11th Spanish-Italian Symposium on Organic Chemistry

SISOC XI

Società Chimica Italiana-Real Sociedad Española de Química

Donostia-San Sebastián, July 13-15, 2016
FICE Building, University of the Basque Country UPV/EHU

_____

BOOK OF ABSTRACTS

SCIENTIFIC COMMITTEE

Bosch, Joan	University of Barcelona
Conte, Valeria	University of Roma (TorVergata)
Farinola, Gianluca	University of Bari
Fernández, Rosario	University of Seville
Gennari, Cesare	University of Milano
González, José Manuel	University of Oviedo
Iesce, Maria Rosaria	University of Napoli "Federico II"
Jiménez-Barbero, Jesús	CICbioGUNE (Bilbao)
Martín, Víctor S.	University of La Laguna-CSIC
Noto, Renato	University of Palermo
Saá, Carlos	University of Santiago de Compostela
Tecilla, Paolo	University of Trieste

ORGANIZING COMMITTEE

(Departamento de Química Orgánica I, Universidad del País Vasco UPV/EHU)

Claudio Palomo (President)
Mikel Oiarbide
Iñaki Ganboa
Rosa López
Antonia Mielgo
Aitor Landa
Silvia Vera

ORGANIZERS

Società Chimica Italiana (SCI)

Real Sociedad Española de Química (RSEQ-GQOR)

SPONSORING

Società Chimica Italiana (SCI)

Real Sociedad Española de Química (RSEQ-GQOR)

—•—•—•—•—•—•—

Eusko Jaurlaritza - Gobierno Vasco

University of the Basque Country UPV/EHU

—•—•—•—•—•—•—

Lilly

Merck

Waters

Oppac

Gilson International

PharmaMar

Mestrelab

Panreac

SISOC I	1992	Valencia
SISOC II	1998	Lecce
SISOC III	2000	Málaga
SISOC IV	2002	Perugia
SISOC V	2004	Santiago de Compostela
SISOC VI	2006	Taormina
SISOC VII	2008	Oviedo
SISOC VIII	2010	Padova
SISOC IX	2012	Tenerife
SISOC X	2014	Firenze

Wednesday, July 13 **Venue: FICE Building**		
8:30	Registration	
	Aula Magna	
9:00	Opening	
	Chairperson: Joan Bosch	
9:30	**IL-1 Paolo M. Scrimin**	
10:00	**IL-2 Carmen Carreño**	
10:30	Coffee break	
	Chairperson: Olga Bortolini	
11:00	**IL-3 Anna Bernardi**	**Aula de Grados**
11:30	**IL-4 Luis Liz-Marzán**	Chairperson: Víctor S. Martín
12:00	**OC-1 María Valle**	**OC-6 Luca Unione**
12:15	**OC-2 Simone Giorgi**	**OC-7 Susan Lepri**
12:30	**OC-3 Eduardo Sánchez-Díez**	**OC-8 Antonio Di Maio**
12:45	**OC-4 Stefania Mirabella**	**OC-9 Daniele Passarella**
13:00	**OC-5 Luca Dell'Amico**	**OC-10 Romen Carrillo**
13:15	Lunch time	

15:00	Posters **P1-P18** (*)	
	Chairperson: Rosario Fernández	
15:30	**IL-5 Cristina Prandi**	**Aula 1.1**
16:00	**IL-6 Aitor Landa**	Chairperson: Valeria Conte
16:30	**OC-11 Valentina Pirovano**	**OC-13 Matteo Tiecco**
16:45	**OC-12 Arkaitz Correa**	**OC-14 Fabrizio Palumbo**
17:00	Coffee break	
	Chairperson: Luciano Mayol	
17:30	**IL-7 Gennaro Piccialli**	**Aula 1.1**
18:00	**IL-8 Francisco Corzana**	Chairperson: Rafael Pedrosa
18:30	**OC-15 Giorgio Bencivenni**	**OC-17 Federica Sabuzi**
18:45	**OC-16 Jordi Mestre**	**OC-18 Alexandre Pinto**
20:30	Welcome cocktail (Palacio Miramar)	

(*) Posters will be displayed from 10:00 to 19:00

Thursday, July 14 Venue: FICE Building	
	Chairperson: Paolo Tecilla
9:00	**IL-9 Mariola Tortosa**
9:30	**IL-10 Miriam Mba**
10:00	**OC-19 Montserrat Martínez**
10:15	**OC-20 Simona Rizzo**
10:30	Coffee break
	Chairperson: Mercedes Amat
11:00	**IL-11 Félix Freire**
11:30	**IL-12 Angelo Nacci**
12:00	**OC-21 Pablo Mauleón**
12:15	**OC-22 Gianluca Farinola**
12:30	**Flash 1-6**
13:15	SISOC management meeting
13:15	Lunch time

15:00	Posters **P19-P35** (*)
	Chairperson: Renato Noto
15:30	**IL-13 Gonzalo Blay**
16:00	**IL-14 Andrea Pace**
16:30	**OC-23 Esteban Urriolabeitia**
16:45	**OC-24 Paolo Tecilla**
17:00	Coffee break
	Chairperson: Carlos Saá
17:30	**IL-15 Raúl San Martín**
18:00	**IL-16 Pier G. Cozzi**
18:30	**Flash 7-10**
21:00	Social Dinner (Restaurante Branka)

(*) Posters displayed from 10:00 to 19:00

Friday, July 15 Venue: FICE Building	
	Chairperson: Jesús Jiménez-Barbero
9:00	**IL-17 Josep Bonjoch**
9:30	**IL-18 Laura F. Cipolla**
10:00	**OC-25 Ignacio Delso**
10:15	**OC-26 Laura Goracci**
10:30	Coffee break
	Chairperson: Enrico Marcantoni
11:00	**IL-19 Rubén Martín**
11:30	**IL-20 Serena Riela**
12:00	**OC-27 Marina Massaro**
12:15	**OC-28 Fernando Pinacho**
12:30	**Flash 11-16**
13:15	Lunch time

15:00	Posters **P36-P52** (*)
	Chairperson: José M. González
15:30	**IL-21 Pedro J. Pérez**
16:00	**IL-22 Claudia Barolo**
16:30	**OC-29 Mª Carmen Nicasio**
16:45	**OC-30 Macarena Poyatos**
17:00	Coffee break
	Chairperson: Roberto Ballini
17:30	**IL-23 Maurizio Prato**
18:00	**Flash 17-20**
18:30	Closing remarks

(*) Posters displayed from 10:00 to 19:00

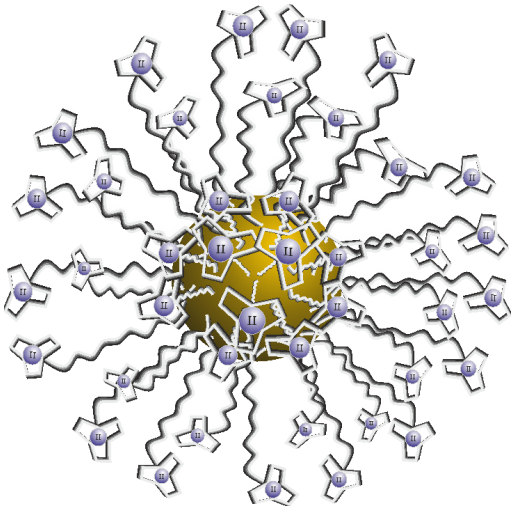
INVITED LECTURES

IL-1

All Happens at the Interface: Monolayer-Protected Gold Nanoparticles and Beyond

Paolo Scrimin
Department of Chemical Scienecs, University of Padova, via Marzolo 1, Padova, Italy
e-mail: paolo.scrimin@unipd.it

Clusters of gold atoms in the range 1-100 nm of diameter are unstable and tend to aggregate to form insoluble materials but becomes very stable once passivated with a monolayer of organic molecules typically anchored on the surface via a Au-S bond. The properties of this monolayer for molecular recognition and as a reaction loci constitute the center of my presentation. In analyzing the examples we have reported with funtionalized monolayers I will show how efficient in molecular recognition and catalysis these systems may become. Several data point out the occurrence of unusual reaction pathways and significant cooperativity between functional groups not observed not only in monomeric equivalent catalysts but also in other aggregation colloids like micelle and vesicles. The picture that emerges is that of an unique environment mimicking several features of enzymatic processes or occurring on proteins.[1]



1. Selected papers and reviews for reference: (a) Pezzato, C.; Scrimin, P.; Prins, L. J. *Angew. Chem. Int. Ed.* **2014**, *53*, 2104–2109; (b) Diez-Castellnou, M.; Mancin, F.; Scrimin, P. *J. Am. Chem. Soc.* **2014**, *136*, 1158-1161; (c) Longo, E.; Orlandin, A.; Mancin, F.; Scrimin, P.; Moretto, A. *ACS Nano* **2013**, *11*, 9933-9939; (d) Mancin, F.; Prins, L. J.; Scrimin, P. *Curr. Opin. Colloid Interface Science* **2013**, *18*, 61–69.

IL-2

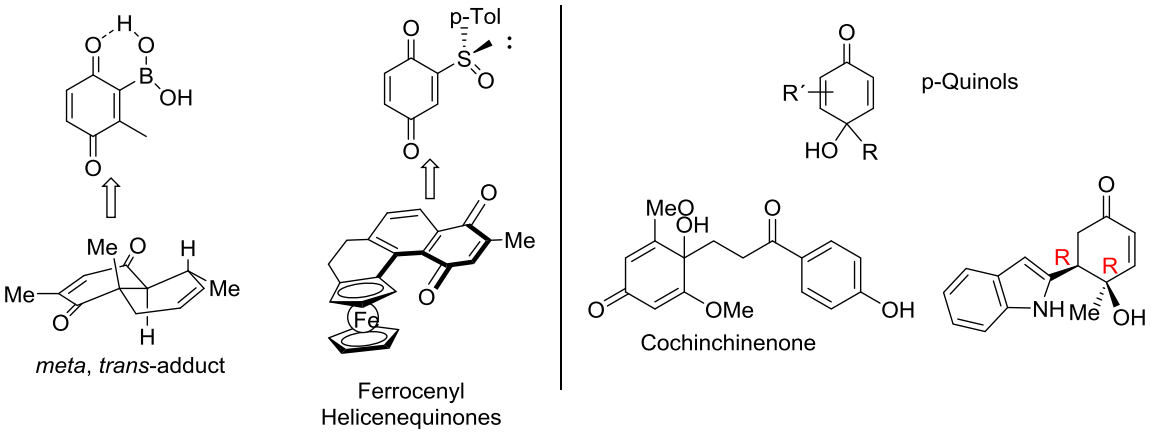
New Synthetic Applications of Quinones and Quinols

María Ribagorda, Antonio Urbano and M. Carmen Carreño
Departamento de Química Orgánica, Universidad Autónoma de Madrid, c/ Francisco Tomás y Valiente 7, Cantoblanco, 28049-Madrid
e-mail: carmen.carrenno@uam.es

This lecture will describe how we are using quinone and p-quinol derivatives to synthesize bioactive molecules and polycyclic structures with helical chirality. Diels-Alder reactions, conjugate additions and Friedel-Crafts reactions were essential processes en route to our targets. Proper choice of the partners allowed domino reactions to occur, opening a rapid access to structurally complex molecules in a highly stereocontrolled manner.

Applications of Oxone® as a source of singlet oxygen, was also been explored and applied to the synthesis of natural p-quinols and polyhydroxylated natural products. Thus, starting from adequately substituted p-alkyl phenols, a new access to angularly oxygenated Angucyclinones was explored. The process was also applied to the total synthesis of natural products such as Cochinchinenone.

The synthesis of enantiopure azobenzenes and their behavior as molecular switches will also be presented.



IL-3

Glycomimetic Antagonists of the Dendritic Cell Receptor DC-SIGN

Anna Bernardi
Department of Chemistry, Università degli Studi di Milano, via Golgi 19, 20133 Milano, Italy
e-mail: anna.bernardi@unimi.it

DC-SIGN (Dendritic Cell-Specific Intercellular adhesion molecule 3-Grabbing Nonintegrin) is a C-type lectin receptor of immature dendritic cells (DC) that recognizes highly mannosylated proteins on pathogen surfaces. It has been shown that various viruses, including HIV, Dengue and Ebola, exploit DC-SIGN to invade the host and fully disseminate the infection.

Inhibition of pathogen interaction using DC-SIGN specific antagonists is an attractive approach to developf novel anti-infective agents. Several groups have recently demonstrated that inhibition of DC-SIGN, either by designed glycoconjugates or by antibodies, prevents pathogen attachment to DC and inhibits the infection of other immune cells at its earliest steps.

Over the past few years, our group has been designing and synthesizing glycomimetic antagonists of mannose-specific C-lectins. The design takes advantage of the 3D structure of known oligosaccharide ligands and of available structural information on the lectin/ligand complexes. The small-molecule monovalent ligands obtained are often endowed with limited protein affinity, but display improved drug-like properties compared to natural sugars. Multivalent presentation on polymeric scaffolds has afforded high-affinity antagonists, and the selectivity of these materials against different C-lectins is being investigated. [1]

The presentation will describe the design and synthesis of the glycomimetic monovalent ligands as well as the optimization of polyvalent constructs that allowed us to achieve high affinity interaction with DC-SIGN. Current research on the structural optimization of the monovalent mimetics will also be described.

1. Ordanini, S. *et al Chem Commun.* **2015**, *51*, 3816 – 3819 and references therein

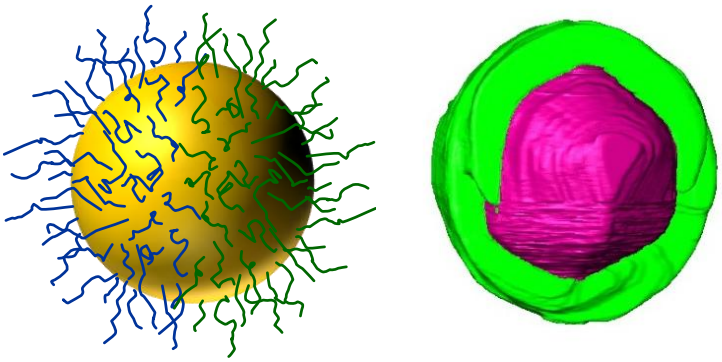
IL-4

Organic Ligands on Inorganic Nanoparticles

Luis M. Liz-Marzán[1,2,3]
[1]*Bionanoplasmonics Laboratory, CIC biomaGUNE, Paseo de Miramón 182, 20009 Donostia-San Sebastián, Spain*
[2]*Ikerbasque, Basque Foundation for Science, 48013 Bilbao, Spain*
[3]*Ciber-BBN, Spain*
e-mail: llizmarzan@cicbiomagune.es

The properties of nanomaterials are largely dependent on the size and morphology of nanoparticles, as well as on their organization within nanostructured materials. A large number of synthetic methods have been developed, which allow an exquisite degree of control over these parameters. One of the most important factors behind particle growth and interparticle interactions is the chemical composition of the nanoparticles' surface, which often involves the presence of organic ligands. These ligands can be used to protect specific crystallographic facets in nanocrystals, to facilitate binding to other molecules or surfaces, but also to direct the assembly of the nanoparticles into well-defined nanostructures.

This lecture will provide an overview of the importance of organic ligands toward nanocrystal growth and manipulation. Some insights will also be provided on the distribution of a mixture of ligands on the nanocrystal surface and in particular on the possibility to generate so-called Janus nanoparticles.

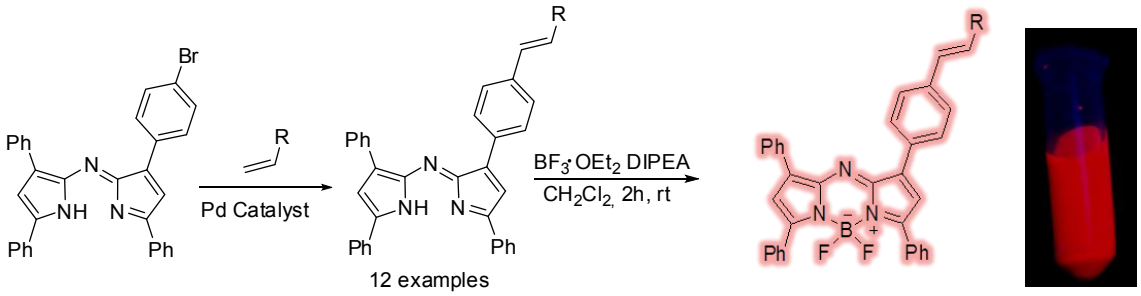


IL-5

Heck Functionalization of Asymmetric Aza-Bodipy Core: Synthesis of Far-Red Infrared Probes for Bioimaging Applications

Stefano Parisotto and Cristina Prandi
Department of Chemistry, University of Turin, via P. Giuria 7, 10125 Torino, cristina.prandi@unito.it

As part of our ongoing work on the synthesis of a new class of plant hormones named Strigolactones and their analogues, we became interested in tracing the bioactive molecules with red emitting BODIPY fluorophores in order to unravel signaling and distribution of Strigolactones *in vivo*.[1]
Strigolactones analogues functionalized with green emitting BODIPY have already been synthetized by our group and observed in plants,[2] however the green auto florescence typical of many plants hampers the application of BODIPY-SLs on a wider base. In addition, the plan of using fluorescent labeled Strigolactones in combination with the GFP tagged receptor of Strigolactones prompted us in investigating new synthetic strategies leading to red emitting asymmetric functionalized BODIPY.
To this purpose we chose to use [3-(4-Bromo-phenyl)-5-phenyl-pyrrol-2-ylidene]-(3,5-diphenyl-1H-pyrrol-2-yl)-amine (Scheme 1), previously synthesized by O' Shea *et al.*[3] as a substrate to optimize Heck functionalization and thus be able to introduce functionalities suitable to hook small active molecules of interest and map their distribution in cells and tissues.



Scheme 1. Heck functionalization of 1,3,5,7-tetraphenyl aza-BODIPY core

1. C. Prandi, H. Rosso, B. Lace, E. G. Occhiato, A. Oppedisano, S. Tabasso, G. Alberto, M. Blangetti *Molecular Plant* **2013,** *6* (1), 113-127.
2. C. Prandi, G. Ghigo, E. G. Occhiato, D. Scarpi, S. Begliomini, B. Lace, G. Alberto, E. Artuso, M. Blangetti *Org. Biomol. Chem.* **2014,** *12* (18), 2960-2968.
3. M. J. Hall, S. O. McDonnell, J. Killoran, D. F. O'Shea *J. Org. Chem.* **2005,** *70* (14), 5571-5578.
4. Y. Ge, D. F. O'Shea *Chem. Soc. Rev*. **2016,** DOI: 10.1039/c6cs00200e, advanced article.

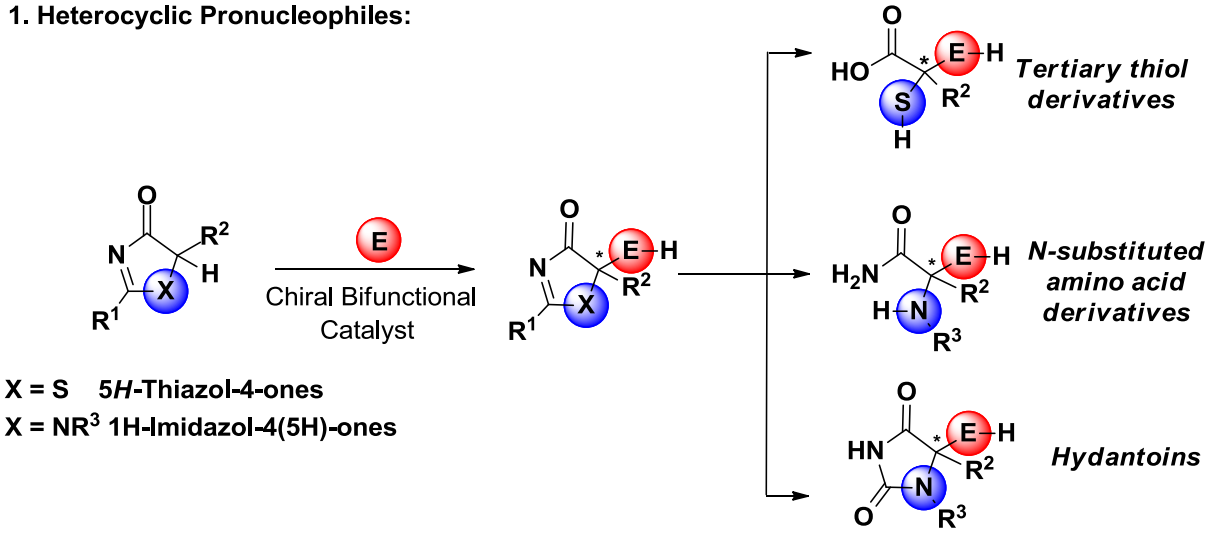
IL-6

New Pronucleophiles for Asymmetric Organocatalytic Reactions: Formation of Quaternary Stereocenters.

Aitor Landa
Departamento de Química Orgánica I, Universidad del País Vasco (UPV-EHU), Manuel de Lardizabal, 3, 20018, San Sebastián
e-mail: a.landa@ehu.es

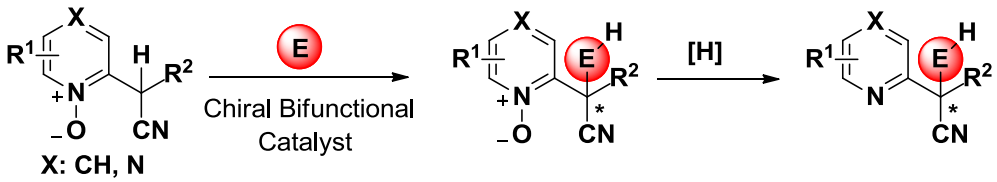
The direct catalytic reaction between an enolizable carbonyl compound and an electrophile under proton-transfer conditions is a relevant transformation in organic synthesis. In this context, whilst chiral tertiary stereocenters have been the subject of most investigations, the synthesis of quaternary stereocenters in optically pure form have remained scarcely explored. A major cause for this deficiency may be the inherent difficulty associated with the stereoselective construction of all carbon quaternary centers.[1] During the last three years, we have developed new procedures for the asymmetric conjugate addition of pronucleophiles (5*H*-thiazol-4-ones, [2] 1*H*-imidazol-4(5*H*)-ones[3] and (cyanomethyl)azaarene *N*-oxides[4]) to electron deficient systems under chiral bifunctional organocatalysis. These advances, involving the elaboration of the obtained adducts to afford optically active tertiary thiols, N-substituted α-amino acids, hydantoins and 2-*tert*-alkyl azaaryl derivatives with a tetrasubstituted stereocenter will be presented in this lecture.

1. Heterocyclic Pronucleophiles:



X = S 5*H*-Thiazol-4-ones
X = NR^3 1H-Imidazol-4(5H)-ones

2. (Cyanomethyl)azaarene *N*-oxides as pronucleophiles:



1. Quasdorf, K. W.; Overman, L. E. *Nature*, **2014**, 181–191.
2. Diosdado, S.; Etxabe, J.; Izquierdo, J.; Landa, A.; Mielgo, A.; Olaizola, I.; López, R.; Palomo, C. *Angew. Chem. Int. Ed.* **2013**, 52, 11846–11851.
3. Etxabe, J.; Izquierdo, J.; Landa, A.; Oiarbide, M.; Palomo, C. *Angew. Chem. Int. Ed.* **2015**, 54, 6883–6886.
4. Izquierdo, J.; Landa, A.; Bastida, I.; López, R.; Oiarbide, M.; Palomo, C. *J. Am. Chem. Soc.* **2016**, 138, 3282−3285.

IL-7

DNA G-Quadruplex: from Nucleic Acid Aptamers to Highly Ordered Supramolecular Structures

Nicola Borbone, Giorgia Oliviero, Stefano D'Errico, Luciano Mayol and Gennaro Piccialli
Department of Pharmacia, University of Naples Federico II, Via D. Montesano 49, 80131, Naples Italy
e-mail: gennaro.piccialli@unina.it

Quadruple helices, or G-quadruplexes, are DNA secondary structures found in guanine rich oligonucleotide sequences, having a natural propensity to self-associate in coplanar arrays of four guanines, stabilized by Hoogsteen hydrogen bonding. The scientific interest towards these particular DNA structures is mainly due to the presence of guanine rich domains, potentially able to form G-quadruplexes, in important regions of the human genome, as gene promoters and telomeres, and to the fact that the G-quadruplexes can constitute the scaffold of aptamers. Aptamers are short DNA or RNA fragments capable to bind with high affinity specific proteins, as for example thrombin or HIV-proteins. On these grounds, aptamers-based synthetic oligonucleotides can represent a new class of pharmacologically interesting molecules, characterized by a high selectivity of action.
Furthermore, the G-quadruplexes can have a potential use in nanotechnology and self assembled supramolecular structures. As a matter of fact, the overall quadruplex scaffold can exhibit several morphologies through intramolecular or intermolecular organization of G-rich oligonucleotide strands, which can form higher-order assemblies by multimerization between G-quadruplex units.
New G-quadruplex aptamers having anti-HIV properties and studies on the multimerization of G-quadruplex scaffold will be also presented

IL-8

Design of novel glycopeptide-based cancer vaccines

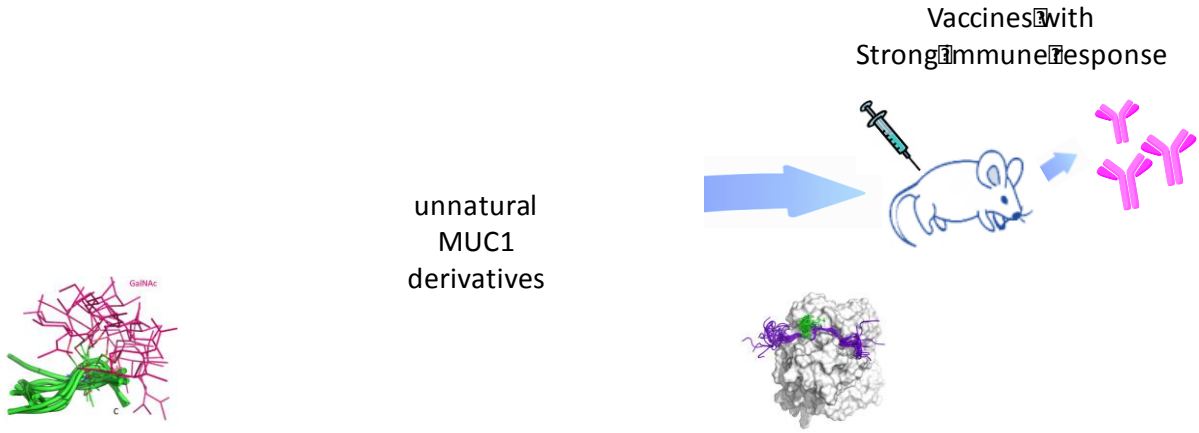
Nuria Martínez-Sáez, Iris A. Bermejo, Jorge Castro-López, Ramón Hurtado-Guerrero, Juan L. Asensio, Jesús Jiménez-Barbero, Jesús. H. Busto, Alberto Avenoza, Jesús M. Peregrina, and Francisco Corzana

Departamento de Química, Universidad de La Rioja, Centro de Investigación en Síntesis Química, Madre de Dios 53, 26006 Logroño, La Rioja

e-mail: francisco.corzana@unirioja.es

Mucin MUC1 is an *O*-glycoprotein overexpressed in various tumors. While in healthy tissues, the peptide sequence of this protein carries complex oligosaccharides, in cancer cells, it shows simple and truncated carbohydrates, such as the Tn antigen (α-*O*-GalNAc-Ser/Thr). These antigens are exposed to the immune system and can interact with it. Due to this unique characteristic, partially glycosylated MUC1 derivatives are attractive antigens for the development of therapeutic vaccines for the treatment of cancer.[1]

Currently, considerable effort is dedicated to synthesize MUC1 derivatives that can elicit strong immune response. However, the identification of the important structural elements involved in the recognition process of MUC1 by anti-MUC1 antibodies remains partly unclear. We are developing a multidisciplinary approach that combines synthesis, X-ray diffraction, nuclear magnetic resonance and molecular modeling to identify these structural features[2,3] (Figure). Our results provide valuable hints for the design of efficacious cancer vaccines.



1. Feng, D.; Shaikh, A. S.; Wang, F. *ACS Chem. Biol.* **2016**, 11, 850−863.
2. Martínez-Sáez, N.; Castro-López, J.; Valero-Gónzalez, J.; Madariaga, D.; Compañón, I.; Somovilla, V. J.; Salvadó, M.; Asensio, J. L.; Jiménez-Barbero, J.; Avenoza, A.; Busto, J. H.; Bernardes, G. J. L.; Peregrina, J. M.; Hurtado-Guerrero, R.; Corzana, F. *Angew. Chem. Int. Ed.* **2015**, *127*, 9968−9972.
3. Martínez-Sáez, N.; Supekar, N. T.; Wolfert, M. A.; Bermejo, I. A.; Hurtado-Guerrero, R.; Asensio, J. L.; Jiménez-Barbero, J.; Busto, J. H.; Avenoza, A.; Boon, G.-J.; Peregrina, J. M.; Corzana, F. *Chem. Sci.* **2016**, *7*, 2294–2301.

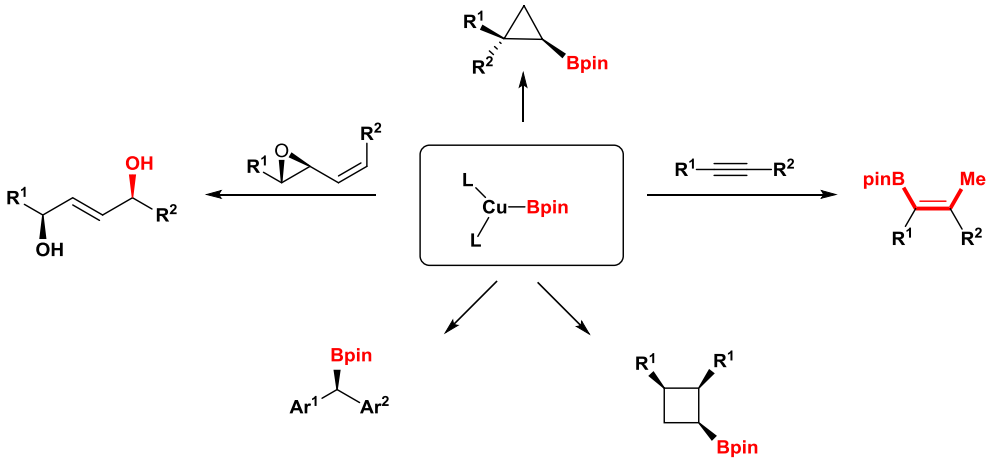
IL-9

Synthesis of Versatil Synthetic Intermediates through Copper-Catalyzed Borylations

Mariola Tortosa

Departamento de Química Orgánica, Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain.
e-mail: mariola.tortosa@uam.es

Boronic esters are versatile synthetic intermediates for the preparation of a wide range of organic molecules.[1] The development of new methods to create C-B bonds in an efficient, inexpensive, and environmentally friendly way is therefore an important challenge in organic chemistry. Traditionally, the methods to form C-B bonds have mostly been based on the electrophilic nature of boron. While this classical approach works well for reactions with nucleophilic partners, it naturally limits the types of boron compounds that can be prepared. Recently, copper-catalyzed borylations have emerged as a new source of nucleophilic boron. The lower price and toxicity of copper versus other transition metals and the unique reactivity of the boryl-copper intermediates make these processes particularly attractive. Inspired by unsolved problems found in the total synthesis of complex molecules, we have used boryl-copper species to synthesize useful synthetic intermediates such as 1,4-diols,[2] trisubstituted alkenes,[3] dibenzylic derivatives[4] and functionalized small rings.[5] Some of these results will be presented in this talk.



[1] Hall, D. In *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*; Hall, D.; Wiley-VCH: Weinheim, Germany, **2005**.
[2] Tortosa M. *Angew. Chem. Int. Ed.* **2011**, *50*, 3950.
[3] Alfaro, R.; Parra, A.; Alemán, J.; García Ruano, J. L.; Tortosa, M. *J. Am. Chem. Soc.* **2012**, *134*, 15165.
[4] Jarava-Barrera, C.; Parra, A.; López, A.; Cruz-Acosta, F.; Collado-Sanz, D.; Cárdenas, D. J.; Tortosa M. *ACS Cat.* **2016**, 6, 442.
[5] (a) Parra, A.; Amenós, L.; Guisan-Ceinos M.; López, A.; Garcia-Ruano, J. L.; Tortosa, M *J. Am. Chem. Soc.* **2014**, *136*, 15833. (b) Guisan-Ceinos, M.; Parra, A.; Martin-Heras V.; Tortosa M. *Angew. Chem. Int. Ed.* **2016**, *accepted manuscript*, DOI: 10.1002/anie.201601976.

IL-10

Peptides as supramolecular templates for the self-assembly of carbon nanostructures in water

Miriam Mba
Department of Chemical Sciences, University of Padova, via Marzolo 1, Padova
e-mail: miriam.mba@unipd.it

The low solubility of carbon nanostructures in water and the need of ordered architectures at the nanoscale level are two major challenges for materials chemistry.

Low Molecular Weight Gelators (LMWG) are self-assembling small molecules that aggregates in solution to form a well-ordered 3D supramolecular network that immobilize the solvent giving a gel.[1] These materials are attracting increasing interest for example in tissue engineering or cell culture, but also in energy-related applications where control over nano-order and morphology plays a key role.[2] Peptides are well known to form supramolecular gels and "de novo" designed peptides open access to a plethora of different morphologies and supramolecular architectures.[3] When functionalized with chromophores or carbon nanostructures, self-assembly of the peptide LMWGs will give a supramolecular architecture in which the functional moieties display a well-defined spatial orientation and disposition.[4] Moreover, the use of water-soluble peptides may be use to increase the solubility in water of organic chromophores and carbon nanostructures, facilitating the access to biomedical applications.[5]

Herein we present our efforts in the use of dipeptides and oligopeptides as templates for the ordered self-assembly of chromophores and carbon nanostructures in water. Covalent and non-covalent approaches will be discussed. The advantages of using mechanochemical non-covalent functionalization of carbon nanostructures will be shown.

