Chimica Organica

ORG-KN-01 A study of the intramolecular interactions of pyridine, thiophene, and furan with standard and perfluorinated aromatic systems in some [3,3]metapara-cyclophanes

Franco Cozzi

Dipartimento di Chimica Organica e Industriale, Universita' degli Studi di Milano, via Golgi 19, 20133 Milano Italy
franco.cozzi@unimi.it

A series of [3,3]meta(heterocyclo)paracyclophanes containing pyridine, thiophene, and furan residues have been synthesized as model compounds for a study of the non-bonding interactions between aromatic and heteroaromatic systems. In these derivatives the heterocyclic rings have been connected through two CH_2SCH_2 bridges to the para positons of a standard benzene ring or of its tetrafluorosubstituted analog. These compounds show enough conformational flexibility to allow the easy flip of the heteroaromatic ring over the benzene platform, a motion that makes the two rings adopt parallel stacked, parallel offset, and hedge-to-face relative dispositions. However they also are rigid enough to feature energy barriers to the interconversion process sufficiently high to be experimentally determined.

The study of the static and dynamic behavior of these model systems has been carried out by a combination of variable temperature NMR and X-ray spectroscopy, and computational methods. It was discovered that the interaction between the heterocyclic and the aromatic rings strongly depends on steric factors and can only partially be rationalized on the basis of polar factors (the polar/π effect).

ORG-KN-02 Dye-Sensitized and Polymeric Bulk Heterojunction Solar Cells: New Generation Organic and Hybrid Materials and Devices

Alessandro Abbotto

[a] Department of Materials Science and Milano-Bicocca Solar Energy Research Center - MIB-Solar, University of Milano-Bicocca, Via Cozzi 53, I-20125, Milano, Italy
alessandro.abbotto@ unimib.it

The Sun is by far the most abundant and cheap source of energy to keep pace with the growing energy demand. Thus, capture of sunlight has attracted an increasing interest in the scientific community. New generation thin film organic and hybrid photovoltaic (PV) technologies - dye-sensitized (DSC) and polymeric bulk heterojunction solar cells (OPV) - own a great potential in terms of low cost-performance trade-off, future development, and scale up to market.
Here we review our activity over the past few years on new generation PV materials and devices. We will describe organic (multibranched polar dyes) and organometallic (polypyridine and cyclometallated complexes) DSC sensitizers, highlighting superior optical and photovoltaic properties,[1] and polymeric electrolytes for quasi-solid-state devices.[2] We have investigated a new family of heteroarylene-vinylene donor-acceptor low-bandgap semiconducting polymers, reaching optimal photophysical and electronic properties closely matching optimized materials-design rules for OPV.[3] Finally, we will present our activity in the fabrication of organic and hybrid PV devices in the recently established research center MIB-Solar, in close interaction with industry.[4]

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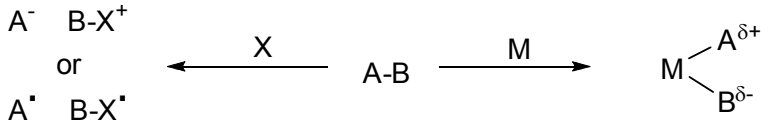
ORG-KN-03 Why not the real thing? Generating high-energy intermediates by photochemical means.

Maurizio Fagnoni, Elisa Fasani, Stefano Protti, Davide Ravelli and Angelo Albini

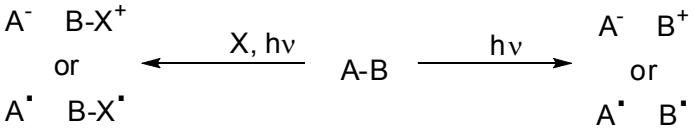
Dipartimento di Chimica, Università di Pavia, v. Taramelli 12, 27100 Pavia, Italy
angelo.albini@unipv.it

The key to most synthetic methods is the generation of a high energy intermediate, typically by homo/heterocleavage of a bond or its weakening, as is the case for the oxidative addition to metal ions.



This either introduces some limitation in the choice of the reagents and in the reaction conditions, or leads to a complexed or in some way stabilized intermediate. As an example, homolytic cleavage is limited to weak bonds, e.g. C-I bonds, and in the ensuing radical reaction a chain carrier is required. Likewise, a metal-complexed fragment may have some cationic character but is very far from a free cation.

In contrast, photochemical excitation or interaction with an excited catalyst via a non-chain process (stoichiometric in photons, although the catalyst is not consumed) exploits the large amount of energy of excited states for arriving at 'the real thing', e.g. free radicals or free ions. And this occurs under unparalleled mild and extremely versatile condtions.



In recent years we have explored two families of such reactions, involving respectively the heterolytic fragmentation of phenyl halides and esters and hydrogen transfer from aliphatic derivatives.

Some examples of the selective synthetic processes obtained and their rationalization based on kinetic data will be presented in order to define the scope and the peculiarity of the method that realizes the 'green' potential of photochemistry in synthesis.

ORG-KN-04 Nitro Compounds and One-Pot Processes: Useful Combination in Organic Synthesis

Alessandro Palmieri

School of Science and Technology, Chemistry Division, Università di Camerino, via S. Agostino 1, 62032, Camerino (MC) – Italy.
alessandro.palmieri@unicam.it

The formation of new carbon-carbon and carbon-heteroatom bonds is the core of organic synthesis, and in this sense, the development of new methodologies, is an essential branch of this science. At the same time, particularly in the last years, there is a diffuse and general request to study new processes that are not only focused on the efficiency of the reaction, but also on their environmental impact. This aspect was rationalized with the "Twelve Principles of Green Chemistry", which are the generally accepted guideline to develop the new eco-sustainable processes [1].

In this context, the one-pot reactions well fit with the green chemistry principles. In fact, a reactant is subjected to successive chemical reactions in just one reactor, avoiding the tedious and expensive work-up and purification of the intermediates, thus saving resources and time [2].

Nitro compounds, thanks to their chemical reactivity, such as the possibility to generate stabilized carbanions under mild reaction conditions, the opportunity to convert the nitro group into other functionalities, or exploit its behavior as a leaving group, have been involved with success, as building blocks in a variety of one-pot processes. In particular we focused our attention to the synthesis of important homo-, heterocycles and other valuable fine chemicals [3].

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ORG-KN-05 Predicting NMR spectra of natural substances by DFT calculations as a tool for structure determination

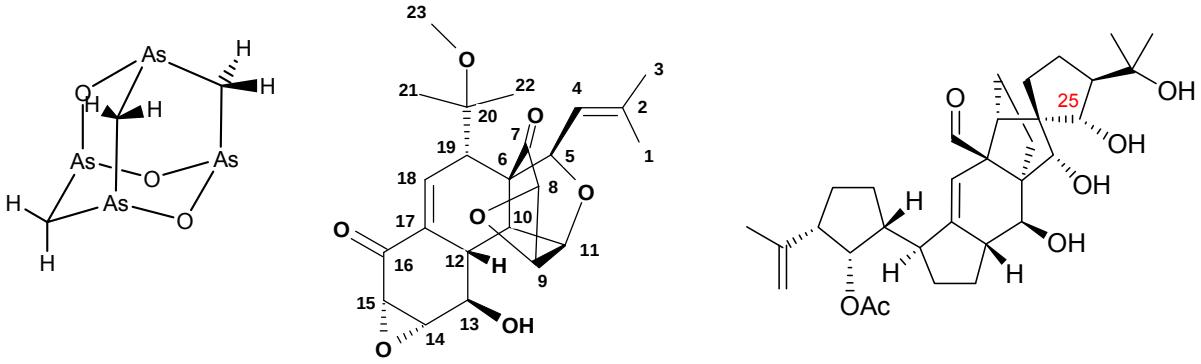
Alessandro Bagno[a]

[a]Department of Chemistry, University of Padova, via Marzolo 1 – 35131 Padova (Italy)
alessandro.bagno@unipd.it

Natural sources supply a fascinating variety of molecules having intricate structures and unusual functionalities. NMR spectroscopy has become a staple methodology for the determination of such complex molecules; however, despite steady technical advancements, this information may not lead to an unambiguous molecular structure. As a result, it is not unusual to see "structure revisions" where a proposed molecular structure is challenged in view of more compelling arguments (often, total synthesis).[1] The conclusive proof of structure is commonly accepted to be the match between the NMR spectrum of the unknown species and of a species deriving from total synthesis (quite often, not a trivial task).

On the other hand, if the NMR spectrum of a molecule whose structure is certain were available, one could work on the problem backwards – from molecular structure to NMR spectrum rather than vice versa as is normally done, which requires *a priori* knowledge of the chemical shifts and coupling constants for all spins of interest.

Density-functional theory (DFT) methods have enabled such computations with great accuracy. Thus, the scope and application of DFT calculations will be presented in several case histories concerning natural substances,[2] including arsenicin A,[3] hexacyclinol [4] and vannusal B.[5]



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ORG-KN-06 L'eccellenza italiana nella produzione dei principi attivi farmaceutici

P. Allegrini

ORG-KN-07 TWENTY FIVE YEARS OF EXPERIENCE AND SUCCESS IN CHIRAL SEPARATION SCIENCE.

Francesco Gasparrini
Dip. di Chimica e Tecnologie del Farmaco, Università di Roma "Sapienza", P.le A. Moro 5, 00185 Roma, Italy.
francesco.gasparrini@uniroma1.it

Chiral molecules are currently at the forefront of strategies for the development of safer, more effective, drugs.
The enantiomers of chiral drugs show significant differences in their activity, pharmacokinetics, pharmacodynamics and potential adverse reactions. This in turn has led stereoselective chromatographic separations becoming an important technique in this area, so several Enantioselective HPLC methods (EHPLC) have been successfully developed in recent years.
Analytical techniques relying on chiral stationary phases (CSPs) are preferred as they offer specific advantages over indirect methods.
An overview is presented of the experimental results obtained by our group in the design, realization and applications of HPLC enantioselective stationary phases based on surface linked selectors.
Recent developments in this area relate to the preparation and applications of very small-particle (sub-2 μm) enantioselective packing materials incorporating the well known Welk-O1 selector (Ultra Fast-*subminute*-EUHPLC).
In addition to chiral phases with a "brush-type" architecture incorporating small to medium-sized selectors, chiral polymeric materials are extensively employed for the preparation of chiral stationary phases for HPLC applications.
A new type of HPLC chiral stationary phases has been realized by the covalent attachment of chiral polymers to mesoporous silica particles. The *"grafting-from approach"*, in which the polymerization process starts from the silica surface, was used to produce a thin, densely packed and ordered layer of chiral polymeric chains (Poly-Brush-DACH-ACR, P-CAP). [1]
A further class of innovative CSPs, incorporating highly preorganized, receptor-like, chiral macrocyclic selectors, was prepared by our group. These silica-bound selectors show unprecedented enantioselection for small peptidic compounds. These materials are well suited for the study of molecular recognition mechanism at receptorial level and featuring extreme enantioselectivity value.
Finally several successful applications of DHPLC in the study of stereodynamic process (enantiomerization, diastereomerization etc.) will be shown.

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ORG-KN-08 Sugars in Biomedicine: ideas, results and perspectives

F. Nicotra

Dipartimento di Biotecnolgie e Bioscienze, Università degli Studi di Milano-Bicocca, Piazza della Scienza 2, 20126 Milano, Italy
Francesco.nicotra@unimib.it

The structural feature of sugars: diversity, polyfunctionality and structural rigidity, make this class of compounds a unique instrument for nature and synthetic chemists. It is now well established that most biomolecular recognition phenomena involve carbohydrates, and disfunction of such processes often leads to relevant pathologies such as cancer.
Glycochemistry is therefore a field of wide interest in biomedicine and a big effort must be performed by chemists to explore new opportunities [1]. Beside the idea to generate agonists or antagonists of glycidic structures involved in pathological processes, sugars can be used as scaffolds to generate libraries of potential drugs, exploiting the diversity and structural rigidity, or can be incorporated in more complex bioactive structure in order to modulate the pharmacokinetic properties .
Furthermore, conjugation of sugars to materials and nanoparticles can provide them properties of impressive biomedidical interest.
Examples of the exploitation of sugars in biomedicine, such as the finding of a dansyl-C-glucoside preventing septic shock [2], the decoration of nanoparticles with glycofused polycyclic compounds for Alzheimer's disease therapy, the generation of glyco-decorated smart biomaterials for tissue engineering [3,4], will be presented end the future perspectives will be discussed.

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ORG-KN-09 A Few Good Reasons to Love the Chemistry of Natural Products

G.Vidari

Dipartimento di Chimica, Via Taramelli 10, 27100 Pavia
e-mail: vidari@unipv.it

Mother Nature still provides organic chemists with a multitude of attractive challenges stimulating different research activities related to the basic and applied sciences of natural products. In this talk the author shall give a brief account of his multidecennial scientific activity in the field. This comprises: the isolation and characterization of new compounds i) from plants collected in extra European countries (Ecuador, Cameroon, Kurdistan) ii) from Italian Basidiomycetes and iii) from insects; iv) the determination of the different biological properties of isolated compounds and their role in the chemical defence system of the producing organisms; v) the functional and structural modification of various active products; vi) the stereoselective total synthesis of monoterpenoids, iridoids, sesquiterpenes, triterpenes, alkaloids, prostaglandins, isoprostanoids, fragrance components. These synthetic activities enabled us to clarify some aspects of the relationship between structure and odour properties of important perfume components, as well as to determine the biological significance of metabolites formed by ROS oxidation of PUFAs occurring in plant tissues and human neuronal membranes. These compounds thus emerged as biomarkers and possible mediators of the so called "oxidative stress", to which severe human diseases are linked. From a stricter chemical point of view, new synthetic methods, based in the chemistry of Si, Pd, B, Re, and Au derivatives, as well as new examples and applications of the Meyer-Schuster rearrangement, and stereoselective biomimetic cyclization and Diels-Alder reactions, have been developed in these studies.

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ORG-KN-10 Mass Spectrometry and the Attractive World of Secondary Metabolism

Francesco De Angelis, Samantha Reale
Dipartimento di Chimica, Ing. Chimica e Materiali, Università dell'Aquila
e-mail: francesco.deangelis@univaq.it

The chemistry of natural organic compounds has always elicited the interest of the researcher, and in the XIX century it was the necessary early base for the establishment of organic chemistry as a separate discipline. Nowadays many of the remarkable advances in this area rely upon specialized spectroscopic techniques which, besides being a sophisticated but relatively easy way for structure elucidation, also allow a deep insight into the most intriguing aspects of the metabolic processes. One of these is advanced mass spectrometry, in its more recently developed configurations like Electrospray Ionization (ESI) and Matrix Assisted Laser Desorption Ionization (MALDI). At the same time, also, very sensitive and selective extraction techniques like Solid-Phase Micro-Extraction (SPME), coupled with the long established GC-MS, are successfully exploited for the study of tiny quantities of secondary metabolites, like those present in tissue fragments and secreting glands of living, small organisms.

Some cases, which have engaged our research group as part of a long lasting interest in this field, will be addressed in the course of the lecture. One Dufour gland producing trial and sexual pheromones, directly resected from one ant [1], or also one leaf fragment from artemisinin-rich (antimalarian drug) *Artemisia annua* cultivars [2], once submitted to SPME-GC-MS released their volatile components giving information on their nature and activity, eventually. The study by ESI-MS of a new microperoxidase from an aquatic microorganism gave information on its oxido-reductive role [3]. Finally an ESI-MS and MALDI-MS approach to *in vitro* produced lignins [4] and melanins [5] were of paramount importance for further understanding the biosynthetic pathways involved in the production of these complex natural biopolymers.

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ORG-OR-01 Oxazolidin-2-one Based Foldamers for the Formation of Supramolecular Materials

Claudia Tomasini[a]

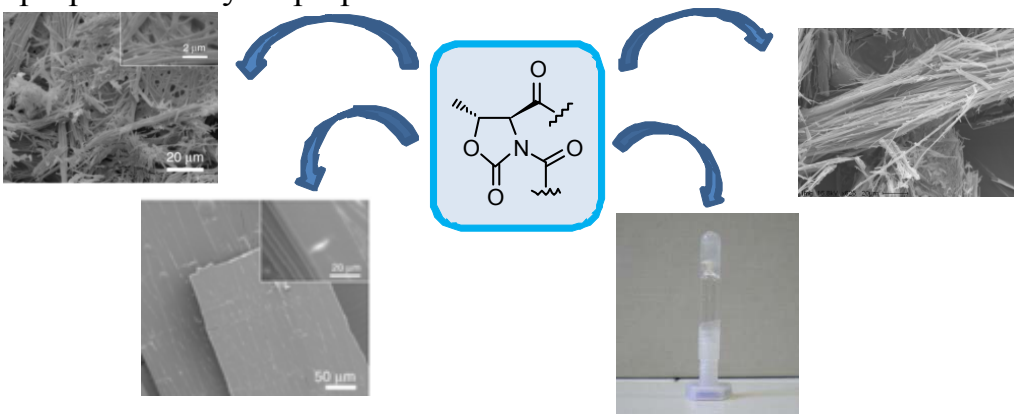
[a] Dipartimento di Chimica "G. Ciamician", Alma Mater Studiorum Università di Bologna, Via Selmi 2, 40126 Bologna, Italy

claudia.tomasini@unibo.it

Foldamers are artificial molecules able to get organized in well defined secondary structures, such as helixes, β-sheets and turns. The essential requirement for an oligomer to be included in the foldamer family is to possess a well defined, repetitive secondary structure, imparted by conformational restrictions of the monomeric unit. These compounds may be composed of any kind of subunits, but most of them contain unusual amino acids and/or aromatic units.

We have recently studied the synthesis, the conformational analysis and the application as supramolecular materials of foldamers containing the 4-carboxy oxazolidin-2-one unit or related molecules, where an imido-type function is obtained by coupling the nitrogen of the heterocycle with the carboxylic acid moiety of the next unit. The imide group is characterized by a nitrogen atom connected to an endocyclic and an exocyclic carbonyl which tend to adopt always the *trans* conformation. As a consequence of this locally constrained disposition effect, these imide-type oligomers are forced to fold in ordered conformations, such as PPII helixes, β-band ribbon spirals, β-sheets and β- or γ-turns and a wide variety of unusual secondary structures are obtained from hybrid foldamers.

In the solid state, some of these compounds form supramolecular materials, such as fibers, layers and gels, that may be used for several applications. The synthetic approach is highly tunable with endless variations, so, simply by changing the design and the synthesis of the foldamer, a supramolecular material with the required properties may be prepared "on demand".



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ORG-OR-02 Ionic Self Assembly in the Design of Fluorinated Ionic Liquid Crystals (ILCs).

Ivana Pibiri,[a] Giacomo Saielli,[b,c] Valerio Causin,[b] Antonio Palumbo Piccionello, [a] Andrea Pace, [a] Silvestre Buscemi.[a]

[a]Dipartimento di Scienze e Tecnologie Molecolari e Biomolecolari - Sez. Chimica Organica "E. Paternò" - Università degli Studi di Palermo, Viale delle Scienze Parco d'Orleans II , Ed. 17, 90128, Palermo, Italy
[b]Dipartimento di Scienze Chimiche - Università di Padova, Via Marzolo, 1 - 35131, Padova Italy
[c]Istituto per la Tecnologia delle Membrane del CNR, Sezione di Padova, Via Marzolo, 1 - 35131, Padova Italy
pibiri@unipa.it

Ionic liquid crystals are a class of compounds containing anions and cations, that combine the properties of liquid crystals and ionic liquids[1].
In the conventional design of ionic liquid crystalline compounds, an ionic core is connected with mesogenic groups *via* chemical covalent bonding . Alternatively, in ionic compounds, strong electrostatic interactions between cation and anion can be used to build up liquid crystalline order at supramolecular level. This general approach, called ionic self-assembly (ISA), allows one to create ionic phases and mesophases with highly organized supramolecular order [2].
In this context, a new series of fluorinated ionic liquids (ILs) and ionic liquid crystals (ILCs) was obtained starting from perfluoro-alkylated carboxylic acids and 1,2,4-oxadiazolyl-pyridine units (Figure 1). Their thermotropic properties were investigated by combined differential scanning calorimetry and polarized optical microscopy.

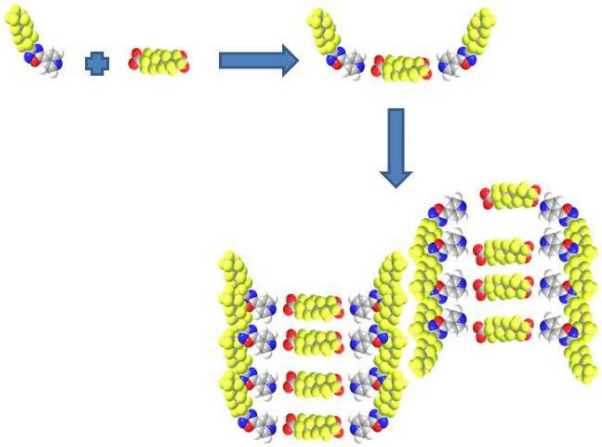

Figure 1.

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ORG-OR-03 Halogen Bonding: A new strategy for pharmaceutical co-crystals

Giancarlo Terraneo,[a,b] Michele Baldrighi,[a] Serena Biella,[a,b] Pierangelo Metrangolo,[a,b] Tullio Pilati,[a] Giuseppe Resnati,[a,b] Marco Saccone [a]

[a] NFMLab- Department of Chemistry, Materials and Chemical Engineering, ''Giulio Natta'', Politecnico di Milano, Via L. Mancinelli 7, 20131 Milan, Italy.

[b] CNST-IIT@POLIMI, Via Pascoli 70/3, 20133 Milan, Italy.

E-mail: giancarlo.terraneo@polimi.it

A large amount of pharmacologically interesting molecules has severe difficulties to become proper drugs because of their bad characteristics in terms of water solubility and/or industrial processability. This derives from both the intrinsic properties of the molecule (logP) and the characteristics of its crystal form (shape, moisture sensitivity, etc.). From the early 90's [1] the co-crystallization of an API (Active Pharmaceutical Ingredient) with an appropriate partner (called CCF - Co-Crystal Former) has represented an original way to overcome in many cases the undesired characteristics of the API itself.

Halogen bonding (XB) [2] is a non-covalent interaction that has proven to be very robust in the creation of several supramolecular architectures [3] and in principle can be successfully used in the design of API co-crystals. Many market drugs contain halogenated APIs (*i.e.* Figure 1), and the halogenated moieties can be exploited for the formation of halogen bonds with CCFs presenting lone-pair possessing residues. In this contribution we will present the first use of halogen bonding in the formation of co-crystals involving halogenated APIs.

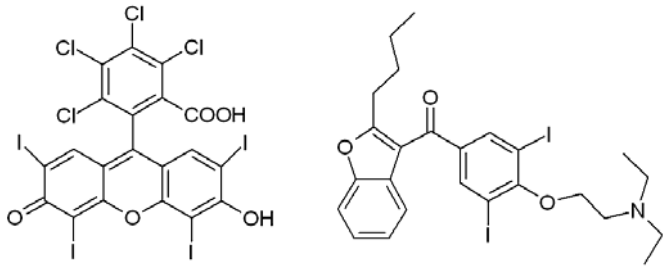

Figure 1: two examples of halogenated API: Rose bengal (left) and Amiodarone (right)

[1] J.A.Zerkowski, C.T.Seto, G.M.Whitesides., *J. Am. Chem. Soc*., **1992**, *114*, 5473.

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[3] P.Metrangolo, F.Meyer, T.Pilati, G.Resnati, G.Terraneo *Angew. Chem. Int. Ed.,* **2008**, *47*, 6114.

ORG-OR-04 Targeting Medically Relevant Lectins with Multivalent Glycocalixarenes

Silvia Bernardi, Alessandro Casnati, Francesco Sansone, Rocco Ungaro
Dipartimento di Chimica Organica e Industriale, Università degli Studi, Parco Area delle Scienze 17/A, 43124 Parma, Italy
E-mail: francesco.sansone@unipr.it

The involvement of carbohydrate-protein recognition processes in numerous pathological events make them an attractive target for the development of new therapeutic strategies. The efficiency of glycosides or mimics in the inhibition of lectin activity strongly depends not only on their proper structural features, but also on their exposition. A multivalent presentation can significantly improve their potency, as in fact often occurs at the biological level, and then help in obtaining new potential biologically active compounds.

For these reasons, since some years we are developing glycoclusters based on calixarenes functionalized with different carbohydrate units depending on the target lectin [1-3]. In particular we focused our attention and efforts towards medically relevant proteins such as plant toxins [2], bacterial lectins [1], human galectins [2,3]. Calixarenes of different sizes, conformational properties, valency and functionalized *via* chemical or chemo-enzymatic procedures with galactose, lactose, LacNAc units or oligosaccharides and mimics have shown their high efficiency and selectivity in the inhibition of different types of lectins.

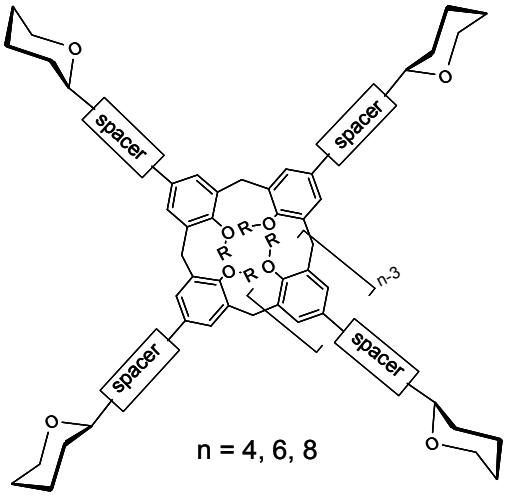


Figure. A general structure of glycocalix[n]arenes.

[1] D. Arosio, M. Fontanella, L. Baldini, L. Mauri, A. Bernardi, A. Casnati, F. Sansone, and R. Ungaro, *J. Am. Chem. Soc.*, *127*, **2005**, 3660.
[2] S. André, F. Sansone, H. Kaltner, A. Casnati, J. Kopitz, H.-J. Gabius, and R. Ungaro, *ChemBiochem*, *9*, **2008**, 1649.
[3] S. André, C. Grandjean, F.-M. Gautier, S. Bernardi, F. Sansone, H.-J. Gabius, and R. Ungaro, *Chem. Commun.*, **2011**, DOI: 10.1039/C1CC11163A.

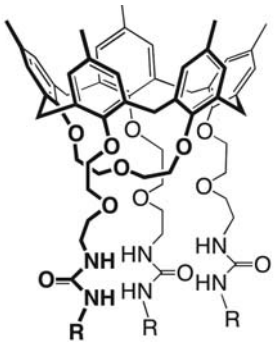
ORG-OR-05 Getting around counterion effects in the complexation of charged species

Calogero Capici,[a] Claudia Gargiulli,[a] Giuseppe Gattuso,[a] Anna Notti,[a] Melchiorre F. Parisi,[a] Sebastiano Pappalardo[b]

[a]Dipartimento di Chimica Organica e Biologica, Università di Messina, Viale F. Stagno d'Alcontres 31, 98166, Messina, Italy
[b]Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria 6, 95125, Catania, Italy
ggattuso@unime.it

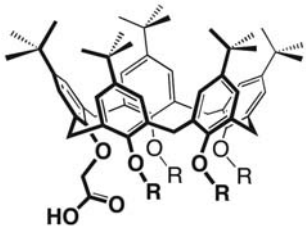
It is commonly accepted that binding of ionic species to neutral receptors is significantly affected by the nature of the counterion of the target charged guest. In low-polarity non-solvating media, saline substrates may tightly associate to form contact ion pairs. As a result, the efficiency is hampered by the reluctance of the target ion to dissociate from its counterion [1].

A first strategy to circumvent this drawback relies on the use of heteroditopic receptors. Calix[5]arene-crown-3 derivatives **1a**,**b**, endowed at their lower rim with alkyl- or arylureido pendant groups, are capable of recognizing (aryl)alkylammonium halides as receptor-separated ion pairs by binding the ammonium cation within the calixarene cavity and the halide anion within the cleft formed by the three urea groups [2].



1a R = *n*-Butyl;
1b R = 1-Naphthyl

An alternative approach takes advantage of ionizable calix[5]arenes (**2a**,**b**) that can selectively transfer protons to 'silent' (di)amines, turning them into active substrates devoid of competitive counterions. This recognition event ultimately yields internally ion-paired *endo*-cavity complexes that effectively harness ion pairing as a stabilizing interaction.



2a R = $(CH_2)_3CH(CH_3)_2$
2b R = $CH_2CO_2C(CH_3)_3$

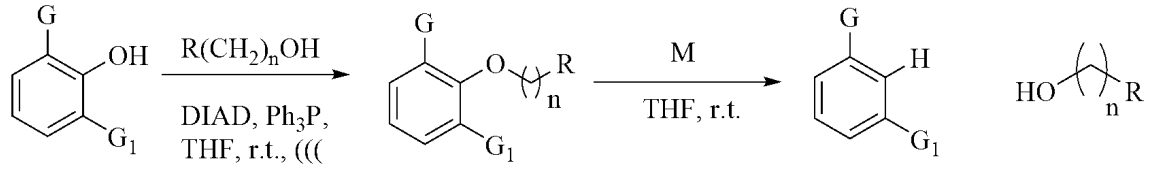
[1] G. Cafeo, G. Gattuso, F.H. Kohnke, A. Notti, S. Occhipinti, S. Pappalardo, and M.F. Parisi, *Angew. Chem. Int. Ed.*, *41*, **2002**, 2122.
[2] C. Capici, R. De Zorzi, C. Gargiulli, G. Gattuso, S. Geremia, A. Notti, S. Pappalardo, M.F. Parisi, and F. Puntoriero, *Tetrahedron*, *66*, **2010**, 4987. G. Gattuso, C. Gargiulli, C. Liotta, A. Notti, M. F. Parisi, I. Pisagatti, and S. Pappalardo, *J. Org. Chem.*, *74*, **2009**, 4350.

ORG-OR-06 New hydroxyl protecting groups removable under SET conditions

Sarah Mocci, Luisa Pisano, Ugo Azzena

Department of Chemistry, University of Sassari, via Vienna 2, 07100- Sassari (Italy)
sarahmocci@uniss.it

The protection of hydroxyl groups plays a central role in many multistep reactions, and there is a need to develop new and efficient protective groups, which can be selectively removed under mild reaction conditions.[1] In this contest, we have studied the protection of several functionalized and non functionalized alcohols, as *m*-terphenyl, *o*-biphenyl and 2,6-dimethoxyphenyl alkyl ethers. Their syntheses were performed under ultrasound stimulated Mitsunobu reaction,[2] as reported in the Scheme. We next investigated the reductive cleavage of these ethers under SET conditions and we obtained regioselective deprotection in the presence of a slight excess of Na or K metal in THF at room temperature.



G = G_1 = Ph
G = G_1 = OCH_3
G = Ph; G_1 = H

Finally we studied the protection/deprotection of chiral secondary alcohols, fucusing at first our attention on the stereochemistry of *m*-terphenyl and *o*-biphenyl ethers. The preliminary results are very interesting indeed the Mitsunobu protection as *m*-terphenyl ethers proceeds with retention of configuration, while the etherification as *o*-biphenyl ethers proceeds with prevalent inversion.

[1] (a) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, **2007.** (b) Kocienski, P. *Protecting Groups*; Georg Thieme Verlag: Stuttgart, **2003.**
[2] Lepore, S. D.; He, Y. *J. Org. Chem*. **2003**, 68, 8261-8263.

ORG-OR-07 3,4-Bis(4-ethynylphenyl)-2,5-diphenylcyclopenta-2,4-dienone based organogels: the importance of a hydroxydimethyl group

Letizia Sambri,[a] Rita Mazzoni,[b] Andrea Baschieri[a]
[a]Unibo, Dip. Chimica Organica "A. Mangini", v.le Risorgimento 4, 40136 Bologna, Italy
[b]Unibo, Dip. Chimica Fisica ed Inorganica, v.le Risorgimento 4, 40136 Bologna, Italy
letizia.sambri@unibo.it

Spontaneous self-assembly of low molecular weight molecules is a powerful tool that allows complex supramolecular structures to be built. This strategy can be successfully applied to the creation of soft materials of technological interest, and of potential application of organic materials in optoelectronics.[1]
During our studies on the synthesis of propargyl functionalized cyclopentadienones as Shvo catalysts[2] ligands, we incidentally observed the formation of an organogel from derivative **1**, which then proved to be able to gel both aromatic and polar solvents by cooling hot solutions. The process is reversible and the gel formation is accelerated by ultrasounds.
The presence of two methyl groups on the propargyl substituent proved to be essential for the gel formation, in fact when they are changed in hydrogen or phenyl groups the gelating ability of the compound vanishes.
The gels are transparent and dark red, and form fiber-like structures. VT-NMR studies furnished interesting informations on the role of the solvent on the gel formation.

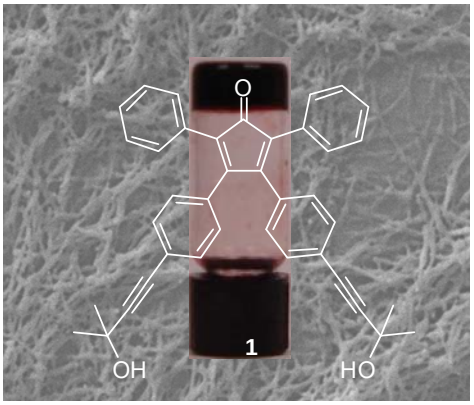


Figure 1: Compound **1** and the SEM image of the corresponding toluene xerogel

[1] a) J. W. Steed, J. L. Atwood, Supramolecular Chemistry; John Wiley & Sons, 2009; b) M. Suzuki, K. Hanabusa, *Chem. Soc. Rev*. **2009**, *38*, 967 and references.
[2] a) B. L. Conley, M. K. Pennington-Boggio, E. Boz and T. J. Williams *Chem. Rev.*, **2010**, *110*, 2294. b) L. Busetto, D. Fabbri, R. Mazzoni, M. Salmi, C. Torri, V. Zanotti, *Fuel*, **2011**, *90*, 1197.
[3] L. Sambri, R. Mazzoni, A. Baschieri, *submitted manuscript*.

ORG-OR-08 Design, Synthesis and Characterization of novel amphiphilic Guanosine-based Nucleolipids

Luca Simeone,[a] Lorenzo De Napoli,[a] Carlo Irace,[b] Antonio Di Pascale,[b] Mariangela Boccalon,[c] Paolo Tecilla[c] and Daniela Montesarchio[a]

[a] Dipartimento di Chimica Organica e Biochimica dell'Università "Federico II" di Napoli, Via Cintia, 4, 80126, Napoli, Italy
[b] Dipartimento di Farmacologia Sperimentale dell'Università di Napoli "Federico II", via D. Montesano 49, 80131 Napoli, Italy;
[c] Dipartimento di Scienze Chimiche dell'Università di Trieste, Via L. Giorgieri, 34127 Trieste, Italy
daniela.montesarchio@unina.it

Hybrid molecules formed by a lipid core covalently linked to a nucleoside, called nucleolipids, occur in eukaryotic and prokaryotic cells and display a variety of biological activities. In order to associate the pharmacological potential of nucleosides with the aggregation properties of vesicle-forming lipids, several nucleolipids have been synthesized.[1] A number of amphiphilic nucleolipids incorporating adenosine, cytosine or uridine have been described; on the contrary, very few guanosine-based nucleolipids are known and almost completely unexplored are their potential applications. Still, lipophilic guanosines play a special role in supramolecular chemistry, being able to generate peculiar architectures in organic solvents based on stacked G-tetrads, stabilized by metal ions, or, in the absence of cations, bidimensional assemblies called G-ribbons.[2-5]

We here describe the design, synthesis, biophysical and biological characterization of a library of novel sugar-modified guanosine derivatives. Decoration with fatty acid chains and diverse hydrophilic groups provided different amphiphilic guanosine analogs, here named **G1**-**G7**. CD studies, ion transport experiments through phospholipids bilayers and *in vitro* screening of their antiproliferative activity showed these amphiphiles as very interesting compounds, with distinctive properties, finely tunable as a function of the ribose substituents.[6]

[1] A.Gissot, M.Camplo, M.W.Grinstaff, and P.Berthélémy, *Org. Biomol. Chem.*, *6*, **2008**, 1324-1333 and literature cited therein.
[2] S.Lena, S.Masiero, S.Pieraccini, and G.P.Spada, *Chem. Eur. J., 15*, **2009**, 7792-7806.
[3] J.T.Davis, and G.P.Spada, *Chem. Soc. Rev.*, *36*, **2007**, 296-313.
[4] I.Yoshikawa, J.Sawayama, and K.Araki, *Angew. Chem. Int. Ed., 47*, **2008**, 1038-1041.
[5] S.Masiero, R.Trotta, S.Pieraccini, S.De Tito, R.Perone, A.Randazzo, and G.P.Spada, *Org. Biomol. Chem.*, *8*, **2010**, 2683-2692.
[6] L.Simeone, D.Milano, L.De Napoli, C.Irace, A.Di Pascale, M.Boccalon, P.Tecilla, and D.Montesarchio, *submitted*.

ORG-OR-09 Steric and Electronic Effects on the Configurational Stability of Phosphorus Centred Three - Bladed Propellers

T. Benincori,[a] V. Bonometti,[b] R. Cirilli,[c] P. Mussini,[b] M. Pierini,[d] T. Pilati,[e] S. Rizzo,[e] F. Sannicolò[f]

[a] Dipartimento di Scienze Chimiche ed Ambientali, Università dell'Insubria, via Valleggio 11, 22100, Como, Italy

[b] Dipartimento di Chimica Fisica ed Elettrochimica, Università di Milano, via Golgi 19, 20133 Milano, Italy

[c] Dipartimento del Farmaco, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161, Roma, Italy

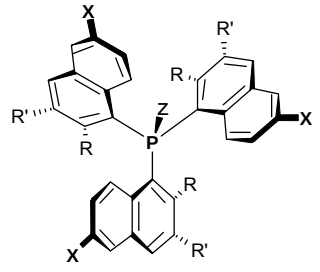
[d] Dipartimento di Chimica e Tecnologie del Farmaco, Università di Roma "La Sapienza", P.le Aldo Moro 5, 00185, Roma, Italy

[e] Istituto di Scienze e Tecnologie Molecolari, Consiglio Nazionale delle Ricerche, via Golgi 19, 20133, Milano, Italy

[f] Università di Milano, Dipartimento di Chimica Organica e Industriale and C.I.MA.I.NA., via Venezian 21, 20133, Milano, Italy

simona.rizzo@istm.cnr.it

A series of tris-aryl phosphanes and phosphane-oxides structurally designed for existing as *residual* enantiomers or diastereoisomers, bearing substituents differing in size and electronic properties on the aryl rings, have been synthesized and characterized (Figure 1). Their electronic properties have been evaluated through theoretical calculations and experimentally on the basis of their electrochemical oxidative potential determined by voltammetry. The configurational stability of *residual* phosphanes, evaluated by dynamic ^{1}H- and ^{31}P-NMR analysis and by dynamic enantioselective HPLC was found rather modest (stereomerization barriers of about 17 kcal m^{-1}), much lower than those shown by the corresponding phosphane-oxides which have been always obtained in an enantiopure state. Their helix reversal barriers could be inferred by off-column kinetics monitored by HPLC (about 28 kcal m^{-1}) on enantiopure antipodes. In accordance with calculations, an unexpectedly low barrier for phosphorous pyramidal inversion was invoked as responsible for the scarce configurational stability of the *residual* tris-arylphosphanes. A strategy for inhibit phosphorous inversion was based on the production of a frame of hydrogen bonds amongst the blades located inside the conical space of the propeller.



Z = O, lone pair X = H, OEt, NO_2, Br, SO_3H
R = OEt, OH, R' = H
R-R' = O-CH_2-CH_2-O, (*S*,*S*)-O-CHMe-CHMe-O, -$OCMe_2O$

Figure 1.

[1] T.Benincori, G.Celentano, T.Pilati, A.Ponti, S.Rizzo, F.Sannicolò, *Angew. Chem. Int. Ed.*, *45*, **2006**, 6193.

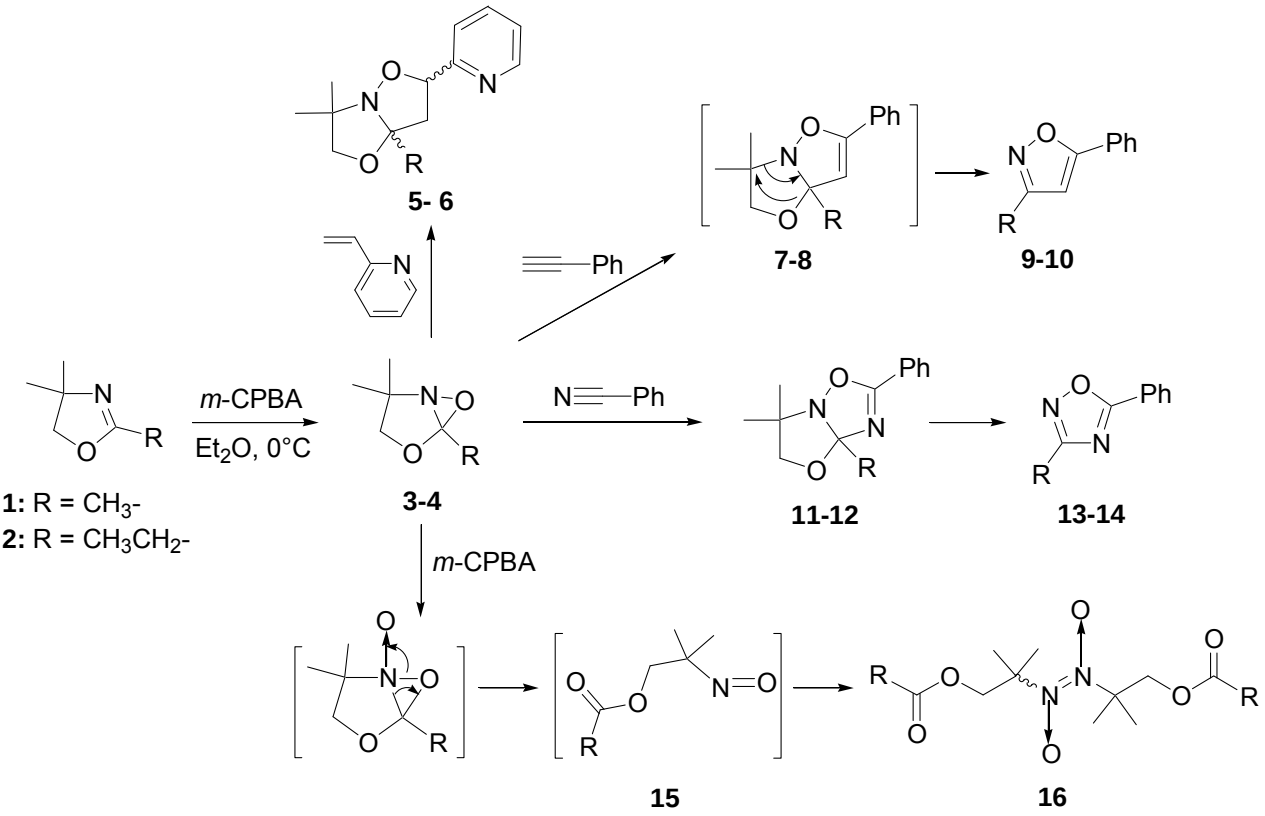
[2] T.Benincori, A.Marchesi, P.R.Mussini, T.Pilati, A.Ponti, S.Rizzo, F. Sannicolò, *Chem. Eur. J.*, *15*, **2009**, 86; *Chem. Eur. J.* **2009**, *15*, 94.

ORG-OR-10 Condensed Oxaziridines: Synthesis of Polyhetero-bicyclo and Azodioxy-Carbonyl Compounds

Serena Perrone, Francesca Rosato, Catia Granito, Luigino Troisi

Dipartimento di Scienze e Tecnologie biologiche ed Ambientali, University of Salento, Via Prov.le Lecce-Monteroni, 73100, Lecce, Italy
E-mail: serena.perrone@unisalento.it

Oxaziridines, very special three-membered heterocycles, are a group of compounds of unusually high reactivity. They are often the scaffold of more complex biologically active molecules, which have been shown to possess antitumor and mutagenic activities [1, 2].
In this contribution we report the synthesis of oxaziridines condensed with heterocycles such as oxazolines, and their reactivity with alkenes, alkynes and nitriles. In addition, in the presence of 3-chloroperbenzoic acid (*m*-CPBA), the condensed oxaziridines are further oxygenated to generate *C*-nitroso (**15**) and subsequently azodioxy-carbonyl compounds (**16**).



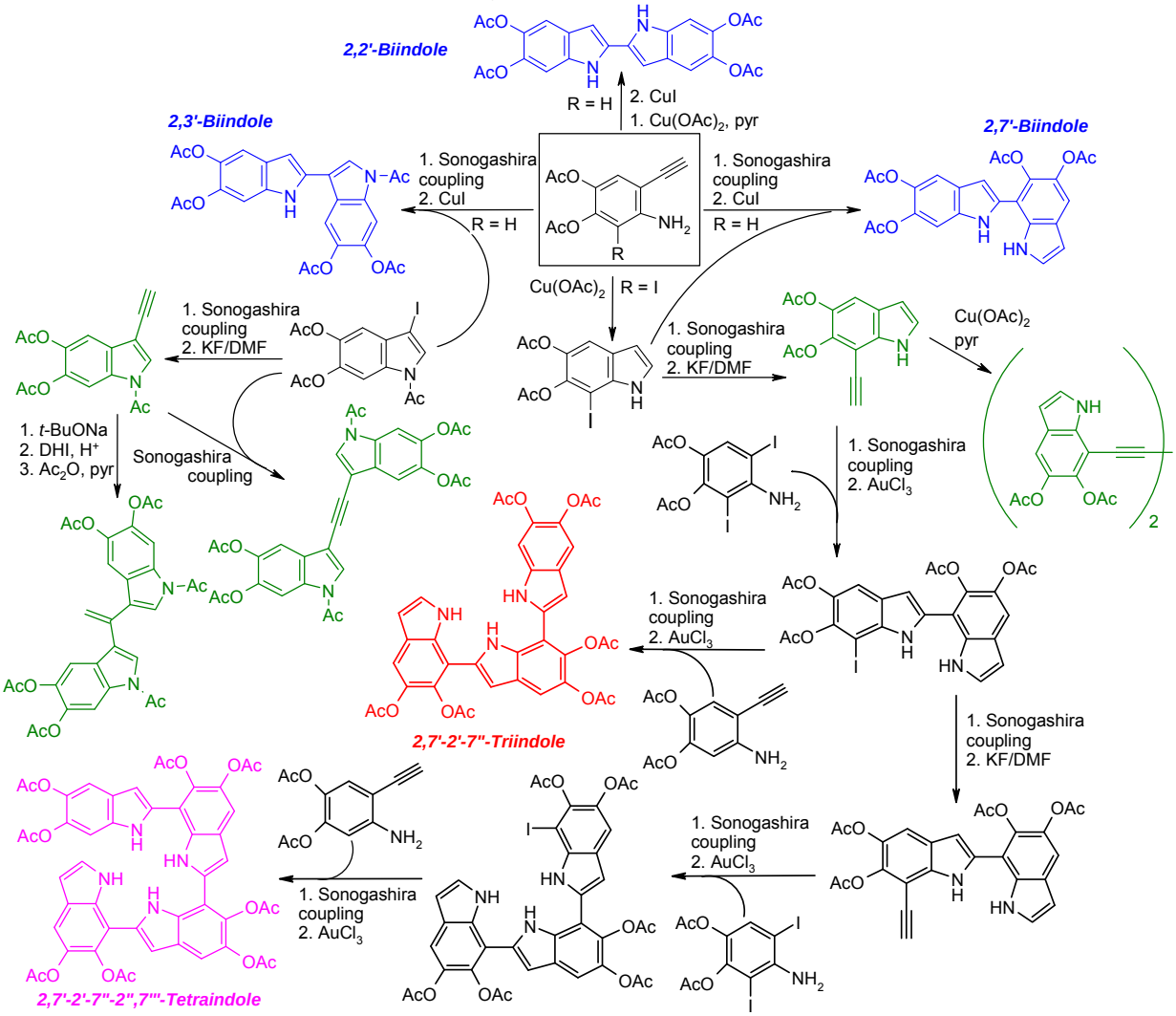
[1] Daniel, J.S.; Chatterj, T.; MacGillivray, L.R.; Gates S. *J. Org. Chem.*, **1998**, *63*, 10027-10030.
[2] Chen, H.; Murray, J.; Kornberg, B.; Dethloff, L.; Rock, D.; Nikam, S.; Mutlib, A.E. *Chem. Res. Toxicol.*, **2006**, *19*, 1341-1350.

ORG-OR-11 Alkynyl routes to 5,6-dihydroxyindole-based oligomers and functionalized π-extended scaffolds

P. Manini, A. Pezzella, A. Napolitano, M. d'Ischia

Dept. Organic Chemistry and Biochemistry, Univ. Naples Federico II, via Cinthia 4, I-80126 Naples. paola.manini@unina.it

The prospects of developing improved models of eumelanin biopolymers and/or novel bioinspired functional materials/scaffolds for application in organoelectronics have incited increasing efforts toward the rational design and synthesis of 5,6-dihydroxyindole (DHI)-based π-electron systems with tailored structural and electronic properties.[1-3] A valuable entry to this goal has derived from the exploitation of alkynyl chemistry for the assembly of novel oligomers[4,5] and the realization of π-extended systems.[6]



[1] M. d'Ischia, A. Napolitano, A Pezzella, P. Meredith and T. Sarna, *Angew. Chem. Int. Ed.*, **2009**, *48*, 3914-3921. [2] A. Pezzella, A. Iadonisi, S. Valerio, L. Panzella, A. Napolitano, M. Adinolfi and M. d'Ischia, *J. Am. Chem. Soc.*, **2009**, *131*, 15270-15275. [3] J. P. Bothma, J. de Boor, U. Divakar, P. E. Schwenn, P. Meredith, *Adv. Mat.*, **2008**, *20*, 3539-42. [4] L. Capelli, P. Manini, A. Pezzella, A. Napolitano and M. d'Ischia, *J. Org. Chem.*, **2009**, *74*, 7191-7194. [5] L. Capelli, P. Manini, A. Pezzella, and M. d'Ischia, *Org. Biomol. Chem.* **2010**, *8*, 4243-4245. [6] L. Capelli, O. Crescenzi, P. Manini, A. Pezzella, V. Barone, and M. d'Ischia, *J. Org. Chem.* **2011**, ASAP.

ORG-OR-12 Novel Organic Dyes for Photovoltaic Applications

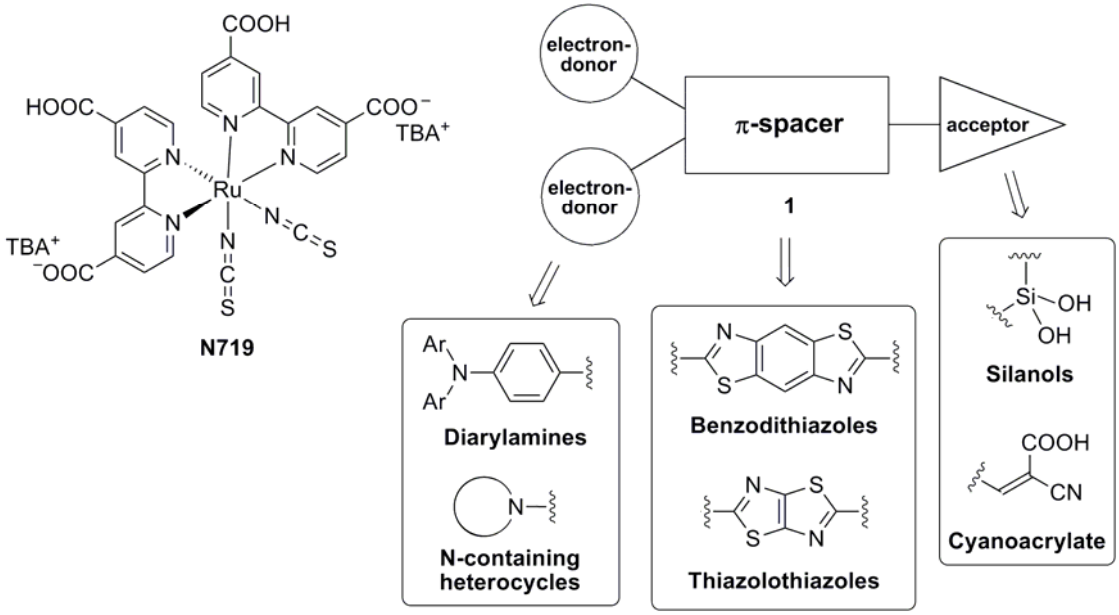
Lorenzo Zani,[a] Gabriella Barozzino Consiglio,[a] Fabio Pedna,[a] Alessandro Mordini,[a] Maurizio Taddei,[b] Riccardo Basosi,[c] Adalgisa Sinicropi,[c] Gianna Reginato*,[a]

[a]CNR-ICCOM, Via Madonna del Piano 10, 50019 Sesto Fiorentino, Florence, Italy; [b]Università degli Studi di Siena, Dipartimento Farmaco Chimico Tecnologico, Via A. Moro 2, 53100 Siena, Italy; [c]Università degli Studi di Siena, Dipartimento di Chimica, Via A. De Gasperi 2, 53100 Siena, Italy.

E-mail: lorenzo.zani@iccom.cnr.it; gianna.reginato@iccom.cnr.it.

Dye-sensitized solar cells (DSC) recently attracted much attention as promising devices for the conversion of sunlight in electric power.[1] Such cells employ dyes, which act as photosensitizers, together with a suitable inorganic semiconductor, such as TiO_2. Historically, the first class of photosensitizers employed in DSC was represented by transition metal complexes, such as the Ru-bipyridyl complex **N719**.[2] More recently, purely organic sensitizers, not containing any metal atom, have emerged as a cheap and efficient alternative.[3] Such substances are often based on a "donor-π-acceptor" architecture, featuring electron-donating and electron-accepting groups separated by a conjugated spacer.

Here, we will present some of the dyes recently prepared in our laboratories, whose general structure (**1**) is shown in the figure.



The synthesis of these compounds will be described together with the results of preliminary experiments conducted on test cells containing the novel sensitizers.

[1] Hagfeldt, A.; Boschloo, G.; Sun, L.; Kloo, L.; Pettersson, H. *Chem. Rev.* **2010**, *110*, 6595.

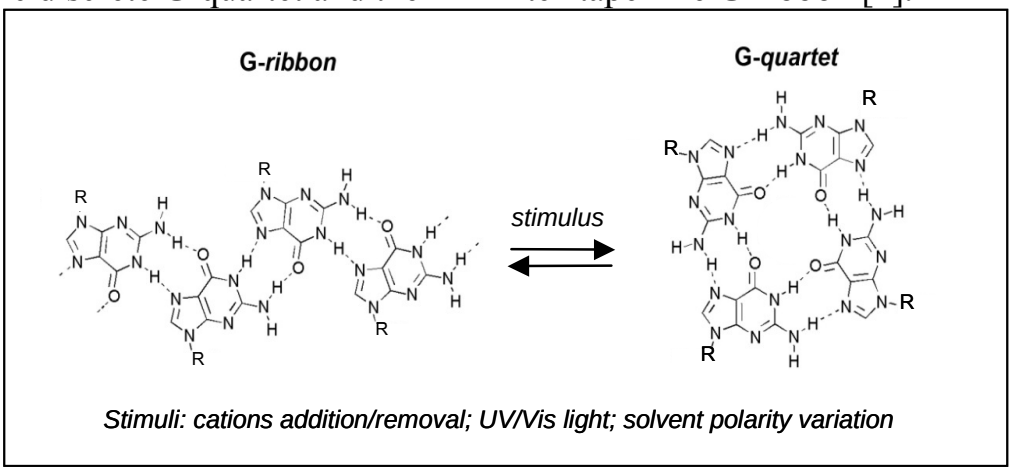
[2] (a) O'Regan, B.; Grätzel, M. *Nature* **1991**, *353*, 737

[3] (a) Mishra, A.; Fisher, M. K. R.; Bäuerle, P. *Angew. Chem. Int. Ed.* **2009**, *48*, 2474. (b) Ooyama, Y.; Harima, Y. *Eur. J. Org. Chem.* **2009**, 2903.

ORG-OR-13 Switching between supramolecular assemblies of guanosine derivatives triggered by external stimuli

Lucia Gramigna, Stefano Masiero, Paolo Neviani, Rosaria Perone, Silvia Pieraccini, Gian Piero Spada
Alma Mater Studiorum – Università di Bologna, Dipartimento di Chimica Organica "A. Mangini", Via San Giacomo 11, I-40126 Bologna, Italy
gianpiero.spada@unibo.it

Depending on the experimental conditions, lipophilic guanosines (LipoG's) can undergo different self-assembly pathways based on different H-bonded motifs, e.g. the cyclic discrete G-quartet and the "infinite" tape-like G-ribbon [1].



The switching between different supramolecular motifs have been obtained by a variety of external stimuli. A first example is represented by chemical stimuli: addition of an alkali metal ion stabilizes the G-quartet while its removal shifts the equilibrium toward the G-ribbon [2].
A second type of stimuli is represented by light: the photocontrolled self-assembly of a modified guanosine nucleobase with a photoactive unit at C8 is obtained [3] selecting the appropriate wavelength. Finally, a lipoG armed with a terthiophene unit undergoes a pronounced variation of its supramolecular organisation by changing the polarity of the solvent [4]: in chloroform the derivative assembles via H-bonding in a Guanosine directed structure, while in the more polar (and H-bond competing) acetonitrile different aggregates are observed, where the terthiophene chains are π-π stacked in a helicoidal arrangement.

[1] J. T. Davis, G. P. Spada, *Chem. Soc. Rev.* **2007**, *36*, 296
[2] A. Ciesielski, S. Lena, S. Masiero, G. P. Spada, P. Samorì, *Angew. Chem. Int. Ed.* **2010**, *49*, 1963-1966
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ORG-OR-14 Multinuclear Magnetic Resonance Spectroscopy in the Structural Investigation of Reactive Intermediates Useful in Stereoselective Synthesis

Biagia Musio and Renzo Luisi
Dipartimento Farmaco-Chimico, Università degli Studi di Bari "Aldo Moro"
Via E. Orabona, 4 – 70125 Bari, Italy
E-mail: bmusio@gmail.com

A challenging aspect in the modern synthetic chemistry, also aimed at shedding light on the reaction mechanisms, concerns the structural characterization of those "reactive intermediates" formed in planned stereoselective synthesis. At the same time, crucial parameters such as reaction time, temperature and concentration need to be faithfully checked and taken into consideration in order to improve the yields and reduce the formation of side-products. Such structural characterization and optimization can be carried out employing in a synergistic and complementary way modern spectroscopic and spectrometric techniques.
In this context, the Multinuclear and Multidimensional Magnetic Resonance Spectroscopy (MMRS) hold the potential to fulfill the gap in knowledge on the structure and dynamics in solution of special reactive intermediates such as polar organometallic derivatives, thought as "fleeting species".

In this lecture will be showed as the MMRS has been used to get insight on the structure in solution of some heterosubstituted organolithium derivatives and to get information about the dynamics at molecular level. [1]

The results coming from this investigation have found application in the development of stereoselective synthetic processes useful for the preparation of new molecular scaffolds and architectures even in highly enantioenriched form [2].

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ORG-OR-15 Multifunctional Peptide Nucleic Acids (PNA) for Alteration of Gene Expression by MicroRNA targeting

Alex Manicardi,[a] Fabio Aimi,[a] Tullia Tedeschi,[a] Stefano Sforza,[a] Rosangela Marchelli,[a] Enrica Fabbri,[b] Nicoletta Bianchi,[b] Roberto Gambari,[b] Roberto Corradini[a]

[a] Dipartimento di Chimica Organica e Industriale, Università di Parma, Parco Area delle Scienze 17/A, 43124, Parma, Italy [b] BioPharmaNet, Dipartimento di Biochimica e Biologia Molecolare, Università di Ferrara, Via Fossato di Mortara n.74, 44100 Ferrara, Italy. *E-mail: roberto.corradini@unipr.it*

Peptide nucleic acids (PNA), and their modification (Figure 1A) are extensively used for targeting mRNA in the antisense approach for the down-regulation of the expression of target genes.[1] Micro-RNA (miR) are regulatory short (19-23 bp) dsRNA which modulate gene expression of highly relevant biological functions such as differentiation, cell cycle and apoptosis, through mRNA degradation. Inhibition of miR activity by specific molecules (anti-miR, figure 1B) has been shown to be of great interest in drug development [2].

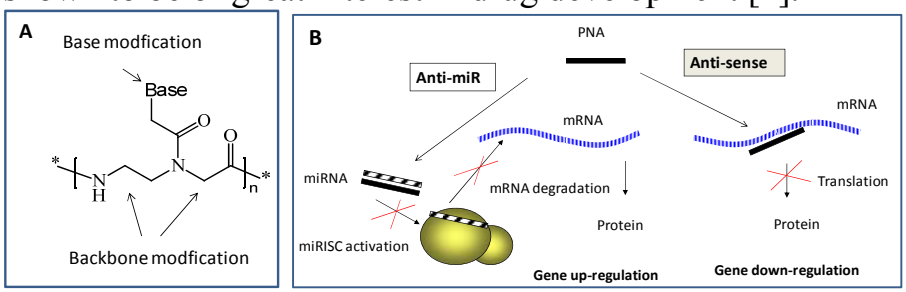

Figure 1.

In the present communication we describe the synthesis of anti-miR PNA either conjugated with a carrier peptide or bearing modified residues along the chain, PNA of high affinity and high specificity for miR210 and miR 221, involved in erythroid differentiation and tumor progression respectively were obtained. Modified PNA showed improved biovailability and effectively entered into tumor cells and exerted anti-miR acivity [2], leading to up-regulation of genes. New strategies for the elaboration of PNA structure during the solid phase synthesis either at the backbone or at the nucleobase level, thus introducing new functionalities for RNA binding or catalysis will also be described.

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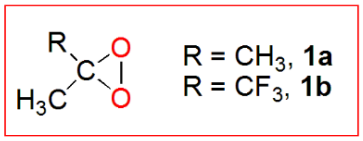
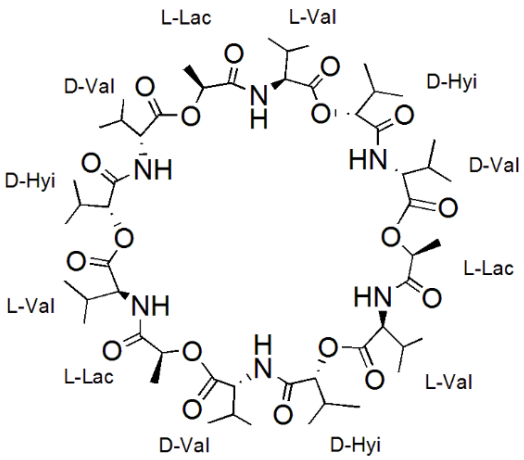
ORG-OR-16 Selective Oxidation of Natural Target Molecules using Methyl(trifluoromethyl)dioxirane

Cosimo Annese, Immacolata Fanizza, Lucia D'Accolti, Caterina Fusco, and Ruggero Curci

Dipartimento di Chmica, Università degli Studi Aldo Moro di Bari, Via Amendola 173, 70126 Bari, Italy
ICCOM-CNR, Dipartimento di Chimica, Università degli Studi Aldo Moro di Bari, Via Amendola 173, 70126 Bari, Italy
Department of Chemistry, Brown University, 324 Brook St., Providence RI, USA
annese@chimica.uniba.it

Over the past two decades, the dimethyldioxirane (DDO) (**1a**) and its trifluoro analog **1b** (TFDO) have fruitfully been employed to accomplish the selective oxyfunctionalization of natural targets such as steroids, vitamine D_3 derivatives, terpenes, as well as amino acids. Besides the extremely mild reaction conditions, dioxiranes **1** offer a number of advantages over other classical oxidation reagents, because their high reactivity is often accompanied by an outstanding selectivity.[1,2]





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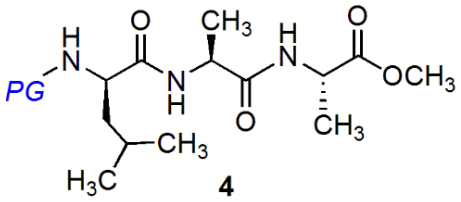

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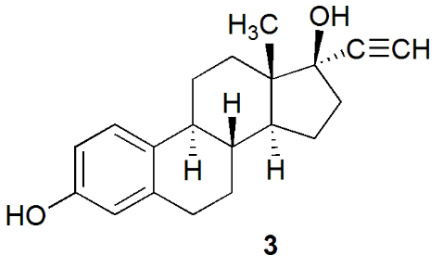

3

We now report on our current investigations in the selective oxidation of target molecules, such as valinomycin (**2**)**,** the steroid **3**, and some model peptides (**4**).

