6$^{\text{èmes}}$ Journées Franco-Italiennes de Chimie

VI$^{\text{e}}$ Giornate Italo-Francesi di Chimica

Marseille

16-17 avril/aprile 2012

Université d’Aix-Marseille, Campus St Charles
(Amphithéâtre des Sciences Naturelles)

Société Chimique de France

Società Chimica Italiana

La section PACA de la Société Chimique de France en collaboration avec les sections Ligurie et Piémont-Val d'Aoste de la Società Chimica Italiana, organise à Marseille les 16 et 17 avril 2012, la sixième édition des Journées Franco-Italiennes de Chimie.

Cet événement, qui a lieu tous les deux ans et qui est organisé en alternance par les deux pays, s'est déroulé en 2002 à Juan-les-Pins, en 2004 à Gênes, en 2006 à Turin, en 2008 à Nice et en 2010 à Gênes.

Ces journées ont un caractère interdisciplinaire et ont établi un contact durable entre les chercheurs de la région Provence-Alpes-Côte d'Azur et ceux des régions de la Ligurie et du Piémont-Vallée d'Aoste, dans le but d'une intégration toujours plus étroite, au niveau européen tant au niveau scientifique que culturel.

L’ensemble des domaines de la chimie sont abordés au cours de ces journées, notamment *la chimie organique et biomédicale, la chimie physique et analytique, la chimie pharmaceutique, la chimie de l’environnement et des produits naturels et la chimie des matériaux.*

Quatre conférences plénières de prestige, quatre conférences invitées, trente communications orales, mettant en avant les jeunes chercheurs, et plus de cent affiches sont présentées.

Nous remercions les sponsors pour leur participation au succès de ces journées, et vous souhaitons des journées marseillaises intéressantes et agréables.

Le comité d’organisation.

La sezione PACA (Provenza, Alpi e Costa Azzurra) della Società Chimica Francese, in collaborazione con le sezioni Liguria e Piemonte-Valle d'Aosta della Società Chimica Italiana, organizza a Marsiglia nei giorni 16 e 17 aprile 2012 la sesta edizione delle Giornate Italo-Francesi di Chimica.

Questa manifestazione, che si svolge alternativamente dai due paesi con cadenza biennale, è stata precedentemente organizzata a Juan-les-Pins (2002), Genova (2004), Torino (2006), Nizza (2008) e Genova (2010).

Le Giornate hanno un carattere interdisciplinare e permettono un rapporto di confronto durevole tra ricercatori della regione francese Provenza, Alpi e Costa Azzurra e quelli delle regioni italiane Liguria, Piemonte e Valle d'Aosta, in vista di una sempre più stretta integrazione scientifica e culturale.

Le presentazioni esplorano tutti i settori della chimica, in particolare la *chimica organica, inorganica, biomedicale, fisica, analitica, farmaceutica, dell'ambiente, dei materiali e industriale.*

Nell'ambito di queste giornate sono previste quattro prestigiose conferenze plenarie, quattro conferenze di relatori invitati dal comitato organizzatore, trenta relazioni orali per le quali sarà data priorità ai giovani ricercatori e più d'un centinaio di poster.

Ringraziamo gli sponsors per la loro partecipazione al successo di queste giornate e vi auguriamo giornate marsigliesi interessanti e piacevoli.

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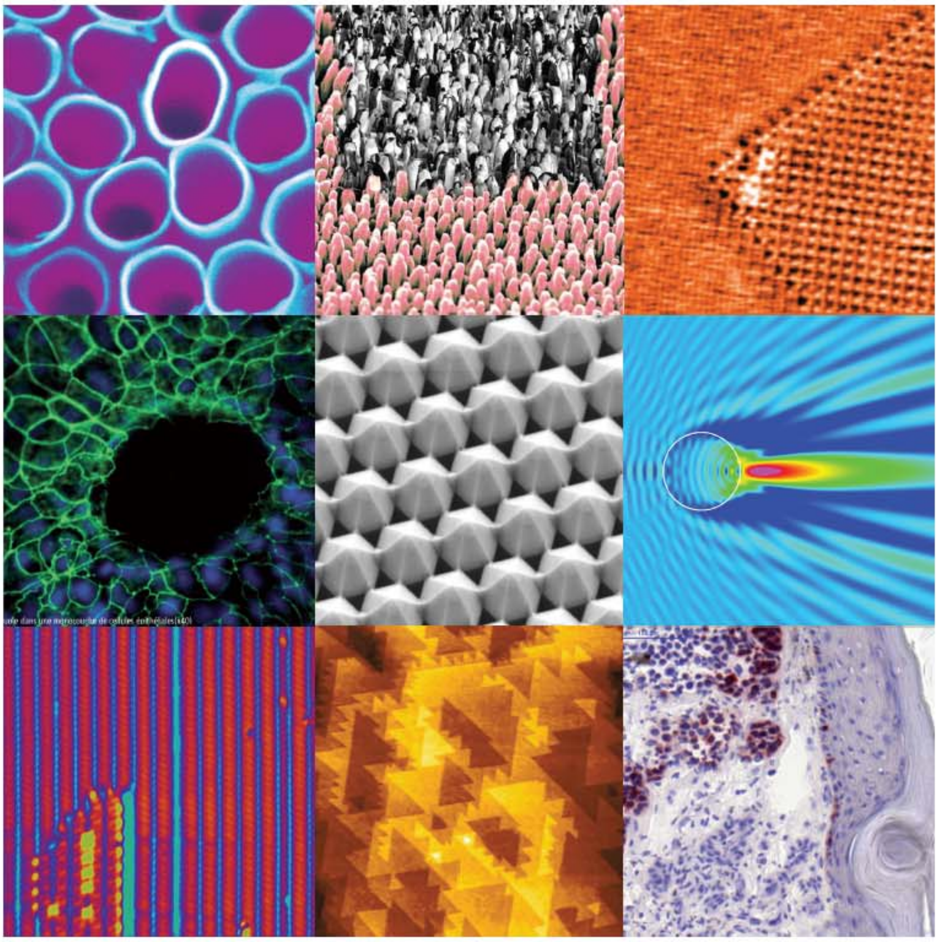
dans une monocouche de cellules endothéliales (x40)

Programme scientifique des $6^{èmes}$ Journées Franco-Italiennes de Chimie
Programma scientifico delle VI^{e} Giornate Italo-Francesi di Chimica

Université d'Aix-Marseille, Campus St Charles
(Amphithéâtre des Sciences Naturelles)

Lundi 16 avril 2012 / Lunedí 16 aprile 2012

8h30 Accueil des participants / Accoglienza dei partecipanti

9h15 Ouverture /Apertura

9h30 Didier GIGMES (PL1)
Nitroxide Mediated Polymerization: From Alkoxyamines to Advanced Polymer Materials

10h15 Fabio MORANA (COM1)
Organocatalytic Asymmetric Synthesis of β-Aryl-β-isocyanoesters

10h30 Daniela PINGRET (COM2)
Compréhension de la dégradation des huiles végétales traitées aux ultrasons

10h45 Jonathan MARTINELLI (COM3)
Redox Sensitive Dendrimeric BetaCD/Gd Chelates supramolecular adducts

11h00-11h30 Pause café – Session affiches / Pausa caffè – Sessione poster (Salle de conférences)

11h30 Davide VIONE (INV1)
Photochemical Processes in Surface Waters

12h00 Gilles LEMIERE (COM4)
$Bi(OTf)_3$-Catalyzed Hydroarylation of Allenes and Dienes

12h15 Anna PIATEK (COM5)
High-performance liquid chromatography determination of (R)-3-hydroxybutyric acid in human plasma

12h30 Didier DEVAUX (COM6)
Effect of the architecture of PEO based polymer electrolytes on their ionic conductivities

12h45 Fabrizio SORDELLO (COM7)
Photocatalytic hydrogen production on Pt-loaded TiO_2 inverse opals

13h00-14h30 Buffet – Session affiches / Pranzo – Sessione poster (Salle de conférences)

14h30 Adriana SACCONE (PL2)
Rare Earths and their Recycling for Energy and Environmental Sustainability

15h15 Fabien RODIER (COM8)
Diastereoselective Access to Spirolactones *via* Rh-Mediated [5+2]-Cycloaddition Reactions. En route to the AC core of Micrandilactone C

15h30 Valentina AINA (COM9)
Novel smart biomaterials for dental and orthopaedic applications: bioactive glasses containing metal nano-particles (NPs) conjugated with molecules of biological interest.

15h45 Laurence CHARLES (COM10)
Ion mobility mass spectrometry: a powerful tool to evidence shape variation of dendrimers upon multiple protonation

16h00 Lisa MONI (COM11)
Synthesis and Biological Evaluation of β-Amyloid and Tau Protein Aggregation Inhibitors for Alzheimer's Disease

16h15 Marlène LEJARS (COM12)
Grafted copolymers based on polydimethylsiloxane and poly(*tert*-butyldimethylsilyl methacrylate) synthesized by the RAFT process: a new class of binders for FRC/SPC hybrid antifouling coatings

16h30-17h00 Pause café – Session affiches / Pausa caffè – Sessione poster (Salle de conférences)

17h00 Sylvain ANTONIOTTI (INV2)
Catalyse, biocatalyse et synthons bio-sourcés

17h30 Yuriy SAKHNO (COM13)
Towards a "surface science model for biology": glycine adsorption on nanohydroxyapatite with well defined surfaces

17h45 Monika SKROBANSKA (COM14)
Phase formation during mechanical alloying of Mg–Ti–Si powders

18h00-18h45 Remise du Prix du Doctorant SCF-PACA et du Prix CDP Innovation 2012 / Premio del Dottorando SCF-PACA e Premio CDP Innovation 2012

18h05 Julien MAURY (COM15)
Aminomethylation of Michael Acceptors: Complementary Radical and Polar Approaches Mediated by Dialkylzincs

18h25 Manjunatha REDDY (COM16)
NMR Methods and Applications for the Study of Complex Mixtures

Mardi 17 avril 2012 – Martedí 17 aprile 2012

9h00 Guido VISCARDI (PLE3)
Dye Sensitized Solar Cells: Fundamentals and Perspectives

9h45 Hamid MARZAG (COM17)
Efficient Synthesis of Aryl *C*-nucleosides through Friedel-Crafts reaction. Post Synthetic Transformations

10h00 Luca BONO (COM18)
On Line SPE - LC-MS/MS Quantification of Triazine Pesticides in Water

10h15 Gilles QUELEVER (COM19)
Novel and efficient synthesis of poly(amino)ester dendrimers

10h30-11h00 Pause café - Session affiches / Pausa caffè – Sessione poster (Salle de conférences)

11h00-11h30 Cédric GARNIER (INV3)
Transfert et spéciation des éléments traces métalliques en zone côtière: approche analytique et modélisation

11h30 Gaia FENOGLIO (COM20)
Non invasive analysis of manuscript covers: portable X-ray Fluorescence enlightening medieval jewellery masterpieces

11h45 Paul BREMOND (COM21)
Chemically Triggered C–ON Bond Homolysis of Alkoxyamines. Quaternization of the Alkyl Fragment

12h00 Stefania ZAPPIA (COM22)
Synthesis and characterization of novel highly photoresponsive nanosensors

12h15 Wilfried RAIMONDI (COM23)
1,2-dicarbonyl compounds as pro-nucleophiles in asymmetric transformations

12h30-14h00 Buffet - Session affiches / Pranzo - Sessione poster (Salle de conférences)

14h00 Remise du Grand Prix de la SCF-PACA 2012 / Grande Premio SCF-PACA 2012
Maurice SANTELLI: Tédicyp, a new ligand for palladium (PL4)

14h45 Valentina PIRRO (COM24)
Multivariate Strategies for Screening Evaluation of Chronic Alcohol Abuse

15h00 Mattia LUCCHINI (COM25)
Biochemical sensors based on magnetic nanoparticles

15h15 Cinzia PASSINI (COM26)
Imprinted Thin Layers for Capillary Electrophoresis

15h30-16h00 Pause café – Session affiches / Pausa caffè – Sessione poster (Salle de conférences)

16h00 Chiara BRULLO (INV4)
Synthesis and Biological Evaluation of New Small Molecules as Multiple Target Inhibitors in the Chemotaxis Process

16h30 Nicolas BALDOVINI (COM27)
The diketonic constituents of *Helichrysum italicum*

16h45 Marta GIORGIS (COM28)
Carnosine analogues containing Phenol substructures

17h00 Ahlem BOUHLEL (COM29)
Access to original spirocyclic derivatives *via* inter- or intramolecular reaction mediated by manganese(III) acetate

17h15 Florence VACANDIO (COM30)
Synthesis and characterization of zirconia nanotubes by electrochemical anodisation of sputtered zirconium thin films

17h30 Clôture des 6èmes Journées Franco-italiennes de Chimie – Chiusura delle VI^{e} Giornate Italo-Francesi di Chimica

CONFERENCES PLENIERES

CONFERENZE PLENARIE

$6^{\text{èmes}}$ *Journées Franco-Italiennes de Chimie*
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

Nitroxide Mediated Polymerization : From Alkoxyamines to Advanced Polymer Materials

Gigmes D.

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Controlled Radical Polymerization (CRP) offers an unique opportunity to obtain well defined co-polymers with predictable molar masses, topologies, end group functionalities and narrow molar masses distribution. Significant advances in every CRP procedure allow now the preparation materials that were difficult to manufacture a decade ago such as bioconjugates, organic/inorganic composites, or surface-tethered copolymers. Among the different techniques currently used in CRP, Nitroxide Mediated Polymerization (NMP) has attracted a renewal of interest because of its simplicity, since in most cases it requires only adding the suitable alkoxyamine to the polymerization system. This presentation will highlight our latest advances in the field of NMP. We will focus more particularly on the development of a highly labile alkoxyamine the so-called MAMA-SG1 or blocbuilder® and its applications in advanced polymer material synthesis. [2]

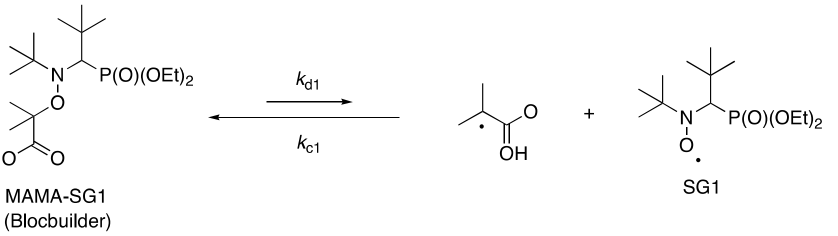

Figure 1

In a second part, we will present that the use of MAMA-SG1, in 1,2 intermolecular addition on an appropriate olefin, represents a key step and a powerful tool for macromolecular architecture synthesis[2].

The potential of this strategy will be illustrated through the preparation of various poly(styrene-*b*-ethylene oxide)-*b*-poly(styrene) triblock copolymers for both elaboration of synthetic nano-porous membrane[3] and polymer electrolyte for lithium metal battery. The interest of this approach will be also demonstrated by the synthesis of a poly(lactide)-*b*-poly(2-hydroxyethyl (meth)acrylate) diblock copolymer[4] designed for the preparation of synthetic tubular guide in nerve repair applications.

[1] Chauvin, F.; Dufils, P-E.; Gigmes, D.; Guillaneuf, Y.; Marque, S. R. A.; Tordo, P.; Bertin, D. *Macromolecules,* **2006***,* 16, 5238-5250

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Didier Gigmes received a PhD in organic chemistry (1998) under the supervision of Prof. Paul Tordo (Marseille, France). Then he completed a postdoctoral fellowship at Elf-Atochem, North America in Pennsylvania (USA) under the guidance of Dr. Gary Silverman. In 2001, he obtained a position of researcher at CNRS to develop the nitroxide-mediated polymerization (NMP) technique. In 2008, he defended his Habilitation at the University of Provence (Marseille, France) and in October 2010, he was appointed Research Director at the CNRS working at Aix-Marseille University (Marseille, France). During the past few years he was working on the development of NMP and especially in the design of a highly efficient alkoxyamine for macromolecular engineering. With his group, his main concerns are focused, on the comprehension of the mechanisms involved in NMP but also the development and use of new methodologies for the synthesis of advanced polymer materials. These materials are designed to find applications in various fields such as health, environment and energy. Up to now, he is the co-author of 100 papers and 7 patents.

PLE2

RARE EARTHS AND THEIR RECYCLING FOR ENERGY AND ENVIRONMENTAL SUSTAINABILITY

A.Saccone

Dipartimento di Chimica e Chimica Industriale, Università di Genova

Rare earth metals consist of 17 elements of the periodic table: the fifteen lanthanides, scandium and yttrium. Rare earths are being used in many applications today. Several “green” technologies depend on them since their unique properties can save weight and increase efficiency in products such as hybrid electric vehicles, generators in wind power plants, low energy light bulbs, etc. These elements are not rare, but, unfortunately, their concentration in ore deposits is often low and their extraction and refining quite difficult. Today China stands for more than 95% of the world supply. Increasing global demand and Chinese reductions in export quotas over the past few years have led to international concerns about future supply shortages. For this reason the recycling of rare earths, very uncommon issue until today, have to be considered to mitigate supply risk.

In this talk the present "state of the art" in recycling of rare earth based materials will be discussed, especially taking into account the recycling of rare earths from magnets.

Adriana Saccone is Full Professor for General and Inorganic Chemistry at the Faculty of Sciences MFN of the University of Genova (Italy), where she gives lectures of Inorganic Chemistry and Advanced Inorganic Chemistry.
- Member of the Senate of the University of Genova
- Coordinator of the Doctorate Course "Science and Chemical Technologies" (from XXVI cycle)
- Member of the Directive Committee of the Divisione di Chimica Inorganica of the Italian Chemical Society.
- Member of the Directive Committee of the Italian Group of Calorimetry and Thermal Analysis (GICAT).
- Formerly Head of the Corso di Laurea in Chemistry and Chemical Technologies and of the Laurea Specialistica in Chemical Sciences of the University of Genova.
- Scientific Editor of the International Journal "Chemistry of Metals and Alloys". Member of the Organizing or Scientific Committees of International and Italian Scientific Meetings and Conferences. She took part both as lecturer and organizer to advanced schools sponsored by the Italian Chemical Society. She has been Guest Editor of a number of special issues of international scientific journals.
- She collaborates with international and national scientific research groups, in particular with: Institut für Physikalische Chemie of the Vienna University; Department of Inorganic Chemistry of the Ivan Franko Università of Lviv (Ucraina); Institute of Materials and Surfaces Science and Engineering, Instituto Superior Técnico, Technical University of Lisboa; Dipartimento di Chimica Strutturale e Stereochimica Inorganica, University of Milan; Dipartimento di Scienza dei Materiali e Ingegneria Chimica, Politecnico of Turin; Dipartimento di Ingegneria Meccanica, University of Padova; Dipartimento di Fisica, University "La Sapienza" of Rome.
- Co-author of more than 180 original publications in refereed international journals and about 200 oral communications or posters presented at a range of national and international conferences, published on Proceedings. She is co-author of a book on Intermetallic Chemistry (Elsevier, Pergamon Materials Series, 2008), of invited chapters on books and about 100 assessments on the properties of binary and ternary alloys taking part of a project of the Max-Planck Institute of Stuttgart (Germany) co-ordinated by the Materials Science International Team (MSIT).

The main fields of research, all concerning the solid state chemistry, are briefly summarized in the following:

- Experimental determination of phase equilibria of binary and complex metallic systems; particular attention is paid to the constitutional properties of the systems formed by the rare earth metals with light elements (Mg, Al, Si, Ge) and with transition elements (Cu, Ag, Au).
- Prevision of phase equilibria and contributions to the systematics of the binary and ternary alloys of the rare earth elements
- Crystallographic characterization of intermetallic phases
- Investigation of physical properties of intermetallic compounds, such as resistivity and susceptibility; electrochemical investigation and corrosion behaviour of Mg-based and Al-based alloys; investigation of the electrocatalytic behaviour of selected binary and ternary systems involving rare earths.
- Investigation of the hydrogen adsorption properties of selected intermetallic compounds.

PLE3

Dye Sensitized Solar Cells: Fundamentals and Perspectives.

Guido Viscardi

Dipartimento di Chimica, via Pietro Giuria 7, Università di Torino, 10125 Torino – Italy.

Solar energy is going to play a crucial role as a clean energy source. Organic photovoltaic cells (OPV) have recently risen great expectations, because they can be produced at low cost in large scale plants. OPVs are conceived as thin films devices, deposited either on flexible or on rigid substrates, made of easy-to-find, no-toxic materials. Their main drawback is its efficiency, significantly lower than that of (poly)crystalline Si, of CdTe and of other thin film cells. A promising alternative is the hybrid device named Dye-Sensitized-Solar-Cell (DSC). Introduced by M. Grätzel [1], a DSC is based on a mesoporous TiO_2 film composed of nanometer sized particles with an adsorbed layer of a sensitizer. Sunlight pumps electrons from a lower (HOMO) to a higher (LUMO) energy level of the sensitizer, and the photogenerated electrons are directly injected from the LUMO level of the sensitizer into the conduction band of TiO_2 on which the dye molecules are grafted.

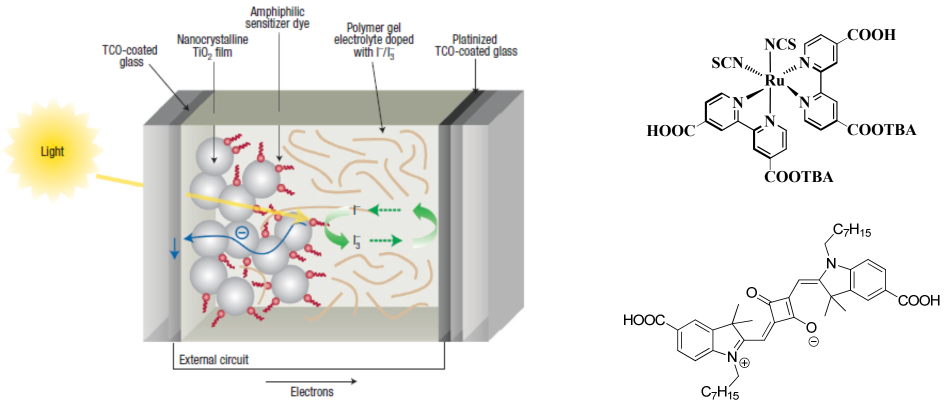

Figure 1: scheme of a DSC (reference 2) and examples of Ru-complex (N719) and squaraine sensitizers.

Ru(II) complexes have been by far the most investigated and efficient sensitizer systems yielding a conversion efficiencies over 12% (AM 1.5) [3]. The industrial interest is large in particular for sustainable architecture; so, in addition to efficiency of photoelectric effect, other improvements are required in terms of lowest costs, durability, aesthetic appreciation and availability of different colors. Much of work has been focused on the sensitizer. Metal-free dyes have been studied: push-pull polyenes, coumarines, squaraines, cyanines [4]. Organic dyes appear interesting owing to high molar absorption coefficients, versatile molecular design and low cost of synthesis and purification. Cobalt complexes have been developed as innovative electrolytes as also gel- and solid-state mixtures.

[1] B. O'Regan, M. Grätzel. Nature. 1991,353, 737.
[2] J.R. Durrant and S.A. Hacque. Nature Materials 2003, 362.
[3] A. Yella, H.-W. Lee, H. N.k Tsao, C. Yi, A. K. Chandiran, M.K. Nazeeruddin, E. W.-G. Diau, C.-Y. Yeh, S.M. Zakeeruddin, M. Graetzel. Science, 2011, 334, 629-634.
[4] Martiniani, A.Y. Anderson, C. Law, B.C. O'Regan, C. Barolo. Chem Commun, 2012, 48, 2406–2408; J. Park, C. Barolo, F. Sauvage, N. Barbero, C. Benzi, P. Quagliotto, S. Coluccia, D. Di Censo, M. Grätzel, M.K. Nazeeruddin, G. Viscardi. Chem Comm 2012, 48, 2782-2784.

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Guido VISCARDI, born in 1957, is full professor in Organic Chemistry next the Sciences Faculty of Turin University. Research fields concern in Heterocyclic Chemistry, Chemistry of Dyes and Applied Organic Chemistry. Novel dyes were synthesized by the preparation of novel heterocyclic intermediates for several applied fields, from the more traditional dyeing process of textiles to more advanced and non-conventional uses as solar energy recovery, micro- and nano-sensors, optoelectronics, analytical chemistry, bio-conjugation, liquid crystals.

He is author of 145 scientific publications, 2 patents, 2 monographs.

PLE4

Tedicyp as ligand for palladium chemistry

Santelli M.

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The lecture deals with the synthesis and use of the *cis*,*cis*,*cis*,1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane (Tedicyp) as ligand for palladium chemistry.

Through the use of $[(\eta^3\text{-}C_3H_5)PdCl]_2$/Tedicyp (1:2) as catalyst, a range of palladium catalyzed coupling reactions (Tsuji-Trost, Sonogashira, Heck, Suzuki reactions) are described. In each case, this catalyst can be used at a very low catalyst loading even for reactions of sterically hindered reagents (turnover numbers up to 10^6 at 10^9 have been reached). More of 3000 compounds including new products have been obtained by this way.

In conclusion, the complex formed by association of Tedicyp and $[(\eta^3\text{-}C_3H_5)PdCl]_2$ seems to possess a fine balance of steric and electronic properties, which allows fast catalytic processes to be achieved with a very wide variety of substrates.

Maurice Santelli received his PhD in chemistry working with Prof. M. Bertrand (homoallenylic participation, non-classical ions). He had a postdoctoral position at the University of Cambridge (U. K.) in 1973–74 (Prof. R. A. Raphael). After an appointment at the University of Oran (Algeria) (1975–77), he is presently emeritus professor of organic chemistry at Aix-Marseille University. His main research areas are physical organic chemistry, electrophilic activation (chemistry of allylsilanes), palladium-chemistry with new ligands, and synthesis of bioactive products (polyunsaturated fatty acids, Prelog-Djerassi lactone, non-natural steroids, vitamine D derivatives...).
He is the authors of about 300 manuscripts.

CONFERENCES INVITEES

CONFERENZE INVITATE

INV1

Photochemical processes in surface waters

Davide Vione,[1] Valter Maurino, Claudio Minero

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Chemical reactions driven by sunlight are important processes in surface freshwaters, where they are involved in the transformation of xenobiotic molecules and of naturally occurring compounds [1]. The relevant reactions are generally distinguished into direct photolysis and indirect photodegradation. Direct photolysis involves molecules that absorb sunlight and are transformed as a consequence. Main molecular factors involved in the process are the direct photolysis quantum yield, namely the ratio of the transformation rate to the absorbed photon flux, and the absorbance values at environmentally significant wavelengths [2]. Indirect phototransformation involves reactive transients such as $^{\bullet}OH$, $CO_3^{-\bullet}$, $^1O_2$ and the triplet states of chromophoric dissolved organic matter (^{3}CDOM*). They are generated by irradiation of photosensitisers such as CDOM (producing ^{3}CDOM*, $^1O_2$ and $^{\bullet}OH$), nitrate and nitrite ($^{\bullet}OH$) [3,4]. The radical $CO_3^{-\bullet}$ is produced *via* oxidation of carbonate/bicarbonate by $^{\bullet}OH$ and, at a lesser extent, upon oxidation of carbonate by ^{3}CDOM* [5]. The transient species formed by irradiated photosensitisers can induce the degradation of naturally occurring compounds and of pollutants. Photochemical transformation kinetics in surface waters can be modelled, on the basis of photochemical reactivity parameters of the relevant molecules (direct photolysis quantum yield and second-order reaction rate constants with $^{\bullet}OH$, $CO_3^{-\bullet}$, $^1O_2$ and ^{3}CDOM*) and of water chemical composition [6,7]. Some results of this approach are presented.

CDOM, the main photosensitiser in surface waters, is a complex mixture of an elevated number of compounds with different origin. The most photoactive fraction is constituted by humic substances (mainly humic and fulvic acids) derived from soil. They are major constituents of the so-called allochthonous CDOM fraction. Other less photoactive organic substances are released by aquatic organisms and constitute the autochthonous CDOM fraction [8]. Molecular size is an important parameter that influences CDOM photoactivity: the fraction smaller than 0.1 μm produces most of the species (*e.g.* ^{3}CDOM* and $^1O_2$) that are available to react with dissolved compounds [9]. In the case of larger-size CDOM fractions, reactive species are probably confined in the hydrophobic core [10]. Overall, the chemical composition of CDOM is largely unknown and model photosensitisers are used as proxies to study some details of specific processes. The use of quinoid compounds as CDOM proxies is very useful in modelling studies [11].

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Davide Vione was born in Moncaliery (Torino, Italy) in 1974. Presently he is Associate Processor in the Department of Chemistry of the University of Torino. His main research interests are the photochemistry of surface and atmospheric waters, heterogeneous photocatalysis and its applications to the environmental and cosmetic fields, advanced oxidation processes (such as Fenton reaction and sonochemistry) applied to waste remediation.

His publication record to date includes 105 ISI articles, 9 book chapters and over 60 congress communications.

INV2

$6^{èmes}$ Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

Catalyse, Biocatalyse, et synthons bio-sourcés

Sylvain Antoniotti

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Environmental concerns in regards of the way of life of developed countries and the growing desire of a sustainable development have stressed the scientific community to provide mankind with solutions to many problems (climate change, air, water, and soil pollutions, diminishing feedstock, threats on biodiversity ...). In the field of chemistry, new concepts and paradigms have been formulated in the nineties and have matured into subfields of chemical sciences, namely green and sustainable chemistry. Catalysis and biocatalysis may "naturally" satisfy many of the 12 principles of green chemistry by offering, in addition to intrinsic assets (small amounts of material used, increase of reaction rates resulting in reduced reaction time or reduced operating temperature), good specificity and selectivity.

We will present our work from the last years on the development of eco-friendly methodologies in organic synthesis based on the use of catalysis, biocatalysis, and renewable starting materials from plants.[1-3]

Review articles:

[1] A.-L. Groussin ; S. Antoniotti., Valuable chemicals by the enzymatic modification of molecules of natural origin: terpenoids, steroids, phenolics and related compounds, *Bioresource Technol.*, **2011**, doi:10.1016/ j.biortech.2011.1010.1050.
[2] S. Antoniotti ; S. Poulain-Martini ; E. Duñach, Electrophilic Functionalization of Non-Activated Olefins Catalyzed by Lewis Superacids, *Synlett*, **2010**, 2973-2988.
[3] S. Antoniotti ; V. Dalla ; E. Duñach, Metal Triflimidates: better than Metal Triflates as Catalysts in Organic Synthesis-the Effect of a Highly Delocalised Counter-Anion, *Angew. Chem. Int. Ed.*, **2010**, *49*, 43, 7860-7888.

Sylvain Antoniotti

Education (U. Nice Sophia Antipolis)

- DEA Chimie Moléculaire 2000 (1/11, mention TB).
- Doctorat es sciences, chimie, 2003 (Dir. E. Dunach). « Oxydation d'époxydes en α-dicétones catalysée par des dérivés du bismuth. Applications en chimie fine. ».
- HDR, 2008. « Catalyses et méthodologie de synthèse organique éco-compatible. ».

Curriculum

- Post-doc, 2003-2004, Rensselaer Polytechnic Institute, Troy, NY, USA (Prof. Jon Dordick). Utilisation d'enzymes pour la synthèse d'oligophénols bioactifs en phase liquide et en phase solide.
- ATER, 2004-2005, ENSCP, aujourd'hui ChimieParisTech (Prof. J.-P. Genêt/Dr V. Michelet). Nouvelles réactions de cycloisomérisation d'alcools et d'acides bis-homo propargyliques par des complexes d'iridium et d'or.
- CR CNRS, 2005-présent, LCMBA, aujourd'hui Institut de Chimie de Nice.

Activités de recherche

33 articles >650 citations, 1 chapitre d'ouvrage, 2 brevets d'invention, 11 confs invitées :
    Méthodologie de synthèse en chimie organique éco-compatible, chimie verte
    Hemisynthèse à partir de substances naturelles renouvelables
    Catalyse organométallique (Bi, Sn, Au), superacides de Lewis
    Catalyse enzymatique (hydrolases, peroxidases, monooxygénases)
    Synthèse biomimétique

INV3

Transfer and speciation of trace metals in coastal environments: analytical and modelling approaches

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Coastal environments are known to be strongly influenced by various continental inputs, leading to potential increase in the different environmental compartments (water column, sediment, biota, …) of inorganic (e.g. metals, metalloids, …) and organic (e.g. PAH, PCB, pharmaceuticals, …) contaminants which are naturally present at trace or ultra-trace levels. Among all these possible sources of marine pollutions, large coastal cities impact is one of the most worrying, especially in the Mediterranean Sea, due to the rapid population increase all around the coasts. These inputs, partly diffusive and strongly linked to weather conditions (e.g. episodic intensive rain events leading to important urban/industrial land weathering) have to be carefully studied to be compared to other contaminant sources as large river or atmospheric inputs. In such context, the evaluation of trace metals dynamic and fate in coastal environments is a complex issue, which needs the use/development of numerous sampling, analytical, experimental and modelling tools.

The present talk will be illustrated by recent results obtained in the framework of different research programs (MARSECO, GIRAC-PACA, CARTOCHIM, PHC COGITO, …) in 3 contrasted Mediterranean coastal areas: (1) the Marseille (France) bay, a large agglomeration directly connected to the open sea, (2) the Toulon bay (France), a semi-closed area presenting an important contamination of its sediments and (3) the Krka river estuary (Šibenik bay, Croatia), a stratified and oligotrophic estuary with ultra-trace levels of metals except in summer due to significant inputs from nautical activities (e.g. antifouling paints).

Cédric Garnier was born in Brest (France) in 1977. After a PhD in environmental chemistry at the Université du Sud Toulon Var (France) obtained in 2004, he was recruited as assistant professor in 2005 at the Institut des Sciences Moléculaires (UMR CNRS 5255, University Bordeaux 1, France). Since 2009, he is assistant professor at the PROTEE laboratory (Université du Sud Toulon Var), defended his Habilitation in 2010 and became leader of the CAPTE research team of the PROTEE laboratory. His main research activities concern the study of trace metal/metalloids dynamic in aquatic systems (such as river, estuary, coastal area and sediments) by the use/development of various analytical and modelling tools, especially based on electrochemical techniques to apprehend metal speciation and binding properties toward organic ligands.
He is the co-author of 25 papers and over 75 congress oral/poster communications."

INV4

Synthesis and biological evaluation of new small molecules as multiple target inhibitors in the chemotaxis process.

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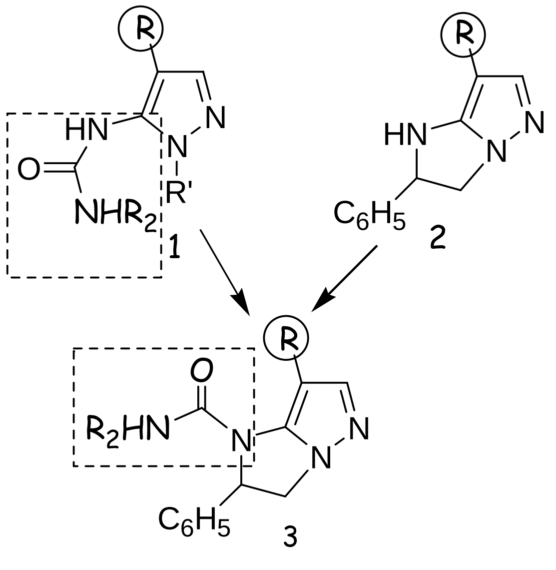
Chemotaxis is a complex process which consists of the neutrophils migration to the site of inflammation. Various chemoattractants can induce chemotaxis, in particular fMLP, and CXC chemokine IL8 (also named CXCL8), which both bind on specific G-protein coupled receptors (FPR and CXCR, respectively). Each step of this patho-physiological event is regulated by downstream signalling molecules, including phosphatidylinositol 3-kinase (PI3K), phospholipase C, mitogen activated protein kinases (MAPKs) and extracellular response kinases 1 and 2 (ERK1/2) [1].

We recently reported many pyrazolyl-urea derivatives (compounds **1**) as very potent *in vitro* inhibitors in the IL8- or in fMLP-OMe-induced chemotaxis. Other compounds showed interesting dual activity [2-3]. Compounds **1** were obtained by functionalization of the suitable 5-amino-1*H*-pyrazole-4-carboxylic acid ethylester N1-substitued with a one-pot reaction using phosgene and the suitable amines or appropriate phenyl isocyanate. By cyclization of the same pyrazole intermediates, we obtained new 2-phenyl-2,3-dihydro-1*H*-imidazo[1,2-*b*]pyrazoles 7-substituted (compounds **2**) which resulted in potent inhibitors of fMLP-OMe chemotaxis [4]. To increase our knowledges about SAR and mechanism of action of these chemotaxis inhibitors, we designed and synthesized compounds **3** including in the same structure the rigid scaffold of compounds **2**, the urea moieties of the most active compounds **1** and the same alkyl substituent at 4 position of pyrazole ring [5].



Further biological studies confirmed that two different chemotaxis mechanisms, in particular the MAPK/ERK and PKC pathways, are involved in compounds **1-3** action. This good versatility represents the most important characteristic of these new molecules, particularly as concerns their pharmacological application.

In fact, the most selective ones could be very useful as pharmacological tools to assess the knowledges about the intracellular mechanism of neutrophil recruitment. Whereas, the dual active compounds are the starting point for the development of new multi-targeted antiinflammatory drugs. All synthesis and biological data will be reported.

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COMMUNICATIONS ORALES

COMUNICAZIONE ORALI

COM1

$6^{èmes}$ Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
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16-17 avril/aprile 2012

Organocatalytic Asymmetric Synthesis of β-Aryl-β-isocyanoesters

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The asymmetric addition of malonates to *in situ* generated *N*-formylimines derived from aromatic aldehydes was achieved under phase-transfer catalysis using *Cinchona* alkaloids derived ammonium quaternary salts. The resulting β-formamido malonates have been efficiently converted into β-aryl-β-isocyanoesters. Their utility in the multicomponent Ugi reaction with chiral cyclic imines has been demonstrated.

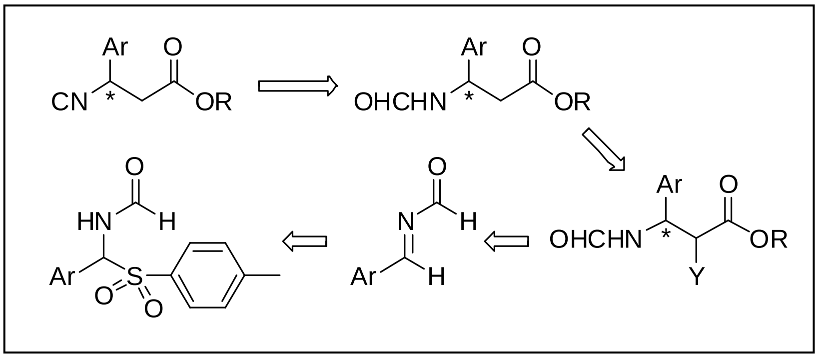

Figure 1 : retrosynthetic design

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6èmes Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
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Compréhension de la dégradation des huiles végétales traitées aux ultrasons

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(2) *Laboratoire de Chimie BioOrganique et des Systèmes Moléculaire Vectoriels, Faculté des Sciences, 33 rue Louis Pasteur, 84000 Avignon, France.*

L'utilisation de technologies innovantes telles que les ultrasons dans l'industrie alimentaire pour la préparation et transformations des aliments devient de plus en plus importante [1]. Cette technologie dite « verte » permet un gain de temps, rendement et efficacité avec une diminution des coûts et déchets nocifs. Cependant, dans le cas des produits riches en lipides, l'apparition d'une odeur de rance est observée et reporté dans la littérature sans que plus d'études se fassent pour vérifier l'impact des ultrasons dans ce type de produit [2]. A partir de l'étude du mécanisme de dégradation des lipides, une étude a été mené afin de comprendre la voie probable par lequel ces composés volatiles ce sont formés lors d'un traitement ultrasonore sur une huile de tournesol modèle. Le traitement aux ultrasons a été avec deux sondes à ultrasons de natures différentes (figure 1) et des paramètres physicochimiques, ainsi que des analyses par GC / MS (chromatographie en phase gazeuse couplée à la spectrométrie de masse) et par RPE (résonance paramagnétique électronique) ont été faits dans les échantillons avant et après traitement ultrasonore. Les résultats nous ont permis de différencier l'impact pour les deux appareils de façon à minimiser la dégradation, ainsi que de trouver la voie possible de dégradation issue de l'application des ultrasons sur les lipides.

Figure 1: Traitement ultrasonore d'une huile.

[1] Chemat F., Zill-e-Huma, et Khan MK. (2011). Applications of ultrasound in food technology: Processing, preservation and extraction. Ultrasonics Sonochemistry, 18 (4), 813-835.
[2] Pingret D., Fabiano-Tixier A-S., Petitcolas E., Canselier J-P., et Chemat F. (2011). First Investigation on Ultrasound-Assisted Preparation of Food Products: Sensory and Physicochemical Characteristics. Journal of Food Science, 76 (2), C287-C292.

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COM3

$6^{èmes}$ Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
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Redox sensitive dendrimeric β-CD/Gd-chelates supramolecular adducts

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The design of responsive ("smart") probes represents one of the most exciting research areas in the development of MRI contrast agents. Their performance can be modulated by changes in the physiological environment such as pH, partial oxygen pressure, metal ion concentration or enzyme activity. We have prepared a new type of Gd-based MRI probe based on a dendrimeric structure hold together by disulfide bonds, that can be cleaved under reducing conditions like those where specific enzymes or high radical concentrations are associated with a disease state (*e.g.* tumors or strokes). The activation of the agent is signaled by a change in the relaxation properties.

The macromolecular architecture of the agent consists of β-cyclodextrin (CD) units attached to a PAMAM-G1 dendrimer through a disulfide bond. Each CD cavity can host a hydrophobic moiety from a Gd-complex, with the binding affinity depending on the nature of the moiety. The formation of the inclusion compounds has been followed *via* relaxometric titration with either Gd-DOTA-MA-Ad or (Gd-AAZTA)$_2$-Ph-Ad (see Figure 1). The two complexes present high affinities (~10^4 and ~10^6 M^{-1}, respectively) for the CD units of the dendrimer through their adamantane pendant group. The MRI contrast effect is sensibly enhanced (up to +70%) upon binding of the Gd-complexes to the polymeric structure. NMRD studies were carried out on both the free complexes and their inclusion compounds. Finally, reduction experiments were run *via* relaxometric technique, as well as investigations on the competition between the paramagnetic dendrimer and human serum albumin for (Gd-AAZTA)$_2$-Ph-Ad: the paramagnetic probes are not displaced by HSA from the dendrimeric structure, thus being potentially suitable for *in vivo* applications.

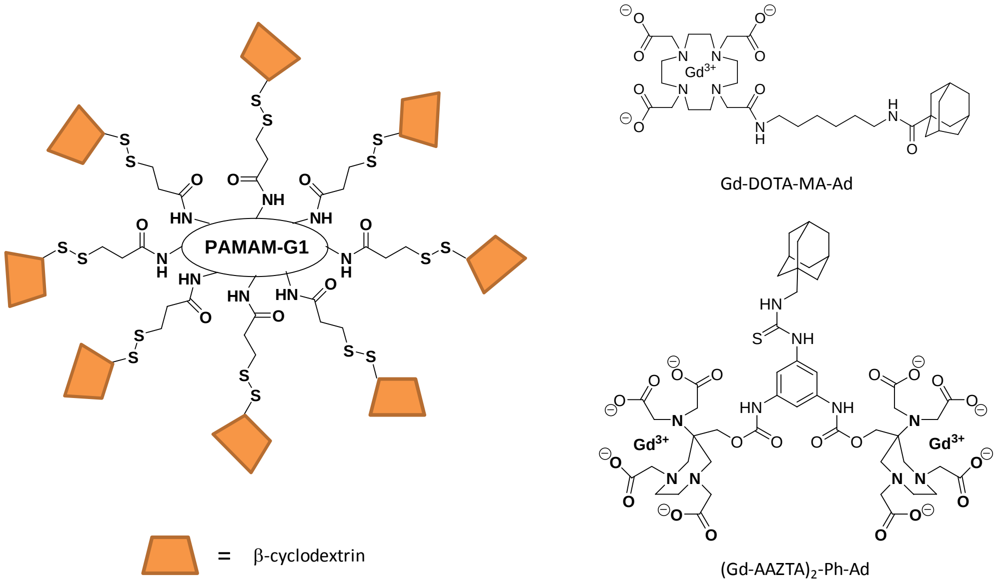

Figure 1 : Structures of PAMAM-CD$_8$ (left), Gd-DOTA-MA-Ad and (Gd-AAZTA)$_2$-Ph-Ad.

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COM4

6èmes Journées Franco-Italiennes de Chimie
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16-17 avril/aprile 2012

Bi(OTf)$_3$-Catalyzed Hydroarylation of Allenes and Dienes

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The development of catalytic, clean, efficient and mild synthetic methods to create C–C bonds remains one of the most important topics in the field of organic chemistry. In this context, catalytic Friedel-Crafts reactions have gained a particular attention.[1] The hydroarylation, namely the addition of an arene C–H bond across a multiple bond, represents the most atom-economical way to functionalize aromatic nuclei since theoretically no waste is produced during the reaction. Although the studies concerning the catalytic hydroarylation of alkynes and alkenes have been well-undertaken, the extensions to related allenes and 1,3-dienes have been more disregarded. Hydroarylation of allenes has been mainly reported using noble transition-metal catalysts based on gold[2] and platinum[3] derivatives. Despite their efficiency, these methodologies require the use expensive catalysts and are limited to the functionalization of electron-rich arenes.

Our group has been interested in the development of new cycloisomerization processes catalyzed by triflate[4] and triflimide[5] metal salts. We found that bismuth(III) triflate could be employed successfully to promote the intra- and intermolecular hydroarylation of allenes and 1,3-dienes. A sequential bis-hydroarylation of the allene moiety was also developed giving access to various interesting polycyclic structures (Figure 1).

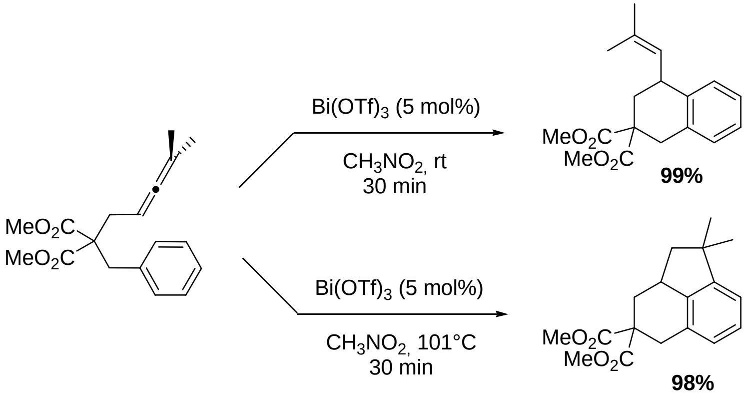

Figure 1 : Intramolecular hydroarylation of allene catalyzed by Bi(OTf)$_3$

[1] Rueping, M.; Nachtsheim, B. J. *Beilstein J. Org. Chem.* **2010**, *6*, 6 and references therein

[2] (a) Tarselli, M. A.; Gagne, M. R. *J. Org. Chem.* **2008**, *73*, 2439; (b) Watanabe, T.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett.* **2007**, *9*, 4821.

[3] Mo, J.; Lee, P. H. *Org. Lett.* **2010**, *12*, 2570.

[4] (a) Cacciuttolo, B.; Poulain-Martini, S.; Duñach, E. *Eur. J. Org. Chem.* **2011**, *2011*, 3710; (b) Godeau, J.; Olivero, S.; Antoniotti, S.; Duñach, E. *Org. Lett.* **2011**, *13*, 3320.

[5] (a) Grau, F.; Heumann, A.; Duñach, E. *Angew. Chem. Int. Ed.* **2006**, *45*, 7285; (b) Ben, O. R.; Affani, R.; Tranchant, M.-J.; Antoniotti, S.; Dalla, V.; Duñach, E. *Angew. Chem., Int. Ed.* **2010**, *49*, 776.