[1] George, M.; Weiss, R. G., *Acc. Chem. Res.* **2006**, *39* (8), 489-497.
[2] Hirst, A. R.; Escuder, B.; Miravet, J. F.; Smith, D. K., *Angew. Chem. Int. Ed.* **2008**, *47* (42), 8002-8018.
[3] Lowik, D. W. P. M.; Leunissen, E. H. P.; van den Heuvel, M.; Hansen, M. B.; van Hest, J. C. M., *Chem. Soc. Rev.* **2010**, *39* (9), 3394-3412.
[4](a) Mba, M.; Moretto, A.; Armelao, L.; Crisma, M.; Toniolo, C.; Maggini, M., *Chem-Eur J* **2011**, *17* (7), 2044-2047. (b) Mba, M.; Jiménez, A. I.; Moretto, A., *Chem. Eur. J.* **2014**, *20* (14), 3888-3893. (c) Bartocci, S.; Morbioli, I.; Maggini, M.; Mba, M., *Journal of Peptide Science* **2015**, *21* (12), 871-878.
[5] Bartocci, S.; Mazzier, D.; Moretto, A.; Mba, M., *Org Biomol Chem* **2015**, *13* (2), 348-352.

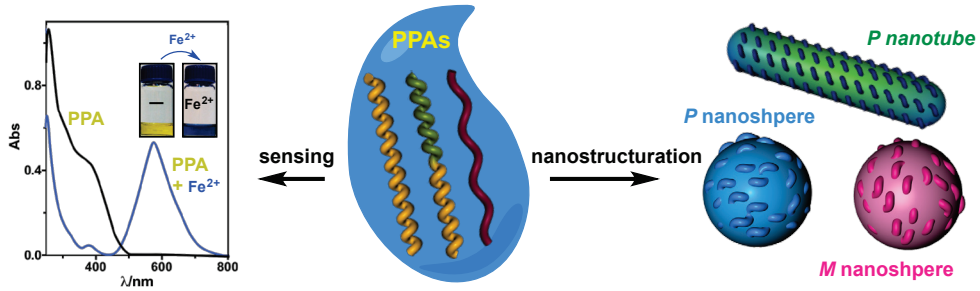
IL-11

Chiral Polymers: Taming the Helix

Félix Freire
Research Centre in Biological Chemistry and Molecular Materials (CIQUS), University of Santiago de Compostela, SPAIN
e-mail: felix.freire@usc.es

Dynamic helical polymers such as poly(phenylacetylene)s (PPAs) present interesting properties due to the possibility of modulating their helical sense once they are obtained.[1] Moreover, the helicity adopted by a PPA is directly related to the conformational composition at the pendant moiety and therefore, the manipulation of this conformational equilibrium by the presence of external stimuli can result in helix inversion or chiral amplification of the initial helical structure adopted by the PPA.

In our group, different polymers were developed to produce these effects. For instance, a PPA containing (*R*)-*a*-methoxy-*a*-phenylacetamide presents a dynamic helical structure when it is dissolved in different organic solvents, yielding a polymer without a helical sense excess and therefore, without optical activity. The different coordination of the pendant group with monovalent or divalent metal ions results in a chiral amplification of the helical structure towards the left of right handed helix respectively due to the presence/absence of cation-p interactions.[2] Moreover, we found that these polymer-metal complexes generate nanospheres where their size and helical sense excess can be tuned by changing the metal/polymer ratio.[3] On the other hand, the ability of these polymers to respond to the presence of external stimuli was used to generate sensors. Thus, we designed polymers that can, for instance: a) classify solvents attending to their polarity or donor character,[4] b) detect the presence of iron(II) and c) anions. Due to our interest in Supramolecular Chemistry and the helical structure of PPAs, we design a polymer that forms stereocomplexes by interlocking enantiomeric helical structures. This fact is possible due to the complementarity and the presence of supramolecular hydrogen bond interactions between the enantiomeric helices.[5]



[1] Yashima E.; Maeda K. Iida, K.; Nagai, K. *Chem. Rev.* **2009**, *109*, 6102-6211.
[2] (a) Freire, F.; Seco, J. M.; Quiñoá, E.; Riguera, R. *Angew. Chem. Int. Ed.* **2011,** *50*, 11692-11696. (b) Arias, S., Freire, F., Quiñoá, E.; Riguera, R. *Polym. Chem.* **2015,** *6*, 4725-4733. (c) Bergueiro, J., Freire, F.; Seco, J. M.; Quiñoá, E.; Riguera, R. *Chem. Sci.* **2014,** *5*, 2170-2176.
[3] (a) Freire, F.; Seco, J. M.; Quiñoá, E.; Riguera, R. *J. Am. Chem. Soc.* **2012**, *134*, 19374-19383. (b) Arias, S.; Freire, F.; Quiñoá, E.; Riguera; R. *Angew. Chem. Int. Ed.* **2014,** *53*, 13720-13724.
[4] Arias, S., Bergueiro, J.; Freire, F.; Quiñoá, E.; Riguera, R. *Small*, **2016**, *12*, 238-244.
[5] (a) Leiras, S., Freire, F.; Seco, J. M.; Quiñoá, E.; Riguera, R. *Chem. Sci.* **2013,** *4*, 2735-2743. (b) Leiras, S., Freire, F.; Quiñoá, E.; Riguera, R. *Chem. Sci.* **2015,** *6*, 246-253. (c) Freire, F.; Quiñoá, E.; Riguera, R. *Chem. Rev.* **2016**, DOI: 10.1021/acs.chemrev.5b00280

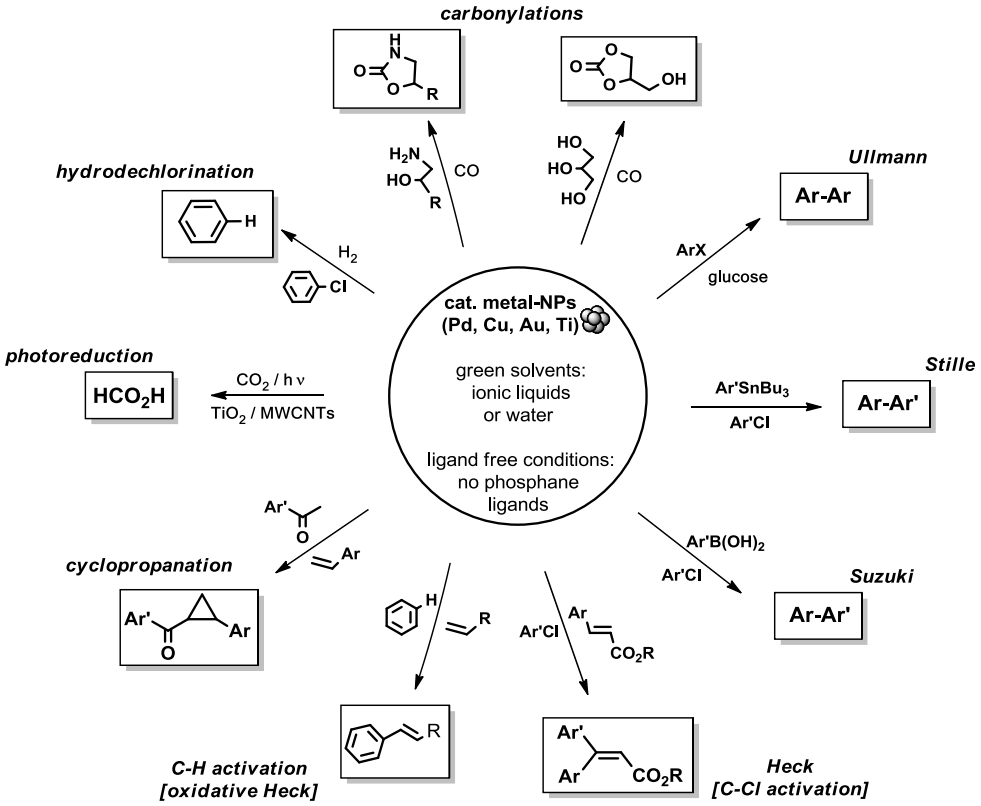
IL-12

Nanostructured Metals for Green Catalysis

Angelo Nacci

Department of Chemistry - University of Bari, Via Orabona 4, 70125 - Bari, Italy
CNR – ICCOM - Department of Chemistry - University of Bari, Via Orabona 4, 70125 - Bari, Italy.
e-mail: angelo.nacci@uniba.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] Nowadays, many researchers are exploiting the high activity and selectivity of nanocatalysts to develop greener and waste-minimized processes.[2]
During the last decade, we exploited nanostructured metal catalysts based on Pd, Cu, Au and Ti to perform a wide range of organometallic reactions (Heck, Suzuki, Ullmann, Stille, carbonylations, cyclopropanations, hydrodehalogenations and CO_2 photoreduction) under environmentally friendly conditions given by the absence of phosphane ligands and using neoteric solvents (ionic liquids, water and so on) as green reaction media.[3]



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

[1] Astruc, D.; Lu, F.; Aranzaes J. R.. Angew. Chem. 2005, 117, 8062; *Angew. Chem. Int. Ed.* **2005**, *44*, 7852.
[2] Pârvulescu, V. I.; Hardacre, C. *Chem. Rev.* **2007**, *107*, 2615.
[3] a) Monopoli, A.; Cotugno, P.; Palazzo, G.; Ditaranto, N.; Mariano, B.; Cioffi, N.; Ciminale, F.; Nacci. A. Adv. Synth. & Catal. **2012**, *354*, 2777–2788, b) Cotugno, P.; Monopoli, A.; Ciminale, F.; Milella, A.; Nacci, A. *Angew. Chem. Int. Ed.* **2014**, *126*, 13511–13837.

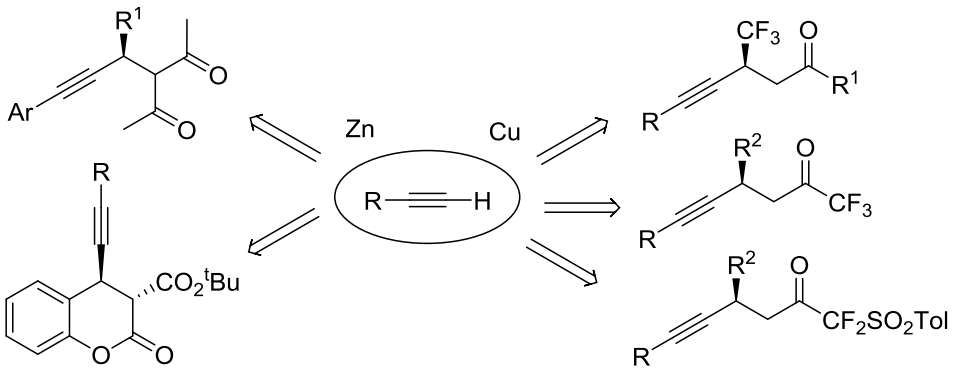
IL-13

Zinc and Copper Catalyzed Enantioselective Conjugate Alkynylation of α,β-Unsaturated Carbonyl Compounds

Gonzalo Blay,* Amparo Sanz-Marco and José R. Pedro*
Departament de Química Orgànica, Facultat de Química, Universitat de València, C/Dr. Moliner 50, 46100-Burjassot (Valencia), Spain
e-mail: gonzalo.blay@uv.es

The interest in the chemistry of alkynes has experienced a progressive growth in the last years.[1] Besides classical procedures based on elimination reactions, the nucleophilic addition of terminal alkynes to electrophilic groups stands as one of the most straightforward methods to introduce the triple bond in organic molecules, many times generating a new stereocenter. Accordingly, considerable success has been obtained in the enantioselective alkynylation of prochiral carbonyl compounds[2] and imines.[3] However, the asymmetric conjugate addition of alkynes to α,β-unsaturated carbonyl compounds has only been developed more recently to give chiral β-alkynyl ketones that are very versatile building blocks.[4]

In this lecture we will disclose our contribution to the development of this reaction using zinc[5] and copper[6] catalysis, as well as some synthetic applications of the resulting β-alkynyl carbonyl compounds.



Acknowledgements: Financial support from MINECO (CTQ2013-47494-P) is gratefully acknowledged. A. S.-M. thanks the MINECO for a predoctoral grant (FPI program).

1. (a) Godoi, B.; Schumacher, R. F.; Zeni, G. *Chem. Rev.* **2011**, *111*, 2937-2980. (b) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2014**, *114*, 1783-1826.
2. Trost, B. M.; Weiss, A. H. *Adv. Synth. Catal.* **2009**, *351*, 963-983.
3. Blay, G.; Monleón A.; Pedro, J. R. *Curr. Org. Chem*. **2009**, *13*, 1498-1539.
4. Selected examples. Cu catalysis: (a) Knopfel, T. F.; Zarotti, P.; Ichikawa, T.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *27*, 9682-9683. (b) Yazaki, R.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 10275-10277. Rh catalysis: (c) Nishimura, T.; Sawano, T.; Hayashi, T. *Angew. Chem. Int. Ed.* **2009**, 4*8*, 8057-8059. (d) Fillion, E.; Zorzitto, A. K. *J. Am. Chem. Soc.* **2009**, *131*, 14608-14609. (e) Dou, X.; Huang, Y.; Hayashi, T. *Angew. Chem. Int. Ed.* **2016**, *55*, 1133-1137.
5. (a) Blay, G.; Cardona, L.; Pedro, J. R.; Sanz-Marco, A. *Chem. Eur. J.* **2012**, *18*, 12966-12969. (b) Blay, G.; Muñoz, M. C.; Pedro, J. R.; Sanz-Marco, A. *Adv. Synth. Catal.* **2013**, *555*, 1071-1076.
6. (a) Sanz-Marco, A.; Garcia-Ortiz, A.; Blay, G.; Pedro, J. R. *Chem. Commun.* **2014**, *50*, 2275-2278. (b) Sanz-Marco, A.; Garcia-Ortiz, A.; Blay, G.; Fernandez, I.; Pedro, J. R. *Chem. Eur. J.* **2014**, *20*, 668-672. (c) Sanz-Marco, A.; Blay, G.; Muñoz, M. C.; Pedro, J. R. *Chem. Commun.* **2015**, *51*, 8958-8961. (d) Sanz-Marco, A.; Blay, G.; Muñoz, M. C.; Pedro, J. R. *Chem. Eur. J.* **2016**, accepted.

IL-14

Juggling with and Taming Fluorinated Azoles in the Heterocyclic Circus

Andrea Pace
Dipartimento di Scienze e Technologie Biologiche Chimiche e Farmaceutiche (STEBICEF), Università degli Studi di Palermo, Viale delle Scienze Ed. 17, 90128 Palermo, Italy.
e-mail: andrea.pace@unipa.it

Azoles are a subset of heteroaromatic compounds which are widely applied in the fields of bioactive compounds and materials science. When the appropriate heterocyclic synthon is available, ring-rearrangements are a successful strategy to obtain target azoles and other heterocyclic compounds.[1] In this context, 1,2,4-oxadiazoles possess a high propensity for thermal or photochemical rearrangements into more stable heterocyclic rings, such as quinazolinones, 1,3,4-oxadiazoles, and 1,2,4-triazoles.[2] Additionally, the introduction of fluorinated groups in the 1,2,4-oxadiazole core can be used to opportunely tune its chemical reactivity, opening the way to new synthetic methodologies towards fluorinated heterocycles.[3] This lecture will focus on the chemistry of oxadiazoles and triazoles from curiosity-driven research to current development and potential applications as bioactive compounds and functional components in fluorinated materials.

1. Vivona, N.; Buscemi, S.; Pibiri, I.; Palumbo Piccionello, A.; Pace, A. in *Handbook of Synthetic Photochemistry* **2010**, *Ch. 12*, pp. 387-416, Ed. Albini, A. and Fagnoni, M. Wiley-VCH Weinheim, Germany.
2. (a) Pace, A.; Pierro, P. *Org. Biomol. Chem.* **2009**, *7*, 4337−4348. (b) Pace, A.; Buscemi, S.; Palumbo Piccionello, A.; Pibiri, I. *Adv. Het. Chem.* **2015**, *116*, 85-136.
3. Pace, A.; Palumbo Piccionello, A.; Pibiri, I.; Buscemi, S.; Vivona, N. in *Fluorine in Heterocyclic Chemistry Vol 1* **2014**, pp. 369-417, Ed. Nenajdenko, V. Springer International Publishing, Switzerland.

IL-15

New copper, palladium and nickel catalytic systems. An evolution towards more efficient procedures

Raul SanMartin
Department of Organic Chemistry II, University of the Basque Country (UPV/EHU), Sarriena auzoa, z/g 48940 Leioa (Spain)
e-mail: raul.sanmartin@ehu.eus

The development of a plethora of transition metal-catalyzed reactions has revolutionized synthetic chemistry. However, there still remain a number of challenges in this prolific field. Challenges related to the use of transmetallating agents, the catalyst amount required, a search for suitable reaction media and more sustainable reagents, recycling of the catalyst, stereoselectivity of the process, etc. These facts apply to copper-, palladium-, and nickel-catalysed cross-coupling reactions, direct arylations and oxidative processes.[1]

Several strategies devised by our group in order to overcome some the aforementioned problems will be described. In this regard, our recent improvements on direct coupling in lieu of procedures involving stoichiometric amounts of transmetallating agents, molecular oxygen as the ideal oxidant, and tailor-designed metallocycles as more convenient metal sources and catalysts will be described.

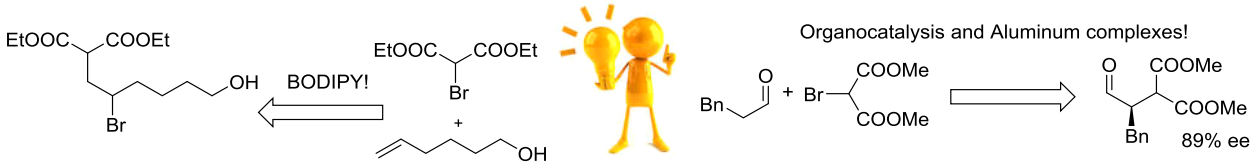
1. See, for example: (a) Wu, X.-F.; Anbarasan, P.; Neumann, H.; Beller, M. *Angew. Chem. Int. Ed*. **2010**, *49*, 9047-9050; (b) Huang, H.; Jiang, H.; Chen, K.; Liu, H. *J. Org. Chem.* **2009**, *74*, 5599-5602.

IL-16

New Directions in Photocatalytic Reactions

Pier Giorgio Cozzi[a]*
[a]*ALMA MATER STUDIORUM, Università di Bologna,*
Dipartimento di Chimica "G. Ciamician",
Via Selmi 2, 40126 Bologna, Italy,
e-mail: piergiorgio.cozzi@unibo.it

Use in light promoted synthetic transformation has recently found a renewed interest,[1] due the mild reaction conditions and the creativity associated with the invention of interesting chemistry.[2]. Through the controlled generation of radical species, catalytic cycle in which metals complexes or organic molecules are involved as promoters were recently investigated [3]
In our research group we are focusing our attention in two different projects associated to photocatalysis:
a) Use of abundant metals for promoting stereoselective photocatalytic reactions.
b) New photocatalytic reactions promoted by BODIPY.
In this lecture, we will present new results in these research areas. We will report photocatalytic reactions promoted by aluminum complexes,[4] and a new, effective, and straightforward generation of radicals for alkene functionalization in the presence of BODIPY.[5] All these investigations are opening new perspective and possibilities in photocatalytic transformations.



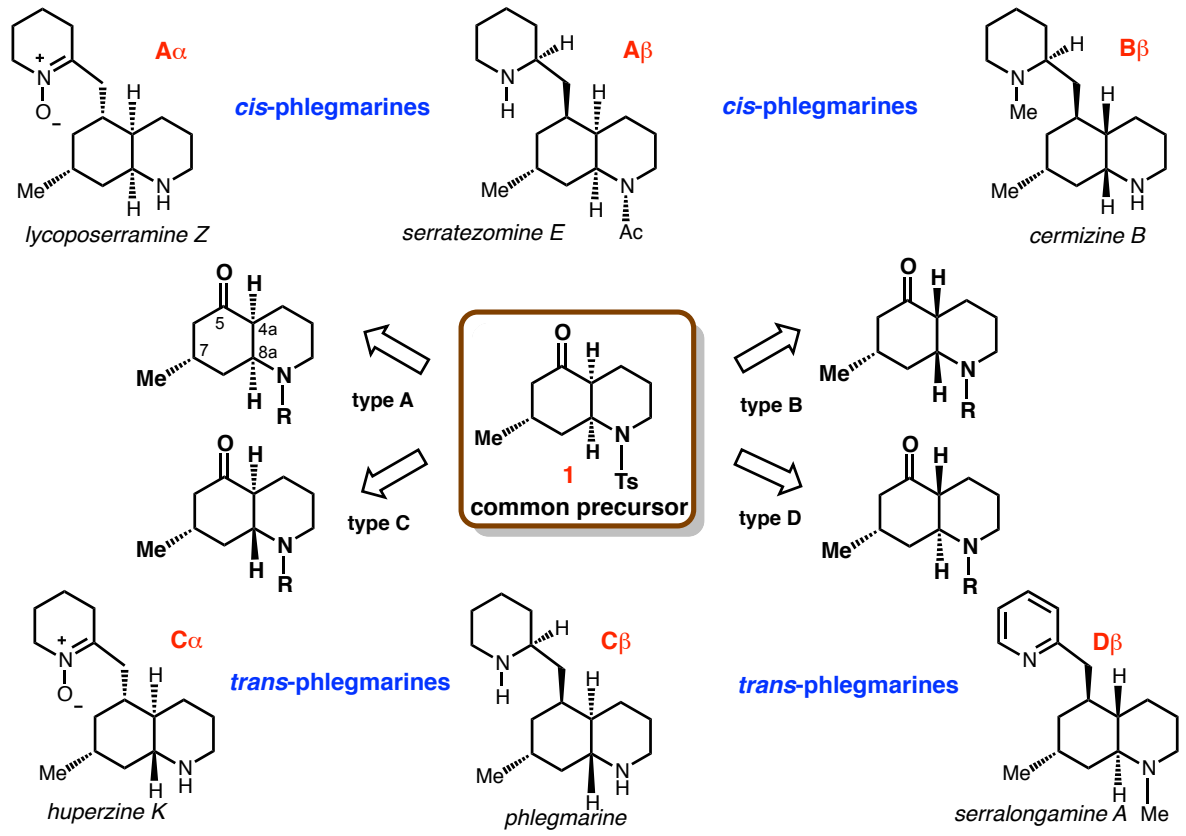
[1] For reviews, see: (a) Svoboda J.; König, B. *Chem.Rev*. **2006**, *106*, 541; (b) Prier, C. K.; Rankic ,D. A.; MacMillan, D. W. C. *Chem. Rev*. **2013**, *113*, 5322; (c) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102; (d) Skubi, K. L.; Yoon, T. P. *Nature* **2014**, *515*, 46.
[2] (a) Nicewicz, D. A.; MacMillan, D. W. C. *Science*, **2008**, *322*, 77; (b) Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 10875; (c) Shih, H.-W.; Vander Wal, M. N.; Grange, R. L.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 13600; (d) DiRocco, D. A.; Rovis, T. *J. Am. Chem. Soc.* **2012**, *134*, 8094; (e) Tarantino, K. T.; Liu, P.; Knowles, R. R. *J. Am. Chem. Soc.* **2013**, *135*, 10022; (f) Du, J.; Skubi, K. L.; Schultz, D. M.; Yoon, T. P. *Science* **2014**, *344*, 392.
[3] (a) Zuo, Z.; Cong, H.; J. Choi, W, Li; Fu, G. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* ***2016***, *138*, 1832; (b) Zuo, Z.; Ahneman, D. T.; Chu, LTerrett, .J. A.; Doyle, A. G.; MacMillan D. W. C. *Science*, **2014**, *345*, 437.
[4] With Andra Gualandi, Luca Mengozzi, Hagos Testfay Kidanu, Antoine Frac, Marianna Marchini, Paola Ceroni.
[5] With Andra Gualandi, Luca Mengozzi, Gian Domenico Magagnano (now in ICIQ, Spain), Marianna Marchini, Paola Ceroni.

IL-17

A Divergent Synthetic Approach to Phlegmarine Alkaloids

Josep Bonjoch
Laboratori de Química Orgànica, Facultat de Farmàcia, Universitat de Barcelona, Av. Joan XXIII s/n, 08028-BarcelonaSpain
e-mail: josep.bonjoch@ub.edu

The phlegmarine alkaloids, a subset of the *lycopodium* alkaloids, are of interest for their biological properties and synthetic challenges. Structurally characterized by a 5,7-disubstituted decahydroquinoline ring and a $C_{16}N_2$ skeleton, they can be classified in four types, according to the relationship of the ring fusion hydrogens with the H-7 in the decahydroquinoline ring. A general strategy for the synthesis of phlegmarine alkaloids has been developed and total syntheses of (+)-lycoposerramine Z, (-)-cermizine B, (+)-serratezomine A, (±)-serralongamine A, and (±)-huperzine N via a common decahydroquinoline have been achieved.[1] Synthetic access to all the different stereochemical arrangements of the decahydroquinoline ring core of phlegmarine alkaloids has been efficiently achieved by the use of organocatalysis, tandem reactions, thermodynamic epimerization, stereodivergent hydrogenation and "pot and time economy" strategies.



1. (a) Bradshaw, B.; Luque-Corredera, C.; Bonjoch, J. *Org. Lett.* **2013**, *15*, 326-329. (b) Bradshaw, B.; Luque-Corredera, C.; Bonjoch, J. *Chem. Commun.* **2014**, *50*, 7099-7102. (c) Bosch, C.; Fiser, B.; Gomez-Bengoa, E.; Bradshaw, B.; Bonjoch, J. *Org. Lett.* **2015**, *17*, 5084-5087. (d) Saborit, G. V.; Bosch, C.; Parella, T.; Bradshaw, B.; Bonjoch, J. **2016**, *81*, 2629-2634.

IL-18

Glycomics and regenerative medicine: new challenges and opportunities for organic chemists

Laura Russo, Antonella Sgambato, Roberto Guizzardi, Laura Cipolla,
Dept. of Biotechnology and Biosciences, University of Milano-Bicocca, P.za della Scienza 2 20126 Milano-Italy
e-mail: laura.cipolla@unimib.it

It is well established that glycans play an essential role in a plethora of biological events,[1] including cellular adhesion and migration, organism development, disease progression, and modulation of immunological responses. Their use as signaling molecules for material surface functionalization to control stem cell growth and differentiation is presently limited, due to the high complexity of their structure, synthesis and chemical manipulation. However, recent data highlight them as promising cues for tissue engineering and regenerative medicine applications.[2] On the other hand, there is great interest in the development of naturally derived biomaterials, including extracellular matrix (ECM) components, such as collagen, elastin and proteoglycans, for many applications such as direct tissue replacement; the ECM complex, in fact, provides a good model for biomaterials design for tissue engineering. Collagen, and other ECM-macromolecules, have been used in the last years as biomaterials for tissue regeneration applications. Given the relevant role played by carbohydrates, they appear as invaluable tools, if suitably exposed at the interface between material surfaces and cells, for the design of innovative smart biomaterials able to direct and control cell fate. Given these premises, different chemoselective strategies have been designed for the bioconjugation of carbohydrate epitopes to ECM proteins and other synthetic polymers, such as PCL. The results of the intraction between neoglycosylated materials and different cell lines will be outlined, highlighting how glycans at the interface between materials and cells may drive their behaviour. For example, neoglucosylated collagen matrices drive F11 neuroblastoma cells to differentiation into active neurons, while different sialylated collagen matrices[3] are able to modulate gene expression toward chondrogenesis or osteogenesis in mMSC.[4]

Acknowledgments.
We gratefully acknowledge FA 2014 and the European Community's programme under Grant Agreement number: 642028 —H2020-MSCA-ITN-2014 “NABBA” for financial support.

1. Ohtsubo, K.; Marth, J.D. *Cell* **2006**, *126* (5), 855-867.
2. Russo, L.; Battocchio, C.; Secchi, V.; Magnano, E.; Nappini, S.; Taraballi, F.; Gabrielli, L.; Comelli, F.; Papagni, A.; Costa, B.; Polzonetti, G.; Nicotra, F.; Natalello, A.; Doglia, S. M.; Cipolla, L. *Langmuir* **2014**, *30* (5), 1336–1342.
3. Russo, L.; Sgambato, A.; Lecchi, M.; Pastori, V.; Raspanti, M.; Natalello, A.; Doglia, S.M.; Nicotra, F.; Cipolla, L. *ACS Chem Neurosci*. **2014**, 5(4), 261-265.
4. Sgambato, A.; Russo, L.; Montesi, M.; Panseri, S.; Marcacci, M.; Caravà, E.; Raspanti, M.; Cipolla, L. *ACS Appl. Mater. Interfaces*, **2015** 10.1021/acsami.5b08270.

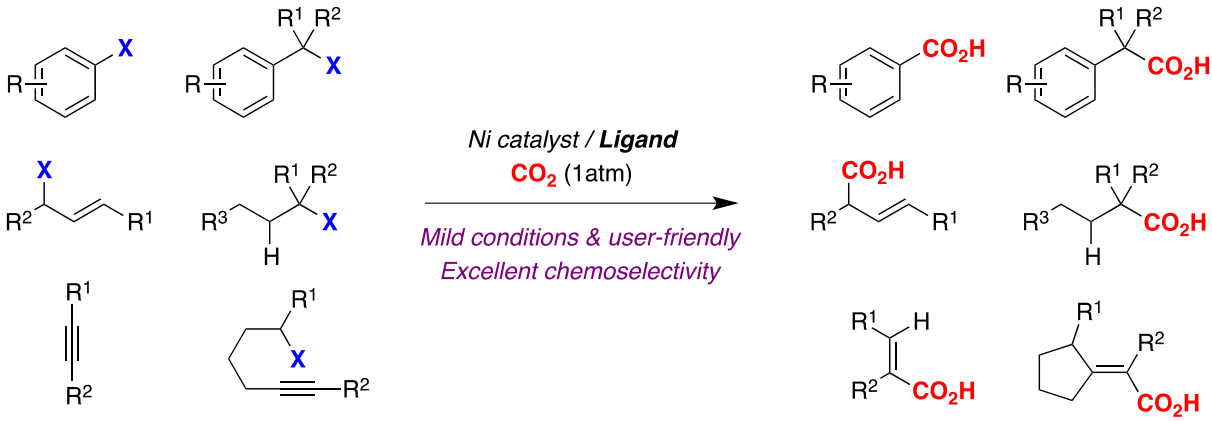
IL-19

Ni-catalyzed Reductive Carboxylation Techniques with CO_2

Ruben Martin
Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology, Av. Paisos Catalans 16, 43007, Tarragona (Spain)
Catalan Institution for Research and Advanced Studies (ICREA), Passeig Lluis Companys 23, 08010, Barcelona (Spain)
e-mail: rmartinromo@iciq.es

The sustainable utilization of available feedstock materials for preparing valuable compounds holds great promise to revolutionize approaches in organic synthesis. In this regard, the implementation of abundant and inexpensive carbon dioxide (CO_2) as a C1 building block, probably the greenest C1 source in nature, has recently attracted a considerable attention.[1] Among the different alternatives in CO_2 fixation, the preparation of carboxylic acids, relevant motifs in a myriad of pharmaceuticals and agrochemicals would provide a rapid an unconventional entry to building blocks in a catalytic fashion.[2] In recent years, our research group has reported some progress directed towards the catalytic reductive carboxylation of organic matter with CO_2 (Scheme 1).[3] These methods are characterized by their simplicity, wide substrate scope, including challenging substrate combinations with particularly sensitive functional groups and a diverse set of substitution patterns.

.



[1] For reviews : (a) Tsuji, Y. ; Fujihara, T. *Chem. Commun.* **2012**, *48*, 9956. (b) Cokoja, M. ; Bruckmeier, C. ; Rieger, B. ; Herrmann, W. A. ; Kühn, F. E. *Angew. Chem. Int. Ed.* **2011**, *50*, 8510.
[2] Maag, H. *Prodrugs of carboxylic acids ;* Springer : New York, **2007**
[3] Recent references : (a) Börjesson, M.; Moragas, T.; Martin, R. *J. Am. Chem. Soc.* **2016**, *In Press.* (b) Wang, X.; Liu, Y.; Martin, R. *J. Am. Chem. Soc.* **2015**, *137*, 6476. (c) Wang, X.; Nakajima, M.; Martin, R. *J. Am. Chem. Soc.* **2015**, *137*, 8924. (d) Moragas, T.; Cornella, J.; Martin, R. *J. Am. Chem. Soc.* **2014**, *136*, 17702. (e) Liu, Y.; Cornella, J.; Martin, R. *J. Am. Chem. Soc.* **2014**, *136*, 11212.

IL-20

Recent Researches on Halloysite Nanotubes a Smart Nanomaterials for Several Applications

Serena Riela
Dipartimento di Scienze e Tecnologie Biologiche Chimiche e Farmaceutiche (STEBICEF), Università degli Studi di Palermo, Viale delle Scienze Parco d'Orleans II Ed-17
e-mail: serena.riela@unipa.it

Halloysite clay are aluminosilicate nanomaterials (HNTs) with an unique combination of hollow tubular nanostructure, large aspect ratio, suitable mechanical strength, high perspectives in terms of functionality, biocompatibility ecocompatibility and wide availability.[1] Moreover, their low cost makes them attractive alternative to the better known carbon nanotubes. As a consequence, in the last years, HNTs have garnered particular interest in material science. HNTs possess different inner and outer surface composition; in particular most of the aluminol groups are located in the halloysite inner surface, whereas the external portions are mainly composed of siloxanes providing a surface available for covalent grafting of organic moieties.[2] This peculiar chemical composition allows different functionalization methods of both surfaces that increase the HNTs application fields.[3]

In this context I report some recent progresses in my research group towards the development of functionalized-HNTs hybrids nanocomposites paying particular attention to the synthesis and characterization of the hybrids as well as their application in particular in drug carrier and delivery.[4]

Figure 1: Some examples of HNT applications.

[1] (a)Lvov, Y.; Wang, W.; Zhang, L.; Fakhrullin, R., Halloysite *Adv. Mater.* **2016,** *28* (6), 1227-1250; (b) Bellani, L.; Giorgetti, L.; Riela, S.; Lazzara, G.; Scialabba, A.; Massaro, M., *Environ. Toxicol. Chem.* **2016**, *doi:10.1002/etc.3412*.