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ORG-OR-17 Water Soluble Functionalized Polymers as New ^{19}F MRI agents

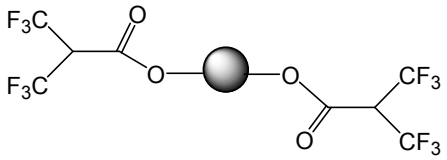
Maurizio Benaglia,[a] Marco Ortenzi,[a] Edoardo Micotti,[b] Carlo Perego,[b] Maria Grazia De Simoni[b]

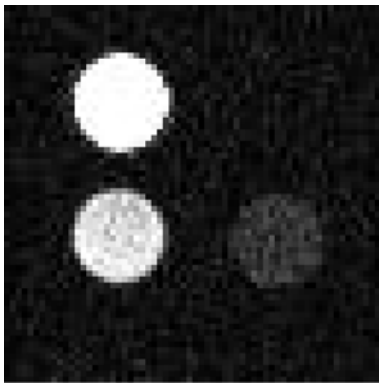
[a]Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milano, Via Venezian, 21 20133 - Milano – Italy
[b]Istituto di Ricerche Farmacologiche Mario Negri, Via La Nasa, 19 20156 - Milano – Italy
E mail: Maurizio.Benaglia@unimi.it

In "multifunctional nanomedicine" the research has been focused towards the development of novel devices that integrate diagnostic and therapeutic functions within the same platform.[1] Multifunctional nanomedicine holds considerable promise as the next generation of medicine, for example in cancer therapy, allowing for the molecular diagnosis of cancer phenotypes, customized therapy to exploit unique cancer targets, and simultaneous treatment and monitoring of therapeutic efficacy.

Our project would like to explore the development of **polymeric materials bearing a fluorinated residue suitable for ^{19}F MRI and that may further implemented with other functions,** a diagnostic or, in the future, even a therapeutic one. Because of the lack of any ^{19}F background in the body, observed signals originating from injected ^{19}F containing agent exhibited an excellent degree of specifity and merging of recorded ^{19}F images on ^{1}H images enables an exact anatomic localization of fluorinated substances as "hot spots". [2]

In a preliminary approach a commercially available polymer was employed as carrier of the fluorinated residue. Polyethylene glycol (PEG) has many positive features: it's a very cheap, atoxic, biocompatible, water soluble polymer that can be easily functionalized by well described standard experimental procedure.[3] The simple condensation of polyethylen glycol with the 2-(trifluoromethyl)-3,3,3-trifluoro-propanoic acid allowed to isolate a new material, bearing an fluorinated moiety. Two different PEGs were employed, having MW of 2000 Dalton and 400 Dalton, to afford two novel polymers, of **2310 Dalton** and **760 Dalton**, respectively, both showing a single ^{19}F signal at NMR in deuterated chloroform and D_2O; both compounds are indeed soluble in water. However when experiments of *in vitro* MR imaging were conducted only with the sample of **760 MW** it was possible to obtain a clear imaging, pointing at the importance of the fluorine content of the carrier. Different images have been obtained for three different concentration to test the sensitivity of the imaging agent (see figure on the right).





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ORG-OR-18 Protein-carbohydrate interactions at host pathogen interface

Alba Silipo

Dipartimento di Chimica Organica e Biochimica, Università di Napoli Federico II, Complesso Universitario Monte Santangelo Via Cintia 4, I-80126 Napoli, Italy
Email: silipo@unina.it

The interactions between proteins and carbohydrates are involved in important biological processes such as recognition of antigenic carbohydrates on the bacterial cell surface by antibodies or initiation of inflammatory response. Understanding of molecular recognition events in protein-carbohydrate systems is pivotal for the elucidation, at molecular level, of the events involved at the heart of biological phenomena and drug discovery process. Nuclear Magnetic Resonance (NMR) spectroscopy is a powerful method for studying protein-ligand interactions in solution. Two techniques, Saturation Transfer Difference (STD) NMR and transferred NOE [1], together provide a picture of ligand binding to a receptor. In this communication, preliminary studies on different systems of protein-carbohydrate interactions at host-pathogen interface will be reported.
By this approach we analyzed the interaction between peptidoglycan (PGN) fragments of bacterial cell wall, named muropeptides, and an eukaryotic-like Ser/Thr membrane kinase, characteristic of Gram positive bacteria. This protein contains an extracellular domain, named PASTA, capable of binding the muropeptides of PGN DAP(*meso*-diaminopimelic acid)-type released into extracellular milieu during bacterial growth [2]. The recognition PASTA-peptidoglycan is the trigger of the germination of dormant bacterial spores because it represents a signal of favorable environmental conditions.
In order to fully describe, at molecular level, this system of interaction we performed NMR experiments on the extracellular domain of kinases from two different Gram positive bacteria, *Bacillus subtilis* and *Staphilococcus aureus*, using as ligands monomeric and dimeric muropeptides deriving from the PGN DAP-type.

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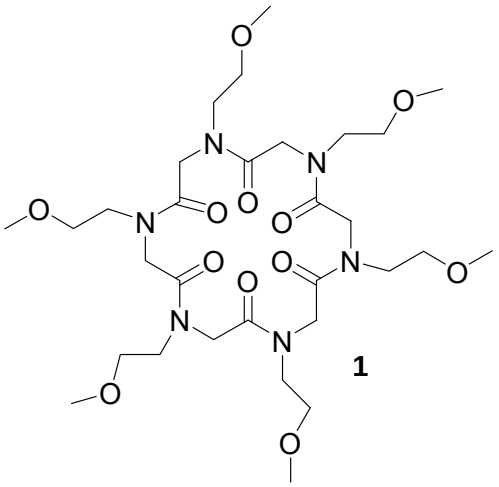
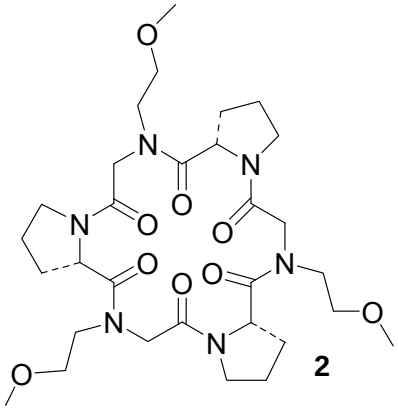
ORG-OR-19 Synthesis and Properties of Cyclic Hexapeptoids

Irene Izzo, [a] **Consiglia Tedesco,**[a] **Chiara De Cola,** [a] **Graziella Ianniello,** [a] **Giovanna Cerasuolo,**[a] **Loredana Erra,**[b] **and Francesco De Riccardis**[a]
[a] Department of Chemistry and Biology, Via Ponte don Melillo, Fisciano (SA), Fax: +39089969603; Tel: +39089969560;
[b]European Synchrotron Radiation Facility, BP 220, 38043 Grenoble, France
e-mail: iizzo@unisa.it

Peptoids, bioinspired peptidomimetics, show unique structural and physical properties. [1] The conformational ordering of their achiral polyimide backbone is dictated by stereoelectronic effects caused by *N*- (and C-) substitution and/or by cyclization. [2]
In this communication the synthesis, X-ray crystallographic investigations and complexation properties of *N*-metoxyethyl cyclic peptoids (*e.g* **1** and **2**) will be reported.



1



2

The elaboration of the linear peptoid precursors was accomplished via an expeditious mixed 'monomer', and 'submonomer' approach on solid phase. The oligomerization of the units was performed on a 2-chlorotrityl resin. Once the construction of the linear oligomers was completed, they were cleaved from the resin, and a head-to-tail macrocyclizations of the linear *N*-substituted oligoglycines proceeded smoothly giving, under high dilution conditions, the desired macrocycles. [3]
In particular for both compounds sodium complex were analyzed by X-ray crystallography, they both have all-*trans* backbone configuration, but the solid state assembly is rather different, **1** gives rise to a 1D coordination polymer, **2** to a discrete molecular complex**.**

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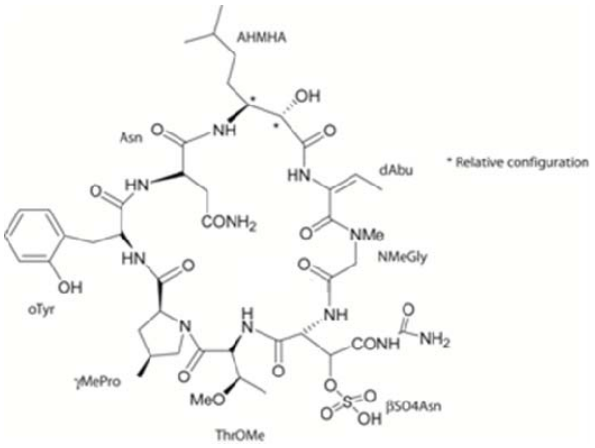
ORG-OR-20 Chemical Proteomics, a Powerful Tool in the Analysis of Perthamide C Cellular Effects

Luigi Margarucci, Maria Chiara Monti, Annalisa Vilasi, Alessandra Tosco, Raffaele Riccio, Stefano Fiorucci, Angela Zampella, Agostino Casapullo

Dipartimento di Scienze Farmaceutiche e Biomediche, Università degli Studi di Salerno, Via Ponte don Melillo, 84084 Fisciano, Italy
E-mail: casapullo@unisa.it

The identification of the biological effects of natural products is becoming crucial to better understand the molecular mechanism of ligand-protein interactions. This is also an essential information to assist the rational development of novel drugs with greater selectivity and/or potency. Here, we describe the application of mass spectrometry-based chemical proteomics to the analysis of perthamide C effects on a cell proteome. Perthamide C is a novel cyclic octapeptide isolated from the polar extract of *Theonella swinhoei*, a marine sponge source of bioactive peptides with interesting biological activities.[1] The combination of mass spectrometry with affinity purification and 1D/2D gel electrophoresis opened the way to a comprehensive picture of perthamide C-induced proteome changes. These results allowed us to speculate on an anti-apoptotic effect of the marine metabolite, mediated through its involvement in several cellular pathways, as finally confirmed by *in vitro* and *in cell* assays.



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ORG-OR-21 Smart Biomaterials for biotechnologies

L. Cipolla, L. Russo, D. Bini, and L. Gabrielli

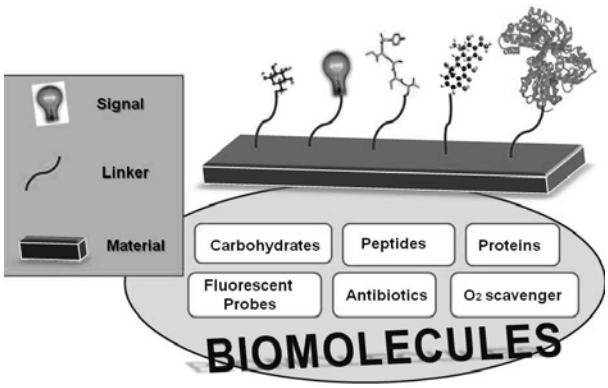
Dipartimento di Biotecnologie e Bioscienze, Università degli Studi di Milano-Bicocca, Piazza della Scienza 2, 20126 Milano, Italy
laura.cipolla@unimib.it

Decoration of nanostructured materials is relevant in a wide variety of applications, including novel tissue engineered scaffolds and devices, site specific drug delivery systems, non-viral gene carriers, biosensor and screening systems, and clinical bio-analytical diagnostics and therapeutics [1]. Through the modification of material surfaces one can control and tailor their properties in a predictable manner, and impart them with biological properties and chemical functionalities to better suit their applications. We wish to report our recent investigations on materials decoration with novel chemical approaches [2-5]. These approaches have been tested taking into accounts different key-points:

a) Chemical nature of the material: organic of natural origin (collagen), polymeric (PP and PCL), inorganic (hydroxyapatite);

b) Chemistry applied to the decoration step: plasma functionalisation, diazo-transfer, silanisation, direct linkage to material functional groups, Huisgen-cycloaddition;

c) Molecules for the (bio)decoration: the different functional groups introduced on material surface are used for the covalent immobilization of small organic molecules.



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Acknowledgments. We gratefully acknowledge Fondazione Cariplo-projects 2010-0378 and 2008/3175, MIUR-project FIRB RBPO68JL9, for financial support.

ORG-OR-22 Diversity-oriented synthesis and chemical genetics to address lead identification in drug discovery

Andrea Trabocchi,[a] Irene Stefanini,[b] Duccio Cavalieri,[b] Antonio Guarna[a]

[a] Department of Chemistry "Ugo Schiff", University of Florence, via della Lastruccia 13, Sesto Fiorentino, Florence, Italy
[b] Department of Pharmacology "Mario Aiazzi Mancini",University of Florence, viale Pieraccini 6, 50139, Florence, Italy
andrea.trabocchi@unifi.it

Chemical genetics is a powerful approach for selecting small molecules possessing the ability to induce a biological phenotype or to interact with a particular gene product, and it is an emerging tool for lead generation in drug discovery. Accordingly, there is a need for robust and versatile synthetic processes capable to generate complex and diverse molecular collections, and Diversity-Oriented Synthesis (DOS) of small molecules is the concept of choice to give access to new chemotypes bearing high structural diversity. Moreover, biological evaluation using cell growth as a phenotypic screening on *Saccharomyces cerevisiae* deletant strains is a powerful tool to identify new chemotypes as hit compounds in the discovery of new antifungal and anticancer agents, and also in the dissection of their mode of action.

Our efforts in this field are focused on the generation of diversity-oriented molecular probes of peptidomimetic nature, and on the evaluation of their ability to induce phenotypic effects with functional implications on a panel of strains of the budding yeast *Saccharomyces cerevisiae* [1]. Recently, we succeeded in generating morpholine-based scaffolds from amino acid and sugar derivatives in a diversity-oriented fashion, and in the successful application of a library of these molecules on a panel of *Saccharomyces cerevisiae* strains, which provided the identification of new chemotypes involved in mitochondria metabolism and respiration [2].

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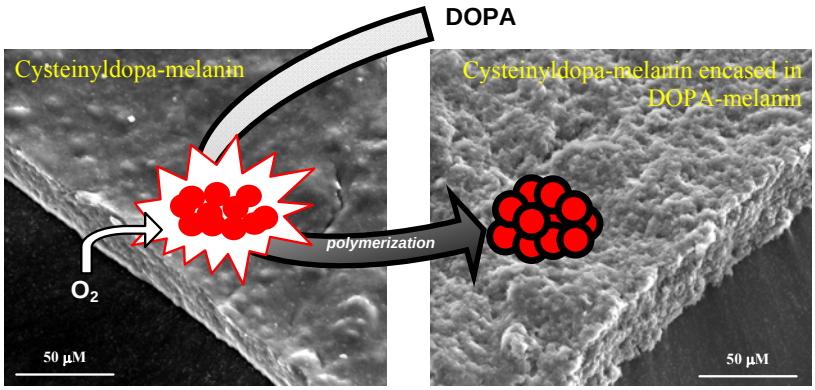
Acknowledgements: financial support from Fondazione Roma and CINMPIS.

ORG-OR-23 A melanin-inspired system promoting aerial polymerization of catecholamines and deposition of nanosized coatings encasing the redox active core: new opportunities for preparation of functional biomaterials.

Alessandra Napolitano,[a] Giorgia Greco, [a] Lucia Panzella, [a] Gennaro Gentile,[b] Maria Emanuela Errico, [b] Cosimo Carfagna,[b] Marco d'Ischia [a]

[a] Dept Org Chem Biochem, Univ Naples "Federico II", via Cinthia 4, I-80126, Naples, Italy.; [b] Natl Counc Res - Inst Chem Technol Polymer, via Campi Flegrei 34, I-80078 Pozzuoli (NA), Italy
E-mail: alesnapo@unina.it

In recent years the opportunity of translating current knowledge of the properties and mechanisms of formation of phenol biopolymers to the design and implementation of innovative functional materials has increasingly been appreciated. Of particular interest are the polymers inspired to eumelanins, the pigments responsible for dark hues of human hair and skin, the pheomelanins typical of the red hair phenotypes, and the black polymers produced by oxidation of dopamine and related catecholamines, the main component of the neuromelanin of substantia nigra of human brain.[1] Melanin precursors, such as DOPA, dopamine and norepinephrine have been used for the preparation of bioactive materials, multifunctional coatings and adhesive films that stick to organic and inorganic surfaces, e.g. silica, dimethyldiethoxysilane emulsions, nanotubes, and even cellular surfaces, for preparation of nanostructures and neuroactive biomaterials.[2] In most of these surface modification processes, however, catecholamine polymerization and coating is induced through a slow autooxidation process subject to substrate and oxygen availability as main determinants of coat thickness. [3]



Herein, we disclose an unprecedented biomimetic chemical system promoting aerial catecholamine polymerization and leading to novel core-shell materials. The new system is built upon the discovery that finely suspended melanin obtained from 5-*S*-cysteinyldopa (CD), a synthetic model for pheomelanins, markedly accelerates the oxygen-dependent polymerization of DOPA and other catecholamines at pH 7.4 leading to deposition of black eumelanin-like polymer

encapsulating the CD-melanin active core. SEM analysis indicated a close similarity of the morphology of the resulting pigment with that of a pure DOPA-melanin sample suggesting encasing of the CD-melanin component into the DOPA-melanin coating. Chemical degradation experiments indicated that, while most of the CD-melanin was readily solubilized and released from the filter by alkaline washings, no CD-melanin was detected in the washings of the DOPA melanin-coated sample, confirming the presence of an insoluble DOPA-washing steps. The oxidative polymerization process is likely mediated by key benzothiazine units through a redox interaction mechanism occurring on the surface of the finely suspended pro-oxidant polymer. These results broaden the field of application of melanin inspired biopolymers indicating methodologies for improving and accelerating coating formation. The presence of cysteine in the CD pigment precursor may allow to use protein residues as an anchor for DOPA to create an encapsulation and functionalization of cell surface with covalently bonded, artificial shells.

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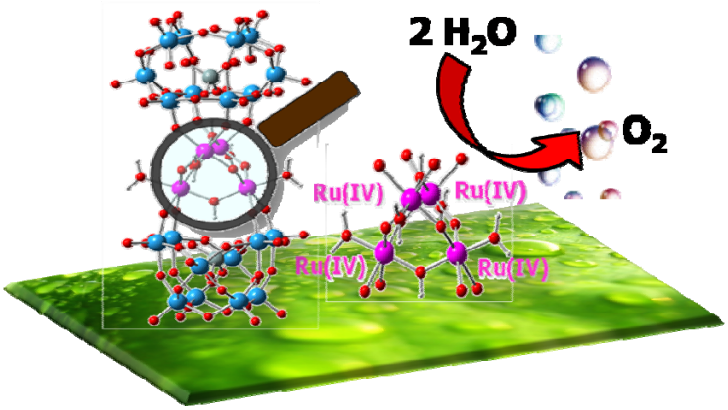
MS-IL-01 Shaping the Beating Heart of Artificial Photosynthesis: Oxygenic Nano-Hybrid Interfaces

Marcella Bonchio[a]

[a] Istituto per la Tecnologia delle Membrane, ITM-CNR sezione di Padova, c/o Dipartimento di Scienze Chimiche, Università degli Studi di Padova, Via Marzolo, 1, 35131 Padova.
e-mail: marcella.bonchio@unipd.it

Water oxidation is the crucial stage in the chemical and molecular sequence of photosynthesis, designed by Nature to convert solar light into chemical energy. The artificial "off-leaf" transposition is a major goal of energy research, aiming at the continuous production of hydrogen as solar fuel, through the photo-catalytic splitting of H_2O.[1] Success in this task primarily depends on the interplay of light-activated multi-electron oxidation and reduction routines and on the invention of stable and robust water oxidation catalysts, liberating oxygen with fast rates, high quantum yield, and long-term activity. Indeed, the Achilles' heel of the chloroplast assembled architecture stems from the intrinsic weakness of the functional components chosen by Nature. The artificial perspective should find its roots on more solid materials. The vision here is to transcend the natural wonder, while being inspired by its key guidelines along the design of a functional system/device, with superior operation stability. We will highlight a recently discovered pathway carved within the class of inorganic metal-oxides displaying a unique mimicry of the PSII enzyme.[2] Furthermore, the shaping of their functions at the interface of specifically tailored carbon nano-structures and/or polymeric scaffolds opens a vast scenario for tuning electron/proton transfer mechanisms in term of rates, distance, geometries and communication between donor/acceptor centers.[3]



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MS-IL-02 Supramolecular Ligands in Transition metal catalysis, evolutionary ligand screening and a first approach to catalyst selection

Joost N.H. REEK
Homogeneous and Supramolecular Catalysis, Van 't Hoff Institute for Molecular Sciences, University of Amsterdam, Nieuwe Achtergracht 166, 1018WV Amsterdam (the Netherlands).
E-mail: reek@science.uva.nl

The interface between supramolecular chemistry and transition metal catalysis has received surprisingly little attention in contrast to the individual disciplines. It provides, however, novel and elegant strategies that lead to new tools for the search of effective catalysts, [1] and as such this has been an important research theme in our laboratories. In this presentation I will focus on supramolecular strategies to make bidentate ligands and compare that to traditional catalyst development. Supramolecular approaches appear ideally suited for the creation of large ligand libraries. The large number of catalyst that become available in this manner, asks for screening strategies and evolutionary approaches. A first academic example of catalyst selection from a mixture will be discussed. In addition, the application of a cofactor strategy will be presented, which is also ideally suited for selection procedures.

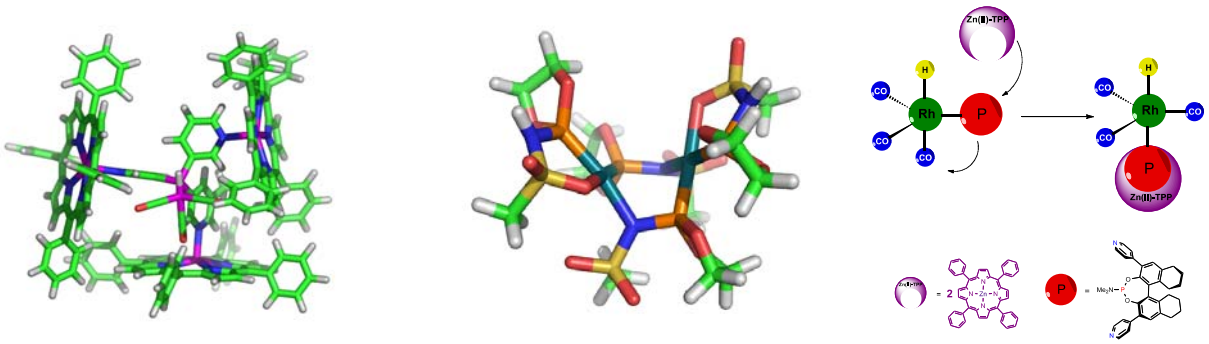

Figure 1: New concepts in TM catalysis: Left) a ligand-template approach to porphyrin encapsulated rhodium catalyst. Middle) dinuclear complexes based on METAMORPhos ligand Right) coordination chemistry steered by supramolecular chemistry.

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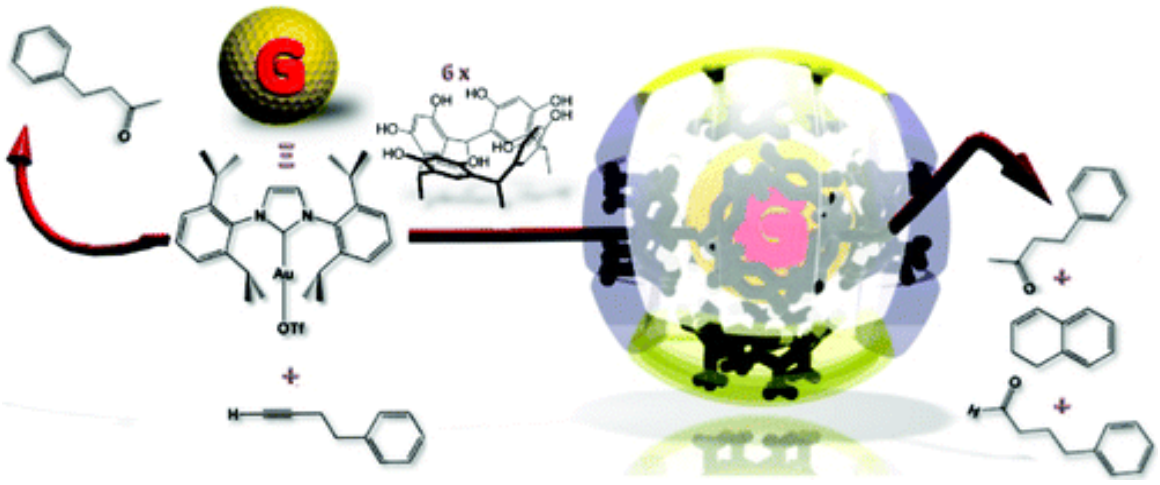
MS-01 Supramolecural Control on Product and Substrate Selectivity via Encapsulation within a Hydrogen Bonded Self-assembled Hexameric Capsule

Giorgio Strukul, Alessandro Scarso*

Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari di Venezia,
Calle Larga S. Marta 2137, 30123, Venezia. *alesca@unive.it*

The impressive chemo, regio and stereoselectivity displayed by enzymes are the result of a large number of weak attractive intermolecular interactions as well as repulsive steric requirements operating between the substrate and the catalytic site. In the latter, recognition phenomena allow also the selective picking of the substrate among a series of similar reagents bearing same functional groups but different size. Overall enzymes control both sides of a chemical transformation, while common organometallic catalysis usually puts its effort prevalently on the right side of the catalytic reaction. Hosting of organometallic catalysts within well defined porous supports led to enhancement of enantioselectivitywhile for catalytic systems working under homogeneous conditions, encapsulation within rigid metal-ligand tetrahedral or square bi-pyramidal assemblies allowed rate acceleration and substrate selective reactions for a series of small reagents.
Herein we report about the simple modification of the product and substrate selectivity properties of an organometallic catalyst via encapsulation in a spherical hexameric self-assembled capsule held together by a seam of sixty hydrogen bonds. The steric requirements imparted by the capsule modify product distribution in the alkyne hydration reaction towards uncommon species and, at the same time, steer substrate selectivity in parallel competitive experiments towards the substrate that better fit the residual space available in the cavity.



MS-02 Rhodium-Catalyzed Asymmetric Hydrogenation of Olefins with PhthalaPhos, a New Class of Chiral Supramolecular Ligands

Luca Pignataro,[a] Michele Boghi,[a] Monica Civera,[a] Stefano Carboni,[b] Umberto Piarulli[b] and Cesare Gennari[a]

[a]Università degli Studi di Milano, Dipartimento di Chimica Organica e Industriale, Istituto di Scienze e Tecnologie Molecolari (ISTM) del CNR, via Venezian 21, 20133 Milano, Italy

[b]Università degli Studi dell'Insubria, Dipartimento di Scienze Chimiche e Ambientali, via Valleggio 11, 22100 Como, Italy

luca.pignataro@unimi.it

Nature makes wide use of non-covalent interactions to build its complex supramolecular architectures and to achieve efficient and selective transformations. In recent years, supramolecular approaches to the development of new enantioselective catalysts have gained momentum [1]. Herein we report the design and synthesis of a novel class of chiral monodentate phosphite ligands, named PhthalaPhos [2], which contain a phthalic acid diamide moiety (Figure 1). Such phthalamide group displays both donor and acceptor hydrogen bonding properties that can give rise to supramolecular interactions both between the ligands and with the substrate. The modular nature of the PhthalaPhos ligands allows to tune their properties by simply varying structural elements such as the linker, the BINOL unit and the ancillary amide group (i.e. the amide not connected to the phosphite group), thus allowing a parallel-combinatorial ligand optimization.

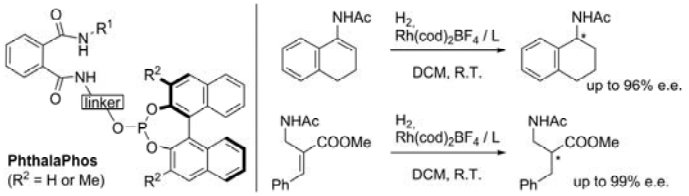


Figure 1

The catalytic properties of the PhthalaPhos library (19 representatives) were tested in the rhodium-catalyzed enantioselective hydrogenation of dehydro aminoesters and *N*-acyl enamides. Excellent results in terms of catalytic activity and stereocontrol were obtained with both benchmark substrates and 'challenging', industrially relevant olefins (Figure 1). Spectroscopic and computational studies, together with control experiments, suggest that the role of the phthalamide group consists in binding and orientating (by hydrogen bonding) the substrate during the catalytic cycle of the hydrogenation process [2b].

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MS-03 Covalent Nano-Clip and Nano-Box Compounds Based on Free Base Porphyrins

Placido Mineo,[a,b] **Emilio Scamporrino**[a]
a) Dipartimento di Scienze Chimiche, Università di Catania. Viale A. Doria, 6 - 95125 Catania,
Italy
b) Istituto per i Processi Chimico Fisici-CNR. Viale F. S. D'Alcontres, 37 - 98158 Messina, Italy
Email: *gmineo@unict.it*

There is an increasing interest in developing smart nanostructures for applications in many different fields, from environmental monitoring to biological, medical and industrial chemistry. For some specific properties (e.g. strong molar absorption, bound metal atoms in pyrrolic cores, extensive aromatic structures, peculiar affinity for neoplastic cells, etc.), porphyrin-derivatives are among the most studied compounds and some applications like chemical and/or biological receptors, artificial sensors for drug determinations, mimesis of biological systems, etc., are already well-defined. Recently, several 3D cyclic oligo-porphyrins with different architectures [e.g. spheres, prisms, regular polyhedra (with a varying number of faces), etc.] have been studied[1]. The properties of these molecules may depend on the size and hydrophobic nature of the cavities inside their 3D structure (for example, suitable to accommodate hydrophobic chemicals).

In the present paper, as the first step in the preparation of water soluble Nano-Clip and Nano-Box compounds, the synthesis and characterization of some novel macromolecular cyclic ethers, constituted by two (Nano-clip, fig. 1) or four (Nano-box, fig. 2) porphyrin units and spaced with methylene bridges, are reported. These compounds, obtained by the reaction between dibromomethane and 5,15-di[p-(9-methoxytriethylenenoxy)phenyl]-10,20-di[p-hydroxyphenyl] porphyrin, have a co-facial (nano-clip) or a four wall-box (nano-box) architecture.

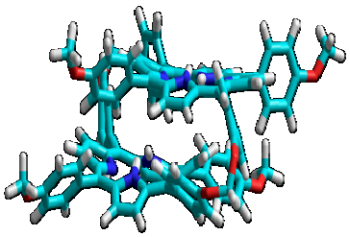
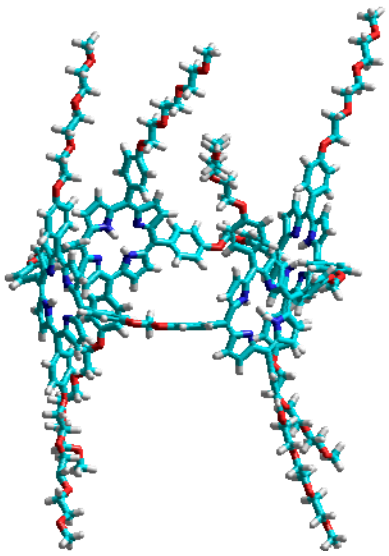


Fig.1



The aim of these syntheses was to obtain molecular systems for the recognition and/or the carriage of bio-molecules. Spectroscopic data of the Nano-clip showed modified Soret and Q-bands, with respect to the monomer and cyclic tetramer, as a probable consequence of a hybrid orbital deformation (HOD) phenomenon involving the two porphyrin π rings forced to a closer co-facial spatial arrangement [2].

A UV-vis titration allowed verification of the easy and reversible protonation of the pyrrolic cores which, by electrostatic repulsion, modifies the spatial distance between the two co-facial porphyrins and, therefore, the cavity size. This reversible modification could be used to change the dimer molecule status from Open to Closed, and facilitate the accommodation or release of suitable chemical species, acting then as a drug carrier.
The tetrameric porphyrin molecule (Nano-box) could also be used as a drug-carrier, forming an inclusion complex with macromolecular drugs, or as a nano-reactor, for the peculiar nano-space conditions inside the box. In this case, ^{1}H-NMR spectroscopic analysis showed a high-field shift of the aromatic and ether protons present in the upper and lower box rims as a specific characteristic of this molecular structure[2]. These compounds differ from previous analogous porphyrinic systems in that their totally covalent structure makes them more versatile potential macromolecular tools.

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MS-04 Novel functionalized PTA ligands, their coordination complexes and use in catalysis

A. Guerriero,[a] L. Gonsalvi,[a] M. Peruzzini,[a] G. Reginato,[a] D. A. Krogstad,[b] N. Six,[c] F. Hapiot,[c] E. Monflier[c]

aICCOM-CNR, Sesto Fiorentino (FI), Italy
bConcordia College at Moorhead, 334F Ivers, Moorhead, Minnesota, USA
cUniversité d'Artois, UCCS-UMR 8181, Lens Cedex, France
E-mail: *antonella.guerriero@iccom.cnr.it*

PTA (1,3,5-triaza-7-phosphaadamantane), the neutral water-soluble and air-stable monodentate phosphine firstly reported by Daigle et al. in 1974 [1], has been used by us and other groups to obtain water-soluble transition metal complexes which have been applied as homogeneous catalysts in aqueous or biphasic systems [2].
The largest part of modifications of PTA has so far involved the P or N atoms, so we focused on the functionalization at one carbon of the upper rim [3]. The optimized derivatization reaction is based on the isolation of the pyrophoric PTA-Li salt, which was then reacted with electrophiles such as aromatic aldehydes and ketones [4]. Thus, new chiral ligands were obtained and used to bind Ir(I) and Ru(II) organometallic moieties. The corresponding complexes were tested as catalysts for hydrogenation reactions under mild conditions. In parallel, modifications of the lower rim of PTA, i.e. alkylations at N atom, were also carried out and the new N-alkylated PTA derivatives so obtained were used as water soluble ligands in biphasic Rh-catalyzed hydroformylations of long-chain olefins in the presence of randomly methylated □-cyclodextrins.[5].
We thank financial contributions from MATTM (PIRODE project), CNR for bilateral CNR-CNRS project, COST Action CM0802 "PhoSciNet", MAE for JRP Cooperation Italy-USA (2008-2010).

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ORG/CTC-KN-01 Bridging the Gap between Theory and Experiment: Modeling Chiroptical Properties and Spectroscopies

Franco Egidi,[1] Julien Bloino,[1] Chiara Cappelli[2]

[1]Scuola Normale Superiore, Piazza dei Cavalieri, 7 I-56126, Pisa, Italy.
[2]Dipartimento di Chimica e Chimica Industriale, Università di Pisa, via Risorgimento, 35 I-56126, Pisa, Italy.
chiara@dcci.unipi.it

The tremendous progress of ab-initio quantum chemistry in the last decades has led to an increasing number of applications of quantum mechanical (QM) approaches to the calculation of chiroptical properties [1-7].
The progress has been so large that a ‘‘renaissance’’ in chiroptical methods due to the accuracy and computational efficiency achieved by ab initio QM methods in reproducing experimental data and predicting new ones has been invoked [8].
In this contribution, some peculiar aspects of the computation of chiroptical properties and spectroscopies are remarked through the analysis of case studies, with special emphasis towards the gaining of calculated data directly comparable to experiments, by the inclusion of solvation and vibrational effects.

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ORG/CTC-KN-02 Structural Basis for the design and synthesis of selective HDAC inhibitors.

Simone Di Micco, Maria Giovanna Chini, Stefania Terracciano, Ines Bruno, Raffaele Riccio, and Giuseppe Bifulco

Dipartimento di Scienze Farmaceutiche e Biomediche dell'Università di Salerno, Via Ponte Don Melillo, 84084, Fisciano (SA), Italy
bifulco@unisa.it

Protein lysine acetylation is a key mechanism in the epigenetic control of gene expression, the regulation of cell metabolism[1,2], and protein deacetylases are potential targets for treating cancer and a range of autoimmune and neurodegenerative diseases[3]. In this context, the HDAC inhibitors have attracted the attention of the researchers as promising anticancer agents [4,5]. Based on sequence phylogeny and function, there are four distinct classes of HDAC: class I (HDAC1, 2, 3 and 8), class IIa (HDAC4, 5, 7 and 9), class IIb (HDAC6 and 10) and class IV (HDAC11) represent Zn^{2+}-dependent amidohydrolases, whereas class III comprises the mechanistically diverse NAD+-dependent sirtuins [6]. In this contribute, we have traced out the structural elements responsible of selective binding in the whole landscape of the HDAC isoforms considered interesting therapeutic targets. In particular, we have rationalized experimental observations and tried to systematically add new insights for a targeted design of selective inhibitors for the different HDAC isoforms. In detail, we have focused our attention on all HDACs zinc dependent enzymes, except HDAC5 and HDAC9-11, for which few information on expression, function in tumor cells, and ligand inhibitory profile are available in literature. The structural analysis was performed by molecular docking calculations, using as ligands known pan and class selective HDAC inhibitors [4]. Based on the obtained structural guidelines, we designed, synthesized and experimentally tested selective inhibitors for HDAC2.

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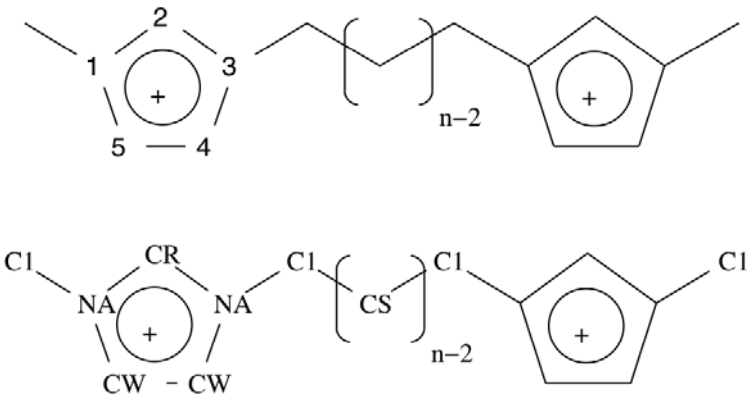
ORG/CTC-OR-01 The Structure of Ionic Liquids Based on Geminal Imidazolium: a Theoretical Study

E. Bodo and R. Caminiti

Dept. of Chemistry and CNISM, University of Rome "La Sapienza", Italy
E-mail: bodo@caspur.it

Among the most exciting and successful materials developed and studied in the last twenty years, ionic liquids [1] are among those that can certainly claim one of the most rich field of applications in industry and in applied technological research. A special class of ILs is have recently been obtained using geminal imidazolium dications [2] that represent a very interesting variation of the cationic partner and that may present various advantages over the traditional mono-cationic ionic liquids in applications such as lubricants, catalyst, solvents and as separation media.



A schematic view of the molecular structures is reported above: we have a linkage chain (whose length can be 3, 6, 9 or 12 for the compounds analyzed in the present work) that connects two imidazolium rings with a net positive charge on them and that are substituted with a methyl group. We have recently [3] analyzed the behavior of such compounds by calculating the structures of the gas phase complexes. We will report these and further results obtained by means of MD simulations.

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ORG/CTC-OR-02 Chemoinformatic strategies in the design of new antibacterials active against multidrug resistant Gram-positive pathogens.

Cosimo G. Fortuna[a], Rosario Musumeci[b], Andrea Pace[c]

[a] Dipartimento di Scenze Chimiche, Università di Catania, Viale A. Doria,6 95125 Catania, Italy

[b]Dipartimento di Medicina Clinica e Prevenzione, Università di Milano-Bicocca, Via Cadore 48, I-20052, Monza (MB), Italy.

[c] Dipartimento di Scienze e Tecnologie Molecolari e Biomolecolari (STEMBIO), Università degli Studi di Palermo, Viale delle Scienze Ed. 17 – Parco D'Orleans II, I-90128, Palermo, Italy.

cg.fortuna@unict.it

Chemoinformatic strategies possess great potentialities in modelling the interactions between biopolymers and ligands. Molecular recognition plays in fact a fundamental role in drug-receptor interactions.

Due to the lack of pharmacological targets, in previous studies [1] we adopted a Virtual Receptor Site (VRS) approach, where ligands interact with a complex receptor of unknown structure, aimed at identifying pieces of the structure which could be valuable for improving the antibacterial activity.

In the design of new drugs it is also very important that they exhibit ADME (Adsorption, Distribution, Metabolism, Elimination) properties warranting an acceptable bioavailability. For this purpose, a new method, called VOLSURF [2], able to correlate 3D molecular structures with physico-chemical properties, and highly efficient in predicting the biological activities, appears to be appropriate.

According to the advances achieved in the past two years due to the availability of the x-ray structures for a few drug targets, molecular modelling by docking of new ligands to the receptor active sites appears nowadays an appropriate strategy in the design of new antibacterials against multidrug resistant strains.

In this context, we adopted a recently developed algorithm called Fingerprints for Ligands and Proteins (FLAP) that can be used to describe proteins and ligands based on a common reference framework [3]. FLAP is able to explore the 3D-pharmacophoric space of ligands and proteins and to provide quantitative information for the complementarity of their interactions to allow ligand-ligand, ligand-protein, or protein-protein comparison. By means of all these chemoinformatic tools, we studied the interactions between synthetically accessible compounds and the crystallographic structure of Linezolid binding protein to identify a scaffold that we could modify introducing different substituents to improve the *in vitro* antibacterial activity.

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ORG/CTC-OR-03 Revisiting Nucleophilic-Electrophilic Mechanisms in Oxidation Reactivity

Giulia Licini,[a] Cristiano Zonta[a]

[a] Dipartimento di Scienze Chimiche, Università di Padova, Via Marzolo 1, 35131, Padova, Italia
cristiano.zonta@unipd.it

Oxidation chemistry has always been one of the most important playgrounds for the interpretation and mastering of reactivity.[1] The interest of scientists has been driven not only by the strong implications that this reactivity plays in biological systems, but also because it represents an essential tool in functional groups transformation. These studies have also deeply contributed to the development of the basic principles of reactivity.
In recent years we have been involved in the study of metal catalysts for oxygen transfer reactions.[2] The experimental results have offered us the possibility to investigate in detail the mechanism of oxidation reactions, and in particular to study the effect of intermolecular interactions in catalysis.[3]
The evaluation of these experimental results, with the support of theoretical calculations, have led to a reinterpretation of the concept of nucleophilic and electrophilic reactivity in oxidation chemistry. This analysis can have implications that go beyond oxidation chemistry

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ORG/CTC-OR-04 L-Arabinose adsorption on a Ru cluster

Remedios Cortese[a], Dario Duca[a], Dmitry Yu. Murzin[b]
[a]Dipartimento di Chimica "S. Cannizzaro" Università di Palermo, Viale delle Scienze, Ed. 17 90128 Palermo, Italy
[b]Department of Chemical Engineering, Åbo Akademi University, Biskopsgatan 8, FI-20500 Turku, Finland
remedios@cccp.unipa.it

Use of bio-mass for energy, chemicals and material supply is one of the key issues of sustainable development, because bio-based resources are both CO_2-neutral and renewable, at variance with fossil fuels. Carbohydrates are the main source of renewables employed for the production of bio-based products. Therefore, chemistry know-how on industrial processes, involving carbohydrates is a subject of basis importance.

Adsorption of the monosacharide L-Arabinose on a ruthenium nanocluster is here presented as an example of a catalytic system of potential industrial interest [1]. L-Arabinose can be found in aqueous solution in 5 tautomeric forms (*i.e.* α or β pyranose, α or β furanose and acyclic species) in equilibrium with each other. All these tautomers show a very large conformational flexibility, which previously has been also analyzed.

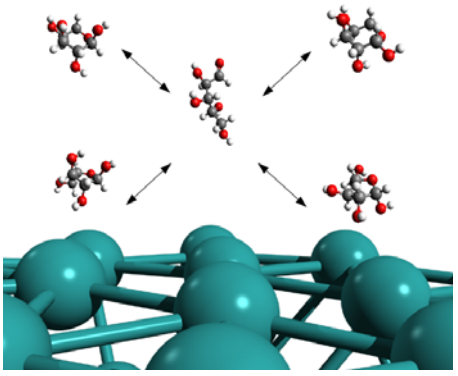

Figure 1. L-Arabinose on Ru surface

The L-Arabinose/Ru system has been investigated into the frame of the density functional theory (DFT). Calculations have been actually performed, using the DFT approach as implemented in SIESTA [2]. This employs linear combination of pseudoatomic orbitals as basis set. The atomic core is replaced by a non-local norm-conserving relativistic Troullier Martins pseudopotential, factorized in the Kleinmann-Bylander form.

The adsorption of different conformers, per each tautomers, on a Ru (0001) surface of the nanocluster have been modeled and analyzed in order to characterize the adsorption points both on the ruthenium surface and in the tautomeric species and to characterize if some of the latter are especially stabilized by the adsorption processes. Since adsorption phenomena could be affected by the adsorbate orientation, three different ways of binding per each conformers were investigated, considering either pyranose or furanose forms, and two for the acyclic forms.

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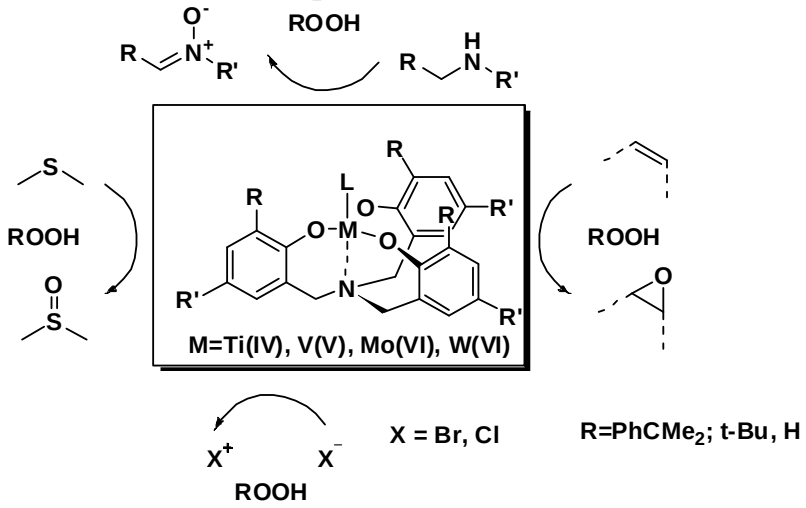
ORG/GC-IL-01 Amino Triphenolates as Privileged Ligands in Catalysis

Cristiano Zonta, Miriam Mba, and Giulia Licini

Dipartimento di Scienze Chimiche, Università degli Studi di Padova, via Marzolo 1, 35131 Padova, Italy
email: giulia.licini@unipd.it

Triphenolamines are highly modular tetradentate molecules that effectively coordinate transition metals and main group elements with podand topology.[1] They form chiral complexes with well defined coordination geometries controlled by the ligand, in particular by the nature of the substituents in *ortho* position to the hydroxy groups, which are able to influence their reactivity and stability. Early transition metal complexes, like Ti(IV), V(V), Mo (VI) and W (VI) complexes have been found to be stable and effective Lewis acids in oxygen transfer processes.[2]



Here we will report on their synthesis, characterization and their reactivity in oxygen transfer reactions. Tuning of metal ion and reaction conditions allows the selective oxidation of different nucleophiles, such as olefins, halogens, sulfur or nitrogen derivatives using aqueous hydrogen peroxide and/or alkyl hydroperoxides as primary oxidants with very low catalyst loadings and high TON's and TOF's. Computational and spectroscopic studies for the elucidation of the reaction mechanism of peroxide activation and oxygen transfer reactions will be also presented.

***Acknowledgements*:** We acknowledge for financial support MIUR, PRIN 2008 project, University of Padova and CARIPARO Fundation (NANO-MODUles Progetto Eccellenza 2009-2010).

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ORG/GC-IL-02 Structural effects on physico-chemical and catalytic properties of functionalized ionic liquids

Cinzia Chiappe and Sunita Rajamani

Dipartimento di Chimica e Chimica Industriale, Via Bonanno 33, 56126 Pisa

During the past decade or so, ionic liquids (molten salts liquid at/or near room temperature) as potential environmentally friendly solvents have been able to gather widespread interest and curiosity from the scientific and engineering community. The number of research publications on investigations of ionic liquids for properties, analysis, and applications has increased exponentially. Almost every named synthesis and many more organic/inorganic/organometallic reactions have been reported in ILs.[1] Effective, and in some cases unique, utilization of ILs as solvents has been demonstrated in a variety of techniques in electroanalysis, separation, spectrometry, and sensing. Nevertheless, thought not reported explicitly, certain drawbacks have also emerged from the aforementioned detailed investigations with ILs; perhaps, the *limited* solubility of a fairly large number of common solutes, including metal salts, [2] or the effects that traces of impurities present in ILs can have on the behavior of many reactions. Alkyl substituted imidazolium, pyridinium and pyrrolinium cations are the most investigated positive components of ILs, generally associated to anions such tetrafluoroborate, hexafluorophosphate and bistriflimide. More recent data have however shown that functionalized ionic liquids (ILs) are able to overcome at least some of the above mentioned weaknesses, offering new possibilities for application in organic synthesis and catalyzed processes. The performance of these systems as solvents and/or catalysts largely depends on cation and anion structure and liquid-state organization.

In this communication, several examples of functionalized ILs will be reported and their properties discussed to highlight the main peculiarities which can be fundamental for a rational design and development of new improved ionic media and catalysts.

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ORG/GC-OR-01 Biomass as Green Alternative for Chemicals and Energy Supply

Chiara Samorì, Paola Galletti, Emilio Tagliavini
Centro Interdipartimentale di Ricerca per le Scienze Ambientali (CIRSA), Università di Bologna, Via Sant'Alberto 163 Ravenna. *chiara.samori3@unibo.it*

Obtaining chemicals from renewable material is of growing importance in facing environmental concerns over fossil fuels consumption. Aquatic and terrestrial biomasses are the main renewable resources available for the supply of both energy and chemical compounds. We have recently developed novel procedures aimed to afford either biofuels or high-value chemicals from biomass. The former goal was achieved through a new improved route to extract biofuels from terrestrial and aquatic vegetables. The latter goal was achieved through the exploitations of some chemicals and materials deriving from the pyrolytic treatment of terrestrial biomass. Levoglucosan is the major product from the pyrolysis of cellulose. We have developed a method for the selective enzymatic acylation of levoglucosan in good yields using both long and short chain vinyl esters and carboxylic acids in green solvents: CH_3CN, a traditional solvent with low ecotoxicity, and room temperature ionic liquids (RTILs). 4-*O*-dodecanoyl levoglucosan, prepared by our route, has shown interesting tensioactive properties [1]. Furfural is a cheap chemical, industrially obtained from the acidic treatment of lignocellulosic raw materials or from the pyrolysis of wood and cellulose. Here furfural has been used as building block for the synthesis of a class of furan-containing quaternary ammonium salts, whose application can be envisioned in the fields of ionic liquid solvents, surfactants or biocides in analogy with benzyl quaternary ammonium salts [2]. Molasses is the viscous by-product of the processing of sugar cane or sugar beets into sugar; from the pyrolysis of molasses we have obtained a porous graphite-reach char which was treated with sulfuric acid to give a stable solid containing a high density of active acidic sites ($-SO_3H$). This catalyst was proved to be more active than conventional solid acid catalyst in several reactions including the esterification of fatty acids. Microalgae are a very attractive source of biofuels, above all because most of them are highly rich in lipids. We have developed a new green procedure to extract the oil from microalgae by using switchable polarity solvents SPS, a new class of liquids that can be turned from a non-ionic form to an ionic liquid, simply by bubbling CO_2 and reconverting the non-ionic form by the addition of N_2. Lipid extraction was carried out with a 1,8-diazabicyclo-[5.4.0]-undec-7-ene (DBU)/alcohol 1:1 mixture under neutral or basic conditions; then, the introduction of CO_2 switched the solvent to the ionic form allowing the separation of the lipid phase. The final bubbling of N_2 reverted the solvent to the non-ionic form, ensuring a full recyclability of both DBU and alcohol components[3].

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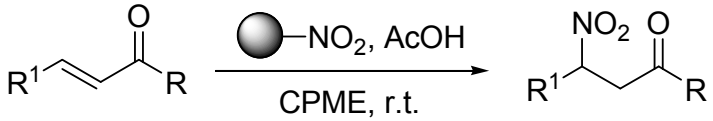
ORG/GC-OR-02 New Ecofriendly Improvements in the Synthesis of Nitro Compounds

Serena Gabrielli,[a] Alessandro Palmieri,[a] Roberto Ballini[a]

[a]Green Chemistry Group, Scuola di Scienze e Tecnologie,divisione Chimica Organica, Università di Camerino, Via S. Agostino 1, 62032 Camerino, Italy Fax: (+) 39 0737402297 e-mail: *serena.gabrielli@unicam.it*

Nitroalkanes are one of the most fundamental classes of substrates in organic chemistry.[1] This is mainly due to the fact that (i) they allow the easy formation of new carbon-carbon and carbon-heteroatom bonds under very mild reaction conditions,[2,3] (ii) the nitro group can be converted into a plethora of other functionalities,[4] and (iii) they are the key starting material for the preparation of a variety of fine chemicals.[5] Thus, the easy accessibility to nitroalkanes remains an important goal, especially for those functionalized ones.[6] In this context, □-nitro ketones **2**, or their protected ones, are important starting materials in organic synthesis, but the classical procedures for their preparations still present important drawbacks from the eco-sustainability point of view. In order to circumvent these problems and based on our experiences, we have now developed an improved eco-friendly, general procedure for the nitration of conjugated enones **1**, under solid supported reagents (SSR) (Figure 1).

Figure 1



1 **2**

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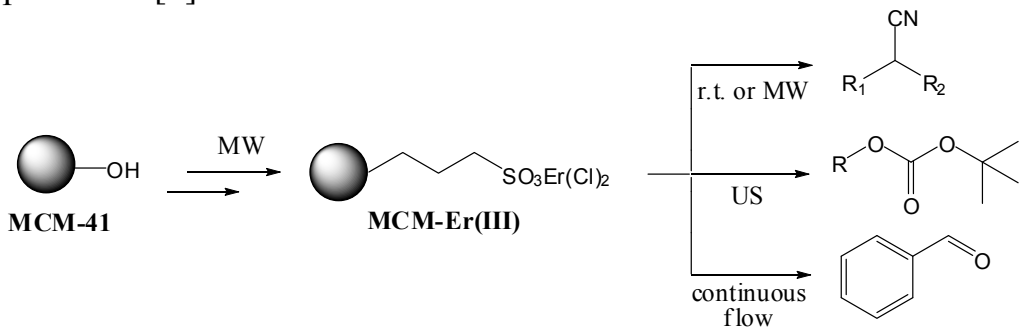
ORG/GC-OR-03 New frontiers in heterogeneous catalysis: synthesis, applications and perspectives of MCM-Er(III) materials.

M. Oliverio,[a] A. Procopio,[a] G. De Luca,[b] M. Nardi,[b] P. Costanzo,[a] R. Paonessa.[a]

[a] Università Magna Græcia di Catanzaro, Campus Salvatore Venuta, 88100 Germaneto (CZ)
[b] Università della Calabria, Ponte Bucci, cubo 12C, 87036 Arcavacata di Rende (CS)
e-mail: m.oliverio@unicz.it

Since the idea of a sustainable chemistry became an urgency for the scientific community, an exponential increasing in the use of heterogeneous recoverable catalysts was registered. Mesoporous silica (MCM) have played a prominent role as inert supporting materials in this field, because of their high specific surface areas, their large pore size and their thermal and chemical stability.[1] The efficiency of non toxic Er(III) salts as Lewis acid catalysts in homogeneous phase was largely explored by our group. This work is focused on the realization and application of a new class of heterogeneous catalysts based on the Er(III) chemistry. The MW-assisted synthesis and characterization, the rationalization of the MW–effect on the system, the application of a new MCM-Er(III) catalyst under non-conventional synthetic methods as US, MW and continuous-flow conditions will be presented.[2]



The versatility and resistance of these supported materials justify the investment in terms of design of more complex catalytic systems. Therefore, preliminary results on the synthesis of a new heterogeneous bifunctional-asymmetric supported catalyst, will be discussed. The new system is characterized by the cooperation between a general Base and an Er(III) Lewis acid, grafted together on the silica surface.

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ORG/GC-OR-04 Greener approach to oxidation reactions with diluted H_2O_2 using continuous flow system

C. Giancarlo Piscopo, Raimondo Maggi , Giovanni Sartori
"Clean Synthetic Methodology Group", Dipartimento di Chimica Organica e Industriale dell'Università, Parma, Italy. *calogerogiancarlo.piscopo@nemo.unipr.it*

One of the major challenges of green chemistry is, undoubtedly, the achievement of more environmentally friendly processes in organic synthesis. An important goal in this field is the development of cleaner and safer synthesis routes for oxidation reactions.[1]

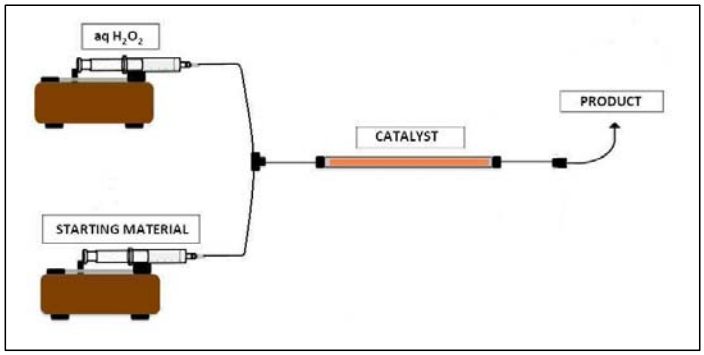

Figure 1

Hence, in the last decades many studies have been devoted to replace common oxidants with aqueous hydrogen peroxide,[2] which is a cheap, mild and environmentally benign reagent since water is formed as the only by-product. Furthermore, continuous processing of catalytic reactions offers significant improvements compared to conventional batch processes due to a precise control of residence time, heat and mass transport.[3]
Here we report two very highly chemoselective oxidation reactions carried out with diluted H_2O_2, and catalyzed by sulfonic resin Amberlite IR-120H, in continuous flow reactors (Figure 1).
Concerning the thioanisole oxidation,[4] by performing the reaction at 22 °C with a stoichiometric amount of 3% aqueous H_2O_2 at a residence time of 25 minutes, methylphenylsulfoxide has been obtained in 90% yield and 100% selectivity. The catalyst can be used for at least 3,000 minutes without any loss of activity. Similar excellent results have been achieved with different aryl alkyl sulfides.
A similar system was developed for the oxidation of methylhydroquinone to the corresponding methylbenzoquinone with 30% aqueous H_2O_2. A mixture of methylhydroquinone and hydrogen peroxide in methanol was passed through the reactor for 360 minutes obtaining the product in 59% yield and 95% selectivity.

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INO/OM-KN-01 Metal-coordinated carbenes: reactive species or robust ligands?

Marino Basato

Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova.
marino.basato@unipd.it

Transition metal carbene complexes have been mainly considered reactive intermediates in several catalytic organic transformations, like for example, the reactions involving the decomposition of diazo compounds (cyclopropanations, C-H insertions, C-C coupling) [1].
However, since the discovery of stable imidazol-2-ylidenes, which were first isolated by Arduengo *et al.* in 1991, much interest has been growing in the chemistry of N-heterocyclic carbenes (NHCs) [2]; in fact, these resulted to be excellent ligands towards transition metal centres both in low and medium-high oxidation state, allowing the synthesis of robust catalysts with negligible carbene dissociation, stable in acidic and oxidative environment.

The dual nature of carbenes can be illustrated by selected examples taken from our recent results involving:
A) reactions of reactive carbene intermediates such as i) insertion of carbenes into C=C, C-H and O-H bonds catalysed by Pt(II) and Rh(II) complexes; ii) reaction of diazo derivatives in presence of olefins to give metathesis and cyclopropanation products catalysed by [RuCl(Cp)(COD)] [3];
B) synthesis of novel di- and tricarbene Pd(II), Pt(II), Cu(I), Ag(I), Au(III) complexes and applications as catalysts in i) Heck reaction, ii) selective hydroarylation of olefins, iii) Ullmann-type arylation [4].
The obtained results show the extraordinary flexibility of the carbene mojety and fully justifies the strong research efforts on this still new and fascinating chemistry.

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INO/OM-KN-02 Stereoselective Gold Catalysis: New Opportunities in Organic Synthesis

Michel Chiarucci, Gianpiero Cera, Marco Bandini

Dipartimento di Chimica "G. Ciamician", Alma Mater Studiorum – Università di Bologna, via Selmi 2, 40126 Bologna, Italy.
marco.bandini@unibo.it

The re-discovery of homogeneous gold(I) catalysis has recently revolutionized the whole organic synthesis scenario, opening up access to unprecedented synthetic manipulations of unfunctionalized unsaturated hydrocarbons under mild and environmental acceptable conditions.[1] At the same time, new opportunities were also created in the "crowded" area of asymmetric catalysis, providing reliable solutions to the preparation of enantiomerically enriched polyfunctionalized molecular architectures in the presence of chiral gold(I) complexes.[2]

In conjunction with our ongoing interests oriented to the catalytic enantioselective decoration of arenes,[3] we have recently reported on the effective gold-mediated direct electrophilic activation of allylic alcohols,[4] in the preparation of functionalized heterocyclic compounds (*i.e. morpholines, indolines, carbazoles*).[5] This consolidated background, along with the use of propargylic alcohols in gold-catalyzed cascade cyclization reactions[6] concur to define new guidelines in organometallic synthesis under noble metal assistance.

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INO/OM-OR-01 Pd/Ln_xO_y (Ln = La, Ce, Pr, Sm, Gd, Dy and Yb): Efficient Precatalysts for a Fast and Green Suzuki-Miyaura Reaction

A. Del Zotto, F. Amoroso, S. Colussi, A. Trovarelli

Dipartimento di Chimica, Fisica e Ambiente dell'Università di Udine, via Cotonificio 108, 33100 Udine, Italy.
alessandro.delzotto@uniud.it

In the last two decades, the Pd-catalyzed C-C bond formation has emerged as an outstanding strategy for building more or less complex organic molecules. Of the commonly used reactions, the Suzuki-Miyaura (SM) coupling has been proven to be the most useful and widely applied [1]. Our efforts have been mainly devoted to the development of new Pd-based catalysts that can efficiently promote the SM reaction in mild and green conditions. The focus of interest is: i) use of safe solvents, ii) room temperature catalysis, iii) reusability of the catalytic system.
In recent work from our group, the Pd/CeO_2 system was found to show very good activity for the SM coupling in water/ethanol mixtures at room temperature [2]. We demonstrated that the "heterogeneous" Pd-containing precatalyst acts as "releaser" of "homeopathic" amounts of a catalytically active soluble form of Pd. Furthermore, we succeeded in recycling the Pd/CeO_2 precatalyst at least ten times without a marked decrease of catalytic activity.
The present work is an extension of the study to different Pd/Ln_xO_y catalyst precursors (Ln = La, Pr, Sm, Gd, Dy and Yb). Interestingly, all novel catalytic systems showed an activity much higher than that exhibited by Pd/CeO_2. The reusability of all precatalysts is also good, in particular for Pd/Sm_2O_3.
Current studies are focused on assessing some crucial features of the mechanism of formation of the "true" catalyst. In particular, the higher catalytic activity of Pd/Ln_2O_3 with respect to Pd/CeO_2 seems to be related to the easier release of Pd particles from the surface of the former precatalyst.

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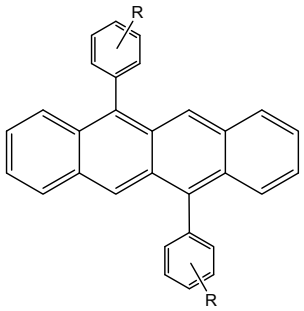
INO/OM-OR-02 New tetracene based materials for organic electronics: organometallic approach to their synthesis.

