.

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MS-IL-01 Shaping the Beating Heart of Artificial Photosynthesis: Oxygenic Nano-Hybrid Interfaces

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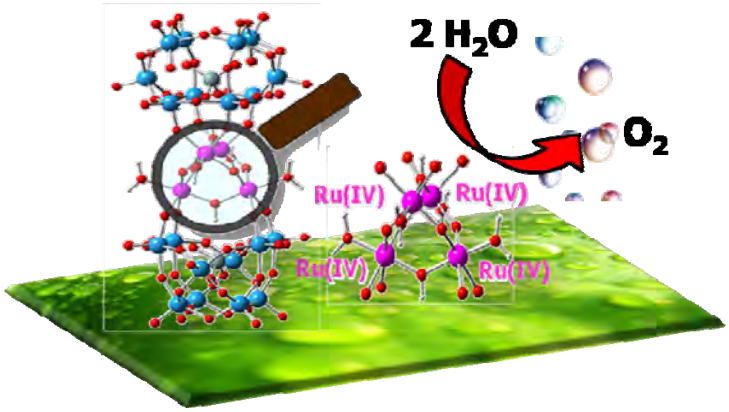
Water oxidation is the crucial stage in the chemical and molecular sequence of photosynthesis, designed by Nature to convert solar light into chemical energy. The artificial "off-leaf" transposition is a major goal of energy research, aiming at the continuous production of hydrogen as solar fuel, through the photo-catalytic splitting of H_2O.[1] Success in this task primarily depends on the interplay of light-activated multi-electron oxidation and reduction routines and on the invention of stable and robust water oxidation catalysts, liberating oxygen with fast rates, high quantum yield, and long-term activity. Indeed, the Achilles' heel of the chloroplast assembled architecture stems from the intrinsic weakness of the functional components chosen by Nature. The artificial perspective should find its roots on more solid materials. The vision here is to transcend the natural wonder, while being inspired by its key guidelines along the design of a functional system/device, with superior operation stability. We will highlight a recently discovered pathway carved within the class of inorganic metal-oxides displaying a unique mimicry of the PSII enzyme.[2] Furthermore, the shaping of their functions at the interface of specifically tailored carbon nano-structures and/or polymeric scaffolds opens a vast scenario for tuning electron/proton transfer mechanisms in term of rates, distance, geometries and communication between donor/acceptor centers.[3]



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MS-IL-02 Supramolecular Ligands in Transition metal catalysis, evolutionary ligand screening and a first approach to catalyst selection

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The interface between supramolecular chemistry and transition metal catalysis has received surprisingly little attention in contrast to the individual disciplines. It provides, however, novel and elegant strategies that lead to new tools for the search of effective catalysts, [1] and as such this has been an important research theme in our laboratories. In this presentation I will focus on supramolecular strategies to make bidentate ligands and compare that to traditional catalyst development. Supramolecular approaches appear ideally suited for the creation of large ligand libraries. The large number of catalyst that become available in this manner, asks for screening strategies and evolutionary approaches. A first academic example of catalyst selection from a mixture will be discussed. In addition, the application of a cofactor strategy will be presented, which is also ideally suited for selection procedures.

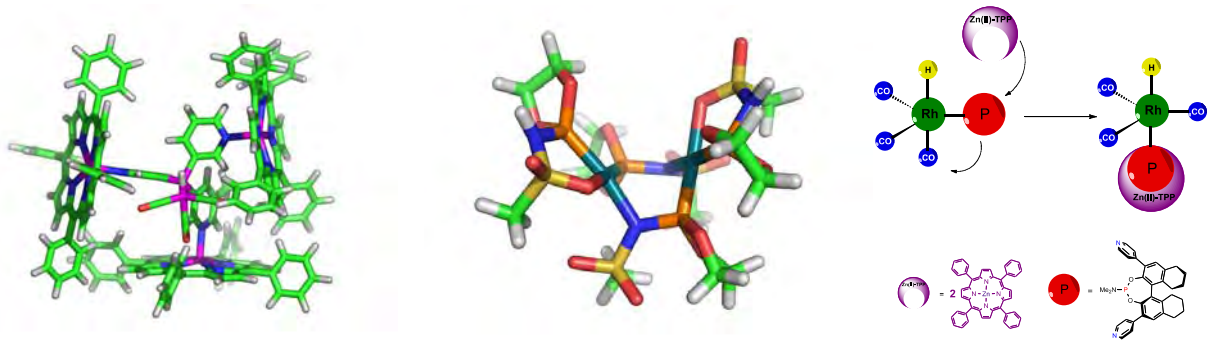

Figure 1: New concepts in TM catalysis: Left) a ligand-template approach to porphyrin encapsulated rhodium catalyst. Middle) dinuclear complexes based on METAMORPhos ligand Right) coordination chemistry steered by supramolecular chemistry.

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MS-01 Supramolecural Control on Product and Substrate Selectivity via Encapsulation within a Hydrogen Bonded Self-assembled Hexameric Capsule

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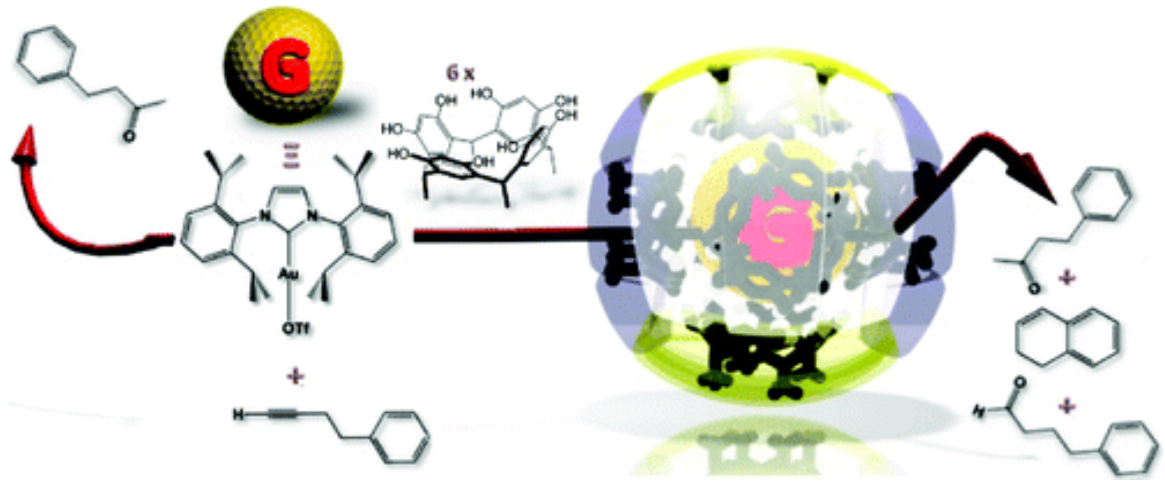
The impressive chemo, regio and stereoselectivity displayed by enzymes are the result of a large number of weak attractive intermolecular interactions as well as repulsive steric requirements operating between the substrate and the catalytic site. In the latter, recognition phenomena allow also the selective picking of the substrate among a series of similar reagents bearing same functional groups but different size. Overall enzymes control both sides of a chemical transformation, while common organometallic catalysis usually puts its effort prevalently on the right side of the catalytic reaction. Hosting of organometallic catalysts within well defined porous supports led to enhancement of enantioselectivitywhile for catalytic systems working under homogeneous conditions, encapsulation within rigid metal-ligand tetrahedral or square bi-pyramidal assemblies allowed rate acceleration and substrate selective reactions for a series of small reagents.
Herein we report about the simple modification of the product and substrate selectivity properties of an organometallic catalyst via encapsulation in a spherical hexameric self-assembled capsule held together by a seam of sixty hydrogen bonds. The steric requirements imparted by the capsule modify product distribution in the alkyne hydration reaction towards uncommon species and, at the same time, steer substrate selectivity in parallel competitive experiments towards the substrate that better fit the residual space available in the cavity.



MS-02 Rhodium-Catalyzed Asymmetric Hydrogenation of Olefins with PhthalaPhos, a New Class of Chiral Supramolecular Ligands

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Nature makes wide use of non-covalent interactions to build its complex supramolecular architectures and to achieve efficient and selective transformations. In recent years, supramolecular approaches to the development of new enantioselective catalysts have gained momentum [1]. Herein we report the design and synthesis of a novel class of chiral monodentate phosphite ligands, named PhthalaPhos [2], which contain a phthalic acid diamide moiety (Figure 1). Such phthalamide group displays both donor and acceptor hydrogen bonding properties that can give rise to supramolecular interactions both between the ligands and with the substrate. The modular nature of the PhthalaPhos ligands allows to tune their properties by simply varying structural elements such as the linker, the BINOL unit and the ancillary amide group (i.e. the amide not connected to the phosphite group), thus allowing a parallel-combinatorial ligand optimization.

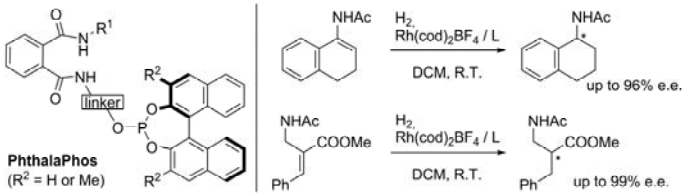

Figure 1

The catalytic properties of the PhthalaPhos library (19 representatives) were tested in the rhodium-catalyzed enantioselective hydrogenation of dehydro aminoesters and *N*-acyl enamides. Excellent results in terms of catalytic activity and stereocontrol were obtained with both benchmark substrates and 'challenging', industrially relevant olefins (Figure 1). Spectroscopic and computational studies, together with control experiments, suggest that the role of the phthalamide group consists in binding and orientating (by hydrogen bonding) the substrate during the catalytic cycle of the hydrogenation process [2b].

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MS-03 Covalent Nano-Clip and Nano-Box Compounds Based on Free Base Porphyrins

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There is an increasing interest in developing smart nanostructures for applications in many different fields, from environmental monitoring to biological, medical and industrial chemistry. For some specific properties (e.g. strong molar absorption, bound metal atoms in pyrrolic cores, extensive aromatic structures, peculiar affinity for neoplastic cells, etc.), porphyrin-derivatives are among the most studied compounds and some applications like chemical and/or biological receptors, artificial sensors for drug determinations, mimesis of biological systems, etc., are already well-defined. Recently, several 3D cyclic oligo-porphyrins with different architectures [e.g. spheres, prisms, regular polyhedra (with a varying number of faces), etc.] have been studied[1]. The properties of these molecules may depend on the size and hydrophobic nature of the cavities inside their 3D structure (for example, suitable to accommodate hydrophobic chemicals).

In the present paper, as the first step in the preparation of water soluble Nano-Clip and Nano-Box compounds, the synthesis and characterization of some novel macromolecular cyclic ethers, constituted by two (Nano-clip, fig. 1) or four (Nano-box, fig. 2) porphyrin units and spaced with methylene bridges, are reported. These compounds, obtained by the reaction between dibromomethane and 5,15-di[p-(9-methoxytriethylenenoxy)phenyl]-10,20-di[p-hydroxyphenyl] porphyrin, have a co-facial (nano-clip) or a four wall-box (nano-box) architecture.

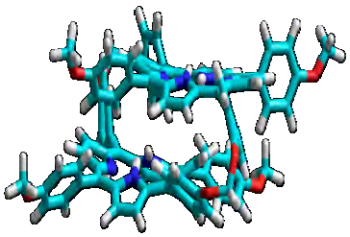
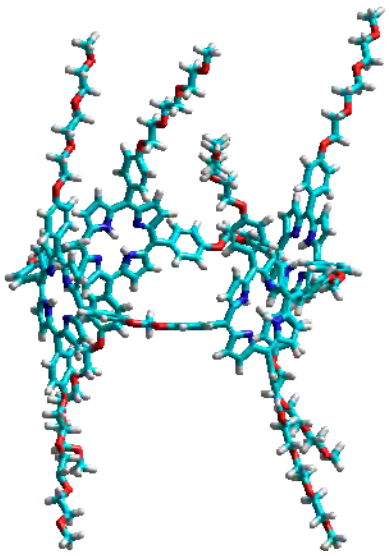


Fig.1



The aim of these syntheses was to obtain molecular systems for the recognition and/or the carriage of bio-molecules. Spectroscopic data of the Nano-clip showed modified Soret and Q-bands, with respect to the monomer and cyclic tetramer, as a probable consequence of a hybrid orbital deformation (HOD) phenomenon involving the two porphyrin π rings forced to a closer co-facial spatial arrangement [2].

A UV-vis titration allowed verification of the easy and reversible protonation of the pyrrolic cores which, by electrostatic repulsion, modifies the spatial distance between the two co-facial porphyrins and, therefore, the cavity size. This reversible modification could be used to change the dimer molecule status from Open to Closed, and facilitate the accommodation or release of suitable chemical species, acting then as a drug carrier.
The tetrameric porphyrin molecule (Nano-box) could also be used as a drug-carrier, forming an inclusion complex with macromolecular drugs, or as a nano-reactor, for the peculiar nano-space conditions inside the box. In this case, ^{1}H-NMR spectroscopic analysis showed a high-field shift of the aromatic and ether protons present in the upper and lower box rims as a specific characteristic of this molecular structure[2]. These compounds differ from previous analogous porphyrinic systems in that their totally covalent structure makes them more versatile potential macromolecular tools.

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MS-04 Novel functionalized PTA ligands, their coordination complexes and use in catalysis

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PTA (1,3,5-triaza-7-phosphaadamantane), the neutral water-soluble and air-stable monodentate phosphine firstly reported by Daigle et al. in 1974 [1], has been used by us and other groups to obtain water-soluble transition metal complexes which have been applied as homogeneous catalysts in aqueous or biphasic systems [2].
The largest part of modifications of PTA has so far involved the P or N atoms, so we focused on the functionalization at one carbon of the upper rim [3]. The optimized derivatization reaction is based on the isolation of the pyrophoric PTA-Li salt, which was then reacted with electrophiles such as aromatic aldehydes and ketones [4]. Thus, new chiral ligands were obtained and used to bind Ir(I) and Ru(II) organometallic moieties. The corresponding complexes were tested as catalysts for hydrogenation reactions under mild conditions. In parallel, modifications of the lower rim of PTA, i.e. alkylations at N atom, were also carried out and the new N-alkylated PTA derivatives so obtained were used as water soluble ligands in biphasic Rh-catalyzed hydroformylations of long-chain olefins in the presence of randomly methylated -cyclodextrins.[5].
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ORG/CTC-KN-01 Bridging the Gap between Theory and Experiment: Modeling Chiroptical Properties and Spectroscopies

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The tremendous progress of ab-initio quantum chemistry in the last decades has led to an increasing number of applications of quantum mechanical (QM) approaches to the calculation of chiroptical properties [1-7].
The progress has been so large that a ‘‘renaissance’’ in chiroptical methods due to the accuracy and computational efficiency achieved by ab initio QM methods in reproducing experimental data and predicting new ones has been invoked [8].
In this contribution, some peculiar aspects of the computation of chiroptical properties and spectroscopies are remarked through the analysis of case studies, with special emphasis towards the gaining of calculated data directly comparable to experiments, by the inclusion of solvation and vibrational effects.

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ORG/CTC-KN-02 Structural Basis for the design and synthesis of selective HDAC inhibitors.

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Protein lysine acetylation is a key mechanism in the epigenetic control of gene expression, the regulation of cell metabolism[1,2], and protein deacetylases are potential targets for treating cancer and a range of autoimmune and neurodegenerative diseases[3]. In this context, the HDAC inhibitors have attracted the attention of the researchers as promising anticancer agents [4,5]. Based on sequence phylogeny and function, there are four distinct classes of HDAC: class I (HDAC1, 2, 3 and 8), class IIa (HDAC4, 5, 7 and 9), class IIb (HDAC6 and 10) and class IV (HDAC11) represent Zn^{2+}-dependent amidohydrolases, whereas class III comprises the mechanistically diverse NAD+-dependent sirtuins [6]. In this contribute, we have traced out the structural elements responsible of selective binding in the whole landscape of the HDAC isoforms considered interesting therapeutic targets. In particular, we have rationalized experimental observations and tried to systematically add new insights for a targeted design of selective inhibitors for the different HDAC isoforms. In detail, we have focused our attention on all HDACs zinc dependent enzymes, except HDAC5 and HDAC9-11, for which few information on expression, function in tumor cells, and ligand inhibitory profile are available in literature. The structural analysis was performed by molecular docking calculations, using as ligands known pan and class selective HDAC inhibitors [4]. Based on the obtained structural guidelines, we designed, synthesized and experimentally tested selective inhibitors for HDAC2.

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ORG/CTC-OR-01 The Structure of Ionic Liquids Based on Geminal Imidazolium: a Theoretical Study

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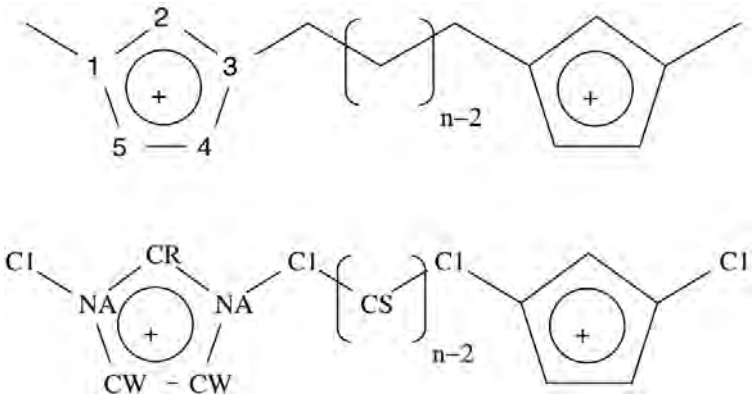
Among the most exciting and successful materials developed and studied in the last twenty years, ionic liquids [1] are among those that can certainly claim one of the most rich field of applications in industry and in applied technological research. A special class of ILs is have recently been obtained using geminal imidazolium dications [2] that represent a very interesting variation of the cationic partner and that may present various advantages over the traditional mono-cationic ionic liquids in applications such as lubricants, catalyst, solvents and as separation media.



A schematic view of the molecular structures is reported above: we have a linkage chain (whose length can be 3, 6, 9 or 12 for the compounds analyzed in the present work) that connects two imidazolium rings with a net positive charge on them and that are substituted with a methyl group. We have recently [3] analyzed the behavior of such compounds by calculating the structures of the gas phase complexes. We will report these and further results obtained by means of MD simulations.

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ORG/CTC-OR-02 Chemoinformatic strategies in the design of new antibacterials active against multidrug resistant Gram-positive pathogens.

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Chemoinformatic strategies possess great potentialities in modelling the interactions between biopolymers and ligands. Molecular recognition plays in fact a fundamental role in drug-receptor interactions.

Due to the lack of pharmacological targets, in previous studies [1] we adopted a Virtual Receptor Site (VRS) approach, where ligands interact with a complex receptor of unknown structure, aimed at identifying pieces of the structure which could be valuable for improving the antibacterial activity.

In the design of new drugs it is also very important that they exhibit ADME (Adsorption, Distribution, Metabolism, Elimination) properties warranting an acceptable bioavailability. For this purpose, a new method, called VOLSURF [2], able to correlate 3D molecular structures with physico-chemical properties, and highly efficient in predicting the biological activities, appears to be appropriate.

According to the advances achieved in the past two years due to the availability of the x-ray structures for a few drug targets, molecular modelling by docking of new ligands to the receptor active sites appears nowadays an appropriate strategy in the design of new antibacterials against multidrug resistant strains.

In this context, we adopted a recently developed algorithm called Fingerprints for Ligands and Proteins (FLAP) that can be used to describe proteins and ligands based on a common reference framework [3]. FLAP is able to explore the 3D-pharmacophoric space of ligands and proteins and to provide quantitative information for the complementarity of their interactions to allow ligand-ligand, ligand-protein, or protein-protein comparison. By means of all these chemoinformatic tools, we studied the interactions between synthetically accessible compounds and the crystallographic structure of Linezolid binding protein to identify a scaffold that we could modify introducing different substituents to improve the *in vitro* antibacterial activity.

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ORG/CTC-OR-03 Revisiting Nucleophilic-Electrophilic Mechanisms in Oxidation Reactivity

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Oxidation chemistry has always been one of the most important playgrounds for the interpretation and mastering of reactivity.[1] The interest of scientists has been driven not only by the strong implications that this reactivity plays in biological systems, but also because it represents an essential tool in functional groups transformation. These studies have also deeply contributed to the development of the basic principles of reactivity.
In recent years we have been involved in the study of metal catalysts for oxygen transfer reactions.[2] The experimental results have offered us the possibility to investigate in detail the mechanism of oxidation reactions, and in particular to study the effect of intermolecular interactions in catalysis.[3]
The evaluation of these experimental results, with the support of theoretical calculations, have led to a reinterpretation of the concept of nucleophilic and electrophilic reactivity in oxidation chemistry. This analysis can have implications that go beyond oxidation chemistry

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ORG/CTC-OR-04 L-Arabinose adsorption on a Ru cluster

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Use of bio-mass for energy, chemicals and material supply is one of the key issues of sustainable development, because bio-based resources are both CO_2-neutral and renewable, at variance with fossil fuels. Carbohydrates are the main source of renewables employed for the production of bio-based products. Therefore, chemistry know-how on industrial processes, involving carbohydrates is a subject of basis importance.

Adsorption of the monosacharide L-Arabinose on a ruthenium nanocluster is here presented as an example of a catalytic system of potential industrial interest [1]. L-Arabinose can be found in aqueous solution in 5 tautomeric forms (*i.e.* α or β pyranose, α or β furanose and acyclic species) in equilibrium with each other. All these tautomers show a very large conformational flexibility, which previously has been also analyzed.

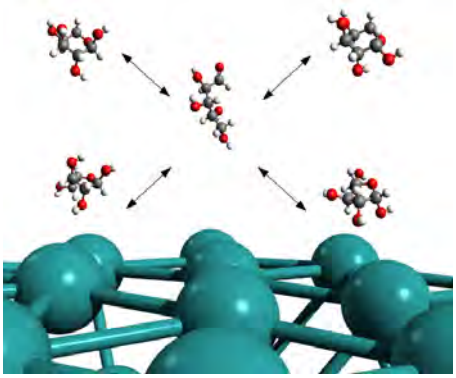

Figure 1. L-Arabinose on Ru surface

The L-Arabinose/Ru system has been investigated into the frame of the density functional theory (DFT). Calculations have been actually performed, using the DFT approach as implemented in SIESTA [2]. This employs linear combination of pseudoatomic orbitals as basis set. The atomic core is replaced by a non-local norm-conserving relativistic Troullier Martins pseudopotential, factorized in the Kleinmann-Bylander form.

The adsorption of different conformers, per each tautomers, on a Ru (0001) surface of the nanocluster have been modeled and analyzed in order to characterize the adsorption points both on the ruthenium surface and in the tautomeric species and to characterize if some of the latter are especially stabilized by the adsorption processes. Since adsorption phenomena could be affected by the adsorbate orientation, three different ways of binding per each conformers were investigated, considering either pyranose or furanose forms, and two for the acyclic forms.

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ORG/GC-IL-01 Amino Triphenolates as Privileged Ligands in Catalysis

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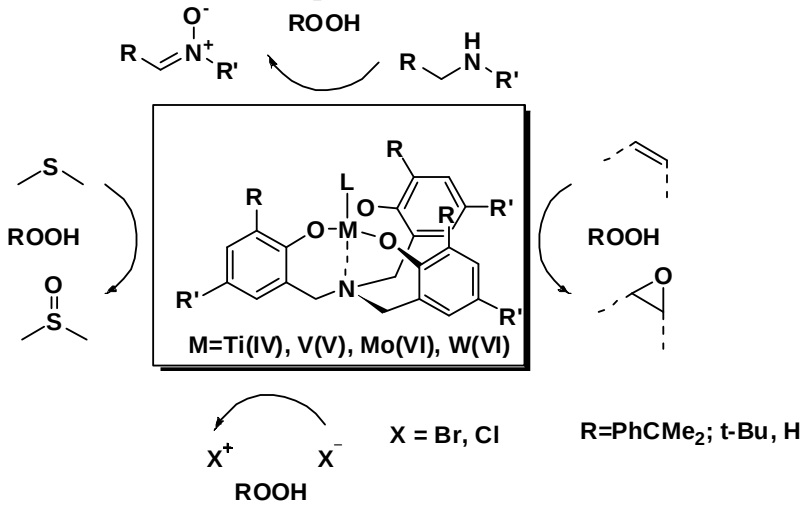
Triphenolamines are highly modular tetradentate molecules that effectively coordinate transition metals and main group elements with podand topology.[1] They form chiral complexes with well defined coordination geometries controlled by the ligand, in particular by the nature of the substituents in *ortho* position to the hydroxy groups, which are able to influence their reactivity and stability. Early transition metal complexes, like Ti(IV), V(V), Mo (VI) and W (VI) complexes have been found to be stable and effective Lewis acids in oxygen transfer processes.[2]



Here we will report on their synthesis, characterization and their reactivity in oxygen transfer reactions. Tuning of metal ion and reaction conditions allows the selective oxidation of different nucleophiles, such as olefins, halogens, sulfur or nitrogen derivatives using aqueous hydrogen peroxide and/or alkyl hydroperoxides as primary oxidants with very low catalyst loadings and high TON's and TOF's. Computational and spectroscopic studies for the elucidation of the reaction mechanism of peroxide activation and oxygen transfer reactions will be also presented.

***Acknowledgements*:** We acknowledge for financial support MIUR, PRIN 2008 project, University of Padova and CARIPARO Fundation (NANO-MODUles Progetto Eccellenza 2009-2010).

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ORG/GC-IL-02 Structural effects on physico-chemical and catalytic properties of functionalized ionic liquids

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During the past decade or so, ionic liquids (molten salts liquid at/or near room temperature) as potential environmentally friendly solvents have been able to gather widespread interest and curiosity from the scientific and engineering community. The number of research publications on investigations of ionic liquids for properties, analysis, and applications has increased exponentially. Almost every named synthesis and many more organic/inorganic/organometallic reactions have been reported in ILs.[1] Effective, and in some cases unique, utilization of ILs as solvents has been demonstrated in a variety of techniques in electroanalysis, separation, spectrometry, and sensing. Nevertheless, thought not reported explicitly, certain drawbacks have also emerged from the aforementioned detailed investigations with ILs; perhaps, the *limited* solubility of a fairly large number of common solutes, including metal salts, [2] or the effects that traces of impurities present in ILs can have on the behavior of many reactions. Alkyl substituted imidazolium, pyridinium and pyrrolinium cations are the most investigated positive components of ILs, generally associated to anions such tetrafluoroborate, hexafluorophosphate and bistriflimide. More recent data have however shown that functionalized ionic liquids (ILs) are able to overcome at least some of the above mentioned weaknesses, offering new possibilities for application in organic synthesis and catalyzed processes. The performance of these systems as solvents and/or catalysts largely depends on cation and anion structure and liquid-state organization.

In this communication, several examples of functionalized ILs will be reported and their properties discussed to highlight the main peculiarities which can be fundamental for a rational design and development of new improved ionic media and catalysts.

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ORG/GC-OR-01 Biomass as Green Alternative for Chemicals and Energy Supply

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Obtaining chemicals from renewable material is of growing importance in facing environmental concerns over fossil fuels consumption. Aquatic and terrestrial biomasses are the main renewable resources available for the supply of both energy and chemical compounds. We have recently developed novel procedures aimed to afford either biofuels or high-value chemicals from biomass. The former goal was achieved through a new improved route to extract biofuels from terrestrial and aquatic vegetables. The latter goal was achieved through the exploitations of some chemicals and materials deriving from the pyrolytic treatment of terrestrial biomass. Levoglucosan is the major product from the pyrolysis of cellulose. We have developed a method for the selective enzymatic acylation of levoglucosan in good yields using both long and short chain vinyl esters and carboxylic acids in green solvents: CH_3CN, a traditional solvent with low ecotoxicity, and room temperature ionic liquids (RTILs). 4-*O*-dodecanoyl levoglucosan, prepared by our route, has shown interesting tensioactive properties [1]. Furfural is a cheap chemical, industrially obtained from the acidic treatment of lignocellulosic raw materials or from the pyrolysis of wood and cellulose. Here furfural has been used as building block for the synthesis of a class of furan-containing quaternary ammonium salts, whose application can be envisioned in the fields of ionic liquid solvents, surfactants or biocides in analogy with benzyl quaternary ammonium salts [2]. Molasses is the viscous by-product of the processing of sugar cane or sugar beets into sugar; from the pyrolysis of molasses we have obtained a porous graphite-reach char which was treated with sulfuric acid to give a stable solid containing a high density of active acidic sites ($-SO_3H$). This catalyst was proved to be more active than conventional solid acid catalyst in several reactions including the esterification of fatty acids. Microalgae are a very attractive source of biofuels, above all because most of them are highly rich in lipids. We have developed a new green procedure to extract the oil from microalgae by using switchable polarity solvents SPS, a new class of liquids that can be turned from a non-ionic form to an ionic liquid, simply by bubbling CO_2 and reconverting the non-ionic form by the addition of N_2. Lipid extraction was carried out with a 1,8-diazabicyclo-[5.4.0]-undec-7-ene (DBU)/alcohol 1:1 mixture under neutral or basic conditions; then, the introduction of CO_2 switched the solvent to the ionic form allowing the separation of the lipid phase. The final bubbling of N_2 reverted the solvent to the non-ionic form, ensuring a full recyclability of both DBU and alcohol components[3].

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ORG/GC-OR-02 New Ecofriendly Improvements in the Synthesis of Nitro Compounds

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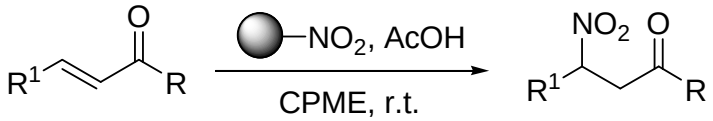
Nitroalkanes are one of the most fundamental classes of substrates in organic chemistry.[1] This is mainly due to the fact that (i) they allow the easy formation of new carbon-carbon and carbon-heteroatom bonds under very mild reaction conditions,[2,3] (ii) the nitro group can be converted into a plethora of other functionalities,[4] and (iii) they are the key starting material for the preparation of a variety of fine chemicals.[5] Thus, the easy accessibility to nitroalkanes remains an important goal, especially for those functionalized ones.[6] In this context, -nitro ketones **2**, or their protected ones, are important starting materials in organic synthesis, but the classical procedures for their preparations still present important drawbacks from the eco-sustainability point of view. In order to circumvent these problems and based on our experiences, we have now developed an improved eco-friendly, general procedure for the nitration of conjugated enones **1**, under solid supported reagents (SSR) (Figure 1).

Figure 1



1 **2**

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ORG/GC-OR-03 New frontiers in heterogeneous catalysis: synthesis, applications and perspectives of MCM-Er(III) materials.

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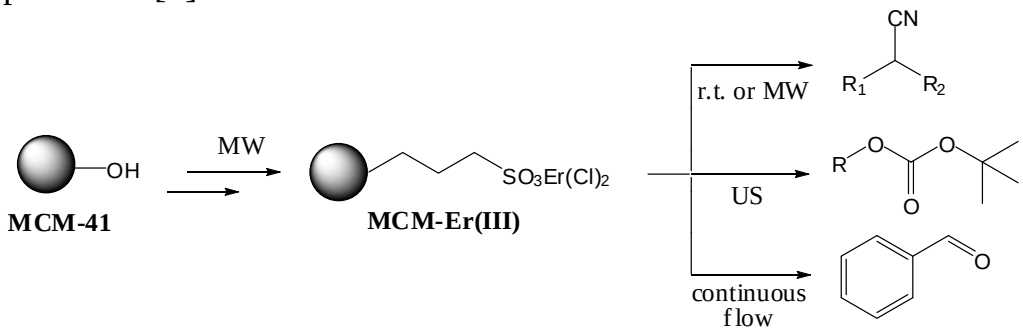
Since the idea of a sustainable chemistry became an urgency for the scientific community, an exponential increasing in the use of heterogeneous recoverable catalysts was registered. Mesoporous silica (MCM) have played a prominent role as inert supporting materials in this field, because of their high specific surface areas, their large pore size and their thermal and chemical stability.[1] The efficiency of non toxic Er(III) salts as Lewis acid catalysts in homogeneous phase was largely explored by our group. This work is focused on the realization and application of a new class of heterogeneous catalysts based on the Er(III) chemistry. The MW-assisted synthesis and characterization, the rationalization of the MW–effect on the system, the application of a new MCM-Er(III) catalyst under non-conventional synthetic methods as US, MW and continuous-flow conditions will be presented.[2]



The versatility and resistance of these supported materials justify the investment in terms of design of more complex catalytic systems. Therefore, preliminary results on the synthesis of a new heterogeneous bifunctional-asymmetric supported catalyst, will be discussed. The new system is characterized by the cooperation between a general Base and an Er(III) Lewis acid, grafted together on the silica surface.

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ORG/GC-OR-04 Greener approach to oxidation reactions with diluted H_2O_2 using continuous flow system

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One of the major challenges of green chemistry is, undoubtedly, the achievement of more environmentally friendly processes in organic synthesis. An important goal in this field is the development of cleaner and safer synthesis routes for oxidation reactions.[1]

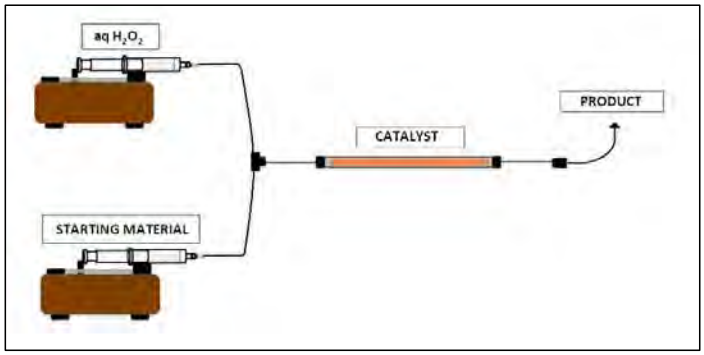

Figure 1

Hence, in the last decades many studies have been devoted to replace common oxidants with aqueous hydrogen peroxide,[2] which is a cheap, mild and environmentally benign reagent since water is formed as the only by-product. Furthermore, continuous processing of catalytic reactions offers significant improvements compared to conventional batch processes due to a precise control of residence time, heat and mass transport.[3]
Here we report two very highly chemoselective oxidation reactions carried out with diluted H_2O_2, and catalyzed by sulfonic resin Amberlite IR-120H, in continuous flow reactors (Figure 1).
Concerning the thioanisole oxidation,[4] by performing the reaction at 22 °C with a stoichiometric amount of 3% aqueous H_2O_2 at a residence time of 25 minutes, methylphenylsulfoxide has been obtained in 90% yield and 100% selectivity. The catalyst can be used for at least 3,000 minutes without any loss of activity. Similar excellent results have been achieved with different aryl alkyl sulfides.
A similar system was developed for the oxidation of methylhydroquinone to the corresponding methylbenzoquinone with 30% aqueous H_2O_2. A mixture of methylhydroquinone and hydrogen peroxide in methanol was passed through the reactor for 360 minutes obtaining the product in 59% yield and 95% selectivity.

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INO/OM-KN-01 Metal-coordinated carbenes: reactive species or robust ligands?

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Transition metal carbene complexes have been mainly considered reactive intermediates in several catalytic organic transformations, like for example, the reactions involving the decomposition of diazo compounds (cyclopropanations, C-H insertions, C-C coupling) [1].
However, since the discovery of stable imidazol-2-ylidenes, which were first isolated by Arduengo *et al.* in 1991, much interest has been growing in the chemistry of N-heterocyclic carbenes (NHCs) [2]; in fact, these resulted to be excellent ligands towards transition metal centres both in low and medium-high oxidation state, allowing the synthesis of robust catalysts with negligible carbene dissociation, stable in acidic and oxidative environment.

The dual nature of carbenes can be illustrated by selected examples taken from our recent results involving:
A) reactions of reactive carbene intermediates such as i) insertion of carbenes into C=C, C-H and O-H bonds catalysed by Pt(II) and Rh(II) complexes; ii) reaction of diazo derivatives in presence of olefins to give metathesis and cyclopropanation products catalysed by [RuCl(Cp)(COD)] [3];
B) synthesis of novel di- and tricarbene Pd(II), Pt(II), Cu(I), Ag(I), Au(III) complexes and applications as catalysts in i) Heck reaction, ii) selective hydroarylation of olefins, iii) Ullmann-type arylation [4].
The obtained results show the extraordinary flexibility of the carbene mojety and fully justifies the strong research efforts on this still new and fascinating chemistry.

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INO/OM-KN-02 Stereoselective Gold Catalysis: New Opportunities in Organic Synthesis

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The re-discovery of homogeneous gold(I) catalysis has recently revolutionized the whole organic synthesis scenario, opening up access to unprecedented synthetic manipulations of unfunctionalized unsaturated hydrocarbons under mild and environmental acceptable conditions.[1] At the same time, new opportunities were also created in the "crowded" area of asymmetric catalysis, providing reliable solutions to the preparation of enantiomerically enriched polyfunctionalized molecular architectures in the presence of chiral gold(I) complexes.[2]

In conjunction with our ongoing interests oriented to the catalytic enantioselective decoration of arenes,[3] we have recently reported on the effective gold-mediated direct electrophilic activation of allylic alcohols,[4] in the preparation of functionalized heterocyclic compounds (*i.e. morpholines, indolines, carbazoles*).[5] This consolidated background, along with the use of propargylic alcohols in gold-catalyzed cascade cyclization reactions[6] concur to define new guidelines in organometallic synthesis under noble metal assistance.

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INO/OM-OR-01 Pd/Ln_xO_y (Ln = La, Ce, Pr, Sm, Gd, Dy and Yb): Efficient Precatalysts for a Fast and Green Suzuki-Miyaura Reaction

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In the last two decades, the Pd-catalyzed C-C bond formation has emerged as an outstanding strategy for building more or less complex organic molecules. Of the commonly used reactions, the Suzuki-Miyaura (SM) coupling has been proven to be the most useful and widely applied [1]. Our efforts have been mainly devoted to the development of new Pd-based catalysts that can efficiently promote the SM reaction in mild and green conditions. The focus of interest is: i) use of safe solvents, ii) room temperature catalysis, iii) reusability of the catalytic system.
In recent work from our group, the Pd/CeO_2 system was found to show very good activity for the SM coupling in water/ethanol mixtures at room temperature [2]. We demonstrated that the "heterogeneous" Pd-containing precatalyst acts as "releaser" of "homeopathic" amounts of a catalytically active soluble form of Pd. Furthermore, we succeeded in recycling the Pd/CeO_2 precatalyst at least ten times without a marked decrease of catalytic activity.
The present work is an extension of the study to different Pd/Ln_xO_y catalyst precursors (Ln = La, Pr, Sm, Gd, Dy and Yb). Interestingly, all novel catalytic systems showed an activity much higher than that exhibited by Pd/CeO_2. The reusability of all precatalysts is also good, in particular for Pd/Sm_2O_3.
Current studies are focused on assessing some crucial features of the mechanism of formation of the "true" catalyst. In particular, the higher catalytic activity of Pd/Ln_2O_3 with respect to Pd/CeO_2 seems to be related to the easier release of Pd particles from the surface of the former precatalyst.

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INO/OM-OR-02 New tetracene based materials for organic electronics: organometallic approach to their synthesis.

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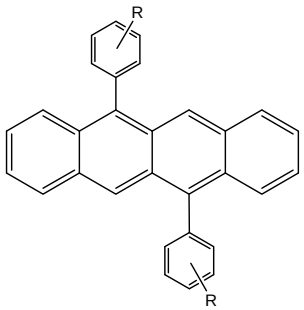
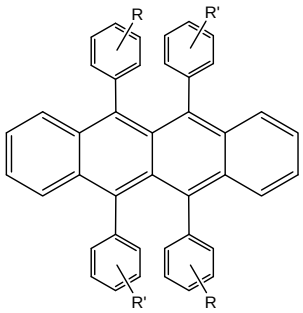
Acene-based organic semiconductors, thanks to their outstanding properties and their good processability, are key molecular materials for the development of organic electronics and derivatives of tetracene represent those where a good compromise between environmental stability and charge transport solid state properties is realised. Among tetracene-based systems, rubrene (5,6,11,12-tetraphenyl-tetracene) showed exceptional high charge carrier mobilities in Organic Field Effect Transistors (OFET) built on single crystals[1] and now represents the state of the art for molecular organic semiconductors.
It is noteworthy that, despite the peculiar and interesting properties of aryl-substituted-tetracenes, few synthetic routes are available (mostly tedious multi steps procedures) and relatively limited examples of molecules belonging to this series are known. This should urge on the organic chemist community to develop synthetic strategies to access to new organic semiconductors belonging to this class with improved transport properties, stability and processability. In principle, these properties (stability against photo-oxidation, solubility and charge carrier mobility) can be optimized by proper chemical modifications both on the tetracene core and on the aryl-substituents and transition metal-catalyzed processes are, from this point of view, particularly appealing both to improve the efficiency and to shorten the synthetic procedures.



5,11-diaryl-tetracenes



5,6,1,11,12-tetraaryl-tetracenes

Here we present our advances on the synthesis of new diaryl- and tetraaryl tetracenes where Pd-mediated cross-coupling reactions represent the key tools both to access to these systems and to prepare strategic precursors. In particular the synthesis of 1,1,3-triaryl-substituted propargyl alcohols, key intermediate for the synthesis of 5,6,11,12 tetra-aryl-substituted tetracenes (Rubrene-like systems) by

copper-free Sonogashira protocol along with their evolution into rubrenes will be described.[2] A new protocol for the preparation of 5,11-diaryl-substituted tetracenes by Suzuki-based cross-coupling reaction from 5,11-di bromo- tetracene in liquid ionic will be also presented.[3] Some properties of the new tetracenes will be discussed.

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INO/OM-OR-03 Organometallic Fuel Cell development: the combined effect of molecular architecture with an high surface area carbon support

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The selective and simultaneous conversion of alcohols and sugars into energy and chemicals is a target of primary importance for the sustainable development. Two established types of fuel cells operating in alkaline media can convert the free energy of alcohols ($R\text{-}CH_2\text{-}OH$) into electrical energy and the corresponding carboxylate product: the direct alcohol fuel cell (DAFC), based on feasible metal electrocatalyst for alcohol oxidation [1] and the enzymatic biofuel cell (EBFC) that utilizes oxidation enzymes such as dehydrogenases in conjunction with an electron transfer mediator [2]. From a mechanistic viewpoint, the conversion of ethanol into energy and acetate resembles the process occurring in a biofuel cell where the electrocatalytic system consists of alcohol- and aldehyde-deydrogenases in combination with a hydrogen/electron transfer mediator. Recently, we introduced a third type of fuel cell operating in alkaline media where the anode catalyst is *a molecular metal complex*. We showed that in this device, named "organometallic fuel cell (OMFC)" a molecular rhodium complex is capable of evolving through fast chemical equilibria in the course of the catalytic cycle to form a specific catalyst for alcohol dehydrogenation, a specific catalyst for aldehyde dehydrogenation and a specific catalyst for the H/electron-transfer [3]. From a practical perspective, a molecular metal complex, soluble in different solvents and hence easily dispersible on very small surfaces, but capable of delivering high power densities upon oxidation of alcohols and sugars, paves the way to the further miniaturization of fuel cells for biological applications as well as biosensors. The combination of *well-defined molecular architecture* with a *matching support* (high surface area carbon black types) might allow for the selective oxidation of polyalcohols into valuable chemicals under waste-free conditions which is hardly achievable by traditional methods.

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INO/OM-OR-04 Microwave-Assisted Aminocarbonylation of Ynamides using catalytic $Fe_3(CO)_{12}$ at Low Pressure of Carbon Monoxide

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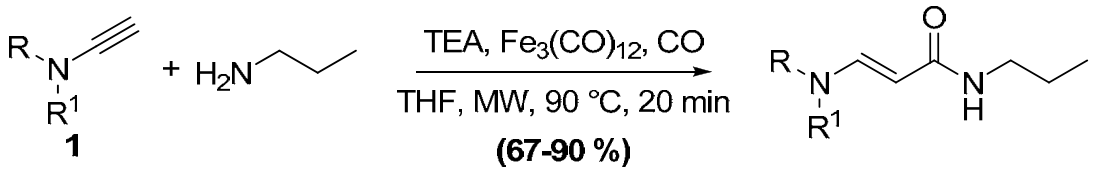
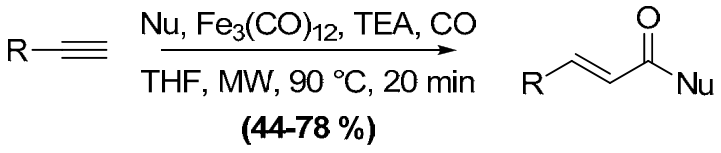
Carbonylation is a wideley applied atom economic reaction providing esters, ketons, carboxylic acids, amides and heterocyclic compounds.[1] Several procedures for the carbonylation of alkene and alkyne derivatives with different catalysts have been investigated but only few reports investigate the use of iron as the catalyst.[2] Iron carbonyl complexes have been increasingly used in organic synthesis in recent years and iron catalysis represents a promising area in the homogeneous catalysis.
Beside our interest on new ecofriendly catalysts for microwave assisted carbonylation reactions using carbon monoxide as a bening source of C, a microwave-assisted procedure for the iron catalyzed carbonylation of ynamides and terminal alkynes was developped.[3]
Starting from ynamides **1** a new class of *E*-acrylamides has been regioselectively synthesized after irradiation with microwaves for only 20 minutes at low pressure of CO (1.3 bar) using $Fe_3(CO)$ and TEA as the catalyst precursors (Scheme 1).



Scheme 1

The same procedure can be easily applied to terminal alkynes giving regioselectively *E*-acryl- and cinnamides. Using alcohols or thiols as nucleophiles *E*-acrylesters and thioesters are obtained in good yields as well (Scheme 2).



Scheme 2

The building blocks obtained by this atomeconomic process are key intermediates in the synthesis of natural products and small bioactive molecules.

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ORG/OM-IL-01 Metal Nanoparticles as Efficient Catalysts in Green Chemistry

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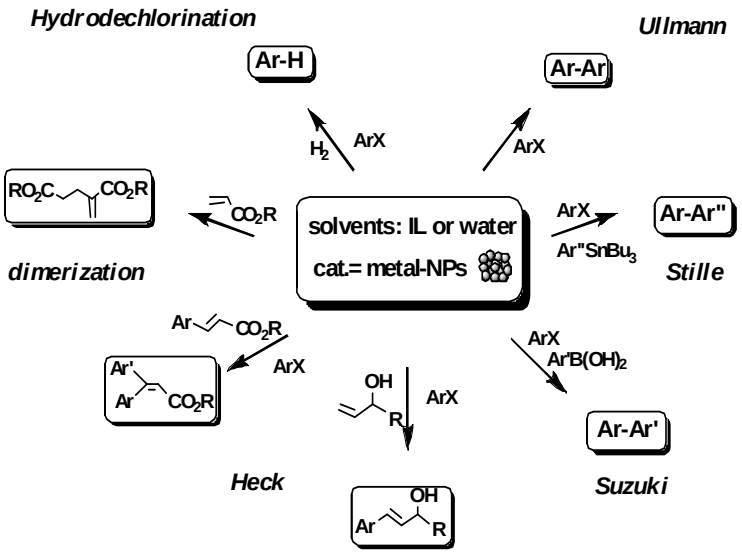
Transition-metal nanoparticles (NPs) are attracting a great deal of attention in almost any scientific and technological field, including catalysis, where nanoscale materials are becoming more prevalent in a wide range of applications such as fuel conversion, pollution abatement and fine chemical production.[1]
An increasing interest is also devoted nowadays to properly exploit the high activity and selectivity of nanocatalysts in order to develop greener and waste-minimized processes. From the Green Chemistry standpoint, new nanocatalysts must be designed to operate under environmentally friendly (for instance phosphine-free) conditions or in neoteric green solvents (e.g. ionic liquids, supercritical fluids, fluorous phases, water and so on).[2]



In this context, during the last decade, we exploited the use of nanostructured metal catalysts based on palladium, copper, and gold, to perform a wide range of C-C bond forming reactions, like for example Heck, Suzuki, Stille, acrylate dimerization, and Ullmann couplings, using tetraalkylammonium ionic liquids and water as green reaction media.[3]

This communication deals with our recent advances in controlling the catalyst performances by choosing appropriately the nature of the ionic liquid or the aqueous medium.

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ORG/OM-IL-02 The Amination of Hydrocarbons Catalysed by Ruthenium Porphyrin Complexes. A Mechanistic Investigation.

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The direct amination of hydrocarbons is a reaction of great synthetic interest due to the biological and pharmaceutical importance of aza-derivatives. We have focused our interest on this class of transformations for ten years using aryl azides as nitrogen sources and metallo porphyrins as catalysts [1]. More recently, we have investigated the catalytic activity of Ru(TPP)CO in C-H bonds aminations and we have isolated and characterised the active bis-imido intermediate Ru(TPP)$(NAr)_2$ (Ar = 3,5-$(CF_3)_2C_6H_3$) (**1**) [2].
To propose a general mechanism for the reaction we have investigated the reactivity of Ru(TPP)CO (**2**) towards several aryl azides, discovering that the nature of the active intermediate strongly depends on the electronic nature of the employed azide. The replacement of 3,5-$(CF_3)_2C_6H_3N_3$ with 4-$CF_3C_6H_4N_3$ in the reaction with Ru(TPP)CO allowed the isolation of the mono-imido complex Ru(TPP)(NAr)CO (Ar = 4-$(CF_3)_2C_6H_4$) (**3**) that showed a good catalytic activity in hydrocarbon aminations. On the other hand, the reaction of Ru(TPP)CO with an aryl azide bearing an electron donating group, 4-^{t}Bu$C_6H_4N_3$, gave a very unstable imido complex (**4**). Complex **4** has been detected by NMR and it rapidly decomposed to the mono-amino compound Ru(TPP)(NH_2Ar)CO (Ar = 4-^{t}BuC_6H_4) (**5**) that was isolated and characterised.

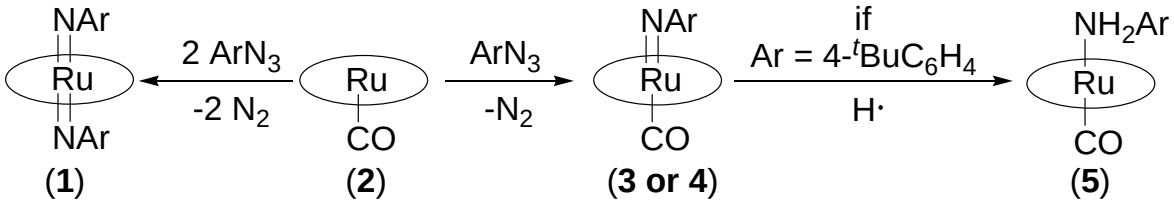

Figure 1

A kinetic study has been also performed to better rationalise the dependence of the reaction mechanism on the nature of the organic azide.

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ORG/OM-OR-01 Cationic Olefin Complexes of Platinum(II): from the Well Established to New Perspectives

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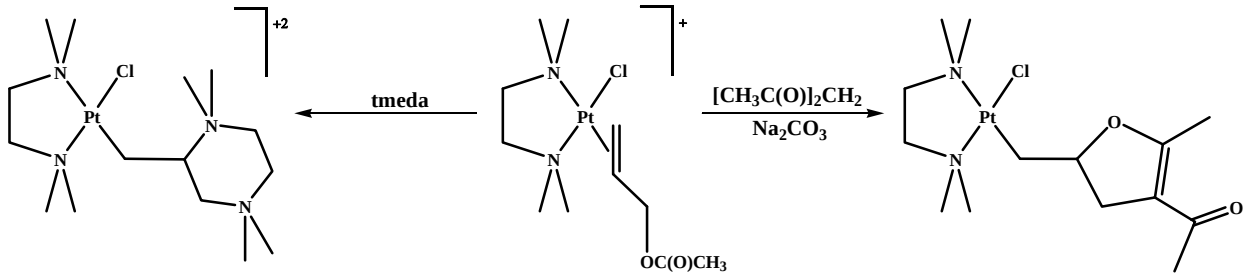
After our first report concerning the complex [PtCl(^{2}-C_2H_4)(N-N)]$^+$, **1**, (N-N = *N*,*N*,*N'*,*N'*-tetramethylethanediamine, tmeda) [1] many properties of this type of species have been clarified.

The obtainment of **1** (the prototype of stable cationic platinum complexes which can contain olefins different from ethene) was a clear experimental proof of the -donating properties of olefins, which could give stable complexes also in the absence of relevant -back-donation from the metal to the unsaturated ligand.

The coordinated olefin is endowed with a good degree of electrophilicity [2] and, in the case of olefins higher than ethene, it can also exhibit Brönsted acidity [3]. Deprotonation can eventually prevail over nucleophilic addition [4].

The dinitrogen ancillary ligand plays an important role in tuning the properties of the complexes; in particular, when tmeda is replaced by an aromatic diimine, the metal becomes more electrophilic and it can compete with the olefin in the reaction with soft nucleophiles [5].

In cationic complexes with allyl acetate, [$PtCl_2$(^{2}-CH_2=$CHCH_2OC(O)CH_3$)(N-N)]$^+$, two reactive sites are present in the coordinated olefin: the allylic carbon and the C=C double bond. Nucleophiles first replace the acetato group and then add to the olefinic bond. In the case of bidentate nucleophiles a heterocycle is built up in the near proximity of the coordination sphere (see Scheme). When the two donor atoms are different, because of the two consecutive reaction steps, only one of the possible isomers is formed.



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ORG/OM-OR-02 Sustainable Oxidations with Tailored Molecular Metal Oxides: Bridging the Gap between Homogeneous and Heterogeneous Catalysis

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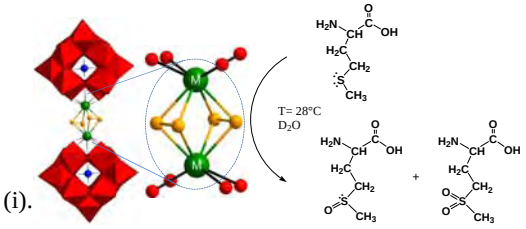
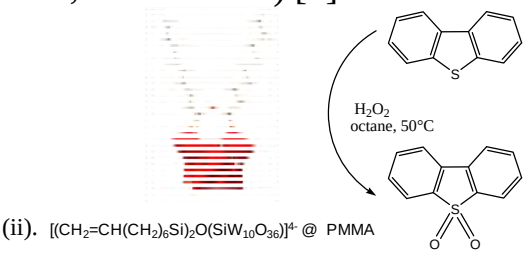
Polyoxometalates (POMs) have been proposed as the homogeneous models of solid metal oxides. Their success of as oxidation catalysts is based on their multi-metallic composition, which is pivotal to access diverse mechanistic pathways and an enhanced stability. The presence of d^0 metals, in particular, can be exploited to activate the non-waste producing oxidant H_2O_2. We present herein two promising strategies to design innovative and sustainable oxidative processes with H_2O_2, involving the use of transition metal substituted POMs (TMSPs) and hybrid organic-inorganic POMs.

(i) The molecular structure of TMSPs, featuring well defined catalytic sites, may be very convenient to study the mechanism and to tune their reactivity. Stable dimeric POM structures containing 4th group transition metals as Zr^{IV} or Hf^{IV}, in particular, form peroxometal-butterflies as active species. They have been used in water to oxidize *L*-methionine (70-99% yields in 20-48 h, at r.t.) and benzyl alcohols (50 min, under MW assisted activation, T_{bulk}=90°C, TOF= 75 h^{-1}) [1].





(ii) Covalent grafting of organic moieties on POMs may implement affinity towards different media, as well as immobilization strategies [2]. POMs functionalized with unsaturated alkyl chains have been used as monomers to prepare methacrylate-based copolymers, by means of radical polymerization. The heterogeneous catalytic material has been used to model a fuel desulfurization process: in octane, dibenzothiophene has been quantitatively converted to the corresponding sulfone in 4h (TOF= 18 h^{-1}).

[1] a) S. S. Mal, N. H. Nsouli, M. Carraro, A. Sartorel, G. Scorrano, H. Oelrich, L. Walder, M. Bonchio, U. Kortz *Inorg. Chem.* 49, **2010**, 7; b) M. Carraro, N. H. Nsouli, H. Oelrich, A. Sartorel, A. Sorarù, S. S. Mal, G. Scorrano, L. Walder, U. Kortz, M. Bonchio *Chem. Eur. J.* **2011**, in press.

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ORG/OM-OR-03 Evaluation of counterion and solvent effect in the single insertion of olefin into the Zr-C bond by low-temperature NMR kinetic studies

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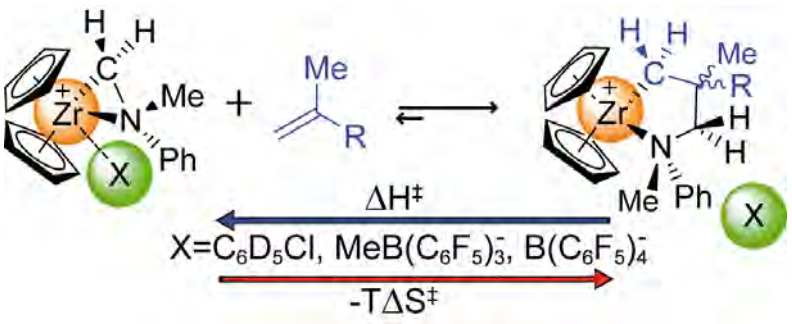
The insertion of olefin into the metal-carbon bond is the elemental step of the Ziegler-Natta catalysis that, in the homogeneous phase, occurs through the initial association of the olefin with the metal cation of the catalytic ion pair. Group IV metallocenium ion pairs polymerize olefins with high rates, but the elevate reactivity of such systems dramatically complicates fundamental kinetic investigations. During our studies on the self-aggregation of zirconocenium ion pairs [1,2], we synthesized some zirconazidirines having ($[Cp_2Zr(\ ^2\text{-}CH_2\text{-}NR_1R_2)][X]$ as general formula that show some remarkable requisites to be used as good models for investigating the single insertion of olefin into the Zr-C bond. In particular, they are able to react stoichiometrically with olefins leading to a five-membered azametallacycle, as represented in figure.



With the aim of obtaining thermodynamic activation parameters of the single insertion and determining as they depend on nature of counterion and solvent, low-temperature kinetic NMR studies of the reaction of 2-methyl-1-heptene with $[Cp_2Zr(\ ^2\text{-}CH_2\text{-}NMePh)][X]$ [**1a**:X^-=$MeB(C_6F_5)_3^-$; **1b**:$B(C_6F_5)_4^-$] ion pairs were performed. Results indicate that, in toluene, $H^{\ddagger}$ is higher for $MeB(C_6F_5)_3^-$ than for $B(C_6F_5)_4^-$ ($H^{\ddagger}$=-4.5 kcal mol^{-1}) but the former better compensates the loss of entropy caused by olefin association ($S^{\ddagger}$=-13 cal mol^{-1} K^{-1}). The two ion pairs **1a-b** behave exactly the same in a toluene/chlorobenzene mixture due to the coordination of a chlorobenzene molecule at the zirconium center that pushes the counterion in the second coordination sphere. $H^{\ddagger}$ (ca 11 kcal mol^{-1}) is higher than in toluene ($H^{\ddagger}$=8.5 kcal mol^{-1} and $H^{\ddagger}$=4.0 kcal mol^{-1} for **1a** and **1b**, respectively) while $S^{\ddagger}$ (ca -26 cal mol^{-1} K^{-1}) is similar to that of **1a** in toluene ($S^{\ddagger}$=-32 cal mol^{-1} K^{-1}).

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ORG/OM-OR-04 Synthesis and application of Tetraferrocenylporphyrins as sensitive materials in photoelectrochemical devices

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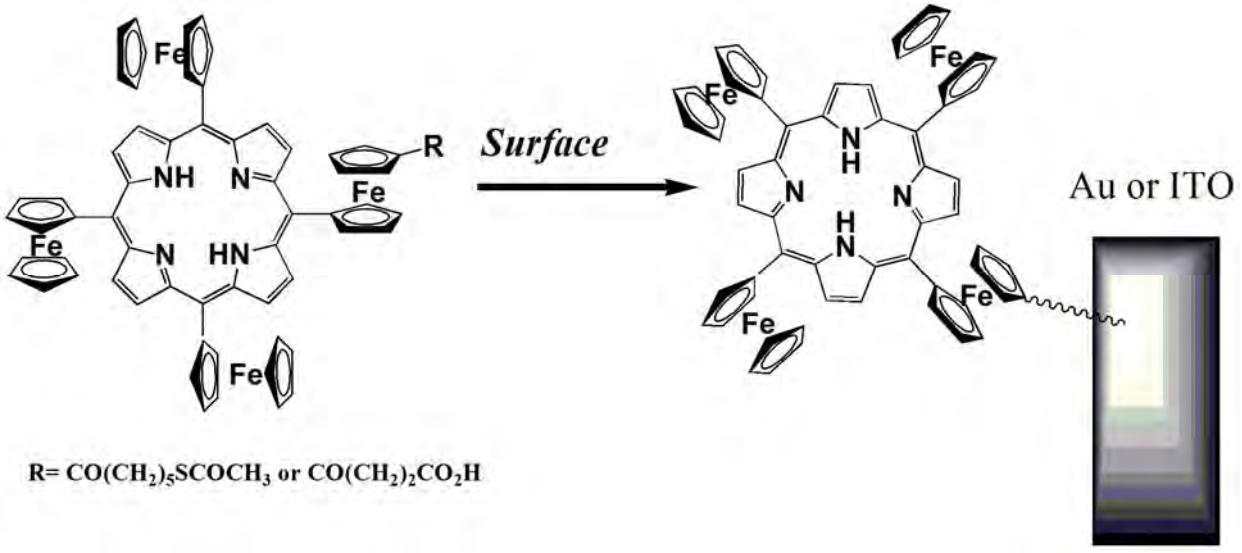
5,10,15,20-tetraferrocenylporphyrins have been object of our interest in different application such as electron transfer reactions [1], mixed-valence states [2], multiredox processes and long-range electronic internal communication [3]. These properties make them suitable for the construction of photochemical devices.

New tetraferrocenylporphyrins containing one functionalized ferrocenyl group were synthetized with the aim to link these molecules on surfaces. A chain with a terminal thioacetate or carboxylic acid was used to obtain functionalized Au or ITO surfaces.



The obtained monolayers were characterized by Uv-vis and electrochemical techniques and used in photoelectrochemical cells. Promising results in terms of photocurrent vs applied potential was obtained and will be discussed in connection with the surface-potential-experimental conditions set.

[1] P. Galloni, B. Floris, L. De Cola, E. Cecchetto, R. M. Williams, *J. Phys. Chem. C* **2007**, *111*, 1517.

[2] V. N. Nemykin, G. T. Rohde, C. D. Barrett, R. G. Hadt, C. Bizzarri, P. Galloni, B. Floris, I. Nowik, R. H. Herber, A. G. Marrani, R. Zanoni, N. M. Loim, *J. Am. Chem. Soc.*, **2009**, *131*, 14969.

[3] V. N. Nemykin, G. T. Rohde, C. D. Barrett, R. G. Hadt, J. R. Sabin, G. Reina, P.Galloni, B.Floris *Inorg. Chem*. **2010**, *49*, 7497.

ORG-FP-01 Ionic tags effect on organic catalyst reactivity

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The insertion of a suitably designed ionic group (tag) in the structure of known catalysts and organocatalysts (Figure 1), allows to obtain two main advantages. The ionic group confers to the molecule a particular solubility profile and so it becomes possible exploit liquid-liquid biphasic reaction condition techniques, where the typical benefits of homogeneous catalysis are combined with the easier procedures for catalyst recovery, typical of heterogeneous catalysis.[1]

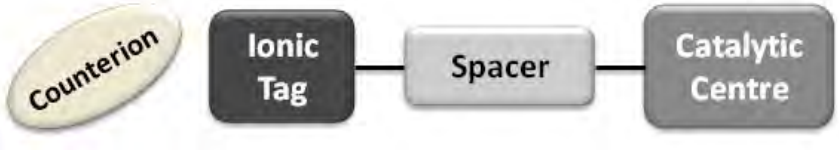
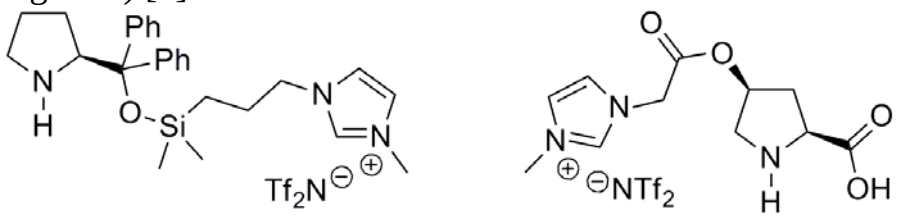


Figure 1

Moreover, catalysts with ionic tags often show an increase of the catalytic performances compared to the equivalent non-ionic catalysts from which they derive.[2] Remarkable activation effects were obtained in the organocatalytic addition reactions of aldehydes to nitroalkenes using catalyst **A** (Figure 2)[3] and in organocatalytic cross-aldol condensations between ketones and aldehydes using catalyst **B** (Figure 2).[4]



A: Michael additions ***B: cross-aldol reactions***

Figure 2

Here the most recent results aimed at rationalizing the effects conferred to reactivity by the presence of ionic tags will be presented, with special attention to the case of organocatalytic enantioselective cross-aldol reactions.

[1] M. Lombardo, C. Trombini, *Synlett* **2010**, 1746-1765.
[2] M. Lombardo, C. Trombini, *Chem. Cat. Chem.* **2010**, *2*, 135-145.
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[4] M. Lombardo, S. Easwar, F. Pasi, C. Trombini, *Adv. Synth. Catal.* **2009**, *351*, 276-282.

ORG-FP-02 Novel and Efficient $CeCl_3 \cdot 7H_2O$/NaI-Catalyzed Sulfenylation of Indoles and Pyrroles

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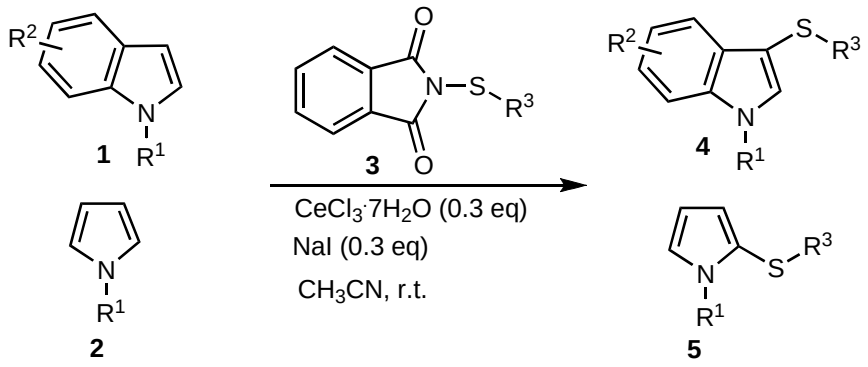
The preparation and manipulation of functionalized low molecular weight heteroaromatic compounds is of increasing importance for obtaining new more potent pharmaceuticals [1]. In particular, 3-sulfenyl indoles (**4**) and 2-sulfenyl pyrrole (**5**) are an important class of compounds due their activity towards the treatment of several deseases [2], and as inhibitors in medicinal chemistry [3]. Most of methods for their preparation are based on electrophilic aromatic sulfenylation, but a considerable number of them have been unsatisfactory because the procedures provide low yields of the desired products, and/or require harsh conditions that are incompatible with sensitive functional groups [4]. In the framework of our ongoing program in the development of Lewis acid-catalyzed reactions by $CeCl_3$ [5], we have developed a new general and efficient methodology for the sulfenylation of indoles **1** and pyrroles **2** by N-(alkylthio)- and N-(arylthio)phthalimides (**3**) in the presence of our combination $CeCl_3 \cdot 7H_2O$/NaI.



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ORG-FP-03 On the phytotoxins produced by *Diplodia cupressi*, pathogenic fungus of cypress

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The fungi associated with different forms canker disease of the Italian cypress (*Cupressus sempervirens* L.) and other species of *Cupressus* in the Mediterranean area belong to the genera *Diplodia*, *Pestalotiopsis*, and *Seiridium*. They cause heavy losses in cypress plantations within forestry and ornamental uses, thus altering of the typical landscapes, and noteworthy loss in the nursery industry. *Diplodia cupressi* produced all known sphaeropsidins A-F along with sphaeropsidones (**1** and **2**) and chlorosphaeropsidone and its 6-epimer (**3** and **4**) [1]. Only preliminary phytotoxic and antifungal activities were investigated for sphaeropsidones due to their limited amount isolated from the fungal culture filtrates.

Recently, a CBS strain of *D. cupressi*, that appeared to be a good producer of both sphaeropsidone and *epi*-sphaeropsidone, yielded adequate amounts of **1**-**4** to determine, by a X-ray diffratometric analysis, the relative configuration of **1** and therefore that of **2**-**4** and to prepare eight key derivatives to carry out a structure-activity relationships study assaying their phytotoxic and antifungal activities.

In this communication will be illustrated the results obtained in the SAR study in order not only to understand their mechanism of action on plants and their true role in pathogenesis, but also to generate new compounds with potential application as fungicides in agriculture.

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ORG-FP-04 Synthesis of functionalized olefins for the preparation of polymeric additives for food packaging

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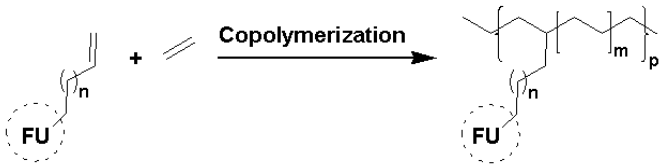
Polyolefins are the plastics most frequently used as food contact materials due to their low cost and low reactivity. However, polyolefins are quite sensitive to oxidation and require to be stabilized by blending with antioxidant additives to inhibit or retard oxidative degradation. The vast majority of commercial available antioxidants are low molecular weight derivatives of sterically hindered monohydroxy phenols. Since their chemical structure is quite different from that of the non polar polymer matrix, two problems can be envisaged: i) the poor solubility of the antioxidants into the polyolefin matrix, which can induce aggregation of the stabilizers and an inhomogeneous distribution; ii) the mobility and volatility of the antioxidants, that can lead to their loss by migration or diffusion from the polyolefin matrix.

Aim of this project is the synthesis of functionalized olefins bearing an antioxidant and/or a HALS (Hindered Amine Light Stabilizers) Functional Unit (**FU**) moiety separated from the double bond by methylene spacers of different lengths. These monomers can be employed as comonomers with ethylene (or propylene) to obtain very stable and solid macromolecular additives where the stabilizers **FU**s are covalently bonded to the polymeric chains. Such macromolecular additives are, in turn, used as masterbatch for the preparation of non-releasing polymeric films for food packaging [2].



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ORG-FP-05 Synthesis and self-organization of novel bock co-polymers for water filtration

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Water channel proteins (**WCP**) are a particular class of transmembrane proteins embedded in the cell membrane that regulate the flow of water and thus the osmotic pressure inside the cell.[1] These proteins can be extracted from living cell or expressly synthesized and incorporated in liable synthetic vesicles or liposomes keeping their activity. More recently water channel protein (also known as Aquaporin) have been incorporated in very stable synthetic block co-polymers opening to the realization of free standing films for water filtration.[2]
For practical application a particularly high fraction of **WCP** have to be functionally incorporated into the synthetic membrane and this depends on the nature of the copolymer used (chemical composition, on structural rigidity).
In this framework, we report the synthesis and characterization of novel poly(methyloxiazoline)block(polydimethyl siloxane)block(polymethyl oxiazoline) co-polymers incorporating rigid and fluorescent perilene diimide units inside the apolar block that offer the possibility to follow their self-aggregation in solution by simple optical spectroscopy techniques.
On the other hand the presence of rigid planar units into the flexible PDMS apolar block offers the chance to study the possible interaction when **WCP** are functionally incorporated.

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ORG-FP-06 Scalable *in situ* diazomethane generation in continuous-flow reactors

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Diazomethane is a highly reactive and selective reagent for the synthesis of pharmaceuticals and fine chemicals [1]. However, its acute toxicity and explosive characteristics strongly discourage a large-scale use in synthesis.