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COM5

$6^{èmes}$ Journées Franco-Italiennes de Chimie
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16-17 avril/aprile 2012

High-performance liquid chromatography determination of (*R*)-3-hydroxybutyric acid in human plasma

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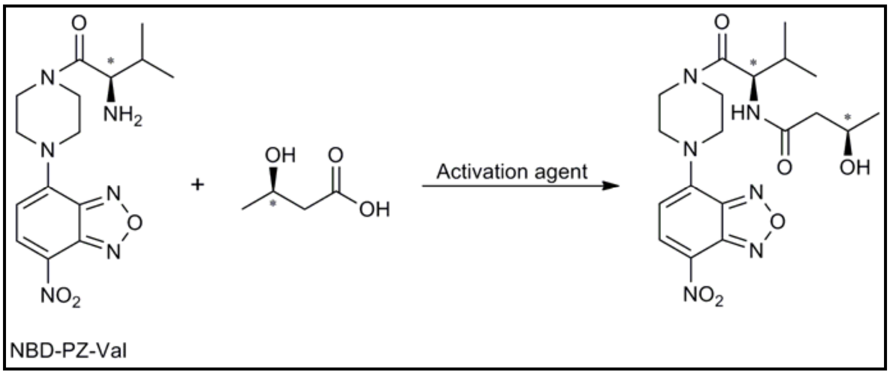
(2) *CNR – Institute of Chemical Methodologies, Rome, Italy*
(3) *Present address: Chemessentia-SRL, Via G. Bovio, 6-28100 Novara, Italy*

The accurate determination of (*R*)-3-hydroxybutyric acid [(*R*)-3-HBA] is important in the diagnosis of diabetes and other metabolic disorders. To this purpose, several methods for the determination of this compound have been reported. These procedures, which are simple and accurate, are based on the enzymatic method of Williamson *et al.*;[1] however, these methods are not sensitive enough and require a large volume of serum sample to obtain reliable value.

More recently, a sensitive method for analyzing (*R*)-3-HBA by gas chromatography-mass spectrometry (GC-MS) has been reported.[2] However, this method requires a specific and expensive instrument that may be out of reach for many laboratories. Given these limitations and on the basis of our previous experience in this field,[3] we have developed and validated a sensitive and convenient high-performance liquid chromatography (HPLC) method. This method is based on the reaction of (*R*)-3-HBA with our chiral derivatization agent (2*S*)-2-amino-3-methyl-1-[4-(7-nitro-benzo-2,1,3-oxadiazol-4-yl)-piperazin-1-yl]-butan-1-one (NBD-PZ-Val) in the presence of the coupling agent *O*-(7-azobenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) and *N*-ethyldiisopropylamine (DIEA) to produce a fluorescent derivative that can easily monitored fluorimetrically at $\lambda_{ex} = 489$ nm and $\lambda_{em} = 532$ nm.

A calibration curve for (*R*)-3-HBA standard solution showed good linearity in the range of 10 to 500 μM with 0.9997 correlation coefficient. The analytical method was successfully applied to human plasma samples from normal healthy subjects.



Scheme: Derivatization reaction of (R)-3-HBA with the chiral reagent NBD-PZ-Val.

[1] Williamson, D.H., Mellanby, J., Krebs, H.A., *Biochem. J.*, **1962**, *82*, 90-96.
[2] Hassan, H.M., Cooper, G.A., *J. Anal. Toxico*l., **2009**, *33*, 502-507.
[3] Cevasco, G., Piatek, A.M., Scapolla, C., Thea, S., *J. Chromatogr. A*, **2011**, *1218*, 787-792.

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6èmes *Journées Franco-Italiennes de Chimie*
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Effect of the architecture of PEO based polymer electrolytes on their ionic conductivities

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Safety is the ever-growing concern battery systems with, for example in liquid electrolyte technologies, the possibility of leaks, flammable reaction products and internal short-circuits. A solution to this problem is the development of solid polymer electrolytes (SPE). Among the dry SPE materials available, poly(ethylene oxide) PEO and its derivatives are the most widely studied because PEO contains ether coordination sites and has a flexible macromolecular structure, which assists in dissociation of salts and improves ionic transport. The major drawback of SPE is that mechanical strength and conductivity generally vary in opposite manner. Ionic conduction in solid polymer electrolytes depends on the movement of polymer chains [1].To improve the mechanical strength of low molecular weight (M_n) PEO, many attempts have been made to graft it to a synthetic backbone to produce block copolymers [2] or comb-like polymers [3]. The idea is that the polymer backbone gives the mechanical stability while preserving locally the high molecular dynamics of the small grafted PEO chains. A better understanding of the mechanism of charge transport in these systems would allow improving the design of the future polymer electrolytes.

The objective of the study is thus to model the ionic conductivity of such polymeric systems doped with the LiTFSI salt depending on their overall architecture (linear or branched). For linear PEO, the impact of the nature of the end-groups (OH or CH_3) and the chain length were studied. At low M_n, the end functions play a crucial role on the dynamics of the polymer chains and notably on the glass transition temperature (T_g). This effect has been introduced accordingly to the free volume theory into the VTF equation and allows predicting the influence of the M_n and end groups. For branched PEO such as poly[(meth)acrylate of ethylene oxide], several lengths of grafted EO as well as different M_n were analysed. In this context, the backbone flexibility is shown to pilot the EO chain dynamics. At last, a predictive model based on a network topological parameter called tortuosity has been developed to fit the experimental data.

References:
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[2] A. Ghosh and P. Kofinas, ECS Transactions 11 (2008) 131-137.
[3] Y-H. Liang, C-C. Wang, C-Y. Chen, European Polymer Journal 44 (2008) 2376-2384.

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COM7

Photocatalytic hydrogen production on Pt-loaded TiO_2 inverse opals

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TiO_2 inverse opals belong to the family of metamaterials and exhibit interesting catalytic properties arising from their peculiar interaction with light [1]. Two different TiO_2 inverse opals with different pore size and two TiO_2 macroporous structures with disordered arrangement of the pores have been tested in the photocatalytic production of hydrogen in aqueous solution with methanol as hole scavenger. To discriminate the effects of slow photons the hydrogen photoproduction experiments were carried out at two different wavelengths: at 365 nm, where the effect of slow photons is maximized, and at 254 nm, where is negligible. The resulting hydrogen production rates suggest a strong effect of the slow light, since at 365 nm the inverse opal samples are more active than the ones lacking of long range structural order, whereas at 254 nm this difference is not observable.

Another parameter that influences the hydrogen production rate is the polymer template used in the synthesis of the TiO_2 powders. The chemical properties of the polymeric sacrificial template determine the nature of the crystalline phases present in the sample and as a consequence they affect also the catalytic performances of the resulting TiO_2 structures.

The effects of the pH and of different organic electron donors on the hydrogen production rate have also been evaluated.

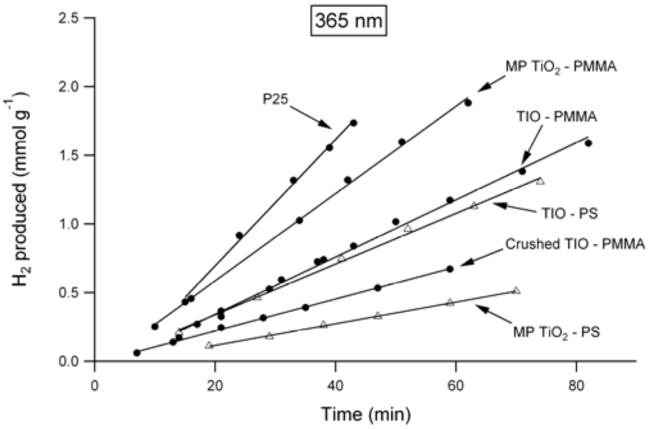

Figure 1 : Hydrogen produced as a function of the irradiation time for suspensions containing 1 g L^{-1} of different TiO_2 powders and 2 mg L^{-1} of Pt in the presence of methanol 0.4 M. The radiation source had an emission maximum at 365 nm

[1] F. Sordello, C. Duca, V. Maurino, C. Minero, Chem. Commun. 47 (2011) 6147-6149.

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COM8

Diastereoselective Access to Spirolactones *via* Rh-Mediated [5+2]-Cycloaddition Reactions. En route to the AC core of Micrandilactone C

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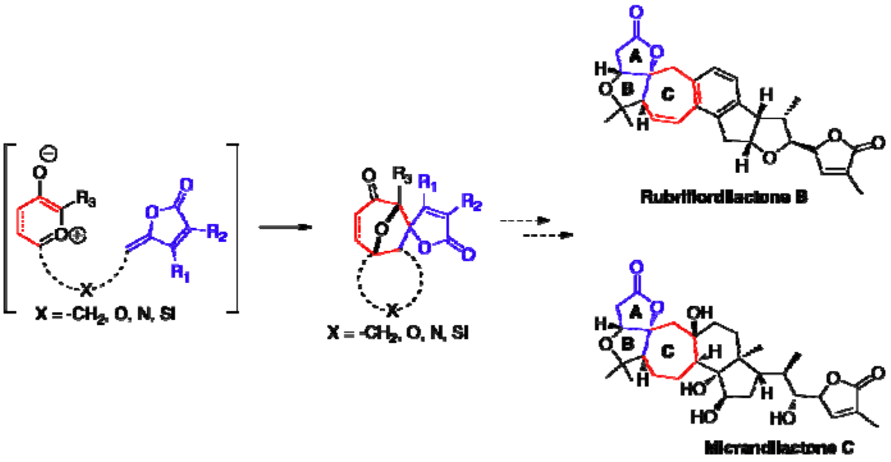
Spirolactones containing natural products are of great interest for two main reasons. First of all they represent a significant synthetic challenge due to the stereoselective installation of the quaternary spiro carbon. Secondly they are often responsible for the biological activities of the molecule.[1] Moreover, the spiro [6.4] ring system is a recurring structural motif in numerous natural products such as micrandilactone C and rubriflordilactone B (two anti-HIV compounds),[2] so we decided to focus on developing an approach toward the AC ring system of these two natural products.

The reactivity of the exocyclic double bond of γ-alkylidenebutenolides was utilized in a rhodium catalyzed [5+2]-cycloaddition and, we were very pleased to observe the formation of the [6.4] complex polycyclic structure containing the desired spirolactone residue with total control of the diastereoselectivity. Further synthetic elaboration led to the AC ring system of micrandilactone C and rubriflordilactone B.



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COM9

Novel smart bio-nanomaterials for dental and orthopaedic applications: bioactive glasses containing metal nano-particles (NPs) conjugated with molecules of biological interest

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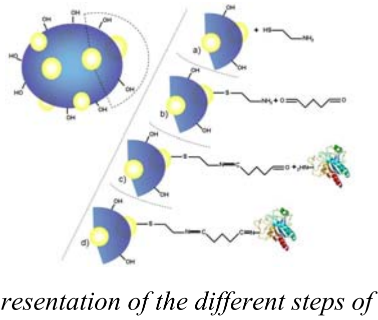
Smart materials hold great promises for social and economic development and are of great relevance in both fundamental research and technological applications. Their design and realization through innovative processes involve complementary expertises, with comparable efforts on both synthetic and analytical sides.

Actually, to meet the ever-increasing demands for performing biomaterials, their surface features have been tailored to achieve an optimal interfacial behaviour toward the hosting tissue. In particular, the introduction of metal nanoparticles (Au, Ag and Cu NPs) onto the glass surface are very useful because NPs can directly act as: *(i)* bactericides (Ag, Cu NPs), *(ii)* imaging agents; moreover, they 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.

In the present contribution, it was demonstrated that bioactive glasses containing Au nanoparticles (AuNPs) can be selectively functionalized with small molecules carrying either amino or thiol groups by simply varying the temperature and pH of the functionalization batch[1,2]. These results should allow production, in a selective way, of different bonds exhibiting different strengths and, consequently, different release times in solution, with a wide range of possible applications. Weak Au-N bonds for drug delivery and strong Au-S bonds for protein immobilization (*i.e.* peroxidises immobilization[2]).



Scheme 1. Schematic representation of the different steps of glass functionalization.

[1] Functionalization of sol gel bioactive glasses carrying Au nanoparticles: selective Au affinity for amino and thiol ligand groups.V. Aina, T. Marchis, E. Laurenti, E. Diana, G. Lusvardi, G. Malavasi, L. Menabue, G. Cerrato, C. Morterra. Langmuir Letter 26 (2010) 18600-10605.

[2] Novel bio-conyugate materials to decrease the oxidative stress in in vitro cellular tests: soybean peroxidase immobilized on bioactive glasses.V. Aina, D. Ghigo, T. Marchis, G. Cerrato, E. Laurenti, C. Morterra, G. Lusvardi, G. Malavasi, L. Menabue. L. Bergandi. J. Mat. Chem. 21 (2011) 10970-10981.

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COM10

Ion mobility mass spectrometry : a powerful tool to evidence shape variation of dendrimers upon multiple protonation

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Dendrimers constitute a class of polymers with well-defined structure and complex architecture bearing unique radiating branching units in the interior and numerous end-groups on the surface. In solution, poly(amido)amine (PAMAM) dendrimers readily assemble with guest molecules, forming stable and uniform nanoscale complexes. The guest release is believed to be promoted upon protonation of inner tertiary amine groups due to the pH decrease experienced by the dendrimer complex while entering the cell endosome.[1] However, this so-called “proton sponge effect” has only been supported by biological tests and remains hypothetical.

Ion mobility spectrometry is a technique which enables gas phase ions to be distinguished based on their shape. Combined with mass spectrometry, it appears as an attractive tool to monitor the dendrimer swelling as its charge state increases. Ion mobility spectrometry actually allows the collision cross section of ions to be experimentally measured. Performing molecular dynamics calculation, these collision cross section values can subsequently be related to conformations adopted by the dendrimer as a function of its protonation state. As a proof of principle, this analytical approach has been applied to two generation 1 PAMAM dendrimers of different geometry (globular- or fan-shape).

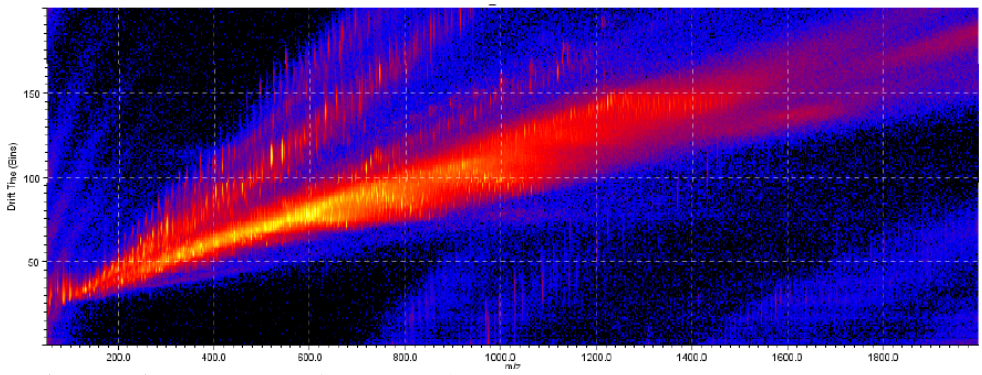

Figure 1 : Driftscope of a PAMAM dendrimer sample

From experimentally measured collision cross sections, it could be concluded that the dendrimer adopt three distinct shapes when electrosprayed in three different charge states and these results could be related to variation of the dendrimer conformation predicted by molecular dynamics calculation. Interestingly, the increase in size experienced by the dendrimer as its protonation state increase strongly depends on the dendrimer geometry.

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[2] Y Liu et al. *J. Am. Chem. Soc.* **2009**, 131: 2798

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COM11

$6^{èmes}$ Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

Synthesis and Biological Evaluation of β-Amyloid and Tau Protein Aggregation Inhibitors for Alzheimer's Disease

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Alzheimer's disease (AD), the most common form of dementia, is a progressive neurodegenerative disease characterized by a loss of memory and cognition. In Alzheimer's disease, the brain contains two types of aggregates: intracellular neurofibrillary tangles (NTF-tau protein) and extracellular senile or "amyloid" plaques consisting of the Aβ peptide, a cleavage product of the membrane protein APP.[1] Both types of aggregates are toxic for neurons, and both are based on the principle of amyloid aggregation, in which fibers are formed from the subunit protein by axial stacking of β strands, generating a cross-β-sheet structure at the core of the filaments. Small organic molecules and peptides have been reported as inhibitors of protein aggregation in vitro, however, a majority of them showed only a moderate inhibition efficiency attributed to their poor ability to interact over the large interface of interaction of proteins during the aggregation process or to interact simultaneously with the multiple binding surfaces.

One strategy for maximizing potency is to present more binding moieties within a single multivalent ligand. Herein we report the synthesis and in vitro study of a novel class of conjugates where the binding motifs (etheroaromatic compounds or peptides) are linked in a well define and control orientation onto a peptidic scaffold (Fig. 1)

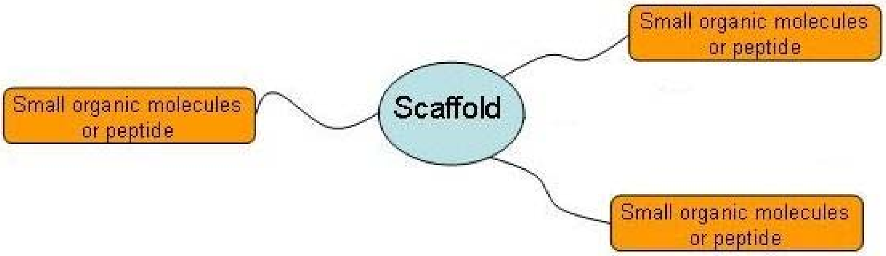

Figure 1

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COM12

Grafted copolymers based on polydimethylsiloxane and poly(*tert*-butyldimethylsilyl methacrylate) synthesized by the RAFT process: a new class of binders for FRC/SPC hybrid antifouling coatings

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Any surface immersed in seawater is rapidly colonized by fouling organisms. This colonization has serious impacts on ship navigation (e.g. increased roughness, increased fuel consumption) and is responsible for the transfer of invasive species from an eco-system to another. Two main antifouling coatings can be applied on ship hulls to limit fouling colonization:

- Self-Polishing Coatings (SPC) [1]: these coatings release toxic biocides into the marine environment by controlled erosion of the surface.
- Fouling Release Coatings [2]: these hydrophobic coatings based on polysiloxanes or fluorinated polymers limit the fouling adhesion strength resulting in the easy removal of fouling at ship speed higher than 10 knots.

The aim of our work is the development of an environmentally friendly FRC/SPC hybrid coating, without biocides, with both the hydrophobic properties of polysiloxanes and a controlled erosion of the coating. Thus, the antifouling efficiency of FRC during idle periods and at low speed could be improved and the impact of biocides into the marine environment reduced.

Tri-alkylsilyl methacrylate monomers can be used for the synthesis of binders for SPC coatings. Indeed, they can be hydrolyzed in seawater which influences the hydrophilic character of the synthesized polymers and consequently its erosion upon time. Hybrid FRC/SPC polymer binders, based on *tert*-butyldimethylsilyl methacrylate (SPC type) and polydimethylsiloxane methacrylate (FRC type) have been synthesized by the RAFT process (Radical Addition-Fragmentation chain Transfer) (Figure 1). Polymers with a controlled molecular weight and a controlled architecture (graft, blocks…) can be synthesized by such controlled radical polymerization process. The FRC/SPC duality of these hybrid polymers has been studied concerning in particular (i) their erosion properties (SPC type) by a kinetic study of their hydrolysis by ^{1}H-NMR and (ii) their hydrophobic properties (FRC type) by contact angle measurements.

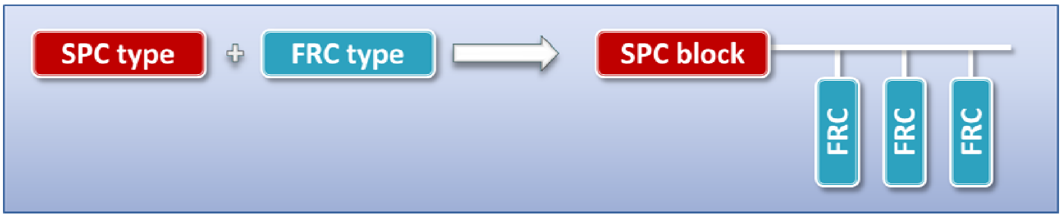

Figure 1 : Synthesis of hybrid FRC/SPC copolymers with controlled architectures.

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[2] Lejars *et al.* “Fouling Release Coatings: a non-toxic alternative to biocidal antifouling coatings”. *Chemical Reviews* (submitted).

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6èmes *Journées Franco-Italiennes de Chimie*
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

Spectroscopic and theoretical Study of Glycine interaction with well defined surfaces of nanohydroxyapatite.

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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.

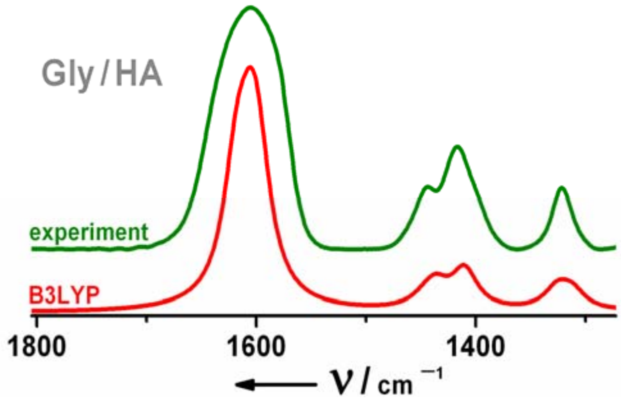

Figure 1.

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These HA nanoparticles were used to investigate the adsorption of non-ionic HOOC-CH_2-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].

[1] A. Rimola, Yu. Sakhno, L. Bertinetti, M. Lelli, G. Martra, and P. Ugliengo, J. Phys. Chem. Lett., 2, 2011, 1390.

$6^{èmes}$ Journées Franco-Italiennes de Chimie
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Phase formation during mechanical alloying of Mg–Ti–Si powders

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One of the most important characteristics of the Ti based alloys is their high specific resistance (high resistance combined with low density) which can be further improved, in the field of structural applications [1], adding elements at low density such as Mg, Si or Al [2]. Ti and Mg are immiscible in the solid state and do not form any intermetallic phases [3]; moreover the boiling temperature of magnesium is lower than the melting temperature of titanium. As a consequence to obtain Ti–Mg based alloys it is necessary to use non-conventional methods, for example mechanical alloying (MA). This technique permits the synthesis of alloys having extremely fine microstructure in equilibrium or non-equlibrium conditions.

The aim of the present work is to investigate phase formation and morphology during mechanical alloying of Mg – Ti – Si samples. The results of four different samples ($Mg_{70}Ti_{10}Si_{10}$, $Mg_{10}Ti_{60}Si_{30}$, $Mg_{20}Ti_{15}Si_{65}$, $Mg_{33}Ti_{33}Si_{34}$) submitted to MA will be presented.

Milling was performed in a planetary ball mill PM 400 type in a 50 mL tungsten carbide jar. The powders were characterized by a scanning electron microscope equipped with an X–ray spectroscopy system to measure their size and to collect information on their morphology and by a vertical X–ray powder diffractometer to check the formation of new phases during milling.

The MA of Mg–Ti–Si powder mixtures leads to multiphase samples containing crystalline binary phases stable in the Mg–Si and in the Ti–Si systems. The Mg_2Si compound was obtained in all samples (without applying any thermal treatment). Different Ti–Si intermetallic phases were instead detected depending on the composition of the initial powders. The intermetallic Ti_5Si_3 phase was formed in two samples, while the intermetallic $TiSi_2$ phase was observed for the equiatomic composition. The time necessary to promote the solid state reactions between pure elements and the completeness of reaction depends on composition. No ternary phases were detected in any of the alloyed powders.

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COM15

Aminomethylation of Michael Acceptors: Complementary Radical and Polar Approaches Mediated by Dialkylzincs

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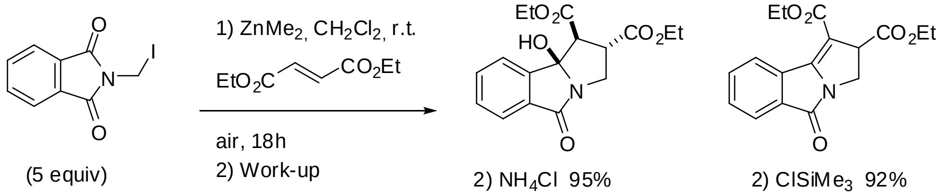
Phtalimidomethyl iodide and substituted maleimidomethyl iodide were used as radical precursors in dialkylzinc mediated tin-free radical addition to diethylfumarate. The reactions led stereoselectively to functionalized indolizidines. The radical mechanism was supported by spin-trapping experiments and rationalized by theoretical calculations. Moreover, radical additions and carbozincation followed by transmetallation with copper (I) were shown to be complementary methods to achieve the formal aminomethylation of activated unsaturated compounds. [1]



[1] J. Maury, D. Mouysset, L. Feray, S. R. A. Marque, D. Siri and M. P. Bertrand *Chem.—Eur. J.* 2012, in press DOI: 10.1002/chem.201102366

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NMR Methods and Applications for the Study of Complex Mixtures

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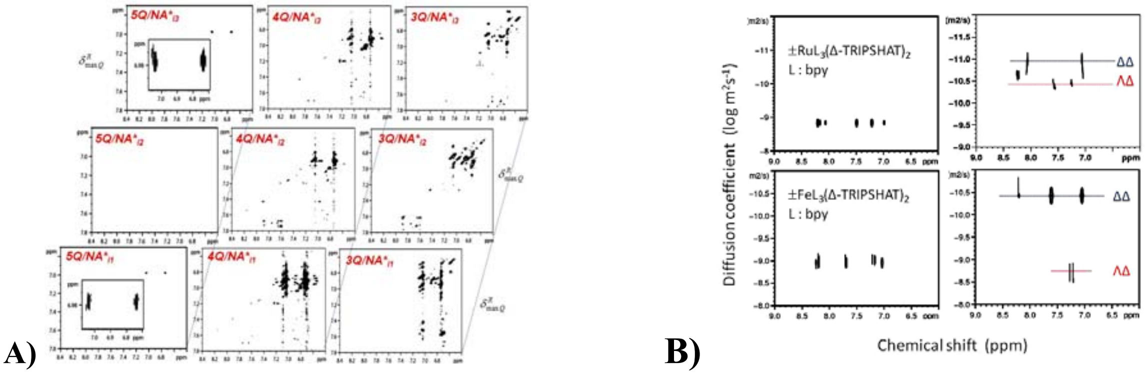
We demonstrate recently introduced high-resolution NMR methods for analysis of synthetic and natural mixtures composed of small-molecules, with a characterization and quantification of their components. Particularly, the present work: introduces a novel approach, **Maximum-Quantum (MaxQ) NMR** for decomposing the spectra of complex mixtures; and it explores the separation capability of labile species (ion pairs) via **Chromatographic NMR**.

MaxQ NMR is an approach in which the highest possible MQ order of a spin system is excited. [1] Since its first chronological demonstration, [1] MaxQ NMR analysis has been successfully applied to demix the mixture composing environmentally relevant compounds (11 poly- and monocyclic aromatic hydrocarbons), [2] to a standard mix of 11 phenolic acids that are commonly used as chromatographic standards [2] and to mixtures of natural of origin [2] (polyphenols in commercial olive oil extract). The characterization of quite a large number of molecular components through the latter approach at detection limits down to µM is a notable result, which has been further explored for measuring concentrations of mixture components [3] and for screening the polyphenols in olive oils of geographical interest (e.g. extra virgin Italian olive oils) and commercial gasoline products.[5] Improvements in MaxQ NMR by means of a combination of non-uniform sampling (NUS), recursive-multidimensional decomposition (R-MDD),[4] and through an accordion excitation scheme are described. [5]

Chromatographic NMR [6] is a tool that combines a chromatography-inspired separation and NMR characterization in one pot. In this work we show that, besides qualitatively reproducing a chromatographic resolution described for the separations of supramolecular entities on bare silica, [7] this method can even outperform the chromatographic separation for selected mixtures. For example, the spectral separation of labile Fe^{2+} diastereoisomeric salts, associated to Δ-TRISPHAT anion using bare silica gel is illustrated herein. [5]



(A) Demonstration of the screening capability of polyphenols through MaxQ NMR on a set of three extra virgin Italian olive oils. (B) Demostration of the separation capability of Chromatographic NMR of supramoleculear entities on bare silica.

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COM17

Efficient Synthesis of Aryl *C*-nucleosides through Friedel-Crafts reaction. Post Synthetic Transformations

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Aryl *C*-glycosides are frequently found in nature and many of these compounds show biologically important behavior. [1] In this context, aryl *C*-glycosylation is one of the most straightforward methods for obtaining these aryl *C*-glycosides. [2] Various routes have been recently developed, among them, the addition of aryl-metallated species to an appropriate activated sugar is the well-reported methodology. However, this strategy led in many cases to low yields and undesired side products. [3] On the other hand, the Friedel–Crafts reaction is an efficient and attractive procedure, which has been particularly developed in pyranose series with aryl donors and glycosyl acceptors. [4] In a previous work, our team has developed a direct coupling of aryl donor and tetra-*O*-acetylribose in the presence of Lewis acid for the synthesis of β-*C*-nucleosides in good yields. [5] In continuation of our studies aimed at the development of efficient synthetic routes of functionnalized aryl and heteroaryl-*C*-nucleosides for their incorporation into oligonucleotides and to assess their biological activities, [6] we herein report a direct ribosylation based on Friedel-Crafts reaction using Lewis acid catalysts (figure I). Further post-synthetic modifications of the aryl-*C*-nucleosides were performed through Sonogashira, Still and Suzuki cross-coupling reactions.

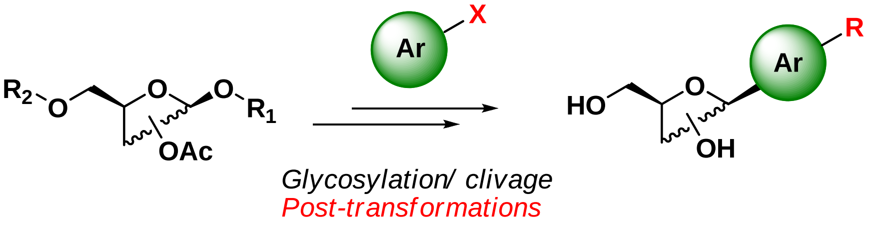

Figure I: Aryl C-glycosylation of sugar series through Friedel-Crafts reaction followed by a post-synthetic transformation

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COM18

6èmes Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

On Line SPE - LC-MS/MS Quantification of Triazine Pesticides in Water

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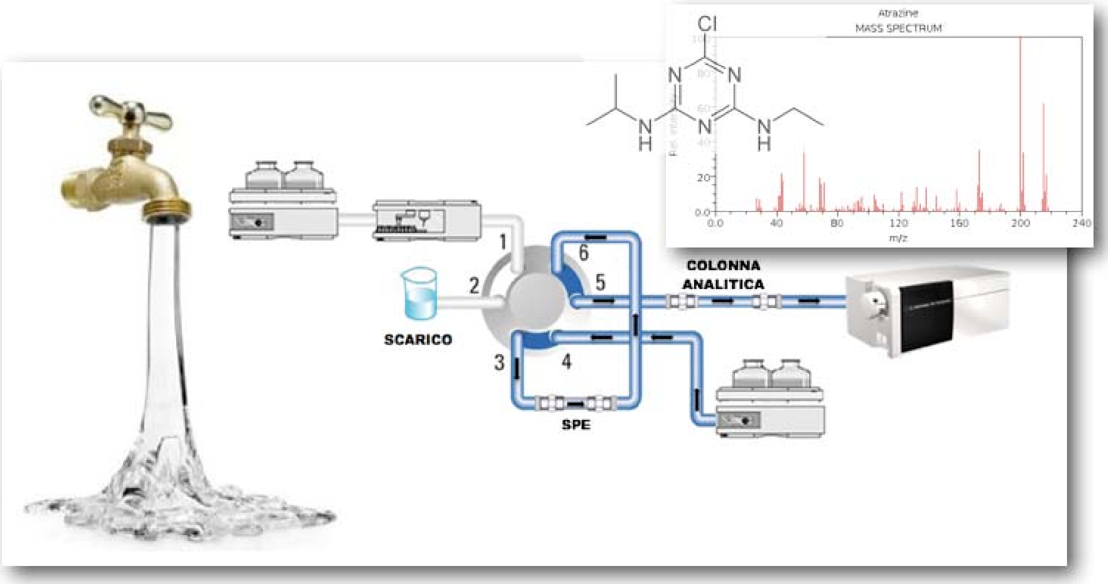
Triazine pesticides represent an important class of pesticides widely used in agriculture. In order to protect quality of drinking and surface waters, a priority list was compiled by the European Union (98/83/EC Water Directive).

A sensitive and selective method based on on-line solid-phase extraction (SPE) coupled to liquid chromatography/electrospray ionization tandem mass spectrometry (LC/ESI-MS/MS) using a triple quadrupole mass spectrometer was developed for the trace-level determination of triazine herbicides in water samples. This method minimizes tedious sample preparation, increases productivity and sample throughput if compared to traditional off-line SPE procedures.

In this work a new kind of LC-MS/MS acquisition mode, triggered Dynamic Multiple Reaction Monitoring (t-DyMRM), for detection and quantification of triazine compouds at low ppt level was used.

Multiresidual MRM analysis of pesticides uses time segmentation, where a method is divided into a series of time segments and predefined sets of MRM transitions are monitored for each segment. As sample complexity increases (e.g. quantifying very low levels of hundreds of pesticide residues in a wide variety matrices), very real practical limitations in the time-segmentation methodology become apparent. Dynamic MRM methods yield equivalent, or better, quality data and results if compared to traditional time segment based methods. Furthermore Triggered MRM (tMRM) combines MRM quantitative analysis with data dependent acquisition which can be used for library searching, identification, and confirmation. The method was applied to different water samples obtaining good recovery, linearity and reproducibility.



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COM19

6èmes Journées Franco-Italiennes de Chimie
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16-17 avril/aprile 2012

Novel and efficient synthesis of poly(amino)ester dendrimers

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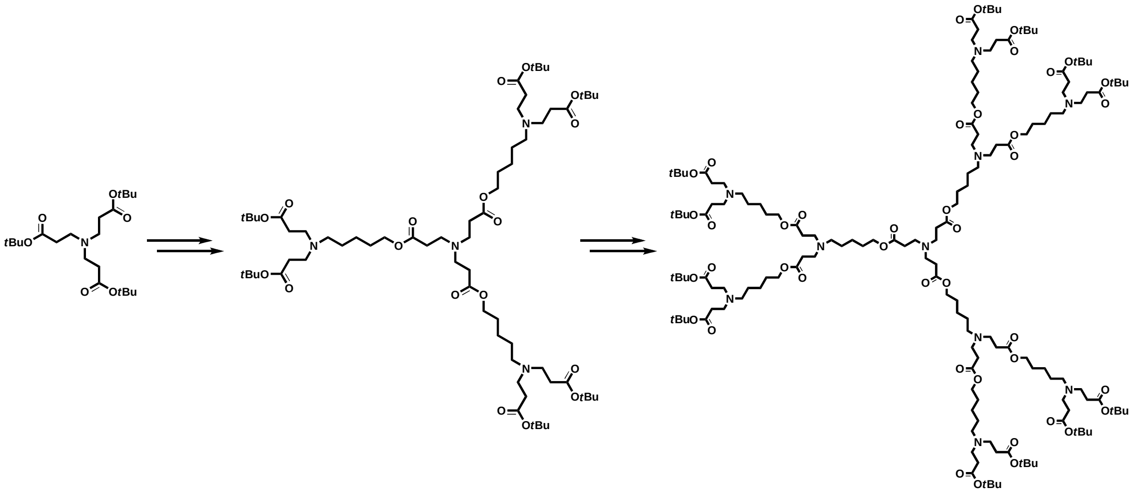
We are working on the design and synthesis of poly(amino)ester dendrimers in the view to develop vectors for drug delivery. Poly(amino)ester dendrimers have particular advantages of biodegradability via hydrolytic cleavage of ester groups, facility for cell uptake via the tertiary amine moieties and ability to compact negatively charged nucleic acids.
On the base of our previous results with PAMAM dendrimers on RNA targeting and RNA delivery [1], we have designed a family of structurally flexible poly(amino)ester dendrimers. In this work, we report the synthesis of such poly(amino)esters, which consists of an iterative four-step sequence involving deprotection of the carboxylic esters followed by activation of the resulting carboxylic acid functions as its cyanomethyl esters, prior to transesterification and solution-phase scavenging of the excess of alcohol [2]. This method was used for the synthesis of poly(amino)ester dendrimers starting from amino containing central core **1** [3].



Synthesis of poly(amino)ester dendrimers

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$6^{èmes}$ *Journées Franco-Italiennes de Chimie*
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

Non invasive analysis of manuscript covers: portable X-ray Fluorescence enlightening medieval jewellery masterpieces

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This work will present the results of p-XRF analysis applied in situ to three XI- XII century manuscripts covers considered as masterpieces of Northern Italy medieval jewellery: the golden and silver valves of *Evangeliario di Ariberto* (Milano), the golden valve of *Pace di Chiavenna* and the golden and silver valves of *Liber Evangeliorium* of Vercelli binding. The golden valves show a sumptuous decoration of golden leaves, plates and filigrees, enamels and casted gems, while the silver ones, probably the covers of the case containing the manuscript, have a more simple and sober aspect, thus reflecting the different meaning and function of the two objects during the liturgy.

The aim of this research is to obtain information on manufacturing techniques and composition of the artefacts, considering possible analogies and differences which may be useful for art historians discussion on manufacture place and artistic connections. XRF analysis was performed with p-XRF in order to determine the composition of the metals and enamels, and quantitative results, obtained using certified standards, undergo data treatment with multivariate analysis. Relationship between composition and material manufacturing was clearly observed, all filigrees showing higher Cu and Ag values respect to sheets and plates. In particular, the Evangelists in *Pace di Chiavenna* shows the highest Au content among the golden sheets, while we underline the higher Ag contents of the central filigree round respect to the external ones, suggesting for this artefact two separate manufacturing of the filigree rounds. Analysis on *Pace di Ariberto* differentiated originals parts from substitutions, presenting lower Au contents, and recognized as *niello* the black decoration on the Christ figure. The *Liber Evangeliorum* cover shows a wider range of compositions for Cu-Au-Ag alloys. The silver sheets of the bottom are in fact brightly reddish because of higher Cu contents, while the golden plates shows high Au contents: the resulting different and contrasting colours are used to obtain a peculiar chromatic effect.

Figure 1 : detail of Liber Evangeliorium of Vercelli with lower plates portraying the Virgin Mary and St. John..

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COM21

Chemically Triggered C–ON Bond Homolysis of Alkoxyamines. Quaternization of the Alkyl Fragment

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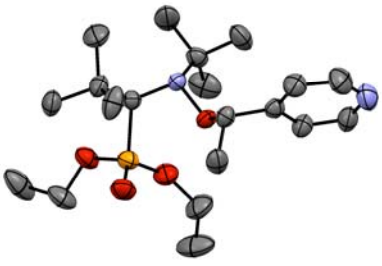
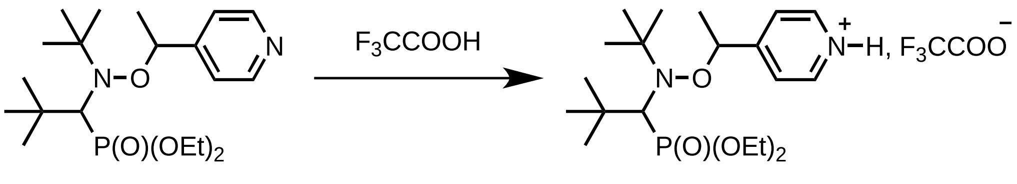
Alkoxyamines $R^1R^2NOR^3$ are efficient initiator/controller for Nitroxide-Mediated Polymerization (NMP), as they can homolyze to give a nitroxide $R^1R^2NO\bullet$ and a radical $R^3\bullet$.[1] However drastic rules are applied for shipping of compounds exhibiting low activation energy E_a of decomposition, and some care must be taken in handling and storage.

Following our program of development of readily homolyzable alkoxyamines, we investigate the chemical activation of alkoxyamines in order to considerably decrease their activation energy.

Rate constants k_d of the C–ON bond homolysis in a new type of alkoxyamines carrying alkyl fragments capable of protonation were measured. A 15-fold increase was reported for the protonated alkoxyamine compared to the non-protonated homologue as predicted.[2] Other types of chemical activation will be discussed.[3]



(SS/RR)-4-pyridylethyl-SG1 alkoxyamine



k_d (80 ºC) = $1.5.10^{-4}$ s^{-1}

E_a = 123.2 $kJ.mol^{-1}$

k_d (80 ºC) = 2.10^{-3} s^{-1}

E_a = 113.6 $kJ.mol^{-1}$

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COM22

Synthesis and characterization of novel highly photoresponsive nanosensors

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In the last decades, colour-changing sensors have been considered with increasing interest for high-performance monitoring of analytes in various applications, including chemical/biological sensing, diagnostics and drug screening, because the colorimetric detection is easy, fast, inexpensive and complex instrumentation is not required[1-2].

Here we propose a promising, flexible approach for the development of highly photoresponsive chemosensors based on the chemisorption of properly-functionalized diacetylenic chains onto pre-formed noble metal nanoparticles, followed by photopolymerization of the monomer outer shell.

The best results have been obtained by using the carboxyl-terminated 10,12-pentacosadiynoic acid (PCDA) self-assembled onto tailored-sized silver nanoparticles (AgNPs) dispersed in water[3].

The spectroscopic properties of these novel probes have been tested as a function of different experimental factors such as the chemical and molecular properties of the stabilizing solution agent, the timescale of the chemisorptions process and the stability of the silver cores before and after their monomer functionalization. On this basis, a well-defined protocol of synthesis and purification of PCDA-coated Ag nanoparticles has been established in order to optimize the polydiacetylene photogeneration in the highly-conjugated blue form.

Moreover, to improve significantly the system specificity toward specific analytes, incorporation in the organic layer of motifs receptive to given target species is necessary. To this end we have undertaken the study of the photopolymerization onto silver nanoparticles of mixtures of differently-functionalized diacetylene monomers carrying accessory end groups suitable for post-derivatization reactions with tailored receptor elements. The preliminary results obtained will be presented and discussed.

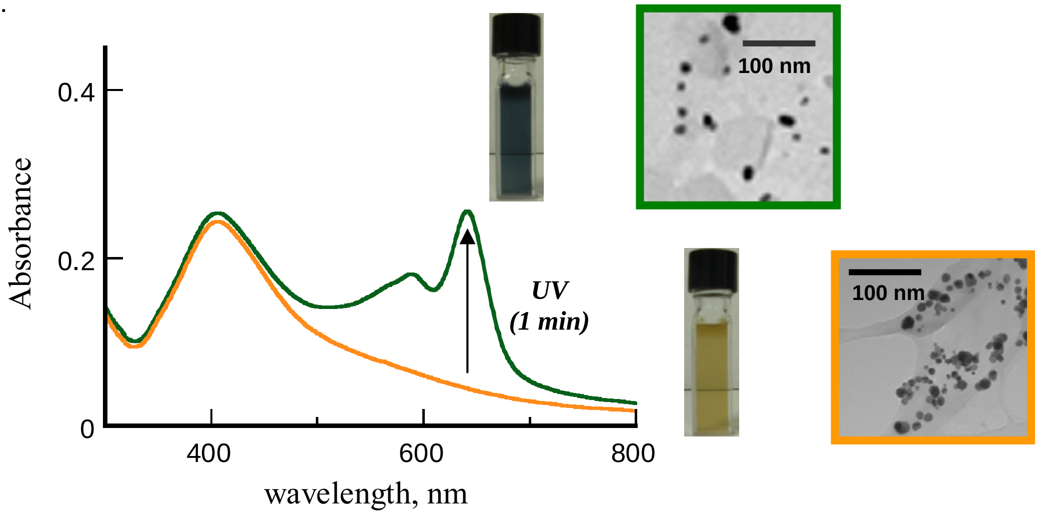

Figure 1 : Absorption spectra of PCDA-coated AgNPs before (orange line) and after (green line) the organic layer photopolymerization and their corresponding images of aqueous suspensions and TEM micrographs.

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COM23

1,2-dicarbonyl compounds as pro-nucleophiles in asymmetric transformations

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Nowadays, the development of eco-compatible processes is becoming more and more important given our planet's environmental situation. To fulfill these ecological and economical needs, the research towards organocatalytic enantioselective methods to access enantiopure molecules has received much attention in the last ten years.[1] Such methodologies have many advantages in terms of efficiency, selectivity and environmental benefits. More particularly, the asymmetric organocatalysed Michael addition of various nucleophiles to nitroolefins represents a very useful reaction as the reaction products can easily be converted into highly functionalised cyclic or acyclic building blocks.

In this context, we became interested in the challenging reactivity of 1,2-dicarbonyl compounds as pronucleophiles in organocatalysed transformations as only few examples have been reported so far.[2] We successfully developed the first enantioselective organocatalysed Michael additions of a-ketoamides and α-ketoesters onto nitroolefins with excellent stereoselectivities and very good yields.3,4 The Michael adducts can be used as versatile synthetic platforms to make five-membered carbo- and heterocycles, as well as six-membered carbocycles with the creation and control of additional stereocenters.

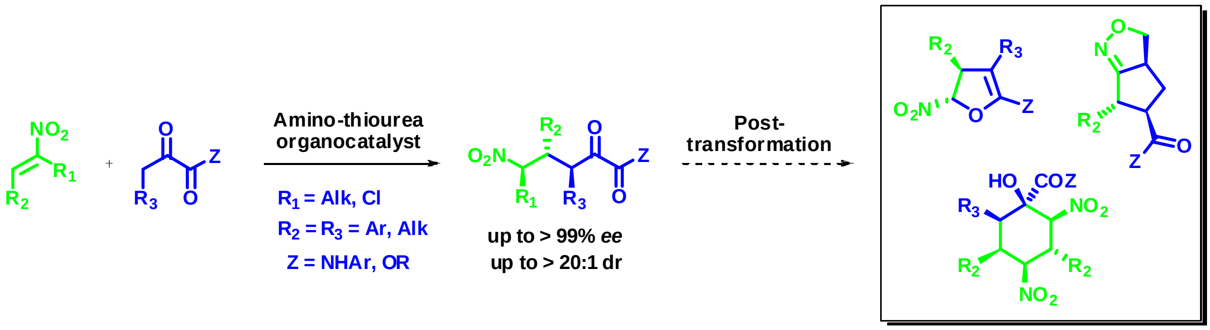

Figure 1: Organocatalysed Michael addition of 1,2-dicarbonyl compounds onto nitroalkenes

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COM24

Multivariate strategies for screening evaluation of chronic alcohol abuse

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An important goal of forensic toxicology and clinical medicine is to identify appropriate biomarkers of ethanol consumption, so as to objectively support the diagnosis of chronic excessive alcohol intake. In the common practice, screening of large population sets are commonly executed by simple and inexpensive immunometric determination of indirect biomarkers, despite their limited specificity and sensitivity. The present study proposes a multivariate model, based on several indirect biomarkers of alcohol abuse, capable of considerably enhancing their diagnostic efficiency, in terms of specificity and sensitivity. Blood samples were collected from 240 healthy non-alcohol abusers and other 183 subjects, objectively classified as non–drinkers (N=62), social drinkers (N=48) and active heavy drinkers (N=73). Five indirect biomarkers of ethanol consumption (AST, ALT, γ-GT, MCV and CDT) were determined. The original biomarkers' values, and some previously proposed mathematical combinations of them, were used to perform ROC curve analysis, which provides a diagnostic performances evaluation of the traditional approach, in terms of discrimination between healthy non-alcohol abusers and active heavy drinkers. The results from the univariate approach were compared with those obtained from a multivariate strategy based on a UNEQ class-model technique. This model was developed by splitting the 423 subjects under study into a training set (N=203) and an evaluation set (N=220). It was found that the UNEQ class-model built on γ-GT, CDT, MCV and AST can noticeably improve the screening potential of indirect biomarkers in the evaluation of alcohol misuse, with respect to the traditional univariate strategy. Moreover, this model can be easily introduced in the clinical routine work. From the present screening evaluation of healthy non-alcohol abusers, only a moderate percentage of subjects (10%÷20% at a fixed 10% or 5% active heavy drinker misrecognition rate) is requested to undergo more expensive and time-demanding confirmation procedures, such as the determination of ethyl glucuronate in head hair, with considerable reduction of work and expenses. The improved capability expressed by this multivariate evaluation make the reappraisal of indirect biomarkers topical, in contrast with the recent trend of considering their use void of practical significance.

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COM25

Biochemical sensors based on magnetic nanoparticles

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The biological and medical use of magnetic nanoparticles (MNP) is at the moment one of the most interesting researches in the field of the nanosized systems due to their possible applications for drug delivery, magnetic hyperthermia and as biological or biochemical sensors[1-2].

In our laboratory, superparamagnetic magnetite (Fe_3O_4) nanoparticles with narrow dimensions distribution ($r_{NP} < 5$ nm) have been synthesized by coprecipitation method[3], and coated with silica (SiO_2) to increase the likeability to an organic molecule: these syntheses were checked by TEM and FE-SEM analyses. The obtained $Fe_3O_4@SiO_2$ MNP were then linked to a fluorescent amine (2-(benzo-2,1,3-oxadiazol-4-ylsulfanyl)-ethanamine) by PMPI (*N*-(*p*-maleimidophenyl)isocyanate) as linker between the core and the fluorescent amine.

The different steps of the process were also followed by spectroscopic methods (fluorescent emission spectrum of the different intermediates), while the increase of the dimensions of the nanoparticles with the different coatings (see Fig.1), were detected by room temperature dynamic magnetic susceptibility analysis.