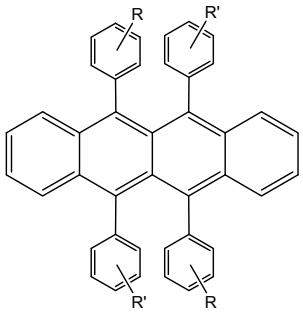
A. Papagni

Dipartimento di Scienza dei Materiali, Università di Milano Bicocca, via R. Cozzi 53, 20125 Milano (Italy)
(e-mail address: antonio.papagni@unimib.it)

Acene-based organic semiconductors, thanks to their outstanding properties and their good processability, are key molecular materials for the development of organic electronics and derivatives of tetracene represent those where a good compromise between environmental stability and charge transport solid state properties is realised. Among tetracene-based systems, rubrene (5,6,11,12-tetraphenyl-tetracene) showed exceptional high charge carrier mobilities in Organic Field Effect Transistors (OFET) built on single crystals[1] and now represents the state of the art for molecular organic semiconductors.
It is noteworthy that, despite the peculiar and interesting properties of aryl-substituted-tetracenes, few synthetic routes are available (mostly tedious multi steps procedures) and relatively limited examples of molecules belonging to this series are known. This should urge on the organic chemist community to develop synthetic strategies to access to new organic semiconductors belonging to this class with improved transport properties, stability and processability. In principle, these properties (stability against photo-oxidation, solubility and charge carrier mobility) can be optimized by proper chemical modifications both on the tetracene core and on the aryl-substituents and transition metal-catalyzed processes are, from this point of view, particularly appealing both to improve the efficiency and to shorten the synthetic procedures.



5,11-diaryl-tetracenes



5,6,1,11,12-tetraaryl-tetracenes

Here we present our advances on the synthesis of new diaryl- and tetraaryl tetracenes where Pd-mediated cross-coupling reactions represent the key tools both to access to these systems and to prepare strategic precursors. In particular the synthesis of 1,1,3-triaryl-substituted propargyl alcohols, key intermediate for the synthesis of 5,6,11,12 tetra-aryl-substituted tetracenes (Rubrene-like systems) by

copper-free Sonogashira protocol along with their evolution into rubrenes will be described.[2] A new protocol for the preparation of 5,11-diaryl-substituted tetracenes by Suzuki-based cross-coupling reaction from 5,11-di bromo- tetracene in liquid ionic will be also presented.[3] Some properties of the new tetracenes will be discussed.

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INO/OM-OR-03 Organometallic Fuel Cell development: the combined effect of molecular architecture with an high surface area carbon support

Manuela Bevilacqua[b], Jonathan Filippi[b], Alessandro Lavacchi[b], Andrea Marchionni[b], Werner Oberhauser[b], Hartmut Schönberg[a], Francesco Vizza[b], Claudio Bianchini[b] & Hansjörg Grützmacher[a]

[a] Department of Chemistry and Applied Biosciences, ETH Hönggerberg, CH-8093 Zürich, Switzerland. [b] Institute of Chemistry of Organometallic Compounds, ICCOM-CNR, Polo Scientifico Area CNR
Via Madonna del Piano 10, I-50019 Sesto Fiorentino, Italy
manuela.bevilacqua@iccom.cnr.it

The selective and simultaneous conversion of alcohols and sugars into energy and chemicals is a target of primary importance for the sustainable development. Two established types of fuel cells operating in alkaline media can convert the free energy of alcohols ($R\text{-}CH_2\text{-}OH$) into electrical energy and the corresponding carboxylate product: the direct alcohol fuel cell (DAFC), based on feasible metal electrocatalyst for alcohol oxidation [1] and the enzymatic biofuel cell (EBFC) that utilizes oxidation enzymes such as dehydrogenases in conjunction with an electron transfer mediator [2]. From a mechanistic viewpoint, the conversion of ethanol into energy and acetate resembles the process occurring in a biofuel cell where the electrocatalytic system consists of alcohol- and aldehyde-deydrogenases in combination with a hydrogen/electron transfer mediator. Recently, we introduced a third type of fuel cell operating in alkaline media where the anode catalyst is *a molecular metal complex*. We showed that in this device, named "organometallic fuel cell (OMFC)" a molecular rhodium complex is capable of evolving through fast chemical equilibria in the course of the catalytic cycle to form a specific catalyst for alcohol dehydrogenation, a specific catalyst for aldehyde dehydrogenation and a specific catalyst for the H/electron-transfer [3]. From a practical perspective, a molecular metal complex, soluble in different solvents and hence easily dispersible on very small surfaces, but capable of delivering high power densities upon oxidation of alcohols and sugars, paves the way to the further miniaturization of fuel cells for biological applications as well as biosensors. The combination of *well-defined molecular architecture* with a *matching support* (high surface area carbon black types) might allow for the selective oxidation of polyalcohols into valuable chemicals under waste-free conditions which is hardly achievable by traditional methods.

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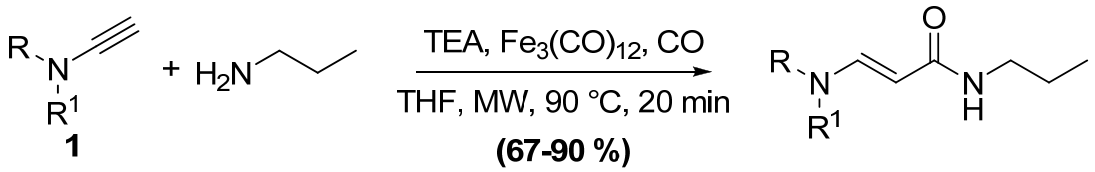
INO/OM-OR-04 Microwave-Assisted Aminocarbonylation of Ynamides using catalytic $Fe_3(CO)_{12}$ at Low Pressure of Carbon Monoxide

Elena Petricci, Marianna Pizzetti, Adele Russo and Maurizio Taddei

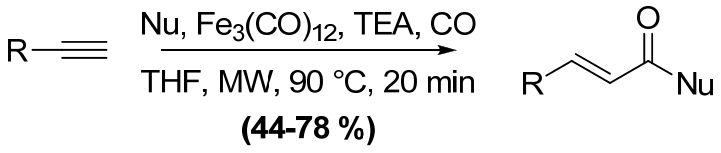
Dipartimento Farmaco Chimico Tecnologico, Università degli Studi di Siena, Via A. Moro,53100, Siena, Italy
pizzetti4@unisi.it

Carbonylation is a wideley applied atom economic reaction providing esters, ketons, carboxylic acids, amides and heterocyclic compounds.[1] Several procedures for the carbonylation of alkene and alkyne derivatives with different catalysts have been investigated but only few reports investigate the use of iron as the catalyst.[2] Iron carbonyl complexes have been increasingly used in organic synthesis in recent years and iron catalysis represents a promising area in the homogeneous catalysis.
Beside our interest on new ecofriendly catalysts for microwave assisted carbonylation reactions using carbon monoxide as a bening source of C, a microwave-assisted procedure for the iron catalyzed carbonylation of ynamides and terminal alkynes was developped.[3]
Starting from ynamides **1** a new class of *E*-acrylamides has been regioselectively synthesized after irradiation with microwaves for only 20 minutes at low pressure of CO (1.3 bar) using $Fe_3(CO)$ and TEA as the catalyst precursors (Scheme 1).



Scheme 1

The same procedure can be easily applied to terminal alkynes giving regioselectively *E*-acryl- and cinnamides. Using alcohols or thiols as nucleophiles *E*-acrylesters and thioesters are obtained in good yields as well (Scheme 2).



Scheme 2

The building blocks obtained by this atomeconomic process are key intermediates in the synthesis of natural products and small bioactive molecules.

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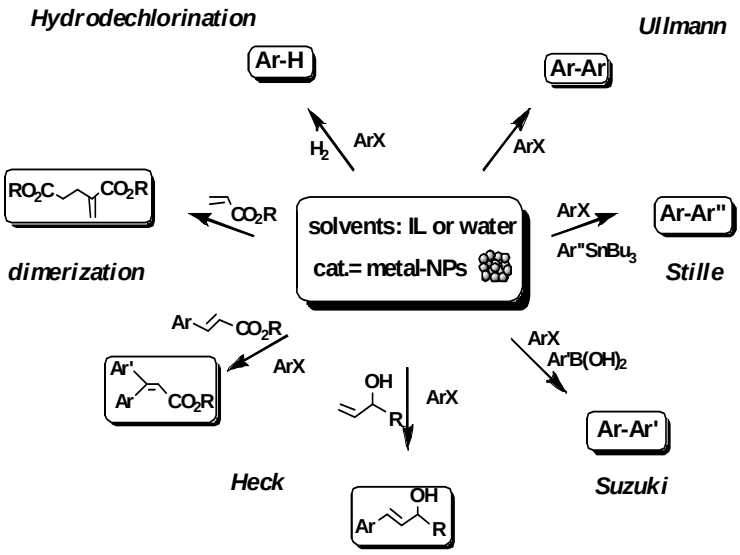
ORG/OM-IL-01 Metal Nanoparticles as Efficient Catalysts in Green Chemistry

[a]Antonio Monopoli, [a] F. Ciminale,[a]P. Cotugno,[a]B. Mariano,[a]G. Antonicelli,[a]N. Cioffi, [a]V. Calo', [a]G. Palazzo and [a,b]A. Nacci
[a]Department of Chemistry - University of Bari, Via Orabona 4, 70126-Bari, Italy
[b]CNR – ICCOM Department of Chemistry Via Orabona 4, 70126-Bari, Italy
E-mail: *antomono@libero.it*

Transition-metal nanoparticles (NPs) are attracting a great deal of attention in almost any scientific and technological field, including catalysis, where nanoscale materials are becoming more prevalent in a wide range of applications such as fuel conversion, pollution abatement and fine chemical production.[1]
An increasing interest is also devoted nowadays to properly exploit the high activity and selectivity of nanocatalysts in order to develop greener and waste-minimized processes. From the Green Chemistry standpoint, new nanocatalysts must be designed to operate under environmentally friendly (for instance phosphine-free) conditions or in neoteric green solvents (e.g. ionic liquids, supercritical fluids, fluorous phases, water and so on).[2]



In this context, during the last decade, we exploited the use of nanostructured metal catalysts based on palladium, copper, and gold, to perform a wide range of C-C bond forming reactions, like for example Heck, Suzuki, Stille, acrylate dimerization, and Ullmann couplings, using tetraalkylammonium ionic liquids and water as green reaction media.[3]

This communication deals with our recent advances in controlling the catalyst performances by choosing appropriately the nature of the ionic liquid or the aqueous medium.

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ORG/OM-IL-02 The Amination of Hydrocarbons Catalysed by Ruthenium Porphyrin Complexes. A Mechanistic Investigation.

Emma Gallo, Daniela Intrieri, Alessandro Caselli, Fabio Ragaini
Dipartimento di Chimica Inorganica Metallorganica e Analitica "L. Malatesta", Via Venezian 21, 20133 Milano, Italia
emma.gallo@unimi.it

The direct amination of hydrocarbons is a reaction of great synthetic interest due to the biological and pharmaceutical importance of aza-derivatives. We have focused our interest on this class of transformations for ten years using aryl azides as nitrogen sources and metallo porphyrins as catalysts [1]. More recently, we have investigated the catalytic activity of Ru(TPP)CO in C-H bonds aminations and we have isolated and characterised the active bis-imido intermediate Ru(TPP)$(NAr)_2$ (Ar = 3,5-$(CF_3)_2C_6H_3$) (**1**) [2].
To propose a general mechanism for the reaction we have investigated the reactivity of Ru(TPP)CO (**2**) towards several aryl azides, discovering that the nature of the active intermediate strongly depends on the electronic nature of the employed azide. The replacement of 3,5-$(CF_3)_2C_6H_3N_3$ with 4-$CF_3C_6H_4N_3$ in the reaction with Ru(TPP)CO allowed the isolation of the mono-imido complex Ru(TPP)(NAr)CO (Ar = 4-$(CF_3)_2C_6H_4$) (**3**) that showed a good catalytic activity in hydrocarbon aminations. On the other hand, the reaction of Ru(TPP)CO with an aryl azide bearing an electron donating group, 4-^{t}Bu$C_6H_4N_3$, gave a very unstable imido complex (**4**). Complex **4** has been detected by NMR and it rapidly decomposed to the mono-amino compound Ru(TPP)(NH_2Ar)CO (Ar = 4-^{t}BuC_6H_4) (**5**) that was isolated and characterised.

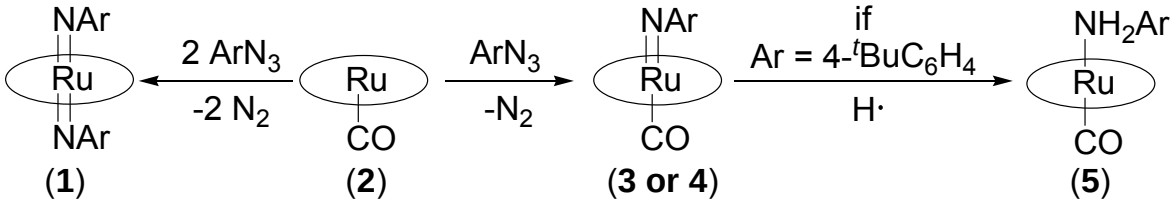

Figure 1

A kinetic study has been also performed to better rationalise the dependence of the reaction mechanism on the nature of the organic azide.

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ORG/OM-OR-01 Cationic Olefin Complexes of Platinum(II): from the Well Established to New Perspectives

Carmen R. Barone, Luciana Maresca, and Giovanni Natile
Dipartimento Farmaco-Chimico, Università degli Studi di Bari "Aldo Moro",
Via E. Orabona, 4 - 70125 Bari, Italy
carmenbarone@farmchim.uniba.it

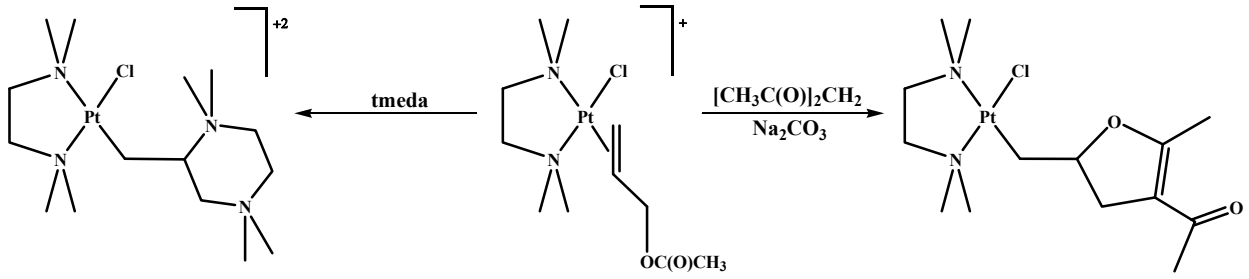
After our first report concerning the complex $[PtCl(\eta^2\text{-}C_2H_4)(N\text{-}N)]^+$, **1**, (N-N = *N*,*N*,*N*′,*N*′-tetramethylethanediamine, tmeda) [1] many properties of this type of species have been clarified.

The obtainment of **1** (the prototype of stable cationic platinum complexes which can contain olefins different from ethene) was a clear experimental proof of the σ-donating properties of olefins, which could give stable complexes also in the absence of relevant π-back-donation from the metal to the unsaturated ligand.

The coordinated olefin is endowed with a good degree of electrophilicity [2] and, in the case of olefins higher than ethene, it can also exhibit Brönsted acidity [3]. Deprotonation can eventually prevail over nucleophilic addition [4].

The dinitrogen ancillary ligand plays an important role in tuning the properties of the complexes; in particular, when tmeda is replaced by an aromatic diimine, the metal becomes more electrophilic and it can compete with the olefin in the reaction with soft nucleophiles [5].

In cationic complexes with allyl acetate, $[PtCl_2(\eta^2\text{-}CH_2{=}CHCH_2OC(O)CH_3)(N\text{-}N)]^+$, two reactive sites are present in the coordinated olefin: the allylic carbon and the C=C double bond. Nucleophiles first replace the acetato group and then add to the olefinic bond. In the case of bidentate nucleophiles a heterocycle is built up in the near proximity of the coordination sphere (see Scheme). When the two donor atoms are different, because of the two consecutive reaction steps, only one of the possible isomers is formed.



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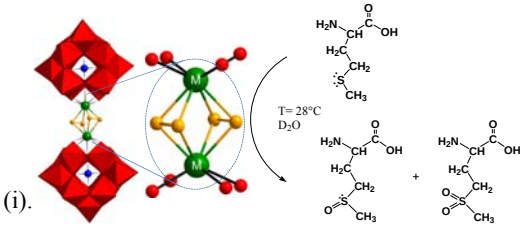
ORG/OM-OR-02 Sustainable Oxidations with Tailored Molecular Metal Oxides: Bridging the Gap between Homogeneous and Heterogeneous Catalysis

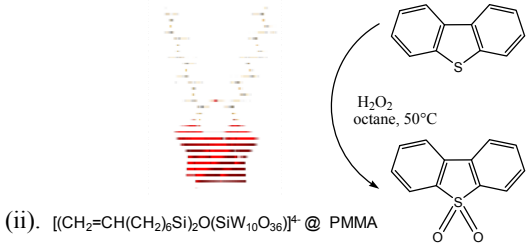
Mauro Carraro, Giulia Fiorani, Antonio Sorarù, Lorenzo Mognon, Andrea Sartorel, Marcella Bonchio, Gianfranco Scorrano

[b] Dipartimento di Scienze Chimiche / ITM-CNR, Unità di Padova Università degli Studi di Padova, Via Marzolo, 1, 35131 Padova *e-mail: mauro.carraro@unipd.it*

Polyoxometalates (POMs) have been proposed as the homogeneous models of solid metal oxides. Their success of as oxidation catalysts is based on their multi-metallic composition, which is pivotal to access diverse mechanistic pathways and an enhanced stability. The presence of d^0 metals, in particular, can be exploited to activate the non-waste producing oxidant H_2O_2. We present herein two promising strategies to design innovative and sustainable oxidative processes with H_2O_2, involving the use of transition metal substituted POMs (TMSPs) and hybrid organic-inorganic POMs.

(i) The molecular structure of TMSPs, featuring well defined catalytic sites, may be very convenient to study the mechanism and to tune their reactivity. Stable dimeric POM structures containing 4th group transition metals as Zr^{IV} or Hf^{IV}, in particular, form peroxometal-butterflies as active species. They have been used in water to oxidize *L*-methionine (70-99% yields in 20-48 h, at r.t.) and benzyl alcohols (50 min, under MW assisted activation, T_{bulk}=90°C, TOF= 75 h^{-1}) [1].





(ii) Covalent grafting of organic moieties on POMs may implement affinity towards different media, as well as immobilization strategies [2]. POMs functionalized with unsaturated alkyl chains have been used as monomers to prepare methacrylate-based copolymers, by means of radical polymerization. The heterogeneous catalytic material has been used to model a fuel desulfurization process: in octane, dibenzothiophene has been quantitatively converted to the corresponding sulfone in 4h (TOF= 18 h^{-1}).

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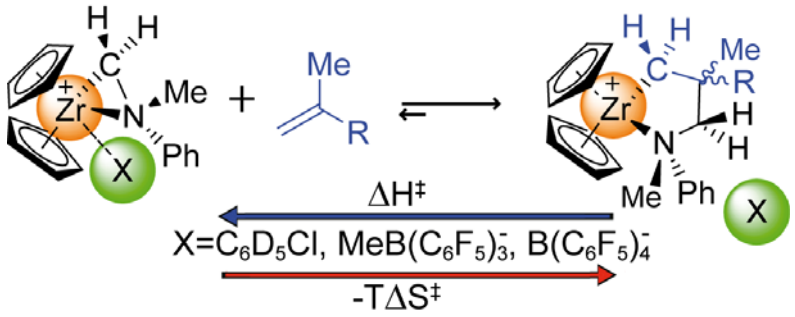
ORG/OM-OR-03 Evaluation of counterion and solvent effect in the single insertion of olefin into the Zr-C bond by low-temperature NMR kinetic studies

Luca Rocchigiani, Gianluca Ciancaleoni, Alceo Macchioni and Cristiano Zuccaccia
Dipartimento di Chimica dell'Università degli Studi di Perugia, Via Elce di Sotto 8, I-06123 Perugia, Italy
luca.rocchigiani@progetti.unipg.it

The insertion of olefin into the metal-carbon bond is the elemental step of the Ziegler-Natta catalysis that, in the homogeneous phase, occurs through the initial association of the olefin with the metal cation of the catalytic ion pair. Group IV metallocenium ion pairs polymerize olefins with high rates, but the elevate reactivity of such systems dramatically complicates fundamental kinetic investigations. During our studies on the self-aggregation of zirconocenium ion pairs [1,2], we synthesized some zirconazidirines having ([$Cp_2Zr(\eta^2$-CH_2-$NR_1R_2)$][X] as general formula that show some remarkable requisites to be used as good models for investigating the single insertion of olefin into the Zr-C bond. In particular, they are able to react stoichiometrically with olefins leading to a five-membered azametallacycle, as represented in figure.



With the aim of obtaining thermodynamic activation parameters of the single insertion and determining as they depend on nature of counterion and solvent, low-temperature kinetic NMR studies of the reaction of 2-methyl-1-heptene with [$Cp_2Zr(\eta^2$-CH_2-NMePh)][X] [**1a**:X^-=$MeB(C_6F_5)_3^-$; **1b**:$B(C_6F_5)_4^-$] ion pairs were performed. Results indicate that, in toluene, $\Delta H^{\ddagger}$ is higher for $MeB(C_6F_5)_3^-$ than for $B(C_6F_5)_4^-$ ($\Delta\Delta H^{\ddagger}$=-4.5 kcal mol^{-1}) but the former better compensates the loss of entropy caused by olefin association ($\Delta\Delta S^{\ddagger}$=-13 cal mol^{-1} K^{-1}). The two ion pairs **1a-b** behave exactly the same in a toluene/chlorobenzene mixture due to the coordination of a chlorobenzene molecule at the zirconium center that pushes the counterion in the second coordination sphere. $\Delta H^{\ddagger}$ (ca 11 kcal mol^{-1}) is higher than in toluene ($\Delta H^{\ddagger}$=8.5 kcal mol^{-1} and $\Delta H^{\ddagger}$=4.0 kcal mol^{-1} for **1a** and **1b**, respectively) while $\Delta S^{\ddagger}$ (ca -26 cal mol^{-1} K^{-1}) is similar to that of **1a** in toluene ($\Delta S^{\ddagger}$=-32 cal mol^{-1} K^{-1}).

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ORG/OM-OR-04 Synthesis and application of Tetraferrocenylporphyrins as sensitive materials in photoelectrochemical devices

Pierluca Galloni,[a] Andrea Vecchi,[a] Alessia Coletti,[a] Barbara Floris,[a] Valeria Conte,[a] Mariano Venanzi,[a] Emanuela Gatto,[a] Martina Tiravia,[a] Victor N. Nemykin[b]

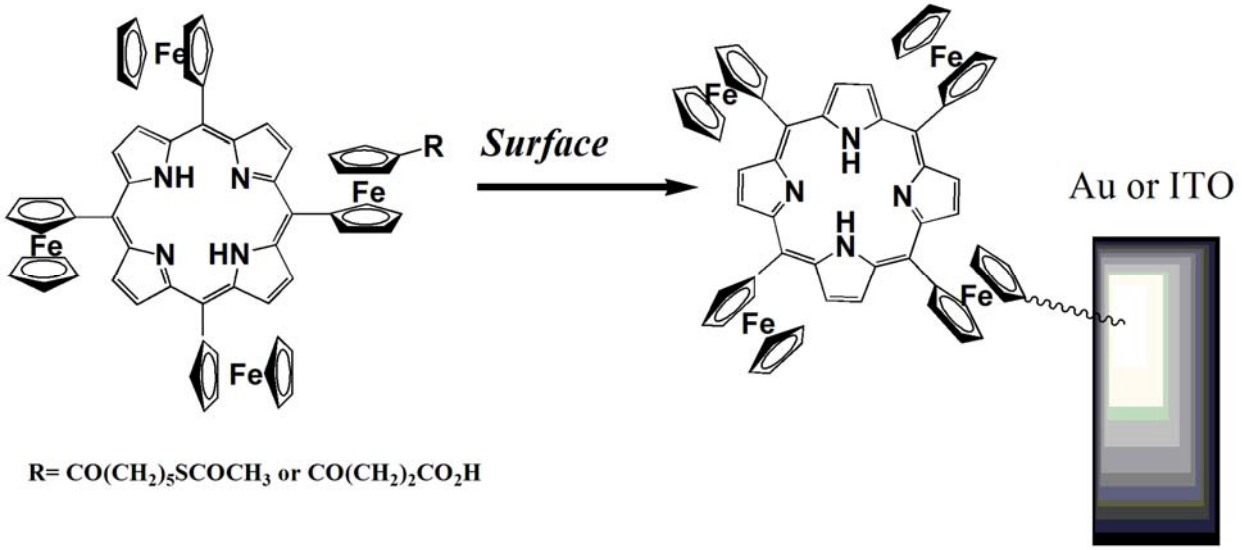
[a]Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma "Tor Vergata", via della ricerca scientifica snc, 00133, Rome, Italy

[b]Department of Chemistry & Biochemistry, University of Minnesota-Duluth, 55812, Duluth, Minnesota USA

galloni@scienze.uniroma2.it

5,10,15,20-tetraferrocenylporphyrins have been object of our interest in different application such as electron transfer reactions [1], mixed-valence states [2], multiredox processes and long-range electronic internal communication [3]. These properties make them suitable for the construction of photochemical devices.

New tetraferrocenylporphyrins containing one functionalized ferrocenyl group were synthetized with the aim to link these molecules on surfaces. A chain with a terminal thioacetate or carboxylic acid was used to obtain functionalized Au or ITO surfaces.



The obtained monolayers were characterized by Uv-vis and electrochemical techniques and used in photoelectrochemical cells. Promising results in terms of photocurrent vs applied potential was obtained and will be discussed in connection with the surface-potential-experimental conditions set.

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[2] V. N. Nemykin, G. T. Rohde, C. D. Barrett, R. G. Hadt, C. Bizzarri, P. Galloni, B. Floris, I. Nowik, R. H. Herber, A. G. Marrani, R. Zanoni, N. M. Loim, *J. Am. Chem. Soc.*, **2009**, *131*, 14969.

[3] V. N. Nemykin, G. T. Rohde, C. D. Barrett, R. G. Hadt, J. R. Sabin, G. Reina, P.Galloni, B.Floris *Inorg. Chem*. **2010**, *49*, 7497.

ORG-FP-01 Ionic tags effect on organic catalyst reactivity

Marco Lombardo, Elisa Montroni, Claudio Trombini

Dipartimento di Chimica "G. Ciamician", Università degli Studi di Bologna, Via Selmi 2, 40126, Bologna, Italy
elisa.montroni2@unibo.it

The insertion of a suitably designed ionic group (tag) in the structure of known catalysts and organocatalysts (Figure 1), allows to obtain two main advantages. The ionic group confers to the molecule a particular solubility profile and so it becomes possible exploit liquid-liquid biphasic reaction condition techniques, where the typical benefits of homogeneous catalysis are combined with the easier procedures for catalyst recovery, typical of heterogeneous catalysis.[1]

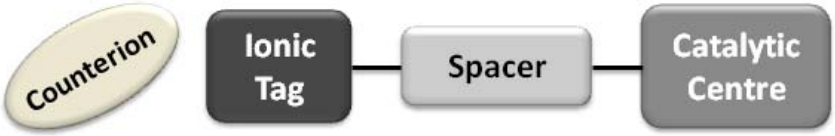
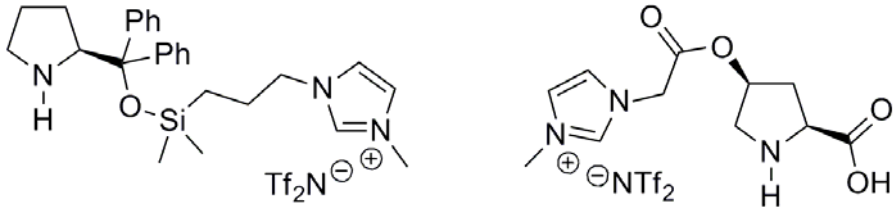


Figure 1

Moreover, catalysts with ionic tags often show an increase of the catalytic performances compared to the equivalent non-ionic catalysts from which they derive.[2] Remarkable activation effects were obtained in the organocatalytic addition reactions of aldehydes to nitroalkenes using catalyst **A** (Figure 2)[3] and in organocatalytic cross-aldol condensations between ketones and aldehydes using catalyst **B** (Figure 2).[4]



A: Michael additions ***B: cross-aldol reactions***

Figure 2

Here the most recent results aimed at rationalizing the effects conferred to reactivity by the presence of ionic tags will be presented, with special attention to the case of organocatalytic enantioselective cross-aldol reactions.

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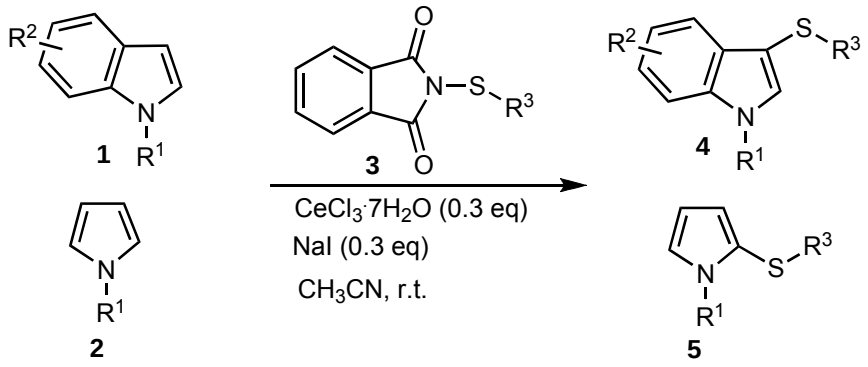
ORG-FP-02 Novel and Efficient $CeCl_3 \cdot 7H_2O$/NaI-Catalyzed Sulfenylation of Indoles and Pyrroles

R. Cipolletti,[a] E. Marcantoni,[a] L. Marsili,[a] S. Menichetti,[b] R. Properzi,[a] C. Viglianisi[b]

[a]School of Science and Technology, Chemistry Division, University of Camerino, via S. Agostino 1, I-62032 Camerino (MC), Italy.
[b]Department of Chemistry "Ugo Schiff", University of Florence, via della Lastruccia 13, I-50019 Sesto Fiorentino (FI), Italy
e-mail: laura.marsili@unicam.it

The preparation and manipulation of functionalized low molecular weight heteroaromatic compounds is of increasing importance for obtaining new more potent pharmaceuticals [1]. In particular, 3-sulfenyl indoles (**4**) and 2-sulfenyl pyrrole (**5**) are an important class of compounds due their activity towards the treatment of several deseases [2], and as inhibitors in medicinal chemistry [3]. Most of methods for their preparation are based on electrophilic aromatic sulfenylation, but a considerable number of them have been unsatisfactory because the procedures provide low yields of the desired products, and/or require harsh conditions that are incompatible with sensitive functional groups [4]. In the framework of our ongoing program in the development of Lewis acid-catalyzed reactions by $CeCl_3$ [5], we have developed a new general and efficient methodology for the sulfenylation of indoles **1** and pyrroles **2** by N-(alkylthio)- and N-(arylthio)phthalimides (**3**) in the presence of our combination $CeCl_3 \cdot 7H_2O$/NaI.



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ORG-FP-03 On the phytotoxins produced by *Diplodia cupressi*, pathogenic fungus of cypress

Marco Masi,[a] Lucia Maddau,[b] Anna Andolfi,[a] Bruno Scanu,[b] Andrea Motta,[c] Angela Tuzi,[d] Antonio Evidente[a]

[a]Dipartimento di Scienze del Suolo, della Pianta, dell'Ambiente e delle Produzioni Animali, Università di Napoli Federico II, via Università 100, 80055 Portici, Italy
[b]Dipartimento di Protezione delle Piante, Università di Sassari, Via E. De Nicola 9, 07100 Sassari, Italy,
[c]Istituto di Chimica Biomolecolare del CNR, Comprensorio Olivetti, Edificio 70, Via Campi Flegrei 34, 80078 Pozzuoli, Italy
[d]Dipartimento di Chimica, Università di Napoli Fedrico II, Complesso Universitario Monte. S. Angelo, Via Cinthia 4, I-80126 Napoli, Italy
E-mail marco.masi@unina.it

The fungi associated with different forms canker disease of the Italian cypress (*Cupressus sempervirens* L.) and other species of *Cupressus* in the Mediterranean area belong to the genera *Diplodia*, *Pestalotiopsis*, and *Seiridium*. They cause heavy losses in cypress plantations within forestry and ornamental uses, thus altering of the typical landscapes, and noteworthy loss in the nursery industry. *Diplodia cupressi* produced all known sphaeropsidins A-F along with sphaeropsidones (**1** and **2**) and chlorosphaeropsidone and its 6-epimer (**3** and **4**) [1]. Only preliminary phytotoxic and antifungal activities were investigated for sphaeropsidones due to their limited amount isolated from the fungal culture filtrates.

Recently, a CBS strain of *D. cupressi*, that appeared to be a good producer of both sphaeropsidone and *epi*-sphaeropsidone, yielded adequate amounts of **1**-**4** to determine, by a X-ray diffratometric analysis, the relative configuration of **1** and therefore that of **2**-**4** and to prepare eight key derivatives to carry out a structure-activity relationships study assaying their phytotoxic and antifungal activities.

In this communication will be illustrated the results obtained in the SAR study in order not only to understand their mechanism of action on plants and their true role in pathogenesis, but also to generate new compounds with potential application as fungicides in agriculture.

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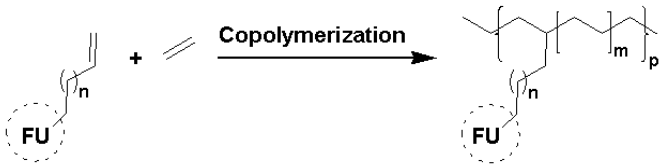
ORG-FP-04 Synthesis of functionalized olefins for the preparation of polymeric additives for food packaging

S. Menichetti,[a] C. Viglianisi,[a] M. C. Sacchi,[b] S. Losio,[b] P. Stagnaro,[c] S. Limbo[d]
[a]Dipartimento di Chimica 'U. Schiff' Universita` di Firenze, Via della Lastruccia 3-13, 50019 Sesto Fiorentino, Firenze, Italy
[b]ISMAC-CNR via E. Bassini 15, 20133 Milano, Italy
[c]ISMAC-CNR via De Marini 6, 16149 Genova, Italy
[d]Dipartimento di Scienze e Tecnologie Alimentari e Microbiologiche, Università degli Studi di Milano, Via Celoria 2, 20133 Milano, Italy
caterina.viglianisi@unifi.it

Polyolefins are the plastics most frequently used as food contact materials due to their low cost and low reactivity. However, polyolefins are quite sensitive to oxidation and require to be stabilized by blending with antioxidant additives to inhibit or retard oxidative degradation. The vast majority of commercial available antioxidants are low molecular weight derivatives of sterically hindered monohydroxy phenols. Since their chemical structure is quite different from that of the non polar polymer matrix, two problems can be envisaged: i) the poor solubility of the antioxidants into the polyolefin matrix, which can induce aggregation of the stabilizers and an inhomogeneous distribution; ii) the mobility and volatility of the antioxidants, that can lead to their loss by migration or diffusion from the polyolefin matrix.

Aim of this project is the synthesis of functionalized olefins bearing an antioxidant and/or a HALS (Hindered Amine Light Stabilizers) Functional Unit (**FU**) moiety separated from the double bond by methylene spacers of different lengths. These monomers can be employed as comonomers with ethylene (or propylene) to obtain very stable and solid macromolecular additives where the stabilizers **FU**s are covalently bonded to the polymeric chains. Such macromolecular additives are, in turn, used as masterbatch for the preparation of non-releasing polymeric films for food packaging [2].



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ORG-FP-05 Synthesis and self-organization of novel bock co-polymers for water filtration

Giuliano Iacobellis, Gianluca M. Farinola,[a] Giuseppe Calamita,[b]

[a]Dipartimento di Chimica - Università di Bari, Via Orabona, 4, 710125, Bari, Italy
[b] Dipartimento di Fisiologia Generale Ambientale - Università di Bari, Via Amendola, 165/A 71012,- Bari, Italy
E-mail iacobellis@chimica.uniba.it

Water channel proteins (**WCP**) are a particular class of transmembrane proteins embedded in the cell membrane that regulate the flow of water and thus the osmotic pressure inside the cell.[1] These proteins can be extracted from living cell or expressly synthesized and incorporated in liable synthetic vesicles or liposomes keeping their activity. More recently water channel protein (also known as Aquaporin) have been incorporated in very stable synthetic block co-polymers opening to the realization of free standing films for water filtration.[2]
For practical application a particularly high fraction of **WCP** have to be functionally incorporated into the synthetic membrane and this depends on the nature of the copolymer used (chemical composition, on structural rigidity).
In this framework, we report the synthesis and characterization of novel poly(methyloxiazoline)block(polydimethyl siloxane)block(polymethyl oxiazoline) co-polymers incorporating rigid and fluorescent perilene diimide units inside the apolar block that offer the possibility to follow their self-aggregation in solution by simple optical spectroscopy techniques.
On the other hand the presence of rigid planar units into the flexible PDMS apolar block offers the chance to study the possible interaction when **WCP** are functionally incorporated.

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ORG-FP-06 Scalable *in situ* diazomethane generation in continuous-flow reactors

Emiliano Rossi[a], Pierre Woehl[b], Michele Maggini[a].

[a] Dipartimento di Scienze Chimiche dell'Università degli Studi di Padova, Via Marzolo 1, 35131, Padova, Italy.
[b] Corning European Technology Center, 7-bis Avenue de Valvins, 77210, Avon, France.
Email: emiliano.rossi@unipd.it.

Diazomethane is a highly reactive and selective reagent for the synthesis of pharmaceuticals and fine chemicals [1]. However, its acute toxicity and explosive characteristics strongly discourage a large-scale use in synthesis.

In this communication we report an optimized continuous generation of diazomethane through the base-induced decomposition of the precursor N-methyl-N-nitrosourea which is safer to store than other diazomethane precursors. Process scale-up was quickly and efficiently achieved on a modular continuous-flow platform that allowed the production and use of diazomethane up to 19 mol d^{-1} at a total flow rate of 53 ml min^{-1}, while maintaining the amount of diazomethane itself in the reactor limited to 6.5 mmol. This process productivity could, at least in principle, fulfill the needs of small pharma or fine chemical companies. Best reaction parameters were first developed on a small-volume flow reactor (0.9-1.35 ml) for minimal reagents consumption. Then a 10-folds production improvement was achieved by increasing the flow reactor dimensions (15-25 ml) with a very limited optimization effort.

In addition, hazardous diazo compounds produced in flow conditions were successfully used to prepare functionalized fullerenes with potential use as acceptor components in polymer-based solar cells.

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ORG-FP-07 Convenient synthetic approach to functionalized quinolines and 1,2,3,4-tetrahydrobenzo[*c*][2,7]naphtyridines

Giacomo Guerrini[a], Maurizio Taddei[b] and Fabio Ponticelli[a]

[a]Dipartimento di Chimica, Università di Siena, Via Aldo Moro 2, 53100 Siena, Italy
[b]Dipartimento Farmaco Chimico Tecnologico, Università di Siena, Via Aldo Moro 2, 53100 Siena, Italy
giacomoguerrini@unisi.it

Following our interest for the preparation of aromatic *ortho*-amino ketones, we reported a convenient photochemical access to this kind of useful molecules that cannot be readly available by a common synthetic strategy, requiring the use of drastic reaction conditions and/or the presence of toxic and expensive reagents. Ortho-amino ketones have been recently used for the synthesis of 1,4 benzodiazepines and quinazolines, [1] two important classes of organic scaffolds.
Hereby we reported the application of aromatic *ortho*-amino ketones for a convenient synthetic access to two more classes of interesting heterocyclic systems: quinolines and naphtyridines.
The former were obtained starting from aromatic anilides irradiated at 254 nm to give the correspondent *ortho*-amino ketones that were subsequently treated with dimethyl-acetylen-dicarboxylate (DMAD) to give the desired products in moderate to good yields. Quinoline is a common structural motif found in many natural products with remarkable pharmacological properties. Members of this family have wide applications in medicinal chemistry, being used as antimalarial (chloroquine and mefloquine), anti-inflammatory, antiasthmatic, antibacterial, and antihypertensive activities: hence continues to spur synthetic efforts regarding their acquisition.[2]
Benzo-condensed quinolines, with particular attention to benzo[*c*][2,7]-naphtyridines, have been recently considered for their wide range of biological activities such as inhibition of phosphoinositide-dependent protein kinase 1 (PDK-1) involved in the progression of some kinds of cancer, release of calcium, antiviral and antimicrobial activity and cytotoxicity. [3] They were obtained in excellent yields for treatment of some quinoline derivatives with potassium carbonate.

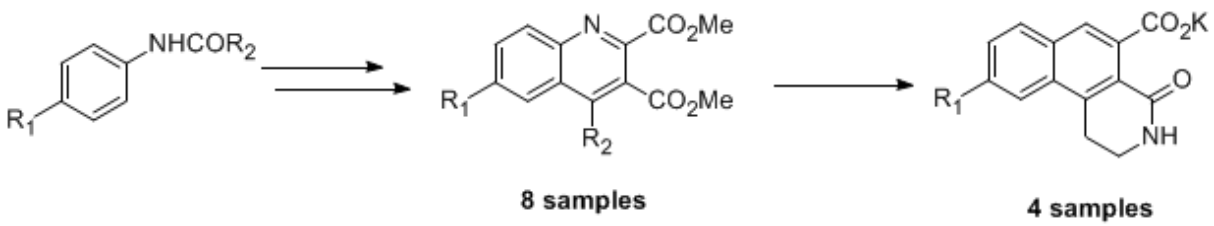

Figure 1.

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ORG-FP-08 Sequence Stereoisomerism in Calixarene-Based Pseudo[3]rotaxanes

C. Talotta, C. Gaeta, T. Pierro, P. Neri

Department of Chemistry and Biology, University of Salerno, Via Ponte don Melillo, I-84084 Fisciano, Salerno, Italy

ctalotta@unisa.it

Very recently we reported that new pseudorotaxane systems can be easily obtained by the *through-the-annulus* threading [1] of scarcely efficient calix[6]arene hosts upon exploiting the inducing effect of the weakly coordinating tetrakis[3,5bis(trifluoromethyl)phenyl]borate (TFPB) anion that gives free "naked" dialkylammonium cations.

This approach was subsequently extended to the preparation of pseudo[3]rotaxane systems in which two calix[6]arene macrocycles are threaded by a bis(benzylalkylammonium) axle [2]. Because of the three-dimensional nonsymmetrical nature of the calix[6]arene wheels, in these instances three sequence stereoisomers [3] could be obtained, which can be termed as head-to-head (H,H), head-to-tail (H,T) and tail-to-tail (T,T) (**Figure 1**). We demonstrated that the stereo-controlled direct preparation of any given sequence stereoisomer can be obtained by exploiting the preference for the *endo*-alkyl complexation over the *endo*-benzyl one. These stereoisomeric pseudo[3]rotaxanes, in analogy to natural informational systems -DNA, RNA and proteins- could allow the design of "*informational devices*" in which each sequence isomer corresponds to a specific physical or chemical output.

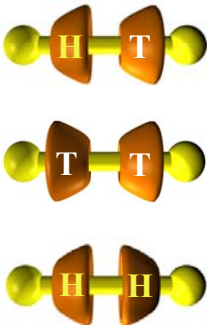

Figure 1

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ORG-PO-01 Synthesis and characterization of dendrimeric polyesters containing peripheral lysine and histidine groups

S. Alfei, S. Castellaro, M. Pocci, F. Lucchesini, V. Bertini
Dipartimento di Chimica e Tecnologie Farmaceutiche e Alimentari, Università di Genova, Via Brigata Salerno, 13 I-16127 Genova, Italy.
alfei@dictfa.unige.it.

Dendrimers are a unique class of polymeric systems characterized by well- defined nanostructured architecture, high symmetry, narrow polydispersity, presence of functional groups at the periphery which can be chemically trans-formed. These structural properties make dendrimers particularly suitable for biomedical applications such as drug delivery, bioimaging, gene therapy [1].
With the aim of preparing non toxic polycation dendrimers to use as non-viral vectors for gene delivery [2], we report in this communication the synthesis of hydrolyzable polyester-based dendrimers of fourth and fifth generation bearing hydroxy end-groups (Figure 1) derived from 2,2-*bis*(hydroxymethyl)propanoic acid, characterized by low toxicity *in vivo*, properly functionalized at the periphery with lysine and histidine groups.

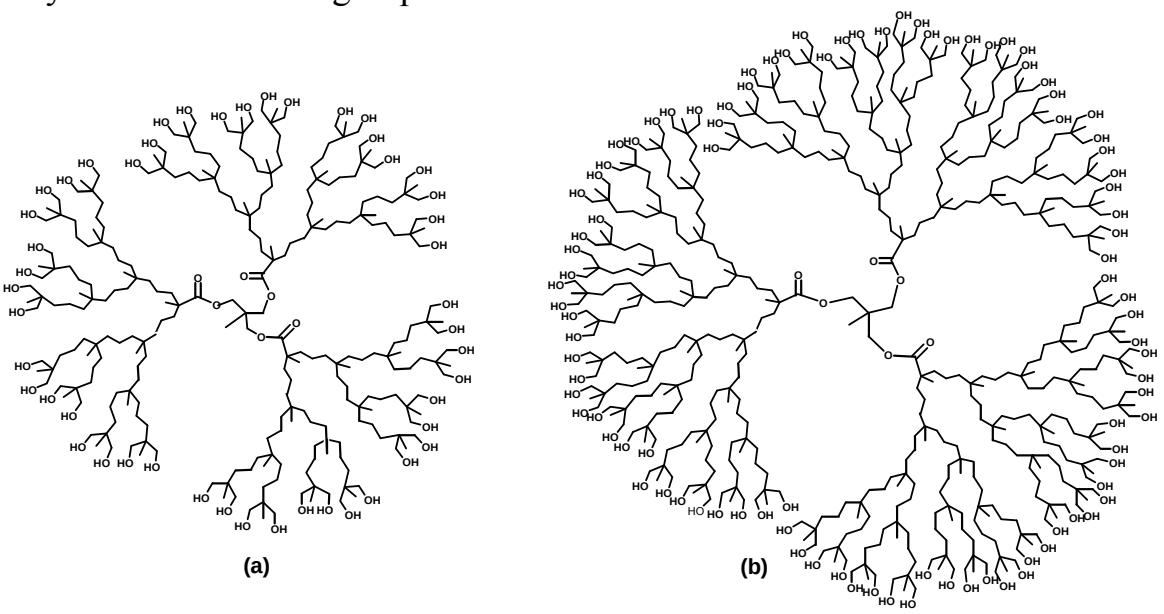

Figure 1. Skeletal structures of dendrimers of 4th (a) and 5th generation (b).

The prepared functionalized dendrimers were characterized through ^{1}H-NMR, potentiometric and volumetric titrations. A very good accordance was observed between theoretical and experimental molecular weight data.

References:
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ORG-PO-02 Aggregation of Pluronics in Ionic Liquids

Guido Angelini, Gabriella Siani, Antonella Fontana, Paolo De Maria, Carla Gasbarri

Dipartimento di Scienze del Farmaco dell'Università G. d'Annunzio di Chieti-Pescara, Via dei Vestini, 66100 Chieti, Italy
g.angelini@unich.it

Pluronics (PEO_y-PPO_x-PEO_y triblock copolymers) self-assemble in water to form mainly micelles with several potential applications [1], such as the improvement of the aqueous solubility of drugs, chemical separations and nanoparticle synthesis

Room temperature ionic liquids (RTILs) are alternative solvents with characteristic properties, such as non-flammability, low volatility, high thermal stability [2]. RTILs can solubilise both hydrophilic and hydrophobic compounds and influence the aggregation properties of amphiphilic molecules.

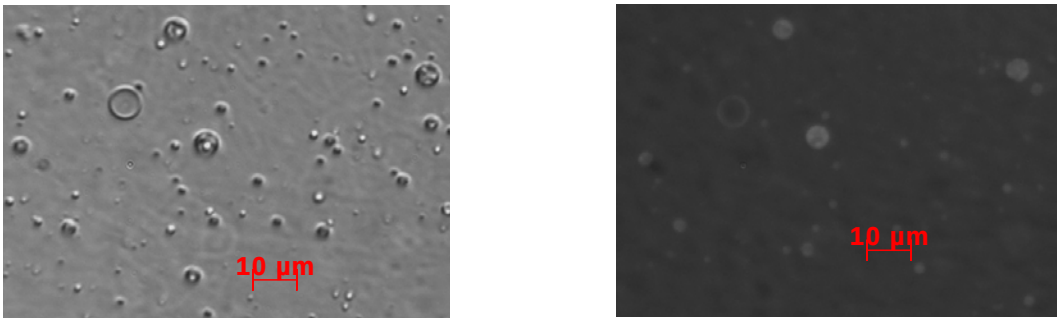

Figure 1.

The aggregation of a series of Pluronics (P85, P105, L121) in some RTILs ($[Bmim^+]$ $[BF_4^-]$, $[Bmim^+]$ $[PF_6^-]$ and $[Bmim^+]$ $[TF_2N^-]$) has been investigated by using different techniques (UV-NIR spectroscopy, optical microscopy).

The critical aggregation concentration (CAC) of the investigated Pluronics has been determined by UV-NIR [3]. The CAC increases in the RTILs in comparison to water, suggesting an higher affinity of the polymers for the ionic liquids. The values of CAC depends on both the nature of the polymer (PEO/PPO ratio) and the permittivity (ε) of the ionic liquid.

Supramolecular structures have been observed by optical microscopy (Figure 1).

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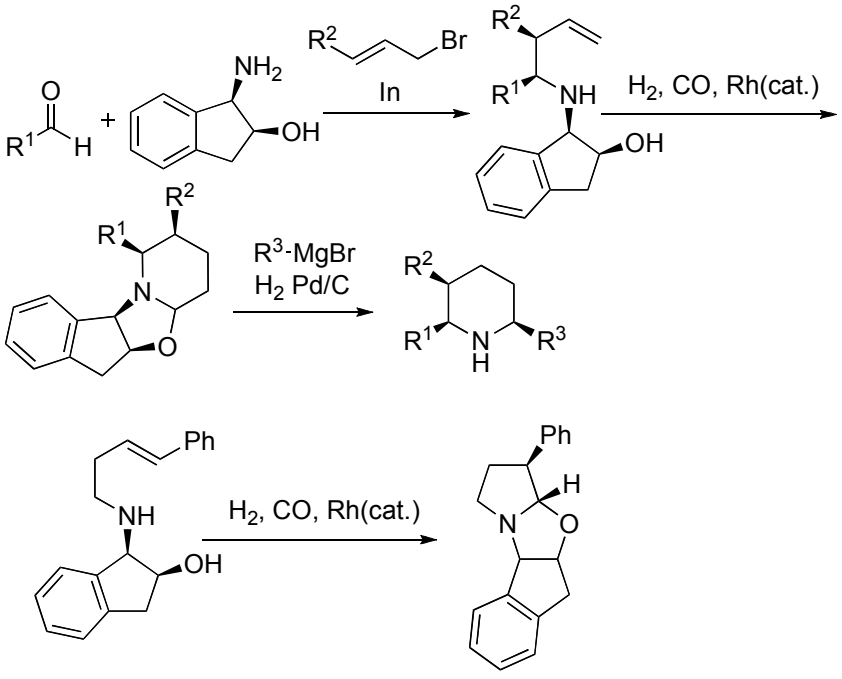
ORG-PO-03 Cyclohydrocarbonylation-Based Strategy toward aza-heterocycles

Giada Arena,[a] André Mann,[b] Jessica Salvadori,[a] Nicolas Girard[b] and Maurizio Taddei [a]

[a] Dipartimento Farmaco Chimico Tecnologico, Università degli Studi di Siena, Via A. Moro 2, 53100 Siena.
[b] Laboratoire d'Innovation Thérapeutique, UMR 7200 CNRS-Université de Strasbourg, Faculté de Pharmacie, 67401 Illkirch, France
arena9@unisi.it

Cyclohydrocarbonylation (CHC) is a versatile strategy for domino or multicomponent synthesis of library of aza-heterocycles.
A series of 2-, 2,3- e 2,6- e 2,3,6- substituted enantiomerically pure piperidines can be prepared by cyclohydrocarbonylation of chiral homoallyl amines, prepared via Indium mediated allylation or crotylation of aldehydes using (S)-2-phenylglycinol or (1*R*,2*S*)-1-amino-2-indanol as chiral auxiliary [1].



A similar procedure can be applied to the synthesis of pyrrolidine derivates with a high level of stereocontrol due to the presence of the aromatic ring.

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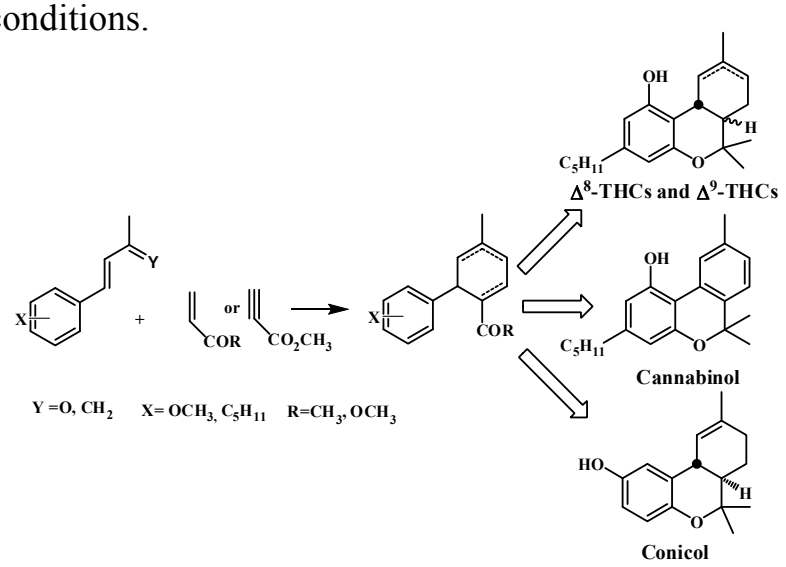
ORG-PO-04 High-Pressure Entry into Cannabinoids Family

Eleonora Ballerini, Lucio Minuti
Dipartimento di Chimica, Università degli Studi di Perugia, via Elce di Sotto 8, 06123, Perugia, Italy
eleonoraballerini@yahoo.it

In recent years, our interest has been focused in developing novel synthetic routes to target molecules incorporating the tetrahydro-6H-benzo[c]chromene system [1]. This structural motif has been proposed as a *privileged structure* since occurs as subunits in a diverse range of bioactive natural products, being capable of interacting with a variety of cellular targets.
Recently, our laboratory reported an high-yielding and environmental safe method for the construction of the *cis*- and *trans*-6a,7,10,10a-tetrahydro-6H-benzo[c]chromene skeleton through the use of a Diels-Alder reaction using coumarins or alkoxybenzylideneacetones as dienophiles [2].
Herein we report the study of the Diels-Alder reaction of alkoxy/alkyl-substituted 1-phenyl-1,3-butadienes with methyl vinyl ketone, methyl acrilate and methyl propriolate in ethanol, water or dichloromethane as reaction medium and/or under high-pressure conditions.



This approach has been used to synthesized a large number of cannabinoid derivatives, including the Δ^9-*cis*- and the Δ^9-*trans*-THCs, the cannabinols and the conicols family . Application of this approach to the synthesis of paracyclophane derivatives that are useful in the field of new materials, will be also reported.

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ORG-PO-05 Anion Binding in Water with Use of Metal-salophen receptors

Silvia Bartocci[a], Antonella Dalla Cort[a], Kristin Bartik[b], Gianpiero Forte[a], Luca Schiaffino [c], Francesco Yafteh Mihan[a]

[a] Dipartimento di Chimica, Università La Sapienza, Piazzale Aldo Moro 5, 00185 Roma.

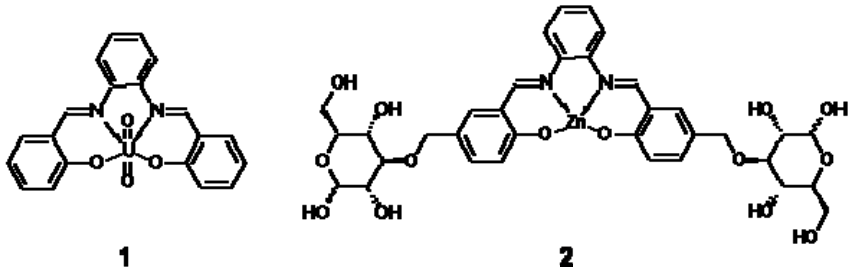
[b] Université libre de Bruxelles, Matières et Matèriaux, Bruxelles, Belgium.

[c] Dipartimento di Scienze e Tecn. Chimiche, Università degli Studi Tor Vergata, 00173 Roma

e-mail: silvia.bartocci@uniroma1.it

Anions are ubiquitous in both the organic and mineral worlds. They play different key roles in biology, and cause dramatic effects as environmental pollutants. Consequently the development of synthetic anion receptors that work in water represents an area of significant current interest in supramolecular chemistry[1] nurtured by the potential practical applications of such systems for the detection and quantification of these species. Obviously the task is quite challenging. The intrinsic peculiarities of anions make their complexation quite different from that of cations. It was initially thought that only positively charged receptors could compete with anion solvation, but recently it has been shown that neutral hosts that rely on hydrogen bond formation and/or on Lewis acidity can also exhibit considerable affinity for anions in water[2].

Here we report that metal-salophen based receptors, structurally simple and easy to prepare, can become protagonists in this field[3]. Different approaches and different strategies have been pursued in order to achieve selective and efficient binding of anions in water. One is the use of micelles (CTABr, CTACl) to solubilize the Uranyl-salophen receptors. Receptor **1**, under these conditions, exhibits high binding affinity towards fluoride anion[3], $K_a>10^4$ M^{-1}. Another is to introduce, on the basic skeleton of the receptor, neutral hydrophilic groups like glucose units. Zn-salophen complex **2** is reasonably soluble in water and behaves as a good receptor for a number of α-aminoacids through carboxylate binding[4].



1 **2**

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[4] Work carried out within the frame of COST Action 1005 « Supramolecular Chemistry in Water »

ORG-PO-06 Multi-metallic molecular catalysts for water oxidation

Irene Bazzan, Serena Berardi, Andrea Sartorel, Mauro Carraro, Gianfranco Scorrano and Marcella Bonchio
Università degli studi di Padova e ITM-CNR, Dipartimento di Scienze Chimiche via Marzolo 1 − 35131 Padova (Italy)
andrea.sartorel@unipd.it

Artificial photosynthesis converts solar light into chemical energy, by the light driven splitting of water into hydrogen and oxygen, and can therefore be considered as a promising route to produce renewable fuels, satisfying the ever increasing global energy demand.[1]
The development of suitable catalysts for water oxidation to dioxygen is nowadays recognized as the bottleneck for the construction of an efficient device for water splitting.[2] Bio-inspired approaches try to mimic the natural machinery of the photosystem II enzyme, which orchestrates low energy pathways leading to oxygen evolution through a catalytically active Mn_4CaO_5 core.
In this communication, we report the development of novel, molecular catalysts for water oxidation to oxygen, incorporating multi-metallic reactive nano-cores[3-5] including also cheap and abundant metals such as Cobalt.[5]
Success in this task has been demonstrated by homogeneous processes under dark and illumination conditions, in combination with ruthenium polypyridine photosensitizers.[6-7]
Optimization of the molecular system and its evolution within functional nano-materials is envisaged for photoelectrochemical water splitting devices.[8]

[1] M Carraro, A Sartorel, FM Toma, F Puntoriero, F Scandola, S Campagna, M Prato, M Bonchio *Top. Curr. Chem.* **2011**, in press.
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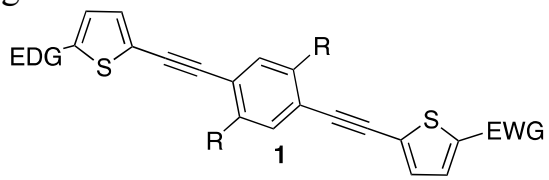
ORG-PO-07 Thiophene- and Imidazole-based π-Conjugated Fluorophores via Selective Pd-catalyzed C-C Bond Formation Reactions

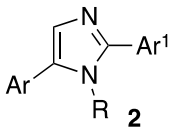
Fabio Bellina and Marco Lessi
Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Risorgimento 35, 56126 Pisa, Italy
bellina@dcci.unipi.it

The development of nanometer-sized fluorophores of precise length showing π-extended conjugation has attracted considerable attention over the past decades. One driving force for the growing interest in this area is the realization that such molecular devices can be used for a variety of applications, ranging from solar energy conversion [1] to optoelectronic devices [2]. Among the molecular fluorophores, thiophene-substituted acetylenes are undoubtedly technologically important materials [3]. In this communication we will describe the preparation of novel push-pull thienyl-substituted 1,4-bis-ethynylbenzenes **1** using selective Pd-catalyzed cross couplings.



1

We will also illustrate our efforts in the application of selective Pd-catalyzed direct C-H arylation protocols [4] to the synthesis of 2,5-diarylimidazoles **2** and bis-imidazoles **3**, two interesting classes of imidazole-based fluorophores.



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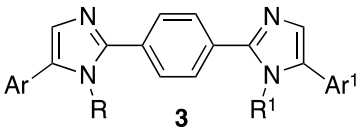

3

Organic fluorophores containing an imidazole core are interesting molecules due to their unique optical properties and relevant thermal stability [5], and could find application also as pH probes [6].

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ORG-PO-08 HIV-Pr inhibitors from stereoselective azidation and click chemistry on monohydroxyethylene cores

Fabio Benedetti, Federico Berti,[a] Pietro Campaner,[a] Lidia Fanfoni,[a] Adrian Ostric,[a] and Biswajit Kumar Singh.[a]

[a]Dipartimento di Scienze Chimiche e Farmaceutiche dell'Università degli Studi di Trieste, Via L.Giorgieri 1, 34127 Trieste, Italy.

lfanfoni@units.it

In connection with our interest in the synthesis of dipeptide isosteres and pseudopeptide HIV-Pr inhibitors, we have developed in the past a methodology for the stereoselective hydroazidation of α,β-unsaturated ketones, to *syn* β-azidoketones.[1] Such products could offer a useful entry point towards stereopure azido-alcohols, and by this route towards libraries of potential HIV-Pr inhibitors (Fig. 1) by exploiting combinatorial chemistry by differential acylation at nitrogen and by the click chemistry strategy[2] at the azido group.

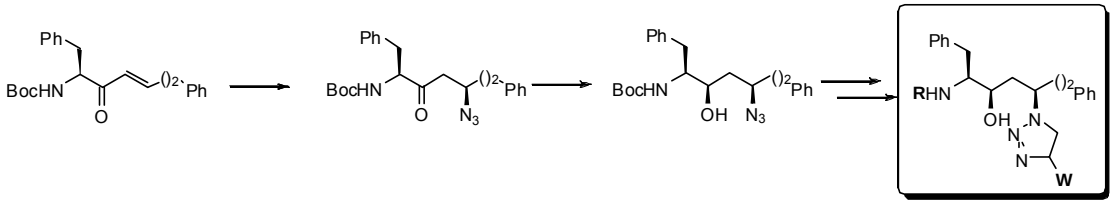
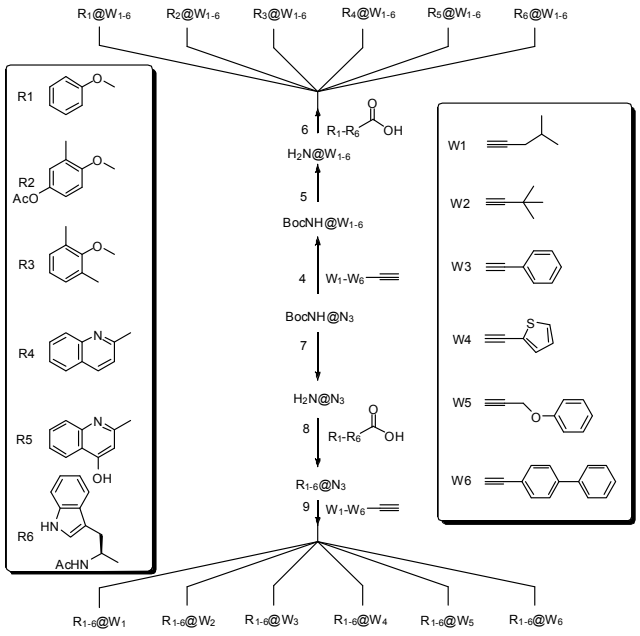


Figure 1.

By this way we have synthesized ten couples of 36 member orthogonal libraries by varying substituents on triazole ring (W) and different lateral chains (R).



Scheme 1.