In this communication we report an optimized continuous generation of diazomethane through the base-induced decomposition of the precursor N-methyl-N-nitrosourea which is safer to store than other diazomethane precursors. Process scale-up was quickly and efficiently achieved on a modular continuous-flow platform that allowed the production and use of diazomethane up to 19 mol d^{-1} at a total flow rate of 53 ml min^{-1}, while maintaining the amount of diazomethane itself in the reactor limited to 6.5 mmol. This process productivity could, at least in principle, fulfill the needs of small pharma or fine chemical companies. Best reaction parameters were first developed on a small-volume flow reactor (0.9-1.35 ml) for minimal reagents consumption. Then a 10-folds production improvement was achieved by increasing the flow reactor dimensions (15-25 ml) with a very limited optimization effort.

In addition, hazardous diazo compounds produced in flow conditions were successfully used to prepare functionalized fullerenes with potential use as acceptor components in polymer-based solar cells.

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ORG-FP-07 Convenient synthetic approach to functionalized quinolines and 1,2,3,4-tetrahydrobenzo[*c*][2,7]naphtyridines

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Following our interest for the preparation of aromatic *ortho*-amino ketones, we reported a convenient photochemical access to this kind of useful molecules that cannot be readly available by a common synthetic strategy, requiring the use of drastic reaction conditions and/or the presence of toxic and expensive reagents. Ortho-amino ketones have been recently used for the synthesis of 1,4 benzodiazepines and quinazolines, [1] two important classes of organic scaffolds.
Hereby we reported the application of aromatic *ortho*-amino ketones for a convenient synthetic access to two more classes of interesting heterocyclic systems: quinolines and naphtyridines.
The former were obtained starting from aromatic anilides irradiated at 254 nm to give the correspondent *ortho*-amino ketones that were subsequently treated with dimethyl-acetylen-dicarboxylate (DMAD) to give the desired products in moderate to good yields. Quinoline is a common structural motif found in many natural products with remarkable pharmacological properties. Members of this family have wide applications in medicinal chemistry, being used as antimalarial (chloroquine and mefloquine), anti-inflammatory, antiasthmatic, antibacterial, and antihypertensive activities: hence continues to spur synthetic efforts regarding their acquisition.[2]
Benzo-condensed quinolines, with particular attention to benzo[*c*][2,7]-naphtyridines, have been recently considered for their wide range of biological activities such as inhibition of phosphoinositide-dependent protein kinase 1 (PDK-1) involved in the progression of some kinds of cancer, release of calcium, antiviral and antimicrobial activity and cytotoxicity. [3] They were obtained in excellent yields for treatment of some quinoline derivatives with potassium carbonate.

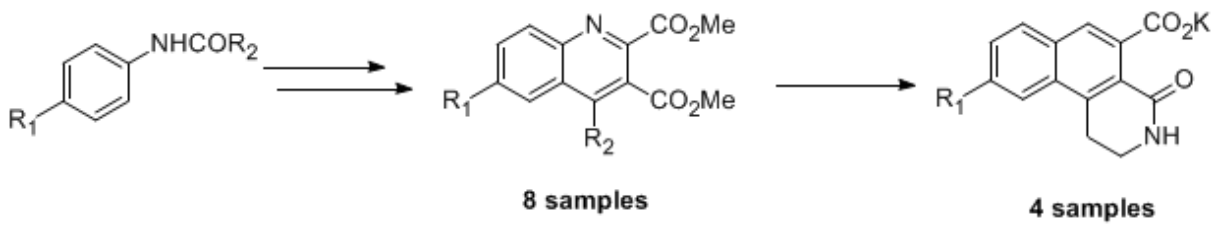

Figure 1.

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[3] a) P.K. Agarwal, S.K. Sharma, D. Sawant, B. Kundu, *Tetrahedron*, **2009**, *65*, 1153-1161. b) K. Kim, A. Wissner, M.B. Floyd Jr., H.L. Fraser, Y.D. Wang, R.G. Dushin, Y.Hu, A.Olland, B. Guo, K. Arndt, *Bioorg. Med. Chem. Lett.*, **2009**, *19*, 5225-5228 and references cited therein.

ORG-FP-08 Sequence Stereoisomerism in Calixarene-Based Pseudo[3]rotaxanes

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Very recently we reported that new pseudorotaxane systems can be easily obtained by the *through-the-annulus* threading [1] of scarcely efficient calix[6]arene hosts upon exploiting the inducing effect of the weakly coordinating tetrakis[3,5bis(trifluoromethyl)phenyl]borate (TFPB) anion that gives free "naked" dialkylammonium cations.

This approach was subsequently extended to the preparation of pseudo[3]rotaxane systems in which two calix[6]arene macrocycles are threaded by a bis(benzylalkylammonium) axle [2]. Because of the three-dimensional nonsymmetrical nature of the calix[6]arene wheels, in these instances three sequence stereoisomers [3] could be obtained, which can be termed as head-to-head (H,H), head-to-tail (H,T) and tail-to-tail (T,T) (**Figure 1**). We demonstrated that the stereo-controlled direct preparation of any given sequence stereoisomer can be obtained by exploiting the preference for the *endo*-alkyl complexation over the *endo*-benzyl one. These stereoisomeric pseudo[3]rotaxanes, in analogy to natural informational systems -DNA, RNA and proteins- could allow the design of "*informational devices*" in which each sequence isomer corresponds to a specific physical or chemical output.

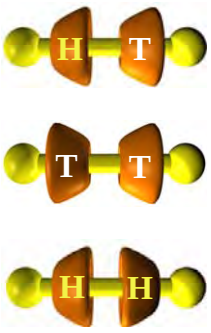

Figure 1

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ORG-PO-01 Synthesis and characterization of dendrimeric polyesters containing peripheral lysine and histidine groups

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Dendrimers are a unique class of polymeric systems characterized by well- defined nanostructured architecture, high symmetry, narrow polydispersity, presence of functional groups at the periphery which can be chemically trans-formed. These structural properties make dendrimers particularly suitable for biomedical applications such as drug delivery, bioimaging, gene therapy [1].
With the aim of preparing non toxic polycation dendrimers to use as non-viral vectors for gene delivery [2], we report in this communication the synthesis of hydrolyzable polyester-based dendrimers of fourth and fifth generation bearing hydroxy end-groups (Figure 1) derived from 2,2-*bis*(hydroxymethyl)propanoic acid, characterized by low toxicity *in vivo*, properly functionalized at the periphery with lysine and histidine groups.

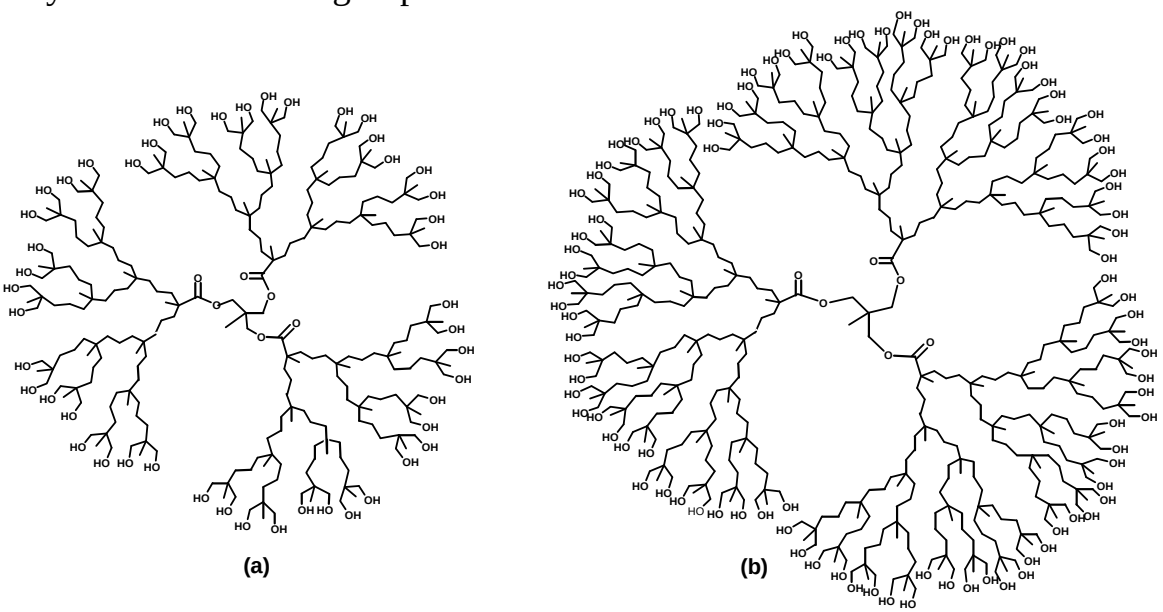

Figure 1. Skeletal structures of dendrimers of 4th (a) and 5th generation (b).

The prepared functionalized dendrimers were characterized through ^{1}H-NMR, potentiometric and volumetric titrations. A very good accordance was observed between theoretical and experimental molecular weight data.

References:
[1] O.Rolland, O-C.Turrin, A-M.Caminade, and J-P.Majoral, *New J. Chem.*, *33*, **2009**, 1809.
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ORG-PO-02 Aggregation of Pluronics in Ionic Liquids

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Pluronics (PEO_y-PPO_x-PEO_y triblock copolymers) self-assemble in water to form mainly micelles with several potential applications [1], such as the improvement of the aqueous solubility of drugs, chemical separations and nanoparticle synthesis

Room temperature ionic liquids (RTILs) are alternative solvents with characteristic properties, such as non-flammability, low volatility, high thermal stability [2]. RTILs can solubilise both hydrophilic and hydrophobic compounds and influence the aggregation properties of amphiphilic molecules.

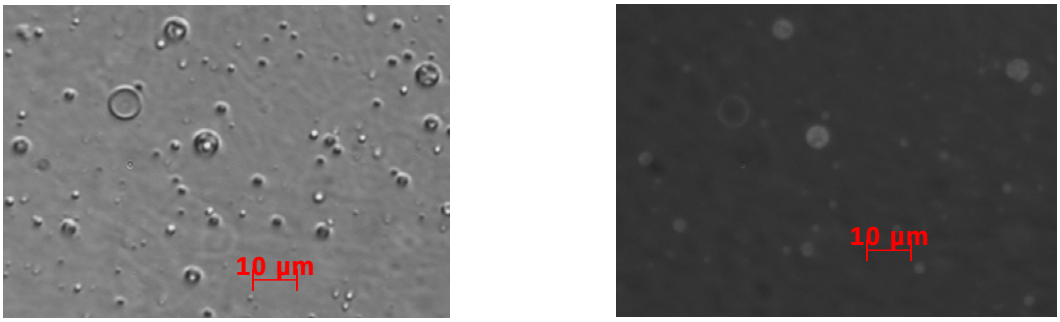

Figure 1.

The aggregation of a series of Pluronics (P85, P105, L121) in some RTILs ($[Bmim^+]$ $[BF_4^-]$, $[Bmim^+]$ $[PF_6^-]$ and $[Bmim^+]$ $[TF_2N^-]$) has been investigated by using different techniques (UV-NIR spectroscopy, optical microscopy).

The critical aggregation concentration (CAC) of the investigated Pluronics has been determined by UV-NIR [3]. The CAC increases in the RTILs in comparison to water, suggesting an higher affinity of the polymers for the ionic liquids. The values of CAC depends on both the nature of the polymer (PEO/PPO ratio) and the permittivity (ε) of the ionic liquid.

Supramolecular structures have been observed by optical microscopy (Figure 1).

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ORG-PO-03 Cyclohydrocarbonylation-Based Strategy toward aza-heterocycles

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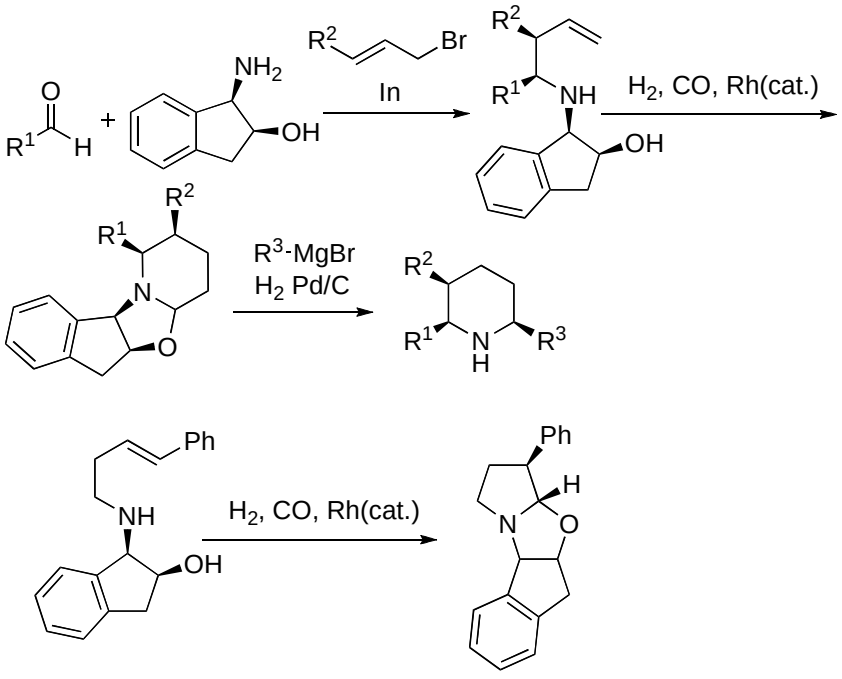
Cyclohydrocarbonylation (CHC) is a versatile strategy for domino or multicomponent synthesis of library of aza-heterocycles.
A series of 2-, 2,3- e 2,6- e 2,3,6- substituted enantiomerically pure piperidines can be prepared by cyclohydrocarbonylation of chiral homoallyl amines, prepared via Indium mediated allylation or crotylation of aldehydes using (S)-2-phenylglycinol or (1*R*,2*S*)-1-amino-2-indanol as chiral auxiliary [1].



A similar procedure can be applied to the synthesis of pyrrolidine derivates with a high level of stereocontrol due to the presence of the aromatic ring.

[1] Arena, G. ; Zill, N.; Salvadori, J.; Girard, N.; Mann, A.;Taddei, M. *Org. Lett*., **2011**, *13*, 2294-2297.

ORG-PO-04 High-Pressure Entry into Cannabinoids Family

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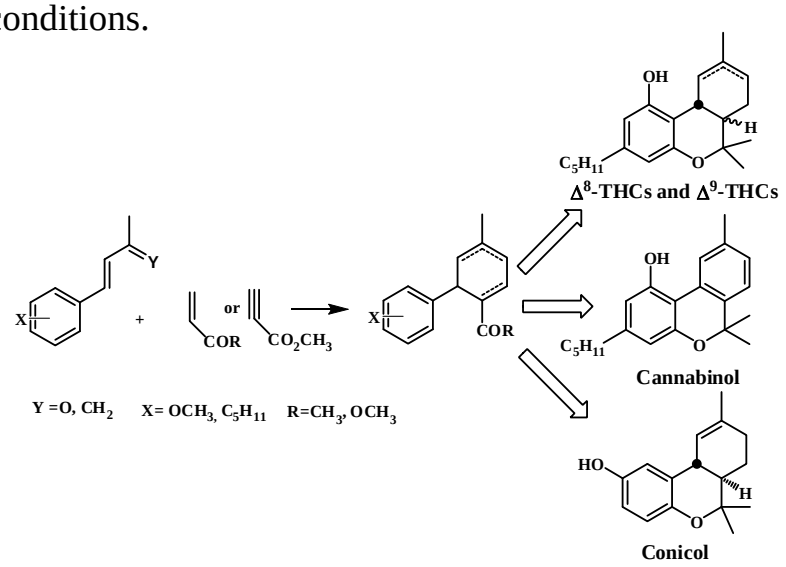
In recent years, our interest has been focused in developing novel synthetic routes to target molecules incorporating the tetrahydro-6H-benzo[c]chromene system [1]. This structural motif has been proposed as a *privileged structure* since occurs as subunits in a diverse range of bioactive natural products, being capable of interacting with a variety of cellular targets.
Recently, our laboratory reported an high-yielding and environmental safe method for the construction of the *cis*- and *trans*-6a,7,10,10a-tetrahydro-6H-benzo[c]chromene skeleton through the use of a Diels-Alder reaction using coumarins or alkoxybenzylideneacetones as dienophiles [2].
Herein we report the study of the Diels-Alder reaction of alkoxy/alkyl-substituted 1-phenyl-1,3-butadienes with methyl vinyl ketone, methyl acrilate and methyl propriolate in ethanol, water or dichloromethane as reaction medium and/or under high-pressure conditions.



This approach has been used to synthesized a large number of cannabinoid derivatives, including the Δ^9-*cis*- and the Δ^9-*trans*-THCs, the cannabinols and the conicols family . Application of this approach to the synthesis of paracyclophane derivatives that are useful in the field of new materials, will be also reported.

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ORG-PO-05 Anion Binding in Water with Use of Metal-salophen receptors

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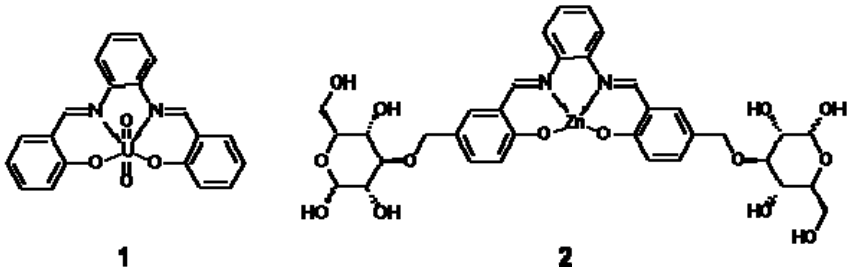
Anions are ubiquitous in both the organic and mineral worlds. They play different key roles in biology, and cause dramatic effects as environmental pollutants. Consequently the development of synthetic anion receptors that work in water represents an area of significant current interest in supramolecular chemistry[1] nurtured by the potential practical applications of such systems for the detection and quantification of these species. Obviously the task is quite challenging. The intrinsic peculiarities of anions make their complexation quite different from that of cations. It was initially thought that only positively charged receptors could compete with anion solvation, but recently it has been shown that neutral hosts that rely on hydrogen bond formation and/or on Lewis acidity can also exhibit considerable affinity for anions in water[2].

Here we report that metal-salophen based receptors, structurally simple and easy to prepare, can become protagonists in this field[3]. Different approaches and different strategies have been pursued in order to achieve selective and efficient binding of anions in water. One is the use of micelles (CTABr, CTACl) to solubilize the Uranyl-salophen receptors. Receptor **1**, under these conditions, exhibits high binding affinity towards fluoride anion[3], $K_a>10^4$ M^{-1}. Another is to introduce, on the basic skeleton of the receptor, neutral hydrophilic groups like glucose units. Zn-salophen complex **2** is reasonably soluble in water and behaves as a good receptor for a number of α-aminoacids through carboxylate binding[4].



1 **2**

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[4] Work carried out within the frame of COST Action 1005 « Supramolecular Chemistry in Water »

ORG-PO-06 Multi-metallic molecular catalysts for water oxidation

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Artificial photosynthesis converts solar light into chemical energy, by the light driven splitting of water into hydrogen and oxygen, and can therefore be considered as a promising route to produce renewable fuels, satisfying the ever increasing global energy demand.[1]
The development of suitable catalysts for water oxidation to dioxygen is nowadays recognized as the bottleneck for the construction of an efficient device for water splitting.[2] Bio-inspired approaches try to mimic the natural machinery of the photosystem II enzyme, which orchestrates low energy pathways leading to oxygen evolution through a catalytically active Mn_4CaO_5 core.
In this communication, we report the development of novel, molecular catalysts for water oxidation to oxygen, incorporating multi-metallic reactive nano-cores[3-5] including also cheap and abundant metals such as Cobalt.[5]
Success in this task has been demonstrated by homogeneous processes under dark and illumination conditions, in combination with ruthenium polypyridine photosensitizers.[6-7]
Optimization of the molecular system and its evolution within functional nano-materials is envisaged for photoelectrochemical water splitting devices.[8]

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ORG-PO-07 Thiophene- and Imidazole-based π-Conjugated Fluorophores via Selective Pd-catalyzed C-C Bond Formation Reactions

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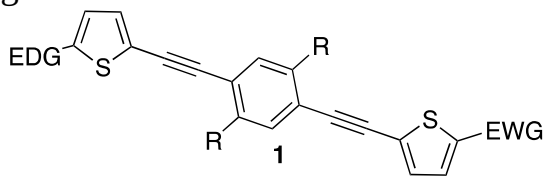
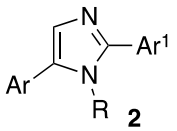
The development of nanometer-sized fluorophores of precise length showing π-extended conjugation has attracted considerable attention over the past decades. One driving force for the growing interest in this area is the realization that such molecular devices can be used for a variety of applications, ranging from solar energy conversion [1] to optoelectronic devices [2]. Among the molecular fluorophores, thiophene-substituted acetylenes are undoubtedly technologically important materials [3]. In this communication we will describe the preparation of novel push-pull thienyl-substituted 1,4-bis-ethynylbenzenes **1** using selective Pd-catalyzed cross couplings.



1

We will also illustrate our efforts in the application of selective Pd-catalyzed direct C-H arylation protocols [4] to the synthesis of 2,5-diarylimidazoles **2** and bis-imidazoles **3**, two interesting classes of imidazole-based fluorophores.



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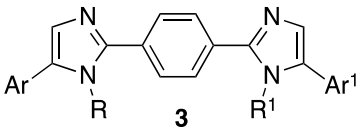

3

Organic fluorophores containing an imidazole core are interesting molecules due to their unique optical properties and relevant thermal stability [5], and could find application also as pH probes [6].

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ORG-PO-08 HIV-Pr inhibitors from stereoselective azidation and click chemistry on monohydroxyethylene cores

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In connection with our interest in the synthesis of dipeptide isosteres and pseudopeptide HIV-Pr inhibitors, we have developed in the past a methodology for the stereoselective hydroazidation of α,β-unsaturated ketones, to *syn* β-azidoketones.[1] Such products could offer a useful entry point towards stereopure azido-alcohols, and by this route towards libraries of potential HIV-Pr inhibitors (Fig. 1) by exploiting combinatorial chemistry by differential acylation at nitrogen and by the click chemistry strategy[2] at the azido group.

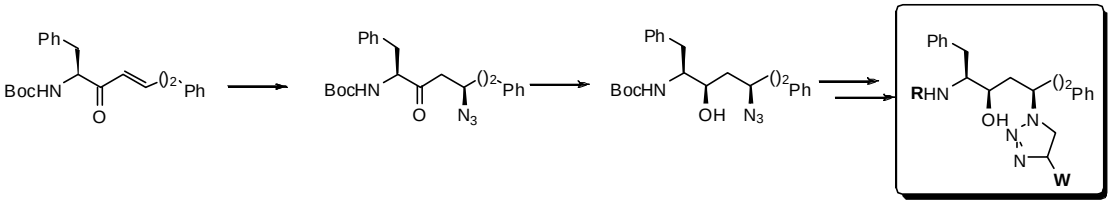
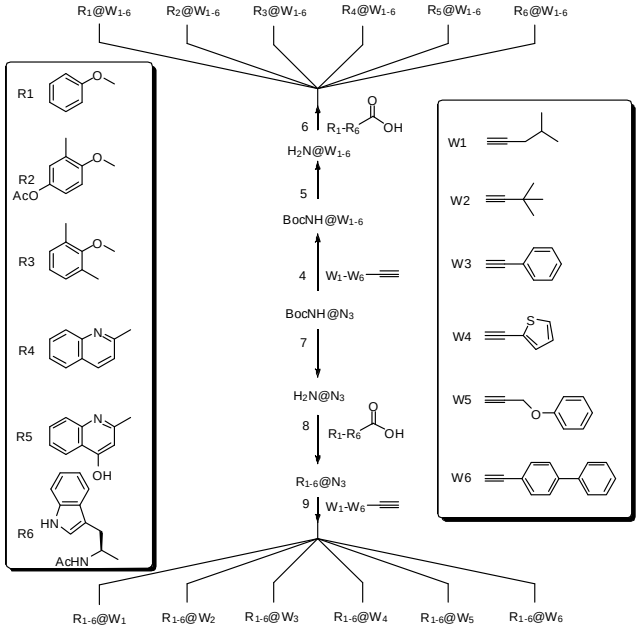


Figure 1.

By this way we have synthesized ten couples of 36 member orthogonal libraries by varying substituents on triazole ring (W) and different lateral chains (R).



Scheme 1.

The libraries were then submitted to a screening for HIV-Pr inhibition. After deconvolution, the most promising compounds were identified and synthesized as optically pure compounds; their anti-HIV-Pr activity was confirmed and their synthesis was optimized.

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ORG-PO-09 Configurational Stability of 2,7-Dihydro-1-Phenyl-Phosphepine-Oxides and Electronic Properties of the Phosphanes

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[c] Dipartimento del Farmaco, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161, Roma, Italy

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[e] Istituto di Scienze e Tecnologie Molecolari, Consiglio Nazionale delle Ricerche, via Golgi 19, 20133, Milano, Italy

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The configurational stability of four chiral 2,7-dihydro-1-phenyl-phosphepine-oxides **1a**-**4a** (Figure 1), differing for the nature of the aromatic rings (carbocyclic or heterocyclic, six- or five-membered) constituting the stereogenic scaffold have been investigated. Unknown compound **4a** was fully characterized by single crystal X-ray analysis. The tendency to enantiomerize has been determined by circular dichroism and on-column enantioselective HPLC methods. Biphenine-oxide **1a** was found the only unstable compound at room temperature, displaying an enantiomerization barrier of about 20 kcal mol^{-1}.

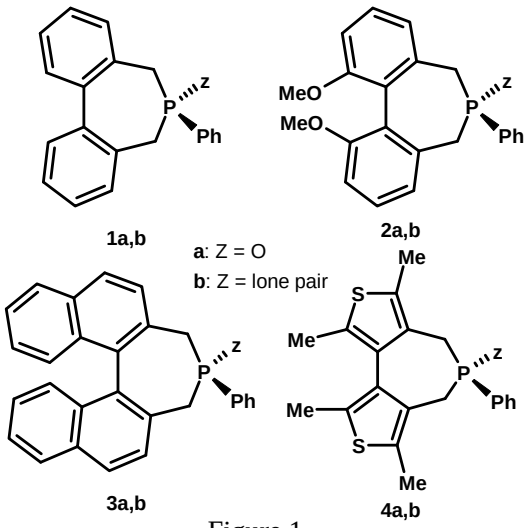

Figure 1.

Also the corresponding phosphanes **1b**-**4b** have been considered in order to perform a comparative evaluation of their electronic availability, which is a crucial parameter affecting both the catalytic activity and stereoselection ability of their metal complexes. Unknown bithienophosphepine **4b** was fully characterized by single crystal X-ray analysis. The quantitative evaluation of the electronic properties was performed by voltammetry, using the electrochemical oxidative peak potential as probe: the higher the value, the electron-poorer the phosphane. The electronic availability was found to decrease along to the sequence: **2b**, **4b**, **3b**, **1b**.

E.Alberico, S.Karandikar, S.Gladiali, *ChemCatChem 22*, **2010**, 1395 and references therein.

ORG-PO-10 Convenient synthesis of novel 1-aryl-dihydroxyisochromans exhibiting antioxidant activity

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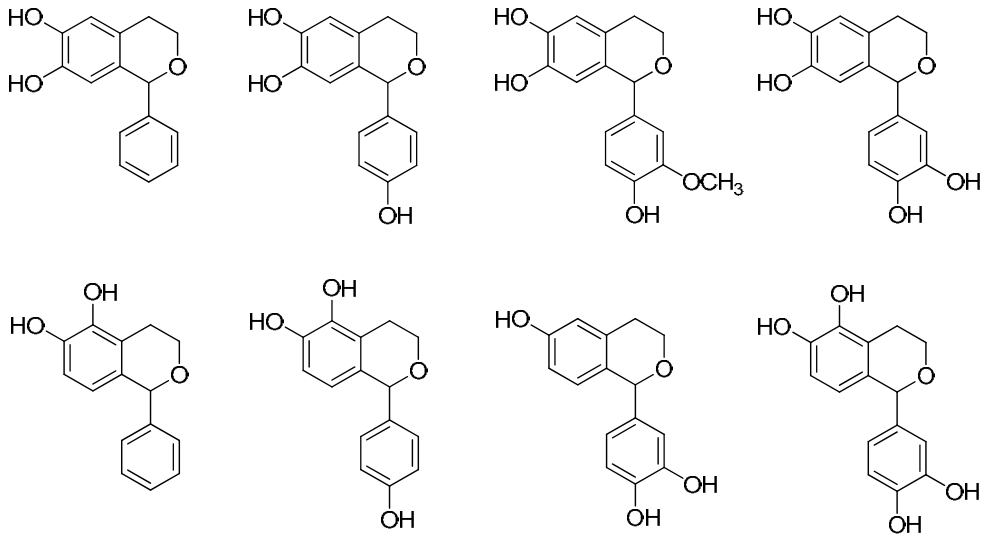
A large panel of 1-aryl-dihydroxyisochromans showing novel patterns of substitution into A or B aromatic rings were synthesized from phenethyl alcohols and substituted benzaldehydes by the oxa-Pictet-Splenger reaction performed in dimethyl carbonate (DMC), an ecofriendly solvent, followed by the regioselective aromatic hydroxylation/oxidative aromatic demethylation with 2-iodoxybenzoic acid (IBX)/sodium dithionite ($Na_2S_2O_4$) system [1].



All 1-aryl-dihydroxyisochromans were tested about their radical scavenging activity toward 2,2-diphenyl-2-picrylhydrazyl radical ($DPPH^{\cdot}$) and compared to the corresponding phenolic or guaiacolic derivatives. Experimental results confirmed the important role of the catecholic moiety for the antioxidant activity.

[1] R. Bernini, F. Crisante, G. Fabrizi, P. Gentili *Tetrahedron* **2011**, *submitted*.

ORG-PO-11 Synthesis of a novel ester of hydroxytyrosol and α-lipoic acid exhibiting an antiproliferative effect on human colon cancer HT-29 cells

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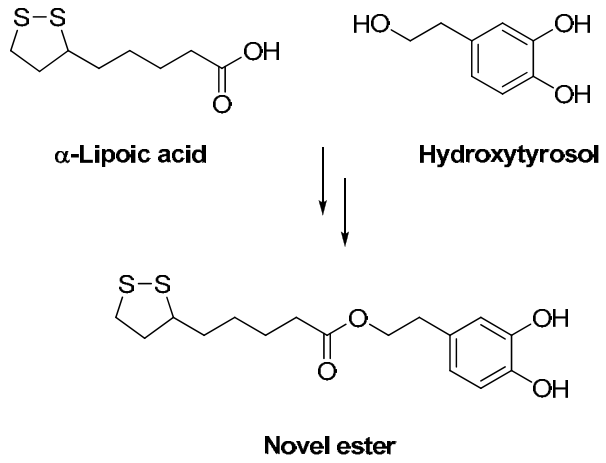
Email: berninir@unitus.it

A novel ester obtained by joining biologically active compounds such as hydroxytyrosol and α-lipoic acid was prepared in satisfactory yield and high purity by a simple and efficient procedure [1].



The effect of the novel ester on the proliferation of the human colorectal adenocarcinoma HT-29 cell line was evaluated. The experimental results showed that it exhibited an antiproliferative effect significantly more potent than the corresponding parent compounds, either singularly or in combination. Moreover, it induced a significantly stronger block of the cell cycle at the G2/M phase than hydroxytyrosol and α-lipoic acid, either singularly or in combination. This result indicates that the inhibition of cancer cell growth was mediated by the induction of a G2/M phase cell cycle arrest.

Further syntheses are currently in progress in our laboratories for the preparation of analogue derivatives to be tested.

[1] R. Bernini, F. Crisante, N. Merendino, R. Molinari, M. C. Soldatelli, F. Velotti *Eur. J. Med. Chem. 46,* **2011**, 439-446.

ORG-PO-12 Chemoselective C-4 Aerobic Oxidation of Catechin Derivatives Catalyzed by the *Trametes villosa* Laccase/1-Hydroxybenzotriazole System: Synthetic and Mechanistic Aspects

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[b] Dipartimento di Chimica and IMC-CNR Sezione Meccanismi di Reazione della Sapienza Università di Roma, La P. le A. Moro 5, I-00185 Roma, Italy
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Catechin derivatives have been oxidized under aerobic conditions in the presence of the *Trametes villosa* laccase/1-hydroxybenzotriazole (HBT) system in buffered water/1,4-dioxane as reaction medium [1]. The oxidation products, flavan-3,4-diols and the corresponding C-4 ketones, are bioactive compounds and useful intermediates for the hemisynthesis of proanthocyanidins, plant polyphenols providing beneficial health properties for humans.

Determinations of oxidation potentials excluded that catechin derivatives could be directly oxidized by laccase Cu(II), while it resulted in the H-abstraction from benzylic positions being promptly promoted by the enzyme in the presence of the mediator HBT, the parent species producing in situ the reactive intermediate benzotriazole-N-oxyl (BTNO) radical. A remarkable and unexpected result for the laccase/HBT oxidative system has been the chemoselective insertion of the oxygen atom into the C-4-H bond of catechin derivatives. Mechanistic aspects of the oxidation reaction have been investigated in detail for the first time in order to corroborate these results. Since the collected experimental findings could not alone provide information useful to clarify the origin of the observed chemoselectivity, these data were expressly supplemented with information derived by suitable molecular modeling investigations. The integrated evaluation of the dissociation energies of the C-H bonds calculated both by semiempirical and DFT methods and the differential activation energies of the process estimated by a molecular modeling approach suggested that the observed selective oxidation at the C-4 carbon has a kinetic origin.

[1] R. Bernini, F. Crisante, P. Gentili, F. Morana, M. Pierini, M. Piras *J. Org. Chem. 76*, **2011**, 820-832.

ORG-PO-13 Heterogeneization of a Basic Ionic Liquid and its Use as Catalyst in Knoevenagel and Michael Reactions.

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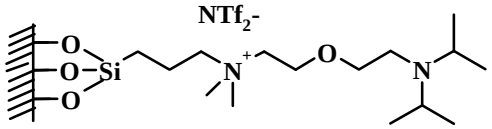
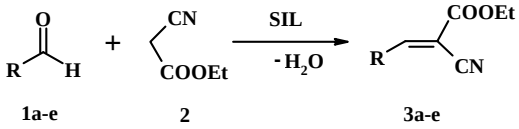
E-mail: antonio.mega@studenti.unipr.it

Careful application of heterogeneous catalysis can help to achieve selective reactions, with minimum waste, thereby rendering more attractive the synthetic processes. Indeed, solid catalysts can be easily separated quantitatively in their active form from the reaction products by a simple filtration and subsequently recycled. C. Hardacre and co-workers [1] reported a new class of ionic liquids containing the non-nucleophilic Hünig's base unit. These ionic liquids were able to promote Knoevenagel reactions in good yields, but some drawbacks were observed employing them supported on silica (SILPs) by simple impregnation. The recyclability of these SILPs was only moderate towards these reactions.

Thus, we decided to anchor a basic ionic liquid on a silica support by covalent bonding, with the purpose of increasing the robustness of the catalyst, making it reusable and expanding its applicability.

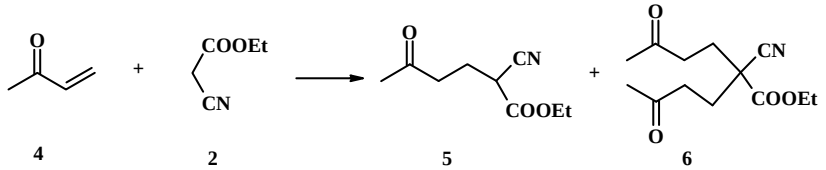


The catalytic activity of the covalently-supported ionic liquid (which, of course, is no longer an ionic liquid) was tested in Knoevenagel and Michael reactions, which are important carbon–carbon bond forming reactions in organic synthesis. The Knoevenagel condensations of various aldehydes were successfully carried out in solventless conditions at 60 °C (yields 88-99%, selectivity 94-99%).



1a-e 2 3a-e

In addition, the catalyst was found to be recyclable many times.
The Michael reaction was examined under different reaction conditions, generating a selective process for the formation of either the single addition product, **5**, or of the double addition product, **6**.



4 2 5 6

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[1] C. Paun, J. Barklie, P. Goodrich, H. Q. N. Gunaratne, A. McKeowna, V. I. Pârvulescu, C. Hardacre, *J. Mol. Catal. A: Chem.*, 269, **2007**, 64.

ORG-PO-14 Viologen-based ionic liquid crystals: effect of the molecular structure on the mesophase stability

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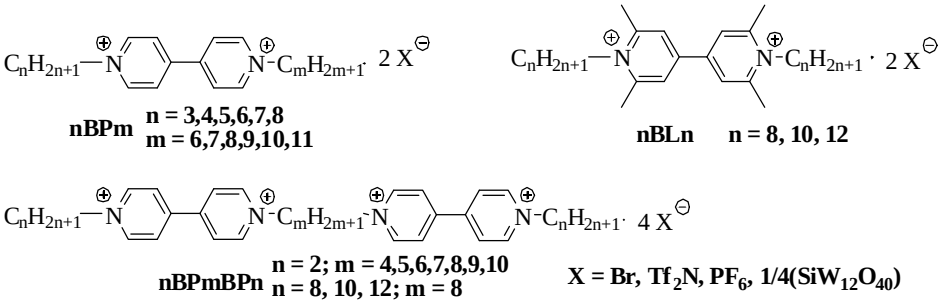
Ionic liquid crystals (ILC) are expected to combine the properties and technological applications of ionic liquids and liquid crystals. We have investigated how structural modifications of the viologen cation (1,1′-dialkyl-4,4′-bipyridinium) affect the stability and temperature range of the ILC mesophases. Thus we report the synthesis and characterization of the compounds of Scheme 1: *i)* non-symmetric viologen salts (nBPm, with n ≠ m); *ii)* symmetric salts of tetramethylviologen (nBLn); dimeric viologen salts (nBPmBPn). In most cases the counteranion is bis(trifluoromethanesulfonyl)amide (Tf_2N^-). The effect of the anion has been considered by studying some salts of Br^-, PF_6^- and dodecatungstosilicate ($SiW_{12}O_{40}^{4-}$). The various phases exhibited by these salts have been characterized by means of TGA, DSC, X-ray diffraction, polarized optical microscopy and solid state NMR[1-2] while HR-NMR, MS spectrometry and cyclic voltammetry have been used to study their behaviour in solution.[3,4] The modulation of the length of the alkyl chains allowed the fine tuning of the transition temperatures and temperature range of stability of the ILCs. Some of the non-symmetric salts show a stable room temperature smectic phase from about 0 °C up to about 130 °C. Moreover, the use of viologen dimers as molecular tweezers for fullerene complexation has been the subject of a computational investigation.[5]



[1] V. Causin, and G. Saielli, *J. Mol. Liq. 145*, **2009**, 41.
[2] V. Causin, and G. Saielli, *J. Mater. Chem.*, *19*, **2009**, 9153.
[3] E. Marotta, F. Rastrelli, and G. Saielli, *J. Phys. Chem. B*, *112*, **2008**, 16566.
[4] G. Saielli, *J. Phys. Chem. A*, *112*, **2008**, 7987.
[5] G. Casella, and G. Saielli, *New J. Chem.*, *35*, **2011**. DOI: 10.1039/C1NJ20117D

ORG-PO-15 Diketopyrrolopyrrole Supramolecular Network

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[a]Dipartimento di Scienze Molecolari e Nanosistemi, [b]Dipartimento di Scienze Ambientali, Informatica e Statistica; Ca' Foscari Venezia, Dorsoduro 2137, I-30123, Venezia.
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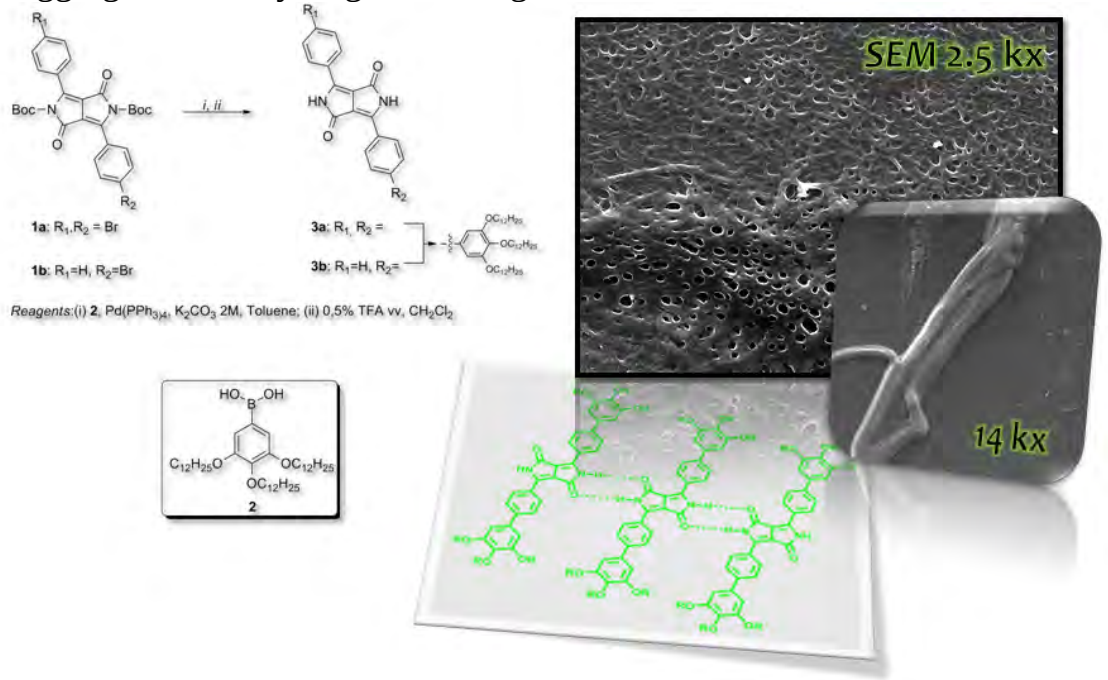
Diketopyrrolopyrrole (**DPP**) is among the most important high performance pigments (Colour Index PR 255). It is used in automotive industries and in general paint and tinting applications. In recent years, research in the **DPP** focused on the synthesis of new derivatives to be used in the field of organic photovoltaic (OPV) applications [1] and as chromophore for near-infrared spectroscopy (NIR).[2] Our research aims to the synthesis of new soluble **DPPs** *via Suzuki cross-coupling*,[3] starting from the dibromide **1**. In the case of **3a**, the SEM image indicates the formation of supramolecular networks in the solid state which was rationalized as due to aggregation via hydrogen bonding as shown below.



[1] (a) B. Walker, C. Kim, T. Q. Nguyen, *Chem. Mater.* **2011**, *23*, 470; (b) B. P. Karsten, R. A. J. Janssen, *Macromol. Chem. Phys.* **2011**, *212*, 515.
[2] (a) G. M. Fischer, E. Daltrozzo, A. Zumbusch, *Angew. Chem. Int. Ed.* **2011**, *50*, 1406; (b) G. M. Fischer, A. P. Ehlers, A. Zumbusch, E. Daltrozzo, *Angew. Chem. Int. Ed.* **2007**, *46*, 3750; (c) G. M. Fischer, M. Isomäki-Krondahl, I. Göttker-Schnetmann, E. Daltrozzo, A. Zumbusch, *Chem. Eur. J.* **2009**, *15*, 4857.
[3] Lincker, F.; Bourgun, P.; Masson, P.; Didier, P.; Guidoni, L.; Bigot, J-Y.; Nicoud, J-F.; Donnio, B.; Guillon, D. *Org. Lett.* **2005**, 7, No. 8, 1505.

ORG-PO-16 α-Diketones as acyl anion equivalents: new enzymatic and non-enzymatic thiamine-promoted routes to aldehyde-ketone coupling

Olga Bortolini, Giancarlo Fantin, Marco Fogagnolo, Pier Paolo Giovannini, Valentina Venturi, Alessandro Massi, Salvatore Pacifico
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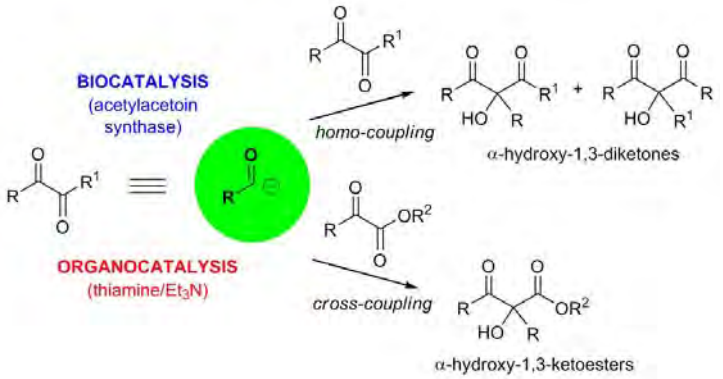
Thiamine diphosphate (ThDP)-depending enzymes are well established biocatalytic tools for the asymmetric synthesis of α-hydroxy carbonyl compounds (acyloins) via carboligation reactions between two carbonyl reagents (*Umpolung* strategy). Recently, we reported the unprecedented enzymatic aldehyde-ketone coupling by using Acetylacetoin synthase (AAS) as the enzyme and, noteworthy, α-diketones as acyl anion sources [1]. In particular, we found that AAS is capable to catalyze in vivo the homo-coupling reaction of various symmetrically and unsymmetrically substituted 1,2-diketones, thus affording a suite of chiral and prochiral tertiary alcohols featuring the α-hydroxy-α-diketone moiety (Figure).

By mimicking the peculiar behavior of ThDP-depending AAS, we have also demonstrated that the sole thiamine hydrochloride-Et_3N couple is able to promote nucleophilic acylations such as the above homo-coupling of α-diketones and the hitherto unreported cross-coupling between α-diketones and α-ketoesters. Both carboligation reactions yield α-hydroxyketone derivatives in a straightforward manner by an effective and benign procedure involving the use of eco-friendly PEG_{400} as the reaction medium. Crucial for the disclosed mode of acyl anion generation is the utilization of dialkyl α-diketone donors with at least an acidic hydrogen adjacent to the carbonyl group. Interestingly, a different reaction pathway (hydride vs. acyl anion transfer) is observed for arylalkyl α-diketone donors.



[1] Giovannini, P. P.; Pedrini, P.; Venturi, V.; Fantin, G.; Medici, A. *J. Mol. Catal. B: Enzym.* **2010**, *64*, 113.
[2] Fantin, G.; Fogagnolo, M.; Giovannin, P. P.; Venturi, V., Massi, A.; Bortolini, O. manuscript submitted.

ORG-PO-17 Peroxide value determination in oils without the use of chlorinated solvents

Augusta Caligiani, Martina Cirlini and Gerardo Palla.

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gerardo.palla@unipr.it

The standard method for peroxide determination in oils requires the reaction of peroxides with potassium iodide (KI) added to samples dissolved in a mixture of acetic acid and chloroform: the last solvent is a problem both for health and environment as it is carcinogenic and highly pollutant. As an alternative, we check other organic solvents and found that the use of ethyl acetate in place of chloroform or dichloromethane allowed reproducible data of the peroxide number for both common food oils(olive oil) and special products such as sunflower ozonized oil used for cosmetics (Cosmoproject Spa), net or mixed with lipophilic or hydrophilic gel. Several experiments were carried out by adding KI to ozonized oil samples used for cosmetics in order to follow the kinetic of decomposition in different solvents. Results from NMR data showed that the degradation rate of ozonides in ethyl acetate or in chlorinated solvents in presence of KI was similar, allowing a complete reaction after standing 16 hours at room temperature. GC-MS data confirmed that the degradation products of ozonides from sunflower oil were mainly aldehydes, iodo-alkanes and furyl derivatives.

Bibl: Official Methods of Analysis of AOAC International, Vol 1, 2

ORG-PO-18 Anion Binding via Charge Assisted Halogen Bond in 2-Iodo-Imidazolium Systems

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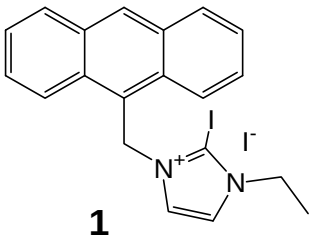
[2] Institute of Molecular Science and Technology, CNR—University of Milan, Milano, Italy

Anion recognition is one of the classical themes in Supramolecular Chemistry since its early age, and still a florid area of research [1]. In the incessant search for novel paradigm for achieving the efficient capture of negatively charged species, researchers have explored many different non-covalent forces, such as electrostatic interactions, metal coordination, hydrogen bonding, anion-π interactions, etc. Among these, halogen bonding (XB), namely any noncovalent interaction involving the positive region of the electrostatic potential surface of halogen atoms [2] has recently drawn considerable attention. XB is, nowadays, a well recognized class of non-covalent interactions. Investigations on XB systems increased in recent years, embracing both experimental and theoretical studies. As to experimental works, crystal engineering studies represent an overwhelming majority. In marked contrast with the abundance of solid state investigations, studies in solution are surprisingly scanty.



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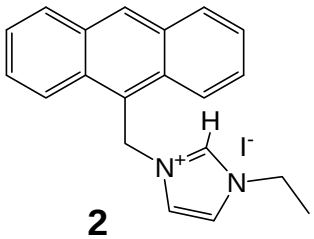

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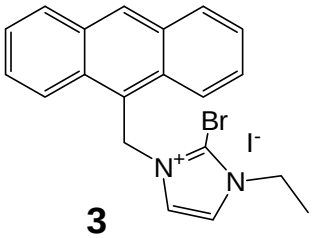

3

Here we report on the study of the anion binding properties of the 2-iodo-imidazolium receptor **1**. Solution studies confirm that the 2-iodo-imidazolium unit provides relatively strong interactions with halide ions and oxo-anions (such as AcO^- and $H_2PO_4^-$) in a competitive solvent such as DMSO. Relevant comparisons were made with the 2-H and with the 2-Br derivatives, compounds **2** and **3**, in order to assess the relative strength of the XB with respect to the HB in the analogue 2-H derivative, and to further verify the occurrence of the XB interaction, respectively.

[1]: P. A. Gale and W. Dehaen, Eds., Anion Recognition in Supramolecular Chemistry, 2010, Springer; Special Issue of *Chem. Soc. Rev.*, **2010**, Issue 10, 3581-4008.

[2]: An IUPAC Task Group set up to examine the definition of halogen bonding has not yet reported, so that given here should be taken as temporary (see www.iupac.org/web/ins/2009-032-1-100 and www.halogenbonding.eu).

ORG-PO-19 PHOTOCHEMISTRY OF ARYL NONAFLATES.

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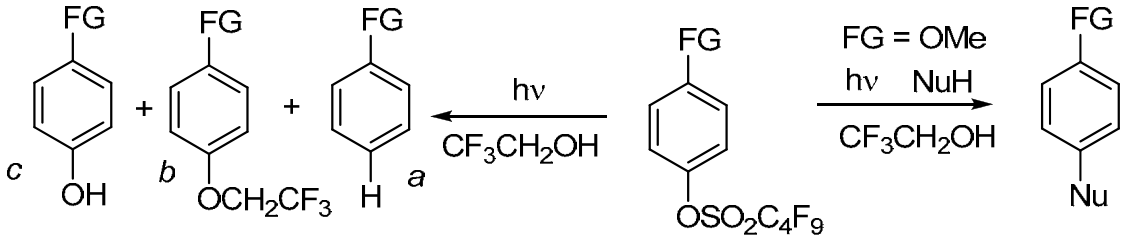
prottistefano@gmail.com

Aryl nonaflates (Ar-$OSO_2C_4F_9$) have recently emerged as promising substrates in transition metal catalyzed cross-coupling reactions for aryl-carbon bond formation[1]. On the other hand, the photoactivation of the Ar-O bond in aromatic sulfonates is likewise possible. In particular, our group demonstrated that irradiation of electron-rich aryl triflates or mesylates in polar or protic solvents in the presence of π nucleophiles (alkenes, aromatics) can be exploited for the development of metal-free, arylation procedure to achieve biphenyls, allyl benzenes and α-arylacetals[2]. In the aim of exploring the synthetic potential of aryl nonaflates in photochemistry, we decided to investigate the photoreactivity of these esters substituted with a NMe_2, OMe or an alkyl group in various solvents and in the presence of π nucleophiles (benzene, mesitylene, allyltrimethylsilane). Preliminary results showed that these compounds have a marked photoreactivity in neat solvent ($\Phi_R > 0.1$) where the competition between three different pathways (reduction (*a*) , solvolysis (*b*) and deprotection (*c*)) can be observed. In addition, the *p*-methoxy derivative could be employed in several Ar-C bond formation reactions procedures, and arylation yields were comparable with those obtained with the corresponding mesylates or triflates.



[1] D. Xu, Z. Hua Liu, W. Jun Tang, J. Mo and L. Jin Xu, *Chin. Chem. Lett.* **2008**, *19*, 1017.
[2] M. De Carolis, S. Protti, M. Fagnoni, and A. Albini, *Angew. Chem. Int. Ed.* **2005**, *44*, 1232; V. Dichiarante, and M. Fagnoni, *Synlett* **2008**, 787.

ORG-PO-20 Exploring the Chemistry of Marine Mollusks: from Chemical Weapons to New Pharmaceutical Leads

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margherita.gavagnin@icb.cnr.it

In recent years the number of identified bioactive natural compounds from marine sources has progressively increased [1]. Sponges, cnidarians and microorganisms are the richest sources in the sea of bioactive natural products, but a significant incidence of activity has been also found in compounds isolated from mollusks [2]. In particular, shell-less gastropod mollusks belonging to the subclass Opisthobranchia revealed to be one of the most interesting group. The survival of these apparently unprotected mollusks is based on a series of defensive strategies, which include the use of deterrent or toxic molecules. Opisthobranchs obtain their chemical "weapons" by either bio-accumulation of selected metabolites from their dietary sources, bio-transformation of dietary compounds, or *de novo* bio-synthesis. Thus they represent a remarkable source of bioactive molecules that have been selected in nature to play fundamental roles for the survival of the organisms that contain them. This reveals an extraordinary library of compounds that could be considered excellent drug candidates.

In continuing our research directed to explore the valuable chemical content of gastropod mollusks, we have examined different species. These studies led us to characterize several novel bioactive molecules (some examples in Fig. 1). Selected results will be presented in this communication.

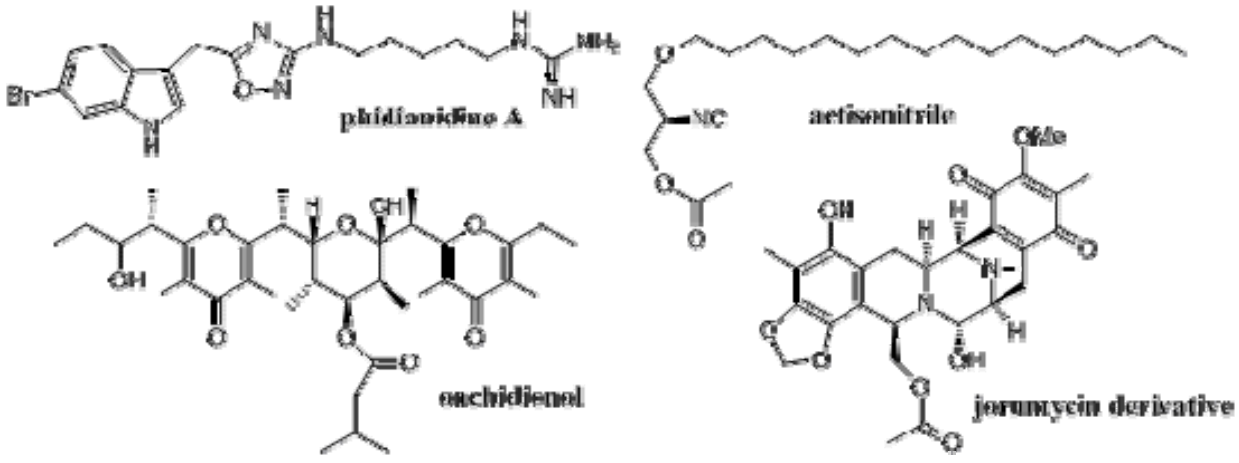

Figure 1.

[1] J.W. Blunt, B.R. Copp, M.H.G. Munro, P.T. Northcote, and M.R. Prinsep, *Nat. Prod. Rep*., *28*, **2011**, 196.
[2] T.F. Molinski, D.S. Dalisay, S.L. Lievens, and J.P. Saludes, *Nat. Rev. Drug Discov.*, *8*, **2009**, 69.

ORG-PO-21 Chiral Macrocycles as Chiroptical Sensors and as Building Blocks for Supramolecular Helical Nanotubes

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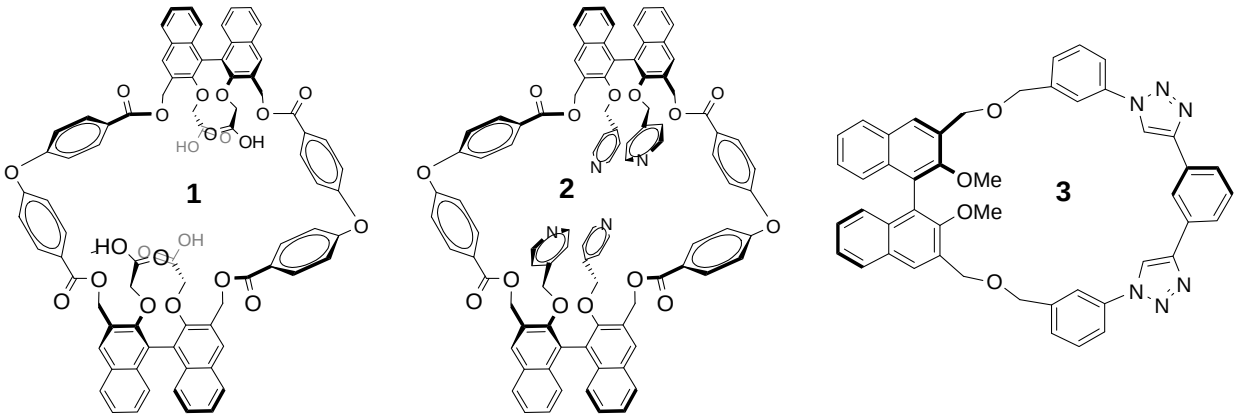
marco.caricato@unipv.it

We present our efforts for the incorporation of BINOL-based molecular modules, acting as a "robust" source of chirality, into homochiral, shape-persistent macrocycles, with function as chiroptical sensors and precursors for supramolecular organic nanotubes.[1] Constructing abiological helices have potential applications in the area of chiral separation, asymmetric catalysis and electrooptic materials. More specifically, we have used several elaborated molecular modules, such as 3,3'-dimethanol-1,1'-binaphthyl with different functionalities in 2,2' positions, and cyclized them via amidation and esterification reactions, and click chemistry.[2]



1 has four carboxylic acid functionalities pointing into the macrocyclic cavity, and it is capable of recognition of Cu^{2+}, Ni^{2+}, Zn^{2+} in physiological conditions, with the binding event which can be detected using CD spectroscopy. Macrocycle **3** is capable of anion recognition given the presence of acidic triazole CH bonds, which can be again detected using CD spectroscopy. The coordination of pyridine fucntionalities with ligand $PdCl_2(CH_3CN)_2$ in macrocycle **2** yield chiral supramolecular nanotubular polymers on surfaces.

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ORG-PO-22 An innovative and easy way to anchor biomolecules onto Superparamagnetic Iron Oxide Nanoparticles (SPIONs) through a bifunctional linker

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Superparamagnetic Iron Oxide Nanoparticles (SPIONs) have demonstrated great promise for diagnostic and therapeutic applications. Thanks to their magnetic properties and to their size, comparable to that of biologically objects, they are very useful for biomedical applications, such as, for example, automated DNA extraction, targeted gene delivery, magnetic resonance imaging (MRI), and magnetic field induced hyperthermia for cancer therapy.[1a-e] For these applications, SPIONs must be coupled with targeting agents, therapeutic drugs, and other functional probes. Hence, the need to develop efficient synthetic strategies for the conjugation of molecules to SPIONs is an important and appealing target.[2] The strategies used can involve passive noncovalent adsorption on the outer particle surface or the formation of a more stable covalent bond by using appropriate heterobifunctional linkers, in which one functional group specifically binds the nanoparticle, while the other reacts with the biomolecule in order to form the new nanoconjugate (Figure 1).
In this communication, the use of an heterobifunctional linkers containing an isocyanate moiety as new functional group able to directly bind SPIONs will be shown.

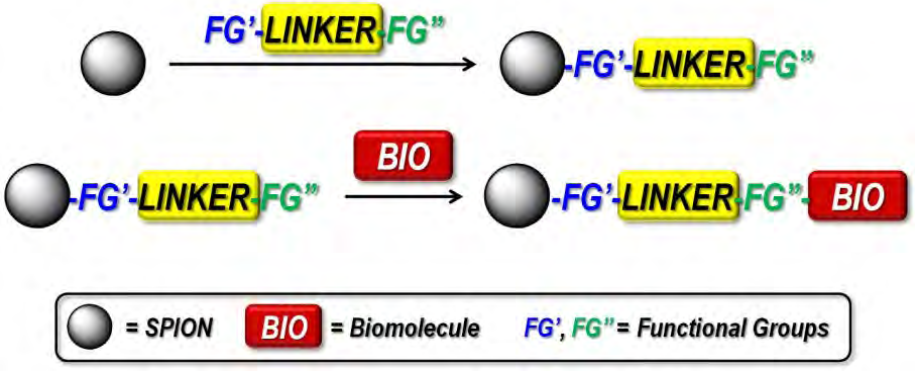

Figure 1

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ORG-PO-23 Halogen bonding in halocarbon-protein complexes

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Halogen bonding (XB) [1] has been extensively described in the context of a variety of self-assembled supramolecular materials with specific structural properties. [2] However, it has so far received only little recognition for its possible role in the stabilization of the interactions between small chemicals and large biomolecules. In this contribution, we provide some examples of halogen bonding occurring between small halogen-substituted ligands and their biological substrates. [3] The crystal structures presented here, where iodine and bromine atoms function as halogen bonding donors and different electron rich sites, such as oxygen and nitrogen, function as halogen bonding acceptors, prove how halogen bonding can occur in biological systems and provide a class of higly directional stabilizing contacts that can be exploited in the process of rational drug design.

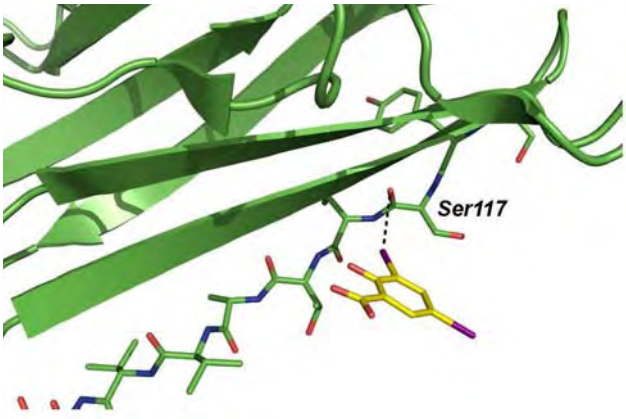

Figure 1: An iodine atom of 3,5-diiodosalicilic acid forms a halogen bonding contact with the Ser117 carbonyl oxygen in the 3,5-diiodosalicylic-transthyretin structure (PDB code = 3B56).

[1] An IUPAC Task Group set up to examine the definition of halogen bonding has not yet reported, so that given here should be taken as temporary (see www.iupac.org/web/ins/2009-032-1-100 and www.halogenbonding.eu).

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ORG-PO-24 Microreactor Technology in the Development of Stereoselective Syntheses

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Microflow devices have been found to be very effective in controlling extremely fast reaction, involving highly unstable intermediates, allowing the introduction of the concept of flash chemistry [1]. Flash chemistry is defined as "*a field of chemical synthesis where extremely fast reactions are conducted in a highly controlled manner to produce desired compounds with high selectivity and reaction times ranging from milliseconds to seconds*". This concept has been successfully applied to several organic reactions involving highly reactive intermediates such as carbanions and carbocations [2]. In fact, functionalized organolithiums or alkoxycarbeniums, widely used in modern synthetic chemistry, are example of reactive intermediates that exhibit high reactivity, giving fast and exothermic reactions, and usually require very low temperature and controlled reaction conditions in order to avoid byproducts and decomposition.
In this communication, it will be reported our recent results on the development of new stereoselective syntheses by using carbanionic and carbocationic intermediates, generated from functionalized aziridines in microreactor systems.

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ORG-PO-25 HENRY REACTION CATALYZED BY COPPER(I) COMPLEXES OF A NEW PYRIDINE CONTAINING MACROCYCLIC LIGAND.

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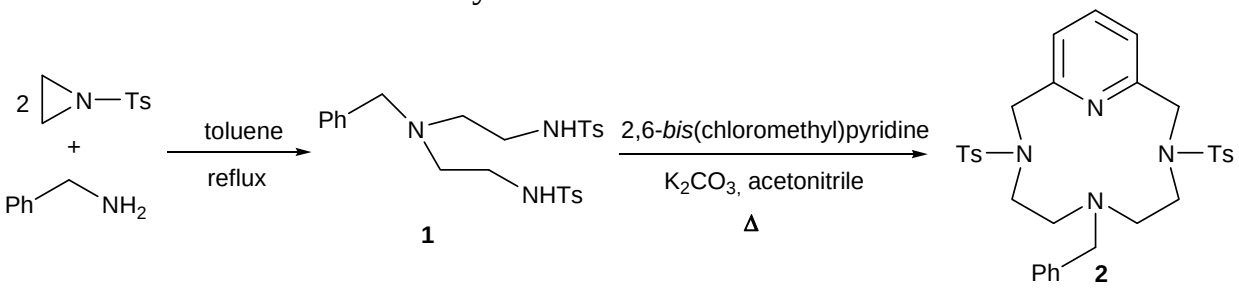
The Henry or nitroaldol reaction has received much attention as a valuable tool for the formation of C-C bonds [1]. The reaction couples nitroalkanes with carbonyl compounds in the presence of a base giving β-nitroalcohols that are useful intermediates in the synthesis of relevant biologically active compounds. Recent studies in our research group demonstrated the efficacy of Cu(I) complexes derived from novel macrocyclic ligands containing a pyridine ring (**PC-L**) in the cyclopropanation reaction of various alkenes [2]. The excellent results obtained prompted us to verify the application of such Cu(I) complexes in the Henry reaction. We report here the synthesis of the new macrocyclic ligand **2** (Scheme 1) and the application of the corresponding Cu(I) complex as Lewis acid catalyst in the condensation between aldehydes and nitroalkanes.



Scheme 1

The best results in terms of chemical yields were obtained with *in situ* formed 1:1 ligand **2**:Cu(OTf) complex (from $[Cu(OTf)]_2 \cdot C_6H_6$) in dichloromethane at room temperature and in the presence of substoichiometric amount of a tertiary amine. Noteworthy, no trace of competitive side-reaction products were ever detected.

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ORG-PO-26 Formation of Gels from Stereoisomeric Pseudopeptides in the Presence of Metal Ions

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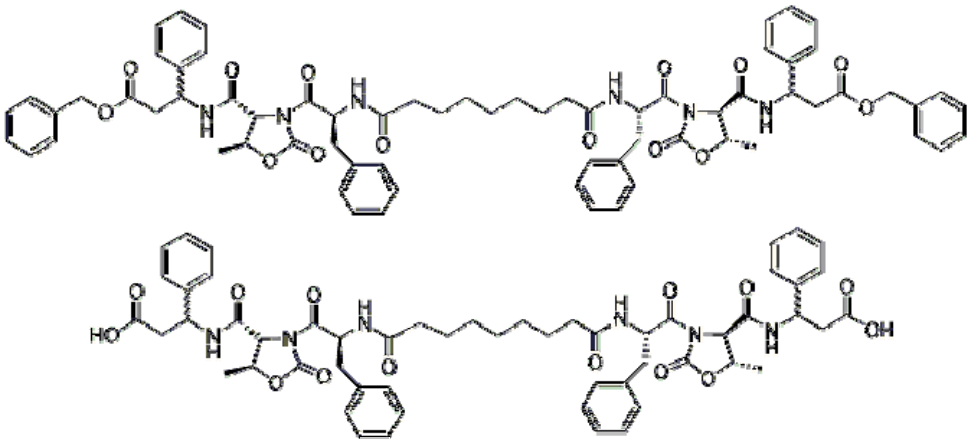
A small library of stereoisomeric pseudopeptides able to make gels in different solvents has been prepared and their attitude to make gels in the presence of several metal ions was evaluated [1]. Four benzyl esters and four carboxylic acids, all containing a moiety of azelaic acid (a long chain dicarboxylic acid) coupled with four different pseudopeptide moieties sharing the same skeleton (a phenyl group one atom apart from the oxazolidin-2-one carboxylic group), were synthesized in solution, by standard coupling reaction. The tendency of these pseudopeptides to form gels was evaluated by using the inversion test of 10 mM solutions of pure compounds and of stechiometric mixtures of pseudopeptides and metal ions. To obtain additional information on the molecular association, the gel samples were left to dry in the air to form xerogels that were further analyzed using SEM and XRD. The formation of gel containing Zn(II) or Cu(II) ions gave good results in term of incorporation of the metal ions, while the presence of Cu(I), Al(III) and Mg(II) gave less satisfactory results. This outcome is a first insight in the formation of stable LMWGs formed by stechiometric mixtures of pseudopeptides and metal ions. Further studies will be carried out to develop similar compounds of pharmacological interest.



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ORG-PO-27 Fluorous-based stationary phases for the HPLC separation of environmentally relevant compounds

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Fluorous-based stationary phases are made of perfluorinated alkyl-chains or perfluorinated aromatic moieties chemically bound to silica gel. They have been employed as separation media in SPE and HPLC due to their unique characteristics of selectivity and retention towards fluorinated and/or halogenated compounds. These properties depend on both solute and stationary phase molecular structure (number of fluorous atoms) and on the mobile phase composition. The selectivity of fluorous-based stationary phases is different from that exhibited by ordinary hydrophobic separation media due to their both hydrophobic and hydrophilic character. Hence, fluorous-based stationary phases seem to be promising separation media for applications in Environmental Analytical Chemistry. In this work, the chromatographic behavior of homologous series of four perfluorinated alkyl-acids (PFAs, C5-C8) often employed as flame retardant additives was studied. Mobile phase composition, column temperature and mobile phase flow velocity were the experimental variables upon which the retention of these compounds was studied on a C_6F_{13} column. Our investigation has revealed an U-shaped retention behavior when the mobile phase composition was changed by 40 to almost 100 % v/v ACN in water, with the lowest capacity factor at around 90% ACN. Van't Hoff plots were employed to correlate variations of enthalpy and entropy of mobile-to-stationary phase transfer with the mobile phase composition and the number of fluorous atoms in the solutes. Additionally, Van Deemter and kinetic plots were used to compare the chromatographic performances of fluorous phases and standard C_{18} media. Due to the low UV sensitivity of PFAs, all measurements were done by LC-ESI/MS. Applications of fluorous-based stationary phases as pre-concentration media and the implementation of an online enrichment/analysis instrumental setup based on these phases are discussed.

ORG-PO-28 Benzothienopyridines: interesting tricyclic compounds, scaffold in pseudopeptides against β-secretase.

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Benzothienopyridines represent a class of tricyclic heteroaromatic compounds of particular interest in medicinal chemistry: in fact their pharmacological activity as antiallergic [1], antibacterical [2] and anxioselective agents [3] has been reported.

In recent years there is an increasing attention on small molecules and their inhibitory activity on BACE 1 [4], β-secretase, has been developed.

With the aim to explore a possible effect in Alzheimer's disease, we prepare 5-amino-4-methoxycarbonyl-2-methyl[1]benzothieno[2,3-*b*]pyridine [6] in an improved synthetic route which passes through the formation of N-(heteroaryl) iminophosphoranes and a tandem aza-Wittig/electrocyclization reaction.

Furthermore this molecule could be use as scaffold for pseudopeptidic structures obtained by coupling with aminoacids or small peptides (figure 1).