This approach confirms the possibility to link an organic or biological molecule to a MNP in order to carry it to the desired target or to use it as biochemical sensor.

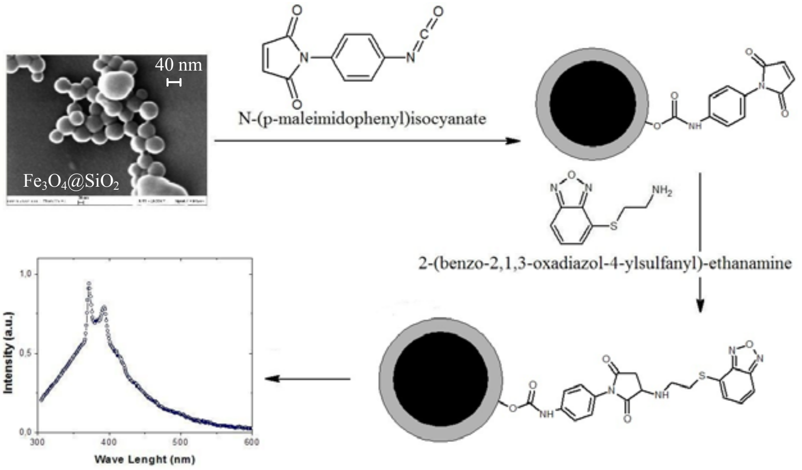

Figure 1:The steps of the linkage process

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COM26

Imprinted Thin Layers for Capillary Electrophoresis

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Non-covalent molecular imprinting is a well-known technique to produce polymeric materials able to selectively recognise and bind a target molecule. The traditional approach concerns the bulk polymerization of imprinted polymers used as stationary phase in liquid chromatography. A recent improvement of imprinting technology is focused on the development of innovative approaches for direct synthesis of polymers with controlled morphology, eliminating the cumbersome steps of grinding, sieving and sedimentation. Most of them involve the polymerization of imprinted support within the confines of the micrometric capillary columns in the form of pseudostationary phase, monolithic material, and thin layer.

In this work, we studied the surface initiation techniques in order to obtain imprinted thin layers prepared in very small devices as capillary columns, with well-defined thickness and reproducibility, and attractive molecular recognition properties.

The three different radical initiators were characterized by a radical mechanism and 'living-like properties' to control better the thickness of the thin layers.

At the beginning, the silica surface of the capillary was chemically modified to add functionalities necessary for the covalent binding of initiators that were at first activated and then attached on the surface. Finally, capillaries were filled with pre-polymerization mixture consisted of template, functional monomer and cross-linker dissolved in a proper amount of solvent, and heat- or light-treated.

To verify the applicability of this technique, two different polymerization mixtures already reported in literature and with well-defined molecular recognition properties were employed to prepare the imprinted capillaries. One used 2,4,5 trichlorophenoxyacetic acid as a model template in a polar polymerization mixture composed of water and methanol to achieve hydrophobic binding site that were able to interact mainly with template or analytes strictly related to the imprinting molecule through hydrophobic interactions. The other is a more classical polymerization mixture based on a hydrophobic solvent, that is chloroform, and warfarin as template. The recognition properties of the imprinted polymer were characterized by hydrophilic interaction, such as hydrogen bonds between the binding sites and the template or structurally related molecules.

Furthermore, the selective recognition properties of these thin imprinted layers are comparable with those observed in bulk format reported in previous works. This feature demonstrates that the capillary format can be used as a valid alternative to more classical format, reducing material consumption and time for the analyses.

Finally this techniques represents an innovative way to develop both classical and more polar polymerization mixture for the screening of the binding properties towards different kinds of templates in capillary electrophoresis.

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COM27

The diketonic constituents of *Helichrysum italicum*

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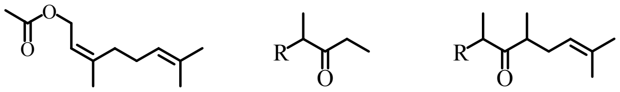
Helichrysum italicum ssp. *italicum* (Asteraceae) is widespread all over the Mediterranean basin. It is sometimes called “curry plant” because of the typical strong spicy smell of its leaves. In the flavour & fragrance industry, this species is used for the production of absolute and essential oil. The composition of the essential oil has been extensively studied, and the main constituent is usually neryl acetate **1**. Despite some controversies, it appears that the characteristic spicy odor of the plant is due to non terpenic 2-methyl-1,3-diketones **2** & **3** which are formally acylated derivatives of pentan-3-one **4** [1] and 4,7-dimethyl-oct-6-en-3-one **5** [2] and have never been observed in other species.



1

2 : R = R'CO
4 : R = H

3 : R = R'CO
5 : R = H

Figure 1 : Structures of several Helichrysum italicum constituents

Up to now, around ten of such diketones could be identified in the essential oil, but it seems possible that trace amounts of other homologous diketones are also present in the plant. Moreover, the individual contribution of each diketone to the global odor profile of the plant is still unknown. In order to answer to these questions, we synthetised a series of diketones by acylation of **4** and **5**, and studied the distribution of these compounds in the essential oils of corsican *H. italicum*. The olfactive impact of these constituents was also evaluated with the help of GC/O experiments.

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[2] Tira, S.; Di Modica, G., *Tetrahedron Letters,* **1967,** *8* (2), 143-148.

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Carnosine analogues containing Phenol substructures

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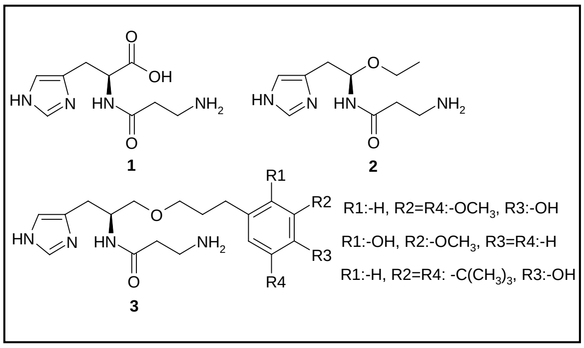
Carnosine **1** is a histidine-containing dipeptide (β-alanyl-L-hystidine) which in humans is principally present in muscle and nerve tissues. It is rapidly cleaved into its constituents, in both cells and serum, under the action of carnosinases, a group of dipeptidases belonging to the family of metalloproteases. At present, the physiological role of carnosine remains unclear. In vitro, it triggers a variety of biological actions [1]. In particular, it exerts protection against oxidative stress, being a scavenger of reactive oxygen species (ROS), which are responsible for oxidative damage of cellular lipids, enzymes, proteins and DNA. In addition, carnosine can trap toxic electrophilic α,β- unsaturated aldehydes (e.g., (*E*) 4-hydroxy-*trans*-2,3-nonenal (HNE) and malondialdehyde) deriving from the oxidation of unsaturated membrane lipids. It protects proteins from glycation, thus inhibiting the formation of toxic advanced glycation end-products (AGEs). Since oxidative stress and AGEs are involved in the development and progression of some cardiovascular and neurodegenerative diseases, as well as in ageing, there is currently great interest in carnosine and its derivatives. One possible limitation in the use of carnosine as a protective drug is that it is rapidly inactivated by carnosinases. A number of carnosinase-stable derivatives were developed, including some new carnosine amides, recently described by our group [2]. These products share a number of properties with carnosine, further, in contrast with the lead, they also display high serum stability. The ether derivative **2**, described in the same work [2], maintains good HNE scavenging properties as well as stability to carnosinase, but loses antioxidant capacity. Since ROS generation is fundamental in the pathogenesis of several diseases we tried to obtain a series of ether-carnosine-derivatives (general structure **3**), endowed with potent antioxidant activity. We chose different phenol functions [3], known for their radical scavenging properties, to be joined to carnosine through an ether bridge. Synthesis, serum stability, ability to scavenge reactive carbonyl species (HNE) as well as preliminary antioxidant activity profile of these products are reported.



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COM29

$6^{èmes}$ Journées Franco-Italiennes de Chimie
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Access to original spirocyclic derivatives *via* inter- or intramolecular reaction mediated by manganese(III) acetate

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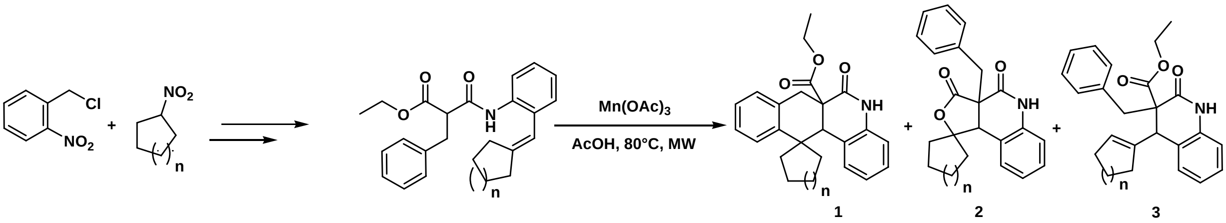
Despite the existence of several synthetic methodologies to obtain spirocyclic compounds,[1] the last decade has seen a large number of patents on spirocyclic scaffold synthesis and applications illustrating the high level of interest in spirocyclic rings in medicinal chemistry.[2] In this purpose, an easily reproducible protocol allowing inter- or intramolecular spirocyclization on β–dicarbonyl structures is described. This multistep synthesis involves an oxidative cyclisation mediated by manganese(III) acetate. This strategy offers a general and practical route to diversify spirocyclic pharmacophores. As examples, highly substituted spirobenzophenanthridin-6(5*H*)-ones **1** and spirolactones **2** were obtained in the same time. This reaction conducted also to 1,2,3,4-tetrahydroquinolinone derivatives **3**.



*Multistep synthesis of spirobenzophenanthridin-6(5H)-one **1**, spirolactone **2**, and tetrahydroquinoline **3**.*

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COM30

SYNTHESIS AND CHARACTERISATION OF ZIRCONIA NANOTUBES BY ELECTROCHEMICAL ANODISATION OF SPUTTERED ZIRCONIUM THIN FILMS

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Zirconia is a particularly interesting material showing good chemical and thermal stability, mechanical strength and good wear resistance. Moreover, zirconia is well known for its ionic conductivity properties: it is an electrical insulator which can become a pure ionic conductor when it is doped. So, the window of applications is wide including solid electrolyte fuel cell, oxygen sensor ... Hence, porous materials are very promising in various fields especially in energy. Indeed, these porous materials have the advantage of large specific surface and would thus reduce the size of electronic components and batteries for example.
Recent works have allowed the synthesis of nano zirconia tubes from electrochemical anodization of zirconium foils. The aim of this work is to develop electrochemical zirconia nanotubes from a thin layer of zirconium.
In a first step, thin films of zirconium were deposited on silicon by cathodic sputtering. These films were then electrochemically anodized in an organic fluoride ions containing electrolyte at various potentials. The effect of potential applied on the morphology and structure of zirconium was characterized by X-ray Diffraction and Scanning Electron Microscope observations. Electrical measurements were performed by Electrochemical Impedance Spectroscopy.

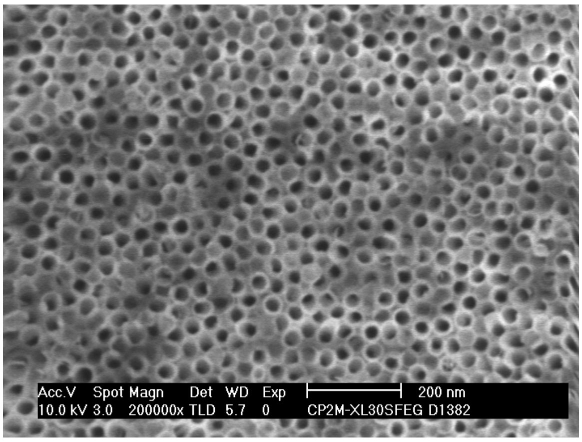

Figure 1 – Top View SEM images of Zirconia nanotubes.

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Journal of the electrochemical society Vol. 157, Issue: 12. Pages: K279-K283 – (2010)

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AFFICHES

POSTERS

$6^{èmes}$ *Journées Franco-Italiennes de Chimie*
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P1

Eléments traces métalliques et métalloïdes dans les romarins sur le massif des Calanques (Marseille): transferts dans les parties consommées et effets sur la composition chimique des huiles essentielles

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Le romarin, *Rosmarinus officinalis* L., est une espèce pérenne largement répandue dans le bassin méditerranéen. Ses propriétés antibactériennes et anti-oxydantes en font une plante largement utilisée en pharmacologie, cosmétique et dans l'industrie agro-alimentaire. Sur le massif des Calanques (Bouches-du-Rhône, France), une pratique courante est la récolte de romarin par les promeneurs et riverains. Cependant, les activités industrielles passées, notamment sur la partie littorale du massif de Marseilleveyre, ont généré une multi-pollution par les éléments traces métalliques et métalloïdes (ETMM). En particulier, l'ancien site industriel de l'Escalette sur le littoral sud-est de la ville de Marseille, est un site idéal d'étude des phénomènes de transfert des ETMM, du fait de son importante contamination en métaux (référencé BASOL, Pb, As, Zn, Cd et Sb principalement). Cet ancien site industriel, recevant du plomb argentifère et abandonné depuis les années 1920, est implanté aux portes du massif des Calanques, futur Parc National.

L'objectif de notre étude a été de déterminer le transfert des ETMM du sol vers les parties aériennes de romarin sur 2 populations naturelles du Massif et d'étudier le risque de transfert de ces ETMM dans les tisanes et les effets de cette contamination sur la composition chimique des huiles essentielles tirées de ses parties aériennes.

Sur le site de l'Escalette, une des zones les plus contaminées en ETMM se situe au niveau de l'ancienne cheminée (site nommé «Escalette»). Afin d'avoir un référentiel de comparaison, un site présentant des conditions quasi-identiques de nature de sol, de climat (altitude, orientation) et de végétation (mattoral), mais très peu contaminé en ETMM, a été choisi (site nommé «Contrôle»). Ainsi sur chacun de ces 2 sites, des prélèvements sur 5 romarins (parties aériennes) d'une même population ont été effectués, ainsi que sur les 5 sols de leurs zones racinaires. Les concentrations en ETMM (Pb, Sb, Zn, Cu, et As) ont été analysées dans les tiges et les feuilles des romarins et dans les sols (minéralisation eau régale et analyses en ICP-AES ou GF-AAS). Des infusions ont été réalisées à partir des sommités fleuries de chaque romarin (50 g sec.L^{-1} ébouillantés pendant 15 min) et les concentrations en ETMM y ont été analysées après filtration (GF-AAS). Afin de savoir si la présence d'ETMM dans le sol peut influencer quantitativement et qualitativement les huiles essentielles, celles-ci ont été extraites à partir des 2 populations de romarins par hydrodistillation (Clevenger) et leur composition analysée par GC-FID et GC/MS.

Les résultats ont confirmé que le site «Escalette» est beaucoup plus contaminé que le «Contrôle» : dans les sols plus de 200 fois pour Pb, As et Sb, et plus de 50 fois pour Zn. Par exemple, pour l'arsenic les concentrations moyennes dans les sols et les feuilles des romarins sont respectivement de 1130 ppm et 0,40 ppm dans la zone contaminées, et de 4,8 ppm et 0,09 ppm respectivement dans la zone peu contaminée. Les facteurs de bioconcentrations FB (concentration dans la partie aérienne / concentration dans sol) sont significativement plus élevés pour les romarins du site non contaminé concernant As, Cu, Sb et Zn. Ils restent cependant très faibles pour As, Pb, Zn et Sb (< 0,05) mais plus importants pour Cu (1,1).

Les concentrations en ETMM dans les infusions sont toutes inférieures aux normes européennes pour les eaux de boisson, mais elles sont significativement plus élevées pour As et Sb dans le cas des romarins poussant en zone contaminée : par exemple pour As de 2,75 ppb et de 0,35 ppb respectivement dans la zone contaminées et celle peu contaminée. Sur le site «Escalette», les taux de transfert en ETMM des feuilles vers les infusions sont de 16,5%, 2,2% et 2,5% pour As, Pb et Sb respectivement.

L'analyse de la composition chimique des huiles essentielles (HE) indique que les romarins des 2 populations correspondent au même chémotype. Ces huiles ont une composition relativement stable puisque 39 composés identifiés sont retrouvés dans toutes les HE obtenues (10 hydrodistillats) et représentent plus de 99% des constituants des HE. Les composés majoritaires sont le camphre, l'α-pinène et le 1,8-cinéole. Une analyse statistique a cependant permis de mettre en évidence une corrélation positive entre la teneur en sesquiterpènes et la concentration en métaux (Pb, Zn, Sn, As), ces composés étant connus pour leurs propriétés anti-oxydantes. Il n'y a pas de transfert des ETMM dans les huiles essentielles.

Cette étude montre un risque limité lié à la consommation de romarin sur le site contaminé si l'on ne prend pas en considération les effets cumulatifs.

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Stimuli-responsive biomaterials for *in-situ* delivery of doxorubicin. Synthesis and physico-chemical characterization

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In the last ten years, new generations of therapeutic biomaterials sensitive to environmental changes, such as pH variation, raised an increasing attention for a more specific and controlled drug release. In the present contribution the attention will be focused on the study of bioactive glasses, a vast class of inorganic biomaterials, of interest for the realisation of prostheses to be used in orthopaedic and dentistry fields. Osteosarcoma, the most frequent primary solid malignancy of bone, is defined by the presence of malignant mesenchymal cells which produce osteoid and/or immature bone. To this purpose, bioactive glasses, due to their ability to bond to bone tissues through the formation of an Hydroxycarbonate apatite (HCA) layer, can be used as bone fillers to replace damages bone tissues.

Our aim is to prepare a bioactive glass to be used as a prosthetic material, but also containing an anti-cancer drug (*e.g.*, doxorubicin, one of the most active agents against osteosarcoma) able to release the drug only in the presence of tumour cells. Exploiting the acidic environment typical of osteosarcoma cells in comparison with neutral/physiological pH characteristic of normal osteoblast/osteoclast cells, the development of a pH-sensitive drug delivery biomaterial allows to: *i)* obtain a specific activity only on the malignant cells, and *ii)* avoid both systemic and local toxicity of the chosen drug.

Data related to the development of new smart biomaterials and to their physico-chemical characterization are reported.

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Electrochemical study of ZnO deposition mechanism

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Oxide materials such as ZnO can be alternative materials to improve the efficiency of energy cells like dye sensitive solar cells or photovoltaic devices. These materials can be obtained separately using several methods included CVD, PVD, hydrothermal and electrochemical methods.

The one-step electrodeposition of ZnO films have been extensively reported [1] using dissolved oxygen at 70°C. Izaki and Omi [2] were the first to report ZnO formation at the cathode by using nitrate ions as oxygen precursor. In this media, the indirect formation of ZnO is induced by the nitrate ions reduction at the cathode surface. The hydroxide ions then produced can react with Zn^{2+} at the viccini of the cathode to precipitate in ZnO. If some papers are already devoted to electrochemical fabrication of ZnO [3, 4], the indirect mechanism of its formation is not totally explained. More precisely it is not clear why the direct Zn^{2+} reduction in Zn can't be obtained.

In this paper we focused on the electrodeposition mechanisms of ZnO formation on vitreous carbon using cyclic voltametry experiments coupling with electrochemical quartz crystal measurements (EQCM). The influence of some deposition parameters (as deposition time, potential, concentration in solution) on the morphology of ZnO thin films was also investigated using X-ray diffraction (XRD), energy dispersive X-ray (EDS) and scanning electron microscopy (SEM).

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P4

Analogues of anthocyanins with a 3',4'-dihydroxy substitution: synthesis and investigation of their structural transformations, binding and hydrogen-donating properties in aqueous solution

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Anthocyanins are naturally occurring glycosides of flavylium (2-phenyl-1-benzopyrylium) ions substituted by hydroxyl and methoxyl groups [1]. They constitute one of the major classes of plant pigments, typically responsible for a wide variety of red to blue colours [2]. One important mechanism of colour stabilisation and variation is metal – anthocyanin binding, a phenomenon restricted to 3',4'-dihydroxyflavylium ions. On the other hand, anthocyanins are also one of the most ubiquitous polyphenol classes in our diet and as such may contribute to the prevention of cardiovascular disease [3]. However, investigating the chemical properties of anthocyanins in line with their activity in plant, food and in humans is somewhat impeded by their difficult extraction and purification from plants and their limited access from commercial sources. Hence glycosides of hydroxylated flavylium ions can be proposed as pertinent anthocyanin analogues. In this work, a simple chemical synthesis of 3',4'-dihydroxy-7-O-β-D-glucopyranosyloxyflavylium chloride (**P2**) and its aglycone (**P1**) (Fig. 1) is reported as well as the ability of the two pigments to undergo proton transfer, add water with subsequent conversion into chalcones, bind Al^{3+} and deliver H-atoms to the DPPH (1,1-diphenyl-2-picrylhydrazyl) radical as a first estimation of their antioxidant activity.

Synthesis: a) regioselective glycosidation of 2,4-dihydroxybenzaldehyde under mildly alkaline phase transfer conditions, b) construction of the flavylium chromophore via acid-catalyzed aldol condensation, c) deprotection and purification.

Structural transformations in water: at equilibrium the quinonoid bases (kinetic products) are present in very minor concentrations (< 10% of the total pigment concentration) compared to the chalcone (thermodynamic product). **P2** appears significantly less acidic than **P1**. By contrast, the thermodynamics of the overall sequence of hydration-ring opening-(*Z*,*E*) isomerisation process is not affected by the β-*D*-glucosyl moiety.

Aluminium complexation: although **P1** and **P2** display similar affinities for Al^{3+} ($K_M = 1 - 2 \times 10^4\ M^{-1}$), the Al^{3+} complex of **P2** is more stable than the one of **P1** due to the higher sensitivity of the latter to water addition and conversion into the corresponding chalcone.

Scavenging of DPPH radical: glycosidation at C7-OH results in a lower rate constant of first H-atom transfer to DPPH and a lower stoichiometry (total number of DPPH radicals reduced per pigment molecule). An interpretation will be provided.

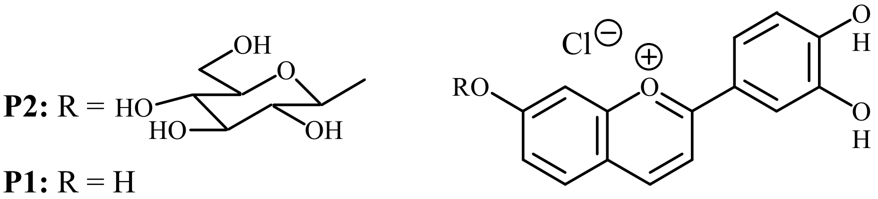

*Figure 1: Structures of **P1** and **P2***

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P5

Instant controlled pressure drop assisted extraction of natural products

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The Instant Controlled Pressure Drop technology, DIC (Détente Instantanée Contrôlée) as an innovative technique has been designed and developed whether on an laboratory, pilot or industrial scale by ABCAR-DIC Process for various applications.
DIC treatment is based on thermo-mecanical effects induced by exposing the raw material to a short period of high saturated steam pressure followed by an abrupt pressure drop toward a vacuum.

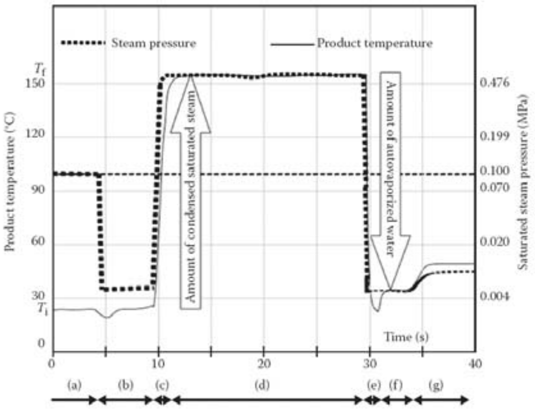

Figure: DIC Pressure and Temperature cycle

Such a pressure drop ($\Delta P/\Delta t$) higher than 0.5 MPa/s, triggers: an autovaporization of volatile compounds, the instantaneous cooling of the product, which stops thermal degradation and a swelling or even rupture of the cell and the secretion element walls

Volatile Molecules

Conventional extraction processes such as Hydrodistillation (HD) and Steamdistillation (SD) are tedious and time consuming. DIC extraction increases the amount of essential oil obtained and reduces the duration. It simultaneously improves the kinetics and the yield. *In the case of thyme oil, a direct oil yield of 4.3% dm was obtained using 9 cycles of DIC in 160 s and at 0.5 MPa compared with 3.5% dm in 7 h for HD and 2.7% in 6 h for SD [1].*

Non volatile Molecules

Another effect of DIC treatment is the expansion of the solid matrix, which acts on solvent extraction. The solvent can easily enter the matter and hence facilitate the extraction of the desired compound. DIC texturing can be considered as a pretreatment that dramatically decreases the solvent extraction time of nonvolatile compounds. *In the case of myrtle leaves, the yield of flavonoids increases with the DIC of 50% (compared with standard solvent extraction) [2].*

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SOME IONIC LIQUIDS AS CATALYST TO TRANSFER SOME SUGAR DERIVATES

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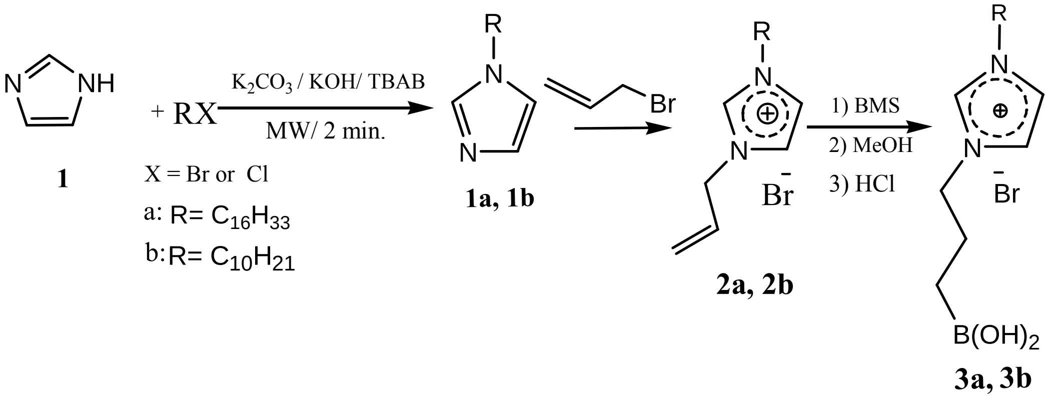
Abstract: The ionic liquids synthesized **3a** and **3b** can be used as transfer agents of glycopyrannosides thanks to their boronic acid function, the imidazolium nucleus and their long carbon chain.

Key words: Ionic liquid, transfer, glycopyranosides, imidazolium.

Glucose is a primary energy source and essential that our bodies need. Its migration through cell membranes is assisted by transporters. Sometimes this process may be defective and lead to serious health problems.[1, 2] In view of improving this transport, we developed some ionic liquids (Fig.1) and studied their capacity to transfer some sugar derivatives. Recent studies have shown the importance of ionic liquids in organic synthesis [3, 4] but their action potential as phase transfer catalysts and / or carriers for hydrophilic substances has not yet been studied.



SCHEME 1 Synthesis of ionic liquids

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P7

Atomic Layer Deposition of nanolaminates for ultracapacitor applications

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Atomic Layer Deposition (ALD) is becoming very attractive in various fields including microelectronics, energy storage, electrocatalysis or green fuel production as fuel cell applications.

ALD is a powerful method to provide conformal and high quality films. In this study, Pt, TiN and Al_2O_3 ultrathin films were deposited on Si plane substrate and into 3D high aspect ratio alumina membranes [1]. Deposition parameters such as temperature, duration, pressure, or deposition mode (thermal ALD, plasma-enhanced ALD and exposure mode) were varied.

The morphology of deposits were analyzed by scanning and transmission electronic microscopies and the surface was analysed by X-ray photoelectron spectroscopy and secondary ion mass spectrometry.

The final aim of this project is to develop a new energy storage system fabricating all-solid ultracapacitors [2]. The conductive and dielectric nanolaminates will be successively deposited into high aspect ratio nanostructures to obtain the capacitance as high as possible and to increase the performances of the nanocapacitors. First resistivity electric measurements of TiN and Al_2O_3 deposits were performed and the results are very promising.

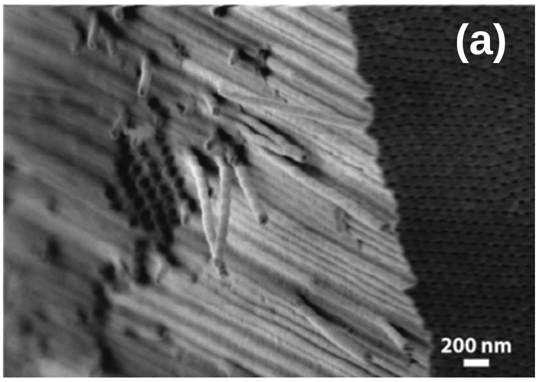

Figure (a): ALD of Pt in Al_2O_3 membranes.

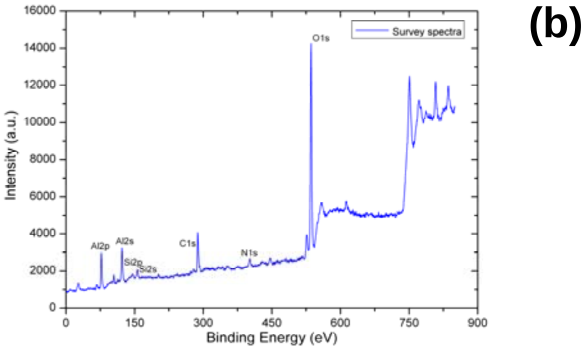

Figure (b): XPS analysis of Al_2O_3 thin films deposited by ALD on Si substrate.

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P8

Cybotactic Effect on Nitrogen and Phosphorus Hyperfine coupling constants for β-phosphorylated nitroxides

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Nitrogen hyperfine coupling constant is used as spectroscopic probes to investigate cybotactic effect. It has been shown that the nitrogen hyperfine coupling constants a_N of **1** (Figure 1) is correlated to the Dimroth-Reichardt solvent polarity constant E_N^T (Figure 2a). This behaviour has been reported for other nitroxides such as **4**. The presence of phosphorus atom in the b position for **4** and **5** involved a hyperfine coupling constant $a_{P\beta}$ between the phosphorus atom and the odd electron which depends on the dihedral angle θ <PCNSOMO>. As a_N increased with solvent polarity on would expect $a_{P\beta}$ increasing keeping θ unchanged. Surptinsing, the reverse effect is observed (Figure 2b) when aPb of 4 and 5 is plotted against E_N^T.

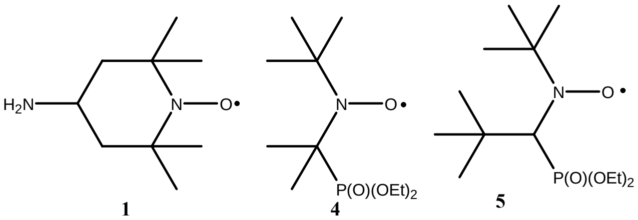

Figure 1. Nitroxides investigated

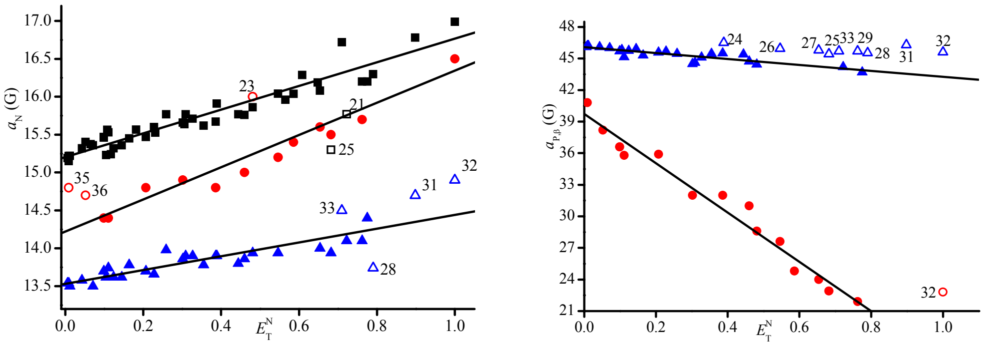

*Figure 4. (a) Plots a_N vs E_T^N in various solvents for **1** (■), **4** (●), and **5** (▲).(b) Plots $a_{P,\beta}$ vs E_T^N in various solvents for **4** (●) and **5** (▲).Empty symbols are for outliers.*

6èmes Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

Vers une approche transverse des processus chimiques et radiochimiques dans l'environnement

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Amélie Leclerc, Pierre-Charles Maria, Hervé Michel, Ilaria Monfardini, Nathalie Sauret,

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Le devenir et l'impact des éléments traces stables et radioactifs dans l'environnement et en particulier dans l'hydrosphère (biotope) est la problématique développée par l'équipe Processus Chimiques et Radiochimiques dans l'Environnement (PCRE, anciennement Laboratoire de Radiochimie et des Sciences Analytiques de l'Environnement) de l'Institut de Chimie de Nice. Au cœur de cette expertise environnementale centrée sur l'hydrosphère, la chimie des éléments traces stables et radioactifs représentant un impact sur le biotope (et l'humain) est une composante essentielle et relativement peu représentée. Par exemple, les actinides issus de la gestion des actions et des politiques du passé, tant dans le domaine civil que militaire, constituent des éléments dont l'impact sociétal est particulièrement fort (gestion des risques nucléaires) et dont la chimie extrêmement riche complexifie l'interprétation des mécanismes mis en jeu.

L'équipe actuelle articule ses projets de recherche autour de trois axes principaux :

- le transfert et comportement des éléments traces dans l'environnement ;
- la chimie et comportement des radioéléments dans l'environnement et son impact sur le vivant ;
- la métabolomique marine le choix de biomarqueurs remarquables.

Nous proposons de décliner ces trois axes suivant une approche transverse qui allie échantillonnage et analyse environnementaux à l'étude de systèmes modèles moléculaires associés. Les méthodologies développées font donc appel à l'analyse de trace, à la spéciation et à l'étude des formes moléculaires.

Il s'agit en résumé (i) de définir la distribution spatio-temporelle des éléments stables et radioactifs, effectuer un travail d'inventaire et d'archivage dans le but de préciser la spéciation en milieu naturel notamment dans le domaine de la chimie aquatique ; (ii) de préciser les mécanismes biochimiques pouvant impliquer des éléments contaminants stables ou radioactifs (radioéléments) ; (iii) d'étudier les voies métaboliques possiblement affectées en ciblant le milieu marin.

Le poster présentera un aperçu des projets initiés ou en cours de développement dans l'équipe ainsi que les méthodologies envisagées.

Le projet de l'équipe PCRE se positionne résolument dans une approche chimique de l'étude des processus de transfert et accumulation dans l'environnement. C'est un développement essentiel dans le contexte actuel de redéploiement des études à caractère fondamental et appliqué sur l'interaction entre les contaminants stables et radioactifs et le biotope environnant, ouvrant des voies de compréhension des processus ultérieurs de contamination.

P10

Analyse de polymères synthétiques à groupements terminaux labiles par spectrométrie de masse MALDI

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La polymérisation radicalaire assistée par nitroxyde (NMP) permet la préparation de copolymères synthétiques de taille contrôlée. Dans cette étude, la synthèse d'un copolymère à bloc poly(oxyde d'éthylène)/polystyrène (POE-*b*-PS) est réalisée en faisant croître le bloc PS à partir d'un homopolymère POE fonctionnalisé avec le nitroxyde SG1 (*N*-(2-méthylpropyl)-*N*-(1-diéthylphosphono-2,2-diméthyl propyl)-*N*-oxyl). Le contrôle analytique de la fonctionalisation du POE est donc fondamental et consiste typiquement à déterminer la masse des groupements terminaux à partir d'un spectre de masse. Cependant, la fragilité de la liaison C-ON qui lie le groupement SG1 au squelette polymérique, et sur laquelle repose le processus NMP, devient un problème majeur pour l'analyse MALDI car le nitroxyde est systématiquement éliminé sous forme radicalaire lors du processus d'ionisation.[1]

Pour produire des adduits oligomériques intacts en phase gazeuse et ainsi assurer la fiabilité de l'analyse des groupements terminaux, les facteurs influant sur la stabilité de la liaison C-ON ont été étudiés. Une étude *ab initio* a montré une augmentation de l'énergie de dissociation de cette liaison lorsque le groupement *tert*-butyl porté par l'azote du nitroxide est substitué par un atome d'hydrogène. Un traitement à l'acide trifluoroacétique a donc été développé pour opérer cette substitution, transformant efficacement le groupement SG1 en un groupement SG1'.[2] Les spectres MALDI-MS obtenus pour les homopolymères POE-SG1' indiquent que le renforcement de la liaison C-ON prédit par les calculs théoriques est suffisant pour permettre la désorption d'adduits intacts du polymère traité.[3]

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P11

Transition rate of aligned coupled electrical dipoles between equivalent stable equilibrium configurations

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In a recent paper [1], an extension of Onsager minimum dissipation principle was proved, yielding the transition probabilities for a mechanical system in the limit of large frictional coefficient γ among states labeled by coordinates α_0 and α_f through a functional integral expression :

$$(1) \qquad K(\alpha_f, t_f / \alpha_0, t_0) = \int_{\alpha_0, t_0}^{\alpha_f, t_f} \mathcal{D}\alpha(t) \, \exp\left\{ -\frac{m\gamma}{4T} \int_{\alpha_0}^{\alpha_f} dt \left(\dot{\alpha} + \frac{1}{m\gamma} U'(\alpha) \right)^2 \right\}$$

where the integral is understood in the sense of Ito. The boundary conditions may be incorporated into the integral by a variable transformation, after discretization [1]. Here it is proposed to apply this principle to evaluate the most probable paths and transition rates of a couple of aligned interacting dipoles between the two equivalent stable equilibrium configurations.

In our previous papers on the same subject (see [2] and refs. therein) it was introduced the appropriate coordinate system which assigns values to the angles defining the mutual orientations of the dipoles. Accordingly the couple of planar vectors $\boldsymbol{\theta}_A$, $\boldsymbol{\theta}_B$ were defined, whose moduli are considered constrained on the region $0 \le \theta_A, \theta_B \le \pi/2$, and consequently the orthogonal transformation to planar vectors $\boldsymbol{\alpha}$, $\boldsymbol{\beta}$, constrained inside the circle $\alpha^2 + \beta^2 \le \pi^2$, and forming an angle ψ between their directions. The expanded dipolar potential energy function $U(\boldsymbol{\alpha},\boldsymbol{\beta})=U(\alpha^2,\beta^2,\sin\psi)$ has the form

$$(2) \qquad \begin{aligned} U(\boldsymbol{\alpha},\boldsymbol{\beta}) = \frac{\mu^2}{R^3}\Big[& -2 + \frac{1}{4}\left(3\alpha^2+\beta^2\right) - \frac{1}{48}\left(3\alpha^4+\beta^4\right) + \frac{1}{1440}\left(3\alpha^6+\beta^6\right) - \\ & - \frac{1}{1440}\left(120 - 7\alpha^2 - 5\beta^2\right)\alpha^2\beta^2 \sin^2\psi \Big] + \text{h.o.t.} \end{aligned}$$

The dipoles are originally assumed confined inside the above defined region and aligned along $\alpha=0$, $\beta=0$. The escape rate may be evaluated by calculating the action variation along the most probable paths leading from the stable equilibrium configuration up to the saddle point [3]. In a first approximation the α and β coordinates are independent, therefore it may be assumed that the α-coordinate has relaxed toward zero and solve the one-dimensional problem for β in the potential $U(\alpha^2=0,\beta^2,\sin\psi)$. At large values of the interaction parameter the configurational dilation factors [2] can be neglected in a first approximation, so that the dynamics is dominated by $U(\beta^2)$. This potential has no maxima if terms up to $O(\beta^6)$ are retained, but an inflexion point with respect to variable β^2 at $\beta^2=10$, which is very close to the true saddle point at $\beta=\pi$. The resulting activation energy from eq. (2) is 10/9 of the exact one. Mean first-passage time techniques are also applicable to this one-dimensional model (see, for instance, ref. [4]).

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P12

Study on the photodegradation of Amidosulfuron and on the behaviour of sulfonylurea herbicides undergoing photodegradation

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Sulfonylurea herbicides are a new generation of pesticides characterised by a molecular structure comprising a sulfonylurea bridge; the different active formulas differ for the two substituents (R1 and R2) on the sulfonylurea bridge.

Sulfonylurea herbicides are extensively widespread for the protection of crops and vegetables because of their low application rates, high selectivity and low persistency in the environment; unfortunately, their low persistence does not always correspond to a lower toxicity, since new species potentially more toxic and stable than the precursor herbicides, can form owing to natural degradation processes [1-2].

Here, the photo-degradation of Amidosulfuron in aqueous solutions (5.00 mg L-1) was studied by HPLC-DAD-MS/MS to identify the degradation products thanks to a photo-irradiation in a solar box for a maximum of 34 days.

ESI and APCI ion sources in both positive (PI) and negative ion (NI) mode were used to obtain complementary information about the metabolites that can form; moreover, a study of the chromatogram acquired in Total Ion Current (TIC) followed by the extraction of the SIM (Selected Ion Monitoring) chromatograms of the most intense m/z signals have enabled the identification of the possible photo-degradation transformation products.

Three degradation products and three impurities were found and studied.

All results were obtained by this approach: six m/z values corresponding to possible metabolites were evidenced. The proposed structures were obtained using the molecular masses identified in the mass spectra from the pseudo-molecular ions according to the Nitrogen rule, the UV-Vis data collected by the DAD detector and the spectrophotometric analyses. When possible, the structures proposed were confirmed by MSn experiments performed by the direct infusion in the mass analyser of the solutions exposed to photodegradation.

To complete this study hydrolysis experiment was carried out and the typical hydrolysis product was be identified.

The results obtained in our laboratories about the photo-degradation of Amidosulfuron are then compared to those obtained in previous works carried out in comparable experimental conditions about Nicosulfuron [3] and Tribenuron Methyl[4], two sulfonylurea herbicides belonging to different classes, and to literature data: hypotheses on the existence of preferential degradation pathways are then drawn, in consequence of the molecular structure of the sulfonylurea pesticide.

At the end, ecotoxicological tests were performed by Vibrio Fisheri to assess the true toxicity of the solution after the degradation process.

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Considerations about the toxicity are drawn since the complete mineralisation of the sample is never reached: the parent pesticides totally degraded or partially transformed into other organic compounds showing at least the same toxicity as the precursor herbicides, if subjected to eco-toxicological tests. To this regard, the usually professed low persistence of sulfonylurea pesticides seems to guarantee no real advantage.

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P13

Laser ablation and microstructuring of polymers designed for 3D-SIP chips

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In the context of miniaturization and integration of nomadic devices, the trend is toward three-dimensional hyperintegration, or 3D-SiP (System in Package), which consists in vertically stacking multiple components, thus realizing a small, heterogeneous, complex system that can "feel, think and talk" (More than Moore approach). As an alternative to classical silicon microelectronics, organic microelectronics is getting more and more attention due to its potential to decrease costs. To produce 3D components, an approach consists in embedding individual silicon-based systems into organic flexible substrates and build a multi-layer structure using through-polymer-via to interconnect the chips. In order to define and implement laser processes to realize 3D building-blocks, we investigated the ablation of polymer by pulsed lasers. To transfer, embed and interconnect chips into an organic matrix, we investigated laser processes for high aspect-ratio via drilling and etching of flat, square cavities. UV nanosecond irradiations are well known for promoting photochemical ablation of polymer, and in this work, we studied the role of nonlinear absorption of polymer material in ultrashort pulse regime. By modifying the chemical composition of the polymer and its thermal degradation properties, laser ablation was improved and peculiar labyrinth like structures were obtained at the bottom of ablation cavities (Figure1).

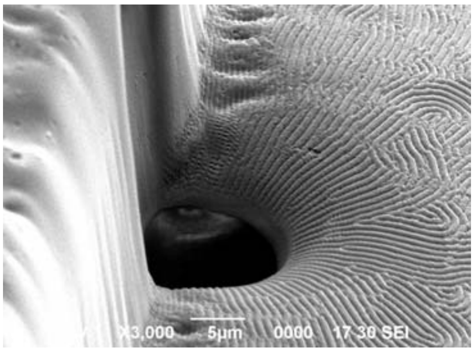

Figure 1 : Ripples obtained at the bottom of an ablation cavity in a p((S-N3)-r-MMA) copolymer.

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Combinatorial peptide libraries with molecular recognition properties towards the mycotoxin patulin

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The determination of food contaminants is based on analytical methods involving the solid phase extraction of the analyte to pre-concentrate it and to remove possible interferents from the matrix. Between the existing approaches, the most widely used is the solid phase immunoextraction with selective antibodies for the analyte of interest. Despite the fact that immunoextraction increases yields and eases the analytical protocol, it suffers from several drawbacks such as a limited load capacity, reduced stability and high costs. All these factors have contributed to the widespread opinion that new synthetic systems mimicking recognition properties of natural ligands, had to be studied and developed. Thus, over the last few years, many efforts have been made to develop alternative extraction methods based on molecularly imprinted polymers and binding peptides. The latter are obtained through a combinatorial approach, selecting from peptide libraries the aminoacidic sequence with the best recognition properties toward the analyte running equilibrium partition experiments. The morphological characteristics of the solid support used for the synthesis of the peptides determine the binding behavior of the material obtained and its application to the analysis of real samples.

In this communication is described the preparation of a hexapeptide library by recursive combinatorial synthesis and the identification of a peptide with sequence His-Ala-Asn-Pro-Arg-Asn, which showed good affinity towards patulin. Performing equilibrium partition experiments between the solid phase and an aqueous solution of patulin at pH 3.6 we were able to obtain the trend of the binding isotherm. The data were interpolated with the Langmuir-Freundlich isotherm to determine the patulin concentration that saturate the binding sites of the solid support (B_{max}) and the dissociation constant of the peptide-mycotoxin complex (k_d). The identification of such a hexapeptide allowed us to prepare an affinity column for patulin and to develop a solid phase extraction protocol for the mycotoxin. It was also evaluated the ability of this affinity column to retain patulin in apple juice real samples.

P15

Polycationic Amphiphilic α-, β-, and γ-Cyclodextrins: Impact of their Structural Nature on Gene Delivery Efficiency

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Success of non viral gene delivery is dependent on the design of efficient vectors. Recently, multifunctional macrocyclic platforms such as calixarenes or cyclodextrins have emerged as suitable tools to condense efficiently DNA into transfectious nanoparticles [1]. With this aim in mind, we have focussed on the use of derivatives elaborated upon cyclodextin scaffolds. In our previously reported results [2], polycationic amphiphilic β-cyclodextrins (β-paCDs) were shown to compact DNA into small monodisperse nanoparticles (CDplexes) (80 nm) with high transfection behaviour and low toxicity on various cell lines. In this study, our interest was particularly concentrated on the modulation of compaction abilities as well as transfection properties of CDplexes resulting from α to γ-paCD. Thus, we synthetized and evaluated α- and γ-paCD homologues of the most efficient β-paCD derivative previously described (figure 1) [2]. Here, we present comparative data on (i) physico-chemical properties (gel electrophoresis, particles size and zeta potential analysis) (ii) transfection efficiency on COS-7 cell line and (iii) cell viability in the whole series of α-, β- and γ-paCD derivatives.