The libraries were then submitted to a screening for HIV-Pr inhibition. After deconvolution, the most promising compounds were identified and synthesized as optically pure compounds; their anti-HIV-Pr activity was confirmed and their synthesis was optimized.

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ORG-PO-09 Configurational Stability of 2,7-Dihydro-1-Phenyl-Phosphepine-Oxides and Electronic Properties of the Phosphanes

T. Benincori,[a] V. Bonometti,[b] R. Cirilli,[c] R. Ferretti, [c] P. Mussini,[b] M. Pierini,[d] T. Pilati,[e] S. Rizzo,[e] F. Sannicolò,[f] L. Vaghi [f]

[a] Dipartimento di Scienze Chimiche ed Ambientali, Università dell'Insubria, via Valleggio 11, 22100, Como, Italy

[b] Dipartimento di Chimica Fisica ed Elettrochimica, Università di Milano, via Golgi 19, 20133 Milano, Italy

[c] Dipartimento del Farmaco, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161, Roma, Italy

[d] Dipartimento di Chimica e Tecnologie del Farmaco, Università di Roma "La Sapienza", P.le Aldo Moro 5, 00185, Roma, Italy

[e] Istituto di Scienze e Tecnologie Molecolari, Consiglio Nazionale delle Ricerche, via Golgi 19, 20133, Milano, Italy

[f] Università di Milano, Dipartimento di Chimica Organica e Industriale and C.I.MA.I.NA., via Venezian 21, 20133, Milano, Italy

roberto.cirilli@iss.it

The configurational stability of four chiral 2,7-dihydro-1-phenyl-phosphepine-oxides **1a**-**4a** (Figure 1), differing for the nature of the aromatic rings (carbocyclic or heterocyclic, six- or five-membered) constituting the stereogenic scaffold have been investigated. Unknown compound **4a** was fully characterized by single crystal X-ray analysis. The tendency to enantiomerize has been determined by circular dichroism and on-column enantioselective HPLC methods. Biphenine-oxide **1a** was found the only unstable compound at room temperature, displaying an enantiomerization barrier of about 20 kcal mol^{-1}.

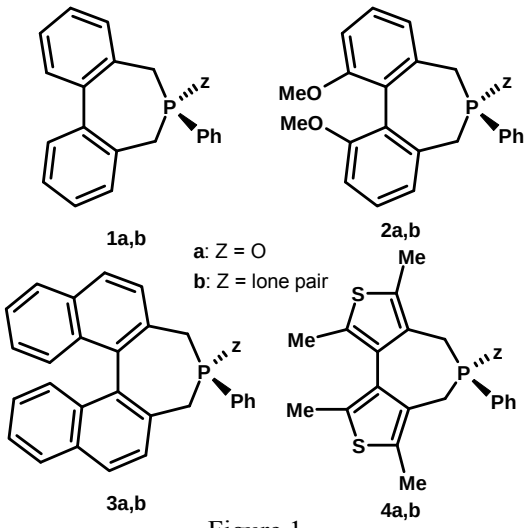


Figure 1.

Also the corresponding phosphanes **1b**-**4b** have been considered in order to perform a comparative evaluation of their electronic availability, which is a crucial parameter affecting both the catalytic activity and stereoselection ability of their metal complexes. Unknown bithienophosphepine **4b** was fully characterized by single crystal X-ray analysis. The quantitative evaluation of the electronic properties was performed by voltammetry, using the electrochemical oxidative peak potential as probe: the higher the value, the electron-poorer the phosphane. The electronic availability was found to decrease along to the sequence: **2b**, **4b**, **3b**, **1b**.

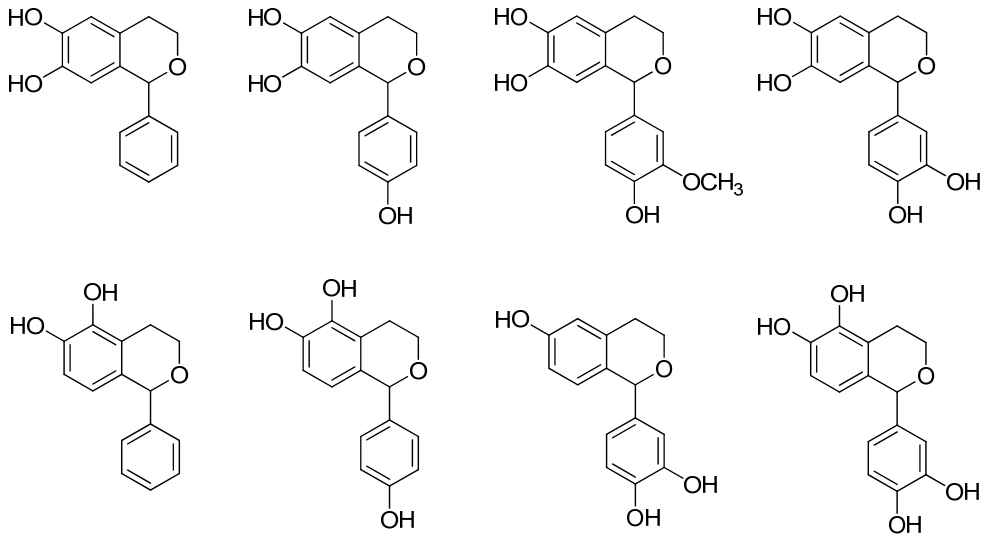
E.Alberico, S.Karandikar, S.Gladiali, *ChemCatChem 22*, **2010***,* 1395 and references therein.

ORG-PO-10 Convenient synthesis of novel 1-aryl-dihydroxyisochromans exhibiting antioxidant activity

Roberta Bernini,[a] Fernanda Crisante,[a] Giancarlo Fabrizi,[b] Patrizia Gentili [c]

[a] Dipartimento di Scienze e Tecnologie per l'Agricoltura, le Foreste, la Natura e l'Energia dell'Università degli Studi della Tuscia, Via S. Camillo De Lellis, 01100 Viterbo, Italy
[b] Dipartimento di Chimica e Tecnologia del Farmaco della Sapienza Università di Roma, P. le A. Moro 5, I-00185 Roma, Italy
[c] Dipartimento di Chimica e IMC-CNR Sezione Meccanismi di Reazione della Sapienza Università di Roma, La P. le A. Moro 5, I-00185 Roma, Italy
Email: berninir@unitus.it

A large panel of 1-aryl-dihydroxyisochromans showing novel patterns of substitution into A or B aromatic rings were synthesized from phenethyl alcohols and substituted benzaldehydes by the oxa-Pictet-Splenger reaction performed in dimethyl carbonate (DMC), an ecofriendly solvent, followed by the regioselective aromatic hydroxylation/oxidative aromatic demethylation with 2-iodoxybenzoic acid (IBX)/sodium dithionite ($Na_2S_2O_4$) system [1].



All 1-aryl-dihydroxyisochromans were tested about their radical scavenging activity toward 2,2-diphenyl-2-picrylhydrazyl radical ($DPPH^{\cdot}$) and compared to the corresponding phenolic or guaiacolic derivatives. Experimental results confirmed the important role of the catecholic moiety for the antioxidant activity.

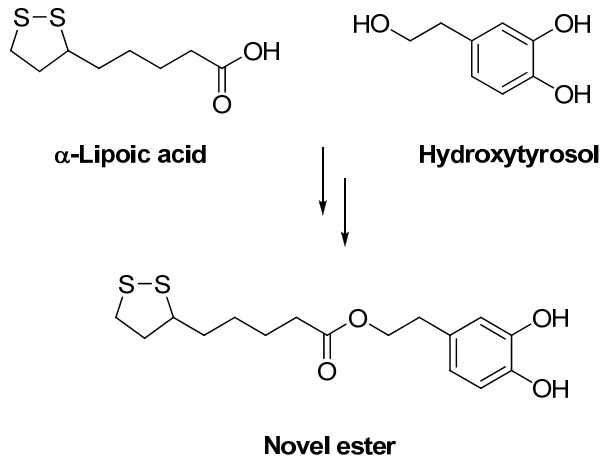
[1] R. Bernini, F. Crisante, G. Fabrizi, P. Gentili *Tetrahedron* **2011**, *submitted*.

ORG-PO-11 Synthesis of a novel ester of hydroxytyrosol and α-lipoic acid exhibiting an antiproliferative effect on human colon cancer HT-29 cells

Roberta Bernini,[a] Fernanda Crisante,[a] Nicolò Merendino,[b] Romina Molinari,[b] Maria Chiara Soldatelli,[b] Francesca Velotti [b]

[a] Dipartimento di Scienze e Tecnologie per l'Agricoltura, le Foreste, la Natura e l'Energia dell'Università degli Studi della Tuscia, Via S. Camillo De Lellis, 01100 Viterbo, Italy
[b] Dipartimento di Scienze Ecologiche e Biologiche dell'Università degli Studi della Tuscia, Via S. Camillo De Lellis, 01100 Viterbo, Italy
Email: berninir@unitus.it

A novel ester obtained by joining biologically active compounds such as hydroxytyrosol and α-lipoic acid was prepared in satisfactory yield and high purity by a simple and efficient procedure [1].



The effect of the novel ester on the proliferation of the human colorectal adenocarcinoma HT-29 cell line was evaluated. The experimental results showed that it exhibited an antiproliferative effect significantly more potent than the corresponding parent compounds, either singularly or in combination. Moreover, it induced a significantly stronger block of the cell cycle at the G2/M phase than hydroxytyrosol and α-lipoic acid, either singularly or in combination. This result indicates that the inhibition of cancer cell growth was mediated by the induction of a G2/M phase cell cycle arrest.

Further syntheses are currently in progress in our laboratories for the preparation of analogue derivatives to be tested.

[1] R. Bernini, F. Crisante, N. Merendino, R. Molinari, M. C. Soldatelli, F. Velotti *Eur. J. Med. Chem. 46,* **2011**, 439-446.

ORG-PO-12 Chemoselective C-4 Aerobic Oxidation of Catechin Derivatives Catalyzed by the *Trametes villosa* Laccase/1-Hydroxybenzotriazole System: Synthetic and Mechanistic Aspects

Roberta Bernini,[a] Fernanda Crisante,[a] Patrizia Gentili,[b] Fabio Morana,[b] Marco Pierini,[c] Monica Piras [c]

[a] Dipartimento di Scienze e Tecnologie per l'Agricoltura, le Foreste, la Natura e l'Energia dell'Università degli Studi della Tuscia, Via S. Camillo De Lellis, 01100 Viterbo, Italy
[b] Dipartimento di Chimica and IMC-CNR Sezione Meccanismi di Reazione della Sapienza Università di Roma, La P. le A. Moro 5, I-00185 Roma, Italy
[c] Dipartimento di Chimica e Tecnologia del Farmaco della Sapienza Università di Roma, P. le A. Moro 5, I-00185 Roma, Italy
Email: berninir@unitus.it

Catechin derivatives have been oxidized under aerobic conditions in the presence of the *Trametes villosa* laccase/1-hydroxybenzotriazole (HBT) system in buffered water/1,4-dioxane as reaction medium [1]. The oxidation products, flavan-3,4-diols and the corresponding C-4 ketones, are bioactive compounds and useful intermediates for the hemisynthesis of proanthocyanidins, plant polyphenols providing beneficial health properties for humans.

Determinations of oxidation potentials excluded that catechin derivatives could be directly oxidized by laccase Cu(II), while it resulted in the H-abstraction from benzylic positions being promptly promoted by the enzyme in the presence of the mediator HBT, the parent species producing in situ the reactive intermediate benzotriazole-N-oxyl (BTNO) radical. A remarkable and unexpected result for the laccase/HBT oxidative system has been the chemoselective insertion of the oxygen atom into the C-4-H bond of catechin derivatives. Mechanistic aspects of the oxidation reaction have been investigated in detail for the first time in order to corroborate these results. Since the collected experimental findings could not alone provide information useful to clarify the origin of the observed chemoselectivity, these data were expressly supplemented with information derived by suitable molecular modeling investigations. The integrated evaluation of the dissociation energies of the C-H bonds calculated both by semiempirical and DFT methods and the differential activation energies of the process estimated by a molecular modeling approach suggested that the observed selective oxidation at the C-4 carbon has a kinetic origin.

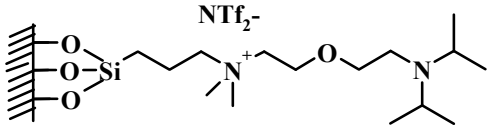
[1] R. Bernini, F. Crisante, P. Gentili, F. Morana, M. Pierini, M. Piras *J. Org. Chem. 76*, **2011**, 820-832.

ORG-PO-13 Heterogeneization of a Basic Ionic Liquid and its Use as Catalyst in Knoevenagel and Michael Reactions.

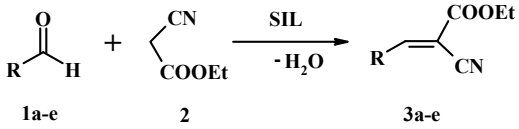
F. Bigi,[a] C. Quarantelli, [a] A. Mega, [a] H.Q.N. Gunaratne,[b] K.R. Seddon [b]
[a] Dipartimento di Chimica Organica e Industriale dell'Universita`, Parco Area delle Scienze17/A,43100Parma, Italy
[b]QUILL Centre, The Queen's University of Belfast, David Keir Building, Belfast BT9 5AG, UK
E-mail: antonio.mega@studenti.unipr.it

Careful application of heterogeneous catalysis can help to achieve selective reactions, with minimum waste, thereby rendering more attractive the synthetic processes. Indeed, solid catalysts can be easily separated quantitatively in their active form from the reaction products by a simple filtration and subsequently recycled. C. Hardacre and co-workers [1] reported a new class of ionic liquids containing the non-nucleophilic Hünig's base unit. These ionic liquids were able to promote Knoevenagel reactions in good yields, but some drawbacks were observed employing them supported on silica (SILPs) by simple impregnation. The recyclability of these SILPs was only moderate towards these reactions.

Thus, we decided to anchor a basic ionic liquid on a silica support by covalent bonding, with the purpose of increasing the robustness of the catalyst, making it reusable and expanding its applicability.

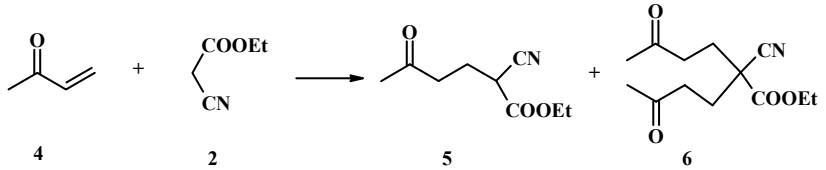


The catalytic activity of the covalently-supported ionic liquid (which, of course, is no longer an ionic liquid) was tested in Knoevenagel and Michael reactions, which are important carbon–carbon bond forming reactions in organic synthesis. The Knoevenagel condensations of various aldehydes were successfully carried out in solventless conditions at 60 °C (yields 88-99%, selectivity 94-99%).



1a-e 2 3a-e

In addition, the catalyst was found to be recyclable many times.
The Michael reaction was examined under different reaction conditions, generating a selective process for the formation of either the single addition product, **5**, or of the double addition product, **6**.



4 2 5 6

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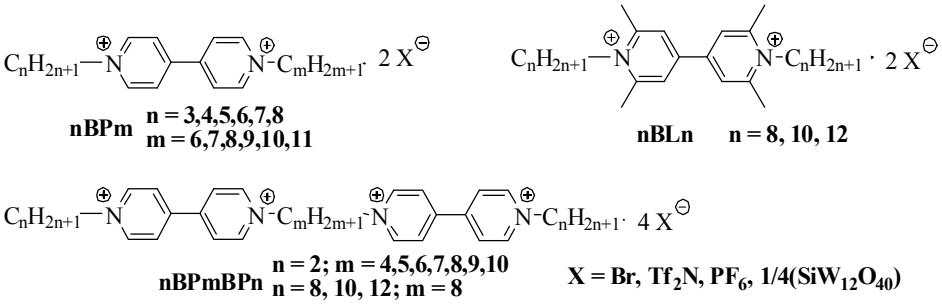
[1] C. Paun, J. Barklie, P. Goodrich, H. Q. N. Gunaratne, A. McKeowna, V. I. Pârvulescu, C. Hardacre, *J. Mol. Catal. A: Chem.*, 269, **2007**, 64.

ORG-PO-14 Viologen-based ionic liquid crystals: effect of the molecular structure on the mesophase stability

Marcella Bonchio,[a] Mauro Carraro,[b] Girolamo Casella,[b] Valerio Causin,[b] Federico Rastrelli,[b] Giacomo Saielli[a]

[a]Istituto per la Tecnologia delle Membrane del CNR, Unità di Padova
[b]Dipartimento di Scienze Chimiche – Università di Padova
Via Marzolo, n. 1, 35131 Padova
e-mail: giacomo.saielli@unipd.it

Ionic liquid crystals (ILC) are expected to combine the properties and technological applications of ionic liquids and liquid crystals. We have investigated how structural modifications of the viologen cation (1,1′-dialkyl-4,4′-bipyridinium) affect the stability and temperature range of the ILC mesophases. Thus we report the synthesis and characterization of the compounds of Scheme 1: *i)* non-symmetric viologen salts (nBPm, with n ≠ m); *ii)* symmetric salts of tetramethylviologen (nBLn); dimeric viologen salts (nBPmBPn). In most cases the counteranion is bis(trifluoromethanesulfonyl)amide (Tf_2N^-). The effect of the anion has been considered by studying some salts of Br^-, PF_6^- and dodecatungstosilicate ($SiW_{12}O_{40}^{4-}$). The various phases exhibited by these salts have been characterized by means of TGA, DSC, X-ray diffraction, polarized optical microscopy and solid state NMR[1-2] while HR-NMR, MS spectrometry and cyclic voltammetry have been used to study their behaviour in solution.[3,4] The modulation of the length of the alkyl chains allowed the fine tuning of the transition temperatures and temperature range of stability of the ILCs. Some of the non-symmetric salts show a stable room temperature smectic phase from about 0 °C up to about 130 °C. Moreover, the use of viologen dimers as molecular tweezers for fullerene complexation has been the subject of a computational investigation.[5]



[1] V. Causin, and G. Saielli, *J. Mol. Liq. 145*, **2009**, 41.
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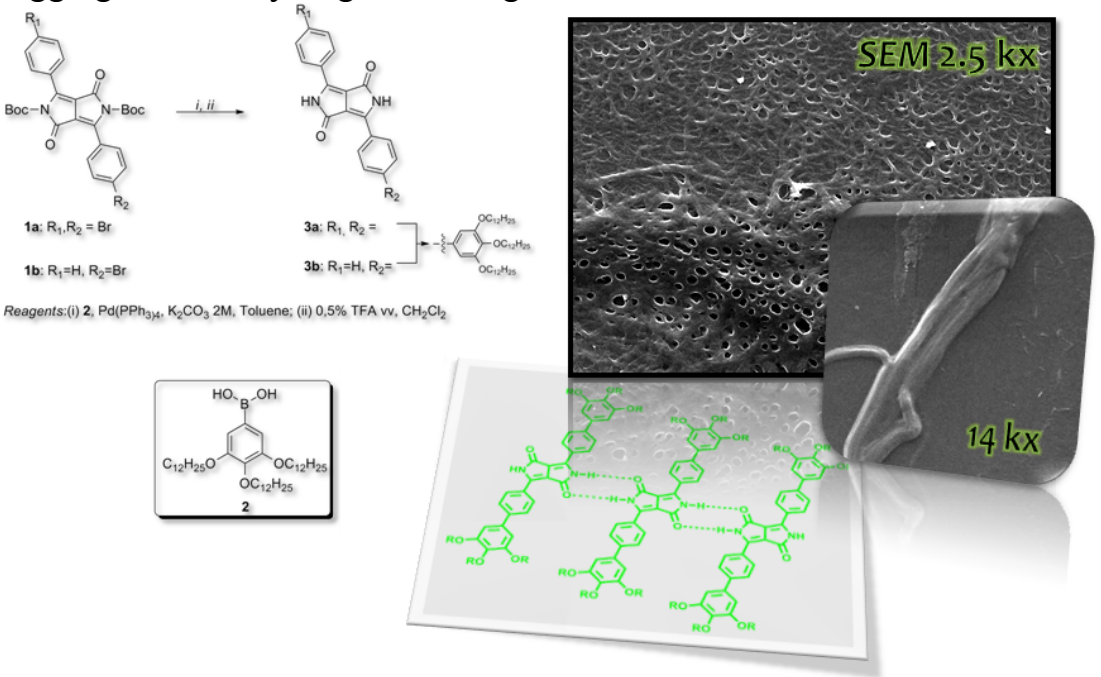
[3] E. Marotta, F. Rastrelli, and G. Saielli, *J. Phys. Chem. B, 112*, **2008**, 16566.
[4] G. Saielli, *J. Phys. Chem. A, 112*, **2008**, 7987.
[5] G. Casella, and G. Saielli, *New J. Chem., 35,* **2011**. DOI: 10.1039/C1NJ20117D

ORG-PO-15 Diketopyrrolopyrrole Supramolecular Network

G. Borsato,[a] R. Beninatto,[a] E. Vagnozzi,[a] O. De Lucchi,[a] F. Fabris,[a] V. Lucchini[b] and E. Zendri[b]

[a]Dipartimento di Scienze Molecolari e Nanosistemi, [b]Dipartimento di Scienze Ambientali, Informatica e Statistica; Ca' Foscari Venezia, Dorsoduro 2137, I-30123, Venezia.
e-mail: gborsato@unive.it

Diketopyrrolopyrrole (**DPP**) is among the most important high performance pigments (Colour Index PR 255). It is used in automotive industries and in general paint and tinting applications. In recent years, research in the **DPP** focused on the synthesis of new derivatives to be used in the field of organic photovoltaic (OPV) applications [1] and as chromophore for near-infrared spectroscopy (NIR).[2] Our research aims to the synthesis of new soluble **DPPs** *via Suzuki cross-coupling,*[3] starting from the dibromide **1**. In the case of **3a**, the SEM image indicates the formation of supramolecular networks in the solid state which was rationalized as due to aggregation via hydrogen bonding as shown below.



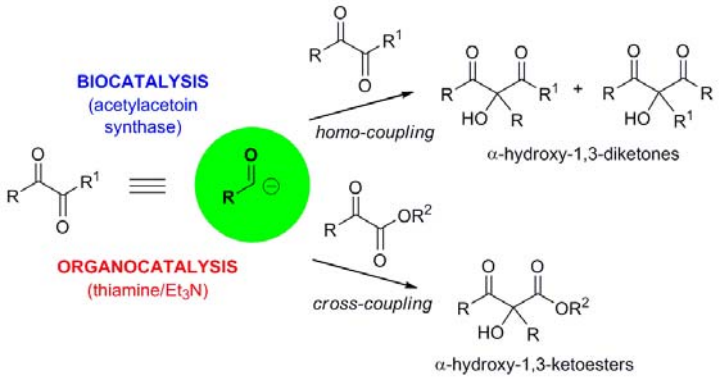
[1] (a) B. Walker, C. Kim, T. Q. Nguyen, *Chem. Mater.* **2011**, *23*, 470; (b) B. P. Karsten, R. A. J. Janssen, *Macromol. Chem. Phys.* **2011**, *212*, 515.
[2] (a) G. M. Fischer, E. Daltrozzo, A. Zumbusch, *Angew. Chem. Int. Ed.* **2011**, *50*, 1406; (b) G. M. Fischer, A. P. Ehlers, A. Zumbusch, E. Daltrozzo, *Angew. Chem. Int. Ed.* **2007**, *46*, 3750; (c) G. M. Fischer, M. Isomäki-Krondahl, I. Göttker-Schnetmann, E. Daltrozzo, A. Zumbusch, *Chem. Eur. J.* **2009**, *15*, 4857.
[3] Lincker, F.; Bourgun, P.; Masson, P.; Didier, P.; Guidoni, L.; Bigot, J-Y.; Nicoud, J-F.; Donnio, B.; Guillon, D. *Org. Lett.* **2005**, 7, No. 8, 1505.

ORG-PO-16 α-Diketones as acyl anion equivalents: new enzymatic and non-enzymatic thiamine-promoted routes to aldehyde-ketone coupling

Olga Bortolini, Giancarlo Fantin, Marco Fogagnolo, Pier Paolo Giovannini, Valentina Venturi, Alessandro Massi, Salvatore Pacifico
Dipartimento di Chimica dell'Università di Ferrara, Via L. Borsari 46, I-44121, Ferrara, Italy
olga.bortolini@unife.it

Thiamine diphosphate (ThDP)-depending enzymes are well established biocatalytic tools for the asymmetric synthesis of α-hydroxy carbonyl compounds (acyloins) via carboligation reactions between two carbonyl reagents (*Umpolung* strategy). Recently, we reported the unprecedented enzymatic aldehyde-ketone coupling by using Acetylacetoin synthase (AAS) as the enzyme and, noteworthy, α-diketones as acyl anion sources [1]. In particular, we found that AAS is capable to catalyze in vivo the homo-coupling reaction of various symmetrically and unsymmetrically substituted 1,2-diketones, thus affording a suite of chiral and prochiral tertiary alcohols featuring the α-hydroxy-α-diketone moiety (Figure).

By mimicking the peculiar behavior of ThDP-depending AAS, we have also demonstrated that the sole thiamine hydrochloride-Et_3N couple is able to promote nucleophilic acylations such as the above homo-coupling of α-diketones and the hitherto unreported cross-coupling between α-diketones and α-ketoesters. Both carboligation reactions yield α-hydroxyketone derivatives in a straightforward manner by an effective and benign procedure involving the use of eco-friendly PEG_{400} as the reaction medium. Crucial for the disclosed mode of acyl anion generation is the utilization of dialkyl α-diketone donors with at least an acidic hydrogen adjacent to the carbonyl group. Interestingly, a different reaction pathway (hydride vs. acyl anion transfer) is observed for arylalkyl α-diketone donors.



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ORG-PO-17 Peroxide value determination in oils without the use of chlorinated solvents

Augusta Caligiani, Martina Cirlini and Gerardo Palla.

Department of Organic and Industrial Chemistry, Parma University, Parco Area delle Scienze 17/A, I-43100 PARMA, Italy
gerardo.palla@unipr.it

The standard method for peroxide determination in oils requires the reaction of peroxides with potassium iodide (KI) added to samples dissolved in a mixture of acetic acid and chloroform: the last solvent is a problem both for health and environment as it is carcinogenic and highly pollutant. As an alternative, we check other organic solvents and found that the use of ethyl acetate in place of chloroform or dichloromethane allowed reproducible data of the peroxide number for both common food oils(olive oil) and special products such as sunflower ozonized oil used for cosmetics (Cosmoproject Spa), net or mixed with lipophilic or hydrophilic gel. Several experiments were carried out by adding KI to ozonized oil samples used for cosmetics in order to follow the kinetic of decomposition in different solvents. Results from NMR data showed that the degradation rate of ozonides in ethyl acetate or in chlorinated solvents in presence of KI was similar, allowing a complete reaction after standing 16 hours at room temperature. GC-MS data confirmed that the degradation products of ozonides from sunflower oil were mainly aldehydes, iodo-alkanes and furyl derivatives.

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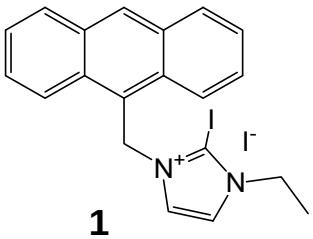
ORG-PO-18 Anion Binding via Charge Assisted Halogen Bond in 2-Iodo-Imidazolium Systems

M. Cametti,[1] P. Metrangolo,[1] T. Pilati,[2] K. Raatikainen,[1] G. Resnati[1] and G. Terraneo[1]

[1] Department of Chemistry, Materials and Chemical Engineering, Polytechnic of Milan, Milano, Italy. email: *massimo.cametti@chem.polimi.it*

[2] Institute of Molecular Science and Technology, CNR—University of Milan, Milano, Italy

Anion recognition is one of the classical themes in Supramolecular Chemistry since its early age, and still a florid area of research [1]. In the incessant search for novel paradigm for achieving the efficient capture of negatively charged species, researchers have explored many different non-covalent forces, such as electrostatic interactions, metal coordination, hydrogen bonding, anion-π interactions, etc. Among these, halogen bonding (XB), namely any noncovalent interaction involving the positive region of the electrostatic potential surface of halogen atoms [2] has recently drawn considerable attention. XB is, nowadays, a well recognized class of non-covalent interactions. Investigations on XB systems increased in recent years, embracing both experimental and theoretical studies. As to experimental works, crystal engineering studies represent an overwhelming majority. In marked contrast with the abundance of solid state investigations, studies in solution are surprisingly scanty.



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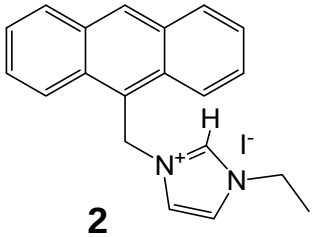

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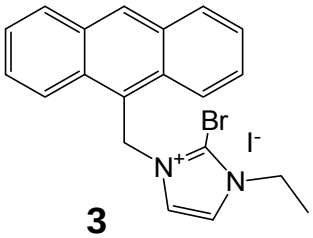

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Here we report on the study of the anion binding properties of the 2-iodo-imidazolium receptor **1**. Solution studies confirm that the 2-iodo-imidazolium unit provides relatively strong interactions with halide ions and oxo-anions (such as AcO^- and $H_2PO_4^-$) in a competitive solvent such as DMSO. Relevant comparisons were made with the 2-H and with the 2-Br derivatives, compounds **2** and **3**, in order to assess the relative strength of the XB with respect to the HB in the analogue 2-H derivative, and to further verify the occurrence of the XB interaction, respectively.

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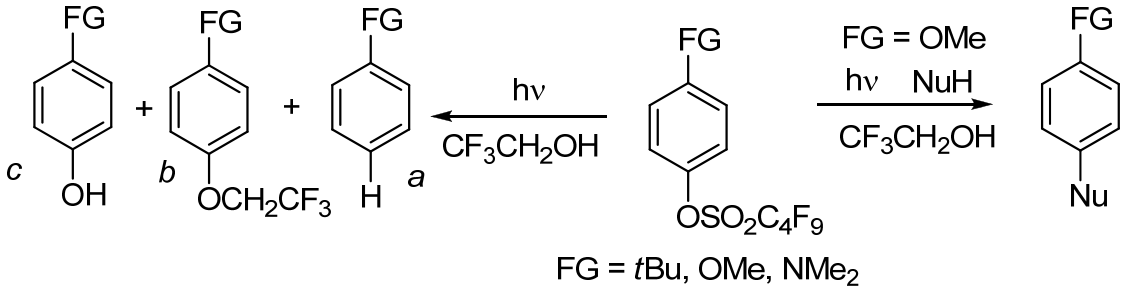
ORG-PO-19 PHOTOCHEMISTRY OF ARYL NONAFLATES.

Veronica Canevari, Stefano Protti, Maurizio Fagnoni, Angelo Albini

Department of Chemistry, University of Pavia, V.Le Taramelli 10, 27100 Pavia (PV)
prottistefano@gmail.com

Aryl nonaflates (Ar-$OSO_2C_4F_9$) have recently emerged as promising substrates in transition metal catalyzed cross-coupling reactions for aryl-carbon bond formation[1]. On the other hand, the photoactivation of the Ar-O bond in aromatic sulfonates is likewise possible. In particular, our group demonstrated that irradiation of electron-rich aryl triflates or mesylates in polar or protic solvents in the presence of π nucleophiles (alkenes, aromatics) can be exploited for the development of metal-free, arylation procedure to achieve biphenyls, allyl benzenes and α-arylacetals[2]. In the aim of exploring the synthetic potential of aryl nonaflates in photochemistry, we decided to investigate the photoreactivity of these esters substituted with a NMe_2, OMe or an alkyl group in various solvents and in the presence of π nucleophiles (benzene, mesitylene, allyltrimethylsilane). Preliminary results showed that these compounds have a marked photoreactivity in neat solvent ($\Phi_R > 0.1$) where the competition between three different pathways (reduction (*a*) , solvolysis (*b*) and deprotection (*c*)) can be observed. In addition, the *p*-methoxy derivative could be employed in several Ar-C bond formation reactions procedures, and arylation yields were comparable with those obtained with the corresponding mesylates or triflates.



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ORG-PO-20 Exploring the Chemistry of Marine Mollusks: from Chemical Weapons to New Pharmaceutical Leads

M. Carbone, E. Mollo, E. Manzo, M.L. Ciavatta, G. Cimino, M. Gavagnin
[a]Istituto di Chimica Biomolecolare, Consiglio Nazionale delle Ricerche, Via Campi Flegrei 34, 80078, Pozzuoli, Napoli, Italy
margherita.gavagnin@icb.cnr.it

In recent years the number of identified bioactive natural compounds from marine sources has progressively increased [1]. Sponges, cnidarians and microorganisms are the richest sources in the sea of bioactive natural products, but a significant incidence of activity has been also found in compounds isolated from mollusks [2]. In particular, shell-less gastropod mollusks belonging to the subclass Opisthobranchia revealed to be one of the most interesting group. The survival of these apparently unprotected mollusks is based on a series of defensive strategies, which include the use of deterrent or toxic molecules. Opisthobranchs obtain their chemical "weapons" by either bio-accumulation of selected metabolites from their dietary sources, bio-transformation of dietary compounds, or *de novo* bio-synthesis. Thus they represent a remarkable source of bioactive molecules that have been selected in nature to play fundamental roles for the survival of the organisms that contain them. This reveals an extraordinary library of compounds that could be considered excellent drug candidates.

In continuing our research directed to explore the valuable chemical content of gastropod mollusks, we have examined different species. These studies led us to characterize several novel bioactive molecules (some examples in Fig. 1). Selected results will be presented in this communication.

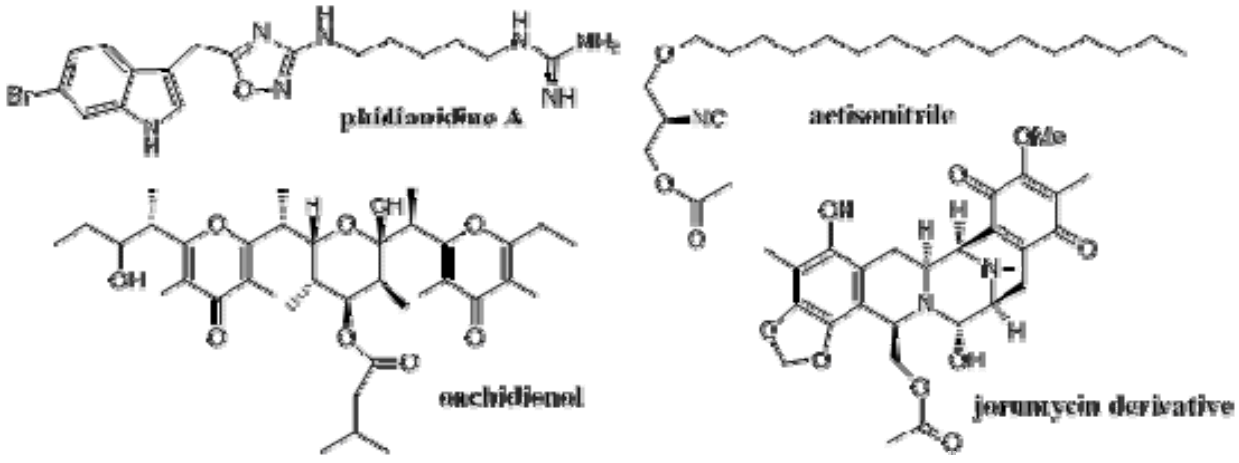

Figure 1.

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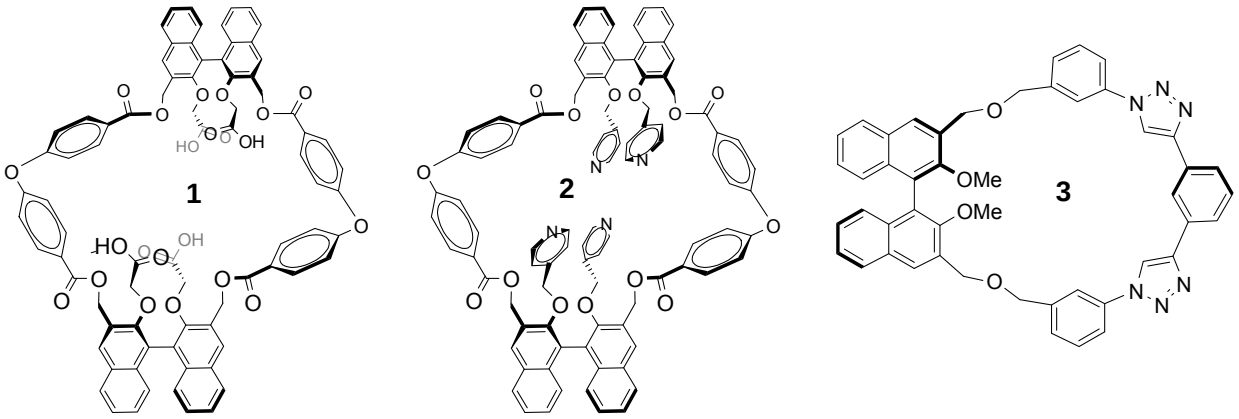
ORG-PO-21 Chiral Macrocycles as Chiroptical Sensors and as Building Blocks for Supramolecular Helical Nanotubes

Marco Caricato,[a] Nerea Jordana Leza[a] and Dario Pasini[a]

[a]Department of Chemistry – University of Pavia –Viale Taramelli, 10 – Pavia – Italy
marco.caricato@unipv.it

We present our efforts for the incorporation of BINOL-based molecular modules, acting as a "robust" source of chirality, into homochiral, shape-persistent macrocycles, with function as chiroptical sensors and precursors for supramolecular organic nanotubes.[1] Constructing abiological helices have potential applications in the area of chiral separation, asymmetric catalysis and electrooptic materials. More specifically, we have used several elaborated molecular modules, such as 3,3'-dimethanol-1,1'-binaphthyl with different functionalities in 2,2' positions, and cyclized them via amidation and esterification reactions, and click chemistry.[2]



1 has four carboxylic acid functionalities pointing into the macrocyclic cavity, and it is capable of recognition of Cu^{2+}, Ni^{2+}, Zn^{2+} in physiological conditions, with the binding event which can be detected using CD spectroscopy. Macrocycle **3** is capable of anion recognition given the presence of acidic triazole CH bonds, which can be again detected using CD spectroscopy. The coordination of pyridine fucntionalities with ligand $PdCl_2(CH_3CN)_2$ in macrocycle **2** yield chiral supramolecular nanotubular polymers on surfaces.

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ORG-PO-22 An innovative and easy way to anchor biomolecules onto Superparamagnetic Iron Oxide Nanoparticles (SPIONs) through a bifunctional linker

Claudio Carrara, Andrea Pizzi, Silvia Sonzini, Emanuela Licandro

Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milano
Via G. Venezian 21, 20133, Milano. *emanuela.licandro@unimi.it*

Superparamagnetic Iron Oxide Nanoparticles (SPIONs) have demonstrated great promise for diagnostic and therapeutic applications. Thanks to their magnetic properties and to their size, comparable to that of biologically objects, they are very useful for biomedical applications, such as, for example, automated DNA extraction, targeted gene delivery, magnetic resonance imaging (MRI), and magnetic field induced hyperthermia for cancer therapy.[1a-e] For these applications, SPIONs must be coupled with targeting agents, therapeutic drugs, and other functional probes. Hence, the need to develop efficient synthetic strategies for the conjugation of molecules to SPIONs is an important and appealing target.[2] The strategies used can involve passive noncovalent adsorption on the outer particle surface or the formation of a more stable covalent bond by using appropriate heterobifunctional linkers, in which one functional group specifically binds the nanoparticle, while the other reacts with the biomolecule in order to form the new nanoconjugate (Figure 1).
In this communication, the use of an heterobifunctional linkers containing an isocyanate moiety as new functional group able to directly bind SPIONs will be shown.

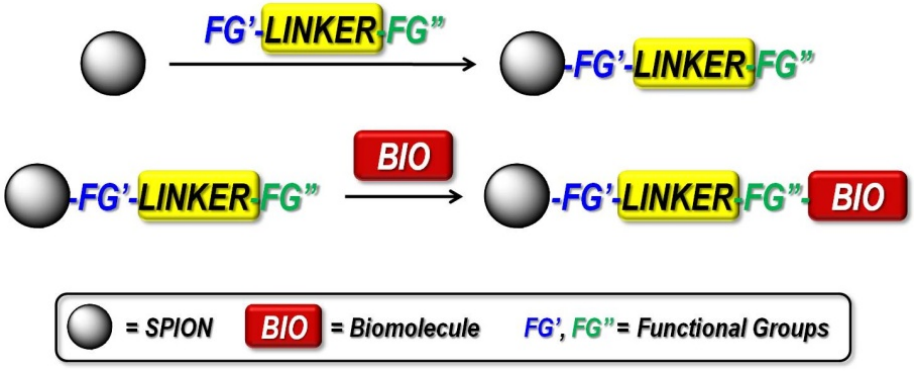

Figure 1

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ORG-PO-23 Halogen bonding in halocarbon-protein complexes

Giuseppe Resnati[a,b], Serena Biella[a,b], Gabriella. Cavallo[b], Pierangelo Metrangolo[a,b], Valentina Nardone[b], Emilio Parisni[b], Tullio Pilati[a], Giancarlo Terraneo[a,b]

[a] NFMLab- Department of Chemistry, Materials and Chemical Engineering, ''Giulio Natta'', Politecnico di Milano, Via L. Mancinelli 7, 20131 Milan, Italy.

[b] CNST-IIT@POLIMI, Via Pascoli 70/3, 20133 Milan, Italy.

E-mail: giueseppe.resnati@polimi.it

Halogen bonding (XB) [1] has been extensively described in the context of a variety of self-assembled supramolecular materials with specific structural properties. [2] However, it has so far received only little recognition for its possible role in the stabilization of the interactions between small chemicals and large biomolecules. In this contribution, we provide some examples of halogen bonding occurring between small halogen-substituted ligands and their biological substrates. [3] The crystal structures presented here, where iodine and bromine atoms function as halogen bonding donors and different electron rich sites, such as oxygen and nitrogen, function as halogen bonding acceptors, prove how halogen bonding can occur in biological systems and provide a class of higly directional stabilizing contacts that can be exploited in the process of rational drug design.

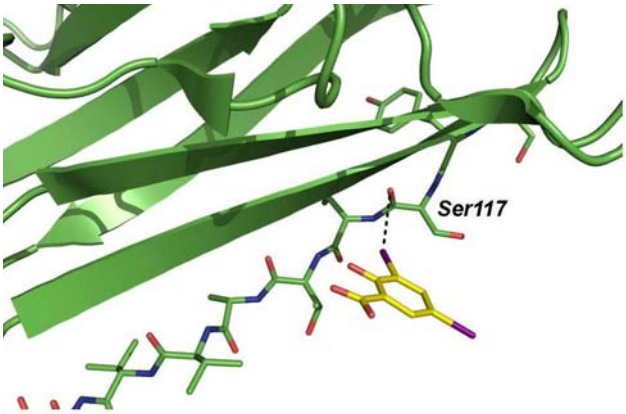

Figure 1: An iodine atom of 3,5-diiodosalicilic acid forms a halogen bonding contact with the Ser117 carbonyl oxygen in the 3,5-diiodosalicylic-transthyretin structure (PDB code = 3B56).

[1] An IUPAC Task Group set up to examine the definition of halogen bonding has not yet reported, so that given here should be taken as temporary (see www.iupac.org/web/ins/2009-032-1-100 and www.halogenbonding.eu).

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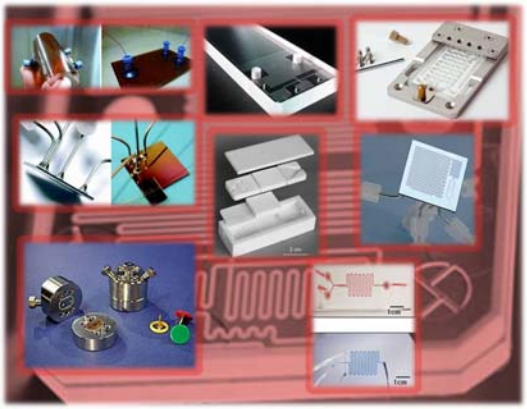
ORG-PO-24 Microreactor Technology in the Development of Stereoselective Syntheses

Laura Carroccia, Piera Trinchera, Biagia Musio, Leonardo Degennaro and Renzo Luisi
Dipartimento Farmaco-Chimico, Università degli Studi di Bari "Aldo Moro"
Consorzio Interuniversitario Nazionale C.I.N.M.P.I.S. , via E. Orabona 4, I-70125, Bari, Italy
laura.carroccia@libero.it

Microflow devices have been found to be very effective in controlling extremely fast reaction, involving highly unstable intermediates, allowing the introduction of the concept of flash chemistry [1]. Flash chemistry is defined as "*a field of chemical synthesis where extremely fast reactions are conducted in a highly controlled manner to produce desired compounds with high selectivity and reaction times ranging from milliseconds to seconds*". This concept has been successfully applied to several organic reactions involving highly reactive intermediates such as carbanions and carbocations [2]. In fact, functionalized organolithiums or alkoxycarbeniums, widely used in modern synthetic chemistry, are example of reactive intermediates that exhibit high reactivity, giving fast and exothermic reactions, and usually require very low temperature and controlled reaction conditions in order to avoid byproducts and decomposition.
In this communication, it will be reported our recent results on the development of new stereoselective syntheses by using carbanionic and carbocationic intermediates, generated from functionalized aziridines in microreactor systems.



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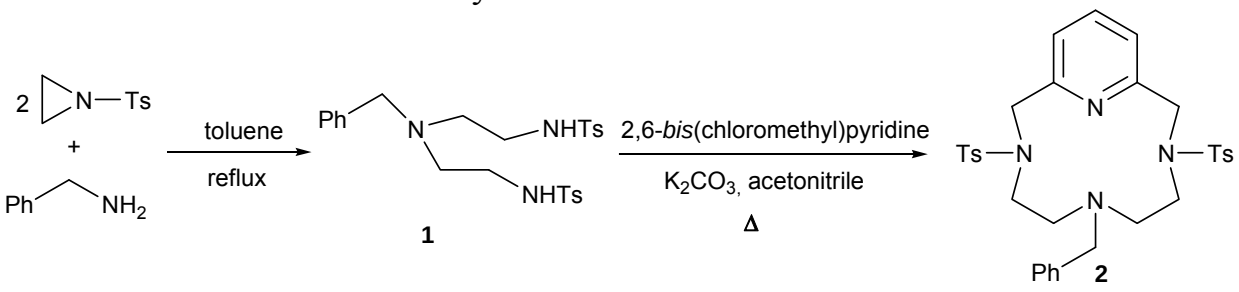
ORG-PO-25 HENRY REACTION CATALYZED BY COPPER(I) COMPLEXES OF A NEW PYRIDINE CONTAINING MACROCYCLIC LIGAND.

A. Caselli,[a] B. Castano,[a] M. Sisti,[b] E. Gallo,[a] F. Ragaini,[a] N. Casati[c]

[a] Dip. CIMA, Università degli Studi di Milano, Via G. Venezian 21, 20133 Milano, Italy;
[b] Dip. Scienze Chimiche e Ambientali, Università degli Studi dell'Insubria, Via Valleggio 11, 22100 Como, Italy;
[c] Diamond light source ltd., Harwell science and innovation campus, Chilton, OX110DE, U.K.
alessandro.caselli@unimi.it; massimo.sisti@uninsubria.it

The Henry or nitroaldol reaction has received much attention as a valuable tool for the formation of C-C bonds [1]. The reaction couples nitroalkanes with carbonyl compounds in the presence of a base giving β-nitroalcohols that are useful intermediates in the synthesis of relevant biologically active compounds. Recent studies in our research group demonstrated the efficacy of Cu(I) complexes derived from novel macrocyclic ligands containing a pyridine ring (**PC-L**) in the cyclopropanation reaction of various alkenes [2]. The excellent results obtained prompted us to verify the application of such Cu(I) complexes in the Henry reaction. We report here the synthesis of the new macrocyclic ligand **2** (Scheme 1) and the application of the corresponding Cu(I) complex as Lewis acid catalyst in the condensation between aldehydes and nitroalkanes.



Scheme 1

The best results in terms of chemical yields were obtained with *in situ* formed 1:1 ligand **2**:Cu(OTf) complex (from $[Cu(OTf)]_2 \cdot C_6H_6$) in dichloromethane at room temperature and in the presence of substoichiometric amount of a tertiary amine. Noteworthy, no trace of competitive side-reaction products were ever detected.

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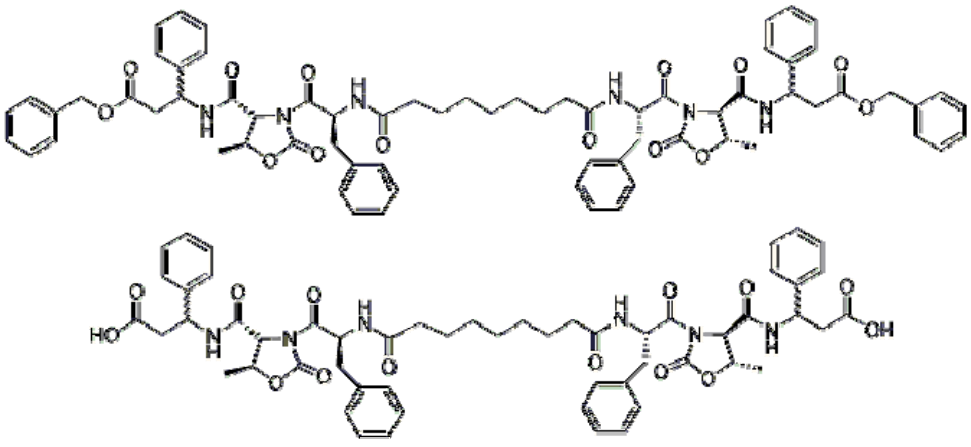
ORG-PO-26 Formation of Gels from Stereoisomeric Pseudopeptides in the Presence of Metal Ions

Nicola Castellucci, Giuseppe Falini and Claudia Tomasini*

Dipartimento di Chimica "G. Ciamician" - Alma Mater Studiorum Università di Bologna - Via Selmi 2, I–40126 Bologna (Italy)
nicola.castellucci2@unibo.it

A small library of stereoisomeric pseudopeptides able to make gels in different solvents has been prepared and their attitude to make gels in the presence of several metal ions was evaluated [1]. Four benzyl esters and four carboxylic acids, all containing a moiety of azelaic acid (a long chain dicarboxylic acid) coupled with four different pseudopeptide moieties sharing the same skeleton (a phenyl group one atom apart from the oxazolidin-2-one carboxylic group), were synthesized in solution, by standard coupling reaction. The tendency of these pseudopeptides to form gels was evaluated by using the inversion test of 10 mM solutions of pure compounds and of stechiometric mixtures of pseudopeptides and metal ions. To obtain additional information on the molecular association, the gel samples were left to dry in the air to form xerogels that were further analyzed using SEM and XRD. The formation of gel containing Zn(II) or Cu(II) ions gave good results in term of incorporation of the metal ions, while the presence of Cu(I), Al(III) and Mg(II) gave less satisfactory results. This outcome is a first insight in the formation of stable LMWGs formed by stechiometric mixtures of pseudopeptides and metal ions. Further studies will be carried out to develop similar compounds of pharmacological interest.



[1] Nicola Castellucci, Giuseppe Falini, Gaetano Angelici, Claudia Tomasini, *Amino Acids*, **2011,** DOI: 10.1007/s00726-011-0908-0

ORG-PO-27 Fluorous-based stationary phases for the HPLC separation of environmentally relevant compounds

Alberto Cavazzini,[a] Roberto Samperi,[b] Chiara Cavaliere,[b] Alessia Ciogli,[c] Francesco Gasparrini,[c] Aldo Laganà,[b] Nicola Marchetti,[a] Luisa Pasti,[a] Francesco Dondi,[a] Claudio Villani[c]

[a] Dipartimento di Chimica, Università di Ferrara, via L. Borsari 46, 44121 Ferrara
[b] Dipartimento di Chimica, Università di Roma "La Sapienza", P.le Aldo Moro 5, 00185 Roma
[c] Dipartimento di Chimica e Tecnologie del Farmaco, Università di Roma "La Sapienza", P.le Aldo Moro 5, 00185 Roma
alberto.cavazzini@unife.it

Fluorous-based stationary phases are made of perfluorinated alkyl-chains or perfluorinated aromatic moieties chemically bound to silica gel. They have been employed as separation media in SPE and HPLC due to their unique characteristics of selectivity and retention towards fluorinated and/or halogenated compounds. These properties depend on both solute and stationary phase molecular structure (number of fluorous atoms) and on the mobile phase composition. The selectivity of fluorous-based stationary phases is different from that exhibited by ordinary hydrophobic separation media due to their both hydrophobic and hydrophilic character. Hence, fluorous-based stationary phases seem to be promising separation media for applications in Environmental Analytical Chemistry. In this work, the chromatographic behavior of homologous series of four perfluorinated alkyl-acids (PFAs, C5-C8) often employed as flame retardant additives was studied. Mobile phase composition, column temperature and mobile phase flow velocity were the experimental variables upon which the retention of these compounds was studied on a C_6F_{13} column. Our investigation has revealed an U-shaped retention behavior when the mobile phase composition was changed by 40 to almost 100 % v/v ACN in water, with the lowest capacity factor at around 90% ACN. Van't Hoff plots were employed to correlate variations of enthalpy and entropy of mobile-to-stationary phase transfer with the mobile phase composition and the number of fluorous atoms in the solutes. Additionally, Van Deemter and kinetic plots were used to compare the chromatographic performances of fluorous phases and standard C_{18} media. Due to the low UV sensitivity of PFAs, all measurements were done by LC-ESI/MS. Applications of fluorous-based stationary phases as pre-concentration media and the implementation of an online enrichment/analysis instrumental setup based on these phases are discussed.

ORG-PO-28 Benzothienopyridines: interesting tricyclic compounds, scaffold in pseudopeptides against β-secretase.

Iole Cerminara[a], Lucia Chiummiento[a], Maria Funicello[a], Paolo Lupattelli[a].

[a]Dipartimento di Chimica "A. M. Tamburro" dell' Università della Basilicata, Via Ateneo Lucano 10, 85100, Potenza, Italy

e-mail: iole.cerminara@gmail.com

Benzothienopyridines represent a class of tricyclic heteroaromatic compounds of particular interest in medicinal chemistry: in fact their pharmacological activity as antiallergic [1], antibacterical [2] and anxioselective agents [3] has been reported.

In recent years there is an increasing attention on small molecules and their inhibitory activity on BACE 1 [4], β-secretase, has been developed.

With the aim to explore a possible effect in Alzheimer's disease, we prepare 5-amino-4-methoxycarbonyl-2-methyl[1]benzothieno[2,3-*b*]pyridine [6] in an improved synthetic route which passes through the formation of N-(heteroaryl) iminophosphoranes and a tandem aza-Wittig/electrocyclization reaction.

Furthermore this molecule could be use as scaffold for pseudopeptidic structures obtained by coupling with aminoacids or small peptides (figure 1).

In the present communication preliminary results will be reported.

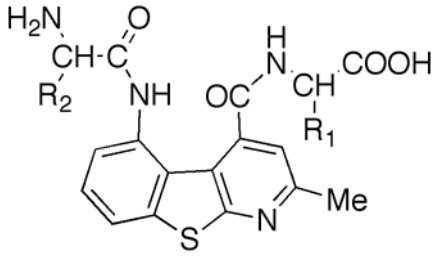


Figure 1

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ORG-PO-29 Products of the aqueous chlorination of the nicotine

Flavio Cermola[a], Marina DellaGreca[a], Maria Rosaria Iesce[a], Marina Isidori[b], Alice Parolisi[a], Lucio Previtera[a], Fabio Temussi[a], Armando Zarrelli[a]
[a]Dipartimento di Chimica Organica e Biochimica dell'Università Federico II, complesso Universitario Monte Santangelo, 80126 Napoli, Italy
[b]Dipartimento delle Scienze della Vita della II Università di Napoli, Via Vivaldi n. 43, 81100, Caserta, Italy

Nicotine is a non prescribed drug to which all members of a tobacco-smoking society are exposed either through direct assumption or second-hand inhalation. FAO projections have foreseen 7.1 million tonnes of tobacco leaves production in the 2010. Nicotine makes up about 5% of tobacco leaves, by weight [1].
During the tobacco manufacturing a certain amount of nicotine is released into the atmosphere, in wastewaters, sent to water treatment facilities, and in tobacco dust, discharged to landfills. Hence 93% of nicotine released is expected to be in water, 4% in the soil, 3% in air [2]. As the manufactured tobacco concerns, only 25% of the total nicotine amount in a cigarette is in the smoke stream while the remaining is lost in the surrounding [3]. Dynamics in indoor and outdoor environments [4], human excretions and the manufacturing process are responsible for the presence of nicotine in surface waters as a result of industrial and municipal discharges [5]. According to its presence in surface waters, analyses on effluents of many sewage treatment plants (STP) show that nicotine survives conventional treatment processes.
However Teijon et al. [6] report that in the Depurbaix STP the nicotine removal was almost quantitative after additional chlorination treatments. Fontela et al. [7] report the same result in a drinking water treatment plant after two chlorination steps. Chlorination therefore seem to be effective in simultaneously removing both pathogens and nicotine from row waters but the possible generation of by-products more resistant to degradation and/or with equal or more toxic effects than nicotine must be considered as well. In a model study of the effects of chlorination on nicotine with hypochlorite the main oxidation and/or chlorination products were identified and their toxicity on different organisms of the freshwater chain, as well as their mutagenic and genotoxic effects, were evaluated.

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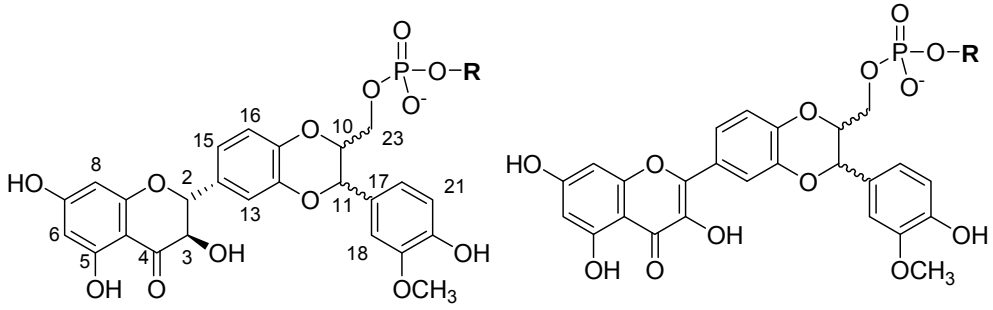
ORG-PO-30 New 23-phosphodiester derivatives of Silybin and DHS: synthesis and preliminary evaluation of antioxidant properties.

Giovanni Di Fabio, Anna Mancino, Marina Della Greca, Jennifer D'Onofrio, Lorenzo De Napoli, Lucio Previtera and Armando Zarrelli
Dipartimento di Chimica Organica e Biochimica, Università degli Studi di Napoli "Federico II", Complesso Universitario di Monte S. Angelo, via Cynthia, 4, 80126 Napoli, Italia.
zarrelli@unina.it

Silybin is the major flavonolignan of silymarin which is widely used as a natural remedy for the treatment of cirrhosis, chronic hepatitis, and liver diseases associated with alcohol consumption and exposure to environmental toxins [1]. Different studies recently made on the antiradical activity of silybin and DHS have elucidated the functional groups responsible for this activity [2]. The results suggest that the C-23 position could be a site for useful modifications aimed to improve the bioactivity of silybin and/or DHS analogues. Recently we describe an efficient synthetic strategy to obtain a variety of new silybin and 2,3-dehydrosilybin (DHS) derivatives in which the 23-hydroxyl group was converted to a sulfate, phosphodiester, or amine group, using a solution-phase approach [3]. The antioxidant properties of the new compounds were evaluated in a cellular model *in vivo* and most of them displayed an antioxidant activity comparable or higher to silybin and DHS. These results confirmed the assumption that modifications in position C–23 do not affect the radical scavenging activity of these analogues.

With the final goal to expand the repertoire of silybin and DHS C-23 modified, we describe here the synthesis and preliminary evaluation of antioxidant properties of a variety of new silybin and DHS conjugated with different labels through a phosphodiester bond The antioxidative properties of the above-synthesized compounds were determined by free radical scavenging (DPPH) assays.



23-phosphodiester silybin modified 23-phosphodiester DHS modified

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ORG-PO-31 Quantitative Correction of Solvent and/or Catalyst Effect on Proton Abstraction Rate Constants of C-H Acids.

Alessia Ciogli,[a] Roberto Cirilli,[b] Roberta Costi,[a] Simona Dei Cicchi,[a] Roberto Di Santo,[a] Sergio Menta,[b] Marco Pierini,[a] Gabriella Siani.[c]

[a] Dipartimento di Chimica e Tecnologie del Farmaco di "Sapienza, Università di Roma", Piazzale Aldo Moro 5, 00185, Rome, Italy

[b] Istituto Superiore di Sanità, Dipartimento del Farmaco, Viale Regina Elena 299, 00161, Rome, Italy

[c] Dipartimento di Scienze del Farmaco dell'Università "G. D'Annunzio", Via dei Vestini 31, 66100, Chieti, Italy

marco.pierini@uniroma1.it

Kinetic determinations commonly find a variety of applications in the field of chemical and material sciences, often providing crucial information about the elucidation of reaction mechanisms, stereolability of chiral species endowed with pharmaceutical or enantio-/diastereo-selective sensorial activity, [1,2] etc. However, it is also not infrequent that an experimentally easy measurement of rate constants can be performed in a medium and with a catalyst different from that in which the datum is instead required. The present communication deals with a procedure of general application developed with the intent to allow a quantitative correction of rate constants of proton abstraction equilibria when the wanted solvent and/or catalyst of the process are different from that in which an experimental value is already available. The attention was focused on the case of C-H acids (ketones), a wide variety of bases of both organic and inorganic nature and three solvents, endowed with very different properties: water, acetonitrile and dichloromethane. The analysis was based on a suitable elaboration of Brønsted equations, from which a couple of final and quite simple mathematical expressions have been derived. Results pointed out that effective corrections of rate constants can be obtained also inserting in the elaborated equations pK_a values of C-H acids and/or basic catalysts (pK_a^{BH+}) estimated in the selected solvents by theoretical approaches, so making the procedure very attractive for a ready and generalized use. Notably is the possibility to employ the method to correct rate constants measured in apolar organic solvents to water, the medium in which compounds of biological interest normally express their activity. This may dramatically extend the range of choice towards kinetic techniques typically operating with organic media or solvents mixtures, such as dynamic chromatography, dynamic electrophoresis and dynamic nuclear magnetic resonance spectroscopy.

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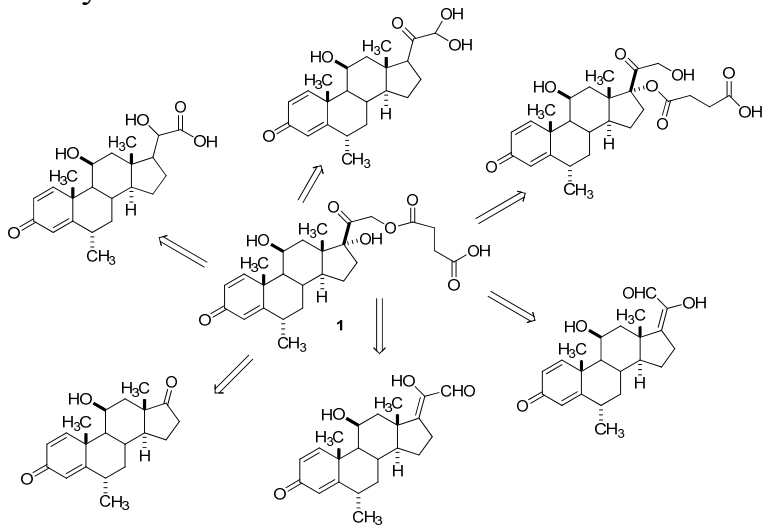
ORG-PO-32 Isolation, Characterization, and Synthesis of Degradation Products of Methylprednisolone Derivatives

R. Cipolletti,[a] D. Galli Angeli,[b] L. Gramaccioni,[b] E. Marcantoni,[a] M. Marcolini,[a] R. Properzi,[a] M. Ricciutelli,[a]

[a]School of Science and Technology, Chemistry Division, University of Camerino, via S. Agostino 1, I-62032 Camerino (MC), Italy.
[b]Analytical Laboratory, via Volta 12, I-60020 Camerata Picena (AN), Italy
e-mail: roberto.cipolletti@unicam.it

Corticosteroids are important synthetically produced glucocorticoids used as anti-inflammatory drugs [1]. Although the active pharmaceutical substances such as methylprednisolone derivatives have been on the market for many years, not much information is available in the literature regarding their degradation behaviours [2]. During the course of our studies on polyfunctional molecules with biological activity, we have been interested in exploring the determination of possible degradation products of methylprednisolone hemisuccinate (**1**), and also their identification. These degradation products are interesting molecules from the pharmaceutical point of view, and are currently under biological evaluation [3]. On the basis of fragmentation pathway and molecular weight obtained by LC-MS results, possible chemical structures can be proposed. Most of them are not sufficiently stable to be isolated, then only by synthesis it is possible to confirm the structures proposed by LC-MS results.