[2]Massaro, M.; Riela, S.; Cavallaro, G.; Gruttadauria, M.; Milioto, S.; Noto, R.; Lazzara, G. *J. Organomet. Chem.*, **2014**, *749*, 410-415.

[3](a)Pasbakhsh, P.; Churchman, G. J.; Keeling, J. L. *Appl. Clay Sci.*, **2013**, *74*, 47-57; (b) Arcudi, F.; Cavallaro, G.; Lazzara, G.; Massaro, M.; Milioto, S.; Noto R.; Riela, S. *J. Phys. Chem. C*, **2014**, *118*, 15095-15101.

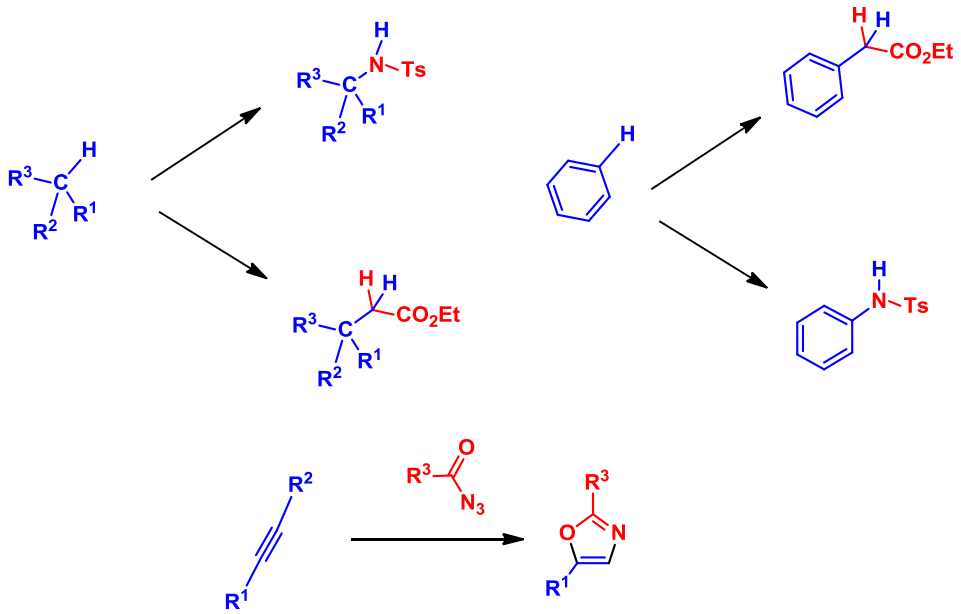
[4](a) Massaro, M.; Riela, S.; Lo Meo, P.; Noto, R.; Cavallaro, G.; Milioto, S.; Lazzara, G. *J. Mater. Chem. B*, **2014**, *2*, 7732-7738; (b) Massaro, M.; Colletti, C. G.; Noto, R.; Riela, S.; Poma, P.; Guernelli, S.; Parisi, F.; Milioto, S.; Lazzara, G., *Int. J. Pharm.* **2015,** *478* (2), 476-485; (c) Massaro, M.; Riela, S.; Baiamonte, C.; Blanco, J. L. J.; Giordano, C.;. Lo Meo, P; Milioto, S.;. Noto, R; Parisi, F.; Pizzolanti, G.; Lazzara G. *RSC Adv.* ***submitted***.

IL-21

Conversion of simple hydrocarbons into functionalized products

Pedro J. Pérez
Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC, CIQSO-Centro de Investigación en Química Sostenible and Departamento de Química, Universidad de Huelva, Campus de El Carmen 21007 Huelva, Spain
e-mail: perez@dqcm.uhu.es

An overview of the transformations developed with group 11 metal-based catalysts involving the transfer of carbene and nitrene units will be presented. Saturated or unsaturated linear hydrocarbons have been converted into esters, amines, cyclopropanes or aziridines. Arenes have also been employed as reactants for some of the previous reactions. Additionally, alkyne-azide [3+2] cycloadditions and related novel transformations have been developed in our laboratory.



IL-22

Functional dyes: from synthesis to applications

Claudia Barolo, Nadia Barbero, Claudio Magistris, Simone Galliano, Roberto Buscaino, Pierluigi Quagliotto and Guido Viscardi
Department of Chemistry, NIS and ICxT Interdepartmental and INSTM Reference Centres, University of Turin, Via Pietro Giuria 7, I-10125 Torino (Italy)
e-mail: claudia.barolo@unito.it

The term "*functional dyes*" has been used to indicate dye or pigment molecules developed for purposes other than the classical coloration of substrates. Starting from the two seminal International Symposium on Functional Dyes on the early nineties the development of this frontier research has been very fast and resulted in the main research line for colorist both in academia and industry starting from the mid nineties.

In this contribution will be presented some example of functional dyes (from UV to IR absorbing dyes), which are useful for hi-tech applications and that were recently developed in our laboratories. Emphasis will be paid to the design of dye molecules[1] and the synthetic approaches (Figure 1)[2] needed for the specific application (ranging from optoelectronics, i.e. Dye-sensitized solar cells, DSCs,[3] or light emitting cells, LEC,[4] to biomedical applications, such as photodynamic therapy, PDT[1], for the treatment of cancer and fluorescent sensors).

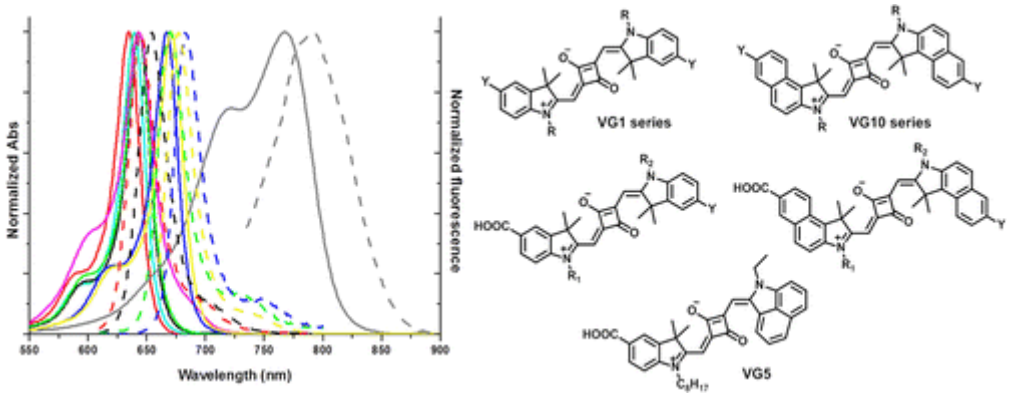


Figure 1: absorption spectra and molecular structures of a series of IR functional dyes for high-tech applications

[1] Barolo, C.; Yum, J.; Artuso, E.; Barbero, N.; Di Censo, D.; Lobello, M. G.; Fantacci, S.; De Angelis, F.; Graetzel, M.; Nazeeruddin, M. K.; Viscardi G. *ChemSusChem* **2013** *6*, 2170-2180

[2] Barbero, N.; Magistris, C.; Park, J.; Saccone, D.; Quagliotto, P.; Buscaino, R.; Medana, C.; Barolo, C.; Viscardi, G. *Org. Lett.* **2015** *17*, 3306-3309.

[3] Saccone, D.; Galliano, S.; Barbero, N.; Quagliotto, P.; Viscardi, G.; Barolo, C. *Eu. J. Org. Chem.* **2016** *13*, 2244-2259.

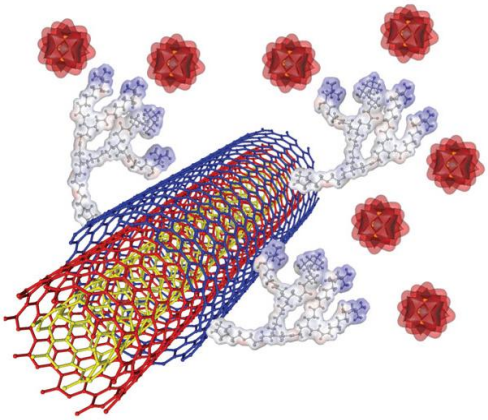
[4] (a) Weber, M. D.; Garino, C.; Volpi, G.; Casamassa, E.; Milanesio, M.; Barolo, C.; Costa, R. D. *Dalton Trans.* **2016** *45*, 8984-8993. (b) Volpi, G.; Garino, C.; Conterosito, E.; Barolo, C.; Gobetto, R.; Viscardi G. *Dyes and Pigments* **2016** *128*, 96-100.

IL-23

Organic materials in electrochemical and photochemical splitting of water

Maurizio Prato
Department of Chemical and Pharmaceutical Sciences, University of Trieste, Italy and CIC BiomaGUNE, San Sebastián, Spain
e-mail: prato@units.it

We have recently demonstrated that the combination of functionalized carbon nanotubes with powerful catalysts for oxidation of water provides very efficient systems. In fact, functionalized carbon nanotubes and graphene act as effective electron transducers, helping the process, which occurs with very high turnover number and turnover frequencies.



After our initial efforts in the electrochemically catalyzed splitting of water, we moved to the more interesting photochemical process. As sensitizer, we started to use perylene bisimides, an old class of compounds extensively studied for their interesting photophysical properties. They absorb light very efficiently and have been widely used as strong acceptors in dyads and triads, in photoinduced electron-transfer reactions.

During this talk, we will describe the synthesis and the properties of novel perylene bis-imide derivatives, with an eye to applications in materials science, including the preparation of photoactive electrodes and water splitting systems.

ORAL COMMUNICATIONS

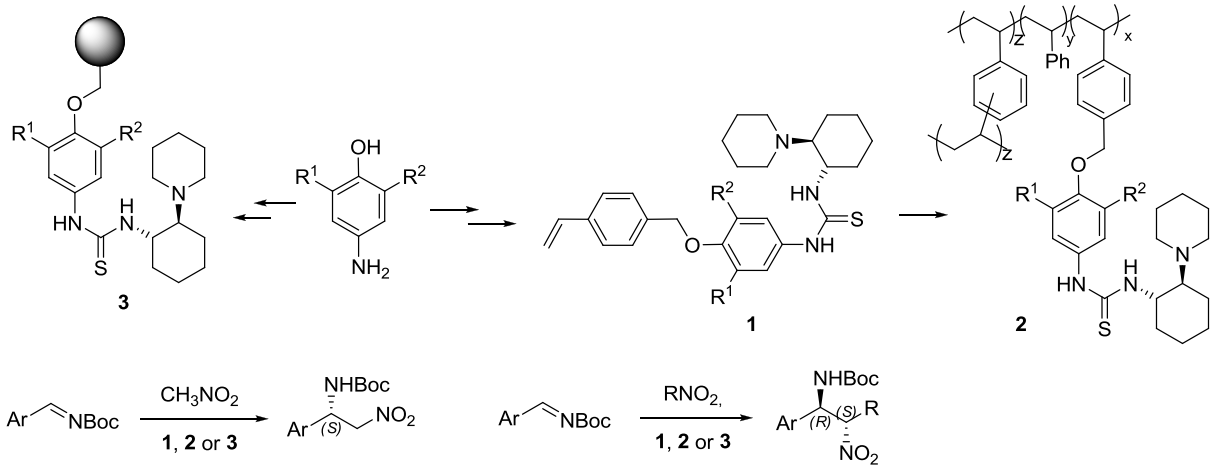
OC-1

Application of New Bifunctional Thioureas in Enantioselective and Diastereoselective Aza-Henry reactions

Rafael Pedrosa*, José M. Andrés*, Mercedes Sánchez and María Valle
Instituto CINQUIMA and departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid, Paseo de Belén, 7, 47011-Valladolid, Spain
e-mail: maria.valle.alvarez@alumnos.uva.es

The asymmetric aza-Henry reaction of nitroalkanes with N-Boc-imines is considered one of the most attractive methods in the formation of β-nitroamines.[1] We became interested in the development of new thiourea catalysts[2] as hydrogen-bond donors and have found that bifunctional thioureas bearing a tertiary amino group derived from trans-1,2cyclohexanodiamines efficiently promote enantio- and diastereoselective aza-Henry additions in neat conditions.

Almost the entire examples found in the literature show the preparation of supported organocatalysts by their anchorage on polymeric commercial materials. We have obtained catalyst **3** from Merrifield resins and catalyst **2** following another less investigated strategy which consists in the bottom-up synthesis by co-polimerization of styryl thiourea **1** and divinylbenzene.



Novel thioureas **1-3** catalyze aza-Henry reactions and the polymeric ones can be easily isolated and recycled without modification of the catalytic activity, obtaining the best results with catalyst **2**.

Acknowledgements: Authors thank MINECO (Project CTQ2014-59870-P) and JC y L (Project VA 064U13) for financial support.

1. (a). T. A. Davis, J. N. Johnston. *Chem. Sci.* **2011**, *2*, 1076.

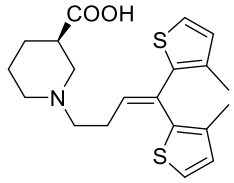
2. (a). R. Munirathinam, J. Huskens, W. Verboom. *Adv. Synth. Catal.* **2015**, *357*, 1093. (b). P. Kasaplar, E. Ozkal, C. Rodríguez-Escrich, M. A. Pericàs. *Green Chem*. **2015**, *17*, 3122. (c). J. M. Andrés, N. de la Cruz, M. Valle, R. Pedrosa *ChemPlusChem* **2016**, *81*, 86.

OC-2

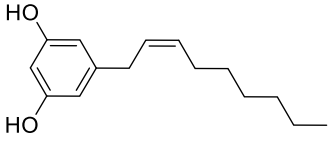
Selective Carbon-Carbon Double Bond Formation in the Synthesis of Small Molecules with Biological Activity

Roberto Ballini, Enrico Marcantoni, Gabriele Lupidi, Pamela Piermattei, Serena Gabrielli and Simone Giorgi
School of Science and Technology, Chemistry Division, University of Camerino, Via S. Agostino 1, 62032 Camerino
e-mail: simone.giorgi@unicam.it

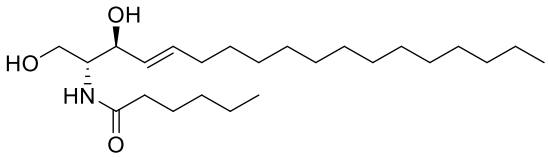
In recent decades, the development of small molecules has had a big impact in pharmaceutical chemistry for the treatment of diseases. The term 'small molecules' has not strict definition, but it is usually used to describe organic molecules which molecular weight is generally under 2000 Daltons, and always less than that of macromolecules such as DNA, RNA and proteins.[1]
Carbon-Carbon double bond is a functional group present in many small molecules. The position and configuration of the double bond give to the molecule characteristic biological activities. All of the molecules represented below possess interesting biological activity, in particular was demonstrated for L-*erythro*-Ceramide and Climacostol that the activity is strictly related to the alkene configuration.[2,3,4]



(R)-Tiagabine



Climacostol



L-*erythro*-Ceramide

We performed the total synthesis of these molecules with high regio- and diastereoselective formation of the double bond obtaining the desired molecules with good yields.[5] There are several benefits associated with the use of small molecules as therapeutic agents including their synthetic accessibility, that is considerably easier than for complex macromolecules.

1 Schreiber, S. L. *Nat. Chem. Biol* **2005**, *1*, 64-66.
2 (a) Janosi, L.; Gorfe, A. *Biophys. J.* **2010**, *99*, 2957-2966. (b) Bielawska, A.; Crane, H. M.; Liotta, D.; Obeid, L. M.; Hannun, Y. A. *J. Biol. Chem.* **1993**, *268*, 26226-26232.
3 (a) Quassinti, L.; Ortenzi, F.; Marcantoni, E.; Ricciutelli, M.; Lupidi, G.; Ortenzi, C.; Buonanno, F.; Bramucci, M. *Chemico-Biol. Int.* **2013**, *206*, 109-116. (b) Perrotta, C.; Buonanno, F.; Zecchini, S.; Giavazzi, A.; Guerra, L.; Belardinelli, M. C.; Picchietti, S.; Fausto, A. M.; Giorgi, S.; Marcantoni, E.; Clementi, E.; Ortenzi, C.; Cervia, D. *Sci. Rep.* **2016**, in press.
4 Frølund, B.; Jørgensen, A.T.; Tagnose, L.; Stensbøl, T. B.; Vestergaard, H. T.; Engblom, C.; Kristiansen, U.; Sanchez, C.; Krogsgaard-Larsen P.; Liljefors, T. *J. Med. Chem.* **2002**, *45*, 2454-2468.
5 (a) Bartoli, G.; Cipolletti, R.; Di Antonio, G.; Giovannini, R.; Lanari, S.; Marcolini, M.; Marcantoni, E. *Org. Biomol. Chem.* **2010**, *8*, 3509-3517. (b) Fiorini, D.; Giuli, S.; Marcantoni, E.; Quassinti, L.; Bramucci, M.; Amantini, C.; Santoni, G.; Buonanno, F.; Ortenzi, C. *Synthesis*, **2010**, *9*, 1550-1556.

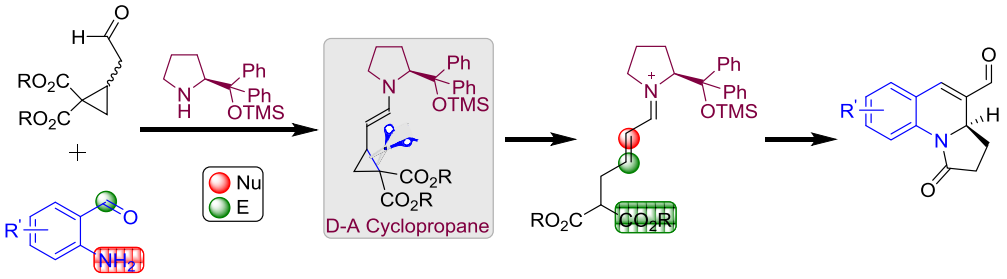
OC-3

Aminocatalysis Mediated Cyclopropane Ring Opening/Aza-Michael/Aldol Domino Reaction. Straightforward Synthesis of Pyrrolo[1,2-α]quinolines

Eduardo Sánchez-Díez, Diana L. Vesga, Efraim Reyes, Uxue Uria, Luisa Carrillo, Jose Luis Vicario

Departamento de Química Orgánica II. Facultad de Ciencia y Tecnología
Universidad del País Vasco/Euskal Herriko Unibertsitatea (UPV/EHU)
P.O. Box 644, 48080 Bilbao (Spain)
e-mail: eduardo.sanchez@ehu.eus

Domino reactions show up as an elegant and efficient strategy in synthetic chemistry. We believe, that properly functionalized Donor−acceptor cyclopropanes can play a key role in the development of this chemistry through the interesting polyfunctional intermediates generated after a ring-opening process. Based on the precendents of organocatalysts to promote domino processes, we have designed a cyclopropaneacetaldehyde[1] that upon condensation with an aminocatalyst renders a Donor-acceptor cyclopropane which will initiate the reaction sequence.



Base on that, we concentrated our efforts on the synthesis of enantioenriched pyrrolo-[1,2-α]quinolines, which are a key structural feature associated with multiple examples of bioactive compounds.[2] After the ring-opening step, an electrophilic α,β-unsaturated iminium ion that would hypothetically react with 2-aminobenzaldeyde leading to the quinoline scaffold would be formed. The pendant arm bearing the ester moiety would allow a final lactamization to form the desired product and include the whole structure of the cyclopropane in the product scaffold. We were delighted to confirm our proposal and obtain the enantioenriched pyrrolo-[1,2-α]quinolines in a one-pot sequence (81-99% ee).

Acknowledgement: The authors thank the Spanish MINECO (FEDER CTQ2014-52107-P) and the Basque Government (IT328-10) and UPV/EHU (UFI QOSYC 11/22 and pre-doctoral fellowship to E.S.) for financial support. Membership in the COST action CM1407 (NatChemDrugs) is also acknowledged.

[1] Halskov, K. S.; Kniep, F.; Lauridsen, V. H.; Iversen, E. H.; Donslund, B. S.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2015**, *137*, 1685-1691.
[2] For a recent review, see: Patel, R. V.; Park, S. W. *Bioorg. Med. Chem* **2015**, *23*, 5247-5263.

OC-4

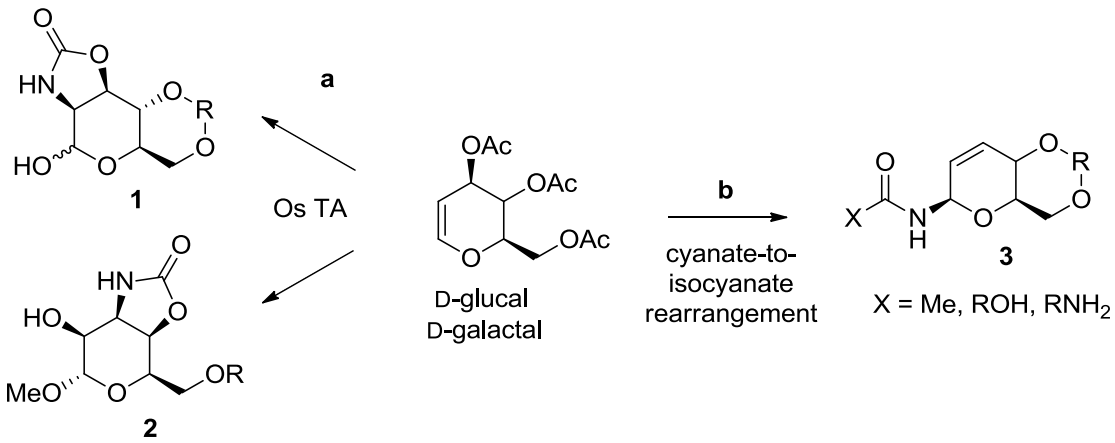
Novel stereoselective syntheses of aminosugars from glycals

Stefania Mirabella, Francesca Cardona and Andrea Goti
Department of Chemistry "Ugo Schiff", University of Firenze, via della Lastruccia 13, Sesto Fiorentino (FI), Italy
e-mail: stefania.mirabella@unifi.it

Amino groups are recurring functionalities in natural products and biologically active compounds, often playing a key role in recognition and interaction with receptors. The stereoselective introduction of amino groups into carbohydrate derivatives to achieve aminosugars represents a challenging and pursued task in organic chemistry. To reach this goal, we exploited a tethered approach, connecting the nitrogen source directly to glycal substrates and unsaturated sugars and performing an intramolecular deliver of the nitrogen atom.

The Donohoe osmium-catalyzed tethered aminohydroxylation (TA)[1] reaction was applied to D-glucal and D-galactal derivatives providing a stereodirected access to 2- and 3-aminosugars protected as oxazolidinones (Scheme a).[2] Complementary results were observed depending on the stage at which the reaction was performed, directly or after a double bond shift consequent to a Ferrier rearrangement.

A stereoselective access to 1-aminosugars from glycals was also achieved taking the advantage of a [3,3] cyanate-to-isocyanate sigmatropic rearrangement[3] (Scheme b). This reaction proceeds under mild conditions, does not require metal catalysis and guarantees efficient chirality transfer. Further functionalization of the obtained *N*-glycosides through a dihydroxylation reaction were also performed with good level of diastereoselectivity.



[1] Donohoe, T. J.; Callens, C. K. A., Lacy A. R., Winter C. *Eur. J. Org. Chem*. **2012**, 655-633.
[2] Mirabella, S.; Cardona, F.; Goti, A. *Org. Lett*. **2015**, 17, 728-731.
[3] Stecko, S. *J. Org. Chem*. **2014**, 79, 6342-6346.

OC-5

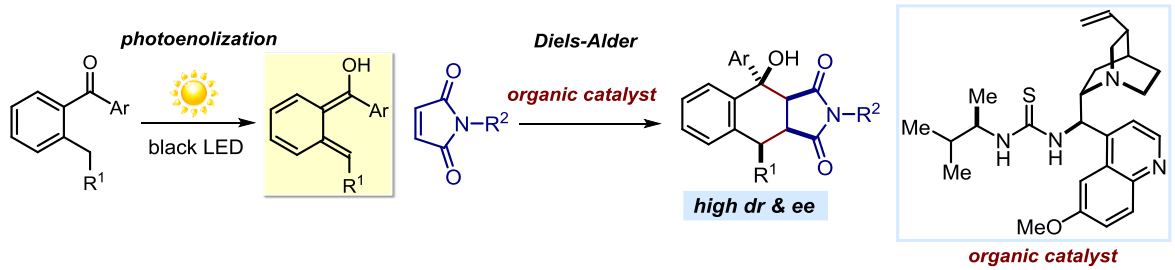
Enantioselective Organocatalytic Diels–Alder Trapping of Photochemically Generated Hydroxy-*o*-Quinodimethanes

Alberto Vega-Peñaloza, Sara Cuadros, Paolo Melchiorre, and Luca Dell'Amico

ICIQ - Institute of Chemical Research of Catalonia, Av. Països Catalans 16, 43007

ldellamico@iciq.es

The photoenolization/Diels–Alder strategy offers straightforward access to synthetically valuable benzannulated carbocyclic products.[1] This historical light-triggered process has never before succumbed to efforts to develop an enantioselective catalytic approach.[2] Herein, we demonstrate how asymmetric organocatalysis provides simple yet effective catalytic tools to intercept photochemically generated hydroxy-*o*-quinodimethanes with high stereoselectivity. We used a chiral organic catalyst, derived from natural cinchona alkaloids, to activate maleimides toward highly stereoselective Diels–Alder reactions. An unconventional mechanism of stereocontrol is operative, wherein the organocatalyst is actively involved in both the photochemical pathway, by leveraging the formation of the reactive photoenol, and the stereoselectivity-defining event.



Scheme 1. Diels-Alder trapping of photochemically generated hydroxy-*o*-quinodimethanes with maleimide derivatives.

The developed strategy shows significant tolerance for structural and electronic variations of the benzophenone derivatives to enable access to a variety of complex tetrahydronaphthalenols, which contain three or four stereogenic centers, with exquisite diastereoselectivity and high enantioselectivity.[3]

L.D. thanks the Marie Curie COFUND action (2014-1-ICIQ-IPMP) for postdoctoral fellowship.

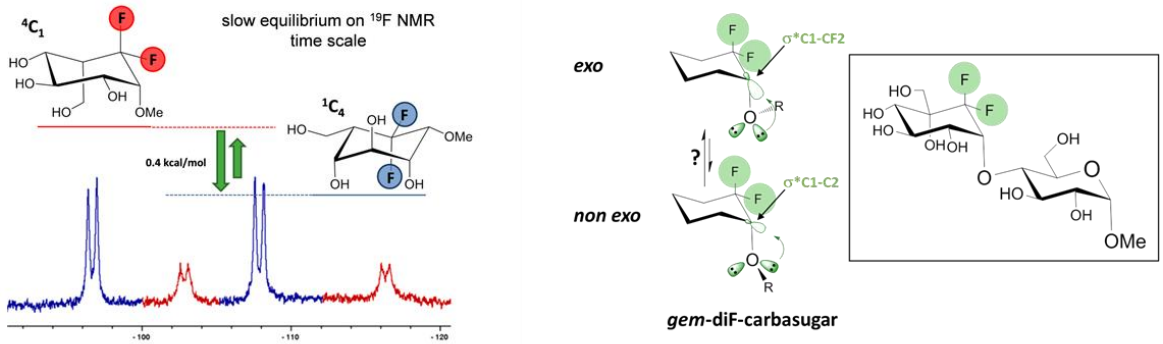
[1] Sammes, P. G., *Tetrahedron* **1976**, *32*, 405–422.
[2] Yang, N. C.; Rivas. C. *J. Am. Chem. Soc.* **1961**, *83*, 2213–2213.
[3] Dell'Amico, L.; Vega-Peñaloza, A.; Cuadros, S.; Melchiorre P. *Angew. Chem. Int. Ed.* **2016**, 128, 3374-3378.

OC-6

Sugars and Proteins: a dynamic interaction

Bixue Xu, Dolores Díaz, F. Cañada, João Sardinha, Sonsoles Martín-Santamaria, Ana Poveda, Jesús Jiménez-Barbero and Luca Unione
Molecular Recognition and Host-Pathogen Interactions, CICbioGUNE, Bizkaia Science and Technology Park bld 801 A, 48160 Derio, Bizkaia Spain
e-mail: lunione@cicbiogune.es

Sugar/protein interactions arise from the delicate interplay between structure, molecular recognition features, and dynamics.[1] Both partners involved in the recognition processes are flexible molecules. Therefore, the effectiveness and specificity of the resulting biochemical response is associated to the plasticity of binding. The sugar code is significantly enriched by the intrinsic flexibility of monosaccharide rings or at higher complexity level, by the flexibility of the interglycosidic linkages.[2] Thus, the access to bio-relevant structures and the possibility of unravelling the origin of sugars flexibility is of paramount importance. However, the access to the experimental values of the energy barriers and free-energy difference for conformer interconversion in water solution has been elusive. Herein, I present detailed studies on structural flexibility in mono- and di-saccharides and mimetics thereof, its consequences in modulating the interaction with biological receptors, as well as approaches to extract the energy values associated to conformer interconversion.[3] I will also provide key findings in the relevance of the stereoelectronic component of the anomeric effect, by demonstrating that CF_2 sugar analogues are able to adopt the natural glycoside conformation, providing new avenues for sugar-based drug design.[4] The combination of fluorine NMR spectroscopy and computational methods allows shedding light on the thermodynamic and kinetic features of the conformational equilibrium in carbohydrates that would have otherwise remained unobserved.



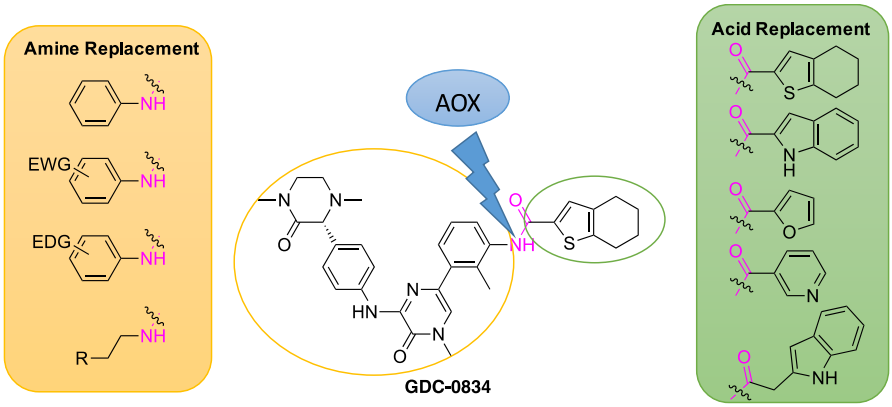
[1] Seeberger, P. H. & Werz, D. B. Synthesis and medical applications of oligosaccharides. *Nature* **2007**, 446, 1046-1051.
[2] Gabius, H. J. & Kayser, K. Introduction to glycopathology: the concept, the tools and the perspectives. *Diagn. Pathol.* **2014**, 9, 4.
[3] Unione, L. Xu, B. et al. Conformational plasticity in Glycomimetics: Fluorocarbamethyl-L-idopyranosides mimic the intrinsic Dynamic behaviour of Natural Idose rings. *Chem. Eur. J.* **2015**, 21, 10513-10521.
[4] Xu, B. Unione, L. et al. gem-Difluorocarbadisaccharides: Restoring the exo-Anomeric Effect. *Angew. Chem. Int. Ed.* **2014**, 53, 9597-9602.

OC-7

Insights into Aldehyde Oxidase metabolism: synthesis and analysis of potential substrates

Martina Ceccarelli, Nicolò Milani, Laura Goracci, Gabriele Cruciani, and Susan Lepri
Department of Chemistry, Biology and Biotechnology, University of Perugia, Via Elce di Sotto 8, 06123 Perugia, Italy
e-mail: susanlepri @gmail.com

One of the major challenge for pharmaceutical companies is knowing the metabolism of drug candidates in the early stages of drug discovery. Nowadays, the development of more reliable models for metabolism prediction is crucial to reduce the risk of failure. Indeed, a significant improvement of the already available models (only based on the most studied CYP450) could be represented by taking into account also non-CYP enzyme. In particular, increasing interest has been aroused by aldehyde oxidase (AOX), playing a key role in Phase I metabolism.[1] Similarly to CYPs, it contributes to oxidation, but in absence of NADPH as co-factor. AOX has a broad substrate specificity, catalysing oxidation not only of aldehydes, but also of nitrogen containing heteroaromatic scaffold.[2] In particular, the aza-heteroaromatic moiety is frequently shared by the majority of drugs, making them susceptible to AOX mediated oxidation.[2] In addition, AOX mediated metabolism has been associated to drug toxicity and drug-drug interactions (DDIs).[3] Moreover, other reactions are ascribed to this enzyme, such as the recently discovered amides hydrolysis[4] on GDC-0834 (Scheme 1).
In the present study, several compounds with potential susceptible moiety towards AOX metabolism were synthesized or acquired, with particular attention focused on amide functionality, to be tested by *in vitro* assays (Scheme 1). The obtained results could help medicinal chemists to design drugs with a reduced risk of failure due to the AOX mediated metabolism. Eventually, these findings can be also used to improve the predictive ability of *in silico* models for metabolism evaluation.



Scheme 1. Design of differently decorated amides inspired to GDC-0834 to investigate AOX mediated amide hydrolysis.

[1] Hutzler, J. M.; Obach, R. S.; Dalvie, D.; Zientek, M. A. *Expert Opin. Drug Metab. Toxicol.* **2013**, *9*, 153-168.
[2] Pryde, D. C.; Dalvie, D.; Hu, Q.; Jones, P.; Obach, R. S.; Tran, T. D. *J. Med. Chem.* **2010**, *53*, 8441-8460.
[3] Beedham, C. *Drug Metab. Rev.* **1985**, *16*, 119-156.
[4] Sodhi, J. K.; Wong, S.; Kirkpatrick, D. S.; Liu, L.; Khojasteh, S. C.; Hop, C. E.; Barr, J. T.; Jones, J. P.; Halladay, J. S. *Drug Metab. Dispos.* **2015**, *43*, 908-915.