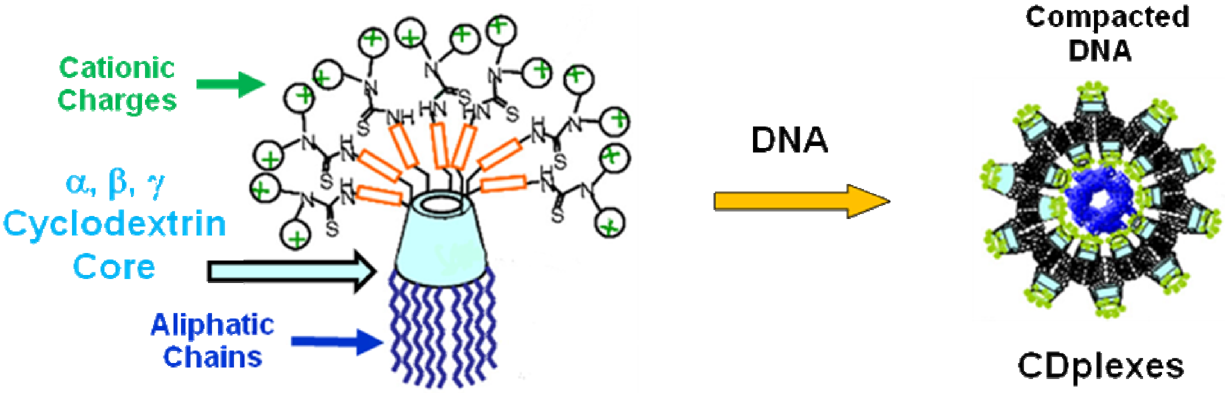

Figure 1: Condensation of DNA with polycationic amphiphilic α, β or γ-cyclodextrins, formation of nanoparticles (CDplexes)

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P16

Organocatalytic Stereoselective Michael Additions with N-Heterocyclic Carbenes

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The organocatalytic properties of 1,3-imidazol(in)-2-ylidene NHCs (e.g. IPr and SIMes) in the Michael addition of 1,3-dicarbonyl compounds to activated olefins have been studied. The reaction was found very efficient and general, allowing the isolation of the Michael adducts in high yield under smooth and clean conditions.[1]

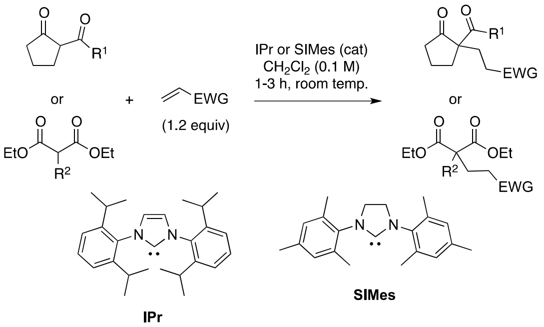

Figure 1 : NHC-catalyzed Michael addition of 1,3-dicarbonyls

The organocatalytic properties of these NHCs were exploited in an efficient and diastereoselective diversity-oriented synthesis of spirolactones and -lactams from cyclic 2-diazo-1,3-diketones through a single *consecutive reaction* taking full advantage of microwave technology and catalysis.[2] The *consecutive* sequence involves a microwave-assisted Wolff rearrangement,[3] a microwave-assisted olefin cross-metathesis[4] and finally, an unprecedented *N*-heterocyclic carbene-catalyzed intramolecular Michael addition. Remarkably, the Hoveyda-Grubbs precatalyst can be iteratively used as the source of the olefin metathesis ruthenium-based catalyst, and the Michael-induced spirocyclization *N*-heterocyclic carbene catalyst. This reaction is a nice example of an attractive concept where the same molecule of precatalyst is the source of both an organometallic and an organic catalyst used successively in a multiple bond-forming transformation.[5]

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P17

Towards the design of nontoxic antifouling solutions from natural products
The case study of naamine A

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Bacterial biofilms cause problems in medical health care since they colonize implants such as artificial joints or catheters while in marine environment, formation of biofilms on immersed substrata, leads to major economic problems which conducted to the use of toxic biocides to eradicate these communities. In this context, design of original compounds which can limit formation of bacterial biofilms is of great need in view of rational use of biocides (and/or antibiotics) as environmentally friendly solutions. Some of the anti-biofilm techniques that are tested todays, are aimed to the discovery of new potential anti-biofilm compounds from marine organisms such as sponges, soft corals or algae.

In this field, our group designed series of naamine A analogs as potential antibiofilm leads and initiated a program aimed to establish structure-activity relationships of such natural products as potential antibiofilm compounds.

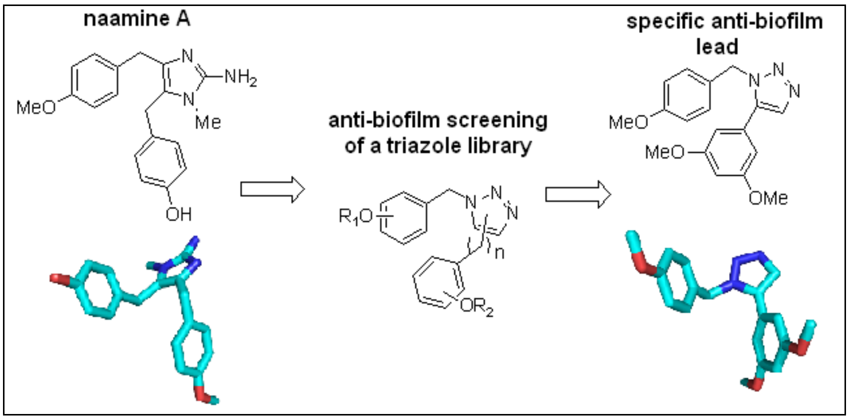

Figure 1 : design of antibiofilm compounds from naamine A

For this purpose "click chemistry" methodologies were retained as interesting high through processes. Results showed that some compounds exhibited non-toxic specific anti-biofilm activities against marine bacterial biofilms.

D. Linares, O. Bottzeck, O. Pereira, A. Praud-Tabariès, Y. Blache. Designing 2-aminoimidazole alkaloids analogs with anti-biofilm activities: Structure–activities relationships of polysubstituted triazoles. *Bioorganic and Medicinal Chemistry Letters*, 2011, 21, 6751-6755

6èmes Journées Franco-Italiennes de Chimie
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Le bleu égyptien
Le premier pigment artificiel

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Pourquoi se concentrer sur les pigments bleus plutôt que sur les pigments jaunes ou rouges ? Il faut s'intéresser à la fabrication de ces pigments pour s'apercevoir qu'ils furent partout et de tous temps artificiels.

Il est largement admis que le bleu égyptien est le premier pigment de synthèse connu. Cependant, aucune source directe d'époque pharaonique ne nous renseigne réellement sur la naissance de ce dernier. Il semble que ce pigment soit apparu en même temps que le verre, vers 2500 ans avant notre ère.

L'hypothèse couramment acceptée est que les Egyptiens auraient cherché à obtenir, pour la décoration pariétale, une teinte bleue égalant l'éclat du lapis-lazuli, minerai que sa rareté réservait à la bijouterie [1]. Le bleu égyptien est l'unique pigment bleu utilisé en peinture murale depuis la IV^{e} dynastie égyptienne (2613-2494 av. JC) jusqu'au moyen-âge. Son utilisation ne s'est pas limitée au territoire égyptien et le pigment a circulé tout autour de la Méditerranée. Malgré son exportation dans tout l'Empire Romain où il est retrouvé très fréquemment dans les fresques de régions les plus diverses et jusqu'en Norvège, son emploi a cessé vers le IX^{e} siècle ap. JC sans raison connue.

Aucune recette égyptienne n'est arrivée jusqu'à nous. Ce n'est qu'à partir de la période hellénistique que nous en trouvons des mentions d'abord chez Théophraste puis au I^{er} siècle après JC chez Pline l'Ancien et Vitruve [2]. Cependant, la recette décrite par ce dernier n'est pas quantitative. Elle dissimule les réelles difficultés de la fabrication et n'est donc pas opérationnelle. La découverte à Pompéi, au début du XIX^{e} siècle, de bleu égyptien sur les peintures murales mais également sous la forme de pigments bruts suscitera un engouement exceptionnel de la part des chimistes qui vont dès lors pendant 2 siècles tenter d'en percer le secret de fabrication [3].

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P19

Al_2O_3 doping influence on crystal growth, structure and superconducting properties of $Y(Ca)Ba_2Cu_3O_{7-y}$ whiskers

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Stacks of Intrinsic Josephson Junctions (IJJs) with atomic size are naturally formed in layered high-T_c superconductors (HTS) such as $Bi_2Sr_2CaCu_2O_{8+\delta}$ (Bi-2212), $La_{2-x}Sr_xCuO_4$ (LSCO) and RE-123 (RE = Y, Eu, Gd, Dy, Ho, Er, Tm, and Lu) [1, 2]. IJJs have been proposed as modular elements in the realization of various cryogenic devices, such as THz emitters/sensors [3], micro-SQUIDs' [4] and quantum bit-computing based on Macroscopic Quantum Tunneling phenomena [5]. HTS whiskers, like the ones belonging to the YBCO system are suitable to realize IJJs because of their highly crystalline nature, excellent superconducting properties and micrometric cross section, envisaging the fabrication of devices with a high degree of miniaturization [1, 6]. Moreover, cationic chemical doping of YBCO whiskers could represent a convenient technique to obtain modulation of the anisotropy and IJJs critical current density. Al_2O_3 doped $Y(Ca)Ba_2Cu_3O_{7-y}$ (YBCO) whiskers were synthesized using a solid-state reaction technique. In these single crystal samples aluminum addition was systematically varied in the nominal cationic stoichiometry of $Y_1Ba_2Cu_3Ca_1Te_{0.5}Al_x$, with $0 \leq x \leq 0.5$. It was observed that moderate amounts of alumina increase the number density of the grown whiskers. X-ray diffraction as well as electrical transport measurements have been performed and the obtained results will be discussed.

Two main results can be summarized: a) the increase in the amount of produced whiskers, can be due to the role played by alumina in the creation of nucleation centers for the whisker growth ; b) the incorporation of Al in the whisker presented a gradient along its profile, with a higher amount at the tip region, thus giving new evidences for the bottom-up growth mechanism.

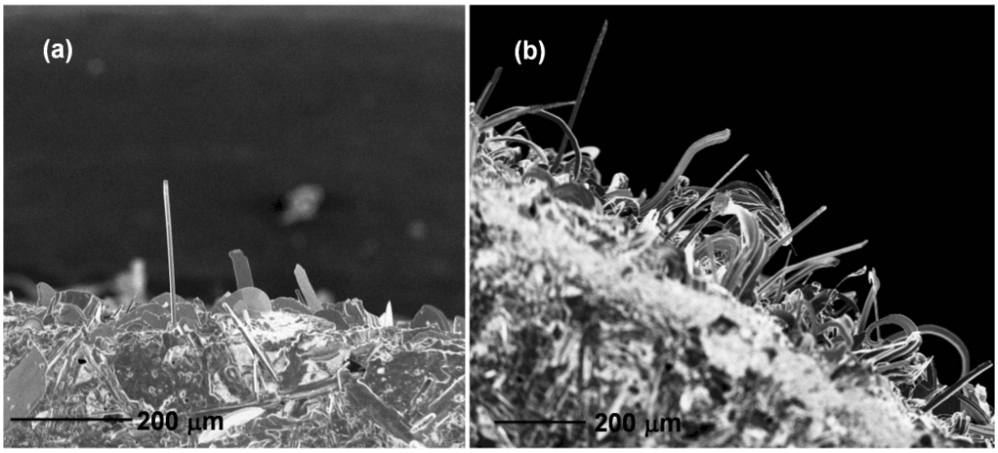

Figure 1 : SEM images of $Y(Ca)Ba_2Cu_3Al_xO_{7-y}$ crystals obtained from two different synthesis. Panel (a) corresponds to x=0 and panel (b) corresponds to x=0.05.

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P20

Memory of Chirality in Cascade Rearrangement of Enedyines: Mechanistic Study.

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We have developed an enantioselective polar-radical cascade rearrangement of enediynes based on memory of chirality phenomenon. The cascade starts with base-promoted 1,3-proton shift, to generate allene **A**. This is followed by Saito-Myers cyclization to make biradical **B**. The latter, undergoes 1,5-hydrogen transfer from the captodative position, which leads to diradical **C**. The cascade ends with the recombination of the rearranged biradical leading two diastereoisomers, with retention of configuration. In the case of alanine, competitive disproportionation leads to alkene **2a.**

The use of GA-SBA15 (mesoporous silica grafted with a tertiary amine group), a recyclable nanocatalyst, has also been explored in this rearrangement.

Deuterium labeling studies of enediyne-connected amino esters reactivity showed that the reaction proceeds according to 1,5- or 1,6- hydrogen abstraction depending on the nature of the parent amino ester. A mechanistic proposal based on theoretical calculations will be discussed, to explain the exclusive regioselectivity of the hydrogen atom shift.

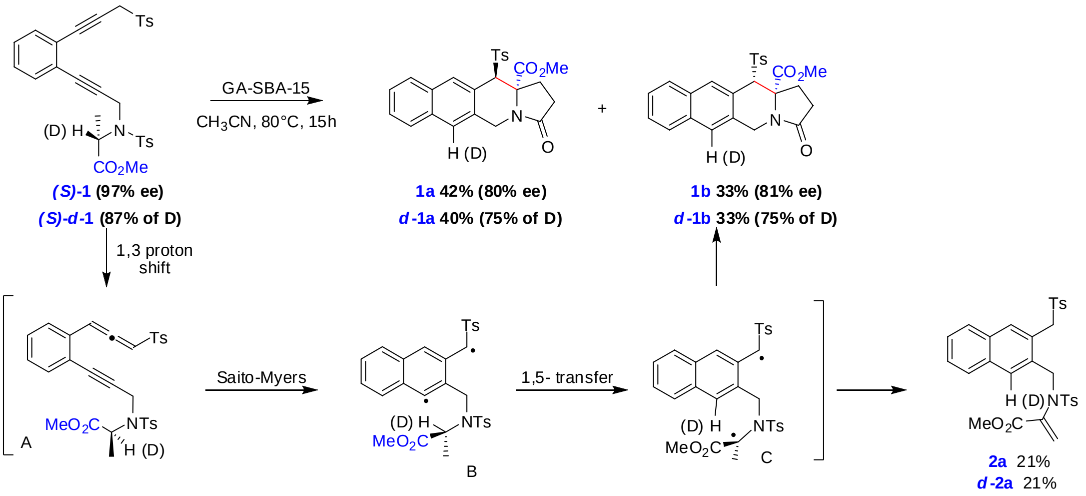

Figure 1 : Cascade rearrangement of alanine ester derived enediyne

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P21

Effect of Si and Ge alloying additions on the passivation characteristics of Fe_3Al intermetallic compound in NaCl solution

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Ordered iron aluminide intermetallics with the composition Fe_3Al and FeAl possess unique properties of high mechanical strength to weight ratio and excellent resistance to high temperature oxidation and sulphidation. Though iron aluminides are mainly developed for the structural applications at elevated temperatures, a number of studies have been concentrated on the aqueous corrosion behaviour of these materials.

The addition of passivity–inducing elements should change the nature of the anodic polarization curve and shift the corrosion potential into the passive range. The corrosion rate decreases significantly in alloyed iron aluminides due to passivity [1].

In a previous work, the effect of silicon and germanium on the passivation properties of $Fe_{75}Al_{25}$ intermetallic compound has been evaluated in 0.25 M H_2SO_4[2]. In this research, the corrosion behavior of the same samples has been studied in 0.1 M NaCl solution by means of potentiodynamic polarization, potentiostatic transients and electrochemical impedance spectroscopy (EIS) techniques. Fe_3Al and $Fe_{70}Al_{25}M_5$ (M = Si, Ge) intermetallic compounds were prepared by arc melting the stoichiometric amounts of pure elements in argon atmosphere. Samples were tested in the as-cast condition. Prior to and after electrochemical tests phase compositions were investigated. All the iron aluminides exhibit a single-phase microstructure after characterization by scanning electron microscopy (SEM) equipped with energy dispersive X-ray spectroscopy (EDXS). X-ray diffraction analysis was also used to determine the crystal structures. Electrochemical studies reveal a clear improvement in the protective properties of passive films formed on $Fe_{70}Al_{25}Si_5$ and $Fe_{70}Al_{25}Ge_5$ intermetallics as compared to $Fe_{75}Al_{25}$. XPS analysis were carried out on the passive films grown after air exposure: Al_2O_3, Fe_2O_3 and SiO_2 or GeO_2 were detected.

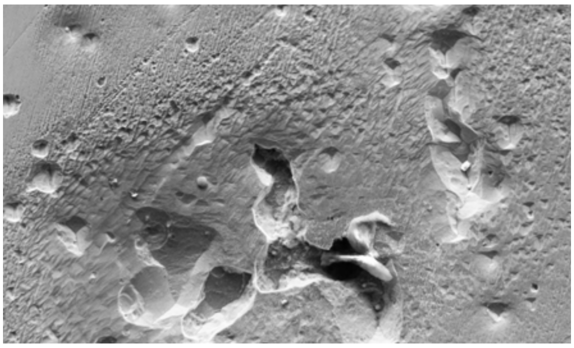

Figure 1 : SEM micrograph SE mode of Fe_3Al binary compound after electrochemical test

[1] S. Frangini, N. De Cristofaro, J. Lascovich, A. Mignone, Corros. Sci., 35 (1993), p. 153
[2] F. Rosalbino, R. Carlini, R. Parodi, G. Zanicchi, Electrochimica Acta, 62, (2012), 305–312

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P22

Strong Structural Effects on Gold Nanoparticles Formation in Ionic Liquids

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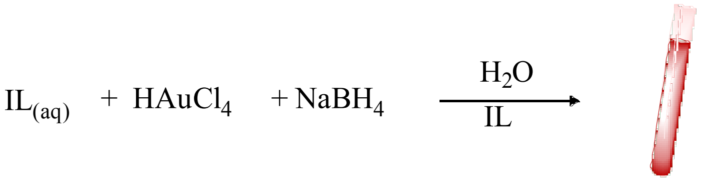
Ionic liquids (ILs) have been the object of an increasing interest in the last ten years for their potential in many chemical fields. In this communication we report on the effects of a set of ILs based on imidazolium, ammonium and phosphonium cation associated at different anions on the formation of gold nanoparticles obtained in water by reduction of $HAuCl_4$.



$$IL_{(aq)} + HAuCl_4 + NaBH_4 \xrightarrow[IL]{H_2O}$$

UV-vis spectroscopy and transmission electron microscopy (TEM) show that there are distinct differences in particle formation and stabilization depending on cation core, alkyl substituent length on cation, anion nature and reducing agent. Stable nanoparticles were obtained both in simple ILs bearing long alkyl chain(s), 1-methyl-3-dodecylimidazolium chloride and trioctylmethylammonium chloride (Aliquat 336) and in functionalized ILs, trioctyl(2,3-dihydroxypropyl)phosphonium chloride and 1-dodecyl-3-thiopropylimidazolium chloride.

Results suggest that there are very specific IL–gold interactions that are responsible for the formation of gold particles with an IL-specific shape, size, and aggregation behavior.

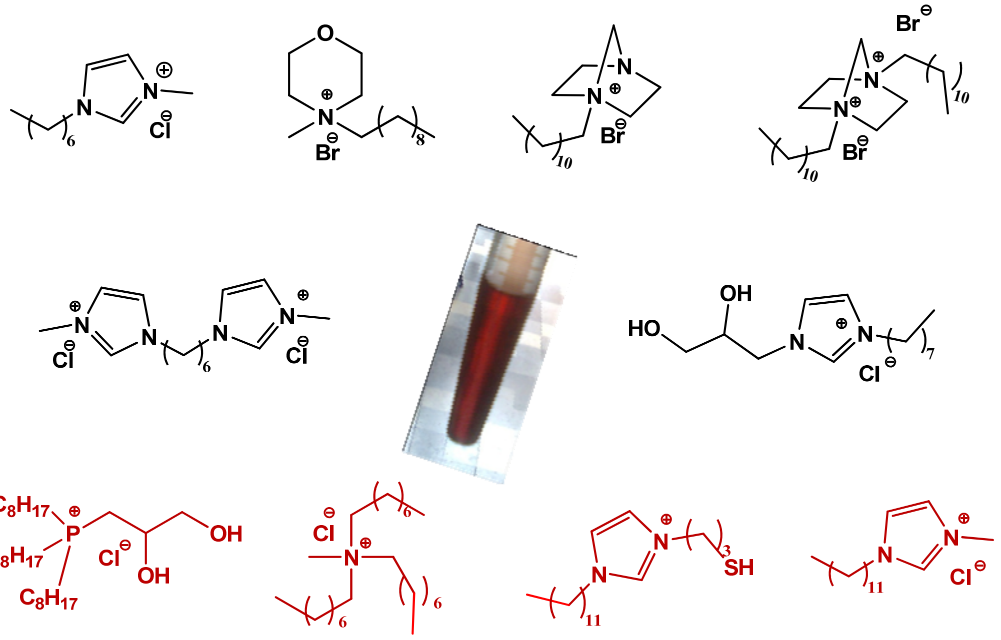


Figure 1 : Tested Ionic liquids

P23

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MULTITARGET DRUGS: NO-DONOR DOXORUBICINS.

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Doxorubicin (DOX), is an antibiotic belonging to the class of antracyclines, used for the treatment of a wide range of cancers, including hematological malignancies, many types of carcinoma, and soft tissue sarcomas. However there are some serious limitation to DOX efficacy in cancer therapy. The one of them is the easy development of the resistance through different mechanisms, the main of which is the overexpression of ATP-Binding Cassette (ABC) transporters, such as P-glycoprotein (Pgp), Multidrug Resistance Related Proteins (MRPs) and Breast-Cancer Resistance Related Protein (BCRP), that actively extrude the drug from tumor cells. Resistance to DOX is often part of a cross-resistance towards several anti-cancer drugs known as Multidrug Resistance (MDR) [1]. The identification of new MDR-reversing agents selectively targeting drug-resistance cells is a field of active investigation, but until now no satisfactory reversing strategies have been identified [2].

In previous works our group showed that nitric oxide can reduce MDR in human cancer cells. Some exogenous NO donors like S-nitrosopenicillamine, sodium nitroprusside and S-nitrosoglutathione, were able to reduce the activity of Pgp and MRPs by nitrating of tyrosine residues, crucial for protein functions with consequent increase of intracellular DOX concentration and toxicity in MDR tumor cells [3]. Lately we demonstrated that another class of NO-donors, 1,2,5-oxadiazole 2-oxides (furoxans), was able to inhibit Pgp and MRP1 transporters in MDCK cells [4]. On these bases new DOX derivatives, in which the antibiotic was joined through an ester linkage to NO-donor moieties were designed (figure 1) [5].

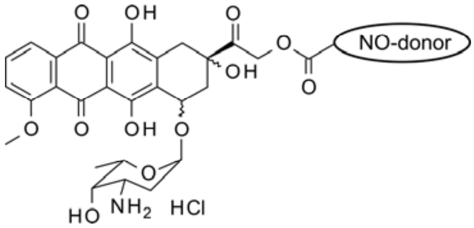

Figure 1

These compounds were studied on doxorubicin-resistant human colon cancer cell populations (HT29-dx). This experimental model have highlighted the ability of NO-donor DOXO to trigger anticancer action and to overcome the drug resistance of the cells, demonstrating that the design of NO-donor antitumor drugs could be a useful strategy to improve efficacy against drug-resistant tumors.

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P24

Electrospray tandem mass spectrometry of dendrimers – Dissociation rules for identification of structural deviations

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The use of tandem mass spectrometry (MS/MS) to identify by-products in dendrimer samples first requires the dissociation behavior of the perfect molecule to be established. Then, any deviation from this behavior as observed in the MS/MS spectrum of a dendritic impurity can be related to a specific structural modification. This methodology was applied here to a new biodegradable poly(amino)ester dendrimer, using electrospray to produce intact protonated molecules in the gas phase. Collision induced dissociation of the protonated perfect dendrimer mainly consists of multiple eliminations of a 2-methyl-1-propene neutral, the number of which indicates the total number of end-groups. Subsequently, a charge-remote mechanism allows both carbon dioxide and ethene to be released. This dissociation sequence is diagnostic of the presence of an intact branch. Loss of an entire arm from the precursor ion is observed as an alternative process.

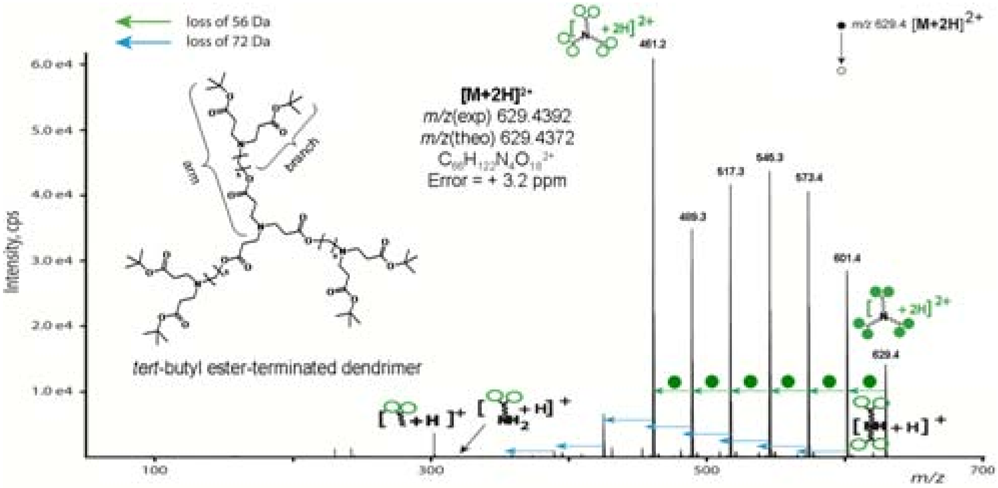

Figure 1 :Electrospray tandem mass spectrum of $[M+2H]^{2+}$ of a tert-butyl ester-terminated dendrimer

Based on these fragmentation rules, and performing high resolution mass measurements, the structure of two defective dendritic by-products present in the dendrimer sample has been accurately characterized.

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P25

Décomposition de l'échange magnétique en DFT dans des systèmes biradicalaires

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Dans le but d'améliorer la compréhension des contributions qui constituent l'interaction d'échange caractérisant les systèmes magnétiques, nous avons menés une étude théorique systématique basée sur l'étude de deux types de modèles :
- des dimères de cuivre [1] reliés par divers groupements pontant de type hydroxo (OH), azoture (N_3), methoxo ($O-CH_3$), aquo (H_2O) et chloro (Cl). L'atome de cuivre (II) possède une configuration électronique de valence de type $3d^9$. Il possède donc un électron célibataire sur sa sous-couche d la plus haute (Fig.1 droite).
- des bis-iminyl-nitroxydes (2IN) de petite taille constitués de deux groupements IN reliés par un système conjugué permettant l'échange magnétique entre les deux groupements nitroxydes (NO) et caractérisés par des couplages ferro- et anti-ferromagnétiques importants (Fig.1 gauche).

Nous avons développé une approche théorique originale basée sur la méthode LSCF [2] permettant d'étudier la décomposition de l'interaction d'échange magnétique en différentes contributions telles que l'intégrale d'échange, l'échange cinétique et le mécanisme de polarisation de spin.
Notre méthode repose sur l'utilisation de la DFT (Density Functional Theory) et sur l'approche de la symétrie brisée [3] (de l'état de bas spin) qui permet de calculer l'interaction d'échange en utilisant la relation de Yamaguchi [4]. Les calculs DFT sont menés avec le logiciel Gaussian 03 modifié pour réaliser cette décomposition.

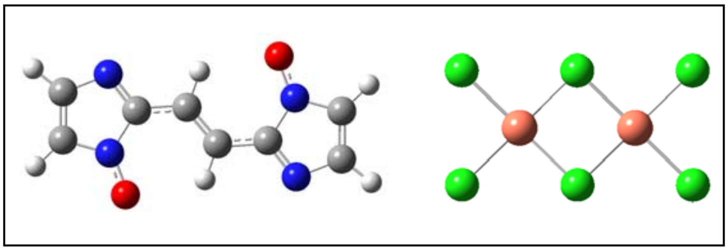

Figure 1 : Bis-iminyl-nitroxyde (2IN) et dimère de cuivre Cu_2Cl_6.

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P26

Laboratory Experiments of Titan Tholins formed by Photochemistry of Cyanopolyynes

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Tholins are complex organic materials produced by irradiation of several carbon and nitrogen rich atmosphere. It has been proposed that *Tholins* could have played an important role in the origin of life on Earth [1]. We investigate the formation of polymer (*Tholins*) from the photolysis of dicyanoacetylene.

As of today, nitriles molecules have been identified in Titan atmosphere. Among these nitriles, the cyanopolyynes (HC_nN) are very important since they are the essential constituents in building block amino acids. It is known that a rich phochemistry takes place in the Titan aerosols, and contributes to the evolution of molecular diversity in this atmosphere. These compounds evolve through polymerization processes in aerosol particles, which grow by coagulation and rain down to the surface of Titan containing water ice.

We present photochemical processes of larger cyanopolyyne formation from small precursor molecules submitted to long wavelength photons. Under UV irradiation cyanopolyynes are known to induce izomerization process (figure 1) [2] and formation of longer cyanopolyynes [3].

We provide the photochemical processes of Titan *Tholins* formation (figure 2) from cyanopolyyne precursor molecules submitted to long wavelength photons. Such photons penetrate down into the stratosphere and troposphere (figure 3). The photoreactivity of the cyanopolyynes with other Titan molecules are also presented. Laboratory experiments involving ultraviolet irradiation of dicyanoacetylene (C_4N_2) trapped in water ice have been conducted and monitored by infrared spectroscopy (FTIR). The irradiation of a C_4N_2/H_2O ice mixture at long wavelenghts has been found to be a possible source of $NH_4^+HCO_3^-$ (ammonium bicarbonate) and $NH_4^+HCOO^-$ (ammonium formate) [4].

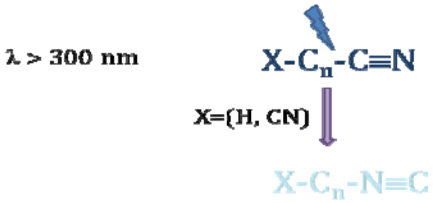

Figure 1: Izomerisation process of cyanopolyynes

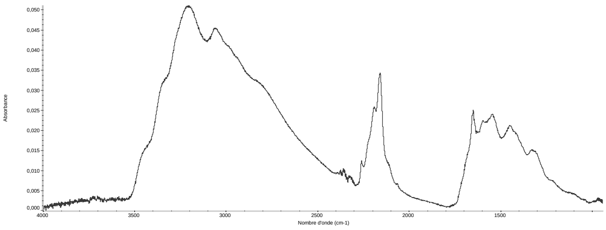

Figure 2: Infrared spectrum of Titan Tholins obtained by photolysis of pure C_4N_2 ice

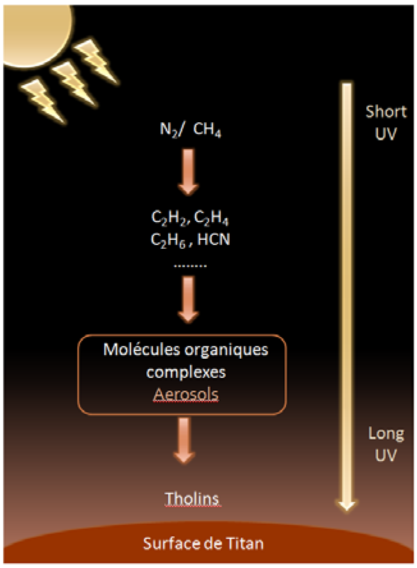

Figure 3: Titan atmosphere and surface composition

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P27

A redox cycle approach to H_2 production by two-step methanol reforming over $CoFe_2O_4$ inverse spinel catalysts. The effect of morphology and redox properties on catalytic performance.

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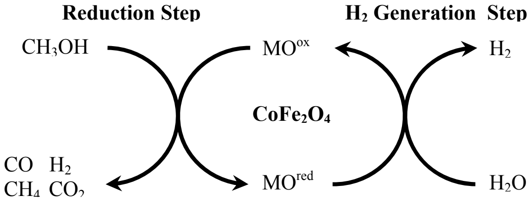
The largest amount of hydrogen produced today derives from processes of steam-reforming and water-gas-shift [1]. Hydrogen production can be performed also by chemical water splitting through a two-step approach by employing a suitable reducing agent and a metal oxide as redox pair MO^{ox}/MO^{red}.



In the present work we studied the catalytic production of pure hydrogen from methanol and water using the spinel-type oxide $CoFe_2O_4$ (cobalt ferrite) as electron carrier. $CoFe_2O_4$ is an interesting material with an inverse spinel structure, and can be readily prepared by co-precipitation of the two oxides in basic media [2]. The final material was obtained by calcinations, and two different calcination temperatures (T_{calc}= 450 and 750°C) have been selected, to yield the corresponding CF450 and CF750 samples. A thorough physico-chemical characterization of the materials as a function of T_{calc} was carried out. In fact, T_{calc} induces some morphological changes in the material, strongly affecting, by aggregation, particles size and so leading to different catalytic performances. Another important aspect, related to T_{calc}, seems to be the surface coke deposition, and this phenomenon should be minimized in order to maximize the hydrogen yield.

This work is aimed at establishing the influence of both crystal size and carbon deposition on the catalytic performance, in order to improve the stability of the material though several RedOx cycles.

Physico-chemical characterization was carried out by means of different analysis techniques, among which X-ray diffraction, HR-TE microscopy, and in situ FTIR spectroscopy.

Combining catalytic results with characterization data, it has been possible to conclude that: (i) the chemical reduction step is strongly influenced by both morphological properties and reaction temperature, (ii) during this step coke is deposited over the catalyst, but different reaction parameters (*i.e.*, time and temperature) can limit the phenomenon, (iii) during the regeneration step with water steam, H_2 and CO_2 are the only products obtained.

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6èmes Journées Franco-Italiennes de Chimie
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Gas-phase phenol methylation over Mg/Me/O catalysts: mechanistic implications due to different acid-base and dehydrogenating properties.

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In recent years a great deal of attention has been devoted to the development of heterogeneous materials with basic properties, which may efficiently catalyse reactions of industrial interest and for which homogeneous bases are currently employed.

Mg/Me mixed oxides, i.e. oxides containing both alkaline-earth metal ions and transition metal ions, have been reported to act as catalysts for many important reactions in fine chemicals industry. One of these reactions is the methylation of phenol.

This work reports about *in-situ* FT-IR charcterization and catalytic reactivity of Mg/Me^{3+} mixed oxides (Me=Cr, Fe, or Al; Mg/Me=2, atomic ratio) in the gas-phase methylation of phenol with methanol. Combining IR spectroscopic data and catalytic tests, we have tried to propose a plausible hypothesis on the actual mechanism occurring in the reaction.

The catalytic behaviour exhibited by the three catalysts differ with regard to both methanol and phenol reactants [1-4]. All investigated systems present a basic-type behaviour with regard to phenol, which dissociates to yield an adsorbed phenolate species, but the distribution of phenolic compounds obtained with the Mg/Al/O catalyst is that typically observed with acid catalysts, with prevailing formation of anisole, when the reaction is carried out below 350°C, and of mono and poly-C-alkylated compounds, when the reaction temperature is above 350°C. On the contrary, the reactivity shown by both Mg/Fe/O and Mg/Cr/O systems is that reported in the literature as typical of mixed oxides possessing basic features. The extent of methanol decomposition into light compounds is maximum in the case of Mg/Fe/O catalysts, due to the pronounced redox behaviour typical of Fe^{3+} species, whereas no methanol dehydrogenation nor decomposition is observed with Mg/Al/O up to 400°C. Reactivity tests and spectroscopic experiments hint for methanol dehydrogenation to formaldehyde as the first step in the ring-methylation of phenol with Mg/Cr/O and Mg/Fe/O: in this case, *o*-cresol and 2,6-xylenol are the only reaction products obtained. On the other hand, with Mg/Al/O systems, for which no methanol dehydrogenation occurs, the formation of anisole is due to the synergistic effect of stronger basic features and the presence of Lewis acidic sites, that facilitate the reaction between phenol and methanol after activation over the two different types of catalytic sites. In conclusion, it can be stated that the different nature of the methylating species, generated by catalytic methanol activation, can determine the different products obtained in the phenol methylation reaction.

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P29

Modeling as a complementary tool to understand arsenic behavior in marine sediments

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Sediments of the Toulon bay (SE, France) are significantly polluted by trace metals, metalloids and organic contaminants, due to historical events (2nd World War...). Contaminant behavior in sediments and transfer to the water column should be investigated to evaluate the risks linked to such pollution. In addition, when analyses did not lead to arsenic speciation, modeling appears to be to be a suitable tool to better understand this element dynamics, by speciation calculus (PHREEQC) and steady-state one dimensional fitting (PROFILE). This work focused on As dynamics in the Toulon Bay by studying two major processes: effect of early diagenesis and the subsequent diffusive flux.

Interface sediment cores were sampled at contrasted locations and seasons, followed by porewater analysis of physico-chemical parameters (pH, Eh, DOC), diagenesis tracers (Fe, Mn, S, Ca, DIC …) and As species. The obtained sediment depth profiles showed a significant variation of Eh, SO_4^{2-}, DOC and arsenic in porewaters between the campaigns. Such observation could result from different diagenesis activities, linked to inputs of labile organic matter (e.g. plankton bloom). Additionally, As appeared to be significantly correlated (R^2 0.89) to the DOC content, indicating a possible association between As and organic matter.

Based on the measured phyco-chemical parameters and the dissolved species concentration (majors, diagenesis tracers, arsenic…), PHREEQC was used to calculate As chemical speciation [1]. Then, PROFILE fitting of diagenesis tracers and As depth profiles allowed the evaluation of their diffusive fluxes at the sediment/water column interface [2]. Finally, As depth profiles were successively simulated by PHREEQC, taking account of solid As concentration, dissolved organic matter, carrier solid phases (clays, calcite, iron oxy(hydroxide), iron (mono)sulfide), and the affinity of these components for each As species.

The As dynamics in Toulon coastal sediment appears to be mainly controlled by its chemical speciation in porewater, immobilization on carrier phase, and interaction with dissolved organic matter (as AsV but also as AsIII). Association of analysis and modeling tools (thermodynamic calculation, reactive transport fitting and sorption simulation) is suitable to better understand trace elements behavior at the sediment/water interface.

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P30

Glycine oligomerization on TiO_2 nanocrystals: from the formation of biopolymers in prebiotic conditions to the potential application in fine chemistry

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The study of interaction of biomolecules with oxides surfaces it is of great interest for the disclosure of peptide bond formation mechanism in prebiotic conditions.[1] In this respect, some efforts have been already done in order to set-up model systems to selectively investigate the surface-small molecules interaction (like in case of Hydroxyapatite[2] or SiO_2 materials[3]). The same approach can be used to study the surface of TiO_2 nanopowders by the combined use of IR spectroscopy and Mass Spectrometry of adsorbed molecules from the vapor phase. Glycine (NH_2CH_2COOH), the simplest amino acid, has been chosen as biomolecule and, because of the deep knowledge of its surface properties,[4-6] the commercial TiO_2 P25 from Degussa has been selected for this research work. This study resulted in the first observation of the formation of long glycine oligomers (up to 17 terms) under the vapor-solid interaction regime, consistent with the Bernal's hypothesis.[7] Additionally, the self-aggregation of polyglycines, as consequence of hydration, to form helical and β-sheet-like structures, has been observed.

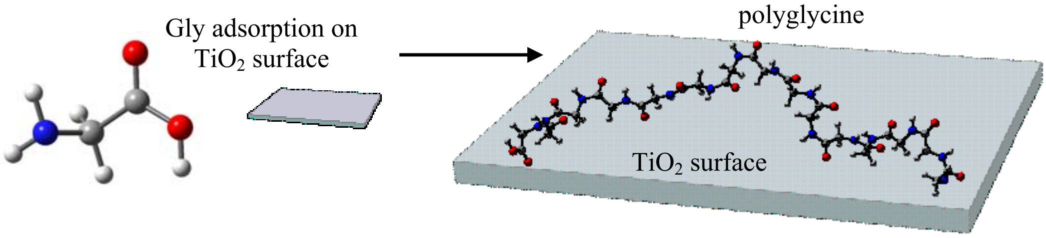

Figure 1. Schematic representation of glycine oligomerization induced by interaction with TiO_2 surface.

To elucidate the reaction mechanism, resulting in the formation of the amide bonds, the interaction between formic acid and pentylamine on the TiO_2 surface was studied.

It was found that the activation of the carboxylic moiety is the result of the formation of carboxylate species, stabilized on the TiO_2 surface, the C atom of which undergoes a nucleophilic attack by the N atom of the amine.

This could represent a new heterogeneous catalyst for promoting amide bond formation, one of the most important reactions in organic chemistry.[8]

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P31

6èmes Journées Franco-Italiennes de Chimie
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Extraction assistée par Ultrasons de Lipides contenus dans les Microalgues à l'aide de terpènes comme alternative à l'hexane

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L'extraction par solvant assistée par ultrasons consiste à traiter sous ultrasons un solide sec ou humide en contact avec un solvant. Dans le cas des microalgues, les ultrasons entraînent une déstructuration des cellules (lyse) et ainsi la libération des composés intracellulaires. Ces expériences relativement courtes permettent de préserver les composés les plus thermolabiles (acides gras poly-insaturés, pigments) des réactions de dégradation traditionnelles. Dans le domaine de l'extraction des lipides, l'utilisateur souhaitant rendre son procédé moins couteux en énergie et moins dangereux, pourra adopter cette nouvelle technologie et choisir également l'utilisation de solvants verts, offrant généralement moins de toxicité que le *n*-hexane. Les terpènes permettent la dissolution des lipides grâce à leurs propriétés chimiques similaires à l'hexane (Tableau 1), ainsi la combinaison des ultrasons et des agrosolvants s'avère donc intéressante pour l'extraction des lipides dans les microalgues.

Le but de cette étude a été de comparer une technique conventionnelle ; la macération à une technique innovante ; l'extraction par solvant assistée par ultrasons avec l'utilisation d'hexane et de trois solvants terpéniques le *d*-limonène, l'*α*-pinène et le *p*-cymène. Ces extractions nous ont permis de déterminer des rendements lipidiques par gravimétrie, ainsi que des profils d'acide gras après analyses en GC/FID. Les résidus de pâte algale après extraction ont été également observés en microscopie optique.

Tableau 1 : Propriétés de l'hexane et des agrosolvants

Propriétés	*n*-hexane	*d*-limonene	α-pinene	*p*-cymene
Poids moléculaire (g/mol)	86.17	136.24	136.24	134.22
Densité (g/ml)	0.660	0.837	0.854	0.856
Point d'ébullition (°C)	68.7	176	155	177
Constante diélectrique (□)	2.0	2.3	2.7	2.3
Impact environnemental	++	-	-	-

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P32

PHOTOCHEMICAL PRODUCTION OF REACTIVE TRIPLET STATES IN WATER SAMPLES FROM MOUNTAIN LAKES, LOCATED BELOW OR ABOVE THE TREELINE

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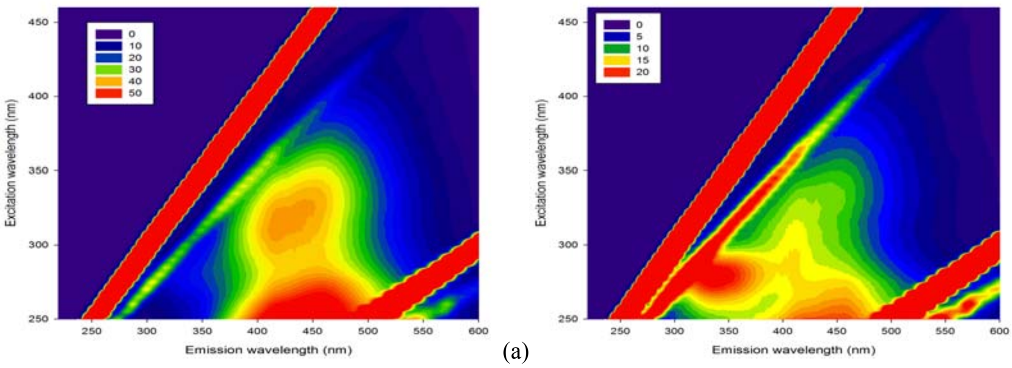
The production of excited triplet states of chromophoric dissolved organic matter (CDOM) was measured upon irradiation of water samples, taken from lakes located in a mountain area (NW Italy) between 1450 and 2750 m above sea level. The lakes are located below or above the tree line and surrounded by different vegetation types (trees, alpine meadows or exposed rocks –no vegetation).

The most photoactive samples belonged to lakes below the tree line and their fluorescence spectra and CDOM optical features suggested the presence of a relatively elevated amount of humic (allochthonous) material[i,ii]. The lowest (negligible) photoactivity was found for a lake surrounded by exposed rocks. Its CDOM showed an important autochthonous contribution (due to in-lake productivity) and considerably lower spectral slope compared to the other samples, suggesting low CDOM molecular weight and/or aromaticity[iii]. Among the samples, CDOM photoactivity (rate of triplet state production under irradiation) decreased with changing vegetation type (in the order trees, meadows, rocks), which could be connected with decreasing contribution from catchment runoff and increasing contribution from autochthonous processes[iv,v] and possibly precipitation[vi].

Interestingly, CDOM in precipitation is poorly photoactive and could contribute to the low photoactivity of samples from lakes located above the tree line, in particular in the presence of exposed rocks[vii].



(a) (b)

Figure 1 : 3D fluorescence excitation-emission matrix (as contour plot) of Lago Nero (a) and della Foppa (b). Fluorescence intensity is scaled from 0 to 50 intensity units for Lago Nero and from 0 to 25 for Lago della Foppa. The linear feature is the signal obtained when excitation equals the emission wavelength.

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Kinetic of transformation of formic acid on titanium dioxide

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The use of heterogeneous photocatalysis for the abatement of persistent pollutants has been increased in the last decades owing its great potential to remove aqueous and air pollutants often till a complete mineralization [1,2.3]. The change of the redox properties of a semiconductor surface as a consequence of the absorption of a photon with energy greater (or equal) than its band gap is at the basis of the photocatalytic process. This phenomenon, called photoexcitation, promotes charge transfer reactions through the semiconductor- media interface. The net result is the oxidation of the dissolved contaminants catalyzed by the irradiated semiconductor [4].

The photocatalytic efficiency is influenced by a wide variety of chemical-physical parameters and the process can involve several mechanisms which have different importance as a function of the adopted experimental conditions and of the catalyst nature. Cause of it, an exhaustive mathematical treatment of the photocatalytic process results very complex and object of debate [5].

Aim of this work was the experimental determination of the influence that the optical parameters of titanium dioxide suspensions have on the photocatalytic efficiency. The evaluation of these parameters for different commercial TiO_2 was carried out determining the light absorption and scattering capacity through the estimation of the *a*-dimensional parameter χ. The χ parameter, defined by Minero et al. [6] takes into account both of the light absorption (κ) and of the scattering (σ) coefficients. The expression for this parameter is

$$\chi = \frac{1}{b}\int_0^b \sqrt{\frac{I(z)}{I_0}}dz$$

where b is the optical path length, $I(z)$ is the radiation intensity at the depth z inside the suspension and I_0 is the incident light intensity.

Optical properties are related to the degradation rate of the photocatalytic process which can be expressed as a function of the χ parameter as follow

$$\frac{rate_{obs}}{C_{cat}} = -k' + \sqrt{2\ln(10)I_0 k' \varepsilon_{abs}}\,\chi$$

where C_{cat} is the catalyst suspension concentration, ε_{abs} is the cross section for the absorption and k' a parameter containing the kinetic constants for the main processes that occur during photocatalytic experiments.

The relationship between the optical parameters and the kinetic of the photocatalytic process was picked out monitoring formic acid transformation in the presence of two different commercial TiO_2 (Degussa P25 and Hombikat UV100) as a function of i) the type and concentration of the catalyst; ii) the substrate concentration. The experimental evidences, reported in Figure 1, showed that the photocatalytic efficiency is directly proportional to the values of the parameter χ as defined in [6].

It was underlined that the formic acid photocatalytic degradation happens through different mechanisms. The relative importance of these different mechanistic paths is strictly related both to the adopted experimental conditions and to the catalyst properties.

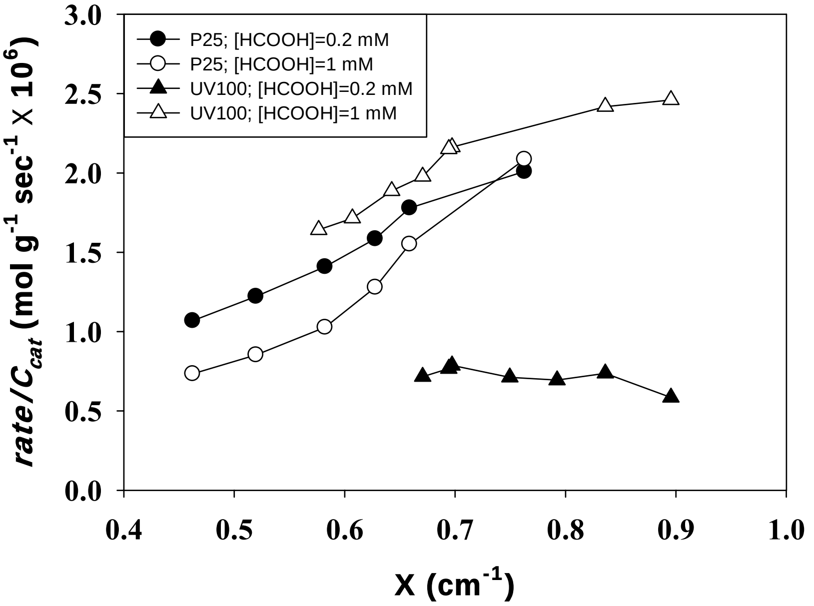

Figure 1: Degradation rate for formic acid as a function of χ values and substrate concentration.