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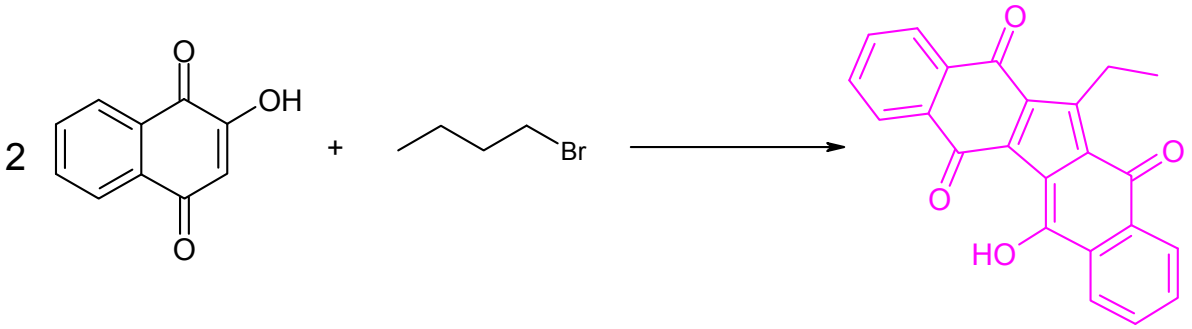
ORG-PO-33 A class of highly delocalized pentacyclic diquinoid compounds with interesting spectroscopic behavior

A. Coletti [a], V. Conte [a], B. Floris [a], S. Lentini [a], P. Galloni [a], O. Bortolini [b], F. Grepioni [c]

[a] Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma"Tor Vergata", via della ricerca scientifica, 00133 Rome, Italy
[b] Dipartimento di Chimica, Università di Ferrara, via Luigi Borsari 46, 44100, Ferrara, Italy
[c] Dipartimento di Chimica "Giacomo Ciamician", Università di Bologna, Via Selmi 2, 40126, Bologna, Italy
e-mail: sara.lentini@uniroma2.it

A new class of pentacyclic diquinoid compounds has been synthesized in a one-pot reaction from two molecules of 2-hydroxynaphthoquinone and 1-bromoalkanes in the presence of ferrocene.
These molecules were isolated as enol tautomer which exhibit an internal hydrogen bond and an extended electronic conjugation; such properties combined with the redox behavior of the quinoid moiety, allow different applications for this peculiar molecule.
In particular the field of light interactions open new routes in the diquinoid utilization as a potential acceptor in electron transfer processes and as a new molecular probe for solvent polarity (VOCs and RTILs) measurements.[1] [2] [3]
The spectroscopic studies of the reference compound (scheme) will be presented and discussed.



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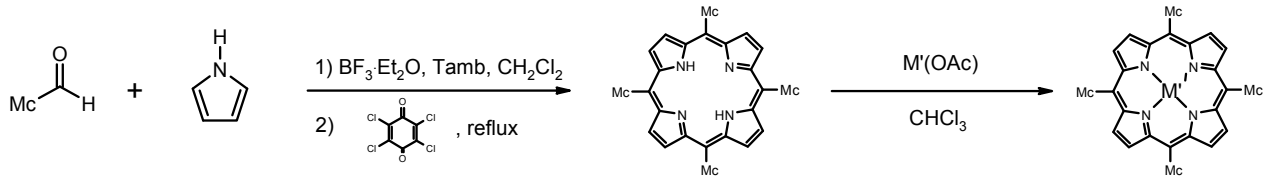
ORG-PO-34 Synthesis, characterization and applications of metallocenylporphyrins

A.Coletti,[a] V.Conte,[a] B.Floris,[a] P.Galloni,[a] E.Gatto,[a] M. Tiravia [a], A.Vecchi,[a] M. Venanzi,[a] V. Nemykin[b]

[a] Dip. Scienze e Tecnologie Chimiche, Università di Roma Tor Vergata
Via della Ricerca Scientifica, 00133, Roma, Italia
[b] Department of Chemistry & Biochemistry, University of Minnesota-Duluth, Duluth, Minnesota 55812
e-mail: andrea.vecchi@uniroma2.it

Metallocenylporphyrins have some peculiar spectroelectrochemical properties: on one hand they show a broader absorption in the visible portion of the spectrum with respect to that of other simple porphyrins; conversely the presence of a metallocenyl moiety enhance their donor character and make accessible more redox processes and mixed-valence states[1-3]. Moreover the metallation of these porphyrins can modulate their redox features.
We have prepared some free base and metal-porphyrins as shown below:



Such features and the possibility to form stable monolayers onto a surface make metallocenyl-porphyrins appealing for the application in photochemical and optoelectronic devices.
The compounds were characterized by UV-vis and electrochemical techniques, both as in solution and as surface-linked species. Differences in behavior will be discussed.

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ORG-PO-35 Heteroaromatic-based organic and organometallic dyes for dye-sensitized solar cells

Carmine Coluccini,[a] Norberto Manfredi,[a] Valentina Leandri,[a] Riccardo Ruffo,[a] Matteo Salamone,[a] Alessia Colombo,[b] Claudia Dragonetti,[b] Stefania Ordanini,[b] Dominique Roberto,[b] Adriana Valore,[b] and Alessandro Abbotto[a]

[a] Department of Materials Science and Milano-Bicocca Solar Energy Research Center - MIB-Solar, University of Milano-Bicocca, Via Cozzi 53, I-20125, Milano, Italy
[b] Dipartimento CIMA "Lamberto Malatesta", University of Milano, Via Venezian 21, I-20133, Milano, Italy
carmine.coluccini@mater.unimib.it

Solar energy is the most abundant clean and renewable energy source but photovoltaic technology has not yet found widespread use due to its high intrinsic costs. Emerging thin-film molecular-based photovoltaic technologies, based on organic and organometallic molecules and polymers, offer a unique promise of cheap, efficient, and robust devices. Amongst the new technologies, dye-sensitized solar cells (DSCs) show one of the best potential of high-conversion efficiency and low-cost manufacturing.
Here we present our recent studies on DSC based on organic and organometallic photosensitizers. The organic sensitizers have an unprecedented multi-branched structure, at variance with the conventional uni-dimensional geometry, for enhanced power conversion efficiencies and stabilities. We also report our most recent studies on a new family of cyclometalated complexes for efficient and more stable devices. In both cases the design of the sensitizer dyes originated from a careful selection of electron-rich and electron-poor aromatic and heteroaromatic fragments in order to tune, and optimize, optical and energetic properties and, in turn, device performance. The new dyes have been completely characterized in their optical and electrochemical properties and investigated in photovoltaic devices. [1]

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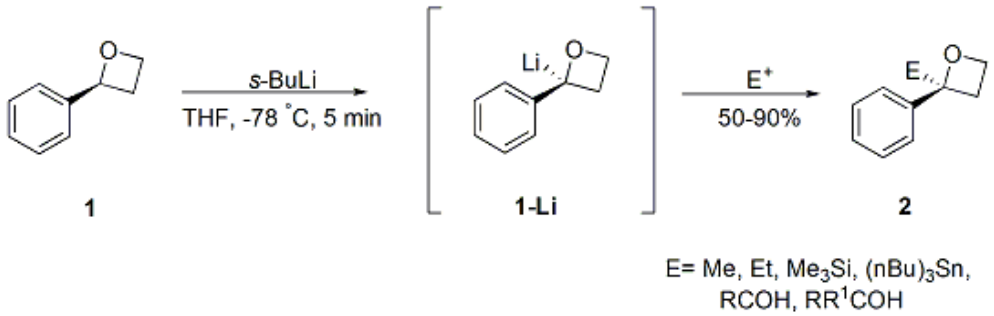
ORG-PO-36 Lithiated 2-Phenyloxetane: A Versatile Intermediate in Organic Synthesis

Donato Ivan Coppi, Filippo Maria Perna, Antonio Salomone, Vito Capriati
Università di Bari "A. Moro", Dipartimento Farmaco-Chimico, Consorzio Interuniversitario Nazionale Metodologie e Processi Innocativi di Sintesi C.I.N.M.P.I.S., Via E. Orabona 4, I-70125, Bari, Italy
donato.coppi8@gmail.com

Oxetanes, the closest homologs to epoxides, are an important group of four-membered cyclic ethers that, as equivalent for the a^3-synthon, can undergo a wide range of chemical transformation; their ring motif is also found in many natural products that exhibit a range of biological activities [1]. The importance of oxetanes as versatile buiding blocks to synthetic and medicinal chemistry as well as to material and agrochemical sciences is dramatically increased over the last ten years with the development of new and efficient methods for their preparation [2].

Despite recent advances, their reactivity toward organometallic reagents has only been scarcely explored. Inspired by intensive interest in the field of α-lithiated oxiranes [3] we became intrigued by the possibility of both generating an α-lithiated oxetane chemically stable on the timescale of its reactions and of investigating its reactivity. Herein, we report a promising route to 2-substituted phenyloxetanes **2** exploiting the nucleophilic reactivity of α-lithio-2-phenyloxetane **1-Li** prepared by means of an hydrogen-lithium exchange from 2-phenyloxetane **1**. Configurational stability of **1-Li** on the time scale of its reactions will also be tackled.



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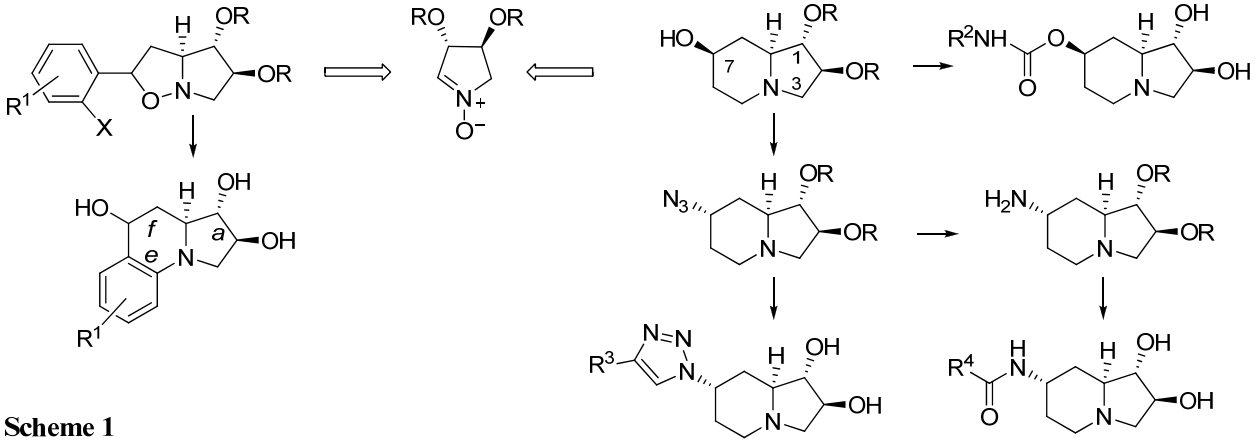
ORG-PO-37 Syntheses of Lentiginosine Derivatives Oriented to Diversity

Franca M. Cordero, Paola Bonanno, Bhushan Khairnar, and Alberto Brandi
Dipartimento di Chimica "Ugo Schiff" dell' Università di Firenze, via della Lastruccia 13, 50019 Sesto Fiorentino (FI), Italy,
E-mail: alberto.brandi@unifi.it

(+)-Lentiginosine [(+)-**1**], an indolizidine alkaloid isolated for the first time by Elbein et al. from the leaves of *Astragalus lentiginosus* in 1990,[1] is the less oxygenated iminosugar able to mimic glucosidase natural substrates and it is a selective inhibitor of amyloglucosidases.[2] The non-natural enantiomer (–)-**1** is a weaker inhibitor than (+)-**1**, and was recently shown to be a caspase-dependent apoptosis inducer on tumor cells of different origin.[3] The important activity of these compounds suggested the synthesis of several differently functionalised derivatives to study their interaction with bioreceptors, with an input deriving also from computational studies. Taking advantage of the highly reliable and selective nitrone 1,3-dipolar cycloaddition, various 7-substituted- and *e*-benzocondensed lentiginosine derivatives were synthesized starting from enantiopure pyrroline *N*-oxides derived from L- and D-tartaric acid (Scheme 1).[4]



Scheme 1

Aspects of the stereoselective synthesis of lentiginosine derivatives will be presented together with the most recent results of biological tests.

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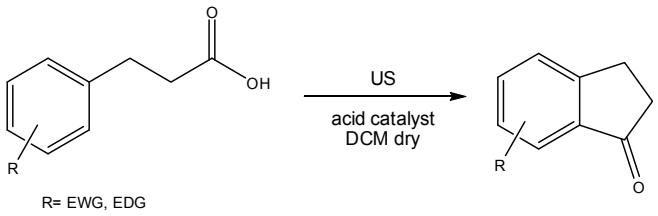
ORG-PO-38 Ultrasounds mediated cyclization of aryl propionic acids: a new route towards indanones.

P. Costanzo,[a] M. Oliverio,[a] F. Ortuso,[a] M. Nardi,[b] R. Paonessa,[a] A. Procopio.[a]

[a] Università Magna Græcia di Catanzaro, Campus Salvatore Venuta, 88100 Catanzaro (CZ)
[b] Università della Calabria, Ponte Bucci, cubo 12C, 87036 Arcavacata di Rende (CS)
e-mail: pcostanzo@unicz.it

Indanones are structural motifs frequently used as synthetic precursors of several biologically active both natural and pharmaceuticals compounds. The indanone plays a pivotal role in the donepezil (Aricept) mediated acetylcholinesterase (ACh) inhibition. The classical way to achieve an indanone moiety is to perform a Friedel-Craft cyclization of aryl propionic acyl chloride or Meldrum's acids.[1] Some examples of cyclization starting from aryl propionic acids has been reported in the literature, but all the procedures need superacids catalysts [2] or drastic reaction conditions [3]. Molecular modelling studies have suggested indanone derivatives, reporting an EWG group on the aromatic cycle, as promising ACh inihibitors.
An efficient ultrasounds-assisted Friedel-Craft cyclization of inactivated aryl propionic acids is presented.



Ultrasounds allow to use a low amount of acid with respect to the procedures reported in the literature and to perform the reaction at room temperature or under slight heating. A comparison between the reaction performed with or without sonication shows that ultrasounds reduce the reaction time and improve the reaction yield giving rise to a pure product even in the case of strongly inactivated starting materials.

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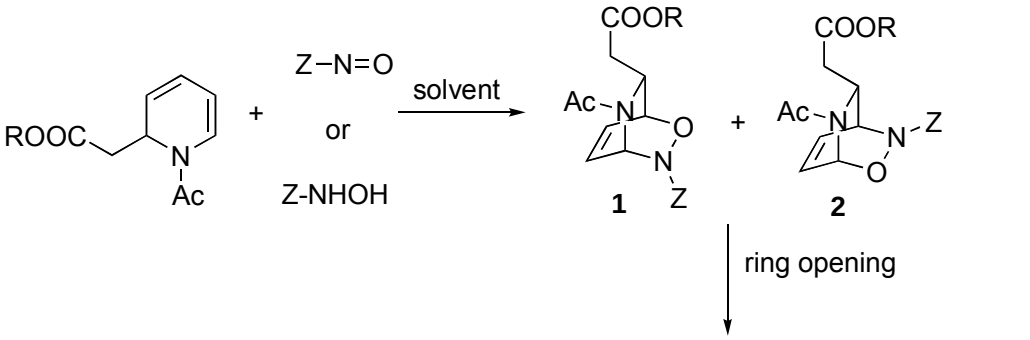
[3] D.-M. Cui, C. Zhang, M. Kawamura and S. Shimada, *Tetrahedron Lett.*, *45*, **2004**, 1741-1745.

ORG-PO-39 Novel Expeditious Synthesis of Unconventional Piperidines

Stefano Crotti,[a] Valeria di Bussolo,[a] Mauro Pineschi*[a]

[a] Dipartimento di Scienze Farmaceutiche, Sede di Chimica Bioorganica e Biofarmacia, Università di Pisa, Via Bonanno 33, 56126 Pisa.
E-mail:pineschi@farm.unipi.it

Nitroso cycloadducts, derived from nitroso Diels-Alder reactions, are valuable synthetic intermediates as they serve as a general scaffold to create unique structural and functional diversity.[1] In our continued interest for the chemistry of these cycloadducts,[2] we have examined the nitroso Diels-Alder of N-acetyl-1,2-dihydropyridyl acetic acid derivatives, very recently obtained by us using a Perkin-acyl Mannich reaction.[3]



The nitroso cycloadducts **1** and **2** were obtained with complete *trans*-stereoselectivity with respect to the C_2 substituent with a regioselectivity that was highly dependant by the nitroso dienophile used. The ring opening of adducts **1** and **2** afforded densely functionalized piperidines with unconventional substitution patterns and showed some interesting features.

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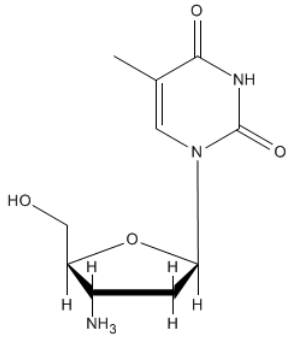
ORG-PO-40 Synthesis, Stability Evaluation and Permeability Study of a Zidovudine-Bile Acid Prodrug

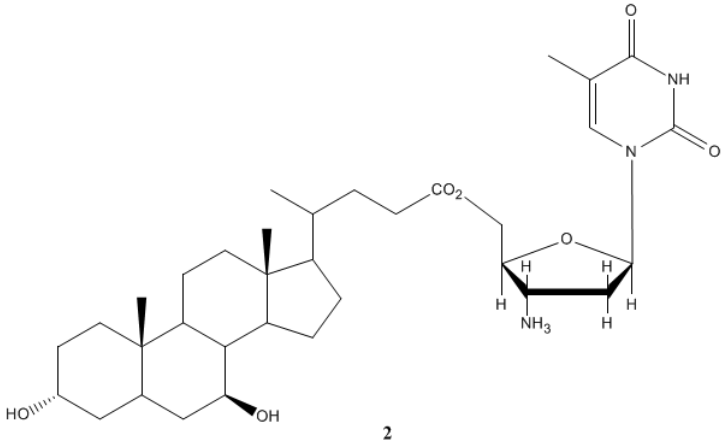
A. Dalpiaz[a], M. Fogagnolo[b], B. Pavan[c], D. Perrone[c] and I. Poppi[b]

[a]Department of Pharmaceutical Sciences, University of Ferrara, via Fossato di Mortara 19, 44121 Ferrara.
[b]Department of Chemistry, University of Ferrara, via L. Borsari 46, 44121 Ferrara.
[c]Department of Biology and Evolution, University of Ferrara, via L. Borsari 46, 44121 Ferrara.
daniela.perrone@unife.it

3'-Azido-3'-deoxythymidine (**1**, AZT, Zidovudine), clinically approved by FDA to treat human HIV infection, is a typical member of the nucleoside analogues. Recently, the well known clinical limitations related with AZT therapy (especially dose-related toxicity and a short half-life in plasma) have prompted the synthesis of different types of 5'-*O*-conjugates of zidovudine [1].



1



2

Based on the large application of bile acids in pharmacology and their amphiphilic structures, we have designed and synthesized the AZT-ursodehoxycholic acid prodrug **2** in an effort to enhance the efficiency of drug delivery. In this prodrug, conjugating moiety is linked to AZT through a 5'-*O*-ester group. The stability in physiological fluids and the *in vitro* permeability of zidovudine-prodrug **2** have been evaluated.

Every detail concerning synthesis, stability and permeability will be discussed.

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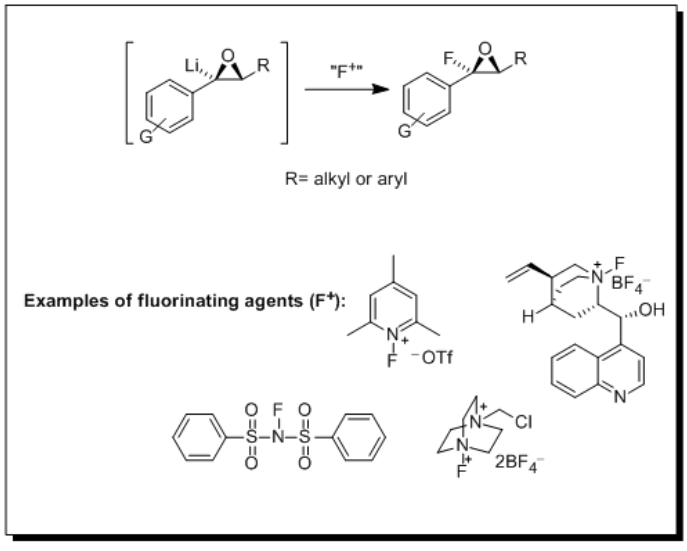
ORG-PO-41 Electrophilic Fluorination of Lithiated Aryloxiranes

Mariangela Dammacco, Filippo Maria Perna, A. Salomone, V. Capriati
Dipartimento Farmaco-Chimico, Università degli Studi di Bari "Aldo Moro"
Consorzio Interuniversitario Nazionale C.I.N.M.P.I.S. , via E. Orabona 4, I-70125, Bari, Italy
E- mail: marydammacco@hotmail.it

Today, the significant expansion in the use of fluorinated chemicals has been attracting more and more the attention of organic, agricultural, medicinal, and material chemists. This is because the replacement of hydrogen by fluorine alters sterically, electronically and lypophilically the properties of the molecule, affecting overall reactivity and stability [1]. In this context, the development of new synthetic fluorinating methodologies of "building blocks", starting from commercially available and cheaply material, is quite interesting and widely pursued.

One of the most fascinating aspects of organofluorine chemistry is the asymmetric synthesis of fluorinated molecules. To date, in particular, only a few methods of synthesis of fluorinated epoxides have been reported [2]. As the oxiranyl anion-based methodology has undoubtedly become a valuable tool for making more functionalized epoxides [3], fluorination of lithiated aryloxiranes has been investigated starting either from configurationally stable and optically active derivatives or from racemic substrates but that can successfully undergo a dynamic resolution.

Asymmetric fluoruration of meso epoxides will also be discussed.



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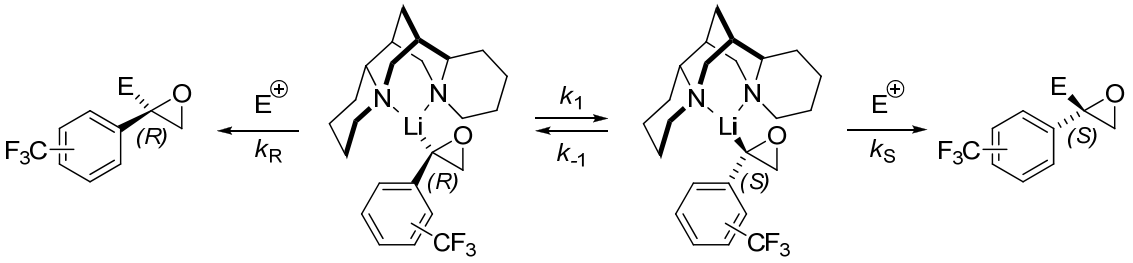
ORG-PO-42 Lithiated Trifluoromethylphenyloxiranes: Solution Structure and Dynamic Resolution

Antonio Salomone, Rosmara Mansueto, Filippo Maria Perna, Saverio Florio and Vito Capriati

Università di Bari "Aldo Moro", Dipartimento Farmaco-Chimico, Consorzio Interuniversitario Nazionale Metodologie e Processi Innovativi di Sintesi C. I. N. M. P. I. S., Via E. Orabona 4, *I*-70125, Bari, Italy
antoniosalomone@gmail.com

Stereoselective substitution of organolithiums represents a powerful methodology in asymmetric synthesis. While it is much convenient to use configurationally stable reagents, it is also possible to carry out an asymmetric synthesis by using stereolabile organolithiums that undergo fast racemization. This goal, usually achieved by exploiting a dynamic resolution of the racemic organolithium, provides an opportunity to obtain enantioenriched products starting from racemic substrates with the aid of external chiral ligands. As part of our research on the reactivity of □-lithiated aryloxiranes, [1] we recently found that although □-lithiated trifluoromethyl-substituted aryloxiranes undergo fast racemization when generated in THF, the employment of hexane/TMEDA dramatically hinders their racemization.[2]



Dynamic Kinetic Resolution: $k_1, k_{-1} >> k_S, k_R$
Dynamic Thermodynamic Resolution: $k_S, k_R >> k_1, k_{-1}$

In this communication, we report preliminary results concerning the dynamic resolution of □-lithiated trifluoromethylstyrene oxides, in the presence of chiral diamine ligands. Solution structure and racemization mechanism will also be discussed in light of DFT calculations and a multinuclear magnetic resonance investigation.

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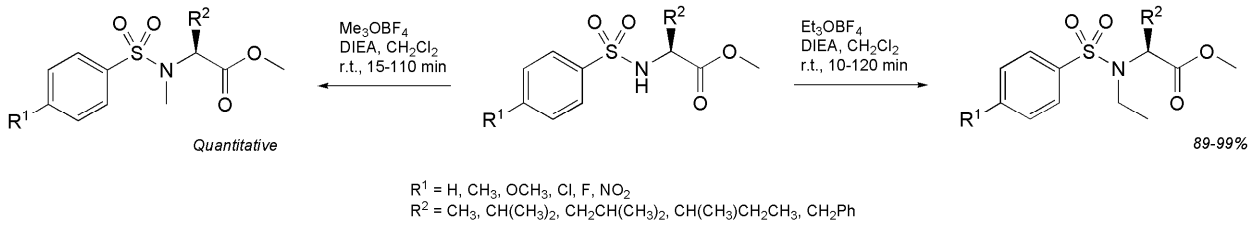
ORG-PO-43 *N*-Alkylation of *N*-Arylsulfonyl-α-Amino Acid Methyl Esters by Trialkyloxonium Tetrafluoroborates

Rosaria De Marco,[a] Maria Luisa di Gioia,[a] Angelo Liguori,[a] Francesca Perri,[a] Carlo Siciliano,[a] and Mariagiovanna Spinella[a]

[a] Dipartimento di Scienze Farmaceutiche, Università della Calabria, Edificio Polifunzionale, I-87036 Arcavacata di Rende (CS) – Italy
E-mail:francesca.perri@unical.it

N-Alkyl-α-amino acids are a representative class of amino acid derivatives. They find applications as synthetic building blocks in medicinal chemistry and are structural constituents of peptidomimetics and naturally occurring bioactive peptides [1]. In particular, the synthesis of *N*-methyl and *N*-ethyl-α-amino acids has received attention for decades [2]. *N*-Methyl-α-amino acids are successfully obtained by reacting *N*-nosyl-α-amino acids with diazomethane [3]. However, the highly toxic nature of this reagent prompted us to exploit new methods in which more safe alkylating species could be used.



Scheme 1

In this communication we present a highly efficient strategy for the rapid, clean, and chemospecific *N*-methylation of a series of differently 4-substituted *N*-arylsulfonyl-α-amino acid methyl esters, performed using trimethyloxonium tetrafluoroborate. *N*-Methylation of the amino acid derivatives is quantitative also in those cases in which diazomethane results to be ineffective. In a similar protocol, *N*-ethylation of the same 4-substituted *N*-arylsulfonyl-α-amino acid methyl esters tested for *N*-methylation is easily realized using triethyloxonium tetrafluoroborate.

[1] C.A.Bewley, and D.J.Faulkner, *Angew.Chem.Int.Ed.*, *37*, **1998**, 2162.
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ORG-PO-44 γ-Hydroxybutenolide Derivatives As Promising Negative Modulators Of Microsomal Prostaglandin E_2 Synthase-1.

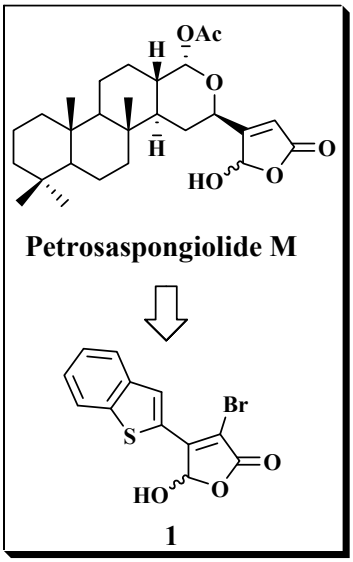
R. De Simone,[a] I. Bruno,[a] O. Werz,[b] R. Riccio.[a]

[a]Department of Pharmaceutical Sciences, University of Salerno, Via Ponte Don Melillo, 84084 Salerno, Italy.
[b]Department of Pharmaceutical Analytics, Pharmaceutical Institute, Eberhard Karls University Tuebingen, Auf der Morgenstelle, D-72076 Tuebingen, Germany.
E-mail: rdesimone@unisa.it

Petrosaspongilide M (PM) is a natural product isolated from the marine sponge *Petrosaspongia nigra* characterized by a γ-hydroxybutenolide ring. It is able to potently inhibit the human synovial phospholipase A_2 (PLA_2) type IIA, the enzyme responsible for triggering the arachidonic acid cascade [1].

In the frame of a previous project involved in the generation of PM-simplified derivatives as potential inhibitors of PLA_2, we identified the interesting compound **1** able to negatively modulate microsomal prostaglandin E_2 synthase-1 (mPGES-1), the enzyme involved in the biosynthesis of PGE_2 from PGH_2 [2,3].

The intriguing biological results shown by this new potent and selective negative modulator of mPGES-1 expression (IC_{50} = 1.80 μM) [2,3] encouraged us to continue our studies and, taking into account Ludi software suggestions, we undertook the synthesis of a new generation of γ-hydroxybutenolides, bearing different molecular decorations in order to amplify the chemical space under investigation.



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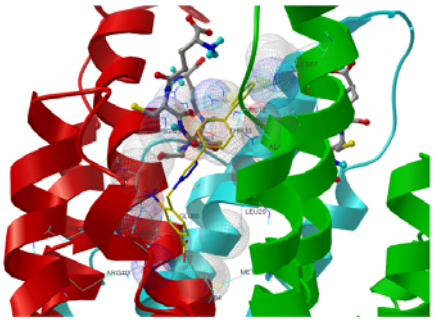
M.D.Guerrero, M.Aquino, I.Bruno, R.Riccio, M.C.Terencio, and M.Paya, *Eur.J.Pharmacol., 620*, **2009**, 112.

ORG-PO-45 Development Of A New Collection Of Trizole-Based Derivatives As Promising Microsomal Prostaglandin E_2 Synthase-1 Inhibitor.

R. De Simone,[a] M. G. Chini,[a] I. Bruno,[a] G. Bifulco,[a] O. Werz,[b] R. Riccio.[a]

[a]Department of Pharmaceutical Sciences, University of Salerno, Via Ponte Don Melillo, 84084 Salerno, Italy.
[b]Department of Pharmaceutical Analytics, Pharmaceutical Institute, Eberhard Karls University Tuebingen, Auf der Morgenstelle, D-72076 Tuebingen, Germany.
e-mail: rdesimone@unisa.it

Microsomal prostaglandin E_2 synthase-1 (*m*PGES-1) enzyme is recently emerged as an attractive target involved in inflammatory diseases [1]. Because of its ability to affect only COX-2-mediated PGE_2 production, *m*PGES-1 inhibitors are supposed to be a promising alternative to non-steroidal anti-inflammatory drugs which are known to be endowed with severe side effects [2].



Despite many efforts have been lavished in this research area, owing to the lack of *m*PGES-1 crystallographic structure in the open active form, very few inhibitors of the enzyme have been identified so far [3]. Hence we decided to choose as model for our investigations microsomal glutathione S-transferase (MGST-1), an enzyme belonging together with *m*PGES-1, to membrane associated proteins in eicosanoid and gluthatione metabolism (MAPEG) family, and showing a high homology sequence with our selected target [4]. On the basis of virtual screening outcomes, we designed and synthesized a collection of potential *m*PGES-1 inhibitors based on 1,4-disubstituted triazole moiety which showed interesting pharmacological profiles. In this frame we discovered a promising hit (IC_{50} = 3.2 μM) [5] which has been subjected to a further structural optimization process, according to molecular modeling suggestions, in order to improve its biological activity.

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R.De Simone, M.G.Chini, I.Bruno, R.Riccio, D.Mueller, O.Werz, and G.Bifulco, *J.Med.Chem*., *54*, **2011**, 1565.

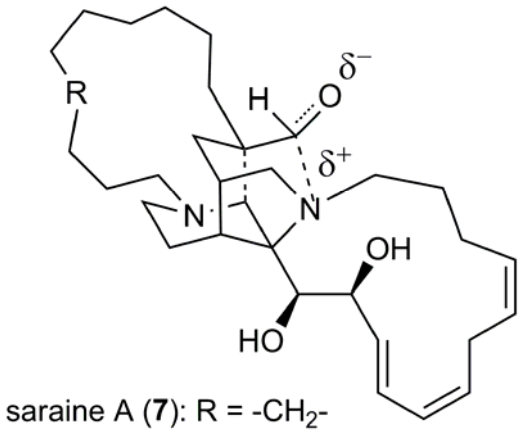
ORG-PO-46 New structural insights into saraines A, B and C, macrocyclic alkaloids from the Mediterranean sponge *Reniera (Haliclona) sarai*.

Andrea Defant,[a] Ines Mancini,[a] Lucija Raspor,[b] Graziano Guella,[a] Tom Turk,[b] Kristina Sepčić [b]

[a] Laboratorio di Chimica Bioorganica, Dipartimento di Fisica, Università di Trento, via Sommarive 14, I-38123 Povo Trento, Italy.
[b] Department of Biology, Biotechnical Faculty, University of Ljubljana, Večna pot 111, 1111 Ljubljana, Slovenia.
defant@science.unitn.it

Saraines A, B and C (Figure 1) are structurally complex diamine alkaloids first isolated from the sponge *Reniera sarai* collected in the bay of Naples [1]. Their peculiar core structure induces an uncommon behaviour responsible of chromatographic and spectroscopic anomalies, and that was explained by a strong "proximity effect" between a tertiary ammine and aldehyde groups, able to be involved into a cyclic zwitterionic form.

On saraines A-C recently isolated from the same sponge collected in the Northern Adriatic Sea, we report now on new structural evidences including: *a)* NMR analysis in different solvents, *b)* electrospray ionization (ESI)-MS spectra showing signals for mixed $[2M+H]^+$ clusters in neutral conditions and $[M+H]^+$ ions in acidic media, *c)* zwitterionic form trapped by conversion to a stable O-methyl ammonium salt derivative, *d)* density functional theory (DFT) calculations on the amine-aldehyde form, resulting in good agreement with Bürgi–Dunitz angle, a model able to forecast the preferred spatial approach in the nucleophilic addition to a carbonyl group.



saraine A (**7**): R = $-CH_2-$

saraine B (**8**): R = $-CH=^{Z}CH-$

saraine C (**9**): R = $-CH=^{Z}CHCH_2-$

Figure 2.

In addition, biological activities including antibacterial, haemolytic and anti-acetilcholinesterase assays were investigated for saraines A-C, in order to clarify their ecological role [2].

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ORG-PO-47 Design, Virtual Screening and Synthesis of Potential Heat Shock Protein 90 (HSP90) inhibitors

Stefania Terracciano, Maria Giovanna Chini, Ines Bruno, Giuseppe Bifulco and Raffaele Riccio

Dipartimento di Scienze Farmaceutiche e Biomediche, Università di Salerno, Via Ponte Don Melillo, 84084, Fisciano (Salerno), Italy
sterracciano@unisa.it

Molecular chaperones are a class of proteins responsible for the correct folding of several cellular "client" proteins which are deeply involved in key physiological functions in human cells. Belonging to this wide proteins family is the heat shock protein 90 (Hsp90), which has recently emerged as a very important target in several human diseases including cancer, neurodegeneration, viral, fungal and microbial infections.[1] In particular, Hsp90 is an ATP-dependent chaperone that plays a central role in regulating the stabilization, activation and degradation of a range of proteins that promote cell growth and survival.[2] These "client" proteins include kinases, steroid hormone receptors, transcription factors, directly involved in malignancy, and also a number of known over-expressed or mutant oncogenic proteins such as Raf-1, mutant BRaf, Akt, HER2, IGF-IR, mutant EGFR and others.[3] On this basis Hsp90 is considered an important target for pathway-oriented drug discovery. With the aim of developing new Hsp90 inhibitors we performed an in silico screening by molecular docking using Autodock-Vina software [4] starting from 176 designed molecules. For our docking calculation, we used the X-ray crystallographic structure of Hsp90 N-terminal domain (pdb code: 2qg0).[5] Following computational docking suggestions, we successfully undertook the synthesis of a collection of new triazole based molecules through "click chemistry" approach as potential Hsp90 inhibitors.

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ORG-PO-48 Stereoselective Synthesis of Diastereoisomeric 6-Deoxy-*N*-Cbz-iminoglycal-derived Vinyl Oxiranes and their Regio- and Stereoselective Behavior in Addition Reactions

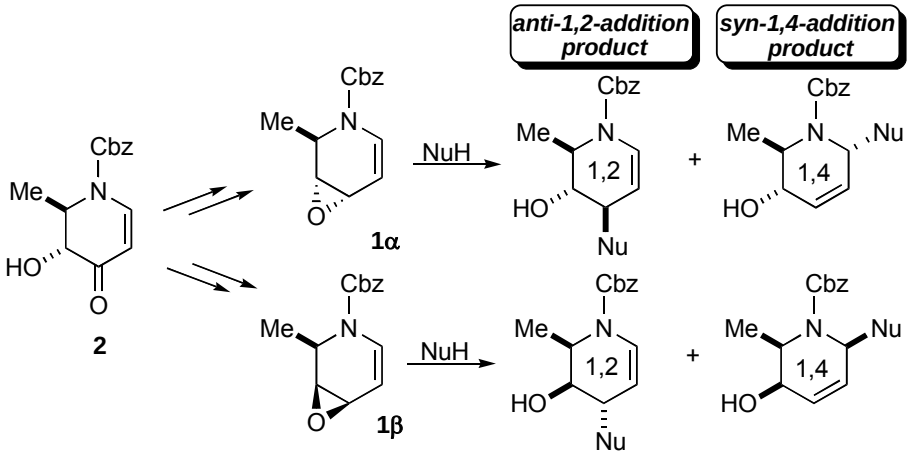
V. Di Bussolo, I. Frau, A. Fiasella[¶] and P. Crotti

Dipartimento di Scienze Farmaceutiche, Università di Pisa
e-mail: *paolo.crotti@farm.unipi.it*

The iminoglycal system can constitute an efficient access to differently substituted azasugars, a class of compounds with potentially interesting biological properties, in particular as inhibitors of enzymatic activity.[1]

In view of their use as precursors of azasugars, the new, diastereoisomeric 6-deoxy-*N*-Cbz-iminoglycal-derived vinyl epoxides **1α** and **1β**,[2] were synthesized starting from a common synthetic intermediate, the *trans* hydroxy ketone **2**, on its own prepared by a racemic application of the Comins' enantioselective protocol.[3]

The regio- and stereoselective behavior of epoxides **1α** and **1β** was examined in addition reactions with *O*-, *N*-, *S*-, and *C*-nucleophiles.



The results have indicated that *1,2-* and/or *1,4-addition products* are obtained, depending on the reaction conditions. In particular, a complete or large 1,4-regio- and *substrate-dependent* stereoselectivity toward corresponding *syn-1,4-addition products* is observed when coordinating nucleophiles are used. On the contrary, the use of non-coordinating nucleophiles leads to the formation of corresponding *anti-1,2-addition products*.

[¶] Present address: Istituto Italiano di Tecnologia (IIT), Genova.

[1] K. Afarinkia, and A. Bahar, *Tetrahedron:Asymmetry*, *16*, **2005**, 1239.
[2] See also: V. Di Bussolo, A. Fiasella, M.R. Romano, L. Favero, M. Pineschi, and P. Crotti, *Org. Lett, 9,* **2007**, 4479.
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ORG-PO-49 Amine-Oxide Surfactant Hydrogels Hybridized with Single-Walled Carbon Nanotubes: Preparation, Rheology and Applications

Antonello Di Crescenzo,[a] Antonio Iannitelli,[a] Raimondo Germani,[b] Gianfranco Savelli,[b] Antonella Fontana[a]

[a]Dipartimento di Scienze del Farmaco, Università "G. d'Annunzio", Via dei Vestini 31, 66100, Chieti, Italy
[b]CEMIN, Centro di Eccellenza Materiali Innovativi Nanostrutturati, Dipartimento di Chimica, Università di Perugia, Via Elce di Sotto 8, 06123, Perugia, Italy
a.dicrescenzo@unich.it

The preparation of hydrogels hybridized with single-walled carbon nanotubes (SWNTs) is very interesting in view of bio-inspired applications, such as the design of biosensors [1]. Due to their superb characteristics, SWNTs can modulate the gel properties acting as reinforcing fillers or increasing the electrical conductivity. In return, SWNTs get a matrix that keeps them separate in a semi-solid state, allowing to overcome the restriction on use.

Amine-oxide surfactants possess a low toxicity and are readily biodegradable; in addition some analogues are able to form viscoelastic solutions based on worm-like micelles [2].

In this work well-dispersed SWNTs were successfully incorporated in supramolecular hydrogels obtained with amine-oxide surfactants (Fig.1). Rheological characterization of the prepared hybrids was performed under oscillating dynamic conditions and highlighted a typical viscoelastic behavior with the measured storage moduli (G′) dominating the loss moduli (G″) by one order of magnitude and exhibiting little frequency dependence over the range of angular frequencies tested. The effects of different SWNT and gelator concentrations employed on the hydrogel properties were assessed. The temperature dependence was studied as well. Dependence of the investigated rheological properties of the hydrogels from the SWNTs concentration evidenced reinforcing intermolecular interactions occurring between the nanotubes and the surfactants.

Fig. 1 Hydrogel of SWNTs prepared with *p*-dodecyloxy-benzyldimethylamine oxide (pDoAO).

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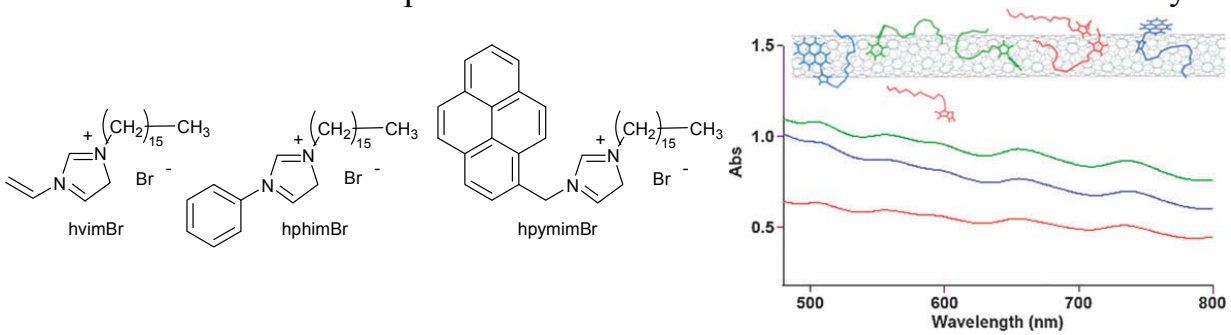
ORG-PO-50 Structural modifications for improving the dispersibility of single-walled carbon nanotubes

Antonello Di Crescenzo,[a] Massimiliano Aschi, [b] Elisa Del Canto,[c] Silvia Giordani[c] and Antonella Fontana[a]

[a]Dipartimento di Scienze del Farmaco, Università "G. d'Annunzio", Via dei Vestini 31, 66100, Chieti, Italy
[b] Dipartimento di Chimica, Ingegneria Chimica e Materiali, Università di L'Aquila, Via Vetoio (Coppito 1), 67010, L'Aquila, Italy.
[c] School of Chemistry/Centre for Research on Adaptive Nanostructures and Nanodevices (CRANN), Trinity College Dublin, Dublin 2, Ireland
fontana@unich.it

The main limitation related to the use of Single-Walled Carbon Nanotubes (SWNTs) is their low solubility in organic and aqueous solvents. It has been previously demonstrated that ionic liquids (ILs) based on the imidazolium cation can disentangle SWNT bundles [1] and that a long-chain imidazolium IL (hvimBr) has the ability to produce stable homogeneous aqueous dispersions of SWNTs [2].

The purpose of the present study is to assess the effect of different moieties in position 3 of the imidazole ring on the dispersing ability of ionic liquid surfactants toward SWNTs, in order to develop new derivatives with ideal features. We demonstrate that aromatic groups enhance the affinity for SWNTs, as confirmed by molecular dynamics simulations, but at the same time render the molecule less water soluble and more prone to self-assembly [3]. NIR-PL, Raman, AFM and vis-NIR absorbance results show that hphimBr has the best features to be used as SWNT water dispersant as it has an optimal hydrophobic/hydrophilic balance which favors adsorption onto the nanotube sidewalls over self-assembly.



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ORG-PO-51 Synthesis of new Pyrrole-Indomethacin derivatives

M. Di Magno,[a] M. A. Loreto,[a] A. Migliorini,[a] S. Panero,[a] M. Polin,[a] J. Serra Moreno[a]

[a]Department of Chemistry, Università "La Sapienza", P.le A.Moro 2, I-00185 Rome, Italy

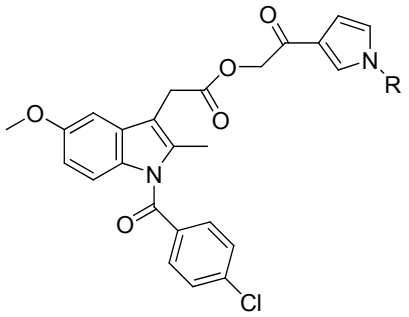
mariaantonietta.loreto@uniroma1.it

Indomethacin (IDMC) is a non-steroidal anti-inflammatory drug (NSAID), which is useful for the treatment of pain and inflammation by inhibiting the cyclooxygenases (COXs) activities. The major drawback of IDMC, if orally ingested, is an undesirable gastric effect. The embedding of IDMC molecules into a biomaterial is a strategy to overcome the undesirable side effects and exploit the possibility of a locally achieved controlled drug release.

Among polymeric biomaterials, PPy is an attractive electroconductive polymer that, properly doped with molecules with pharmacological activity, combines biological compatibility with good electroconductivity [1], becoming a good candidate as smart biomaterial [2].

At the present our attention is focussed on the synthesis of novel pyrrole monomers functionalized with IDMC (Py-IDMC) to obtain new electroconductive and bioactive polymers.

In order to achieve this purpose we synthesized ester **1** and "reverse ester" **2**, where IDMC is covalently bound, through a spacer chain, to the properly functionalized Py.



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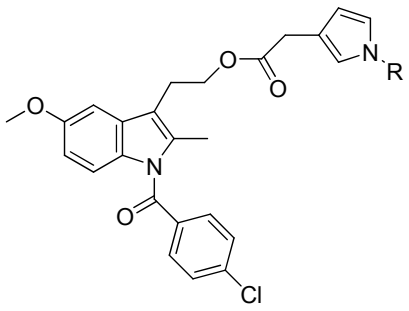

2

These products will be subjected to electropolymerization assay and biological and toxicological tests. Our efforts will address new Py-IDMC derivatives where the spacer is a glycolamide moiety [3].

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Acknowledgement. We thank the University "La Sapienza" of Rome for financial support. (Ateneo Founds Project 2010)

ORG-PO-52 Design, synthesis and biological evaluation of non peptide integrin antagonists via Copper (I) Catalyzed Azide-Alkyne Cycloaddition

Pierangelo Fabbrizzi,[a] Gloria Menchi,[a] Andrea Trabocchi,[a] Antonio Guarna,[a] Anna Bottoncetti,[b] Alberto Pupi,[b] Silvia Raspanti.[b]

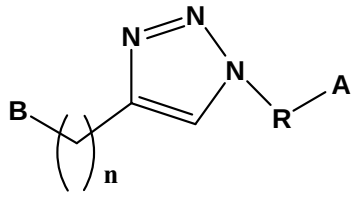
[a] Department of Chemistry "U. Schiff" – University of Florence, Via della Lastruccia, 13 I – 50019 Sesto Fiorentino (FI), Italy.

[b] Department of Clinical Physiopathology, Nuclear Medicine Unit – University of Florence, Viale G. Pieraccini 6, I – 50134 Firenze, Italy.

pfabbrizzi@gmail.com

Integrins are cell surface ahdesion proteins that play main roles in cell-cell and cell-matrix interactions. Subgroup αvβ3 is involved in angiogenesis and tumor cell migration, interacting with vitronectin on the extracellular matrix mainly through the recognition of the tripeptide sequence RGD (Arg-Gly-Asp).[1] That sequence was first incorporated into various linear and cyclic peptides, recently, research has been focused on the synthesis of selective non peptide integrin antagonists, because of their enhanced metabolic stability, bioavailability and biological absorption.

In recent years Sharpless and Kolb[2] proposed the triazole ring as a non-classical bioisostere of peptidic bond. Triazolic rings can be synthesized via an high yield reaction that can be performed in simple conditions, the so-called CuAAC (Copper (I) catalyzed azide-alkyne cycloaddition), the main reaction of the "Click Chemistry" concept[3]. Considering also the stability of such ring, we focused our synthetic efforts in producing a library of triazole derivatives bearing isosteres of the basic and acidic groups of the RGD sequence. After a first library of compounds was synthesized and their biological effects were evaluated,[4] other structures were then designed, synthesized and evaluated also as radiolabeled compounds for imaging applications.



B: Basic Isostere A: Acidic Isostere

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ORG-PO-53 Production of fumonisin analogues in *Fusarium verticillioides* broth cultures under different growth parameters.

C. Falavigna[1], C. Dall'Asta[1], G. Galaverna[1], P. Battilani[2], A. Dossena[1]

[1] Dipartimento di Chimica organica e Industriale, Università degli Studi di Parma, Viale delle Scienze 17/A, 43124 Parma
[2] Istituto di Entomologia e Patologia Vegetale; Via Emilia Parmense
arnaldo.dossena@unipr.it

Fumonisins are a group of structurally related mycotoxins that are mainly produced by *Fusarium verticillioides*. This fungus is one of the most common molds colonizing maize crops throughout the world before harvesting, during the time between harvesting and drying, and during storage. Fumonisins are most frequently found in maize and maize-based foodstuffs and feedstuff, and less
commonly in other grains. These compounds show toxic effects in animals and humans. Moreover, the consumption of fumonisin contaminated maize has been associated statistically with the high incidence of esophageal cancer in rural areas of South Africa, China and Italy.
The fumonisin analogues that have been characterized since 1988 can be classified into four main groups, identified as the fumonisin series A, B, C, and P. The fumonisin B (FB) analogues, comprising toxicologically important FB1, FB2 and FB3, are the most abundant naturally occurring fumonisins, with FB1 predominant, and are usually found at the highest levels. Apart from the FB series, some of the other analogues may occur in naturally contaminated maize, at relatively low levels (<5% of the total fumonisin present).
The present study aimed to evaluated the production of the main fumonisins as well as of their minor analogues in *Fusarium* colture broth under different growth conditions (a_w, time, temperature), in order to better define the biosynthetic pathway of these compounds and the factors which may inhibit/elicitate their production. All the main compounds were identified and by LC-ESI-MS/MS and the fragmentation patterns have been fully characterised. Exact mass measurements were performed by LTQ-Orbitrap.

ORG-PO-54 Phenolic content and radical scavenging ability of wild fruits of *Rubus* species and related jam and seeds from Calabria

Alessia Fazio, Bartolo Gabriele, Pierluigi Plastina

Department of Pharmaceutical Sciences, University of Calabria, 87036 Arcavacata di Rende (CS), Italy
a.fazio@unical.it

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

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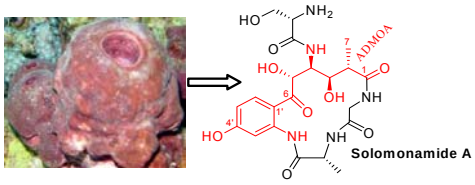
ORG-PO-55 Solomonamides A and B: two unprecedented cyclic peptides from the marine sponge *Theonella swinhoei*

C. Festa[a], S. De Marino[a], V. Sepe[a], M. V. D'Auria[a], G. Bifulco[b], M. Bucci[c], A. Zampella[a]

[a] Dipartimento di Chimica delle Sostanze Naturali, Università di Napoli "Federico II", via D. Montesano 49, 80131 Napoli, Italy;
[b]Dipartimento di Scienze Farmaceutiche, Università di Salerno, via Ponte don Melillo, 84084 Fisciano (SA), Italy;
[c]Dipartimento di Farmacologia Sperimentale, Università di Napoli "Federico II", via D. Montesano 49, 80131 Napoli, Italy
carmen.festa@unina.it



Theonella swinhoei represent one of the most prolific source of innovative secondary metabolites, belonging to more than nine biosynthetic classes [1]. Among these, surely the peptides represent the most significant group, with unusual chemical structures and intriguing biological activities.

In the course of our search for novel metabolites from this sponge, we have isolated two new cyclic peptides, named solomonamides A and B. Solomonamide A is composed of three conventional amino acid residues, alanine, glycine and serine, and a 4-amino(2'-amino-4'-hydroxyphenyl)-3,5-dihydroxy-2-methyl-6-oxohexanoic acid (ADMOA) unit which is unprecedented in natural products. Solomonamide B differs from solomonamide A for the presence of the 4-amino-6-(2'-amino-4'-hydroxyphenyl)-3-hydroxy-2-methyl-6-oxohexanoic acid residue (AHMOA) instead of ADMOA residue.

Structural characterization was elucidated on the basis of comprehensive 1D and 2D NMR tecniques and hight-resolution mass spectrometry. A combinated approach, involving Marfey's method [2], QM *J* based analysis and DFT $J/^{13}C$ calculations [3], was used for establishing the absolute configuration of the entire molecules.

Solomonamide A showed an interesting *in vivo* anti-inflammatory activity reducing carrageenan induced mouse paw oedema [4].

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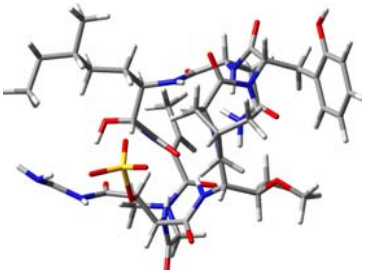
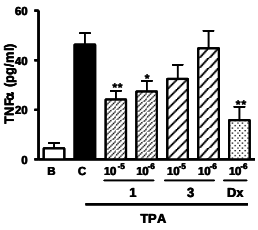
ORG-PO-56 Perthamides C-F, potent human antipsoriatic cyclopeptides

C. Festa[a], S. De Marino[a], V. Sepe[a], M. V. D'Auria[a], G. Bifulco[b], R. Andrés[c], M. C. Terencio[c], M. Payá[c], A. Zampella[a].

[a] Dipartimento di Chimica delle Sostanze Naturali, Università di Napoli "Federico II", via D. Montesano 49, 80131 Napoli, Italy;
[b]Dipartimento di Scienze Farmaceutiche, Università di Salerno, via Ponte don Melillo, 84084 Fisciano (SA), Italy;
[c]Department of Pharmacology, University of Valencia and Center of Molecular Recognition and Technological Development (IDM), Av. V. Andrés Estelles s/n 46100, Burjassot, Valencia, Spain
carmen.festa@unina.it

Psoriasis is a chronic autoimmune inflammatory skin disorder affecting approximately 2-3% of the general population in Europe and North America. Cutaneous and systemic overexpression of various proinflammatory cytokines (TNF-α, IL-8, IFN-□, etc) has been demonstrated in psoriatic patients [1].
Pursuing the chemical investigation of the polar extracts of the Solomon marine sponge *Theonella swinhoei*, we isolated two new cyclic octapeptides, perthamides E and F, together with a large amount of perthamide C [2].
Structural characterization were performed by interpretation of NMR and MS data and the absolute configuration of the AHMOA (3-amino-2-hydroxy-6-methyloctanoic acid) residue in perthamides E and F was proposed on the basis of quantum chemical calculation of NMR chemical shifts [3].
Perthamides C and E are endowed with anti-inflammatory activity inhibiting TNF-□ and IL-8 release in primary human keratinocytes cells and therefore could represent potentially leads for the treatment of psoriasis.





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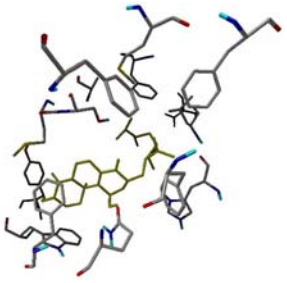
ORG-PO-57 Towards new ligands of nuclear receptors. Discovery of malaitasterol A, an unique bis-secosterol from marine sponge *Theonella swinhoei*

Valentina Sepe,[a] Maria Valeria D'Auria,[a] Simona De Marino,[a] Raffaella Ummarino,[a] Giuseppe Bifulco,[b] Barbara Renga[c], Stefano Fiorucci,[c] Angela Zampella[a]

[a]Dipartimento di Chimica delle Sostanze Naturali, Università di Napoli "Federico II", via Domenico Montesano 49, 80131, Napoli, Italy
[b]Dipartimento di Scienze Farmaceutiche, Università di Salerno, via Ponte Don Melillo, 84084, Fisciano (SA), Italy
[c]Dipartimento di Medicina Clinica e Sperimentale, Università di Perugia, Via Gerardo Dottori 1, S. Andrea delle Fratte, 06132, Perugia, Italy
valentina.sepe@unina.it

In our studies of bioactive compounds from sponges collected from the Solomon Islands, we found a single specimen of the sponge *Theonella swinhoei* as an extraordinary source of new metabolites. Analysis of the polar extracts afforded anti-inflammatory peptides [1], [2], and two sulfated sterols, solomonsterols A and B [3], potent leads in the treatment of immune-driven inflammatory bowel diseases. Investigation of the apolar extracts uncovered a new sterol, which we named malaitasterol A [4].



The structural elucidation of malaitasterol A, which features an unprecedented bis-secosteroid skeleton has been solved through extensive 2D NMR analysis, ESI-MS data and DFT ^{13}C chemical shift calculations.
The pharmacological analysis demonstrated that malaitasterol A is a potent agonist of pregnane-X-receptor and the putative binding mode has been obtained through docking calculations.
In this poster the structure of the new sterol, its pharmacological evaluation and the potential of this study will be focused.

[1]. Festa, C.; De Marino, S.; Sepe, V.; Monti, M. C.; Luciano, P.; D'Auria, M. V.; Debitus, C.; Bucci, M.; Vellecco, V.; Zampella, A. *Tetrahedron* **2009**, *65*, 10424-10428.
[2]. Festa, C.; De Marino, S.; Sepe, V.; D'Auria, M.V.; Bifulco, G.; Debitus, C., Bucci, M.; Vellecco, V.; Zampella, A. *Org. Lett. 13,* **2011**, 1532-1535.
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ORG-PO-58 Chirality effects on the structure of basket resorcarene/nucleoside complexes by gas-phase IR action spectroscopy.

Antonello Filippi[a], Caterina Fraschetti[a], Susanna Piccirillo[b], Flaminia Rondino[a], Bruno Botta[a], Ilaria D'Acquarica[a], Andrea Calcaterra[a], Maurizio Speranza[a]

[a] Dipartimento di Chimica e Tecnologie del Farmaco, Università "La Sapienza", 00185 Roma, Italy
[b] Dipartimento di Scienze e Tecnologie Chimiche, Universita` di Roma "Tor Vergata", Roma, Italy
antonello.filippi@uniroma1.it

Enantioselectivity is a selection phenomenon acting at molecular level. It is responsible of many highly specific biological processes in living systems and implicated in a great number of chiral synthetic processes. Although it intrinsically requires optically active species involved in intimate diastereomeric interactions, other environmental factors may also be important for its efficiency in solution, e.g. solvation, counterion, pH, ionic strength, etc, whose contribution can only be evidenced when their effects can be excluded, i.e. in the gas phase.
In the last decades development of high pressure sources such as electrospray (ESI), nano-electrospray (nano-ESI), atmosferic pressure chemical ionization (APCI), enabled the study of molecular systems up to protein dimensions by means of mass spectrometric devices, i.e. in the absence of environmental effects perturbing the intrinsic gas-phase enantioselectivity. This kind of investigations of have been greatly improved in the last years by introducing a tunable infrared (IR) laser beam into an ion trap (IT) or an ion cyclotron resonant (ICR) mass spectrometer, where selected ions can be isolated long enough to allow their absorbance spectrum be collected. The IR spectum is recorded by measuring the intensity of the fragment ions generated by MultiPhoton induced Dissociation (IRMPD) of the precursor ion.
Despite detailed information on the structure and the conformation of covalent diastereomeric species[1] and their metal ion adducts,[2] has been gathered by IRMPD action spectroscopy,[3] no similar investigations have been performed on non-covalent supramolecular systems, where specific

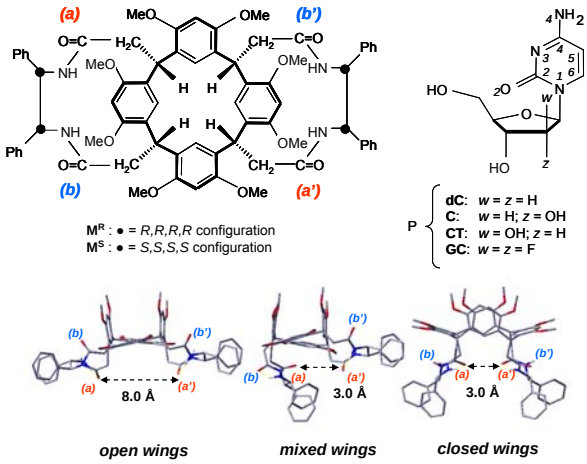

Chart 1

configuration-dependent interactions and the orientation of the host/guest functionalities may affect their enantioselectivity, as well as their IR spectrum.
Herein we present the first IRMPD investigation of chiral non-covalent supramolecular systems, which may provide a first insight into the nature of intrinsic configuration-dependent interactions in chiral receptor/molecule aggregates. As chiral receptor mimics, we selected the bis(diamido)-bridged basket resorcin[4]arene enantiomers ($\mathbf{M^R}$ or $\mathbf{M^S}$) in the flattened cone conformation, whose joint chiral pendants exhibit the amidocarbonyl groups *a/a'* pointing inward and the *b/b'* ones outward the chiral cavity (Chart 1).[4] Pyrimidine nucleosides (P) were used as chiral guests since previous studies showed their marked propensity to proton bonding to $\mathbf{M^R}$ and $\mathbf{M^S}$.[5] Among the nucleoside investigated, cytarabine (**CT**) is an epimer of cytidine (**C**),[5] while gemcitabine (**GC**) is the *gem*-difluoro derivative of 2'-deoxycytidine (**dC**). The experimental data have been analyzed by comparison with theoretical results of model systems.

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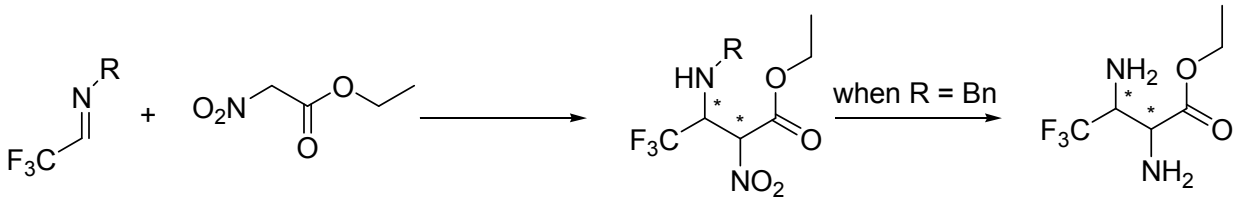
ORG-PO-59 Aza-Henry Reactions of Trifluoromethyl Schiff Bases

Stefania Fioravanti, Lucio Pellacani, Paolo Antonio Tardella, Maria Cecilia Vergari
Dipartimento di Chimica, Università degli Studi di Roma "La Sapienza", P.le Aldo Moro 5, I-00185 Roma
stefania.fioravanti@uniroma1.it

The development of new methodologies to form carbon-carbon bonds is a key goal in the progress of organic synthesis, especially where multiple stereocenters are created simultaneously in a single operation with complete control of the reaction course. The maximum challenge is the control of contiguous stereocenters in flexible acyclic molecules [1].