In the present communication preliminary results will be reported.

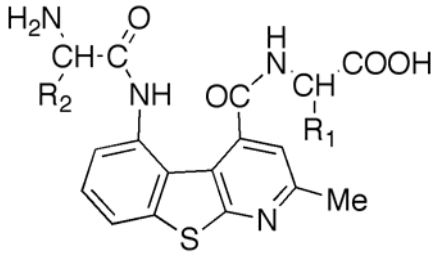

Figure 1

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ORG-PO-29 Products of the aqueous chlorination of the nicotine

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Nicotine is a non prescribed drug to which all members of a tobacco-smoking society are exposed either through direct assumption or second-hand inhalation. FAO projections have foreseen 7.1 million tonnes of tobacco leaves production in the 2010. Nicotine makes up about 5% of tobacco leaves, by weight [1].
During the tobacco manufacturing a certain amount of nicotine is released into the atmosphere, in wastewaters, sent to water treatment facilities, and in tobacco dust, discharged to landfills. Hence 93% of nicotine released is expected to be in water, 4% in the soil, 3% in air [2]. As the manufactured tobacco concerns, only 25% of the total nicotine amount in a cigarette is in the smoke stream while the remaining is lost in the surrounding [3]. Dynamics in indoor and outdoor environments [4], human excretions and the manufacturing process are responsible for the presence of nicotine in surface waters as a result of industrial and municipal discharges [5]. According to its presence in surface waters, analyses on effluents of many sewage treatment plants (STP) show that nicotine survives conventional treatment processes.
However Teijon et al. [6] report that in the Depurbaix STP the nicotine removal was almost quantitative after additional chlorination treatments. Fontela et al. [7] report the same result in a drinking water treatment plant after two chlorination steps. Chlorination therefore seem to be effective in simultaneously removing both pathogens and nicotine from row waters but the possible generation of by-products more resistant to degradation and/or with equal or more toxic effects than nicotine must be considered as well. In a model study of the effects of chlorination on nicotine with hypochlorite the main oxidation and/or chlorination products were identified and their toxicity on different organisms of the freshwater chain, as well as their mutagenic and genotoxic effects, were evaluated.

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ORG-PO-30 New 23-phosphodiester derivatives of Silybin and DHS: synthesis and preliminary evaluation of antioxidant properties.

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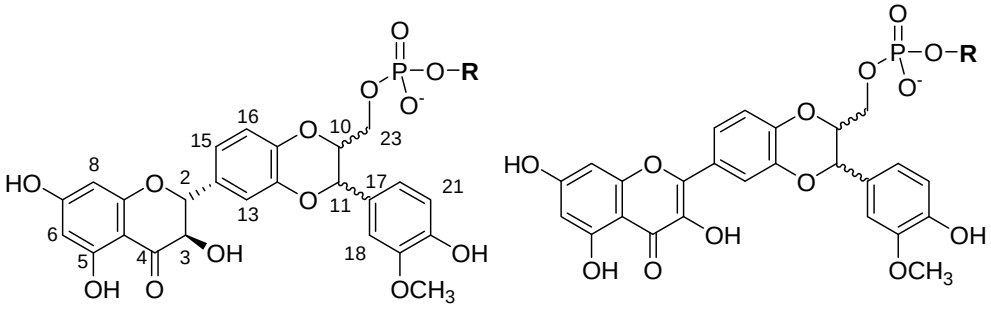
Silybin is the major flavonolignan of silymarin which is widely used as a natural remedy for the treatment of cirrhosis, chronic hepatitis, and liver diseases associated with alcohol consumption and exposure to environmental toxins [1]. Different studies recently made on the antiradical activity of silybin and DHS have elucidated the functional groups responsible for this activity [2]. The results suggest that the C-23 position could be a site for useful modifications aimed to improve the bioactivity of silybin and/or DHS analogues. Recently we describe an efficient synthetic strategy to obtain a variety of new silybin and 2,3-dehydrosilybin (DHS) derivatives in which the 23-hydroxyl group was converted to a sulfate, phosphodiester, or amine group, using a solution-phase approach [3]. The antioxidant properties of the new compounds were evaluated in a cellular model *in vivo* and most of them displayed an antioxidant activity comparable or higher to silybin and DHS. These results confirmed the assumption that modifications in position C–23 do not affect the radical scavenging activity of these analogues.

With the final goal to expand the repertoire of silybin and DHS C-23 modified, we describe here the synthesis and preliminary evaluation of antioxidant properties of a variety of new silybin and DHS conjugated with different labels through a phosphodiester bond The antioxidative properties of the above-synthesized compounds were determined by free radical scavenging (DPPH) assays.



23-phosphodiester silybin modified 23-phosphodiester DHS modified

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ORG-PO-31 Quantitative Correction of Solvent and/or Catalyst Effect on Proton Abstraction Rate Constants of C-H Acids.

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Kinetic determinations commonly find a variety of applications in the field of chemical and material sciences, often providing crucial information about the elucidation of reaction mechanisms, stereolability of chiral species endowed with pharmaceutical or enantio-/diastereo-selective sensorial activity, [1,2] etc. However, it is also not infrequent that an experimentally easy measurement of rate constants can be performed in a medium and with a catalyst different from that in which the datum is instead required. The present communication deals with a procedure of general application developed with the intent to allow a quantitative correction of rate constants of proton abstraction equilibria when the wanted solvent and/or catalyst of the process are different from that in which an experimental value is already available. The attention was focused on the case of C-H acids (ketones), a wide variety of bases of both organic and inorganic nature and three solvents, endowed with very different properties: water, acetonitrile and dichloromethane. The analysis was based on a suitable elaboration of Brønsted equations, from which a couple of final and quite simple mathematical expressions have been derived. Results pointed out that effective corrections of rate constants can be obtained also inserting in the elaborated equations pK_a values of C-H acids and/or basic catalysts (p$K_a^{BH^+}$) estimated in the selected solvents by theoretical approaches, so making the procedure very attractive for a ready and generalized use. Notably is the possibility to employ the method to correct rate constants measured in apolar organic solvents to water, the medium in which compounds of biological interest normally express their activity. This may dramatically extend the range of choice towards kinetic techniques typically operating with organic media or solvents mixtures, such as dynamic chromatography, dynamic electrophoresis and dynamic nuclear magnetic resonance spectroscopy.

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ORG-PO-32 Isolation, Characterization, and Synthesis of Degradation Products of Methylprednisolone Derivatives

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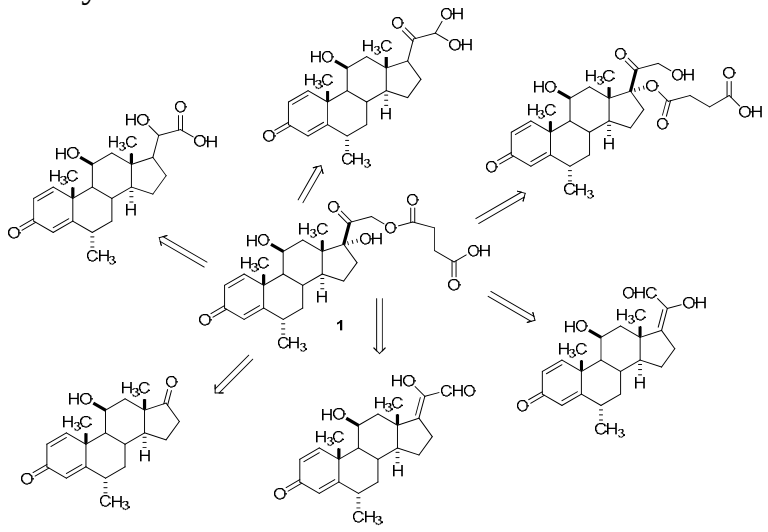
Corticosteroids are important synthetically produced glucocorticoids used as anti-inflammatory drugs [1]. Although the active pharmaceutical substances such as methylprednisolone derivatives have been on the market for many years, not much information is available in the literature regarding their degradation behaviours [2]. During the course of our studies on polyfunctional molecules with biological activity, we have been interested in exploring the determination of possible degradation products of methylprednisolone hemisuccinate (**1**), and also their identification. These degradation products are interesting molecules from the pharmaceutical point of view, and are currently under biological evaluation [3]. On the basis of fragmentation pathway and molecular weight obtained by LC-MS results, possible chemical structures can be proposed. Most of them are not sufficiently stable to be isolated, then only by synthesis it is possible to confirm the structures proposed by LC-MS results.



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ORG-PO-33 A class of highly delocalized pentacyclic diquinoid compounds with interesting spectroscopic behavior

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[b] Dipartimento di Chimica, Università di Ferrara, via Luigi Borsari 46, 44100, Ferrara, Italy
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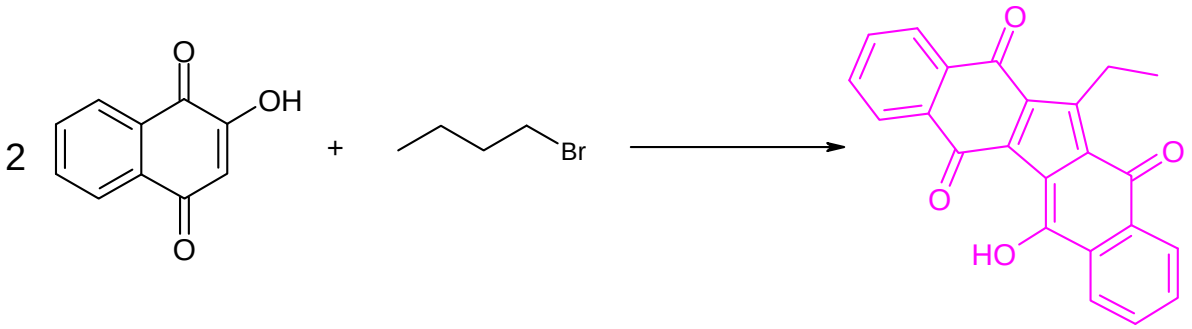
A new class of pentacyclic diquinoid compounds has been synthesized in a one-pot reaction from two molecules of 2-hydroxynaphthoquinone and 1-bromoalkanes in the presence of ferrocene.
These molecules were isolated as enol tautomer which exhibit an internal hydrogen bond and an extended electronic conjugation; such properties combined with the redox behavior of the quinoid moiety, allow different applications for this peculiar molecule.
In particular the field of light interactions open new routes in the diquinoid utilization as a potential acceptor in electron transfer processes and as a new molecular probe for solvent polarity (VOCs and RTILs) measurements.[1] [2] [3]
The spectroscopic studies of the reference compound (scheme) will be presented and discussed.



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ORG-PO-34 Synthesis, characterization and applications of metallocenylporphyrins

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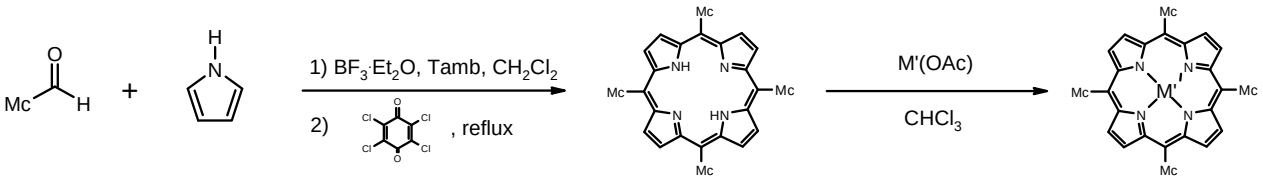
Metallocenylporphyrins have some peculiar spectroelectrochemical properties: on one hand they show a broader absorption in the visible portion of the spectrum with respect to that of other simple porphyrins; conversely the presence of a metallocenyl moiety enhance their donor character and make accessible more redox processes and mixed-valence states[1-3]. Moreover the metallation of these porphyrins can modulate their redox features.
We have prepared some free base and metal-porphyrins as shown below:



Such features and the possibility to form stable monolayers onto a surface make metallocenyl-porphyrins appealing for the application in photochemical and optoelectronic devices.
The compounds were characterized by UV-vis and electrochemical techniques, both as in solution and as surface-linked species. Differences in behavior will be discussed.

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ORG-PO-35 Heteroaromatic-based organic and organometallic dyes for dye-sensitized solar cells

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Solar energy is the most abundant clean and renewable energy source but photovoltaic technology has not yet found widespread use due to its high intrinsic costs. Emerging thin-film molecular-based photovoltaic technologies, based on organic and organometallic molecules and polymers, offer a unique promise of cheap, efficient, and robust devices. Amongst the new technologies, dye-sensitized solar cells (DSCs) show one of the best potential of high-conversion efficiency and low-cost manufacturing.
Here we present our recent studies on DSC based on organic and organometallic photosensitizers. The organic sensitizers have an unprecedented multi-branched structure, at variance with the conventional uni-dimensional geometry, for enhanced power conversion efficiencies and stabilities. We also report our most recent studies on a new family of cyclometalated complexes for efficient and more stable devices. In both cases the design of the sensitizer dyes originated from a careful selection of electron-rich and electron-poor aromatic and heteroaromatic fragments in order to tune, and optimize, optical and energetic properties and, in turn, device performance. The new dyes have been completely characterized in their optical and electrochemical properties and investigated in photovoltaic devices. [1]

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ORG-PO-36 Lithiated 2-Phenyloxetane: A Versatile Intermediate in Organic Synthesis

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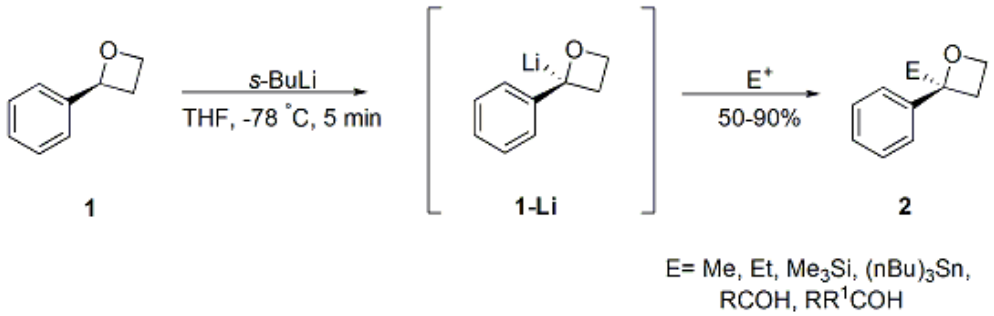
Oxetanes, the closest homologs to epoxides, are an important group of four-membered cyclic ethers that, as equivalent for the a^3-synthon, can undergo a wide range of chemical transformation; their ring motif is also found in many natural products that exhibit a range of biological activities [1]. The importance of oxetanes as versatile buiding blocks to synthetic and medicinal chemistry as well as to material and agrochemical sciences is dramatically increased over the last ten years with the development of new and efficient methods for their preparation [2].

Despite recent advances, their reactivity toward organometallic reagents has only been scarcely explored. Inspired by intensive interest in the field of α-lithiated oxiranes [3] we became intrigued by the possibility of both generating an α-lithiated oxetane chemically stable on the timescale of its reactions and of investigating its reactivity. Herein, we report a promising route to 2-substituted phenyloxetanes **2** exploiting the nucleophilic reactivity of α-lithio-2-phenyloxetane **1-Li** prepared by means of an hydrogen-lithium exchange from 2-phenyloxetane **1**. Configurational stability of **1-Li** on the time scale of its reactions will also be tackled.



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ORG-PO-37 Syntheses of Lentiginosine Derivatives Oriented to Diversity

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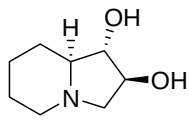
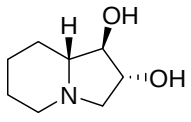
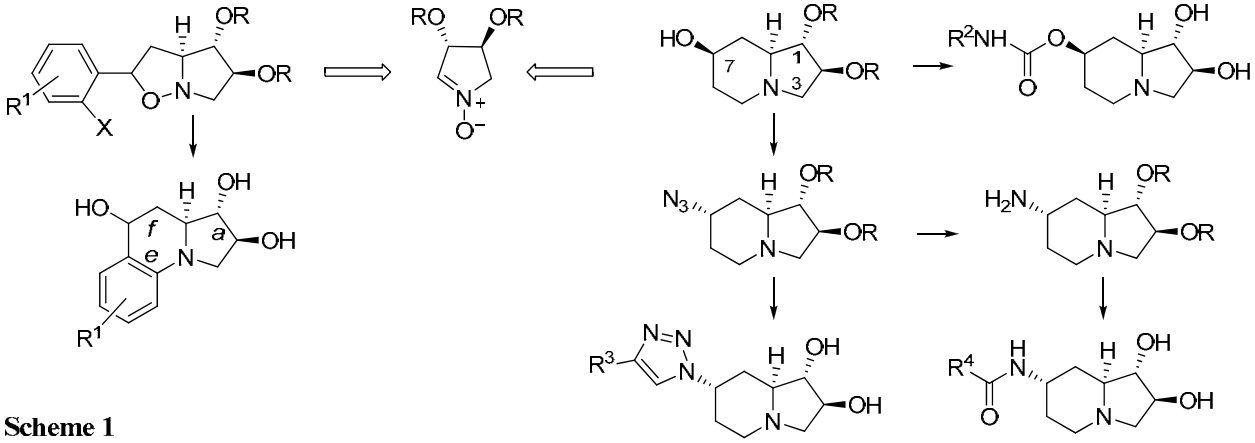
(+)-Lentiginosine [(+)-**1**], an indolizidine alkaloid isolated for the first time by Elbein et al. from the leaves of *Astragalus lentiginosus* in 1990,[1] is the less oxygenated iminosugar able to mimic glucosidase natural substrates and it is a selective inhibitor of amyloglucosidases.[2] The non-natural enantiomer (–)-**1** is a weaker inhibitor than (+)-**1**, and was recently shown to be a caspase-dependent apoptosis inducer on tumor cells of different origin.[3] The important activity of these compounds suggested the synthesis of several differently functionalised derivatives to study their interaction with bioreceptors, with an input deriving also from computational studies. Taking advantage of the highly reliable and selective nitrone 1,3-dipolar cycloaddition, various 7-substituted- and *e*-benzocondensed lentiginosine derivatives were synthesized starting from enantiopure pyrroline *N*-oxides derived from L- and D-tartaric acid (Scheme 1).[4]



(+)-**1**
natural alkaloid
amyloglucosidase inhibitor



(-)-**1**
non-natural
proapoptotic



Scheme 1

Aspects of the stereoselective synthesis of lentiginosine derivatives will be presented together with the most recent results of biological tests.

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ORG-PO-38 Ultrasounds mediated cyclization of aryl propionic acids: a new route towards indanones.

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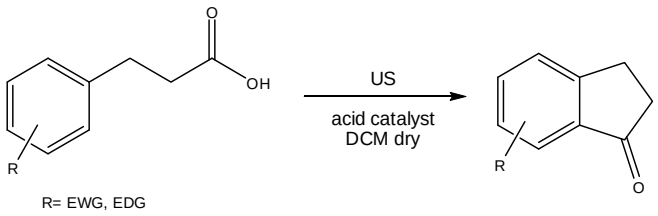
Indanones are structural motifs frequently used as synthetic precursors of several biologically active both natural and pharmaceuticals compounds. The indanone plays a pivotal role in the donepezil (Aricept) mediated acetylcholinesterase (ACh) inhibition. The classical way to achieve an indanone moiety is to perform a Friedel-Craft cyclization of aryl propionic acyl chloride or Meldrum's acids.[1] Some examples of cyclization starting from aryl propionic acids has been reported in the literature, but all the procedures need superacids catalysts [2] or drastic reaction conditions [3]. Molecular modelling studies have suggested indanone derivatives, reporting an EWG group on the aromatic cycle, as promising ACh inihibitors.
An efficient ultrasounds-assisted Friedel-Craft cyclization of inactivated aryl propionic acids is presented.



Ultrasounds allow to use a low amount of acid with respect to the procedures reported in the literature and to perform the reaction at room temperature or under slight heating. A comparison between the reaction performed with or without sonication shows that ultrasounds reduce the reaction time and improve the reaction yield giving rise to a pure product even in the case of strongly inactivated starting materials.

References:

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ORG-PO-39 Novel Expeditious Synthesis of Unconventional Piperidines

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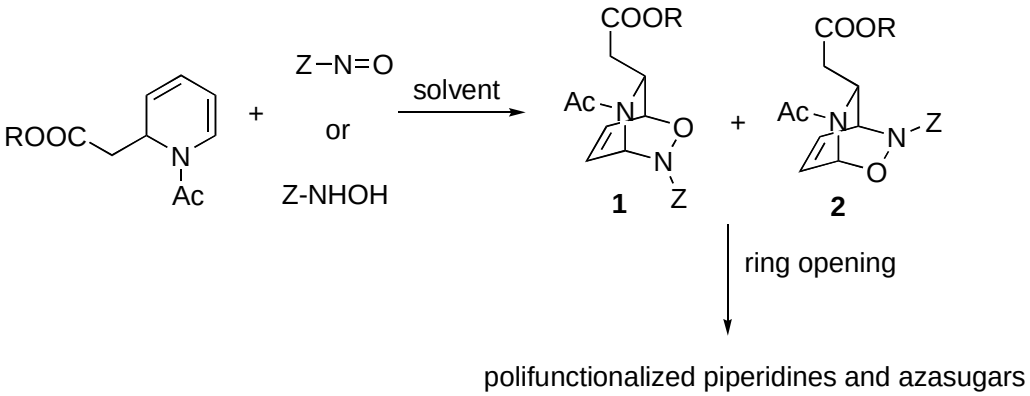
Nitroso cycloadducts, derived from nitroso Diels-Alder reactions, are valuable synthetic intermediates as they serve as a general scaffold to create unique structural and functional diversity.[1] In our continued interest for the chemistry of these cycloadducts,[2] we have examined the nitroso Diels-Alder of N-acetyl-1,2-dihydropyridyl acetic acid derivatives, very recently obtained by us using a Perkin-acyl Mannich reaction.[3]



The nitroso cycloadducts **1** and **2** were obtained with complete *trans*-stereoselectivity with respect to the C_2 substituent with a regioselectivity that was highly dependant by the nitroso dienophile used. The ring opening of adducts **1** and **2** afforded densely functionalized piperidines with unconventional substitution patterns and showed some interesting features.

[1] B. S. Bodnar, M. J. Miller, *Angew. Chem. Int. Ed.* **2011**, DOI: 10.1002/anie.201005764.
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[3] Manuscript submitted.

ORG-PO-40 Synthesis, Stability Evaluation and Permeability Study of a Zidovudine-Bile Acid Prodrug

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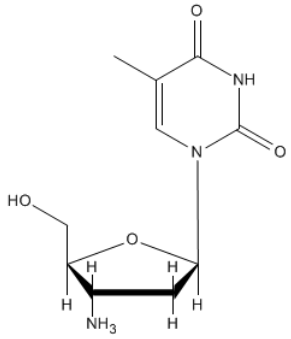
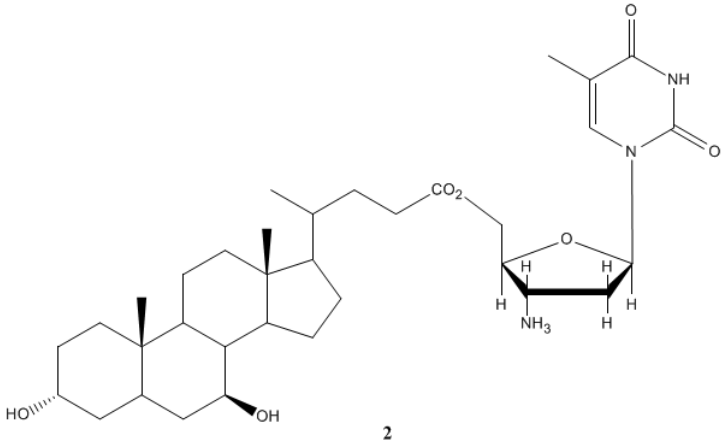
3'-Azido-3'-deoxythymidine (**1**, AZT, Zidovudine), clinically approved by FDA to treat human HIV infection, is a typical member of the nucleoside analogues. Recently, the well known clinical limitations related with AZT therapy (especially dose-related toxicity and a short half-life in plasma) have prompted the synthesis of different types of 5'-*O*-conjugates of zidovudine [1].



1



2

Based on the large application of bile acids in pharmacology and their amphiphilic structures, we have designed and synthesized the AZT-ursodehoxycholic acid prodrug **2** in an effort to enhance the efficiency of drug delivery. In this prodrug, conjugating moiety is linked to AZT through a 5'-*O*-ester group. The stability in physiological fluids and the *in vitro* permeability of zidovudine-prodrug **2** have been evaluated.

Every detail concerning synthesis, stability and permeability will be discussed.

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ORG-PO-41 Electrophilic Fluorination of Lithiated Aryloxiranes

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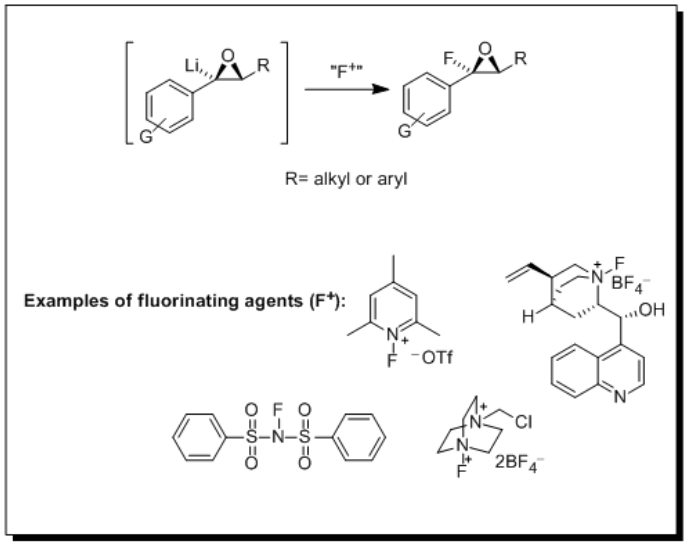
Today, the significant expansion in the use of fluorinated chemicals has been attracting more and more the attention of organic, agricultural, medicinal, and material chemists. This is because the replacement of hydrogen by fluorine alters sterically, electronically and lypophilically the properties of the molecule, affecting overall reactivity and stability [1]. In this context, the development of new synthetic fluorinating methodologies of "building blocks", starting from commercially available and cheaply material, is quite interesting and widely pursued.

One of the most fascinating aspects of organofluorine chemistry is the asymmetric synthesis of fluorinated molecules. To date, in particular, only a few methods of synthesis of fluorinated epoxides have been reported [2]. As the oxiranyl anion-based methodology has undoubtedly become a valuable tool for making more functionalized epoxides [3], fluorination of lithiated aryloxiranes has been investigated starting either from configurationally stable and optically active derivatives or from racemic substrates but that can successfully undergo a dynamic resolution.

Asymmetric fluoruration of meso epoxides will also be discussed.



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V. Capriati, S. Florio, R. Luisi, *Chem. Rev.*, *108*, **2008**, 1918; (b) V. Capriati, S. Florio, A. Salomone, In *Topics in Stereochemistry, 26*, **2010,** R. E. Gawley, Ed., Verlag Helvetica Chimica Acta: Zürich.

ORG-PO-42 Lithiated Trifluoromethylphenyloxiranes: Solution Structure and Dynamic Resolution

Antonio Salomone, Rosmara Mansueto, Filippo Maria Perna, Saverio Florio and Vito Capriati

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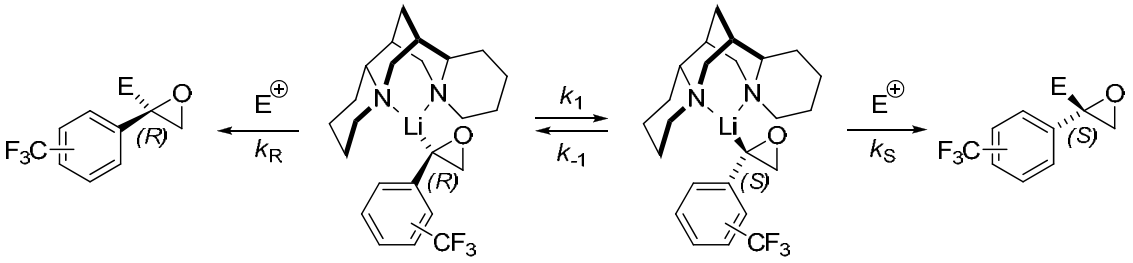
Stereoselective substitution of organolithiums represents a powerful methodology in asymmetric synthesis. While it is much convenient to use configurationally stable reagents, it is also possible to carry out an asymmetric synthesis by using stereolabile organolithiums that undergo fast racemization. This goal, usually achieved by exploiting a dynamic resolution of the racemic organolithium, provides an opportunity to obtain enantioenriched products starting from racemic substrates with the aid of external chiral ligands. As part of our research on the reactivity of -lithiated aryloxiranes, [1] we recently found that although -lithiated trifluoromethyl-substituted aryloxiranes undergo fast racemization when generated in THF, the employment of hexane/TMEDA dramatically hinders their racemization.[2]



Dynamic Kinetic Resolution: $k_1, k_{-1} >> k_S, k_R$
Dynamic Thermodynamic Resolution: $k_S, k_R >> k_1, k_{-1}$

In this communication, we report preliminary results concerning the dynamic resolution of -lithiated trifluoromethylstyrene oxides, in the presence of chiral diamine ligands. Solution structure and racemization mechanism will also be discussed in light of DFT calculations and a multinuclear magnetic resonance investigation.

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ORG-PO-43 *N*-Alkylation of *N*-Arylsulfonyl-α-Amino Acid Methyl Esters by Trialkyloxonium Tetrafluoroborates

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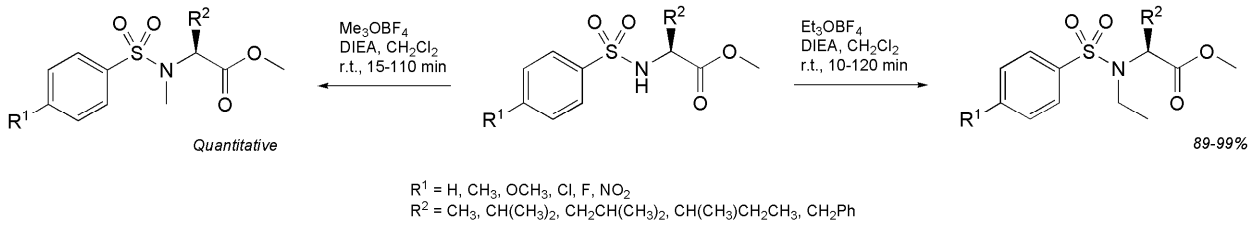
N-Alkyl-α-amino acids are a representative class of amino acid derivatives. They find applications as synthetic building blocks in medicinal chemistry and are structural constituents of peptidomimetics and naturally occurring bioactive peptides [1]. In particular, the synthesis of *N*-methyl and *N*-ethyl-α-amino acids has received attention for decades [2]. *N*-Methyl-α-amino acids are successfully obtained by reacting *N*-nosyl-α-amino acids with diazomethane [3]. However, the highly toxic nature of this reagent prompted us to exploit new methods in which more safe alkylating species could be used.



Scheme 1

In this communication we present a highly efficient strategy for the rapid, clean, and chemospecific *N*-methylation of a series of differently 4-substituted *N*-arylsulfonyl-α-amino acid methyl esters, performed using trimethyloxonium tetrafluoroborate. *N*-Methylation of the amino acid derivatives is quantitative also in those cases in which diazomethane results to be ineffective. In a similar protocol, *N*-ethylation of the same 4-substituted *N*-arylsulfonyl-α-amino acid methyl esters tested for *N*-methylation is easily realized using triethyloxonium tetrafluoroborate.

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ORG-PO-44 γ-Hydroxybutenolide Derivatives As Promising Negative Modulators Of Microsomal Prostaglandin E_2 Synthase-1.

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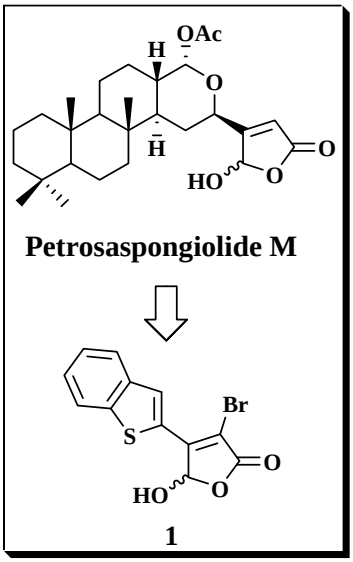
Petrosaspongilide M (PM) is a natural product isolated from the marine sponge *Petrosaspongia nigra* characterized by a γ-hydroxybutenolide ring. It is able to potently inhibit the human synovial phospholipase A_2 (PLA_2) type IIA, the enzyme responsible for triggering the arachidonic acid cascade [1].

In the frame of a previous project involved in the generation of PM-simplified derivatives as potential inhibitors of PLA_2, we identified the interesting compound **1** able to negatively modulate microsomal prostaglandin E_2 synthase-1 (mPGES-1), the enzyme involved in the biosynthesis of PGE_2 from PGH_2 [2,3].

The intriguing biological results shown by this new potent and selective negative modulator of mPGES-1 expression (IC_{50} = 1.80 μM) [2,3] encouraged us to continue our studies and, taking into account Ludi software suggestions, we undertook the synthesis of a new generation of γ-hydroxybutenolides, bearing different molecular decorations in order to amplify the chemical space under investigation.



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M.D.Guerrero, M.Aquino, I.Bruno, R.Riccio, M.C.Terencio, and M.Paya, *Eur.J.Pharmacol.*, *620*, **2009**, 112.

ORG-PO-45 Development Of A New Collection Of Trizole-Based Derivatives As Promising Microsomal Prostaglandin E_2 Synthase-1 Inhibitor.

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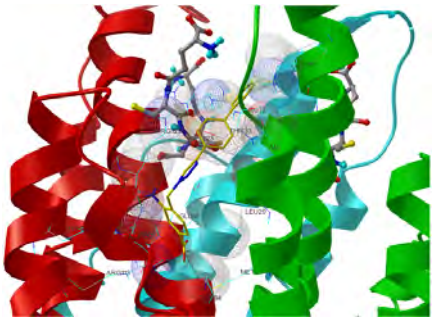
Microsomal prostaglandin E_2 synthase-1 (*m*PGES-1) enzyme is recently emerged as an attractive target involved in inflammatory diseases [1]. Because of its ability to affect only COX-2-mediated PGE_2 production, *m*PGES-1 inhibitors are supposed to be a promising alternative to non-steroidal anti-inflammatory drugs which are known to be endowed with severe side effects [2].



Despite many efforts have been lavished in this research area, owing to the lack of *m*PGES-1 crystallographic structure in the open active form, very few inhibitors of the enzyme have been identified so far [3]. Hence we decided to choose as model for our investigations microsomal glutathione S-transferase (MGST-1), an enzyme belonging together with *m*PGES-1, to membrane associated proteins in eicosanoid and gluthatione metabolism (MAPEG) family, and showing a high homology sequence with our selected target [4]. On the basis of virtual screening outcomes, we designed and synthesized a collection of potential *m*PGES-1 inhibitors based on 1,4-disubstituted triazole moiety which showed interesting pharmacological profiles. In this frame we discovered a promising hit (IC_{50} = 3.2 μM) [5] which has been subjected to a further structural optimization process, according to molecular modeling suggestions, in order to improve its biological activity.

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ORG-PO-46 New structural insights into saraines A, B and C, macrocyclic alkaloids from the Mediterranean sponge *Reniera (Haliclona) sarai*.

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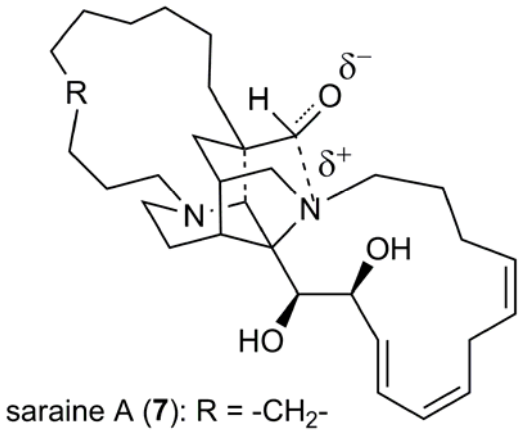
Saraines A, B and C (Figure 1) are structurally complex diamine alkaloids first isolated from the sponge *Reniera sarai* collected in the bay of Naples [1]. Their peculiar core structure induces an uncommon behaviour responsible of chromatographic and spectroscopic anomalies, and that was explained by a strong "proximity effect" between a tertiary ammine and aldehyde groups, able to be involved into a cyclic zwitterionic form.

On saraines A-C recently isolated from the same sponge collected in the Northern Adriatic Sea, we report now on new structural evidences including: *a)* NMR analysis in different solvents, *b)* electrospray ionization (ESI)-MS spectra showing signals for mixed $[2M+H]^+$ clusters in neutral conditions and $[M+H]^+$ ions in acidic media, *c)* zwitterionic form trapped by conversion to a stable O-methyl ammonium salt derivative, *d)* density functional theory (DFT) calculations on the amine-aldehyde form, resulting in good agreement with Bürgi–Dunitz angle, a model able to forecast the preferred spatial approach in the nucleophilic addition to a carbonyl group.



saraine A (**7**): R = $-CH_2-$

saraine B (**8**): R = $-CH\overset{Z}{=}CH-$

saraine C (**9**): R = $-CH\overset{Z}{=}CHCH_2-$

Figure 2.

In addition, biological activities including antibacterial, haemolytic and anti-acetilcholinesterase assays were investigated for saraines A-C, in order to clarify their ecological role [2].

[1] G.Cimino, C.A.Mattia, L.Mazzarella, R.Puliti, G. Scognamiglio, A.Spinella, E.Trivellone, *Tetrahedron*, *45*, **1989**, 3863.
A.Defant, I.Mancini, L.Raspor, G.Guella, T.Turk, K.Sepčić, *Eur.J.Org.Chem.*, **2011** in press.

ORG-PO-47 Design, Virtual Screening and Synthesis of Potential Heat Shock Protein 90 (HSP90) inhibitors

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Dipartimento di Scienze Farmaceutiche e Biomediche, Università di Salerno, Via Ponte Don Melillo, 84084, Fisciano (Salerno), Italy
sterracciano@unisa.it

Molecular chaperones are a class of proteins responsible for the correct folding of several cellular "client" proteins which are deeply involved in key physiological functions in human cells. Belonging to this wide proteins family is the heat shock protein 90 (Hsp90), which has recently emerged as a very important target in several human diseases including cancer, neurodegeneration, viral, fungal and microbial infections.[1] In particular, Hsp90 is an ATP-dependent chaperone that plays a central role in regulating the stabilization, activation and degradation of a range of proteins that promote cell growth and survival.[2] These "client" proteins include kinases, steroid hormone receptors, transcription factors, directly involved in malignancy, and also a number of known over-expressed or mutant oncogenic proteins such as Raf-1, mutant BRaf, Akt, HER2, IGF-IR, mutant EGFR and others.[3] On this basis Hsp90 is considered an important target for pathway-oriented drug discovery. With the aim of developing new Hsp90 inhibitors we performed an in silico screening by molecular docking using Autodock-Vina software [4] starting from 176 designed molecules. For our docking calculation, we used the X-ray crystallographic structure of Hsp90 N-terminal domain (pdb code: 2qg0).[5] Following computational docking suggestions, we successfully undertook the synthesis of a collection of new triazole based molecules through "click chemistry" approach as potential Hsp90 inhibitors.

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ORG-PO-48 Stereoselective Synthesis of Diastereoisomeric 6-Deoxy-*N*-Cbz-iminoglycal-derived Vinyl Oxiranes and their Regio- and Stereoselective Behavior in Addition Reactions

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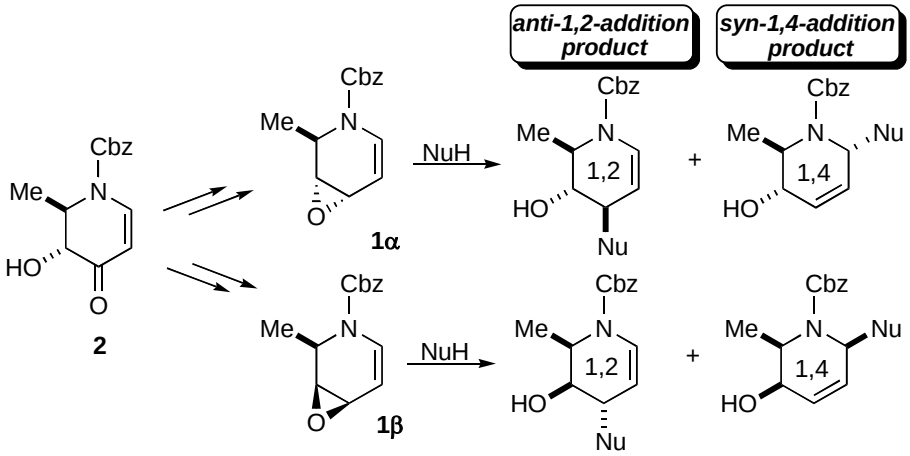
The iminoglycal system can constitute an efficient access to differently substituted azasugars, a class of compounds with potentially interesting biological properties, in particular as inhibitors of enzymatic activity.[1]

In view of their use as precursors of azasugars, the new, diastereoisomeric 6-deoxy-*N*-Cbz-iminoglycal-derived vinyl epoxides **1α** and **1β**,[2] were synthesized starting from a common synthetic intermediate, the *trans* hydroxy ketone **2**, on its own prepared by a racemic application of the Comins' enantioselective protocol.[3]

The regio- and stereoselective behavior of epoxides **1α** and **1β** was examined in addition reactions with *O*-, *N*-, *S*-, and *C*-nucleophiles.



The results have indicated that *1,2-* and/or *1,4-addition products* are obtained, depending on the reaction conditions. In particular, a complete or large 1,4-regio- and *substrate-dependent* stereoselectivity toward corresponding *syn-1,4-addition products* is observed when coordinating nucleophiles are used. On the contrary, the use of non-coordinating nucleophiles leads to the formation of corresponding *anti-1,2-addition products.*

[¶] Present address: Istituto Italiano di Tecnologia (IIT), Genova.

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ORG-PO-49 Amine-Oxide Surfactant Hydrogels Hybridized with Single-Walled Carbon Nanotubes: Preparation, Rheology and Applications

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The preparation of hydrogels hybridized with single-walled carbon nanotubes (SWNTs) is very interesting in view of bio-inspired applications, such as the design of biosensors [1]. Due to their superb characteristics, SWNTs can modulate the gel properties acting as reinforcing fillers or increasing the electrical conductivity. In return, SWNTs get a matrix that keeps them separate in a semi-solid state, allowing to overcome the restriction on use.

Amine-oxide surfactants possess a low toxicity and are readily biodegradable; in addition some analogues are able to form viscoelastic solutions based on worm-like micelles [2].

In this work well-dispersed SWNTs were successfully incorporated in supramolecular hydrogels obtained with amine-oxide surfactants (Fig.1). Rheological characterization of the prepared hybrids was performed under oscillating dynamic conditions and highlighted a typical viscoelastic behavior with the measured storage moduli (G′) dominating the loss moduli (G″) by one order of magnitude and exhibiting little frequency dependence over the range of angular frequencies tested. The effects of different SWNT and gelator concentrations employed on the hydrogel properties were assessed. The temperature dependence was studied as well. Dependence of the investigated rheological properties of the hydrogels from the SWNTs concentration evidenced reinforcing intermolecular interactions occurring between the nanotubes and the surfactants.

Fig. 1 Hydrogel of SWNTs prepared with *p*-dodecyloxy-benzyldimethylamine oxide (pDoAO).

[1] V.S. Gavalas, S.A. Law, J.C. Ball, R. Andrews and L.G. Bacas, *Anal. Biochem., 329,* **2004,** 247.
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ORG-PO-50 Structural modifications for improving the dispersibility of single-walled carbon nanotubes

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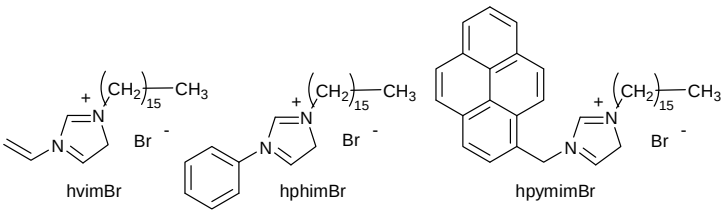
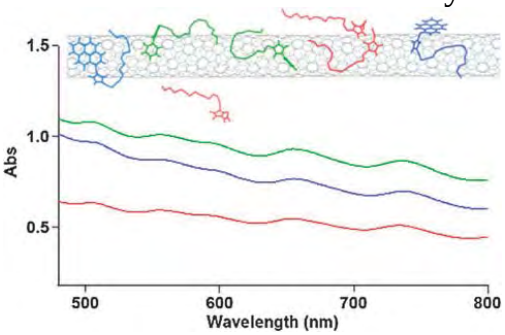
The main limitation related to the use of Single-Walled Carbon Nanotubes (SWNTs) is their low solubility in organic and aqueous solvents. It has been previously demonstrated that ionic liquids (ILs) based on the imidazolium cation can disentangle SWNT bundles [1] and that a long-chain imidazolium IL (hvimBr) has the ability to produce stable homogeneous aqueous dispersions of SWNTs [2].

The purpose of the present study is to assess the effect of different moieties in position 3 of the imidazole ring on the dispersing ability of ionic liquid surfactants toward SWNTs, in order to develop new derivatives with ideal features. We demonstrate that aromatic groups enhance the affinity for SWNTs, as confirmed by molecular dynamics simulations, but at the same time render the molecule less water soluble and more prone to self-assembly [3]. NIR-PL, Raman, AFM and vis-NIR absorbance results show that hphimBr has the best features to be used as SWNT water dispersant as it has an optimal hydrophobic/hydrophilic balance which favors adsorption onto the nanotube sidewalls over self-assembly.





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ORG-PO-51 Synthesis of new Pyrrole-Indomethacin derivatives

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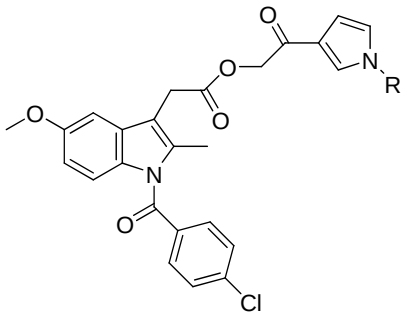
Indomethacin (IDMC) is a non-steroidal anti-inflammatory drug (NSAID), which is useful for the treatment of pain and inflammation by inhibiting the cyclooxygenases (COXs) activities. The major drawback of IDMC, if orally ingested, is an undesirable gastric effect. The embedding of IDMC molecules into a biomaterial is a strategy to overcome the undesirable side effects and exploit the possibility of a locally achieved controlled drug release.

Among polymeric biomaterials, PPy is an attractive electroconductive polymer that, properly doped with molecules with pharmacological activity, combines biological compatibility with good electroconductivity [1], becoming a good candidate as smart biomaterial [2].

At the present our attention is focussed on the synthesis of novel pyrrole monomers functionalized with IDMC (Py-IDMC) to obtain new electroconductive and bioactive polymers.

In order to achieve this purpose we synthesized ester **1** and "reverse ester" **2**, where IDMC is covalently bound, through a spacer chain, to the properly functionalized Py.



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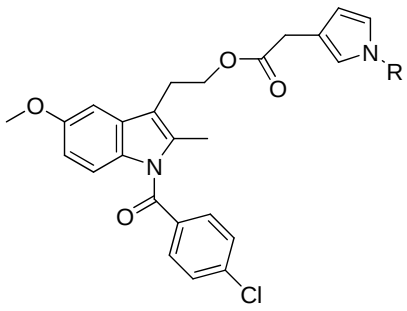

2

These products will be subjected to electropolymerization assay and biological and toxicological tests. Our efforts will address new Py-IDMC derivatives where the spacer is a glycolamide moiety [3].

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ORG-PO-52 Design, synthesis and biological evaluation of non peptide integrin antagonists via Copper (I) Catalyzed Azide-Alkyne Cycloaddition

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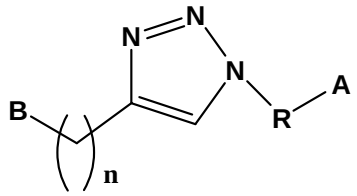
Integrins are cell surface ahdesion proteins that play main roles in cell-cell and cell-matrix interactions. Subgroup $\alpha v\beta 3$ is involved in angiogenesis and tumor cell migration, interacting with vitronectin on the extracellular matrix mainly through the recognition of the tripeptide sequence RGD (Arg-Gly-Asp).[1] That sequence was first incorporated into various linear and cyclic peptides, recently, research has been focused on the synthesis of selective non peptide integrin antagonists, because of their enhanced metabolic stability, bioavailability and biological absorption.

In recent years Sharpless and Kolb[2] proposed the triazole ring as a non-classical bioisostere of peptidic bond. Triazolic rings can be synthesized via an high yield reaction that can be performed in simple conditions, the so-called CuAAC (Copper (I) catalyzed azide-alkyne cycloaddition), the main reaction of the "Click Chemistry" concept[3]. Considering also the stability of such ring, we focused our synthetic efforts in producing a library of triazole derivatives bearing isosteres of the basic and acidic groups of the RGD sequence. After a first library of compounds was synthesized and their biological effects were evaluated,[4] other structures were then designed, synthesized and evaluated also as radiolabeled compounds for imaging applications.



B: Basic Isostere A: Acidic Isostere

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ORG-PO-53 Production of fumonisin analogues in *Fusarium verticillioides* broth cultures under different growth parameters.

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Fumonisins are a group of structurally related mycotoxins that are mainly produced by *Fusarium verticillioides*. This fungus is one of the most common molds colonizing maize crops throughout the world before harvesting, during the time between harvesting and drying, and during storage. Fumonisins are most frequently found in maize and maize-based foodstuffs and feedstuff, and less
commonly in other grains. These compounds show toxic effects in animals and humans. Moreover, the consumption of fumonisin contaminated maize has been associated statistically with the high incidence of esophageal cancer in rural areas of South Africa, China and Italy.
The fumonisin analogues that have been characterized since 1988 can be classified into four main groups, identified as the fumonisin series A, B, C, and P. The fumonisin B (FB) analogues, comprising toxicologically important FB1, FB2 and FB3, are the most abundant naturally occurring fumonisins, with FB1 predominant, and are usually found at the highest levels. Apart from the FB series, some of the other analogues may occur in naturally contaminated maize, at relatively low levels (<5% of the total fumonisin present).
The present study aimed to evaluated the production of the main fumonisins as well as of their minor analogues in *Fusarium* colture broth under different growth conditions (a_w, time, temperature), in order to better define the biosynthetic pathway of these compounds and the factors which may inhibit/elicitate their production. All the main compounds were identified and by LC-ESI-MS/MS and the fragmentation patterns have been fully characterised. Exact mass measurements were performed by LTQ-Orbitrap.

ORG-PO-54 Phenolic content and radical scavenging ability of wild fruits of *Rubus* species and related jam and seeds from Calabria

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Small berries are rich sources of bioactive compounds such as flavonoids, phenolic acids and vitamin C, which are known to display potential health-promoting effects [1]. Blackberry is an edible fruit produced by several species of the *Rubus* genus of the *Rosaceae* family. In this study, we have determined the chemical composition, the phenolic content, and the antioxidant activity of Southern Italy blackberries (*Rubus ulmifolius* Schott) growing wild in Calabria. In particular, the studies were extended to two anatomically distinct parts of fruit, the pulp and the seeds and a derived product such as jam. The fruits were picked randomly from different parts of wild bushes on mountain slopes at an altitude of 1000 m above sea level (C.da Pallone, Cosenza). The freeze-dried fruits were crushed in a mortar and were sieved using a 60 mesh screen to achieve the separation of seeds from the pulp. One part of the pulp was directly analyzed, while another part was cooked to make jam. Total lipids were extracted from ground seeds (5 g) with hexane at 90°C for 2 h (22% yield w/w). The fatty acid composition was then determined by GLC after a direct transesterification procedure [2] carried out in methanol-benzene with acetyl chloride. The most represented fatty acids were linoleic and linolenic acids (89,6%). The methanolic extract of defatted seed flour showed a strong radical scavenging activity determined using DPPH test (97%). On the other hand, the antioxidant activity of two phenolic fractions extracted from the pulp (ethyl acetate extract containing phenolic acids and flavonol glicosides, and acidic methanol extract containing anthocyanins) was lower than that of seeds (70% and 69% respectively). The processing of the berries into jam, prepared by cooking 50 g of pulp with 25 g of sugar and 1,25 g of pectins for 3 min, led to a significant loss of radical scavenging activity (50 %). HPLC-UV/vis and HPLC-ESI analyses were used to determine anthocyanin and phenolic composition. The results indicated that cyanidin-3-glucoside was the major anthocyanin in the pulp while the most abundant non-anthocyanin phenolic was epicatechin. The main phenolic compound detected in the metanolic extract of the seeds was free ellagic acid.

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ORG-PO-55 Solomonamides A and B: two unprecedented cyclic peptides from the marine sponge *Theonella swinhoei*

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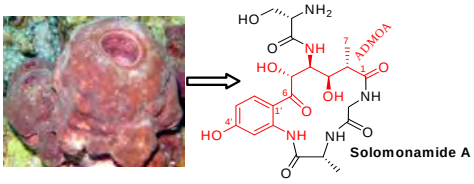

Theonella swinhoei represent one of the most prolific source of innovative secondary metabolites, belonging to more than nine biosynthetic classes [1]. Among these, surely the peptides represent the most significant group, with unusual chemical structures and intriguing biological activities.

In the course of our search for novel metabolites from this sponge, we have isolated two new cyclic peptides, named solomonamides A and B. Solomonamide A is composed of three conventional amino acid residues, alanine, glycine and serine, and a 4-amino(2'-amino-4'-hydroxyphenyl)-3,5-dihydroxy-2-methyl-6-oxohexanoic acid (ADMOA) unit which is unprecedented in natural products. Solomonamide B differs from solomonamide A for the presence of the 4-amino-6-(2'-amino-4'-hydroxyphenyl)-3-hydroxy-2-methyl-6-oxohexanoic acid residue (AHMOA) instead of ADMOA residue.

Structural characterization was elucidated on the basis of comprehensive 1D and 2D NMR tecniques and hight-resolution mass spectrometry. A combinated approach, involving Marfey's method [2], QM *J* based analysis and DFT $J/^{13}C$ calculations [3], was used for establishing the absolute configuration of the entire molecules.

Solomonamide A showed an interesting *in vivo* anti-inflammatory activity reducing carrageenan induced mouse paw oedema [4].

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ORG-PO-56 Perthamides C-F, potent human antipsoriatic cyclopeptides

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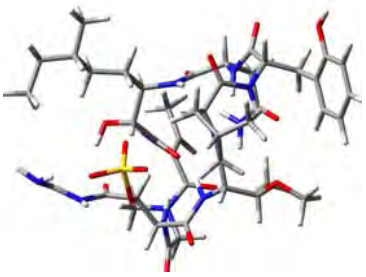
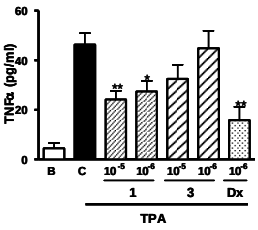
Psoriasis is a chronic autoimmune inflammatory skin disorder affecting approximately 2-3% of the general population in Europe and North America. Cutaneous and systemic overexpression of various proinflammatory cytokines (TNF-α, IL-8, IFN- , etc) has been demonstrated in psoriatic patients [1].
Pursuing the chemical investigation of the polar extracts of the Solomon marine sponge *Theonella swinhoei*, we isolated two new cyclic octapeptides, perthamides E and F, together with a large amount of perthamide C [2].
Structural characterization were performed by interpretation of NMR and MS data and the absolute configuration of the AHMOA (3-amino-2-hydroxy-6-methyloctanoic acid) residue in perthamides E and F was proposed on the basis of quantum chemical calculation of NMR chemical shifts [3].
Perthamides C and E are endowed with anti-inflammatory activity inhibiting TNF- and IL-8 release in primary human keratinocytes cells and therefore could represent potentially leads for the treatment of psoriasis.





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ORG-PO-57 Towards new ligands of nuclear receptors. Discovery of malaitasterol A, an unique bis-secosterol from marine sponge *Theonella swinhoei*

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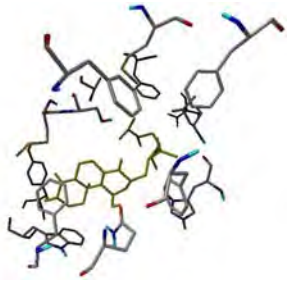
In our studies of bioactive compounds from sponges collected from the Solomon Islands, we found a single specimen of the sponge *Theonella swinhoei* as an extraordinary source of new metabolites. Analysis of the polar extracts afforded anti-inflammatory peptides [1], [2], and two sulfated sterols, solomonsterols A and B [3], potent leads in the treatment of immune-driven inflammatory bowel diseases. Investigation of the apolar extracts uncovered a new sterol, which we named malaitasterol A [4].



The structural elucidation of malaitasterol A, which features an unprecedented bis-secosteroid skeleton has been solved through extensive 2D NMR analysis, ESI-MS data and DFT ^{13}C chemical shift calculations.
The pharmacological analysis demonstrated that malaitasterol A is a potent agonist of pregnane-X-receptor and the putative binding mode has been obtained through docking calculations.
In this poster the structure of the new sterol, its pharmacological evaluation and the potential of this study will be focused.

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ORG-PO-58 Chirality effects on the structure of basket resorcarene/nucleoside complexes by gas-phase IR action spectroscopy.

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Enantioselectivity is a selection phenomenon acting at molecular level. It is responsible of many highly specific biological processes in living systems and implicated in a great number of chiral synthetic processes. Although it intrinsically requires optically active species involved in intimate diastereomeric interactions, other environmental factors may also be important for its efficiency in solution, e.g. solvation, counterion, pH, ionic strength, etc, whose contribution can only be evidenced when their effects can be excluded, i.e. in the gas phase.
In the last decades development of high pressure sources such as electrospray (ESI), nano-electrospray (nano-ESI), atmosferic pressure chemical ionization (APCI), enabled the study of molecular systems up to protein dimensions by means of mass spectrometric devices, i.e. in the absence of environmental effects perturbing the intrinsic gas-phase enantioselectivity. This kind of investigations of have been greatly improved in the last years by introducing a tunable infrared (IR) laser beam into an ion trap (IT) or an ion cyclotron resonant (ICR) mass spectrometer, where selected ions can be isolated long enough to allow their absorbance spectrum be collected. The IR spectum is recorded by measuring the intensity of the fragment ions generated by MultiPhoton induced Dissociation (IRMPD) of the precursor ion.
Despite detailed information on the structure and the conformation of covalent diastereomeric species[1] and their metal ion adducts,[2] has been gathered by IRMPD action spectroscopy,[3] no similar investigations have been performed on non-covalent supramolecular systems, where specific

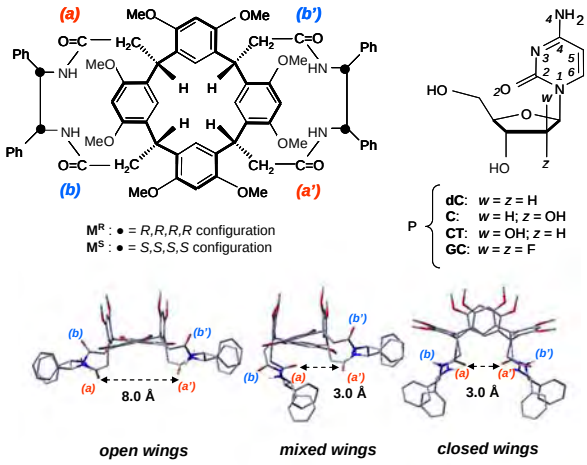

Chart 1

configuration-dependent interactions and the orientation of the host/guest functionalities may affect their enantioselectivity, as well as their IR spectrum.
Herein we present the first IRMPD investigation of chiral non-covalent supramolecular systems, which may provide a first insight into the nature of intrinsic configuration-dependent interactions in chiral receptor/molecule aggregates. As chiral receptor mimics, we selected the bis(diamido)-bridged basket resorcin[4]arene enantiomers ($\mathbf{M}^{\mathbf{R}}$ or $\mathbf{M}^{\mathbf{S}}$) in the flattened cone conformation, whose joint chiral pendants exhibit the amidocarbonyl groups *a/a'* pointing inward and the *b/b'* ones outward the chiral cavity (Chart 1).[4] Pyrimidine nucleosides (P) were used as chiral guests since previous studies showed their marked propensity to proton bonding to $\mathbf{M}^{\mathbf{R}}$ and $\mathbf{M}^{\mathbf{S}}$.[5] Among the nucleoside investigated, cytarabine (**CT**) is an epimer of cytidine (**C**),[5] while gemcitabine (**GC**) is the *gem*-difluoro derivative of 2'-deoxycytidine (**dC**). The experimental data have been analyzed by comparison with theoretical results of model systems.

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ORG-PO-59 Aza-Henry Reactions of Trifluoromethyl Schiff Bases

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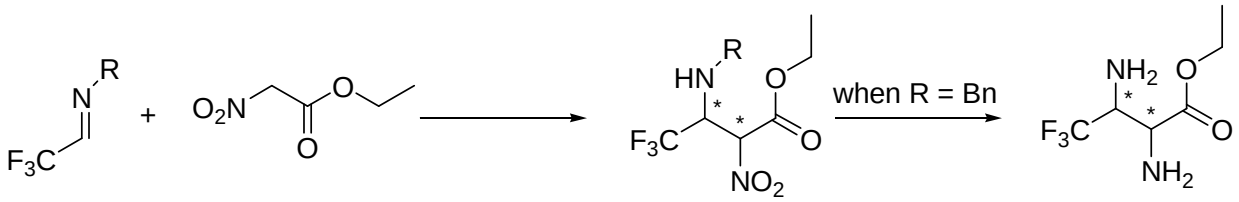
The development of new methodologies to form carbon-carbon bonds is a key goal in the progress of organic synthesis, especially where multiple stereocenters are created simultaneously in a single operation with complete control of the reaction course. The maximum challenge is the control of contiguous stereocenters in flexible acyclic molecules [1].

The synthesis of , -diamino acids, having two vicinal chiral centers, has recently emerged as a stimulating and active area of research, because this structural motif is present in many different bioactive natural products and therapeutic agents. The presence of a trifluoromethyl group can enhance the potentiality of these compounds as versatile building blocks for the synthesis of new potential surrogates of peptidic units, able to modulate conformational, physico-chemical and biological properties [2].

We here report the first successful attempts to obtain , -diamino -trifluoromethyl esters by an aza-Henry reaction [3] between different trifluoromethyl imines [4] and ethyl nitroacetate.



The reduction reaction leads to new non proteinogenic amino acid derivatives. Furthermore, when R is an L- or D- -amino ester residue, a diastereoselective reaction will give new fluorinated molecules, potential surrogates in known peptidic entities.

Italian MIUR and Università degli Studi di Roma "La Sapienza" are gratefully acknowledged for financial support (PRIN 2007FJC4SF_005)

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ORG-PO-60 Novel Heterocyclizations Leading to Thiophene and Benzothiophene Derivatives

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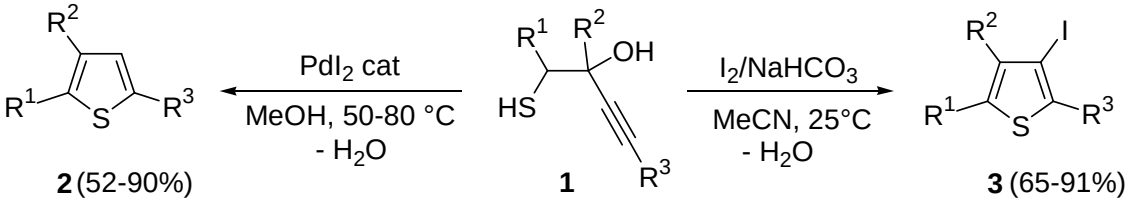
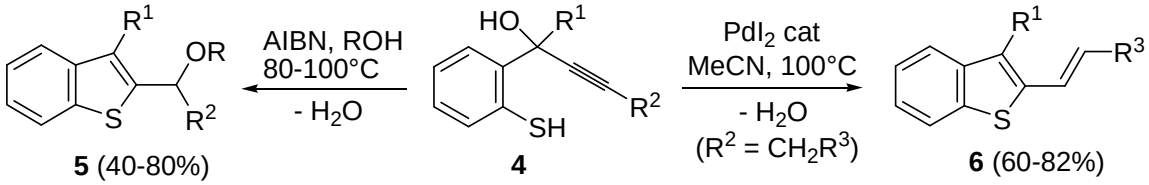
Thiophenes and benzothiophenes are very important classes of heterocyclic compounds. A variety of molecules containing the thiophene or benzothiophene ring display a wide range of biological activity and find extensive application as pharmaceuticals or fragrance compounds. Moreover, they are useful synthetic intermediates, for example, in the preparation of new materials.
In this communication, we will report a novel synthetic approaches to thiophene (**2**, **3**) and benzothiophene (**5**, **6**) derivatives based on *S*-heterocyclization of readily available 1-mercapto-3-yn-2-ols **1** (Scheme1) and 1-(2-mercaptophenyl)-2-yn-1-ols **4** (Scheme 2), respectively.



Scheme 1



Scheme 2

ORG-PO-61 Design of new potential linezolid-like antibacterials

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Although new antibacterials such as linezolid, a fluorinated oxazolidinone introduced in clinical practice since 2000, are active against resistant microorganisms such as MRSA[1] VRE and PNSSP, resistance to this antibiotic has recently been reported [2,3]. The attention in recent papers is also focused on the resistance of fluoroquinolones against Gram negative bacteria. In this context it would be desirable a chemoinformatic optimization, followed by synthesis and biological tests on structures such as linezolid or fluoroquinolones to overcome resistance and hopefully limit side effects.
We here report molecular modelling by means of computational procedures such as: (a) ALMOND to correlate the changes in chemical structures with antibacterial activities [4]; (b) VOLSURF to correlate 3D molecular structures with pharmacokinetic and physicochemical properties [5,6]; (c) docking of new ligands to the receptor active sites by means of FLAP that can be used to describe proteins and ligands based on a common reference framework. In this context we identified a new synthesizable scaffold that is expected to exhibit high antibacterial activity against Gram-negative resistant pathogens.

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ORG-PO-62 Antimicrobial photodynamic therapy: synthesis, conformational properties and antibacterial activity of peptide-porphyrin conjugates

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The worldwide rise of antibiotic resistance stimulates the search for new strategies for controlling bacterial infections based on the use of agents different from the common antibiotics. Two promising approaches are the application of photodynamic therapy (PDT) and of cationic antimicrobial peptides (CAMP) in the treatment of localized infection.

PDT [1] involves the use of non-toxic dyes or photosensitizers (PS), that can generate reactive oxygen species upon exposure to light in the presence of oxygen. It is well establish that singlet oxygen is produced as the main species responsible for cell death.

CAMP [2] are components of the innate defense mechanism of many organisms. They are short peptides (10-50 amino acids), with an overall positive charge (generally +2 to +9) and a substantial proportion (≥30%) of hydrophobic residues. These properties permit the peptide to fold into an amphipathic structure, often upon contact with membranes, and ensures accumulation at the poly-anionic microbial cell surfaces.

In general neutral, anionic or cationic PS molecules can efficiently kill Gram-positive bacteria, whereas Gram-negative bacteria are less susceptible to phodynamic killing and only cationic porphyrins can induce their photo-inactivation. On the contrary CAMP exhibit a broad spectrum of antimicrobial activity and do not easily induced resistance compared to conventional antibiotics. Thus the use of CAMP in combination with PDT is expected to enhance the effectiveness of PDT.

Recently we have shown that the conjugation of apidaecin 1b, a 18-residue peptide, to a 5(4'-carboxyphenyl)-10,15,20-triphenylporphyrin (cTPP) photosensitizer afforded a new antibacterial agent, with a broader spectrum activity with respect to that of the two individual components or a mixture of them [3].

Here, we present the synthesis of a new conjugate between cTPP and the membrane active peptide magainin 2 and a preliminary investigation of its antibacterial activity, in the dark and under light-activation. Moreover, the conformational properties of the porphyrin-peptide conjugates will be compared to those of the parent peptides and an interpretation of the circular dichroism spectra

with respect to the assembling of these systems in aqueous environment will be presented.

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ORG-PO-63 A New Approach to Functionalized Isoquinoline and Isochromene by Carbonylation of (2-Alkynyl)benzylideneamine Derivatives

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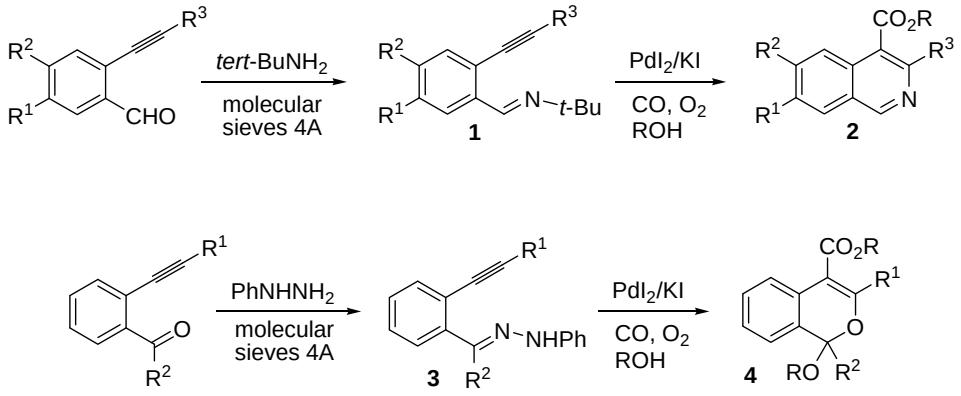
The Pd-catalyzed oxidative carbonylation of simple functionalized alkynes is one of the most versatile methods for the direct synthesis of carbonylated heterocyclic derivatives. We report here on some new synthetic approaches to functionalized nitrogen or oxygen carbonylated heterocycles by PdI_2-catalyzed oxidative carbonylation of (2-alkynylbenzylidene)amine derivatives, obtained by condensation of the corresponding 2-alkynylbenzaldehydes with amines or hydrazines.

In particular, we have found that *tert*-butyl-(2-alkynylbenzylidene)amines **1** selectively afford isoquinoline-4-carboxylic esters **2**, ensuing from *N*-cyclization (Eq. 1), while *N*-[2-(alkynyl)benzylidene]-*N*-phenylhydrazines **3** lead to isochromene-4-carboxylic esters **4** through water attack to the imino group of the followed by *O*-cyclization (Eq. 2).

Reactions were carried out in alcoholic solvents at 80-100 °C and under 20-80 atm (at 25 °C) of a 4:1 mixture of CO-air, in the presence of PdI_2 (2-10 mol %) in conjunction with KI (KI/PdI_2 molar ratio = 10). In the case of imines, the use of a dehydrating agent, such as a trialkyl orthoformate, was necessary in order to obtain satisfactory yields of isoquinolines.



ORG-PO-64 Enhanced Probes for Catalytic Signal Amplification for the Detection of Enzyme Activity

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The detection of low levels of proteins and other biomarkers is of crucial importance for an early diagnosis of diseases [1]. The large interest in the development of chemical-sensing methodologies, complementary or as alternative to biological assays, is due to the simple detection protocols and easy structural modifications of the system adapting for a wide variety of targets.
Recently, we report on the application of a catalytic amplification process for the detection of proteases [2-5]. This approach lead to a highly sensitive assay, since the enzymatic conversion of a single substrate molecule lead to the formation of a multitude of reporter molecules through a cascade of chemical events, each of them magnifying the previous one. A central role is played by gold nanoparticles covered with a catalytic self-assembled organic monolayer (Au-MPC) (Figure 1). In the first event an enzyme hydrolyses a peptide substrate, which acts as an inhibitor for the catalytic monolayer. Upon hydrolysis, the catalytic activity of the monolayer is restored, which results in the production of large quantities of a yellow reporter molecule. The main limit of this system relies on the low turn over frequency of our substrate (HPNPP), together with a relatively low binding affinity of HPNPP to the Au NPs. Our aim is the improvement of these two parameters, by acting on the nature of the substrate and in particular on the leaving group, in order to enhance the cleavage rate and the binding affinity for the Au-MPC.