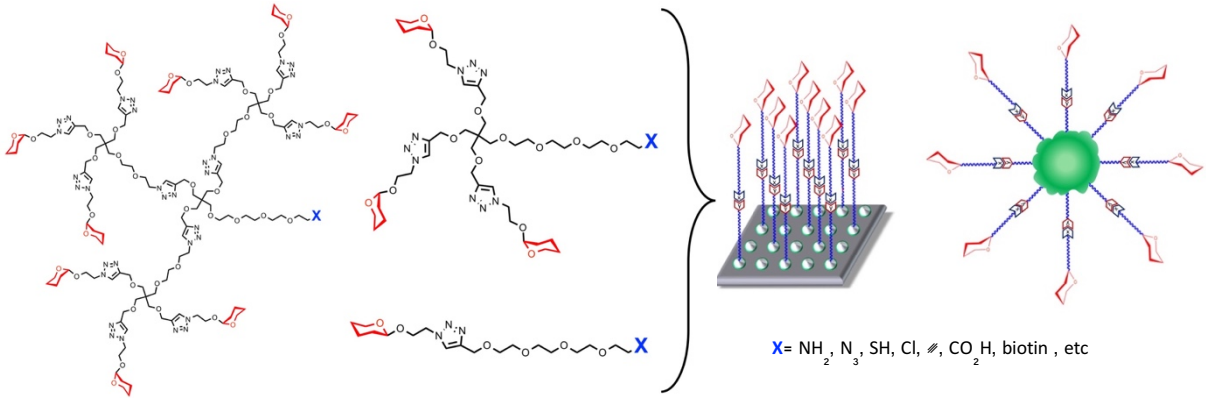
OC-8

Synthesis of dendritic carbohydrate multivalent systems to study biological interaction with lectins

Antonio Di Maio,[a] José J. Reina,[a] Javier Ramos-Soriano,[a] Rute C. Figueiredo,[b] Blanka Didak,[c] Ludovic Landemarre,[c] and Javier Rojo[a]

a) Glycosystems Laboratory, Instituto de Investigaciones Químicas (IIQ), CSIC – Universidad de Sevilla, Américo Vespucio, 49, 41092, Seville, Spain; b) Departamento de Química, Universidade Federal de Ouro Preto, Rua Costa Sena, 171, Centro, 35400-000, Ouro Preto, Minas Gerais, Brazil; c) GLYcoDiag, rue de Chartres, 45071 Orléans, France
e-mail: antoniod.maio@iiq.csic.es

Multivalency plays a major role in biological processes that involves protein–oligosaccharide recognition events particularly with lectins such as MBL, DC-SIGN, defensins etc.[1] The search for high-affinity ligands to study such interactions involves the combination of carbohydrate ligands with different scaffolds for a multivalent presentation of these ligands. These multivalent systems, appropriately functionalized for their conjugation to surfaces, particles or proteins allows the construction of useful tools to address biological studies.



In order to obtain these structures, our laboratory have set up and developed procedures for the synthesis of dendrimeric molecules[2] as well as rapid and efficient strategies to achieve the preparation of the desired carbohydrates units.[3] The versatility of these methods permits the functionalization of the focal point with several functional groups to immobilize these dendrons on different scaffold as described in the Figure using different approaches.
In this way, it is possible to prepare glyconjugates than can be used as very useful tools to study sugar-protein interaction.

Acknowledgements: This work was supported by Ministerio de Economía y Competitividad (MINECO) project CTQ2014-52328-P, co-financed by European Regional Development Fund (ERDF). and EU H2020-MSCA-ITN-2014-642870 (Immunoshape). JJR thanks to CSIC for a JAEdoc contract and JRS thanks MINECO for a FPU fellowship. RCF acknowledge Fundación Carolina for financial support.

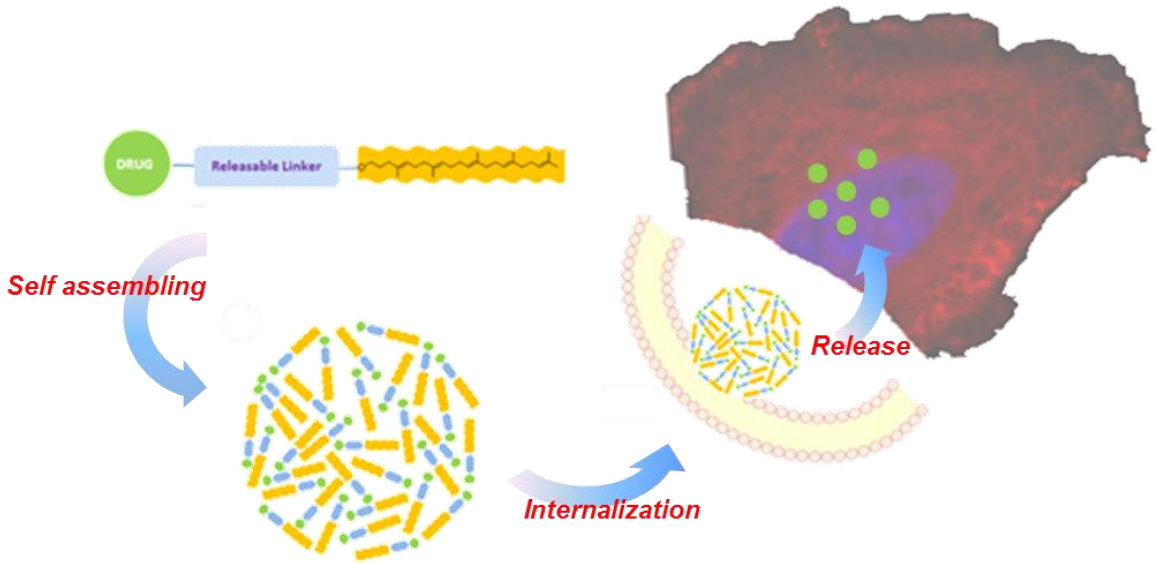
[1] Buzás, E.I.; György, B.; Pásztói, M.; Falus, A.; Gabius, H.J.. *Autoimmunity*, **2006**, *39*, 691-704.
[2] a) Muñoz, A. et al. *Nature Chem.*, ***2016***, *8*, 50-57 b) Varga, N. *et al. Biomaterials*, **2014**, *13*, 4175-4184 c) Ribeiro-Viana, R.; et al. *Nature Comm., 3,* **2012**, 2302.
[3] Reina, J-J.; Di Maio, A.; Ramos-Soriano, J.; Figueiredo, R.-C.; Rojo, J.; *Org. Biomol. Chem.*, **2016**,*14*, 2873-2882

OC-9

Self-assembling drug-conjugates to face cancer

Daniele Passarella
Dipartimento di Chimica, Università degli Studi di Milano, Via Golgi 19, 20133 Milano, Italy
daniele.passarella@unimi.it

Our continuous interest in the field of chemical approaches to target cancer cells moved us to study the preparation of a novel classes of conjugate compounds using natural products with anticancer properties as building blocks. In previous efforts we used squalene tail as self-assembling inducer[1] and a disulphide containing linker to secure the release of the drugs after cell internalization.[2] Subsequently we demonstrated the possibility to generate hetero and fluorescent nanoparticles by mixing a paclitaxel-squalene conjugate and fluorescein-squalene conjugate.[3] In the light of facing the high demanding issue of resistance due to cancer stem cells[4] we studied the formation of cyclopamine-paclitaxel containing nanoparticles and we had the way to detect the internalization by confocal microscopy and super-resolution.[5] Our efforts are actually focused on: a) new combination of drugs to overcome drug resistance, b) new self-assembling inducers, c) new hetero-nanoparticles and c) new drug-conjugates deriving by modification of active natural products.



References:

1. G. Fumagalli, C. Marucci, M. Christodoulou, D. Passarella *et al.* *Drug Discovery Today* accepted
2. S. Borrelli, A. D. Passarella *et al. Eur.J.Med.Chem* 2014, *85*, 179
3. S. Borrelli, G. Fumagalli, D. Passarella *et al.* *ChemPlusChem* **2015**, *80*, 47
4. P.A. Sotiropoulou, C. Herold-Mende, D. Passarella *et al.* *Drug Discovery Today* **2014**, *19*, 1547
5. G. Fumagalli, P. Sotiropoulou, D. Passarella *et al.* *ChemPlusChem* **2015**, *9*, 1380

OC-10

Self-Immolative Molecular Capsules

Romen Carrillo
Departamento de Química Orgánica, Instituto Universitario de Bio-Orgánica "Antonio González", Universidad de La Laguna, Astrofísico Fco. Sánchez, 2, Apdo. Correos 456, 38200 – La Laguna, Spain
e-mail: rocarril@ull.es

Covalent molecular capsules are not versatile: Although they are strong and resistant even to aggressive chemical environments, they cannot release their cargos under a suitable stimulus. In other words, they are not responsive systems. And that is an important drawback for their usage as carriers. In this communication we will report a way to overcome such a disadvantage: Building a self-immolative capsule.

Self-immolative moieties are structural units that "sacrifice themselves" in order to let the function of the whole system to be carried out.[1] Traditionally they are based on the inherent instability of 4-hydroxybenzyl ethers or analogous molecules. This kind of moieties have been already used in pro-drugs, sensors and in dendrimers. We thought that an optimal solution to design a responsive covalent capsule would be to place a self-immolative moiety in a specific area of its structure.

Indeed, our responsive covalent capsule displays a self-immolative lid, which is removed under the right stimulus, allowing thus the releasing of the cargo. The base of the capsule was built over a CTV scaffold, which allows for an efficient encapsulation of biologically relevant ionic pairs such as taurine and GABA.[2] Therefore, when the stimulus is present, the capsule is disassembled and the guest is released.

Such a proof of concept is currently being focused towards drug delivery, with water-soluble, biocompatible capsules.

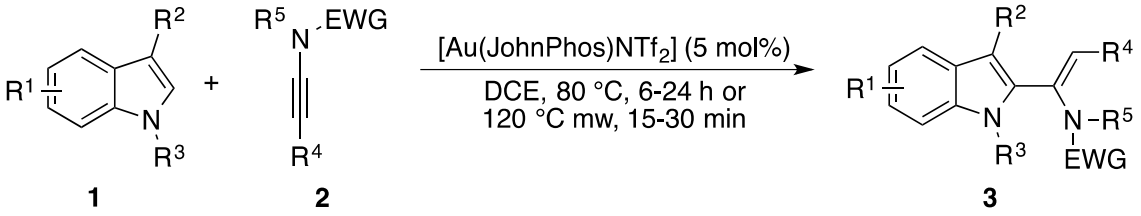
[1] (a) Gnaim, S.; Shabat, D. *Acc. Chem. Res*. **2014**, *47*, 2970−2984. (b) Roth, M. E.; Green, O.; Gnaim, S.; Shabat, D. *Chem. Rev*. **2016**, *116*, 1309-1352.
[2] Perraud, O.; Robert, V.; Gornitzka, H.; Martinez, A.; Dutasta, J.-P. *Angew. Chem. Int. Ed*. **2012**, *51*, 504 –508.

OC-11

Gold-Catalyzed *cis*-Hydroarylation reactions of Ynamides with Indoles: Regio- and Stereoselective synthesis of a new class of 2-vynilindoles

Valentina Pirovano, Marco Negrato, Giorgio Abbiati, Monica Dell'Acqua, Elisabetta Rossi
. *Dipartimento di Scienze Farmaceutiche, Sezione di Chimica Generale e Organica "A. Marchesini", Università degli Studi di Milano, Via Venezian 21, 20133 Milano, Italy*
e-mail: valentina.pirovano@unimi.it

In the last years, among unsatured compounds, ynamides have emerged a versatile building block, becoming a widely exploited starting material in organic synthesis.[1] This class of molecules is characterized by the presence of a nitrogen atom directly connected to a C-sp of an alkyne. As consequence, a strong polarization of the triple bond is observed, enabling a reactivity characterized by high level of regio- and/or steroselection. Recently, gold-catalysts have been employed in reactions involving ynamides in particular for the synthesis of heterocycles.[2] In fact, after activation of the triple bond by the gold species, nucleophilic attack, usually on the C_α, is favored with the formation of a vinyl-gold intermediate that can evolve in other transformations. Thus, in accordance to our interest in gold-catalyzed functionalization on indole ring,[3] we decided to test the possibility of using a simple 3-substituted indole as nucleophile in the reaction with an ynamide. The reaction, conducted in the presence of a gold(I) catalyst led to (*Z*)-(3-methyl-indol-2-yl)-2-vinyl benzensulfonamide **3** as product.



1 **2** **3**

[1] For some recent reviews on the use of ynamides see: (a) Evano, G.; Theunissen, C.; Lecomte, M. *Aldrichimica Acta* **2015**, *48*, 59–70; (b) Wang, X. -N; Yeom, H. -S.; Fang, L. -C.; He, S.; Ma, Z. -X.; Kedrowski, B. L.; Hsung, R. P. *Acc. Chem. Res.* **2014**, *47*, 560-578; (c) Evano, G.; Coste, A.; Jouvin, K. *Angew. Chem. Int. Ed.* **2010**, *49*, 2840-2859; (d) DeKorver, K. A.; Li, H.; Lohse, A. G.; Hayashi, R.; Lu, Z.; Zhang, Y.; Hsung, R. P. *Chem. Rev.* **2010**, *110*, 5064-5106.

[2] For some selected examples see: (a) Liu, J.; Chen, M.; Zhang, L.; Liu, Y. *Chem. Eur. J.* **2015**, *21*, 1009-1013; (b) Zhou, A. -H.; He, Q.; Shu, C.; Yu, Y. -F.; Liu, S.; Zhao, T.; Zhang, W.; Lu, X.; Ye, L. -W.; *Chem. Sci.* **2015**, *6*, 1265-1271; (c) Xin, Z.; Kramer, S.; Overgaard, J.; Skydstrup, T. *Chem. Eur. J.* **2014**, *20*, 7926-7930; (d) Karad, S. N.; Liu, R. -S. *Angew. Chem. Int. Ed.* **2014**, *53*, 9072-9076.

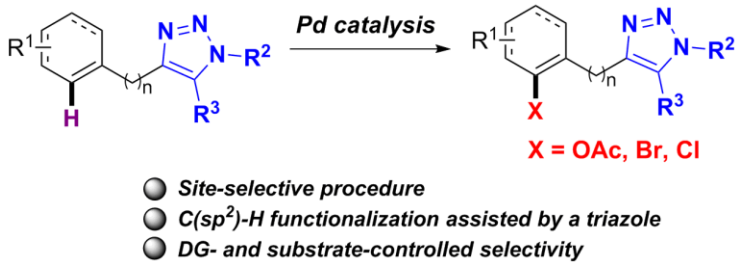
[3] (a) E. Rossi, G. Abbiati, M. Dell'Acqua, M. Negrato, A. Paganoni, V. Pirovano, *Org. Biomol. Chem.* **2016**, accepted manuscript; (b) V. Pirovano, D. Facoetti, M. Dell'Acqua, E. Della Fontana, G. Abbiati, E. Rossi, *Org. Lett.* **2013**, *15*, 3812–3815.

OC-12

Click & Go!

Aitziber Irastorza, Asier Goitia and Arkaitz Correa*
Department of Organic Chemistry-I, University of the Basque Country (UPV-EHU), Joxe Mari Korta R&D Center, Av. Tolosa 72 -20018 Donostia-San Sebastián.
arkaitz.correa@ehu.eus

Owing to its high metabolic stability, hydrogen bonding capability and amide bioequivalence, 1,2,3-triazole core is a privileged structure of wide presence in a vast array of relevant compounds in distinct research areas such as crop protection, medicinal chemistry and material sciences.[1] One of the most practical methods for the assembly of 1,2,3-triazoles is widely referred to as a "*click process*" involving a Cu-catalyzed azide-alkyne [3+2] cycloaddition (CuAAC) to furnish 1,4-disubstituted triazoles.[2] However, despite their widespread important applications and the existence of modular syntheses, 1,2,3-triazoles have been overlooked in organic chemistry and their powerful and unique properties have not yet been exploited. In this communication, selective Pd-catalyzed C(sp^2)−H functionalization events of 4-substituted-1,2,3-triazoles will be described. Unlike previous metal-catalyzed C−H functionalization processes, which preferentially occur at the activated heterocyclic C−H bond,[3] the regioselective oxygenation and halogenation of the C(sp^2)−H bond is now achieved featuring an unconventional role of such simple triazole scaffold as a modular and selective directing group.[4]



Acknowledgements. A.I. thanks Gobierno Vasco for a predoctoral fellowship. A.C. thanks MINECO for a Ramón y Cajal research contract (RYC-2012-09873). We are grateful to the Gobierno Vasco (ELKARTEK_KK-2015/0000101) and UPV/EHU (GIU15/31) for financial support. Prof. J. M. Aizpurua is kindly acknowledged for providing equipment and laboratory facilities.

[1] (a) Thirumurugan, P.; Matosiuk, D.; Jozwiak, K. *Chem Rev.* **2013**, *113*, 4905. (b) Astruc, D.; Liang, L.; Rapakousiou, A.; Ruiz, J. *Acc. Chem. Res.* **2012**, *45*, 630. (c) Chu, C.; Liu, R. *Chem. Soc. Rev.* **2011**, *40*, 2177. (d) Lau, Y. H.; Rutledge, P. J.; Watkinson, M.; Todd, M. H. *Chem. Soc. Rev.* **2011**, *40*, 2848. For a themed issue, see: (e) *Chem. Soc. Rev.* **2010**, *39*, 1231.
[2] (a) Haldón, E.; Nicasio, M. C.; Pérez, P. J. *Org. Biomol. Chem.* **2015**, *13*, 9528. (b) Ackermann, L.; Potukuchi, H. K. *Org. Biomol. Chem.* **2010**, *8*, 4503. (c) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952.
[3] (a) Lesieur, M.; Lazreg, F.; Cazin, C. S. J. *Chem. Commun.* **2014**, *50*, 8927. (b) Ackermann, L.; Althammer, A.; Fenner, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 201. (c) Ackermann, L.; Vicente, R.; Born, R. *Adv. Synth. Catal.* **2008**, *350*, 741. (d) Chuprakov, S.; Chernyak, N.; Dudnik, A. S.; Gevorgyan, V. *Org. Lett.* **2007**, *9*, 2333. (e) Iwasaki, M.; Yorimitsu, H.; Oshima, K. *Chem. Asian. J.* **2007**, *2*, 1430. (f) Jiang, H.; Feng, Z.; Wang, A.; Liu, Z.; Chen, Z. *Eur. J. Org. Chem.* **2007**, 1227.
[4] Irastorza, A.; Aizpurua, J. M.; Correa, A. *Org. Lett.* **2016**, *18*, 1080.

OC-13

Characterizations and synthetic applications of zwitterionic deep eutectic solvents

Matteo Tiecco, Raimondo Germani, Fabio Cardellini
Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia, Via Elce di Sotto 8-I, 06124 Perugia, Italy
e-mail: matteotiecco@gmail.com

The search for low toxicity reaction media has been investigated thoroughly, especially to find alternatives to organic solvents. One of these alternatives is represented by Ionic Liquids (ILs) formed by organic cations and organic or inorganic anions, which are liquid at temperatures under 100°C[1]. These reaction media have many advantages compared to typical organic solvents such as low vapour pressure and high recycle capability. Unfortunately ILs show also many "green" disadvantages because of their low biodegradability and low biocompatibility and therefore low sustainability; moreover the synthesis and purification of these media often requires extensive use of organic solvents. For these reasons, more biocompatible novel systems have gained relevance in recent years, like Deep Eutectic Solvents (DESs). DESs are a novel family of organic media generally liquid at temperatures lower than 100°C. DESs show chemico-physical properties similar to the traditionally used ionic liquids; however they are less toxic and more biodegradable[2]. DESs can be prepared by mere mixing high-melting-point quaternary ammonium or phosphonium salts with neutral compounds, which are able to form hydrogen-bond interactions, as alcohols, amides, carboxylic acids, phenols, polyols or carbohydrates. The strong interaction between the hydrogen-bond donor compound and the anion, provided by the salt, leads to a considerable reduction in the melting point of the mixture.
In this work we report the preparation and the characterization of novel classes of zwitterionic DESs. The first class is represented by mixtures of trimethylglicine with aromatic and aliphatic carboxylic acids[3]; the second class is formed by (1S)-(+)-10-camphorsulfonic acid (CSA) and differently structured sulfobetaines with aliphatic, aromatic and amphiphilic moieties, and they are liquid at room temperature (RTDESs)[4]. A DES from this second class (3-(cyclohexyldimethylammonio)propane-1-sulfonate and CSA mixture) was successfully used both as reaction media and catalyst in Carbon-Carbon bond formation via Claisen-Schmidt reaction[5]. The advantages of the use of this DES in this probe reaction are represented by: the green properties of the media and its low toxicity; the absence of harmful acids to catalyse the aldol condensation because of the camphorsulfonic acid composing the DES mixture; the recycling and the re-use of the DES in subsequent reaction cycles; the mild conditions and the excellent conversions and yields observed.

1. Welton, T., *Chemical reviews* **1999,** *99* (8), 2071-2084.
2. Alonso, D. A.; Baeza, A.; Chinchilla, R.; Guillena, G.; Pastor, I. M.; Ramón, D. J., *European Journal of Organic Chemistry* **2016**.
3. Cardellini, F.; Tiecco, M.; Germani, R.; Cardinali, G.; Corte, L.; Roscini, L.; Spreti, N., *RSC Advances* **2014,** *4* (99), 55990-56002.
4. Cardellini, F.; Germani, R.; Cardinali, G.; Corte, L.; Roscini, L.; Spreti, N.; Tiecco, M., *RSC Advances* **2015,** *5* (40), 31772-31786.
5. Tiecco, M.; Germani, R.; Cardellini, F., *RSC Advances* **2016,** *6*, 43740 - 43747.

OC-14

Hydrogen Abstraction for Photoactive Cholesterol Derivatives

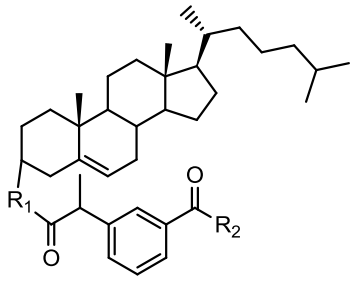
Fabrizio Palumbo[1], Isabel M. Morera[1], Francisco Bosca[1], Inmaculada Andreu[2] and Miguel A. Miranda[1]

[1] *Instituto de Tecnología Química UPV-CSIC, Departamento de Química, Universitat Politecnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain*

[2] *Unidad Mixta de Investigación IIS La Fe-UPV, Hospital Universitari i Politecnic La Fe, Avenida de Fernando Abril Martorell 106, 46026 Valencia, Spain*

e-mail: fpalumbo@itq.upv.es

Cholesterol (Ch) is the most important lipidic building block in cell membranes. Its oxidation in cells can be induced *via* free radicals (Type I) or singlet oxygen (Type II). The former generally involves hydrogen abstraction (HA) of an allylic hydrogen at carbon C7 and can be achieved by photosensitizing agents such as nonsteroidal antiinflammatory drugs (NSAIDs), in combination with UVA light. In this context, ketoprofen (KP) is a NSAID that contains the benzophenone chromophore and displays a n,π* triplet excited state, whereas suprofen (SP) is a related drug that includes the 2-benzoylthiophene chromophore and has a π,π* lowest triplet excited state. With this background, the goal of the present work is to synthesize the photoactive cholesterol derivatives KP-NHCh,[1] KP-Ch[2] and SP-Ch[3], using KP and SP as photosensitizers, in order to follow the primary intramolecular hydrogen abstraction from the Ch backbone.



KP-NHCh:
R_1 = -NH-, R_2 = -Phenyl
KP-Ch:
R_1 = -O-, R_2 = -Phenyl
SP-Ch:
R_1 = -O-, R_2 = - Thiophene

The HA for KP-NHCh, KP-Ch and SP-Ch has been studied by combining steady-state photolysis, laser flash photolysis (LFP) and photo-CIDNP experiments. Thus, KP-NHCh and KP-Ch are appropriate models for clean Type I Ch oxidation, whereas the SP derivatives are suitable systems for investigation of both Type I and Type II mechanisms, since they can be used to photogenerate both biradicals and singlet oxygen. Moreover, the obtained results clearly indicate that Ch hydrogen abstraction is strongly dependent on the lipophilicity of the employed solvent, the specific orientation of the reactants and the electronic nature of the involved triplet excited state.

[1] Neshchadin, D.; Palumbo, F.; Sinicropi, M. S.; Andreu, I.; Gescheidt, G.; Miranda, M. A., *Chem. Sci.* **2013**, *4*, 1608-1614
[2] Andreu, I.; Palumbo, F.; Tilocca, F.; Morera, I. M.; Boscá, F.; Miranda, M. A., *Org. Lett.* **2011**, *13*, 4096-4099.
[3] Palumbo, F.; Boscá, F.; Morera, I. M.; Andreu, I.; Miranda, M. A., *Beilstein J. Org. Chem.* **2016**, Accepted.

OC-15

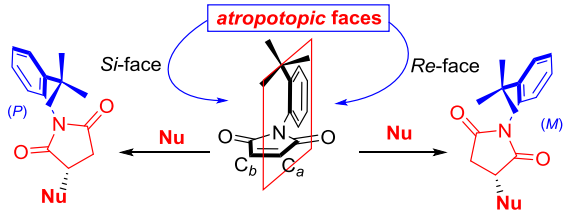
The Remote Control of Axial Chirality Through Aminocatalytic Desymmetrization of *N*-Arylmaleimides

Nicola Di Iorio, Paolo Righi, Andrea Mazzanti, Michele Mancinelli, and Giorgio Bencivenni*

[1]*Dept. of Industrial Chemistry "Toso Montanari", School of Science, University of Bologna, Viale del Risorgimento 4, 40136 Bologna,*

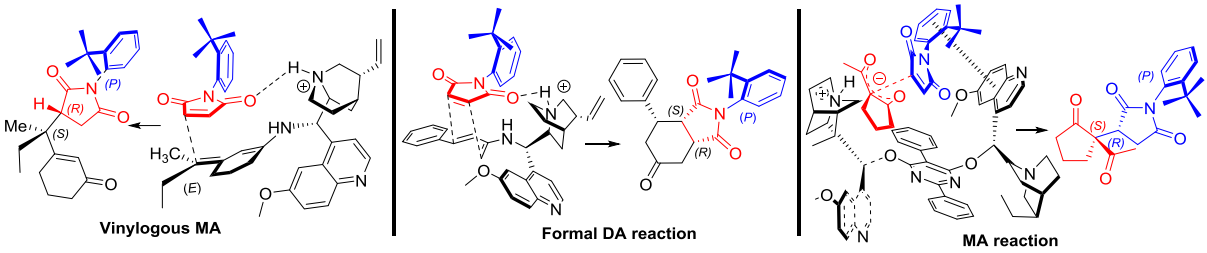
e-mail: giorgio.bencivenni2@unibo.it

N-(2-*tert*-butylphenyl)maleimides are a class of compounds having a hindered rotation of the C_{Ar}-N single bond.[1] This implies the existence of a plane of symmetry which can be desymmetrized through nucleophilic addition at one of the two carbon atoms of the double bond, with the generation of a stereogenic axis in the resulting succinimide (Scheme 1).



Scheme 1

The necessary requirement for the remote control of the stereogenic chiral axis, is the selective recognition by the organocatalyst of the different *Re* atropotopic or *Si* atropotopic side of the maleimide's symmetry plane. This idea was applied to important asymmetric organic reactions such as the vinylogous Michael addition of cyclohexenones,[2] the formal Diels-Alder reaction of α,β-unsaturated ketones[3] and the Michael type reaction of carbon nucleophiles[4] (Scheme 2).



Scheme 2

The results obtained allowed us to establish the efficiency of cinchona alkaloid catalysts to transfer the stereochemical information to both prochiral centers several bonds away and a more distant prochiral axis thus realizing two simultaneous stereochemical events: the generation of two contiguous stereocenters and the remote control of an axial chirality.

[1] Curran, D. P.; Qi, H.; Geib, S. J.; DeMello, N. C.; *J. Am. Chem. Soc.* **1994**, *116*, 3131.
[2] Di Iorio, N.; Righi, P.; Mazzanti, A.; Mancinelli, M.; Ciogli, A.; Bencivenni, G.; *J. Am. Chem. Soc.*, **2014**, 136, 10250.
[3] Eudier, F.; Righi, P.; Mazzanti, A.; Ciogli, A.; Bencivenni, G.; *Org. Lett.* **2015**, *17*, 1728.
[4] Di Iorio, N.; Champavert F.; Erice, A.; Righi, P.; Mazzanti, A.; Bencivenni, G.; *Tetrahedron* **2016**, doi: 10.1016/j.tet.2016.02.052.

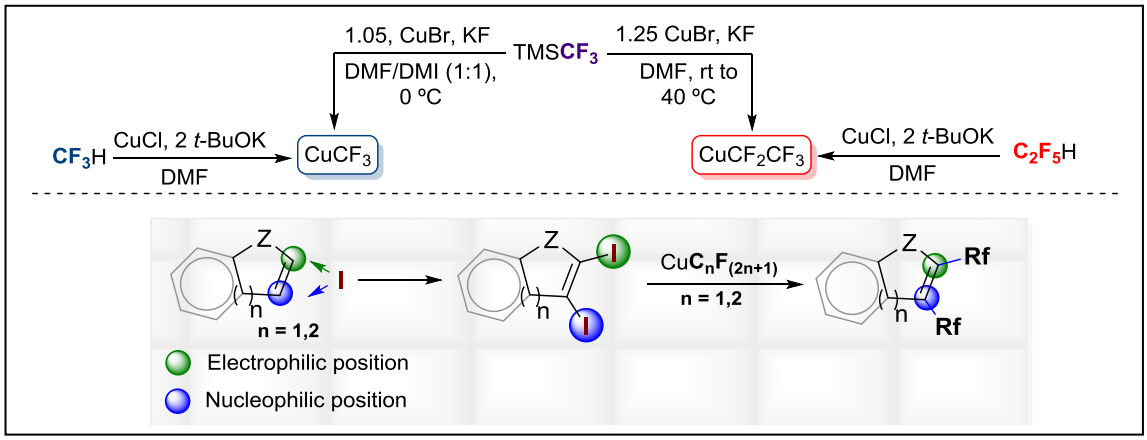
OC-16

Regioselective Trifluoromethylation and Pentafluoroethylation of Electron-Rich Alkenes Using $Cu(CF_2)_nCF_3$ Reagents

Jordi Mestre,[a] Anton Lishchynskyi[b]
Vladimir Grushin,[b] Sergio Castillón,[a] and Omar Boutureira,[a]
[a] Departament de Química Analítica i Química Orgànica, Universitat Rovira i Virgili, C/ Marcel·lí Domingo s/n, 43007, Tarragona, Spain; [b] Institute of Chemical Research of Catalonia (ICIQ) Avgda. Països Catalans 16, 43007, Tarragona, Spain;
jordi.mestre@urv.cat

Fluorine chemistry has long been in the spotlight of drug discovery since the incorporation of fluorine or fluorinated groups drastically enhance the chemical, physical, and biological properties of the non-fluorinated parent molecules.[1]

Here we present complementary methods for the preparation of $Cu(CF_2)_nCF_3$ reagents from either HCF_3[2] or $TMSCF_3$ and their application in a cross-coupling strategy that exploits regioselective positioning of a Csp^2–I bond for the introduction of CF_3 and CF_2CF_3 into ubiquitous electron-rich alkenes present in natural products including glycals, nucleosides and indoles.



[1]Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev*. **2008**, *37*, 320-330.

[2]Zanardi, A.; Novikov, M. A.; Martin, E.; Benet-Buchholz, J.; Grushin, V. V. *J. Am. Chem. Soc.;* **2011**, *133*, 20901–20913.

OC-17

Light-driven water splitting using KuQuinones photocatalysts

Pierluca Galloni, Barbara Floris, Valeria Conte and Federica Sabuzi

Dipartimento di Scienze e Tecnologie Chimiche, Università degli Studi di Roma Tor Vergata
Via della ricerca scientifica, 00133, Roma, Italy
e-mail: federica.sabuzi@uniroma2.it

Water splitting is a strongly endoergonic process, which requires the participation of four electrons and four protons and the formation of a new O−O bond. Consequently, it is characterized by important kinetic barriers, and the use of a catalyst is crucial to activate the splitting. Photosystem II constitutes in nature a successful model for water oxidation[1] indeed, the use of sunlight to perform water splitting appears to be a valid approach.
Few years ago we developed a one-pot procedure for the synthesis of novel pentacyclic quinoid compounds, called KuQuinones (KuQs)[2], starting from easily available and cheap precursors. These compounds are able to harvest light in the visible region of the spectrum due to their pentacyclic and conjugated structure. Thanks to these interesting properties, we studied their ability to act as sensitive material in photoelectrochemical devices, using KuQs-functionalized ITO as working electrode and triethanolamine (TEOA) as sacrificial electron donor in solution[3]. These features suggested the potential application of such novel compounds both as dyes and as electrons acceptor moiety also in the water-oxidation process. In this regard, a stable and high anodic photocurrent signal was detected in basic solution, according to the mechanism proposed in Figure 1. In this contribution, the general synthetic procedure of KuQuinones and preliminary results for the photoelectrochemical water oxidation will be presented.

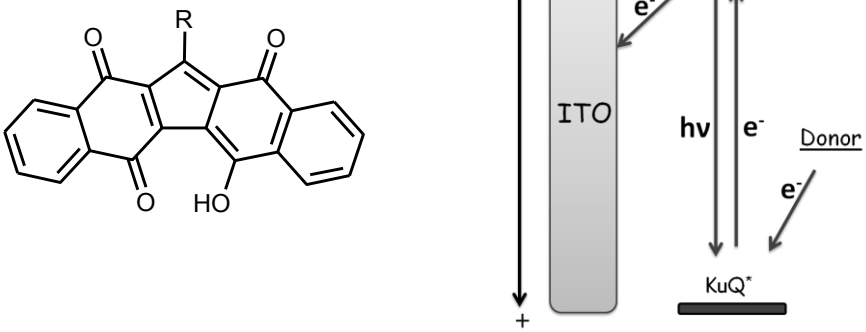


Figure 1. Structure of KuQs (left) and proposed mechanism for the photoelectrochemical cell (right).