The synthesis of □,□-diamino acids, having two vicinal chiral centers, has recently emerged as a stimulating and active area of research, because this structural motif is present in many different bioactive natural products and therapeutic agents. The presence of a trifluoromethyl group can enhance the potentiality of these compounds as versatile building blocks for the synthesis of new potential surrogates of peptidic units, able to modulate conformational, physico-chemical and biological properties [2].

We here report the first successful attempts to obtain □,□-diamino □-trifluoromethyl esters by an aza-Henry reaction [3] between different trifluoromethyl imines [4] and ethyl nitroacetate.



The reduction reaction leads to new non proteinogenic amino acid derivatives. Furthermore, when R is an L- or D-□-amino ester residue, a diastereoselective reaction will give new fluorinated molecules, potential surrogates in known peptidic entities.

Italian MIUR and Università degli Studi di Roma "La Sapienza" are gratefully acknowledged for financial support (PRIN 2007FJC4SF_005)

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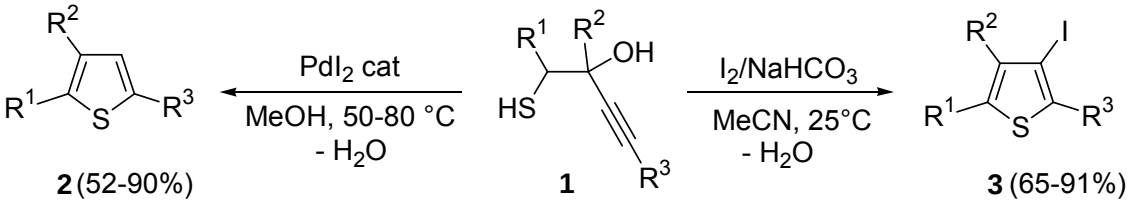
ORG-PO-60 Novel Heterocyclizations Leading to Thiophene and Benzothiophene Derivatives

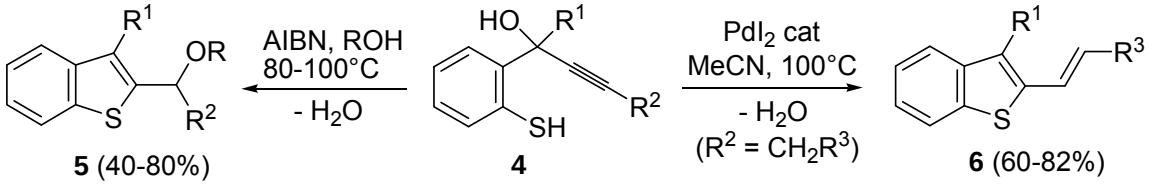
Raffaella Mancuso,[a] Bartolo Gabriele,[b] Lucia Veltri,[a] Vito Maltese,[a] Giuseppe Salerno[a]

[a] Dipartimento di Chimica, Università della Calabria, 87036 Arcavacata di Rende (CS), Italy.
[b] Dipartimento di Scienze Farmaceutiche, Università della Calabria, 87036 Arcavacata di Rende (CS), Italy.
raffaella.mancuso@unical.it

Thiophenes and benzothiophenes are very important classes of heterocyclic compounds. A variety of molecules containing the thiophene or benzothiophene ring display a wide range of biological activity and find extensive application as pharmaceuticals or fragrance compounds. Moreover, they are useful synthetic intermediates, for example, in the preparation of new materials.
In this communication, we will report a novel synthetic approaches to thiophene (**2**, **3**) and benzothiophene (**5**, **6**) derivatives based on *S*-heterocyclization of readily available 1-mercapto-3-yn-2-ols **1** (Scheme1) and 1-(2-mercaptophenyl)-2-yn-1-ols **4** (Scheme 2), respectively.



Scheme 1



Scheme 2

ORG-PO-61 Design of new potential linezolid-like antibacterials

G. Fisichella, C.G. Fortuna, G. Musumarra

Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria, 6, 95125 Catania
gabriele.fisichella@hotmail.com

Although new antibacterials such as linezolid, a fluorinated oxazolidinone introduced in clinical practice since 2000, are active against resistant microorganisms such as MRSA[1] VRE and PNSSP, resistance to this antibiotic has recently been reported [2,3]. The attention in recent papers is also focused on the resistance of fluoroquinolones against Gram negative bacteria. In this context it would be desirable a chemoinformatic optimization, followed by synthesis and biological tests on structures such as linezolid or fluoroquinolones to overcome resistance and hopefully limit side effects.
We here report molecular modelling by means of computational procedures such as: (a) ALMOND to correlate the changes in chemical structures with antibacterial activities [4]; (b) VOLSURF to correlate 3D molecular structures with pharmacokinetic and physicochemical properties [5,6]; (c) docking of new ligands to the receptor active sites by means of FLAP that can be used to describe proteins and ligands based on a common reference framework. In this context we identified a new synthesizable scaffold that is expected to exhibit high antibacterial activity against Gram-negative resistant pathogens.

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ORG-PO-62 Antimicrobial photodynamic therapy: synthesis, conformational properties and antibacterial activity of peptide-porphyrin conjugates

E. Frezza, [a] V. Sella,[a] R. Dosselli,[b] S. Campestrini,[a] E. Reddi,[b] A. Ferrarini[a] and M. Gobbo[a]

[a] Dipartimento di Scienze Chimiche, Università di Padova, via F. Marzolo 1, 35131 Padova, Italy
[b] Dipartimento di Biologia, via U. Bassi 58/B, 35129 Padova, Italy
E-mail: marina.gobbo@unipd.it

The worldwide rise of antibiotic resistance stimulates the search for new strategies for controlling bacterial infections based on the use of agents different from the common antibiotics. Two promising approaches are the application of photodynamic therapy (PDT) and of cationic antimicrobial peptides (CAMP) in the treatment of localized infection.

PDT [1] involves the use of non-toxic dyes or photosensitizers (PS), that can generate reactive oxygen species upon exposure to light in the presence of oxygen. It is well establish that singlet oxygen is produced as the main species responsible for cell death.

CAMP [2] are components of the innate defense mechanism of many organisms. They are short peptides (10-50 amino acids), with an overall positive charge (generally +2 to +9) and a substantial proportion (≥30%) of hydrophobic residues. These properties permit the peptide to fold into an amphipathic structure, often upon contact with membranes, and ensures accumulation at the poly-anionic microbial cell surfaces.

In general neutral, anionic or cationic PS molecules can efficiently kill Gram-positive bacteria, whereas Gram-negative bacteria are less susceptible to phodynamic killing and only cationic porphyrins can induce their photo-inactivation. On the contrary CAMP exhibit a broad spectrum of antimicrobial activity and do not easily induced resistance compared to conventional antibiotics. Thus the use of CAMP in combination with PDT is expected to enhance the effectiveness of PDT.

Recently we have shown that the conjugation of apidaecin 1b, a 18-residue peptide, to a 5(4'-carboxyphenyl)-10,15,20-triphenylporphyrin (cTPP) photosensitizer afforded a new antibacterial agent, with a broader spectrum activity with respect to that of the two individual components or a mixture of them [3].

Here, we present the synthesis of a new conjugate between cTPP and the membrane active peptide magainin 2 and a preliminary investigation of its antibacterial activity, in the dark and under light-activation. Moreover, the conformational properties of the porphyrin-peptide conjugates will be compared to those of the parent peptides and an interpretation of the circular dichroism spectra

with respect to the assembling of these systems in aqueous environment will be presented.

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ORG-PO-63 A New Approach to Functionalized Isoquinoline and Isochromene by Carbonylation of (2-Alkynyl)benzylideneamine Derivatives

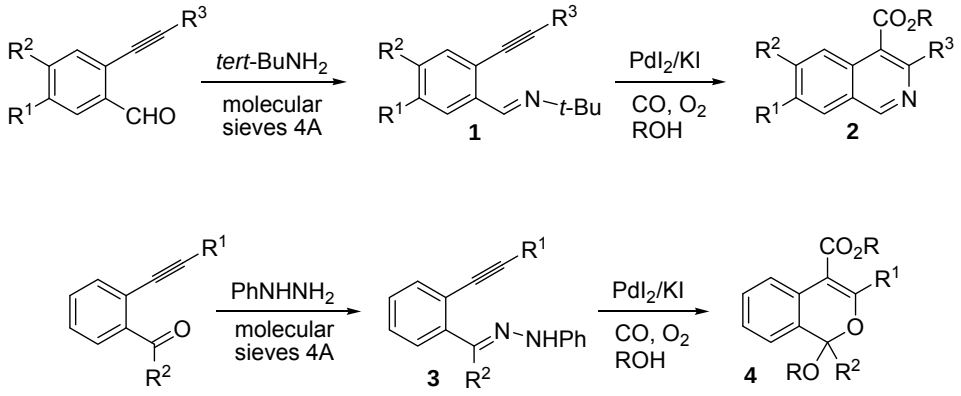
Bartolo Gabriele,[a] Lucia Veltri,[b] Vito Maltese,[b] Rosella Spina,[b] Raffaella Mancuso,[b] and Giuseppe Salerno[b]

[a] Dipartimento di Scienze Farmaceutiche, Università della Calabria, 87036 Arcavacata di Rende (CS), Italy; Fax: +39 0984 492044; E-mail: b.gabriele@unical.it
[b] Dipartimento di Chimica, Università della Calabria, 87036 Arcavacata di Rende (CS), Italy
metalsoviet@tiscali.it

The Pd-catalyzed oxidative carbonylation of simple functionalized alkynes is one of the most versatile methods for the direct synthesis of carbonylated heterocyclic derivatives. We report here on some new synthetic approaches to functionalized nitrogen or oxygen carbonylated heterocycles by PdI_2-catalyzed oxidative carbonylation of (2-alkynylbenzylidene)amine derivatives, obtained by condensation of the corresponding 2-alkynylbenzaldehydes with amines or hydrazines.

In particular, we have found that *tert*-butyl-(2-alkynylbenzylidene)amines **1** selectively afford isoquinoline-4-carboxylic esters **2**, ensuing from *N*-cyclization (Eq. 1), while *N*-[2-(alkynyl)benzylidene]-*N*-phenylhydrazines **3** lead to isochromene-4-carboxylic esters **4** through water attack to the imino group of the followed by *O*-cyclization (Eq. 2).

Reactions were carried out in alcoholic solvents at 80-100 °C and under 20-80 atm (at 25 °C) of a 4:1 mixture of CO-air, in the presence of PdI_2 (2-10 mol %) in conjunction with KI (KI/PdI_2 molar ratio = 10). In the case of imines, the use of a dehydrating agent, such as a trialkyl orthoformate, was necessary in order to obtain satisfactory yields of isoquinolines.



ORG-PO-64 Enhanced Probes for Catalytic Signal Amplification for the Detection of Enzyme Activity

Patrizia Galzerano, Cristian Pezzato, Paolo Scrimin, Leonard J. Prins

Department of Chemical Sciences, University of Padova, Padova, Italy. *patrizia.galzerano@unipd.it*

The detection of low levels of proteins and other biomarkers is of crucial importance for an early diagnosis of diseases [1]. The large interest in the development of chemical-sensing methodologies, complementary or as alternative to biological assays, is due to the simple detection protocols and easy structural modifications of the system adapting for a wide variety of targets.
Recently, we report on the application of a catalytic amplification process for the detection of proteases [2-5]. This approach lead to a highly sensitive assay, since the enzymatic conversion of a single substrate molecule lead to the formation of a multitude of reporter molecules through a cascade of chemical events, each of them magnifying the previous one. A central role is played by gold nanoparticles covered with a catalytic self-assembled organic monolayer (Au-MPC) (Figure 1). In the first event an enzyme hydrolyses a peptide substrate, which acts as an inhibitor for the catalytic monolayer. Upon hydrolysis, the catalytic activity of the monolayer is restored, which results in the production of large quantities of a yellow reporter molecule. The main limit of this system relies on the low turn over frequency of our substrate (HPNPP), together with a relatively low binding affinity of HPNPP to the Au NPs. Our aim is the improvement of these two parameters, by acting on the nature of the substrate and in particular on the leaving group, in order to enhance the cleavage rate and the binding affinity for the Au-MPC.

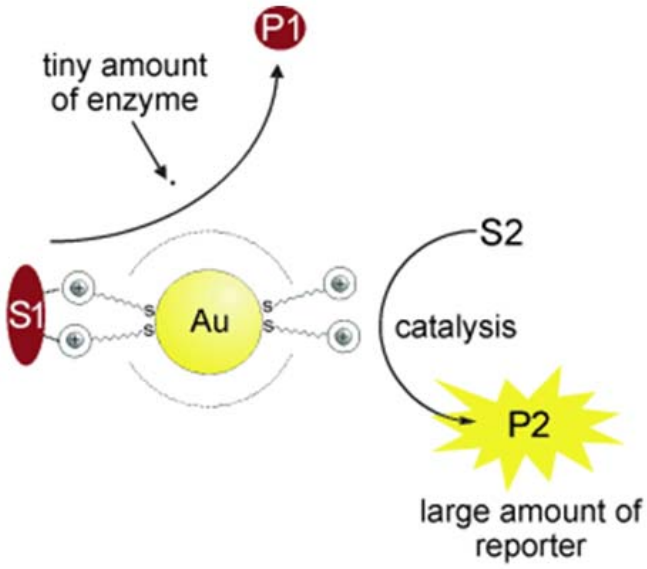


Figure 1. Catalytic signal amplification using functionalized nanoparticles.

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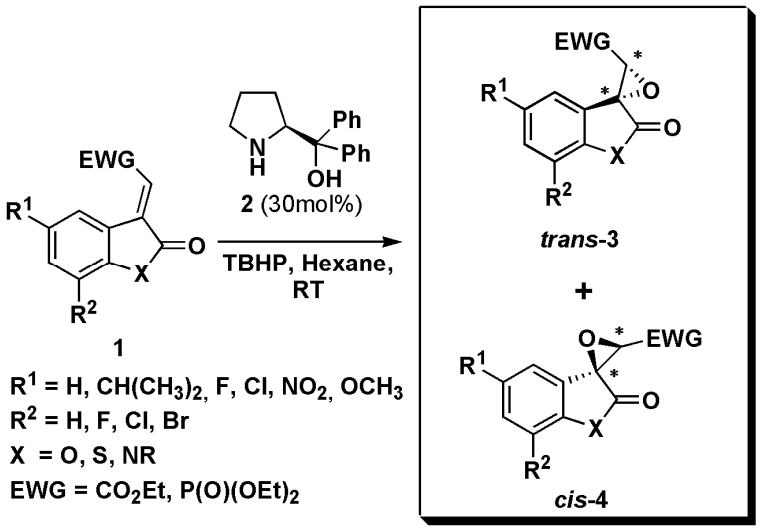
ORG-PO-65 Proline Derivatives in Asymmetric Nucleophilic Epoxidation: a Novel Organocatalytic Approach to Spiroepoxy Esters

Gambacorta, A.,[a] Gasperi, T.[a], Palumbo, C.,[b] Loreto, M.A.,[b] Migliorini, A.[b] and Tofani, D.[a]
[a]Department of Mechanical and Industrial Engineering, University of "Roma Tre", Via della Vasca Navale 79, I-00146 Rome, Italy;
[b]Department of Chemistry, University of Roma "La Sapienza", P.le A. Moro, 5, I-00185 Rome, Italy.
gambacor@uniroma3.it

Asymmetric epoxidation has always been an hunted goal for organic chemists. After the Sharpless's breakthrough, only over the last years, have systems been described which allow the asymmetric epoxidation of electron-poor olefins [1]. In particular, organocatalytic strategies have been taking on more and more importance [2].Within this context, pursuing previous studies on biologically relevant isatine systems [3] and prompted by the amazing results on α,β-unsaturated ketones [4] we envisioned the opportunity to exploit the diphenyl prolinol **2**/TBHP system to perform a stereoselective organocatalytic epoxidation of α-alkylideneoxindoles **1** (X=NR) bearing a further electron-withdrawing group [EWG=CO_2Et, $P(O)(OEt)_2$] on the exocyclic double bond. Herein, we account for the achievement of the desired spiroepoxides **3** and **4** in quite good enantioselectivity (up to 86%*ee*), with the formation of a quaternary stereocenter. Moreover, extension of such procedure to novel alkylidene analogs **1** (X=O,S), should broad the substrate scope and better clarify the operating mechanistic pathway.



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ORG-PO-66 Effect of Concentration and Temperature on Vesicles Formed by a New Sultaine Surfactant

Carla Gasbarri[a], Antonella Fontana[a], Paolo De Maria[a], Guido Angelini[a], Gabriella Siani[a], Giorgio Cerichelli[b], Marco Chiarini[c]

[a]Dipartimento di Scienze del Farmaco dell'Università G. d'Annunzio di Chieti-Pescara, Via dei Vestini, 66100 Chieti, Italy

[b]Dipartimento di Chimica, Ingegneria Chimica e Materiali dell'Università degli Studi de L'Aquila, Via Vetoio, 67010 Coppito, L'Aquila, Italy

[c]Dipartimento di Scienze degli Alimenti dell'Università degli Studi di Teramo, Via Lerici, 64023 Mosciano Sant'Angelo, Teramo, Italy

c.gasbarri@unich.it

The formation of micelles, bilayers or vesicles in aqueous solution depends on the structural properties of the surfactant [1].

Vesicles can act as drug delivery systems in many biotechnological applications. To be suitable as a carrier, surfactant vesicle should have high affinity for the biological membranes and high stability under physiological conditions to release its content in a controlled way [2].

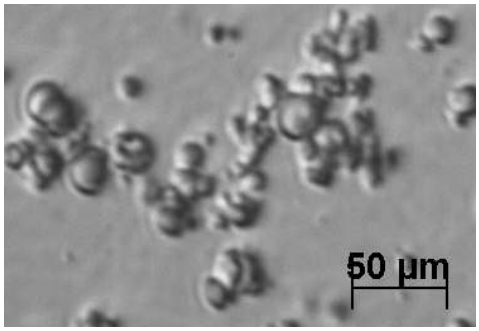

Figure 1.

Sultaine surfactants are characterized by low irritancy and non denaturizing-protein effect. The aggregation behaviour of a new synthesized sultaine has been studied in buffer solution at pH 7.4 [3]. Spontaneously formed vesicles can be observed by optical microscopy (Fig.1). The sultaine transition temperature has been determined by DSC and Nile Red fluorescence.

Two critical vesicular concentrations (CVC_1 and CVC_2) have been fluorimetrically found and two kind of aggregates have been identified and investigated: vesicles above the CVC_1 and closely packed aggregates above the CVC_2. The sultaine vesicles formed above the CVC_1 decreases their stability from 25 to 75°C due to the membrane association promoted at high temperature.

Dynamic Laser Light Scattering and fluorescence measurements confirm the presence of larger aggregates above the CVC_2 due to the vesicles assembly promoted at high sultaine concentration.

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ORG-PO-67 Synthesis of PNA in non conventional media

Clelia Giannini[a], Laura Poletti[a], Matteo Fusari[a]

[a]Dipartimento di Chimica Organica e Industriale, Via Venezian 21, 20133, Milano, Italy
clelia.giannini@unimi.it

The growing awareness of the urgent need for greener, more sustainable technologies has focused the scientific attention on the use of alternative reaction media that circumvent the problems associated with the traditional volatile organic

solvents (VOCs). The use of non conventional reaction media also provides opportunities to facilitate the recovery and the recycling of the reaction solvent [1].
Among the most promising alternatives to classical organic solvents, ionic liquids (ILs) have been intensely studied in the recent years as potential environmentally benign reaction media due to their lack of measurable vapour pressure and high thermal and chemical stability [2].
Recently, room temperature Ionic liquids (RTILs) have been used as solvents in the preparation of several classes of biomolecules such as oligosaccharides [3] and peptides [4].
In this communication we report a preliminary study on the use of ILs as solvents in the preparation of peptide nucleic acids (PNAs) [5].
The optimization of the reaction conditions, as well as the recycling of the ILs and the use of microwave will be discussed.

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ORG-PO-68 CONTROL OF RAPIDLY-ISOMERIZING ORGANOLITHIUMS BY USING MICROREACTOR TECHNOLOGY

Arianna Giovine[a], Aiichiro Nagaki[b], Jun-ichi Yoshida[b], Biagia Musio[a] and Renzo Luisi[a]

[a] Dipartimento Farmaco-Chimico, Università degli Studi di Bari
Consorzio Interuniversitario Nazionale C.I.N.M.P.I.S. , via Orabona 4, 70125, Bari, Italy
[b] Department of Synthetic Chemistry and Biological Chemistry

Graduate School of Engineering, Kyoto University, Nishikyo-ku Kyoto, Japan
giovinearianna@libero.it

The concept of flash chemistry[1], chemical synthesis in which extremely fast reactions are conducted in a highly controlled manner by using a flow microreactor system, has been successfully applied to various organic reactions including those producing undesired byproducts in subsequent reactions, highly exothermic reactions that are difficult to control, and reactions in which a reactive intermediate easily decomposes in conventional reactors.
It has been demonstrated that microreactors are particularly useful in organolithium-mediated synthesis allowing the generation of lithiated intermediates at higher temperatures and the control of stereolabile intermediates [2].
In this context we envisaged that the solvent-promoted racemization [3] and thermally induced isomerization of lateral-lithiated aziridines, recently investigated in our laboratory, could be a suitable system to be studied by using a flow microreactor system consisting of micromixers and microtube reactors (Figure 1).

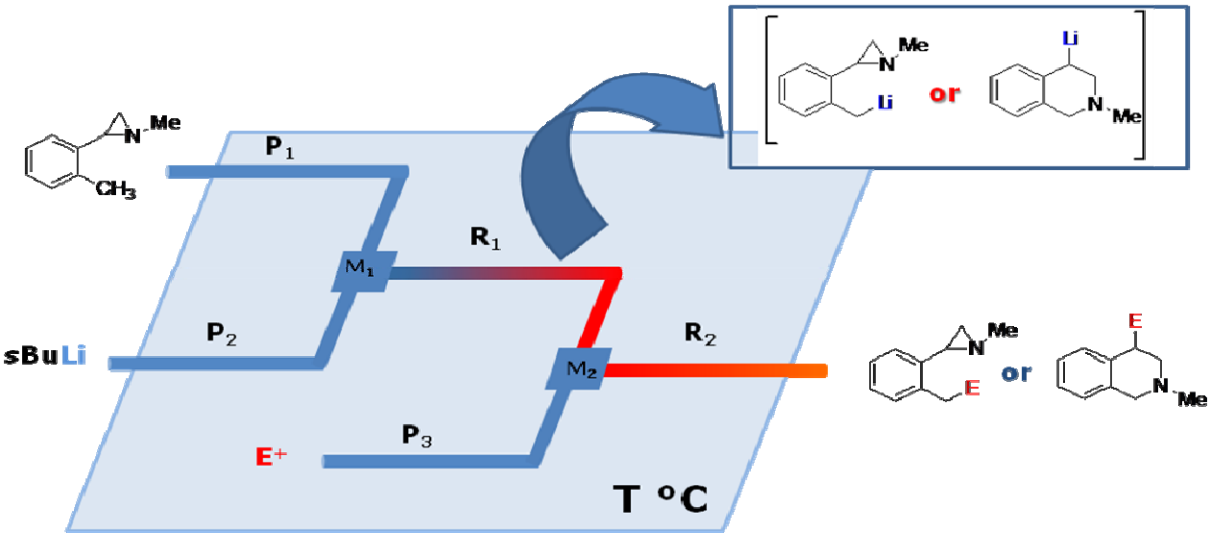

Figure 1

In this communication it will be reported that the exquisite control of the reaction parameters, realized into the microreactors, enabled us to set up the synthesis of either laterally functionalized aziridines or functionalized tetrahydroisoquinolines.

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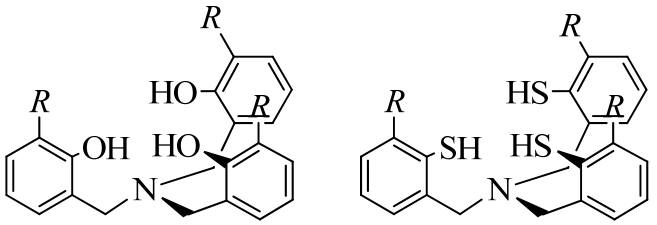
ORG-PO-69 Towards new ligands for metal complexation and catalysis

B. Gjoka, F. Romano, M. Mba, C. Zonta*, G. Licini*

Università di Padova, Dipartimento di Scienze Chimiche, Via Marzolo 1, 35131, Padova, Italy.
e-mail : *blerina.gjoka@studenti.unipd.it*

Recently, we developed an efficient synthesis of triphenolamine **1** [1]. They can form stable metal complexes with a wide variety of transition and main group elements [2] such as Ti(IV) [3], V(V) [4] and Mo(VI) [5] which achieved noteworthy catalytic properties in the oxidations of sulfides, secondary amines, halides and olefines. As an extension of our work, we examinated the use of their analougues *tri*-thiofenolamino systems. It is known that many metallo-enzymes contain molybdenum atom centers coordinated to sulfur atoms. Key step for the introduction of sulfur atom is the Newmann-Kwart rearrangement, which is a valuable synthetic technique to convert phenols in thiophenols. Herein we will report the synthetic strategy for the preparation of the new parent compound **2** and their coordination chemistry with transition metals such as molybdenum (Mo) or vanadium (V).



1 **2**

R = H, Me, Ph, *t*-Bu

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ORG-PO-70 Sali di imidazolio multistrato supportati covalentemente: attività catalitica per la produzione di carbonati ciclici in $scCO_2$ e nuovi supporti per catalizzatori di palladio

M. Gruttadauria,[a] F. Giacalone,[a] A.M.P. Salvo,[a] P. Agrigento,[a] L.F. Liotta,[b] V. La Parola,[b] C. Aprile,[c] P. P. Pescarmona,[d] R. Noto[a]

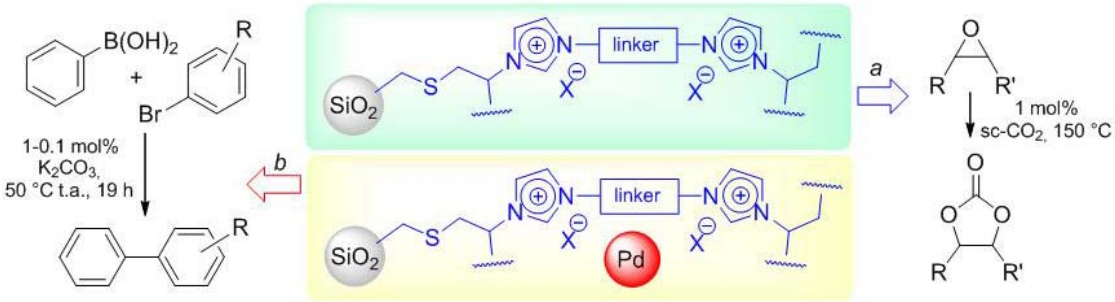
[a] (STEMBIO) Sez. Chimica Organica "E. Paternò", Università di Palermo, Viale delle Scienze, Ed. 17, 90128, Palermo, Italy.

[b] ISMN-CNR, Via Ugo la Malfa 153, 90146 Palermo, Italy.

[c] Département de Chimie, Unité de Chimie des Nanomatériaux (UCNANO), Facultés Universitaires Notre-Dame de la Paix, Rue de Bruxelles 61, B-5000 Namur, Belgium.
[d] Centre for Surface Chemistry and Catalysis, K.U. Leuven, Kasteelpark Arenberg 23, 3001 Heverlee, Belgium.
mgrutt@unipa.it

I liquidi ionici supportati (SILP) hanno trovato interessanti applicazioni sia nel campo delle reazioni catalizzate da metalli che in organocatalisi [1]. Inoltre, i SILP sono stati efficacemente impiegati in reazioni di apertura di epossidi in CO_2 supercritica per fornire carbonati ciclici [2]. I liquidi ionici vengono generalmente supportati covalentemente attraverso la modificazione dei gruppi funzionali presenti sulla superficie del supporto, conducendo in tal modo alla formazione di un monostrato di liquido ionico supportato. Gli esempi di SILP legati covalentemente, in maniera tale da ottenere dei multistrato, sono rari.

In questa comunicazione viene riportato un metodo per preparare dei sali di imidazolio supportati covalentemente e il loro impiego come: *a*) catalizzatori riciclabili per la reazione di epossidi con CO_2 supercritica per fornire carbonati ciclici, e *b*) supporti per nanoparticelle di palladio e l'impiego di tali materiali come catalizzatori riciclabili per la reazione di Suzuki in ambiente acquoso fra acidi boronici e bromuri arilici.



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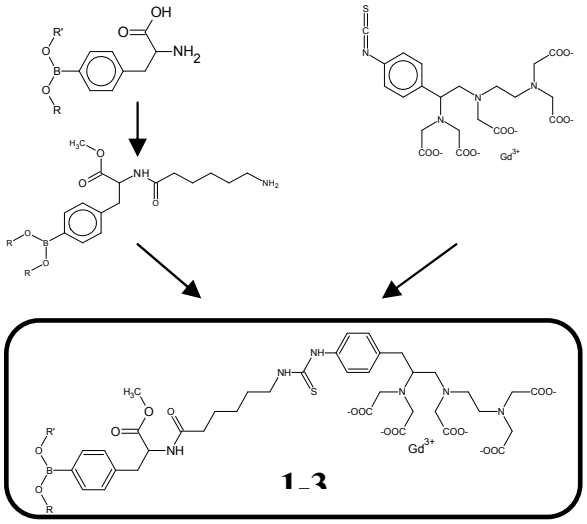
ORG-PO-71 SYNTHESIS OF MOLECULAR NANOMAGNETS USED IN THE BNCT FOR THE TREATMENT OF HEPATIC TUMOR

C. Guanci,[a] A. Porta,[a] M. Bonora,[b] F. Borsa,[b] M. Corti,[b] G. Zanoni,[a] G. Vidari[a]
[a]Dipartimento di Chimica dell' Università di Pavia, Via Taramelli 12, 27100, Pavia, Italy; [b]Dipartimento di Fisica "A. Volta" dell' Università di Pavia, Via Bassi 6, 27100, Pavia, Italy

e-mail: claudia.serenag@libero.it

Boron Neutron Capture Therapy (BNCT) is a binary therapy based on the property of the 10B isotope to capture neutrons and to produce energy through a nuclear reaction inside cells, inducing apoptosis. A bimetallic molecule enriched in 10B and including a Gd complex, useful for MRI study would permit to monitor the distribution of the compound in cancer affected tissues and, in this way, to better direct the neutron beam [1]. Subject of this communication is the short synthesis of novel compounds **1-3** consisting of three units: i) *p*-10borono-L-phenylalanine, which, being similar to the natural amino acid, would promote the preferential absorption of the compound in tumour cells [2]; ii) a linker derived from 6-amino-caproic acid, connecting the two bimetallic moieties through a thioureido linkage; iii) a Gd3+-DTPAcomplex. The entire molecules have readily been assembled.

1H and 10B NMR and MRI investigation of boron and gadolinium-boron compounds in boron neutron capture therapy.The synthesis and the magnetic properties of **1-3** will be discussed in this communication.



1 : R = H,
R' = H
2 : R = H,
R' = Me
3 : R = Me.

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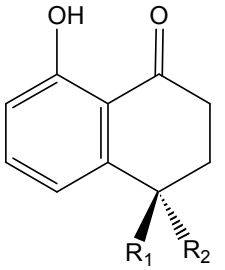
ORG-PO-72 Assignment of Absolute Configuration to Natural Phytotoxic Naphthalenone Pentaketides by Computational Analysis of Optical Rotation and ECD spectra.

Giuseppe Mazzeo[a], Alessio Cimmino[b], Laura Mugnai[c], Angel M. Villegas-Fernández[b], Anna Andolfi[d], Diego Rubiales[b], Antonio Evidente[d] and Stefano Superchi[a].

[a]Dipartimento di Chimica, Università della Basilicata, via Nazario Sauro 85,-85100 Potenza, Italy. [b]Institute for Sustainable Agriculture, CSIC, Apdo 4084,

14080 Cordoba, Spagna. [c] Dipartimento di Biotecnologie-Patologia Vegetale, Università di Firenze, Piazzale delle Cascine 28, 50144 Firenze, Italy. [d]Dipartimento di Scienze del Suolo, della Pianta, dell'Ambiente e delle Produzioni Animali, Università di Napoli Federico II, Via Università 100, 80055 Portici, Italy
e-mail: stefano.superchi@unibas.it

The computational simulation of optical rotation (OR) and electronic circular dichroism (ECD) is nowadays widely used for the assignment of the molecular absolute configuration (AC) of both synthetic and natural occurring chiral molecules This approach was herein employed to assign the absolute configuration of regiolone and isosclerone (**1**), two enantiomeric bioactive pentaketide napthalenones produced by fungi and plants and for which the configurational assignment was still matter of debate.



(-)-**1** (4*R*)-Regiolone R_1=OH, R_2=H
(+)-**1**(4*S*)-Isosclerone R_1=H, R_2=OH

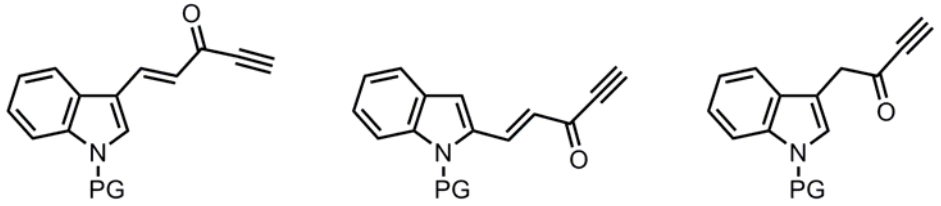
A DFT/B3LYP/TZVP conformational analysis was therefore carried out on (*S*)-**1** allowing to sort out four populated conformers within a 4 kcal mol^{-1} range. The ECD spectra and OR values were then calculated at TDDFT/CAM-B3LYP/TZVP level for each conformer and Boltzmann averaged over the conformers' population. The comparison of the experimental and theoretical OR's and ECD spectra allowed to unambiguously establish a (*R*)/(-) (*S*)/(+) relationship between absolute configuration and optical rotation of regiolone/isosclerone. The AC appear to be close related to the phytotoxicity.

ORG-PO-73 Synthesis of 3-substituted aroylindole compounds by cycloaddition of nitrosoarenes with conjugated alkynones

G. Ieronimo,[a] G Palmisano,[a] K. M. Nicholas,[b] A. Penoni[a]

[a] Dipartimento di Scienze Chimiche ed Ambientali, Università degli Studi dell'Insubria, 22100, Como – Italy; [b] Department of Chemistry and Biochemistry, University of Oklahoma, Norman, OK - USA 73019
gabriella.ieronimo@uninsubria.it

Many synthetic approaches were studied so far to achieve indolization procedures starting from different nitrogen containing precursors.[1] Our general interest in this topic lead us to disclose a novel and regioselective indole synthesis by annulation reaction between nitro- and nitrosoarenes with alkynes. Indoles, *N*-hydroxy- and *N*-alkoxyindoles were afforded in moderate to excellent yields and good regioselectivity.[2] This synthetic strategy was used to prepare natural products like meridianins, marine indole alkaloids known as kinase inhibitors.[3] Using conjugated alkynones as starting materials the reaction proceeded with the regioselective formation of 3-acylindoles and/or *N*-hydroxy-3-acylindoles.[4]



More recently and starting from conjugated alkynones with a preformed indole fragment we focused our attention on the preparation of bis-indole compounds as target molecules. This class of products can be furtherly used as starting material to achieve indolecarbazole derivatives and other complex molecules with biological activity.

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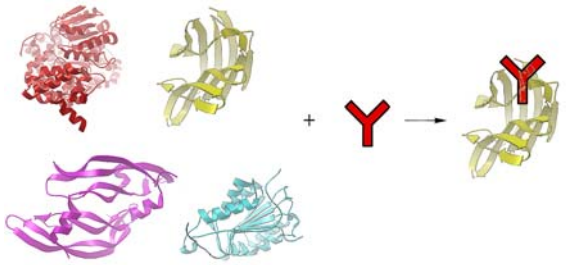
ORG-PO-74 Re-evaluation of the biological activity of natural compounds: the role of the Inverse Virtual Screening as a useful in silico tool.

Gianluigi Lauro, Milena Masullo, Angela Perrone, Sonia Piacente, Raffaele Riccio, Giuseppe Bifulco

Dipartimento di Scienze Farmaceutiche e Biomediche dell'Università di Salerno, Via Ponte Don Melillo, 84084, Fisciano (SA), Italy
glauro@unisa.it

A small library of natural compounds belonging to different chemical classes (flavonoids, cycloartanes, chalcones, xanthones, iridoids) and mainly known for their monoamine oxidase inhibitory effects [1-2], was screened on a panel of targets involved in the genesis and progression of cancer [3].
The re-investigation of their potential activity was achieved through the Inverse Virtual Screening approach [4-5] using the Autodock-Vina software [6]. The variability of the binding sites of the different targets, representing a fundamental parameter in the evaluation and comparison of the predicted binding energies, was overcomed applying a normalization of all the values [7].
Most of the results of the screening showed the selection of biological targets not explored for these classes of compounds until now. On the other hand, the interaction with an amineoxidase target was underlined, essentially confirming the robustness of the method. The subsequent biological tests could confirm the reliability of the Inverse Virtual Screening approach and its effective applicability for a re-evaluation of the activity of these compounds.



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ORG-PO-75 GUANIDINIUM-BASED CALIX[4]ARENES FOR GENE DELIVERY

Lomazzi Michela,[a] Bagnacani Valentina,[a] Sansone Francesco,[a] Donofrio Gaetano,[b] Casnati Alessandro,[a] Ungaro Rocco[a]

[a]Dipartimento di Chimica Organica e Industriale, Università degli Studi di Parma, Parco Area delle Scienze 17/a, 43124 Parma
[b]Dipartimento di Salute Animale, Università degli Studi di Parma, Via del Taglio 8, 43126 Parma, Italy

michela.lomazzi@gmail.com

The possibility to fight several diseases through gene therapy can find a significant improvement through the development of selective and efficient gene delivery systems [1].

In alternative to viruses, many classes of compounds are studied as non-viral vectors for cell transfection [2]. In general, although they are less efficient than viruses, they show low toxicity, low immunogenicity and can be rather easily modified in order to improve their biological properties.

In this context we have synthesized new vectors based on calix[4]arene scaffolds, functionalized with guanidinium moieties and lipophilic chains [3-5]. These macrocyclic compounds generate electrostatic interactions/hydrogen bonds with DNA, while hydrophobic interactions among calixarene skeleton lead to the formation of different types of aggregates, as Atomic Force Microscopy and spectroscopic studies show. We herein also report transfection and cytotoxicity studies on this new class of non-viral vectors [4,5].

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ORG-PO-76 Cyanuric chloride-catalyzed Beckmann rearrangement of ketoximes in biodegradabile ionic liquids

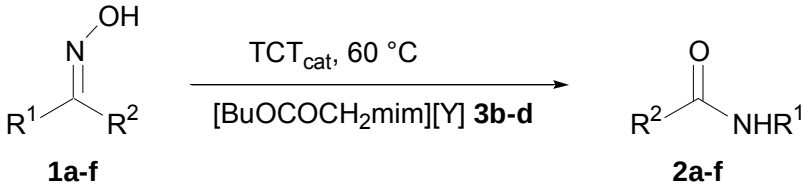
Angelamaria Maia,[a] Dario Landini,[b] Domenico Albanese.[b]

[a]Ist. di Scienze e Tecnologie Molecolari-CNR, Via Golgi 19, 20133 Milano, Italy
[b]Dip. di Chimica Organica e Industriale, Via Venezian 21, 20133 Milano, Italy
angelamaria.maia@istm.cnr.it

Biodegradable ionic liquids (ILs) represent a potential more ecosustainable alternative to traditional ILs that, due to their excellent stability and often water solubility, could determine a possible accumulation in the environment [1].

The incorporation of an ester group into the IL side chain is found to significantly improve the IL biodegradation since it provides a site for possible enzymatic cleavage [1]. However, the favourable biodegradability must be balanced by the required stability of the solvent and practical applicability. In particular, the presence of the ester moiety in the IL could represent a drawback in reactions performed under high basicity or acidity conditions.

We have proved that biodegrable imidazolium-based ILs of this type (**3b-d**) can be successfully utilized as the alternative to traditional ILs even in the Beckmann rearrangement that is known to require strongly acidic and dehydrating media[2]. The procedure is mild and suitable for both aromatic (**1a-e**) and aliphatic (**1f**) ketoximes affording the rearrangement products (**2a-f**) in good to quantitative yields. Our findings are of particular interest in view of a possible scale-up of this fundamental reaction. These ILs, in fact, are not only biodegradable but they can be recovered and reused several times.



1a-f **2a-f**

1,2a $R^1 = R^2 =$ Ph
1,2b R^1 = Ph, R^2 = Me
1,2c R^1 = 4-C_6H_4-OH, R^2 = Me
1,2d R^1 = 4-C_6H_4-Cl, R^2 = Me
1,2e R^1 = 2-C_6H_4-OMe, R^2 = Me
1,2f $R^1 – R^2 = (CH_2)_{11}$

3b, Y = ClO_4^-
3c, Y = BF_4^-
3d, Y = PF_6^-

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ORG-PO-77 New Mesoporous Materials for a Controlled Progesterone Release

Lucia Veltri[a], Bartolo Gabriele[b], Giuseppe Salerno[a], Luigi Pasqua[c], Flaviano Testa[c]

[a] Dipartimento di Chimica, [b] Dipartimento di Scienze Farmaceutiche, and [c] Dipartimento di Ingegneria Chimica e dei Materiali Università della Calabria, 87036 Arcavacata di Rende (CS)

lucia.veltri@unical.it

We have synthesized two novel mesoporous materials in order to design a drug delivery system able to increase the oral bioavailability of drugs. In particular, we have functionalized SBA-15 silica with β-cyclodextrin residues by two different synthetic approaches, leading to the materials **SC1** and **SC2** (Figure 1).

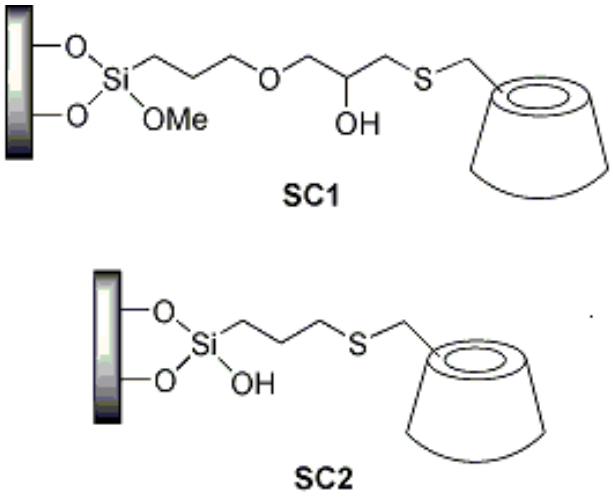

Figure 1

Progesterone was selected as model drug and loaded into both **SC1** and **SC2**. The materials before and after progesterone loading were characterized by TGA, N-2 sorption analysis and small angle X-ray diffraction (XRD). The results showed that the **SC2** material had a better capacity for loading progesterone and retained the drug more efficiently: the release after 2 h in acidic media (at pH = 1, as in the stomach) was only 30%, and reached 99% after 12 h at pH = 6.8 (pH in the intestine). This results show that **SC2** is a good candidate for a controlled delivery of progesterone *in vivo*.

ORG-PO-78 Dynamic High-Performance Liquid Chromatography of Chiral Stereolabile Compounds: the conformational stereoisomers of Tri-O-thymotide.

Rocchina Sabia, Marco Pierini, Stefano Levi Mortera, Francesco Gasparrini, Claudio Villani

Università degli Studi di Roma "La Sapienza", P.le A. Moro 5, 00185 Roma - Italy
claudio.villani@uniroma1.it

Dynamic high performance liquid chromatography on enantioselective stationary phases is a well-established technique to investigate chiral molecules with labile stereogenic elements that result in stereoinversion processes occuring on the time scale of the separation process. Kinetic parameters for on-column interconversions can be extracted from exchange-deformed experimental peak profiles by computer simulation. The technique has been used in a wide range of temperatures and is complementary in scope to dynamic nuclear magnetic resonance spectroscopy.[1-3]

Here we report the first HPLC resolution of the conformational enantiomers of tri-O-thymotide (TOT), a macrocyclic trilactone existing in fast-exchanging multiple chiral conformations.[4] Variable chromatography on brush type chiral stationary phases showed dynamic features due to on-column interconversions in the temperature range between 25 and -15 °C. These features are consistent with the known energy barrier measured by NMR for the major, propeller shaped conformational enantiomers of TOT. Cryo-HPLC at column temperature as low as -80 °C allowed us to resolve the enantiomers of the minor, helix shaped conformational enantiomers of TOT.

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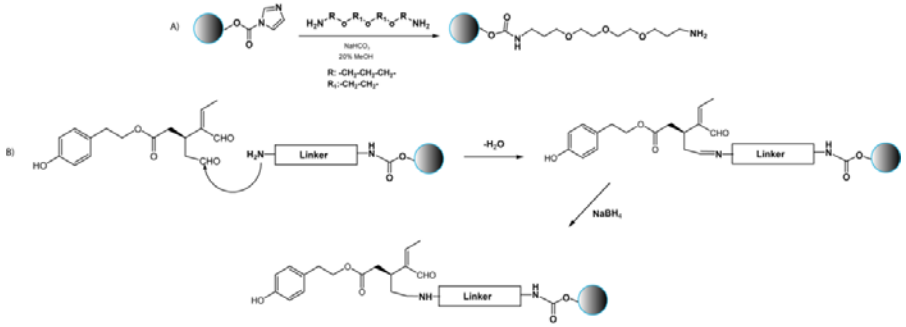
ORG-PO-79 Towards the Identification of Oleocanthal Cellular Interactome by Chemical Proteomics

Luigi Margarucci, Maria Chiara Monti, Alessandra Tosco, Raffaele Riccio and Agostino Casapullo

Dipartimento di Scienze Farmaceutiche e Biomediche, Università degli Studi di Salerno, Via Ponte don Melillo, 84084, Fisciano, Italy
E-mail: lmargarucci@gmail.com

Oleocanthal (OLC), the dialdehydic form of (-) deacetoxy-ligstroside aglycon responsible for the bitter taste of olive oil, has been recently supposed to interfere within important pathways of relevant human diseases, such as inflammation[1] and Alzheimer (AD)[2]. Otherwise, OLC exact mechanism of action at cellular level still remain unknown. In recent years, mass-spectrometry-based chemical proteomics has been applied to the macromolecular target discovery under physiological condition[3]. The procedure usually requires three steps, beginning with the chemical modifications of the matrix beads with a spacer bound to the molecule of interest, followed by the isolation of the potential targets, through affinity chromatography of the crude cell extract and SDS-PAGE of the eluting proteins, and the identification by MS of the interacting target (s) . The last step is the pharmacological evaluation of the compound by *in vitro* and/or *in vivo* based assays[4].



Here we report the investigation of the interactome of OLC through the application of the above mentioned chemical proteomics based experiment. These experiments combined with an opportune in vitro/in vivo assays allowed us to enlarge our knowledge on the therapeutic properties of OLC.

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ORG-PO-80 Advanced oxidation of binary mixtures of volatile organic compounds induced by air atmospheric plasma

Ester Marotta, Milko Schiorlin, Cristina Paradisi
Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova, Italy
ester.marotta@unipd.it

Advanced oxidation of volatile organic compounds (VOCs) induced by atmospheric plasma is developing as a powerful means for air purification. In such plasmas, which are conveniently produced by corona discharges in air at room temperature and atmospheric pressure, the oxidative decomposition of VOCs is promoted by reactions with the species produced by ionization, excitation and dissociation of air and water molecules (mainly $^{\bullet}OH$, O_3, H_3O^+, $O_2^{+\bullet}$, NO^+, $O_2^{-\bullet}$). Despite some well-established technological implementations, fundamental knowledge of the underlying chemical processes is still limited and the majority of studies so far have involved simplified models of contaminated air consisting of a single VOC in a synthetic mixture of N_2 and O_2 [1].

The aim of our research is to characterize the reactions and the mechanisms underlying VOCs decay in these systems [2]. Particular attention is given to the ions produced within the plasma and to their reactions, which are generally neglected in the literature in favour of radical decomposition routes. Furthermore, in a step towards a more realistic air model, we have recently undertaken the study of mixtures of two different VOCs to investigate on possible competition and entrainment effects. The experiments are performed with a large flow reactor, in which corona discharges can be produced by the application of dc or pulsed voltage. Chemical diagnostics includes on-line analysis with FT-IR and GC coupled with different detectors. Additional experiments are conducted with an APCI (Atmospheric Pressure Chemical Ionization) mass spectrometer in which the introduction system has been suitably modified to introduce gaseous and volatile compounds diluted in air. This is the ideal system to monitor the ions produced by corona discharge in air. In the case of air containing a single VOC the ionic species are generally formed by ion/molecule reactions of the VOC with the background ions coming from air; in the case of binary mixtures of VOCs additional ionic species can be observed coming from reactions between ions formed from one of the VOCs with molecules of the second one.

The results from this integrated approach obtained with various binary mixtures of CCl_2=CCl_2, CCl_4, C_6H_{14} and CH_3OH will be presented and discussed with regard to the process efficiency and mechanism.

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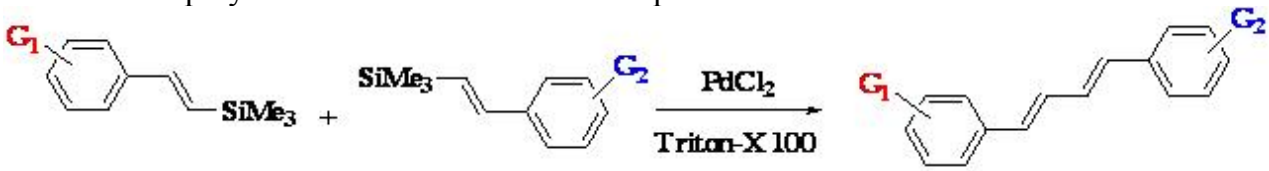
ORG-PO-81 Stereoselective "One-Pot" Procedure for the Synthesis of Unsymmetrically 1, 4-Disubtituted 1, 3-Butadienes in water

C. Martinelli [1], S. R. Cicco[1], G. M. Farinola[2], R. Rubino [2], F. Naso[2]
[1] CNR ICCOM, Dipartimento di Chimica, Università degli Studi di Bari, I-70126
[2]Dipartimento di Chimica, Università degli Studi di Bari, via Orabona, 4 I-70126
martinelli.carmela@chimica.uniba.it

Stereodefined conjugated polyenes and aryl polyenes constitute a common structural motif in natural products and useful building blocks in organic synthesis. In recent years, polyenes containing electron-releasing and electron-withdrawing substituents within one molecule (push-pull polyenes) have attracted considerable attention due to their interesting photophysical and photochemical properties and their use as models for quantum-chemical calculations and simulations. For these reasons, a great deal of research works were devoted to the development of efficient and stereoselective methodologies to synthesize diene skeleton with different end groups. The conventional approach to the synthesis of dienic system involves the palladium catalyzed cross-coupling reactions of alkenylmetals with haloalkenes or olefin coss-metathesis reactions. In particular, a plethora of synthetic methods employing a large number of organometallic reagents, such as indium, rhodium and nickel have been developed for the preparation of symmetrical and unsymmetrical 1,3-dienes. Very recently, unsymmetrical 1,4-disubstituted 1,3-butadienes were prepared by silicon-based cross-coupling reactions and by Stille/Suzuki-Miyaura coupling sequences [1] by using a bis-metallo 1,3-butadiene. This approach allows to design and easily realize more complex butadienic systems. As a part of our research efforts in the development of efficient synthetic strategies for obtaining organic materials for photonics and electronics, we have recently reported a palladium-catalyzed homocoupling reaction of unsaturated silanes in micellar conditions for the synthesis of symmetrically α-ω disubstituted stereodefined all *trans* dienes in mild conditions and in good yields [2]. The use of water as reaction solvent in combination with surfactant has emerged as an important tool in the formation of carbon-carbon bond by organometallic methodologies. As a further extension of our "*green*" methodology, we examined the application of the palladium-catalyzed dimerization reaction of unsaturated silanes to the synthesis of unsymmetrically 1,4-disubstituted 1,3-butadienes in mild conditions and in water as the only solvent. In this connection herein, we report the first example of a "one-pot" palladium-catalyzed cross coupling reaction (Scheme 1) as an efficient methodology to obtain unsymmetrically disubstituted polyenes in water and at room temperature.



G_1 (electron-withdrawing groups) : NO_2- , PhCO- , F-
G_2 (electron-donating groups) : MeO- , $(Me)_2$ N- , MeS-

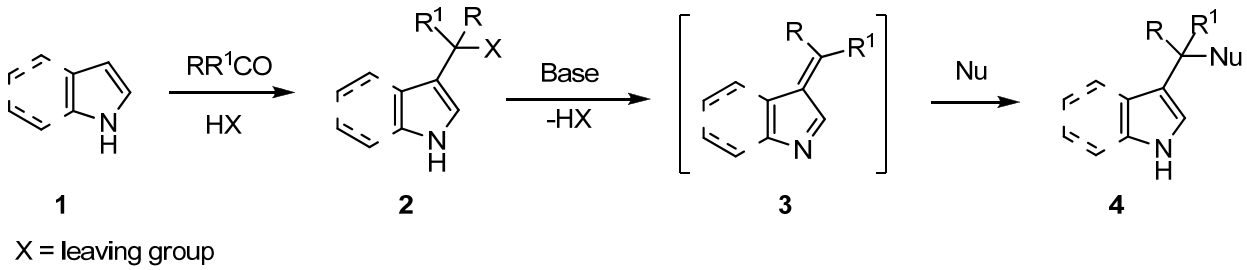
Scheme 1

[1] R. S.Coleman, M. C. Walczak *Org. Lett*. **2005**, *7*, 11;
[2] S. R. Cicco, G. M. Farinola, C. Martinelli, F. Naso, M. Tiecco *Eur. J. Org. Chem*. **2010**, 2235.

ORG-PO-82 3-Alkylidene Intermediates in the Synthesis of Functionalized Nitrogen Containing Heterocyclic Compounds.

Fabio Martinelli, Alessandro Palmieri and Marino Petrini
School of Science and Technology, Chemistry Division, Università di Camerino, via S.Agostino, 1, 62032, Camerino (MC) – Italy.
alessandro.palmieri@unicam.it

Functionalization of azoles at 3-position is commonly attained exploiting a Friedel-Crafts (F-C) reaction using electron-poor alkenes and acid promoters. Some limitations inherent to the F-C process can be easily surmounted using a strategy involving alkylidene intermediates **3** which actually act as vinylogous imino derivatives and can be made to react with a wide range of nucleophilic reagents [1].



1 **2** **3** **4**

Recently, we have introduced 3-(1-arylsulfonylalkyl) azoles **2** (X=SO_2Ar) as readily available precursors for reactive intermediate **3**. Reactants **2** are readily obtained by three components, coupling azoles **1** with aldehydes and arenesulfinic acids. Elimination of the arylsulfinic group can be carried out under basic or acid conditions allowing the reaction of the electrophilic intermediate with a wide array of nucleophilic reagents. Organometallics, stabilized carbon nucleophiles, heteronucleophiles can be made to react with compounds **2**.

The nature of the azole substrate **1** amenable for this process ranges from traditional functionalized indoles to indazoles. Pyrroles can be also profitably used in this strategy accounting that for a proper regioselectivity control at C3, a suitable directing group must be inserted on nitrogen. The reaction conditions studied for this transformation allow the utilization of homogeneous as well as heterogeneous promoters. Solid bases such as KF on basic alumina have been proved particularly effective in many processes using stabilized carbanions [2]. The mild reaction conditions required for the activation of these sulfonyl azoles also enabled their utilization in asymmetric synthesis [3].

[1] A.Palmieri, M.Petrini and R.R.Shaikh, *Org.Biomol.Chem.* **2010**,*8*, 1259.
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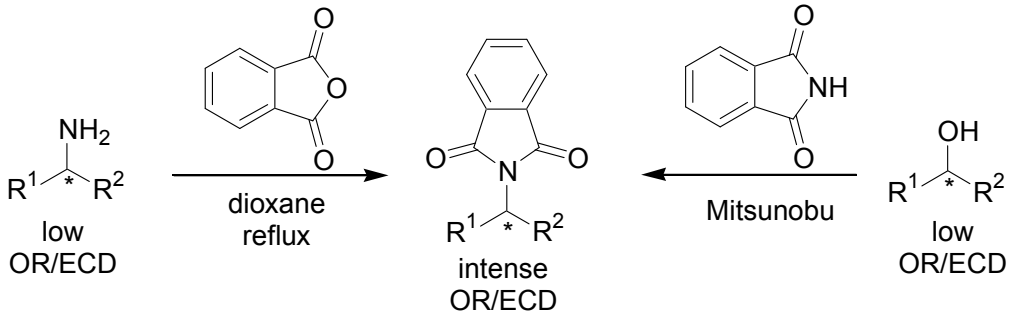
ORG-PO-83 Assignment of absolute configuration to aliphatic amines and alcohols by enhancement of their chiroptical properties and computational prediction of ECD spectra.

Giuseppe Mazzeo, Daniele Padula, Ernesto Santoro, Carlo Rosini, and Stefano Superchi.

Dipartimento di Chimica “Antonio. M. Tamburro”, Università della Basilicata, via Nazario Sauro 85; 85100 Potenza, Italy.
e-mail: gi.mazzeo@tiscali.it

The computational simulation of optical rotation (OR) and electronic circular dichroism (ECD) is nowadays widely used for the assignment of the molecular absolute configuration (AC). However, some problems still remain in the treatment of transparent chiral molecules such as aliphatic amines and alcohols. Such compounds, lacking of typical UV-vis chromophores, display small ORs and/or weak ECD signals, making unreliable any computational simulation. In this communication we will show how this problem can be solved by transforming amines and α-aminoacids in the corresponding chromophoric *N*-substituted phtalimides [1]. These derivatives show much higher chiroptical properties, making then possible an AC assignment by a computational treatment. The same transformation into *N*-substituted phtalimides can be also obtained from chiral alcohols through Mitsunobu reaction with phthalimide, thus allowing to achieve an enhancement of the chiroptical response also with these substrates.



Experimental chiroptical properties (OR, ORD, and ECD) of *N*-phtalimides were then compared with the calculated ones at the TDDFT/B3LYP/6-31G* level of theory, thus arriving at a reliable AC assignment for chiral amines, aminoacids, and alcohols.

[1] F. Kazmierczak, K. Gawronska, U. Rychlewska, J. Gawronski, *Tetrahedron: Asymmetry*, **1994**, *5*, 527.

ORG-PO-84 Synthesis of isoxazolidinyl-bisphosphonates with potential biological activity

A. Melicchio,[a] O. Bortolini,[b] A. De Nino,[a] L. Maiuolo,[a] I. Mulani,[a] B. Russo[a]

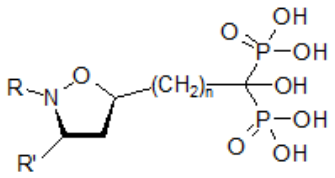
[a]Dipartimento di Chimica, Università della Calabria, Via Bucci 12 C, 87036, Rende (CS) Italy

[b]Dipartimento di Chimica, Università di Ferrara, Via Borsari 46, 44100, Ferrara (FE) Italy
alessandro.melicchio@unical.it

In the last years the development of organophosphoric chemistry has been characterized by a great interest on bisphosphonates and bisphosphonic acids. The significant pharmacological properties of these compounds make them of great interest: they showed a considerable cytotoxic activity against several human cell lines and therefore they could be successfully employed as anticancer drugs [1]. Moreover, these compounds are actually in use for the treatment of many bone diseases, such as Paget's disease, myeloma, bone metastases and osteoporosis [2].

Bisphosphonates can be considered as stable analogues of pyrophosphate (P-O-P), that is implied in the physiological regulation of bone calcification and resorption. Recently several analogues of these molecules have been synthesised in the last years [3].

In this communication we describe the synthesis of isoxazolidines by 1,3-dipolar cycloaddition reactions between suitable nitrones and substituted vinyles, by microwaves irradiation. The cycloadducts obtained, after appropriate functionalization, were converted in their correspondent bisphosphonic derivatives. As well as in the zoledronate, these compounds present an oxydrilic group, which increases the affinity for calcium even further owing to the ability of such derivatives to acts as tridentate ligands. They also have a different alkyl chain length on which is anchored a bisphosphonic group, that could modulate the potency of inhibition of bone resorption.



R= Bn- R'= *o*-Cl-C_6H_4-, *o*-F-C_6H_4-, C_6H_5- n= 0, 1, 2

R= Me- R'= C_6H_5- n= 0

[1] V.Stresing, F.Daubiené, I.Benzaid, H.Monkkonen, P.Clézardin, *Cancer Letters, 257*, **2007**, 16-35.

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(b) H.Fleisch, *Ann. Med*., *29*, **1997**, 55-62.
L.Widler, K.A.Jaeggi, M.Glatt, K.Muller, R.Bachmann, M.Bisping, A.Born, R.Coretesi, G.Guiglia, H.Jeker, R.Klein, U.Ramseier, J.Schmid, G.Schreiber, Y.Seltenmeyer and J.R.Green, *J. Med. Chem., 45*, **2002**, 3721.

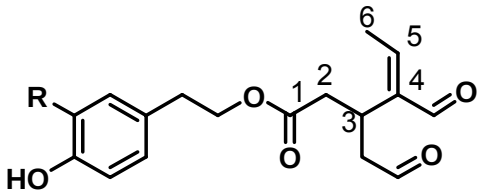
ORG-PO-85 Anti-inflammatory effect of oleopentanedialdheydes on primary human vascular endothelial cells

M. Nardi,[a] A. Caruso,[c] S. Fiorentini.[c] A. Cozza,[c] A. Procopio,[b] G. Sindona [a]

[a]Department of Chemistry University of Calabria Ponte Bucci, cubo 12C, 87036 Arcavacata di Rende (CS) Italy ,
[b]Department of Pharmacobiology University of Magna Græcia, Complesso Ninì Barbieri, 88021 Roccelletta di Borgia (CZ), Italy.
[c]Department of Applied and Experimental Medicine, Section of Microbiology University of Brescia Piazzale Spedali Civili, 1, 25123 Brescia, Italy
nardi@unical.it

Olive oil represents a typical lipid source of the Mediterranean diet, whose intake has been associated with a low incidence of cardiovascular diseases, mostly due to the presence of several phenolic compounds which have anti-oxidant and anti-inflammatory properties. In this work we showed that *oleopentadial* (**1**) [2-(3,4-hydroxyphenyl)ethyl(3S,4E)-4-formyl-3-(2-oxoethyl)hex-4-enoate], a minor component of virgin olive oil, displays potent anti-inflammatory properties and anti-endothelial activation properties.

The molecule corresponds to the hydroxylated form of a dialdehyde, named *oleocanthal* (2), present in minor amounts in olive oil, [1] whose anti-inflammatory properties have been recently disclosed.[2].



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

The easy access to the molecule prompted [3] us to investigated the anti-inflammatory effect of oleopentanedial in a cell model we developed to mimic inflammatory injury of endothelium. This was based on the production of the proinflammatory chemokine MCP-1, following in vitro stimulation of primary human endothelial cells. Pre-treatment of cells with oleopentanedial resulted in a dose-dependent inhibition of MCP-1 secretion. The effect of oleopentanedial on MCP-1 expression was observed at the transcriptional level. Functional data have shown that OLPD diminished monocyte adhesion to HUVECs. These results point on the use of oleopentanedial as a novel drug aimed to prevent or reduce inflammation of endothelium.

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ORG-PO-86 Dimensional encapsulation of halogen-bonded supramolecular anions in non porous onium salts.