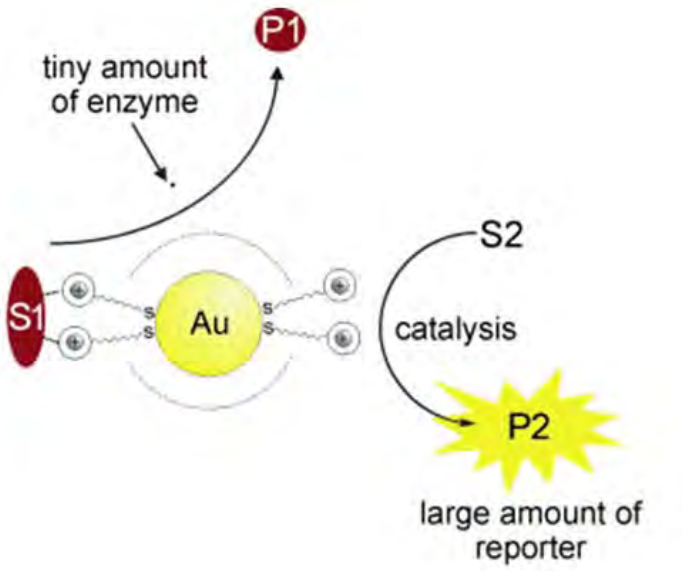

Figure 1. Catalytic signal amplification using functionalized nanoparticles.

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Financial support from the European Research Council under the Seventh Framework Programme (FP7/2007–2013)/ERC of the European Community (Starting Grant agreement no. 239898) is acknowledged.

ORG-PO-65 Proline Derivatives in Asymmetric Nucleophilic Epoxidation: a Novel Organocatalytic Approach to Spiroepoxy Esters

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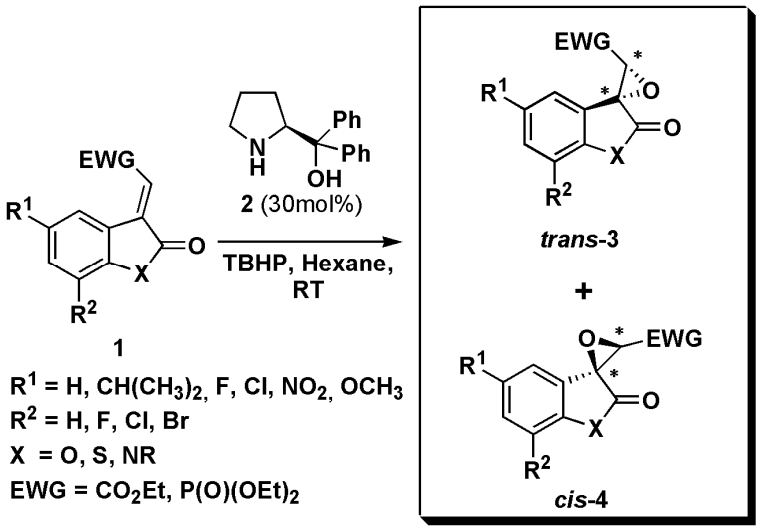
Asymmetric epoxidation has always been an hunted goal for organic chemists. After the Sharpless's breakthrough, only over the last years, have systems been described which allow the asymmetric epoxidation of electron-poor olefins [1]. In particular, organocatalytic strategies have been taking on more and more importance [2].Within this context, pursuing previous studies on biologically relevant isatine systems [3] and prompted by the amazing results on α,β-unsaturated ketones [4] we envisioned the opportunity to exploit the diphenyl prolinol **2**/TBHP system to perform a stereoselective organocatalytic epoxidation of α-alkylideneoxindoles **1** (X=NR) bearing a further electron-withdrawing group [EWG=CO_2Et, $P(O)(OEt)_2$] on the exocyclic double bond. Herein, we account for the achievement of the desired spiroepoxides **3** and **4** in quite good enantioselectivity (up to 86%*ee*), with the formation of a quaternary stereocenter. Moreover, extension of such procedure to novel alkylidene analogs **1** (X=O,S), should broad the substrate scope and better clarify the operating mechanistic pathway.



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ORG-PO-66 Effect of Concentration and Temperature on Vesicles Formed by a New Sultaine Surfactant

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The formation of micelles, bilayers or vesicles in aqueous solution depends on the structural properties of the surfactant [1].

Vesicles can act as drug delivery systems in many biotechnological applications. To be suitable as a carrier, surfactant vesicle should have high affinity for the biological membranes and high stability under physiological conditions to release its content in a controlled way [2].

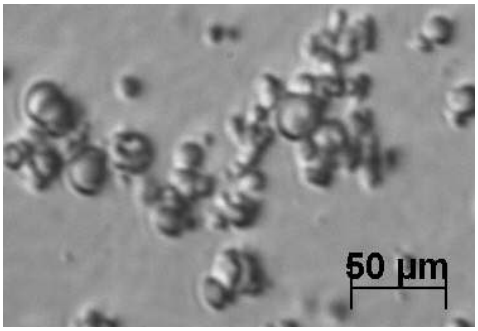

Figure 1.

Sultaine surfactants are characterized by low irritancy and non denaturizing-protein effect. The aggregation behaviour of a new synthesized sultaine has been studied in buffer solution at pH 7.4 [3]. Spontaneously formed vesicles can be observed by optical microscopy (Fig.1). The sultaine transition temperature has been determined by DSC and Nile Red fluorescence.

Two critical vesicular concentrations (CVC_1 and CVC_2) have been fluorimetrically found and two kind of aggregates have been identified and investigated: vesicles above the CVC_1 and closely packed aggregates above the CVC_2. The sultaine vesicles formed above the CVC_1 decreases their stability from 25 to 75°C due to the membrane association promoted at high temperature.

Dynamic Laser Light Scattering and fluorescence measurements confirm the presence of larger aggregates above the CVC_2 due to the vesicles assembly promoted at high sultaine concentration.

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ORG-PO-67 Synthesis of PNA in non conventional media

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The growing awareness of the urgent need for greener, more sustainable technologies has focused the scientific attention on the use of alternative reaction media that circumvent the problems associated with the traditional volatile organic

solvents (VOCs). The use of non conventional reaction media also provides opportunities to facilitate the recovery and the recycling of the reaction solvent [1].
Among the most promising alternatives to classical organic solvents, ionic liquids (ILs) have been intensely studied in the recent years as potential environmentally benign reaction media due to their lack of measurable vapour pressure and high thermal and chemical stability [2].
Recently, room temperature Ionic liquids (RTILs) have been used as solvents in the preparation of several classes of biomolecules such as oligosaccharides [3] and peptides [4].
In this communication we report a preliminary study on the use of ILs as solvents in the preparation of peptide nucleic acids (PNAs) [5].
The optimization of the reaction conditions, as well as the recycling of the ILs and the use of microwave will be discussed.

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ORG-PO-68 CONTROL OF RAPIDLY-ISOMERIZING ORGANOLITHIUMS BY USING MICROREACTOR TECHNOLOGY

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The concept of flash chemistry[1], chemical synthesis in which extremely fast reactions are conducted in a highly controlled manner by using a flow microreactor system, has been successfully applied to various organic reactions including those producing undesired byproducts in subsequent reactions, highly exothermic reactions that are difficult to control, and reactions in which a reactive intermediate easily decomposes in conventional reactors.
It has been demonstrated that microreactors are particularly useful in organolithium-mediated synthesis allowing the generation of lithiated intermediates at higher temperatures and the control of stereolabile intermediates [2].
In this context we envisaged that the solvent-promoted racemization [3] and thermally induced isomerization of lateral-lithiated aziridines, recently investigated in our laboratory, could be a suitable system to be studied by using a flow microreactor system consisting of micromixers and microtube reactors (Figure 1).

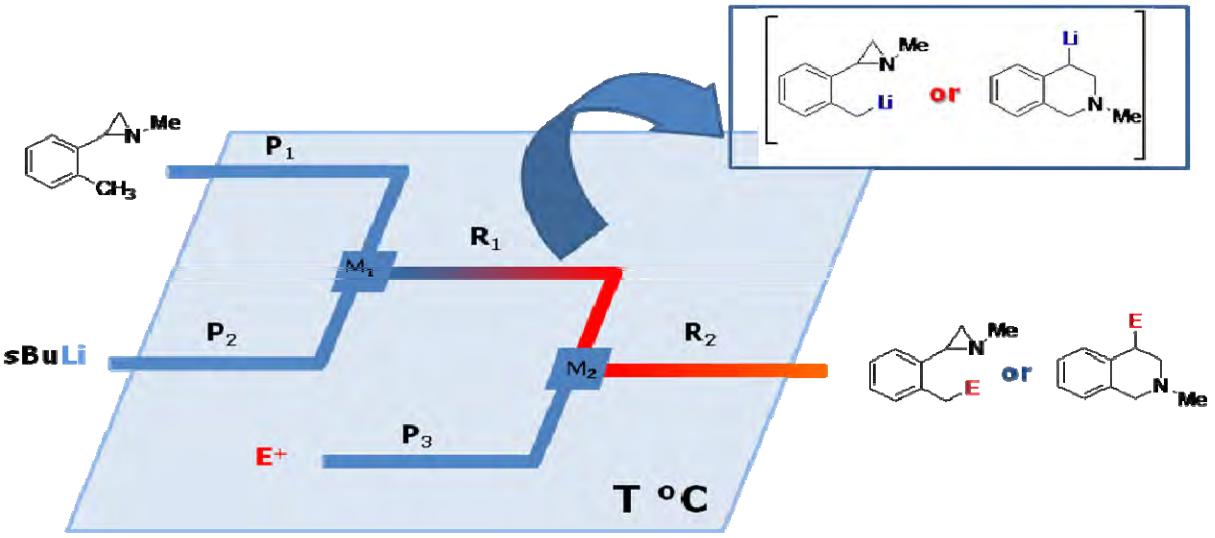

Figure 1

In this communication it will be reported that the exquisite control of the reaction parameters, realized into the microreactors, enabled us to set up the synthesis of either laterally functionalized aziridines or functionalized tetrahydroisoquinolines.

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ORG-PO-69 Towards new ligands for metal complexation and catalysis

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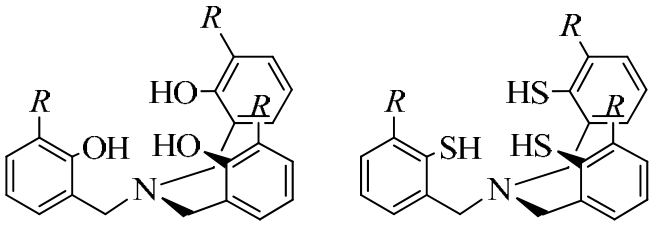
Recently, we developed an efficient synthesis of triphenolamine **1** [1]. They can form stable metal complexes with a wide variety of transition and main group elements [2] such as Ti(IV) [3], V(V) [4] and Mo(VI) [5] which achieved noteworthy catalytic properties in the oxidations of sulfides, secondary amines, halides and olefines. As an extension of our work, we examinated the use of their analougues *tri*-thiofenolamino systems. It is known that many metallo-enzymes contain molybdenum atom centers coordinated to sulfur atoms. Key step for the introduction of sulfur atom is the Newmann-Kwart rearrangement, which is a valuable synthetic technique to convert phenols in thiophenols. Herein we will report the synthetic strategy for the preparation of the new parent compound **2** and their coordination chemistry with transition metals such as molybdenum (Mo) or vanadium (V).



1 **2**

R = H, Me, Ph, *t*-Bu

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Acknowledgements: We acknowledge financial support from MIUR, PRIN 2008 project, University of Padova, Fondazione Cariparo (Nano-Mode, Progetti di Eccellenza 2010) and COST ACTION D40 'Innovative Catalysis – New Processes and Selectivities.

ORG-PO-70 Sali di imidazolio multistrato supportati covalentemente: attività catalitica per la produzione di carbonati ciclici in $scCO_2$ e nuovi supporti per catalizzatori di palladio

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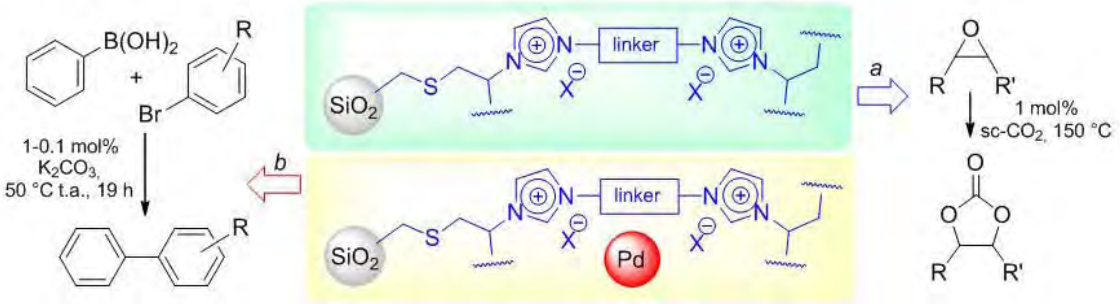
I liquidi ionici supportati (SILP) hanno trovato interessanti applicazioni sia nel campo delle reazioni catalizzate da metalli che in organocatalisi [1]. Inoltre, i SILP sono stati efficacemente impiegati in reazioni di apertura di epossidi in CO_2 supercritica per fornire carbonati ciclici [2]. I liquidi ionici vengono generalmente supportati covalentemente attraverso la modificazione dei gruppi funzionali presenti sulla superficie del supporto, conducendo in tal modo alla formazione di un monostrato di liquido ionico supportato. Gli esempi di SILP legati covalentemente, in maniera tale da ottenere dei multistrato, sono rari.

In questa comunicazione viene riportato un metodo per preparare dei sali di imidazolio supportati covalentemente e il loro impiego come: *a*) catalizzatori riciclabili per la reazione di epossidi con CO_2 supercritica per fornire carbonati ciclici, e *b*) supporti per nanoparticelle di palladio e l'impiego di tali materiali come catalizzatori riciclabili per la reazione di Suzuki in ambiente acquoso fra acidi boronici e bromuri arilici.



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ORG-PO-71 SYNTHESIS OF MOLECULAR NANOMAGNETS USED IN THE BNCT FOR THE TREATMENT OF HEPATIC TUMOR

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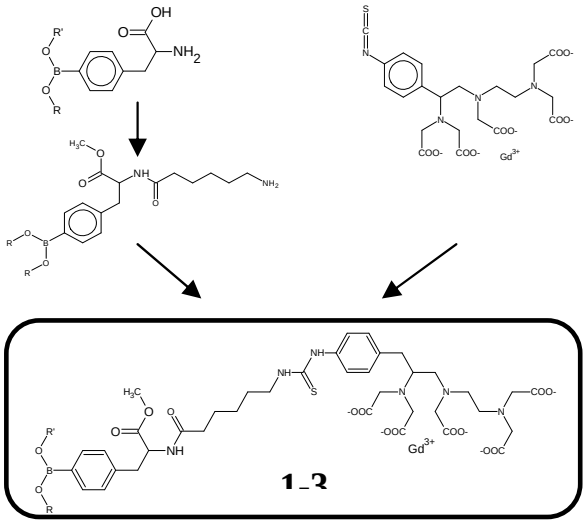
Boron Neutron Capture Therapy (BNCT) is a binary therapy based on the property of the 10B isotope to capture neutrons and to produce energy through a nuclear reaction inside cells, inducing apoptosis. A bimetallic molecule enriched in 10B and including a Gd complex, useful for MRI study would permit to monitor the distribution of the compound in cancer affected tissues and, in this way, to better direct the neutron beam [1]. Subject of this communication is the short synthesis of novel compounds **1-3** consisting of three units: i) *p*-10borono-L-phenylalanine, which, being similar to the natural amino acid, would promote the preferential absorption of the compound in tumour cells [2]; ii) a linker derived from 6-amino-caproic acid, connecting the two bimetallic moieties through a thioureido linkage; iii) a Gd3+-DTPAcomplex. The entire molecules have readily been assembled.

1H and 10B NMR and MRI investigation of boron and gadolinium-boron compounds in boron neutron capture therapy.The synthesis and the magnetic properties of **1**-**3** will be discussed in this communication.



1 : R = H,
R’ = H
2 : R = H,
R’ = Me
3 : R = Me.

[1] M.Bonora et al., 1H and 10B NMR and MRI investigation of boron and gadolinium-boron compounds in boron neutron capture therapy. *et al*., *Appl. Radiat. Isotopes*, **2011,** *Article in Press.*

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ORG-PO-72 Assignment of Absolute Configuration to Natural Phytotoxic Naphthalenone Pentaketides by Computational Analysis of Optical Rotation and ECD spectra.

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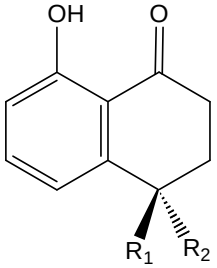
The computational simulation of optical rotation (OR) and electronic circular dichroism (ECD) is nowadays widely used for the assignment of the molecular absolute configuration (AC) of both synthetic and natural occurring chiral molecules This approach was herein employed to assign the absolute configuration of regiolone and isosclerone (**1**), two enantiomeric bioactive pentaketide napthalenones produced by fungi and plants and for which the configurational assignment was still matter of debate.



(-)-**1** (4*R*)-Regiolone R_1=OH, R_2=H
(+)-**1**(4*S*)-Isosclerone R_1=H, R_2=OH

A DFT/B3LYP/TZVP conformational analysis was therefore carried out on (*S*)-**1** allowing to sort out four populated conformers within a 4 kcal mol^{-1} range. The ECD spectra and OR values were then calculated at TDDFT/CAM-B3LYP/TZVP level for each conformer and Boltzmann averaged over the conformers' population. The comparison of the experimental and theoretical OR's and ECD spectra allowed to unambiguously establish a (*R*)/(-) (*S*)/(+) relationship between absolute configuration and optical rotation of regiolone/isosclerone. The AC appear to be close related to the phytotoxicity.

ORG-PO-73 Synthesis of 3-substituted aroylindole compounds by cycloaddition of nitrosoarenes with conjugated alkynones

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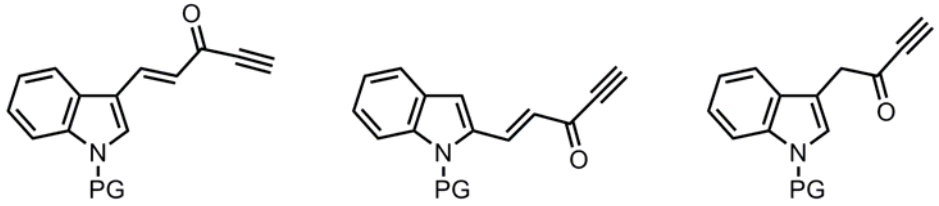
Many synthetic approaches were studied so far to achieve indolization procedures starting from different nitrogen containing precursors.[1] Our general interest in this topic lead us to disclose a novel and regioselective indole synthesis by annulation reaction between nitro- and nitrosoarenes with alkynes. Indoles, *N*-hydroxy- and *N*-alkoxyindoles were afforded in moderate to excellent yields and good regioselectivity.[2] This synthetic strategy was used to prepare natural products like meridianins, marine indole alkaloids known as kinase inhibitors.[3] Using conjugated alkynones as starting materials the reaction proceeded with the regioselective formation of 3-acylindoles and/or *N*-hydroxy-3-acylindoles.[4]



More recently and starting from conjugated alkynones with a preformed indole fragment we focused our attention on the preparation of bis-indole compounds as target molecules. This class of products can be furtherly used as starting material to achieve indolecarbazole derivatives and other complex molecules with biological activity.

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ORG-PO-74 Re-evaluation of the biological activity of natural compounds: the role of the Inverse Virtual Screening as a useful in silico tool.

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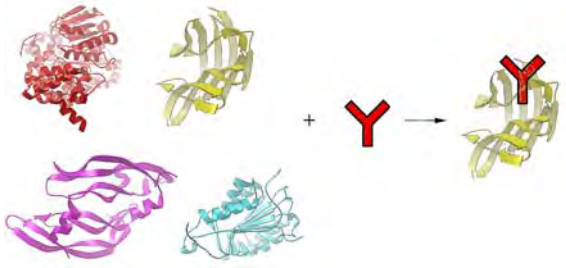
A small library of natural compounds belonging to different chemical classes (flavonoids, cycloartanes, chalcones, xanthones, iridoids) and mainly known for their monoamine oxidase inhibitory effects [1-2], was screened on a panel of targets involved in the genesis and progression of cancer [3].
The re-investigation of their potential activity was achieved through the Inverse Virtual Screening approach [4-5] using the Autodock-Vina software [6]. The variability of the binding sites of the different targets, representing a fundamental parameter in the evaluation and comparison of the predicted binding energies, was overcomed applying a normalization of all the values [7].
Most of the results of the screening showed the selection of biological targets not explored for these classes of compounds until now. On the other hand, the interaction with an amineoxidase target was underlined, essentially confirming the robustness of the method. The subsequent biological tests could confirm the reliability of the Inverse Virtual Screening approach and its effective applicability for a re-evaluation of the activity of these compounds.



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ORG-PO-75 GUANIDINIUM-BASED CALIX[4]ARENES FOR GENE DELIVERY

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The possibility to fight several diseases through gene therapy can find a significant improvement through the development of selective and efficient gene delivery systems [1].

In alternative to viruses, many classes of compounds are studied as non-viral vectors for cell transfection [2]. In general, although they are less efficient than viruses, they show low toxicity, low immunogenicity and can be rather easily modified in order to improve their biological properties.

In this context we have synthesized new vectors based on calix[4]arene scaffolds, functionalized with guanidinium moieties and lipophilic chains [3-5]. These macrocyclic compounds generate electrostatic interactions/hydrogen bonds with DNA, while hydrophobic interactions among calixarene skeleton lead to the formation of different types of aggregates, as Atomic Force Microscopy and spectroscopic studies show. We herein also report transfection and cytotoxicity studies on this new class of non-viral vectors [4,5].

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ORG-PO-76 Cyanuric chloride-catalyzed Beckmann rearrangement of ketoximes in biodegradabile ionic liquids

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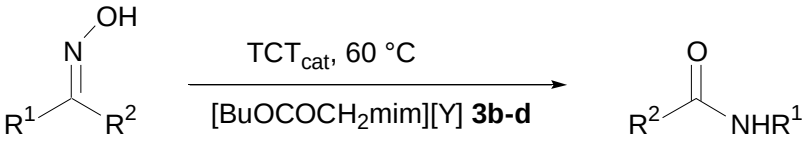
Biodegradable ionic liquids (ILs) represent a potential more ecosustainable alternative to traditional ILs that, due to their excellent stability and often water solubility, could determine a possible accumulation in the environment [1].

The incorporation of an ester group into the IL side chain is found to significantly improve the IL biodegradation since it provides a site for possible enzymatic cleavage [1]. However, the favourable biodegradability must be balanced by the required stability of the solvent and practical applicability. In particular, the presence of the ester moiety in the IL could represent a drawback in reactions performed under high basicity or acidity conditions.

We have proved that biodegrable imidazolium-based ILs of this type (**3b-d**) can be successfully utilized as the alternative to traditional ILs even in the Beckmann rearrangement that is known to require strongly acidic and dehydrating media[2]. The procedure is mild and suitable for both aromatic (**1a-e**) and aliphatic (**1f**) ketoximes affording the rearrangement products (**2a-f**) in good to quantitative yields. Our findings are of particular interest in view of a possible scale-up of this fundamental reaction. These ILs, in fact, are not only biodegradable but they can be recovered and reused several times.



1a-f **2a-f**

1,2a $R^1 = R^2 =$ Ph
1,2b R^1 = Ph, R^2 = Me
1,2c R^1 = 4-C_6H_4-OH, R^2 = Me
1,2d R^1 = 4-C_6H_4-Cl, R^2 = Me
1,2e R^1 = 2-C_6H_4-OMe, R^2 = Me
1,2f $R^1 – R^2 = (CH_2)_{11}$

3b, Y = ClO_4^-
3c, Y = BF_4^-
3d, Y = PF_6^-

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ORG-PO-77 New Mesoporous Materials for a Controlled Progesterone Release

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We have synthesized two novel mesoporous materials in order to design a drug delivery system able to increase the oral bioavailability of drugs. In particular, we have functionalized SBA-15 silica with β-cyclodextrin residues by two different synthetic approaches, leading to the materials **SC1** and **SC2** (Figure 1).

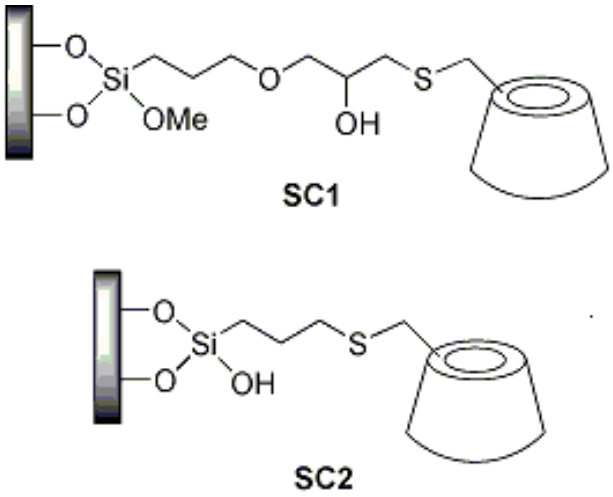

Figure 1

Progesterone was selected as model drug and loaded into both **SC1** and **SC2**. The materials before and after progesterone loading were characterized by TGA, N-2 sorption analysis and small angle X-ray diffraction (XRD). The results showed that the **SC2** material had a better capacity for loading progesterone and retained the drug more efficiently: the release after 2 h in acidic media (at pH = 1, as in the stomach) was only 30%, and reached 99% after 12 h at pH = 6.8 (pH in the intestine). This results show that **SC2** is a good candidate for a controlled delivery of progesterone *in vivo*.

ORG-PO-78 Dynamic High-Performance Liquid Chromatography of Chiral Stereolabile Compounds: the conformational stereoisomers of Tri-O-thymotide.

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Dynamic high performance liquid chromatography on enantioselective stationary phases is a well-established technique to investigate chiral molecules with labile stereogenic elements that result in stereoinversion processes occuring on the time scale of the separation process. Kinetic parameters for on-column interconversions can be extracted from exchange-deformed experimental peak profiles by computer simulation. The technique has been used in a wide range of temperatures and is complementary in scope to dynamic nuclear magnetic resonance spectroscopy.[1-3]

Here we report the first HPLC resolution of the conformational enantiomers of tri-O-thymotide (TOT), a macrocyclic trilactone existing in fast-exchanging multiple chiral conformations.[4] Variable chromatography on brush type chiral stationary phases showed dynamic features due to on-column interconversions in the temperature range between 25 and -15 °C. These features are consistent with the known energy barrier measured by NMR for the major, propeller shaped conformational enantiomers of TOT. Cryo-HPLC at column temperature as low as -80 °C allowed us to resolve the enantiomers of the minor, helix shaped conformational enantiomers of TOT.

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ORG-PO-79 Towards the Identification of Oleocanthal Cellular Interactome by Chemical Proteomics

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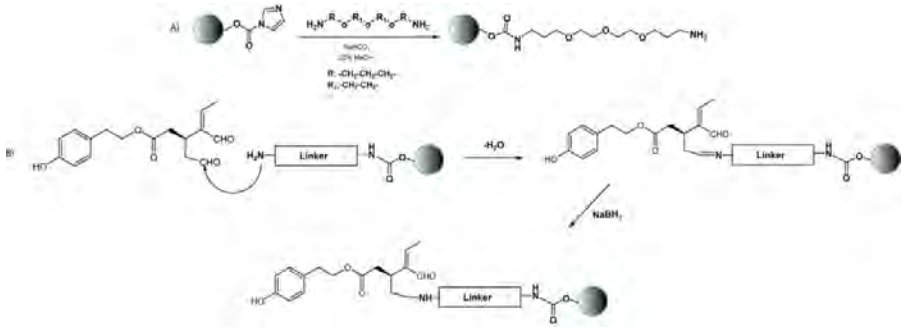
Oleocanthal (OLC), the dialdehydic form of (-) deacetoxy-ligstroside aglycon responsible for the bitter taste of olive oil, has been recently supposed to interfere within important pathways of relevant human diseases, such as inflammation[1] and Alzheimer (AD)[2]. Otherwise, OLC exact mechanism of action at cellular level still remain unknown. In recent years, mass-spectrometry-based chemical proteomics has been applied to the macromolecular target discovery under physiological condition[3]. The procedure usually requires three steps, beginning with the chemical modifications of the matrix beads with a spacer bound to the molecule of interest, followed by the isolation of the potential targets, through affinity chromatography of the crude cell extract and SDS-PAGE of the eluting proteins, and the identification by MS of the interacting target (s) . The last step is the pharmacological evaluation of the compound by *in vitro* and/or *in vivo* based assays[4].



Here we report the investigation of the interactome of OLC through the application of the above mentioned chemical proteomics based experiment. These experiments combined with an opportune in vitro/in vivo assays allowed us to enlarge our knowledge on the therapeutic properties of OLC.

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ORG-PO-80 Advanced oxidation of binary mixtures of volatile organic compounds induced by air atmospheric plasma

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Advanced oxidation of volatile organic compounds (VOCs) induced by atmospheric plasma is developing as a powerful means for air purification. In such plasmas, which are conveniently produced by corona discharges in air at room temperature and atmospheric pressure, the oxidative decomposition of VOCs is promoted by reactions with the species produced by ionization, excitation and dissociation of air and water molecules (mainly $^{\bullet}OH$, O_3, H_3O^+, $O_2^{+\bullet}$, NO^+, $O_2^{-\bullet}$). Despite some well-established technological implementations, fundamental knowledge of the underlying chemical processes is still limited and the majority of studies so far have involved simplified models of contaminated air consisting of a single VOC in a synthetic mixture of N_2 and O_2 [1].

The aim of our research is to characterize the reactions and the mechanisms underlying VOCs decay in these systems [2]. Particular attention is given to the ions produced within the plasma and to their reactions, which are generally neglected in the literature in favour of radical decomposition routes. Furthermore, in a step towards a more realistic air model, we have recently undertaken the study of mixtures of two different VOCs to investigate on possible competition and entrainment effects. The experiments are performed with a large flow reactor, in which corona discharges can be produced by the application of dc or pulsed voltage. Chemical diagnostics includes on-line analysis with FT-IR and GC coupled with different detectors. Additional experiments are conducted with an APCI (Atmospheric Pressure Chemical Ionization) mass spectrometer in which the introduction system has been suitably modified to introduce gaseous and volatile compounds diluted in air. This is the ideal system to monitor the ions produced by corona discharge in air. In the case of air containing a single VOC the ionic species are generally formed by ion/molecule reactions of the VOC with the background ions coming from air; in the case of binary mixtures of VOCs additional ionic species can be observed coming from reactions between ions formed from one of the VOCs with molecules of the second one.

The results from this integrated approach obtained with various binary mixtures of CCl_2=CCl_2, CCl_4, C_6H_{14} and CH_3OH will be presented and discussed with regard to the process efficiency and mechanism.

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ORG-PO-81 Stereoselective "One-Pot" Procedure for the Synthesis of Unsymmetrically 1, 4-Disubtituted 1, 3-Butadienes in water

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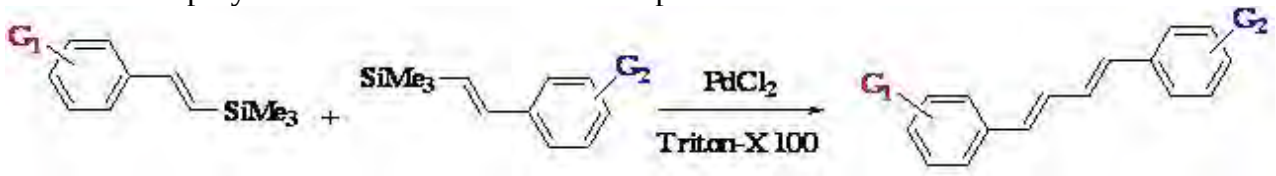
Stereodefined conjugated polyenes and aryl polyenes constitute a common structural motif in natural products and useful building blocks in organic synthesis. In recent years, polyenes containing electron-releasing and electron-withdrawing substituents within one molecule (push-pull polyenes) have attracted considerable attention due to their interesting photophysical and photochemical properties and their use as models for quantum-chemical calculations and simulations. For these reasons, a great deal of research works were devoted to the development of efficient and stereoselective methodologies to synthesize diene skeleton with different end groups. The conventional approach to the synthesis of dienic system involves the palladium catalyzed cross-coupling reactions of alkenylmetals with haloalkenes or olefin coss-metathesis reactions. In particular, a plethora of synthetic methods employing a large number of organometallic reagents, such as indium, rhodium and nickel have been developed for the preparation of symmetrical and unsymmetrical 1,3-dienes. Very recently, unsymmetrical 1,4-disubstituted 1,3-butadienes were prepared by silicon-based cross-coupling reactions and by Stille/Suzuki-Miyaura coupling sequences [1] by using a bis-metallo 1,3-butadiene. This approach allows to design and easily realize more complex butadienic systems. As a part of our research efforts in the development of efficient synthetic strategies for obtaining organic materials for photonics and electronics, we have recently reported a palladium-catalyzed homocoupling reaction of unsaturated silanes in micellar conditions for the synthesis of symmetrically α-ω disubstituted stereodefined all *trans* dienes in mild conditions and in good yields [2]. The use of water as reaction solvent in combination with surfactant has emerged as an important tool in the formation of carbon-carbon bond by organometallic methodologies. As a further extension of our "*green*" methodology, we examined the application of the palladium-catalyzed dimerization reaction of unsaturated silanes to the synthesis of unsymmetrically 1,4-disubstituted 1,3-butadienes in mild conditions and in water as the only solvent. In this connection herein, we report the first example of a "one-pot" palladium-catalyzed cross coupling reaction (Scheme 1) as an efficient methodology to obtain unsymmetrically disubstituted polyenes in water and at room temperature.



G_1 (electron-withdrawing groups) : NO_2- , PhCO- , F-
G_2 (electron-donating groups) : MeO- , $(Me)_2$ N- , MeS-

Scheme 1

[1] R. S.Coleman, M. C. Walczak *Org. Lett*. **2005**, *7*, 11;
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ORG-PO-82 3-Alkylidene Intermediates in the Synthesis of Functionalized Nitrogen Containing Heterocyclic Compounds.

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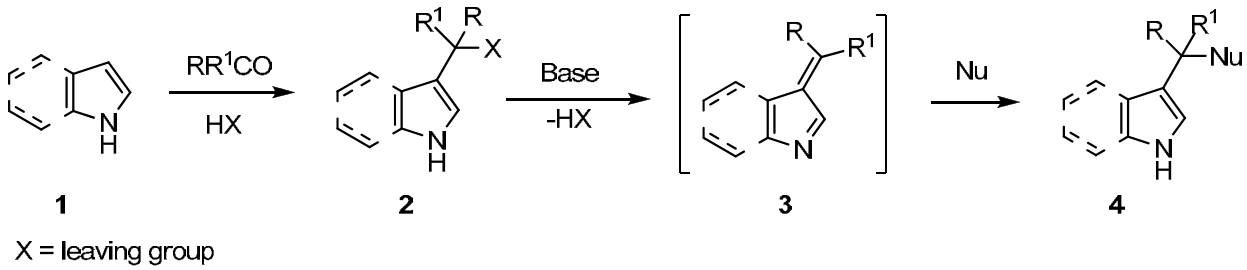
Functionalization of azoles at 3-position is commonly attained exploiting a Friedel-Crafts (F-C) reaction using electron-poor alkenes and acid promoters. Some limitations inherent to the F-C process can be easily surmounted using a strategy involving alkylidene intermediates **3** which actually act as vinylogous imino derivatives and can be made to react with a wide range of nucleophilic reagents [1].



Recently, we have introduced 3-(1-arylsulfonylalkyl) azoles **2** (X=SO_2Ar) as readily available precursors for reactive intermediate **3**. Reactants **2** are readily obtained by three components, coupling azoles **1** with aldehydes and arenesulfinic acids. Elimination of the arylsulfinic group can be carried out under basic or acid conditions allowing the reaction of the electrophilic intermediate with a wide array of nucleophilic reagents. Organometallics, stabilized carbon nucleophiles, heteronucleophiles can be made to react with compounds **2**.

The nature of the azole substrate **1** amenable for this process ranges from traditional functionalized indoles to indazoles. Pyrroles can be also profitably used in this strategy accounting that for a proper regioselectivity control at C3, a suitable directing group must be inserted on nitrogen. The reaction conditions studied for this transformation allow the utilization of homogeneous as well as heterogeneous promoters. Solid bases such as KF on basic alumina have been proved particularly effective in many processes using stabilized carbanions [2]. The mild reaction conditions required for the activation of these sulfonyl azoles also enabled their utilization in asymmetric synthesis [3].

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ORG-PO-83 Assignment of absolute configuration to aliphatic amines and alcohols by enhancement of their chiroptical properties and computational prediction of ECD spectra.

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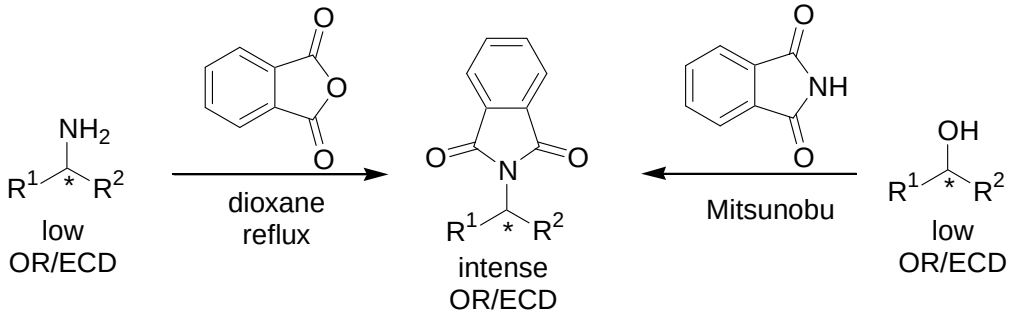
The computational simulation of optical rotation (OR) and electronic circular dichroism (ECD) is nowadays widely used for the assignment of the molecular absolute configuration (AC). However, some problems still remain in the treatment of transparent chiral molecules such as aliphatic amines and alcohols. Such compounds, lacking of typical UV-vis chromophores, display small ORs and/or weak ECD signals, making unreliable any computational simulation. In this communication we will show how this problem can be solved by transforming amines and α-aminoacids in the corresponding chromophoric *N*-substituted phtalimides [1]. These derivatives show much higher chiroptical properties, making then possible an AC assignment by a computational treatment. The same transformation into *N*-substituted phtalimides can be also obtained from chiral alcohols through Mitsunobu reaction with phthalimide, thus allowing to achieve an enhancement of the chiroptical response also with these substrates.



Experimental chiroptical properties (OR, ORD, and ECD) of *N*-phtalimides were then compared with the calculated ones at the TDDFT/B3LYP/6-31G* level of theory, thus arriving at a reliable AC assignment for chiral amines, aminoacids, and alcohols.

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ORG-PO-84 Synthesis of isoxazolidinyl-bisphosphonates with potential biological activity

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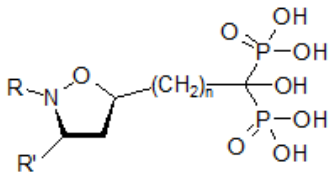
In the last years the development of organophosphoric chemistry has been characterized by a great interest on bisphosphonates and bisphosphonic acids. The significant pharmacological properties of these compounds make them of great interest: they showed a considerable cytotoxic activity against several human cell lines and therefore they could be successfully employed as anticancer drugs [1]. Moreover, these compounds are actually in use for the treatment of many bone diseases, such as Paget's disease, myeloma, bone metastases and osteoporosis [2].

Bisphosphonates can be considered as stable analogues of pyrophosphate (P-O-P), that is implied in the physiological regulation of bone calcification and resorption. Recently several analogues of these molecules have been synthesised in the last years [3].

In this communication we describe the synthesis of isoxazolidines by 1,3-dipolar cycloaddition reactions between suitable nitrones and substituted vinyles, by microwaves irradiation. The cycloadducts obtained, after appropriate functionalization, were converted in their correspondent bisphosphonic derivatives. As well as in the zoledronate, these compounds present an oxydrilic group, which increases the affinity for calcium even further owing to the ability of such derivatives to acts as tridentate ligands. They also have a different alkyl chain length on which is anchored a bisphosphonic group, that could modulate the potency of inhibition of bone resorption.



R= Bn- R'= *o*-Cl-C_6H_4-, *o*-F-C_6H_4-, C_6H_5- n= 0, 1, 2

R= Me- R'= C_6H_5- n= 0

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ORG-PO-85 Anti-inflammatory effect of oleopentanedialdheydes on primary human vascular endothelial cells

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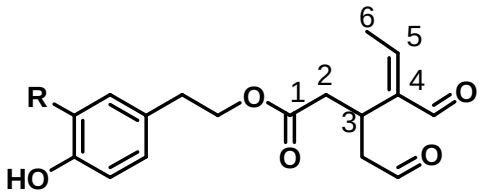
Olive oil represents a typical lipid source of the Mediterranean diet, whose intake has been associated with a low incidence of cardiovascular diseases, mostly due to the presence of several phenolic compounds which have anti-oxidant and anti-inflammatory properties. In this work we showed that *oleopentadial* (**1**) [2-(3,4-hydroxyphenyl)ethyl(3S,4E)-4-formyl-3-(2-oxoethyl)hex-4-enoate], a minor component of virgin olive oil, displays potent anti-inflammatory properties and anti-endothelial activation properties.

The molecule corresponds to the hydroxylated form of a dialdehyde, named *oleocanthal* (2), present in minor amounts in olive oil, [1] whose anti-inflammatory properties have been recently disclosed.[2].



1. R= OH; Oleopentanedial
2. R= H; Oleocanthal

The easy access to the molecule prompted [3] us to investigated the anti-inflammatory effect of oleopentanedial in a cell model we developed to mimic inflammatory injury of endothelium. This was based on the production of the proinflammatory chemokine MCP-1, following in vitro stimulation of primary human endothelial cells. Pre-treatment of cells with oleopentanedial resulted in a dose-dependent inhibition of MCP-1 secretion. The effect of oleopentanedial on MCP-1 expression was observed at the transcriptional level. Functional data have shown that OLPD diminished monocyte adhesion to HUVECs. These results point on the use of oleopentanedial as a novel drug aimed to prevent or reduce inflammation of endothelium.

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ORG-PO-86 Dimensional encapsulation of halogen-bonded supramolecular anions in non porous onium salts.

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Halogen bonding, namely any noncovalent interaction involving the positive region of the electrostatic potential surface of halogen atoms [1], has increasingly facilitated the assembly of diverse host-guest molecules. In this contribution, we show that a well-known class of organic salts, bis(trimethylammonium) alkane diiodides, can be applied to different fields and for different purposes as intrinsically non-porous materials showing very selective separation behaviour.
Firstly, we present how bis(trimethylammonium) alkane diiodides can reversibly encapsulate -diiodoperfluoroalkanes and I_2 through intermolecular interactions between the host’s I^- anions and the guest’s terminal iodine substituents. The process is highly selective and forms an $I^-\cdots GUEST\cdots I^-$ superanion that is matched in length to the chosen dication [2,3]. We will also report that using hexamethonium iodide and bromide we were able to isolate various trihalides and mixed trihalides such as Br_3^-, I_2Cl^- and Br_2Cl^- from solution and the gas phase with high selectivity and reversibility [4]. (Figure 1)

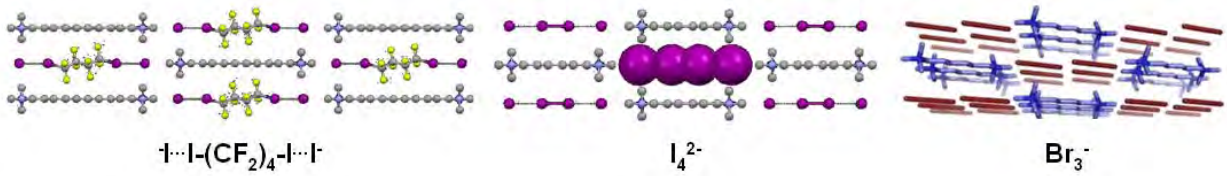

Figure 1: Crystal packing of the complex between organic onium salts and guest molecules

[1] An IUPAC Task Group set up to examine the definition of halogen bonding has not yet reported, so that given here should be taken as temporary (see www.iupac.org/web/ins/2009-032-1-100 and www.halogenbonding.eu).
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ORG-PO-87 Synthesis of isoxazolidine-substituted bisphosphonates by 1,3-dipolar cycloaddition reactions

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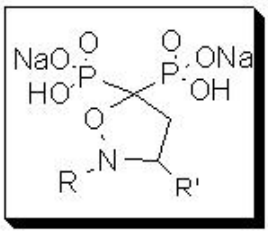
Geminal bisphosphonates (BPs) are structural and stable analogues of naturally occurring pyrophosphates, and an involved in the treatment of several skeletal problems associated to low bone density and osteogenesis imperfect. Further more, effecting on diseases as osteoporosis, Paget's disease and tumor bone diseases [1]. The studies on the inhibitory potency of cyclic nitrogen-containing bisphosphonates indicate that the presence of two geminal phosphonate groups is responsible for interaction with the molecular target [2].

We have developed an efficient method for the preparation of substituted isoxazolidines by 1,3-dipolar cycloaddition with dipolarophile and suitable nitrone, under microwave irradiation, in the absence of solvent [3].

In this communication we describe an efficient and general synthetic approach to bisphosphonates bearing in geminal position a substituted isoxazolidine ring. In fact we investigated the 1,3-dipolar cycloadditions of nitrones with tetraethylvinylidene-1,1-biphosphonate by MW irradiation, obtaining a set of isoxazolidine-substituted bisphosphonates.



R = Me R' = Ph, *o*-Cl-C_6H_4, 3- pyridyl, 2-furyl

R = Bn R' = Ph, *p*-OH-C_6H_4, *o*-Cl-C_6H_4, *o*-F-C_6H_4

Studies on the biological potential and comparison with the bisphosphonates of well established activity are currently under way.

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ORG-PO-88 Synthesis of S-acetyl molecular semiconductors for self-assembling processes

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The functionalization with the thiol group is widely adopted to produce individual molecules with the ability to chemically bind to noble metals or to a number of inorganic materials. This approach is extensively used to fabricate monolayer thin films on metal surfaces (SAMs) or on inorganic nanoparticles or metal-molecule-metal junctions [1]. These assemblies are useful for the study and conprehension of the electronic properties of ordered nanometric aggregates.
In this communication, we wish to present our recent research dealing with the synthesis of conjugated molecules functionalized with pending thiol groups. We recently synthesized a new family of S-acetyl oligoarylenedithiols characterized by a chelating disposition of the two thiol functionalities on the head ring and the presence of terminal substituents exerting different electron effect [2]. In parallel studies, these ligands demonstrated their ability to chemically bind to gold crystalline surfaces *via* both sulfur atoms and adopting a perpendicular disposition of the aromatic backbone with respect to the gold surface [3]. We later synthesized the corresponding tetrathiol molecular wires, having the base structure of oligo(*p*-aryleneethynylene)s (OAEs), that were obtained *via* palladium catalyzed convergent Sonogashira route [4]. The oligomers present interesting emissive properties, and processes of polymerization of these materials are presently under investigation.

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ORG-PO-89 Synthesis of novel derivatives of Resveratrol and screening for potential cancer chemopreventive activities

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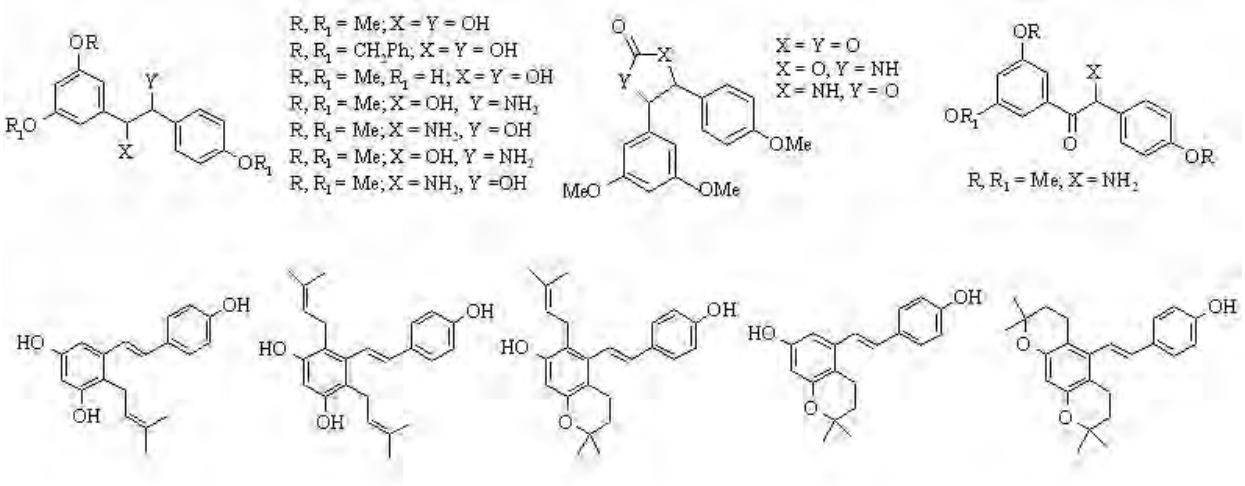
Resveratrol (*trans*-3,4',5-trihydroxystilbene) has attracted the attention of the biomedical researchers because of its beneficial physiological effects it produces. Positive effects of resveratrol has been observed in the field of cardiovascular diseases[1] and neurodegenerative disorders.[2] It has been also identified as a potent cancer chemopreventive agent in assays representing the three major stages of carcinogenesis (i.e. tumor initiation, promotion and progression).

We have synthesized a variety of Resveratrol analogues by chemical modification of the parent trihydroxy stilbene skeleton (Figure 1). The compounds were screened for cancer chemopreventive potential using a series of bioassays relevant for the prevention of carcinogenesis in humans (inhibition of cytochrome P450 1A; determination of NAD(P)H:quinone reductase activity; scavenging of radicals; inhibition of cyclooxygenase activity; inhibition of NO synthase; antiestrogenic and estrogenic activity).[3]

Figure 1.



Acknowledgment. MIUR e Universita' degli Studi di Milano (PRIN 2007 – 2007K29W5J)

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ORG-PO-90 Synthesis and Biological Evaluation of 1,2,4-Oxadiazole Analogues of Linezolid

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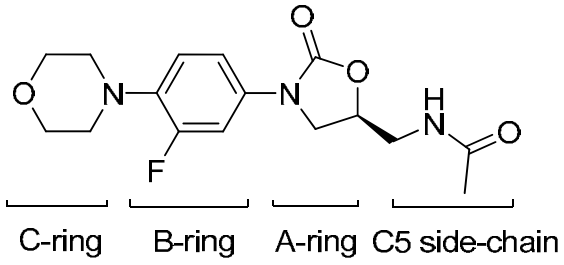
1,2,4-Oxadiazoles are known bioactive heterocycles whose activity has been often associated to their bioisosterism with amide or ester functionalities [1]. As preliminary results of a research project on the molecular design of heterocycle-based antibacterials to contrast Multi-Drug Resistance (MDR)[2], we report the synthesis and the biological evaluation of a series of Linezolid (see Figure) analogues, where a 1,2,4-oxadiazole moiety has been introduced to replace either the oxazolidinone heterocyclic core (A-Ring) or the morpholine moiety (C-Ring).



Linezolid **1**

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[2] Financial support from Italian MIUR within the "FIRB-Futuro in Ricerca 2008" Program - Project **RBFR08A9V1 –** CUP: **B71J10000120001** is gratefully acknowledged.

ORG-PO-91 Synthesis of New Fluorinated Low Molecular Weight (LMW) Gelators.

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Gel formation represents an attractive research area due to the unique properties of this type of soft materials which present many applications in the biomedical field [1]. In this field low molecular weight (LMW) gelators essentially form physical gels in which the molecules are self-assembled into three-dimensional structures, held together by non-covalent interactions [1]. The tendency to self-assemble of fluorinated systems has been also used in order to promote hydrogel formation from various polymers, while only few examples of fluorinated LMW hydrogelators have been reported [2].
In this communication we present a new family of fluorinated 1,2,4-oxadiazoles as Low Molecular Weight (LMW) gelators. These compounds are able to form thermal- and pH-sensitive “smart-hydogels” with a lamellar supramolecular assembly (Fig. 1) and *organogel*s in DMSO with a fibrillar network.

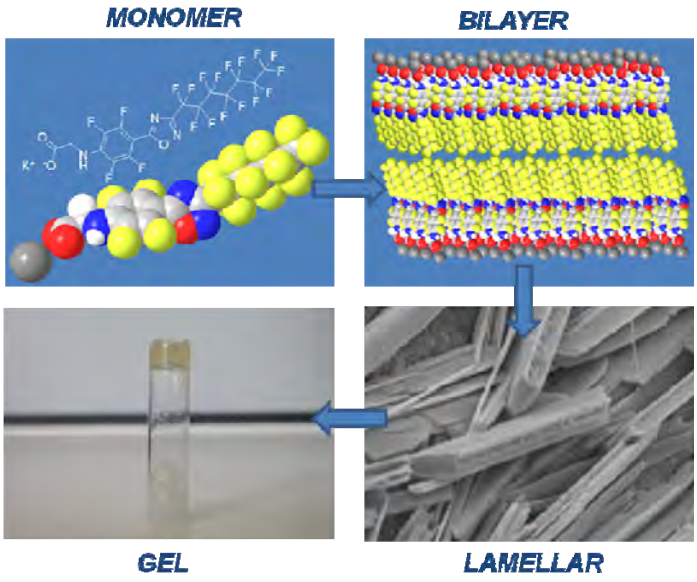

Figure 1.

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ORG-PO-92 Reactivity of decafluoroazobenzene towards aromatic amines: a new entry to tetrafluorophenazines.

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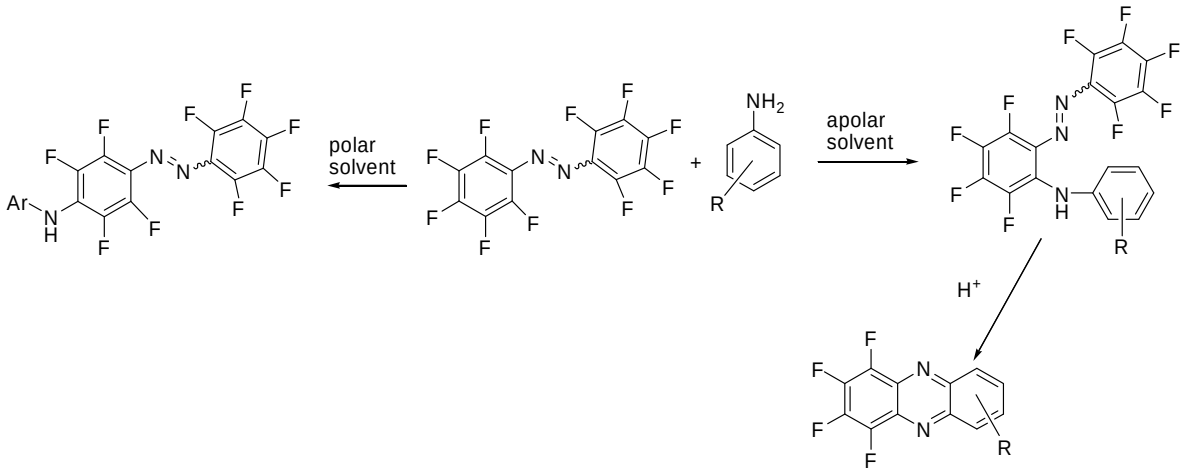
In the last decade the interest for fluorinated aromatic molecules for applications in materials science experienced a huge growth. Indeed, fluorinated aromatic molecules are potential n-type semiconductors, with applications in electroluminescent devices (OLED), transistor, photovoltaic cells and other optoelectronic devices. Our research activities are focused on the synthesis of fluorinated heteroaromatic molecules, with potential application as n-type semiconductors.[1] Recently, we have reported the synthesis of 1,2,3,4-tetrafluoro-acridines and octafluoroacridones starting from decafluorobenzophenone and aromatitic amines.[2] As an extension of this work, here we report on the reactivity of decafluoroazobenzene (prepared by oxidation of pentafluoraniline with lead tetraacetae) towards aromatic nucleophilic substitution with aromatic amines. It was observed that the polarity of reaction medium plays an important role on *ortho/para* regioselectivity and the *ortho*-aniline-substituted-nonafluoroazobenzene is the preferred in low polar solvent such as 1,2,dichloroethane or decaline while only the *para* isomer is obtain in polar solvent such as DMSO. The treatment of *ortho*-aniline-substituted-nonafluoroazobenzene derivatives with trifluoroacetic acid affords the corresponding 1,2,3,4-tetrafluorophenazine derivatives in good yields.



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ORG-PO-93 Parallel kinetic resolution or kinetic resolution of a planar chiral ferrocenylketone through asymmetric reductions

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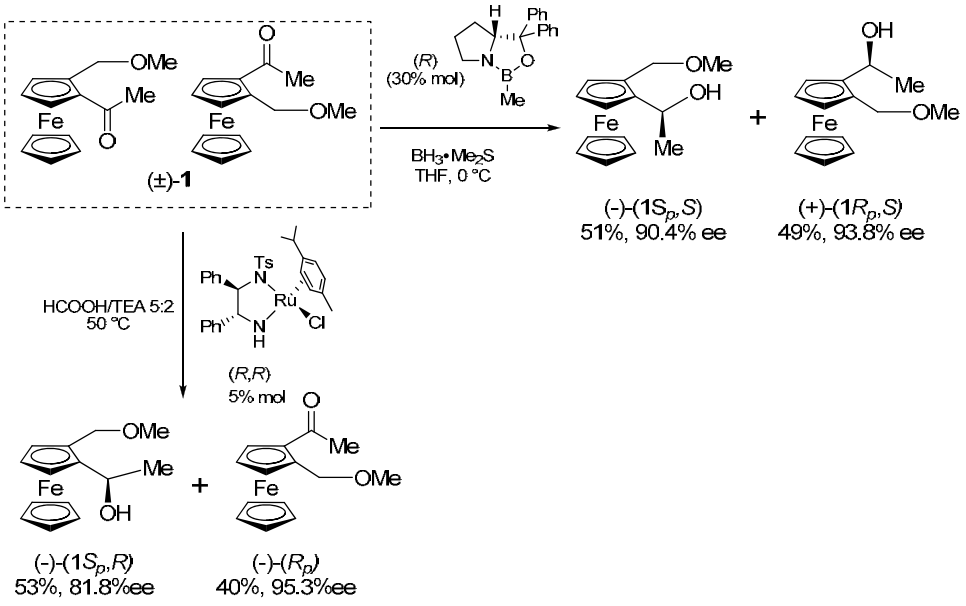
Planar chiral ferrocenes, mainly 1,2-disubstituted ferrocenylderivatives, constitute an important class of ligands active in asymmetric catalysis [1]P. Racemic 1-acetyl-2-methoxymethylferrocene (±-**1**), as a model compound, was subjected to asymmetric reduction with two different methods and complementary results were obtained [2,3]. When the reduction of this ferrocenylketone takes place in the presence of a chiral oxazaborolidine catalyst and BHR_{3R}•$MeR_{2R}S$ as hydrogen source, both enantiomers of the substrate were converted with comparable reaction rate and selectivity. The corresponding diastereoisomeric ferrocenylalcohols were obtained in a 1:1 ratio and >90% enantiomeric excess, this reaction profile being related with a parallel kinetic resolution with high $ds R_{1R}$ and $ds R_{2R}$ diastereofacial selectivities.
On the contrary, the transfer hydrogenation of (±)-1-acetyl-2-methoxymethylferrocene with HCOOH/triethylamine in the presence of Noyori's catalyst proceeded under the classical kinetic resolution fashion, so that the formed (1*Sp,R*)-1-hydroxyethyl-2-methoxymethylferrocene or unreacted ketone could be obtained in highly enantiopure form slight before or beyond 50% of the substrate conversion, respectively.



The alcohol with (1*Rp,S*) or (1*Sp,R*) configuration is not easily accessible by the diastereoselective metalation/electrophilic quenching sequence, routinely applied in the synthesis of planar chiral ferrocenes, so that the described procedures gave a valuable access to this useful starting material for the synthesis of homochiral related derivatives.

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ORG-PO-94 Host-guest polymers with enhanced photoresponsivity assembled by halogen bonding

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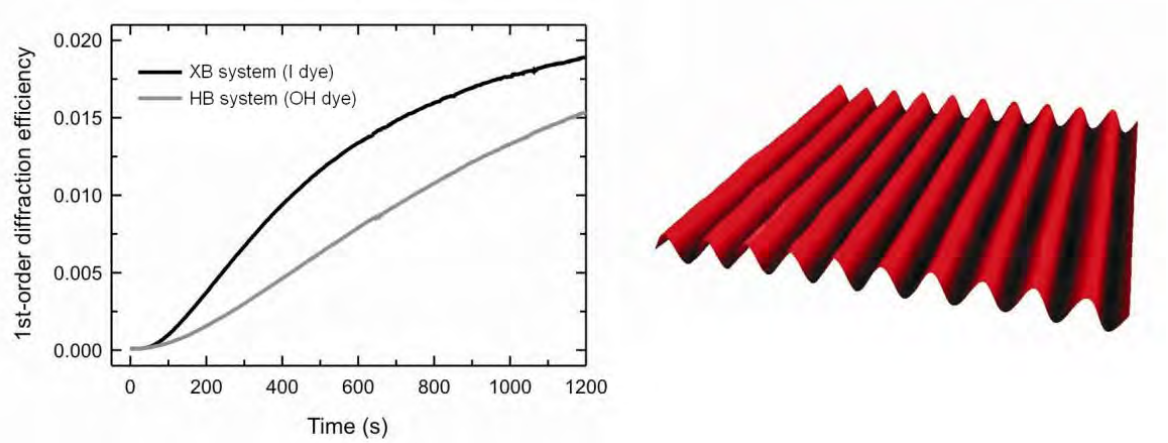
We prepared photoresponsive host-guest materials by halogen bond (XB) [1] coupling of halogenated azo-dyes with poly(4-vinylpyridine). These systems proved to be optimal substrates for the optical inscription of surface relief gratings (SRG), and in some cases outperformed analogous hydrogen bonded materials in such respects as inscription speed, grating depth and diffraction efficiency (see figure below).



The materials were modelled by small molecule complexes in DFT calculations and experimental investigations, suggesting that XB directionality plays a major role in determining the SRG inscription performance. Furthermore, the nature of XB allowed us to perform a systematic study on the role of polymer-dye coupling strength, which was varied by simple substitution of the halogen atom involved [2].

[1] Metrangolo P., Meyer F., Pilati T., Resnati G., Terraneo G., *Angew. Chem. Int. Ed.*, *47*, **2008**, 6114.
[2] Politzer, P., Lane, P., Concha, M.C., Ma, Y., Murray, J.S., *J. Mol. Model.*, *13*, **2007**, 305.

ORG-PO-95 A Novel Synthetic Approach to Oleocanthal, a Natural Anti-inflammatory Agent from Olive Oil

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Oleocanthal (**6a**), a compound isolated from extra virgin olive oil, is a potent non-steroidal anti-inflammatory agent, similar to ibuprofen [1], and a powerful anti-oxidant similar to α-tocopherol. It is suggested that long-term consumption of small quantities of oleocanthal from olive oil may be responsible in part for the low incidence of heart disease associated with the Mediterranean diet. Moreover, activation of TRPA1 by oleocanthal is most likely responsible for the "peppery" taste of olive oil. Only one, rather long, synthesis has been published so far, starting from the chiral pool [2]. In this paper we have developed a new straightforward approach to **6a**, using lactone **1** as the chiral starting building block. Preparative enantioselective HPLC separation provided either enantiopure enantiomers of **1**. In the scheme reported below we show the main steps of the synthesis of the methyl derivative **6b**, as a proof of our synthetic strategy.
Our next aim will be the synthesis of oleocanthal itself (**6a**), following the same route, avoiding the use of protective group.

[1] G.Beauchamp, R.Keast, D.Morel, J.Liu, J.Pika, Q.Han, C.Lee, A.B.III Smith, and P.Breslin, *Nature*, *437*, **2005**, 45-46.
[2] A.B.III Smith, J.B.Sperry, and Q.Han, *J. Org. Chem.*, *72*, **2007**, 6891-6900.

ORG-PO-96 Novel fluorescent silica nanoparticles for heavy metal ions chemical sensing

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Nanotechnology is a fast-growing area, involving the fabrication and use of nano-sized materials and devices. Nanocomposite materials play a key role in this field and, in particular, silica nanoparticles represent a very interesting class of materials for several reasons. Indeed, they are hydrophilic, biocompatible, not sensitive to microbial attack and their morphology and porosity is not dependent on pH changes. Moreover, they are available in well defined size and with external surface bearing reactive functional groups, such as amino groups, that allow easy anchoring of a variety of molecules with specific functions, such as organic dyes, drugs and molecular receptors, thus representing useful nano-structured templates for the fabrication of devices for chemical sensing, bioimaging or drug delivery [1]. Here we report our recent results on the synthesis, the photophysical characterization and the application in chemical sensing of some of the first examples of fluorescent silica nanoparticles functionalized with organic conjugated oligomers, such as oligofluorenes and oligoarylenethienylenes, as well as with organic molecules interacting with heavy metal ions such as Hg^{2+}, Pb^{2+}, Ni^{2+} (Figure 1).

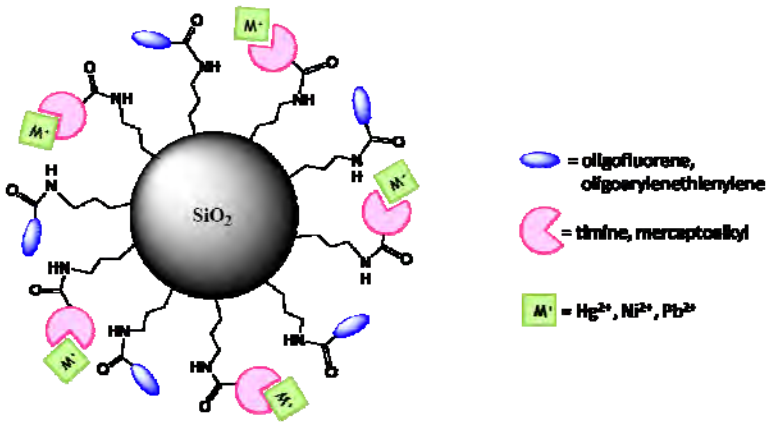

Figure 1.

These materials are potentially useful for heavy metal sensing, allowing detection limit 10^{-7} M and linear fluorescence I/I_0 quenching response for Hg^{2+}, according to the Stern-Volmer law.

[1] L. Wang, K. Wang, S. Santra, X. Zhao, L. R. Hilliard, J. E. Smith, Y. Wu and W. Tan, *Anal. Chem.*, 1, **2006**, 647.

ORG-PO-97 Synthesis of analogues of ochratoxin A

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The mycotoxin ochratoxin A (OTA, Figure 1, **1a**, R = Bn) is a secondary metabolite that occurs in raw and improperly stored food products. In particular, it has been found in cereals, coffee, cocoa, grape juice, beer, and wine [1,2]. OTA has been reported to be nephrotoxic, mutagenic, genotoxic, teratogenic, hepatotoxic, neurotoxic, and immunotoxic, in both animals and humans [3,4]. Several structure-activity relationship studies have been carried out in order to determine the role of each functional group played in OTA toxicity and the question whether the amino acidic moiety plays a role has also been raised [5].

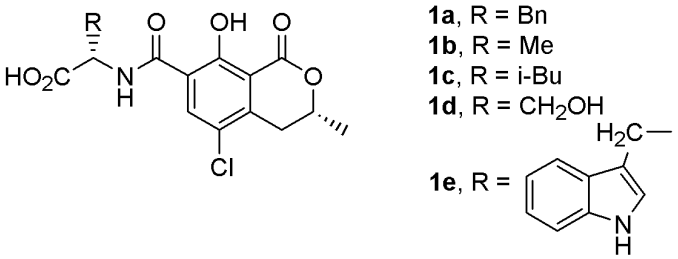

Figure 1

In this communication, we expanded the scope of our previous work on the synthesis of ochratoxin A [6] to the preparation of several OTA analogues, differing for the amino acidic residue. The key step of the synthetic strategy consisted of the condensation reaction between suitably protected amino acid and ochratoxin α (OTα), carried out in the presence of EDC•HCl and HOBt as coupling agents. In particular, OTA alanine (**1b**, R = Me), leucine (**1c**, R = i-Bu), serine (**1d**, R = CH_2OH) and tryptophane (**1e**, R = 3-indolylmethyl) analogues were prepared in satisfactory yields, and will be useful for further toxicological studies.

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[2] E.Anli, and M.Bayram, *Food Rev. Int.*, *25*, **2009**, 214.
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[4] K.R.N.Reddy, B.Salleh, B.Saad, H.K.Abbas, C.A.Abel, W.T.Shier, *Toxin Reviews*, *29*, **2010**, 3.
[5] B.Cramer, H.Harrer, K.Nakamura, D.Uemura, and H.-U.Humpf, *Bioorg. Med. Chem.*, *18*, **2010**, 343.
[6] B.Gabriele, M.Attya, A.Fazio, L.Di Donna, P.Plastina, and G.Sindona, *Synthesis*, *11*, **2009**, 1815.

ORG-PO-98 “One-injection” absolute configuration determination of five acyl-homoserine lactones from *Methylobacterium mesophilicum*

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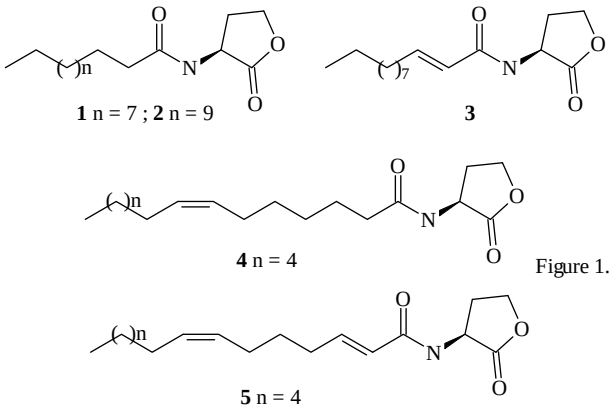

Figure 1.

Brazil has the largest orange orchards in the world and holds an important slice of the international concentrated orange juice market. However, the orchards suffer from several plagues and diseases. There are evidences that the Gram negative bacterium *Methylobacterium mesophilicum* plays a role in the economic relevant citrus variegated chlorosis disease. In the last years, it has been demonstrated that many bacteria employ chemical communication mechanisms known as *quorum sensing* to regulate the expression of important virulent phenotypes against hosts [1]. Therefore, the aim of this work was to characterize the main signaling substances produced by *M. mesophilicum,* belonging to the acyl-homoserine lactones group. The signaling metabolites were purified from 8 l of CHOI3 fermentation media and a mixture (1.1 mg) of five substances was isolated (Figure 1). The absolute configuration determination of these substances proved to be difficult, due to the minute amounts available and the extensive overlap of the saturated and unsaturated homologues on chiral stationary phases by GC-FID analysis. To overcome this problem, a simple and elegant hydrogenation procedure was employed, converting all the unsaturated substances into the saturated ones **1** and **2**. The natural products and derivatives mixture was successfully analyzed by GC-FID with chiral stationary phase, in comparison with racemic and enantiopure synthesized standards. All five substances were characterized as (*S*) enantiomers at the lactone ring with just one injection, and no traces of (*R*) ones were detected. None of these substances had their absolute configuration previously characterized [1].

[1] Pomini, A. M. et al. *J. Nat. Prod.* 72, **2009**, 2125.

Acknowledgments: Fapesp, CNPq.