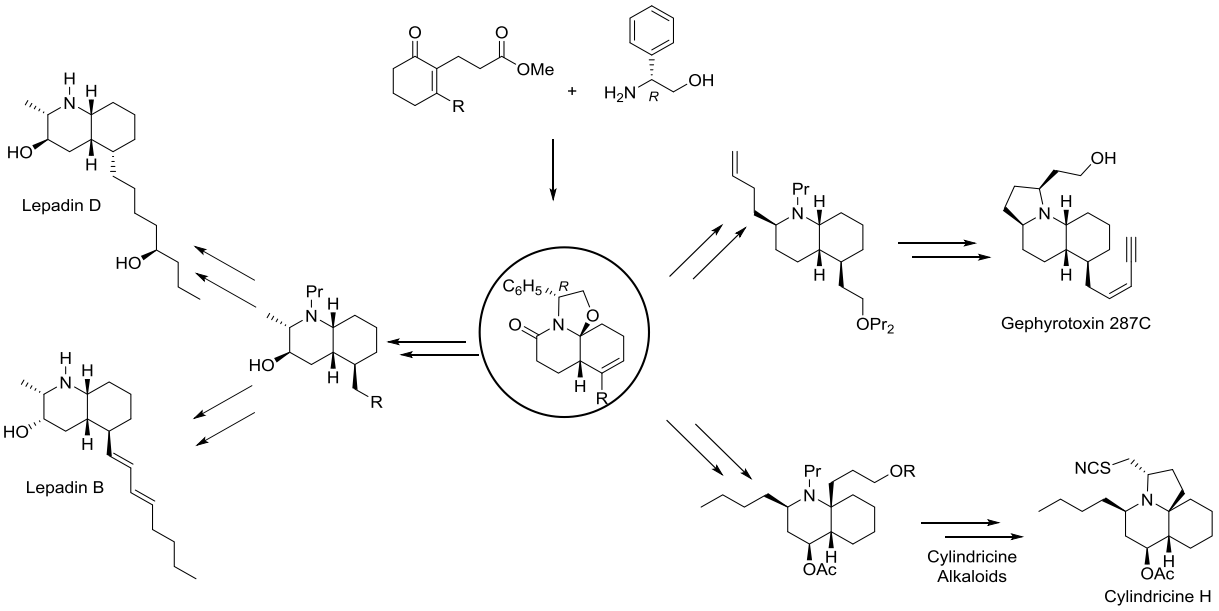
[1] Herrero, C.; Lassalle-Kaiser, B.; Leibl, W.; Rutherford, A. W.; Aukauloo, A. *Coord. Chem. Rev*. **2008**, *252*, 456-468.
[2] Coletti, A.; Lentini, S.; Conte, V.; Floris, B.; Bortolini, O.; Sforza, F.; Grepioni, F.; Galloni, P. *J. Org. Chem*. **2012**, *77*, 6873-6879.
[3] Sabuzi, F.; Armuzza, V.; Conte, V.; Floris, B.; Venanzi, M.; Galloni, P.; Gatto, E. *J. Mat. Chem. C* **2016**, *4*, 622-629.

OC-18

Enantiopure Tricyclic Lactams for the Total Synthesis of Decahydroquinoline Alkaloids

Alexandre Pinto, Miriam Piccichè, Rosa Griera, Joan Bosch and Mercedes Amat
Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Barcelona
e-mail: alexgregorio@ub.edu

The decahydroquinoline motif is widespread in nature and decahydroquinoline alkaloids constitute an important, ever-expanding, group of natural products, which exhibit a wide range of biological activities. They have been isolated mainly from marine (tunicates and flatworms) and animal (amphibians and arthropods) sources, rather than from plants. However, their isolation from natural sources in only scarce amounts and their interesting biological activities have stimulated several synthetic efforts from various groups, including our own, in attempts to develop efficient synthetic routes for these alkaloids.[1]



Our studies on the use of phenylglycinol-derived chiral tricyclic lactams as versatile synthetic platforms for the total synthesis of different families of *cis*-decahydroquinoline alkaloids will be presented.

Acknowledgments: Financial support from the Spanish MICINN/FEDER (CTQ 2015-65354-R and BES-2013-064292), AGAUR, Generalitat de Catalunya (2014-SGR-0155) and networking contribution from the COST action CM-1407.

1. Amat, M., Pinto, A., Griera, R., Bosch, J., *Chem. Eur. J.*, **2015**, *21*, 12804-12808

OC-19

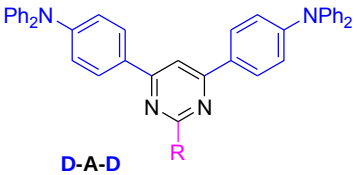
Synthesis, Photophysical and Electrochemical Properties of Push-Pull Structures with a Pyrimidine Core

Cristina Pérez-Caaveiro,[†] María Moreno Oliva,[‡] Juan T. López Navarrete,[‡] José Pérez Sestelo,[†] Luis A. Sarandeses[†] and M. Montserrat Martínez[†]

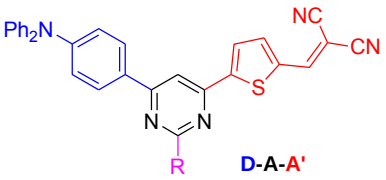
[†]*Departamento Química Fundamental and Centro de investigaciones Científicas Avanzadas (CICA), Universidade da Coruña, E-15071 A Coruña, Spain, and* [‡]*Departamento de Química Física, Universidad de Málaga, Campus de Teatinos s/n, E-29071 Málaga, Spain*

e-mail: mmartinezc@udc.es

Conjugated donor–acceptor (D-A) chromophores, also called push-pull chromophores, have found numerous applications in telecommunication and electro-optical devices. Among them, the pyrimidine ring with its highly π-deficient aromatic character is a good candidate for incorporation as an electron-withdrawing moiety into push-pull scaffolds that favor intramolecular charge transfer (ICT).[1] Herein, we report the synthesis and properties of a series of pyrimidine-core extended π-systems with D-A-D and D-A-A' configuration, in which the donor is a *N*,*N*-diphenylaminophenyl group and the A' is a 2-thiophenyl dicyanovinyl moiety.



D-A-D
(1–3)



D-A-A'
(4–6)

Compound (D-A-D)	λ_{em}^{max} (nm, $CHCl_3$)	Stokes shift (nm)	Φ_f	τ (ns)	$E_g^{opt.}$ (eV)	Compound (D-A-A')	λ_{em}^{max} (nm, $CHCl_3$)	Stokes shift (nm)	Φ_f	τ (ns)	$E_g^{opt.}$ (eV)
1, R = H	485	94	0.49	3.79	2.88	**4**, R = H	510	124	0.02	5.49	1.75
2, R = Cl	510	104	0.42	4.17	2.72	**5**, R = Cl	545	159	6.0E–03	6.19	1.68
3, R = 2-Py	481	90	0.28	3.67	2.85	**6**, R = 2-Py	507	117	1.0E–03	4.96	1.75

The synthesis of the target molecules was carried out by sequential palladium catalyzed cross-coupling reactions of chloropyrimidines with triorganoindium reagents (R_3In).[2] D-A-D compounds (**1**–**3**) displayed absorption wavelengths in the UV region and emission bands with maxima at 481–510 nm with Stokes shifts ~100 nm, fluorescence lifetime (τ) up to 4.17 ns, fluorescence quantum yields up to 0.49 and solvatochromism. The D-A-A' π-systems (**4**–**6**) emitted in the cyan-green region (507–545 nm) with large Stokes shifts (117–159 nm), and exhibit fluorescence lifetime up to 6.19 ns. The redox properties by cyclic voltammetry (CV) for D-A-D compounds exhibit a two-electron reversible oxidation process assigned for the strong electron-donating triphenylamine moieties, whereas for D-A-A' π-systems only one-electron reversible process was observed.

Acknowledgements: We are grateful to the Ministerio de Economía y Competitividad (CTQ2012- 31200 and CTQ2015-68369-P) for financial support.

1. (a) A. Mishra, P. Bäuerle. *Angew. Chem. Int. Ed.* **2012**, *51*, 2020−2067. (b) Achele, S.; Plé, N. *Curr. Org. Synth.* **2012**, *9*, 163−187.
2. Martínez, M. M.; Pérez-Caaveiro, C.; Peña-López, M.; Sarandeses, L. A.; Pérez Sestelo, J. *Org. Biomol. Chem.* **2012**, *10*, 9045−9051.

OC-20

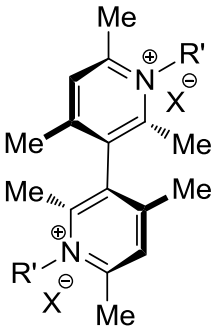
"Inherently Chiral" Ionic Liquids:New Media for Chiral Voltammetry

Francesco Sannicolò,Patrizia Romana Mussini, Serena Arnaboldi,Voichita Mihali,Roberto Cirilli,Alessandra Forni,Armando Gennaro,Abdirisak Ahmed Isse,Marco Pierini and Simona Rizzo

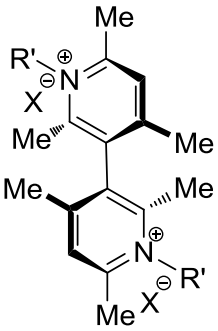
Istituto di Scienze e Tecnologie Molecolari, Consiglio Nazionale delle Ricerche, Via Golgi 19, 20133 Milano (Italy)
e-mail: simona.rizzo@istm.cnr.it

In "inherently chiral" molecular materials the coincidence of the stereogenic element with the molecular portion responsible for their specific properties was shown to result in outstanding enantioselectivity as electrode surfaces.We successfully experimented this concept in designing chiral organic semiconductors employed as highly stereoselective electrode surfaces.[1]

In this work inherently chiral ionic liquids ICILs **1** have been prepared starting from 3,3'-bicollidine, which can be synthesized from inexpensive reagents, separated into stable enantiomers by crystallization of the diastereeomeric salts with D- and L-*O*,*O*-dibenzoyltartaric acids, and converted into long-chain dialkyl salts with melting points below room *T*. All the steps of the sequence have been scaled up to several tenths of grams.



(*R*)-1



(*S*)-1

R, R' = Et X = BF_4
R, R' = Oct X = $(CF_3SO_2)_2N$
R = Oct, R' = Me X = $(CF_3SO_2)_2N$

In this work inherently chiral ionic liquids ICILs **1** have been prepared starting from 3,3'-bicollidine, which can be synthesized from inexpensive reagents, separated into stable enantiomers by crystallization of the diastereeomeric salts with D- and L-*O*,*O*-dibenzoyltartaric acids, and converted into long-chain dialkyl salts with melting points below room *T*. All the steps of the sequence have been scaled up to several tenths of grams.

Both the new inherently chiral ILs and shorter family terms (solid at room *T*), employed as low concentration additives in commercial achiral ionic liquids, afford outstanding enantiodiscrimination of the oxidation peaks of structurally different chiral probes (L- and D-DOPA and their methyl esters, (*R*)- and (*S*)-*N*,*N*-dimethyl-1-ferrocenylethylamines and the antipodes of a chiral oligothiophene) on achiral electrodes, comparable to that obtained on inherently chiral electrodes and regularly increasing with additive concentration.

[1]F. Sannicolò, S. Arnaboldi, T. Benincori, V. Bonometti, R. Cirilli, L. Dunsch, W. Kutner, G. Longhi, P. R. Mussini, M. Panigati, M. Pierini, S. Rizzo, *Angew. Chem. Int. Ed.***2014**, 53, 2623; S. Arnaboldi, T. Benincori, R. Cirilli, W. Kutner, M. Magni P.R. Mussini, K. Noworyta; F. Sannicolò, *Chemical Science***2015**, *6*, 1706.

This work was supported by Fondazione Cariplo (reg. No 2011-1851) and C.N.R..

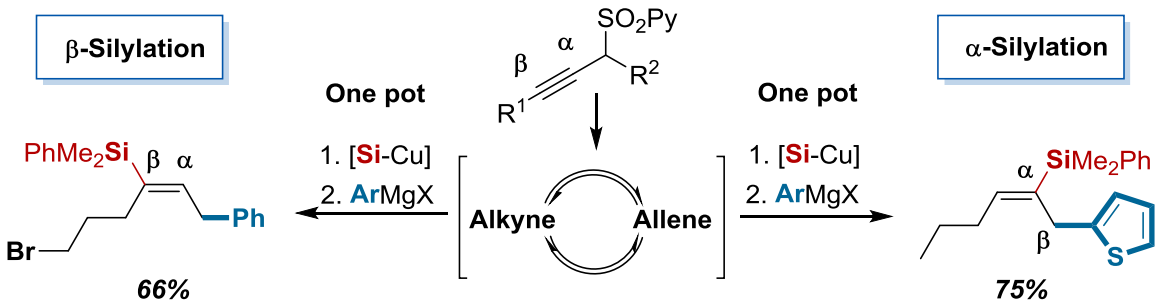
OC-21

Regioselective Cu-Catalyzed Silylation and Borylation of Alkynes

P. Mauleón,* A. García Rubia, Shin Ho Kim, J. A. Romero Revilla, R. Gómez Arrayás,* J. C. Carretero*

Department of Organic Chemistry, Universidad Autónoma de Madrid
c/ Fco. Tomás y Valiente 7, Cantoblanco 28049, Madrid (Spain).
e-mail: pablo.mauleon@uam.es

The Cu-catalyzed silylation of terminal and internal alkynes bearing a 2-pyridyl sulfonyl group (SO_2Py) at the propargylic position affords a breadth of vinyl silanes in good yields and excellent regio- and stereocontrol under mild conditions. The directing SO_2Py group is essential in terms of reaction efficiency and chemoselectivity. Importantly, this group also provides the ability to reverse the regiochemical outcome of the reaction, opening the access to either regioisomer without modification of the starting substrate by virtue of an in situ base-promoted alkyne to allene equilibration which takes place prior to the silylcupration process.[i] Furthermore, removal of the directing SO_2Py enables further elaboration of the silylation products. In particular, a one-pot tandem alkyne silylation/allylic substitution sequence, in which both steps are catalyzed by the same Cu species, opens up a new approach for the access to either formal hydrosilylation regioisomer of unsymmetrical aliphatic-substituted internal alkynes from propargyl sulfones.[1]



The application of this strategy to other Cu-catalyzed borylation processes, as well as rare intramolecular tandem carboborylation reactions, will also be discussed.

1. García Rubia, A.; Romero Revilla, J. A.; Mauleón, P.; Gómez Arrayás, R.; Carretero, J. C. *J. Am. Chem. Soc.* **2015**, *137*, 6867-6865.

OC-22

Synthesis of Semiconducting Polymers for Plastic Solar Cells *via* Direct C-H Bond Arylation of Heterocyclic Monomers

Giuseppe Marzano[1], Francesco Carulli[2], Francesco Babudri[1], Andrea Pellegrino[3], Silvia Luzzati[2], Riccardo Po[3] and Gianluca M. Farinola[1]

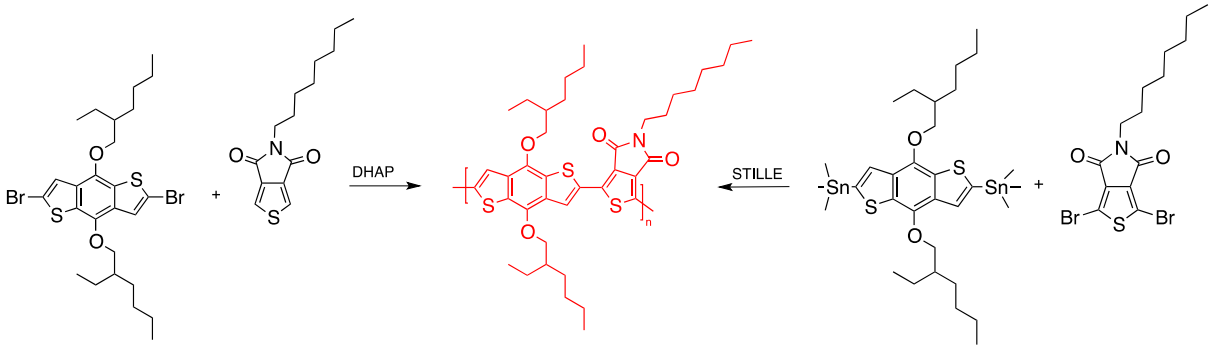
[1]*Dipartimento di Chimica, Università di Bari Aldo Moro, Via E. Orabona 4, Bari, Italy.*
[2]*Istituto per lo Studio delle Macromolecole, CNR-ISMAC, Via E. Bassini 33, Milano, Italy.*
[3]*Istituto Eni Donegani, Eni S.p.A., Via G. Fauser 4, Novara, Italy*

e-mail: gianlucamaria.farinola@uniba.it

The most performing conjugated polymers for Organic Photovoltaics (OPVs) are usually synthesized *via* Pd-catalyzed cross-coupling reactions of organometallic reagents, and the Stille coupling polymerization is frequently the protocol of choice.[1] On the other hand, the highly toxic organo-tin compounds and the stoichiometric amount of metal-containing wastes produced by this reaction do not comply with industrial scalability. In this context, Direct (Hetero)Arylation Polymerization (DHAP) *via* C-H bond activation represents a simpler and greener synthetic tool compared to conventional cross-coupling reactions, avoiding the use of toxic organometallic reagents which can strongly limit large scale processes of industrial interest.[2,3]

The communication will discuss the synthesis of one of the most promising polymers for plastic solar cells, (poly[(benzo[1,2-b:4,5-b']dithiophene)-alt-(4H-thieno[3,4-c]pyrrole-4,6(5 H)-dione) **PBDTTPD**, *via* $Pd(PPh_3)_4$-catalyzed Direct (Hetero)Arylation Polymerization (DHAP). Molecular weight distribution, thermal stability and embedded metal impurities of the polymer obtained with this protocol favourably compare with those of the same material prepared by the Stille polycondensation. In addition, the polymer synthesized *via* DHAP is demonstrated to outperform the Stille reference material in photovoltaic devices under the same processing conditions.

Our results undoubtedly confirm the potential of DHAP as a straightforward and scalable synthetic approach to semiconducting polymers for plastic solar cells.



[1] Marzano, G.; Ciasca, C.V.; Babudri, F.; Bianchi, G.; Pellegrino, A.; Po, R.; Farinola, G.M. *Eur. J. Org. Chem* **2014**, *30*, 6583-6614.
[2] Mercier, G.L. ; Leclerc, M. *Acc. Chem. Res.* **2013**, *46*, 1597−1605.
[3] Marzano, G.; Kotowski, D.; Babudri, F.; Musio, R.; Pellegrino, A.; Luzzati, S.; Po, R.; Farinola, G.M. *Macromolecules* **2015**, *48*, 7039-7048.

OC-23

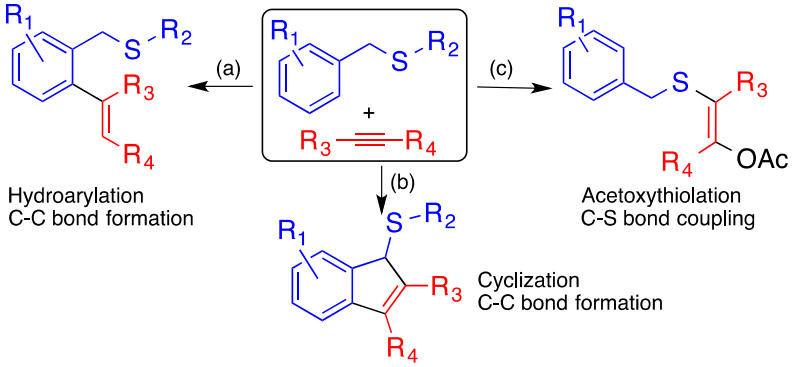
C-H functionalization of benzylthioethers catalyzed by Ru/Cu derivatives: synthetic scope and mechanistic possibilities

Sara Ruiz,[a] Pedro Villuendas,[a] Agustí Lledós,[b] and Esteban P. Urriolabeitia[a]
[a]*ISQCH, CSIC-Universidad de Zaragoza, Pedro Cerbuna 12, 50009 Zaragoza (Spain)*
[b]*Departament de Quimica, Edifici Cn, Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallés, Barcelona (Spain)*
e-mail: esteban@unizar.es

The site-selective activation of C-H bonds promoted by transition metals is currently one of the most powerful tools for the tailored building of complex organic molecules.[1] The selectivity required by the reaction is sometimes achieved according to electronic or steric biases. However, when two or more positions are very similar and their discrimination is not possible, the use of directing groups provides a general solution.[2] Due to this fact hundreds of directing groups are known, almost all of them based on N- and O-bonding atoms. In clear contrast the use of S-directing groups is scarce, in spite of the interest of many S-containing molecules, due to problems related with the deactivation of the catalysts after S-bonding.

In this contribution we show that the use of S-directing groups in Ru/Cu catalysis is perfectly compatible. We have studied the coupling of benzylthioethers with internal alkynes, and we found a highly versatile process. By fine tuning of the reaction conditions we have observed either the hydroarylation of the alkyne (only one C-H bond activation, path a) or the oxidative coupling of the arene and the alkyne (double C-H bond activation, path b) affording indene derivatives. On the other hand, when benzylmercaptane is used as starting material, the selective acetoxythiolation of the alkyne is observed (path c).

All these results have been rationalized on the basis of the respective reactions mechanisms, which have been fully determined by DFT methods.



1. (a) *C-H Bond Activation and Catalytic Functionalization I*, Dixneuf, P. H.; Doucet, H. Eds., *Top. Organomet. Chem.* **2016**, *55*, 1-260. (b) *C-H Bond Activation and Catalytic Functionalization II*, Dixneuf, P. H.; Doucet, H. Eds., *Top. Organomet. Chem.* **2016**, *56*, 1-207.
2 (a) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936. (b) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788.

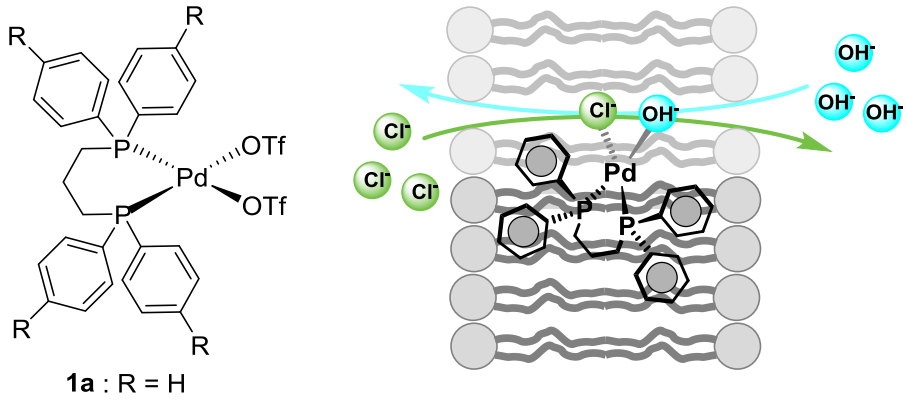
OC-24

Chloride transport across phospholipid membranes mediated by diphosphine-metal complexes

Massimo Tosolini, Gabriele Balducci, Elisabetta Iengo and Paolo Tecilla
Department of Chemical and Pharmaceutical Sciences, University of Trieste, Via Giorgieri 1, I-34127, Trieste, Italy.
e-mail: ptecilla@units.it

There is a growing interest in the potential biological activity of synthetic *trans*-membrane anion transporters[1] mainly related to the fact that defects in anion-transport proteins can lead to a number of diseases known as "channelopathies", the best known being cystic fibrosis (CF), a severe illness caused by impairment of chloride transport through the CFTR anion channel in epithelial cell membranes. It has been proposed that synthetic anion carriers may supply to the deficient chloride transport in ill cells and some experimental evidences have started to appear in the literature.[2]

We have recently reported that a simple Pd(II)–diphosphine complex (**1a**) is able to efficiently transport chloride anions across a phospholipid bilayer acting with a carrier mechanism in which the metal complex resides in the membrane and shuttles the ions across the membrane, by exchanging chloride with OH^- (see Figure). [3]



With the aim to better understand the mechanism of action and to optimize the transport efficiency of this new class of anion transporters we are now exploring several mutations of the diphosphine ancillary ligand. In particular we are tuning the electronic properties of the ligand by adding electron-donor or electron-withdrawing residues (R = OCH_3, CF_3, CN), its lipophilicity (R = CH_3, *n*-butyl), as well as we are testing different metal ions such as Ni(II) and Cu(I). The results of these studies will be presented and discussed.

1. Gale, P. A.; Busschaert, N.; Haynes, C. J. E.; Karagiannidis L. E.; Kirby, I. L. *Chem. Soc. Rev.*, **2014**, *43*, 205−241.
2. Li; H.; Valkenier; H.; Judd, L. W.; Brotherhood. P. R.; Hussain, S.; Cooper, J. A.; Jurček. O.; Sparkes, H. A.; Sheppard, D. N.; Davis. A. P. *Nat. Chem.*, **2016**, 8, 24−32
3. Milano, D.; Benedetti, B.; Boccalon, M.; Brugnara, A.; Iengo, E.; and Tecilla P.; *Chem. Commun.*, **2014**, *50*, 9157–9160.

OC-25

Design and synthesis of fungal transglycosylase ihibitors

Pedro Merino,[a] Tomás Tejero,[a] Ramón Hurtado-Guerrero,[b] Fernando Gomollón,[a] Beatriz García-Carrilero,[a] Jorge Castro[b] and Ignacio Delso[a]
a. Departamento de Síntesis y Estructura de Biomoléculas. Instituto de Síntesis Química y Catálisis Homogénea (ISQCH). Universidad de Zaragoza-CSIC. 50009 Zaragoza, Spain
b. Instituto de Biocomputación y Fisica de Sistemas complejos (BIFI), BIFI-IQFR (CSIC) Joint Unit, Universidad de Zaragoza 50018 Zaragoza, Aragón, Spain
e-mail: idelso@unizar.es

Fungi cell wall remodeling is controlled by the equilibrium between glycoside hydrolases, glycosyltransferases, and transglycosylases. Family 72 glycoside hydrolases (GH72) are ubiquitous in fungal organisms and are known to possess significant transglycosylase activity, producing elongated β-(1,3) glucan chains. Among them are the Gas (in *S. cerevisiae*), Gel (in *A. fumigates*) or Phr and Pga (in *C. albicans*), and all of them with a well conserved catalytic site. The only protein whose structure has been resolved within this family is *Sc*Gas2,[1] which will be our model for ligands and inhibitors design.
In this communication, the design and synthesis of novel ligands for ScGas2 will be presented. Our approach is based on the modification of β-(1,3) glucans, the enzyme natural substrate, by introducing additional groups to increase the number of protein-ligand interactions with the surrounding residues, in order to enhance the binding affinity.

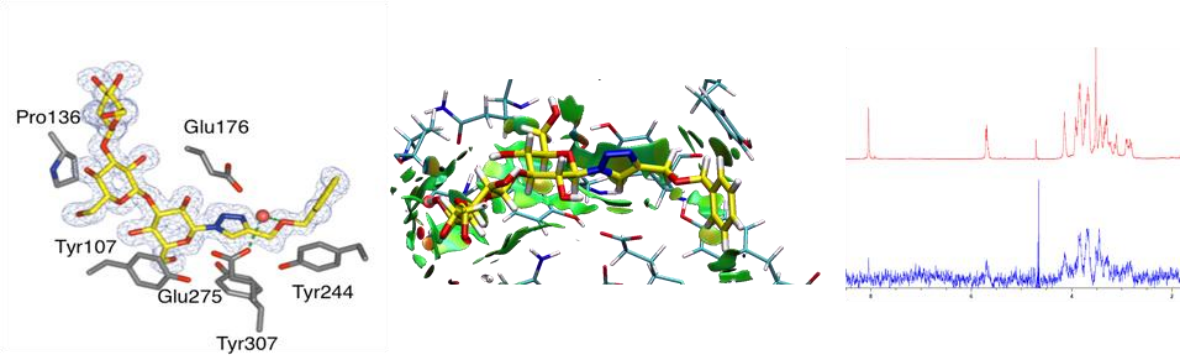


Figure 1. Crystallographic structure of ScGas2-ligand complex (left). Representation of the NCI in the complex (center). STD spectrum (right)

The study of the protein-ligand interactions with several techniques (Figure 1), such as saturation transfer difference NMR experiments (STD-NMR), molecular docking, molecular dynamics, non-covalent-interaction calculation (NCI) and X-ray diffraction of protein complexes will be also discussed.[2]

[1] Hurtado-Guerrero R., Schuettelkopf A.W., Mouyna I., Ibrahim A.F.M., Shepherd S., Fontaine T., Latge J.P., van Aalten, D.M.F. *J. Biol. Chem*, **2009**, 284, *8461-8469* and articles cited therein
[2] Delso I., Valero-Gonzalez J., Marca E., Tejero T., Hurtado-Guerrero R., Merino P. *Chem. Biol. Drug Des*., **2016**, 87, *163-170*

OC-26

Discovery of inhibitors of a novel drug/proton antiporter in human brain endothelial hCMEC/D3 cell line by a pharmacophore-based approach

Laura Goracci[a], Hélène Chapy[b,c,d], Philippe Vayer[e], Yannick Parmentier[e], Pierre-Alain Carrupt[f], Xavier Declèves[b,c,d], Jean-Michel Scherrmann[b,c,d], Salvatore Cisternino[b,c,d], Gabriele Cruciani[a]

[a]*Department of Chemistry, Biology and Biotechnology, University of Perugia, 06123, Perugia, Italy*

[b]*Variabilité de réponse aux psychotropes, INSERM, U1144, 75006 Paris, France.*

[c]*Université Paris Descartes, UMR-S 1144, Paris, F-75006, France*

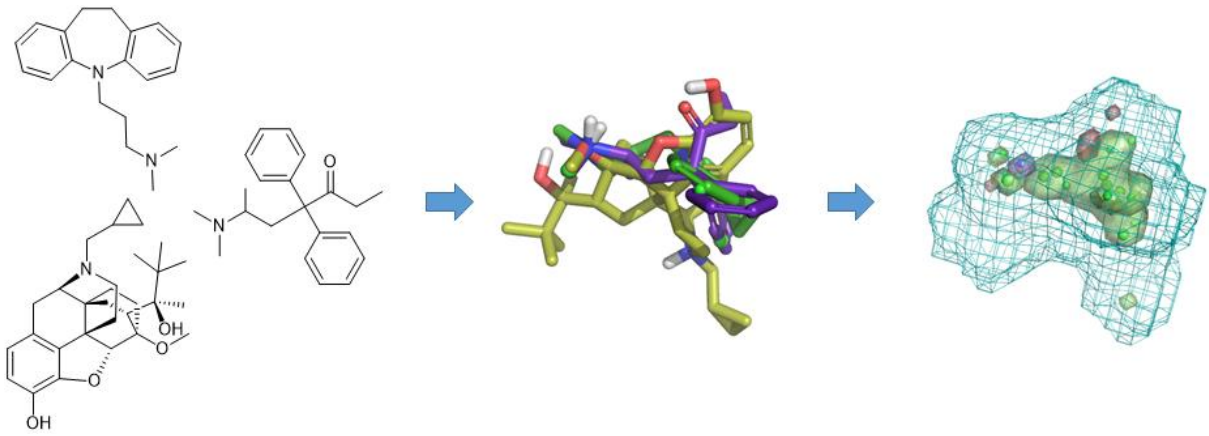
[d]*Université Paris Diderot, UMR-S 1144, Paris, F-75013, France*

[e]*Laboratoire Servier, Département de recherche biopharmaceutique, 45000, Orléans, France*

[f]*Université de Genève – Laboratoire de Pharmacochimie, CH-1211, Genève, Switzerland*

e-mail: laura.goracci@unipg.it

Drug transporters play a key role in governing absorption, distribution, and elimination (ADE) of drugs. The blood-brain barrier (BBB) regulates movement of compounds particularly by specific carrier-mediated systems. Recently, a new proton-antiporter of unknown structure was functionally evidenced *in vitro* and *in vivo*.[1] The aim of this study was to establish a pharmacophore model for inhibitors of this antiporter, since the identification of strong inhibitors is fundamental in studying the pharmacological role of this antiporter. Starting from a dataset of about 30 selected compounds with known inhibition effect (i.e. strong, medium, weak, non-inhibitors) against specific transporter substrates in the human cerebral endothelial hCMEC/D3 cell line, a pharmacophore model for inhibitors was generated. The pharmacophore obtained was used as a template for virtual screening of four xenobiotic and endogenous compound databases. Thus, the hypothetical hit/candidate compounds were tested *in vitro* to determine their inhibition capacity.[2] The pharmacophore model for the new antiporter inhibitors proved to be a good predictor of known inhibitors and allowed the identification new good inhibitors. Moreover, the chemical features of strong inhibitors have been described for the first time.



1. Chapy, H.; André, P.; Declèves, X.; Scherrmann, J.M.; Cisternino, S. *Br. J. Pharmacol.* **2015**, 172, 4714-25.
2. Chapy, H.; Goracci, L.; Vayer, P.; Parmentier, Y.; Carrupt, P. A.; Decleves, X.; Scherrmann, J. M.; Cisternino, S.; Cruciani, G. *Br. J. Pharmacol.* **2015**, *172*, 4888-904.

OC-27

Halloysite Nanotubes as Support for Metal-Based Catalysts

Marina Massaro,[a] Giuseppe Cavallaro,[b] Carmelo G. Colletti,[a] Giuseppe Lazzara,[b] Stefana Milioto,[b] Renato Noto,[a] Filippo Parisi,[b] Serena Riela[a]

[a]*Dipartimento di Scienze e Tecnologie Biologiche, Chimiche e Farmaceutiche (STEBICEF),*
[b]*Dipartimento di Fisica e Chimica*
Università degli Studi di Palermo, Viale delle Scienze, Parco d'Orleans II, Ed. 17
e-mail: marina.massaro@unipa.it

Halloysite nanotubes (HNTs) are a natural, biocompatible, environmental friendly and cheap double-layered aluminosilicate mineral that has a predominantly hollow tubular structure. The general stoichiometry of halloysite is $Al2Si2O_5 \cdot 4(H_2O)$. The layer units consist of a tetrahedral SiOH sheet stacked with an edge shared octahedral AlO_6 sheet with an internal aluminol group AlOH. A water layer exists between the adjacent two layers.[1]

Thanks to their structural features, HNTs are suitable for a potential application as support for catalytic composites.