Pierangelo Metrangolo,[a,b] Lorenzo Meazza,[b] Javier Martí-Rujas,[b] Luca Colombo,[a] Tullio Pilati,[a] Giuseppe Resnati,[a,b] Giancarlo Terraneo [a,b]

[a] NFMLab- Department of Chemistry, Materials and Chemical Engineering, ‘‘Giulio Natta’’, Politecnico di Milano, Via L. Mancinelli 7, 20131 Milan, Italy.
[b] CNST-IIT@POLIMI, Via Pascoli 70/3, 20133 Milan, Italy.
E-mail:pierangelo.metrangolo@polimi.it

Halogen bonding, namely any noncovalent interaction involving the positive region of the electrostatic potential surface of halogen atoms [1], has increasingly facilitated the assembly of diverse host-guest molecules. In this contribution, we show that a well-known class of organic salts, bis(trimethylammonium) alkane diiodides, can be applied to different fields and for different purposes as intrinsically non-porous materials showing very selective separation behaviour.
Firstly, we present how bis(trimethylammonium) alkane diiodides can reversibly encapsulate □□□-diiodoperfluoroalkanes and I_2 through intermolecular interactions between the host’s I^- anions and the guest’s terminal iodine substituents. The process is highly selective and forms an $I^-\cdots GUEST\cdots I^-$ superanion that is matched in length to the chosen dication [2,3]. We will also report that using hexamethonium iodide and bromide we were able to isolate various trihalides and mixed trihalides such as Br_3^-, I_2Cl^- and Br_2Cl^- from solution and the gas phase with high selectivity and reversibility [4]. (Figure 1)

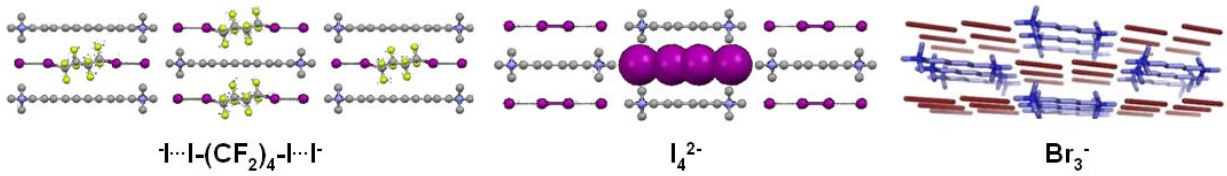

Figure 1: Crystal packing of the complex between organic onium salts and guest molecules

[1] An IUPAC Task Group set up to examine the definition of halogen bonding has not yet reported, so that given here should be taken as temporary (see www.iupac.org/web/ins/2009-032-1-100 and www.halogenbonding.eu).
[2] P.Metrangolo, Y. Carcenac; M.Lahtinen, T.Pilati, K.Rissanen, A.Vij, G.Resnati *Science* **2009**, *323*, 1461.
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ORG-PO-87 Synthesis of isoxazolidine-substituted bisphosphonates by 1,3-dipolar cycloaddition reactions

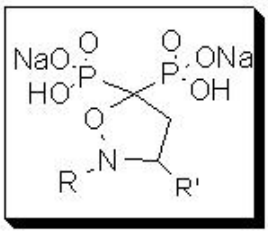
I. Mulani,[a] O. Bortolini,[b] A. De Nino,[a] L. Maiuolo,[a] A. Melicchio, [a] B. Russo[a]

[a]Dipartimento di Chimica, Università della Calabria, Via Bucci 12 C, 87036, Rende (CS) Italy.
[b]Dipartimento di Chimica, Università di Ferrara, Via Borsari 46, 44100, Ferrara (FE) Italy.
iqbal.mulani@unical.it

Geminal bisphosphonates (BPs) are structural and stable analogues of naturally occurring pyrophosphates, and an involved in the treatment of several skeletal problems associated to low bone density and osteogenesis imperfect. Further more, effecting on diseases as osteoporosis, Paget's disease and tumor bone diseases [1]. The studies on the inhibitory potency of cyclic nitrogen-containing bisphosphonates indicate that the presence of two geminal phosphonate groups is responsible for interaction with the molecular target [2].

We have developed an efficient method for the preparation of substituted isoxazolidines by 1,3-dipolar cycloaddition with dipolarophile and suitable nitrone, under microwave irradiation, in the absence of solvent [3].

In this communication we describe an efficient and general synthetic approach to bisphosphonates bearing in geminal position a substituted isoxazolidine ring. In fact we investigated the 1,3-dipolar cycloadditions of nitrones with tetraethylvinylidene-1,1-biphosphonate by MW irradiation, obtaining a set of isoxazolidine-substituted bisphosphonates.



R = Me R' = Ph, *o*-Cl-C_6H_4, 3- pyridyl, 2-furyl

R = Bn R' = Ph, *p*-OH-C_6H_4, *o*-Cl-C_6H_4, *o*-F-C_6H_4

Studies on the biological potential and comparison with the bisphosphonates of well established activity are currently under way.

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ORG-PO-88 Synthesis of S-acetyl molecular semiconductors for self-assembling processes

Alessandra Operamolla,[a] Omar Hassan Omar,[b] Roberta Ragni, [a] Francesco Babudri, [a] Gianluca M. Farinola [a]

[a] Dipartimento di Chimica, Università degli Studi di Bari "Aldo Moro", via Orabona 4, I-70126 Bari
[b] Istituto di Chimica dei Composti Organometallici CNR-ICCOM, Dipartimento di Chimica, via Orabona 4, I-70126 Bari
a.operamolla@chimica.uniba.it

The functionalization with the thiol group is widely adopted to produce individual molecules with the ability to chemically bind to noble metals or to a number of inorganic materials. This approach is extensively used to fabricate monolayer thin films on metal surfaces (SAMs) or on inorganic nanoparticles or metal-molecule-metal junctions [1]. These assemblies are useful for the study and conprehension of the electronic properties of ordered nanometric aggregates.
In this communication, we wish to present our recent research dealing with the synthesis of conjugated molecules functionalized with pending thiol groups. We recently synthesized a new family of S-acetyl oligoarylenedithiols characterized by a chelating disposition of the two thiol functionalities on the head ring and the presence of terminal substituents exerting different electron effect [2]. In parallel studies, these ligands demonstrated their ability to chemically bind to gold crystalline surfaces *via* both sulfur atoms and adopting a perpendicular disposition of the aromatic backbone with respect to the gold surface [3]. We later synthesized the corresponding tetrathiol molecular wires, having the base structure of oligo(*p*-aryleneethynylene)s (OAEs), that were obtained *via* palladium catalyzed convergent Sonogashira route [4]. The oligomers present interesting emissive properties, and processes of polymerization of these materials are presently under investigation.

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ORG-PO-89 Synthesis of novel derivatives of Resveratrol and screening for potential cancer chemopreventive activities

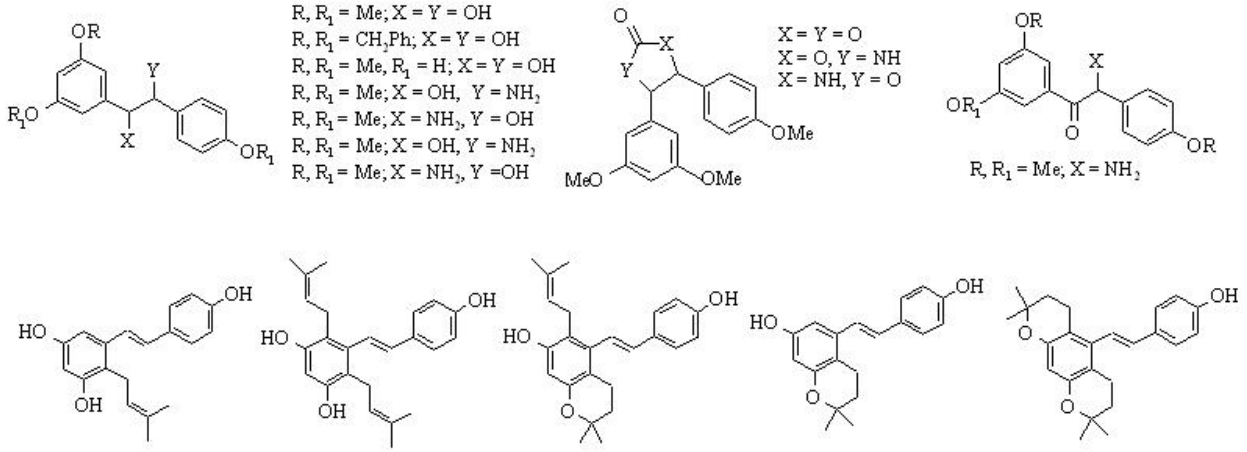
F. Orsini [a], L.Verotta[a], R. Pagliarin[a], C. Gerhauser[b], K. Klimo[b]
[a] Dipartimento di Chimica Organica e Industriale, via Venezian 21, 20133 Milano,

Italy
[b] German Cancer Research Center, 69120 Heidelberg, Germany
e-mail: fulvia.orsini@unimi.it

Resveratrol (*trans*-3,4',5-trihydroxystilbene) has attracted the attention of the biomedical researchers because of its beneficial physiological effects it produces. Positive effects of resveratrol has been observed in the field of cardiovascular diseases[1] and neurodegenerative disorders.[2] It has been also identified as a potent cancer chemopreventive agent in assays representing the three major stages of carcinogenesis (i.e. tumor initiation, promotion and progression).

We have synthesized a variety of Resveratrol analogues by chemical modification of the parent trihydroxy stilbene skeleton (Figure 1). The compounds were screened for cancer chemopreventive potential using a series of bioassays relevant for the prevention of carcinogenesis in humans (inhibition of cytochrome P450 1A; determination of NAD(P)H:quinone reductase activity; scavenging of radicals; inhibition of cyclooxygenase activity; inhibition of NO synthase; antiestrogenic and estrogenic activity).[3]

Figure 1.



Acknowledgment. MIUR e Universita' degli Studi di Milano (PRIN 2007 – 2007K29W5J)

[1] G. Petrovski, N. Gurusamy, and D. K. Das, *Ann. N. Y. Acad. Sci.,* 1215, **2011**, 23.
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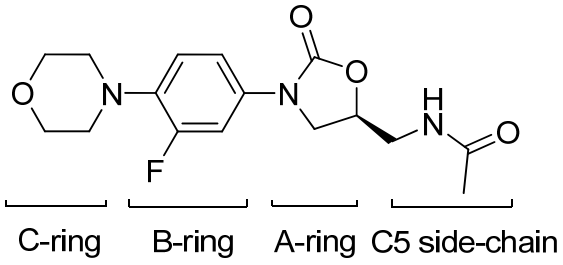
ORG-PO-90 Synthesis and Biological Evaluation of 1,2,4-Oxadiazole Analogues of Linezolid

Andrea Pace,[a] Rosario Musumeci,[b] Cosimo Gianluca Fortuna[c]

[a] Dipartimento di Scienze e Tecnologie Molecolari e Biomolecolari – Sez. Chimica Organica "E. Paternò" – Università degli Studi di Palermo, Viale delle Scienze, Ed. 17, 90128 Palermo, Italy
[b] Dipartimento di Medicina Clinica e Prevenzione, Università di Milano-Bicocca - Edificio U8 - Via Cadore 48, 20052 Monza (MB), Italy.
[c] Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria,6 95125 Catania
pace@unipa.it

1,2,4-Oxadiazoles are known bioactive heterocycles whose activity has been often associated to their bioisosterism with amide or ester functionalities [1]. As preliminary results of a research project on the molecular design of heterocycle-based antibacterials to contrast Multi-Drug Resistance (MDR)[2], we report the synthesis and the biological evaluation of a series of Linezolid (see Figure) analogues, where a 1,2,4-oxadiazole moiety has been introduced to replace either the oxazolidinone heterocyclic core (A-Ring) or the morpholine moiety (C-Ring).



Linezolid **1**

[1] A. Pace, and P. Pierro, *Org. Biomol. Chem., 7,* **2009**, 4337.
[2] Financial support from Italian MIUR within the "FIRB-Futuro in Ricerca 2008" Program - Project **RBFR08A9V1 –** CUP: **B71J10000120001** is gratefully acknowledged.

ORG-PO-91 Synthesis of New Fluorinated Low Molecular Weight (LMW) Gelators.

Antonio Palumbo Piccionello, Annalisa Guarcello, Andrea Pace, Ivana Pibiri, Silvestre Buscemi.

Dipartimento di Scienze e Tecnologie Molecolari e Biomolecolari- Sez. Chimica Organica "E. Paternò", Università di Palermo, Viale delle Scienze – Parco d'Orleans II, I-90128 Palermo.
E-mail: apalumbo@unipa.it

Gel formation represents an attractive research area due to the unique properties of this type of soft materials which present many applications in the biomedical field [1]. In this field low molecular weight (LMW) gelators essentially form physical gels in which the molecules are self-assembled into three-dimensional structures, held together by non-covalent interactions [1]. The tendency to self-assemble of fluorinated systems has been also used in order to promote hydrogel formation from various polymers, while only few examples of fluorinated LMW hydrogelators have been reported [2].
In this communication we present a new family of fluorinated 1,2,4-oxadiazoles as Low Molecular Weight (LMW) gelators. These compounds are able to form thermal- and pH-sensitive "smart-hydogels" with a lamellar supramolecular assembly (Fig. 1) and *organogel*s in DMSO with a fibrillar network.

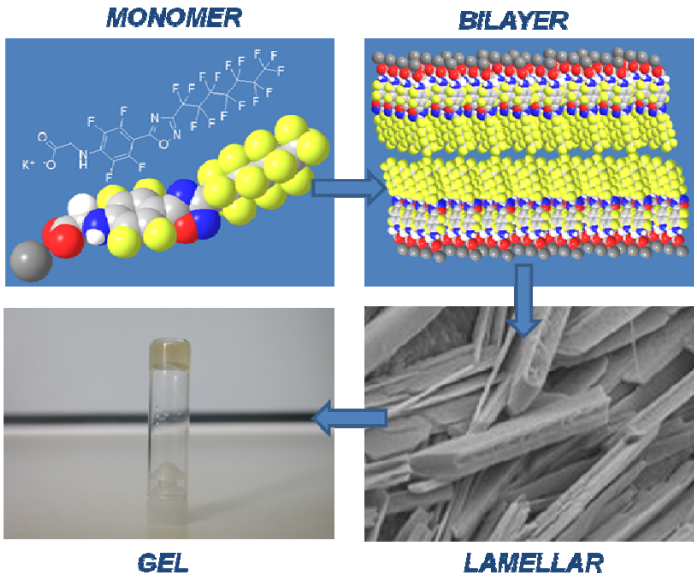


Figure 1.

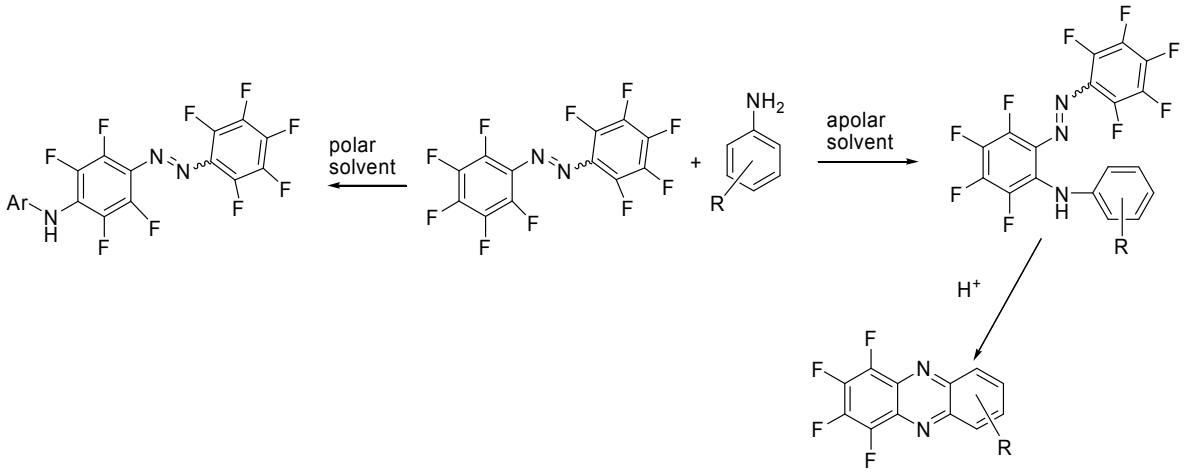
[1] a) L.A. Estroff, and A.D. Hamilton, *Chem. Rev., 104*, **2004**, 1201. b) M. de Loos, B.L. Feringa, and J.H. van Esch, *Eur. J. Org. Chem.,* **2005**, 3615.
[2] see for example: a) A. Palumbo Piccionello, A. Pace, S. Buscemi, N. Vivona, and G. Giorgi, *Tetrahedron Lett., 50*, **2009**, 1472. b) S. Buscemi, G. Lazzara, S. Milioto, and A. Palumbo Piccionello, *Langmuir, 25*, **2009**, 13368.

ORG-PO-92 Reactivity of decafluoroazobenzene towards aromatic amines: a new entry to tetrafluorophenazines.

Antonio Papagni[1], Massimo Moret,[1] Luciano Miozzo[1], Ramona Gironda[1], Matteo Parravicini[1], Stefano Bergantin[1], Francesca Bettinelli[1] and Andrea Burini[1]

[1]Dipartimento di Scienza dei Materiali, Università di Milano Bicocca, Via Cozzi 53, 20125 Milano.
antonio.papagni@unimib.it

In the last decade the interest for fluorinated aromatic molecules for applications in materials science experienced a huge growth. Indeed, fluorinated aromatic molecules are potential n-type semiconductors, with applications in electroluminescent devices (OLED), transistor, photovoltaic cells and other optoelectronic devices. Our research activities are focused on the synthesis of fluorinated heteroaromatic molecules, with potential application as n-type semiconductors.[1] Recently, we have reported the synthesis of 1,2,3,4-tetrafluoro-acridines and octafluoroacridones starting from decafluorobenzophenone and aromatitic amines.[2] As an extension of this work, here we report on the reactivity of decafluoroazobenzene (prepared by oxidation of pentafluoraniline with lead tetraacetae) towards aromatic nucleophilic substitution with aromatic amines. It was observed that the polarity of reaction medium plays an important role on *ortho/para* regioselectivity and the *ortho*-aniline-substituted-nonafluoroazobenzene is the preferred in low polar solvent such as 1,2,dichloroethane or decaline while only the *para* isomer is obtain in polar solvent such as DMSO. The treatment of *ortho*-aniline-substituted-nonafluoroazobenzene derivatives with trifluoroacetic acid affords the corresponding 1,2,3,4-tetrafluorophenazine derivatives in good yields.



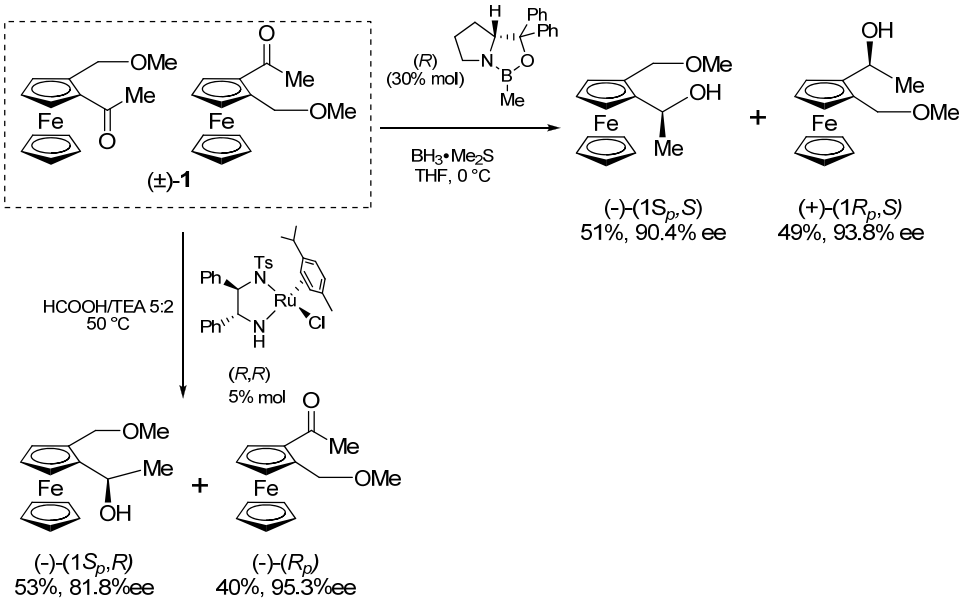
[1] M. Miozzo, A. Papagni, G. Casalbore-Miceli, P. Del Buttero, C. Girotti, M. Moret, S. Trabattoni, *Chem. Mater.* **16** (2004), 5124.
[2] Del Buttero, P.; Gironda, R.; Moret, M.; Papagni, A.; Parravicini, M.; Rizzato, S.; Miozzo, L., *European Journal of Organic Chemistry* (2011), 2265-2271.

ORG-PO-93 Parallel kinetic resolution or kinetic resolution of a planar chiral ferrocenylketone through asymmetric reductions

Sonia Pedotti and Angela Patti

Istituto di Chimica Biomolecolare del CNR ,Via PaoloGaifami 18, I-95126 Catania – Italy
e-mail: sonia.pedotti@icb.cnr.itUT

Planar chiral ferrocenes, mainly 1,2-disubstituted ferrocenylderivatives, constitute an important class of ligands active in asymmetric catalysis [1]P. Racemic 1-acetyl-2-methoxymethylferrocene (±-**1**), as a model compound, was subjected to asymmetric reduction with two different methods and complementary results were obtained [2,3]. When the reduction of this ferrocenylketone takes place in the presence of a chiral oxazaborolidine catalyst and BHR_{3R}•$MeR_{2R}S$ as hydrogen source, both enantiomers of the substrate were converted with comparable reaction rate and selectivity. The corresponding diastereoisomeric ferrocenylalcohols were obtained in a 1:1 ratio and >90% enantiomeric excess, this reaction profile being related with a parallel kinetic resolution with high $ds R_{1R}$ and $ds R_{2R}$ diastereofacial selectivities.
On the contrary, the transfer hydrogenation of (±)-1-acetyl-2-methoxymethylferrocene with HCOOH/triethylamine in the presence of Noyori's catalyst proceeded under the classical kinetic resolution fashion, so that the formed (1*Sp,R*)-1-hydroxyethyl-2-methoxymethylferrocene or unreacted ketone could be obtained in highly enantiopure form slight before or beyond 50% of the substrate conversion, respectively.



The alcohol with (1*Rp,S*) or (1*Sp,R*) configuration is not easily accessible by the diastereoselective metalation/electrophilic quenching sequence, routinely applied in the synthesis of planar chiral ferrocenes, so that the described procedures gave a valuable access to this useful starting material for the synthesis of homochiral related derivatives.

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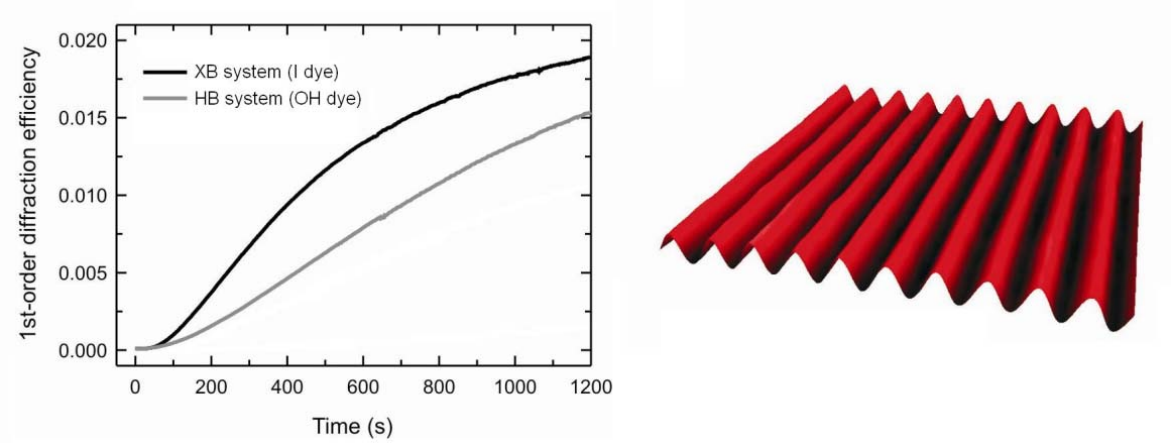
ORG-PO-94 Host-guest polymers with enhanced photoresponsivity assembled by halogen bonding

Arri Priimagi[a], Gabriella Cavallo[b], Alessandra Forni[c], Roberto Milani[b], Mikael Gorynsztejn–Leben[a], Pierangelo Metrangolo[d], Matti Kaivola[a], Giuseppe Resnati[d]

[a] Department of Applied Physics, Aalto University of Science and Technology, P.O. Box 13500, FI-00076 Aalto, Finland.
[b] Center for Nano Science and Technology @Polimi, Istituto Italiano di Tecnologia, Via Giovanni Pascoli, 70/3, 20133 Milano, Italy.
[c] CNR – ISTM, Università degli Studi di Milano, V. Golgi, 19, 20133 Milano, Italy.
[d] NFMLab, DCMIC "Giulio Natta", Politecnico di Milano; via Mancinelli, 7, I-20131 Milano, Italy.
roberto.milani@iit.it

We prepared photoresponsive host-guest materials by halogen bond (XB) [1] coupling of halogenated azo-dyes with poly(4-vinylpyridine). These systems proved to be optimal substrates for the optical inscription of surface relief gratings (SRG), and in some cases outperformed analogous hydrogen bonded materials in such respects as inscription speed, grating depth and diffraction efficiency (see figure below).



The materials were modelled by small molecule complexes in DFT calculations and experimental investigations, suggesting that XB directionality plays a major role in determining the SRG inscription performance. Furthermore, the nature of XB allowed us to perform a systematic study on the role of polymer-dye coupling strength, which was varied by simple substitution of the halogen atom involved [2].

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ORG-PO-95 A Novel Synthetic Approach to Oleocanthal, a Natural Anti-inflammatory Agent from Olive Oil

E.G. Peviani, A. D'Alfonso, M. Valli, A. Porta, G. Zanoni, G. Vidari

Dipartimento di Chimica, Via Taramelli 10, 27100 Pavia
e-mail: elena_giulia@hotmail.it

Oleocanthal (**6a**), a compound isolated from extra virgin olive oil, is a potent non-steroidal anti-inflammatory agent, similar to ibuprofen [1], and a powerful anti-oxidant similar to α-tocopherol. It is suggested that long-term consumption of small quantities of oleocanthal from olive oil may be responsible in part for the low incidence of heart disease associated with the Mediterranean diet. Moreover, activation of TRPA1 by oleocanthal is most likely responsible for the "peppery" taste of olive oil. Only one, rather long, synthesis has been published so far, starting from the chiral pool [2]. In this paper we have developed a new straightforward approach to **6a**, using lactone **1** as the chiral starting building block. Preparative enantioselective HPLC separation provided either enantiopure enantiomers of **1**. In the scheme reported below we show the main steps of the synthesis of the methyl derivative **6b**, as a proof of our synthetic strategy.
Our next aim will be the synthesis of oleocanthal itself (**6a**), following the same route, avoiding the use of protective group.

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[2] A.B.III Smith, J.B.Sperry, and Q.Han, *J. Org. Chem.*, *72*, **2007**, 6891-6900.

ORG-PO-96 Novel fluorescent silica nanoparticles for heavy metal ions chemical sensing

Pinto Vita,[a] Gianluca M. Farinola,[a] Antonio Cardone,[b] Roberta Ragni.[a]

[a] Dipartimento di Chimica, Università degli Studi di Bari, Via Orabona 4, 74125, Bari, Italy
[b] CNR ICCOM , Dipartimento di Chimica, Università degli Studi di Bari, Via Orabona 4, 74125, Bari, Italy
vita.pinto@uniba.it

Nanotechnology is a fast-growing area, involving the fabrication and use of nano-sized materials and devices. Nanocomposite materials play a key role in this field and, in particular, silica nanoparticles represent a very interesting class of materials for several reasons. Indeed, they are hydrophilic, biocompatible, not sensitive to microbial attack and their morphology and porosity is not dependent on pH changes. Moreover, they are available in well defined size and with external surface bearing reactive functional groups, such as amino groups, that allow easy anchoring of a variety of molecules with specific functions, such as organic dyes, drugs and molecular receptors, thus representing useful nano-structured templates for the fabrication of devices for chemical sensing, bioimaging or drug delivery [1]. Here we report our recent results on the synthesis, the photophysical characterization and the application in chemical sensing of some of the first examples of fluorescent silica nanoparticles functionalized with organic conjugated oligomers, such as oligofluorenes and oligoarylenethienylenes, as well as with organic molecules interacting with heavy metal ions such as Hg^{2+}, Pb^{2+}, Ni^{2+} (Figure 1).

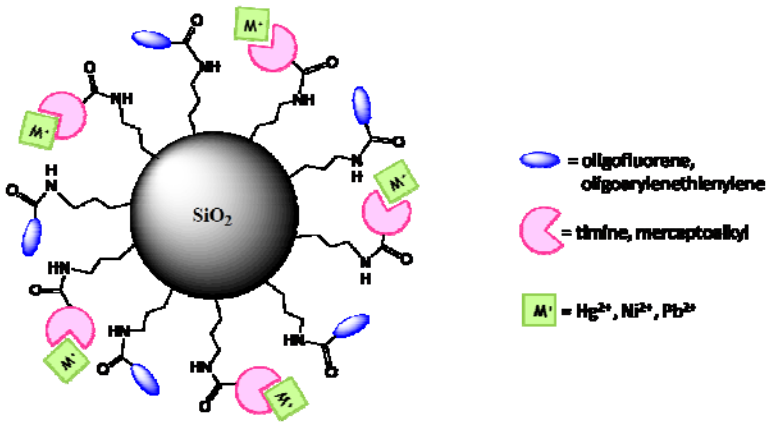

Figure 1.

These materials are potentially useful for heavy metal sensing, allowing detection limit 10^{-7} M and linear fluorescence I/I_0 quenching response for Hg^{2+}, according to the Stern-Volmer law.

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ORG-PO-97 Synthesis of analogues of ochratoxin A

Pierluigi Plastina,[a] Alessia Fazio,[a] Mohamed Attya,[b] Giovanni Sindona,[b] and Bartolo Gabriele[a]
[a] Dip. di Sc. Farmaceutiche dell'Università della Calabria, 87036, Rende, Italy
[b] Dip. di Chimica dell'Università della Calabria, 87036, Rende, Italy
E-mail: p.plastina@unical.it

The mycotoxin ochratoxin A (OTA, Figure 1, **1a**, R = Bn) is a secondary metabolite that occurs in raw and improperly stored food products. In particular, it has been found in cereals, coffee, cocoa, grape juice, beer, and wine [1,2]. OTA has been reported to be nephrotoxic, mutagenic, genotoxic, teratogenic, hepatotoxic, neurotoxic, and immunotoxic, in both animals and humans [3,4]. Several structure-activity relationship studies have been carried out in order to determine the role of each functional group played in OTA toxicity and the question whether the amino acidic moiety plays a role has also been raised [5].

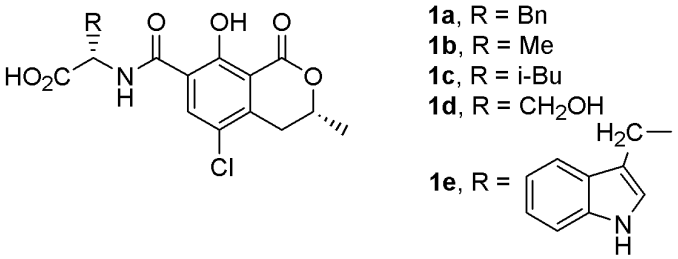

Figure 1

In this communication, we expanded the scope of our previous work on the synthesis of ochratoxin A [6] to the preparation of several OTA analogues, differing for the amino acidic residue. The key step of the synthetic strategy consisted of the condensation reaction between suitably protected amino acid and ochratoxin α (OTα), carried out in the presence of EDC•HCl and HOBt as coupling agents. In particular, OTA alanine (**1b**, R = Me), leucine (**1c**, R = i-Bu), serine (**1d**, R = CH_2OH) and tryptophane (**1e**, R = 3-indolylmethyl) analogues were prepared in satisfactory yields, and will be useful for further toxicological studies.

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[4] K.R.N.Reddy, B.Salleh, B.Saad, H.K.Abbas, C.A.Abel, W.T.Shier, *Toxin Reviews*, *29*, **2010**, 3.
[5] B.Cramer, H.Harrer, K.Nakamura, D.Uemura, and H.-U.Humpf, *Bioorg. Med. Chem.*, *18*, **2010**, 343.
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ORG-PO-98 "One-injection" absolute configuration determination of five acyl-homoserine lactones from *Methylobacterium mesophilicum*

Armando M. Pomini[a,b], Pedro L. R. Cruz[a], Cláudia Gai[c], Welington L. Araújo[c] and Anita J. Marsaioli[b]

[a] Chemistry Institute, University of Campinas, 13083-970, Campinas, SP, Brazil; [b] Chemistry Department, University of Maringá, 87020-900, Maringá, PR, Brazil; [c] Genetics Department, University of São Paulo, 13400-970, Piracicaba, SP, Brazil. *ampomini@uem.br*

Brazil has the largest orange orchards in the world and holds an important slice of the international concentrated orange juice market. However, the orchards suffer from several plagues and diseases. There are evidences that the Gram negative bacterium *Methylobacterium mesophilicum* plays a role in the economic relevant citrus variegated chlorosis disease. In the last years, it has been demonstrated that many bacteria employ chemical communication mechanisms known as *quorum sensing* to regulate the expression of important virulent phenotypes against hosts [1]. Therefore, the aim of this work was to characterize the main signaling substances produced by *M. mesophilicum,* belonging to the acyl-homoserine lactones group. The signaling metabolites were purified from 8 l of CHOI3 fermentation media and a mixture (1.1 mg) of five substances was isolated (Figure 1). The absolute configuration determination of these substances proved to be difficult, due to the minute amounts available and the extensive overlap of the saturated and unsaturated homologues on chiral stationary phases by GC-FID analysis. To overcome this problem, a simple and elegant hydrogenation procedure was employed, converting all the unsaturated substances into the saturated ones **1** and **2**. The natural products and derivatives mixture was successfully analyzed by GC-FID with chiral stationary phase, in comparison with racemic and enantiopure synthesized standards. All five substances were characterized as (*S*) enantiomers at the lactone ring with just one injection, and no traces of (*R*) ones were detected. None of these substances had their absolute configuration previously characterized [1].

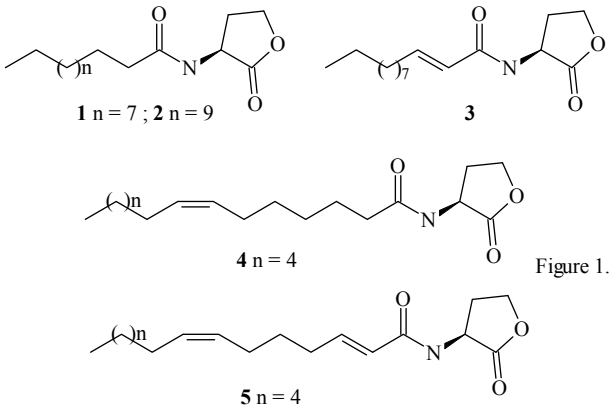

Figure 1.

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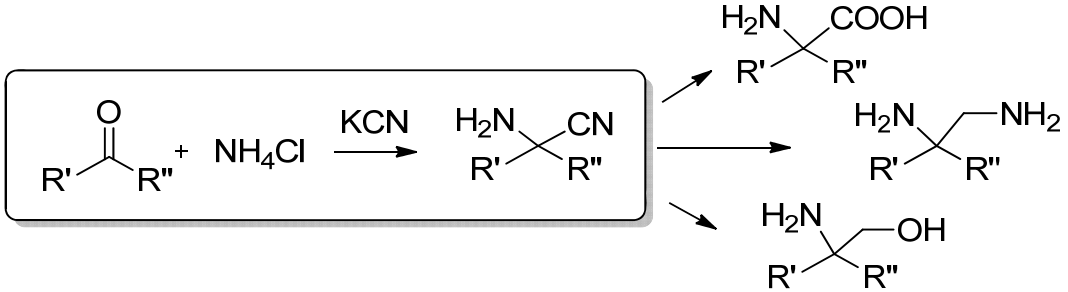
Acknowledgments: Fapesp, CNPq.

ORG-PO-99 Catalyst-free Strecker reaction in water: a simple and efficient protocol using acetone cyanohydrin as cyanide source

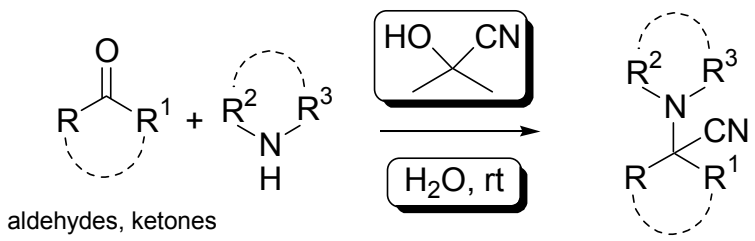
Matteo Pori, Paola Galletti, Daria Giacomini
matteo.pori2@unibo.it

The Strecker reaction is known since 1850[1] and the classic procedure involves the reaction between a carbonyl compound, NH_4Cl, and KCN to give α-aminonitriles[2] which are versatile intermediates for the synthesis of highly functionalized compounds, such as 1,2-diamines, 2-amino alcohols, and α-aminoacids.



The most common cyanide sources for the Strecker reaction like HCN, TMSCN, Bu_3SnCN, Et_2AlCn, K_4FeCN_6 are generally expensive, unsafe and their contribution to atom economy[3]is poor. We choose an economical and relatively safe reagent, the acetone cyanohydrin, that seems to be a good compromise between cost, toxicity and also atom economy.

We studied a simple, convenient, and practical method for the synthesis of α-aminonitriles[4] through a one-pot three-component reaction of a carbonyl compound, amine, and acetone cyanohydrin in H_2O.



Reactions proceed very efficiently without any catalyst at room temperature with high chemoselectivity and giving in some cases the expected α-aminonitrile pure just after direct separation from H_2O.

The protocol is particularly efficient on both aliphatic or aromatic aldehydes, cyclic ketones, in combination with primary and secondary amines. We extended the study to the the synthesis of unusual α-aminonitriles derived from 1,2-diamines and secondary amines.

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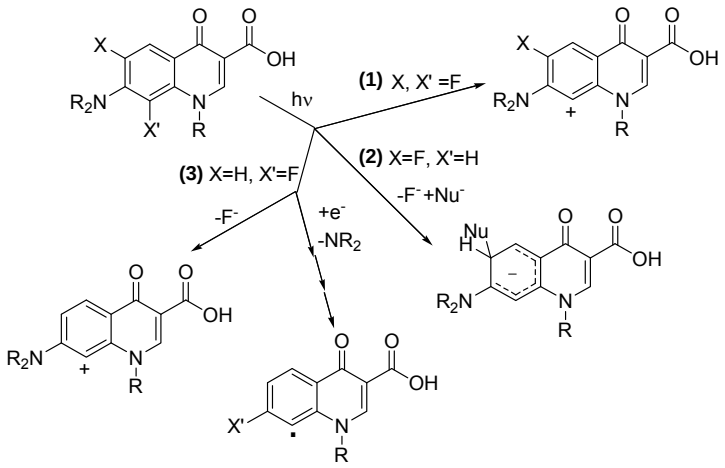
[2] Optaz T., *Synthesis*, **2009,** 12, 1941–1959
[3] Trost. B. M., *Angew. Chem. Int. Ed. Engl*, **1995**, 34 (3), 259–281;
[4] Galletti P., Pori M., Giacomini D., *European Journal of Organic Chemistry*, in press, DOI: 10.1002/ejoc.201100089

ORG-PO-100 UNEXPECTED PATHS IN THE PHOTOCHEMISTRY OF A 8-FLUOROQUINOLONE

L. Pretali,[a] D. Dondi,[a] E. Fasani,[a] A. Albini[a]
[a]Dipartimento di Chimica dell'Università degli Studi di Pavia, via Taramelli 10, 27100, Pavia, Italy.
E-mail: luca.pretali@unipv.it

The largely used antimicrobic fluoroquinolones are often phototoxic. In particular those bearing a fluorine atom in 8 position showed to be strongly photoreactive and are known to cause severe side effects upon light exposure, ranging from skin sensitivity to carcinogenicity.[1] This has stimulated the interest in their photochemistry, which has revealed unusual aspects.[2] In particular, 6,8-difluoro-7-aminoquinolones (1) undergo a selective photo S_N1 process with formation of the cation in 8 in the triplet state. This in turn inserts into C-H bonds, adds to C=C bonds or, in the presence of a donor, is reduced. In contrast, 6-fluoro-7-amino derivatives (2) undergo a S_N2 reaction. Looking for a generalization, we synthesized a 8-fluoro-7-amino derivative (3). This behaves as (1) in a non reducing medium, but in the presence of a donor loses the amino group exhibiting a 'pseudo-benzyne' behavior. In fact, in the presence of a donor, such as pyrrole or iodide, the entire piperazine moiety was lost, and a fluorine atom was found in the place of it. New products were isolated and characterized and a plausible reaction mechanism was proposed which took into account the new experimental results. This hypothesis was strengthened by a computational analysis of the reaction mechanism. This further confirms the rich photochemistry of heteroaromatics and in particular of fluoroquinolones and shows how it is possible to change and, to some extent, drive the reactivity of such compounds by introducing appropriate target modifications on the aromatic scaffold.



[1] L.Marrot, J.P.Belaidi, C.Jones, P.Perez, L.Riou, A.Sarasin, and J.R.Meunier, J. R. *J. Invest. Dermatol*., 121, **2003**, 596. L.J.Martinez, R.H.Sik, and C.Chignell, *Photochem. Photobiol*., 67, **1998**, 399.N.Wagai, and K.Tawara, *Arch. Toxicol*., 66, **1992**, 392.
[2] E.Fasani, S.Monti, I.Manet, F.Tilocca, L.Pretali, M.Mella, and A.Albini, *Org. Lett.*, 11(9), **2009**, 1875. L.Pretali, E.Fasani, D.Dondi, M.Mella, and A.Albini, *Tetrahedron. Lett.*, 51(36), **2010**, 4696.

ORG-PO-101 Selective synthesis of aminoalcohols by hydroxyalkylation of amines in alcohol or in cyclic ether cosolvents: a new domino radical mechanism promoted by $TiCl_4$-Zn/t-BuOOH.

Simona Prosperini, Nadia Pastori, Alessandra Ghilardi, Angelo Clerici and Carlo Punta
Dipartimento di Chimica, Materiali e Ingegneria Chimica "G. Natta", Politecnico di Milano, Sezione Chimica,Via Mancinelli 7, I-20131 Milano, Italy.
corresponding author: simona.prosperini@gmail.com

Following the radical route, we report a new and fast domino synthesis of 1,2-aminoalcohols under mild conditions. The free-radical reaction of aliphatic and aromatic amines with alcohol cosolvents is promoted by means of the $TiCl_4$-Zn/*t*-BuOOH system [1]. According to the proposed mechanism [2], the amine reacts with two molecules of alcohol in an electrophilic-nucleophilic cascade process.

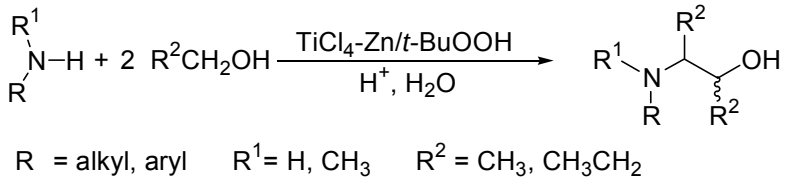


Figure 3 Radical domino reaction between of an amine with two molecules of alcohol, triggered by $TiCl_4$-Zn/t-BuOOH

This procedure, if compared with the $TiCl_3$/*t*-BuOOH-mediated protocol previously reported[3], appears to be more selective, of more general applicability and affords the desired products in higher yields. Besides, with the same catalytic system it was possible to promote the reaction of primary arylamines with two molecules of cyclic ether, leading to the formation of a wider range of functionalized aminoalcohols [2].

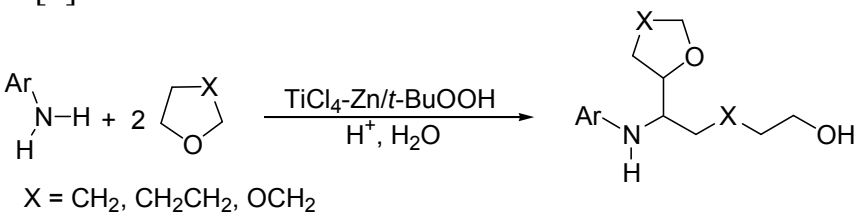


Figure 4 Radical domino reaction of a primary arylamine with two molecules of cyclic ether triggered by $TiCl_4$-Zn/t-BuOOH

[1] N. Pastori, C. Greco, A. Clerici, C. Punta and O. Porta, *Org. Lett.*, 12, **2010**, 3898-3901.
[2] S. Prosperini, N. Pastori, A. Ghilardi, A. Clerici and C. Punta, *Org. Biomol. Chem.*, 6, **2011**, 3759-3767.
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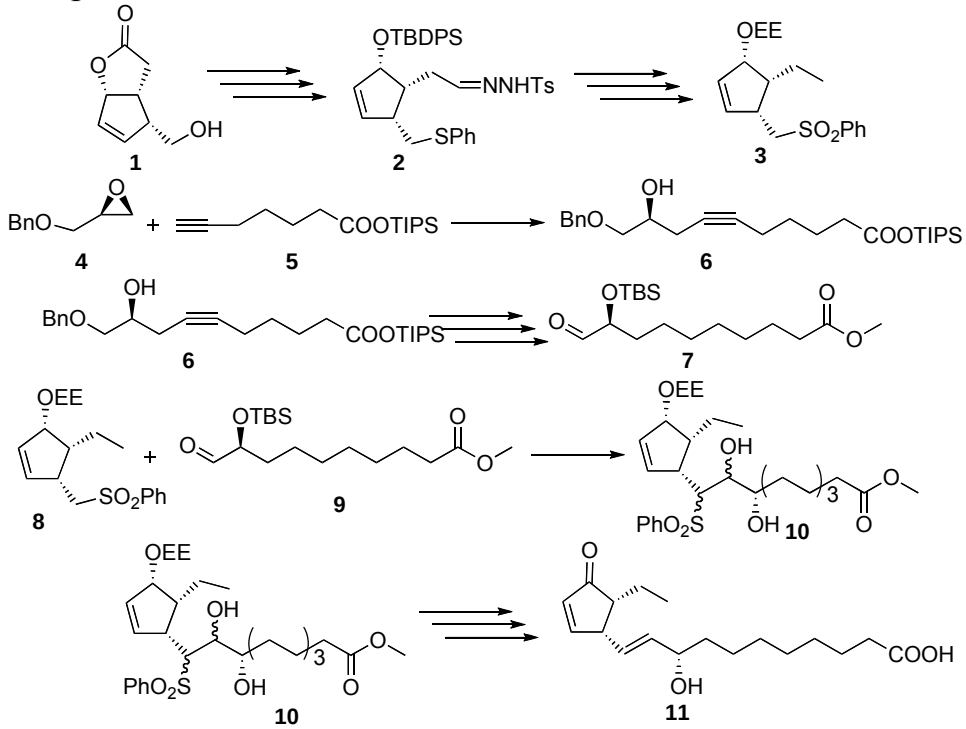
ORG-PO-102 Enantioselective total synthesis of Phytoprostane A1 type II

M. Quaroni, A. Negri, G. Forni, M. Valli, A.Porta, G.Zanoni, G.Vidari

Dipartimento di Chimica, Via Taramelli 10, 27100 Pavia
e-mail: matteo.valli@unipv.it

Plants utilize linoleic and linolenic acids to produced C_{18}-isoprostanoids (phytoprostanes, PP) via non-enzymatic, free radical-catalysed pathways similar to isoprostane synthesis in animals [1]. The cyclopentenone-phytoprostanes PPA and PPB up-regulate gene expression, especially for enzymes involved in the response to challenges by foreign organisms or external conditions, triggering phytoalexin production, while they down-regulate genes involved in cell division and growth. Moreover, PP are present in vegetable oils and have been detected in plasma; therefore, the biological properties of phytoprostanes in terms of potential effects on human cells need to be investigated using material only available by total synthesis. In this communication we report the first enantioselective synthesis of phytoprostane A1 type II (**11**), as shown in the Scheme reported below. The cyclopentenone core of **11** was prepared from enantiopure lactone **1** [2], while the lateral chains were installed using intermediates obtained from commercially available compounds.



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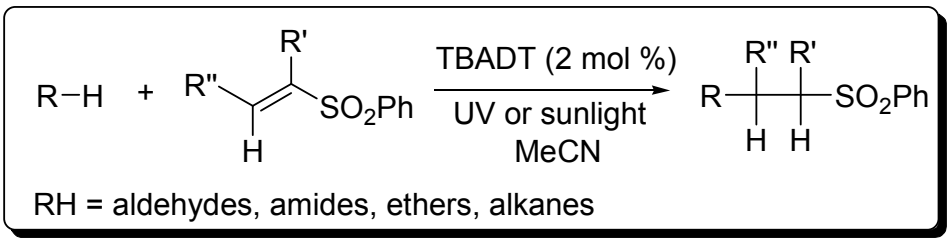
[2] Zanoni, G.; Porta A.; Brunoldi, E., Vidari, G.; *J. Org. Chem.*; **2006**, *71*, 8459.

ORG-PO-103 TETRABUTYLAMMONIUM DECATUNGSTATE PHOTOCATALYZED SYNTHESIS OF SULFONES.

Davide Ravelli, Sara Montanaro, Maurizio Fagnoni, Angelo Albini

Department of Chemistry, University of Pavia,V.Le Taramelli 12, 27100 Pavia
fagnoni@unipv.it

The sulfone moiety plays a useful role in the synthesis of organic molecules due to its easy functionalization and its leaving group aptitude. [1] Vinyl sulfones (e.g. phenyl vinyl sulfone), on the basis of their electrophilic character, can easily undergo conjugate radical additions to give substituted sulfones.
An appealing and atom-economical way to generate substituted alkyl radicals is by a C-H activation reaction and this can be accomplished by having recourse to photocatalysis. In the last years we developed the reactions of a new photocatalyst namely tetrabutylammonium decatungstate ((*n*-$Bu_4N)_4W_{10}O_{32}$), TBADT)). [2] When in the excited state, this abstracts chemoselectively a hydrogen from a C-H bond in several classes of organic molecules including alkanes. The resulting C-centered radicals have been successfully exploited in conjugate radical additions to electron-poor olefins under mild green tin-free conditions. [3]
Thus, (UV or sunlight) irradiation of a mixture containing the hydrogen donor (RH), the unsaturated (substituted) sulfone and catalytic amounts of TBADT allowed the preparation of various substituted sulfones in up to 90% yield.



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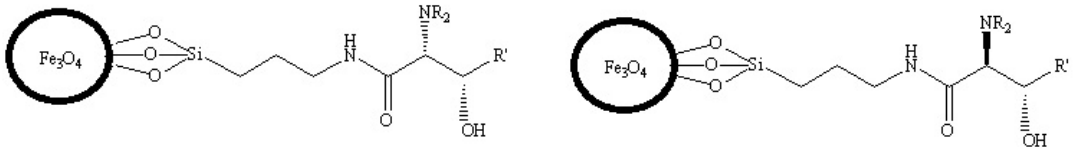
ORG-PO-104 Preparation of magnetite nanoparticles functionalized with optically active 1,2-amino alcohols.

G. Righi,[a] A. Mari,[b] M.S. Maglione,[b] C. Tatangelo,[b] L. Suber[c]

[a]CNR-ICB, Dip.di Chimica, Sapienza Università di Roma, P.le A. Moro 5, 00185 Roma, Italy
[b]Dip.di Chimica, Sapienza Università di Roma, P.le A. Moro 5, 00185 Roma, Italy
[c]CNR-ISM, Area della Ricerca, Via Salaria km 29.500, 00016 Monterotondo Scalo, Italy.
alessandra.mari@uniroma1.it

Recently, the use of magnetic nanoparticles led to the development of new catalysts that combine advantages of both homogeneous and heterogeneous catalysis [1]. In fact, nanoparticles with appropriate surface coatings are readily dispersible in organic solvents and, owing to their small size, have very high surface areas. Thus nanoparticles can be used as novel supports for asymmetric catalysts, with activity close to the homogeneous one. In addition, nanoparticle magnetic decantation allows a simple recovery of the catalyst from the reaction mixture and its reuse, as in the case of heterogeneous catalysts.
In this context, we report on the synthesis of magnetite nanoparticles functionalized with optically active amino alcohols, a class of compounds largely employed in asymmetric catalysis [2].
Magnetite nanoparticles were prepared using the organic phase thermal decomposition method.[3]
The synthesis of the amino alcoholic chains was based on the regio- and stereocontrolled opening of enantiopure functionalized epoxides. A triethoxysilane group was introduced at the end of the chains and used for the covalent anchoring to the nanoparticle surface.



The novel "chiral" nanoparticles will be tested as magnetically decantable asymmetric catalysts, at first in the addition of organozinc compounds to aldehydes. The catalytic system will be optimized modifying both the stereochemistry of the amino alcoholic fragment and the steric hindrance of the R and R' groups.

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ORG-PO-105 Synthesis of novel conjugated oligomers for labeling applications

P.Rinaldi[a], O.Hassan Omar[b], A.Operamolla[a], G.M.Farinola[a] ,F.Babudri[a]

[a] Dipartimento di Chimica dell'Università di Bari, Via Orabona, 70126, Bari, Italy
[b] CNR ICCOM, Dipartimento di Chimica dell'Università di Bari, Via Orabona, 70126, Bari, Italy
paolo.rinaldi83@alice.it

The research in luminescent organic semiconductor markers for biosensing applications is currently proceeding at a rapid pace[1].
Oligo(*p*-aryleneethynylene)s (OAEs) have emerged as molecular building blocks for the design and fabrication of optoelectronic systems, including chemical and biological sensors[2]. These materials possess interesting semiconducting and optical properties arising from the presence of triple C-C bonds which confer rod-like structure and high conjugation to the resulting system.
In this communication we report the synthesis of oligo(*p*-aryleneethynylene)s with unsymmetrical functionalization on the external rings and various central cores, that are endowed with terminal carboxyl groups to tether biomolecules by formation of amidic bonds. Our synthetic approach is based on palladium catalyzed organometallic methodologies, which appear selective and tolerant of a number of functional groups [3]. In particular, for the cross-coupling of terminal arynes with aryl halides we adopted either the classic Cassar-Heck-Sonogashira reaction and the Mori procedure. Moreover the absorption and emission spectra of the resulting oligomers were recorded and evaluated in order to get information about the influence of the structure of the selected central core and of the different terminal substituents on the overall optical properties.

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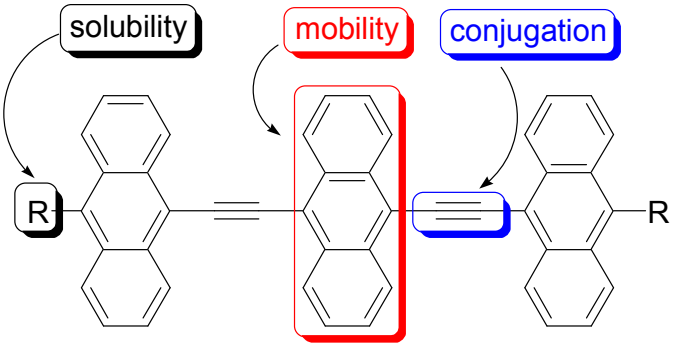
ORG-PO-106 9,10-*ter*-Anthrylene-Ethynylenes: New Semiconductors for Solution Processed Organic Field-Effect Transistors

Giuseppe Romanazzi,[a] Gian Paolo Suranna,[a] Serafina Cotrone,[b] Luisa Torsi,[b] Francesco Marinelli,[b] Davide Altamura,[c] Cinzia Giannini,[c] Piero Mastrorilli[a]
[a] Dipartimento di Ingegneria delle Acque e di Chimica (DIAC), Politecnico di Bari, via Orabona 4, 70125 Bari, Italy
[b] Dipartimento di Chimica, Università degli Studi Aldo Moro di Bari, via Orabona 4, 70125 Bari, Italy
[c] Istituto di Cristallografia (IC-CNR), via Amendola 122/O, 70126 Bari, Italy
E-mail: g.romanazzi@poliba.it

The research on soluble organic semiconductors to be employed in electronic devices such as organic field-effect transistors (OFETs) benefits from the continuous improvement of the available synthetic tools necessary for their preparation [1,2]. However, focused synthetic efforts are still required to conceive new organic structures aiming at gaining more insight into the structure-property relations for these materials. In this presentation, the preparation and properties of soluble 9,10-*ter*-anthrylene-ethynylenes (**Figure 1**) through combined Negishi and Sonogashira cross-couplings will be addressed.



Alkyl functionalised
A1 : R = *n*-Butyl
A2 : R = *n*-Octyl
A3 : R = 2-Ethylhexyl
A4 : R = *n*-Decyl
Ester functionalised
E1 : R = carboethoxy
E2 : R = carbobutoxy
E3 : R = carbooctoxy

Figure 1.

The optical, electrochemical, and thermal properties of the oligomers **A1-4** and **E1-E3** will be discussed as well as STM and XRD investigations aimed at elucidating their order in thin films. Results on their semiconducting properties will also be presented: the top contact OFETs fabricated exhibited hole mobilities up to $5.5 \cdot 10^{-2}$ $cm^2 \cdot V^{-1} \cdot s^{-1}$ and on/off ratios higher than 10^4. The good performances in OFETs of **A1-4** and especially of the polar functionalised **E1-E3** make these materials promising as active layers for OFET sensing applications [3].

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ORG-PO-107 Wacker Oxidation in Ionic Liquids

Angelo Sanzone[a], Cinzia Chiappe[a], Paul Dyson[b]

[a]Dipartimento di Chimica e Chimica Industriale dell'Università di Pisa, via Bonanno 33, I-56122, Pisa, Italy.

[b]Institut des Sciences et Ingénierie Chimiques, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland.

E-mail : angelo.sanzone@ns.dcci.unipi.it

A series of hydrophilic N,N-dimethylpyrrolidinium and N,N-dimethylpiperidinium-based ionic liquids (ILs) have been prepared and applied as reaction media in the Wacker oxidation of styrene by hydrogen peroxide using $PdCl_2$ as catalyst.[1,2] The efficiency of these ILs was compared with hydrophilic and hydrophobic imidazolium systems (including those with nitrile functionalities).

The nature of the ionic liquid strongly influences the product distribution. In particular, in hydrophobic ILs relevant amounts of 1,3-dipheyl-1-butene arising from styrene dimerization were detected in addition to the expected phenylmethylketone. The formation of 1,3-dipheyl-1-butene may be attributed to the formation of Pd(0) species from "ClPdOH" (probably formed during the Wacker process) in a side-reaction.

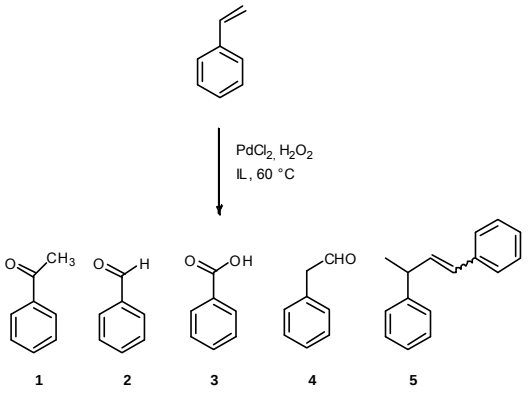

Figure 1. Isolated reaction products.

Consequently, the ability of the IL to favor or disfavor the reoxidation of "ClPdOH" to "ClPdOOH" by hydrogen peroxide giving an homogeneous phase or a biphasic system appears to be the main factor affecting selectivity.

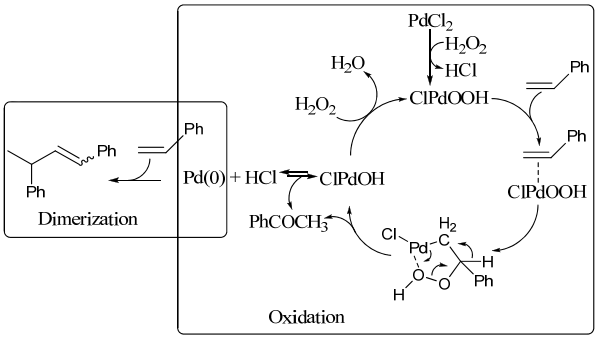

Figure 2. Proposed mechanism for competitive palladium catalyzed styrene oxidation and dimerization.

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ORG-PO-108 Synthesis of Chiral Phosphites and Their Application in the Asymmetric Addition of Dimethylzinc to Alkylidenmalonates

Patrizia Scafato, Valeria Marchitiello, Laura Pisani, Stefano Superchi

Dipartimento di Chimica dell'Università della Basilicata, via N. Sauro, 85, 85100, Potenza, Italy
patrizia.scafato@unibas.it

The asymmetric conjugate addition of dimethylzinc to α,β-unsaturated carbonyl compounds is an efficient and direct method to obtain a methyl substituted stereogenic centre, a structural motif which often plays an important role in determining the biological activity of numerous natural compounds [1].
Acyclic □□□-unsaturated esters are generally not reactive towards dialkylzinc reagents but, in any case, chiral 3-methylesters can be achieved by asymmetric addition of dimethylzinc to alkylidenmalonates followed by direct demethoxycarbonylation of the addition products [2].
We decided to prepare herein new chiral phosphites [3] and to explore their efficiency as ligands in the copper-catalyzed asymmetric conjugate addition of dimethylzinc to diethyl 3-phenylpropylidenmalonate with the aim to disclose new synthetic applications of this procedure. In particular we focused our attention on the development of new route to some floral fragrances like Phenoxanol, Citralis and Nitrile Citralis, in optically active form, choosing 3-phenylpropylidenmalonate as starting substrate on which to test the asymmetric addition.

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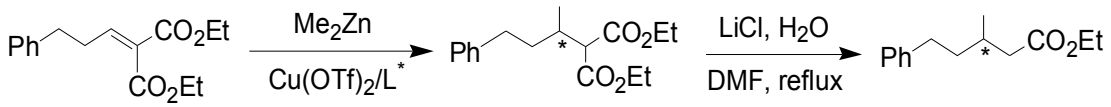

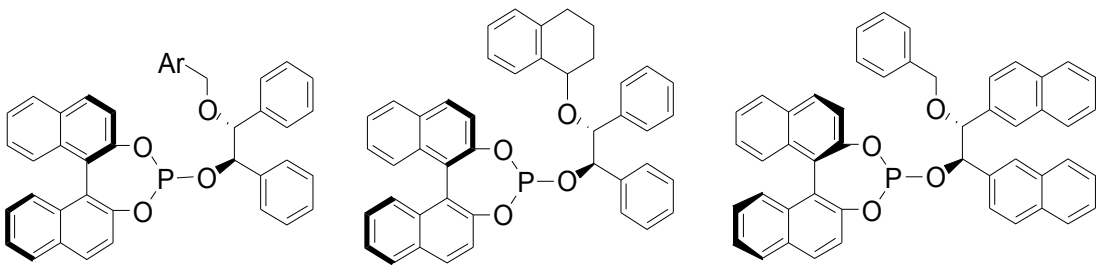

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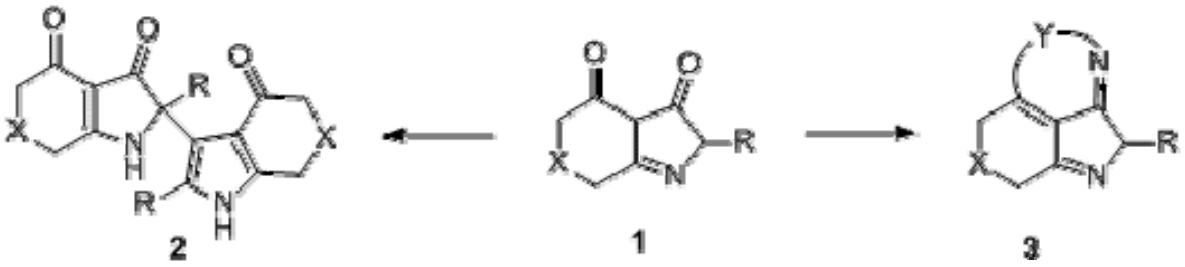
ORG-PO-109 Indole-3,4-dione as promising scaffold for the synthesis of antiviral compounds

A. Scala,[a] M. Cordaro,[a] A. Mazzaglia,[b] F. Risitano,[a] and G. Grassi [a]

[a] Dipartimento di Chimica Organica e Biologica, Università, Vill.S.Agata I-98166 Messina, Italy
[b] ISMN-CNR, c/o Dipartimento di Chimica Inorganica, Chimica Fisica e Chimica Analitica, Università, Vill.S.Agata I-98166 Messina, Italy
e-mail: scala@isengard.unime.it

In recent years, indole-based compounds are reported to exhibit broad-spectrum chemotherapeutic properties such as antiviral, antitubercular, antifungal, and antibacterial activities. Due to their biological relevance, they attract special attention as building blocks for the synthesis of new therapeutic agents.
In the framework of our studies dealing with the design of useful polifunctionalized N,O-heterocycles, we recently reported [1] a class of water soluble indole-3,4-diones **1** as promising lead compounds for antiherpetic drug development. Furthermore, these molecules were successfully entrapped in amphiphilic β-cyclodextrin nanoparticles, to increase the bioavailability and modulate the drug delivery [2].
Based on these findings, we further extended our investigation to synthesize more complex molecular architectures **2** and **3**, starting from the indoledione scaffold **1**.
The modulation of reactants and reaction conditions allowed a good skeletal diversity.