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Enhancing the Relaxivity of Gd-based Contrast Agents: a new Gd-AAZTA Dimer for MRI Applications

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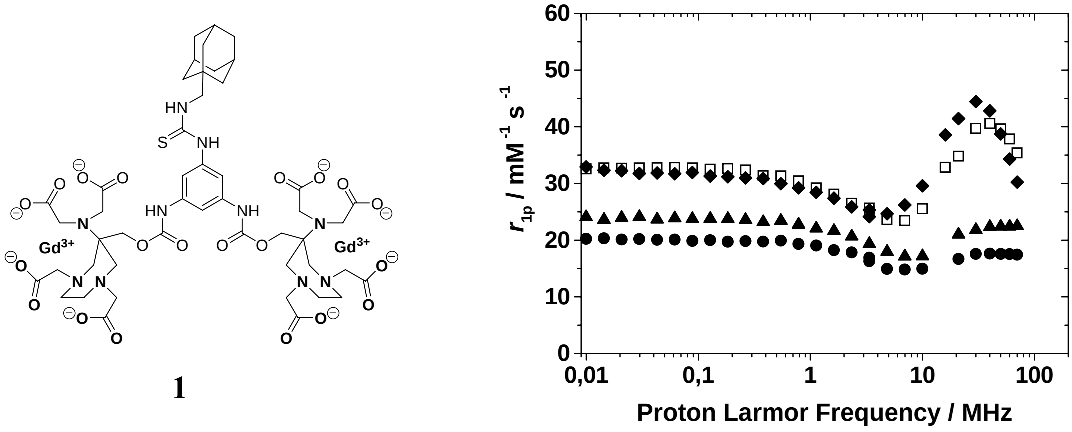
Magnetic Resonance Imaging (MRI) is a powerful diagnostic technique that allows the non invasive acquisition of high-resolution images of tissues and organs without exposure to ionizing radiation. In many cases the potential of this technique may be further improved by the use of suitable contrast agents (CA), and paramagnetic Gd^{III}-complexes are by far the most used ones.[1] There is an ongoing interest in producing high-relaxivity Gd-based MRI contrast agents to overcome the low sensitivity issue inherent to MRI. The lengthening of the reorientational correlation time (τ_R) for systems with two fast exchanging water molecules is one possible way to increase the relaxivity of Gd^{III}-CAs. This may be obtained either by increasing the size of the complex or by forming reversible adducts between a suitably functionalized complex and a macromolecular substrate. A new dimeric derivative of the Gd^{III}-chelate with the heptadentate ligand AAZTA bearing an adamantane moiety has been synthesized (**1**). Its relaxivity (r_{1p}=16.7 mM^{-1} s^{-1}, at 20 MHz and 298 K) is comparable and even higher than that of other Gd^{III}-dimers reported in the literature with two coordinated, fast exchanging, water molecules (q = 2) on each metal ion.[2] Furthermore, an efficient relaxation enhancement can be achieved through the interaction of the adamantane group with slowly tumbling macromolecular substrates. In fact the complex forms high-molecular-weight host-guest adducts with β-cyclodextrin (βCD) and poli-βCD, and also interacts strongly (K_A=1.17·10^4 M^{-1}) with hydrophobic binding sites on human serum albumin (HSA). A detailed relaxometric study on both the dimer **1** and its adducts with βCD, poli-βCD and HSA will be illustrated.



*Chemical structure of (Gd-AAZTA)$_2$-Ph-Ad (**1**)(left), and overlapping of 1/T_1 NMRD profiles (298 K) of 0.1 mM solutions of **1** (●) and its adducts with βCD (▲), p-βCD (□) and HSA (♦)(right).*

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P35

Theoretical Study of a Key Step in the Natural Biosynthesis of Flavonoids

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In each living system, the concentration of functional biological entities (e.g. proteins, enzymes, peptides…) is incredibly high. Though most of them are located in separate compartments in the cell, depending on their structure or function, each individual entity is led to show with others spatial proximity, or even close contacts, due to diffusion movements for instance. Thus, some transient complex-structures may appear and, depending on the affinity they exhibit for each other, may subsist during sufficiently long timescales that may lead to new functional systems.

Recent investigations put forward the existence of a supramolecular complex in the course of flavonoid production in which the successive enzymes remain in interaction. Indeed, it is now recognized that the mechanisms underlying the biosynthesis of natural products involve the creation of such transient structures, built around several proteins or enzymes. The product of an enzymatic reaction becoming the substrate for the neighbour enzyme, it just has to "jump" from an active site to the next one, diminishing the time lost during diffusion processes and the energy lost during solvation and desolvation processes, leading then to enhance the catalytic efficiency.

Accessing to a precise description of the overall structures of such macromolecular assemblies has then become a key-point to understand the underlying biological mechanisms but also for developing new therapeutic strategies. Our goal in this project is to simulate the various phenomena in this complex, including the chemical transformations but also the way products and substrates are transferred from the active site of an enzyme to the following. To this end, a broad spectrum of theoretical methods is used to unravel the mechanisms and interactions at different levels of complexity: QM and QM/MM methodologies are applied to decipher the reaction mechanisms, Molecular Dynamics procedures help in describing, both structurally and energetically, the interactions between substrate-cofactors and enzymes and up-to-date Protein-Protein docking protocols aim at building protein-protein complex structures.

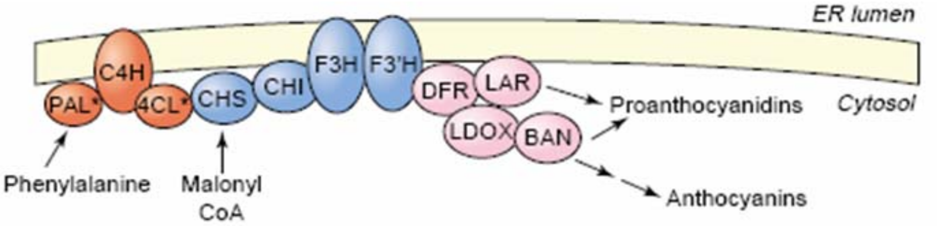

Figure 1 : Transient Macromolecular Complex involved in the Course of Flavonoids Biosynthesis

In a first approach of this study, will be presented our recent investigations concerning DFR enzymatic activities : the substrate-Enzymes interactions as well as reactions mechanisms will be depicted.

P36

6èmes Journées Franco-Italiennes de Chimie
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Proton-Conducting Cross-Linked Sulfonated Aromatic Polymers for Fuel Cells Application

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Thermal stability, hydration and mechanical properties of thermally cross-linked Sulfonated Aromatic Polymers (SAPs) with high ionic exchange capacity (IEC) were measured and compared to untreated samples. The formation of cross-linking greatly stabilizes SAPs in terms of thermal, mechanical, and hydrolytic degradation: they can resist in water even at a temperature of 145 °C with improved mechanical properties. Elemental analysis, acid-base titration, and FTIR spectra consistently indicate that the SAP microstructure stabilization is related to cross-linking of the polymer chains by SO_2 bridges, which is promoted by temperature. The analysis by stress–strain tests and Dynamic Mechanical Analysis shows also a large increase of glass transition temperature and mechanical strength. The new method for introducing a certain degree of covalent bonds between adjacent polymeric chains by heat treatment of cast membranes is really economic, since the cross-linking reaction can be performed directly after membrane casting [1-3]. Due to its simplicity, it is furthermore very suitable for industrial preparation of cross-linked membranes, because the procedure can be easily up-scaled. However, a delicate balance still exists between the hydrophilic character of membranes and their properties.

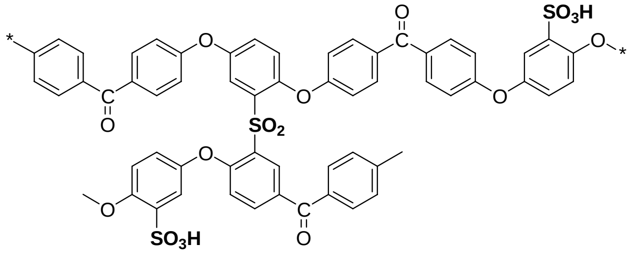

Figure 1: A typical structure of cross-linked sulfonated aromatic polymer

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First-Principles Study of Silver Nanocage Clusters

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Noble metal nanoparticles have attracted considerable interest in the scientific and technological community due to their peculiar electronic and optical properties[1]. In particular, these systems have great potentials in the development of optics devices as well as for medical applications, in the diagnostic[2] and therapy[3] fields. For example, in the photothermal therapy these nanoparticles, if properly functionalized, can be target to specific cells like the cancer ones. In this way, due to their plasmonic properties, nanoparticles can efficiently convert photons into heat, thus enabling the thermal ablation of the targeted cells. However, since biological tissues are transparent in the near infrared (NIR) region, the noble metal nanoparticles need to be tailored in order to have strong absorption in this spectral windows. A similar situation holds when nanoparticles are used as contrast agent for imaging diagnostic, where their scattering properties are exploited.

For this reason, great efforts have been invested in developing synthetic methods to control the parameters that dictate the nanostructure applicability like; shape, stability, composition and size. In this framework, theoretical investigations can serve as a bridge to correlate, for example, the electronic properties of these systems, with the structural ones[4,5] as well as their compositions, in order to tune the nanoparticle absorption wavelengths. Initially, due to the large number of electron involved first principles approach have been applied to small clusters, with less than 20 atoms, while, for larger clusters, semiempirical Hamiltonians or Mie scattering models were used. In the latter case, the discrete dipole approximation models should be satisfied and the systems properties become closer to the bulk ones. In each case the model structures were based on *classic* shapes like icosahedral or tetrahedral solid cores. Recently, due to the plasmonic absorption properties of *non classic* structures in the NIR region, shapes like nanorods and nanocages have acquired more interest while improvements in the understanding of the structure/electronic properties was achieved using time-dependent (TD-) and independent density functional theory (DFT) studies[6] by which the size dependence of the dielectric constant can be taken into account. In this communication, for achieve new insights on these systems, we present the results of a DFT study related to structure stability and optical properties of Ag_{60} clusters with nanocages or hollow nanorods shapes. These systems will be compared with some planar clusters as representative models of typical crystallographic Ag planes. The clusters structural properties are investigated using the B3LYP hybrid functional by analysing the binding energy and at the same time are tested the performances of different pseudopotentials. On this basis, the optical properties of the differently shaped Ag_{60} clusters are studied through TD-B3LYP calculations, and, for these hollow shapes, the role of the 3d, 4s and 4p atomic orbitals will be discussed. We have found that, as far as the hollow spherical-shaped clusters are concerned, the results of the theoretical modelling are in nice agreement with the Ag nanocages experimental data. For the medium to large sized clusters here considered, the analysis of their electronic structures combined with those of the allowed optical excitation nature (in function of molecular orbitals excitations) clearly indicates that the predicted transitions in the infrared region are due to the rising of a plasmonic excitation.

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Iridium Soft Salts: a New Approach for OLEDs Design?

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Organic Light-Emitting Diodes (OLEDs) are attractive as a next generation display due to their significant potential applications in solid state lighting source and flat panel or flexible displays. OLEDs using phosphorescent materials such as iridium complexes are among the most widely investigated. However, one major drawback of neutral iridium complexes originates from their low to moderate synthetic yields, therefore rendering iridium complexes less attractive for low fabrication cost. Recently, use of ion-paired iridium (III) complexes in OLEDs opened the possibility to develop highly efficient devices while enabling the preparation of both cationic and anionic partners of the ion-paired complexes in quasi-quantitative yields.[1] In this communication, we will present our recent research efforts devoted to the preparation of a series of ion-paired iridium complexes comprising mononuclear and dinuclear cationic complexes used for the design of red, blue, green and white-emitting devices.[2,3] By chemical engineering, easy color tunability could be obtained by modifying the ligand architecture of both the cationic and the anionic complexes.[4]

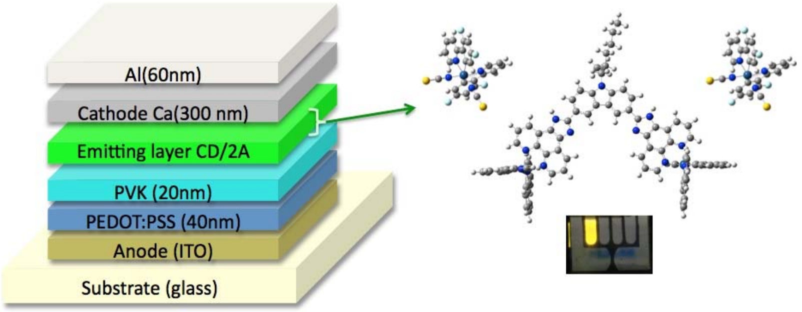

Figure 1 : Soft salts-based OLEDs

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P39

Synthèse de dérivés boroniques à partir d'halogénures organiques par voie catalytique

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Récemment au laboratoire a été décrit un mode de préparation de dérivés benzylboroniques par voie catalytique [1]. Le procédé décrit permet d'accéder en une seule étape, avec de bons rendements, aux esters benzylboroniques pinacoliques à partir des dérivés benzylhalogénés correspondants par une catalyse au magnésium. Ce processus met en jeu des quantités catalytiques de magnésium (10% molaire) là où les méthodes classiques utilisent des métaux nobles et/ou des quantités stœchiométriques.

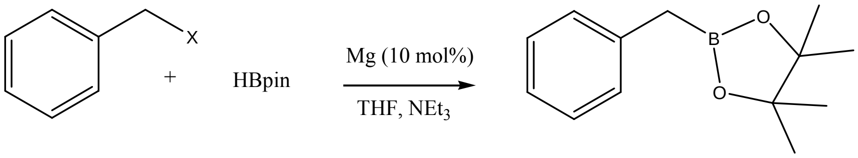

Figure 1 : Préparation de dérivés benzylboroniques en présence de Mg catalytique

Les études mécanistiques et théoriques de cette réaction ont mis en évidence le rôle essentiel de la stabilité du réactif de "Grignard" qui se forme *in situ*, et de l'agent boratant (HBpin) pour permettre le recyclage efficace du magnésium.

L'objet de cette nouvelle étude est d'appliquer et d'adapter cette méthodologie aux dérivés arylhalogénés pour accéder aux esters arylboroniques. Il s'agit dans un premier temps de déterminer les potentiels rédox des différents halogénures d'aryles ainsi que de leurs dérivés magnésiens afin dévaluer leur capacité de recyclage du magnésium en présence de l'agent boratant.

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Elaboration des copolymères à blocs à base de poly(diméthylsiloxane) par procédé RAFT

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L'apparition des méthodes de polymérisation radicalaire contrôlée est une grande révolution dans le domaine des polymères. Ces méthodes permettent de synthétiser des polymères avec un contrôle des masses molaires, des fonctions en bout de chaîne, de la structure moléculaire et de faibles indices de polymolécularité. Des architectures macromoléculaires complexes, par exemple en étoile, greffées, dendritiques, peuvent être obtenues avec diverses compositions, ainsi que la synthèse de copolymères à blocs, alternés, et à gradient. Parmi les méthodes de polymérisation radicalaire contrôlée, la méthode RAFT (Reversible Addition Fragmentation chain Transfer) est de plus en plus utilisée car elle est applicable à une large gamme de monomère et de solvant, elle peut être menée en masse, en solution y compris dans l'eau ou en milieux dispersés.[1]

Les poly(diméthylsiloxane)s (PDMS) possèdent des propriétés intéressantes comme une stabilité élevée en température et sous irradiation UV, des températures de fusion et de transition vitreuse faibles, une énergie de surface de l'ordre de 20-23 (mJ/m^2) [2] et une bonne perméabilité aux gaz. De plus, ils sont non toxiques, respectueux de l'environnement et biocompatibles.[3]

Dans cette étude, des copolymères à blocs à base de PDMS et de méthacrylate d'alkyle ou trialkylsilyle ont été synthétisés par le procédé RAFT à partir d'un macro-agent de transfert de chaîne de type PDMS. Le caractère contrôlé de ce procédé a été démontré par RMN-^{1}H et TD-SEC. L'incompatibilité des deux blocs a été mise en évidence par DSC.

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P41

Mixed-Ligand Pd catalytic systems to promote cross coupling for synthesizing bioactive triazole nucleoside analogues

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In our quest for biologically active triazole nucleosides,[1] we are interested in synthesizing *N*-arylaminotriazole nucleosides, which exhibit potent anticancer activity with novel modes of action.[2] We first explored Cu-mediated C-N coupling, which offered only limited success with narrow substrate scope (*Scheme A*).[3] Our further effort led to the discovery of highly reactive Pd/ligand systems using the phosphor ligands, Synphos and Xantphos, for selective C-N coupling with 5- and 3-bromotriazole acyclonucleoside isomers, respectively (*Scheme B*).[4] Recently, we have developed a mixed-ligand system of Pd/Synphos/Xantphos, which is strikingly powerful and efficient, allowing for unparalleled substrate scope and high product yields as well as promotion of C-Cl bond activation for C-N coupling (*Scheme C*).[5] Currently, we are developing mixed-ligand Pd catalyst to synthesize structurally novel and biologically active *S*-arylthiotriazole nucleosides, which are otherwise difficult to achieve.

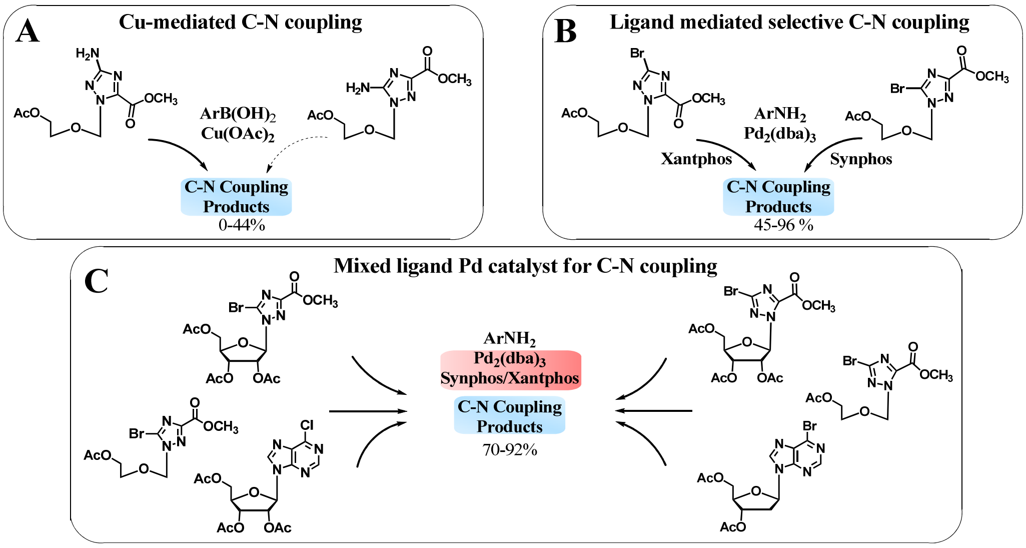

*Figure 1 : Different strategies explored for synthesizing N-arylaminotriazole nucleosides via C-N coupling. (**A**): Cu mediated C-N coupling; (**B**) Ligand-mediated selective C-N coupling; (**C**) Mixed-ligand Pd catalyst.*

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Sequential processing of 2D covalent networks on metal substrates

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The chemistry of boronic acids is currently one of the ways used for the formation of covalent organic 3D networks (COF). Our goal is to apply this concept to the formation of two-dimensional organic nanostructures on metal surfaces to prepare organic nanoporous masks of various sizes.

Previous work carried out in our laboratory on the molecule of 1,4-Benzene DiBoronic Acid (BDBA) led to the STM observation of 2D covalent honeycomb-like nanoporous networks with 15Å pores.[1] However due to the irreversibility of the covalent bond formation, defects are present in the polymer film.

To improve the regularity of the 2D network, a promising approach consists in controlling the kinetics of formation by use of two successive reactions. In this aim, we recently combined two reactions that significantly varied by their mechanisms, each reaction being activated in a specific range of temperature i.e. formation of the boroxine rings by dehydration at room temperature followed by C-C bond formation via an Ullmann coupling at temperature higher than 200°C (Fig. 1).

Herein, we present our results obtained during the sequential polymerization of 1-Bromo Benzene 4-Boronic Acid (BBBA) on Au(111) surface (Fig. 1).[2] Using the above-mentioned stepwise approach, a polymer network of higher quality with 23Å hexagonal pores was thus obtained.

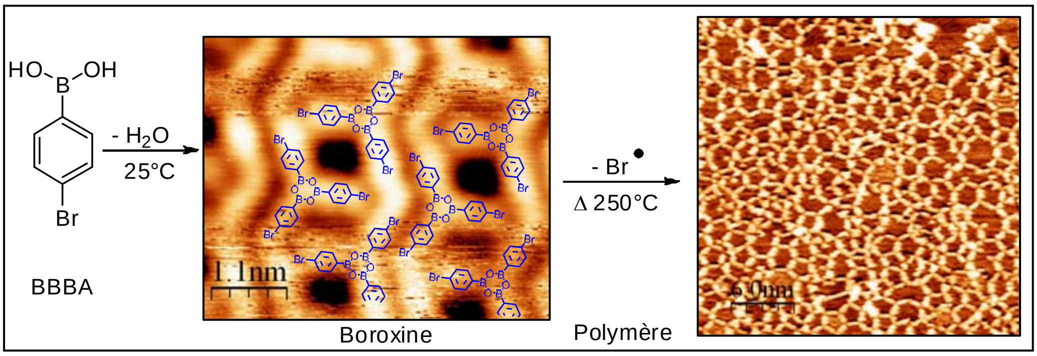

Figure 1 : Polymerization mechanism and BBBA network STM images of the boroxine and polymer phases on Au (111)

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Rationalization of dye uptake on TiO_2 glasses for DSSC solar cells by chemometric approach

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Dyes are one of the key elements of dye sensitized solar cells (DSSC). Understanding the chemical properties at the molecular levels of the dyes and the features of the interactions governing polyene-diphenylaniline dye (D5) uptake on TiO_2 surface is of paramount importance for DSSC characterization and further development.

From structural information seems that D5 bonded to titanium oxide in the working DSSC devices suffers of the presence of strong intermolecular interactions between the phenyl groups of the chromophores; this evidence is of paramount importance during the dye grafting process, where aggregation of dyes should be avoided. Also after the grafting onto the surface of 25 nm sized titanium oxide, lateral interactions between neighboring bonded D5 molecules play an important role in self-absorption and charge recombination processes, that could lower the yield of electron injection into titanium oxide conduction band, with an overall smaller efficiency of the DSSC cell.

A chemometric approach of Factorial Experimental Design was used in the determination of the amount of uptake of D5 dye on TiO_2 surface, in order to obtain information about the correlations between the three variables governing the uptake itself, i.e. D5 concentration, dispersant (cheno-deoxycholic acid, *CDCA*) concentration and contact time. A 2^3 Full Factorial Design was performed allowing to evaluate, at the same time, the principal and the interaction effects of three variables. The obtained Ordinary Least Squares (OLS) regression model shows that large uptakes can be obtained, as expected, when *CDCA* is present if the contact time is high, but, surprisingly, in absence of *CDCA* if the contact time is small. This behaviour can be related to the effects of the intermolecular interactions.

Synthèse de Nouveaux Complexes de Difluorure de Bore avec des Ligands β-Dicétonates à Conjugaison Etendue

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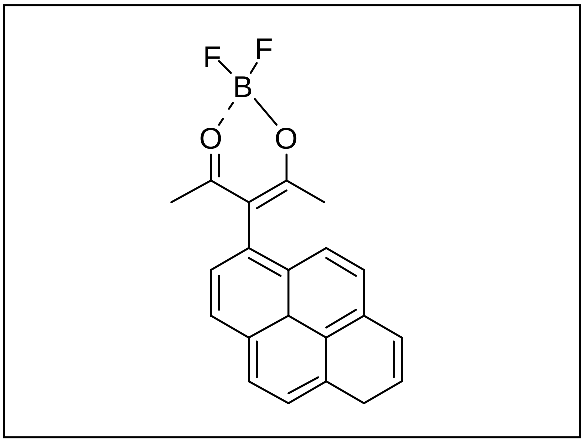
Les dérivés de β-dicétones, comme l’acétylacétone (acacH), sont particulièrement bien connus en chimie de coordination pour l’obtention de complexes métalliques à propriétés optiques et électroniques. Nous présentons la conception et la synthèse d’une série de ligands dérivés de acacH et fonctionnalisés en différentes positions par des motifs π-conjugués ou aromatiques. La préparation de leurs complexes avec l’unité BF2 et des résultats préliminaires sur les propriétés physico-chimiques des chélates dioxaborine seront décrits.



Synthesis of Ni nanoparticles/porous silica hybrid materials and their applications in hydrogen storage

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Hydrogen is a promising energy carrier. Nevertheless, for its efficient storage, some technological and scientific key problems still need to be unlocked. One of them concern the reversibility of the storage: hydrogen and the porous material need to develop specific interactions leading to not only large adsorbed amounts of gas but also to a desorption that is not too expensive from an energetic point of view [1]. In this context, mesoporous silicas presenting large pores were first synthesized using the sol-gel process, and then functionalized with metallic nanoparticles. Nickel nanoparticles incorporated as transition metals are known to develop the specific interactions with hydrogen that are mentioned above. Porous materials before and after the incorporation of the nanoparticles were characterized using conventional techniques such as N_2 sorption at 77K, TEM and ICP-MS. Then, H_2 adsorption properties were studied at 77K and at low pressure ($p<1$bar) using a Tian-Calvet type isothermal microcalorimeter coupled with a manometric device built in house [2]. This apparatus allows both the construction of the isotherms (adsorbed amounts as a function of pressure) and the determination of the adsorption enthalpies as a function of surface coverage. A theoretical modelling of hydrogen adsorption properties on these porous materials was also performed. In light of these results and those found in the literature, a novel type of hybrid material combining a large number of requirements is then proposed.

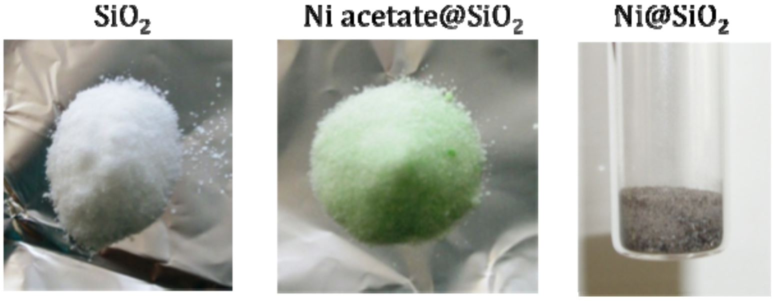

Figure 1: Pictures of as-prepared mesoporous silica (white); after incorporation of Ni acetate (green) and of Ni nanoparticles (black)

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[2] P.L. Llewellyn, G. Maurin, *C. R. Chim.*, 8 (2005) 283–302.

P46

Beryllium in interaction with benzene, graphene and graphite: an in-depth analysis of the electronic structure

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Although beryllium is found to physisorbed on graphene, it chemically binds in a bi-layer of graphite. This difference in bonding is modelled by the interaction with a beryllium atom and a monomer or a dimer of benzene, and then analysed at different level of theory: DFT, MP2, CCSD(T) and CASSCF.

It is found that the Be- π system interaction can be cast in a short-range and a long-range part. In the long-range part, an excellent agreement is found between MP2/CCSD(T) calculations and some DFT functionals (PBE-vdw and M06); in that case, the ground state is in a molecular electronic configuration. In the short-range part, a strong Jahn-Teller distortion is found and a charge transfer occurs from beryllium to the benzene molecules. The electronic ground state is ionic, while the molecular electronic configuration belongs to an excited state.

At the end of the work, the difference in the nature of bonding between graphene and the bilayer of graphite is understood, and DFT is found to well reproduce the post-HF results in the whole range of the interaction.

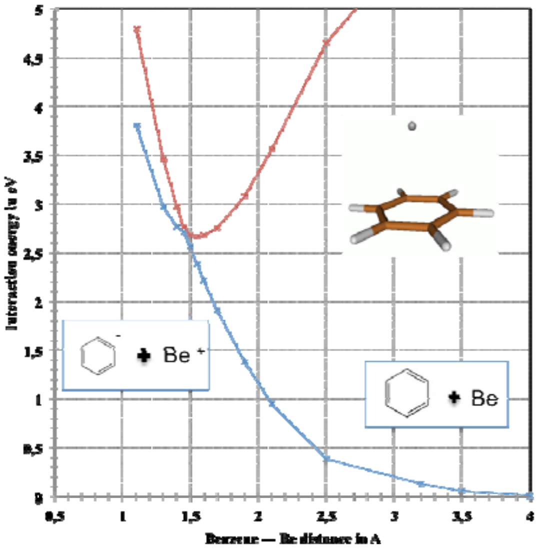

Figure 1 : Beryllium atom in interaction with benzene : CAS-SCF potential energy surfaces. Ground state in blue. First excited state in red.

P47

Scouting new molecular targets for CFTR therapy: the HSC70/BAG-1 complex. A computational study.

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Cystic fibrosis (CF) is a multiorgan genetic disorder caused by the loss of function of the CF transmembrane conductance regulator (CFTR) [1]. Loss of function of CFTR results in viscous secretions of the exocrine glands in multiple organ systems and elevated sweat chloride levels. At present, the respiratory complications are responsible for the majority of mortality associated with this disease.

Since the discovery of the *CFTR* gene in 1989 [2], a major effort has been directed to develop causative therapies for CF. These included gene-replacement strategies and a number of alternative approaches [3] among which potentiators, compounds that stimulate pre-activated CFTR channel activity and correctors, agents that rescue cell-surface expression of mutated/defective CFTR, in particular ΔF508-CFTR, the most abundant protein mutation.

More recently increasing attention has been devoted to those molecular chaperones that assist the protein folding processes within the cell. Among them, HSC70 has been identified as an important molecular target involved in the ΔF508-CFTR cystic fibrosis. HSC70 associates ΔF508-CFTR to a much greater extent than WT-CFTR and after this step, it recruits other co-chaperones (BAG1, CHIP) and performs the ubiquitination and proteosomal degradation of the protein.

Un to now, several X-ray data concerning the HSC70:BAG1 complexes become available. Thus, we performed an "in silico" investigation focused to explore which different amino acid residues are involved in the binding of ATP, the natural substrate, and the co-crystallized ligands at the HSC70/BAG-1 interface. In particular, we focused our attention on NSC71948, a mixture of two components, which has been discovered as acting on the HSC70:BAG1 assembly, displaying an IC_{50} of 0.9 - 0.1 μM in the in vitro HSC70:BAG-1interaction assay [4].

The derived key interactions, which resulted to be effective on the HSC70:BAG1 inhibition, have been successively employed to evaluate, through docking procedures, a number of compounds recently described as CFTR correctors.

The obtained results, being in agreement with the experimental data, allowed us to reasonably hypothesize (for the examined compounds) a mode of binding highlighting interesting perspectives for expedite the development of new CFTR correctors.

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[3] Amaral MD, Kunzelmann K, (2007) Molecular targeting of CFTR as a therapeutic approach to cystic fibrosis. Trends Pharmacol Sci 7: 334–341.
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P48

Usefulness of Au µwire electrode for Cu speciation: A study in estuarine waters using voltammetric techniques with comparison to the classical Hg drop

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Copper is an important essential/toxic trace metal to organisms in natural waters such as seawater, where its potential bioavailability is dictated by its chemo-physical form. Electrochemistry allows one to distinguish to some extent between these physical forms. Pseudopolarography is a pre-concentration technique that allows great sensitivity for a number of trace metal species, including copper – distinct anodic stripping voltammograms (ASV) are built up to construct a pseudopolarogram. This often shows several waves of signal intensity as the potential becomes more negative, where both labile and inert species can be distinguished. Speciation is conducted by relating the thermodynamic strength of complexation of the metal with ligands which have a specified shift in halfwave potential, giving a distinctive 'shape'. We compare the speciation of Cu by pseudopolarography using the historically utilized hanging mercury drop electrode (HMDE) [1] and the newly developed vibrating gold microwire electrode (VGME) [2] onsite in unaltered waters collected in Martinska estuary, Croatia, July 2011.

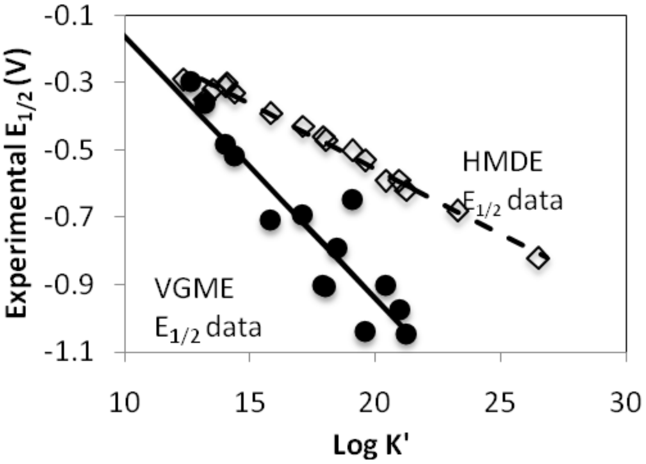

Figure 1 : Comparison of model compounds in UV digested seawater using the VGME [2] *and the HMDE* [1].

Figure 1 shows a comparison in terms of model compounds such as EDTA in UV digested seawater for the two electrodes with some significant differences. It is interesting to see if the analysis of real samples conducted with both in the same natural waters at the same time is consistent.

[1] Croot et al. (1999) Marine Chemistry 67, 219-232.
[2] Gibbon-Walsh et al. (2012) Physical chemistry, in preparation.

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P49

Comparative study on the chemical composition of the tunisian *Aplysia depilans* at different stages of development.

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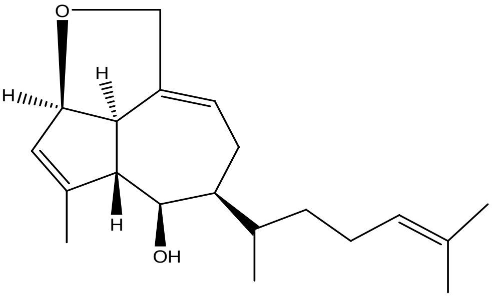
Sea hares are slow moving soft bodied opistobranch mollusks lacking a shell for protection. They rely on a variety of defensive strategies to get protected against predators, with the secretion of ink and opaline cryptic coloration, distastefulness of skin and body wall, withdrawal and escape. During their ontogeny, sea hares may also use one or several chemical strategies to avoid predation, depending on the developmental stage. Few studies dealt with the chemical defenses of *Aplysia* through the different stages of its life cycle.

In this study, we compared the chemical fingerprints of the adult *Aplysia depilans* (skin and organs) with its egg masses.

Four different compounds identified from the chemical profiles obtained by HPLC-DAD-ELSD, were mainly present in the adult *Aplysia* (skin and organs) but absent in the eggs.

One other compound found in the organs and the egg masses, was absent in the skin. This suggested that this compound may originate from the diet of the animal, to be then incorporated in the eggs.

The chemical process: extraction, isolation, and structural elucidation (1D and 2D NMR, MS); allowed us to identify the major metabolite of *A. depilans* as Dictyol A (**1**), previously identified in *Dictyota dichotoma*, a brown algae grazed by *Aplysia*.



Dictyol A (1)

Figure 1 : Dictyol A

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6èmes Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
Marseille – Campus St Charles
16-17 avril/aprile 2012

Propargylic radicals from Dialkylzinc

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The conversion of propargylic or allenic radicals into derivatives directly usable in organic synthesis remains a challenge. We propose a radical methodology to meet this challenge without tin that we developed in our laboratory using dialkylzincs under aerobic conditions.[1] The allenyl zincs obtained can be trapped by various electrophilic centers to drive molecules functionalize more complex. In this poster presentation, we discuss some of the results obtained in this chemistry in our laboratory.

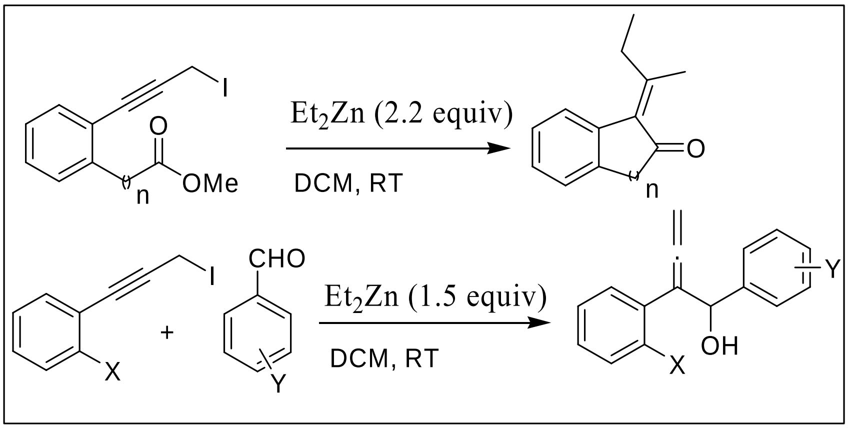

Figure 1

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P51

Design and synthesis of new RNA ligands that bind HIV-1 TAR RNA

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It is currently admitted that RNAs play a key role in biological processes in living cells and are considered as the essential regulators of many steps of gene expression. Furthermore, many viruses such as HIV, HCV, influenza and flaviviruses are encoded by a unique RNA molecule that serves as the main genetic material. Therefore, small molecules that bind specifically to particular RNA sequences and structures and disturb RNA function could be powerful tools for understanding and controlling gene expression.[1] TAR sequence in the HIV RNA genome, is a highly conserved region of viral RNA essential for viral replication since it interacts with proteins and cofactors initiating genome replication. New ligands that would be able to interact with TAR RNA and inhibit its interaction with protein TAT and other cofactors would lead to the inhibition of viral replication (Figure 1A). In this work, we conceived and synthesized new compounds containing different RNA binding domains: (i) a modified nucleobase able to form specific hydrogen bonds with a AU base pair in the duplex region of the target RNA and (ii) amino acids or aminoglycosides which are known to bind TAR RNA with high affinity. These RNA binding motifs are coupled using different spacers, such as a 2'-deoxyribose (nucleosides analogues) and other linear linkers of different length (non-nucleoside analogues).

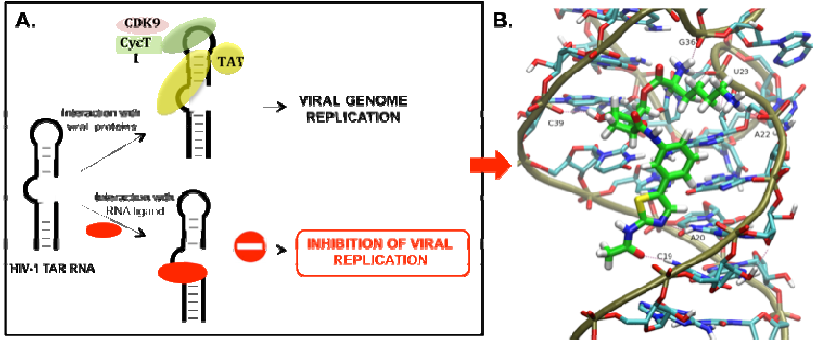

Figure 1. A. *HIV-1 TAR RNA normally interacts with TAT protein and other cofactors leading to viral genome replication (top) but the presence of efficient TAR ligands could change RNA conformation and eventually inhibit viral replication (bottom).* ***B.*** *Molecular modeling showing the interaction of the new synthesized RNA ligands with the target RNA.*

These different RNA recognition domains altogether act cooperatively in order to bind the target with both strong affinity (Kd = 2-30 µM) and selectivity. We suggest that these molecules interact with the target RNA at the stem-bulge junction as supported by molecular modeling (Figure 1B). Some of these compounds showed also a very good viral inhibition in cells infected with HIV-1 and no toxicity toward non-infected cells. The strategy presented here could be applied to other important RNA targets and could become a general approach to discover new antiviral and anticancer drugs.

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P52

One-pot Chemoselective Bis-Suzuki-Miyaura Cross-Coupling Reactions: Efficient Access to 3,9-Di(hetero)aryl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one Derivatives

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The 4*H*-pyrido[1,2-*a*]pyrimidin-4-one ring is a successful scaffold for the development of biologically interesting molecules. Their pharmacological activities in wide biological areas have been reported in the literature.[1-3] In connection with our studies, directed by the interest of microwave heating in Suzuki-Miyaura cross-coupling reactions[4] and the synthesis of 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones as potential biologically active compounds, we have developed an extremely efficient one-pot chemoselective double Suzuki-Miyaura coupling on the 7,9-dichloro-3-iodo-4*H*-pyrido[1,2-*a*]pyrimidin-4-one derivative.

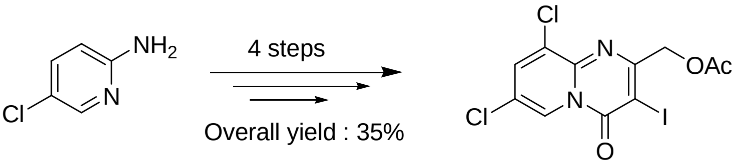

Figure 1 : Synthesis of the starting material

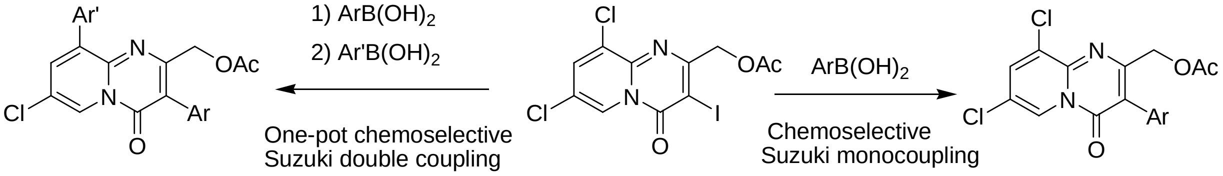

Figure 2 : Chemoselective Suzuki-Miyaura cross-coupling reactions

The structure of synthesized 4*H*-pyrido[1,2-*a*]pyrimidin-4-ones and the methodologies employed will be reported and discussed.

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P53

Relation between mechanical properties of proton-conducting polymers macromolecular structure, additives and thermal treatments

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Proton-Conducting Polymers attract attention as possible electrolytes for Proton Exchange Membrane Fuel Cells. Objective of the current development is to obtain a suitable proton-conducting polymer for use at intermediate temperatures (typically 120°C) and under low relative humidity and to improve long-term durability.

Mechanical properties are fundamental for durability under fuel cell conditions. We have recently investigated polymer membrane characteristics by tensile tests and Dynamic Mechanical Analysis. [1-4]

In this presentation, we will discuss the influence of materials composition, manufacture and thermal treatments on the static and dynamic mechanical performance [5]. One important requirement for high durability is to remain during fuel cell operation below the yield stress, where plastic deformation starts. One way of improvement is to enhance the membrane stiffness, characterized by Young modulus, and yield stress by development of composite and cross-linked membranes. Relevant examples will be given.

[1] M. L. Di Vona et al. Chem. Mater., 20, 4327 (2008)
[2] E. Sgreccia et al., J. Power Sources, 178, 667 (2008)
[3] E. Sgreccia et al., J. Power Sources, 195, 7770 (2010)
[4] M.L. Di Vona et al., J. Membrane Sci., 354, 134 (2010).
[5] P. Knauth, M. L. Di Vona, Solid State Proton Conductors : Properties and Applications in Fuel Cells, Wiley, 2012.

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P54

Rapid and efficient synthesis of 2-substituted-tetrahydropyrido[3,4-*b*] quinoxalines using TDAE strategy

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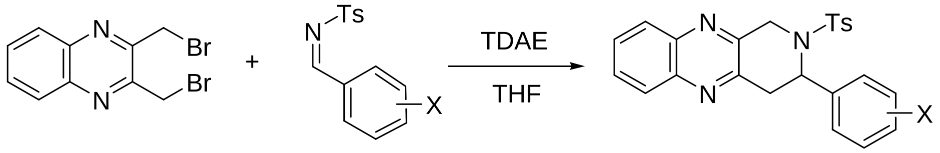
The quinoxaline derivatives show very interesting biological properties,[1] such as antibacterial,[2] antiviral,[3] anticancer,[4] antifungal, antihelmintic, antileishmanial,[5] anti-HIV,[5] insecticidal, anti–inflammatory activites.[6] Many drug candidates bearing quinoxaline core structures are in clinical trials. Among them, the XK469 ((±)-2-[4-(7-chloro-2-quinoxaliny)oxy]phenoxy propionic acid) was known as antineoplastic quinoxaline topoisomerase II inhibitor and possesses antitumor activity especially against murine and human solid tumors.[7]

On the other hand, the tetra- and dihydropyrido[3,4-*b*]pyrazine derivatives exhibited interesting biological activity as anticancer agents. In spite of the great interest that could represent combined structures presenting the quinoxaline and the tetrahydropyridine nucleus, few synthesis of tetra-hydropyrido[3,4-*b*]quinoxaline derivatives have been reported.[8]

Since 2003, we have shown that from *o*- and *p*-nitrobenzyl chloride, Tetrakis(DimethylAmino)Ethylene (TDAE) could generate a nitrobenzyl carbanion which is able to react with various electrophiles as aromatic aldehydes, α-ketoester, ketomalonate, α-ketolactam and sulfonimine derivatives.[9] We report herein an original and efficient synthesis of new substituted 2-tosyl-1,2,3,4-tetrahydropyrido[3,4-*b*]quinoxalines based on the TDAE strategy from the reaction between 2,3-bis(bromomethyl)quinoxaline and sulfonimine.



X = H, 2-Cl, 2-Br, 2-Me, 2-OMe, 2-CF_3
3-F, 3-Br, 3-OMe, 4-Me, 4-OMe

56-68%

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Proton-conducting hydrated acidic polymers: relations between polymer microstructure and proton mobility

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Sulfonated Aromatic Polymers (SAP) are alternative polymer electrolytes for Proton Exchange Membrane Fuel Cells. Objective of the development is to obtain a suitable proton-conducting polymer for use at intermediate temperatures (typically 120°C) and under low relative humidity and to improve long-term durability.
In our recent work, we focus on the study of physico-chemical properties of various SAP, including Sulfonated Poly-Ether-Ether-Ketone (SPEEK) with various Degree of Sulfonation, Sulfonated PolyPhenylSulfone (SPPSU), and cross-linked derivatives, obtained by innovative synthesis procedures or by optimized thermal annealing. [1-4]
In this presentation, we will discuss the proton mobility in the acid solutions present inside the polymer matrix. [5] These data are obtained from water uptake isotherms and proton conductivity measurements by impedance spectroscopy. The presence of the polymer matrix is observed in several aspects. The decrease of proton mobility $u(H^+)$ with increasing proton concentration $c(H^+)$ can be described by power laws (Figure 1). It is related to the proton localization near sulfonate groups and space charge effects. The effect on proton mobility can be discussed taking into account the tortuosity of the membranes and the percolation threshold of the nanometric aqueous channels inside the matrix as phenomenological parameters. [6]

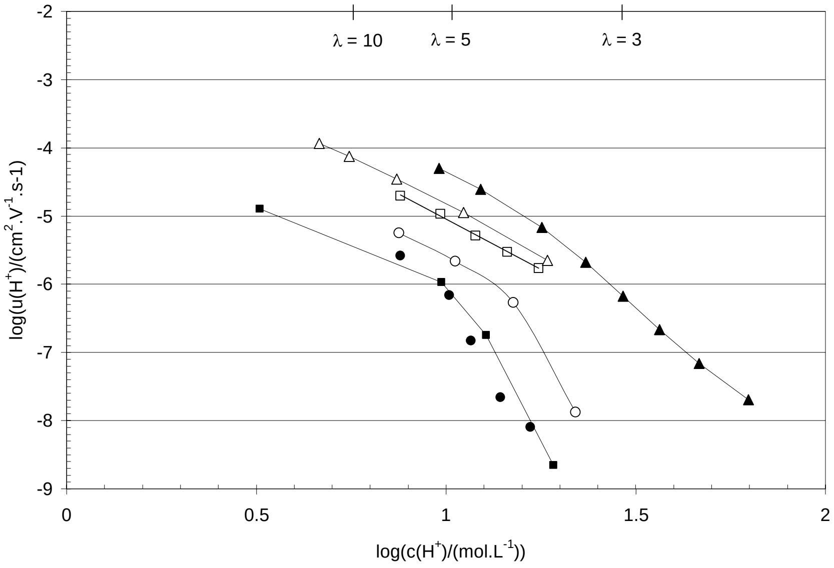

Figure 1.

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6èmes Journées Franco-Italiennes de Chimie
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Caractérisation physico-chimique de l'adhésion à l'interface substrat organique/peinture poudre

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Dans le domaine automobile et aéronautique, l’étape de mise en peinture garantie une protection de base et assure l’esthétisme du produit final. Cette étape est fortement impactée par un champ de contraintes règlementaires récent qui oblige les industriels à revoir leurs moyens de mise en œuvre et le choix des produits. Ces contraintes réglementaires sont de plusieurs types : REACH qui vise à éliminer les produits dangereux pour la santé, la limitation du taux de Composés Organiques Volatiles (COV) pour les peintures en phase solvant organique... Les peintures poudres sont une réponse à ces contraintes réglementaires tout en maintenant le niveau de performance.

De nombreux paramètres seront testés afin d'optimiser l'adhérence de ce type de revêtement: le moyen de mise en œuvre, le procédé d'application de la peinture poudre, le système de réticulation, l'état de surface du substrat, le traitement de surface...