Recently, we reported the synthesis of novel palladium-based catalytic systems using halloysite nanotubes modified with imidazolium or triazolium moieties as supports for PdNPs and we successfully employed these supported catalysts in the Suzuki reaction under microwave irradiation.[2]

Herein we report an efficient strategy to prepare HNTs-based catalyst through direct chemical grafting with stimuli-responsive polymer (PNIPAAM) coordinating PdNPs. The HNT-PNIPAAM/PdNPs was tested as catalyst in the Suzuki reaction under microwave irradiation.[3]

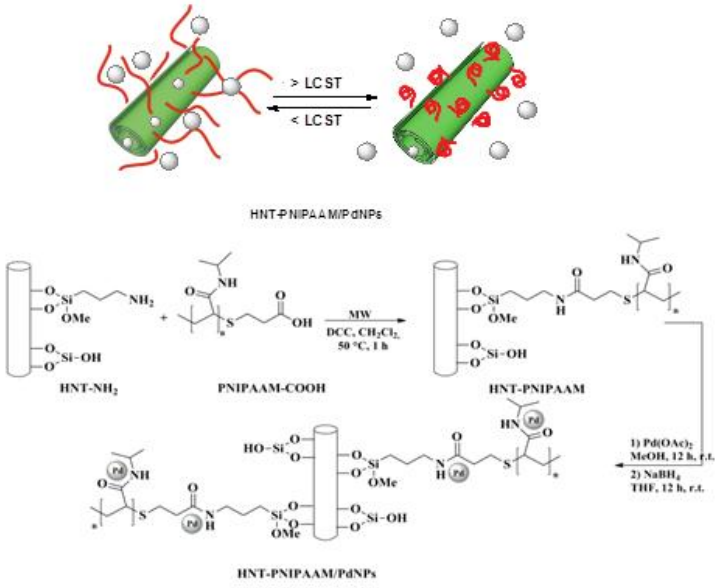


Figure 1. Schematic representation of the synthesis of HNT-PNIPAAM/PdNPs catalyst.

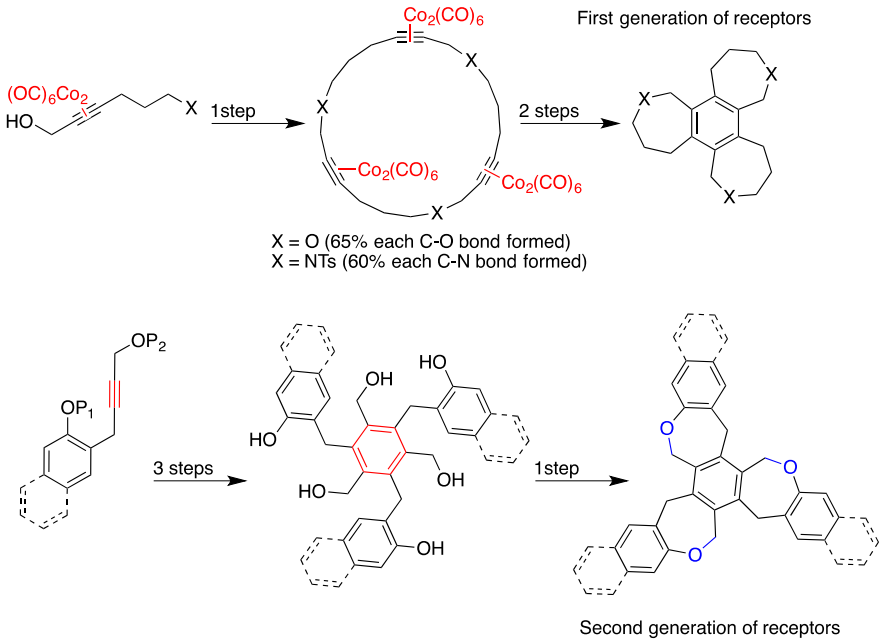
[1]Lvov, Y.; Wang, W.; Zhang, L.; Fakhrullin, R., Halloysite *Adv. Mater.* **2016,** *28* (6), 1227-1250.
[2](a) M. Massaro, S Riela, G. Cavallaro, M. Gruttadauria, S. Milioto, R. Noto, G. Lazzara *J. Organomet. Chem.* **2014**, *749*, 410-415; (b) M. Massaro, S Riela, G. Lazzara, M. Gruttadauria, S. Milioto, R. Noto *Appl. Organomet. Chem.* **2014**, *28*, 234-238.
[3]M. Massaro, S. Riela, G. Cavallaro, C.G. Colletti, S. Milioto, R. Noto, F. Parisi, G. *J. Mol. Catal. A* **2015**, *408*, 12-19.

OC-28

Design and Synthesis of new Structures for Molecular Recognition

Fernando Pinacho Crisóstomo
Instituto Universitario de Bio-Orgánico Antonio González, Avda Astrofísico Francisco Sánchez 2, La Laguna
e-mail: fpinacho@ull.edu.es

The benzocyclotrimers is a new class of compounds that proved to be suitable for molecular recognition purposes. These compounds are C_3 symmetric fused cyclic compounds with a benzene ring at the center forming a small cavity. Recently, our group has disclosed a methodology able to synthesize two new benzocyclotrimers analogs within few synthetic steps and studied the ability to recognize ammonium ions in gas phase.[1] Based on this precedent, we designed a second generation of receptors for tetramethylammonium ion recognition in gas and solution phase.[2] Starting from one these receptors, we are currently performing structural modifications that will confer it water solubility and it will also open up the possibility to use it as scaffold to synthesize new molecular capsules.



1. Carrillo, R.; Martín, T.; López-Rodríguez, M.; Pinacho Crisóstomo, F. *Org. Lett.* **2014**, *16*, 552–555.
2. Carrillo, R.; Hynes, M. J.; Martín, V. S.; Martín, T.; Pinacho Crisóstomo, F. *Org. Lett.* **2015**, *17*, 2912–2915.

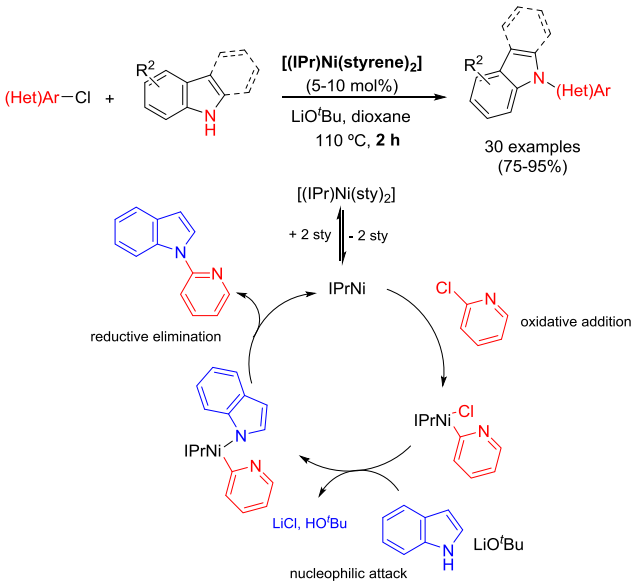
OC-29

The First Nickel-Catalyzed Arylation of Indoles and Carbazoles

Silvia G. Rull,[a] Manuel R. Fructos,[a] Tomás R. Belderrain[a] and M. Carmen Nicasio[b]
[a]*Laboratorio de Catálisis Homogénea, Unidad Asociada al CSIC, CIQSO- Centro de Investigación en Química Sostenible, and Departamento de Química, Universidad de Huelva, 21007, Huelva (Spain)*
[b]*Departamento de Química Inorgánica, Universidad de Sevilla, Aptdo 1203, 41071, Sevilla, (Spain)*
e-mail: mnicasio@us.es

N-arylindoles are pharmaceutically valuable compounds due to their interesting biological activities, including antifungal, antiviral and antipsychotic, among others.[1] The most direct synthetic route to the N-arylindole core is the metal-mediated C-N coupling between an aryl halide and the indole ring. Copper and to a lesser extent palladium are the metal of choice to achieve this transformation.[2]

Recently, we became interested in developing a nickel-based methodology for C-N cross-coupling reactions.[3] We reported that the Ni(0) complex [(IPr)Ni(styrene)$_2$] (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) efficiently catalyzed the coupling of aryl tosylates with cyclic secondary amines and anilines.[3b] Herein, we disclose the first efficient Ni-based protocol for the N-arylation of indoles and carbazoles with (hetero)aromatic chlorides.[4] The procedure provides selectively N-(hetero)arylation products in good to high yields, in short reaction times and without adding an excess of ligands (Scheme 1). Mechanistic studies carried out support a Ni(0)/Ni(II) pathway for this transformation.



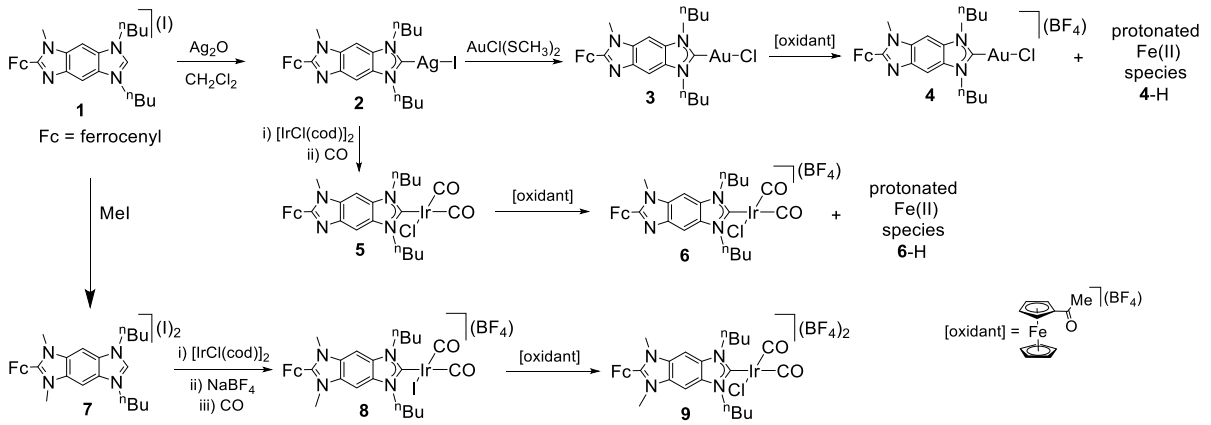
[1] Li, S.-M. *Nat. Prod. Rep*. **2010**, *27*, 57.
[2] Joucla, L.; Djiakovitch, L. *Adv. Synth. Catal*. **2009**, *351*, 673.
[3] (a) Iglesias, M. J.; Prieto, A.; Nicasio, M. C. *Adv. Synth. Catal*. **2010**, *352*, 1949; (b) Iglesias, M. J.; Blandez, J. F.; Fructos, M. R.; Prieto, A.; Álvarez, E.; Belderrain, T. R.; Nicasio, M. C. *Organometallics* **2012**, *31*, 6312.
[4] Rull, S. G.; Blandez, J. F.; Fructos, M. R.; Belderrain, T. R.; Nicasio, M. C. *Adv. Synth. Catal*. **2015**, *357*, 907. (Very Important Paper; Inside Cover)

OC-30

Fc-based N-heterocyclic carbenes for the design of redox-switchable catalysts

Susana Ibáñez, Dmitri Gusev, Eduardo Peris and Macarena Poyatos
Institute of Advanced Materials (INAM), Universitat Jaume I,
Av. Vicente Sos Baynat s/n, 12071-Castellón, Spain
e-mail: poyatosd@uji.es

In traditional design of homogeneous catalysts, the choice of a ligand is based on its steric and electronic properties. This is due to the notion that the ligand plays a spectator role. However, some of the properties of a metal complex may be influenced by essentially ligand-based reactivity.[1] For example, the introduction of a *redox-active* functionality within a ligand framework potentially allows the reactivity and selectivity of complexed metal centers to be modulated through the electrochemical switching of the redox center.[2] In this context, we have designed imidazolium salts **1** and **7**, in which the redox-active fragment is connected to the NHC ligand precursor unit through a polyaromatic system. Ferrocenyl-imidazolium salt **1** has been used for the preparation of related NHC Ag(I), Au(I) and Ir(I)-based complexes (Scheme 1). Aiming to oxidize complexes **3** and **5**, they were reacted with acetylferrocenium tetrafluoroborate that is quantitatively transformed in acetylferrocene, yielding mixtures of the oxidized compounds **4** and **6** along with the protonated Fe(II) species **4**-H and **6**-H, respectively. In order to avoid the protonation of the ligand and to quantify the modification of its donating character upon the introduction of a positive charge, dicationic salt **7** was prepared and used as precursor in the preparation of complex **8**. Complex **8** was also oxidized, generating complex **9**. The catalytic activity of the Au(I) complexes has been studied in two benchmark gold-catalyzed reactions, namely hydroamination of phenylacetylene with arylamines and cyclization of alkynes with furans, in which the addition of an oxidant to the reaction vessel afforded a significant improvement.



1. Crabtree, R. H. *New J. Chem.* **2011**, *35*, 18.
2. (a) Luca, O. R.; Crabtree, R. H. *Chem. Soc. Rev.* **2013**, *42*, 1440; (b) Blanco, V.; Leigh, D. A.; Marcos, V. *Chem. Soc. Rev.* **2015**, *44*, 5341.

FLASH PRESENTATIONS

Flash-1

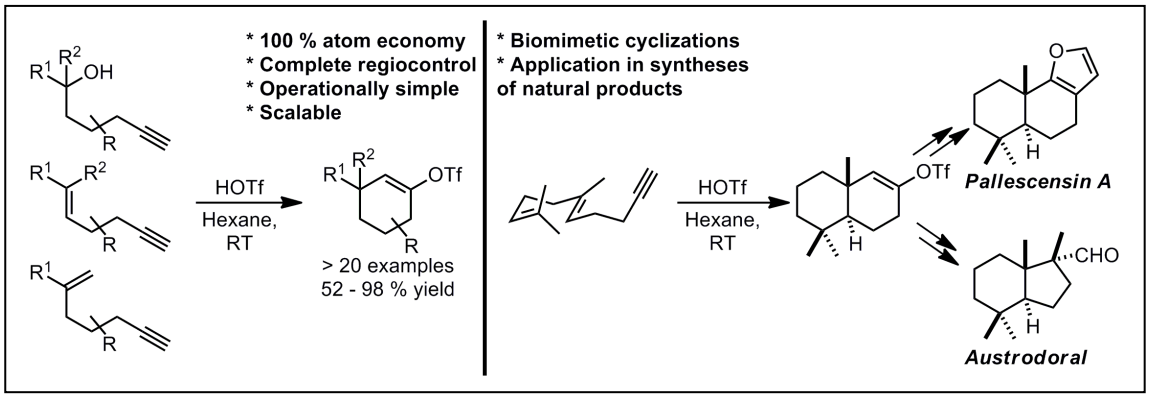
Synthesis of Cyclic Alkenyl Triflates by a Cationic Cyclization Reaction

Pilar Pardo, Alicia Galván, Francisco J. Fañanás, Félix Rodríguez and Pedro Alonso

Departamento de Química Orgánica e Inorgánica de la Universidad de Oviedo, Julián Clavería, 8, 33006, Oviedo

palonsofig@gmail.com

Cyclic alkenyl triflates are useful intermediates in organic synthesis usually synthesized from ketones through a reaction involving enolization and trapping with a triflating agent.[1] This sequence suffers from some stereochemical drawbacks owing to the basic conditions required. Herein, we describe a new Brønsted acid-mediated cationic cyclization reaction of enyne derivatives (or alkynols) to access cyclic alkenyl triflates. This new atom-economical process is high yielding, scalable, technically very simple, proceeds without the need of any metallic reagent or catalyst, and more importantly, it complements and challenges conventional methodologies. We also show the straightforward syntheses of two terpenes by using a new biomimetic cationic polycyclization reaction in the key step of the synthetic routes.[2]



[1] J. E. McMurry, W. J. Scott, *Tetrahedron Lett.*, **1983**, *24*, 979-982.

[2] P. Alonso, P. Pardo, A. Galván, F. J. Fañanás, F. Rodríguez; *Angew. Chem. Int. Ed.*, **2015**, *54*, 15506-15510.

Flash-2

A Unified Strategy for the Enantioselective Synthesis of the Alkaloids of the Madangamine Group

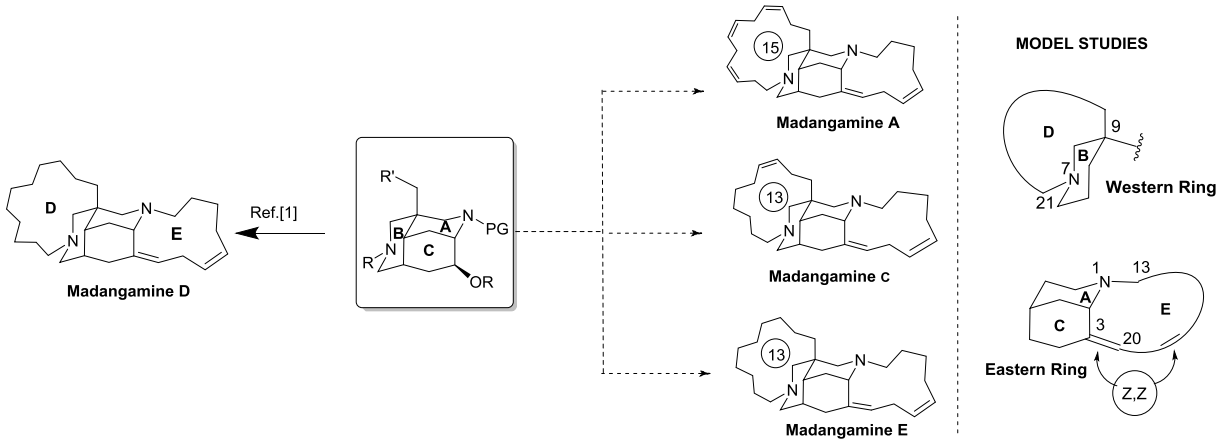
Celeste Are, Roberto Ballette, Maria Pérez, Elena Casetta, Joan Bosch and Mercedes Amat

Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Barcelona

e-mail: cele.are@ub.edu

Madangamine alkaloids constitute a small group of complex pentacyclic alkaloids isolated from marine sponges of the order Haposclerida. Structurally, these alkaloids have an unprecedented skeletal type, characterized by a diazatricyclic core (ABC rings) and two linear carbon bridges. The peripheral macrocyclic ring D is different in each madangamine, in size as well as in degree and position of unsaturation, whereas ring E is identical in madangamines A-E.

In the context of our studies on the enantioselective synthesis of complex piperidine-containing natural products from phenylglycinol-derived bicyclic lactams, we have developed a unified strategy to access the variety of alkaloids of this group.



Our strategy involves the formation of the macrocyclic rings after the construction of the highly functionalized central core. In 2014, we accomplished the enantioselective synthesis of madangamine D, which represents the first and to date the only total synthesis of an alkaloid of the madangamine group.[1] We are currently studying the construction of the D-ring of more complex members of this family, and we are also exploring different strategies to optimize the construction of the complex E ring in order to complete the enantioselective synthesis of other members of this family.

Acknowledgment: Financial support from the Spanish MICINN/FEDER (CTQ 2015-65384-R) and the Generalitat de Catalunya (2014-SGR-0155).

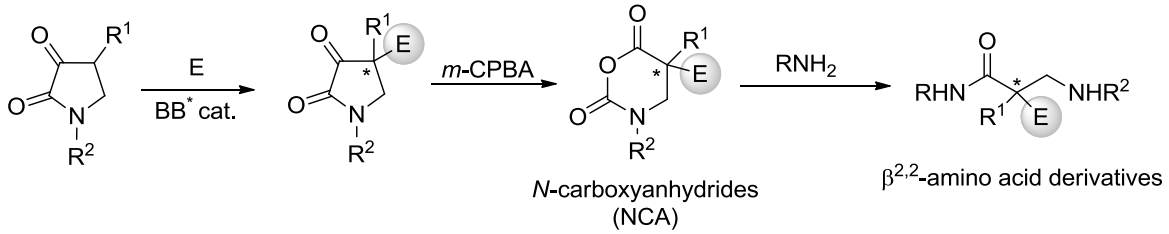
[1] Ballette, R.; Pérez, M.; Proto, S.; Amat, M.; and Bosch, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 6202-6205; Amat, M.; Pérez, M.; Ballette, R.; Proto, S.; Bosch, J. In *The Alkaloids: Chemistry and Biology*, Knölker, H. J. Ed.; Elsevier, 2015, Vol. 74, Chap. 3, p.159

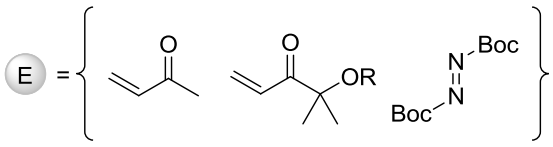
Flash-3

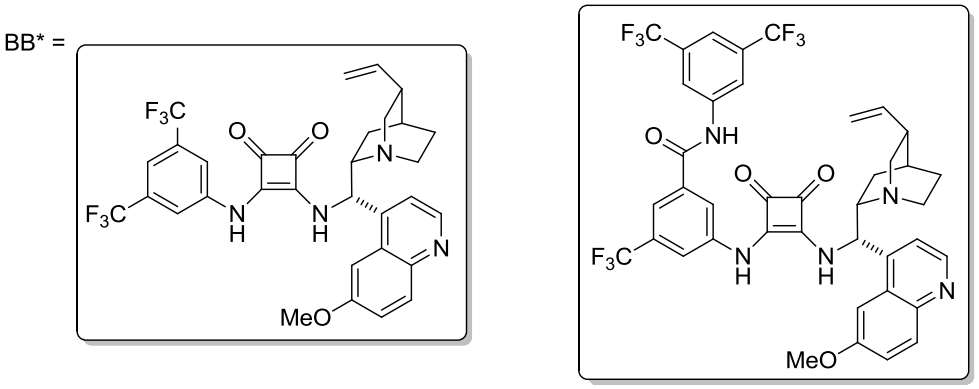
2,3-Dioxopyrrolidines as Michael donors in enantioselective organocatalytic conjugate additions

Eider Badiola, Ana Vázquez, Yurre Olaizola, Antonia Mielgo and Claudio Palomo
Departamento de Química Orgánica I, Facultad de Química, Universidad del País Vasco
Manuel Lardizabal 3, 20018 Donostia, Spain
e-mail: eider.badiola@ehu.eus

Enantioenriched pyrrolidinone skeletons are of great biological and pharmaceutical interest;[1] however, little is known about the asymmetric synthesis and reactions of chiral 2,3-dioxopyrrolidines. Herein we present the first application of these small heterocycles as Michael donors in enantioselective organocatalytic conjugate additions catalyzed by bifunctional Brønsted bases. For instance, the Michael reaction of these substrates with vinyl ketones, α'-oxy enones and di-*tert*-butyl azodicarboxylates provides adducts in very good yields and stereoselectivities and, apart from being biologically interesting, they are also precursors of $\beta^{2,2}$-amino acids. Specifically, through their transformation into NCAs followed by ring opening $\beta^{2,2}$-amino acids, esters and amides can be easily affordable.







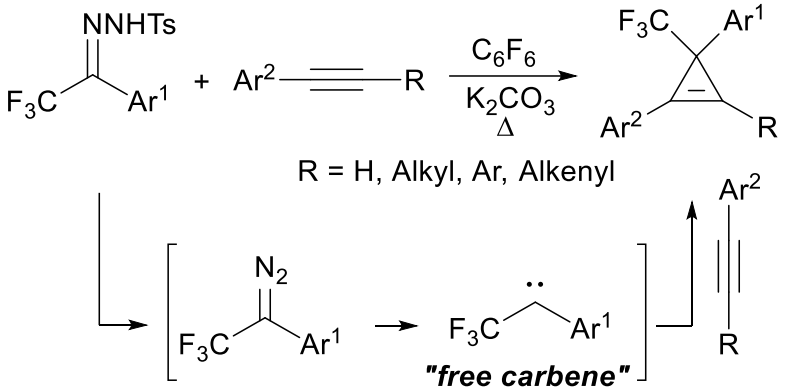
[1] a) Thiel, P.; Kaiser, M.; Ottmann, C. *Angew. Chem. Int. Ed*. **2012**, *54*, 2012. b) Paraskar, A. S.; Sudalai, A. *Tetrahedron* **2006**, *62*, 4907. c) Corey, E. J.; Zhang, F.-Y. *Org. Lett*. **2000**, *2*, 4257.

Flash-4

Synthesis of 1, 3-diaryl-3-trifluoromethyl-cyclopropenes by transition-metal-free reaction of 2, 2, 2-trifluoroacetophenone tosylhydrazones with alkynes: the trifluoromethyl group effect

Azucena Jiménez, M. Carmen Pérez-Aguilar, María Paz Cabal, Carlos Valdés and Raquel Barroso
Organic e Inorganic chemistry department
University of Oviedo
Avenida Julián Clavería, 8, 33006 Oviedo, Asturias. Spain
UO188972@uniovi.es

1,3-Diaryl-3-trifluoromethylcyclopropenes and 2-aryl- or 2-alkyl-1,3-diaryl-3-trifluoromethylcyclopropenes are prepared in a very simple way by reaction between 1,1,1-trifluoroacetophenone tosylhydrazones and terminal or internal alkynes, respectively, in a base promoted process that does not require the presence of any metal catalyst[1]. The essential role of the trifluoromethyl group, which enables the formation of the cyclopropenes instead of the expected pyrazoles[2], has been computationally investigated, suggesting the participation of a free carbene.



Flash-5

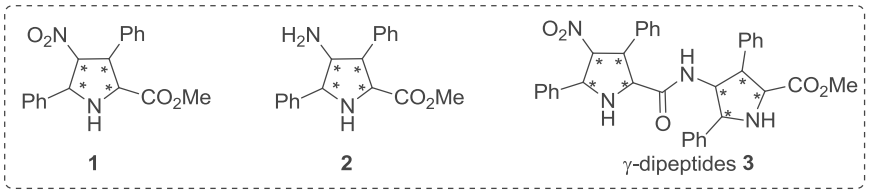
DENSELY SUBSTITUTED PYRROLIDINES AS USEFUL ORGANOCATALYSTS

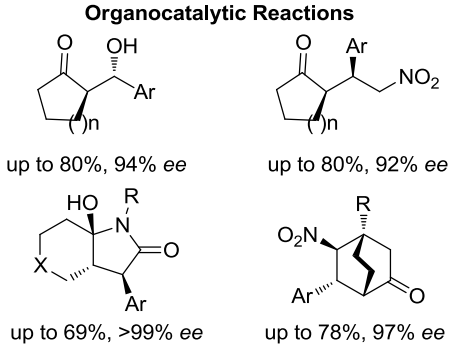
Tamara Bello, Mª de Gracia Retamosa, Andrea Ruiz-Olalla, Maddalen Agirre, Fernando P. Cossío*

Organic Chemistry Department I, University of the Basque Country (UPV-EHU) Joxe Mari Korta Building Avda. Tolosa 72, and International Physics Center (DIPC), P.K. 1072, 20018, Donostia – San Sebastián, Spain

tamara.bello@ehu.es

Our group has developed an efficient methodology via (3+2) cycloaddition[1], hydrolysis, hydrogenation and peptide coupling to synthesize densely substituted unnatural L- and D-Proline derivatives **1**, **2** and **3**. Encouraged by the efficiency of Proline-based organocatalysts in several C-C bond transformations, these new densely substituted pyrrolidines have been used as organocatalysts in aldol, Michael reactions[2] and, more recently, a novel catalytic cyclization. Aside these previous studies, several organocatalysts **3** have shown their usefulness in asymmetric Diels-Alder reactions.





[1] Conde, E.; Bello, D.; de Cózar, A.; Sánchez, M.; Vázquez, M. A.; Cossío, F. P. *Chem. Sci.* **2012**, *3*, 1486.

[2] Retamosa, M.G.; de Cózar, A.; Sánchez, M.; Miranda, J.I.; Sansano, J.M.; Castelló, L.M.; Nájera, C.; Jiménez, A.I.; Sayago, F.J.; Cativiela, C., Cossío, F.P. *Eur. J. Org. Chem*. **2015**, 2503. b) Ruiz-Olalla, A.; Retamosa, M. G.; Cossío, F. P. J. Org. Chem. 2015, 80, 5588.

Flash-6

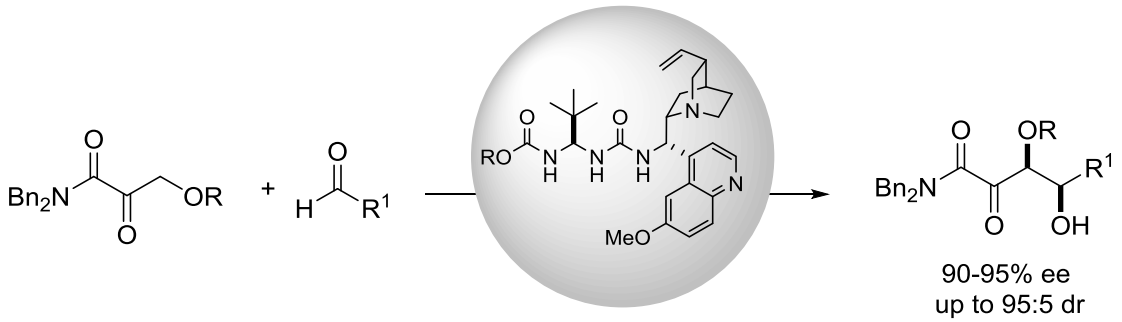
α-Ketoamides as pronucleophiles in organocatalytic carbon-carbon bond forming reactions

Rosa López, Claudio Palomo and Haizea Echave
Department of Química Orgánica I, Facultad de Química UPV-EHU, Paseo Manuel de Lardizabal 3, 20018 Donostia-San Sebastián.
e-mail: haizea.echave@ehu.es

1,2-Dicarbonyl compounds such as pyruvic acid and phosphoenolpyruvate are employed as C_3 donor units in aldolase promoted biosynthesis of ulosonic acids and sialic acids.[1] Despite this synthetic interest, however, the utilization of pyruvates in the realm of chemical synthesis, has been mainly limited to their use as electrophilic counterparts due to the inherent high reactivity of the α,β-dicarbonyl function against nucleophilic1,2-additions.[2]

On the other hand, the developtment of catalyts that exhibit high activity, high stereoselectivity and broad substrate scope is of current interest in organic synthesis. Organocatalysts that combine a site with a Brønsted base (BB) character and another site with hydrogen-bond donor ability have emerged as the most powerful tools to achieve this goal. In this context, we have recently reported ureidopeptide-based Brønsted bases as new sub-family of organocatalysts. These compounds which are distinguised by the presence of an N,N-diacylaminal unit and an urea moiety, both in close proximity to an additional stereodirecting group, have already shown to be very effective in promoting stereoselective carbon-carbon bond forming reactions.[2,3]

In this talk, further progress in the use of these ureidopeptide derived catalysts in challenging transformations will be presented. Specifically, organocatalyzed cross aldol reactions applied to the stereoselective synthesis of polifunctionalized fragments[4] along with some preliminary results for the analogous Mannich reaction.



1. a) M. F. Utter, D. B. Keech, *J. Biol. Chem.* **1963**, *238*, 2603–2608; b) D. Voet, J. G. Voet, in Biochemistry, 3rd ed.,Wiley, New York, **2004**.
2. W. Raimondi, D. Bonne, J. Rodriguez, *Angew. Chem. Int. Ed.* **2012**, *51*, 40–42.
3. a) S. Diosdado, J. Etxabe, J. Izquierdo, A. Landa, A. Mielgo, I. Olaizola, R. López, C. Palomo, *Angew. Chem. Int. Ed.* **2013**, *52*, 11846. b) S. Diosdado, R. López, C. Palomo, *Chem. Eur. J.* **2014**, *20*, 6525.
4. H. Echave, R. López, C. Palomo, *Angew. Chem. Int. Ed.* **2016**, *55*, 3364–3368.

Flash-7

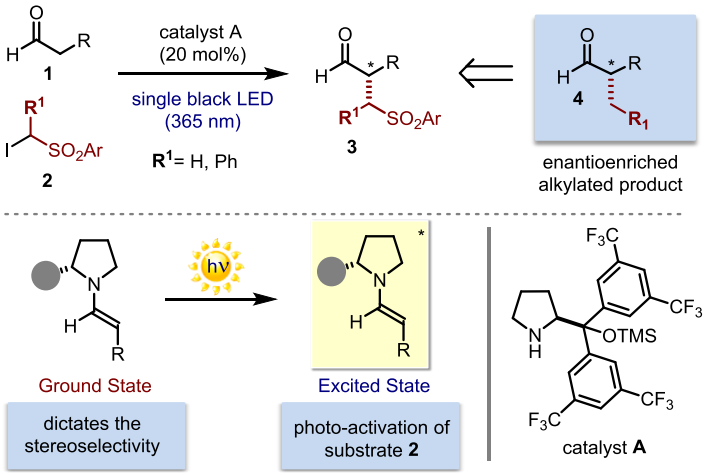
Photochemical Enantioselective Alkylation of Aldehydes with α-Iodo Sulfones

Giacomo Filippini[†], Mattia Silvi[†] and Paolo Melchiorre[†‡]

[†] *ICIQ - Institute of Chemical Research of Catalonia, Av. Països Catalans 16, 43007 (Tarragona, Spain),* [‡]*ICREA - Catalan Institution for Research and Advanced Studies, Pg. Lluís Companys 23, 08010 (Barcelona, Spain)*

gfilippini@iciq.es

Visible light photo-organocatalysis has recently emerged as a powerful activation strategy for the implementation of enantioselective chemical transformations. Our research group has demonstrated that key transient intermediates of organocatalytic processes, in the ground state or in the excited state, can actively participate in the photo-excitation of organic substrates without the need for an external photosensitizer.[1] This reactivity enabled the development of light-driven stereoselective α-alkylations of carbonyl compounds which could not be realized under thermal activation. We are interested in further expanding this light-mediated activation strategy to develop the enantioselective coupling of aldehydes (**1**) and α-iodo sulfones (**2**, Scheme 1). Chiral enamines, generated by condensation of aldehyde **1** with the commercially available chiral secondary amine catalyst **A**, can directly reach an electronically excited state upon light absorption triggering the formation of reactive radical species from the organic halide **2**. Simultaneously, the ground state chiral enamine provides effective stereochemical induction for the enantioselective alkylation process. Product **3** bears a stereogenic centre decorated with a sulfone moiety that can subsequently be converted into a methyl or a benzyl group allowing for the development of a stereoselective formal alkylation of aldehydes.