ORG-PO-99 Catalyst-free Strecker reaction in water: a simple and efficient protocol using acetone cyanohydrin as cyanide source

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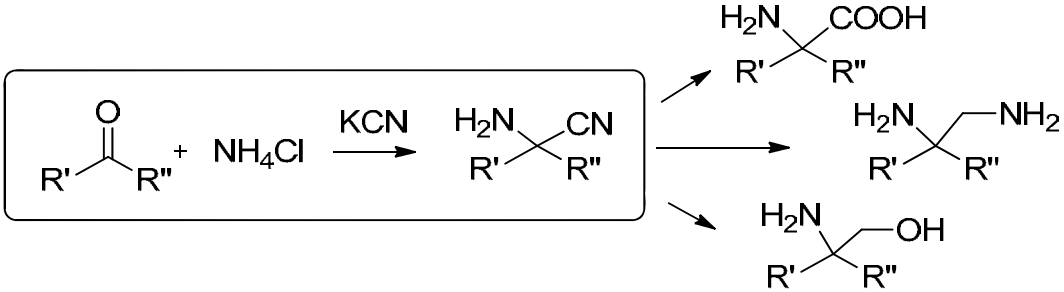
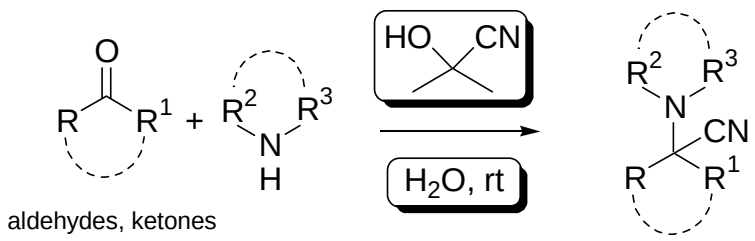
The Strecker reaction is known since 1850[1] and the classic procedure involves the reaction between a carbonyl compound, NH_4Cl, and KCN to give α-aminonitriles[2] which are versatile intermediates for the synthesis of highly functionalized compounds, such as 1,2-diamines, 2-amino alcohols, and α-aminoacids.



The most common cyanide sources for the Strecker reaction like HCN, TMSCN, Bu_3SnCN, Et_2AlCn, K_4FeCN_6 are generally expensive, unsafe and their contribution to atom economy[3]is poor. We choose an economical and relatively safe reagent, the acetone cyanohydrin, that seems to be a good compromise between cost, toxicity and also atom economy.

We studied a simple, convenient, and practical method for the synthesis of α-aminonitriles[4] through a one-pot three-component reaction of a carbonyl compound, amine, and acetone cyanohydrin in H_2O.



Reactions proceed very efficiently without any catalyst at room temperature with high chemoselectivity and giving in some cases the expected α-aminonitrile pure just after direct separation from H_2O.

The protocol is particularly efficient on both aliphatic or aromatic aldehydes, cyclic ketones, in combination with primary and secondary amines. We extended the study to the the synthesis of unusual α-aminonitriles derived from 1,2-diamines and secondary amines.

[1] Strecker A., *Annalen der Chemie und Pharmazie*, **1850,** *75* (1), 27–45;
[2] Optaz T., *Synthesis*, **2009,** 12, 1941–1959
[3] Trost. B. M., *Angew. Chem. Int. Ed. Engl*, **1995**, 34 (3), 259–281;
[4] Galletti P., Pori M., Giacomini D., *European Journal of Organic Chemistry*, in press, DOI: 10.1002/ejoc.201100089

ORG-PO-100 UNEXPECTED PATHS IN THE PHOTOCHEMISTRY OF A 8-FLUOROQUINOLONE

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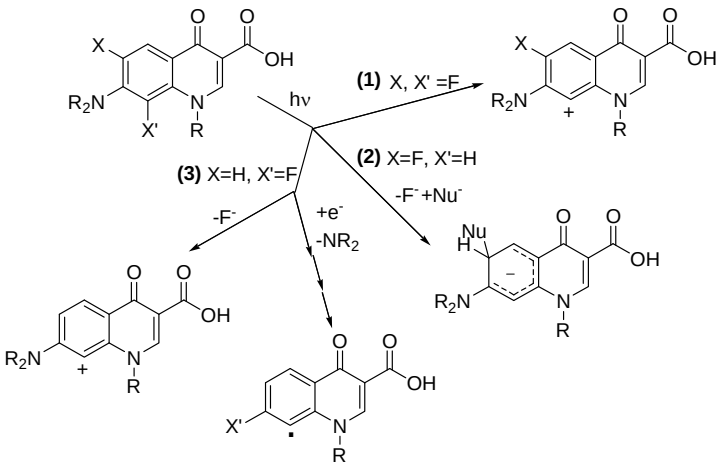
The largely used antimicrobic fluoroquinolones are often phototoxic. In particular those bearing a fluorine atom in 8 position showed to be strongly photoreactive and are known to cause severe side effects upon light exposure, ranging from skin sensitivity to carcinogenicity.[1] This has stimulated the interest in their photochemistry, which has revealed unusual aspects.[2] In particular, 6,8-difluoro-7-aminoquinolones (1) undergo a selective photo S_N1 process with formation of the cation in 8 in the triplet state. This in turn inserts into C-H bonds, adds to C=C bonds or, in the presence of a donor, is reduced. In contrast, 6-fluoro-7-amino derivatives (2) undergo a S_N2 reaction. Looking for a generalization, we synthesized a 8-fluoro-7-amino derivative (3). This behaves as (1) in a non reducing medium, but in the presence of a donor loses the amino group exhibiting a 'pseudo-benzyne' behavior. In fact, in the presence of a donor, such as pyrrole or iodide, the entire piperazine moiety was lost, and a fluorine atom was found in the place of it. New products were isolated and characterized and a plausible reaction mechanism was proposed which took into account the new experimental results. This hypothesis was strengthened by a computational analysis of the reaction mechanism. This further confirms the rich photochemistry of heteroaromatics and in particular of fluoroquinolones and shows how it is possible to change and, to some extent, drive the reactivity of such compounds by introducing appropriate target modifications on the aromatic scaffold.



[1] L.Marrot, J.P.Belaidi, C.Jones, P.Perez, L.Riou, A.Sarasin, and J.R.Meunier, J. R. *J. Invest. Dermatol*., 121, **2003**, 596. L.J.Martinez, R.H.Sik, and C.Chignell, *Photochem. Photobiol*., 67, **1998**, 399.N.Wagai, and K.Tawara, *Arch. Toxicol*., 66, **1992**, 392.
[2] E.Fasani, S.Monti, I.Manet, F.Tilocca, L.Pretali, M.Mella, and A.Albini, *Org. Lett.*, 11(9), **2009**, 1875. L.Pretali, E.Fasani, D.Dondi, M.Mella, and A.Albini, *Tetrahedron. Lett.*, 51(36), **2010**, 4696.

ORG-PO-101 Selective synthesis of aminoalcohols by hydroxyalkylation of amines in alcohol or in cyclic ether cosolvents: a new domino radical mechanism promoted by $TiCl_4$-Zn/t-BuOOH.

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corresponding author: simona.prosperini@gmail.com

Following the radical route, we report a new and fast domino synthesis of 1,2-aminoalcohols under mild conditions. The free-radical reaction of aliphatic and aromatic amines with alcohol cosolvents is promoted by means of the $TiCl_4$-Zn/*t*-BuOOH system [1]. According to the proposed mechanism [2], the amine reacts with two molecules of alcohol in an electrophilic-nucleophilic cascade process.

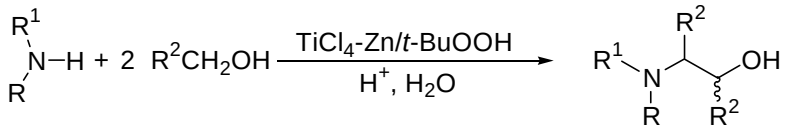

Figure 3 Radical domino reaction between of an amine with two molecules of alcohol, triggered by $TiCl_4$-Zn/t-BuOOH

This procedure, if compared with the $TiCl_3$/*t*-BuOOH-mediated protocol previously reported[3], appears to be more selective, of more general applicability and affords the desired products in higher yields. Besides, with the same catalytic system it was possible to promote the reaction of primary arylamines with two molecules of cyclic ether, leading to the formation of a wider range of functionalized aminoalcohols [2].

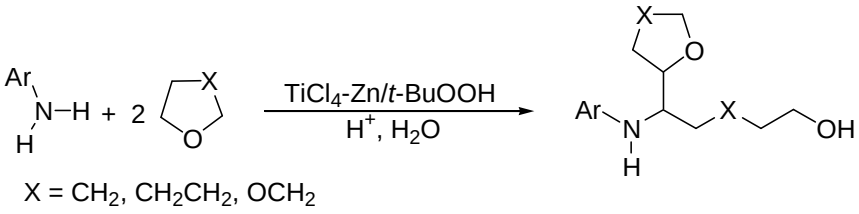

Figure 4 Radical domino reaction of a primary arylamine with two molecules of cyclic ether triggered by $TiCl_4$-Zn/t-BuOOH

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ORG-PO-102 Enantioselective total synthesis of Phytoprostane A1 type II

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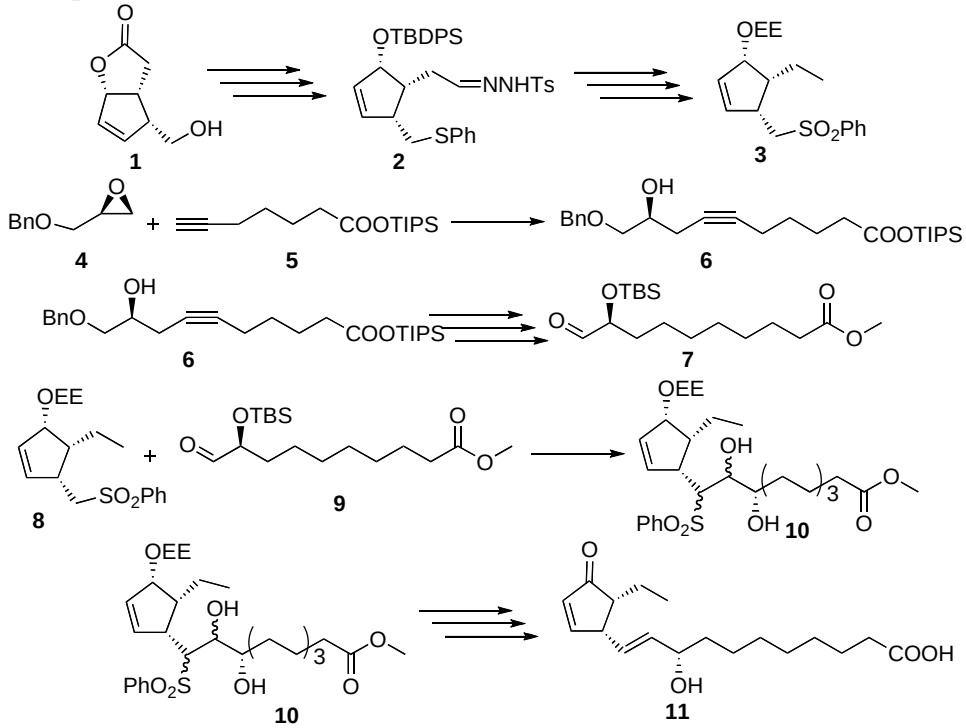
Plants utilize linoleic and linolenic acids to produced C_{18}-isoprostanoids (phytoprostanes, PP) via non-enzymatic, free radical-catalysed pathways similar to isoprostane synthesis in animals [1]. The cyclopentenone-phytoprostanes PPA and PPB up-regulate gene expression, especially for enzymes involved in the response to challenges by foreign organisms or external conditions, triggering phytoalexin production, while they down-regulate genes involved in cell division and growth. Moreover, PP are present in vegetable oils and have been detected in plasma; therefore, the biological properties of phytoprostanes in terms of potential effects on human cells need to be investigated using material only available by total synthesis. In this communication we report the first enantioselective synthesis of phytoprostane A1 type II (**11**), as shown in the Scheme reported below. The cyclopentenone core of **11** was prepared from enantiopure lactone **1** [2], while the lateral chains were installed using intermediates obtained from commercially available compounds.



[1] Muller M. J.; *Plant Biol.*; **2004**, *7*, 441.
[2] Zanoni, G.; Porta A.; Brunoldi, E., Vidari, G.; *J. Org. Chem.*; **2006**, *71*, 8459.

ORG-PO-103 TETRABUTYLAMMONIUM DECATUNGSTATE PHOTOCATALYZED SYNTHESIS OF SULFONES.

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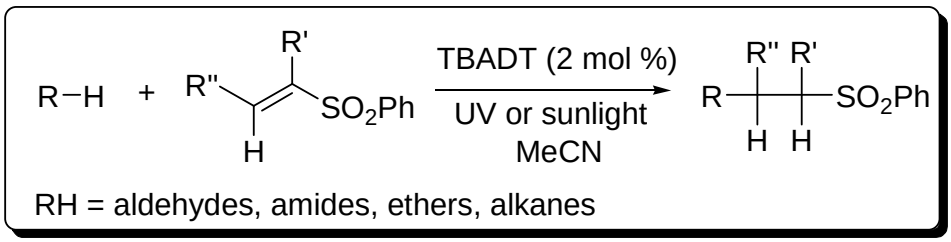
The sulfone moiety plays a useful role in the synthesis of organic molecules due to its easy functionalization and its leaving group aptitude. [1] Vinyl sulfones (e.g. phenyl vinyl sulfone), on the basis of their electrophilic character, can easily undergo conjugate radical additions to give substituted sulfones.
An appealing and atom-economical way to generate substituted alkyl radicals is by a C-H activation reaction and this can be accomplished by having recourse to photocatalysis. In the last years we developed the reactions of a new photocatalyst namely tetrabutylammonium decatungstate ((*n*-$Bu_4N)_4W_{10}O_{32}$), TBADT)). [2] When in the excited state, this abstracts chemoselectively a hydrogen from a C-H bond in several classes of organic molecules including alkanes. The resulting C-centered radicals have been successfully exploited in conjugate radical additions to electron-poor olefins under mild green tin-free conditions. [3]
Thus, (UV or sunlight) irradiation of a mixture containing the hydrogen donor (RH), the unsaturated (substituted) sulfone and catalytic amounts of TBADT allowed the preparation of various substituted sulfones in up to 90% yield.



[1] El-Awa, A.; Noshi, M. N.; Mollat du Jourdin, X.; Fuchs, P. L. *Chem. Rev.* **2009**, 109, 2315-2349.
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ORG-PO-104 Preparation of magnetite nanoparticles functionalized with optically active 1,2-amino alcohols.

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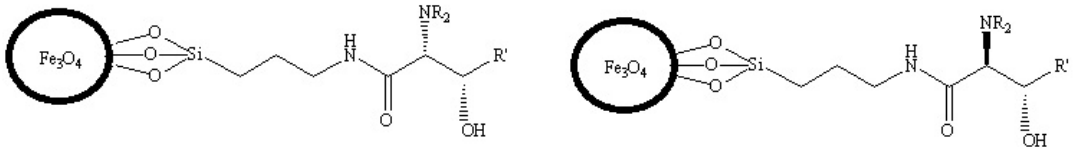
Recently, the use of magnetic nanoparticles led to the development of new catalysts that combine advantages of both homogeneous and heterogeneous catalysis [1]. In fact, nanoparticles with appropriate surface coatings are readily dispersible in organic solvents and, owing to their small size, have very high surface areas. Thus nanoparticles can be used as novel supports for asymmetric catalysts, with activity close to the homogeneous one. In addition, nanoparticle magnetic decantation allows a simple recovery of the catalyst from the reaction mixture and its reuse, as in the case of heterogeneous catalysts.
In this context, we report on the synthesis of magnetite nanoparticles functionalized with optically active amino alcohols, a class of compounds largely employed in asymmetric catalysis [2].
Magnetite nanoparticles were prepared using the organic phase thermal decomposition method.[3]
The synthesis of the amino alcoholic chains was based on the regio- and stereocontrolled opening of enantiopure functionalized epoxides. A triethoxysilane group was introduced at the end of the chains and used for the covalent anchoring to the nanoparticle surface.



The novel "chiral" nanoparticles will be tested as magnetically decantable asymmetric catalysts, at first in the addition of organozinc compounds to aldehydes. The catalytic system will be optimized modifying both the stereochemistry of the amino alcoholic fragment and the steric hindrance of the R and R' groups.

[1] S. Roy et al. *Org. Biomol. Chem. 7*, **2009**, 2669
[2] J. L.Vicario et al. *Current Organic Chemistry, 9*, **2005**, 219

ORG-PO-105 Synthesis of novel conjugated oligomers for labeling applications

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paolo.rinaldi83@alice.it

The research in luminescent organic semiconductor markers for biosensing applications is currently proceeding at a rapid pace[1].
Oligo(*p*-aryleneethynylene)s (OAEs) have emerged as molecular building blocks for the design and fabrication of optoelectronic systems, including chemical and biological sensors[2]. These materials possess interesting semiconducting and optical properties arising from the presence of triple C-C bonds which confer rod-like structure and high conjugation to the resulting system.
In this communication we report the synthesis of oligo(*p*-aryleneethynylene)s with unsymmetrical functionalization on the external rings and various central cores, that are endowed with terminal carboxyl groups to tether biomolecules by formation of amidic bonds. Our synthetic approach is based on palladium catalyzed organometallic methodologies, which appear selective and tolerant of a number of functional groups [3]. In particular, for the cross-coupling of terminal arynes with aryl halides we adopted either the classic Cassar-Heck-Sonogashira reaction and the Mori procedure. Moreover the absorption and emission spectra of the resulting oligomers were recorded and evaluated in order to get information about the influence of the structure of the selected central core and of the different terminal substituents on the overall optical properties.

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ORG-PO-106 9,10-*ter*-Anthrylene-Ethynylenes: New Semiconductors for Solution Processed Organic Field-Effect Transistors

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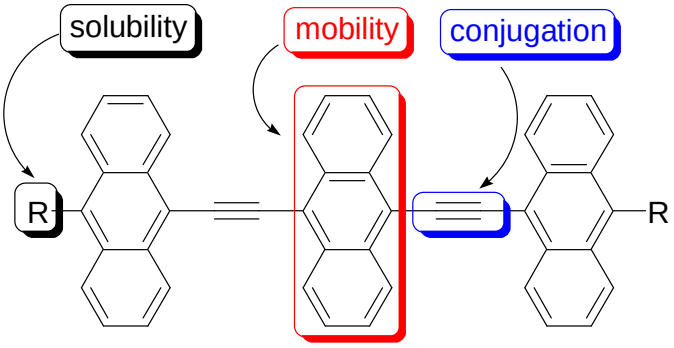
The research on soluble organic semiconductors to be employed in electronic devices such as organic field-effect transistors (OFETs) benefits from the continuous improvement of the available synthetic tools necessary for their preparation [1,2]. However, focused synthetic efforts are still required to conceive new organic structures aiming at gaining more insight into the structure-property relations for these materials. In this presentation, the preparation and properties of soluble 9,10-*ter*-anthrylene-ethynylenes (**Figure 1**) through combined Negishi and Sonogashira cross-couplings will be addressed.



Alkyl functionalised
A1 : R = *n*-Butyl
A2 : R = *n*-Octyl
A3 : R = 2-Ethylhexyl
A4 : R = *n*-Decyl
Ester functionalised
E1 : R = carboethoxy
E2 : R = carbobutoxy
E3 : R = carbooctoxy

Figure 1.

The optical, electrochemical, and thermal properties of the oligomers **A1-4** and **E1-E3** will be discussed as well as STM and XRD investigations aimed at elucidating their order in thin films. Results on their semiconducting properties will also be presented: the top contact OFETs fabricated exhibited hole mobilities up to $5.5 \cdot 10^{-2}$ $cm^2 \cdot V^{-1} \cdot s^{-1}$ and on/off ratios higher than 10^4. The good performances in OFETs of **A1-4** and especially of the polar functionalised **E1-E3** make these materials promising as active layers for OFET sensing applications [3].

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ORG-PO-107 Wacker Oxidation in Ionic Liquids

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A series of hydrophilic N,N-dimethylpyrrolidinium and N,N-dimethylpiperidinium-based ionic liquids (ILs) have been prepared and applied as reaction media in the Wacker oxidation of styrene by hydrogen peroxide using $PdCl_2$ as catalyst.[1,2] The efficiency of these ILs was compared with hydrophilic and hydrophobic imidazolium systems (including those with nitrile functionalities).

The nature of the ionic liquid strongly influences the product distribution. In particular, in hydrophobic ILs relevant amounts of 1,3-dipheyl-1-butene arising from styrene dimerization were detected in addition to the expected phenylmethylketone. The formation of 1,3-dipheyl-1-butene may be attributed to the formation of Pd(0) species from "ClPdOH" (probably formed during the Wacker process) in a side-reaction.

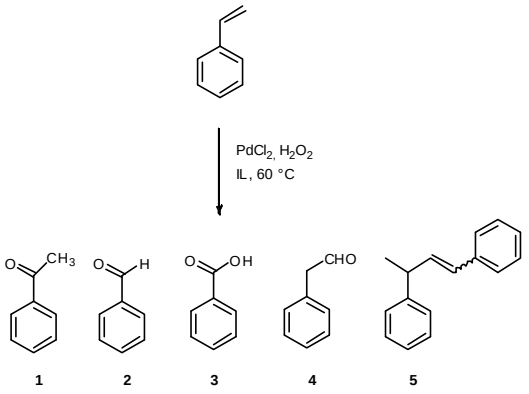

Figure 1. Isolated reaction products.

Consequently, the ability of the IL to favor or disfavor the reoxidation of "ClPdOH" to "ClPdOOH" by hydrogen peroxide giving an homogeneous phase or a biphasic system appears to be the main factor affecting selectivity.

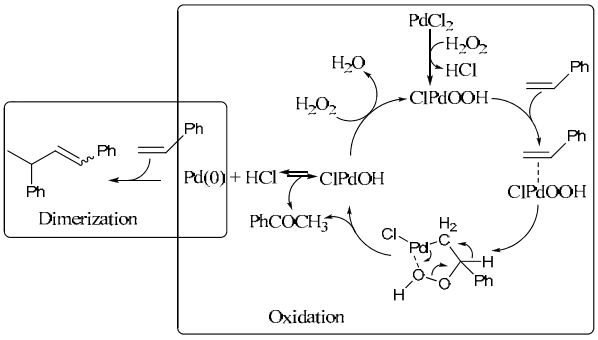

Figure 2. Proposed mechanism for competitive palladium catalyzed styrene oxidation and dimerization.

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ORG-PO-108 Synthesis of Chiral Phosphites and Their Application in the Asymmetric Addition of Dimethylzinc to Alkylidenmalonates

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The asymmetric conjugate addition of dimethylzinc to α,β-unsaturated carbonyl compounds is an efficient and direct method to obtain a methyl substituted stereogenic centre, a structural motif which often plays an important role in determining the biological activity of numerous natural compounds [1].
Acyclic -unsaturated esters are generally not reactive towards dialkylzinc reagents but, in any case, chiral 3-methylesters can be achieved by asymmetric addition of dimethylzinc to alkylidenmalonates followed by direct demethoxycarbonylation of the addition products [2].
We decided to prepare herein new chiral phosphites [3] and to explore their efficiency as ligands in the copper-catalyzed asymmetric conjugate addition of dimethylzinc to diethyl 3-phenylpropylidenmalonate with the aim to disclose new synthetic applications of this procedure. In particular we focused our attention on the development of new route to some floral fragrances like Phenoxanol, Citralis and Nitrile Citralis, in optically active form, choosing 3-phenylpropylidenmalonate as starting substrate on which to test the asymmetric addition.

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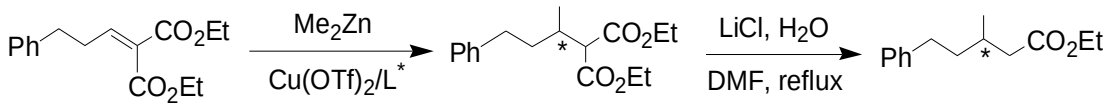

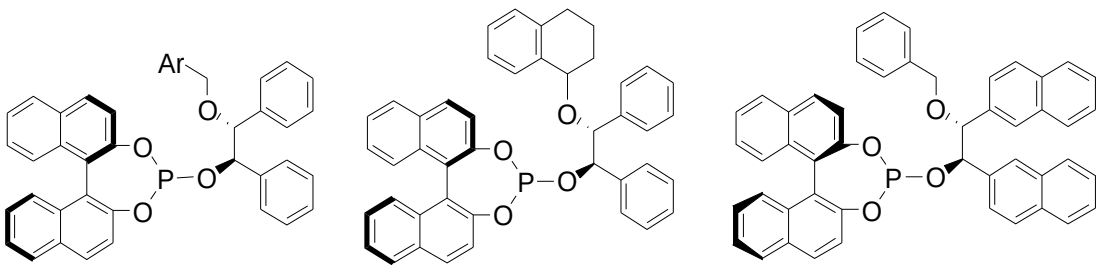

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ORG-PO-109 Indole-3,4-dione as promising scaffold for the synthesis of antiviral compounds

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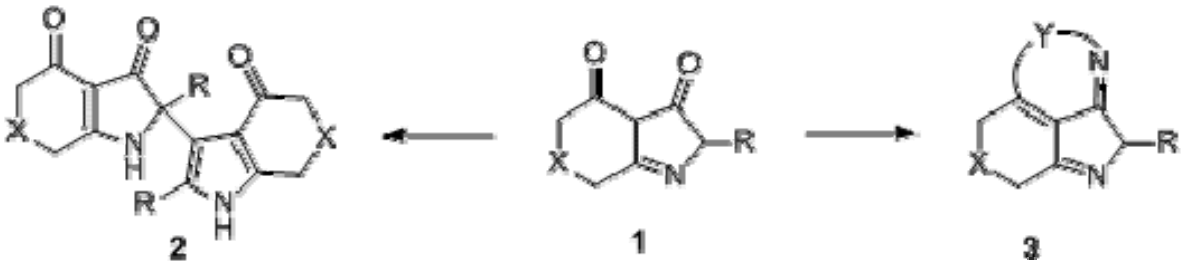
In recent years, indole-based compounds are reported to exhibit broad-spectrum chemotherapeutic properties such as antiviral, antitubercular, antifungal, and antibacterial activities. Due to their biological relevance, they attract special attention as building blocks for the synthesis of new therapeutic agents.
In the framework of our studies dealing with the design of useful polifunctionalized N,O-heterocycles, we recently reported [1] a class of water soluble indole-3,4-diones **1** as promising lead compounds for antiherpetic drug development. Furthermore, these molecules were successfully entrapped in amphiphilic β-cyclodextrin nanoparticles, to increase the bioavailability and modulate the drug delivery [2].
Based on these findings, we further extended our investigation to synthesize more complex molecular architectures **2** and **3**, starting from the indoledione scaffold **1**.
The modulation of reactants and reaction conditions allowed a good skeletal diversity.



Synthetic and mechanicistic details of these transformations will be presented. In particular, a kinetic study of the base-promoted aldol condensation leading to **2** was carried out by UV-Vis absorption. Finally, antiviral activity of the novel chemical libraries was evaluated.

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ORG-PO-110 Influence of Structural Variations in Cationic and Anionic Moieties on Polarity of Ionic Liquids

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The polarity of a series of ionic liquids (ILs) arising from quaternarization of N-methylmorpholine, N-methylpyrrolidine, N-methylpiperidine, N-methylazepane, 4-hydroxy-1-methylpiperidine, 1,2-dimethylimidazole and 1-methylimidazole with simple alkyl chains and/or hydroxyl (mono or dihydroxyl) functionalized alkyl chains and having as counteranion bistriflimide, dicyanamide or nitrate anion has been investigated using solvatochromic dyes and expressed in terms of E_T^N and Kamlet-Taft parameters (dipolarity/polarizability (π*), hydrogen-bond donor acidity (α) and hydrogen-bond basicity (β)). Significant variations of polarity were observed on changing anion and cation combination. Nevertheless, the E_T^N and α values resulted strongly anion-dependent; independently on cation core and substituent on going from bistriflimide to dicyanamide a significant decrease in E_T^N and α values was observed. On the other hand, the alkyl chain length has only a moderate effect on these parameters; however, both an increase or decrease in E_T^N and α values was observed on increasing the alkyl chain length depending on cation core. In the case of cyclic onium salts the size of the cation ring affected the α parameter: the IL based on seven-member ring system, N-methyl-N-butylazepanium (also named N-methyl-N-butylhexamethyleneiminium) $[HME_{1,4}][Tf_2N]$ has high polarity values comparatively to analogous ILs based on five and six member ring cations. The introduction of the OH groups on the cation alkyl chain increases polarity; the effect is substantial for the first OH group and more moderate for the second. Finally, also thermosolvatochromism (changes in solvatochromic properties with change in temperatures) was studied for four dihydroxyl functionalized ILs. The use of principal component analysis (PCA) allow us to better estimate the effects of functionalization and anion-cation association. Furthermore PCA shows that there are only two statistical independent parameters between the ones here considered.

ORG-PO-111 Development of chiral arginine-based PNA microarrays for the selective identification of tomato DNA

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In food analysis, DNA recognition can be extremely useful for tracing the origin of a food product or for evidencing undeclared ingredients, even if present in very small amounts. Among the different DNA markers which might be addressed, Single Nucleotide Polymorphisms (SNPs)[1], which consist in single nucleobase changes within the genome, can be used as specific targets to identify a given food or a specific variety. Surface techniques, and in particular microarray-based platforms [2], turned out to be extremely interesting. Such methods usually rely on the recognition of a DNA target by hybridization with a single strand oligonucleotide probe immobilized onto a surface. The development of PNA-based surface systems allowed to obtain more efficient assays, in terms of selectivity in the recognition of point mutation, robustness and sensitivity [3]. Arginine-based PNAs (Arg-PNAs), recently reported [4] demonstrated their enhanced recognition properties, in terms of binding affinity and mismatch recognition, in solution and on microarray platforms.

Here we show the design and the development of a model Arg-PNA microarray produced for the simultaneous identification of several SNPs, characteristic of different tomato varieties. The design and synthesis of highly selective arginine-based monomer containing PNAs (Arg-PNAs) are reported together with their binding properties in solution and on a microarray surface. In order to define the best design for arginine PNAs for performing selective DNA recognition on surface, two peptide nucleic acids (PNAs) containing three adjacent modified chiral monomers (chiral box) were first synthesized. The chiral monomers contained either a C2- or a C5-modified backbone, synthesized starting from D- and L-arginine, respectively (2D- and 5L-PNA). The 5L-chiral-box-PNA showed the highest Tm with full-match DNA, whereas the 2D-chiral-box-PNA showed the highest sequence selectivity. The PNAs were spotted on microarray slides and then hybridized with Cy5-labeled full match and mismatched oligonucleotides. The results obtained showed a signal intensity in the order achiral >2D-chiral box >5L-chiral box, whereas the full-match/mismatch selectivity was higher for the 2D chiral box [5]. According to these results, seven different PNA probes containing a 2D arginine chiral box were prepared for SNP discrimination in defined sequences of tomato genome. The seven probes were tested in solution and on microarray surface in model

experiments using oligonucleotide mixtures simulating different sequences of the seven tomato varieties [6]. The strenght and the limitations of such a system for SNP recognition will be thoroughly discussed.

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ORG-PO-112 Solvent effects on the keto-enol tautomerization reaction. A thermodynamic study in some organic solvents and ionic liquids

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Organic reactions are commonly performed in solution so that one of the most important parameter for the success of a reaction is the choice of the "best" solvent. Indeed solvents may have a strong influence on reaction rates and equilibria.[1]

Solvent effects on the keto-enol tautomerism have been extensively studied.[1] Recently, the equilibrium constants for the keto-enol interconversion of 2-nitrocyclohexanone (2-NCH) have been reported in water,[2] some organic solvents and ionic liquids (ILs).[3] Due to their peculiar properties, ILs may behave quite differently from conventional molecular solvents. According to these studies [2,3] the enol form of 2-NCH appears to be predominant in apolar solvents while the keto form prevails upon transfer to water, aprotic polar organic solvents and ILs.

In this work the temperature dependence of the tautomeric equilibrium constant for 2-NCH has been studied by UV-visible spectroscopy in five organic solvents, spanning a wide range of permittivity values, , their binary mixtures, and in some ILs in the temperature range 298 to 333 K. The thermodynamic parameters, G^0, H^0 and S^0, for the interconversion reaction have been derived. In the case of molecular solvents a good correlation was found between H^0 and . An attempt to include the studied ILs in the same correlation fails. The nature of the ILs anion seems to play a fundamental role as H^0 is < 0 for $[TF_2N]$- based ILs while it is > 0 for $[BF_4]$- based ILs.

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ORG-PO-113 Microstructured glass reactors and LED illumination: photochemistry as good as it can get

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Light emitting diodes (LEDs) are interesting cold light sources with very high power conversion (80-90%) and narrow emission bands. They find application in consumer electronic devices and lighting. LED light has only found limited use in photochemistry because of the difficulty to obtain low-cost diodes that emit in the deep UV region. However, since new materials for LED applications is rapidly filling this gap, LED-driven photochemistry has the potential to become an important tool to access selective and efficient chemical syntheses.
In this presentation we show how organic photochemists and material scientists can benefit from LEDs through the use of microstructured glass reactors. To this end, we present two examples that best encompass the most interesting features of LED illumination: (i) low power consumption, resulting in economical and environmental friendly processes and (ii) narrow emission bands, resulting in highly selective reaction paths.
(i) Low-power commercial white LED arrays can be used for the quantitative conversion of reagents in photocycloadditions thanks to their high efficiency and the optimal geometry of glass microreactors. The reduced thickness of the microfluidic channel, ensures a uniform illumination of the reaction mixture, reduced reaction times and high space time yields (see figure 1). (ii) Illumination of small (3 nm) silver nanoparticles (AgNPs) results in a growth along preferential directions, depending on the wavelength of the radiation. This effect can be used to produce AgNPs with specific shapes and plasmonic properties that depend on the excitation wavelength used (see figure 2). In this case, microfluidic reactors allow to quickly produce AgNPs that can be functionalized with thiols or used immediately for surface enhanced raman spectroscopy (SERS) analysis.

Figure 1 - Photochemical microreactor with white LED illumination

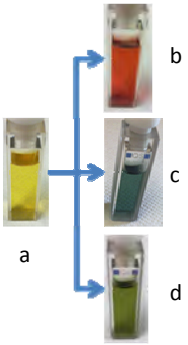

Figure 2 - AgNP seeds (a) and AgNP after illumination at 455 nm (b), 540 nm (c) and 505 nm (d)

ORG-PO-114 O, Se Acetals as Reagents for the Protection of Alcohols

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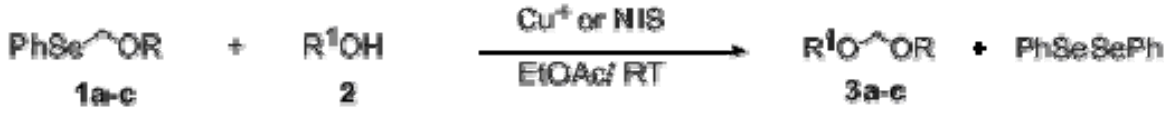
Among the organoselenium compounds the *O, Se* acetals are interesting intermediates because they are precursors of -alkoxyalkyl radicals, -selenocarbenium ions, -alkoxyalkyl lithium derivatives and -alkoxycarbenium ions [1]. It is known that phenylseleno glycosides are versatile glycosyl donors in glycosylation reactions after activation of the selenium atom [2]. We report that C-Se bond in the mixed *O, Se* acetals **1a-c** can be heterolitically cleaved by the action of copper(I) or iodonium ions. If an alcohol **2** is present in the reaction medium, the corresponding acetals **3a-c** where obtained in good to excellent yields. This is a simple and chemoselective method for the protection of alcohols as methoxymethyl-, methoxyethoxymethyl- and 2-(trimethylsilyl)ethoxymethyl ether derivatives [3]. Furthermore the method is compatible with many functional groups and the selenium can be recovered as diphenyl diselenide in almost suitable yield at the end of the procedure.



R= Me, $MeOCH_2CH_2$ or $(Me)_3SiCH_2CH_2$
NIS= *N*-iodosuccinimide

Financial support from MIUR, National Projects PRIN 2007, Consorzio CINMPIS, Bari and University of Perugia is gratefully acknowledged.

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ORG-PO-115 Development of drug-branched peptides complexes for cancer cells tracing and killing

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The aim of this project is to convert 'conventional' cancer drugs, that usually show lack of selectivity and systemic toxicity, in drug-carrier complexes, specifically channelled into tumour cells and able to fulfil its cytotoxic action *in situ*. Peptides, synthesized as dendrimers, are especially suitable for in vivo use due to their stability in human plasma [1]. The realization of these drug delivery systems can be obtained synthesizing a 'smart' linker that manage, at one end, to be bound to the peptide immobilized on a resin and at the other end to the anticancer drug by a 'cleaver' link suitable for different releasing rates.

After internalization into tumor cells the free drug is releasing in situ from the linker by a simple hydrolysis or by specific enzymes. We have chosen to work with different classes of anticancer drugs (antimetabolites, bioreductive drugs, estrogen derivatives, inhibitors of mitosis and platinum complexes), showing different mechanisms of action, in order to potentially provide useful treatments for a wide spectrum of tumours [2]. The synthetic efforts directed towards the optimization of the linkers structure and the attempts to achieve multi-drug carriers are investigating at the moment and will be discussed in this communication.

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ORG-PO-116 Straightforward access and easy functionalization of naphtha- and anthradithiophenes

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Acenes have optical and electronic properties that are desirable for applications in organic-based electronic devices such as organic field-effect transistors (OFETs) and organic light-emitting diodes (OLEDs). Incorporating heteroarenes, such as thiophene, into these frameworks is part of an ongoing effort to prepare new materials with improved device performances [1].

In this communication we will describe a simple strategy for the preparation of naphtha- and anthradithiophenes that exploits easily available alkylaryl- or diarylalkynes as starting materials and two consecutive one-pot electrophilic processes for the introduction of the sulfur atom and the closure of the thiophene ring. This procedure allows the preparation of 3-chloro-substituted thioacene derivatives that can be further functionalised, with different metal catalysed cross coupling reactions, taking advantage of the heterocyclic carbon-chlorine bond [2].

The applicability, limitation and scope of this new procedure, as well as the reasonable mechanisms involved in the transformation will be presented.

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ORG-PO-117 Zinc Oxide: a new Tool for the Solvent- Free Regioselective C- Arylsulfonation of Indoles.

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Aryl sulfones and sulfoxides are interesting functional groups present in a wide variety of compounds in the field of drugs and pharmaceuticals.
In particular, indolyl aryl sulfones have emerged as powerful anti-HIV-1agents [1] or as efficient carcinogenesis modulators with a pleiotropic mode of action [2]. (Figure 1) Although the direct aryl sulfonylation of aromatic systems is well known in the literature, the indolyl aryl sulfones are generally prepared by indirect methods which involve the oxidation of indol-3-yl sulfides to the corresponding sulfone [3].Thus, in view of their importance, in the present research we illustrate a mild and versatile direct one-pot approach for the aryl sulfonation of 1*H*- indoles. (Figure 2)

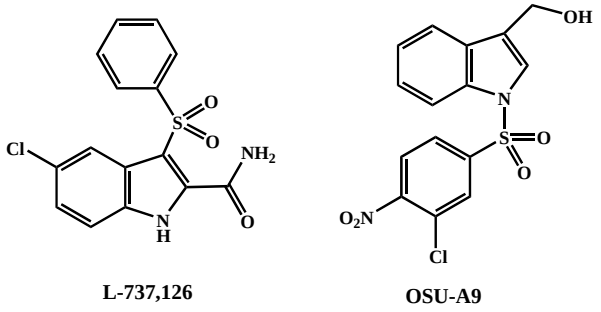

Figure 1

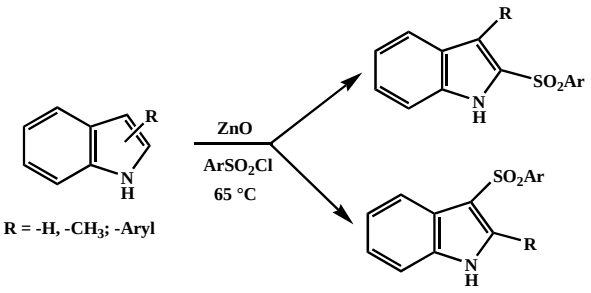

Figure 2

The highly regioselective reaction, carried out in solvent-free conditions and in the presence of ZnO, provided all the C- indolyl aryl sulfones in good yields and short reaction times. Moreover, all the involved parameters have been investigated, paying particular attention at the role of the oxide and the effect of the substituents on the aromatic rings.

Acknowledgements. This work was supported by Progetto Di Ricerca Fondamentale o di Base “Processi e metodologie innovative orientate alla preparazione di sistemi eterociclici bioattivi” (L. R. n° 7, 2007, Bando 2008).
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ORG-PO-118 One-Pot Ester Synthesis from Allyl or Benzyl Halides and Alcohols by Pd-Catalyzed Carbonylation

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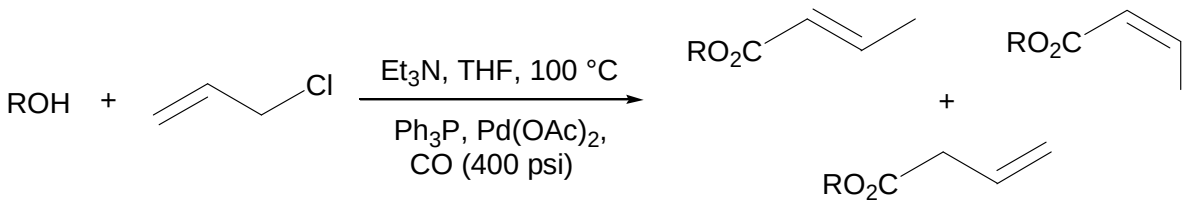
Esters are widely found among all naturally occurring compounds, and are also greatly important intermediates in organic synthesis [1].
The ester bond is one of the most common linkages in organic chemistry and could be formed by different strategies using acids, anhydrides or chlorides with alcohols as starting substrates [2]. The reactions proceed with or without the help of a base or an acid and also with or without a metallic catalysis [3]; among metals used as catalyzers one of the most common is Palladium.

In this contribution we report a mild and efficient one-pot synthesis of esters based on the Pd-catalyzed alkoxy- and aryloxycarbonylation of allylic or benzylic halides. The methodology is applied to primary, secondary and tertiary alcohols as well as to phenol derivatives. The *O*-protection of some biologically relevant molecules is also reported.



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ORG-PO-119 New HIV-1 Protease Inhibitor bearing a benzothiophene as the P2-ligand: easy structure and effective activity.

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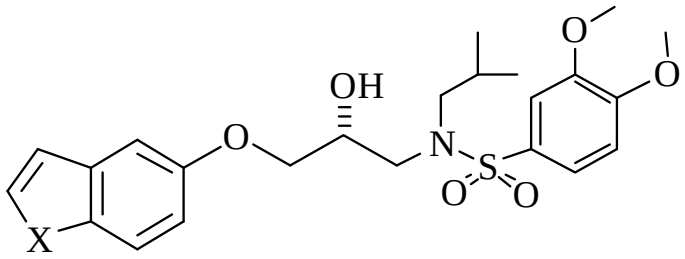
Since protease inhibitors (PIs) have been employed to combat AIDS, HIV infection has definitely become more manageable [1]. However some complex issues associated to these drugs remain unsolved. This has led scientific community to seek novel structures able to overcome such problems [2]. Working on this direction, we recently demonstrated the positive effect of a heteroaromatic group in a series of new thienyl ring containing analogues of two approved PIs, Nelfinavir and Saquinavir [3]. Moreover, we also reported the facile synthesis and the biological evaluation of a new non-peptidic PI (**1**) with an IC50 of 1 μM [4]. On the basis of this result, we have therefore been really intrigued by understanding the actual importance of the NH indolic function regarding the efficiency of **1**. Thus, we alternatively introduced a methyl or a benzyl group on the nitrogen and then switched the heteroatom to oxygen or sulfur. As it is highlighted in figure 1 we have found that the heteroaromatic moiety plays a crucial role in the biological activity of our molecules. Particularly the presence of a benzothiophene affords a significant improvement in IC50. In the present communication we report in detail the results of our investigation.



Inhibitor	X	IC50 (μM)
1	NH	1
2	NMe	>1000
3	NBn	>1000
4	O	130
5	S	0.06

Figure 1

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ORG-PO-120 From Cinchona alkaloids catalysts to Chiral Solvating Agents for NMR spectroscopy

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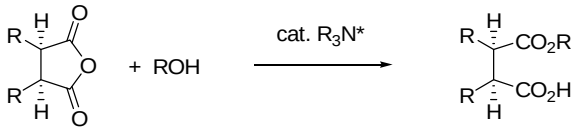
Cinchona alkaloids play a key role in several chiral recognition processes. Their efficiency and versatility as chiral auxiliaries in catalysis and in the direct spectroscopic and chromatographic determination of enantiomeric excesses have been recognized since long time. In particular 9-*O*-ether derivatives of quinidine are valuable organocatalysts employed in the asymmetric alcoholysis of *meso*-anhydrides (Scheme 1).



Scheme 1

In an attempt to give a contribution to the knowledge of such a desymmetrization process, we carried out an accurate NMR investigation on the ground state conformation of mono and bis-9-*O*-pyridazine and anthraquinone derivatives of quinidine in the reaction solvent and in the presence of the reactants (cis-1,2,3,6-tetrahydrophthalic anydride and alcohol) or the reaction products. In the course of this investigation the potential of the alkaloid derivatives as chiral solvating agent for the in situ determination of the enantiomeric excesses of the reaction products was also demonstrated, and further confirmed by examining several mixtures containing different alkaloid derivatives and products of the asymmetric alkoholysis (Figure 2).

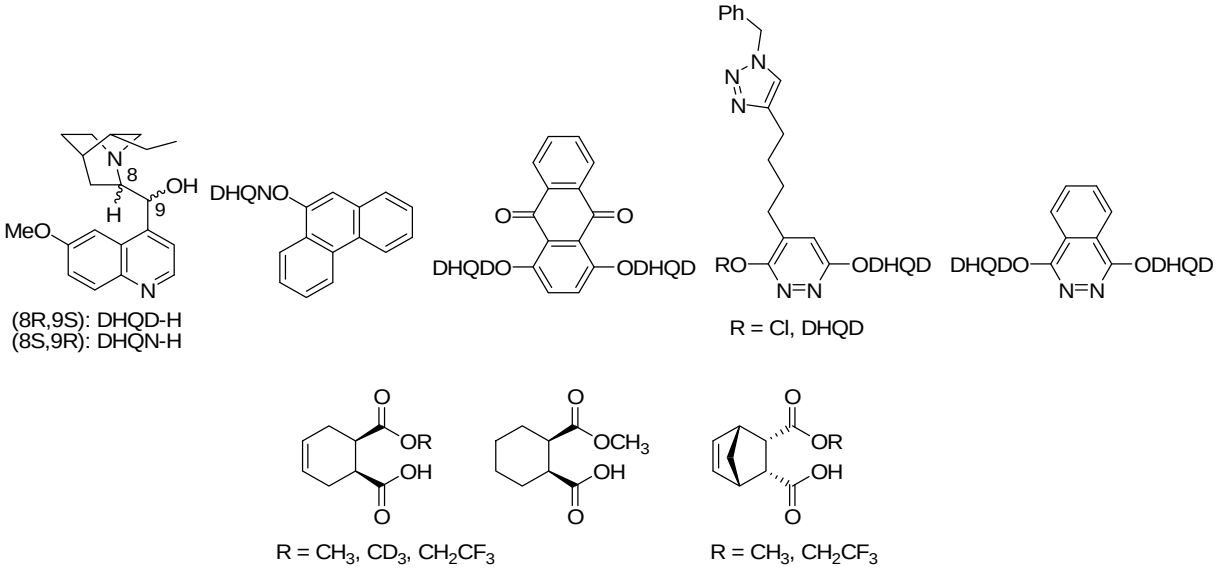


Figure 2

ORG-PO-121 The First Enantioselective Synthesis of a D_2-Neurofuran

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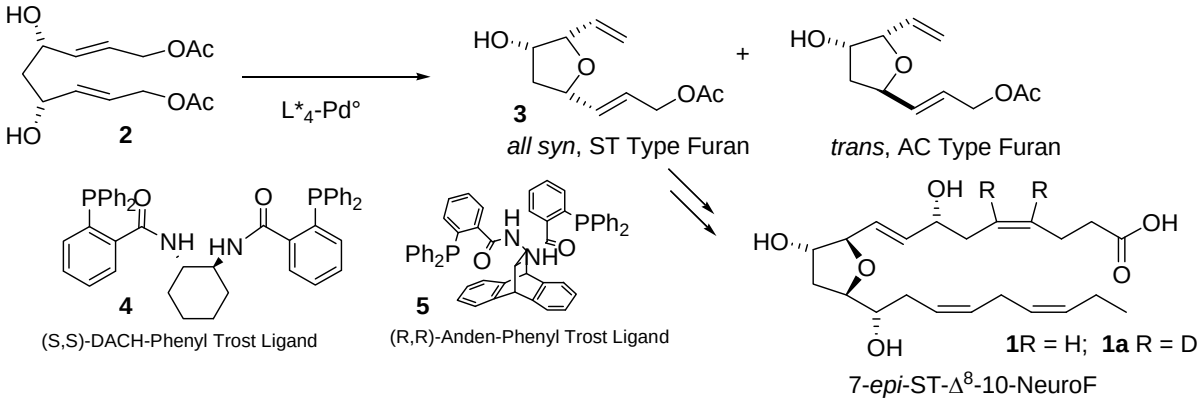
Neurofurans [1] are C-22 compounds formed, under extensive oxidative stress conditions, by ROS, free radical mediated, peroxidation of docosahexaenoic acid (DHA) esterified to neuronal phospholipids. Measurement of the neurofurans may ultimately prove useful in diagnosis, timing and selection of dose in the treatment and chemoprevention of neurodegenerative diseases, such as Alzheimer's and Parkinson's. Moreover, biological activities of neurofurans are still unknown, as well as their possible interferences with the DHA signalling pathway.

In this work we report the first total synthesis of a neurofuran, namely 7-*epi*-ST-Δ^8-10-NeuroF (**1**). The synthesis features the optimization of a general approach to the 3-hydroxy-1,2-dialkyl trisubstituted heterocyclic core, which is based on the desymmetrization of *meso*-diol **2**. Thus, the all-*syn*-furan **3** was obtained in good diastereo- and enantioselectivity via Trost's Pd(0)-catalysed allylic etherification of **2**, using the DACH and Anden chiral ligands **4** and **5**. Subsequently, the two side chains were installed with complete stereocontrol. In particular, hydrogenation of an alkyne unit with the Lindlar catalyst allowed for the preparation of **1** as well as the 4,5-D_2-derivative **1a**.



Our synthetic pathway can readily be extended to the preparation of other neurofurans, including T-labelled derivatives, for the study of their metabolism *in vivo*.

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ORG-PO-122 CHEMICAL SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME STYRYLHETEROCYCLES

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The stilbene scaffold is known to hold several biological activities (antioxidant, antiinflammatory, antifungal) considered beneficial for human health [1]. Resveratrol (*trans*-3, 4', 5-trihydroxystilbene) is a naturally occurring polyphenol stilbenoid found in grapes and in a multitude of dietary plants. This molecule is synthesized by plants in response to environmental stress and fungal infections and is known to be involved in defense mechanisms [2].

In this work we present the synthesis of different styrylheterocycles (2÷3-furyl, 2÷3-thienyl, 4-pyridyl derivatives) through Wittig reaction using LiOH as base [3]. We also studied the antifungal activities of these molecules against *Botrytis cinerea*, a phytopatogenic fungus that attacks flowers, fruits, leaves, and stems of more than 200 plant species, the antioxidant properties of the synthesized molecules and their possible control action on Ochratoxin A (OTA) biosynthesis.

OTA is a mycotoxin produced by several species of fungi belonging to *Aspergillus* and *Penicillium* genera naturally occurring in a variety of food commodities. OTA has been shown to be carcinogenic, nephrotoxic and teratogenic to animals and is suspected to be involved in tumors of the upper urinary tract in humans [4]. OTA biosynthesis is influenced by the presence of peroxides in the environment and some antioxidants like resveratrol inhibits it [5].

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ORG-PO-123 Panchromatic *trans*-di-thiocyanato Ru(II) sensitizer for dye-sensitized solar cells

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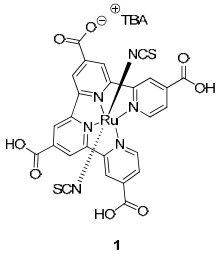
The heart of a DSC is a mesoporous titania film composed of nanometer sized particles with a monomeric layer of a sensitizer [1]. 2,2′-Bipyridine-based Ru(II) complexes have been by far the most investigated and efficient systems [2] (i.e. N3 and N719) yielding a conversion efficiencies over 11% (AM 1.5) [3]. The optimal sensitizer for DSCs should be panchromatic with an absorption spectrum extended throughout the visible and the NIR region. The aim of this research is to produce tetradentate ligands that provide stable *trans* configuration in the corresponding panchromatic Ru (II) complexes. Quaterpyridine ligands are suitable for this purpose and they are still largely unexplored [4]. The main drawback until now has been the long synthetic pathway to get the ligands as well as the repeated purification steps required by the corresponding complexes.

Here we report a new easy and reliable synthetic pathway for the quaterpyridine ligand and the related panchromatic *trans*-Ru(II) complex **1** that can be simply transferred to the analogous compounds. The purification step has been settled upon a standard chromatographic silica column giving a highly pure complex with an overall photovoltaic conversion efficiency of 6.30% at standard AM 1.5 sunlight, that is the best efficiency reported up to now for tetradentate ligand-based Ru(II) complexes. In addition, a photocurrent, 19 mA/cm2 at standard 1.5 sunlight, was obtained by tuning the used electrolyte.



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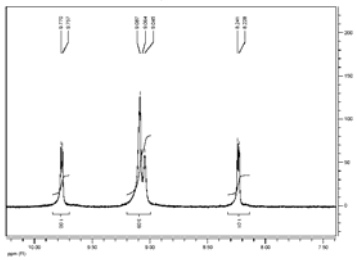

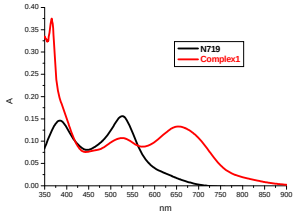

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ORG-PO-124 Synthesis, Structure and Biological Activity of Sulfated Tri Maltose α,α and α,β C-C-linked Dimers

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Large efforts have been addressed to isolating sequences of natural oligosaccharides, which possess a significant biological function, and to preparing synthetic oligosaccharides, that have been designed to mimic the natural ones. We moved to building up mixed O/C malto-oligosaccharides and to check whether or not their sulphated forms would mimic natural malto-oligosaccharide. Sulfated tri maltose C-C-linked dimers (α,α and α,β STMCs) were prepared by halo-maltotriose electroreduction [1] on silver cathode followed by sulfation. The sugar chains of these mimics are characterised by the presence of an interglycosidic C-C bond which are less vulnerable to metabolic processing then their O-analogues and for this reason have been studied as drug candidates and inhibitors of carbohydrate processing enzymes. The presence of the interglycosidic C-C bond is an important feature because, as shown by a molecular modelling conformational analysis, it modifies the geometry of the sugar chains and makes their conformation rigid. Actually, the conformational flexibility of oligosaccharides is critical in determining their binding to protein and consequently their bioactivity.

Development of compounds that target both heparanase and selectins is emerging as promising approach for cancer therapy. The P-selectin specificity of STMCs was defined by the anomeric linkage of the C-C bond. α,β SMTC is an effective inhibitor of P-selectin *in vivo* and attenuated metastasis both on B16-BL6 melanoma cells and on MC-38 carcinoma cells indicating that inhibition of tumor cell interaction with the vascular endothelium is critical for cancer dissemination. α,α SMTC attenuated metastasis in B16-BL6 melanoma cells, expressing high levels of heparanase, but it is not an inhibitor of P-selectin and did not attenuate metastasis on MC-38 carcinoma cells. [2]

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ORG-PO-125 Synthesis of *N*,*N*-dialkylaminobenzonitriles and halo-(*N*,*N*-dialkyl) benzamidines by reaction of halobenzonitriles with lithium amides.

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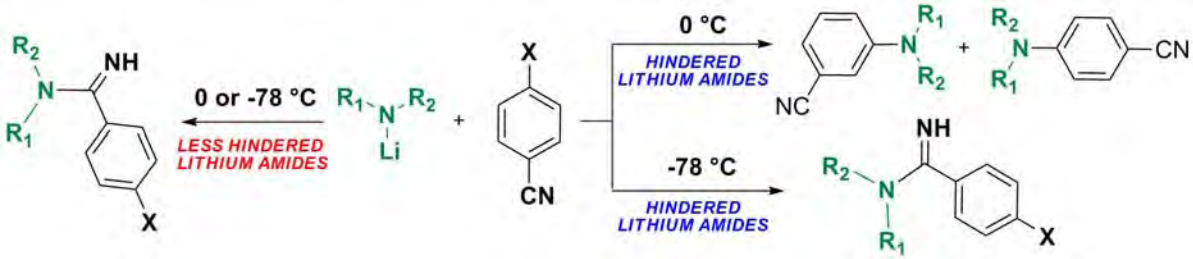
Aminobenzonitriles are important targets in organic synthesis, due to their application as electron donor–acceptor (EDA) molecules, as probes to study material properties [1], for the development of optical switches, and for the potential conversion of photon energy into electricity. The photodynamics of some 4-(dialkylamino)benzonitriles have been studied by time-resolved X-ray diffraction [2-3], femtosecond UV/Vis and mid-IR absorption spectroscopy, both on single crystal or solubilized in polar/non polar solvents [4-5], because these compounds often undergo dual fluorescence and fast intramolecular charge transfer (ICT) reactions. Various starting materials and synthetic strategies, mainly based on transition-metal catalytic processes [6], are used to prepare these compounds. Herein, we report a simple approach to *N*,*N*-dialkylaminobenzonitriles by reacting halobenzonitriles with hindered lithium amides.

3- and 4-*N*,*N*-dialkylaminobenzonitriles and 4-chloro-(*N*,*N*-dialkyl)benzamidines were isolated by reacting 4-chlorobenzonitrile with hindered lithium amides under thermodynamic (0 °C) and kinetic control conditions (-78 °C), respectively (Figure). As previously reported [7], a benzyne mechanism seems to be confirmed when *N*,*N*-dialkylaminobenzonitriles are formed. Only benzamidines were isolated in fair to high yields at both 0 °C and -78 °C with not hindered lithium amides. Exploitation and mechanistic rationale of the reaction of different halobenzonitriles will be reported.



Figure

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ORG-PO-126 Enantioselective bio-reduction of prochiral ketones by the non-conventional yeast *Kluyveromyces marxianus*

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Optically active molecules are important building blocks for the synthesis of many chemicals and biologically active compounds. Among the known catalysts, isolated enzymes have some advantages over conventional methods in the asymmetric synthesis, such as chemo-, regio-, and stereo-selectivity, together with very mild reaction conditions [1].
The asymmetric synthesis accomplished by using whole-cells has also further advantages [2, 3] because all the necessary cofactors and all required substances for their regeneration are present in their natural environment, thus making the catalytic system more efficient [4].
Many research groups have focused their attention on looking for non-conventional yeasts, to study in comparison to the deeply investigated *Saccharomyces cerevisiae* [5].
For several years our interests focused on using non-conventional yeasts to prepare new EPCs: among these, thermotolerant *Kluyveromyces marxianus CBS 6556*, not widely investigated in asymmetric synthesis, was preliminarly and successfully used by us for the stereoselective bioreduction of prostereogenic keto-esters to prepare optically active building-blocks in the synthesis of pharmacologically active compounds [6, 7]. These studies allowed also the isolation of an unkown ADH from this yeast [8], able to mediate the highly stereoselective bioreduction of prostereogenic 3-oxo esters. Herein, we report the continuation of such studies, in which the *Kluyveromyces marxianus CBS 6556* is used in the bioreduction of various prochiral ketones, with the aim to deepen its substrate specificity, turnover rate, regio- chemo- and enantioselectivity.

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ORG-PO-127 Synthesis and characterization of long-chain carboxylic acids with fluorescent end-groups as organic building-blocks for self-assembly on noble-metal nanostructures.

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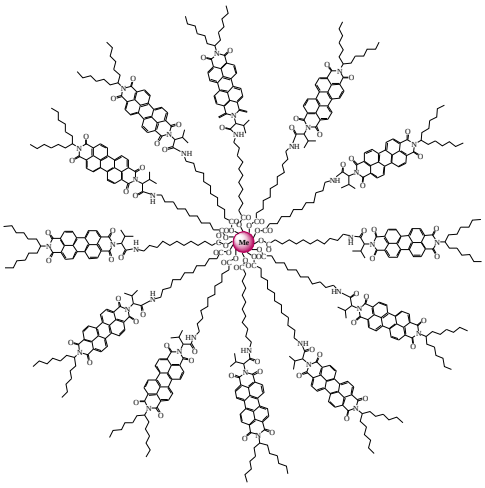
Self-Assembled Monolayers (SAMs) of organic compounds can be prepared through the adsorption of suitable organic molecules from solution onto metal planar surfaces (2-D SAMs) or three-dimensional nanoparticles (3-D SAMs).

The photophysical properties of the 3-D nanohybrids so obtained are closely related to the nature of the groups situated at the end of the organic chain: in particular, fluorescent end-groups provide the material with unique optical properties than can be exploited for various applications, such as biosensors and photovoltaic and optoelectronic devices.



Thiols, disulfides and carboxylic acids are extensively used to prepare SAMs on noble metals [1]. In the case of SAMs on Ag, long-chain carboxylic acids allow better results in terms of stability of the obtained nanohybrids [2-4].

In the communication we present our recent results on the synthesis and on the absorption and emission characterization of long-chain carboxylic acids possessing a chiral aminoacid residue (introduced to allow their study by circular dichroism, useful to get information on their spatial arrangement on the surface of the nanoparticles) and endowed with a fluorescent end-group (e.g. perylene in the figure), and on the preparation and characterization of the noble-metal nanohybrids obtained from them.

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ORG-PO-128 Phytochemical Analysis of Tomato Roots

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Plants are a rich source of biologically active compounds which often act as natural barriers against the attack of pathogens and determine plant resistance or susceptibility to pests. Numerous plant species have been already reported to contain metabolites with biocidal activity and there is a continuous effort in discovering new natural sources [1] for compounds toxic to phytoparasites.

Tomato represents an important agricultural crop, typical of the mediterranean areas, which can undergo to high yield loss due to phytonematodes. As a part of a research program [2] aimed to discover natural biocides from plant extracts, we have evaluated the phytochemical profile of tomato roots resistant and susceptible to nematodes.

We applied a metabolomic approach based on the use of HPLC/PDA/ELSD, LC/MS and NMR. The analytical study showed that the methanolic extract obtained from the plant roots was rich in glycoalkaloids, phenolic compounds and primary polar metabolites such as organic acids and amino acids. Content of these metabolites is discussed and related to nematode resistance or susceptibility of the investigated tomato roots.

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ORG-PO-129 Heterogeneous catalysis in the synthesis of tetrahydrocannabinol analogues

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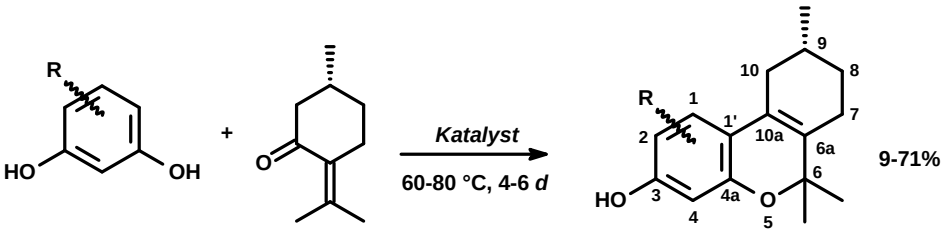
Tetrahydrocannabinols are important natural occurring compounds that recently have found some important applications in pain therapy [1].
Despite a wide range of syntheses of natural tetrahydrocannabinols and analogues reported in the literature since 1940 [2], a lack in the field of heterogeneous synthetic approach to tetrahydrocannabinols and analogues exists. We investigated the possibility to synthesize tetrahydrocannabinol analogues starting from (*R*)-(+)-pulegone and several resorcinol derivatives via heterogeneous catalysis.



To achieve this project we used different heterogeneous solid acid catalysts, such as α-zirconium sulphophenyl phosponate/methanphosphonate [3], ytterbium triflate [4] and supported sulfuric acid on silica gel [5]. Interesting results were obtained and a comparison of the activity between the different solid acid catalysts is possible. In all entries the reaction showed a particular regioselectivity towards 3-hydroxy derivatives and a possible reaction mechanism can be also hypothesized.

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ORG-PO-130 Multicomponent reactions beyond the iminium ion trail: total synthesis of arzanol, the anti-inflammatory principle of eternelle (helicrysum italicum l.)

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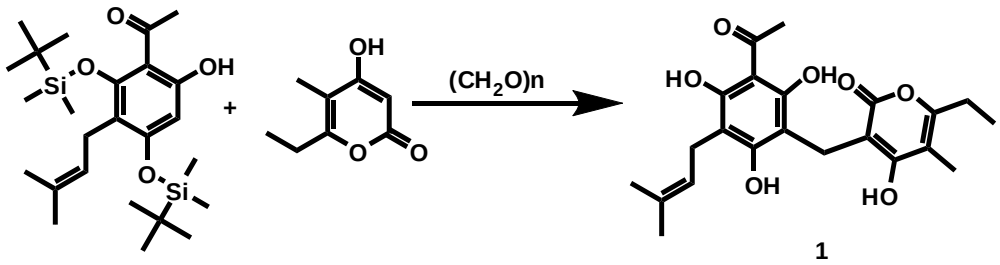
Multicomponent reactions (MCR) are based on the combination of more than two starting materials, and are characterized by high atom economy. Therefore, they represent a premium strategy compared to one-pot reactions. Most MCR are based on the formation of amide and ester bonds, do not generally involve the generation of more than two carbon-carbon bonds, and are triggered by nucleophilic attack to an iminium ion. Non-iminium ion based MCR have not yet received systematic attention, despite their relevance in polyphenolic chemistry. To fill this gap, we have started a methodology study aimed at the generation, in a MCR-fashion, of aryl-heteroarylmethanes, an important class of natural products.
Our interest for this class of compounds was fostered by the remarkable bioactivity of the prenylated phloroglucinyl(pyronyl)methane arzanol (**1**) the major anti-inflammatory, antibiotic, and anti-oxidant principle of everlasting (*Helichrysum italicum*).[1] With the ultimate aim of developing a total synthesis of **1** and related heterodimeric pyrones, we have embarked in a systematic study on the synthesis of *gem*-(β-dicarbonyl)arylmethanes, evaluating the possibility of obtaining this type of compound in a multicomponent fashion by combination of a carbonyl derivative with equimolar amounts of a β-dicarbonyl and an electron-rich aromatic derivative.[2] We will present our methodological studies in the area and their application to the total synthesis of arzanol and to the generation of analogues.



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ORG-PO-131 Photocontrol of the direction of Threading/Dethreading in Pseudorotaxanes

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The design, synthesis and operation of supramolecular systems that exhibit controllable motions of their components is a topic of great interest in nanoscience and constitute a fundamental premise for the construction of molecular machines and motors. Rotaxanes are a class of supramolecular systems in which a ring encloses another rod-like component having bulky end groups too large to let the ring pass through. Pseudorotaxanes share the same supramolecular arrangement but have less bulky end groups that permit fast slippage and extrusion of the ring component[1]. In previous work we have shown how to control the rate of threading/dethreading motions (i.e. rotaxane-likeness) of a pseudorotaxane system (*E,E*-**1**$H^+ \cdot PF_6$) exploiting the photoisomerization of its azobenzene end groups[2]. In this work we present a more elaborate system that allows the control of the direction of threading/dethreading motions. The system is composed of a benzylamine axle terminated with two different end groups: an azobenzene unit at one end and a cyclopentane at the other (*E*-**2**$H^+ \cdot PF_6$). The axle is able to rapidly thread in solution through a dibenzo24crown8 ether (**DB24C8**) wheel from the azobenzene end to yeld a (2)pseudorotaxane[3]. Irradiation of *E*-**2**$H^+ \cdot PF_6$ with 457nm light induces quantitative photoisomerization to the *Z* stereoisomer forcing the system to dethread, under the influence of an appropriate input, from the cyclopentane end. The detailed kinetic analysis carried out show that the photoisomerization of the azobenzene end group of **2**$H^+ \cdot PF_6$ allow the control of the direction of threading and dethreading. The ability to control the direction of threading/dethreading is an essential step toward the ambitious goal of extracting useful work from the molecular motions of this kind of supramolecular systems.

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ORG-PO-132 New Benzothiadiazole- Containing Polymers as Donor in Bulk Heterojunction Solar Cells

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The scientific interest devoted to poly(arylene-vinylene)s (PAV) is currently looking forward to their use in solar cells [1]. The use of vinylene-linked donor and acceptor units could in fact bring about advantages connected with the extension of the conjugation length with respect to the corresponding poly(arylene)s. Aiming at exploiting the benzothiadiazole (BTZ) building block in PAV donor-acceptor architectures, we have carried out the Suzuki-Heck copolymerization, that allows access to several PAV architectures by a palladium catalysed copolymerization between aryl dibromides and potassium vinyl-trifluoroborate.[2] The reaction was applied to the preparation of novel random PAVs embodying BTZ in different amounts with respect to 9,9-bis(2-ethylhexyl)fluorene or 1,4-bis(2-ethylhexyloxy)benzene.

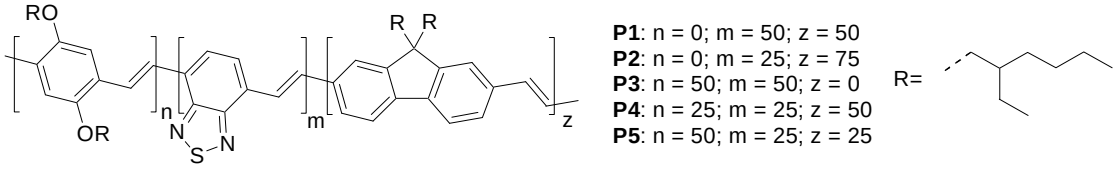

Figure 1.

The optical, electrochemical, and thermal properties of the polymers **P1-5** will be discussed as well as their photovoltaic properties that were investigated in BHJ devices with configuration: ITO/PEDOT-PSS/**P1-5**:PCBM/Al. The terpolymer **P5** resulted the most efficient (PCE = 0.4%, V_{oc} = 0.76 V) and its performances could be justified in terms of the good film forming properties of the polymer/PCBM blend, as indicated by AFM investigations. These results allowed us to conceive a modification of the above mentioned polymeric architecture obtained extending either the benzothiadiazole (**P6**) or the fluorene (**P7**) conjugation with thienyl groups, obtaining an improved PCE for **P6** (0.59%, V_{oc}=0.67V).

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ORG-PO-133 $NiSiO_2$ catalyst immobilisation on glass microreactor for Kumada Corriu continuous flow reaction

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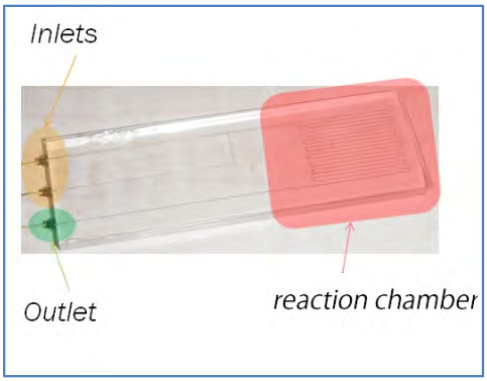
I

n the last decade new generation of chemists are exploiting continuous-flow microreactor as innovative tool for chemical synthesis. This technology appears really promising in the field of catalytic reactions. With smaller volume of solvents, they are less wasteful[1-3]. Moreover reactions can be carried out significantly faster than those in batch, with increases both in yield and selectivity.

In this work we describe a new method for the deposition of Ni-SiO_2 catalyst in a multichannel micro reactor and demonstrate its performances for the production of biaryl compounds.