L'enjeux est ici la compréhension des mécanismes d’adhésion de ce type de revêtement sur substrat organique. Pour se faire différentes techniques de caractérisation de l'interface sont envisagées : la spectroscopie infrarouge à transformée de Fourier (IRTF), le microscope électronique à balayage (MEB) couplé à l'analyse EDX, le microscope à force atomique (AFM) et la microanalyse thermique (µTA).

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Synthesis and SAR Studies of Marine 3-Alkylpyridinium Salts and Analogs

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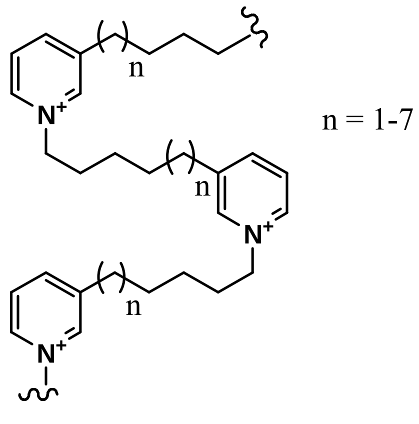
3-Alkylpyridinium salts (3-APAs) are common secondary metabolites isolated from marine Haplosclerid sponges. Two major groups of 3-APAs metabolites with fully saturated alkyl chains have been identified to date: linear and macrocyclic structures. Each group can be further divided according to the number of pyridinium rings in the molecule. Most of the linear compounds are constituted by only one pyridine unit, excepted viscosaline (**1**), a potent antibacterial derivative, and the halitoxins (**2**). The group of cyclic 3-APAs is dominated by dimeric compounds with two pyridine moieties, e.g. cyclostelletamine A (**3**) and haliclamine A (**4**).

Despite their rather simple structure, 3-alkylpyridinium salts display a broad variety of biological properties, such as: cytotoxic, antibacterial, antitumoral and antifouling activities. However, the entire pharmaceutical potential of these molecules is still understudied due to the difficulties to prepare them and the lack of SAR studies.

We present here an original synthesis of linear oligomers as well as higher oligo- and polymeric alkylpyridinium salts, especially from the viscosaline family. We also report a part of the SAR studies realized on them.



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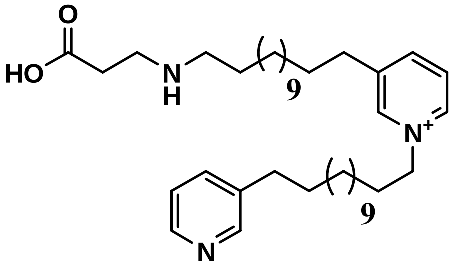

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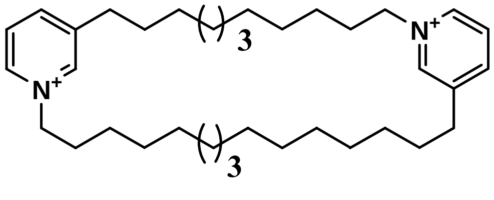

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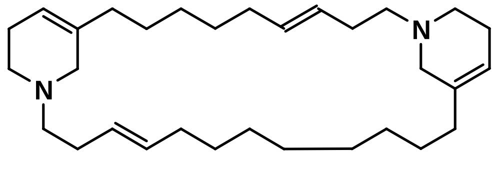

(4)

Figure 1 : Linear and cyclic 3-Alkylpyridinium salts

Green ultrasound-assisted extraction of carotenoids based on the bio-refinery concept using sunflower oil as an alternative solvent

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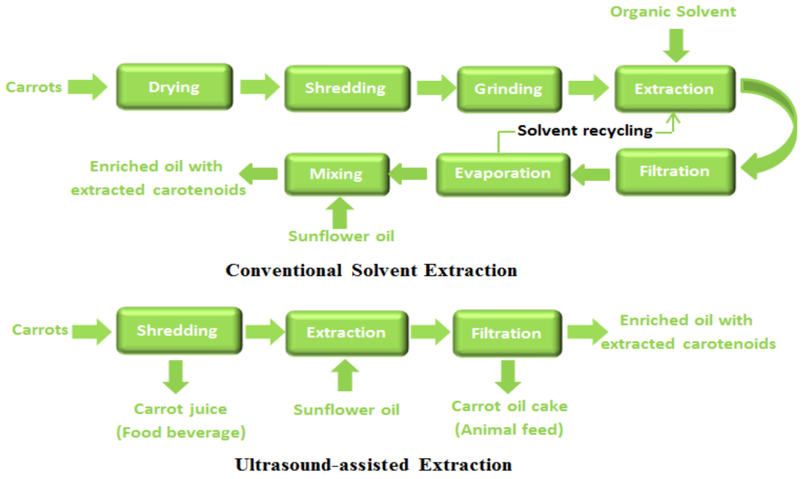
Green Extraction, based upon the principles of Green Chemistry, Green Engineering and the Bio-refinery concept, has arisen as a new trend in natural resource extraction techniques. The carotenoids are one of the most interesting groups of natural antioxidant compounds in fruits and vegetables. Although various innovative techniques, such as the use of microwaves and supercritical fluids, have been developed and applied to the extraction of these components in plant resources, no extraction technique can be considered a truly green, inexpensive and easily carried out method for the extraction of carotenoids.

In this work, sunflower oil was applied, as a substitute to organic solvents, in the green ultrasound-assisted extraction of carotenoids from fresh carrots; a process which is in line with Green Extraction and Bio-refinery concepts. On one hand, the processing procedures of ultrasound-assisted extraction (UAE) and conventional solvent extraction (CSE) were compared as the following flow charts shown. The new green UAE process could not only make the CSE process safer and more compact and highly efficient, but may also has other various advantages such as generation of co-products or by-products that can be put to other uses. On the other hand, the UAE conditions for the subsequent comparison of the two extraction methods were optimized using reference data from UPLC-DAD-MS chromatography. Meanwhile, the kinetics of the ultrasound-assisted carotenoid extraction was studied with different carrot/oil ratios (ranging from 10% to 30%) and at different temperatures (20°C, 40°C). The UAE performed under optimal extraction conditions (carrot/oil ratio 1:5, 40°C, 35min) gave the best results.



Conventional Solvent Extraction

Ultrasound-assisted Extraction

Figure 1 : Processing procedures for conventional solvent extraction and ultrasound-assisted extraction based on the bio-refinery concept

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P59

Synthesis and characterization of mixed rare earth oxycarbonates and oxides.

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In recent years, research on new materials for application in optoelectronic field (for example fluorescent lamps, high efficiency phosphors and persistent phosphors) has been significantly developed. Promising compounds are the mixed rare earths oxycarbonates and the mixed oxides doped with one or more optically active lanthanide ions [1].
Oxycarbonate ($RE_2O_2CO_3$, RE=rare earth) can exist in three forms: monoclinic, cubic, hexagonal. Hexagonal form is the most suitable to host doping ions, but its synthesis is strictly correlated with the synthetic route especially for temperature, atmosphere and treatment time. To date we successfully synthesized $Gd_2O_2CO_3$ in hexagonal form, doped with Eu^{3+}, Dy^{3+} or Ho^{3+}, which presents interesting optical characteristics. Synthesis consist in a thermal treatment of raw materials (mixed oxalates or oxides) in a fluent CO_2 atmosphere with a *flux* of molten salts [2].
Also mixed oxides present particular features: for example the mixed system CeO_2/Gd_2O_3 presents a complete solubility between the two rare earth oxides at any grade of concentration [3,4]. In this system an insertion at high temperature of an optically active lanthanide ion may be possible.

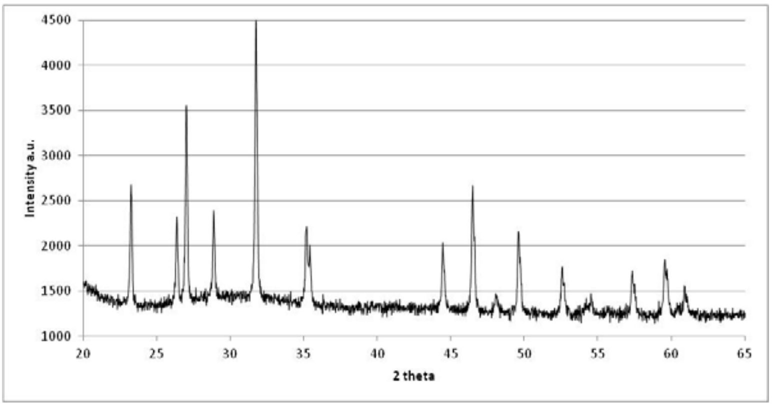

Figure 1 : XRD spectrum of $Gd_2O_2CO_3$:Eu in hexagonal form

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P60

Enantioselective organocatalytic Michael addition of cyclobutanones to nitroalkenes

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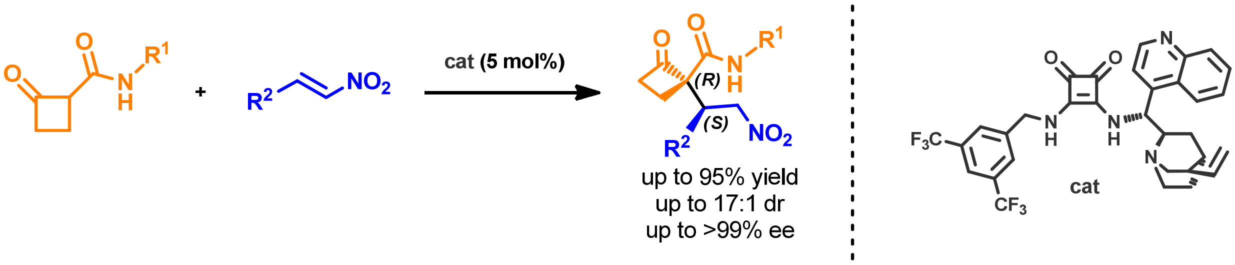
Cyclobutanes have been known for more than a century and their use as synthetic intermediates has only been developed since the 1970's.[1] Their versatile reactivity is the result of the inherent strain associated with the four-membered ring. Cyclobutanes are incorporated in a number of natural products (*e.g.* caryophyllane sesquiterpenes),[2] and stereoselective methods to access such scaffolds are of value.

Organocatalysis has emerged over the past decade as a thriving area of organic synthesis.[3] Although cyclic ketones have been prominently studied, examples of organocatalytic transformations involving cyclobutanones are rare and stereoselectivity remains an issue.[4]

In connection with our research program on applications of 1,3−dicarbonyl compounds,[5] we have developed the first diastereo- and enantioselective organocatalytic Michael additions with cyclobutanones. In this communication we will present our work with a special emphasis on the role of the 4-membered ring in both the substrate and the catalyst.



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P61

Methodological developments in synthetic chemistry and mass spectrometry for the production of bio-sourced materials

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An increasing attention is currently drawn to polymers from renewable resources, such as cellulose, in order to minimize our dependency towards petroleum-based products, as well as for environmental concerns. Although natural polymers have inherent biodegradability properties, they suffer from major drawbacks: their moisture sensitivity and their poor mechanical properties dramatically limit their application. Properties of natural polymers can be significantly improved by blending them with synthetic polymers, providing efficient compatibilizers are available.

A compatibilizer should exhibit similar physico-chemical properties as compared to the two polymers to be blended. However, grafting synthetic blocks onto natural polymeric chains has faced two main issues: a limited knowledge of mechanisms underlying reactivity of functional groups in natural macromolecules to be grafted and the lack of efficient analytical methods to characterize the complex structure of the so-obtained co-polymers [1]. Alternatively, selected oligosaccharides of smaller size and higher solubility with respect to cellulose can be functionalized to allow the growth of polymeric chain using nitroxide-mediated polymerization (NMP) [2].

An efficient optimization of synthetic strategies requires adequate analytical methods to be developed in a concerted manner. Here, a synthetic route based on nitroxide-mediated polymerization is implemented to allow the growth of polystyrene at low temperature, while mass spectrometry is used to characterize the structure of intermediates and final products.

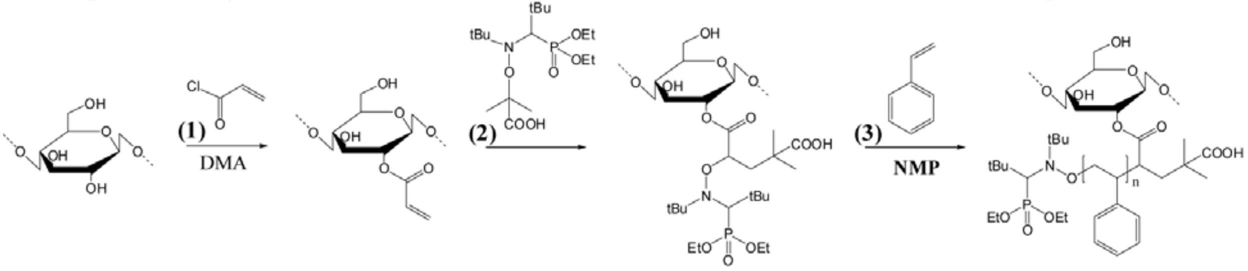

Figure 1: synthetic strategies to produce compatibilizers from oligo-saccharides : (1) grafting of acrylate moiety (2), 1,2-addition of an alkoxyamine and (3) controlled growing of styrene

Preliminary results are presented here for small size sugars, glucose and cellobiose. Optimization of experimental conditions is discussed for both synthesis and analysis, allowing the number of substituted OH groups in the saccharide substrate to be controlled and monitored.

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P62

Influence of grinding time on solvent-free MALDI efficiency: a combined mass spectrometry / solid-state NMR study

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MALDI has quickly emerged as the method of choice for polymer ionization since it mostly allows singly charged oligomer adducts to be produced, leading to more simple mass spectra as compared to electrospray. However, a major issue that limits widespread applications of MALDI-MS is the poor knowledge of fundamental processes underlying the desorption/ionization process. As a result, development of MALDI sample preparation methods remains rather empirical and becomes challenging when it comes to complex polymeric systems. In a previous work, we demonstrated the capabilities of solid state NMR to provide detailed insight in the structuring of the sample to be laser irradiated.

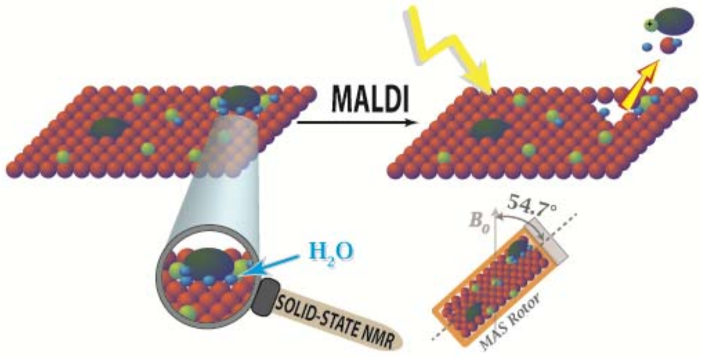

Figure 1 : Solid state NMR to study the MALDI sample

In the present study, molecular organization of MALDI samples was studied by solid-state NMR to account for the different quality of MALDI data as a function of the grinding time used in the solvent-free preparation procedure.[2] This sample preparation method overcomes the drawbacks associated with the use of solvents while providing high quality MALDI data.

The system investigated here was composed of 2,5-DHB as the matrix, a small poly(ethylene oxide) (PEG) as the analyte and cesium chloride as the cationizing agent. Grinding the three components in the solid state was found to promote the formation of a matrix/analyte complex for short grinding times. A matrix/salt complex was also generated when the grinding time was increased, which could be related to an optimal MALDI process. Water molecules were evidenced in this 2,5- DHB/CsCl complex and their presence in the grinding atmosphere was shown to be necessary for this complex to form.

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$6^{èmes}$ Journées Franco-Italiennes de Chimie
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Study of fragmentation pathways of SG1, a persistent free radical ion in tandem MS

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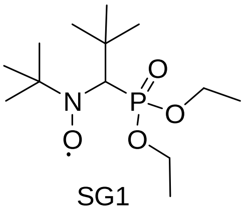
Nitroxides are an important class of organic free radicals employed in various applications such as organic synthesis, spin labeling, controlled radical polymerization… In our group, we are mainly interested in the use of nitroxides as control agent for Nitroxide Mediated Polymerization (NMP)[1-2]. This technique is now recognized as a particularly efficient approach toward reaching a high degree of control over the molar mass distribution, chain end functionalities and macromolecular architectures. During our investigations, we were particularly interested in the study of the MS/MS dissociation behavior of N-tert-butyl N-(1-diethylphosphono-2,2-dimethylpropyl) nitroxyl radical (SG1) produced as a gas phase radical cation upon electrospray ionization (ESI). Indeed, beside Electron Spin Resonance (ESR), mass spectrometry is a method of choice for precise characterization of nitroxide compounds [3].



SG1

In this study, SG1 was investigated using electrospray ionization high resolution mass spectrometry and tandem mass spectrometry in positive mode. Accurate m/z values of the precursor and of the product ions were measured. Geometry optimizations were performed using the hydrid B3LYP density functional theory (DFT) approach as implemented in Gaussian 03.

Dissociation of gas phase ions such as the electrosprayed protonated SG1 could be envisaged to proceed via charge- or radical-induced reactions or according to pathways which involve neither the charge nor the radical. A crucial piece of information to understand product ion formation is the location of the charge. Theoretical calculation indicated that the proton was located on the nitroxide oxygen. Starting from this conformation, mechanisms could be proposed to account for all MS/MS data and were supported by theoretical calculation and accurate mass measurements. A radical-induced reaction was found to imply a β-cleavage, giving rise to the release of the diethyl-phosphite radical or of the *t*-butyl radical. In contrast, elimination of isobutylene from the *t*-butyl group in α-position of the nitrogen would proceed according to a charge-induced pathway.

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P64

New materials as efficient solid electrolytes for lithium batteries

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Energy management and storage are technological challenges for the development of renewable energies. Most current commercial batteries use liquid or liquid-base electrolytes that limit their thermal stability, energy density and safety. These limitations could be considerably offset by the use of solid polymer electrolyte. Lithium metal polymer technology would be a major innovation in this field.

The major drawback of solid polymer electrolytes is the decrease of the ionic conductivity with increasing mechanical strength. For example, poly(ethylene oxide) (PEO) presents a high ionic conductivity in the melted; nevertheless, below its melting temperature, crystalline regions interfere with ion transport and induce a low ionic conductivity. Since ~~a~~ few years, increasing research efforts have been focused on block copolymers as BAB block copolymers, where A is a PEO block and B a polymer which ~~is~~ provides the mechanical strength. These materials are interesting because of their self-assembly properties which lead to well ordered structures and generate solid-like mechanical properties. However, these systems present a high power limitation due to the low transport number t^+ of lithium cations into the PEO matrix.

In this work, we have synthesized a new type of BAB symmetric triblock copolymers with a A block consisting of a linear PEO as template for lithium ion conduction, and a B block consisting of a poly(styrene trifluoromethyl sulfonamide) lithium salt, P(STFSILi). [1] These copolymers were synthesized by Nitroxide-Mediated Polymerization (NMP) from the PEO based alkoxyamine of 35000 g/mol. The obtained materials present excellent mechanical properties, a good ionic conductivity at 60°C and a high transport number. [2]

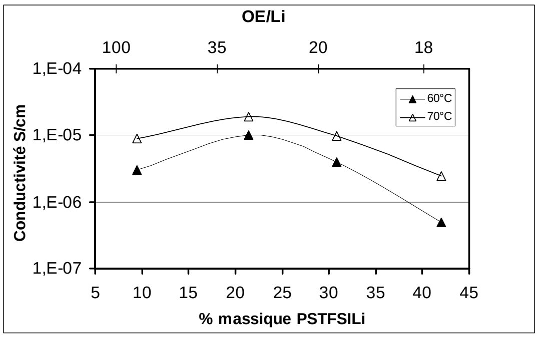

Figure 1: ionic conductivity for polyanionic copolymers P(STFSILi)-b-PEO-b-P(STFSILi) versus -CH_2-CH_2-O-/Lithium ratios at different temperatures.

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P65

New class of NO-donor soluble aspirins

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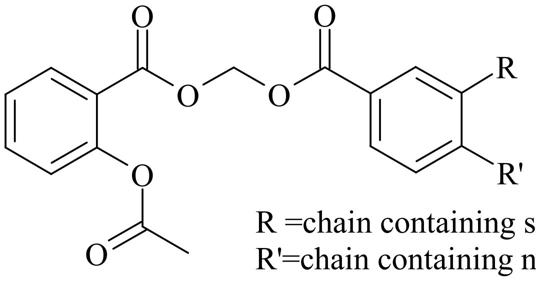
Non-stereoidal anti-inflammatory drugs (NSAIDs) are the most commonly used agents for the treatment of pain and inflammation. The prototype of NSAIDs is Aspirin (ASA), which, in addition to anti-inflammatory and analgesic properties, displays antithrombotic effects and, consequently, protects against ischemic vascular disorders, including myocardial and cerebral infraction. It exerts also some beneficial effects against colorectal cancer.[1] The most important limit in the use of this drug is its strong gastrotoxicity due to systemic and local irritant effects, the latter tightly associated with the presence in the molecule of a free carboxylic group. An obvious strategy to reduce the local gastric drawback was the masking of this function through co-drug formation. The problem with this approach is the high enzymatic lability of the *o*-acetyloxy group in these products. This is due to the loss of the negative charge which is present in aspirin following dissociation of its carboxylic function (pK_a=3.5). Consequently a large part of these substances are not true co-drugs since are rapidly metabolised to salicylates and salicylic acid in human serum without any formation of relevant amount of ASA. Another strategy to decrease the gastrotoxicity of ASA was to combine the drug with nitric oxide (NO)-donor moieties. Indeed it is known that NO is able to display gastrosparing actions through a number of mechanisms.[2] In addition it is able to maintain micro and macrovascular homeostasis as well as to trigger anti-inflammatory and analgesic effects. A number of NO-donor moieties have been joined through an ester linkage to the carboxylic group of the drug. They include substructures containing nitrooxy functions, furoxan, and *N*-diazeniumdiolate moieties.

On these bases we designed a new series of aspirin co-drugs obtained by conjugating NO-donor nitrooxy moieties, containing solubilising groups, to the carboxylic function of ASA through a $–CH_2$-O-(C=O)- bridge. This double ester moiety was chosen in view of its rapid hydrolysis in serum. All the aspirin derivatives were characterized for their human serum and buffered solutions stability; antiaggregatory and NO-dependent vasodilator properties of these new compounds were studied as well.



R =chain containing solubilising groups
R'=chain containing nitrooxy function

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P66

β-Fragmentation of Tertiary Alkoxyl Radicals. G3(MP2)-RAD and Natural Bond Orbital (NBO) Investigations.

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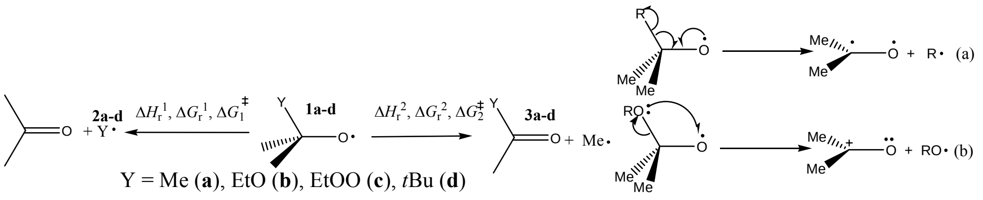
β-fragmentation of alkoxyl radical is a well known radical reaction since decades. However, the effect of heteroatom in the position b has not been investigated by high level calculation. Therefore, G3(MP2)-RAD and NBO approaches were combined to investigate the different pathways of fragmentation for alkoxyl radicals (Figure 1a). Our investigation showed that two mechanisms were possible (Figure 1b): the conventional b-fragmentation mechanism (route a) ot a heterolityc process concerted to electron transfer (route b)

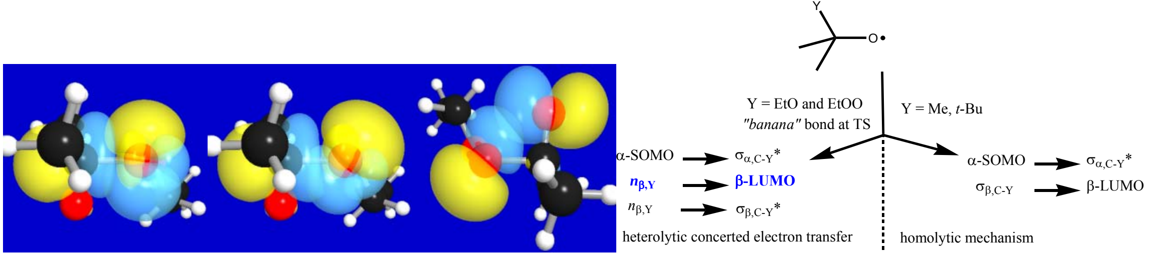


(a) *(b)*

Figure 1a. The two possible pathways of β–fragmentation. ***(b)*** *Two mechanisms for the β-fragmentation of alkoxyl radicals*

NBO investigation (Figure 2) showed for route b that an interaction between the lone pair of the oxygen on the position β $n_{\mathrm{p,OO}}$ and the SOMO was occurring (so-called banana bond) as well as an interaction of the same lone pair and the antibonding orbital of the cleaved bond $\sigma^*_{C—OO}$.

It led us to propose the electronic manifold displayed in Figure 4d.



(a) (b) (c) (d)

Figure 4. *NBO view at TS of* ***1c*** *(a) of spin-orbital α for antibonding orbital $\sigma^*_{C—OO}$ and lone pair of OO $n_{p,OO}$, (b) of spin-orbital β for antibonding orbital $\sigma^*_{C—OO}$ and lone pair of OO $n_{p,OO}$, (c) of spin-orbital β for the β-LUMO orbital at the radical centre and lone pair of OO $n_{p,O}$ overlapping to form a "banana" bond. (d) Electronic manifold for the β-fragmentation of alkoxyl radicals.*

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P67

Phenol phototransformation sensitised by photoactive quinones

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Quinone compounds are important photosensitisers in surface waters and in airborne particles [1,2]. They absorb a significant fraction of the sunlight spectrum (UV and in many cases also visible radiation), and absorption induces the formation of the excited singlet states that can evolve into triplet states by an often efficient inter-system crossing. Triplet states are chemically reactive and can sensitise the transformation of easily oxidised molecules upon electron or hydrogen abstraction, or upon energy transfer [3].

In this work, we have studied the transformation of phenol as model oxidisable compound in the presence of quinones that are commonly found in airborne particles, such as 2-ethylanthraquinone (EtAQ), benzanthracene-7,12-dione (BAD), 5,12-naphthacenequinone (NQ), 9,10-anthraquinone(AQ), and 2,6-dihydroxyanthraquinone (DAQ). The quinone compounds were deposited on glass spheres (9-13 µm average diameter) upon evaporation of dichloromethane solutions, to simulate their occurrence on particulate matter and to overcome their limited water solubility. The sphere-loaded quinones were irradiated separately in aqueous suspension in the presence of phenol, under a solar simulator as a proxy of environmental conditions, and under a blue lamp to enable easier calculation of the quantum yields. The time evolution of phenol was monitored by HPLC-UV in the aqueous phase after filtration, that of the quinones by GC-MS after CH_2Cl_2 extraction of the sphere-loaded filters and the aqueous solution. Negligible phenol was found in the CH_2Cl_2 extracts.

EtAQ was the most active quinone to sensitise phenol transformation under simulated sunlight, enabling a complete kinetic study of its reaction pathways with phenol. A reaction scheme involving competition between phenol and ground-state EtAQ for reaction with triplet EtAQ is proposed, accounting for the experimental data of phenol and EtAQ transformation rates as a function of phenol concentration. Phenoxyphenols and dihydroxybiphenyls were detected as phenol transformation intermediates, suggesting the formation of the phenoxy radical upon phenol oxidation by triplet EtAQ. Under the adopted conditions, EtAQ mostly underwent transformation of the alkyl lateral chain.

In the case of blue-light irradiation, the quantum yield of phenol transformation was the highest for AQ and the lowest for DAQ. Such a different behaviour could be explained with a density functional theory (DFT) study of the spin density distribution in AQ and DAQ triplet states, by use of the B3LYP hybrid functional [4]. The results show that most of the spin density in triplet AQ is localised on a carbonyl group, which is the most likely site to be involved in reaction with phenol to give phenoxyl and a semiquinone radical. In contrast, most of the DAQ spin density in the triplet state is distributed on the aromatic skeleton of the molecule, which is little likely to be involved in chemical reactions. Photoactive EtAQ has similar spin distribution as AQ in the triplet state, suggesting an interesting correlation between electronic properties and photosensitising effects in quinone compounds.

Acknowledgements
Financial support by MIUR – PRIN 2009 (project 20092C7KRC-ARCTICA) is kindly appreciated.

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P68

Etudes dirigées vers la synthèse totale des (+)-déoxytédanolide et (+)-13-déoxytédanolide

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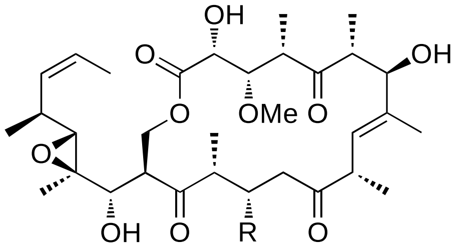
En 1984, Schmitz *et al.*[1] ont isolé d'une éponge des Caraïbes, la *Tedania ignis*, un nouveau macrolide dénommé le (+)-tédanolide. Ce produit naturel, comme tous les macrolides, possède un macrocycle de type lactone. Il diffère, cependant, des autres à un double niveau : 1) son site de lactonisation est éloigné de la fin du squelette carboné, 2) il jouit d'une macrolactone à 18 chaînons construite à partir d'un carbonyle en C1 et d'un groupement hydroxyle primaire en C17, alors que, habituellement, il s'agit d'un groupement hydroxyle secondaire. En 1991, Fusetani *et al*,[2] au cours de leur programme d'extraction de nouveaux métabolites cytotoxiques présents dans les microorganismes marins japonais, ont isolé, à partir d'une éponge japonaise, la *Mycale adhaerens,* un analogue au (+)-tédanolide, le (+)-13-déoxytédanolide. Ces deux métabolites présentent d'excellentes activités anti-tumorales *in-vitro* et *in-vivo* et, récemment, il a été montré que le (+)-13-déoxytédanolide inhibé la synthèse des protéines en se fixant sur la large sous-unité S60 des ribosomes. Les importantes activités biologiques de ces deux métabolites et leurs complexités structurales nous ont poussé à travailler sur ces deux cibles en utilisant en outre les savoirs faire du laboratoire dans la chimie de l'étain.



R = OH : (+)-tédanolide
R = H : (+)-13-déoxytédanolide

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P69

Inverse suspension polymerization: A promising method in the elaboration of ionic imprinted polymer

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Ion imprinted polymers (IIPs) are useful for selective adsorption of metal ions. Ionic imprinting technology involves the preparation of porous polymer matrix able to recognize a particular metal ion. Suspension polymerization has been used to synthesize IIPs in a spherical bead format [1]. The "classical" approach involves stirring an organic phase containing the monomers, a porogen solvent and the initiator within an aqueous phase. However, the choice of the components is limited in this aqueous approach due to the interactions between the water and ionic complexes.

In this work, nickel imprinted beads were prepared using inverse suspension polymerization as a new method. The imprinted beads were prepared (Fig. 1) by using nickel(II) as the template, N-(4-vinyl)-benzyl iminodiacetic acid (VbIDA) as the ligand and ethylene glycol dimethacrylate (EDMA) as the crosslinker. The non-imprinted polymers were prepared in the same conditions as IIPs without the metal ion template. The recognition and selectivity properties of IIPs were investigated by varying the weight ratio of VbIDA/EDMA. The good leaching properties of IIPs prove the good accessibility inside the polymer matrix. The optimal selectivity of IIP compared to non imprinted polymer (NIP) was obtained for a 10% ratio of VbIDA/EDMA. Increasing the ratio of the complexing monomer leads to higher adsorption capacities. Nevertheless, it also induces a decrease in surface area. These results show the necessity to find a compromise for between the ligand and the crosslinker proportions. These selective polymers can be used for solid-phase extraction applications

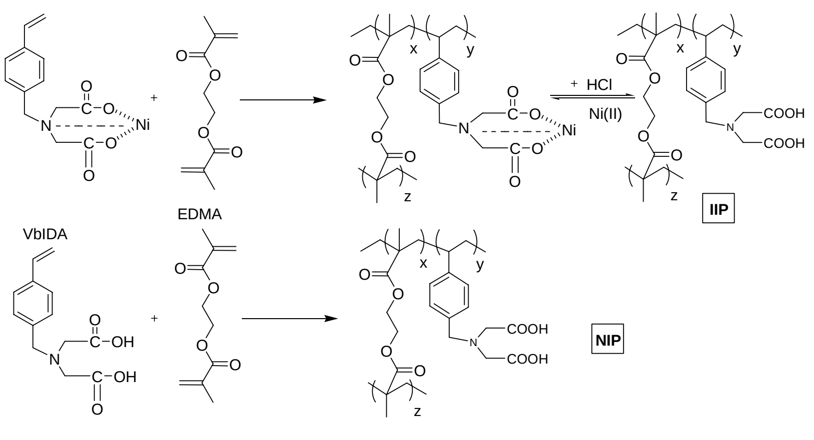

Figure 1 : Schematic illustration of IIPs and NIPs synthesis.

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TiO_2 nanoparticles with (101) predominant crystallographic face: chemical-physics characterization and photocatalytical properties

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Photocatalytic properties of titanium dioxide can have several potential multisectorial applications (refractory pollutants abatement, production of smart materials with self cleaning and self sterilizing properties, photovoltaics, photoproduction of chemicals (e.g Hydrogen by solar water photosplitting) in mild conditions).[1] The photocatalytic properties are strictly related both to the intrinsic properties of the materials (crystallographic exposed facets, allotropic form, reconstruction, hydroxylation, surface defectivity) and to the extrinsic properties (pH, ionic strength, adsorption, surface complexation with redox inert ligand (e.g. F^- [2]), coupling with *ad hoc* adsorbent materials…). Recently, a wide attention was focused on the role that the different crystallographic faces of anatase (the most photo-active allotropic form of TiO_2) have in the photocatalytic process [3]. At the basis of these studies there is the possibility to synthesize micro and nanomaterials with well defined exposed crystallographic faces. Furthermore, it has been demonstrated that the surface complexation of anatase surface with the redox inert fluoride anion can be n efficient tool to explore the role of the surface properties on the photocatalytic performances [4].

This work was aimed to the synthesis of TiO_2 anatase nanoparticles with predominant (101) facets by hydrothermal hydrolysis of the titanium triethanolamine complex (TiO_2-HT). The material was characterized by a multimodal approach: the morphology and the crystallographic phase were investigated by XRD, HR-TEM, measuring of the BET specific surface area and FT-IR spectroscopy of adsorbed CO (the frequency of νCO adsorbed at the surface is strictly function of the crystallographic face where CO is adsorbed). The photocatalytic activity of the synthesized material was tested both pristine and fluorinated toward the degradation of phenol, formic acid and hydrogen peroxide. The photocatalytic production of hydroxyl radicals were investigated by EPR spectroscopy by using DMPO as efficient $^\bullet$OH probe. The experimental evidences were compared with those obtained with TiO_2 Degussa P25, a landmark in the photocatalytic field.

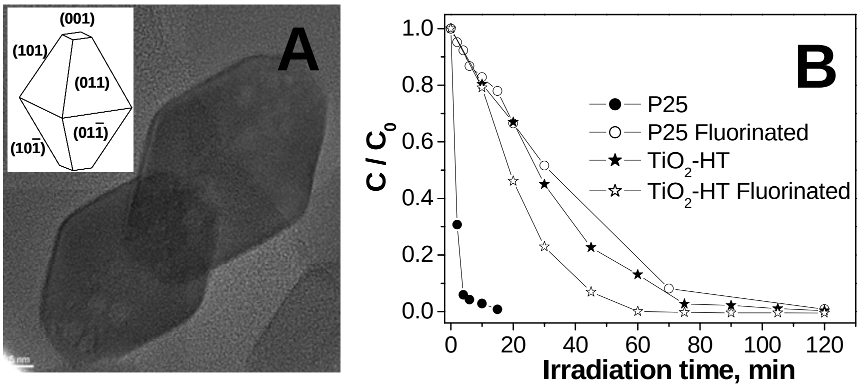

Figure 1: A)HR-TEM micrography of TiO_2-HT (original magnification x300K) Inset: scheme of the crystallographic planes o af anatase crystal); B) H_2O_2 photocatalytic degradation on TiO_2-HT and P25 both pristine and fluorinated.

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The characterization emphasized the predominant presence of the (101) facets on TiO_2-HT and confirmed the overwhelming presence of (101) facets on P25 TiO_2 accompanied with a high density of sites in low coordination conditions. TiO_2-HT showed a high photoactivity, its different behavior in the presence and in the absence of fluoride can be related to the high crystalline degree and consequently low density of sites in low coordination conditions. These sites showed strong adsorbing properties toward organic substrates and their presence promotes efficient photocatalytic transformation mechanisms presumably through direct hole transfer.

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Quantification of the Photocatalytic Self Cleaning Ability of Non Transparent Porous Samples: Development of a New Analytical Method

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A new method for the quantitative evaluation of the photocatalytic self cleaning (SC) properties of non transparent materials is proposed. The analytical method is based on the covering of the tested surface with a defined amount of dye and on the evaluation of the reflectance spectra of the sample as a function of the irradiation time. The calibration of the spectral properties, made spreading different dye amounts over the surface allowed the quantification of the substrate concentration and, consequently the evaluation of the self cleaning profile for the tested material. The method was tested with seven different white and colored pigments by using Methylene Blue (MB), Rhodamine B (RB) and Metanil Yellow (MY) as organic substrates. Furthermore, the SC properties of cement samples obtained with different concentration of photocatalytic or non photocatalytic white/yellow pigments were tested by using the here developed method.

The main first intermediates of the MB photocatalytic degradation formed at the solid/solid interface were recognized. Despite of the MB degradation in solution that happens predominantly with the cleavage of the central ring of the MB structure and secondarily with the N-demethylation of the two symmetric dimethyl amino groups, at the solid/solid interface a prevalence of the latter mechanism can be envisaged. A different degradation mechanism and different photoactivities were also observed at the solid/solid and solid/electrolyte interface during the photocatalytic degradation of Metanil Yellow on the tested pigments. The experimental evidences emphasized the inapplicability of tests carried out in aqueous suspension for the accurate evaluation of the self cleaning ability of photocatalytic materials. The use of SC tests that assess the photocatalytic transformation of organic compounds at the solid/solid surface is mandatory. The test here proposed resulted quite simple to use, reproducible, fast, and applicable without the use of complex analytical tools. The SC test proposed is a promising candidate as standard method for the quantification of the photocatalytic SC ability of non transparent materials.

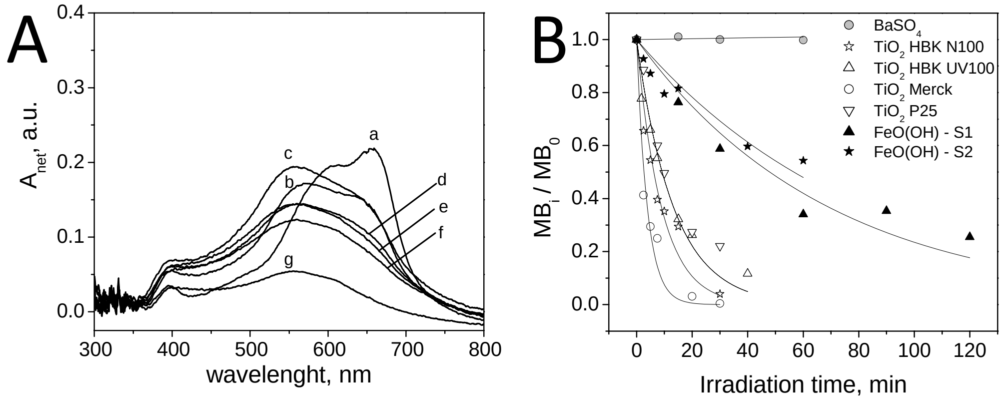

Figure 1: Self Cleaning test with Methylene blue: A) Evolution of the surface spectra at different irradiation times on TiO_2 Hombikat N100; B) Decoloring profiles observed on the tested pigments

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Influence of nitrogen speciation on the total nitrogen measurement in waters by different analytical techniques

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Analytical methodologies for the determination of Total Dissolved Nitrogen (TDN) are based on a conversion step able to transform with high selectivity all the nitrogen species into a defined compound that is then quantified. Nitrogen is a key nutrient in natural waters and accurate TDN measurements are relevant to assess the status of water bodies, local and global nutrient cycling as well as the efficacy of water remediation treatments. [1,2]

A crucial requirement to meet accuracy is the quantitative recovery of all organic and inorganic nitrogen species during the conversion step. Absolute recovery assessment of the Dissolved Organic Nitrogen (DON) fraction is impracticable due to the sheer complexity of the Dissolved Organic Matter (DOM), being composed of a poorly characterized pool of substances of biological origin (urea, aminoacids and peptides, aminopolysaccarides, nucleobases, fulvic and humic acids). Moreover, nitrogen containing xenobiotics can be of importance in contaminated waters. A way to partially overcome this problem is the assessment of N recovery for model molecules representative of N speciations pertinent to DOM and xenobiotics.[3] Despite the importance of N recovery in TDN determination, systematic studies concerning its dependence on organic N speciation and on the nature of the conversion step are scarce. Quantitative recoveries were demonstrated only for a limited selection of organic compounds.

In this work, the N recoveries of two widely employed analytical methodologies that use different conversion steps for the determination of TDN (High Temperature Catalytic Oxidation, HTCO, and Persulfate Digestion, PD) were assessed on a set of selected nitrogen-containing compounds, representative of the structures of both DOM and common contaminants.

Aminoacids, urea and its acyclic derivatives, nucleobases except guanine and uric acid give quantitative N recoveries, whereas azide ions, hydrazine and azo dyes give almost no recovery with either method. Partial recovery with both methods is showed by organic compounds containing triazole rings. S-triazine compounds, guanine and uric acid give satisfactory recoveries only with HTCO. Low recoveries are generally due to poor selectivities during the conversion step, with the formation of nitrogen compounds other than NO (HTCO) and nitrate (PD). A notable exception to this rule is the incomplete mineralization of s-triazine rings by using PD, with formation of cyanuric acid.[4] The results show that in many instances the TDN measurements give systematically low results depending on N speciation. Incomplete organic N recovery is mainly associated to the presence of azo compounds and heterocycles of anthropogenic origin. TDN data of polluted and waste waters must be considered with care. When comparing measurement methods, PD could give lower results than HTCO even for samples containing only organic matter of

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biological origin. Finally, the estimation of dissolved nitrogen fluxes and pools from TDN measurements can be affected by uncertainties larger than previously thought.

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Synthesis of novel nucleoside analogues with a methylene cyclopropane skeleton

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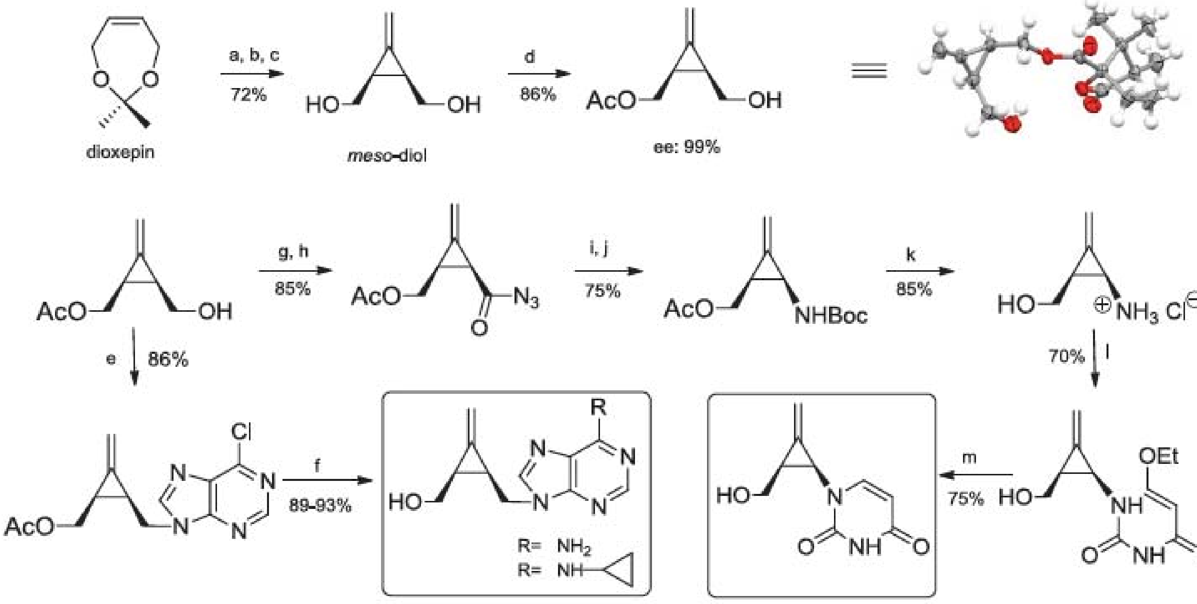
The enzymatic desymmetrization of methylenecyclopropane diol or its corresponding diacetate derivative, generated from a [2+1] cycloaddition between dioxepin and methylchlorocarbene, is achieved. After screening commercial lipases, the two enantiomers of acetic acid 2-hydroxymethyl-3-methylene-cyclopropylmethyl ester are obtained in high yields and excellent enantioselectivities by using PFL in organic solvent. The absolute configuration of the desymmetrization products was established unambiguously by X-Ray analysis using a camphanate derivative as chiral reference. Using these enantiopure building blocks, an enantioselective synthesis of novel nucleoside analogues is accomplished.[1]



Reagents and conditions: (a) 1,1-dichloroethane, *n*-BuLi, −35°C ; (b) *t*-BuOK; (c) HCl (2M); (d) PFL, vinyl acetate; (e) Ph_3P, DIAD, 6-chloropurine; (f) Cyclopropylamine–MeOH (1:5), or NH_3/MeOH; (g) CrO_3, H_2SO_4 ; (h) $(COCl)_2$, NaN_3 ; (i) benzene reflux ; (j) *t*BuOH ; (k) HCl ; (l) N-(chlorocarbonyl)isocyanate, ethyl vinyl ether, Et_3N; (m) H_2SO_4 (2M).

The biological properties of these analogues is under evaluation by Pr. C. Pannecouque (Rega Institute, Belgium) against HIV-1, HIV-2 and other viruses.

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P74

One-pot Crabbé homologation-radical cascade cyclisation and one-pot diazoester coupling-cascade rearrangement of enediynes with memory of chirality.

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The concept of memory of chirality describes a phenomenon in which the "the chirality of a starting material having a chiral sp^3 carbon is preserved in the reaction product even though the reaction proceeds at the chiral carbon as a reaction center through reactive intermediates such as carbanions, singlet monoradicals, biradicals, or carbenium ions".[1] Meanwhile, cascade processes have gained popularity due to the ever growing interest for efficient selective syntheses of complex molecules from an ecologically and economically favorable point of view.[2] We have recently reported the enantioselective cascade rearrangement of enediynes leading to heterocycles bearing quaternary stereogenic centers with the memory of chirality phenomenon.[3] In this context, we explored the tandem Crabbe homologation-radical rearrangement of terminal enediynes leads, in a one-pot procedure, to the enantioselective synthesis of six- and seven-membered ring α-aminoesters bearing a quaternary stereocenter based on the phenomenon of memory of chirality.[4] On the other hand, the Cu-catalyzed reaction of enediynes with diazoesters leads to cyclic amino esters bearing two contiguous quaternary stereogenic centers through a one-pot five-step cascade with memory of chirality.[5] The details will be presented.

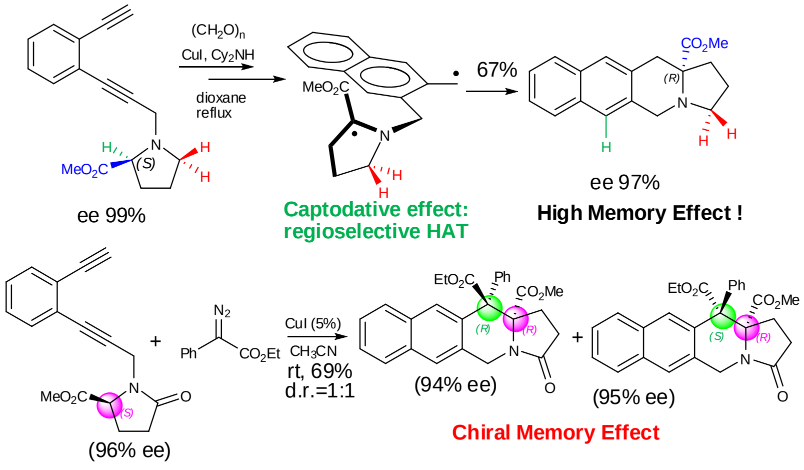

Figure 1 : One-pot protocols

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[4] S. Mondal, M. Nechab, N. Vanthuyne, M. P. Bertrand *Chem. Commun.*, **2012**, *48*, 2549.
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P75

Interaction between Lewis superacids catalysts and organic ligands: A quantitative approach of affinity scales using mass spectrometry

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Metal triflates and triflimidates behave as "Lewis superacids" and are currently employed as catalysts in the domain of organic synthesis [1,2]. Their superacidic character is often correlated to the efficiency of their catalytic activity. Several hypotheses about the nature of the reaction intermediates involved have been made, but in most of the cases the reaction mechanism remains unclear.