Scheme 1. Formal photo-organocatalytic enantioselective methylation of aldehydes.

Acknowledgements: This work was supported by the ICIQ Foundation, MINECO (project CTQ2013-45938-P and Severo Ochoa Excellence Accreditation 2014-2018, SEV-2013-0319), and by the European Research Council (ERC 278541 - ORGA-NAUT).

[1] (a) Arceo, E.; Jurberg, I. D.; Álvarez-Fernández, A.; Melchiorre, P. *Nature Chem.* **2013**, *5*, 750. (b) Woźniak, Ł; Murphy, J. J.; Melchiorre, P. *J. Am. Chem. Soc.* **2015**, *137*, 5678-5681. (c) Silvi, M.; Arceo, E.; Jurberg, I. D.; Cassani, C.; Melchiorre, P. *J. Am. Chem. Soc.* **2015**, *137*, 6120-6123.

Flash-8

Computational Study of Metal-catalyzed Cyclizations

Béla Fiser, [†] Juan M.Cuerva, [‡] Enrique Gómez-Bengoa*,[†]
[†]*Department of Organic Chemistry I, University of the Basque Country/UPV-EHU, Donostia-San Sebastián, Spain-20018,* [‡]*Department of Organic Chemistry, University of Granada, Granada, Spain-18071*
e-mail: bela.fiser@ehu.es, jmcuerva@ugr.es, enrique.gomez@ehu.es

Baldwin´s rules for ring closure have become a useful tool for chemists and were applied efficiently in the last decades since their publication in 1976 [1]. On the one hand, they were originally limited (specially for nucleophilic additions) to first row elements taking into account the differences in geometries, bond lengths and even mechanisms for second- and higher-row elements. On the other hand, the rules, or at least the nomenclature, have been assumed to be applicable to transition metal-promoted reactions, especially for insertions of Palladium intermediates in Heck-type reactions [2,3]. Nevertheless, a systematic study of their validity in these metal-including systems has not been reported yet. In this work, a set of intramolecular carbometalations of alkenes and alkynes have been investigated using density functional theory (DFT). The size of the formed rings varied between 3-7 and the effect of different metals were studied involving group 10-12 elements (Figure 1).

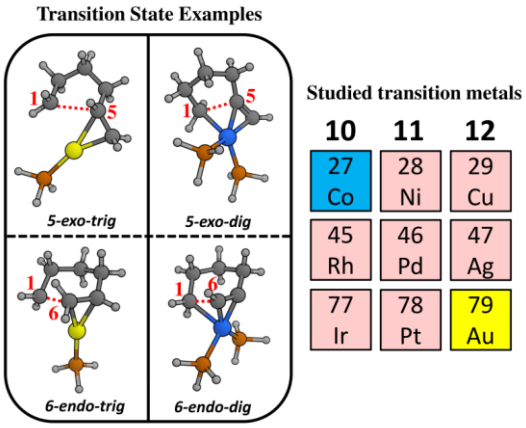


Figure 1 Studied transition metals and example transition states (*5-exo-* & *6-endo-trig* with gold (yellow); *5-exo-* & *6-endo-dig* with cobalt (blue)).

Pd-mediated alkylmetalations of alkenes clearly shows a concordance with postulated rules. Similar trends were found for the other two Group 11 elements (Ni and Pt). Group 10 (Co, Ru, Rh) and 12 (Cu, Ag, Au) serve to explore the trend and generality of the conclusions.

Acknowledgements: Financial support by the FP7 Marie Curie Actions of the European Commission via the ITN ECHONET Network (MCITN-2012−316379) and from the University of the Basque Country UPV/EHU is gratefully acknowledged.

1 Baldwin, J. E. *Chem. Commun*. **1976**, 734.
2 De Meijere, A.; Bräse, S. *J. Organomet. Chem*. **1999**, *576*, 88.
3 Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev*. **2006,** *106*, 4644.

Flash-9

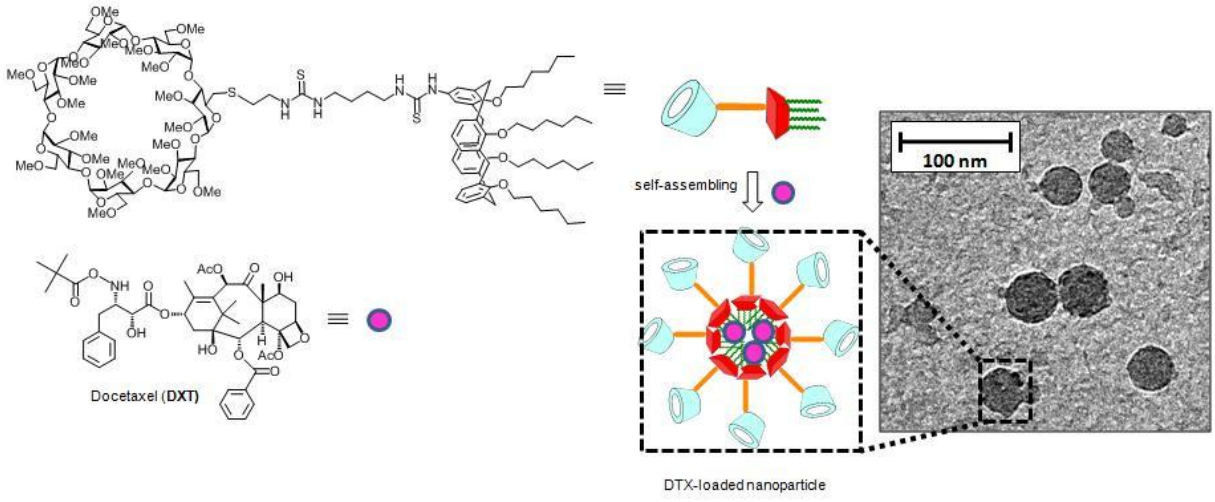
Docetaxel-loaded nanoparticles based on cyclodextrin-calixarene heterodimers for prostate cancer.

Francesco Sansone,[b] Carmen Ortiz Mellet,[a] Alessandro Casnati,[b] Valentín Ceña,[c] José M. García Fernández[d] and Laura Gallego-Yerga,[a]

a) Departamento Química Orgánica, Facultad de Química, Universidad de Sevilla, E-41012 Sevilla, Spain; b) Dipartimento di Chimica, Università degli Studi di Parma, I-43124 Parma, Italy; c) Laboratorio de Farmacología, Facultad de Medicina,Universidad de Castilla-La Mancha, Avda. de Almansa, E-02006, Sevilla, Spain; d) Instituto de Investigaciones Químicas (IIQ), CSIC – Universidad de Sevilla, E-41092 Sevilla, Spain.

e-mail: lgallego@us.es

Docetaxel is one of the most common therapeutic option for various kinds of cancers. However, its clinical applications are limited by its low water solubility and its toxicity to normal cells, resulting in severe side effects. We have developed nanoparticle systems able to solubilize docetaxel in physiological media and improve its delivery and its activity in cancer cells. These nanocarriers are based on heterodimers of calix[4]arene (CA_4),[1] which are functionalized with alkyl chains at its lower rim, and water-soluble β-cyclodextrin (βCD)[2] scaffolds. The amphiphilicity of these systems give them the capacity of self-assembling in water media to form well-ordered nanostructures: nanospheres (NS) and nanocapsules (NC). Both structures consist on an inner core, formed by the CA_4 providing a lipidic matrix where docetaxel can be encapsulated, and a external hydrophilic surface exposing the βCD moieties which allows the nanoparticle solubilization.[3] Cryo-TEM (Transmision Electron Microscopy) images confirmed the nanometric size and the spherical morphology of the loaded particles. In vitro studies have demostrated the capacity of these nanosystems to provide a sustained release of docetaxel and its potential in nanomedicine for the treatment of prostate cancer: the docetaxel-loaded nanoparticles exhibited a potent anti-cancer activity in LnCap cells (early stage human prostate cancer cells).



[1] Sansone, F.; Casnati, A. *Chem. Soc. Rev*. **2013**, *42*, 4623-4639.

[2] (a) Martínez, A.; Ortiz Mellet, C.; García Fernández, J. M. *Chem. Soc. Rev*. **2013**, *42*, 4746-4773; (b) Ortiz Mellet, C.; García Fernández, J. M.; Benito, J. M. *Chem. Soc. Rev*. **2011**, *40*, 1586-1608.

[3] Gallego Yerga, L.; Lomazzi, M.; Sansone, F.; Ortiz Mellet, C.; Casnati, A.; García Fernández, J. M.; *Chem. Commun.* **2014**, *50*, 7440-7443.

Flash-10

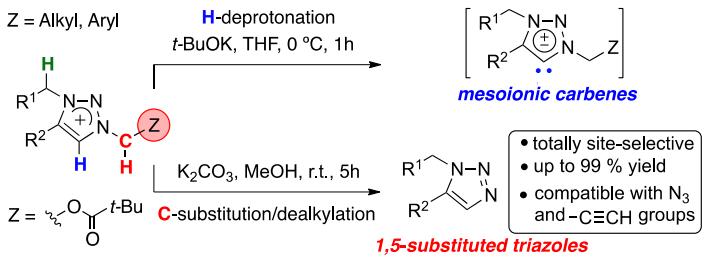
Site-Selective N-Dealkylation of 1,2,3-Triazolium Salts: a Metal-free Route to 1,5-Substituted 1,2,3-Triazoles and Related Bistriazoles.

Aitziber Irastorza, Zaira Monasterio and Jesus M. Aizpurua*

Departamento de Química Orgánica-I, Universidad del País Vasco UPV/EHU, Joxe Mari Korta R&D Center, Avda Tolosa-72, 20018 San Sebastián, Spain.

e-mail: airastorza87@gmail.com

A variety of 1,5-substituted 1,2,3-triazoles[1] incorporating "click"-compatible[2] functional groups, can be easily synthesized from 1-pivaloyloxymethyl-1,2,3-triazoles[3] following a site-selective N-alkylation/N-dealkylation sequence in the N3 position. The method, which is metal-free and operationally very simple, takes advantage of the enhanced electrophilicity generated by the triazolium moiety on the pivaloyloxymethyl intermediates. These triazole intermediates[4] are synthetized in presence of functionalized alkyl triflates. Later on, and to obtain the 1,5 disubstituted 1,2,3-triazoles, a nucleophile-promoted N1-dealkylation of the acidic intermediate triazolium salts is carried out. The azide and alkyne groups incorporated by N-alkylation can be submitted to further CuAAC and Huisgen cycloadditions[5] to provide bis(1,2,3-triazoles) with unprecedented 1,5/1,4 substitution patterns.



[1] (a) Kwok, S. W.; Fotsing, J. R.; Fraser, R. J.; Rodionov, V. O.; Fokin, V. V. *Org. Lett.* **2010**, *12*, 4217. (b) Zhang, L.; Chen, X.; Xue, P.; Sun, H. H. Y.; Williams, I. D.; Sharpless, K. B.; Fokin, V. V.; Jia, G. *J. Am. Chem. Soc.* **2005**, *127*, 15998. (c) Li, Y.; Qi, X.; Lei, Y.; Lan, Y. *RCS Adv.* **2015**, *5*, 49802.

[2] (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596. (b) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952.

[3] (a) Loren, J. C.; Krasinski, A.; Fokin, V. V. Sharpless, K. B. *Synlett* **2005**, 2847.

[4] Schulze, B.; Schubert, U. S. *Chem. Soc. Rev.* **2014**, *43*, 2522.

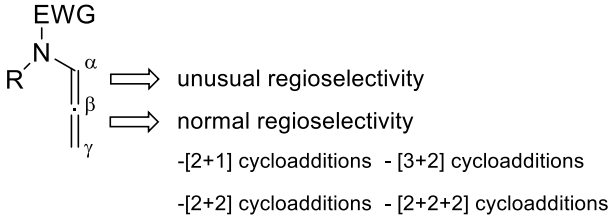
[5] (a) Monasterio, Z.; Sagartzazu-Aizpurua, M.; Miranda, J. I.; Reyes, Y.; Aizpurua, J. M. *Org. Lett.* **2016**, *52*, 788.

Flash-11

Gold Catalyzed [3+2] Cycloaddition Reaction of Vinyldiazo Compounds and N-Allenamides

Enol López and Luis A. López
Departamento de Química Orgánica e Inorgánica, Universidad de Oviedo, c/ Julián Clavería, 8, 33006, Oviedo, Spain.
E-mail: uo215264@uniovi.es

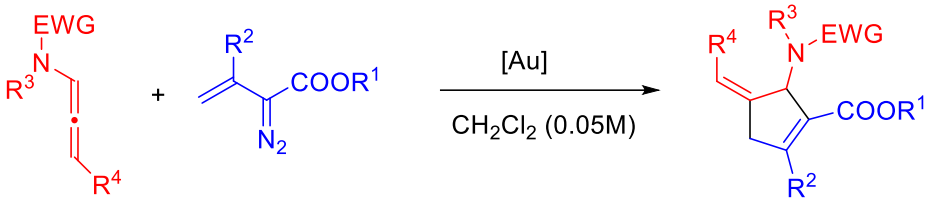
Many selective transition metal-catalyzed cycloaddition reactions of N-allenamides have been reported in the last decades.[1] However, gold complexes have only recently been recognized as useful catalysts in this type of transformations. Whereas the participation of the terminal bond represents the most common regioselectivity pattern,[2] the involvement of the C_α=C_β bond is extremely unusual in gold-catalyzed cycloaddition reactions of this type of allenic scaffolds (Scheme 1).



Scheme 1. Regioselectivity patterns in Gold Catalyzed [n+2] cycloadditions.

On the other hand, metal catalyzed transformations of stabilized vinyldiazo derivatives have received in the last years great attention. However, to the best of our knowledge, the cycloaddition reaction between vinyldiazo compounds and allene derivatives remains unexplored. In this regard, we thought that the recent introduction of gold-catalysts as efficient catalysts in transformations involving vinyldiazo compounds could pave the way for a successful coupling with N-allenamides.

In this communication, we report the gold-catalyzed [3+2] cycloaddition of vinyldiazo compounds and allenamides (Scheme 2).[3]



Scheme 2.Gold catalyzed [3+2] cicloaddition of vinyl diazo derivatives and allenamides.

Notably, the participation of the C_α=C_β bond represents, as stated before, an infrequent regioselectivity pattern in gold-catalyzed cycloadditions involving allenamides. From a mechanistic point of view, these results are consistent with the initial activation of the diazo reagent. This hypothesis has been supported by a computational study.

[1] Yu. S., Ma, S., *Angew. Chem. Int. Ed*. **2012**, 51, 3074.
[2] See for example, Suárez-Pantiga, S., Hernández-Díaz, C., Rubio, E., González, J. M., *Angew. Chem. Int. Ed.*, **2012**, 51, 11552.
[3] López, E., González, J., López, L.A. *Adv. Synth. Cat.*, **2016**, *358*, 1428.

Flash-12

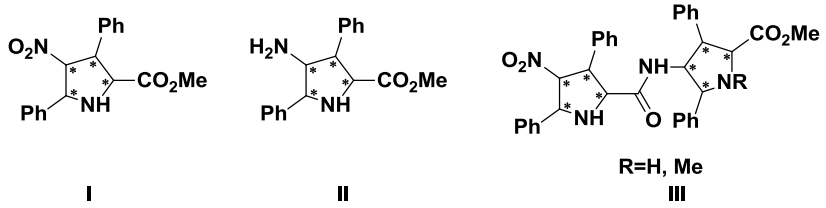
γ-Dipeptides Based On Densely Substituted Pyrrolidines As Suitable Organocatalysts For Michael And Michael-Henry-Acetalization Reactions

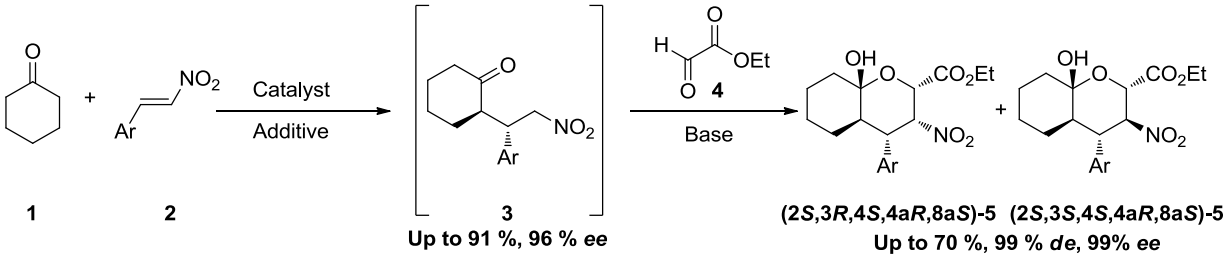
Andrea Ruiz-Olalla, Tamara Bello, Maria de Gracia Retamosa, Fernando. P. Cossío* and Maddalen Agirre

Departamento de Química Orgánica I, Universidad del País Vasco-Euskal Herriko Unibertsitatea and Donosita International Physics Center (DIPC), Pº Manuel de Lardizabal 3, 20018 Donostia-San Sebastián (Spain).

maddalen.agirre@ehu.es

The synthesis of distinct chiral tetrahidropyran (THP) skeletons has developed great interest due to its wide abundance in biologically active natural products and pharmaceuticals.[1] In recent years, several synthetic procedures have been promoted to prepare the chiral THP moiety.[1c] Special remark deserve the asymmetric organocatalytic cascade reactions in which up to five contiguous stereogenic centers are synthesized in a high stereoselective manner.[2] Our group has developed an efficient methodology via (3+2) cycloaddition,[3] hydrolysis, hydrogenation and peptide coupling to synthesize densely substituted L- and D- Proline derivatives I, II and III. Encouraged by the efficiency of Proline based organocatalysts in Michael reactions[4,5] we decided to extend the catalytic activity of the two best γ-dipeptides towards previously cited process. In an early stage, we observed promising results yielding the desired products with excellent diastereo- and enantiomeric excess.





[1] a) Bielitza, M.; Pietruszka, J. *Angew. Chem. Int. Ed*. **2013**, *52*, 10960. b) Nising, C.F.; Bräse, S. *Chem. Soc. Rev*. **2008**, *37*, 1218. c) Clarke, P.A.; Santos, S. *Eur. J. Org. Chem*. **2006**, 2045.

[2] a) Ishikawa, H.; Sawano, S.; Yasui, Y.; Shibata, Y.; Hayashi, Y. *Angew. Chem. Int. Ed*. **2011**, *50*, 3774. b) Han, B.; Xie, X.; Huang, W.; Li, X.; Yang, L.; Peng, C. *Adv. Synth. Catal*. **2014**, *356*, 3676. c) Chauhan, P.; Mahajan, S.; Raabe, G.; Enders, D. *Chem. Commun*. **2015**, *51*, 2270. d) Gurubrahamam, R.; Cheng, Y.-S.; Chen, K. *Org. Lett*. **2015**, *17*, 430.

[3] Conde, E.; Bello, D.; de Cózar, A.; Sánchez, M.; Vázquez, M.A.; Cossío, F.P. *Chem. Sci*. **2012**, *3*, 1486.

[4] Ruiz-Olalla, A.; Retamosa, M.G.; Cossío, F.P. *J. Org. Chem*. **2015**, *80*, 5588.

[5] Ruiz-Olalla, A.; Retamosa, M.G.; Agirre, M.; Cossío, F.P. *Manuscript in preparation.*

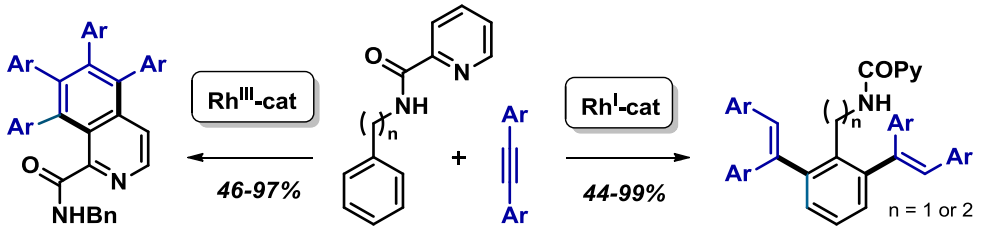
Flash-13

Rh^{I}/Rh^{III} Catalyst-Controlled Divergent Aryl/Heteroaryl C–H Bond Functionalization of Picolinamides with Alkynes

Ángel Manu Martínez, Javier Echavarren, Inés Alonso, Nuria Rodríguez,* Ramón Gómez Arrayás* and Juan C. Carretero*

Departamento de Química Orgánica, Universidad Autónoma de Madrid, C/ Francisco Tomás y Valiente, 7, Campus de Cantoblanco. 28049. Madrid
e-mail: angelm.martinez@uam.es

Recent progress on rhodium-catalyzed C–H bond functionalization has opened new possibilities for an ideal chemical synthesis enabling straightforward formation of new C–C bonds without previous functionalization steps. [1] However, investigations of catalyst controlled divergent C–H functionalizations of distinct C–H bonds are relatively uncommon, yet highly appealing.[2] The concept herein presented illustrates a divergent high site-selective control in the direct functionalization of both aryl and heteroaryl C–H bonds of *N*-substituted picolinamide substrates.[3] By simply switching the oxidation state of the Rh^{I}/Rh^{III} catalyst precursor, it is possible to access either isoquinoline derivatives or *ortho*-olefinated benzylamine and phenethylamine derivatives, respectively.[4]



Experimental mechanistic studies based on isolation and X-ray characterization of Rh^{I} and Rh^{III} picolinamide complexes and deuterium labeling studies as well as DFT theoretical calculations have been performed to explain the factors that influence this switchable site-selectivity control for both Rh^{I} and Rh^{III} catalytic systems.

1. For reviews, see: (a) Bouffard, J., Itami, K. *Top. Curr. Chem*. **2010**, *292*, 231. (b) Colby, D. A., Tsai, A. S., Bergman, R. G., Ellman, J. A. *Acc. Chem. Res*. **2012**, *45*, 814.
2. For elegant examples, see: (a) Campeau, L.-C., Chipper, D. J., Fagnou, K. *J. Am. Chem. Soc.*, **2008**, *130*, 3266. (b) Dooley, J. D., Chidipudi, S. R., Lam, H. W. *J. Am. Chem. Soc.*, **2013**, *135*, 10829. (c) Dooley, J. D., Reddy Chidipudi, S., Lam, H. W. *J. Am. Chem. Soc.*, **2013**, *135*, 10829.
3. Martínez, Á. M., Echavarren, J., Alonso, I., Rodríguez, N., Gómez Arrayás, R., Carretero, J. C. *Chem. Sci.*, **2015**, *6*, 5802.
4. For selected examples of Rh^{III}-catalyzed C–H activation of heterocycles containing basic nitrogen, see: (a) Fukutani, T., Hirano, K., Satoh, T., Miura, M. *J. Org. Chem.*, **2011**, *76*, 2867. (b) Martínez, Á. M., Rodríguez, N., Gómez Arrayás, R., Carretero, J. C. *Chem. Commun.*, **2014**, *50*, 6105. For C–H vinylation of (hetero)arenes with alkynes, see: (c) Schipper, D. J., Hutchinson, M., Fagnou, K. *J. Am. Chem. Soc.*, **2010**, *132*, 6910. (d) Shibata, T., Matsuo, Y. *Adv. Synth. Catal.*, **2014**, *356*, 1516. (e) Zhou, M.-B., Pi, R., Hu, M., Yang, Y., Song, R.-J., Xia, Y., Li, J.-H. *Angew. Chem. Int. Ed.*, **2014**, *53*, 11338.

Flash-14

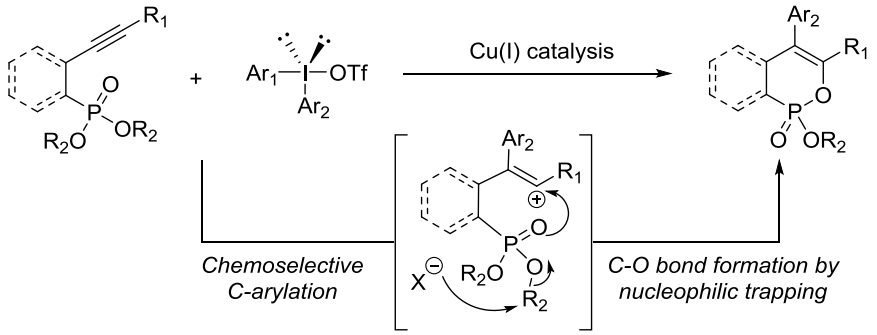
Copper-Catalyzed Cascade Reactions Towards Cyclic Phosphonates

Borja Pérez-Saavedra, Eduardo Laga, Carlos Saá and Martín Fañanás-Mastral
Centro de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) e Departamento de Química Orgánica, Universidade de Santiago de Compostela, 15782 Santiago de Compostela
borja.perez.saavedra@rai.usc.es

Organic phosphonates represent a highly important class of compounds with a wide range of applications in biology, agriculture and synthetic organic chemistry. In particular, cyclic phosphonates have demonstrated antitumor activity and are inhibitors of various enzymes, such as β-lactamases or pancreatic cholesterol esterase.[1] Therefore, the development of new methods for the synthesis of this kind of phosphorous heterocycles is highly desirable.

Diaryliodonium salts are air- and moisture-stable, non-toxic and easy to prepare compounds which have recently gained considerable attention as mild and selective arylating reagents in organic synthesis.[2] These hypervalent iodine compounds have been employed in the copper(I)-catalyzed electrophilic carboarylation of alkynes[3] and in the oxygen-arylation of phosphonates to obtain mixed aryl alkyl phosphonates.[4]

Here we report a novel copper(I)-catalyzed cyclization of alkynyl phosphonates which allow for the synthesis of six-membered arylated cyclic phosphonates under mild conditions. This cascade reaction probably involves an initial chemoselective electrophilic alkyne arylation which generates a vinyl cation which is trapped by the nucleophilic addition of the oxygen atom of the phosphoryl group. Substitution on various positions of the phosphonate is well tolerated and several aryl groups can be introduced with total chemo- and regioselectivity.



Aknowledgements: This work was supported by MINECO (projects CTQ 2014-59015R, CTQ2015-62724-ERC, RYC-2012-11749), the ERDF and the Xunta de Galicia (project GRC 2014/032). We also thank the ORFEO-CINQA network (CTQ 2014-5192 REDC). Borja Pérez-Saavedra thanks Fundación Segundo Gil Dávila for a predoctoral grant.

[1] (a) Kaur, K.; Adediran, S. A.; Lan, M. J. K.; Pratt, R. F. *Biochemistry*, **2003,** *42*, 1529-1536. (b) Li, B.; Zhou, B.; Lu, H.; Ma, L.; Peng, A. Y. *Eur. J. Med. Chem.* **2010**, *45*, 1955–1963.
[2] Merritt, E. A.; Olofsson, B. *Angew. Chem. Int. Ed.* **2009**, *48*, 9052-9070.
[3] Walkinshaw, A. J.; Xu, W.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 12532−12535.
[4] Fañanás-Mastral, M.; Feringa, B. L. *J. Am. Chem. Soc.* **2014**, *136*, 9894−9897.

Flash-15

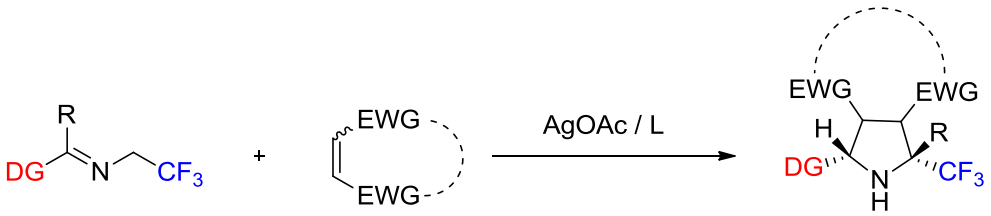
Stereoselective Ag-Catalyzed 1,3-Dipolar Cycloaddition of Activated Trifluoromethyl-Substituted Azomethine Ylides

Alberto Ponce, Javier Corpas, Inés Alonso, Javier Adrio*, Juan Carlos Carretero*

Dpto. de Química Orgánica, Universidad Autónoma de Madrid, Madrid, tfno. : +34914974709; e-mail: alberto.ponce@estudiante.uam.es

The pyrrolidine ring is ubiquitous in natural products and biologically active compounds[1]. In particular, modified proline derivatives have been extensively used to control the conformation of peptides for structure-activity relationship studies[2]. On the other hand, it is well documented that the replacement of hydrogen atoms with fluorine atoms in organic compounds may result in a clear improvement of their biological properties[3]. For instance, the introduction of one or several fluorine atoms proximal to an amine moiety decreases its basicity, which can result in an improvement in the metabolic stability and a reduction in the toxicity of the compound[4].

Herein we report an efficient method for the preparation of 2-trifluoromethyl pyrrolidines by a silver-catalyzed 1,3-dipolar cycloaddition of fluorinated azomethine ylides and activated olefins. Broad scope and high levels of diastereoselectivity have been achieved by using AgOAc/PPh_3 as the catalyst system. The high efficiency of the cycloaddition relies on the presence of a metal-coordinating group on the imine moiety, such as an ester or heteroaryl group. Examples of the catalytic asymmetric version of this cycloaddition has been developed by using (*R*)-Taniaphos as a chiral ligand.



DG = CO_2R or heteroaryl; 60-95% yield

L = PPh_3, 35 examples
(typically *endo* selective)
L = (*R*)-Taniaphos, 86-92% *ee*

1. (a) Kuhnert, M.; Blum A.;Steuber, H.; Diederich, W.E. *J. Med. Chem.* **2015**, *58*, 4845; (b) Roughley, S.D.; Jordan, A.M. *J. Med. Chem.* **2011**, *54*, 3451.
2. (a) Song, B.; Bomar, M.G.; Kibler, P.; Kodukula, K.; Galande, A.K. *Org. Lett.* **2012**, *14*, 732; (b) Whitby, L.R.; Ando, Y.; Setola, V.; Vogt, P.K.; Roth, B.L.; Boger, D.L. *J. Am. Chem. Soc.* **2011**, *133*, 10184.
3. (a) Gouverneur, V.; Muller, K. *Fluorine in Pharmaceutical and Medicinal Chemistry: From Biophysical aspects to Clinical Applications*, Imperial College Press, London, UK, **2012**; (b) Ojima, I. *Fluorine in Medicinal Chemistry and Chemical Biology*, Blackwell Publishing, West Sussex, **2009**; (c) Begue, J.P.; Bonnet- Delpon, D. *Bioorganic and Medicinal Chemistry of Fluorine*, Wiley, Hoboken, **2008**.
4. (a) Chaume, G.; Bebeau, O.; Lesot, P.; Brigaud, T. *J. Org. Chem.* **2010**, *75*, 4135.; (b) Schlosser, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 1496; (c) Schlosser, M. *Angew. Chem. Int. Ed.* **1998**, *110*, 1538.

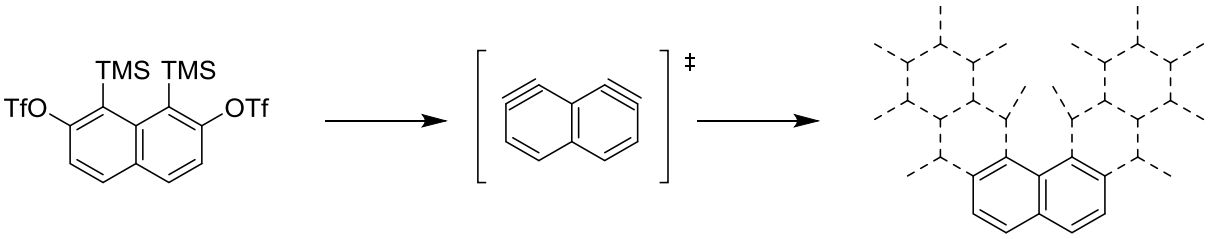
Flash-16

Building angular polycyclic aromatic compounds by aryne chemistry

Iago Pozo, Agustín Cobas, Diego Peña, Enrique Guitián and Dolores Pérez
Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS), Universidade de Santiago de Compostela
iago.pozo@rai.usc.es

Bisaryne synthons are useful building blocks for the construction of large, extended polycyclic aromatic compounds (PACs).[1] Generation of these reactive species in the presence of an adequate partner leads to two sequential cycloaddition reactions in a single synthetic operation, whereas the selective fluoride treatment results in new structurally complex aryne precursors.

Herein we report the reactivity of 1,8-bis(trimethylsilyl)naphthalene-2,7-diyl bistriflate, an efficient precursor of the novel 1,7-naphthodiyne synthon. This methodology allows an efficient synthesis of naphtho[2,3-*a*]tetraphenes and many other interesting PACs.



1. (a) Schuler, B.; Collazos, S.; Gross, L.; Meyer, G.; Pérez, D.; Guitián, E.; Peña, D. *Angew. Chem. Int. Ed.* **2014**, *53*, 9004. (b) Rodríguez-Lojo, D.; Pérez, D.; Peña, D.; Guitián, E. *Chem. Commun*, **2015**, *51*, 5418.

Flash-17

ALKYNYLSILANES AS ALKYNYLATING AGENTS IN THE PRESENCE OF GOLD(I) CATALYSTS

José Manuel González, Alfredo Ballesteros and Belén Rubial
Dpto. de Química Orgánica e Inorgánica e Instituto Universitario de Química Organometálica "Enrique Moles", Universidad de Oviedo, C/ Julián Clavería 8, 33006
e-mail: rubialbelen@uniovi.es

The carbophilic nature of gold(I) complexes[1] makes them suitable agents to activate the **C-Si** bond in alkynylsilanes,[1,2] affording a gold(I) acetylide and a TMSX species in which X is the counteranion in the gold complex. When X is a non-coordinating counteranion, this species is highly electrophilic. Due to the affinity of silicon to form bonds with oxygen atoms,[3] this species could be used to activate or increase the electrophilicity of some oxygenated groups, allowing the corresponding alkynylation reaction.

This strategy has being succesfully applied to a variety of substrates to afford the corresponding alkynylated compounds.[4] A good scope of substituents and functional group tolerance has being observed. Further achievements in order to obtain enantioselective transformations have also being made.