Silica supported nickel catalyst (Ni/SiO_2) is prepared by sol-gel technique and immobilized inside a glass microreactor. Tetraethoxysilane (TEOS) and nickel nitrate hexahydrate ($Ni(NO_3)_2 \cdot 6H_2O$) are used as precursors. A mesoporous silica matrix with a high specific surface area (387 m^2/g) and average pore size in the range of 11 nm is obtained.

Its catalytic activity is demonstrated in a room temperature cross-coupling Kumada Corriu reaction. The obtained yields and reaction times of biaryl compound, compared with those of traditional batch reaction processes, confirme once again the advantages of on-chip organic synthesis.

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ORG-PO-134 Decarboxylative Cassar-Sonogashira Coupling Reactions. Synthesis of a key intermediate of Erlotinib

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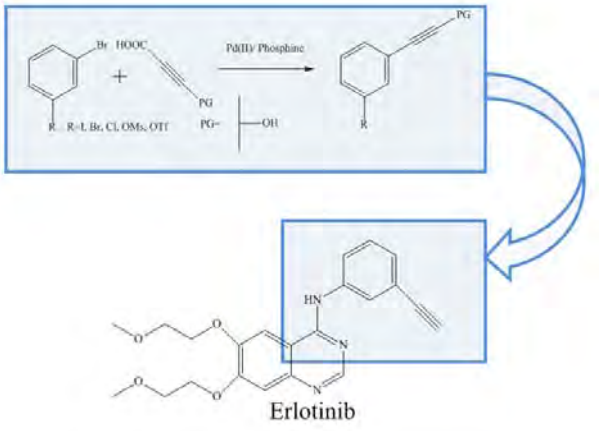
In recent years, the development of decarboxylative coupling reactions of propiolic acid derivatives on aryl halides and pseudohalides [1] emerged as a convenient approach to the synthesis of acetylenic compounds with respect to the conventional Cassar-Sonogashira coupling reaction of terminal alkynes. In the last years, several optimized protocols for decarboxylative couplings of alkynyl carboxylic acids with aryl and benzyl halides with low catalyst loading [2] and Pd-free decarboxylative cross-couplings catalyzed by copper [3] were reported. The coupling reaction of propiolic acid derivatives usually gives disubstituted symmetrical and unsymmetrical acetylenes [4], while the preparation of terminal alkynes by using this approach, at the best of our knowledge, has not been reported.



Herein, we present a protocol for the preparation of terminal alkynes from propiolic acid which was applied to the synthesis of the active pharmaceutical ingredient Erlotinib [5].

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[5] The process is object of two prioritary italian patent applications MI2010A001878, MI2011A000464 and related US and EP applications.

ORG-PO-135 Synthesis and Self-Assembly of Oligo(p-phenylenevinylene) Peptide Conjugates in Water

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Self-assembly (SA) of functionalized oligo(*p*-phenylenevinylene)s (**OPV**) gives organogels with interesting photophysical properties and potential applications in light-emitting diodes, light-harvesting systems or thermal imaging [1]. Organized, robust molecular structures are difficult to obtain by π-π stacking alone, therefore, a variety of promoters able to establish additional noncovalent interactions, such as directional hydrogen bonds, have recently received increasing attention. Among them, we have envisaged the use of peptide amphiphiles, made of a π-conjugated unit and carefully selected peptide sequences. These structures have a strong tendency to form well-defined secondary structures and to self-assemble in water [2].
Here we present the synthesis of a new OPV ω-amino acid that has been incorporated into two β-sheet-forming sequences through solid-phase protocols. The resulting peptide hybrids are soluble in water and reversibly self-assemble to a stable, fluorescent hydrogel upon pH changes [3].

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ORG-PO-136 2,3-dihydro-1H-indan-1-one: useful building blocks for the synthesis of novel molecular photo-switches.

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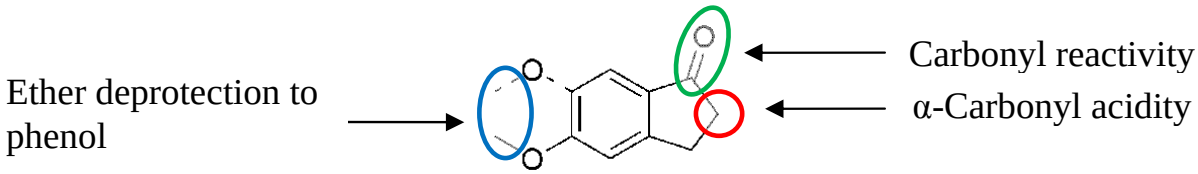
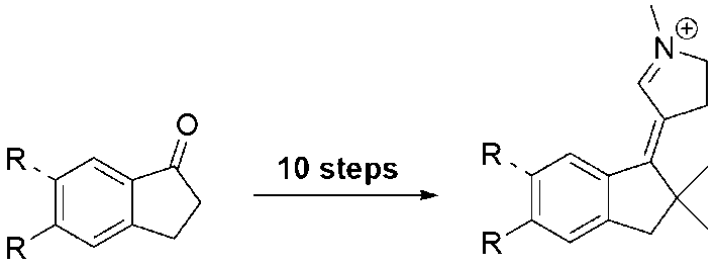
Following our interest in the synthesis of novel biomimetic photo-switches[1] we explored the reactivity and the possibility of functionalization of an important class of molecules, indan-1-ones. These molecules have three functionalizable sites due to the presence of a carbonyl group and one or two methoxy groups in position 5 and 6 that can be deprotected to phenol and alkylated.



Starting from this molecular scaffold we got a library of functionalized indan-1-ones that have been employed in the synthesis[2] of some new photo-isomerizable molecular switches.



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Chimica dei Sistemi Biologici

CSB-KN-01 Il trasporto intracellulare target-selettivo

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Negli ultimi anni numerosi gruppi di ricerca hanno rivolto il loro interesse agli studi dei meccanismi di trasporto di farmaci per il trattamento di gravi patologie: è noto che la membrana plasmatica è caratterizzata da una elevata selettività che la rende impermeabile alle molecole che non utilizzano meccanismi di riconoscimento specifici e/o meccanismi passivi. Per migliorare il delivery intracellulare, sono apparsi in letteratura numerosi studi riguardanti l'identificazione di sistemi innovativi di natura peptidica ma, in particolare, è l'utilizzo di nano particelle che ha attratto molta attenzione per le loro potenziali applicazioni nel trasporto di principi attivi. Verranno presentati studi sulla progettazione, sintesi e caratterizzazione di una nuova classe di molecole capaci di target specifico su cellule tumorali e/o di attraversare in maniera efficace le membrane cellulari; in particolare l'attenzione è stata rivolta ad aggregati sopra-molecolari di natura peptidica e liposomiale utilizzabili come vettori per il rilascio intracellulare di molecole bioattive volte al miglioramento della tecniche terapeutiche e diagnostiche attualmente in uso.

CSB-KN-02 Design and Synthesis of DC-SIGN antagonists

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DC-SIGN (Dendritic Cell-Specific Intercellular adhesion molecule 3-Grabbing Nonintegrin), a specific C-type lectin recognizing pathogen-cell surface glycoproteins, is probably the first trans-membrane receptor on immature dendritic cells (DC) which encounters invading pathogens and binds a number of diverse pathogen-associated molecular patterns. Normally, this binding event triggers internalization of the DC-SIGN-pathogen complex followed by lysosomal degradation of the pathogen and conjugation of the resulting fragments with MHC-II to initiate an adaptive immune response from T cells. Some pathogens, however, have been reported to take advantage of this mechanism, as they appear to deter DC maturation through DC-SIGN-mediated signalling and inhibit antigen presentation to T cells. In particular, van Kooyk's group has shown that HIV-1 enters DC via DC-SIGN avoiding lytic degradation [1]. By doing so, HIV-1 not only escapes the host immune system, but also is presented directly to T cells, which enables fully disseminated HIV-1 infection. Inhibition of pathogen interaction using DC-SIGN specific antagonists is considered as a plausible concept for the development of novel anti-infective agents. Several groups have recently demonstrated that inhibition of DC-SIGN, either by designed glycoconjugates or by antibodies, prevents pathogen attachment to DC and inhibits the infection of other immune cells at its earliest steps [2,3].
Our group has been active in this area and, in collaboration with the European network Carmusys [4], has developed two groups of mannose-based and fucose-based glycomimetic ligands that inhibit DC-SIGN mediated HIV infection in cellular and tissue models.
The presentation will deal with the design and synthesis of these molecules, as well as on the structural studies detailing their interaction with the target lectin.

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CSB-KN-03 Target therapy in anticancer treatment: the HDACi journey.

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In anticancer research, during the last 15 years, more and more efforts have been devoted to the identification and development of NCE targeting specific pathways. The development challenge is the identification of medicines with less toxicity, being specific, and to be used in combination with really cytotoxic products. The biological targets, however, were proteins/enzymes involved in several basic function of the cell like damage repair (i.e. HSP90 or PARP). metabolism (i.e. mTOR, PI3K or AKT) or replication (HGAC).
Among these specific targets, HDACi was until a few years ago one of the main area of interest. Two molecules have been approved by the FDA, Zolinza (Vorinostat by Merck) in 2006 and Istodax (Romidepsin by Glouchester Pharmaceutical in 2009). Both products have been approved in the same niche area, single agents against Cutaneous T-cell lymphoma. The scientific community is still waiting the first approved combination of these drugs.
The research activities on HDACi started when the biological function of HDAC was not completely clear as well as the mode of action of these enzymes. There is still ongoing a debate on the in vitro screening tests and on the pan (3 class of Zn(II), 11 enzymes) HDAC inhibitors versus the selective ones. We are going to discuss Sigma-tau journey in the fields of zinc(II) HDAC inhibitors [1a-h].

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CSB-KN-04 Identification the molecular determinants of amyloid fibril formation *in vivo*

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In 2003 it was reported for the first time that the effect of mutations on the conversion of fully or partially unfolded proteins into amyloid fibrils can be rationalised, and even predicted, on the basis of a number of physico-chemical factors including hydrophobicity, propensity to form β-sheet structure and charge. Since then, ca. 15 algorithms have been published, with predictions largely consistent with experimental data.
The next challenge was to test the validity of these principles in living algorithms and identify the additional physico-chemical and biological factors that determine the aggregation behaviour of proteins *in vivo*. Following the increasing evidence that inclusion bodies accumulating in *E. coli* consist of amyloid-like fibrils, we expressed in *E. coli* cells a C-terminally truncated variant of the N-terminal domain of the HypF protein from E. coli (HypF-N). Expression was carried out at low levels, in a controlled manner and resulted in a folding-incompetent form, due to the lack of the C-terminal residues (as desired). Western blotting assays allowed the measurement of the protein fractions remained soluble and aggregating after expression. The analysis was repeated on 20 mutants of the same C-terminally truncated form of HypF-N, each carrying a single amino acid substitution. This allowed the effect of the mutation on the *in vivo* aggregation to be measured.
The experimentally obtained data were compared with theoretical predictions using algorithms previously tested and validated using only *in vitro* data. The analysis showed a good correlation between the experimentally measured aggregation propensities of the mutants *in vivo* and of the corresponding values calculated from the algorithms. The analysis was thus extended to variants of the amyloid β peptide (Aβ) previously expressed in *E. coli* as peptides fused to the green fluorescent protein (GFP) to measure quantitatively their tendency to aggregate after expression in *E. coli*. The experimental data of aggregation propensity in vivo were again consistent with all tested algorithms, raising the possibility that algorithms previously tuned from *in vitro* data are also largely applicable for aggregation data *in vivo*.

CSB-OR-01 Dopamine receptor agonists and Levodopa modulate protein levels in human T lymphocytes.

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Dopamine receptor agonists and Levodopa are used to treat symptoms in patients affected by Parkinson's Disease (PD) to counteract dopamine (DA) loss at the striatum level [1]. (T)-Lymphocytes express some features of the dopaminergic system (they express tyrosine hydroxylase, dopamine receptors and transporters, and store catecholamines into vesicles [2]), so their functions or activation can be regulated by dopamine. Several effects of dopamine on immune cells have been described [3,4], but none of these studies focus on proteome modifications of human T-cells.

In the attempt to establish if T-cells undergo modifications at the protein level after administration of DA agonists or Levodopa in human subjects, we enrolled 9 PD patients under DA agonist therapy and 5 PD patients DA agonist free. We compared two-dimensional electrophoresis maps of total proteins from T-cells and we identified 7 proteins whose level was significantly different in the two groups considered. Eleven among these patients were treated with Levodopa; indeed, we found levels of 4 spots correlating with the dose of Levodopa assumed daily by patients.

These findings demonstrate that DA stimulation (either by Levodopa or DA agonists) has important effects on T-cell proteome in patients under long term treatment. Therefore, therapies acting on the dopaminergic system have additional effects on the immune system that cannot be neglected. In this view, studies that assert alterations in lymphocytes of PD patients have to take into account the therapy administered to patients.

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CSB-OR-02 RGD-based peptides targeting $\alpha_{IIb}\beta_3$ and $\alpha_v\beta_3$ integrin receptors: an NMR point of view

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Integrins are transmembrane receptors that link the cytoskeleton to the extracellular matrix (ECM),[1] mediating cell–cell and cell–matrix adhesion and providing the traction for cell mobility and invasion.[1] Integrin $\alpha_v\beta_3$ and $\alpha_v\beta_5$ expression is correlated with disease progression in various tumor types (melanoma, prostate, glioblastoma) while the platelet integrin $\alpha_{IIb}\beta_3$ plays a key role in adhesion of platelet to protein-coated surfaces and in platelet/platelet aggregation (thrombus formation). The two integrins show a similar drug-receptor site and bind to the Arg-Gly-Asp (RGD) motif of ligands as primary recognition sequence. The conformation of the RGD sequence is critical for the specificity of this recognition. Since the RGD motif occurs in many extracellular matrix ligands, the recognition specificity is expected to be modified by other residues and to depend on the conformation of the RGD sequence.
Detailed comparison to different ligands of the same integrin binding site could shed light on the essential elements that determine their interaction, specificity and affinity, and allow the rational design of new antagonists.
Our work focuses on the application of NMR techniques[2] (STD and tr-NOESY) for understanding at atomic level the diverse mechanisms of recognition between peptidomimetics and the binding sites of integrins $\alpha_v\beta_3$ and $\alpha_{IIb}\beta_3$. The data allow us to identify (by STD) the portions of the ligands in closest contact with the protein and to define (by trNOESY) the preferred conformation of the bound ligands.
The properties of integrins embedded into cell membranes may differ from those of purified receptors, therefore, we show that the interaction between a small library of RGD-peptidomimetics[3] and membrane-bound proteins can be observed by NMR directly in a H_2O-buffer-suspension of living cells, without the need of isolating the protein receptor. We performed the NMR experiments on a suspension of ECV304, bladder cancer cells in which the integrin $\alpha_v\beta_3$ is highly expressed, or in the presence of whole human platelets (where integrin $_{IIb}$ $_3$ is the most abundant platelet cell surface glycoprotein).
The NMR data are interpreted with the aid of docking calculations affording an improved understanding of integrin-ligand interactions.

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CSB-OR-03 Molecular and supramolecular structure of elastin model peptides containing (2S,4R)-4- hydroxy-proline

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The hydroxylation of some proline residues by prolyl-4-hydroxylase to form (2S,4R)-4-hydroxyproline (Hyp) (Figure 1) is the most common post-translational modification in animals. In particular, it is fundamental in the biosynthesis of collagen, where it plays a critical role in stabilizing the triple helix structure, conferring the correct structure and mechanical strength to collagen fibers. Conversely, in elastin where up to 33 % of proline are Hyp, the possible role for this modification has not been identified.

Recent studies obtained by enzymatic digestion were able to identify the position of proline hydroxylation in skin elastin [1]. In order to investigate the possible role of Hyp in the molecular and supramolecular structure of elastin, we chemically synthesized some elastin–related model peptides containing Hyp. We analyzed them by Circular dichroism (CD), Nuclear Magnetic Resonance (NMR) spectroscopy in order to found out the possible role of Hyp in defining the conformational ensemble populated by elastin peptides and compared them to the related proline-containing peptides. Furthermore, supramolecular studies highlighting the ultrastructure of the self-assembled aggregates, carried out by AFM and TEM microscopies, were presented.

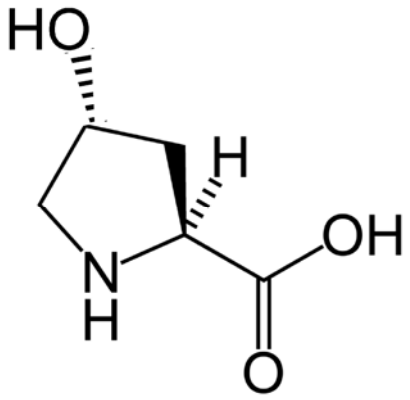

Figure 1: (2S,4R)-4-hydroxyproline

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CSB-OR-04 The Fully-Extended, Peptide Conformation: in Search of Stabilizing Features

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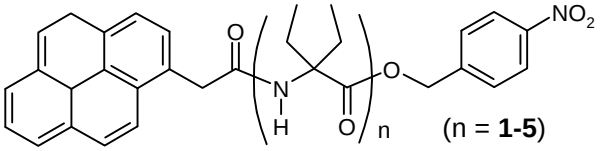
The highly crystalline nature of the peptides rich in C -tetrasubstituted residues was exploited to characterize in detail the fully-extended (2.0_5-helix) by X-ray diffraction analyses. Multiple, consecutive C_5 conformations were observed in homo-peptides made up of residues with both side chains longer than a methyl. This is for instance the case of $C^{\alpha,\alpha}$-diethylglycine (Deg), the residue used in this study. Interestingly, the axial translation per residue in the 2.0_5-helix is about 3.70 Å, the longest possible for a single amino acid, thus making this conformation extremely attractive for its use as a spacer or a bridge [1]. In this communication we describe our recent efforts aimed at detecting conditions and features able to stabilize the 2.0_5-helix. We synthesized and characterized in solution and in the crystal state a variety of Deg homo-peptides. Our findings can be summarized as follows: (i) either an ester or a tertiary amide (both lacking the N-H group) at the peptide C-terminus is compatible with the 2.0_5-helix; (ii) a primary or a secondary amide at the C-terminus promotes 3_{10}-helix formation; (iii) the nature of the solvent is crucial for biasing the peptide secondary structure towards the 2.0_5- or the 3_{10}-helix. This latter conclusion, in particular, was obtained through time-resolved fluorescence experiments on Deg homo-peptides bearing a pyrenylacetyl fluorophore at the N-terminus and a *para*-nitrobenzyloxy quencher at the C-terminus.



Our analysis shows that the peptides are predominantly fully extended in $CHCl_3$, but folded in MeCN or MeOH.

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CSB-OR-05 Diiron-oxo protein models: the role of turns in stabilizing α-helical harpins

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Turns represent portions of protein chains, where the structure doubles back on itself in a hairpin-like conformation. Important for molecular recognition, turns significantly help to stabilize the fold of proteins. Numerous studies have been carried out on the role of turns in four-helix bundle protein structures, showing that amino acid sequences of inter-helical turns influence the stability and even the fold of helical proteins [1].

Previously, we developed minimal models of diiron-oxo proteins, named DFs, using a *de novo design* strategy. The first model, DF1, idealizes the approximate *C*2 symmetry of the parent natural proteins. It is made up of two helix-loop-helix (α2) motifs, able to assembly into an antiparallel four-helix bundle, with the loops on opposite sides of the bundle. DF1 contains a Glu4His2 liganding environment for the diiron center, housed within the center of the bundle [2]. The structural analysis carried out on DF1 and several variants revealed that these minimal models are rigid scaffolds able to tolerate significant changes in the amino acid sequence, without affecting their overall fold. In fact, all the DFs share the same four-helix bundle structure and active site ligand environment as in natural diiron-oxo proteins [3]. Therefore, they could provide an excellent framework for understanding the factors that stabilize inter-helical turns. In this respect, we have designed two new DF variants, DF3 [4] and L9G/L13G-DF1 that differ in the loop sequence connecting the two helices.

The structural and thermodynamic characterization of these models will be presented. The analysis of all the data shows that the turn conformation is dictated by the structural context within the protein, whose overall stability is, in concert, strictly related to the turn conformation.

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CSB-OR-06 Structural and functional aspects of a metallopeptidase from "Mycobacterium tuberculosis" involved in pathological processes

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Zinc metallopeptidases of bacterial pathogens are widely distributed virulence factors and represent promising pharmacological targets. The impact of zinc metallopeptidases on the pathogenesis of *Mycobacterium tuberculosis* (Mtb) has been addressed only recently, identifying Zmp1 as a virulence factor of *Mycobacterium tuberculosis*.

We have cloned, expressed and purified Zmp1, a zinc metallopeptidase belonging to the neprilysin (M13) family. Substrate specificity of Zmp1 was investigated by peptide array method. Several sequences derived from biologically relevant proteins were identified as possible substrates, including the neuropeptides bradykinin, neurotensin and neuropeptide FF. Further, subsequences of other small bioactive peptides were found among most frequently cleaved sites, e.g. insulin and apelin. We determined the specific cleavage site within neuropeptides by mass spectrometry techniques. Hydrophobic amino acids, mainly phenylalanine and isoleucine, were overrepresented at position P1'.

X-ray structure of Zmp1 has been solved, unraveling an oval shape with dimensions of about 78 Å for the major axis and 60 Å for the minor one. The overall structure is composed by two mainly α-helical lobes (red and blue); the enzyme catalytic site is located between the two lobes and is accessible via two oppositely positioned small opening on the protein surface.

Interestingly, this enzyme shows an optimum activity toward a synthetic substrate at moderately acidic pH values (i.e. 6.3), which corresponds to those reported for Mtb phagosome where this enzyme should exert its pathological activity. In addition, the enzymatic mechanism of Zmp1 toward these neuropeptides has been characterized, displaying some differences with respect to the synthetic substrate and indicating that the enzyme adapts its enzymatic action to different substrates.

CSB-OR-07 γ sulphate PNA (S-PNA): a new PNA analogue with strong antigéne activity

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The research of stable and biologically active DNA mimics has promoted studies on Peptide Nucleic Acids (PNAs), nucleic acid analogues showing high stability to enzyme degradation and strong affinity and specificity of binding toward DNA and RNA [1]. Several PNA analogues have been obtained so far in the attempt to overcome solubility, uptake and aggregation issues [2,3]. Studies on PNA oligomers demonstrated that preorganization is a requisite to increase the affinity of binding toward complementary nucleic acids while the presence of positive charges on the backbone increases their cellular uptake. Encouraged by these results and with the aim to develop a new PNA analogue more DNA-like in terms of polarity, charge and solubility we undertook studies on PNAs having a sulphate moiety in the gamma position of the backbone. Studies on sulphate PNA add a new brick to our knowledge on the effect of charge on the secondary structure, stability of the hybrids and potential of the modified oligomer to be biologically active. The sulphate group is, in fact, very similar to the phosphate of DNA, in geometry, steric hindrance, polarity. In this work, we investigated sulphate PNAs. We set up protocols for the synthesis of sulphate PNA monomers and oligomers. The conformational preferences of the monomers and the oligomers were explored, together with the ability and selectivity in the DNA binding. We focused on a homopyrimidine oligomer designed to interfere with the transcription of the proto-oncogene ErbB2, a cell membrane surface-bound receptor tyrosine kinase normally involved in the signal transduction pathways leading to cell growth and differentiation. Interestingly, the sulphate PNAs were found to be potent antigéne molecules, inhibiting the transcription of the target gene.

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CSB-OR-08 Catalytic specificity of heme-protein models

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Mimicking enzymes with alternative molecules represents an important objective in synthetic biology, aimed to obtain new chemical entities for specific applications[1].New biocatalysts, designed to mimic the main structural and functional features of enzymes, may find applications in different fields, such as biocatalysis, biosensor technology, decontamination and detoxification of industrial wastes, drug and food processing. Moreover, they are basic in elucidating structure-function relationship of enzymes. The design of metalloenzymes has been recognized as being an intricate challengesince both the requirements of protein structure and metal ion coordination should be fulfilled[2]. Moreover, metalloenzymes with asymmetrical coordination centre have rarely been mimicked.

Peptide-based models seem valuable candidates for mimicking metalloenzymes [3]. Their structures are smaller than native proteins, making them easier to be used for practical applications. However, their size is such to allow sufficient chemical diversity for the construction of functional sites.In this perspective, aclass of heme-peptide conjugates, named Mimochromes, have been developed in our laboratory to investigate the effects of peptide chain composition and folding in modulating the properties of the metal ion into the porphyrin ring [4]. The main features of these molecules are the covalent structure and the sandwich motif, with two helical peptides surroundings the heme on both faces. Here we presentan evolution, through design and redesign, of this class of molecules, Fe(III)-Mimochrome VI [5].This molecule embodies some of the key elements for peroxidase-like activity: it is stable, water soluble and it exhibits mono-hystidyl-coordination to the heme. Studies on its peroxidase-like activity and specificity, using various reducing substrates, will be presented.

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CSB-OR-09 New neutral liposomal delivery systems of genetic material

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Complexes of DNA with lipid vesicles or synthetic polymers offer an attractive alternative to viral vectors in genetic material delivery. As a matter of fact it is today current opinion among scientists that synthetic carriers must be considered as the future of a safe and efficient Human Gene Therapy. With the aim of developing new lipid-based DNA carriers, in recent years we have studied structure and phase behavior of ternary water suspensions of self assembled complexes composed by zwitterionic lipids, DNA and metal divalent ions[1-3]. Divalent metal cations promote the DNA condensation with liposomes, acting as bridges between the phosphate groups of both DNA and polar heads of lipids. The ternary complexes obtained show structures similar to the ones of the lipoplexes, with the important advantage of the absence of toxicity, being formulated with phospholipids that naturally occur in the cell membrane. In order to improve the ability of liposomes to complex DNA, our strategy has been to develop liposomal systems containing neutral lipids functionalized with complexing agents able to coordinate bivalent metals. The presence of this moiety allows to obtain more stable complexes of plasmidic DNA and ensures a higher control of the surface charge of liposomes. In this perspective we have prepared and studied mixtures of neutral commercial lipids with some newly synthesized amphiphilic lipids, which have been characterized by means of syncrothron x–ray diffraction, dynamic light-scattering and zeta potential.

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CSB-OR-10 3D-Structure Activity Relationships of new simple antimalarial endoperoxides.

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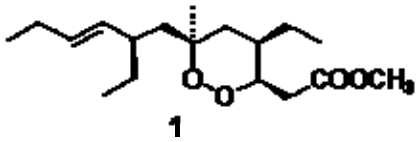
Although the association of chloroquine derivatives with analogues of artemisinin is giving some good results, the therapeutic choices are still too limited for the large and poor malaria market. Indeed, artemisinin therapeutic value is limited by the modest oral availability and high cost of synthesis. Therefore, there is an urgent need of new and economically affordable antimalarial drugs with high efficacy against resistant strains and broad stage mode of action. In this context, it is our aim to contribute to the development of novel antimalarial agents possessing the endoperoxide pharmacophore. The lack of a definitive proof about these drugs modus operandi limits the design of new synthetic derivatives. In the course of our ongoing search for antimalarial lead compounds from marine sources, we have reported that plakortin (**1**), simple endoperoxide containing polyketides, possessed a significant in vitro antimalarial activity particularly on CQ resistant Pf strains [1]. On the basis of a multidisciplinary approach including chemical and computational studies as well as in vitro pharmacological assays, we refined our knowledge on the putative antimalarial action mechanism of molecules belonging to the plakortin family [2]. The hypothesized mechanism of action accounts for the structure-activity relationships of other endoperoxyketal polyketides [3] and newly synthesized derivatives [4]. Thus, our study not only allowed the identification of the structural requirements necessary for antimalarial activity but also provided a tool for subsequent structural modifications.



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CSB-OR-11 Insulin-degrading-enzyme is an heat shock protein and affects neuroblastoma proliferation.

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Insulin-degrading-enzyme (IDE) is an highly conserved and ubiquitous zinc metalloprotease involved in the degradation of substrates such as insulin and β-amyloid (Aβ)[1-3]. In the last decade, the identification of novel substrates (*i.e.* ubiquitin) and its involvement in several biological functions, as steroid signaling and Varicella Zoster virus infection, has cast light that IDE is a multifunctional protein with relevant roles in several physiopathological processes [4-6].

In this work we demonstrate that IDE level is upregulated after cell exposure to different stress conditions, envisaging an Heat Shock Protein-like behavior. We also show that IDE is highly expressed *in vivo* in tumor biopsy of the Central Nervous System (SNC). Additionally, IDE-silencing specifically inhibits neuroblastoma proliferation, triggering cell death. Therefore, we propose a novel role as heat shock protein for IDE, involved in the regulation of tumorigenesis in SNC.

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CSB-OR-12 Advanced Drug Screening platforms by Inkjet printing

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In this work, we show a low-cost, speed, microarray-based drug screening platform that employs inkjet printing drug dispensing on an enzymatic-rich surface.

Mixtures of a model substrate (D-glucose)/inhibitor (D-glucal) couple have been inkjet printed on a target enzymatic monolayer (glucose oxidase) linked to a functionalized silicon oxide solid surface [1].

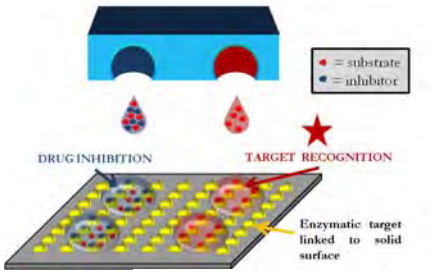

Figure 1.

It has been possible to fabricate microarrays with quality factors as high as those of conventional pin printing spotting. By a simple horseradish-based colorimetric enzymatic assay, the detection of biological activity at the single spot has been proved. The figure shows a scheme of the platform: molecular inks of the enzymatic substrate or a substrate/inhibitor mixture are dispensed on the enzymatic-rich surface with detection at the single spots. Optical intensity measurements showed a competitive inhibition mechanism at the solid-liquid interface, along with overcompeting effects at lower inhibitor concentrations [2]. This methodology is extended to CYP450 enzymes like CYP3A4, one of the main targets for the phase I drug metabolism. In this respect, sol-gel enzymatic encapsulation strategies inside a polymer matrix prepared by MTMOS (methyltrimethoxysilane) precursors [3] or alginate are envisioned. The evaluation of the biological activity is realized via a fluorescent-based assay. In conclusion, we show how inkjet printing methodologies may investigate interesting physico-chemical activities of functional biomolecules at a solid surfaces including their interaction and reaction behavior. Moreover, if coupled with a simple and generalized detection method they may satisfy speed, low-cost, miniaturized and high-throughput screening needs by dispensing entire chemical libraries on solid supported biological targets.

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CSB-OR-13 Amyloidogenesis of EX30-derived human tropoelastin polypeptide sequences

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Amyloid fibers are associated to a large number of diseases such as, for example, Alzheimer's dementia (AD). Many evidences link AD to vascular diseases, while only few data connect amyloids, atherosclerosis and aging via deposits in the aortic intima. Recent results demonstrate that the C-terminal region of human tropoelastin sequence is able to give rise to amyloid-like fibers in vitro, when isolated from the entire protein [1]. Furthermore, it has been demonstrated that the process is favored by sodium taurocholate presence, mimicking the presence of cholesterol. On this basis, it is tempting to speculate that in vascular diseases, under high concentration of lipids, some N- and C-terminal sequences, released from elastin by enhanced proteolytic activity, could aggregate because of mutated microenvironment to form amyloids (whose formation is also favored by lipids) that constitutes the "elastotic material" described in several reports. In order to demonstrate this hypothesis, we synthetized and studied four polypeptide sequences, resulted from the cleavage of human skin elastin by enzymes such as MMP-12 and pepsin [2], all of them self-contained in human tropoelastin gene exon30 coded sequence (EX30D), in order to assess their potential amyloidogenic behavior. We demonstrated that the longest EX30D polypeptide, among those synthetized, is amyloidogenic.

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CSB-OR-14 Corroles: interaction with Polynucleotides.

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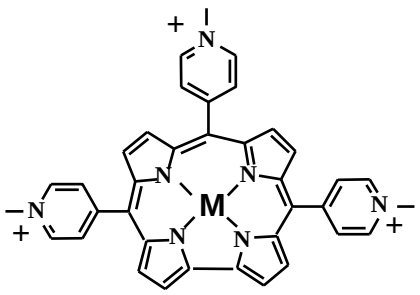
Synthetic porphyrins have been a useful tool to fully understand the complex reactions performed by these macrocycles in biological systems.[1] Furthermore, the attempt to mimic the peculiar chemistry operated by natural porphyrins opened the way to their possible exploitation in a wide range of practical applications. [2]
However, a similar possibility is rarely found with regards to porphyrin analogues, macrocycles having some modification in the molecular skeleton with respect to that of the parent porphyrin.[2] Distinguishable from the core structure of porphyrin by the absence of one of the four meso-positions, corroles contain three "pyrrole-type" hydrogens and a direct pyrrole–pyrrole link.



M = 3H, Ge

The synthesis of pyridyl-substituted corrole has been rarely reported [3]. There are only a few reports about a corrole with positively charged substituents. [4] The corrole with three remote positive charges displayed significantly better efficacy in inhibiting tumour progression and metastasis in animal models than analogous porphyrins. CD, UV-visible absorption and Fluorescence studies with tricationic water-soluble corrole, (TMPC), show that this species can serve as probes to discriminate between single and double strand conformations of polynucleotides poly A and poly C. Furthermore the Germanium (GeTMPC) derivate is able to discriminate between single strand of polyadenilic acid and polycytosine acid, forming extended assemblies in presence of polyA single strand.

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CSB-OR-15 G-quadruplexes and their interactions: a physico-chemical approach

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Guanosine-rich nucleic acid sequences can adopt unusual DNA secondary structures with biological significance, the G-quadruplexes [1]. These structures are four-stranded helical complexes, composed of stacks of G-tetrads, cyclic arrays of four guanine bases which are connected by Hoogsteen hydrogen bonding. The formation of G-quadruplexes requires the presence of metal cations that selectively bind to guanine O6 carbonyl groups in the central cavity generated by the stacked layers of G-tetrads.
Sequences with propensity to form G-quadruplexes have been identified in many regions of human genome. Several pieces of experimental evidence have proven that the 3′ single-stranded overhang of telomeric DNA in eukaryotic cells may adopt this peculiar structure [2]. It has been shown that the formation of G-quadruplexes by telomeric DNA inhibits telomerase activity, with implications in apoptosis and cancer. In addition, some small molecules able to bind G-quadruplex structures alter telomere functions, leading to marked inhibition of tumour cells growth [3]. Recent studies have shown the high density of GC-rich sequences in the promoter region of oncogenes that can transiently unwind and form single-stranded tracts, eventually folding into G-quadruplexes, thus supporting the biological importance of these structures in the control of gene expression [4].
In view of biomedical applications, the understanding of the energetic aspects concerning the structure and stability of G-quadruplexes has achieved new importance in the last years. Moreover, design and development of drugs that selectively bind to a G-quadruplex structure, can be greatly enhanced by detailed knowledge of the thermodynamics of binding to the target [5,6].
In this context, we investigated, with a physico-chemical approach, the G-quadruplex structures and their interaction with proteins and a variety of molecules with high pharmacological interest.

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CSB-OR-16 Site-specific protein double labeling by expressed protein ligation: applications to repeat proteins

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In the last years, the use of labeled proteins has expanded significantly in life sciences. Labeled proteins are nowadays indispensable tools for a wide spectrum of applications in biophysics and chemical biology. The ability to introduce into proteins new functionalities such as post-translational modifications, biophysical and biochemical probes provides a means by which to characterize and modulate protein function or to endow these macromolecules of new useful properties. So far, different protein engineering approaches, based on the use of both chemistry and/or molecular biology, have been developed. We describe a synthetic strategy, based on expressed protein ligation [1], to prepare proteins in high purity and homogeneity in which two different molecular probes are incorporated specifically at any desired position. Proteins are sequentially labeled in solution, with the advantage that large excess of probes are not required and the labeled fragments are not restricted to peptide synthesis length-limitation. This strategy was applied to selectively label a repeat protein, CTPR3 (*Consensus* TetratricoPeptide Repeat) [2], with a fluorophores pair in different positions along the protein sequence. The doubly labeled proteins were prepared at high purity and homogeneity as required for single molecule FRET studies. Remarkably, this approach can be adapted to the introduction of more than two molecular probes.

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CSB-OR-17 siRNAs bearing aromatic residues in the 3'-overhang region

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RNA interference (RNAi) is a biological process whereby small interfering RNA (siRNA) and microRNA (miRNA) silence gene expression in a sequence-specific manner [1]. These effectors regulate gene expression through the RNA-induced silencing complex (RISC). It has been suggested that RISC preferentially selects and incorporates one of two strands of the siRNA duplex depending on its thermodynamic features and that the off-target effects of siRNAs can be correlated to the T_m of the duplex [2]. The problem of unwanted incorporation of the passenger strand into RISC could be address altering the thermodynamic asymmetry of the duplex by using specific chemical modifications [3, 4]. Structural studies have revealed that the 3'-overhang region of the guide strand of siRNA is recognized by the PAZ domain and is accommodated into its hydrophobic binding pocket. We expected that aromatic-based modifications in 3'-overhang would enhance RISC selection of antisense strands of siRNA duplexes, reducing off-target effects induced by sense strands.
In this study, we report the synthesis of siRNAs bearing diphenylpropylamine, tyramine and tryptamine units at the 3'-end of sense and antisense strands. We found thermodynamic stability of the conjugates was increased by these modifications. Furthermore, but not surprisingly, the modified duplexes were found to retain RNA-like A-type conformation. We also assessed the nuclease resistance of the modified siRNAs and found it was similar to those of unmodified siRNAs. These results prompted us to investigate the silencing activity of the siRNAs possessing the aromatic moiety in the 3'-end by *in vitro* experiments in mammalian cells.

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CSB-OR-18 Characterization of copper(II) and zinc(II) complexes with the N-terminal domain of Nerve Growth Factor

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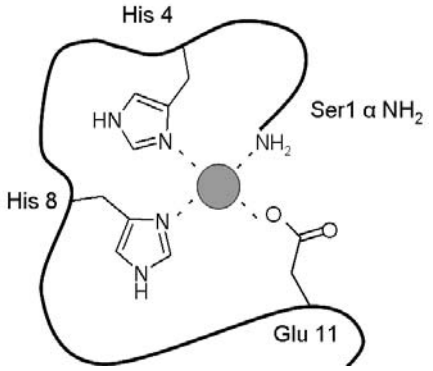
Nerve growth factor (NGF) is a protein involved in development and survival of specific neuronal populations [1]. In Alzheimer's Disease (AD), the lack of trophic support guaranteed by NGF has been observed in the same areas involved in learning and memory. Some d-block metal ions have been proposed to play a crucial role in AD and, intriguingly, NGF performs its activity in the same brain areas affected by metal dys-homeostasis in pathological conditions [2].
As N-terminal residues of NGF are crucial for the activity of this protein, the peptide fragment encompassing the sequence 1-14 of the human NGF, named NGF(1-14), was synthesized and its copper(II) and zinc(II) complexes characterized by means of potentiometric and spectroscopic (UV-vis, CD, NMR and EPR) techniques. The predominant Cu^{2+} complex species in the pH range 5.5-7.4 is the $[CuLH_{-1}]$, in which Cu^{2+} is bound to an amino, an amide and an imidazole nitrogen atom donors (NH_2, N^-, N_{Im}) in a highly distorted environment, due to the presence of an apical oxygen atom of the carboxylate and/or an imidazole nitrogen. Otherwise, Zn^{2+} is bound to two imidazole nitrogen atoms and to the Glu11 carboxylate group in acidic region, whereas Ser1 amino group is involved in the metal coordination above pH 6.5 (Figure 1). Beside to be the first anchoring site for Cu^{2+} and to be involved in Zn^{2+} coordination at physiological pH, the free amino group plays a key role which is stressed by biological essays. Indeed, a synergic proliferative effect has been observed after co-treatment with NGF(1-14) and Cu^{2+} or Zn^{2+} on SHSY5Y neuroblastoma cell line, but this effect was not observed after co-treatment with metals and the N-acetylated form of the peptide fragment, suggesting an important correlation between biological activity and coordination environment.



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CSB-OR-19 Stabilization of G-quadruplex DNA structures by specific ligands and study of their binding affinity and selectivity with mass spectroscopy

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G-quadruplexes are a family of nucleic acids secondary structures stabilized by G-tetrads, coplanar quartets of guanines held together by a cyclic arrangement of eight unconventional hydrogen bonds (Hoogsteen bonds).[1] DNA G-quadruplex can be formed by G-rich strands as the telomeric sequences. Telomeric single-strand DNA is the substrate of telomerase, an enzyme necessary for telomeric replication, which is over-expressed in most cancer cells and participates in tumors genesis. The formation and stabilation of a telomeric G-quadruplex blocks telomerase activity and offers an original strategy for new anti-cancer agents. In the last 25 years, several families of compounds have been identified which specifically bind to the telomeric quadruplex. These derivatives, called "G-quadruplex DNA ligands", are able to block telomeric replication in cancer cells and to cause replicative senescence and/or apoptosis after a few cell cycles. All these molecules are characterized by an aromatic core, which favours stacking interactions with the G-tetrads, and, in most cases, by basic side chains (positively charged under physiological conditions), which interact with the quadruplex loops and helix grooves.[1].

In our research group, a great interest is devoted to study the stabilization of telomeric G-quadruplex structures by small organic molecules, in particular perylene [2] and coronene [3] derivatives, aza-truxenes [4] and alkaloids related to natural compounds such as berberine [5] and taspine.

The affinity of these ligands at various concentrations towards different DNA structures has been studied by ESI-MS measurements [6,7]. This technique allows the transfer of non covalently bound complexes into the gas phase without the disruption of the complex itself. So, the determination of stoichiometry and modes and energies of interaction can be carried out performing mass spectra of samples containing both DNA and varying their ratio. We have found that these molecules are able to bind and stabilize G-quadruplex DNA oligomers.

The selectivity for these structures with respect to duplex DNA, a fundamental topic for the biological evaluation and the pharmacological application of these ligands as potential chemotherapeutic agents, has also been investigated by competition experiments in which there were both quadruplex and duplex DNA structures [7].

Significant biological data about *in vitro* and *in vivo* activity of these ligands will be presented. The correlation between these data and ESI-MS measurements will be also discussed.

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CSB-OR-20 Understanding secreted aspartic proteinase 2 from *C. Albicans* binding with bicyclic peptidomimetic inhibitors by molecular docking

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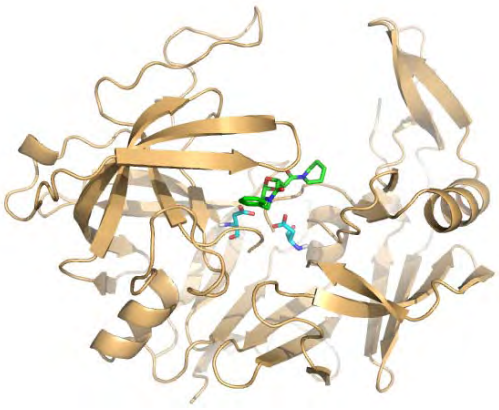
Candida albicans is an opportunistic fungal pathogen that causes even severe systemic infections especially in immunodeficient individuals [1]. Although a certain number of antifungal agents are available, the need for new drugs against *C. albicans* is escalating due to the development of resistance against available drugs. Secreted Aspartic Proteinases (SAPs) activity appears to be a main virulence factor of this fungus, allowing it to adhere and invade host tissues, therefore this family of enzymes offers a potential target for drug intervention in infections. Particularly, SAP2 has been recognized as a crucial virulence factor for vaginal infection and both reversible and irreversible inhibitors have been reported accordingly [2].



We recently reported on the identification of a novel class of small-molecule peptidomimetic SAP2 inhibitors based on 6,8-dioxa-3-azabicyclo[3.2.1]octane scaffold, which showed antifungal activity against *C. Albicans* [3]. In particular, we selected two hit candidates, which proved to be effective both *in vitro* and *in vivo* against drug-resistant *C. albicans* strains. With aim to give more insight into the binding mode and the structural requirements of these compounds for the inhibitory activity towards SAP2, we carried out a structural study by molecular modelling and enzyme inhibition assays, also taking into account the four possible stereoisomers of the two lead compounds.
Through this computational analysis, performed using the automated docking program AutoDOCK 4.0, we gain insight into the possible orientation of these compounds in enzyme catalytic site and the various structural factors and interactions responsible for their inhibitory potency.

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CSB-OR-21 SOLID-PHASE SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF NOVEL NUCLEOSIDE-TETHERED DINUCLEAR PLATINUM(II) COMPLEXES

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Cis-diamminedichloroplatinum(II), commonly known as cisplatin, is a well-known antitumour drug currently used in the treatment of testicular, ovarian, bladder head/neck, lung, and cervical cancers. Unfortunately it has several major drawbacks.
Recent studies concluded that it is possible to overcome the cross-resistance to cisplatin and its analogues using polinuclear compounds. For these reasons, in the last decades some research groups focused their attention on the design and synthesis of new polinuclear platinum complexes where the metal centres are separated by an aliphatic unbranched amine linking ligand. In the light of these studies, we chose to prepare, according to a solid phase approach already employed by us,[1] three new dinuclear platinum complexes, where both platinum moieties are installed on a modified nucleoside acting as ligand. The dinuclear platinum compounds were obtained in good yields starting from a commercially available nucleoside (inosine) and were tested against four different human tumor cell lines. One complex proved to be more cytotoxic than cisplatin against MCF7 cancer cell line in a short-term exposure assay.[2]

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CSB-OR-22 Porphyrins as Proteasome Inhibitors: a new activity for an old molecule.

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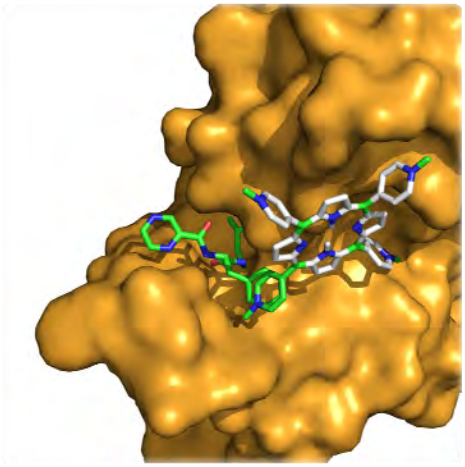
Inhibition of proteasome activity represent a promising anticancer strategy [1]. Proteasome plays a critical role in modulating intracellular levels of proteins involved in cell cycle regulation, it regulates tumor suppressor genes, oncogenes, and the activity of signal transduction pathways.



Porphyrins, very versatile molecules, are also used in PDT cancer therapy [2]. In this study we have tested their efficiency to inhibit proteasome. Chymotriptic, caspasic and tryptic activities on purified 20S, cell extract of 20 S and 26S samples have shown that cationic porphyrins are efficient reversible proteasome inhibitors. Their IC50 values are, in fact, in the range of 10^{-7}M; i.e. they are 100 times more active than lactacystin and MG132.
Spectroscopic results parallel the enzymatic behaviour and molecular modeling suggests that active porphyrins can effectively dock into the proteasome chymotryptic site by electrostatic interactions bridging the residues Thr1 with porphyrin positive groups.

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CSB-OR-23 Clioquinol Glycoconjugates as Potential Anti-Cancer Prodrugs

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Clioquinol (CQ) is a lipophilic chelator of copper, zinc and iron. Several recent studies have generated interest in CQ as a modulator of metal homeostasis in neurodegenerative disorders and cancer. *In vitro* and *in vivo* studies have demonstrated that CQ shows an anti-cancer activity at low micromolar concentration. The mechanism by which it induces cell death in the malignant cells is not completely understood, although some experimental evidences suggest a role of CQ as a copper dependent and/independent proteasome inhibitor [1].
The glycoconjugation has been investigated as a potential strategy to achieve selectivity and the drug glycoconjugates can be recognized by specific receptors such as glucose transporters or galectins, over-expressed in the cancer cells [2].
Thus, following preferential up-take of glycoconjugate compounds, they are subject to hydrolysis by specific β-glycosidases, allowing to liberate the active aglycone part which exerts its anticancer activity [3].
In this scenario, we report the synthesis of conjugates of 8-hydroxyquinoline and clioquinol with glucose and galactose. The derivatives were synthesized starting from protected α-anomer glycosyl bromide by a biphasic reaction, using a phase transfer catalyst. The conjugates obtained were characterized by NMR and UV spectroscopy and ESI-MS.
To evaluate the effect of the glycoconjugation, the clioquinol derivatives were tested in a neuroblastoma cell line, SH-SY5Y. The biological activity of the compounds was analysed by viability test like MTT assay and the selectivity of these compounds to induce cancer cells death was also tested.

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CSB-OR-24 Short Peptaibiotics as New Antimicrobial and Antitumor Agents: Synthesis, Conformational Analysis, Antimicrobial and Cytotoxic Evaluations of Trichogin GA IV and Selected Analogues thereof

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Trichogin GA IV, isolated from the fungus *Trichoderma longibrachiatum* [1], is the prototype of lipopeptaibols, a sub-class of short-length peptaibiotics exhibiting membrane-modifying properties. Its primary structure is as follows:

n-Oct-Aib[1]-Gly-Leu-Aib-Gly-Gly-Leu-Aib-Gly-Ile[10]-Lol

where *n*-Oct is *n*-octanoyl, Aib is α-aminoisobutyric acid, and Lol is the 1,2-amino alcohol leucinol. Using a variety of techniques we demonstrated that this peptaibol is predominantly folded in a mixed 3_{10}-/α- helical conformation with a clear, albeit modest, amphiphilic character [2]. In this work, we synthesized by solution and solid-phase methodologies a set of trichogin GA IV analogues in which the four Gly residues, lying on the poorly hydrophilic face of the helical structure, are substituted by one, two, three, and four strongly hydrophilic Lys residues. The conformational preferences of these analogues were assessed by CD and 2D-NMR techniques in aqueous, organic, and membrane-mimetic environments. We tested the role played by the markedly increased amphiphilicity on the peptide bioactivity, performing fluorescence leakage experiments in model membranes, and checking protease resistance, antibacteral and antifungal activities, cytotoxicity, and hemolysis. The cytotoxicity of trichogin GA IV and its analogues was tested using three *in vitro* cell-based assays: (i) Human red blood cells lysis. (ii) Cell mortality assays in total human blood leukocytes and in separate sub-populations. (iii) Cell mortality of three tumor-derived stable cell lines (HeLa, A541, A431). Our data show that some of our trichogin analogues are active against tumor cells, leaving the leukocytes unaffected.

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CSB-OR-25 Interaction of cisplatin with copper transport proteins: in vitro and in-cell NMR studies

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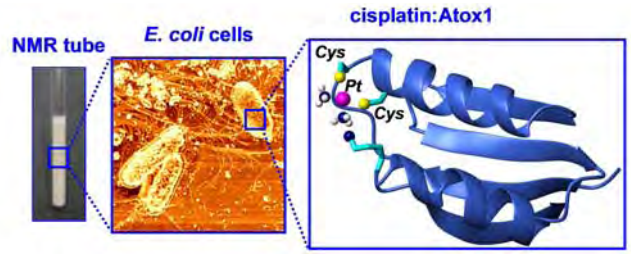
The anticancer drug cisplatin (*cis*-$[PtCl_2(NH_3)_2]$) exploits the cellular transport routes for essential copper (Cu) ions. The Cu permease Ctr1, located on the plasma membrane, is involved in cisplatin uptake, whereas the Menkes and Wilson Cu ATPases regulate cisplatin efflux and vesicular sequestration. In addition, the cytosolic Cu chaperone Atox1 has been found to translocate to the nucleus where it acts as a Cu-dependent transcription factor, thus representing a candidate nuclear carrier for cisplatin. In the nucleus, cisplatin forms adducts with DNA which are at the basis of its antitumor activity [1].

We investigated the coordination properties of Cu(I)-binding motifs of Ctr1 and Atox1 towards different Pt complexes by NMR spectroscopy and circular dichroism, and we determined the stoichiometry of adducts by ESI-MS [2,3]. Cisplatin binds to methionine-rich motifs of Ctr1 and to cysteine motifs of Atox1, but only in the latter case the drug retains its ammine ligands essential for antitumor activity. A combined approach using *in-cell* NMR and ICP-MS was used to probe intracellular drug delivery and the interaction of cisplatin with the dithiol motif of Atox1 in living *E. coli* cells, aiming to obtain detailed molecular information in a physiological environment.

Atox1 overexpression is shown to have a cytoprotective role against cisplatin toxicity by reducing the extent of DNA platination and subsequent cell morphology alterations, and improving cell viability.

The structural characterization of adducts of cisplatin with Cu transport proteins provides the basis for unraveling the effect of Pt-based drugs on Cu homeostasis and may contribute to the rational design of novel and more effective anticancer agents overcoming drug resistance and adverse side-effects.



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CSB-OR-26 Molecular recognition in fatty acid binding proteins: NMR interaction studies with lipids, lipophilic drugs, and liposomes

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Lipid trafficking in cells is a complex and dynamic process that affects many aspects of cellular function. The distribution of bioactive lipids to different cellular compartments appears to be coordinated by lipid chaperones known as fatty acid binding proteins (FABPs), a group of molecules that is also strongly linked to metabolic and inflammatory pathways [1].

FABPs have been shown to reversibly bind hydrophobic ligands, such as saturated and unsaturated long-chain fatty acids, bile acids, eicosanoids and other lipids. Some of the proteins have also displayed ability to bind a variety of exogenous molecules. Although the overall three-dimensional structure is conserved between isoforms, significant differences in ligand selectivity, binding affinity and binding mechanism are found [2].

The binding features of FABPs appear difficult to be captured, although recent studies have set important milestones in the atomic-level description of FABP/ligand interactions. NMR spectroscopy in particular proved an extremely powerful method to characterize these systems in terms of structure, dynamics, binding mechanisms and chemical equilibria, revealing very intriguing features of some members of the family such as binding cooperativity and site-selectivity [3].

The interactions of bile salts to specific FABP carriers have been extensively investigated in our laboratory applying a variety of NMR techniques and are here summarized. Recent results from studies addressing the role of bio-membranes in regulating ligand uptake and release are presented [4]. Finally, we describe lipid-based drugs which were found to be specifically bound by FABPs and displayed attractive features for applications in magnetic resonance imaging [5].

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CSB-OR-27 NMR based studies of stability and dynamics of different forms of BS-RNase

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The development of drugs that can overcome tumor resistance and minimize toxic effects to normal cells is one of the main targets of cancer therapy [1]. Several ribonucleases seem to be a good candidates because of their strong cytotoxic activity towards malignant tumour cells.

Among ribonucleases, bovine seminal ribonuclease (BS-RNase) is the one that shows some of the most interesting features. This is the only mammalian dimeric ribonuclease and it has been proposed that the interchange (swapping) of N-terminal helices is often associated with new biological functions including cytotoxic activity.The current hypothesis linking the swapping to the antitumor activity is that the entanglement of N-terminal tails hinders the neutralizing effect of the cytosolic ribonuclease inhibitor (RI), a protein extremely abundant in mammalian cells that protects endogenous RNA by binding with very high affinity endogenous ribonucleases. Thanks to two disulfide bonds bridging the two identical subunits of BS-RNase, the native protein exists as an equilibrium mixture of two isoforms, MxM and M=M, with and without exchange respectively, which show only minor structural differences in their X-ray structures, located essentially at level of the 16-22 hinge regions, *i.e*. the loop connecting the dislocating arm to the main body of the protein. High resolution NMR experiments allow a fine characterization of the structural and dynamical properties of the different forms that the BS-RNase adopts in solution, i.e. monomer, swapped and un-swapped dimers and can be helpful to define the mechanism of interconversion and, perhaps, to design mutants with improved biological activity. Here we present recent results based on relaxation, H/D exchange and chemical stability NMR experiments acquired on both monomeric and dimeric forms of BS-RNase. Our data suggest a possible mechanism for domain swapping of natural BS RNase.

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CSB-OR-28 Unfolding pathway characterization in prokaryotic zinc-finger domains.

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We have recently characterized the prokaryotic Cys_2His_2 zinc-finger domain[1,2], identified in Ros protein from *Agrobacterium tumefaciens*, demonstrating that, though possessing a similar zinc coordination sphere, this domain is structurally very different from its eukaryotic counterpart (Figure 1).

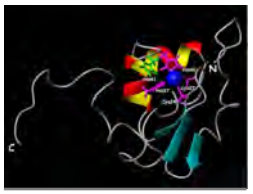

Fig 1 : The prokaryotic zinc-finger domain

A large number of Ros homologues have been found in different bacteria, having mostly a high sequence identity with Ros protein, which, surprisingly, does not comprise the zinc coordination sphere. We have demonstrated that the prokaryotic zinc-finger domain in Ros homologues can either change the coordination sphere or lose the metal while still preserving the DNA binding activity[3,4]. Here we report a thermodynamic and kinetic study of the Ros protein and of one of its zinc lacking homologues unveiling interesting differences in the mechanism of folding of the two proteins. In light of these findings, the role of the zinc ion in the stability and folding of the prokaryotic zinc-finger domains is discussed.

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CSB-PO-01 DNA G-quadruplex binders with a xanthene scaffold

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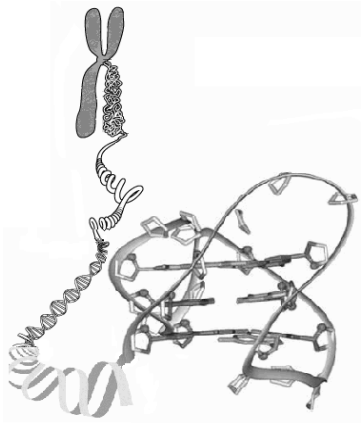
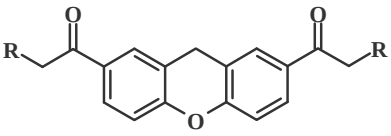
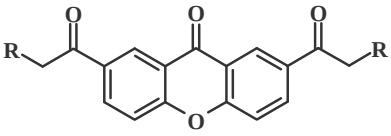


G-quadruplex structures at telomeres (region of repetitive DNA sequence at the end of a chromosome) are likely to play a relevant role, both from the structural and the functional point of view [1]. In fact, molecules able to induce G-quadruplex structures are intensively studied for their ability to inhibit telomerase, as possible therapeutic antitumoral agents [2]. In our research group, a great interest is devoted to study the formation of telomeric G-quadruplex structures by small organic molecules, in particular perylene [3,4] and coronene [5] derivatives and alkaloids related to the natural compound berberine [6]. Recently, we have synthesized the proposed xanthene and xanthone derivatives to test an additional simple aromatoid moiety. The affinity of these ligands at various concentrations towards different DNA structures, was study by ESI-MS measurements [5]. This technique allows the transfer of non covalently bound complexes into the gas phase without the disruption of the complex itself and therefore the determination of the stoichiometry and, in particularly favourable cases, modes and energies of interaction [7]. So, we have found that these molecules are able to bind and stabilize G-quadruplex DNA oligomers. Moreover, we have also studied the selectivity of these compounds for G-quadruplex over duplex DNA. In fact, the selectivity is surely a highly relevant topic and could be related to the specificity of the biological activity of these compounds.



Disubstituted xanthene



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CSB-PO-02 Studies on Temporin B analogues

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Temporins are antimicrobial peptides produced and secreted by the granular glands of the European red frog *(Rana temporaria*).[1] They are amphipathic helical peptides, 10–14 amino acids long, containing only 1 or 2 positively charged amino acids (R or K). Most of them selectively interact with bacterial membranes, being active against Gram positive bacteria, and are not toxic to eukaryotic cells.These peptides, as most of the AMPs, are highly membrane-active and have been hypothesized to fold upon interaction with bacterial membranes. The mechanism of action hypothesized for TL and TB after studies carried out on membrane models, leads to the hypothesis that the peptides first associate to the bacterial membrane; upon interaction, the peptides fold, intercalate the phospholipid bilayer and aggregate forming toxic oligomers, following a pathway similar to that observed the formation of amyloid fibers. [2]
In this study we focused on analogues of temporin B, obtained either after substitution of one or two amino-acids by an alanine and by lengthening the sequence, with the aim to widen our understanding of the factors which determine the interaction of the peptide with the bacterial membrane and their influence on the peptide secondary structure and antimicrobial activity. We investigated the antimicrobial activity of the peptides against Gram positive and Gram negative bacteria, their secondary structure by CD. Interestingly the analogue named G6AKK, with a +4 charge, was found active also against Gram negative bacteria. The interaction of this peptide with the LPS from Salmonella and E.coli was investigated by CD, fluorescence and NMR. The results obtained argue for a close relationship between the composition of the bacterial membrane and the strength of the peptide-membrane interaction which in turn determines the peptide folding and antimicrobial activity.

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CSB-PO-03 Turning ubiquitin into a glass-adhesive and lipid-soluble amyloid

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Ubiquitin (Ub) is involved in the pathways for eliminating misfolded proteins. Failure of this process leads to formation of amyloid aggregates enriched with Ub, that are a hallmark of most neurodegenerative disorders [1]. Amyloid fibril formation is preceded by structural changes in native proteins leading to sticky, partially misfolded intermediates. Although these species are considered to be the primary toxic species, very little is known about their conformational features.
The early steps of the aggregation process can be catalyzed by metal ions. We have shown by NMR that Cu^{II} destabilizes Ub [2] and triggers its aggregation [3] and we were able to determine the crystal structure of Ub in the presence of Zn^{II} [4]. On the basis of the detailed knowledge of the effects of metal coordination, we produced a Ub mutant (E16V), specifically designed to neutralize a negative charge at one edge β-strand, which, to some extent, can mimic metal binding. In water at 37 °C E16V is soluble and folded. In contrast, in water/trifluoroethanol (80:20, v/v) E16V undergoes a time-dependent increase in β-sheet content which drives the protein to interact with ANS hydrophobicity probe and to form amyloid-like deposits on a quartz surface. When added to anionic (but not to zwitterionic) phospholipid liposomes, E16V forms β-rich oligomers able to penetrate the bilayer and to react with the A11 antibody, which specifically recognizes amyloid oligomers [5].
The trapping of E16V oligomers prospects the possibility of using the Ub mutant as a model system for elucidating the structural features of amyloid most toxic species.

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CSB-PO-04 Hydroxymethylferrocene/β-Cyclodextrin inclusion complex: preparation and characterization in aqueous solution and in solid state

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Cyclodextrins (CDs) are cyclic oligosaccharides consisting of six (α-CD), seven (β-CD), eight (γ-CD) or more D-glucopyranose units linked by α-1,4 bonds in a toroidal structure. The inside cavity of β-CD is hydrophobic and the outside is hydrophilic. Due to their structural features, they are capable to include a wide variety of molecules of appropriate size and polarity into their cavity forming inclusion complexes [1]. CDs-drugs inclusion complexes have recently gained interest in the pharmaceutical field due to the enhanced solubility, stability and bioavailability of the drug [2]. Molecular encapsulation may occur both in solid and in solution state.

Ferrocene (Fc) is an organometallic compound consisting of two planar and parallel cyclopentadienyl rings and an iron atom. The biorganometallic and medicinal chemistry of ferrocene has been extensively reviewed recently [3]: the synthesis, characterization and antitumor activities of different CD inclusion complexes containing one of the ferrocene derivatives have been recently described [4].

In this work, we report the preparation and caracterization of inclusion complex between hydroxymethylferrocene (FeMeOH) and β-CD in solid state and in aqueous solution. A solid binary system was prepared in a 1:1 stoichiometric by different techniques such as physical mixture, co-precipitation, kneading, and freeze-drying. These products were characterized using powder X-ray diffractometry (XRPD) and Fourier transform-infrared spectroscopy (FT-IR).

The results obtained indicate the formation of an inclusion complex of FeMeOH with β-CD in the solid state. The effect of β-CD on the aqueous solution and dissolution rate of FeMeOH were also investigated. Our results indicate that the solubility of FeMeOH is significantly increased in presence of β-CD and its phase solubility profile is classified as AL- type, indicating a stoichiometry 1:1 inclusion complexes [5].

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CSB-PO-05 β-hairpin stabilization through click chemistry

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The β-hairpin is an especially interesting naturally occurring scaffold used by many proteins for biomolecular recognition, and thus is an attractive tool for mimetic design [1], in fact the β-Hairpins constitute an important class of connecting protein secondary structures, such structures are the simplest form of β -sheets, the motif consists of two strands that are adjacent in primary structure oriented in an antiparallel arrangement, where the N-terminus of one sheet is adjacent to the C-terminus of the next, and linked by a short loop of two to five amino acids. In this review we explore the possibility to stabilize a β -hairpin conformation through an intramolecular side-chain to side-chain cyclization which will should also improve resistance to proteolytic degradation. We focus on the well know click chemistry reaction which brings to the formation of a 1,2,3, triazole linkage between alkyne and azide reactive groups. Furthermore, we analyzed the relationships between β -hairpin stability and side chain length of the reacting groups. The β -hairpin model system we chosen was the Trpzip2 peptide, and we analyzed the contribution to β -hairpin stability of the 1,2,3 triazole linkage in a nonhydrogens bonded position (NHB). The alkyne and azide amino acids were introduced in position 4 and 9 of Trpzip2 respectively. Trp11 was replaced with valine in order to assess the contribution in absence of aromatic contribution and Trp2 was left as spectroscopic probe. As alkyne amino acids were inserted propargylglycine (Pra), homopropargylglycine (Hpg) and bishomopropargylglycine (Bpg). On the other strand the following azide amino acids were introduced: L-beta azidoalanine, L-gamma-azidohomoalanine and L-delta-azidoornithine. The synthesized and purified linear peptides, were cyclized by the CuAAC reaction and purified prior to the spectroscopic characterization. Linear and cyclic peptides were analyzed by a combination of CD and NMR techniques.

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CSB-PO-06 A novel dual function peptide for gold nanoparticles stabilization and integrin targeting

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Over the past decade gold nanoparticles have attracted much interest since they are versatile agents with a variety of biomedical applications including drug and gene delivery[1]. Several stabilizing agents, that interact with nanoparticle surface, are usually added to improve their stability. Recently, we reported peptide sequences displaying thiol group (GC) as capping agents for gold nanoparticles preparation [2]. A special feature of these peptides is that they do not lead to particle aggregation by cross-linking.
In this framework we designed a novel dual function peptide (RGD-$(GC)_2$) encompasses a RGD motif for $\alpha_v ß_3$ targeting [3] and a GC motif to stabilise the gold nanoparticles. The nanoparticles Au@RGD-$(GC)_2$ functionalized with the peptide were characterised by UV-visible, ATR-FTIR and NMR spectroscopies, confocal and TEM microscopies. The cellular uptake of Au@RGD-$(GC)_2$ gold particles into U87 cells were investigated by confocal microscopy in comparison with Au@$(GC)_2$ as control. A quantitative determination of the uptaken nanoparticles were carried out by measuring the brightness of the images of both systems that highlighted the importance of the RGD sequence of the peptide. In order to understand if the receptor-mediated entrance was favourite, TEM experiments with Au@RGD-$(GC)_2$ and Au@$(GC)_2$ nanoparticles were carried out.

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CSB-PO-07 Harpin oligonucleotides forming G-quadruplexes: new aptamers with potential anti-HIV activity

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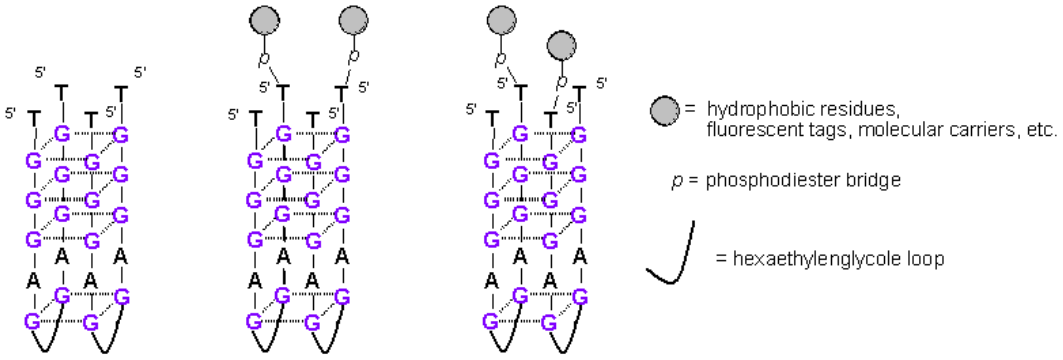
Several G-rich synthetic oligodeoxyribonucleotides (ODNs) have shown promising biological properties, ranging from anticancer to anti-HIV activities. G-quadruplex formation was found to be a crucial prerequisite in determining these biological effects [1]. Aptamers exhibiting anti-HIV activity represent an important class of potential therapeutics [2]. Recently we described the synthesis and characterization of new d(TGGGAG) ODNs, conjugated with different aromatic groups at the 5'-end through a phosphodiester bond [3]. The modified sequences showed a parallel stranded tetramolecular G-quadruplexes CD profile and a pronounced anti-HIV-1 activity.

Herein, with the aim to use d(TGGGAG) as a lead sequence for a more effective anti-HIV agent, we propose the fully automated synthesis of new ODNs containing two d(TGGGAG) sequences whose 3-ends are joint by an hexaethylenglycole loop. CD analysis was undertaken on the 3'-3' linked d(TGGGAG) *hairpins* in comparison with the corresponding unmodified oligomers. Besides, in order to study the influence of the conjugation at the ends of the *harpin* chains on their ability to stabilize quadruplex structures and on their anti-HIV activity, different conjugated oligomers have been studied.



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CSB-PO-08 Synthesis and characterization of a mini-library of new conjugated d(TGGGAG) oligonucleotides with potential anti-HIV activity.

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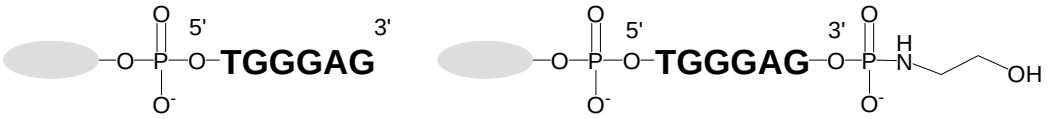
In the search for ODNs endowed with relevant antiviral properties, Hotoda and coworkers [1] investigated a series of G-quadruplex-forming ODNs, finally focusing on modified d(TGGGAG) ODNs conjugated with aromatic residues at the 5-end. These were found to exhibit potent anti-HIV activity associated with low cytotoxicity when carrying at the 5′-end bulky aromatic residues. Recently we described a general approach to obtain a mini library of new d(TGGGAG) ODNs, conjugated with different aromatic groups at the 5'-end through a phosphodiester bond [2]. Several modified sequences showed pronounced anti-HIV-1 activity and they showed high binding affinities for the HIV-1 envelope gp120 and gp41. In these structures the 5-end residues play a major role on the G-quadruplex stability, dramatically enhancing stability of the quadruplex complexes (ΔTm>20°C).

With the final goal to expand the repertoire of accessible end-modified G-rich ODNs, and to get a more complete picture of their structure-activity relationships, we describe herein the synthesis and characterization of a mini-library of new d(5'TGGGAG3') carrying hydrophobic groups at the 5'-end and 2-hydroxyethylphosphate group at the 3'-end, connected through phosphodiester and phosphoramidate bonds, respectively. In order to study the influence of the conjugation at the ends of the oligonucleotide chains on their ability to form quadruplex structures, a CD analysis was undertaken on the conjugated oligomers in comparison with the corresponding unmodified d(TGGGAG) oligomer.