Electrospray Ionization Mass Spectrometry (ESI-MS) is one of the most performing tools for the study of chemical reactions [3]. The ESI soft ionization conditions are suitable to detect all the species present in a reaction medium, directly from solution to the gas phase. It can afford therefore reaction mechanism insights through identification and characterization of reaction intermediates. Preliminary investigations showed that such triflates and triflimidates metal salts have a particular behavior. In presence of a Lewis base, such Lewis superacids produce a mass spectrum corresponding to a complex of the general formula: $[M^{n+}(OTf^{-})_{n-1}(L)_2]^+$ (or $[M^{n+}(NTf_2^{-})_{n-1}(L)_2]^+$) [4]. A competition methodology between two different ligands, allowed the construction of qualitative scales by ESI-MS [3,5] through an unusual mass spectrometric behavior.

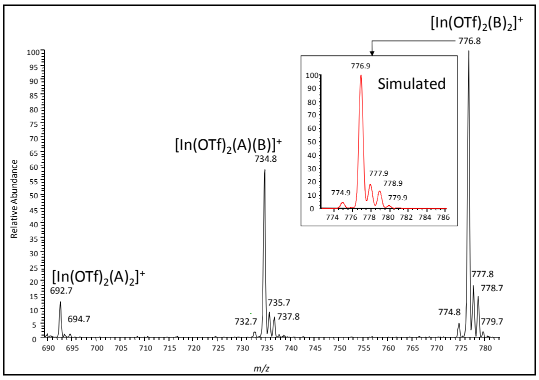

Figure 1 : ESI mass spectrum obtained for ligands competition toward In(III)

We present, in this communication, the results obtained for quantitative relative affinity scales. We developed a methodology based on the relation between concentrations and intensity ratios. We showed that the relative affinity α of ligands toward the catalyst can be extracted from these relations intensity vs. concentration. The nature of the affinity parameter α emerges as a type of equilibrium constant. As the thermodynamic significance of the affinity remains open, quantum chemical investigations were carried out. Gibbs energy of the competition equilibria between similar ligands were calculated using DFT calculations.

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P76

$6^{èmes}$ Journées Franco-Italiennes de Chimie
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On the High Pressure Hydrothermal Synthesis of Zinco - Silicate Zeolites

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In this study we present the high pressure hydrothermal synthesis (100MPa to 300MPa) of zincosilicate zeolites with Li^+ or Na^+ as charge compensating cation.

In nature, Gaultite is the only silicate based zeolite known with Zn occupying framework positions (VSV, Si/Zn=3.5). The mineral gaultite $|Na_{26}H_6\ (H_2O)_{44}|\ [Zn_{16}Si_{56}O_{144}]$ is formed under natural hydrothermal conditions. Under these conditions very few examples of silicate framework types are known where Zn is introduced into the framework instead of Al.

Most synthesis techniques producing Zn-zeolites with Na^+ as charge compensating cation use autogenous pressure with gel precursor, or more recently the vapor phase transport (VPT) [1]. This study aims to present high pressure hydrothermal synthesis of zincosilicate VPI-7 (synthetic analogue of gaultite) for the first time (maximum synthesis temperature: 300°C).

Li-zincosilitate zeolites have been obtained in the same way as Na-zincosilicate materials, but at lower temperature (T_{max}=150°C) and with different stoichiometry for optimum product gain (Si/Zn=2.75). While VPI-7 crystal structure and corresponding zeolite channel system is known [2-3], Li-zincosilitate zeolite materials properties have to be deduced from its physical and chemical characteristics. The lack of thermal stability of the structure is evidenced by TGA combined with XRD. Concerning the properties of the void system, no adsorption measurement is possible due to insufficient thermal stability during dehydration.

We present the high pressure hydrothermal synthesis of micro-crystals and small single crystals. Solid state NMR ^3Li investigations show that charge compensating cations (Li^+) are surrounded only by water molecules. RAMAN measurements indicate 10-membered rings as entrance of the channel system while TG analyses reveal three steps of dehydration corresponding to three crystallographic different water molecules.

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P77

6èmes Journées Franco-Italiennes de Chimie
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Synthèse de dendrimères poly(amino)esters biodégradables par chimie « Click »

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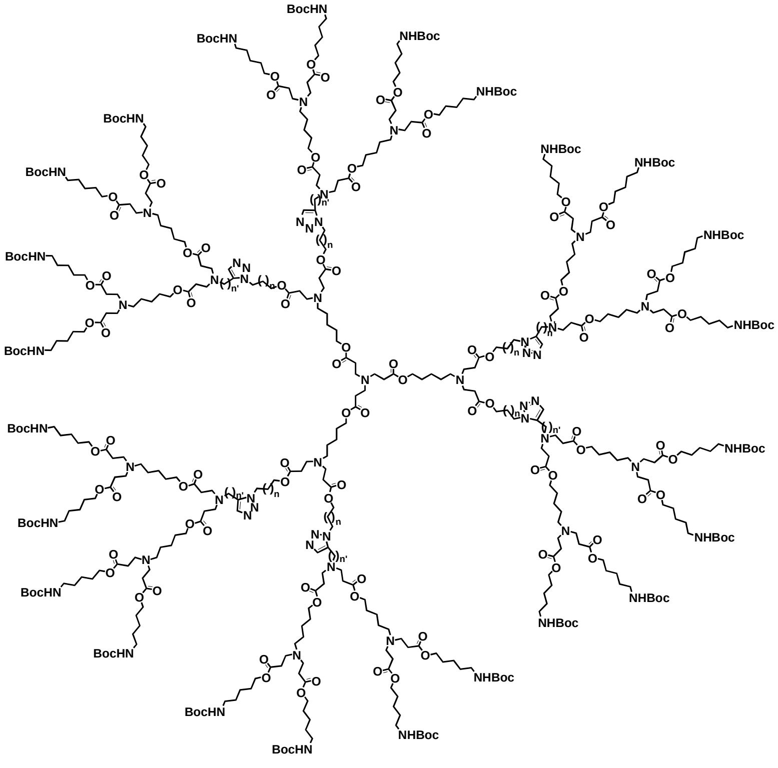
Nous travaillons sur l'élaboration et la synthèse de dendrimères poly(amino)esters afin de développer de nouveaux vecteurs pour la délivrance de matériel génétique.[1] Sur la base des résultats que nous avons obtenus précédemment pour la synthèse et le transport d'ARN et d'ADN par des dendrimères poly(amido)amines (PAMAM), nous avons envisagé la conception de nouveaux dendrimères de type poly(amino)ester. Ces dendrimères présentent en effet l'avantage d'être biodégradables par clivage des fonctions esters, tout en favorisant la pénétration cellulaire *via* leurs amines tertiaires et leur capacité à compacter les acides nucléiques chargés négativement.

Pour ce faire, différentes voies de synthèse sont envisageables, utilisant les principes de la chimie en solution, déjà mis en œuvre dans notre laboratoire.[2] Cependant cette méthode ne permet pas la synthèse de dendrimères de hautes générations. Pour obtenir de plus hautes générations, nous envisageons donc d'élaborer des dendrons pour les connecter ensuite par chimie « click », impliquant une cycloaddition azoture-alcyne catalysée par des ions cuivre [3] et obtenir ainsi des dendrimères poly(amino)esters possédant 24, 48 ou 96 fonctions périphériques.



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P78

Étude catalytique de différents sels de bismuth de type sulfonamide et de bis-sulfonimide pour la réaction d'alkylation de Friedel-Crafts intramoléculaire

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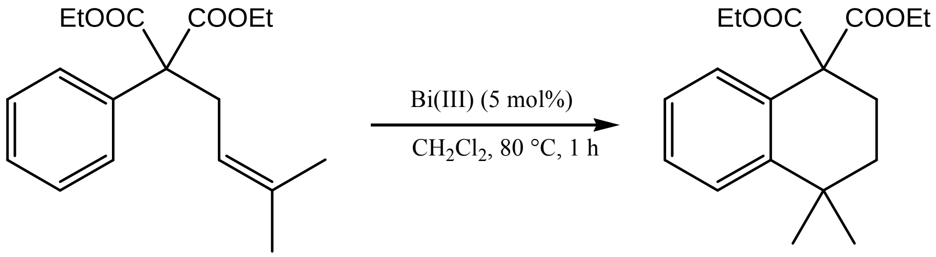
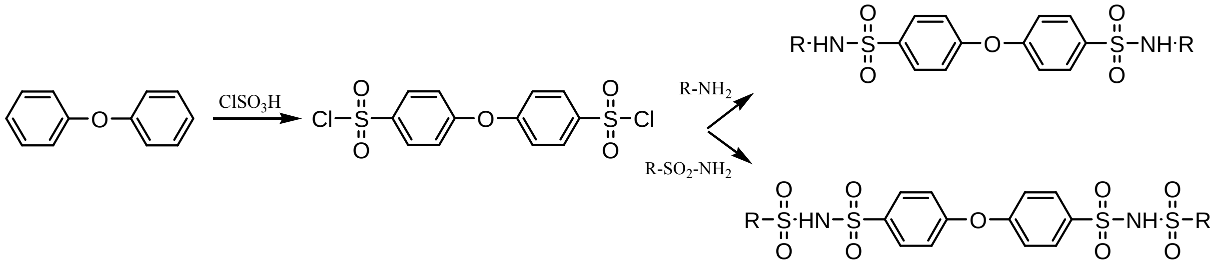
Une étude récente réalisée au laboratoire a porté sur l'influence de l'acidité de Lewis sur la réaction d'alkylation de Friedel-Crafts intramoléculaire (équation 1).[1] La comparaison de l'activité catalytique de différents sels métalliques a montré que le triflate et le triflimidure de bismuth (III) permettait d'obtenir les meilleurs résultats.



Equation 1 : Réaction d'alkylation de Friedel-Crafts intramoléculaire

Nous nous sommes intéressés à la synthèse de nouveaux acides portant des groupements sulfonamide ou bis-sulfonimide, dérivés du diphényle éther, afin de disposer d'une large gamme de composés d'acidité croissante (équation 2). Puis, des sels de Bi (III) avec ces divers acides analogues des triflates ont été obtenus. La préparation des sels de bismuth a été réalisée par voie sonochimie.[2] Les sels ont par la suite été utilisés comme catalyseurs de la réaction d'alkylation de Friedel-Crafts (équation. 1) pour évaluer l'influence de l'acidité de l'anion du catalyseur sur l'activité catalytique et le rendement de la réaction de couplage.



Equation 2 : Synthèse de composés portant une fonction sulfonamide ou bis-sulfonimide

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Synthesis of pyrazolo[3,4-*d*]pyrimidine derivatives endowed with activity against the T315I Abl mutation

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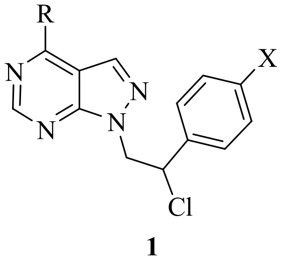
Chronic myelogenous leukemia (CML) is a disease characterized by the presence of the Philadelphia chromosome, that encodes for the constitutively active cytoplasmatic tyrosine kinase (TK) Bcr-Abl. Currently, both selective (e.g. imatinib and nilotinib) and multitarget inhibitors (e.g. dasatinib) are successfully used in CML therapy [1]. Nevertheless, different mechanisms, including mutations in the kinase domain of the enzyme and Bcr-Abl gene amplification, can lead to the onset of resistances, especially in the advanced phases of the disease. In particular, the T315I mutation (substitution of threonine 315 with isoleucine) remains the most difficult to be overcome and is connected with the worst prognosis in CML patients, being therefore referred as the the Achilles' heel of TK inhibitors [2].

Very interestingly, some C6-unsubstituted pyrazolo[3,4-*d*]pyrimidines synthesized by my research group showed good activity against the T315I Abl mutation [3, 4]. On the basis of these promising results, we synthesized molecules **1**, bearing in C4 the amino groups resulted the most active in the previous studies, and generally introducing a halogen atom on the para position of the N1 phenyl ring, since it is connected to an improved of activity (*Figure 1*). Preliminary data available on these molecules showed activity against the T315I Abl in the nanomolar range, encouraging other studies.

Synthesis, enzymatic results and SAR consideration will be reported in the poster session.



1

R = amino groups

X = H, F, Br

Figure 1 : general structure of synthesized molecules.

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P80

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Enantioselective Cyclopentannulation Reactions Mediated by Bifunctional N-Heterocyclic Carbenes

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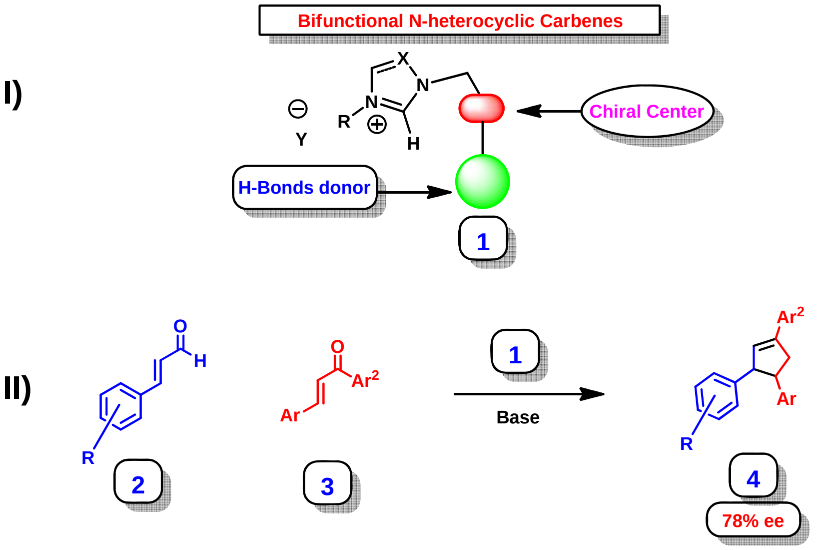
Since the first isolation and characterisation of a stable N-heterocyclic carbene (NHC) by Arduengo twenty one years ago,[1] NHCs have become extremely popular ligands in organometallic but they are also used as organocatalysts.[2] Recently, Nair and co-workers described the synthesis of racemic *trans*-1,3,4,-triarylcyclopentenes by an annulation reaction from enals and chalcones catalysed by imidazolium-derived NHCs, *via* homoenolate equivalent.[3] The groups of Bode and Scheidt have also reported related annulations reactions.[4]

In this work a series of original chiral bifunctional NHCs **1** have been synthesised.[5] These catalysts have proved to be efficient in the enantioselective annulation reaction between enals and chalcones. These results will be discussed.



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P81

Cascade Rearrangement of Enediynes with Memeory Of Chirality

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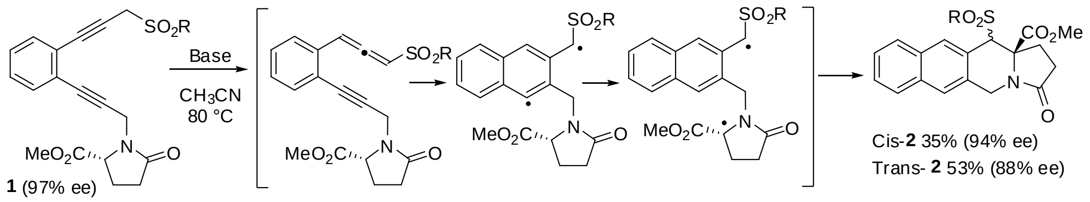
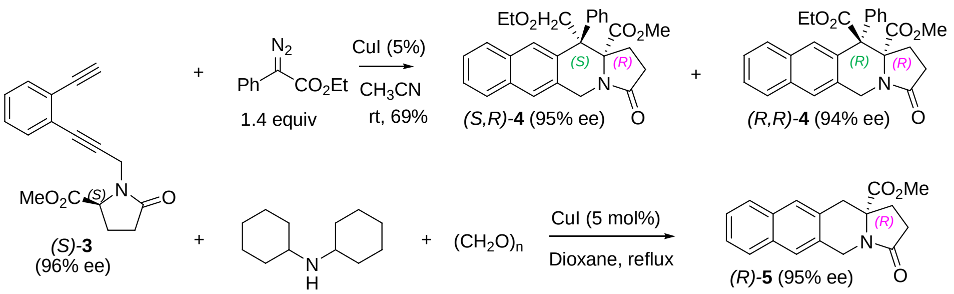
During the past decade, Memory of Chirality (MOC) has emerged as a powerful tool in organic synthesis.[1] This technique allows the enantioselective construction of a chiral tetrasubstituted stereocenters. We have recently developed a polar/radical crossover cascade rearrangement of enediynes **1** bearing a sulfone moiety as the precursor of an intermediate enyne-allene (scheme 1).[2] The reaction proceeded with retention of the configuration of the starting material to afford tetracyclic heterocycle **2** with a high memory effect.



Scheme 1

Heterocyclic analogues of aspartic esters **4** bearing two contiguous quaternary stereogenic centers were also shown to be readily available through the copper-catalyzed cascade reaction of terminal enediynes **3** with diazoesters (scheme 2).[3]



Scheme 2

In order to overcome the lack of diastereoselectivity which is the main drawback of this process, we devised a tandem Crabbé homologation-radical rearrangement of terminal enediynes leading, in one-pot, to six- and seven-membered ring α-aminoesters **5** (scheme 2).[4]

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Indagini archeometriche su materiali vitrei liguri dell'età del Ferro

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Il materiale vitreo della Liguria antica risulta ancora poco conosciuto dal punto di vista della caratterizzazione chimica, della produzione, della lavorazione e della diffusione.
In questo lavoro si presentano i risultati delle analisi effettute su oggetti vitrei provenienti dalla necropoli dell'età del Ferro di Genova. Si tratta di cinque pedine da gioco e di una oinochoe attualmente esposti nel Museo di Archeologia Ligure a Genova Pegli.

Le analisi sono state eseguite *in loco*, utilizzando metolodologie non distruttive: la spettrofotometria in luce visibile in riflettanza e la fluorescenza dei raggi X (XRF).
I quattro colori dei vetri: blu, bianco, nero e giallo, sono stati misurati con uno spettrofotometro Minolta CM-2600d. I dati che provengono dalle misure di riflettanza relative allo spazio colore L*a*b* sono stati elaborati in derivata seconda per mettere meglio in evidenza l'andamento delle curve spettrali.

Sono stati riconosciuti i principali ioni cromofori presenti nei vetri. Le diverse tonalità di blu e blu-turchese sono state ottenute mediante l'uso di ossido di cobalto e ossido di rame (II) in diverse proporzioni. La quantità maggiore del Co si riscontra nel fondo della oinochoe, che appare quasi nero. I bianchi sono stati ottenuti dall'ossido di antimonio Sb_2O_3 usato sia per opacizzare, sia per colorare i vetri. Il colore giallo si trova solo nella oinochoe ed è accompagnato da valori molto alti di piombo e dalla presenza del sopracitato ossido di antimonio, che ha portato alla formazione, durante il processo di fusione, di antimoniato di piombo giallo. Infine il colore nero è legato all'utilizzo di ioni ferro.

P83

Antitubercular and antiprotozoal activities of quinolizidinyl/pyrrolizidinylalkyliminophenazines

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(2) Department of Pharmaceutical Sciences «Pietro Pratesi», Milan University, Via L. Mangiagalli 25, 20133 Milano, Italy

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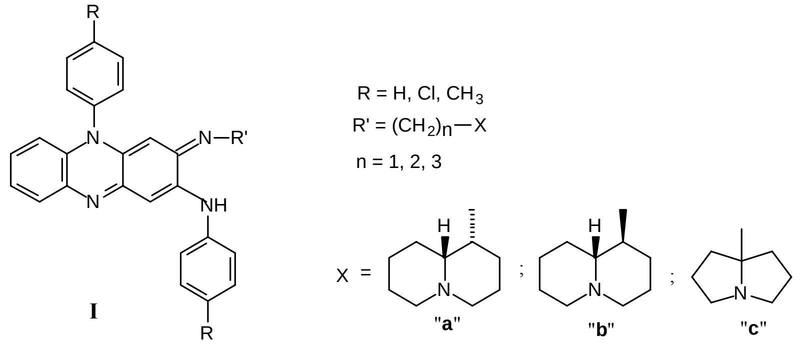
The increasing occurrence of tuberculosis due to MDR strains brought to the pressing need of the development of new agents. Among the numerous substances under study, a significative place is represented by the Riminophenazines, of which clofazimine [I: R = Cl; R' = $CH(CH_3)_2$] is the best known. This drug, originally conceived as an antitubercular, was instead introduced in the polychemiotherapy of leprosy, also due to its antiinflammatory action. Clofazimine and its analogues showed activity against MDR strains of Mycobacterium tuberculosis [1-3].

On the ground of these premises it has been deemed of interest to consider the substitution of the isopropyl residue of clofazimine and its analogues with quinolizidinyl/pyrrolizidinylalkyl chains, as represented by the general structure I. The presence of the basic bicyclic moieties could be noteworthy both for the antitubercular activity and for the modulation of the pharmacokinetic profile.



The synthesized substances were tested for their action on strains of Myc. tuberc., H37Rv, H37Ra, Myc. bovis, Myc. avium, and on some clinical strains. The most active compounds, belonging to the series with R = Cl, showed a MIC = 0.5 μg/mL on the majority of the strains employed.

A number of the above compounds have also been studied for their activity against Trypanosoma rhodesiensis, Tryp. cruzi and Leishmania donovani.

[1] Reddy, V. M.; Nadadhur, G.; Daneluzzi, D.; O'Sullivan, J. F.; Gangadharam, P. R. J. Antituberculosis Activities of Clofazimine and Its New Analogs B4154 and B4157. *Antimicrob. Agents Chemother.* **1996**, *40*, 633-636.

[2] Reddy, V. M.; O'Sullivan, J. F.; Gangadharam, P. R. J. Antimycobacterial activities of riminophenazines. *J. Antimicrob. Chemother.* **1999**, *43*, 615-623.

[3] Kamal, A.; Azeeza, S.; Malik, M. S.; Shaik, A. A.; Rao, M. V. Efforts Toward the Development of New Antitubercular Agents: Potential for Thiolactomycin Based Compounds. *J. Pharm. Pharmaceut. Sci.* **2008**, *11*, 56s-80s.

P84

Synthesis of novel nucleoside analogues with a methylene cyclopropane skeleton

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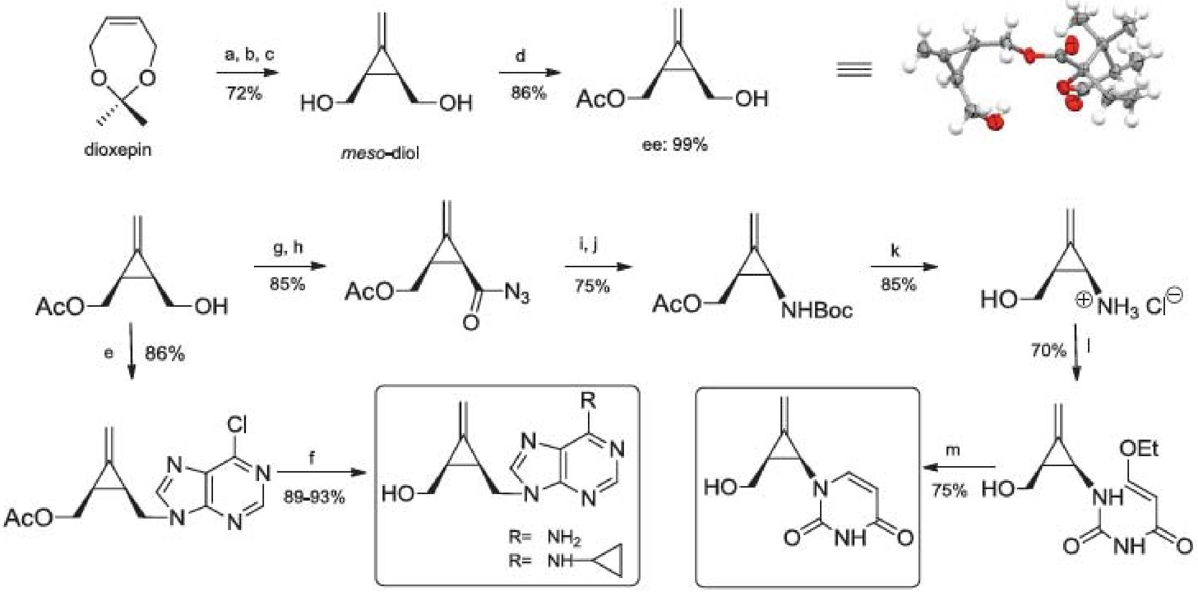
The enzymatic desymmetrization of methylenecyclopropane diol or its corresponding diacetate derivative, generated from a [2+1] cycloaddition between dioxepin and methylchlorocarbene, is achieved. After screening commercial lipases, the two enantiomers of acetic acid 2-hydroxymethyl-3-methylene-cyclopropylmethyl ester are obtained in high yields and excellent enantioselectivities by using PFL in organic solvent. The absolute configuration of the desymmetrization products was established unambiguously by X-Ray analysis using a camphanate derivative as chiral reference. Using these enantiopure building blocks, an enantioselective synthesis of novel nucleoside analogues is accomplished.[1]



Reagents and conditions: (a) 1,1-dichloroethane, *n*-BuLi, –35°C ; (b) *t*-BuOK; (c) HCl (2M); (d) PFL, vinyl acetate; (e) Ph_3P, DIAD, 6-chloropurine; (f) Cyclopropylamine–MeOH (1:5), or NH_3/MeOH; (g) CrO_3, H_2SO_4 ; (h) $(COCl)_2$, NaN_3 ; (i) benzene reflux ; (j) *t*BuOH ; (k) HCl ; (l) N-(chlorocarbonyl)isocyanate, ethyl vinyl ether, Et_3N; (m) H_2SO_4 (2M).

The biological properties of these analogues is under evaluation by Pr. C. Pannecouque (Rega Institute, Belgium) against HIV-1, HIV-2 and other viruses.

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[1] Obame, G.; Pellissier, H.; Vanthuyne, N.; Bongui, J.-B.; Audran, G. *Tetrahedron Lett.* 2011, *52*, 1082-1085

P85

Germyl cations with Ge-S bonds: an experimental and theoretical study on the gaseous $F_nGe(SH)_{3-n}^+$ (n = 0-2)

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The study of gas chemistry allows to gather information regarding the intrinsic reactivity and properties of 'naked' species, which are not easily attainable in the condensed phase. This is, in particular, the case of ionic species, which usually display strong interactions with the solvent and/or counter ions. In this context, we have recently focused our attention on germyl cations, $R_1R_2R_3Ge^+$. These species are interesting reactive intermediates [1], and their 'naked' form is readily yielded by gas phase electron ionisation of various eligible precursors, such as germanium hydrides and fluorides. Starting from the GeF_3^+ precursor, it is possible to form novel germyl cations of the general formula $F_nGe(Nu)_{3-n}^+$, through the reaction with a neutral H-containing nucleophile, resulting in the thermodynamically favoured release of HF [2]. Following this reaction pathway, we have studied the consecutive formation of $F_2Ge(HS)^+$ and $FGe(HS)_2^+$ by ion trap mass spectrometry and high-level *ab initio* calculations. Although Ge-S ion species in the gas phase are already known, germyl cations with such connectivities are still unexplored. In the present communication, thermochemical and kinetic factors related to their formation were investigated.

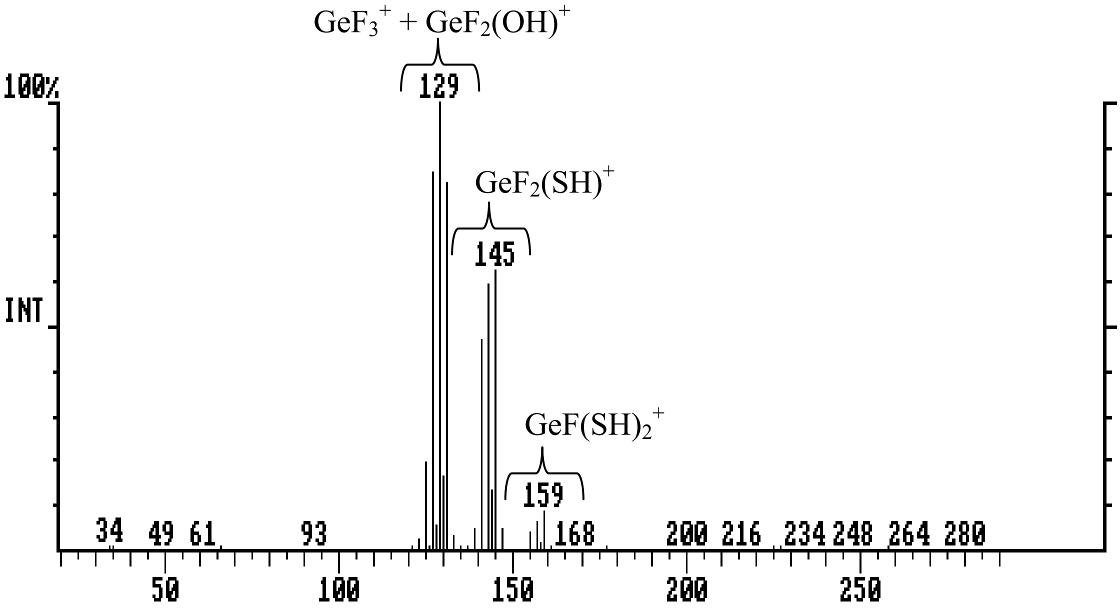

Figure 1 : Time-delayed mass spectrum (t =30 ms) from isolated GeF_3^+ in a GeF_4/H_2S mixture.

[1] V.Y. Lee and A. Sekiguchi, *Organometallic compounds of low-coordinated Si, Ge, Sn, and Pb: from phantom species to stable compounds*. Wiley, Chichester (2010).

[2] P. Antoniotti, E. Bottizzo, L. Operti, R. Rabezzana, S. Borocci and F. Grandinetti, "Gas-phase chemistry of ionized and protonated GeF_4: a joint experimental and theoretical study", *J. Mass Spectrom.* **46**, 465-477 (2011).

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P86

$6^{èmes}$ Journées Franco-Italiennes de Chimie
Giornate Italo-Francesi di Chimica 2012
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Cyclic diterpenoids isolated from surface and whole-cell extracts of the Mediterranean brown seaweed *Dictyota dichotoma*.

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As all substrata immersed in the sea, marine organisms could be colonized by a wide diversity of eukaryotes and prokaryotes **[1].** This natural process called "*biofouling*" is initiated by bacterial attachment to a surface, then bacteria develop into a complex three dimensional community named biofilm. However, some marine organisms, such as the Mediterranean brown alga *Dictyota dichotoma,* appeared to be relatively free from biofilms. Investigations in the field of chemical ecology proved the roles of secondary metabolites from host organisms in deterring the settlement of colonizers. In this work, we have focused our attention on the exploration of substances present at the algal surface in order to design new bio-inspired and non-toxic antifouling agents.

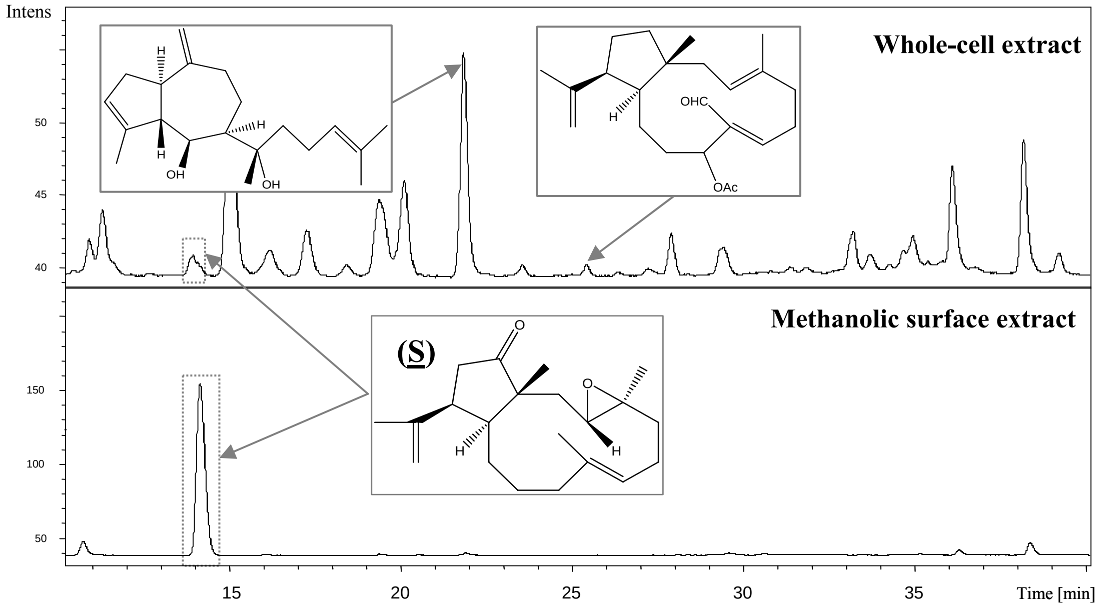

Figure 1: ELSD Chromatograms of methanolic surface and whole-cell extracts with cyclic diterpenoids isolated from Dictyota dichotoma.

This study described the isolation of several diterpenoids from thalli and surfaces of specimens of *D. dichotoma* collected on the French Mediterranean coast (Carqueiranne, Var). Various solvents have been assessed for the extraction of algal surface substances. Methanolic surface extracts have shown the presence of a major dolabellane diterpene (**S**). This compound was unambiguously identified by comparison of the LC-DAD/ELSD/MS^n data of surface extracts with those of the resulting pure metabolites obtained from the whole thallus extract. Diterpene **S** was previously described from *D. dichotoma* and its stereochemistry has been recently revised **[2]**. The chemical structures of the other cyclic diterpenoids from the whole-thallus extracts of *D. dichotoma* were elucidated on the basis of spectral data analyses (MS, 1D and 2D NMR) and comparison with literature.

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Our main objective, following the identification of *D. dichotoma* secondary metabolites, is to explore the chemical mediation of interactions between this alga and associated biofilms by the assessment of the deterrent effects of those metabolites against several marine bacterial strains.

[1] Steinberg & De Nys (2002). *J. Phycol.* **38**: 621-629
[2] Ioannou *et al*. (2011). *J. Nat. Prod*. **74**: 213-222.

P87

$6^{èmes}$ Journées Franco-Italiennes de Chimie
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Preparation of polyaniline/MWNT composites by in situ emulsion polymerization

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Since their discovery in 1991, carbon nanotubes have led to an explosion of research in nanoscience and nanotechnology. They attracted the attention of researchers due to their remarkable properties, their interesting electrical, mechanical, physical and thermal conductivity behavior. In addition, their manufacturing process becomes more basic and less expensive.

On the other hand, the Nobel Prize in Chemistry for 2000 was awarded to three scientists- Alan G. MacDiarmid Alan J. Heeger, and Hideki Shirakawa for their discovery of conductive polymers [1]. Among the conducting polymers, polyaniline is relatively popular due to the low cost of its monomer, its ease of preparation and its easily tunable electrical properties by both electrochemical and chemical methods.

The ability to combine CNT with conducting matrices especially PANI is a very recent area of study. Figure 1 illustrates that this topic has attracted consistently growing interest among researchers worldwide in the last decade. One main reason for this fact is that common applications of the two components offer the possibility to observe synergetic effects.

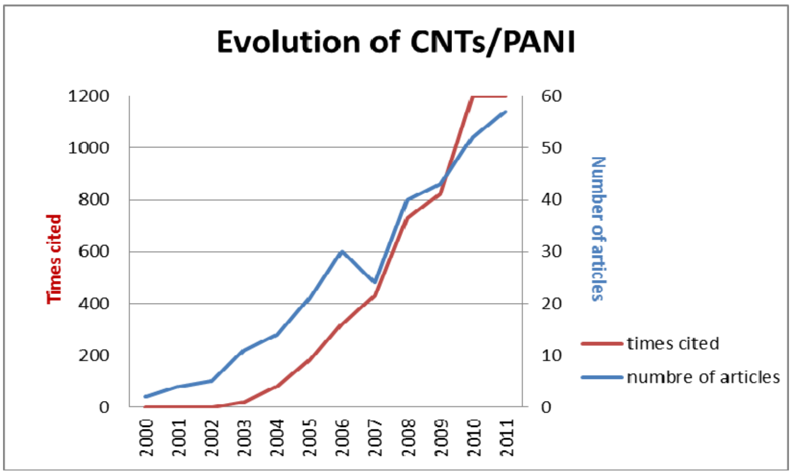

Figure 1 : Evolution of CNT/PANI: number of articles and times cited

Our aim was to synthesize polyaniline-multiwall carbon nanotubes via a new in situ emulsion polymerization technique using decylphosphonic acid DcPA as a surfactant. The structure and morphology of the binary composites will be investigated by a variety of techniques including scanning electron microscopy SEM, thermogravimetric analysis TGA, fourier transform infrared spectroscopy FTIR, ultraviolet-visible spectroscopy UV-Vis, Raman spectroscopy and X-ray diffraction XRD.

[1] Shirakawa H. The discovery of polyacetylene film: the dawning of an area of conductiong polymers. Angew Chem Int Ed 2001; 40:2574-80.

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[*] contact : oueiny@univ-tln.fr

P88

$6^{èmes}$ Journées Franco-Italiennes de Chimie
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Greffage d'une sonde fluorescente sur la Matière Organique Naturelle Standard et caractérisation du produit à des fins d'utilisation environnementale

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L'objectif de ce travail est de greffer une sonde fluorescente pour marquer les matières organiques naturelle (MON) dans le but de suivre leur évolution dans un sol ou une colonne de sol sans pour autant être gêné par sa fluorescence intrinsèque. Pour cela, il a été nécessaire de choisir des sondes fluorescentes qui possèdent un domaine de fluorescence différent de celui de la MON (250&350/420nm) et qui peuvent être greffées sur les matières organiques sans modification importante des propriétés. Le couplage du FITC (Fluorescéine Iso Thio Cyanate) à température ambiante a été appliqué (Figure 1). Le greffage est caractérisé au moyen de la spectroscopie UV-Visible [1], de la fluorescence [2], la RMN, IRTF, la micropH-métrie et le quenching de fluorescence. Ces deux dernières techniques de mesure permettront également de quantifier les sites actifs de la MON lors d'expériences de complexation métallique en laboratoire ou in-situ.

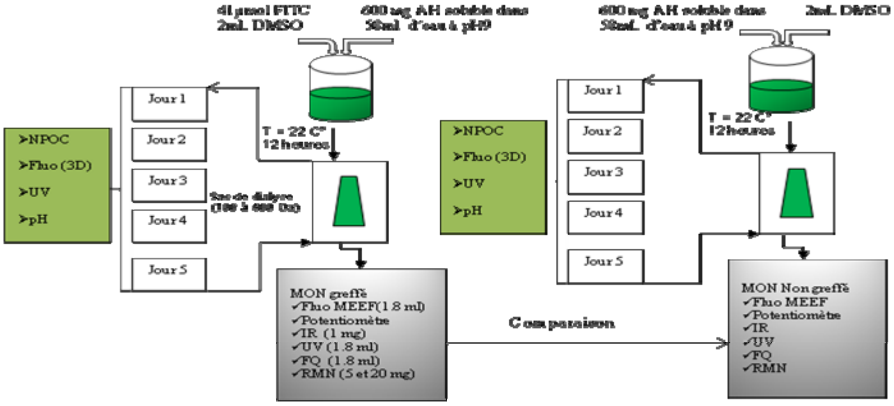

Figure 1 : Le protocole expérimental

Résultats : Par IRTF les groupements thiols R-SH qui sont responsable sur l'AH greffé d'une bande assez faible vers 2460 cm^{-1} sont d'identifiés. La spectroscopie de fluorescence montre que la sonde (Em=520 nm, Ex=489 nm) est associée avec l'acide humique (Em=450 nm, Ex =280 nm). Le suivi du NPOC (Carbone Organique Dissout), de l'UV et de la fluorescence pendant la dialyse montre qu'il est nécessaire de 5 jours pour éliminer le FITC n'ayant pas réagit.

[1] **Perdue, E.M. & Ritchie, J.D.** (2003) Dissolved organic matter in freshwaters. In *Surface and ground water, weathering and soils*, Vol. 5, pp. 273-318. Edited by J.I. Drever. Oxford: Elsevier-Pergamon.

[2] **Sierra, M.M.D., M. Giovanela, E. Parlante and E.J. Soriano-Sierra.** 2005. Fluorescence fingerprint of fulvic and humic acids from varied origins as viewed by single-scan and excitation/emission matrix techniques. Chemosphere 58:715–733.

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P89

6èmes Journées Franco-Italiennes de Chimie
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Simulation de la dynamique des contaminants métalliques dans un mélange eau douce-eau de mer sous 2 régimes climatiques

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Laboratoire PROTEE, Université du Sud Toulon Var, BP 20132, 83957 La Garde, France

Les écosystèmes côtiers en mer Méditerranée sont fortement influencés par les apports continentaux, provenant des principaux fleuves et également des petits fleuves côtiers. La présente étude porte sur la compréhension de la dynamique des éléments traces métalliques issus des rejets de l'agglomération Marseillaise (≈1.7M Ha) dans un gradient de salinité. L'originalité du système Marseillais réside dans la diversité de ses apports au milieu côtier : mélange des effluents de la ville avec les eaux des rivières, directement rejeté en mer via 2 émissaires. Ces apports en particules, éléments nutritifs et contaminants sont caractérisés par de fortes variabilités spatiales et temporelles, en partie contrôlées par les spécificités du climat Méditerranéen. Dans l'optique d'une optimisation des prélèvements de terrain et d'une compréhension globale des mécanismes chimiques contrôlant la dynamique des métaux traces dans la zone des rejets, il est indispensable d'appréhender le système sous 2 régimes climatiques (temps sec vs. temps de pluie).

Des expériences de remobilisation en laboratoire ont permis d'étudier la cinétique des échanges entre phases dissoute et particulaire en fonction de la salinité. Pour simuler la dynamique par temps sec, de l'eau des émissaires a été prélevée et diluée à différents ratios dans de l'eau de mer filtrée afin de couvrir la gamme de salinité. Chaque flacon FEP est agité par retournement, une aliquote est prélevée et filtrée au bout de 15min, 1h et 6h de temps de contact. Le même protocole a été élaboré dans le but de simuler le mélange au cours d'une crue, en ajoutant des particules de laisse de crue à l'eau des émissaires (MES≈800mg.L^{-1}) et en intégrant un prélèvement à 24h de temps de contact.

Pour les 2 expériences, l'analyse du carbone organique dissous présente une évolution conservative, témoignant d'une simple dilution de l'eau douce dans l'eau de mer pour ce paramètre. En revanche, l'analyse par voltamétrie des métaux traces dissous montre un relargage des métaux dans la phase dissoute à faible salinité, témoignant d'une évolution non-conservative de ces éléments (Figure 1). De plus cette étude montre que les mécanismes contrôlant l'évolution des métaux dans un gradient de salinité, tels que l'adsorption ou le relargage, sont dépendants du temps et du métal étudié. Enfin, cette simulation en laboratoire a permis de mettre en évidence une contamination plus importante de la phase dissoute (relargage) et a montré qu'une filtration des échantillons sur le terrain après le prélèvement est nécessaire dans ce type de système, pour ne pas sous estimer la contamination.

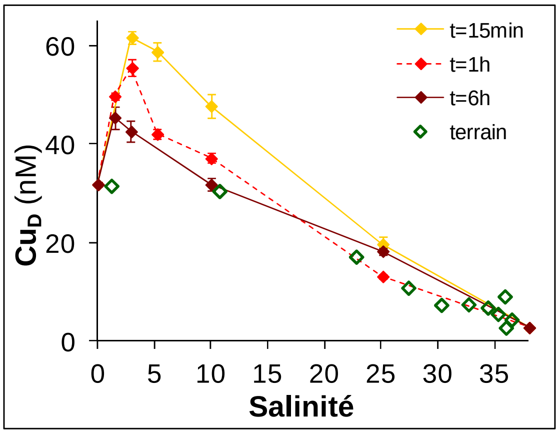

Figure 1 : Cinétique de remobilisation du cuivre dissous par temps sec en fonction de la salinité.

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P90

Synthesis and Characterization of Molecular Relay in Photovoltaic Cells

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Dye-sensitized solar cells (DSCs) have attracted significant attention as low-cost alternatives to conventional solid-state photovoltaic devices. In these cells, the most successful charge-transfer sensitizers employed are zinc porphyrin complexes, yielding over 12% solar-to-electric power conversion efficiencies.[1] The majority of these complexes reported to date show absorption in the visible region at around 448 nm ranges. Essential for efficient conversion of solar energy by DSSC is the spectral match of the sensitizer absorption to the solar radiation, and in this regard, metal compounds such as zinc and ruthenium complexes are inadequate due to the lack of absorption and the low molar extinction coefficients in the far-red/near-IR region. Therefore a study of new compounds with sensitivity in the NIR region is required.

Among the NIR dyes, squaraine dyes are well-known for their remarkable optical behavior because of strong absorption from charge transfer between electron-deficient central squaric core and each side of substituent in the red to near infrared region.[2]

Nevertheless, DSCs show overall efficiencies not comparable to the standard silicon cells. One of the approaches used to overcome these defects is the developing of new sensitizer systems with extended absorption and spectral sensitivity. In fact, it is also possible to exploit energy transfer couples (matching between donor emission and acceptor absorption)[3] QDs have already demonstrated to be very efficient in the photon capture (absorb on a large spectral region), greater than the molecular dyes currently used in DSSCs.[4] Moreover a revolutionary improvement can be achieved by multiple exciton generation (MEG) processes, leading to quantum efficiency larger than 100%.

Förster resonance energy transfer (FRET) has been already demonstrated in a variety of optoelectronic applications and recently in DSSCs as well.[5] Usually the traditional dyes used in DSSCs suffer from their low molar extinction coefficients or limited absorption spectrum region.[6] Using FRET to transfer energy form donor (QDs) to acceptor (Dyes) inside the DSSCs paves a new way for enhancing the photovoltaic performance of DSSCs.

[1] A. Yella, *et al., Science.*, **2011**, *334*, 629-634.
[2] J. J. McEwen, *et al.*, *Chem. Comm..* **2009**, 6339-6351.
[3] (a) J. I. Basham, *et al.*, *ACS nano,* **2010**, *4*, 1253-1258. (b) G. K. Mor, *et al.*, *Nano Lett.*, **2010**, *20*, 2387-2394.
[4] (a) R. Klajn, *et al.*, *Angew. Chem. Int. Ed.*, **2009**, *48*, 7035-7039. (b) M. H. Stewart, *et al.*, *J. Am. Chem. Soc.*, **2010**, *132*, 9804-9813.
[5] (a) B. E. Hardin, *et al.*, *Nat. Photonics*, **2009**, *3*, 406-411. (b) K. Shankar, *et al.*, ACS Nano, **2009**, *3*, 788-794.
[6] A. Hagfeldt, *et al.*, *Chem. Rev.*, **2010**, *110*, 6595-6663.

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$6^{èmes}$ *Journées Franco-Italiennes de Chimie*
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Métaux et métalloïdes dans les Astragales de Marseille sur le massif des Calanques : transferts dans les parties aériennes et biomarqueurs de stress

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2. *Aix-Marseille Université, Laboratoire Chimie Environnement (FRE CNRS 3416), 3 Place Victor Hugo, Case 29, 13331 Marseille, France*

L'activité industrielle du XIXème siècle a laissé des traces dans le paysage de l'agglomération marseillaise. Ainsi, de nombreuses friches industrielles n'ont pas fait, à ce jour, l'objet d'une réhabilitation. La dépollution de ces sites est souvent complexe, plus particulièrement quand la friche industrielle se situe sur une zone protégée pour sa biodiversité. C'est le cas de l'ancienne usine de l'Escalette dont la friche est intégrée dans le périmètre du futur Parc des Calanques.

Des études précédentes ont montré la polluo-tolérance d'une espèce végétale protégée, *Astragalus tragacantha* L., l'Astragale de Marseille, qui pousse spontanément dans les environs de l'ancienne usine. En effet, au niveau des populations de cette espèce sur le massif des Calanques, les analyses de sol ont montré la récurrence d'une contamination en plomb et en arsenic qui peut être liée à l'activité de cette usine.