Synthetic and mechanicistic details of these transformations will be presented. In particular, a kinetic study of the base-promoted aldol condensation leading to **2** was carried out by UV-Vis absorption. Finally, antiviral activity of the novel chemical libraries was evaluated.

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ORG-PO-110 Influence of Structural Variations in Cationic and Anionic Moieties on Polarity of Ionic Liquids

Cinzia Chiappe, Christian Silvio Pomelli, Sunita Rajamani

Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via del Risorgimento, 35- 56126 Pisa, Italy
cris@dcci.unipi.it

The polarity of a series of ionic liquids (ILs) arising from quaternarization of N-methylmorpholine, N-methylpyrrolidine, N-methylpiperidine, N-methylazepane, 4-hydroxy-1-methylpiperidine, 1,2-dimethylimidazole and 1-methylimidazole with simple alkyl chains and/or hydroxyl (mono or dihydroxyl) functionalized alkyl chains and having as counteranion bistriflimide, dicyanamide or nitrate anion has been investigated using solvatochromic dyes and expressed in terms of E_T^N and Kamlet-Taft parameters (dipolarity/polarizability (π*), hydrogen-bond donor acidity (α) and hydrogen-bond basicity (β)). Significant variations of polarity were observed on changing anion and cation combination. Nevertheless, the E_T^N and α values resulted strongly anion-dependent; independently on cation core and substituent on going from bistriflimide to dicyanamide a significant decrease in E_T^N and α values was observed. On the other hand, the alkyl chain length has only a moderate effect on these parameters; however, both an increase or decrease in E_T^N and α values was observed on increasing the alkyl chain length depending on cation core. In the case of cyclic onium salts the size of the cation ring affected the α parameter: the IL based on seven-member ring system, N-methyl-N-butylazepanium (also named N-methyl-N-butylhexamethyleneiminium) $[HME_{1,4}][Tf_2N]$ has high polarity values comparatively to analogous ILs based on five and six member ring cations. The introduction of the OH groups on the cation alkyl chain increases polarity; the effect is substantial for the first OH group and more moderate for the second. Finally, also thermosolvatochromism (changes in solvatochromic properties with change in temperatures) was studied for four dihydroxyl functionalized ILs. The use of principal component analysis (PCA) allow us to better estimate the effects of functionalization and anion-cation association. Furthermore PCA shows that there are only two statistical independent parameters between the ones here considered.

ORG-PO-111 Development of chiral arginine-based PNA microarrays for the selective identification of tomato DNA

Stefano Sforza, Tullia Tedeschi, Alessandro Calabretta, Mariangela Bencivenni, Alex Manicardi, Roberto Corradini, Rosangela Marchelli

Dipartimento di Chimica Organica e Industriale, Università di Parma, Parco Area delle Scienze 17a, I-43124, Parma, Italy.
stefano.sforza@unipr.it; rosangela.marchelli@unipr.it

In food analysis, DNA recognition can be extremely useful for tracing the origin of a food product or for evidencing undeclared ingredients, even if present in very small amounts. Among the different DNA markers which might be addressed, Single Nucleotide Polymorphisms (SNPs)[1], which consist in single nucleobase changes within the genome, can be used as specific targets to identify a given food or a specific variety. Surface techniques, and in particular microarray-based platforms [2], turned out to be extremely interesting. Such methods usually rely on the recognition of a DNA target by hybridization with a single strand oligonucleotide probe immobilized onto a surface. The development of PNA-based surface systems allowed to obtain more efficient assays, in terms of selectivity in the recognition of point mutation, robustness and sensitivity [3]. Arginine-based PNAs (Arg-PNAs), recently reported [4] demonstrated their enhanced recognition properties, in terms of binding affinity and mismatch recognition, in solution and on microarray platforms.

Here we show the design and the development of a model Arg-PNA microarray produced for the simultaneous identification of several SNPs, characteristic of different tomato varieties. The design and synthesis of highly selective arginine-based monomer containing PNAs (Arg-PNAs) are reported together with their binding properties in solution and on a microarray surface. In order to define the best design for arginine PNAs for performing selective DNA recognition on surface, two peptide nucleic acids (PNAs) containing three adjacent modified chiral monomers (chiral box) were first synthesized. The chiral monomers contained either a C2- or a C5-modified backbone, synthesized starting from D- and L-arginine, respectively (2D- and 5L-PNA). The 5L-chiral-box-PNA showed the highest Tm with full-match DNA, whereas the 2D-chiral-box-PNA showed the highest sequence selectivity. The PNAs were spotted on microarray slides and then hybridized with Cy5-labeled full match and mismatched oligonucleotides. The results obtained showed a signal intensity in the order achiral >2D-chiral box >5L-chiral box, whereas the full-match/mismatch selectivity was higher for the 2D chiral box [5]. According to these results, seven different PNA probes containing a 2D arginine chiral box were prepared for SNP discrimination in defined sequences of tomato genome. The seven probes were tested in solution and on microarray surface in model

experiments using oligonucleotide mixtures simulating different sequences of the seven tomato varieties [6]. The strenght and the limitations of such a system for SNP recognition will be thoroughly discussed.

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ORG-PO-112 Solvent effects on the keto-enol tautomerization reaction. A thermodynamic study in some organic solvents and ionic liquids

Gabriella Siani,[a] Guido Angelini,[a] Carla Gasbarri,[a] Paolo De Maria,[a] Antonella Fontana,[a] Marco Pierini,[b] Cinzia Chiappe.[c]

[a] Dipartimento di Scienze del Farmaco, Università "G. D'Annunzio", Via dei Vestini, 31, 66100, Chieti, Italy
[b] Dipartimento di Chimica e Tecnologia del Farmaco, Università "La Sapienza", P.le Aldo Moro, Roma, Italy
[c] Dipartimento di Chimica e Chimica Industriale, Università degli Studi, Via Risorgimento 35, Pisa, Italy
siani@unich.it

Organic reactions are commonly performed in solution so that one of the most important parameter for the success of a reaction is the choice of the "best" solvent. Indeed solvents may have a strong influence on reaction rates and equilibria.[1]

Solvent effects on the keto-enol tautomerism have been extensively studied.[1] Recently, the equilibrium constants for the keto-enol interconversion of 2-nitrocyclohexanone (2-NCH) have been reported in water,[2] some organic solvents and ionic liquids (ILs).[3] Due to their peculiar properties, ILs may behave quite differently from conventional molecular solvents. According to these studies [2,3] the enol form of 2-NCH appears to be predominant in apolar solvents while the keto form prevails upon transfer to water, aprotic polar organic solvents and ILs.

In this work the temperature dependence of the tautomeric equilibrium constant for 2-NCH has been studied by UV-visible spectroscopy in five organic solvents, spanning a wide range of permittivity values, □, their binary mixtures, and in some ILs in the temperature range 298 to 333 K. The thermodynamic parameters, □G^0, □H^0 and □S^0, for the interconversion reaction have been derived. In the case of molecular solvents a good correlation was found between □H^0 and □. An attempt to include the studied ILs in the same correlation fails. The nature of the ILs anion seems to play a fundamental role as □H^0 is < 0 for $[TF_2N]$- based ILs while it is > 0 for $[BF_4]$- based ILs.

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ORG-PO-113 Microstructured glass reactors and LED illumination: photochemistry as good as it can get

Simone Silvestrini[a], **Christian Corrado De Filippo**[a], **Tommaso Carofiglio**[a], **Michele Maggini**[a]
[a]Dipartimento di Scienze Chimiche, Università di Padova, via Marzolo 1, 35131 Padova (PD) Italy.
simone.silvestrini@unipd.it

Light emitting diodes (LEDs) are interesting cold light sources with very high power conversion (80-90%) and narrow emission bands. They find application in consumer electronic devices and lighting. LED light has only found limited use in photochemistry because of the difficulty to obtain low-cost diodes that emit in the deep UV region. However, since new materials for LED applications is rapidly filling this gap, LED-driven photochemistry has the potential to become an important tool to access selective and efficient chemical syntheses.
In this presentation we show how organic photochemists and material scientists can benefit from LEDs through the use of microstructured glass reactors. To this end, we present two examples that best encompass the most interesting features of LED illumination: (i) low power consumption, resulting in economical and environmental friendly processes and (ii) narrow emission bands, resulting in highly selective reaction paths.
(i) Low-power commercial white LED arrays can be used for the quantitative conversion of reagents in photocycloadditions thanks to their high efficiency and the optimal geometry of glass microreactors. The reduced thickness of the microfluidic channel, ensures a uniform illumination of the reaction mixture, reduced reaction times and high space time yields (see figure 1). (ii) Illumination of small (3 nm) silver nanoparticles (AgNPs) results in a growth along preferential directions, depending on the wavelength of the radiation. This effect can be used to produce AgNPs with specific shapes and plasmonic properties that depend on the excitation wavelength used (see figure 2). In this case, microfluidic reactors allow to quickly produce AgNPs that can be functionalized with thiols or used immediately for surface enhanced raman spectroscopy (SERS) analysis.

Figure 1 - Photochemical microreactor with white LED illumination

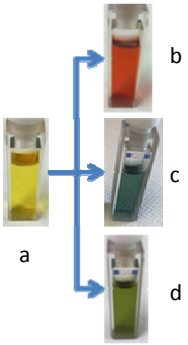


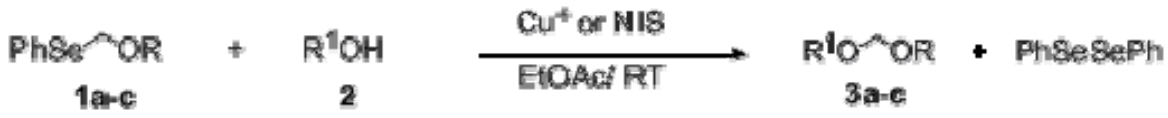
Figure 2 - AgNP seeds (a) and AgNP after illumination at 455 nm (b), 540 nm (c) and 505 nm (d)

ORG-PO-114 O, Se Acetals as Reagents for the Protection of Alcohols

Andrea Temperini, Diego Annesi, Lorenzo Testaferri and Marcello Tiecco

Dipartimento di Chimica e Tecnologia del Farmaco, Sezione di Chimica Organica. Università di Perugia, via del Liceo 1, 06123-Perugia, Italy, *tempa@unipg.it*

Among the organoselenium compounds the *O*, *Se* acetals are interesting intermediates because they are precursors of □-alkoxyalkyl radicals, □-selenocarbenium ions, □-alkoxyalkyl lithium derivatives and □-alkoxycarbenium ions [1]. It is known that phenylseleno glycosides are versatile glycosyl donors in glycosylation reactions after activation of the selenium atom [2]. We report that C-Se bond in the mixed *O*, *Se* acetals **1a-c** can be heterolitically cleaved by the action of copper(I) or iodonium ions. If an alcohol **2** is present in the reaction medium, the corresponding acetals **3a-c** where obtained in good to excellent yields. This is a simple and chemoselective method for the protection of alcohols as methoxymethyl-, methoxyethoxymethyl- and 2-(trimethylsilyl)ethoxymethyl ether derivatives [3]. Furthermore the method is compatible with many functional groups and the selenium can be recovered as diphenyl diselenide in almost suitable yield at the end of the procedure.



R= Me, $MeOCH_2CH_2$ or $(Me)_3SiCH_2CH_2$
NIS= *N*-iodosuccinimide

Financial support from MIUR, National Projects PRIN 2007, Consorzio CINMPIS, Bari and University of Perugia is gratefully acknowledged.

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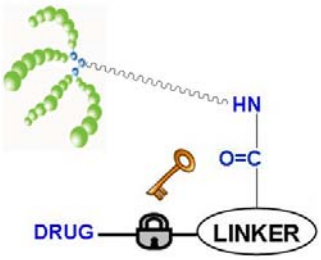
ORG-PO-115 Development of drug-branched peptides complexes for cancer cells tracing and killing

Eleonora Tenori[a], Stefano Menichetti[a], Chiara Falciani[b], Luisa Bracci[b]

[a]Dipartimento di Chimica 'Ugo Schiff', Università di Firenze, Via della Lastruccia 3-13, 50019, Sesto Fiorentino (FI), Italy
[b]Dipartimento di Biologia Molecolare, Università di Siena, Via Fiorentina 1, 53100 Siena, Italy
eleonora.tenori@unifi.it

The aim of this project is to convert 'conventional' cancer drugs, that usually show lack of selectivity and systemic toxicity, in drug-carrier complexes, specifically channelled into tumour cells and able to fulfil its cytotoxic action *in situ*. Peptides, synthesized as dendrimers, are especially suitable for in vivo use due to their stability in human plasma [1]. The realization of these drug delivery systems can be obtained synthesizing a 'smart' linker that manage, at one end, to be bound to the peptide immobilized on a resin and at the other end to the anticancer drug by a 'cleaver' link suitable for different releasing rates.



After internalization into tumor cells the free drug is releasing in situ from the linker by a simple hydrolysis or by specific enzymes. We have chosen to work with different classes of anticancer drugs (antimetabolites, bioreductive drugs, estrogen derivatives, inhibitors of mitosis and platinum complexes), showing different mechanisms of action, in order to potentially provide useful treatments for a wide spectrum of tumours [2]. The synthetic efforts directed towards the optimization of the linkers structure and the attempts to achieve multi-drug carriers are investigating at the moment and will be discussed in this communication.

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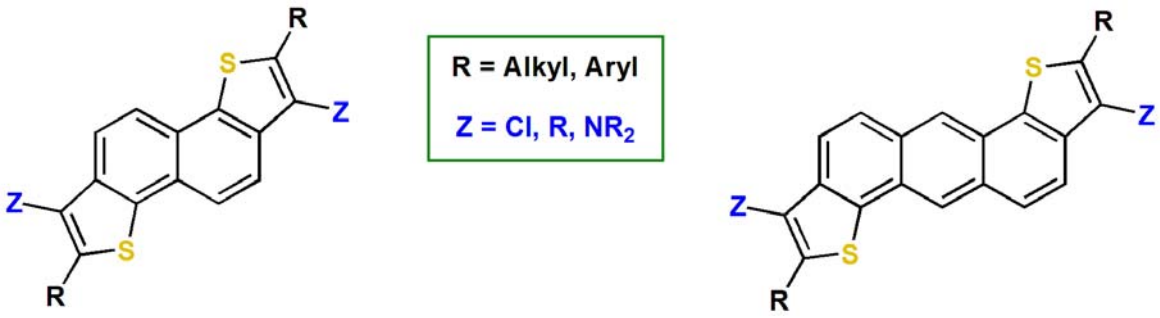
ORG-PO-116 Straightforward access and easy functionalization of naphtha- and anthradithiophenes

Stefano Menichetti, Caterina Viglianisi, Sara Piantini

Dipartimento di Chimica 'U. Schiff' Universita` di Firenze, Via della Lastruccia 3-13, 50019 Sesto Fiorentino, Firenze, Italy
stefano.menichetti@unifi.it

Acenes have optical and electronic properties that are desirable for applications in organic-based electronic devices such as organic field-effect transistors (OFETs) and organic light-emitting diodes (OLEDs). Incorporating heteroarenes, such as thiophene, into these frameworks is part of an ongoing effort to prepare new materials with improved device performances [1].

In this communication we will describe a simple strategy for the preparation of naphtha- and anthradithiophenes that exploits easily available alkylaryl- or diarylalkynes as starting materials and two consecutive one-pot electrophilic processes for the introduction of the sulfur atom and the closure of the thiophene ring. This procedure allows the preparation of 3-chloro-substituted thioacene derivatives that can be further functionalised, with different metal catalysed cross coupling reactions, taking advantage of the heterocyclic carbon-chlorine bond [2].



The applicability, limitation and scope of this new procedure, as well as the reasonable mechanisms involved in the transformation will be presented.

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ORG-PO-117 Zinc Oxide: a new Tool for the Solvent- Free Regioselective C- Arylsulfonation of Indoles.

Graziella Tocco,[a] Michela Begala[a]
[a] Dipartimento Farmaco Chimico Tecnologico, Via Ospedale 72, 09124, Cagliari, Italy
toccog@unica.it

Aryl sulfones and sulfoxides are interesting functional groups present in a wide variety of compounds in the field of drugs and pharmaceuticals.
In particular, indolyl aryl sulfones have emerged as powerful anti-HIV-1agents [1] or as efficient carcinogenesis modulators with a pleiotropic mode of action [2]. (Figure 1) Although the direct aryl sulfonylation of aromatic systems is well known in the literature, the indolyl aryl sulfones are generally prepared by indirect methods which involve the oxidation of indol-3-yl sulfides to the corresponding sulfone [3].Thus, in view of their importance, in the present research we illustrate a mild and versatile direct one-pot approach for the aryl sulfonation of 1*H*- indoles. (Figure 2)

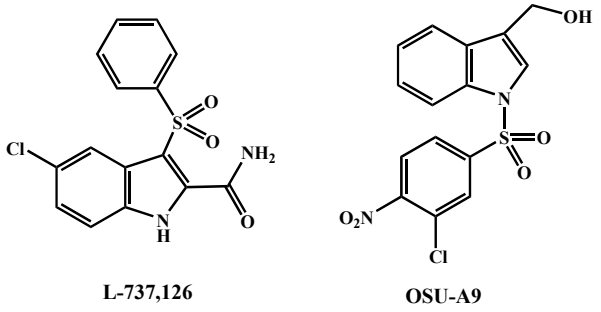

Figure 1

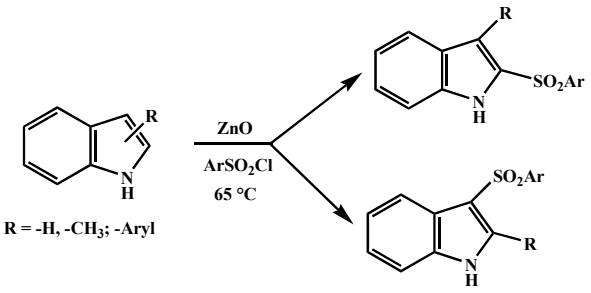

Figure 2

The highly regioselective reaction, carried out in solvent-free conditions and in the presence of ZnO, provided all the C- indolyl aryl sulfones in good yields and short reaction times. Moreover, all the involved parameters have been investigated, paying particular attention at the role of the oxide and the effect of the substituents on the aromatic rings.

Acknowledgements. This work was supported by Progetto Di Ricerca Fondamentale o di Base "Processi e metodologie innovative orientate alla preparazione di sistemi eterociclici bioattivi" (L. R. n° 7, 2007, Bando 2008).

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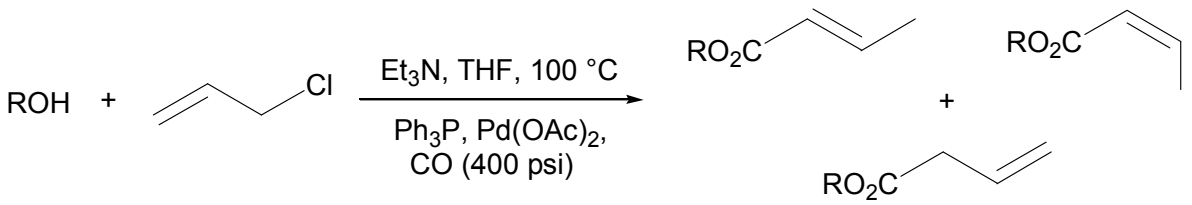
ORG-PO-118 One-Pot Ester Synthesis from Allyl or Benzyl Halides and Alcohols by Pd-Catalyzed Carbonylation

Sara Tommasi, Serena Perrone, Francesca Rosato, Antonio Salomone, Luigino Troisi

Dipartimento di Scienze e Tecnologie biologiche ed Ambientali, University of Salento, Via Prov.le Lecce-Monteroni, 73100, Lecce, Italy
E-mail: sara_tommasi@hotmail.it

Esters are widely found among all naturally occurring compounds, and are also greatly important intermediates in organic synthesis [1].
The ester bond is one of the most common linkages in organic chemistry and could be formed by different strategies using acids, anhydrides or chlorides with alcohols as starting substrates [2]. The reactions proceed with or without the help of a base or an acid and also with or without a metallic catalysis [3]; among metals used as catalyzers one of the most common is Palladium.

In this contribution we report a mild and efficient one-pot synthesis of esters based on the Pd-catalyzed alkoxy- and aryloxycarbonylation of allylic or benzylic halides. The methodology is applied to primary, secondary and tertiary alcohols as well as to phenol derivatives. The *O*-protection of some biologically relevant molecules is also reported.



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ORG-PO-119 New HIV-1 Protease Inhibitor bearing a benzothiophene as the P2-ligand: easy structure and effective activity.

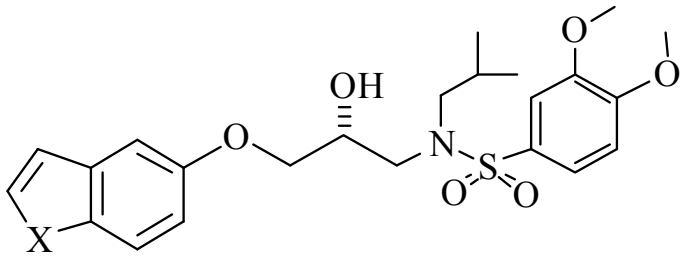
Francesco Tramutola[†], Lucia Chiummiento[†], Maria Funicello[†], Paolo Lupattelli[†], Adrian Ostric[‡].

[†]Dipartimento di Chimica "A.M. Tamburro", Università degli Studi della Basilicata, Via dell' Ateneo Lucano 10, 85100 Potenza, Italy.

[‡]Dipartimento di Scienze Chimiche, Università degli Studi di Trieste, Via Giorgieri 1, 34127 Trieste, Italy.

francesco.tramutola@unibas.it

Since protease inhibitors (PIs) have been employed to combat AIDS, HIV infection has definitely become more manageable [1]. However some complex issues associated to these drugs remain unsolved. This has led scientific community to seek novel structures able to overcome such problems [2]. Working on this direction, we recently demonstrated the positive effect of a heteroaromatic group in a series of new thienyl ring containing analogues of two approved PIs, Nelfinavir and Saquinavir [3]. Moreover, we also reported the facile synthesis and the biological evaluation of a new non-peptidic PI (**1**) with an IC50 of 1 μM [4]. On the basis of this result, we have therefore been really intrigued by understanding the actual importance of the NH indolic function regarding the efficiency of **1**. Thus, we alternatively introduced a methyl or a benzyl group on the nitrogen and then switched the heteroatom to oxygen or sulfur. As it is highlighted in figure 1 we have found that the heteroaromatic moiety plays a crucial role in the biological activity of our molecules. Particularly the presence of a benzothiophene affords a significant improvement in IC50. In the present communication we report in detail the results of our investigation.



Inhibitor	X	IC50 (μM)
1	NH	1
2	NMe	>1000
3	NBn	>1000
4	O	130
5	S	0.06

Figure 1

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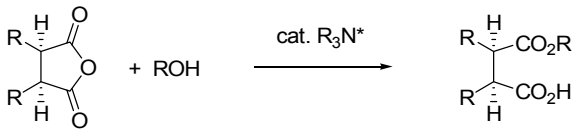
ORG-PO-120 From Cinchona alkaloids catalysts to Chiral Solvating Agents for NMR spectroscopy

Gloria Uccello Barretta, Federica Balzano, Beatrice Di Nicola, Alessandro Mandoli

Dipartimento di Chimica e Chimica Industriale dell'Università di Pisa, Via Risorgimento 35, 56126 Pisa, Italy
gub@dcci.unipi.it

Cinchona alkaloids play a key role in several chiral recognition processes. Their efficiency and versatility as chiral auxiliaries in catalysis and in the direct spectroscopic and chromatographic determination of enantiomeric excesses have been recognized since long time. In particular 9-*O*-ether derivatives of quinidine are valuable organocatalysts employed in the asymmetric alcoholysis of *meso*-anhydrides (Scheme 1).



Scheme 1

In an attempt to give a contribution to the knowledge of such a desymmetrization process, we carried out an accurate NMR investigation on the ground state conformation of mono and bis-9-*O*-pyridazine and anthraquinone derivatives of quinidine in the reaction solvent and in the presence of the reactants (cis-1,2,3,6-tetrahydrophthalic anydride and alcohol) or the reaction products. In the course of this investigation the potential of the alkaloid derivatives as chiral solvating agent for the in situ determination of the enantiomeric excesses of the reaction products was also demonstrated, and further confirmed by examining several mixtures containing different alkaloid derivatives and products of the asymmetric alkoholysis (Figure 2).

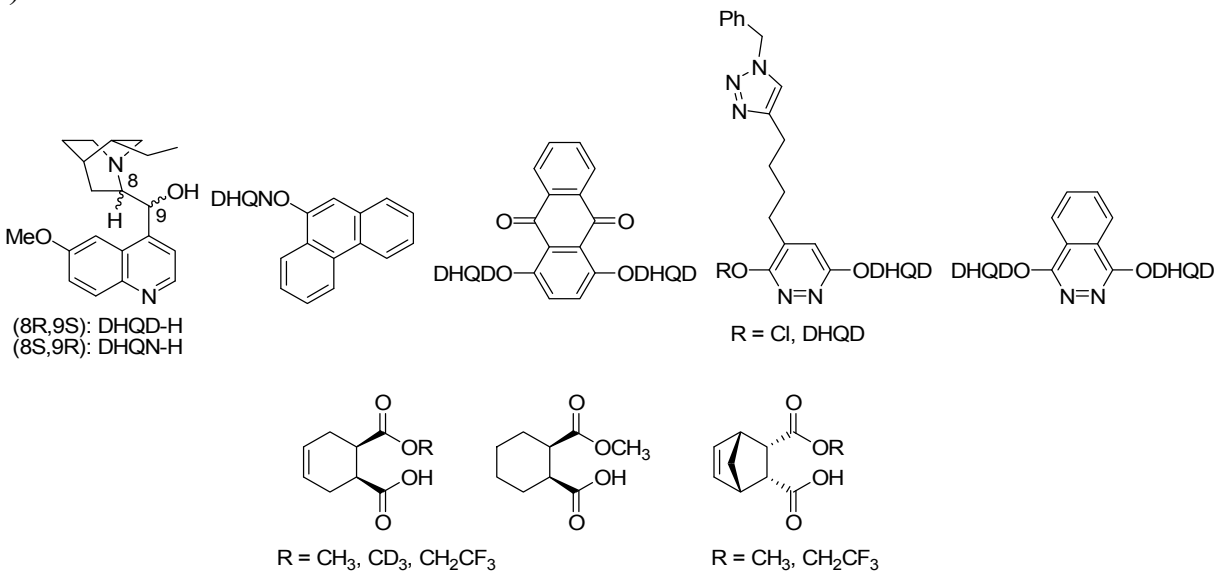


Figure 2

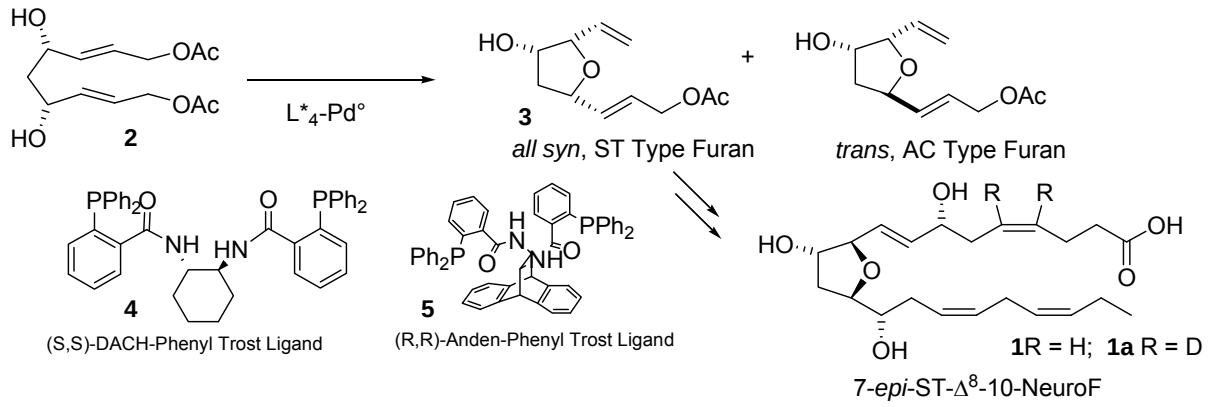
ORG-PO-121 The First Enantioselective Synthesis of a D_2-Neurofuran

M. Valli, P. Bruno, A. Porta, G. Zanoni, G. Vidari

Dipartimento di Chimica dell' Università di Pavia, Via Taramelli 12, 27100 Pavia, Italy
e-mail: alessio.porta@unipv.it

Neurofurans [1] are C-22 compounds formed, under extensive oxidative stress conditions, by ROS, free radical mediated, peroxidation of docosahexaenoic acid (DHA) esterified to neuronal phospholipids. Measurement of the neurofurans may ultimately prove useful in diagnosis, timing and selection of dose in the treatment and chemoprevention of neurodegenerative diseases, such as Alzheimer's and Parkinson's. Moreover, biological activities of neurofurans are still unknown, as well as their possible interferences with the DHA signalling pathway.

In this work we report the first total synthesis of a neurofuran, namely 7-*epi*-ST-Δ^8-10-NeuroF (**1**). The synthesis features the optimization of a general approach to the 3-hydroxy-1,2-dialkyl trisubstituted heterocyclic core, which is based on the desymmetrization of *meso*-diol **2**. Thus, the all-*syn*-furan **3** was obtained in good diastereo- and enantioselectivity via Trost's Pd(0)-catalysed allylic etherification of **2**, using the DACH and Anden chiral ligands **4** and **5**. Subsequently, the two side chains were installed with complete stereocontrol. In particular, hydrogenation of an alkyne unit with the Lindlar catalyst allowed for the preparation of **1** as well as the 4,5-D_2-derivative **1a**.



Our synthetic pathway can readily be extended to the preparation of other neurofurans, including T-labelled derivatives, for the study of their metabolism *in vivo*.

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ORG-PO-122 CHEMICAL SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME STYRYLHETEROCYCLES

Angela Viglianti[a], Roberto Antonioletti[b], Alessandra Ricelli[b], Francesca Massi[a], Francesco Caruso[b], Leonora Mendoza[c], Andrea Leonelli[a]

[a]Department of Chemistry, Sapienza University of Rome, P.le Aldo Moro,5– 00185 Roma; [b]Institute of Biomolecular Chemistry-CNR, P.le Aldo Moro,5 – 00185 Roma; [c]Faculty of Chemistry and Biology, Santiago University, Avenida Bernardo O'Higgins 3363, Santiago, Chile.
email: angela.viglianti@uniroma1.it

The stilbene scaffold is known to hold several biological activities (antioxidant, antiinflammatory, antifungal) considered beneficial for human health [1]. Resveratrol (*trans*-3, 4', 5-trihydroxystilbene) is a naturally occurring polyphenol stilbenoid found in grapes and in a multitude of dietary plants. This molecule is synthesized by plants in response to environmental stress and fungal infections and is known to be involved in defense mechanisms [2].

In this work we present the synthesis of different styrylheterocycles (2÷3-furyl, 2÷3-thienyl, 4-pyridyl derivatives) through Wittig reaction using LiOH as base [3]. We also studied the antifungal activities of these molecules against *Botrytis cinerea*, a phytopatogenic fungus that attacks flowers, fruits, leaves, and stems of more than 200 plant species, the antioxidant properties of the synthesized molecules and their possible control action on Ochratoxin A (OTA) biosynthesis.

OTA is a mycotoxin produced by several species of fungi belonging to *Aspergillus* and *Penicillium* genera naturally occurring in a variety of food commodities. OTA has been shown to be carcinogenic, nephrotoxic and teratogenic to animals and is suspected to be involved in tumors of the upper urinary tract in humans [4]. OTA biosynthesis is influenced by the presence of peroxides in the environment and some antioxidants like resveratrol inhibits it [5].

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ORG-PO-123 Panchromatic *trans*-di-thiocyanato Ru(II) sensitizer for dye-sensitized solar cells

Viscardi Guido,[a] Barolo Claudia,[a] Artuso Emma,[a] Quagliotto Pierluigi,[a] Barbero Nadia,[a] Park Jinhyung,[a] Bonandini Luca,[a] Claudio Magistris,[a] Buscaino Roberto,[a] Yum Jun-Ho,[b] Nazeeruddin Mohammad Khaja,[b] Grätzel Michael.[b]

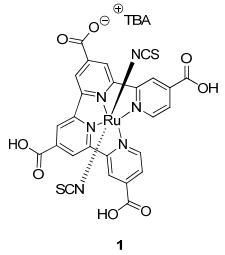
[a] Dip. di Chimica Generale e Chimica Organica and NIS Interdepartmental Center of Excellence, Università degli Studi di Torino, C.so M. d'Azeglio 48, 10125, Torino, Italy

[b] Laboratory for Photonics and Interfaces, ISIC, SB, Swiss Federal Institute of Technology, CH - 1015 Lausanne, Switzerland

guido.viscardi@unito.it

The heart of a DSC is a mesoporous titania film composed of nanometer sized particles with a monomeric layer of a sensitizer [1]. 2,2′-Bipyridine-based Ru(II) complexes have been by far the most investigated and efficient systems [2] (i.e. N3 and N719) yielding a conversion efficiencies over 11% (AM 1.5) [3]. The optimal sensitizer for DSCs should be panchromatic with an absorption spectrum extended throughout the visible and the NIR region. The aim of this research is to produce tetradentate ligands that provide stable *trans* configuration in the corresponding panchromatic Ru (II) complexes. Quaterpyridine ligands are suitable for this purpose and they are still largely unexplored [4]. The main drawback until now has been the long synthetic pathway to get the ligands as well as the repeated purification steps required by the corresponding complexes.

Here we report a new easy and reliable synthetic pathway for the quaterpyridine ligand and the related panchromatic *trans*-Ru(II) complex **1** that can be simply transferred to the analogous compounds. The purification step has been settled upon a standard chromatographic silica column giving a highly pure complex with an overall photovoltaic conversion efficiency of 6.30% at standard AM 1.5 sunlight, that is the best efficiency reported up to now for tetradentate ligand-based Ru(II) complexes. In addition, a photocurrent, 19 mA/cm2 at standard 1.5 sunlight, was obtained by tuning the used electrolyte.



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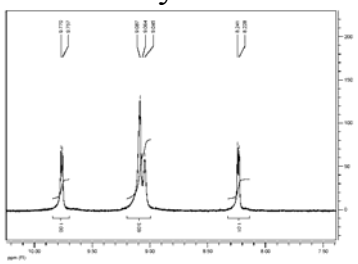

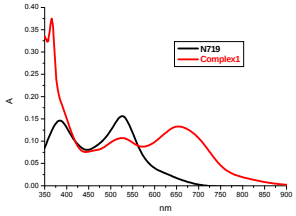

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ORG-PO-124 Synthesis, Structure and Biological Activity of Sulfated Tri Maltose α,α and α,β C-C-linked Dimers

E. Vismara,[a] A. Valerio,[a] L. Borsig,[b] I. Vlodavsky,[c] A. Naggi,[d] S. Pacifico,[d] G.Torri.[d]

[a]Dipartimento di Chimica, Materiali e Ingegneria Chimica 'G.Natta' Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milano, Italy.

[b]Zürich Center for Integrative Human Physiology, Institute of Physiology, University of Zürich, 8057 Zürich, Switzerland.

[c]Cancer and Vascular Biology Research Center, Bruce Rappaport Faculty of Medicine, Technion, Haifa, Israel.

[d]Istituto di Ricerche Chimiche e Biochimiche "G. Ronzoni" via G. Colombo 81, 20133 Milano, Italy.

elena.vismara@polimi.it

Large efforts have been addressed to isolating sequences of natural oligosaccharides, which possess a significant biological function, and to preparing synthetic oligosaccharides, that have been designed to mimic the natural ones. We moved to building up mixed O/C malto-oligosaccharides and to check whether or not their sulphated forms would mimic natural malto-oligosaccharide. Sulfated tri maltose C-C-linked dimers (α,α and α,β STMCs) were prepared by halo-maltotriose electroreduction [1] on silver cathode followed by sulfation. The sugar chains of these mimics are characterised by the presence of an interglycosidic C-C bond which are less vulnerable to metabolic processing then their O-analogues and for this reason have been studied as drug candidates and inhibitors of carbohydrate processing enzymes. The presence of the interglycosidic C-C bond is an important feature because, as shown by a molecular modelling conformational analysis, it modifies the geometry of the sugar chains and makes their conformation rigid. Actually, the conformational flexibility of oligosaccharides is critical in determining their binding to protein and consequently their bioactivity.

Development of compounds that target both heparanase and selectins is emerging as promising approach for cancer therapy. The P-selectin specificity of STMCs was defined by the anomeric linkage of the C-C bond. α,β SMTC is an effective inhibitor of P-selectin *in vivo* and attenuated metastasis both on B16-BL6 melanoma cells and on MC-38 carcinoma cells indicating that inhibition of tumor cell interaction with the vascular endothelium is critical for cancer dissemination. α,α SMTC attenuated metastasis in B16-BL6 melanoma cells, expressing high levels of heparanase, but it is not an inhibitor of P-selectin and did not attenuate metastasis on MC-38 carcinoma cells. [2]

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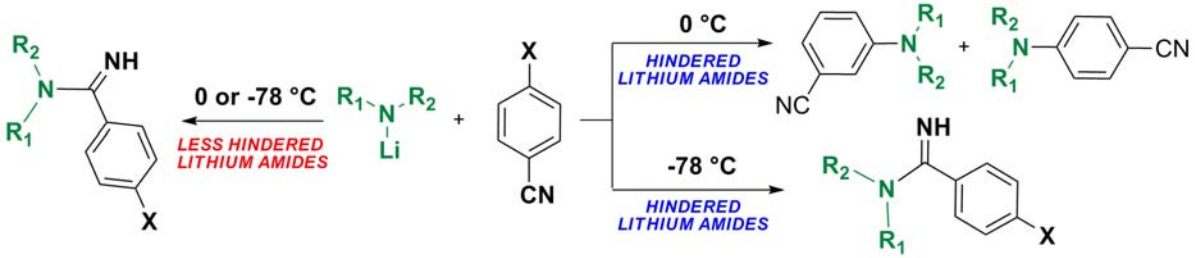
ORG-PO-125 Synthesis of *N*,*N*-dialkylaminobenzonitriles and halo-(*N*,*N*-dialkyl) benzamidines by reaction of halobenzonitriles with lithium amides.

Paola Vitale, Leonardo Di Nunno, Antonio Scilimati
Dipartimento Farmaco-Chimico, Università degli Studi di Bari "A. Moro"
Via E. Orabona, 4, 70125, Bari, Italy
paola.vitale@farmchim.uniba.it

Aminobenzonitriles are important targets in organic synthesis, due to their application as electron donor–acceptor (EDA) molecules, as probes to study material properties [1], for the development of optical switches, and for the potential conversion of photon energy into electricity. The photodynamics of some 4-(dialkylamino)benzonitriles have been studied by time-resolved X-ray diffraction [2-3], femtosecond UV/Vis and mid-IR absorption spectroscopy, both on single crystal or solubilized in polar/non polar solvents [4-5], because these compounds often undergo dual fluorescence and fast intramolecular charge transfer (ICT) reactions. Various starting materials and synthetic strategies, mainly based on transition-metal catalytic processes [6], are used to prepare these compounds. Herein, we report a simple approach to *N*,*N*-dialkylaminobenzonitriles by reacting halobenzonitriles with hindered lithium amides.

3- and 4-*N*,*N*-dialkylaminobenzonitriles and 4-chloro-(*N*,*N*-dialkyl)benzamidines were isolated by reacting 4-chlorobenzonitrile with hindered lithium amides under thermodynamic (0 °C) and kinetic control conditions (-78 °C), respectively (Figure). As previously reported [7], a benzyne mechanism seems to be confirmed when *N*,*N*-dialkylaminobenzonitriles are formed. Only benzamidines were isolated in fair to high yields at both 0 °C and -78 °C with not hindered lithium amides. Exploitation and mechanistic rationale of the reaction of different halobenzonitriles will be reported.



Figure

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ORG-PO-126 Enantioselective bio-reduction of prochiral ketones by the non-conventional yeast *Kluyveromyces marxianus*

Paola Vitale, Filippo Maria Perna, Maria Grazia Perrone, Antonio Scilimati

Dipartimento Farmaco-Chimico, Università degli Studi di Bari "A. Moro", Via E. Orabona, 4, 70125, Bari, Italy
paola.vitale@farmchim.uniba.it

Optically active molecules are important building blocks for the synthesis of many chemicals and biologically active compounds. Among the known catalysts, isolated enzymes have some advantages over conventional methods in the asymmetric synthesis, such as chemo-, regio-, and stereo-selectivity, together with very mild reaction conditions [1].
The asymmetric synthesis accomplished by using whole-cells has also further advantages [2, 3] because all the necessary cofactors and all required substances for their regeneration are present in their natural environment, thus making the catalytic system more efficient [4].
Many research groups have focused their attention on looking for non-conventional yeasts, to study in comparison to the deeply investigated *Saccharomyces cerevisiae* [5].
For several years our interests focused on using non-conventional yeasts to prepare new EPCs: among these, thermotolerant *Kluyveromyces marxianus CBS 6556*, not widely investigated in asymmetric synthesis, was preliminarly and successfully used by us for the stereoselective bioreduction of prostereogenic keto-esters to prepare optically active building-blocks in the synthesis of pharmacologically active compounds [6, 7]. These studies allowed also the isolation of an unkown ADH from this yeast [8], able to mediate the highly stereoselective bioreduction of prostereogenic 3-oxo esters. Herein, we report the continuation of such studies, in which the *Kluyveromyces marxianus CBS 6556* is used in the bioreduction of various prochiral ketones, with the aim to deepen its substrate specificity, turnover rate, regio- chemo- and enantioselectivity.

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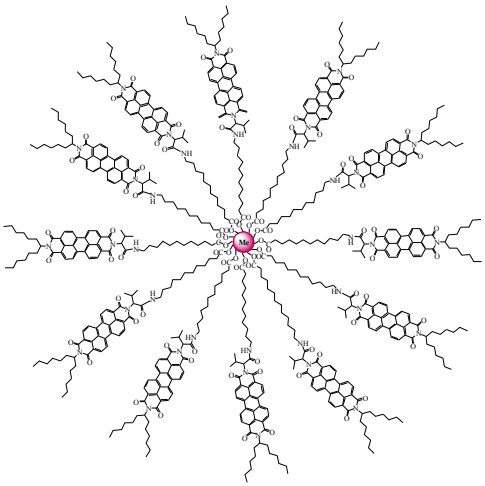
ORG-PO-127 Synthesis and characterization of long-chain carboxylic acids with fluorescent end-groups as organic building-blocks for self-assembly on noble-metal nanostructures.

Stefania Zappia, Marina Alloisio, Anna Demartini, Giovanni Petrillo, Sergio Thea.
Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Genova, via Dodecaneso 31, 16146, Genova
stefaniazappia@libero.it

Self-Assembled Monolayers (SAMs) of organic compounds can be prepared through the adsorption of suitable organic molecules from solution onto metal planar surfaces (2-D SAMs) or three-dimensional nanoparticles (3-D SAMs).

The photophysical properties of the 3-D nanohybrids so obtained are closely related to the nature of the groups situated at the end of the organic chain: in particular, fluorescent end-groups provide the material with unique optical properties than can be exploited for various applications, such as biosensors and photovoltaic and optoelectronic devices.



Thiols, disulfides and carboxylic acids are extensively used to prepare SAMs on noble metals [1]. In the case of SAMs on Ag, long-chain carboxylic acids allow better results in terms of stability of the obtained nanohybrids [2-4].

In the communication we present our recent results on the synthesis and on the absorption and emission characterization of long-chain carboxylic acids possessing a chiral aminoacid residue (introduced to allow their study by circular dichroism, useful to get information on their spatial arrangement on the surface of the nanoparticles) and endowed with a fluorescent end-group (e.g. perylene in the figure), and on the preparation and characterization of the noble-metal nanohybrids obtained from them.

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ORG-PO-128 Phytochemical Analysis of Tomato Roots

Pascale R.[a], Argentieri MP. [a], D'Addabbo T. [b], Leonetti P. [b], Arnesano F. [a], Luisi R. [a], Avato P. [a]

[a]Dipartimento Farmaco-Chimico, Università, Via Orabona 4, I-70125 Bari, Italy
[b]Istituto per la Protezione delle Piante, CNR, Via Amendola 165/a, I-70126 Bari, Italy
rossanapascale@farmchim.uniba.it

Plants are a rich source of biologically active compounds which often act as natural barriers against the attack of pathogens and determine plant resistance or susceptibility to pests. Numerous plant species have been already reported to contain metabolites with biocidal activity and there is a continuous effort in discovering new natural sources [1] for compounds toxic to phytoparasites.

Tomato represents an important agricultural crop, typical of the mediterranean areas, which can undergo to high yield loss due to phytonematodes. As a part of a research program [2] aimed to discover natural biocides from plant extracts, we have evaluated the phytochemical profile of tomato roots resistant and susceptible to nematodes.

We applied a metabolomic approach based on the use of HPLC/PDA/ELSD, LC/MS and NMR. The analytical study showed that the methanolic extract obtained from the plant roots was rich in glycoalkaloids, phenolic compounds and primary polar metabolites such as organic acids and amino acids. Content of these metabolites is discussed and related to nematode resistance or susceptibility of the investigated tomato roots.

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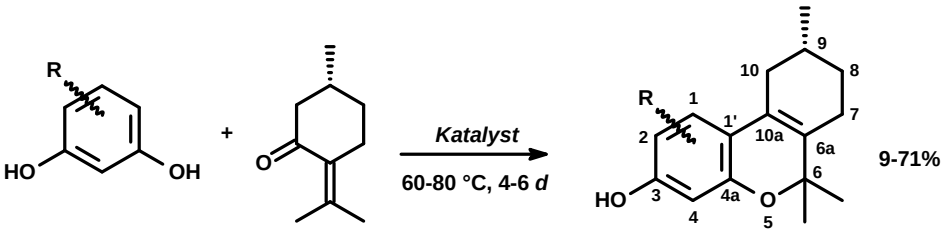
ORG-PO-129 Heterogeneous catalysis in the synthesis of tetrahydrocannabinol analogues

Ornelio Rosati,[a] Massimo Curini,[a] Maria Carla Marcotullio,[a] Federica Messina,[a] Claudia Chiesi.[a]

[a] Dipartimento di Chimica e Tecnologia del Farmaco, Università degli Studi, Via del Liceo 06123 Perugia, Italy

ornros@unipg.it

Tetrahydrocannabinols are important natural occurring compounds that recently have found some important applications in pain therapy [1].
Despite a wide range of syntheses of natural tetrahydrocannabinols and analogues reported in the literature since 1940 [2], a lack in the field of heterogeneous synthetic approach to tetrahydrocannabinols and analogues exists. We investigated the possibility to synthesize tetrahydrocannabinol analogues starting from (*R*)-(+)-pulegone and several resorcinol derivatives via heterogeneous catalysis.



To achieve this project we used different heterogeneous solid acid catalysts, such as α-zirconium sulphophenyl phosponate/methanphosphonate [3], ytterbium triflate [4] and supported sulfuric acid on silica gel [5]. Interesting results were obtained and a comparison of the activity between the different solid acid catalysts is possible. In all entries the reaction showed a particular regioselectivity towards 3-hydroxy derivatives and a possible reaction mechanism can be also hypothesized.

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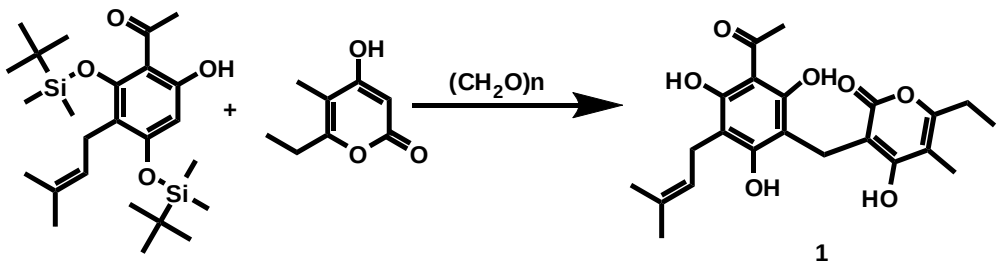
ORG-PO-130 Multicomponent reactions beyond the iminium ion trail: total synthesis of arzanol, the anti-inflammatory principle of eternelle (helicrysum italicum l.)

L. Cicione, A. Minassi*, G. Appendino

DiSCAFF, Via Bovio6, 28100 Novara, Italy,
cicione@pharm.unipmn.it

Multicomponent reactions (MCR) are based on the combination of more than two starting materials, and are characterized by high atom economy. Therefore, they represent a premium strategy compared to one-pot reactions. Most MCR are based on the formation of amide and ester bonds, do not generally involve the generation of more than two carbon-carbon bonds, and are triggered by nucleophilic attack to an iminium ion. Non-iminium ion based MCR have not yet received systematic attention, despite their relevance in polyphenolic chemistry. To fill this gap, we have started a methodology study aimed at the generation, in a MCR-fashion, of aryl-heteroarylmethanes, an important class of natural products.
Our interest for this class of compounds was fostered by the remarkable bioactivity of the prenylated phloroglucinyl(pyronyl)methane arzanol (**1**) the major anti-inflammatory, antibiotic, and anti-oxidant principle of everlasting (*Helichrysum italicum*).[1] With the ultimate aim of developing a total synthesis of **1** and related heterodimeric pyrones, we have embarked in a systematic study on the synthesis of *gem*-(β-dicarbonyl)arylmethanes, evaluating the possibility of obtaining this type of compound in a multicomponent fashion by combination of a carbonyl derivative with equimolar amounts of a β-dicarbonyl and an electron-rich aromatic derivative.[2] We will present our methodological studies in the area and their application to the total synthesis of arzanol and to the generation of analogues.



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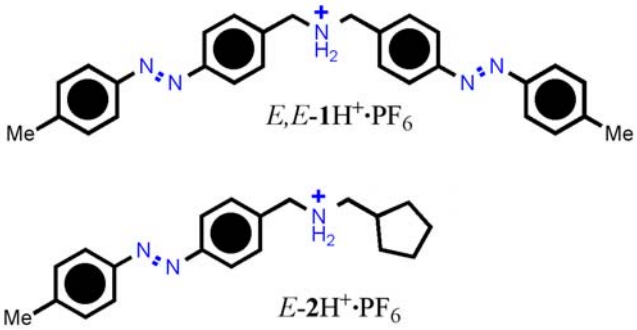
ORG-PO-131 Photocontrol of the direction of Threading/Dethreading in Pseudorotaxanes

Massimo Baroncini[a], Serena Silvi[a], Alberto Credi[a], Margherita Venturi[a]

[a] Department of Chemistry "G. Ciamician", University of Bologna via Selmi 2 40126 Bologna, Italy.
baroncini@isof.cnr.it



The design, synthesis and operation of supramolecular systems that exhibit controllable motions of their components is a topic of great interest in nanoscience and constitute a fundamental premise for the construction of molecular machines and motors. Rotaxanes are a class of supramolecular systems in which a ring encloses another rod-like component having bulky end groups too large to let the ring pass through. Pseudorotaxanes share the same supramolecular arrangement but have less bulky end groups that permit fast slippage and extrusion of the ring component[1]. In previous work we have shown how to control the rate of threading/dethreading motions (i.e. rotaxane-likeness) of a pseudorotaxane system (*E,E*-**1**$H^+ \cdot PF_6$) exploiting the photoisomerization of its azobenzene end groups[2]. In this work we present a more elaborate system that allows the control of the direction of threading/dethreading motions. The system is composed of a benzylamine axle terminated with two different end groups: an azobenzene unit at one end and a cyclopentane at the other (*E*-**2**$H^+ \cdot PF_6$). The axle is able to rapidly thread in solution through a dibenzo24crown8 ether (**DB24C8**) wheel from the azobenzene end to yeld a (2)pseudorotaxane[3]. Irradiation of *E*-**2**$H^+ \cdot PF_6$ with 457nm light induces quantitative photoisomerization to the *Z* stereoisomer forcing the system to dethread, under the influence of an appropriate input, from the cyclopentane end. The detailed kinetic analysis carried out show that the photoisomerization of the azobenzene end group of **2**$H^+ \cdot PF_6$ allow the control of the direction of threading and dethreading. The ability to control the direction of threading/dethreading is an essential step toward the ambitious goal of extracting useful work from the molecular motions of this kind of supramolecular systems.

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ORG-PO-132 New Benzothiadiazole- Containing Polymers as Donor in Bulk Heterojunction Solar Cells

Giovanni Allegretta,[a,b] Roberto Grisorio,[b,c] Piero Mastrorilli,[b] Gian Paolo Suranna,[b] Marco Mazzeo,[c] Giuseppe Gigli, Silvia Colella,[a,c] Giovanna Melcarne[a,c]

[a] National Nanotechnology Laboratory CNR – Istituto Nanoscienze U.O.S. Lecce, Italy (I). [b] Università del Salento, scuola superiore ISUFI, Lecce, (I). [c] Department of Innovation Engineering, Università del Salento, Campus Universitario, Lecce, (I). [d] Department of Water Engineering and of Chemistry, Polytechnic of Bari (I)
E-mail: r.grisorio@poliba.it

The scientific interest devoted to poly(arylene-vinylene)s (PAV) is currently looking forward to their use in solar cells [1]. The use of vinylene-linked donor and acceptor units could in fact bring about advantages connected with the extension of the conjugation length with respect to the corresponding poly(arylene)s. Aiming at exploiting the benzothiadiazole (BTZ) building block in PAV donor-acceptor architectures, we have carried out the Suzuki-Heck copolymerization, that allows access to several PAV architectures by a palladium catalysed copolymerization between aryl dibromides and potassium vinyl-trifluoroborate.[2] The reaction was applied to the preparation of novel random PAVs embodying BTZ in different amounts with respect to 9,9-bis(2-ethylhexyl)fluorene or 1,4-bis(2-ethylhexyloxy)benzene.

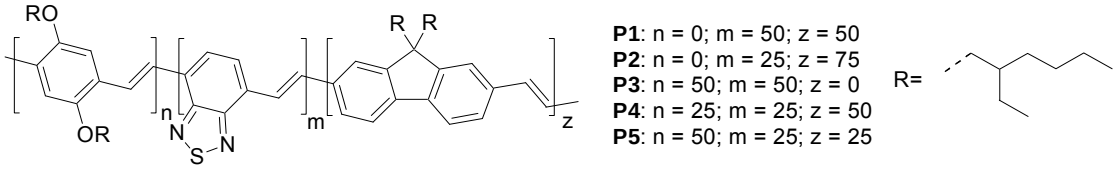

Figure 1.

The optical, electrochemical, and thermal properties of the polymers **P1-5** will be discussed as well as their photovoltaic properties that were investigated in BHJ devices with configuration: ITO/PEDOT-PSS/**P1-5**:PCBM/Al. The terpolymer **P5** resulted the most efficient (PCE = 0.4%, V_{oc} = 0.76 V) and its performances could be justified in terms of the good film forming properties of the polymer/PCBM blend, as indicated by AFM investigations. These results allowed us to conceive a modification of the above mentioned polymeric architecture obtained extending either the benzothiadiazole (**P6**) or the fluorene (**P7**) conjugation with thienyl groups, obtaining an improved PCE for **P6** (0.59%, V_{oc}=0.67V).

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ORG-PO-133 $NiSiO_2$ catalyst immobilisation on glass microreactor for Kumada Corriu continuous flow reaction

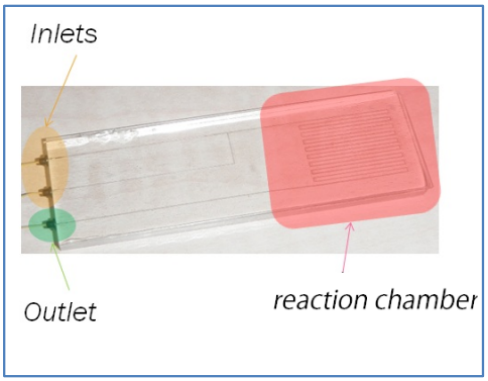
Lucia Marra*[a] , Vincenzo Fusillo[b] , Charlotte Wiles[b], Paul Watts[b], Ross Rinaldi[a] and Valentina Arima[a],

[a] National Nanotechnology Laboratory (CNR- Istituto di Nanoscience) - Distretto Tecnologico ISUFI - Università del Salento, via Arnesano, 73100 Lecce, Italy
[b] Department of Chemistry, University of Hull, Cottingham Road, Hull, UK HU6 7RX
Corresponding author: lucia.marra@unisalento.it

I

n the last decade new generation of chemists are exploiting continuous-flow microreactor as innovative tool for chemical synthesis. This technology appears really promising in the field of catalytic reactions. With smaller volume of solvents, they are less wasteful[1-3]. Moreover reactions can be carried out significantly faster than those in batch, with increases both in yield and selectivity.

In this work we describe a new method for the deposition of Ni-SiO_2 catalyst in a multichannel micro reactor and demonstrate its performances for the production of biaryl compounds.



Silica supported nickel catalyst (Ni/SiO_2) is prepared by sol-gel technique and immobilized inside a glass microreactor. Tetraethoxysilane (TEOS) and nickel nitrate hexahydrate ($Ni(NO_3)_2 \cdot 6H_2O$) are used as precursors. A mesoporous silica matrix with a high specific surface area (387 m^2/g) and average pore size in the range of 11 nm is obtained.

Its catalytic activity is demonstrated in a room temperature cross-coupling Kumada Corriu reaction. The obtained yields and reaction times of biaryl compound, compared with those of traditional batch reaction processes, confirme once again the advantages of on-chip organic synthesis.

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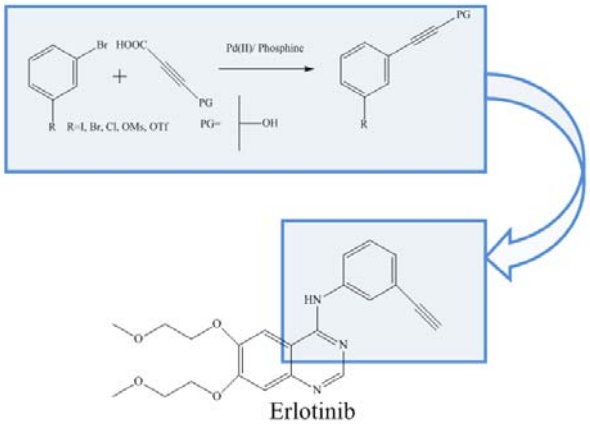
ORG-PO-134 Decarboxylative Cassar-Sonogashira Coupling Reactions. Synthesis of a key intermediate of Erlotinib

Caporale A.[a, b], Tartaggia S.[a] , Fabris F.[a] , Castellin A.[b] and De Lucchi O.[a]

[a] Dipartimento di Scienze Molecolari e Nanosistemi, Calle Larga S. Marta, Dorsoduro 2137, 30123 Venezia
[b] F.I.S. Fabbrica Italiana Sintetici, Via Milano 26b, 36075 Montecchio Maggiore (Vicenza)
e-mail: andrea.caporale@unive.it

In recent years, the development of decarboxylative coupling reactions of propiolic acid derivatives on aryl halides and pseudohalides [1] emerged as a convenient approach to the synthesis of acetylenic compounds with respect to the conventional Cassar-Sonogashira coupling reaction of terminal alkynes. In the last years, several optimized protocols for decarboxylative couplings of alkynyl carboxylic acids with aryl and benzyl halides with low catalyst loading [2] and Pd-free decarboxylative cross-couplings catalyzed by copper [3] were reported. The coupling reaction of propiolic acid derivatives usually gives disubstituted symmetrical and unsymmetrical acetylenes [4], while the preparation of terminal alkynes by using this approach, at the best of our knowledge, has not been reported.



Herein, we present a protocol for the preparation of terminal alkynes from propiolic acid which was applied to the synthesis of the active pharmaceutical ingredient Erlotinib [5].

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ORG-PO-135 Synthesis and Self-Assembly of Oligo(p-phenylenevinylene) Peptide Conjugates in Water

Miriam Mba,[a] Alessandro Moretto,[a] Lidia Armelao,[b] Marco Crisma,[c] Claudio Toniolo[a] and Michele Maggini[a]

[a] Department of Chemical Sciences, University of Padova, Italy.
[b] ISTM-CNR, INSTM, Dept. of Chemical Sciences, University of Padova, Italy
[c] ICB, CNR, Padova Unit, Dept. of Chemical Sciences, University of Padova, Italy
miriam.mba@unipd.it

Self-assembly (SA) of functionalized oligo(*p*-phenylenevinylene)s (**OPV**) gives organogels with interesting photophysical properties and potential applications in light-emitting diodes, light-harvesting systems or thermal imaging [1]. Organized, robust molecular structures are difficult to obtain by π-π stacking alone, therefore, a variety of promoters able to establish additional noncovalent interactions, such as directional hydrogen bonds, have recently received increasing attention. Among them, we have envisaged the use of peptide amphiphiles, made of a π-conjugated unit and carefully selected peptide sequences. These structures have a strong tendency to form well-defined secondary structures and to self-assemble in water [2].
Here we present the synthesis of a new OPV ω-amino acid that has been incorporated into two β-sheet-forming sequences through solid-phase protocols. The resulting peptide hybrids are soluble in water and reversibly self-assemble to a stable, fluorescent hydrogel upon pH changes [3].

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ORG-PO-136 2,3-dihydro-1H-indan-1-one: useful building blocks for the synthesis of novel molecular photo-switches.

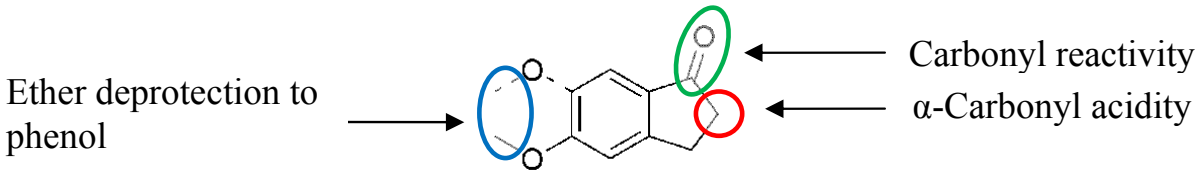
Giacomo Guerrini[a], Riccardo Rossi Paccani[a], Fabio Ponticelli[a] and Massimo Olivucci[a,b]

[a] Dipartimento di Chimica, Università di Siena, Via Aldo Moro 2, 53100 Siena, Italy

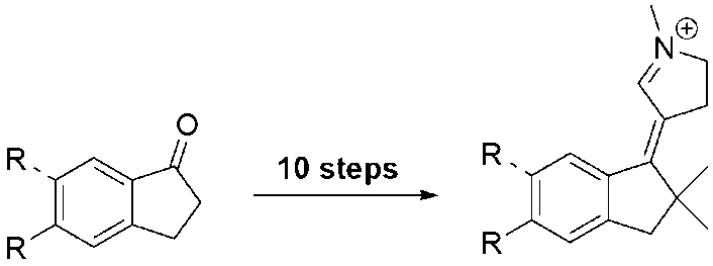
[b] Department of Chemistry, Bowling Green State University , Bowling Green, Ohio 43403, United States

giacomoguerrini@unisi.it

Following our interest in the synthesis of novel biomimetic photo-switches[1] we explored the reactivity and the possibility of functionalization of an important class of molecules, indan-1-ones. These molecules have three functionalizable sites due to the presence of a carbonyl group and one or two methoxy groups in position 5 and 6 that can be deprotected to phenol and alkylated.



Starting from this molecular scaffold we got a library of functionalized indan-1-ones that have been employed in the synthesis[2] of some new photo-isomerizable molecular switches.



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