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CSB-PO-09 Characterization of VEGFR-2 extracellular domains: a tool for new VEGF receptors binder molecules

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Angiogenesis is the process characterized by the formation of new blood capillaries from preexisting vessels, resulting from a complex balance between positive and negative regulators. The most important pro-angiogenic factor is the Vascular Endothelial Growth Factor (VEGF) that regulates blood and lymph vessel formation through activation of two receptor tyrosine kinases, VEGFR-1 and VEGFR-2 [1]. The extracellular portion of VEGF receptors consists of seven immunoglobulin homology domains, which, upon ligand binding, promote receptor dimerization. Dimerization involves domain 4 (D4) and initiates transmembrane signaling, which activates the intracellular tyrosine kinase domains of the receptors [2, 3]. Furthermore, there are structural and biochemical evidences demonstrating that homotypic contacts between the most membrane-proximal Ig-like domain of the extracellular portion (D7) of VEGF receptors play a critical role in VEGF-induced activation and cell signaling *via* VEGF receptors [4]. VEGFR-2 is considered to be the major mediator of several effects of VEGF-A on endothelial cells (ECs) and the predominant transducer of signals required for physiological and pathological angiogenesis [5]. VEGFR-2 regulates ECs proliferation, survival, migration and vascular permeability. In case of pathological conditions associated with angiogenesis, the inhibition of the VEGF/VEGFRs pathway is a promising anti-angiogenic treatment which has already found therapeutic application for example in oncology. Compounds targeting VEGF receptors could be employed in the antiangiogenic therapy as well as in angiogenesis imaging [6]. In this respect, new molecular entities as peptides have already been reported to bind to the extracellular region of VEGF receptors, acting as agonists or antagonists of their activity [7, 8]. In this report we present the expression and purification of D4 and D7 extracellular domains of VEGFR-2 and their preliminary structural characterization, in order to identify new molecules able to bind and inhibit VEGF receptors signaling.

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CSB-PO-10 Heparin-binding hemagglutinin HBHA from Mycobacterium tuberculosis affects actin polymerisation

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Mycobacterium tuberculosis (Mtb) is the etiological agent of tuberculosis (TB), the leading cause of death in the world from a bacterial infectious disease.
Dissemination from the site of primary infection involves interactions of Mtb with epithelial cells through a virulence factor called heparin-binding haemagglutinin, HBHA [1]. This is a surface exposed protein, that mediates binding of mycobacteria to epithelial cells through its C-terminal lysine rich domain, which interacts with heparan sulphate proteoglycans at the cell surface [2]. Also HBHA can cross epithelia cell layers and enter the cytoplasm. Once inside the cytosol, HBHA, but not its truncated from (HBHAΔC) induces a reorganisation of actin cytoskeleton [3]. This finding is very important in light of the newly recognised ability of Mtb to escape from the phagosome into the cytosol, where it replicates and causes cell damage that is instrumental for bacterial spread and infection of other cells. Indeed, HBHA-deficient strains are hampered in their ability to disseminate from the lungs to other tissues. Previously, using Single Molecule Force Spectroscopy, it was shown that both HBHA and HBHAΔC are able to bind actin [4], a finding that does not explain why only full-length HBHA is able to induce cytoskeleton reorganisations [3]. We here reported the actin binding capabilities studies of both HBHA and HBHAΔC. To this aim, we investigated actin filament nucleation and polymerisation, two crucial steps in intracellular organelle movements, in response to HBHA and HBHAΔC [5]. Results provide an explanation to the ability of HBHA to affect cytoskeleton morphology and strengthen the concept that HBHA is involved in Mtb pathogenesis at different dissemination levels.

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CSB-PO-11 Clickable functionalization of liposomes with gH625 peptide from Herpes simplex virus type I for intracellular delivery

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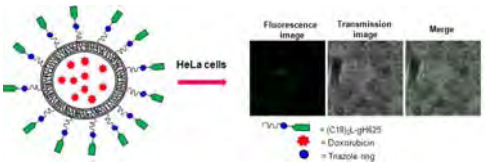
Liposomes externally modified with the nineteen residues gH625 peptide, previously identified as a membrane-perturbing domain in the gH glycoprotein of *Herpes simplex* virus type I [1], have been prepared in order to improve intracellular uptake of an encapsulated drug. An easy and versatile synthetic strategy, based on click chemistry [2], has been used to bind, in a controlled way, several copies of the hydrophobic gH625 peptide on the external surface of DOPG based liposomes. DLS measurements indicate an increase of liposomes diameter of approximately 30% after peptide introduction, and confirm the positioning of the coupled peptides on the liposome external surface. Liposomes have been loaded with the cytotoxic drug doxorubicin. Their ability to penetrate inside cells, promoted by gH625 peptide, has been evaluated by confocal microscopy experiments. Results suggest that liposomes functionalized with gH625 may act as promising intracellular targeting carriers for efficient delivery of drugs, such as chemotherapeutic agents, into tumour cells.



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CSB-PO-12 Secondary Structures in D,L-Alternating Peptides: a Model to Design Macromolecular Architectures.

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In protein structures, distinct secondary structural elements, such as helices and strand, are assembled into a compact fold that is stabilized by a complex network of tertiary interactions. In attempt to design synthetic polypeptide mimics for protein structures, a specifically designed patterning of polar and apolar residues along the synthetic sequence is generally employed in order to direct the orientation of secondary structural elements. We are pursuing an alternate approach to the construction of complex polypeptide structures in which a primary goal has been to design molecules of defined shape that are soluble in poorly interacting organic solvents. In this approach, the driving forces that determine polypeptide-chain folding are enthalpic in nature and consist primarily of hydrogen bonding and van der Waals interactions.
Alternating D,L-peptides are able to assume specific conformations including, among others, various kinds of single and double stranded β-helical structures, predicted also on theoretical ground, and α-extended chains that can aggregate through parallel or antiparallel H bonds and yeld pleated (or rippled) sheet. The stability of each structure depends on the influence of various structural factors, such as the length of the peptide chain, the nature of the lateral substituents and of the end groups, the solvents and the specific pattern of configuration (DLD or LDL) which may modify the conformational properties of the D,L-alternating peptide. The computational and spectroscopic integrated study of interparticles and collective interaction for this synthetic peptides allowed us to known the properties of different new structures.

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CSB-PO-13 A Study of Conformational Constraint Bioactive Peptides: Exploring Intermolecular Interaction and Self-assembling

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Hollow structures containing pockets and pores formed by oligopeptides and proteins are involved in numerous biological processes. Except for a small number of hollows associated with secondary structures, most voids in nature are associated with tertiary and quaternary structures of proteins. One of the most important aspect of natural hollow structures is the exquisite complementarity between their sizes and functions and those of the corresponding guest molecules, process, and reactions. With their complementarity, natural cavities and pores provide microenviroments that lead to a specific binding, catalysis, transportation, and other functions. Since the discovery of crown ether, many macrocycles have been created as host for various guests. The majority of synthetic macrocycles and their acyclic analogs have flexible backbones and thus collapsible cavities. On another front, peptidomimetic oligomers that fold into secondary structures have attracted intense interest on D,L-alternating oligopeptides. Most of these oligomers fold into secondary structures stabilized by multiple interactions that require the participation of both backbones and side chains, with overwhelming majority being helical conformations.

Hollow crescents based on backbone-rigidified oligopeptides. While most cavities and pore are associated with the tertiary and quaternary structures, some helical oligopeptides are known to contains pores. For example, the antibiotic oligopeptides Gramicidin A folds into a β-helix containing a small (~4Å across) pore. Inspired by gramicidin A and valinomicin we started a project to develop unnatural oligopeptides that folds in hollow helical conformation (β-helix) and analogues cyclic peptides that have rigid β-ring conformation. Chemical composition and surrounding medium contribute together to determine in D,L-alternating peptide specific preferences for some of the several conceivable kinds of β-helices. Looking to the example by nature pore-, or cavity-containing secondary structures, work described in this paper stemmed from the development of D,L-alternating stereo-co-oligopeptides containing any cyclic residues insert in well-defined positions of the main chain. This cyclic unit immobilize the curvature into the corresponding backbones, leads an enforced helical (or ring with cyclic peptides) conformation. As a result, a variety of reliably folded, modifiable scaffold can now be constructed. The well-defined crescent helical conformation contain noncollassable internal cavities having multiple, introverted amide bonds. Changing the backbone curvature by tuning the cyclic unit (geometry and/or position) leads to crescents ring dimension or helical with cavities of tunable sizes. We synthesized a series of molecules inserting cyclic units in well-defined position obtaining the designed, natural-like hollow structure. The computational and spectroscopic integrated study of these models allowed us to identify different new structures that will be discussed.

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CSB-PO-14 Design and synthesis of a HCA-PNA conjugates based focused mini-library

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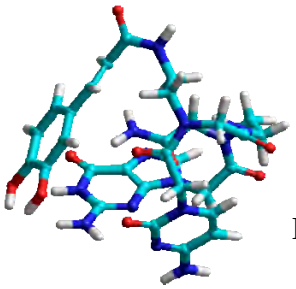
The structures and functions of natural products suggest that structural complexity of molecules is correlated with their biological activity. DOS (Diversity-Oriented Synthesis) is the facile preparation of library of structurally complex and diverse compounds from simple starting materials, typically through the use of "split-pool" combinatorial chemistry, in contrast to TOS (Target-Oriented Synthesis) which aims to prepare a specific target compound [1]. Computational chemistry and molecular modeling represent tools for the combinatorial library design and compound selection. Several virtual libraries containing all possible combinations of cores and appendages have been described [2]. Molecular descriptors are applied to virtual library in order to select the set of compounds to synthesize, for biological screening and medicinal chemistry lead generation. Hydroxycinnamic acid (HCA)-peptide conjugates exhibit a synergistically enhanced antioxidative activity [3]. Herein, we describe the design and synthesis of a focused mini-library of PNA-caffeic acid (CA) dimers conjugates. According to X^{n} rule (X=building blocks, n=coupling numbers), we have designed a virtual library consisting of 16 CA-PNA_2 conjugates. On the basis of calculated Log P, Log S and HyperChem analysis, we have selected the compounds with the best chemical-physical properties and positive interaction between PNA and CA residues. The selected PNA_2-CA conjugates were synthesized by conventional Fmoc chemistry on solid-phase synthesizer and characterized by NMR and MALDI-TOF analysis. Antioxidative activity studies are in progress by DPPH radical scavenging test and lipid peroxidation test with ferric thiocyanate method.



Molecular modeling of GA-HCA conjugate

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CSB-PO-15 A peptide derived from Herpes Simplex Virus type 1 glycoprotein H: membrane translocation and applications to the delivery of quantum dots

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Cell membranes are impermeable to most molecules not actively imported by living cells, including practically all macromolecules and even small molecules whose physiochemical properties prevent passive membrane diffusion. However, over the past decades, we have seen the development of increasingly sophisticated methodology for intracellular drug delivery. Cell-penetrating peptides (CPPs), representing different families of short peptides believed to enter cells by penetrating cell membranes, have attracted a great interest in the hope of enhancing gene therapy, vaccine development, and drug delivery. Nevertheless, to achieve an efficient intracellular delivery, further strategies to bypass the endocytotic pathway need to be investigated. We report on a novel peptide molecule derived from glycoprotein gH of Herpes simplex type I virus (gH625) which is able to traverse the membrane bilayer and to transport a cargo into the cytoplasm. In the present study, to accurately measure the fraction of internalised peptide, We also report confocal microscopy experiments showing the cellular uptake of gH625. In order to assess the ability of the peptide gH625 to deliver drugs inside the cell, we used quantum dots (QDs) as a model cargo. We showed that cargo molecule quantum dots, almost unable to traverse the membrane bilayer on their own, can gain constitutive access to the cell internal compartment and mainly by a non endocytotic route.

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CSB-PO-16 Copper (II) interactions with VEGF peptide fragments encompassing the VEGFR-2 binding site.

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Angiogenesis, the formation of new capillaries from existing vasculature, is a critical process in normal physiology as well as several pathophysiologies. Angiogenesis has long been associated with a heightened sensitivity to copper, but the formation of molecular species containing the metal ion with the main angiogenic agents and their roles remain elusive. The Vascular Endothelial Growth Factors (VEGFs) are the most important and extensively studied angiogenic regulators involved in multiple signaling networks. Though it has been shown that copper (II) is able to induce VEGF expression and wound healing [1] no chemical interaction results have been reported.
We investigated the copper VEGF binding features and here report the synthesis of two peptide fragments encompassing the VEGF residues, 73-101 and 84-101, that include VEGF protein β5-β6 loop aminoacid region. This domain contains the overlapping VEGF binding sites to VEGFR-2. These VEGF fragments could compete with the whole, native protein to trigger the cascade pathway involved in the angiogenesis process and contribute to clarifying the role of copper(II) in the same path. It is interesting to underline that these chosen sequences include three His residues, that are known to be preferential sites for copper(II) binding. Thus a combined spectroscopic (CD, EPR, UV, Vis) and potentiometric investigation of their copper(II) complexes was performed. Futherrmore, the functional interaction of Cu^{2+} ion with VEGF fragments and the whole VEGF protein were tested by measuring the effects on the proliferation and migration phenomena of HUVEC cells.

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CSB-PO-17 Structural characterization of proteins involved in biofilm formation

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Lactobacillus plantarum is a major component of the urogenital and intestinal microflora of most mammals, including humans. Among the probiotics it is one of the most used in processes of conservation and food processing and one of the most studied for its involvement in the immune stimulation and balancing of the intestinal microflora. We have identified within the genome of *L. plantarum* WCFS1 three unknown open reading frame proteins named Flm1, Flm2, Flm3. Interestingly, their amino acid sequences show a significant percentage of identity with the protein BrpA (biofilm regulator protein A). Chatfield et al. [1] have suggested that BrpA is located outside the cell and involved in maintaining the structure of the cell wall through the regulation of autolysines. Interestingly BrpA, as well as Flm1, Flm2, Flm3 contain a highly conserved sequence that is called *LytR-cpsA-psr*. The LytR-CpsA-Psr family of cell envelope-associated transcriptional attenuators has gained attention upon the discovery that members of this family influence various virulence factors as well as antibiotic resistance of important human pathogens. Moreover the LytR-CpsA-Psr family seems to play a role in bacterial cell envelope maintenance [1,2]. The function and structure of the LytR-CpsA-Psr domain, however, is still not known and information about this domain to date are based only on phenotypic characterizations. Here we report the preliminary structural and functional characterization of LytR-CpsA-Psr domain of the Flm1, Flm2 and Flm3 proteins in order to gain insight into the structure and the function of this interesting domain.

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CSB-PO-18 Synthesis and Antioxidant Properties of Benzoxanic Nitrones and Nitroxides

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New benzoxazinic nitrones were recently synthesized and tested as spin trapping agents [1] and it was found that they efficiently scavenge all C- and O-centered radicals. From these nitrones the corresponding nitroxides were also prepared and both nitrones and nitroxides were tested as antioxidants in biological systems. In particular, the antioxidant activity of these compounds was assessed in the oxidation of methyl linoleate micelles in aqueous dispersions induced by AAPH by following the conjugate dienes formation and in the oxidation of phosphatidylcholine liposomes by measuring the TBARS production.

1 **2**

a X = H
b X = OCH_3

Compounds **1a,b** and **2a,b** were also compared with well known antioxidants (TEMPO, PBN, Trolox) and with indolinic nitroxides whose antioxidant activity was extensively studied and demonstrated in the past by our group. [2]
The results obtained clearly indicate that nitroxides **2a,b** are very good antioxidants in both the systems used and they are much better than the indolinic ones (longer lag time in conjugated dienes formation and higher % inhibition of TBARS production). Nitrones **1a,b** are also good inhibitor of TBARS production but they have a “retardation” effect [3] when the formation of conjugated dienes is followed (no lag time, but slower rate of oxidation).

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CSB-PO-19 Evolution of classical zinc finger domains

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Cys_2His_2 zinc-finger domain is one of the most important eukaryotic structural motifs involved in protein–DNA interactions. It is a small domain consisting of 30 aa in which a zinc ion, crucial for its stability, is tetrahedrally coordinated by two cysteines and two histidines. Its amino acid consensus sequence is $(F/Y)XCX_{2-5}CX_3(F/Y)X_5\psi X_2HX_{3-5}H$, where X represents any amino acid and ψ is any hydrophobic amino acid; ψ forms with the other two hydrophobic residues (F/Y) a small hydrophobic core that together with the zinc ion stabilizes a compact 3D structure with a ββα fold.
This eukaryotic domain is also present in several prokaryotic proteins, but with some structural differences. The first prokaryotic Cys_2His_2 zinc finger domain has been identified in the transcriptional regulator Ros[1] from *A. tumefaciens.* Its globular domain consists of 58 amino acids arranged in a βββαα topology and it is stabilized by an extensive hydrophobic core (15 aa) [2]. To date, a large number of homologues have been found in different bacteria, with a high sequence identity to the Ros protein [3,4].
Here, a model for the distribution and the evolution of zinc finger domains in bacteria and eukaryotes is proposed. Zinc finger domain-containing proteins are equally distributed among diverse Alphaproteobacteria, with distinct amino acid compositions in specific families. In some cases, the zinc-finger domain can either change the coordination sphere or lose the metal while still preserving the DNA binding activity. To investigate a possible correlation between prokaryotic and eukaryotic zinc-finger domains, we conducted two separate phylogenetic analyses, one including all retrieved domain sequences and the second including only domains of prokaryotic proteins and their homologues. Our analysis allows to speculate that there is an evolutionary link between the two kingdoms, based on bacteria-to-eukaryota horizontal gene transfer (HGT).

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CSB-PO-20 Characterization of the metal binding site in prokaryotic zinc-finger: structure and dynamics of Ros87_H42A

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Ros protein from *A. tumefaciens* is the first prokaryotic classical zinc finger protein. Ros87, a mutant of Ros wild-type obtained by deletion of the first fifty-five amino acids, which is soluble and contains the zinc finger domain, is still able to bind DNA[1]. The NMR structure of Ros87[2] consists of a very well defined globular domain, in which the zinc ion is tetrahedrally coordinated by Cys-24 and Cys-27 and by His-37 and His-42, and two disordered tails at the N- and C-terminal region. Ros87 globular fold has ββββαα topology and it is stabilized by an extended hydrophobic core of 15 amino acid. These new features define a novel fold never found in literature. The mutant H42A of Ros87 (in which the second coordinating histidine is mutated to alanine) is still able to bind the specific DNA sequence. Moreover, HSQC-J18 experiment demonstrated that in H42A the zinc ion is tetrahedrally coordinated by Cys-24, Cys-27, His-37 and His-41[1] because when His-42 is mutated in Ala, His-41 is able to occupy the fourth position of the zinc coordination, changing its tautomeric form from the N_{e2}-H tautomer, observed in the wild-type protein, to the N_{1}-H tautomer. We report here the complete NMR structural, dynamic and functional characterization of Ros87_H42A mutant in order to investigate the properties of this zinc coordination site.

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CSB-PO-21 Molecular and supramolecular structure of elastin model peptides containing (2S,4R)-4- hydroxy-proline

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The study deals essentially with the synthesis and the structural analysis of nanostructured polypeptides with potential interest in the field of biomaterials science.
Taking advantage of the unique abundance of repetitive sequences in elastomeric proteins, it is planned the synthesis of polypeptides of different size and alternative sequences, followed by crosslinking reaction in order to obtain polymeric material with elastic features. Several elastic proteins was considered as natural models for the design of elastic biomaterials. Common feature of the elastomeric proteins such as elastin, abductin, and resilin is the high content of glycine residues in their sequences, which ensures high flexibility to the monomer chains; they differ for the presence of other aminoacid residues. *[1]*.
Elastomeric protein inspired biomaterial are of paramount interest, for their intrinsic elastic properties, as well as for their straightforward design. The ease of polymer design is due to the presence of small-sized repetitive sequences in elastomeric proteins, such as for example the elastin-related repeats: VPGXG or XGGZG (x,Z= hydrophobic aminoacids).*[2]*.
In elastin they are mainly hydrophobic residues, like valine, leucina, proline, alanina, while in abductin and resilin other residues are present. Other features distinguishing the two proteins are the size (elastin and resilin are constituted by ca 750 and 621 residues respectively, while abductin by 136 aminoacids) and the type of crosslinks. The chemical syntheses of the polypeptides was be carried out by solid phase peptide synthesizer and classical solution synthesis, and in some cases polycondensations $(VPGVG)_{10}$.
We study the effect of hydroxylation on some peptide like (VPGVG) and exon 18 (*) of elastin change prolyne with (2S,4R)-4- hydroxy-proline.

Peptide	Sequence
$(VHypGVG)_{10}$	VHypGVG VHypGVG VHypGVG VHypGVG VHypGVG VHypGVG VHypGVG VHypGVG VHypGVG VHypGVG
Esone 18 H	GAAAGLVPGGPGFGPGVVGVPGAGVPGVGVPGAGIPVVPGAGIPGAAV (*)

Esone 18 H

AFM study effettued on exon 18 mostred fiber similar to other AFM microscopies on exon like 30_18 or exon 26. (Figure 1)

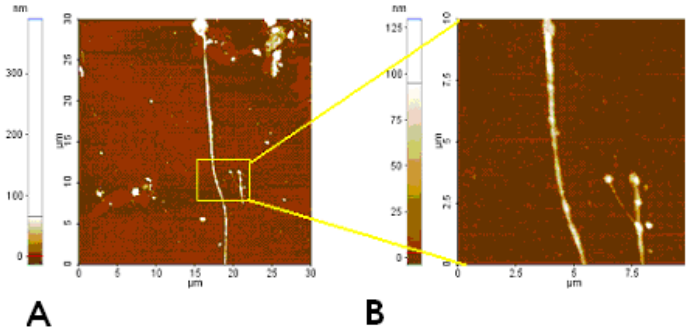

Figure 1: Exon 18. AFM images of pit refilling after water depositing *on wafer silicio (100) (A) and zoom (B).*

AFM study effettued on exon 18 H mostred aggregated dissimilar to exon 18 and elastin in general

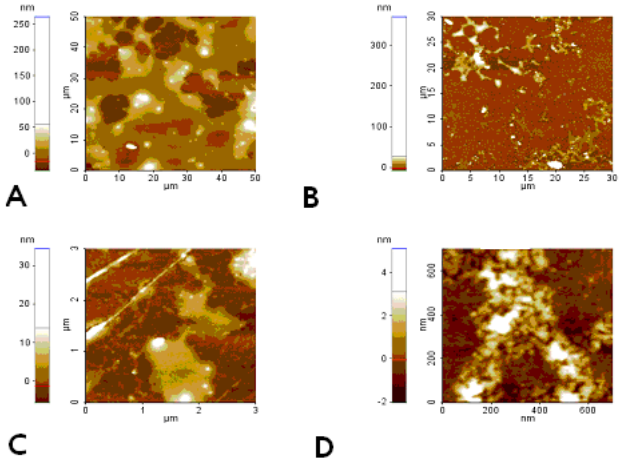

Figure 2: Exon 18 H. AFM images of pit refilling after water depositing *on wafer silicio (100) (A) and zoom (B).), (B,C,D) AFM images after incubation (50 ° for 48 h).*

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CSB-PO-22 Copper(II) and zinc(II) interaction with Aβ42: effects of metal binding on peptide's aggregation rate and morphology of the aggregates.

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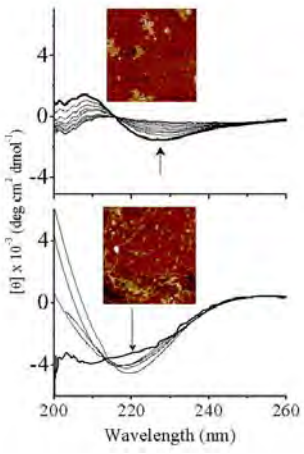
Altered levels of zinc(II) and copper(II) in different brain districts have been implicated in various aspects of Alzheimer's diseases.[1] In particular, it is well established that metal ions play a major role in the self-assembling of Aβ, but their effects on fibrillogenesis and morphology of peptide aggregates are not fully elucidated yet and conflicting results are reported in the literature.[2] In the attempt to shed light on these debated issues, two slightly different monomerization protocols were developed to mimic "seeded" and "unseeded" Aβ(1-42) assembling. Then, metal effects on the peptide aggregation and morphology were comparatively investigated by CD, ThT fluorescence and SFM techniques. Our results indicate that unlike copper(II) which promotes the formation of amorphous aggregates, zinc(II) is quite able to convert soluble Aβ peptides into amyloid-like structures. The obtained results might contribute to set up a hypothesis that correlates metals' coordination modes and different aggregate morphologies as well as in vitro toxicities towards neuronal cell cultures.



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CSB-PO-23 Insights on channel selectivity from the structural and functional characterization of the Kv1.3 channel blocker Tc32.

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The utility of toxins in biomedical research, diagnosis, and therapy is widely recognized. Unfortunately their use is limited by an inadequate target discrimination. Thus, the search for target-specific toxins is of primary relevance. The fact that despite the incredible number of toxins present in the animal kingdom, only a limited number of molecular scaffolds has been selected, is a clear evidence of the importance of the nature and spatial orientation the side chains. The description and understanding of the contact surface between the toxin and the channel entrance appears to be the target for the rationale design of selective and high affinity drugs.

Tc32 toxin from the scorpion *Tityus cambridgei* has been reported to have a clear inhibitory effect on Kv1.3 K^+ channel [1]. This channel, member of the *Shaker* family [2], carries a large proportion of the outward current not only in leucocytes [3] but also in a variety of neuronal cells [4].

In the present work, Tc32 has been cloned and expressed in a soluble and active form for the first time, employing a new protocol we devised [5]. Tc32 activity has been characterized by electrophysiological assays on a distinct subpopulation of periglomerular cells of olfactory bulb and its 3D solution structure determined by ^{1}H-NMR spectroscopy. The structure reveals it exhibits an α/β scaffold typical of the members of the α-KTx family. A structural comparison with the other members of α-KTx 18 subfamily is presented following molecular modeling calculations, and docking simulations to Kv1.1 and Kv1.3 channels.

Our data point out Tc32 as a good lead molecule for the development of new molecules suited for research, diagnosis and therapy.

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CSB-PO-24 Insight into the C-terminal domain of h-Prune: a biochemical and structural characterization

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H-prune has been identified as one of the determinants of metastasis in breast cancer [1]. This protein is a member of the DHH superfamily and its overexpression is correlated to tumor aggressiveness and development of metastasis. H-prune has a phosphodiesterase activity (cAMP-PDE) and inhibition of this activity by dipyridamole can abolish cell motility [2]. The metastatic suppressor Nm23-H1 has been characterized as one of the most important interaction partner of h-prune. In vivo data have shown that binding of Nm23-H1 to h-prune inhibits its function and induces the formation of metastasis. Sequence and limited proteolysis analyses have identified three domains in h-prune: the DHH domain (residues 10-180), the DHHA2 domain (215-330), encompassing the residues responsible for substrate binding and important for specificity, and a C-terminal domain (residues 330-453, named Prune-C), homologue to cortexillin which contains regions rich in prolines and possible coiled-coils [3]. A biochemical study was started on h-prune. Prune-C was the only domain to be obtained stable and soluble with respect to the other h-prune domains (DHHA and DHHA2). A western blotting analysis revealed that it is sufficient to bind the Nm23-H1 endogenous protein. Therefore a structural characterization has been performed by circular dichroism, light scattering and limited proteolysis. An uniformly labeled N^{15} and C^{13} C-prune sample has been prepared and used for NMR structural analyses. At last, by using NMR spectoscopy, we determined the three-dimensional structure of C-terminal Prune (residues 353-453) and mapped the minimal region of interaction with nm23-H1. By making use of a multidisciplinary experimental approach this study provides the basis for the rational design of molecules able to take part in the interaction between H-prune and Nm23-H1 for future therapeutic specific applications in cancer and can contribute to the identification, validation and development of novel anti-metastatic agents.

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CSB-PO-25 ELUCIDATION OF THE ACTION MECHANISM OF NEW ANTIMALARIAL ENDOPEROXIDES: A DFT INVESTIGATION TO SUPPORT DRUG DESIGN.

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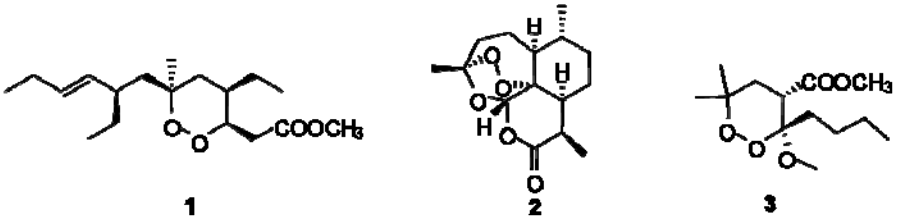
Malaria is a global health threat for about 40% of the world population, mainly located in the tropical and subtropical areas where every thirty seconds a child affected by this disease is destined to die. The therapeutic choices are still too limited for the large and poor malaria market and there is an urgent need of new and economically affordable antimalarial drugs. In this context, through a multidisciplinary approach, we designed new antimalarials based on the dioxane scaffold of plakortin (**1**).



1 **2** **3**

As the mechanism of action of antimalarial endoperoxides is not well understood yet, we performed a density functional study aiming to elucidate thermodynamic and kinetic features of our new lead compound **3** compared to reference compounds plakortin (**1**) and artemisinin (**2**). In details, the possibility of the dissociative electron transfer induced by Fe(II)-heme in the first step of the process was verified through the theoretical evaluation of the antimalarial redox potential E°. The combination of density functional theory and polarizable continuum model (PCM) of the solvent assures to obtain E° reliable values [1] against the demonstrated limits of usual experimental procedures [2]. Besides, to validate the through-space H-shift mechanism of action hypothesized in our previous studies [3], we identified the molecular species involved in the process with the aim to trace the reaction pathway. With this purpose, a DFT investigation of pre-reactive complexes, transition states and radical intermediates was performed considering all the coordination modes of iron to the endoperoxide function and different spin states of the metal.

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CSB-PO-26 The X-ray structural view of the complex between human alpha thrombin and a DNA aptamer directed to exosite II

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The aim of anticoagulant/antithrombotic therapy in cardiovascular disease is to prevent fibrin deposition and platelet aggregation, halting current and future ischemic episodes. The limitations to the effectiveness of the most commonly used agents (heparin, coumadin and aspirin) have led to the development of new anticoagulant compounds. In particular, aptamers represent an attractive approach because of their high specificity and low immunogenicity. The best known example is the Thrombin Binding Aptamer (TBA), namely $^{5'}$GGTTGGTGT-GGTTGG$^{3'}$[1]. TBA and its derivatives [2] adopt a G-quadruplex structure [2-6] and inhibit thrombin activity by blocking the fibrinogen binding site (exosite I) [3-6]. Biological properties of TBA are strictly dependent on its tertiary structure. Other antithrombotic aptamers have been identified using the SELEX process and partially characterized. Among them HD22, namely $^{5'}$GTCCGTGGTAGGGCAG-GTTGGGGTGAC$^{3'}$, is particularly interesting. It presents a 15-nucleotide core sequence that has striking similarity to TBA, and it has been reported to adopt a mixed duplex/quadruplex structure [7]. Remarkably HD22 binds thrombin with much higher affinity than TBA and has been shown to bind exosite II instead of exosite I [7]. No structural data on thrombin-HD22 complex has been reported so far. We have solved the X-ray structure of the thrombin-HD22 complex, with the aim to understand the molecular details of the interaction between the two molecules and to investigate the differences with respect to thrombin-TBA complex, whose structure we have recently determined at high resolution. These results could help the design of a new class of aptamers with an improved capability to modulate thrombin function.

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CSB-PO-27 Non-covalent interactions in organotin(IV) derivatives of 5,7-ditertbutyl- and 5,7-diphenyl-1,2,4-triazolo[1,5-a]pyrimidine as recognition motifs in crystalline self- assembly and their *in vitro* antistaphylococcal activity.

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Non-covalent interactions are known to play a key role in biological compounds due to their stabilization of the tertiary and quaternary structure of proteins [1]. Ligands similar to purine rings, such as triazolo pyrimidine ones, are very versatile in their interactions with metals and can act as model systems for natural bio-inorganic compounds [2]. A considerable series (twelve novel compounds are reported) of 5,7-ditertbutyl-1,2,4-triazolo[1,5-a]pyrimidine (**dbtp**) and 5,7-diphenyl-1,2,4-triazolo[1,5-a]pyrimidine (**dptp**) were synthesized and investigated by FT-IR and ^{119}Sn Mössbauer in the solid state and by ^{1}H and ^{13}C NMR spectroscopy, in solution [3]. The X-ray crystal and molecular structures of $Et_2SnCl_2(dbtp)_2$ and $Ph_2SnCl_2(EtOH)_2(dptp)_2$ were described, in this latter pyrimidine molecules are not directly bound to t[illegible] through N(3), to the -OH group of the ethanol moieties. T[illegible] aromatic interactions involving pyrimidine and phenyl rings in both complexes drives their self-assembly. Non-covalent interactions involving aromatic rings are key processes in both chemical and biological recognition, contributing to overall complex stability and forming recognition motifs. It is noteworthy that in $Ph_2SnCl_2(EtOH)_2(dptp)_2$ π–π stacking interactions between pairs of antiparallel triazolopyrimidine rings mimick base-pair interactions physiologically occurring in DNA (Fig.1).

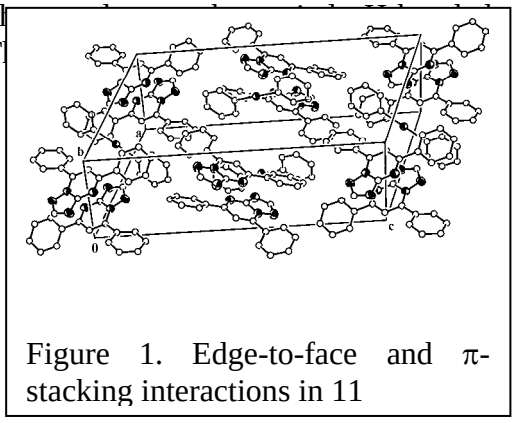

Figure 1. Edge-to-face and π-stacking interactions in 11

Mössbauer spectra suggest for $Et_2SnCl_2(dbtp)_2$ a distorted octahedral structure, with C-Sn-C bond angles lower than 180°. The estimated angle for $Et_2SnCl_2(dbtp)_2$ is virtually identical to that determined by X-ray diffraction. $Ph_2SnCl_2(EtOH)_2(dptp)_2$ is characterized by an essentially linear C-Sn-C fragment according to the X-ray all-trans structure.

The compounds were screened for their *in vitro* antibacterial activity on a group of reference staphylococcal strains susceptible or resistant to methicillin and against two reference Gram-negative pathogens [4] . We tested the biological activity of all the specimen against a group of staphylococcal reference strains (*S. aureus* ATCC 25923, *S. aureus* ATCC 29213, methicillin resistant *S. aureus* 43866 and *S. epidermidis* RP62A) along with Gram-negative pathogens (*P. aeruginosa* ATCC9027 and *E. coli* ATCC25922). $Ph_2SnCl_2(EtOH)_2(dptp)_2$ showed good antibacterial activity with a MIC value of 5 μg mL^{-1} against *S. aureus* ATCC29213 and also resulted active against methicillin resistant *S. epidermidis* RP62A.

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CSB-PO-28 Structural studies of proteins in the intracellular environment: design and characterization of suitable cell systems

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The ability to transfer complex molecules, like proteins, within cells represents a field of considerable scientific interest for both basic research and applied. Recently, the direct transfer of macromolecules in animal cells was obtained through the so-called "cell-penetrating peptides" (CPP), characterized by the property to move across cell membranes. Using advanced methods of NMR, molecular and cellular biology, it was possible to merge these peptides to proteins of interest so as to facilitate their internalization and then to obtain heteronuclear multidimensional NMR spectra of macromolecules *in vivo* at high resolution, both in eukaryotes than in prokaryotes [1]. In this way, it was possible to analyze in detail a number of intracellular events such as conformational changes and dynamic binding events between biological molecules. This study is aimed at obtaining a construct of the C-terminal domain of protein h-prune as a fusion product with a peptide for cellular internalization. The human protein h-prune, belonging to the DHH phosphoesterase protein family, induces cell motility and enhances cancer metastases and through its C-terminal region it interacts with many partners [2]. This strategy involved the use of a portion of the glycoprotein H of herpes simplex virus type 1 (HSV-1) involved in the complex mechanism of fusion between the virus envelope and host cell membrane. Biochemical and NMR spectroscopy studies showed that alpha-helical nature of this peptide is important for the interaction of the membranes and that the aromatic residues in the sequence are essential to ensure the merger [3]. The nucleotide sequence of the peptide was amplified from the genome of HSV-1 and then fused to the sequence encoding the C-terminal domain of h-prune.
Different cell strains of *E. coli*, conditions of temperature, time of induction were examined to optimize the expression levels. Size exclusion chromatography, ESI-MS spectrometry and CD analyses were used to characterize CPP-prune-C. The internalization in tumor cells was evaluated by FACS. In the future it will be essential to carry out studies of NMR *in vitro* of protein "CPP-prune-C" to obtain structural information as a starting point for subsequent experiments of *in vivo* NMR.

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CSB-PO-29 Novel supramolecular aggregates based on monoolein or diolein as target selective contrast agents.

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Magnetic Resonance Imaging (MRI) is a very powerful diagnostic imaging technique [1] giving very resolved images; unfortunately its sensitivity is very poor. During the last years, dendrimers, polymers, and supramolecular aggregates, such as micelles and liposomes, [2] all of them containing a high number of stable gadolinium(III) complexes, have been proposed as very effective contrast agents in MRI. In these high molecular weight compounds, the rotation motion of the Gadolinium complexes is slowed down with the effect of enhancing the relaxivity for each single Gd(III) complex in the compound. In order to obtain new contrast agents with enhanced properties, recently we studied supramolecular aggregates characterized by the presence of a large amount of Gadolinium complexes and of bioactive peptides exposed on their surface [3]. Here we report novel supramolecular aggregates consisting of monoolein (MO) or diolein (DO) with reversed mesophases. These particles, also termed "sponge" nanoparticles, are assumed to consist of a core of L2-(reversed micelle) phase which is stabilized by a shell of L3-(sponge) phase. In order to obtain target selective MRI contrast agents, MO or DO compositions were enriched with $(C18)_2$DTPA(Gd) monomer (from 1% to 20%) and with 3% of $(C18)_2$-Peg3000-folic acid monomer. Gadolinium amphiphilic monomer $(C18)_2$DTPA(Gd) was synthesized according to solid-phase procedures, and aggregates at several weight ratios were formulated by sonication and homogenization procedures. Structural properties of aggregates were defined by Cryo-TEM and DLS techniques. Moreover, relationship between structure and relaxometric behaviour of the sponges was clarified by HNMR and DNMR studies. Preliminary studies on the cellular uptake of sponges by confocal microscopy and by MRI are now in progress on human ovarian adenocarcinoma cell lines overespressing folate receptors.

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CSB-PO-30 Bombesin labelled Liposomes as target selective delivery system for Doxorubicin

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Conventional doxorubicin (DOX) is an established cytotoxic agent for many cancer types, in particular breast cancer. However, irreversible cardiotoxicity has been one of the primary dose-limiting toxicities for this drug [1]. A successful strategy for reducing the cardiotoxicity associated with conventional doxorubicin involves encapsulation into liposomes, which alters the tissue distribution and pharmacokinetics of these agents with the objective of maintaining efficacy and improving the therapeutic index [2]. All liposomal doxorubicin formulations (e.g. Caelyx®/Doxil®) presently marketed are based on non-specific liposomes. To increase therapeutic efficacy of the encapsulated drug and reduce potential toxic side effects on non-target cells, we suggest nanovectors decorated by Bombesin peptide able to deliver a constant dose of chemo-therapeutic agent directly and selectively to cancer cells over an extended period of time. The Bombesin receptor subtype 2 (GRPR) has been found overexpressed by tumor cell lines of several human tumors (ovarian cancers, breast cancers and prostate cancer) [3]. Many studies demonstrate that both the fourteen-residues Bombesin peptide (BN) and its eight-residues C-terminal peptide sequence ([*7-14*]BN) can be used to target these receptors. [7-14]BN containing liposomes were obtained by mixing the synthetic monomer MonY-Peg27(DTPA)-BN and two commercial phospholipid DPPC or DSPC. The development of best liposome formulation and of DOX loading procedures were reported. The cellular uptake and cytotoxicity of the targeted liposomal DOX with respect to the non-specific liposomal DOX, were evaluated in vitro on tumor PC-3 cell lines.

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CSB-PO-31 Antioxidant effect of nitroxide functionalized lipids in liposomes peroxidation

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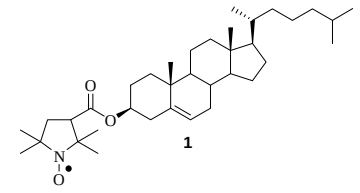
Liposomes are biodegradable and nonimmunogenic vesicular structures made of amphipatic phospholipids which can encapsulate both hydrophilic and hydrophobic materials; because of their versatility they are used as carriers in drugs and gene delivery systems. Polyunsaturated fatty acids present in the bilayer are susceptible to oxidative damage which can alter some important properties like fluidity and permeability and can cause system delivery destruction. The mechanism of lipids oxidative degradation may involve free radical reactions that lead to changes in the unsaturated systems present and eventually to the degradation of the lipid chains. In order to maintain their physical, chemical and functional properties, liposomes need to be protected by antioxidant compounds that can delay or prevent oxidation upon reaction with radical species. Nitroxide radicals are known to protect against oxidative processes in different media and under different stress conditions [1]. As part of our ongoing research in the field of non viral vectors for DNA delivery [2] we synthesized the neutral non zwitterionic lipids 1 and 2 which bear a nitroxide function able to react with radical species. Multilamellar liposomes were prepared by mixing the new lipids with PC and other commercial neutral zwitterionic lipids. Lipid peroxidation was induced by thermal decomposition of the free radical generator AAPH and evaluated using the TBARS assay. The results obtained clearly indicate that both lipids efficiently inhibit PC peroxidation and are better antioxidants than nitroxides (higher % inhibition of TBARS production). In view of a possibile use of liposomes as DNA transfection agents, the liposomes containing nitroxide lipids were complexed with DNA in the presence of bivalent Ca^{++} cations. Ternary complexes formation was investigated by means of synchrotron X-ray diffraction and the antioxidant effect of the functionalized lipids was also studied in these systems.



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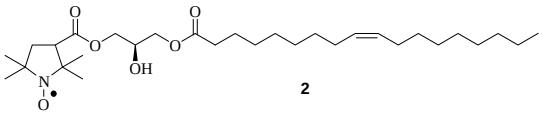

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Chimica Teorica e Computazionale

CTC-KN-01 The polarizability and hyperpolarizability of C and BN nanotubes.
A quantum-mechanical simulation.

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The polarizability, the first and second hyperpolarizability of BN and Carbon nanotubes of the (n,0) family have been evaluated by using a quantum-mechanical approach, a Gaussian basis set and the CRYSTAL code [1]. The Coupled Perturbed Hartree-Fock or Kohn-Sham Self Consistent perturbative schemes [2-3] have been implemented and applied to tubes of increasing radius (from (6,0) to (60,0)) [4,5]. The pure electronic and the ionic contributions have been evaluated, the latter through the FF-NR (finite field nuclear relaxation) scheme proposed by Bishop and Kirtman [6,7]. Longitudinal and transverse components of the three tensors are considered. Five different Hamiltonians (Hartree-Fock, LDA, PBE, PBE0 and B3LYP) are compared. The evolution with the tube radius is considered, and the trend towards the limit of infinite radius (that is, the hexagonal BN or the graphene monolayer) explored.

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CTC-KN-02 Steady-state and time-resolved spectroscopy by excited state ab-initio dynamics

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We discuss our recent progress in simulating steady-state and time resolved spectroscopy by equilibrium and non equilibrium excited state ab-initio dynamics. In particular, we debate the capability of excited state Born-Oppenheimer dynamics[1,2] to properly describe the solvent reorganization following a sudden change of the local electric field, due to electronic excitation of a solute. The focus is on optical spectroscopy and on the potentiality of solvatochromic fluorophores to act as molecular probes.[3,4] Study cases are illustrated.

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CTC-KN-03 Modeling molecule-based devices using Density Functional Theory

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The performances of Density Functional Theory (DFT) and Time-Dependent DFT (TD-DFT) for the prediction of photophysical properties of molecule based devices are here reviewed taking as an example two classes of compounds used either as Photochemical Molecular Devices (PMDs) or as dyes in dye-sensitized solar cells (DSSCs). In the case of PMDs the topology adopted for the novel systems proposed derives from that of acceptor dyads devised to produce charge separated states constituted by an electron withdrawing moiety (A) covalently linked to a photosensitizer (P). Both the properties of existing dyads as well as those of new acceptor units eventually functionalized with magnetic substituents, will be analyzed. In this case various mechanisms of magnetic coupling, as a function of the topology of the acceptor units, will be discussed. The performances of different approaches in reproducing both magnetic coupling and spectral properties will be reviewed. [1-5]. In the case of DSSCs, the performances of DFT and TD-DFT for the study of the photophysical properties of dyes in complex environments (i.e. when adsorbed on semiconductor, such ZnO and TiO_2) are shown via two examples [6-7]. A general protocol for the in-silico optimization of dyes for DSSCs applications is proposed [8].

Finally, some possible methodological developments based on the use of a Spin Flip approach will be discussed.

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CTC-KN-04 Oxygen activation by oxides at the nanoscale

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The properties of materials change when the dimensions are reduced at the nanometer level. This is true also for oxide materials in the form of ultrathin films on metals or of nanoparticles. Here we discuss three cases, all related to the capability to activate oxygen molecules and facilitate oxidation processes by nano-oxides. In doing this we combine DFT calculations with sophisticated experiments. The first two cases deal with oxide ultrathin films. We report recent results which show the spontaneous formation of superoxo radical anions, O_2^-, by simple adsorption of molecular oxygen on 2-3 layers of MgO grown on Mo(100) [1]. The process involved is the spontaneous tunnelling of electrons trough the MgO thin film and the process is of general importance in the field of oxidative catalysis.

The second example is related to monolayer FeO(111) films grown on Pt(111) which efficiently promote low temperature CO oxidation [2,3]. The proposed mechanism includes adsorption of O_2, formation of O_2^-, and oxidation of the bilayer FeO film to a trilayer O-Fe-O film. Under CO and O_2 pressures, this system catalyses CO oxidation to CO_2 via a Mars – van Krevelen type mechanism. The reaction is possible only thanks to the high flexibility of the FeO thin layer, a typical property of ultrahin oxide films not present in bulk surfaces.

The last example is related to oxygen activation on stoichiometric and reduced CeO_2 nanoparticles. The interaction of O_2 with the regular CeO_2(111) surface is very weak, while a strong bond occurs with O vacancies (reduced ceria). On O vacancies (two-electron centers), however, only peroxo, O_2^{2-}, and not superoxo species form. We show that superoxo ions can form on reduced ceria nanoparticles where single excess electrons are localized on low-coordinated Ce^{3+} ions. The interaction of O_2 with these one-electron centers leads to the formation of paramagnetic O_2^- ions [4,5].

These three examples show the importance of dimensionality on the catalytic properties of oxide materials.

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CTC-KN-05 The Excited State Decay in DNA: Quantum Mechanical Calculations on Realistic Polynucleotide Models

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The dynamical properties of the excited states of DNA and of nucleobases have been extensively investigated in the last years, triggering a very lively scientific debate, especially concerning the decay in single and double DNA strand [1,2]. In the last years we have tried to describe, at a Quantum Mechanical level, systems as close as possible to those studied by experimentalists.[3-8] For example, we have studied the excited state decay of a meaningful model of polyAde-polyThy double strand (the Ade_2-Thy_2 tetramer) in aqueous solution.[6,7]
By characterizing the main excited state decay routes of a tetra-nucleotides $(dA)_4Na_3$, fully treated at the QM level, we have recently obtained an unifying description of the dynamics in A-based polynucleotides, giving account of all the main available experimental results, showing that their behaviour is ruled by the equilibrium between 'neutral' and 'charge transfer' excimers.
The study of the most significant decay routes in dinucleotides of Thymine $(dT)_2$ provides instead useful insights on the effects ruling the formation of cyclo-butane dimers and of 6-4 adducts, i.e. the most significant lesions formed in DNA following the UV absorption.

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CTC-KN-06 Computer Simulation Study of Dynamic Crossover Phenomena in Supercooled Nanoconfined Water

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In order to study the dynamic crossover phenomena in nanoconfined water, we performed a series of molecular dynamics (MD) computer simulations of water clusters adsorbed in zeolites, which are microporous crystalline aluminosilicates, whose channels and cavities are of nanometric dimensions.
We used a sophisticated empirical potential for water, including the full flexibility of the molecule and of the aluminosilicate framework was included in the calculations [1,2].
The results of the simulations of water confined in a variety of zeolites (worm-like clusters in silicalite[1], spherical nano-clusters in zeolite A [3], cross-linked nanowires in NaX and ice-like nanotubes in $AlPO_4$-5 and SSZ-24 [1]) at different temperatures and coverage (*loading*) are discussed in connection with the experimental data. Preliminary results of Car-Parrinello MD simulations of water in vermiculite clay are also shown.
In particular, dynamic crossover phenomena are found for the adsorbed water in all the considered cases, in spite of the different shape and size of the clusters, even when the confinement hinders the formation of tetrahedral hydrogen bonds for water molecules. They were evidenced by inspecting the trends of rotational relaxation constants and of spectral contributions to vibrational spectra *vs.* temperature.
Dynamical crossover temperatures were detected around 220 K and 160 K, corresponding to those found experimentally in many hydrated systems, such as aqueous solutions, oxide surfaces, clays, proteins and cement paste. Based on a detailed analysis of the single-molecule dynamical behaviour, hypotheses about the possible dynamic crossover mechanisms are proposed.

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CTC-KN-07 Theoretical Modelling of Electron Transfer Reactions in Complex Molecular Systems.

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Modeling of electron transfer (ET) reactions in complex atomic-molecular environment have always represented a challenge for computational-theoretical physical chemistry. The main reason for that probably resides in the fact that many of the experimental observations regarding ET thermodynamics and kinetics usually involve purely quantum events, i.e. the electron dynamics, somewhat coupled with the classical and semi-classical atomic-molecular degrees of freedom.
As a consequence a physically coherent modeling of this kind of reactions should take into account different events occurring on very different energy and time scales. If one wants to avoid brute-force dynamical calculations to this problem, which are still far from providing reasonable numbers for molecular systems with more than a couple of atoms with few electrons, alternative theoretical and computational tools are necessary. The most popular and efficient approach to address ET reactions rely on the seminal work of Marcus and much of the kinetics is modeled within the framework of the Fermi Golden rule. In this respect a huge amount of computational data have been, and are still being produced. However, despite the successes of Marcus theory, probably further efforts are still necessary for improving our ability of reproducing the complexity of the experimental observable. In particular the coupling with the atomic-molecular fluctuations might be not always reducible to simple analytical forms.
In the last few years we have been working for developing a new computational-theoretical methodology, somewhat complementary to Marcus model, essentially based on a joint application of Molecular Dynamics simulations and Quantum-Chemical calculations and making use of the basic concept of the Diabatic Perturbed Energies to approximate the evolution of the Electron Transfer. In this talk the theoretical basis of the method and two applications, one concerning the equilibrium properties of ET reaction and the other one focused on the modeling of non-equilibrium (kinetics) observables, will illustrated and commented.

CTC-OR-01 Roto-vibrational Characterization of Heavier Protonated A*rgonons* by the Relativistic CCSD(T) Method

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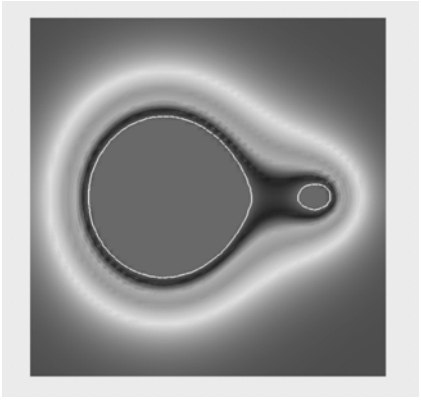

Already in 1933 Pauling inferred the existence of a peculiar chemistry for the heavier inert gas, [1] namely for Kr and Xe and potentially for the radioactive Rn. He also suggested to name them *argonons* (*Rg*s), to move out their claimed nobility and/or inertia. In fact, the first ionization energies of the heavier *Rg*s are in-between those of B and N, being that of H smaller than that of Kr but larger than that of Rn and Xe. H*Rg*X species, with X non-hydrogenic atoms, have been characterized spectroscopically, [2] showing a significant although not dominant RgH^+ component, further investigated deeply. [3]

The electronic structure and the spectroscopic roto-vibrational properties of protonated heavier *Rg* species (RgH^+) have been here calculated, employing a fully relativistic coupled-cluster approach with single and double excitations and a perturbative treatment for triple excitations [CCSD(T)]. Roto-vibrational constants have been obtained by the Dunham analysis performed on the calculated potential energy curves, showing a very good agreement with the available KrH^+ e XeH^+ experimental data. This clearly allows for confidence in the calculated results obtained for the experimentally not characterized RnH^+ species that, as a consequence, could be used for designing spectroscopic experiments, never realized so far. The parameters calculated at relativistic level were compared to the corresponding ones, got without considering relativistic effects. In addition to the expected behavior – concerning the dissociation paths ($Rg + H^+$ and $Rg^+ + H$) characterizing the different RgH^+ species ascribable to the *argononic* potential energy behavior and spin-orbit coupling – the comparison among the protonated *Rg*s also reveals relativistic effects i) on the fundamental vibration frequencies, ii) on the dipole moments and finally iii) on various higher order spectroscopic properties, referable to the differences present in the potential energy curves.

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CTC-OR-02 Carbon dioxide internal energy exchange in earth and planetary atmospheres and hypersonic flows

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The vibrational energy exchange occurring in collisions involving small molecules is largely responsible for energy relaxation and state population of gas phase, and therefore plays a key role in determining the energy balance of planetary atmospheres (see e.g. [1]).
Carbon dioxide is an important component of planetary atmospheres. Being a triatomic molecule, the exchange of internal energy upon collision can be relevant and is a key step in its contribution to the energy balance of the atmospheres. Therefore the behaviour of CO_2 in inelastic collisions with itself or other species such as N_2 and CO deserves considerable interest and finds interesting applications in plasma chemistry and hypersonic aerodynamics.
The first step of the study has been concerned with the assemblage of an appropriate Force Field. To this end electronic structure calculations have been performed at a CCSD(T) level to integrate previous MP2 results [2]. Related information has been used to build a semiempirical potential energy surface (PES) that makes use of a recently introduced bond-bond approach [3].
Due to the important effects of long range interactions on vibrational relaxation and excitation, intermolecular interactions have been formulated using a well tested bond-bond interaction model [3], which reproduces with accuracy short and log range parts of the intermolecular interactions.
The resulting PES has been exported into the VENUS [4] program, and extended ensembles of quasi-classical trajectories (QCT) have been run for the CO_2 + CO_2 collisions in a wide range of energies. Results are targeted to calculate state-to-state vibrational exchange cross sections and thermal rate coefficients. These quantities are the necessary input of kinetic models of use in gas dynamics, aircraft re-entry studies, and many other technological applications.

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CTC-OR-03 ONIOM calculations for electronic excited states.

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The accurate evaluation of electronic transition energies and properties requires the use of computationally expensive methods like the equation of motion coupled cluster singles and doubles (EOM-CCSD). However, the scaling of such methods often makes the study of molecules larger than 10–15 heavy atoms prohibitive, and more approximate approaches must be pursued. The ONIOM (Our own N-layer Integrated molecular Orbital molecular Mechanics) hybrid method, where the system is partitioned into regions which are treated with different levels of theory, represents a promising approach to completely characterize valence excited states of large molecules that cannot be entirely studied with a conventional high-accuracy method. In this contribution we present a series of results that validate the ability of ONIOM(QM:QM) to compute accurate transition energies and oscillator strengths compared to EOM-CCSD [1-3]. We test the effect of various choices of partitioning, low level methods and basis sets, as well as how the link atom bond length can affect the results. ONIOM is compared to conventional calculations with the CIS, TDHF and TDDFT methods. It is shown that the best accuracy-computational time combination is obtained with ONIOM(EOM:TDDFT).

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CTC-OR-04 NMA in aqueous solution using a portable intermolecular potential

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Molecular Dynamics were carried for N-methylacetamide (NMA) in water out using a modified DL_POLY 2.20 molecular modeling package[1]. The system was investigated by running a series of simulations on a different X_{NMA}.
The MD simulations were performed with AMBER[2] charges for the NMA system and forthe water we have used the intermolecular potential for non rigid molecules[3].
Initial configurations for each ofthe concentrations were obtained by placing the correct numbers of *trans*-NMA and water molecules randomly on approximately
30 Angstroms lattice.The total intermolecular interaction was assembled by adding the corresponding electrostatic (V_{el}) and non electrostatic (V_{nel}) contributions. V_{el} is expressed in terms of Coulomb potential of the punctual charge distribution of different molecules while V_{nel} is expressed in terms of effective potentials formulated as an Improved Lennard Jones (ILJ) function[4]:

$$V_{ILJ} = \varepsilon \left[\frac{m}{m-n(r)} \left(\frac{r_m}{r}\right)^{n(r)} - \frac{n(r)}{m-n(r)} \left(\frac{r_m}{r}\right)^{m} \right] \quad n(r) = \beta + 4.0 \left(\frac{r}{r_m}\right)^2$$

in which the additional β parameter, with respect to the usual formulation of the Lennard Jones (LJ) potential, removes most of inadequacies of the LJ function.

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CTC-OR-05 Structure and Dynamics in Y:$BaZrO_3$ Protonic Conductor

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Yttrium-doped barium zirconate protonic conductor seems to be a good candidate as electrolyte ceramic materials for high technological devices [1]. *Ab initio* computational models of singly and doubly substituted Y:$BaZrO_3$ structure have been built and tested. Only in presence of two nearest neighbour yttrium atoms, the relative energy di erences of stable protonic sites reproduced the correct order of magnitude of activation energy values related to the proton hopping.
Ab initio results on $BaZrO_3$ derivatives were the basis of MD simulations performed on yttrium-doped barium zirconate. Dynamics simulations showed a peculiar oxygen sub-network that changed its characteristics up to a temperature value, which depended on the yttrium content. Protonated models having neighbouring yttrium atoms were able to mimic the experimental activation energies characterizing protonic conduction, while oxygen atoms could be grouped into three clusters with peculiar structural features. In particular, two clusters behaved like a multilevel trap for the proton, delaying the di usion of the latter across the material bulk. A characteristic of these traps was the very large number of proton hopping events, occurring per time unit among oxygens surrounding yttrium atoms.

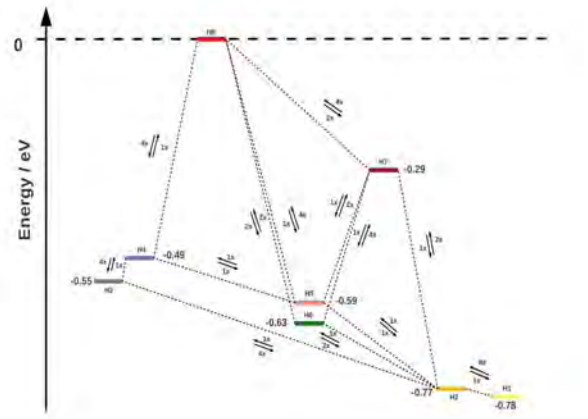

Figure 1. Energy diagram for doubly doped systems.

These results, finally, suggest that yttrium clustering, inferred for Y:$BaCeO_3$ systems [2], seems to also occur for the Y:$BaZrO_3$ derivatives; eventually, protonic conduction in these materials could be improved avoiding such clustering, that is preventing the formation of protonic traps.

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CTC-OR-06 Coverage-dependent reactivity toward oxygen of Iron Phthalocyanine on Ag(110)

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In the last decade, non-precious metal compounds able to catalyze the oxygen reduction reaction (ORR) have attracted a great deal of attention as a consequence of their potential technological application as cost-effective replacement for Pt-based catalysts in low-temperature fuel cells. Actually, it is well known that Iron porphyrins (P) and phthalocyanines (Pc) can promote the reduction of O_2 to H_2O, even though their catalytic activity is lower than that of precious metal compounds and they are almost inert when supported on a substrate other than edge-plane graphite [1].
In this communication, we present a combined experimental and computational study of an ordered network of FePc adsorbed on Ag(110), able to react with O_2. The system was characterized by means of XPS, XAS and STM techniques as well as by Density Functional calculations on slab models of the adsorbed phases. The FePc molecules self-organize on the Ag(110) surface at room temperature. Two different assemblies were observed: the FePc submonolayer exhibited a c(10×4)/p(10×4) arrangement whilst, in the proximity of one monolayer, a more compact (1 4, 4 -3) phase emerged [2]. Furthermore, it was found that, at low-coverage, the FePc units react with O_2 inducing a dramatic change of the STM intramolecular features. Interestingly, such a reaction did not take place at higher coverages. The theoretical modeling of the FePc/ Ag(110) interface ultimately shows that the reactivity of FePc toward oxygen is ruled by the Fe local environment.

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CTC-OR-07 Modeling proton transfer in Proton Exchange Membrane Fuel Cells: a combined DFT/MD approach

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The performances of Proton Exchange Membrane Fuel Cells (PEMFCs) are strongly influenced by the proton conductivity of the solid electrolyte. The N-heterocycles based polymers are today the most promising materials to improve the effectiveness of these systems. A protocol based on Density Functional Theory (DFT) to study azole-based systems is proposed [1]. A detailed theoretical investigation performed on Poly(4-vinyl-imidazole) (P4VI) indicates that the commonly accepted mechanism (Grotthuss) could be hindered in this system because of the backbone constraint. Classical Molecular Dynamic simulations support an alternative mechanism of conduction hypothesized. This latter involves a rotation of the protonated imidazole, constituting the rate-limiting step, before each proton transfer reaction between adjacent azole-moieties can take place (Figure 1). These new insights into the mechanism of conduction are relevant for a rational design of modified azole-based systems used in PEMFCs.

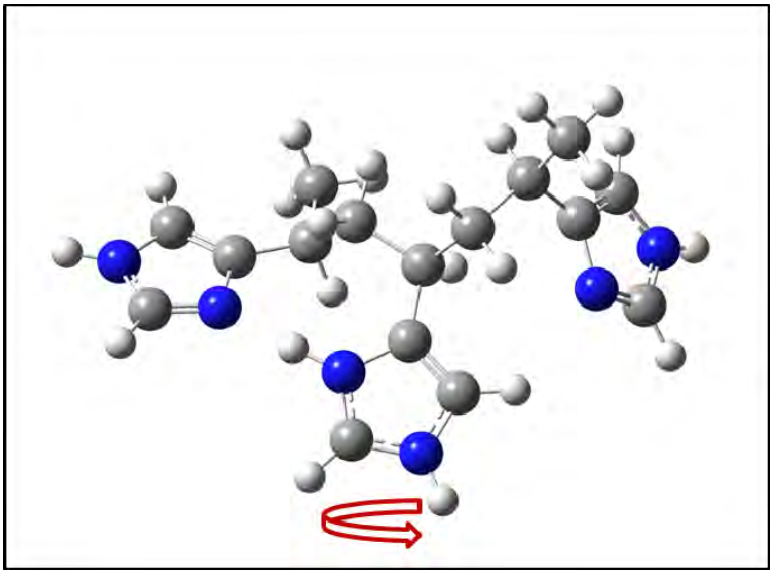

Figure 1

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CTC-OR-08 Tuning charge transfer in model bio-inspired porphyrin-carotene dyads

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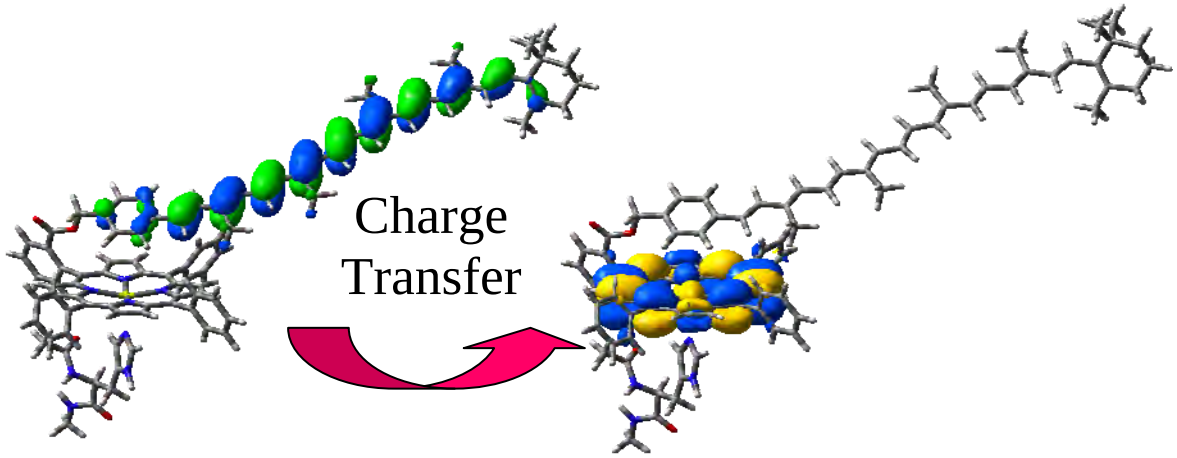
We present a computational study on model bio-inspired donor-acceptor (DA) dyads formed by a carotenoid (C) covalently linked to a tetraphenylporphyrin (TPP) at the *ortho* position of one of the TPP phenyl rings [1]. The mutual orientation of the components and their distance closely resembles the geometry of the dyad chlorophyll-peridinin in PCP [2]. Dyadic systems are intensively studied for potential application in the construction of organic solar cells and development of efficient photocatalytic systems for the solar energy conversion for the unique advantages they offer with regard to synthetic feasibility. The recent progress in computational methodologies, especially the development of DFT rooted methods suitable to describe charge transfer (CT) processes, allow to perform systematic investigations *in silico* of those molecular features which might be important to design high performance bio-inspired artificial devices.



Focussed on CT process, this study aims (i) at better understanding the effect of slight chemical modifications on the absorption spectra, in particular on the lowest CT bands, as well as (ii) at gaining deeper insight on the role of H_2O and hystidine (Hys) in the biological system. The coordination of H_2O or Hys might occur in two different positions: it can be sandwiched between the carotene and the porphyrin ring or can be coordinated to the metal under the porphyrin plane. The effect of different metals of biological interest is also investigated to rationalize the fine tuning of the CT process.

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CTC-OR-09 Mechanistic Insight into Protonolysis of Dimethylplatinum Complexes. A DFT Study

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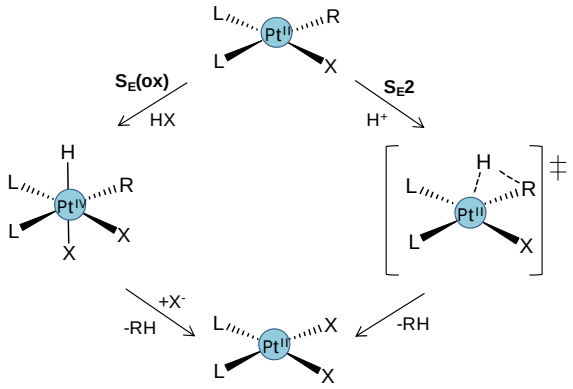
Development of catalysts able to selectively transform hydrocarbons to value-added products is among the most fundamental challenges in chemistry. The understanding of the mechanism of the protonolysis of the Pt-C bond of alkyl Pt(II) complexes, as the *microscopic reverse* of C-H bond activation process, can be considered a part of the efforts devoted to shed light on the mechanistic aspects of alkane C-H bond activation. To date it is still a difficult challenge to obtain experimentally direct and accurate insight in the mechanistic pathways of chemical reactions due to the very short lifetime of key intermediates. Obviously this holds also for the reaction we are addressing here. Computational studies do not suffer from these limitations and provide therefore a valuable complementary tool with respect to experimental studies. The outcomes of a detailed theoretical investigation, aiming to give a contribution to the debate on the mechanism of the electrophilic cleavage of the Pt-C bond, are presented. Energy profiles have been calculated, and compared with experimental observations, for the protonation and subsequent methane elimination reactions of a series of dimethylplatinum(II) complexes as a function of the nature of the ancillary ligands and solvent. The possibility to rationalize and predict the preference for a stepwise oxidative, $S_E(ox)$, or a concerted, S_E2, route has been examined. Theoretical calculations suggest that HOMO nature, *d* metal based or σ-bond localized, is the main factor in determining the preferred protonation site, platinum or carbon atom, and then the preferred protonolysis mechanism.



Scheme

CTC-OR-10 Possible mechanistic paths of the enzymatic activity of GPx

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Glutathione peroxidases (GPx, Fig. 1) belong to a widespread family of proteins that, over the years, have been discovered in almost all kingdoms of life.[1] They catalyze the reduction of H_2O_2 or organic hydroperoxides to water or corresponding alcohols, thus mitigating their toxicity.[2] The global reaction is ROOH+2GSH → GSSG+ROH+H_2O, where GSH indicates glutathione. In the GPx family the active site SeCys or Cys is surrounded by highly conserved residues (Asn, Gln and Trp) forming the catalytic tetrad. One of the main open questions is about the specific role of either SeCys or Cys in the catalysis: it is not yet clear why selenium rather than sulphur has been chosen by nature selection given that a complex and energetically very expensive co-traslational insertion machinery for SeCys is needed.

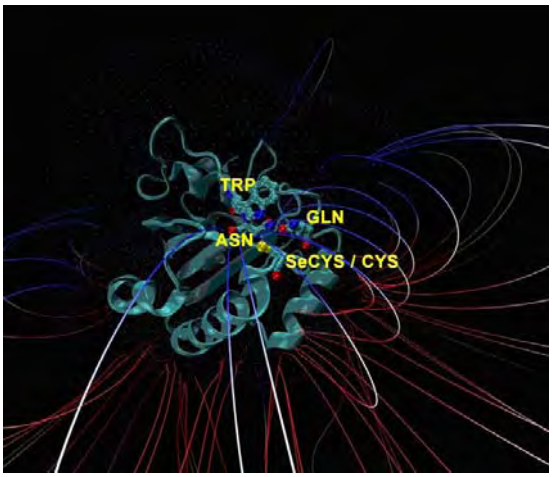

Fig. 1 GPx

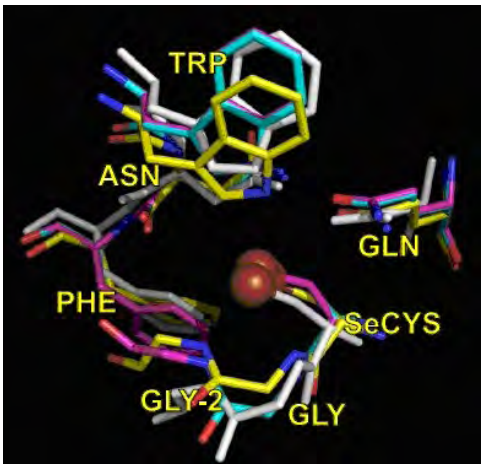

Fig. 2 Model catalytic site

The basic catalytic scheme involves three main steps, i.e. (i) O-O bond cleavage and formation of selenenic/sulphenic acid Se/S-OH and ROH; (ii) formation of a seleno-sulfide (disulfide) intermediate and elimination of H_2O; (iii) formation of the disulfide product and regeneration of the catalyst.
We present a detailed investigation of different possible paths of the reduction of H_2O_2 catalyzed by Se-based as well as S-based GPxs with the aim of validating at quantum chemistry (DFT) level the experimental findings obtained by recent mass spectrometry and biochemistry methods (enzymatic kinetics); a core of seven aminoacids has been identified, which suitably represents the GPx core (Fig. 2). From our results a complex energy landscape emerges, where novel mechanistic paths are possible and novel perspectives on the intriguing behaviour of GPx can be outlined.

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CTC-OR-11 H_β-termination mechanisms in living catalysis of polyolefin at *ab-initio* level

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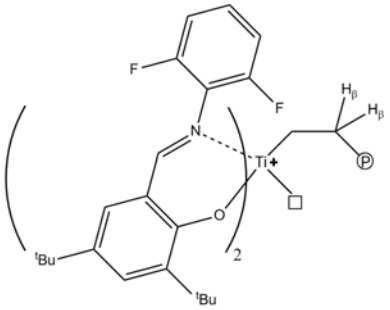
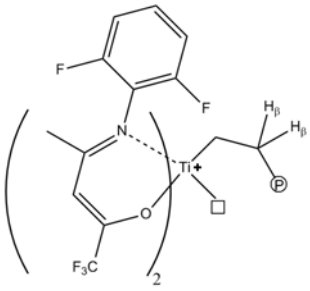
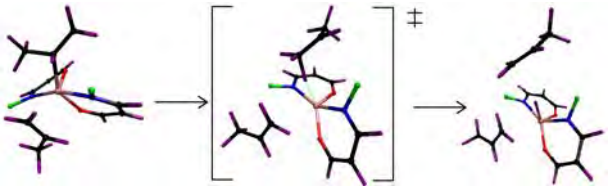
Fujita[1] has been the first to highlight the living behavior of Ti-bis(phenoxyimine) catalysts in the polymerization of ethylene, and proposed the role of an hydrogen-bond between aromatic *o*-fluorine and H of the growing chain in the H -transfer inhibition. Coates[2] demonstrated the living behavior of non fluorinated catalysts, showing an active role of the chelating ligands in this context.