Pour mieux comprendre la situation paradoxale du développement de cette plante rare et protégée sur des sols pollués, la présente étude s'est intéressée au suivi du transfert de métaux et métalloïdes dans les parties aériennes (minéralisation eau régale et analyses en ICP-AES ou GF-AAS) de 15 individus sur 3 populations autour du site de l'Escalette (Montredon, Maronaise et Callelongue, respectivement à 0,6 ; 1,3 et 1,75 km de l'ancienne usine). L'état physiologique des individus a été suivi d'une part sur le terrain, en mesurant de manière non-destructive les teneurs en chlorophylles et en flavonols (mesures de fluorescence Multiplex®, Force A), et d'autre part au laboratoire, en mesurant dans des échantillons de parties aériennes, les teneurs en proline et en chlorophylles totales (dosages spectrophotométriques).

Les résultats montrent que les 3 populations sont soumises à la pollution de l'ancienne usine même celle de Callelongue, pourtant considérée comme hors de portée des impacts directs de la pollution. Ceci peut être lié à l'utilisation des résidus d'exploitation de l'usine (scories) comme matériau de construction pour la route et les stationnements littoraux allant à Callelongue.

Des métaux et des metalloïdes ont été détectés dans les parties aériennes dans les 3 populations même si les concentrations restent très faibles. Seule la teneur en fer est plus élevée pour les échantillons de parties aériennes prélevés à Callelongue comparée à celle à Montredon. Aucune différence dans les teneurs en chlorophylles et en proline dosées au laboratoire, n'a été observée entre les 3 populations. Cependant, les mesures non-destructives effectuées sur les populations *in situ* font apparaître des valeurs de chlorophylles et de flavonols significativement plus faibles pour la population de Callelongue. Ces analyses non-destructives plus sensibles ouvrent une perspective d'étude des espèces rares *in situ* et permettent de réaliser un plus grand nombre de répétitions analytiques.

Cette étude a permis d'avancer sur une meilleure compréhension des effets d'une multi-pollution sur l'état physiologique de l'Astragale de Marseille et de plus, elle a permis de montrer que cette espèce n'accumule pas de métaux et métalloïdes dans ses parties aériennes, limitant le risque de transfert au réseau trophique.

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P92

One-Pot Asymmetric Cyclocarbohydroxylation for the Enantioselective Synthesis of Functionalized Cyclopentanes

Wilfried Raimondi, Damien Bonne* et Jean Rodriguez*

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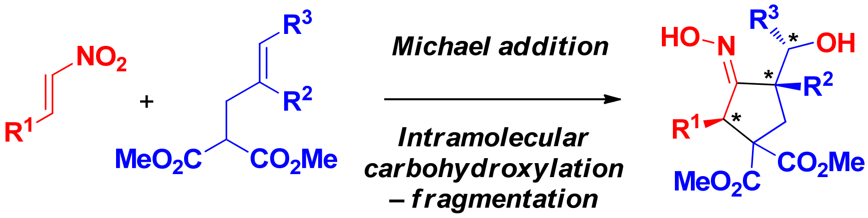
The development of organocatalytic enantioselective methods to access enantiopure molecules has received many attention for the last ten years due to the many advantages in term of efficiency, selectivity and environmental benefits offer by organocatalysis.[1] When the methodology involves simple starting materials and is associated with one-pot multiple bond-forming transformations (MBFTs),[2] the resulting tools are particularly useful to reach high level of structural complexity and functional diversity.

In this context, we present our results on the organocatalytic enantioselective Michael addition between simple acyclic achiral 2-substitued malonates and nitroalkenes followed by an in situ [3+2]-cycloaddition–fragmentation allowing the easy synthesis of densely functionalized cyclopentanes bearing up to three stereogenic centers with very high enantioselectivity and total diastereoselectivity.[3]

We have also identified two structurally different organocatalysts that can lead to both enantiomers of the desired cyclopentane. The high efficiency and the practical simplicity of the method make it an important way for the stereoselective formation of highly substituted five-membered ring systems.



up to 99 % yield
up to 98 % ee
dr > 99 : 1

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P93

Antioxidant (DiOHF) and antidiabetic association in treatment of STZ-induced diabetic rats.

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Diabetes mellitus is a metabolic disease characterized by hyperglycemia resulting from impaired insulin secretion and/or action. Moreover, diabetes is associated with endothelial dysfunction and oxidative stress [1]. Non-insulin dependent diabetes mellitus is widely treated with anti-diabetic drugs having hypoglycemic action such as biguanides or sulfonylureas. However these compounds are known to be associated with an increase of myocardial infarction risk. [2]

The synthetic flavonol -3',4'-dihydroxyflavonol- (DiOHF) is a powerful antioxidant showing a cardioprotective activity when perfused in control and postischemic isolated hearts [3]. Moreover DiOHF can restore endothelium-dependent relaxation in small mesenteric arteries prepared from diabetic rats [4], improves the diastolic function and reduces the myocyte hypertrophy [5]. However, no data are still available when ischemia is induced after DiOHF *in vivo* treatment (*per os*).

With the aim to design more efficient antidiabetic drugs, two new hybrids molecules have been synthesized in our laboratory, associating antidiabetic groups to the DiOHF moiety. We then evaluated the performance of the new compounds compared to reference antidiabetic commercial drugs. Compounds were administrated *in vitro* (during the isolated heart perfusion) or *per os* (for 6 weeks before sacrifice) to STZ-induced diabetic rats. We compared their effect (i) on blood in glycemia limitation, (ii) on LDH (lactate deshydrogenase) release, taken as a tissue damage marker and (iii) on cardioprotection using an ischemia-reperfusion model on isolated rat heart.

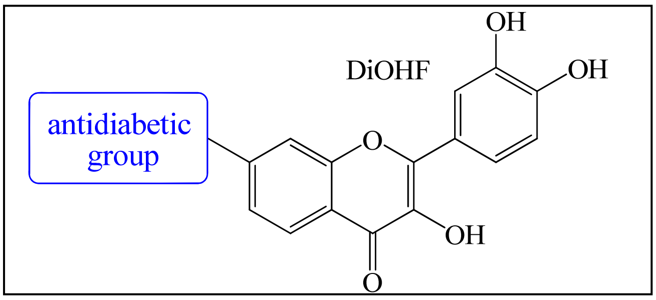

Figure 1 : DIOHF-antidiabetic hybrid structure

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P94

Ageing studies and characterization of polysaccharide plant gums with Thermally Assisted Hydrolysis and Methylation

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In the present work standard monosaccharides, disaccharides and polysaccharides were analyzed by Thermally Assisted Hydrolysis and Methylation (THM) to understand which product can be used as markers for identification of these materials. Pyrolysis under strong alkaline conditions in the presence of methylating reagent (TMAH) was found to cause the formation of metasaccharinic and isosaccharinic acids, characteristics for each monosaccharide and differing according the types of glycosidic linkages. All the markers were identified on the basis of their mass spectra, characterized by the presence of the intense signal at m/z 129 [1].

Different conditions were varied to optimize the method: pyrolysis temperature, concentration of alkaline reagent and contact time between sample and reagent. The optimized method was applied to the study of several plant gums [2], with particular aim to recognize this class of materials in samples coming from artistic and archaeological handiworks. Principal monosaccharide markers were identified in the pyrograms and used to obtain gum classification with application of multivariate data analysis (Figure 1)

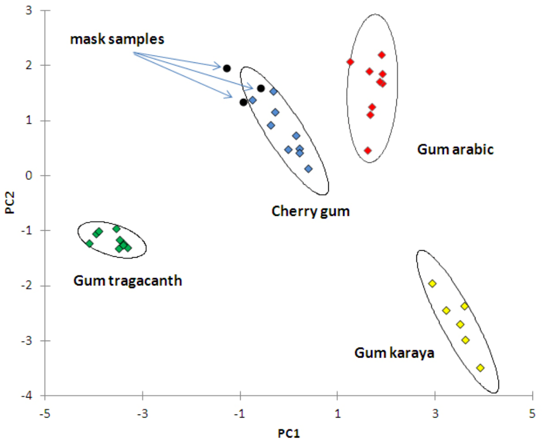

Figure 1 : classification of plant gums with Principal Component Analysis

Effects of artificial accelerated ageing were also investigated. Gums were submitted to photoxidation, alone and in the presence of metallic pigments, and it was demonstrated that these polysaccharides are very stable to oxidative processes. Plant gums were also stable under mild thermoxidative conditions. Only enzymatic treatment and ozonolysis induced strong changes in the molecular components of the plant gums.

As example of application, samples from ancient Egyptian cartonnage were analyzed, confirming that THM coupled with chemometric data analysis is a suitable procedure to identify plant gums even in very low concentrations and with a minimum amount of sample, that is the principal aim of the present work.

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P95

Synthesis and SAR studies of merbarone analogues as novel antiproliferative agents

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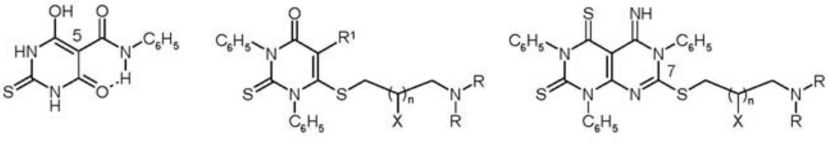
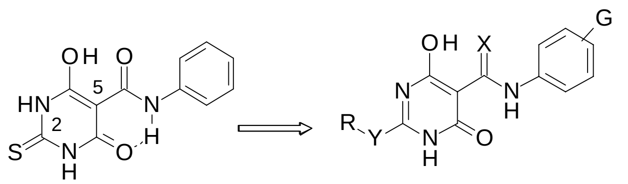
Topoisomerases II (TopoII) are nuclear enzymes that can change the topological state of DNA through the breaking and re-joining of both DNA strands(1). The activity of TopoII is critical for DNA processing progression and its impairment or alteration lead to cell death.(2) These evidences pointed TopoII enzymes as privileged target for the treatment of human cancers. TopoII targeting agents can be divided into two classes: poisons and catalytic inhibitors. TopoII poisons increase the physiological concentration or lifetime of topoII-DNA cleavage complexes whereas the catalytic inhibitors interfere with the catalytic cycle of the enzyme.
Merbarone is a thiobarbituric TopoII inhibitor that showed antitumor activity in NCI screening. However, *in vivo* studies highlighted a general lack of antitumor activity potentially ascribable to the high ionizability (and poor bioavailability) of this compound at physiological pH. With the aim of preparing merbarone analogues endowed with improved pharmacodynamic and pharmacokinetic properties, a series of pyrimidine **I** and pyrimidopyrimidine **II** (Figure 1) analogues have been previously synthesized.(3) In NCI screening, a number of derivatives belonging to series **I** and **II** showed potent antiproliferative activity against leukemia and prostate cell lines (GI_{50} up to 0.01 μM).



Merbarone **I**, R^1 = COOEt, Ph, COMe **II**

Figure 1. *Chemical structures of merbarone and its analogues* ***I*** *and* ***II****.*

With the aim to further extend the SAR study on merbarone analogues, a second generation of derivatives has been synthesized (Figure 2).



Merbarone

X = O, S
Y = S, NH
G = H, 4-Cl, 2,4-Cl_2, 4-NO_2
R = H, alkyl, (aryl)alkyl or aminoalkyl chains

Figure 2. *General structures of new merbarone analogues*

The modification strategy involved the anilido moiety at position 5 and/or the 2-thiocarbonyl group. The prepared close merbarone congeners were tested for their antiproliferative activity in cell based assays. Furthermore, enzymatic test on isolated TopoIIα enzyme were carried out.

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Organocatalyzed Desymmetrization of *Meso* Primary Diols

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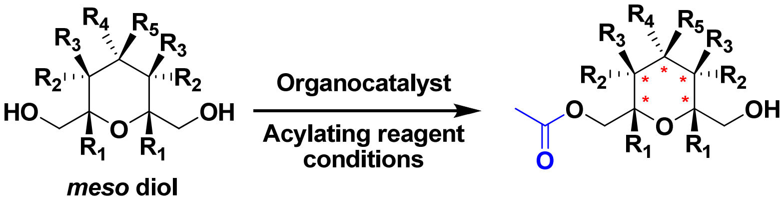
The synthesis of complex targets with numerous stereogenic centers leads to increase the number of enantioselective steps. A strategy to obtain building blocks bearing several stereogenic centers in single enantioselective step consists into the desymmetrization of *meso* precursors.

Our attention is turned on highly functionalized tetrahydropyran (THP) rings because it is present in numerous biological active products [1]. An efficient and versatile synthetic pathway for elaboration of *meso* primary diols derived from THP was proposed in our laboratory. In order to circumvent the limitations of enzymatic desymmetrization (poor tolerance toward the structural variations of the substrates)[2], the first example of enantioselective desymmetrization of *meso* primary diols using chiral DMAP was developed in our laboratory.



Asymmetric desymmetrization of meso diols.

Encouraging results with high yields and high level of enantioselectivities will be presented.

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P97

Highly enantioselective organocatalytic construction of all-carbon quaternary stereocenters by Michael addition with β-ketoamides

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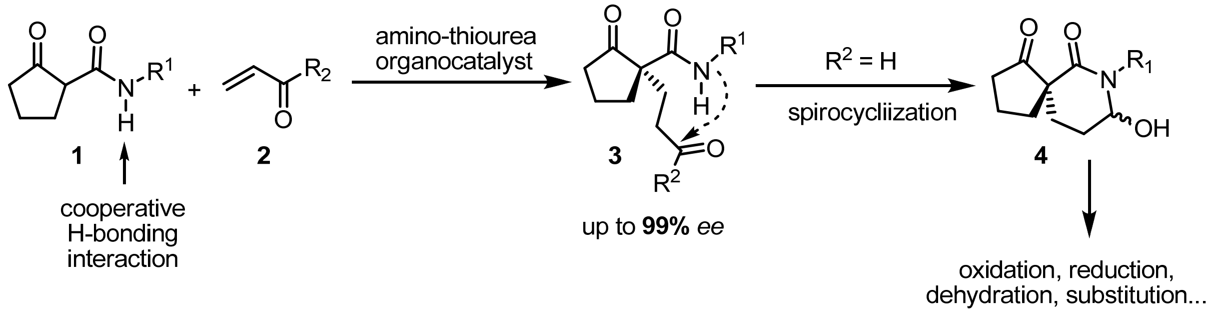
The enantioselective construction of quaternary centers is one of the most demanding key steps in the stereocontrolled synthesis of complex natural and/or pharmaceuticals products.[1] In particular, the generation of all-carbon quaternary stereocenters constitutes a formidable challenge due to additional steric hindrance issues.[2] In this context, the asymmetric conjugate addition represents a powerful tool for the elaboration of these particular stereocenters. In the last decade, extensive studies have been devoted to the development of organocatalytic systems to perform such transformations with excellent enantioselectivities,[3] employing simple substrates.

In this way, our research interest in ketoamides led us to develop the first organocatalytic enantioselective conjugate addition of α-substituted β-ketoamides **1** to enones **2** using an amino-thiourea bifunctional catalyst, involving an unprecedented cooperative effect of the amide function in the activation process. (cf scheme 1).[4],[5] The corresponding adducts **3** containing a highly functionalized all-carbon quaternary stereocenter are obtained in good yields and high to excellent enantiomeric excesses. Moreover, the synthetic advantage of the additional amide function is illustrated through an efficient enantioselective domino Michael/ spirocyclization sequence leading to chiral scaffolds **4** of high synthetic interest.



Scheme 1 *Organocatalyzed enantioselective construction of all-carbon quaternary centers.*

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$6^{èmes}$ *Journées Franco-Italiennes de Chimie*
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MULTIVALENT GLYCOASTERISK LIGANDS AS PROBES AND INHIBITORS OF SOME LECTIN-CARBOHYDRATE INTERACTIONS

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A growing interest in carbohydrate chemistry and glycobiology appeared in the last years, because of their roles played in fundamental life processes (cancer, inflammation, AIDS, cell-cell adhesion, etc.). In view of those findings, carbohydrate-lectin recognition represents an important field of study. For better understanding those interactions, selective inhibitions and a control of lectin assemblies are often necessary. We thus synthesized a novel class of colored, luminescent, UV-responsive glycosylated asterisks to investigate the so-called "carbohydrate cluster effects". They are effective inhibitors against several lectins, near the nanomolar scale. We will also present our new coronene-based asterisk ligands. We will put forward the concept of a multivalent ligand with a dual function, as a biological probe (sensor) and as an inhibitor. Inhibition of biofilms formation will also be a subsequent goal.

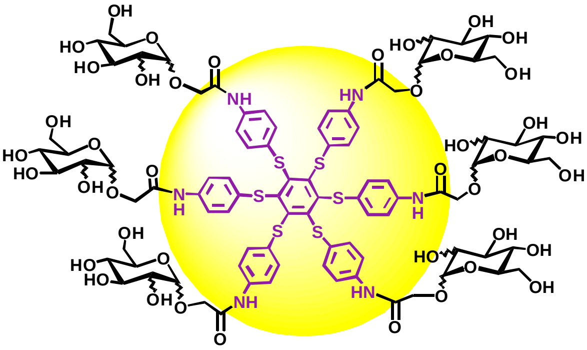

Figure 1: Benzene-cored glycoasterisks

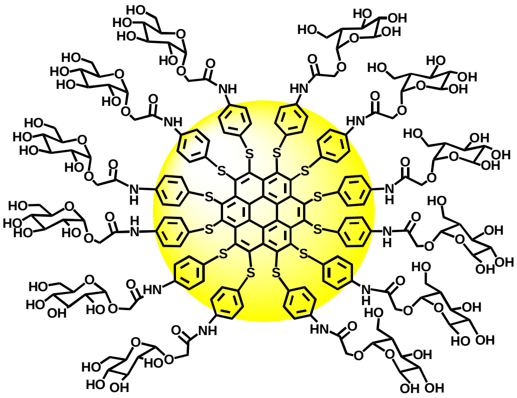

Figure 2: Coronene-cored glycoasterisks

Keywords: Synthetic ligands, multivalency, carbohydrates, lectins, dendrimers, sulfur.
Acknowledgements: CNRS, Aix-Marseille Université, ANR 08-PCVI-0028 "Glycoasterix"

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Esterification, encapsulation and therapeutic applications of sesame oil

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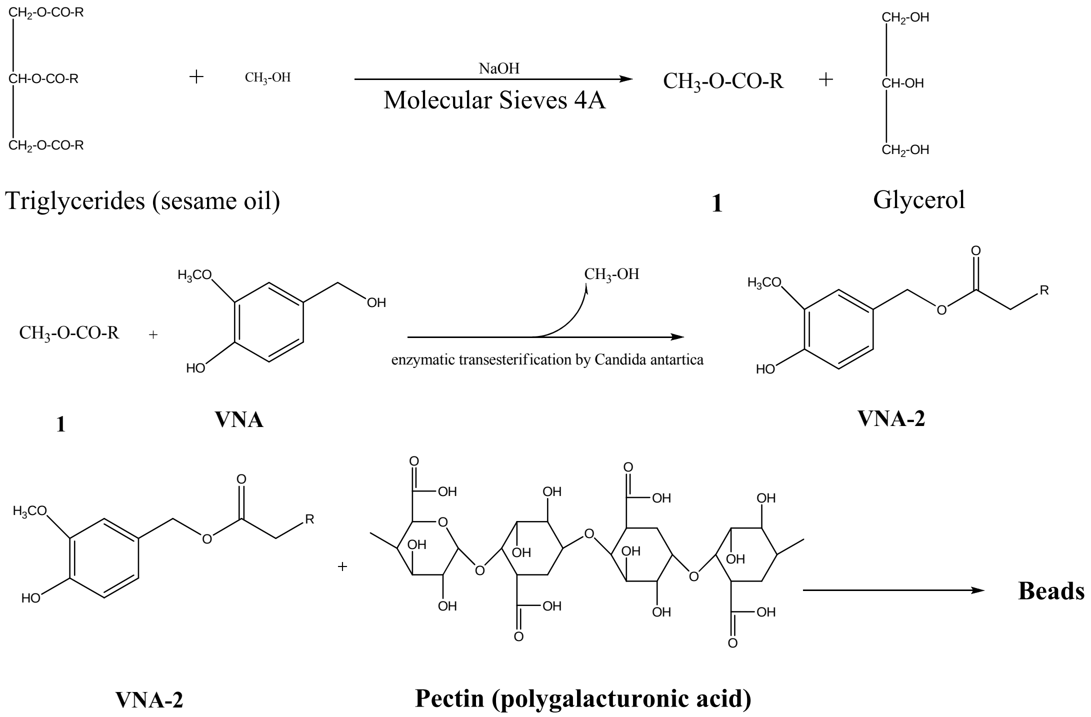
Natural or transformed sesame oil is of great interest for food, cosmetic and pharmacological fields, beeing a biological resource rich in unsaturated fatty acids with also an unsaponifiable fraction rich in protein and antioxidants. Sesame oil can also be used as substrate for the enzymes, antibiotics or pesticides production by bioprocesses. With the aim to valorize it, we esterified sesame oil and supplemented it in antioxidants, as described by Alencar in our laboratory, and then encapsulated it in pectin beads in the presence of calcium chloride or zinc. These beads were then tested for their gastroresistance, and the release of the encapsulated oil was evaluated by *in vitro* dissolution studies to determine the most suitable formulation for controlled release of antioxidants. Finally, we followed the release of the esterified fraction at various pH corresponding to target organs (stomach, intestine) and measure its antioxidant activity in each medium. Antioxidants assays were performed using the supernatant phase of dissolution media. Results of *in vitro* studies indicates that the vanillic ester of sesame oil conserves its antioxidant capacity after beads dissolution and that calcium chloride formulated beads could be the best adapted for intestinal release.



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P100

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EXPEDITIVE SYNTHESES OF FUNCTIONALIZED HELICENES AND APPLICATIONS

Terrasson V., Peresutti R., Hoff B., Barth C., Henry C., Roy M.,
Félix, G. and Gingras, M.*

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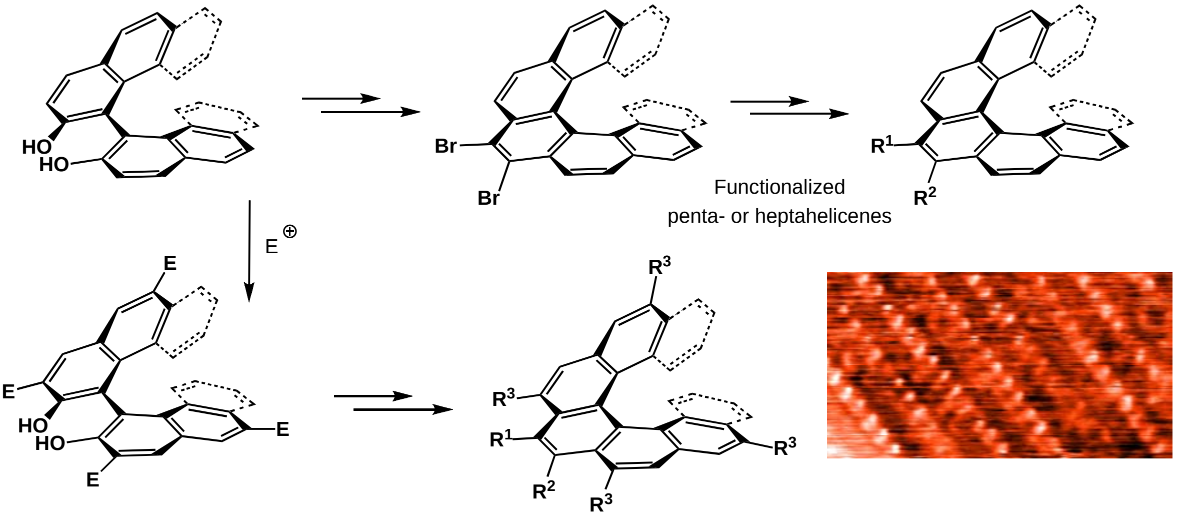
Helicenes are not only aesthetic and intriguing helicoidal polyaromatic compounds, often studied in theoretical chemistry because of their distorted π-system, but they became the centerfold of newly expanding research topics in the fields of asymmetric catalysis, advanced materials (dendrimers, conductors, polymers, liquid crystals, SAMs and films, etc.), molecular electronics, optics (OLED, chiroptical switches, NLO, etc.) and supramolecular helicoidal chemistry.[1] In spite of efforts and early results in the synthesis of functionalized helicoidal structures, numerous applications and improvements are still sought in helicene chemistry, mainly because of the need for practical preparations on a larger scale. The heptahelicene series and higher homologs were somewhat neglected. The purpose of this work is to investigate a practical and efficient synthesis of [5]- and [7]-helicenes using benzylic couplings and their subsequent functionalization employing some metal-catalyzed reactions.[2] Helicenes with a high number of chemical functions can also be prepared by electrophilic substitutions. Among some applications, we present our results on AFM studies concerning the deposition of those helicene molecules on insulating surfaces under ultra-high vacuum, showing interesting organizational behaviour toward chiral surfaces.



(Noncontact AFM in UHV on 7-cyano-[5]-Helicene on Suzuki [NaCl:Cd2+(001)])

Figure 1 : Efficient synthesis of functionalized penta- or heptahelicenes and AFM studies.

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P101

Blind Source Separation of processing of highly overlapping DOSY datasets

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One way to identify molecules in a mixture is the use of PFGSE ("DOSY") experiments, which provide a means of tagging the components by their mobilities, if the spread of these latter is sufficiently large and the processing effective.[1] We explored here the separation performance of Blind Source Separation (BSS),[2] an approach that allows estimating the spectra of N unknown sources (the spectra of the pure components) from a series of P mixed spectra[3] (the single traces of the DOSY dataset in this case). We explored two different BSS approaches, Independent Component Analysis[4] and NNSC,[5] which uses non-negative matrix factorization (NMF) with an additional sparse coding (SC). We did not introduce any parametric modeling of the sources or of the mixing matrix (e.g. the exponential behavior of the PFGSE decay). The results (***estimated sources*** and ***diffusion coefficients***) on a mixture of *sucrose* and *maltotriose*, characterized by a high level of spectral overlap, are shown in the Figure (for NNSC). Thus, hyperparametric BSS can provide excellent separation and calculation of the diffusion constants. The effect of hyperparametrization on the separation and applications to more complex mixtures will be illustrated.

Acknowledgment Grants ANR-08-BLAN-273 ; Region PACA (APO-G-2009)

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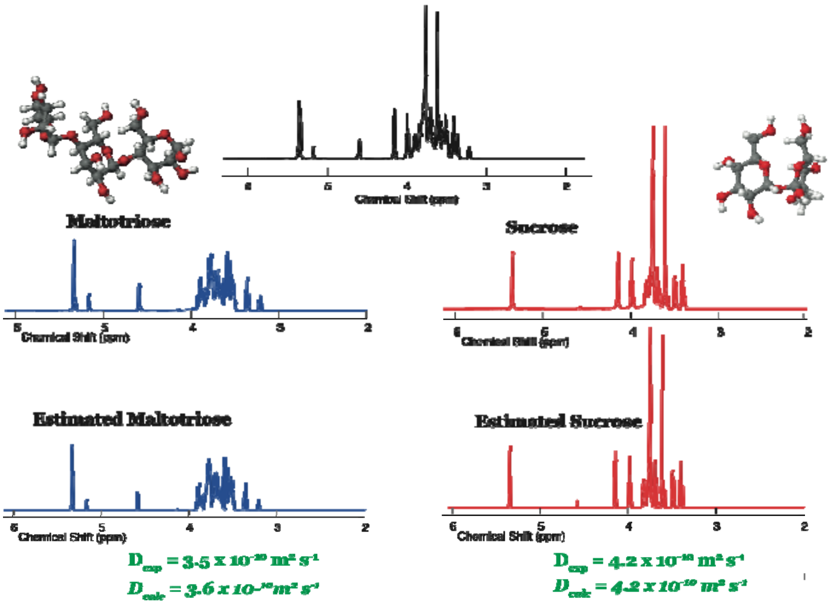

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P102

6èmes Journées Franco-Italiennes de Chimie
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Self-Assembled Calixborate Macrocyclic Anion Receptors

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Since the pioneering work of Sato et *al.*,[1] and Alcalde et *al.*[2] much attention has been paid to imidazolium derivatives for anion receptors. Structures based on imidazolium recognition sites are of particular interest due to their strong and tunable hydrogen binding abilities and their positively charged imidazolium moieties, which facilitate their use as anion receptors. Incorporation of such moieties into a macrocyclic molecular system can give rise to the formation of preorganised structures which can allow cooperative hydrogen bonding interactions to take place from several binding sites.[3]

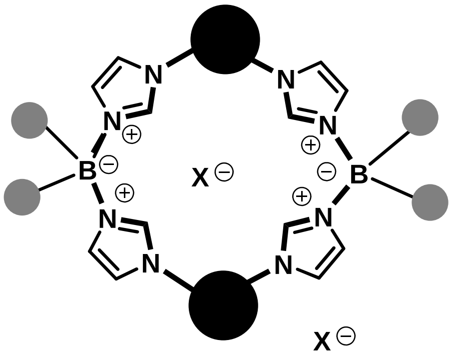

Figure 1 : Designed cationic macrocyclic calixborate anion receptors

Well designed macrocyclic calixborates were synthesized in high yield and their anion binding ability was evaluated by ^{1}H NMR, X-ray crystallography and high-resolution mass spectroscopy. These new macrocycles display high binding affinity for halides and oxoanions.

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P103

AFM tip catalyzed local surface alkene epoxidation

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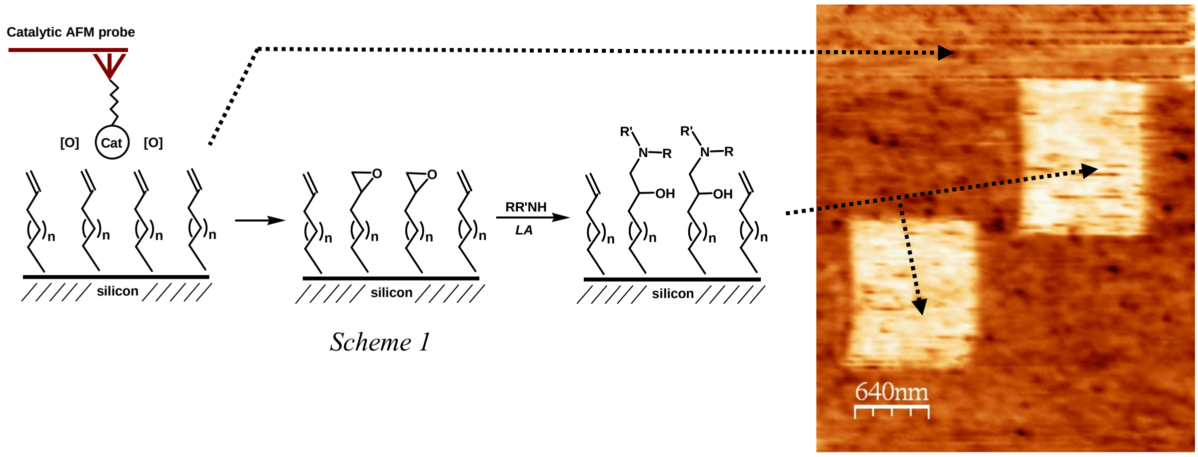
Scanning probe (STM and AFM) nanolithography belongs to the most important methods for creation of nanoobjects on the surface with sub-100 nm resolution. It is generally based on the direct diffusion transfer (Dip-Pen nanolithography) and mechanic or electrical destruction of the surface. Limited reports on the AFM catalyzed chemical surface modification was achieved using AFM probes coated with metals (Pd and Pt – azide hydrogenation[1] and alkene hydrosilylation[2]), metal oxides (Cu_2O, alkyne-azide "click" reaction[3]) and absorbed metal nanoparticles (Pd NPs, Suzuki and Heck cross-coupling[4]).

We report herein the first use of the AFM tip with *immobilized homogeneous catalyst* for spatially controlled epoxidation of the surface terminal alkene groups (Figure 1).



Scheme 1

Figure 1. AFM topography image of the surface after local epoxidation of two 1 µm squares on the alkene terminated SAM followed by the reaction of the epoxide groups with secondary amine

The reaction was carried out in the solution of the epoxidation agent by the direct contact of catalytic AFM probe with alkenyltrichlorosilane SAM on silicon within the appropriate force range (Scheme 1). After treatment of resulting surface with a secondary amine in the presence of a Lewis acid, AFM imaging revealed the positive surface topographic change roughly corresponding to the length of amine molecule *in the epoxidized area only* thus indicating the formation of aminoalcohol domains on the alkene SAM. The concept used in this work could be attractive for the controlled 3D fabrication of various types of nanodevices.

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Nanoconfinement and Surface Effect on Radical Lifetime

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Structured mesoporous silicas can be considered as nanoreactors. These materials have high thermal and chemical stabilities and are easily functionalized. Nanoconfinement has recently proved to be performant in changing the chemical outcome of some organic reactions.[1] The challenge of this study is to explore the influence of nanoconfinement on thiyl radical lifetime. Mesoporous silicas were used for this purpose. Influence of both presence of mesoporous silica and thiol immobilization on mesoporous silica on the spin adducts lifetime is discussed.

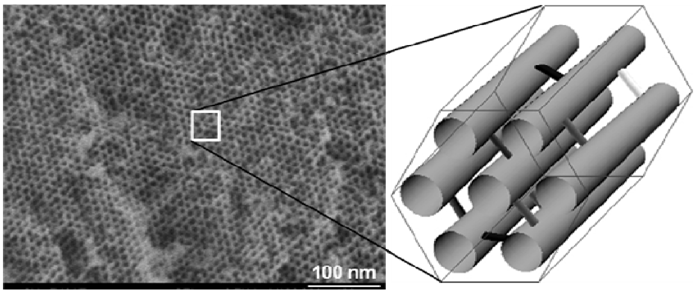

Figure 1 : mesoporous silica SBA-15 (TEM)

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P105

6èmes Journées Franco-Italiennes de Chimie
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Evolution chimique de la matière interstellaire dans des analogues de glaces interstellaire.

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Les grains de poussière interstellaire dont la taille est de l'ordre de 0,1 µm sont constitués d'un coeur de silicates ou de matières carbonées. Lors de leur transit dans le milieu interstellaire ils peuvent se retrouver dans certaines régions appelées nuages moléculaires denses où les principaux éléments que contiennent ces nuages (H, O, N, C..) peuvent s'accréter, puis se combiner entre eux pour produire des molécules comme H_2O, CO, CO_2, H_2CO, CH_3OH, NH_3…qui vont recouvrir la surface de ces grains en formant des glaces interstellaires « primitives ».

Ces grains vont alors se transformer sous l'action des rayonnements et du réchauffement lors de l'évolution du nuage moléculaire dense vers la formation d'un système planétaire. Ces processus énergétiques vont altérer la composition chimique du manteau de glace pour conduire à la formation de molécules de plus en plus complexes qui vont former un résidu organique réfractaire probablement analogue à un grain de type cométaire.

Notre but consiste à suivre l'évolution chimique des grains et des glaces interstellaires que ce soit d'un point de vue thermique ou avec des irradiations par des photons (λ>120 nm) ou des atomes d'hydrogène. Nous identifions les espèces formées en nous appuyant sur des techniques spectroscopiques (IRTF et spectrométrie de masse).

Ces analyses ont vocation à prédire les types de composés détectable dans des comètes. Ces données seront très utiles pour l'interprétation des données collectées par la mission Rosetta. Pour l'instant nos études ont porté sur la molécule de formaldehyde en réaction avec d'autre molécules présentent sur les grains. On arrive alors à un réseau de réaction relativement complexe (Figure 1).

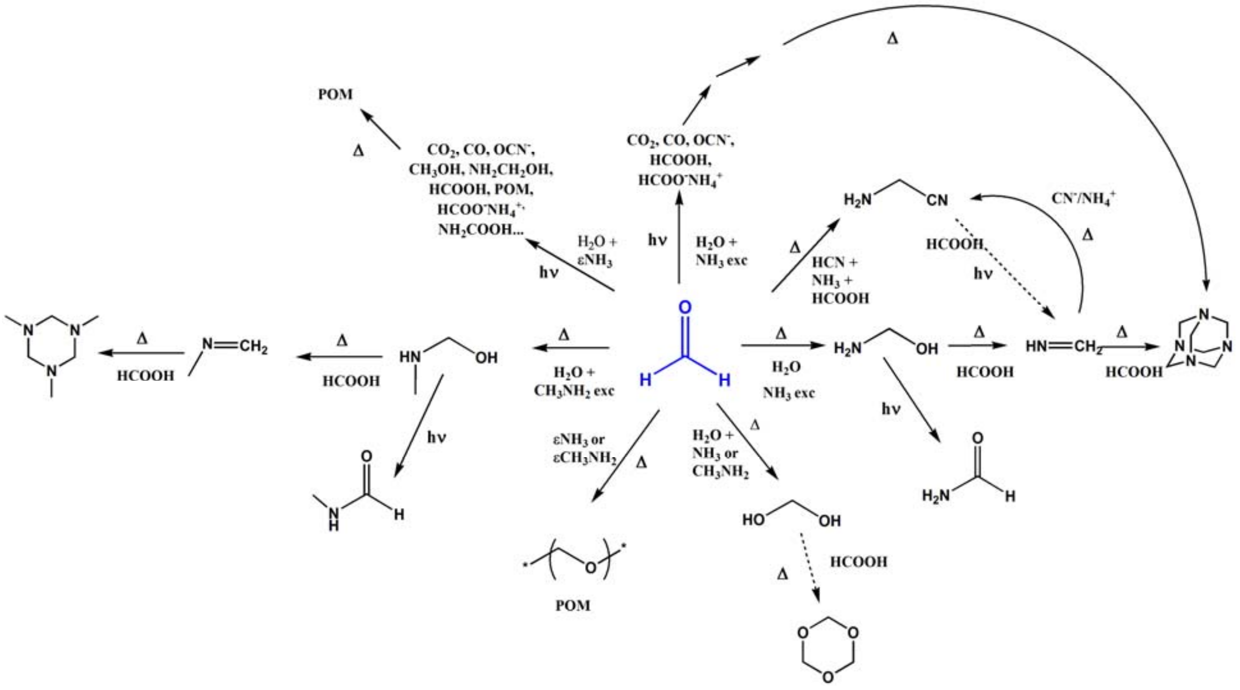

Figure 1 : Exemple de réactions possibles dans les conditions du milieu interstellaire à partir du formaldehyde.

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P106

Antibody and Ligand conjugated dendrimers for targeted siRNA delivery

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Dendrimers are a class of well-defined nano-structured macromolecules possessing spherical architecture with unique radiating branching units and end groups on the surface.[1] We have recently demonstrated that structurally flexible poly(amido)amine (PAMAM) dendrimers[2] are effective nanovectors for siRNA delivery[3] in various disease models.[4] This promising result encourages us to undertake further investigation on targeted siRNA delivery using dendrimers conjugated with specific ligands or antibodies, which can recognize the corresponding receptors or proteins expressed on the cell surface. In this way, siRNA can be delivered specifically to the cells of interest, leading to targeted delivery, which can further improve the delivery efficiency and reduce the toxicity by avoiding non-specific interactions and at lower doses. Here, we will report the design and synthesis of dendrimer conjugates with antibodies and a dendron bearing multiple ligands, respectively, in the view to achieving potent and efficient targeting. Biological evaluation of these dendrimer conjugates is currently underway for targeted siRNA delivery in prostate cancer models *in vitro* and *in vivo*.

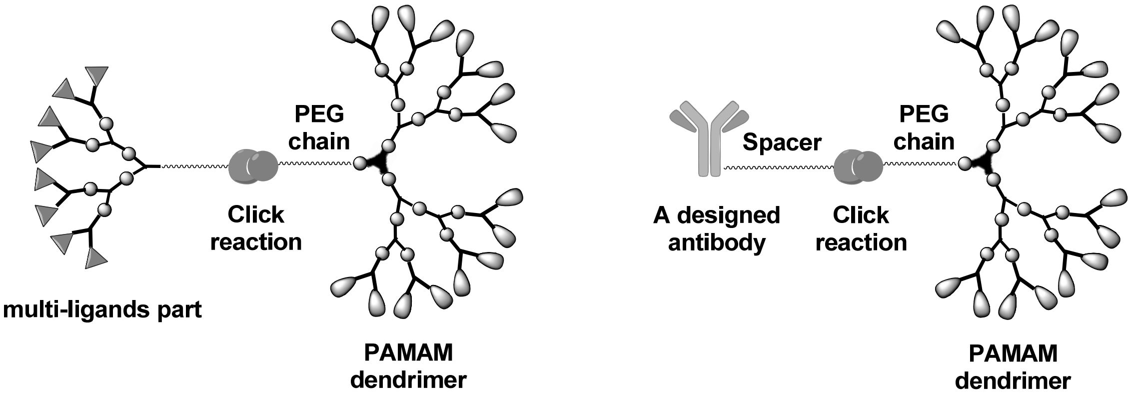

Figure: Ligands or antibody conjugated PAMAM dendrimers

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Affinity columns with nonmetabolizable 2-OG tags for identifying new 2-OG receptors

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2-Oxoglutaric acid 2-OG (Figure 1), a key intermediate of the Krebs cycle, plays important roles in various organisms.1 Recently, we have demonstrated for the first time in vivo that 2-OG serves as nitrogen starvation signal in cyanobacteria using non-metabolizable chemical probes.2-4 In order to further identify the 2-OG receptors and construct the 2-OG signaling pathways in cyanobacteria, we have newly exploited affinity chromatography approach utilizing affinity columns bearing non-metabolizable 2-OG mimics. By making harness of the modern click chemistry, we have successfully attached non-metabolizable 2-OG analogs onto the resin via either a hydrophobic or a hydrophilic linker. Preliminary biological evaluation demonstrated that the so obtained affinity resins are able to retain NtcA, a known 2-OG receptor, not only in the pure protein form but also in the whole cell lysate. We will present here the preparation of 2-OG affinity resins and their biological assessment as well as our further plan to implement these affinity columns in identification of 2-OG binding proteins in cyanobacteria in the view to constructing the complex signaling pathways involving 2-OG.

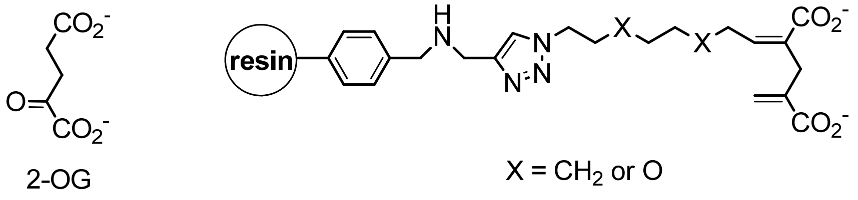

Figure 1 : 2-OG and two examples of resins with 2-OG ligands.

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P108

Design of patentable tyrosine kinase inhibitors using a computational approach.

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Receptor tyrosine kinases (RTKs) are the cell-surface receptors for many growth factors and hormones. Tyrosine kinases represent a super family of enzymes that play a key role in tumor growth, survival and metastasis. Aberrant RTK activation has been linked to the development of several human cancers. Inhibition of RTK pathways has become an interesting approach for the discovery of new anticancer drugs.[1] For example, Imatinib-mesylate (Gleevec) is actually used for the treatment of chronic myelogenous leukemia (CML). However, the selectivity of these compounds is very low since they inhibit the action of a range of kinases in non-specific way and disturbs cellular functions.[2] Moreover, side effects and drug resistance continue to be serious problems.

The aim of the present work is to validate our drug-discovery approach based on molecular modeling studies and crystallographic experimental data for the synthesis and selection of potent and specific ligands of pharmacologically validated RTK targets.

In this context, chemoinformatics has become a valuable tool for medicinal chemists and we assessed the potential of the software platform developed by Oribase Pharma in drug design. Two main chemoinformatic platforms have been dealt with: (1) MedChem-Decision® for assessment of docking and chemical feasibility of new compounds, and (2) EZ-Design® for the virtual library design and profiling.

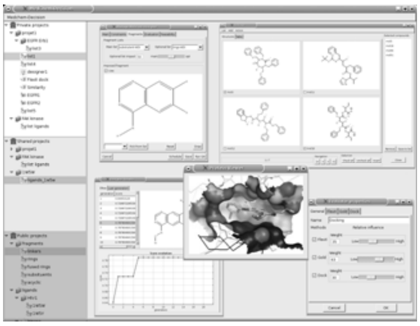

Figure 1: MedChem-Decision®

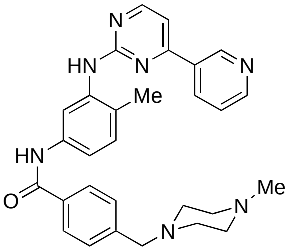

Figure 2: Chemical structure of Gleevec

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P109

Amphiphilic dendrimers for siRNA delivery

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Dendrimers have intriguing features for drug delivery because of their unique properties of high drug payload confined within a compact nanoscale volume and their well-defined structure, regular branching units and the possibility to have different terminal functionalities to impart various physicochemical properties. [1] We have recently developed structurally flexible dendrimers for nucleic acid delivery. [2-7] They can behave as amphiphilic molecules, if their core, repeating or terminal unit is properly modified. Amphiphlic dendrimers, marrying the characteristic of dendrimers and the bio-mimicry of lipids, become particularly appealing as nanovectors for drug delivery in nanomedicine. We will report on the synthesis, characterization and biological evaluation of the amphiphilic dendrimers recently developed in our group as drug delivery platform for the delivery of siRNA to treat adrogene-independent prostate cancer.

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6èmes Journées Franco-Italiennes de Chimie
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Synthesis and spectroscopic properties of dendron-like perylene bisimide/phenyleneethynylene polymers for photovoltaic applications

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Perylene and its derivatives, in particular mono- and bis-imides, combine a strong absorption in the visible region with a very high fluorescence quantum yield and a high stability. Because of these appealing properties, these derivatives have been utilized in various electronic and optical applications such as the fabrication of fluorescent solar collectors, photovoltaic cells[1] and light-emitting diodes (LEDs).[2]

On their side, conjugated materials, in particular, phenyleneethynylenes (PE) have attracted the attention of many researchers due to their strong photo and electroluminescent properties.[4] The efficiency of PE solar cells is however usually low due to the limited absorption range. The introduction of the perylene bisimide derivatives in PE systems should thus lead to an increase of the photovoltaic response by suitably modulating the chemical structure of the materials.

In this work, we report on the synthesis of phenylenethynylene polymers (*Figure 1*) in which perylene bisimide dendrons of one, two and three generation are introduced in the lateral chains. The chemical structure was corroborated by ^{1}H, ^{13}C, APT, DEPT-135 NMR, Raman, FTIR, UV-Vis, and fluorescence spectroscopy. X-Ray diffraction patterns are consistent with a supramolecular assembly in bilayers as found previously in cholesteryl PE oligomers.[5] The optical properties in solution are promising for photovoltaic applications due to a larger absorption range with respect to alcoxy substituted PE.

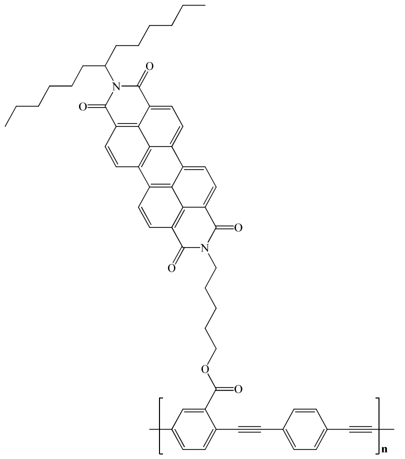

Figure 1: the motif of the first generation perylene bisimides/phenyleneethynylene polymer

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P111

Natural processes occurring in small lakes from Terra Nova Bay Antarctica

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Several small lakes are present in Terra Nova Bay, East Antarctica. This area represents one of the most uncontaminated terrestrial ecosystems on earth and for this reason it is considered as one of the most suitable places for estimating the natural presence, concentration and variability of organic and inorganic compounds with a minimum level of anthropogenic influence. In this work nine lacustrine ecosystems, belonging to four areas of Terra Nova Bay (Edmonson Point, Carezza, Gondwana and Tarn Flat), were investigated in order to gain insight into the natural processes regulating species distribution and to point out the occurrence of possible present or future local and/or global anthropogenic contamination [1]. Major, minor and trace elements were determined in freshwater, algae, mosses and (for one site) lichens, using atomic emission and absorption spectroscopy and mass spectrometry with inductively coupled plasma source. No evidence of a detectable contamination by metals was found in the investigated area. Lake water composition was found to be influenced by the following main factors : marine spray, which gives rise to an increase of alkali and alkaline earth metals; weathering of rocks and sediments, which is a source of minor and trace elements ; input of meltwater ; presence of biological activity ; lake geographical position, such as altitude and distance from the sea, which in turn influence the extent of marine spray and the extent of meltwaters immission. Algae have generally higher concentrations of elements than mosses, probably because they can assimilate nutrients and other elements from waters. The calculation of enrichment factors confirmed the capability of algae to bio-accumulate elements from waters. Data were treated with chemometric techniques ; principal component analysis showed interesting correlations, for instance among elements of marine origin and among lithogenic ones. Hierarchical cluster analysis (HCA) highlighted differences and similarities among the investigated lakes.

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INDEX

INDICE

NOTES / NOTE