Recently, Mecking[3] showed that the simpler catalyst Ti-bis(enolatoimine) with *o*-fluorinated aryl groups is able to achieve a living behavior and proposed via NMR studies a key role of the H-bonds between *o*-F and either H atoms or Ti in the suppression of the H -termination.
In our recent works[4,5], we analyzed via DFT a number of models for Ti-bis(phenoxyimine) and Ti-phenoxyarylpyridine catalysts and studied the insertion mechanism and the role of F interactions.
Currently, we are investigating the mechanism of H -transfer inhibition, necessary to achieve the living polymerization behavior. We studied both Fujita's and Mecking's catalysts with living or non-living behaviors.
Ab-initio calculations were performed on parallel platform using GAUSSIAN09.
Minimum energy profiles have been computed, in which one or two selected internal coordinate(s) are scanned. In all cases, the stationary points (minima and transition states) were localized and energy barriers of activation determined.
A deep investigation of the different termination mechanisms has been performed, and insight about the reasons for each of them taking place is proposed.



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CTC-OR-12 Natural and Artificial Photosynthesis: Computational Studies

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Nature has solved the difficult problem of efficient light-driven, four-electron oxidation of water to O_2, by means of a Mn-based catalyst embedded in the Phostosystem II (PSII), a ~350 kDa complex of 20 proteins. The Mn_4CaO_5 cluster of the oxygen-evolving complex (OEC) of PSII is composed of inexpensive earth-abundant metals (Mn and Ca) and features high turnover rates that are still unmatched by artificial water splitting systems. Elucidating its detailed molecular structure and the catalytic mechanism of photosynthetic water oxidation is crucial for developing new biomimetic catalysts for renewable solar-energy conversion.

Computational modeling studies, including density functional theory (DFT) combined with quantum mechanics/molecular mechanics (QM/MM) hybrid methods, have proposed chemically satisfactory models of the fully ligated OEC Mn-cluster that are maximally consistent with experimental results [1]. Mechanistic investigations of the water-splitting reaction of the OEC have been fundamentally informed by structural studies of oxomanganese complexes. In particular, the $[H_2O(terpy)Mn(O)_2Mn(terpy)OH_2]$(terpy is 2,2′:6′,2"-terpyridine) complex, is a multi-turnover homogeneous water-oxidation catalyst and an excellent functional model of the OEC [2].

This talk summarizes our recent advances on studies of PSII and biomimetic oxomanganese complexes for artificial photosynthesis. Our computational studies [3,4], including DFT, QM/MM methods, classical Molecular Dynamics (MD) and Monte Carlo simulations, are based on the recent crystal structure of PSII at 1.9 Å resolution [5]. We have introduced a novel model for the OEC resting state [3] and elucidated the structural/functional role of chloride cofactor in PSII [4]. The implications of these findings on the water-splitting mechanism in both homogenous and enzymatic reactions will be discussed.

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CTC-OR-13 Monomeric and Collective Deactivation Mechanisms in Photoexcited DNA Investigated by a Quantum Dynamical Approach.

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Sunlight is essential to life but it is also a potential carcenogenic agent, and evolution has selected highly photostable molecules to encode the genomic information. Their photostability is ensured by highly efficient decay pathways that are able to transform the electronic excitation into vibrational energy and finally into heat. The deactivation mechanisms of the single nucleobases after the $\pi\pi^*$ excitation has been deeply investigated experimentally and show multi-exponential features ranging from fs to ps timescales [1]. Here we report the results of our recent static [2] and quantum dynamics investigation of the role of $n\pi^*$ in the decay of Uracil derivatives both in gas-phase [3] and in different solvents [4-5]. Potential energy surfaces have been characterized by TD-DFT, while solvent effect has been accounted by mixed atomistic/continuum models.
The understanding of the dynamics of isolated nucleobases is the necessary pre-requisite for a full comprehension of the deactivation processes in the real bio-polymers, where nonetheless inter-bases interactions modify the efficiency of the single-base decays and open new competitive pathways. In fact long-living excited states, up to the nanosecond timescale have been identified in DNA oligomers, while they are absent in single nucleobeases [6]. Recently, we performed TD-DFT studies in water solution of the excited states of adenine stacked dimers [7], and of tetramers made up of adenine-thymine base-pairs [8]. From these data we derived a vibronic Hamiltonian to study, at quantum dynamical level, the interplay between excitonic and charge-transfer states in the decay mechanism, and we applied it to dimers and oligomers [9]. Quantum dynamical calculation have been carried through traditional Lanczos based propagation schemes and/or a self-made implementation of MCTDH method [10]

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ORG/CTC-KN-01 Bridging the Gap between Theory and Experiment: Modeling Chiroptical Properties and Spectroscopies

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The tremendous progress of ab-initio quantum chemistry in the last decades has led to an increasing number of applications of quantum mechanical (QM) approaches to the calculation of chiroptical properties [1-7].
The progress has been so large that a ‘‘renaissance’’ in chiroptical methods due to the accuracy and computational efficiency achieved by ab initio QM methods in reproducing experimental data and predicting new ones has been invoked [8].
In this contribution, some peculiar aspects of the computation of chiroptical properties and spectroscopies are remarked through the analysis of case studies, with special emphasis towards the gaining of calculated data directly comparable to experiments, by the inclusion of solvation and vibrational effects.

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ORG/CTC-KN-02 Structural Basis for the design and synthesis of selective HDAC inhibitors.

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Protein lysine acetylation is a key mechanism in the epigenetic control of gene expression, the regulation of cell metabolism[1,2], and protein deacetylases are potential targets for treating cancer and a range of autoimmune and neurodegenerative diseases[3]. In this context, the HDAC inhibitors have attracted the attention of the researchers as promising anticancer agents [4,5]. Based on sequence phylogeny and function, there are four distinct classes of HDAC: class I (HDAC1, 2, 3 and 8), class IIa (HDAC4, 5, 7 and 9), class IIb (HDAC6 and 10) and class IV (HDAC11) represent Zn^{2+}-dependent amidohydrolases, whereas class III comprises the mechanistically diverse NAD+-dependent sirtuins [6]. In this contribute, we have traced out the structural elements responsible of selective binding in the whole landscape of the HDAC isoforms considered interesting therapeutic targets. In particular, we have rationalized experimental observations and tried to systematically add new insights for a targeted design of selective inhibitors for the different HDAC isoforms. In detail, we have focused our attention on all HDACs zinc dependent enzymes, except HDAC5 and HDAC9-11, for which few information on expression, function in tumor cells, and ligand inhibitory profile are available in literature. The structural analysis was performed by molecular docking calculations, using as ligands known pan and class selective HDAC inhibitors [4]. Based on the obtained structural guidelines, we designed, synthesized and experimentally tested selective inhibitors for HDAC2.

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ORG/CTC-OR-01 The Structure of Ionic Liquids Based on Geminal Imidazolium: a Theoretical Study

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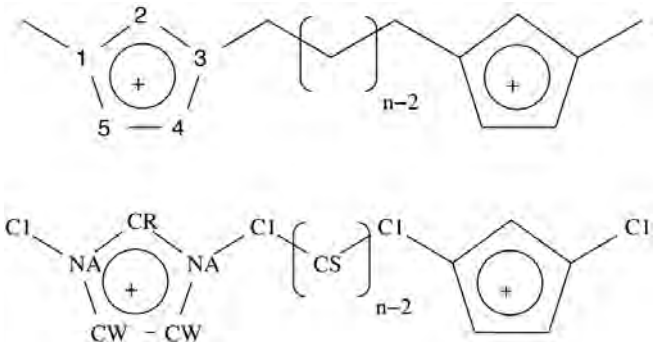
Among the most exciting and successful materials developed and studied in the last twenty years, ionic liquids [1] are among those that can certainly claim one of the most rich field of applications in industry and in applied technological research. A special class of ILs is have recently been obtained using geminal imidazolium dications [2] that represent a very interesting variation of the cationic partner and that may present various advantages over the traditional mono-cationic ionic liquids in applications such as lubricants, catalyst, solvents and as separation media.



A schematic view of the molecular structures is reported above: we have a linkage chain (whose length can be 3, 6, 9 or 12 for the compounds analyzed in the present work) that connects two imidazolium rings with a net positive charge on them and that are substituted with a methyl group. We have recently [3] analyzed the behavior of such compounds by calculating the structures of the gas phase complexes. We will report these and further results obtained by means of MD simulations.

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ORG/CTC-OR-02 Chemoinformatic strategies in the design of new antibacterials active against multidrug resistant Gram-positive pathogens.

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Chemoinformatic strategies possess great potentialities in modelling the interactions between biopolymers and ligands. Molecular recognition plays in fact a fundamental role in drug-receptor interactions.
Due to the lack of pharmacological targets, in previous studies [1] we adopted a Virtual Receptor Site (VRS) approach, where ligands interact with a complex receptor of unknown structure, aimed at identifying pieces of the structure which could be valuable for improving the antibacterial activity.
In the design of new drugs it is also very important that they exhibit ADME (Adsorption, Distribution, Metabolism, Elimination) properties warranting an acceptable bioavailability. For this purpose, a new method, called VOLSURF [2], able to correlate 3D molecular structures with physico-chemical properties, and highly efficient in predicting the biological activities, appears to be appropriate.
According to the advances achieved in the past two years due to the availability of the x-ray structures for a few drug targets, molecular modelling by docking of new ligands to the receptor active sites appears nowadays an appropriate strategy in the design of new antibacterials against multidrug resistant strains.
In this context, we adopted a recently developed algorithm called Fingerprints for Ligands and Proteins (FLAP) that can be used to describe proteins and ligands based on a common reference framework [3]. FLAP is able to explore the 3D-pharmacophoric space of ligands and proteins and to provide quantitative information for the complementarity of their interactions to allow ligand-ligand, ligand-protein, or protein-protein comparison. By means of all these chemoinformatic tools, we studied the interactions between synthetically accessible compounds and the crystallographic structure of Linezolid binding protein to identify a scaffold that we could modify introducing different substituents to improve the *in vitro* antibacterial activity.

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ORG/CTC-OR-03 Revisiting Nucleophilic-Electrophilic Mechanisms in Oxidation Reactivity

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Oxidation chemistry has always been one of the most important playgrounds for the interpretation and mastering of reactivity.[1] The interest of scientists has been driven not only by the strong implications that this reactivity plays in biological systems, but also because it represents an essential tool in functional groups transformation. These studies have also deeply contributed to the development of the basic principles of reactivity.
In recent years we have been involved in the study of metal catalysts for oxygen transfer reactions.[2] The experimental results have offered us the possibility to investigate in detail the mechanism of oxidation reactions, and in particular to study the effect of intermolecular interactions in catalysis.[3]
The evaluation of these experimental results, with the support of theoretical calculations, have led to a reinterpretation of the concept of nucleophilic and electrophilic reactivity in oxidation chemistry. This analysis can have implications that go beyond oxidation chemistry

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ORG/CTC-OR-04 L-Arabinose adsorption on a Ru cluster

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Use of bio-mass for energy, chemicals and material supply is one of the key issues of sustainable development, because bio-based resources are both CO_2-neutral and renewable, at variance with fossil fuels. Carbohydrates are the main source of renewables employed for the production of bio-based products. Therefore, chemistry know-how on industrial processes, involving carbohydrates is a subject of basis importance. Adsorption of the monosacharide L-Arabinose on a ruthenium nanocluster is here presented as an example of a catalytic system of potential industrial interest [1]. L-Arabinose can be found in aqueous solution in 5 tautomeric forms (*i.e.* α or β pyranose, α or β furanose and acyclic species) in equilibrium with each other. All these tautomers show a very large conformational flexibility, which previously has been also analyzed.

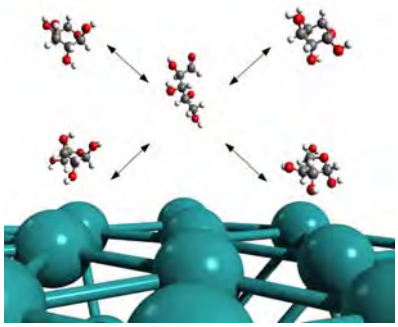

Figure 1. L-Arabinose on Ru surface

The L-Arabinose/Ru system has been investigated into the frame of the density functional theory (DFT). Calculations have been actually performed, using the DFT approach as implemented in SIESTA [2]. This employs linear combination of pseudoatomic orbitals as basis set. The atomic core is replaced by a non-local norm-conserving relativistic Troullier Martins pseudopotential, factorized in the Kleinmann-Bylander form.

The adsorption of different conformers, per each tautomers, on a Ru (0001) surface of the nanocluster have been modeled and analyzed in order to characterize the adsorption points both on the ruthenium surface and in the tautomeric species and to characterize if some of the latter are especially stabilized by the adsorption processes. Since adsorption phenomena could be affected by the adsorbate orientation, three different ways of binding per each conformers were investigated, considering either pyranose or furanose forms, and two for the acyclic forms.

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CTC-PO-01 Computation of the lineshape of electronic spectra in solution within polarizable continuum models: Accounting for both vibrational structure and inhomogeneous broadening

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Starting from the Marcus´s relationships connecting the inhomogeneous broadening with the solvent reorganization energy and exploiting recent developments in Polarizable Continuum Model [1] and PCM/TD-DFT calculations namely state-specific (SS) treatment [2], we propose a procedure to estimate the polar broadening of optical transitions. When applied to a representative molecular probe, coumarin C153 in different solvents, our approach provides for the polar broadening values fully consistent with the experimental ones. For the first time fully ab initio vibrationally resolved absorption spectra in solution (Figure 1) are computed (including both Duschinsky and Herzberg Teller effects, with a method developed in our group [3]) and obtaining spectra for coumarin C153 in remarkable agreement with experiments [4]. Such an agreement allows us to critically compare the relevance of all the vibrational and medium effects that produce the observed lineshapes in gas phase and in different solvents.

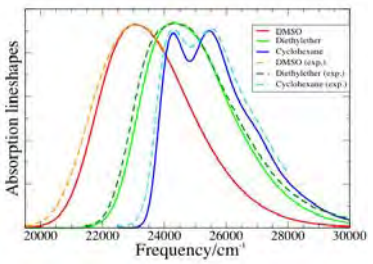

Figure 1.

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CTC-PO-02 Theoretical investigation of magnetic properties in Cu(II) complexes with bridging azide ions

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The property of the azide ion to act as a bridging ligand has been recently exploited in the formation of crystals of crown ether complexes, such as those formed by [Cs([18]-crown-6)$(N_3)_2$], where two azide ions form a linkage between two cesium cations each coordinated by crown ether [1].
In this work, using a computational approach at DFT level, we report some preliminary results obtained in investigating the possibility of forming similar complexes in which, instead of the cesium ion, is present the copper(II) ion.
It is known indeed that the azide ion can bind transition metal atoms to form binuclear complexes, such as [Cu_2(tetramethylethylenediammine)(N_3)(OH)]$(ClO_4)_2$, which show different magnetic properties depending on the kind of coordination [2]. In particular, when the azido group acts as bridging ligands with end-on coordination the resulting binuclear complexes show a ferromagnetic behaviorar and, conversely, when it is coordinated in an end-to-end fashion an antiferromagnetic coupling results.
Therefore, for these complexes the exchange coupling constant J has been estimated as the energy difference between the state of high spin and a broken symmetry singlet state [3].
All results obtained here may be useful for designing new compounds with magnetic properties applicable in the field of single molecular magnets.

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CTC-PO-03 Computational modelling of *de novo* formation of DibenzoFuran: investigation of oxidative pathways of Pyrene and BenzoDibenzoFuran

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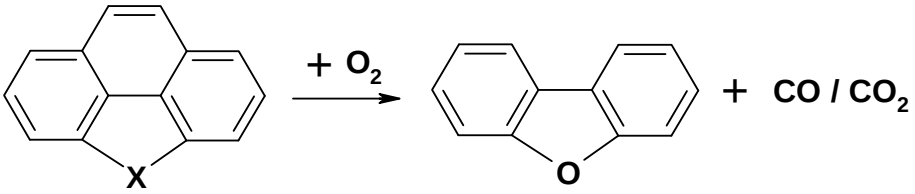
Municipal solid waste (MSW) incineration leads to the production of significant amounts of polychlorinated dibenzo-*p*-dioxins (PCDD) and dibenzofurans (PCDF).[1]
PCDD/Fs are formed in the combustion processes through two main pathways: one involving reactions in the gas phase of precursors, such as chlorinated phenols and chlorobenzenes, in the 400-800 °C range; the second one operates in the 200–400 °C range and mainly involves the so called *de novo* synthesis, which proceeds through burn off of a carbonaceous matrix present in the fly ash with simultaneous oxidation and chlorination reactions. The *de novo* synthesis is the dominating route in the PCDD/F formation in flue gas cooling sections of industrial scale incinerators.[2]
Here we present a theoretical investigation of the oxidative pathways of Pyrene (**1**) and Benzo DibenzoFuran (**2**) that can lead to DibenzoFuran formation. These two systems have been chosen as model compounds of the carbonaceous matrix present in the fly ash.



(**1**) **X**: CH=CH Pyrene
(**2**) **X**: O Benzo DibenzoFuran

Optimized geometries and harmonic vibrational frequencies of reactants, intermediates, products and transition states have been calculated at the PBE1PBE/6-311G** level. IRC calculations have been used to link reactants and products with their transition states. On the basis of previous theoretical studies on benzene[3] and dibenzofuran[4] oxidation, the investigated mechanism involves the initial formation of a radical species (**R**$^{\bullet}$) that, reacting with molecular oxygen, yields a peroxyl radical (**R**-OO$^{\bullet}$). In (**1**) and (**2**), this key-intermediate evolves toward the products following similar paths but involving different energetic barriers.

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CTC-PO-04 Role of IRMOF-3 Zn_4O Vertices in Knoevenagel Condensation

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The Knoevenagel (*Knvgl*) condensation, employed to produce alkenes, involves couple of molecules singly having carbonyl groups and α acidic hydrogen atoms. It has been recently reported that the third member of the Isoreticular Metal Organic Framework family (IRMOF-3) [1] may behave as a basic catalyst, active in the *Knvgl* condensation [2]. The lattice structure of this family of solids is based on Zn_4O moieties (inorganic vertices) and poly-topic linkers, derived by functionalizing 1,4 Benzendicarboxylate (BDC) derivatives.

Within the density functional theory (DFT) framework we already studied structural and basic properties of IRMOF-3 derivatives. Moreover, the mechanism of the catalytic cycle for the *Knvgl* condensation of benzaldehyde and ethyl cyanoacetate was analyzed. The investigation of local chemical properties and of a plausible reaction route for the aniline and dimethyl-2-aminoterephtalate (DM2AT) *Knvgl* catalytic condensation has been also performed, in order to clarify the effects of the inorganic vertices on the amine moieties. Aniline and DM2AT, were chosen for modeling the effects of increasing complexity around the basic sites, characterizing the IRMOF-3 system.

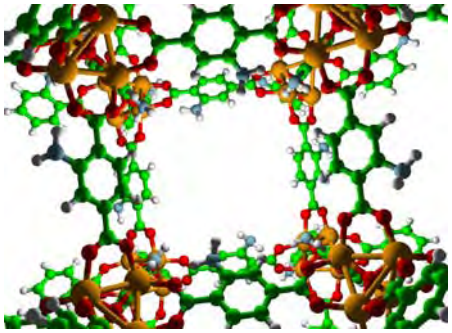

Figure 1. IRMOF-3 cage

The basicity of aniline-like amino moieties grew, along with the catalytic activity, when incorporated into MOF structures. However, the basicity of this class of catalysts did not depend on the charge density present on the nitrogen atom of the aminic group. On the contrary, the basicity was for the most part referable to the IRMOF-3 conjugate acid stabilization, determined by interactions involving the inorganic vertices. Besides this, a direct involvement of the inorganic vertices in the catalytic mechanism could be also pointed out.

These findings, highlighting the active role of the inorganic vertices in the IRMOF-3 activity, are here discussed.

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CTC-PO-05 Time Dependent Density Functional Theory of X-Ray absorption spectroscopy of metal oxides

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The Time Dependent Density Functional Theory (TD-DFT) has been employed to calculate the core electron excitations in metal oxides. From a computational point of view the simulation of the X-Ray Absorption Spectra (XAS) in such systems is an open problem both as concerns the best computational approach and the modelling of the system. Here we present the TD-DFT results obtained for the series of the alkaline-earth oxides (MgO, CaO, SrO e BaO) and the closed shell transition metal oxides TiO_2 and V_2O_5. The XAS spectra have been calculated at the metal K, L and Oxygen K edges. Cluster models to mimic the bulk are considered, embedded within an array of point charges to simulate the Madelung potential. Comparison with experimental data allows a precise assessment of the performances of the method, which appears competitive and suitable to reproduce the measurements. The configuration mixing explicitly included in the TDDFT scheme appears mandatory for a correct reproduction of the oscillator strength distribution in the metal 2p spectra. The origin of the theoretical spectral features is investigated with the help of the partial density of the virtual states (PDOS) calculated to each core hole considered, allowing to discuss the spectral features in terms of the nature of the virtual final states.

CTC-PO-06 Investigating the ion conduction mechanism of the hERG potassium channel

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The hERG channel (Kv11.1) encoded by the human *ether-à-go-go*-related gene KCNH2 [1] is an inward rectifier voltage-gated potassium channel which displays a remarkable low conductance at physiological voltage and K^+ concentrations [2]. In this study, the ion conduction mechanism of hERG was investigated at a fully atomistic detail on a state of the art homology model of the channel [3] by means of the Umbrella Sampling method [4] combined with Path Collective Variables [5]. In apparent disagreement with previous findings based on studies performed on high and moderate conductance channels, no knock-on mechanism was observed in our simulations, and a relatively high energetic barrier (of about 6 kcal mol^{-1}) was found instead (Fig. 1). This barrier is indeed in accordance with a low conductance behavior, and it can be explained in terms of a series of distinctive structural features displayed by the hERG channel.

The achieved results might be useful to provide a predictive framework to assess the impact of point mutations on the conduction functionality of the channel.

To investigate such a possibility, the wild-type ion conduction energetics was compared with that of the G628S mutant, which is known to cause a congenital form of arrhythmia by impairing the ion permeation of the channel.

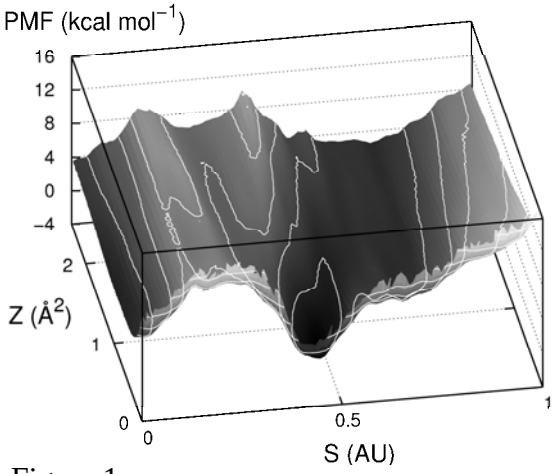

Figure 1.

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CTC-PO-07 Combined Docking and Molecular Dynamics of agonists and antagonists 5-HT_{2C} G-coupled Receptor

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Serotonin (5-hydroxyptamine or 5-HT) through its various class of receptors regulates body temperature, sleep, mood, appetite, pain, anxiety, sex, cognition, smooth muscle growth, gastrointestinal and cardiovascular activities and peripheral secretions [1].
Thus these receptors are target for a variety of drug therapies, including antipsychotic principles.
Among this class, there is the 5-HT_2 family (5-HT_{2a}, 5-HT_{2b}, 5-HT_{2c}). In particular, 5-HT_{2C} receptor, which is mainly expressed in brain, is target of drugs for schizophrenia, depression and glaucoma and it plays an active role in regulating the sleep-wake cycle [2].
5-HT_{2C} receptor variants, due to genetic polymorphisms causing aminoacidic changes, affect treatment efficacy and are involved in treatment-induced side effects as metabolic syndrome and bodyweight gain.
By using a combined automated docking/molecular dynamics protocol [5], we want to assess if polymorphic receptor variants could have altered ligand binding affinity. These changes could explain at molecular level the results obtained in association studies and even help to resolve contradictory associations.
In particular, we docked the natural ligand and several agonists and antagonists to the wild type homology modeled 5-HT_{2C} receptor [3-4]. Then, we repeated the docking using the mutated receptor and comparing the relative agonists' and antagonists' binding energy, pointing out the differences in the corresponding non-covalent interactions at the active site.
This study will be also extended inserting the complexes 5-HT_{2C} receptor-drug into the lipid bilayer of the cellular membrane.

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CTC-PO-08 A theoretical model for the study of the time-resolved fluorescence

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The development of ultrafast laser techniques promoted the study of inherently dynamical phenomena. Nowadays we are able to freeze a far-from-equilibrium system, to observe several snapshots of a chemical reaction and to study the solvent reorganization on both the nuclear and the electronic time scales. Femtochemistry is now a reality.[1] Moreover, advances in the molecular design and bio-sensoristic applications encouraged the development of ad hoc modeled molecules to probe peculiar properties of the environment.[2]
In this new scientific area the computational and theoretical chemistry is essential to analyse and guide the experiment. Relating the spectroscopic behavior to the atomistic re-organisation of a far-from-equilibrium system becomes one of the principal aims of the modern theoretical chemistry. Here we present an integrated theoretical approach to study the time evolution of solute-solvent interactions, or, more in general, of a molecular probe environment. Our approach is based on excited states ab-initio molecular dynamics performed by time-dependent density functional theory.[3-5] In our opinion, this model can provide an invaluable support to the description of ultra-fast phenomena (sub-ps time scale), when the Born-Oppenheimer approximation is still suitable.

As study case, we focussed on the solvation dynamics of the N-methyl-6-oxyquinolinium betaine, in particular on the simulation of its time-resolved Stoke-shift.[6] In spite of a complex solvent dynamics, we observe that the first solvation shell molecules dynamics is ruled by high frequency collective bulk motions. Our results are in good agreement with the experimental counterparts.

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CTC-PO-09 Hydroxymatairesinol Oxidation to Oxomatairesinol on Gold

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The natural product 7-hydroxymatairesinol (HMR) is a member of lignans. The latter form a class of phenolic compounds possessing 2,3-dibenzylbutane skeleton. HMR is abundant in the knots of Norway spruce (Picea Abies), both as (7R,8R,8'R)-(-)-7-allo-hydroxymatairesinol (RRR-HMR) and (7S,8R,8'R)-(-)-7-allo-hydroxymatairesinol (SRR-HMR) diastereoisomers, undergoing isomeric equilibria [1]. HMR can be selectively oxidized to another lignan, oxomatairesinol (oxoMAT) that, due to its antioxidative activity and UV-protection properties, is valuable in cosmetic, pharmaceutical and textile industry. Either RRR-HMR or SRR-HMR can be transformed by oxidative dehydrogenation to oxoMAT. SRR-HMR is the most reactive species [2]. Clearly, the reaction of HMR to oxoMAT is a selective oxidation of a secondary alcohol to the corresponding ketone. Nano-sized gold clusters exhibited excellent activity and selectivity in this kind of reaction [3]. In this work, with the aim of understanding the elementary steps governing the aerobic dehydrogenation of HMR to oxoMAT on gold, adsorption of molecular species – such as O_2, RRR-HMR, SRR-HMR and oxoMAT – on a Au_{28} gold cluster, has been studied by using a DFT approach. The computed kinetic and structural results, related to the binding process, show that molecular oxygen adsorb on the Au_{28} cluster, acting as an electron acceptor able to activate the HMR dehydrogenation. In this context, a reaction mechanism is proposed, especially considering structural and steric properties of the HMR diastereoisomers adsorbed over the gold cluster, which are able to point out and explain their, experimentally found, different reactivity.

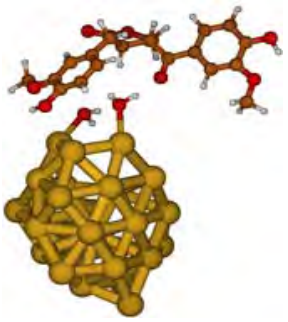

Figure 1. oxoMat on gold

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CTC-PO-10 C K-edge NEXAFS Spectra of Model Systems for C_2H_4 on Si (100): a DFT Simulation

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Adsorption of organic molecules on semiconductor surfaces has been attracting a growing attention for its importance in emerging technologies. Since the properties of the resulting materials are largely dependent on the organic/semiconductor interface, fundamental research on the covalent bonding of molecules with the surface can provide useful information. Problems that have been addressed include the structure of the resulting systems and the spectroscopic measurements, often in concert with theoretical calculations, can assess the orientation and geometry of the molecular adsorbate. NEXAFS spectroscopy is widely used to characterize adsorbate structures on surfaces since it allows to investigate the adsorption mode as well as the extent of the adsorbate-substrate interaction, through the comparison between the spectra of the free and adsorbed molecules. Here we present a DFT simulation of the NEXAFS spectra of ethylene adsorbed on a regular Si (100) surface, considering several adsorption models. Cluster models have been employed to mimic the molecule-surface system for the spectra simulation. Surface models with and without the adsorbed molecule have been optimized by means of periodic slab DFT calculations. Angle dependent spectra have been also calculated and compared with available polarization dependent NEXAFS experiments, revealing the suitability of this technique to derive the adsorption configuration of the molecule on the surface.

CTC-PO-11 Dyes for fluorescence encoding: lifetimes and quantum yields by a combined experimental and theoretical study.

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Due to the advance of techniques based on fluorescence encoding, a renewed interest in synthesis strategies [1] and spectroscopic characterization of common fluorophores [2,3] has been recently shown in literature.

Although the most important features of the optical behaviour, including fluorescence quantum yield and lifetime, are usually well known for commercially available chromophores, a deep understanding of the photophysical behaviour is not fully assessed. On the other hand, an high degree of comprehension is nowadays required for a full control/design of modern optical devices.
In this combined experimental and theoretical work we analyze the fluorescence signatures (lifetime, quantum yield and band peak) of several commonly used rhodamine and pyronin dyes.

In particular we combine Fluorescence Lifetime Imaging Microscopy [4] data with calculations based on the Time-Dependent Density Functional Theory [5] to analyze and interpret the fluorescence signatures (lifetime, quantum yield and band peak) of the chromophores under study.
Our procedure is validated by calculated quantum yields values in good agreement with the experimental counterparts. [6]

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CTC-PO-12 Theoretical study of near edge x-ray absorption fine structure spectra of metal phtalocyanines at C and N K-edges

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Copper phtalocyanine (CuPc), nickel phtalocyanine (NiPc) and metal-free phtalocyanine (H_2Pc) have been considered in this work. Density Functional calculations have been performed in order to assess the relationships between the electronic structure and the most salient NEXAFS spectral features. We have first addressed the description of the electronic structure of the systems under study at the ground state level, in order to establish the nature of the virtual valence molecular orbitals involved in the core excitations, in particular as concerns the relative contributions of ligand and metal atomic sites. Second, we have calculated the NEXAFS spectra, including the relaxation effects upon formation of the core hole by means of the Transition State (TS) scheme, with the aim to compare the results with respect to the experiment as well as to discuss the effect of the presence and the nature of the metal on the spectra.

CTC-PO-13 Theoretical study on the wt-GFP absorption

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Our work is included among the studies of biological macromolecules with specific chemical-physical properties in order to use them in biological, biotechnological or medical applications.[1]
In this field GFPs are non-invasive biosensors ideal to be used in biological systems thanks to their main features.
Our contribution regards the theoretical study of wt-GFP absorption in both its neutral and anionic form and the analysis of the protein environmental influence on the isolated chromophore.
In order to gain these results we used the time-dependent density functional theory (TD-DFT) to describe the electronic excited states of GFP and a quantum mechanical-molecular mechanics approach to study the relationship between the protein structure and the optical properties. For the isolated chromophores we have conducted TD-DFT calculations both in vacuum and in solvents using the conductor-like polarizable continuum model (CPCM).
First of all, as ambiguous conclusions emerge from previous works,[2] we have verified that TD-DFT can accurately describe the S_0-S_1 transition in wt-GFP giving results comparable with the more well-established multi-determinantal methods.
Our results support the idea that the protein environment has a fundamental role in GFP absorption, determining a not negligible red shift with respect to the isolated chromophore. The reliability of our analysis is proven by results in good agreement with the experimental counterparts.[3]

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CTC-PO-14 A theoretical protocol for the determination of the metal-site structure in metalloprotein superfamilies

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NMR spectroscopy is a powerful experimental tool used for the determination of protein structure [1]. NMR chemical shifts accurately reflect the local chemical environment at atomic resolution and are sensitive to many different factors including contacts between residues, hydrogen bonding and proximity to aromatic rings. Several papers have appeared which suggest that reasonably accurate protein structures can be determined directly from chemical shifts [2-4].

In the present work we aim at developing a protocol that employs ab initio computation of chemical shifts as a tool for the structural validation of metal binding site(s) in metalloproteins. EF-hand calcium-binding proteins represent a suitable test application, since accurate databases of structural and NMR properties are available. We have adopted a hybrid quantum mechanical (QM) / molecular mechanical (MM) approach, namely the ONIOM method as implemented in the Gaussian package. In essence, the system is partitioned into two "layers": the molecular region which is immediately adjacent to NMR-active nucleus under investigation is treated at the QM (DFT) level of theory, whereas the rest of the biomacromolecular system is modeled by partial charges from the Amber force field. The frontier between the two layers is based on a hydrogen link-atom scheme and electrostatic interactions between the two layers are accounted for by means of an electronic-embedding implementation. A prototypical EF-hand calcium-binding protein, Calbindin D9k, was employed to perform a systematic exploration of the convergence of computed NMR chemical shifts with respect to the number and nature of residues included in the QM partition. This allows to determine an optimal balance between the high accuracy issuing from the choice of a sufficiently large QM region and the computational costs.

Once a satisfactory partition scheme has been devised, more realistic computations were sought by including motional averaging effects. The procedure requires to perform a classical MD simulation of the biomacromolecule (in explicit solvent); snapshots are extracted at regular time intervals and the results of QM/MM calculations performed on each frame are averaged.

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Spettrometria di Massa

DSM-IL-01 Gas Phase Reactivity of Bioorganic Ions

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The study of properties and reactivity of organic and bioorganic ions in the gas phase is an interesting challenge [1]. Radical cations, even-electron cations or anions can be easily formed by a wide range of ionization techniques and their intrinsic properties and reactivity, free from solvation and reticular forces, can be studied by different methodologies. Further to structural characterization, regio and stereochemistry can be investigated together with chiral recognition, conformation, spectroscopic properties. Decomposition reactions, both unimolecular or induced by photons, electrons or collisions, together with ion/molecule and ion/ion reactions can be carried out and their pathways can be elucidated together with their kinetic and thermodynamic features.

Different approaches and methodologies used in studying the gas phase reactivity of bioorganic ions, taken from the literature and from own research activity [2-3], will be presented.

The gas phase behavior of radical cations and of even-electron positively and negatively charged species produced by perfluoroalkyltriazines has been studied. Their decomposition reactions are strictly dependant upon their structure and type of ion. In particular, protonated species show competitive hydration/elimination reactions involving nucleophilic addition of water [4].

The second study concerns the characterization of a cyclic peptide and the study of its reactions owing to collisions and infrared multiphoton dissociations. The rationalization of the different pathways has been carried out by theoretical calculations.

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DSM-KN-01 Infrared spectroscopy and structure elucidation of mass selected ions

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The survey of gaseous ions by vibrational spectroscopy is a rapidly growing field, taking advantage from the development of widely tunable infrared laser sources. The so-obtained IR multiple photon dissociation (IRMPD) spectroscopy may now easily cover a wide portion of the vibrational spectrum ranging from the mid-IR (fingerprint region) to the X-H (X = C,N,O) stretching region. This methodology, combined with kinetic studies of ion molecule reactions, offers a powerful tool to obtain information about ion structure and dynamics [1]. In this communication an overview is given of few systems studied recently.
The interaction of simple anions with unsaturated molecules bearing electron withdrawing groups may lead either to covalently bound complexes or to non-covalent adducts. IRMPD spectroscopy allows to discriminate between alternative structures for the adducts between RO- (R= H,CH3,C2H5) and halide ions with neutrals such as trinitrobenzene and CF2=CF2.
The post-translational modifications known to severely affect the behavior of an aminoacid residue in a biological matrix may be similarly revealed by characterististic vibrational signatures. An example is shown in Figure 1 where protonated nitrotyrosine displays highly active modes assigned to asymm and symm stretching of the nitro group. Potential interest may thus be envisioned also for diagnostic purposes.

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DSM-KN-02 Diagnostica ed analisi chimica per il monitoraggio del nostro intervento sul manufatto artistico

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Le sofisticate strumentazioni analitiche oggi disponibili trovano sempre più frequente utilizzo nel campo della conservazione e restauro dei Beni Culturali, allo scopo di acquisire informazioni a vari livelli..
Innanzitutto, per lo studio della composizione del manufatto, dei suoi materiali originariamente costitutivi e di quelli eventualmente aggiunti nel passaggio dell'opera attraverso i secoli. In secondo luogo, per lo studio dei processi di degrado che inevitabilmente avvengono nel tempo, a carico dei materiali dell'opera. In terzo luogo, per il monitoraggio dell'intervento di restauro dell'opera stessa, quando necessario. Quest'ultimo aspetto, sebbene di importanza fondamentale al fine di preservare il più fedelmente possibile i valori materiali e di forma dell'opera, è purtroppo quello che fin'ora ha ricevuto la minor attenzione.
In particolare, tra tutte le operazioni passive e attive della conservazione e del restauro, speciale attenzione merita quella genericamente, e imprecisamente, definita "pulitura" di opera policrome e non, proprio per il suo carattere peculiare: intrinsecamente irreversibile, in quanto mirata alla rimozione di materiali, presenta il più alto rischio di interagire con l'opera, di modificarne quindi la composizione, la morfologia e la percezione da parte dell'osservatore.
Se condotta col semplice monitoraggio sensoriale del controllo visivo, come ancor oggi troppo spesso accade, l'assenza di fenomeni macroscopicamente percepibili (solubilizzazione di materiali, perdita di colore…) induce l'operatore a ritenere di aver compiuto un'operazione selettiva, a minima interferenza coi materiali costitutivi dell'opera. Troppo spesso, se valutata con criteri analitici più oggettivi, la stessa operazione mostrerebbe invece un ben diverso grado di interazione: un'irreversibile modificazione del manufatto.
Questo è particolarmente accentuato per opere policrome mobili, come dipinti su tela e tavola e sculture lignee policrome, che sono manufatti compositi: successioni di strati, originari e aggiunti successivamente, in parte compenetratisi. I materiali organici di questi strati, con l'invecchiamento tendono ad acquisire proprietà (dimensioni molecolari, polarità e acidità) sempre più simili a seguito di processi chimici, principalmente ossidativi e idrolitici; gli strati, di conseguenza, divengono difficilmente differenziabili, a scapito della selettività dell'intervento di rimozione.
Nella presentazione si prenderanno in considerazione casi rappresentativi di intervento, discutendo i materiali utilizzati e le tecniche analitiche impiegate per il monitoraggio. Infine, sarà esemplificata una considerazione di importanza fondamentale: sempre più numerose divengono le tecniche analitiche per lo studio dei Beni Culturali, e tutte sono potenzialmente utili. Per esserlo però davvero, occorre che il dato analitico ottenuto sia correttamente interpretato e contestualizzato. Questo spetterebbe a figure professionali dotate di entrambi i tipi di conoscenze e competenze: quelle scientifiche/analitiche e quelle inerenti l'opera d'arte e il restauro. Sfortunatamente, queste figure professionali sono ancora largamente inesistenti…

DSM-OR-01 Determination by ICP-MS of silver concentrations in different dressings used in burns care and evaluation of their release kinetics

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Silver in the ionic form of silver nitrate has been used for the treatment of chronic wounds, ulcers, burns and infections since mediaeval times. Recently the interest in using silver to heal wounds has increased due to the rise of antibiotic resistant bacteria, so that several different silver dressings have been commercialized and are now widely used in burns centres. The dressings are typically composed of a polymeric scaffold impregnated with metallic or ionic silver, the declared silver concentrations are at percentage levels. Different mineralization methods were developed to determine the total silver concentration in the dressings by Inductively Coupled Plasma-Mass Spectrometry (ICP-MS). The instrument parameters and the experimental conditions were optimized using ammonia solution to obtain the best signal stability and to reduce the memory effect of silver. The samples were analyzed using both external calibration and isotope dilution analysis (IDA). Our results confirm the declared silver concentrations in the dressings. After chemical characterization, we assessed the kinetics of silver release in different matrices of increasing complexity:: ultra pure water, normal saline solution (made in house from silver free analytical grade 0.9% m/v NaCl) and a serum substitute (Hit serum substitute, STEMCELL technologies, Vancouver, Canada). These matrices represent the possible environments in which the silver can act during the routine application of the dressings. The concentration of silver released in ultra pure water represents the simplest matrix for studying silver release. The saline solution chemically simulates the wound environment, in which a considerable fraction of the available ionic silver could precipitate from solution as insoluble silver chloride. The serum substitute contains human serum albumin, insulin and transferrin and reflects the protein composition and concentration observed in human serum. We used this solution to assess if these proteins, and particularly albumin, could enhance the solubility of silver by shifting the equilibrium towards more silver in solution by actively competing with chloride as a complexing agent.

DSM-OR-02 CHARACTERIZATION OF CARBONYL BY-PRODUCTS DURING UNIBLU-A OZONATION BY LC-ESI/Qq/TOF/MS AND IC-ESI/Qq/TOF/MS

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Ozonation is one of the most effective chemical oxidation technologies to remediate textile wastewater containing bio-recalcitrant dyes and other persistent organics [1]. However, even though dyes removal by ozonation is often achieved successfully, their complete oxidation is seldom obtained. Therefore, ozonation by-products should usually be expected in ozonation effluents [2].

QqTOF/ESI/MS both in single and tandem MS, coupled to liquid chromatography (HPLC) and ion chromatography (IC), was employed for the characterization of several intermediate as well as end by-products formed during an extensive ozonation of hydrolyzed Uniblu-A (Uniblu-OH), i.e the compound found in the spent bath resulting from dyeing process employing the reactive dye Uniblu-A. The obtained results demonstrated the effectiveness of accurate mass measurement to identify low molecular weight ozonation by-products arising from by-products formed in the early stage of the ozonation process [3]. For achieving such a goal QqTOF/ESI/MS was interfaced to LC, employing a preliminary derivatization step with 2,4-dinitrophenylhydrazine, or to IC. In addition, the employment of spectral accuracy [4] was investigated to identify by-product structures as well as to get detailed information about their fragmentation patterns.

Most of by-products were characterized by mono or double CO_2 and water losses consistent with assignment to aldheydes-, keto- and poli-hydroxylated carboxylic acids of low molecular weight.

The employed experimental approach also allowed the identification of both nitrogen- and sulphur-containing carbonyl by-products. This result is of environmental relevance for the balance of both organic nitrogen and sulphur, as these atoms do not undergo complete mineralization. Owing to the complexity of the reactions occurring during ozonation, it was possible to assess the presence of correlations between different identified by-products which in turn decompose, through decarboxylation and further oxidation, to smaller homologues and then to complete mineralization.

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DSM-OR-03 Sheep cheeses and cashmere pullovers: MS-certified authenticity through peptide analysis

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The authenticity of quality products is an issue of paramount importance in many fields. In foods, the authenticity is usually intended as the adherence to defined production methods, the use of particular ingredients or a production done in a well defined place. Typical examples include olive oils produced starting from defined cultivars, cheeses produced in mountain regions, cheeses produced with milk of defined species, sausages and cheeses having a defined ripening period, fruits and vegetables of defined varieties. But also in other fields, authenticity is important. As an example, dresses of pure cashmere wool are usually considered of very high quality as compared to similar garments made of standard sheep wool. In all these cases, the detection of potential frauds and the objective assessment of authenticity are essential, also because of the high market price of the "authentic" quality products

In the present communication, it will be shown how the use of the MS analysis of proteolytic peptides can rapidly and reliably provide a tool for determining the authenticity of food and non-food products at the molecular level.

Proteolytic peptides, generated from the casein breakdown which takes place during the production and the ageing of cheeses, can be used as markers for the mammalian species from which the milk is produced. In particular, LC/ESI-MS analysis of homologous, but not identical, proteolytic peptides derived from α_{S1}-casein allows to rapidly and reliably assess the presence of cows' milk in cheeses supposedly made only from sheep milk [1] or water-buffalo milk [2].

Enzymatic digestion of keratin extracted from wool's dresses and peptide analysis by LC/ESI-MS allows to determine not only the presence of wool derived from different species (Yak, Cashmere, Sheep) but also to assess the relative percentage of usage.

In all these cases MS-based analysis allow to obtain objective data on the specified products more reliably than currently applied methodologies.

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DSM-OR-04 Molecular characterization of bio-oil through mass spectrometry: GC-MS and APPI FTICR MS analysis.

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The increasing demand for petroleum by emerging economies, the predicted shortage of fossil fuels, as well as related environmental concerns, are pushing up the search for new sources of liquid fuels. It is expected that a significant part of future renewable fuels will be represented by biomass resources.
In this work GC-MS and FTICR MS direct analysis have been used to characterize a Bio-Oil sample obtained by thermochemical conversion of waste biomass. The bio-oil has a high percentage of carbon and a high content of etheroatoms, in particular nitrogen and oxygen.
The sample has been first analyzed in GC-MS with a single quadrupole mass spectrometer. Although the gas chromatographic separation yields a partial coelution of many different compounds, the main classes of compounds have been identified, considering the electron ionization mass spectra.
Direct analysis through APPI-FTICR MS, recently utilized for the molecular characterization of crude oil,[1] has been used for the characterization of bio-oil. The ion source is connected to a LTQ-FT Ultra (Thermo Scientific) instrument with a FT-ICR cell surrounded by a 7 Tesla magnet. Photoionization[2] is very effective for the ionization of low-medium polarity and aromatic molecules. The spectrum has been acquired in positive mode with an average resolving power of 400000. Very high mass accuracy together with high resolution allows the attribution of thousands of molecular formulas per mass spectra. In this bio-oil mass spectrum we have assigned a molecular formula to more than 6000 peaks through a custom built software (ISOMASS).
The main classes found contains one or two nitrogen atoms and 0-2 oxygen atoms(N2,O1N2,O1N1,O2N1) (Fig.1). By GC-MS we have detected some molecules with the same DBE value as those found in the APPI spectrum, but with lower molecular weight. Using these two MS techniques we have made structural hypothesis for some of these classes.

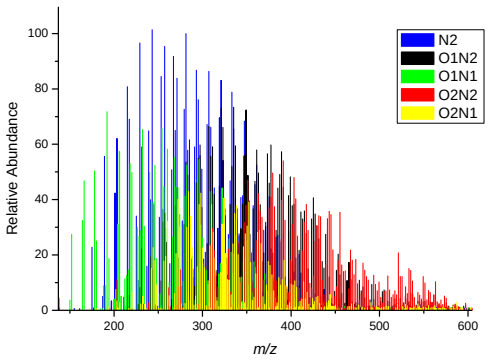

Fig.1 : Bio oil APPI positive mass spectrum.

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DSM-OR-05 Maldi –Tof Mass Spectrometry as a tool for the detection of sheep and goat milk adulterations

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Adulteration consists of the addition or the removal of some components in food in order to obtain a larger profit without significantly changing the product. It includes all the actions aimed at modifying the analytical composition of food. Due to economic convenience unscrupulous producers prefer substituting expensive raw materials with more abundant and cheaper ingredients.
Besides the utilization of casein or powdered milk for the production of cheeses and the selling of skimmed milk and semi-skimmed milk instead of whole milk, common fraud in the milk and dairy field is the illegal addition of cow's milk to goat's and sheep's milk and of goat's milk to sheep's milk.
These practices have commercial, ethical and also serious sanitary consequences because consumers can be exposed to allergens as for example cow's milk proteins, especially αs1- casein (αs1-CN) and β-lactoglobulin. Sheep's and goat's milk differs from cow's milk in terms of allergenic properties.
In order to protect human health and the product quality, European Union (EU) has developed a specific policy relevant to the authenticity of foodstuffs.
Regulation EC 178/ 2002 aims to protect consumers and to defend consumer rights to food safety and accurate information. Indeed, a strict number of modifications such as the addition of certain minerals, vitamins, proteins and changes in the fat content are officially allowed.
Analytical techniques employed in the dairy food quality control are near-infrared (NIR), mid-infrared (MIR), nuclear magnetic resonance (NMR) spectroscopies, liquid chromatography (HPLC) [1], immunoenzymatic assay, polymerase chain reaction (PCR), electrophoresis and sensory analyses. These techniques are time consuming and labor intensive so they can't be used for routine analyses. A possible alternative could be represented by mass spectrometry (MS) techniques; among the soft ionization techniques, Matrix assisted Laser Desorption Ionization (MALDI)-time of flight (ToF) has recently shown to be a useful tool for the detection of milk adulterations through the study of intact proteins [2].
Here, we propose a fast and sensitive method to detect cow's milk adulteration in sheep's and goat's milk and goat's milk adulteration in sheep's milk.
In particular, the tryptic digestion has been performed on milk samples as such and intentionally adulterated at levels of 50%, 20%, 10% and 5% and the resultant digests have been analyzed by means of MALDI TOF MS using the new MALDI matrix 4-Chloro-α-cyanocinnamic acid [3].
Many peptide markers of cow's proteins (β-lactoglobulin, α-S1- and α-S2 caseins) and goat's protein (κ-casein) have been identified in adulterated fresh milk and commercial milk samples.

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DSM-OR-06 *In mesopore* protein digestion a new strategy for mass spectrometry-based proteomics

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As a part of an on going project aimed to the development of convenient and sensitive procedures for proteomics applications [1-3], our group has recently rationally designed and developed a new enzymatic mesoreactor for ultrafast protein digestion [4].
The high surface areas, the ordered periodicity of the pores with controllable dimensions and morphology, render mesoporous silicate (MPS) optimal supports for a great variety of catalysts, from small molecules catalysts (such as metals, metal complexes, metal oxides) to large molecule catalysts such as enzymes.
MPS SBA-15 together with N-(2-aminoethyl)-3-aminopropyl and aminopropyl (indicated as AAPTES and APTES, respectively) functionalized derivatives were prepared with pore dimensions of about 4 nm, slightly larger than the diameter of trypsin (3.8 nm), to obtain a well-fitting physical entrapment. Myoglobin was added to trypsin meso-reactor, with a molar enzyme/substrate ratio of 1:3. Within 1 min of digestion, a rich pattern of proteolytic fragments was obtained for SBA-15-AAPTES and SBA-15-APTES, which allowed unambiguous myoglobin identification. The best performance was achieved for trypsin adsorbed in SBA-15-AAPTES with 100% sequence coverage obtained in just 1 min.
The effect of organic functionalities such as AAPTES and APTES grafted on SBA-15 on in situ-proteolysis are examined. In addition we address the suitability of these bionanocatalysts, for a convenient "proteomic scale" procedure consisting of few sample-handling steps, with increased proteolytic efficiency (1000 times faster and an improved performance compared to the conventional *in solution* procedure), making them promising for high-speed and high-throughput protein identification.

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DSM-OR-07 APULIAN TABLE GRAPES: A COMBINED STUDY BY DIRECT INFUSION HIGH-RESOLUTION MASS SPECTROMETRY AND NUCLEAR MAGNETIC RESONANCE

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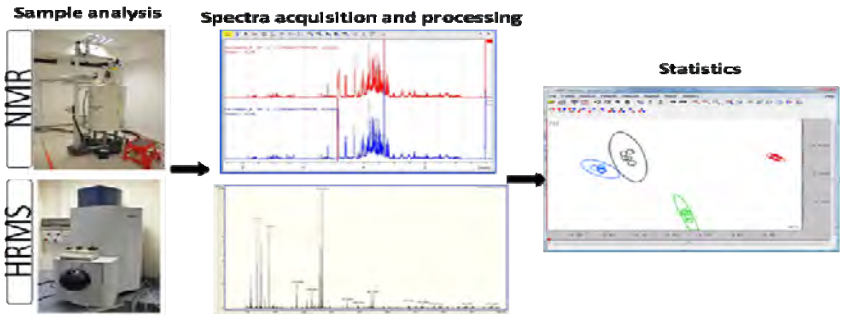
In the table grapes world market, Italy is the fourth largest producer and the second largest exporter. Apulia is in first place of the national context with approximately 70% of annual production. Efficient cultural practices, currently adopted to improve the quality of the table grape, are dependent on the skills of the growers and the use of robust scientific tools for quality control of the table grape is quite rare in the production stages. Even though the direct infusion HRMS and the solution NMR have been proven as fast and reliable techniques for the characterization of food matrices and fruit juices such as grapes and grape juices [1], these spectroscopic methods have not yet been applied to studies on the table grape. This contribution describes the results of a combined study on Apulian table grapes by direct infusion HRMS and NMR. The application of multivariate statistical analysis will also be discussed in order to show the potentialities of HRMS and NMR as discriminating techniques for quality control of the Apulian table grapes.



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DSM-OR-08 High-Throughput Protein Glycomics by Glycoblotting and MALDI mass spectrometry.

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The complex sugar chains of glycoproteins and glycolipids are believed to play important roles in the control of cellular functions and in recognition between the cell and its cellular and fluid environment. Protein glycosylation has long been recognized as a common post-translational modification and has been increasingly recognized as one of the most prominent biochemical alterations associated with malignant transformation and tumorigenesis. Thus, detailed knowledge of protein glycosylation at the proteomics level involving structural information of both the glycan microheterogeneity and the backbone peptide sequence, is of growing importance in clinical research [1].
However, the enrichment and direct determination of individual glycopeptides derived from naturally or engineered glycoproteins in vivo have not been routinely possible to date, because they typically require tedious and time-consuming separation of the glycosylated peptides from extremely complex mixtures before analysis [2, 3]. These limitations, resulting in reduced identifications of proteins and posttranslational modifications, have led to the development of alternative "off-gel" strategies. The "front-end" approaches and its specific implementations, including chemical probes, can selectively tag and facilitate subsequent isolation of a target protein subpopulation such as glycosylated proteins. In particular, any technique that sequesters a glycoprotein bearing a reducing oligosaccharide from a sample and allowing its further manipulation while immobilized on a solid phase support, represents an automated method that greatly facilitates glycoproteomic analysis of a wide range of naturally occurring and engineered glycoproteins.
The proposed method reduces proteome complexity by segregating the *N*-linked glycoproteins by the conjugation of glycoproteins via hydrazide chemistry using commercial fischer-type-functionalized gel and the specific release of formerly *N*-linked glycosylated peptides via peptide-*N*-glycosidase treatment. A single analysis leads to the identification of the glycoprotein, the site(s) of N-linked glycosylation and the characterization of the N-linked carbohydrates by high throughput MS and MS/MS analysis.

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DSM-OR-09 Fragmentation pathways of synthetic peptides investigated by infrared multiphoton dissociation (IRMPD) and Fourier-transform ion cyclotron mass spectrometry (FTICR MS)

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Over the last two decades, there has been a tremendous effort towards the application of mass spectrometry to the field of proteomics/peptidomics, in large part because of the success of tandem mass spectrometry for elucidation of primary sequences and modifications of peptides and proteins [1, 2, 3]. Several ion activation methods have been developed in this context, including collision induced dissociation (CID) which is the most widely used due to its relatively well-understood underpinnings [4]. In most MS/MS experiments, protonated peptides are excited collisionally to induce dissociation (CID) and the fragment ion spectrum is used to elucidate peptide sequences [3]. Here, electrospray ionization and tandem mass spectrometry (ESI-MS/MS) using Fourier-Transform ion cyclotron resonance (FTICR) MS and infrared multiphoton dissociation (IRMPD) was used to perform the characterization of two autoinducing peptide precursors CVGIW and LVMCCVGIW involved in the *quorum sensing* of *L. plantarum* [5]. The IRMPD experiments were performed using a 20 W in-built CO_2 laser (70 ms at 60% energy). Both protonated peptides dissociate to produce *b* and *a* ions as well as abundant fragments arising from further backbone fragmentations (immonium and especially internal ions) or loss of small neutrals. For most fragment ions, the mass resolution defined as $m/\Delta m$ (Δm is the full peak width at half-maximum) achieved >100000 was more than sufficient to resolve the isotopes of the ions and to determine the charge states from the isotope spacing, with routine sub-ppm mass accuracies (-0.5 ppm). Reversed phase liquid chromatography with ESI coupled to a hybrid quadrupole linear ion trap (LTQ) and Fourier-transform ion cyclotron-resonance mass spectrometry (FTICR-MS) was employed for the identification of CVGIW and its dimeric form in cell-free culture of *L. plantarum WCFS1* grown in Wayomonth's Medium Broth (formulation without sulphur organic compounds).

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DSM-OR-10 1,8-bis(Dimethyl-Amino)Naphthalene / 9-Aminoacridine Binary Matrix for Direct Analysis of Intact *Gram-positive* Bacteria by MALDI – TOF – MS

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Lipids and phospholipids (PLs) are important components of all biological cell membranes involved in many significant metabolic and biochemical processes such as energy production and storage, formation and functioning of cellular membranes, and signal transduction [1-3]. Perturbations in the environment and cellular activity can change dramatically the lipid metabolic network affecting the cell's lipidome. For instance, thermophilic and mesophilic bacteria grown at different temperatures have been shown to alter the fatty acid composition of their membrane lipids. This change in lipid composition could influence the cell membrane integrity in Gram-positive micro-organisms during freezing [4]. Thus a simple and reliable strategy for comparative lipidomics could be of great interest for complementing biochemical studies [5]. However, in some cases such as *Gram positive* bacteria, obtaining a lipid extract is not a very straightforward procedure. In fact, these bacteria are characterized by having, as part of their cell wall structure, a thick peptidoglycan (heteropolymers of glycan strands) layer as well as polysaccharides and/or teichoic acids which makes difficult the phospholipid extraction [6]. Then a rapid and sensitive method providing all required compositional information on intact bacteria in a single experiment would be of outstanding interest.
Here, we demonstrate the effectiveness of a strong base, 1,8-bis(dimethyl-amino)naphthalene (DMAN; proton sponge) combined with 9-aminoacridine (9AA) as a novel matrix for the direct lipid analysis of whole cell bacteria by MALDI-TOF-MS. Initially, a standard of phosphatidylglycerol was analyzed using DMAN and 9AA separately or in combination as matrix. In all cases only deprotonated analytes signals were observed in the negative-mode MALDI-TOF/MS spectra with the complete absence of matrix-related signals. Then, DMAN/9AA was successfully applied to the analysis of whole cell *Lactobacillus sanfranciscensis* microorganisms. Different components were sensitively identified from a single spot including free acids, glycolipids, phosphatidylglycerols (PGs), glycolipids and cardiolipins. Compared with the single components, the DMAN/9-AA binary matrix provided better results using a lower laser energy, leading to better resolution and reduced fragmentation and a good intra-spot and spot-to-spot repeatability. This method could be very useful in food safety chain since it allows to rapidly verify if the concentration and preservation technologies employed for lactic acid bacteria used as starter cultures in the food industries can cause cell damage or loss of viability to various degrees.

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DSM-OR-11 Exploring the frontiers of synthetic eumelanin polymers by high resolution Matrix Assisted Laser-Desorption Ionization Mass Spectrometry

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The rapidly developing new trends in material sciences and nanotechnologies are the reason for a growing interest in melanin research.[1] Melanins are important bio-polymers comprising functional components of the human pigmentary system. Eumelanin, in particular, is a heterogeneous polymer derived by the enzymatic oxidation of tyrosine with tyrosinase/O_2 via 5,6-dihydroxyindole (DHI) and its 2-carboxylic acid (DHICA). The photoprotective action, the ion-exchange as well as the prooxidant and antioxidant activities, and also electrical transmission are recognized to be prominent functions of the eumelanin macromolecules.[2] Under the technological point of view, the peculiar physicochemical properties of eumelanins make this molecular system a good candidate for the realization of new bio-inspired functional soft materials, with structure-based physical-chemical properties.[3]

An unprecedented breakthrough into the mechanism of synthetic eumelanin buildup has derived from a detailed investigation of the oxidative polymerization of DHI and its N-methyl derivative (NMDHI) by linear and reflectron MALDI-MS.

Regular collections of oligomers of increasing masses, spanning the entire *m/z* ranges up to 5000 Da (>30-mer) and 8000 Da (> 50-mer) for the two buiding blocks, respectively, were disclosed. It is the first time that the in vitro polymerisation of dihydroxyindoles to form synthetic eumelanins is explored up to its high mass limits, giving at the same time information on the polymerisation mode, whether it follows a stepwise pattern (being this the conclusion in our case) or a staking sequencing of small sized entities.

It is highlighted, also, the influence of the N-methyl substituent on the polymerization process, this opening the way to the production of N-functionalized, synthetic eumelanin-inspired soft materials, for possible future technological applications.

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DSM-PO-01 Characterization of α_{s2}-casein variants in donkey's milk

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Clinical investigations demonstrate that donkey's milk represents a safe and valid alternative to cow's milk for infants affected by cow's milk protein allergy [1]. Although it is reasonable to assume that the reduced allergenic properties of donkey's milk are related to structural differences of its protein components with respect to bovine milk, the mechanism of the tolerance of donkey's milk has not yet been clarified at molecular level. Indeed, the knowledge of the protein composition of equidae milk has been very scant until recent years. In the last years, the investigations carried out in our laboratory on the protein fraction of a individual donkey's milk samples allowed us to improve the knowledge of its protein composition by the identification and characterization of the primary structure of several previously unknown proteins [2, 3, 4, 5].

In the frame of our research line, we report here the determination of the primary structure of four α_{s2}-CNs variants carried out by coupling RP-HPLC and 2DE analyses, enzymatic digestion by trypsin, chimotrypsin and protease V8, and mass spectrometry characterization. The contemporary presence of four variants of α_{s2}–CN in an individual milk sample seems more and more typical of equine milk CNs and appears correlated with the intron/exon structure of their correlated genes, which consists of a large number of short exons that may undergone to differential splicing events and therefore originate numerous isoforms with different amino acid length.

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DSM-PO-02 A mass spectrometry-based proteomic approach for the identification and quantification of potential biomarkers in prostate cancer.

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Prostate cancer (PCa) is the most commonly diagnosed invasive cancer and the second leading cause of cancer-related death among men in Western countries [1]. In the early diagnosis of the disease a crucial role is played by the prostate-specific antigen (PSA), whose value increases in the presence of cancer (> 4 ng/ml). Recent studies show that indeed there is no safe limit value below which it can be assumed that prostate cancer is absent (2). Moreover, the value of PSA has low specificity in differentiating malignant from benign conditions, resulting in overtreatment (3). The identification of new biomarkers that allow early detection of cancer, distinguishing between indolent and aggressive form, and are specific to PCa and PCa recurrence are an urgent, unmet medical need.

The aim of this project is the analysis of differential proteome through the study of tumoral and normal prostate tissue of patients with PCa, to identify potential tissue biomarkers for PCa. Prostate tissue specimens from patient with PCa were collected and analyzed to identify proteomics-based biomarkers useful for prostate cancer diagnosis. We analyzed the tumoral and non tumoral tissue from the same individuals. The hydrosoluble tissue protein extraction and protein chemical fractionation were performed to study the sub-proteome components. Moreover, to remove the high abundant proteins, as albumin, immunoglobulin and transferrin, we developed an alternative methods compatible with a mass-spectrometry analysis. The low molecular weight proteins were proteolitically digested with trypsin, fractionated using a reversed-phase (C18) cartridges and the eluate was analyzed by MALDI-TOF mass spectrometry and MS/MS for protein identification. Differential expression analysis between Normal and Tumoral PCa tissue will be performed in order to identify potential biomarkers in prostate cancer.

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DSM-PO-03 Characterization of the acyl chains of sulfoquinovosyldiacylglycerols (SQDGs) by LC-ESI - tandem mass spectrometry

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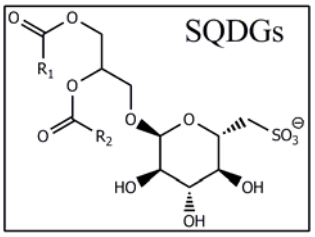
Sulfoquinovosyldiacylglycerols (SQDGs), commonly referred to as the "plant sulfolipids", were first discovered by Benson *et al*. in 1959 [1] and have since been found to exist in all photosynthetic organisms [2]. In contrast to most naturally occurring organosulfur compounds (including sulfur containing lipids), where sulfur occurs in a sulfate ester (C-OSO_3^-), SQDGs contain a very stable and strongly acidic sulfonic acid group, with sulfur linked to the carbon at the 6 position of glucose. Recently, 23 SQDGs have been identified during a global characterization of photosynthetic glycerolipids in a marine alga by LC-ESI-qToF-MS [3]. In the present work LC-ESI-MS/MS based on a linear ion trap mass analyzer (LTQ) has been applied to the characterization of SQDGs in plant leaf extracts. The chain length, degree of unsaturation and positional distribution of the fatty acids (FAs) attached to the primary (*sn*-1) and secondary (*sn*-2) hydroxyl groups of the glycerol moiety were established for 22 SQDGs, starting from negative ion CID-MS/MS spectra. In particular, ions corresponding to neutral losses of either free FA substituents ($[M\text{-}H\text{-}R_xCOOH]^-$) or of their ketenes ($[M\text{-}H\text{-}R_xCH{=}C{=}O]^-$) were exploited to identify the SQDGs acyl chains. Subsequently, their abundances were studied at different collisional energies. It was observed that the peak intensity of $[M\text{-}H\text{-}R_xCOOH]^-$ ions was higher than that of $[M\text{-}H\text{-}R_xCH{=}C{=}O]^-$ ones and this feature was attributed to the gas phase acidity of SQDG ions, making the neutral loss of the acid moieties easier than that of ketenes. Comparing the abundance of fragment ions, it was possible to establish the position of the *sn*-glycerol-bound FA chains (i.e., *sn*-1 vs. *sn*-2) [4,5], along with the fatty acyl composition within all SQDGs investigated.



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DSM-PO-04 Determination of Endocrine Disruptors in Water Samples with Mass Spectrometry - Liquid Chromatography Techniques

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Endocrine-disrupting compounds (EDs) [1] are chemicals that can mimic or block the actions of natural hormones in living organisms, incuding humans, and impair their normal functioning such as growth, metabolism and reproduction. Growing attention recently paid to safety of drinking water makes the development of sensitive and rapid analytical methods necessary to identify these micropollutants.

Different analytical methods [2], based on liquid chromatography - mass spectrometry techniques, were developed for the determination of six EDs: Nonylphenol (NP), Bisphenol A (BPA), estrone (E1), 17β-estradiolo (E2), estriol (E3) and 17α-etynilestradiol (EE2) in acqueos matrix (tap water, river water, waste water).

Both Ion Trap (Varian 500 MS) and Triple Quadrupole mass analyzer (Agilent 6430) were used and the chromatographic separation was optimized testing several commercial columns. A derivatizion reaction with dansyl chloride [3] was also developed to improve sensitivity for hormone molecules.

The analytical method were applied to real water samples, collected with traditional sampling and using passive samplers (POCIS).

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DSM-PO-05 Identification and Structural Characterization of Potentially Active Side Products in the Synthesis of 2-Arylbenzofuran Derivatives by GC/MS and Tandem Mass Spectrometry

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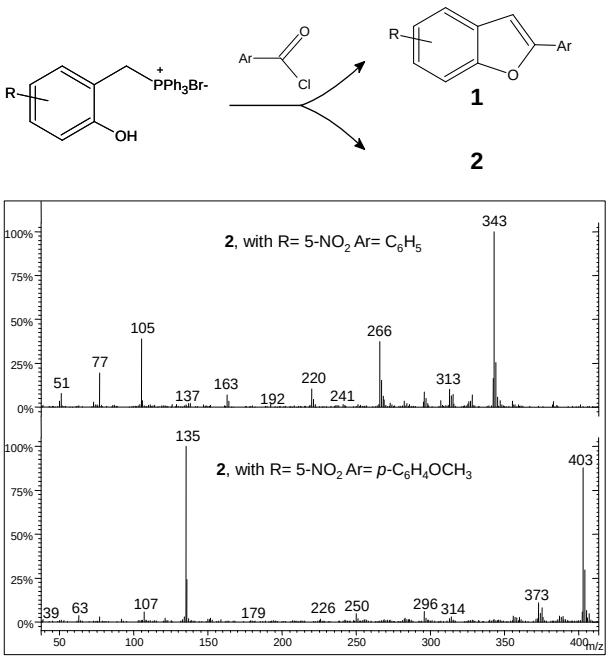
trans-Resveratrol is a natural phenolic component of *Vitis vinifera L.* (Vitaceae). It has shown a number of biological activities, including protection against coronary heart disease, as a result of different effects: significant antioxidant activity, modulation of lipoprotein metabolism, vasodilatatory and platelet antiaggregatory properties. Recently we have reported the synthesis of a series of resveratrolo-coumarine hybrids that showed interesting vasorelaxant and platelet antiaggregatory activities [1,2].

In an attempt to prepare more active heterocyclic derivatives which incorporate the nucleus of the resveratrol, we synthesised a new series of 2-arylbenzofurane derivatives by an intramolecular Wittig reaction starting from the appropriate triphenylphosphonium salt and the corresponding aroyl chloride. The desired Wittig reagent was readily prepared from the conveniently substituted 2-hydroxy-benzyl alcohol and triphenylphosphine hydrobromide (**Figure 1**) [3].

However, while developing our methodology, we observed, together with the desired 2-arylbenzofurane derivatives with the general stricture **1**, the formation of the side products **2** in a ratio ranging from 2:1 to 8:1.

To get insight on the structure and on the mechanism of formation of these side reaction products, we decided to undertake a mass spectrometric study using an ion trap mass spectrometer operating under both EI and CI conditions. In particularly, MS/MS experiments were performed on the molecular ions and on the diagnostic fragment ions generated by the side products **2** as well as by the side product synthesised from labelled starting aroyl chloride. The data so obtained were consistent with the aroyl-benzofurane structure, a scaffold of many pharmaceutical drug candidates [4], thus allowing us to discover and develop a new and convenient approach to the preparation of this class of active compounds.



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DSM-PO-06 Comparative analysis of plasma endogenous metabolite in mice exposed to smoke or air.

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The present study was aimed at investigating whether exposure of mice to cigarette smoke induces qualitative or quantitative changes in the endogenous metabolites. Plasma samples of four different mouse strains (C57BL/6J, CD1, BalbC and 129Sv) were analyzed by LC-MS/MS, FIA-MS/MS and GC-MS methods in order to monitor several metabolite classes such as amino acids, lipids, biogenic amines and energy metabolism intermediates.
The final purpose was the selection of the most suitable mouse model to be used for chronic obstructive pulmonary disease (COPD) studies. COPD is defined as a preventable and treatable disease, whose pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases. Current pharmacotherapy options are for treatment of symptoms only, and none of the existing medications is able to reverse the gradual decline in lung function that is characteristic for COPD. Therefore there is an urgent need for novel therapy for better manage the disease.
Mice were exposed to smoke (10 cigarettes/day, 3 days), using a nose-only inhalation system. Control animals followed the same procedures but were exposed to air. Plasma samples were collected 3 h or 24 h after the last exposure to smoke or air.
The most pronounced changes in term of metabolite concentration seen 3 h after exposure. Smoke caused systemic oxidative stress measured as an increase of methionine sulfoxidation. Furthermore, the energy metabolism (e.g. lactate production) was clearly affected by smoke in a strain-dependent way. Moreover, smoke influenced plasma amino acid levels and the metabolism of biogenic amines (putrescine) and lipids (acylcarnitines, free fatty acids).
Mice of strains BalbC and 129Sv seemed to be most susceptible to smoke exposure: these two strains might be used as animal models for smoke-related respiratory disorder studies.

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