[1] Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed.* **2007**, *46*, 3410-3449
[2] Cicak, H.; Vancik, H.; Mihalic, Z. *J. Org. Chem.* **2010**, *75*, 6969-6972.
[3] Weinhold, F.; West, R. *Organometallics* **2011**, *30*, 5815-5824.
[4] Rubial, B.; Ballesteros, A.; González, J. M. *Adv. Synth. Catal.* **2013**, *355*, 3337-3343.

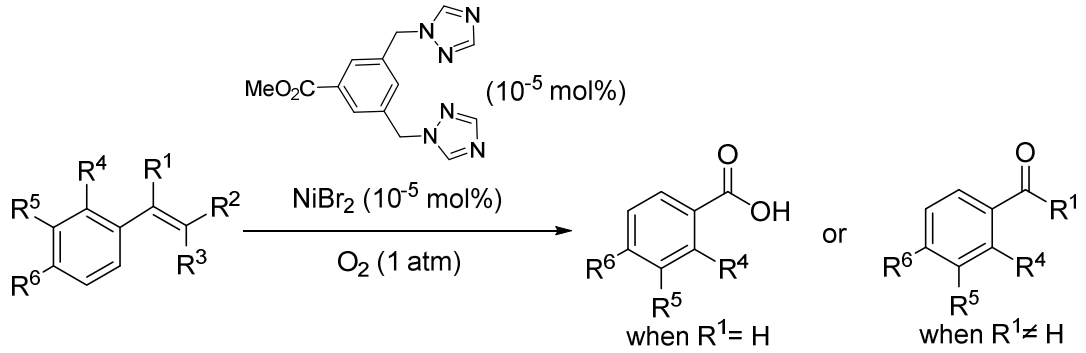
Flash-18

Efficient nickel-catalysed aerobic cleavage of aromatic alkenes

Raul SanMartin, María Teresa Herrero, Esther Domínguez and Garazi Urgoitia
Kimika Organikoa II Saila, Zientzia eta Teknologia Fakultatea, Euskal Herriko Unibertsitatea, PO Box 644, 48080 Bilbao, Spain
e-mail: raul.sanmartin@ehu.eus

Oxidative ozonolysis has been traditionally the main procedure for the cleavage of alkenes into carboxylic acids and carbonyl compounds.[1] This potentially hazardous protocol has been occasionally replaced with the use of stoichiometric amounts of other metal reagents,[2] and later on with the combination of catalysts and non-metallic oxidants.[3] Oxygen is a sustainable oxidizing agent and therefore, a valuable option for the oxidative cleavage of alkenes. However, the oxygen-mediated direct transformation of alkenes into carboxylic acids has been scarcely explored to date.[4]

Herein, we wish to present a general, selective method for the aerobic oxidative cleavage of styrene derivatives into carboxylic acids and ketones. Mono-, di-,tri- and tetrasubstituted aromatic olefins are oxidatively cleaved by this reproducible protocol, also suitable for larger scale (1.5 g) reactions.



Further details about reaction scope and experimental conditions will be discussed.

Acknowledgments This research was supported by the Basque Government (IT-774-13), the Spanish Ministry of Economy and Competitiveness (CTQ2013-46970-P) and the University of the Basque Country (UFI QOSYC 11/12). G.U thanks the University of the Basque Country for a postdoctoral scholarship. Technical and human support provided by SGIker of UPV/EHU is gratefully acknowledged.

[1] Larock, R. C. in: Comprehensive Organic Transformations, Wiley-VCH, New York, 2nd ed., 1999, pp 1213–1215.
[2] See for example: a) Kaneda, K. ; Haruna, S.; Imanaka, T. ; Kawamoto, K.; *J. Chem. Soc. Chem. Commun.* **1990**, 1467; b) Albarella, L.; Giordano, F.; Lasalvia, M.; Piccialli, V.; Sica, D. *Tetrahedron Lett*. **1995**, *36*, 5267; c) Yang, D.; Zhang, C. *J. Org. Chem*. **2001**, *66*, 4814.
[3] Some examples in: a) Shaikh, T. M.; Hong, F.-E. *Adv. Synth. Catal*. **2011**, *353*, 1491; b) Islam, S. M.; Paul, S.; Mobarok, M.; Roy, A. S.; Mondal, P. *Transition Met. Chem*. **2013**, *38*, 7; c) Moorthy, J. N.; Parid, K. N. *J. Org. Chem*. **2014**, *79*, 1143; d) Parida, K. N.; Moorthy, J. N. *Tetrahedron* **2014**, *70*, 2280
[4] a) Zhang, A.; Li, L. ; Li, J.; Zhang, Y.; Gao, S. *Catal. Commun*. **2011**, *12*, 1183; b) Rak, M. J.; Lerro, M.; Moores, A. *Chem. Commun*. **2014**, *50*, 12482.

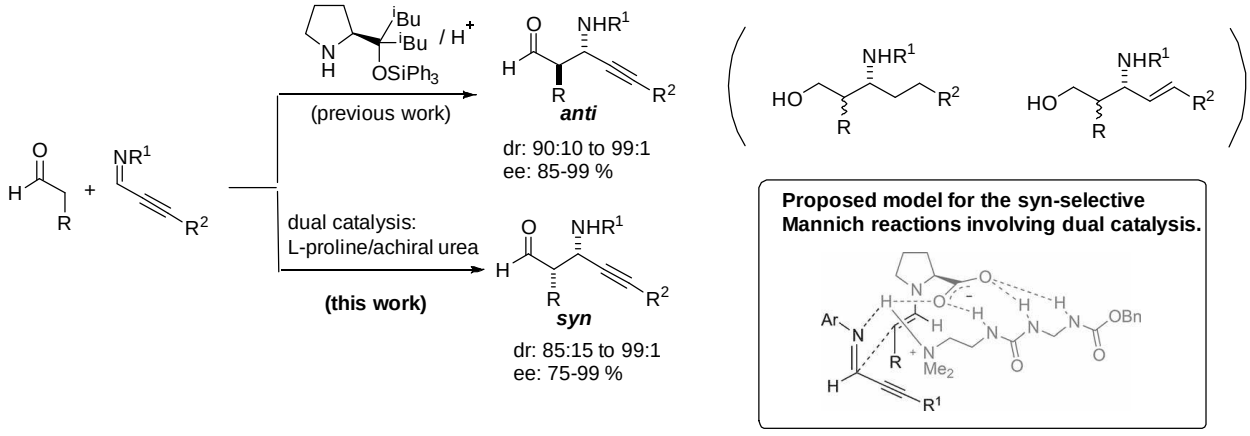
Flash-19

Asymmetric Synthesis of Functionalized Propargylic Amines: *Anti and Syn* Selective Mannich Reaction of Aldehydes with Propargylic Imines

Irati Lapuerta, Mikel Oiarbide and Claudio Palomo, Silvia Vera

Departamento de química orgánica I, Facultad de Químicas
Universidad del País Vasco, Paseo Manuel Lardizabal nº3, 20018
e-mail:*Silvia.vera@ehu.es*

Quite recently we described new asymmetric methodology based on an amine-catalyzed direct Mannich reaction of aldehydes with *C*-alkynyl imines[1]. The method not only proceeds under very mild reaction conditions, but also adducts with two contiguous stereogenic centers and several sites amenable for further synthetic manipulation are afforded. Notably, simple reduction of the alkynyl to the alkyl or alkenyl moieties established new routes to otherwise difficult to prepare Mannich adducts, such as those formally derived from highly enolizable imines or azadienes, respectively. In our previous studies, reactions were promoted by a prolinol silyl ether catalyst and Mannich adducts with *anti* relative configuration were obtained as major diastereomers. In order to have full access to adducts with either stereoconfiguration, we set to find a route to the stereocomplementary *syn* adducts. The stuty resulted the direct *syn*-selective and highly enantioselective Mannich reaction of aldehydes with alkynyl imines based in a dual proline-achiral aminal/urea catalysis system.[2]



[1] Gómez-Bengoa, E., Garcia, J.M, Jimenez S., Lapuerta I., Mielgo, A., Odriozola, J. M. Otazo, I., Razkin, J., Urruzuno I, **Vera S,** and Palomo C.; *Chem. Science*, **2013**, *4*, 3198-3204

[2] I. Lapuerta, **S. Vera**, M. Oiarbide, C. Palomo, *Chem. Eur. J*. **2016,** *22*, 7229-7237

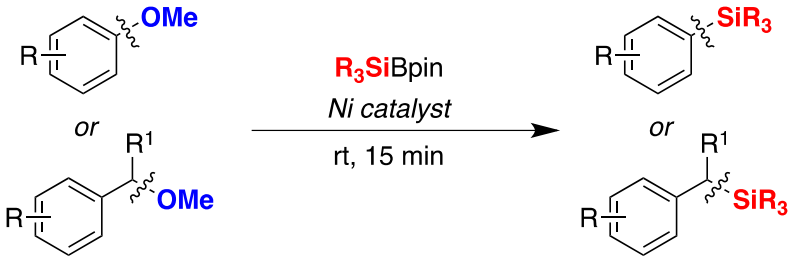
Flash-20

Ligand-Free Ni-Catalyzed Silylation of C(sp^2)– & C(sp^3)–OMe Bonds

Masaki Nakajima,* Cayetana Zarate,* and Ruben Martin
Institute of Chemical Research of Catalonia (ICIQ),
Av. Països Catalans, 16, Tarragona, 43007, Spain
e-mail: rmartinromo@iciq.es; czarate@iciq.es
*These authors contributed equally to this work

While the field of cross-coupling has reached remarkable levels of sophistication, the vast majority of processes are still being conducted with organic halide counterparts.[1] Drawbacks associated to their toxicity and the limited accessibility of densely functionalized aryl halides have prompted chemists to develop powerful, yet practical, alternatives. Among these, utilizing aryl methyl ethers as coupling partners would be particularly rewarding, as they are the simplest derivatives in the phenol series as well as readily accessible from common commercial sources.[2] However, the high activation energy required for effecting C–OMe bond cleavage has become a daunting challenge when devising catalytic techniques using aryl methyl ethers. At present, the vast majority of cross-coupling reactions using aryl methyl ethers remains confined to C–C bond formation utilizing stoichiometric amounts of highly reactive organometallic species, high temperatures and/or protocols based on the employment of rather expensive supporting ligands.[2] As part of our interest in C–OMe cleavage,[3] we have developed a novel Ni-catalyzed silylation of C(sp^2)– and C(sp^3)–OMe bonds. This method is characterized by an unprecedented reaction rate and exceptionally mild ligand-free conditions.[4]

Ni-catalyzed ligand-free silylation of C(sp^2)– & C(sp^3)–OMe bonds



(1) Diederich, F., de Meijere, A., Eds. *Metal-Catalyzed Cross-Coupling Reactions*; Wiley-VCH: Weinheim, 2004.

(2) (a) Tobisu, M.; Chatani, N. *Acc. Chem. Res.* **2015**, *48*, 1717. (b) Cornella, J.; Zarate, C.; Martin, R. *Chem. Soc. Rev.* **2014**, *43*, 8081.

(3) (a) Zarate, C.; Manzano, R.; Martin, R. *J. Am. Chem. Soc.* **2015**, *137*, 6754. (b) Cornella, J.; Gómez-Bengoa, E.; Martin, R. *J. Am. Chem. Soc.* **2013**, *135*, 1997. (c) Álvarez-Bercedo, R.; Martin, R. *J. Am. Chem. Soc.* **2010**, *132*, 17352.

(4) Nakajima, M.; Zarate, C.; Martin, R. *Manuscript in preparation*.

POSTERS

Poster-1

SYNTHESIS OF ISOXAZOLIDINYL-*gem*-BISPHOSPHONIC ACIDS AS FPPS LIGANDS

Vincenzo Algieri,[a,b] Antonio De Nino,[a] Loredana Maiuolo,[a] Beatrice Russo,[a] Ignacio Delso,[b,c] and Pedro Merino.[b]

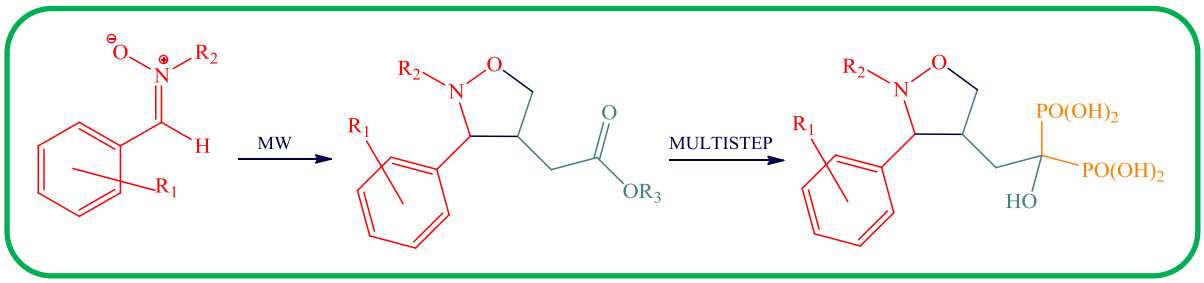
[a] *Dipartimento di Chimica e Tecnologie Chimiche-CTC, Università della Calabria, Ponte Bucci cubo 12/C, 87036, Arcavacata di Rende (CS), IT.*

[b] *Departamento de Síntesis y Estructura de Biomoléculas, Instituto de Síntesis Química y Catálisis Homogénea, U. de Zaragoza-CSIC, 50009 Zaragoza, Spain.*

[c] *Servicio de RMN, Centro de Química y Materiales de Aragón, U. de Zaragoza-CSIC, 50009 Zaragoza, Spain.*

e-mail: vincenzo.algieri@unical.it

The discovery of new pharmacological agents is one of the biggest challenges for current research. One of these is the synthesis of functionalized isoxazolidine rings with biological activity. Isoxazolidines mimic natural nucleosides exerting antitumor activity.[1] The addition of a *gem*-bisphosphonate group on the heterocyclic ring increases the cytotoxicity of the obtained substrates that can be applied in clinical treatment of bone metastases and osteoporosis.[2,3] In particular, this class of molecules inhibits the Farnesyl Pyrophosphate Synthase (FPPS), a key enzyme in the isoprenoid biosynthesis pathway and a target of bisphosphonates for treatment of bone-related disorders.[4] Purpose of this work is the synthesis of isoxazolidinyl-*gem*-biphosphonic acids with potential pharmacological activity. The synthesis is carried out in two phases (Scheme 1): the first step involves the formation of the isoxazolidine nucleus with *solvent free* methodologies, while the second step provides the introduction of geminal bisphosphonate group on the cycle by a multistep reaction synthesis.



Scheme 1

The reaction products were obtained with high yields and an excellent regio- and diastereoisomeric ratio. Finally, these products have been subjected to STD Nuclear Magnetic Resonance studies that show an enzymatic inhibition comparable at the zoledronic acid, drug actually in use for clinical treatment of bone deseas.

1. a) O. Bortolini, M. D'agostino, A. De Nino, L. Maiuolo, M. Nardi, G. Sindona. *Tetrahedron*, **2008**, 64, 8078-8081.
b) O. Bortolini, I. Mulani, A. De Nino, L. Maiuolo, A. Melicchio, B. Russo, D. Granchi, *Current Organic Synthesis*, **2014**, 11, 461-465.
2. E. Guenin, D. Ledoux, O. Oudar, M. Kraemer, *Anticancer Research*, **2005**, 25, 1139-1146.
3. K. Thomson, JE Dunford, MJ Rogers, *Biochem. Biophys. Res. Commun.* **2002**, 290, 869-873.
4. Russell, R.G.G.; Watts, N.B.; Ebetino, F.H.; Rogers, M.J. *Osteoporos. Int.* **2008**, *19*, 733.

Poster-2

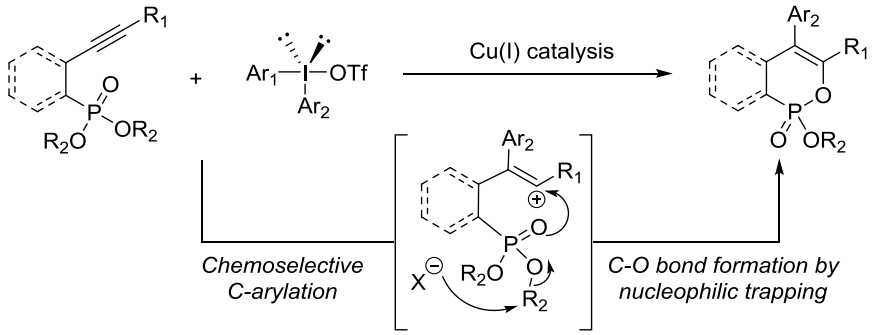
Copper-Catalyzed Cascade Reactions Towards Cyclic Phosphonates

Borja Pérez-Saavedra, Eduardo Laga, Carlos Saá and Martín Fañanás-Mastral
Centro de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) e Departamento de Química Orgánica, Universidade de Santiago de Compostela, 15782 Santiago de Compostela
borja.perez.saavedra@rai.usc.es

Organic phosphonates represent a highly important class of compounds with a wide range of applications in biology, agriculture and synthetic organic chemistry. In particular, cyclic phosphonates have demonstrated antitumor activity and are inhibitors of various enzymes, such as β-lactamases or pancreatic cholesterol esterase.[1] Therefore, the development of new methods for the synthesis of this kind of phosphorous heterocycles is highly desirable.

Diaryliodonium salts are air- and moisture-stable, non-toxic and easy to prepare compounds which have recently gained considerable attention as mild and selective arylating reagents in organic synthesis.[2] These hypervalent iodine compounds have been employed in the copper(I)-catalyzed electrophilic carboarylation of alkynes[3] and in the oxygen-arylation of phosphonates to obtain mixed aryl alkyl phosphonates.[4]

Here we report a novel copper(I)-catalyzed cyclization of alkynyl phosphonates which allow for the synthesis of six-membered arylated cyclic phosphonates under mild conditions. This cascade reaction probably involves an initial chemoselective electrophilic alkyne arylation which generates a vinyl cation which is trapped by the nucleophilic addition of the oxygen atom of the phosphoryl group. Substitution on various positions of the phosphonate is well tolerated and several aryl groups can be introduced with total chemo- and regioselectivity.



Aknowledgements: This work was supported by MINECO (projects CTQ 2014-59015R, CTQ2015-62724-ERC, RYC-2012-11749), the ERDF and the Xunta de Galicia (project GRC 2014/032). We also thank the ORFEO-CINQA network (CTQ 2014-5192 REDC). Borja Pérez-Saavedra thanks Fundación Segundo Gil Dávila for a predoctoral grant.

[1] (a) Kaur, K.; Adediran, S. A.; Lan, M. J. K.; Pratt, R. F. *Biochemistry*, **2003,** *42*, 1529-1536. (b) Li, B.; Zhou, B.; Lu, H.; Ma, L.; Peng, A. Y. *Eur. J. Med. Chem.* **2010**, *45*, 1955–1963.
[2] Merritt, E. A.; Olofsson, B. **2009**, *48*, 9052-9070.
[3] Walkinshaw, A. J.; Xu, W.; Suero, M. G.; Gaunt, M. J. *J. Am. Chem. Soc.* **2013**, *135*, 12532−12535.
[4] Fañanás-Mastral, M.; Feringa, B. L. *J. Am. Chem. Soc.* **2014**, *136*, 9894−9897.

Poster-3

Steric Shielding vs. σ–π Orbital Interactions in Triplet–Triplet Energy Transfer

Inmaculada Andreu, Fabrizio Palumbo, Isabel Morera, Francisco Bosca and Miguel A. Miranda

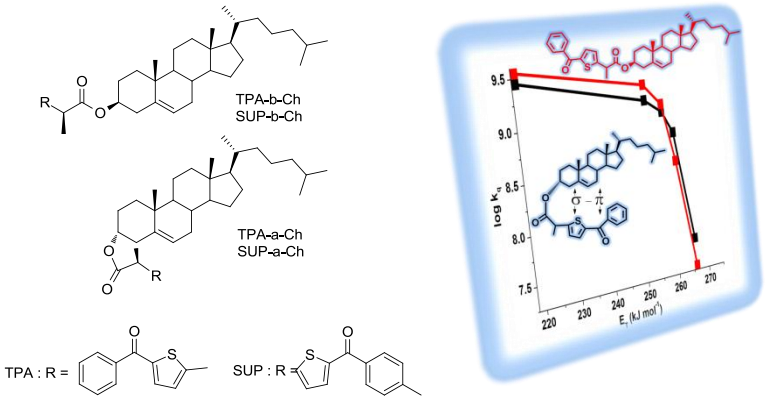
[1] *Instituto de Tecnología Química UPV-CSIC, Universitat Politècnica de València, Avenida de los Naranjos, 46022 Valencia, Spain*

[2] *Departamento de Química, Universitat Politècnica de València, Camino de Vera s/n, 46022 Valencia, Spain*

[3] *Unidad Mixta de Investigación IIS Hospital La Fe-UPV, Avenida de Fernando Abril Martorell 106, 46026 Valencia, Spain*

e-mail: iandreur@qim.upv.es

Triplet excitation energy can be transferred between two chromophores by the Dexter mechanism, which is based on an electron exchange through orbital overlap of the donor excited state and the acceptor ground state.[1] The rate constants of diffusion-controlled triplet–triplet energy transfer (TTET) are affected by steric hindrance (shielding) as demonstrated using aromatic ketones as donors.[2] However, the influence of non-covalent σ–π orbital interactions on TTET through tuning of the donor excitation energy remains basically unexplored. Thus, in the present work, we have investigated intermolecular TTET using donor moieties covalently linked to a rigid cholesterol (Ch) scaffold. For this purpose, diaryl ketones of π,π* electronic configuration tethered to α- or β-Ch were prepared from tiaprofenic acid (TPA) and suprofen (SUP).



The obtained systems TPA-α-Ch, TPA-β-Ch, SUP-α-Ch and SUP-β-Ch were submitted to photophysical studies (laser flash photolysis and phosphorescence), in order to delineate the influence of steric shielding and σ–π orbital interactions on the rate of TTET to a series of energy acceptors.[3] Actually, fine tuning of the donor triplet energy significantly modifies the rate constants of TTET in the absence of diffusion control. The experimental results are rationalized by means of theoretical calculations using first principles methods based on DFT as well as molecular dynamics. This principle should be applicable to a wide variety of chromophores, and the concept could be extended to related processes, such as photoinduced electron transfer.

[1] M. A. Baldo and S. R. Forrest, *Phys. Rev. B*, **2000**, *62*, 10958–10966

[2] J. C. Scaiano, W. J. Leigh, M. A. Meador and P. J. Wagner, *J. Am. Chem. Soc.*, **1985**, *107*, 5806–5807

[3] I. Andreu, I. Morera, F. Palumbo, G. Sastre, F. Bosca, M. A. Miranda *Chem. Sci.*, **2015**, *6*, 4035–4041

Poster-4

Combined Experimental and Computational Study of Enantioselective Intermolecular a-amidoalkylation reactions of bicyclic hydroxylactams and enamides

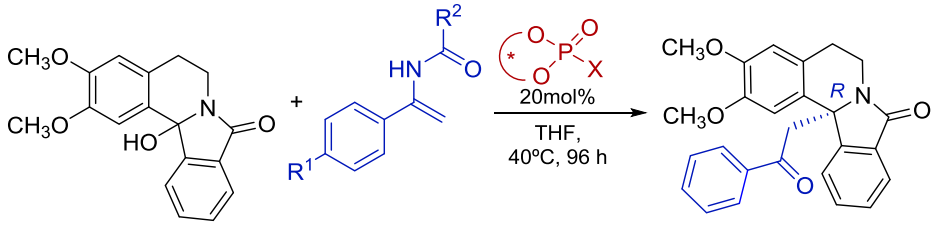
Ana Linares, Sonia Arrasate, Humberto González Díaz, Esther Lete, Nuria Sotomayor, and Eider Aranzamendi

Departamento de Química Orgánica II, Facultad de Ciencia y Tecnología, Universidad del País Vasco / Euskal Herriko Unibertsitatea (UPV/EHU), Apdo. 644, 48080 Bilbao, Spain

e-mail: eider.aranzamendi@ehu.eus

The intermolecular α-amidoalkylation reaction is a very useful carbon-carbon bond-forming process in organic chemistry.[1] It has been widely applied to the sterecontrolled functionalization of nitrogen heterocycles, as the reaction of the cyclic *N*-acyliminium ion intermediates, generated *in situ*, is usually highly diastereoselective. The possibility of using a broad variety of nucleophiles confers upon the reaction a very wide scope, and it has been employed in the natural product and pharmaceutical syntheses. In this context, we reported[2] α-amidoalkylation of indoles with bicyclic α-hydroxylactams for the generation of a quaternary stereocenter in the preparation of 12b-substituted isoindoloisoquinolines (*ee* up to 95%) using BINOL-derived Brønsted acids. The α-amidoalkylation reaction occurs through the formation of chiral phosphate/bicyclic quaternary *N*-acyliminium ion pair. There was experimental evidence to propose that hydrogen-bonding interactions of the phosphate ion-paired intermediate to the indole N–H could potentially be involved. Hence, the BINOL derived phosphoric acid would be acting as a bifunctional catalyst interacting also with the nucleophile.

In order to expand the scope of the procedure, we have evaluated enamides with a free N-H group as nucleophiles in this type of enantioselective α-amidoalkylation reactions. Besides, we have used quantitative structure-reactivity relationship (QSRR) methods[3] for the prediction of the enantioselectivity of these reactions. This study would help to understand how different parameters affect the stereochemical outcome and thus help us to design or choose the adequate catalyst or experimental conditions for a given reaction without engaging in a long term, empirical investigation. Details will be given.



1. For a review: Martínez-Estibalez, U.; Gómez-SanJuan, A.; García-Calvo, O.; Aranzamendi, E.; Lete, E.; Sotomayor, N. *Eur. J. Org. Chem.* **2011**, 3610-3633.
2. Aranzamendi, E.; Sotomayor, N.; Lete, E. *J. Org. Chem.* **2012**, *77*, 2986-2991.
3. Blázquez-Barbadillo, C.; Aranzamendi, E.; Coya, E.; Lete, E.; Sotomayor, N.; González-Díaz, H. *RSC Adv.* **2016**, *6*, 38602-38610.

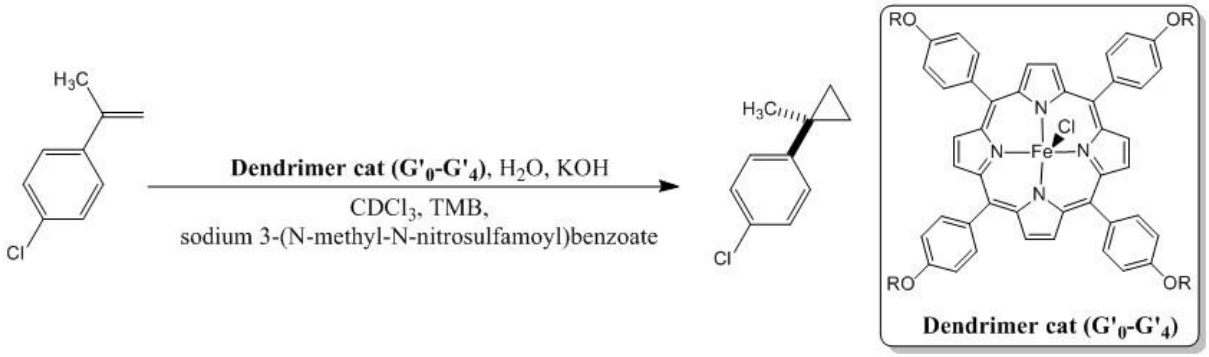
Poster-5

(Metallo)-dendrimers as catalysts of cyclopropanation reactions

*Iosune Arrastia[b,d], Petr Vins[a], Abel de Cózar[b,c,d], Iván Rivilla[b], Katerina Nováková[e], Ronen Zangi[b,c], Josef Cvacka[e], Ana Arrieta[b], Pavel Drasar[a], José I. Miranda[f] and Fernando P. Cossío[b,d,]**

[a] University of Chemistry and technology in Prague, Czech Republic. [b] Dpto. de Química Orgánica I, and Centro de Innovación en Química Avanzada (ORFEO-CINQA), UPV/EHU, Donostia, Spain, [c] Ikerbasque, Basque Foundation for Science, Bilbao, Spain. [d] DIPC, Donostia, Spain. [e] Institute of Organic Chemistry and Biochemistry AS CR, Prague, Czech Republic, [f] SGIker, NMR Facility, UPV/EHU, Donostia, Spain.
e-mail: mireniosune.arrastia@ehu.es

(Metallo)-dendrimers are macromolecular entities which possess interesting properties in homogeneous catalysis.[1]
In this way, experimental and computational studies were carried out on dendrimers possessing a Fe(porphyrin) catalytic core and polyether dendritic arms.
The catalytic activity of this kind of compound was tested with regard to the reaction of cyclopropanation of substituted styrene with diazometane (Scheme 1).[2]



Scheme 1

Our results suggest that these macromolecules are efficient catalysts for the cyclopropanation reaction of other alkenes under safe conditions.[3]
In addition, we have seen that the reaction rate depends on the dendrimer generation used, decreasing considerably with the transition to third- and fourth-generation (G'_3-G'_4). From Molecular Dynamics (MD) calculations data and Diffusion-Ordered NMR Spectroscopy (DOSY) experiments, we attribute this distinct behavior to cooperative effects, generated via aggregation of dendritic units.
Acknowledgements: Financial support by Ministry of Education, Youth and Sports of the Czech Republic, Czech Foundation, DIPC, Ministerio de Economía y Competitividad of Spain, FEDER and Basque Government are gratefully acknowledged.

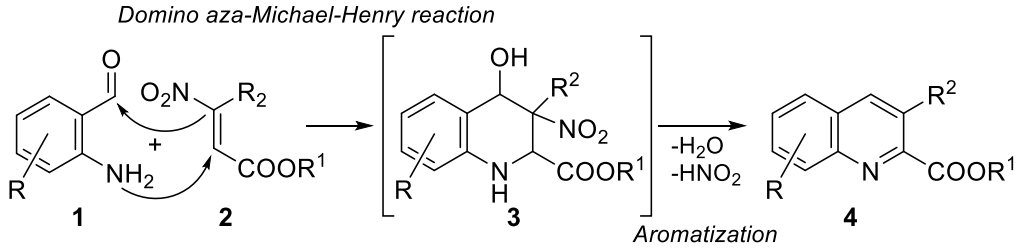
[1] Astruc, D; Boisselier, E.; Ornelas, C. *Chem. Rev.* **2010**, *110*, 1857-1959.
[2] Morandi, B.; Carreira, E.M. *Science* **2012**, *335*, 1471-1474.
[3] Vins, P.; de Cózar, A.; Rivilla, I.; Novakova, K.; Zangi, R.; Cvacka, J.; Arrastia, I.; Arrieta, A.; Drasar, P.; Miranda, J.I.; Cossío, F.C. *Tetrahedron* **2016**, *72*, 1120-1131.

Poster-6

β-Nitroacrylates and *o*-Aminoaldehydes: Useful Building Blocks to Synthesize Quinoline-2-carboxylates under Heterogeneous Conditions

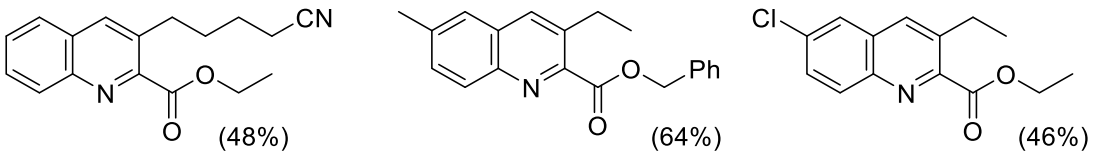
Serena Gabrielli, Alessandro Palmieri, Susanna Sampaolesi and Roberto Ballini
School of Science and Technology, Chemistry Division
University of Camerino, Via S. Agostino 1, 62032 Camerino
e-mail: roberto.ballini@unicam.it

Over the years β-nitroacrylates demonstarted to be valuable building blocks of higly functionalized materials, and in particular, key precursors of heterocycle systems.[1] Following our studies on the chemistry of this class nitro derivatives,[2] we found a new reactivity of β-nitroacrylates with *o*-aminoaldehydes to provide quinoline-2-carboxylates in a one-pot way. The idea was to develop the process exploiting four different reactions: (i) an *aza*-Michael addition between the 2-aminobenzaldheydes **1** and β-nitroacrylates **2**, (ii) an intramolecular to give the benzopiperidines **3**, (iii) elimination of water, and (iv) nitrous acid elimination to provide the title targets **4** (Scheme 1).



Scheme 1. Our idea

The domino *aza*-Michael-Henry reaction proceeds under promoter-free and solvent-free conditions, at 70°C, to give the intermediate **3**, which is directly treated at 50°C with acetonitrile and supported BEMP to provide the quinoline-2-carboxylates **4**. By our approach, it has been possible to prepare title compounds in good overall yields (37-64%), introducing different substituent in 3-position as well as in the benzene ring (Scheme 2).



Scheme 2. Some representative examples

1. (a) Ballini, R.; Palmieri, A.; Talaq, M.A.; Gabrielli, S. *Adv. Synth. Catal.* **2009**, *351*, 2611-2614. (b) Ballini, R.; Gabrielli, S.; Palmieri, A. *Synlett* **2009**, 965-967. (c) Palmieri, A.; Gabrielli, S.; Cimarelli, C.; Ballini, R. *Green Chem.* **2011**, *13*, 3333-3336. (d) Palmieri, A.; Gabrielli, S.; Parlapiano, M.; Ballini, R. *RSC Adv.* **2015**, *5*, 4210-4213.
2. (a) Ballini, R.; Gabrielli, S.; Palmieri, A. *Curr. Org. Chem.* **2010**, *14*, 65-83. (b) Palmieri, A.; Gabrielli, S.; Ballini, R. *Green Chem.* **2013**, *15*, 2344-2347.

Poster-7

New G-wires DNA nanostructures from G-rich oligonucleotides incorporating a 3'-3' inversion of polarity site

Giorgia Oliviero,[1] Stefano D'Errico,[1] Fabrizia Nici,[1] Brunella Pinto,[1] Principia Dardano,[2] Ilaria Rea,[2] Luca De Stefano,[2] Gennaro Piccialli[1,3] and Nicola Borbone[1]

[1]*Department of Pharmacy, University of Naples Federico II, Via D. Montesano 49, 80131 Napoli, Italy*

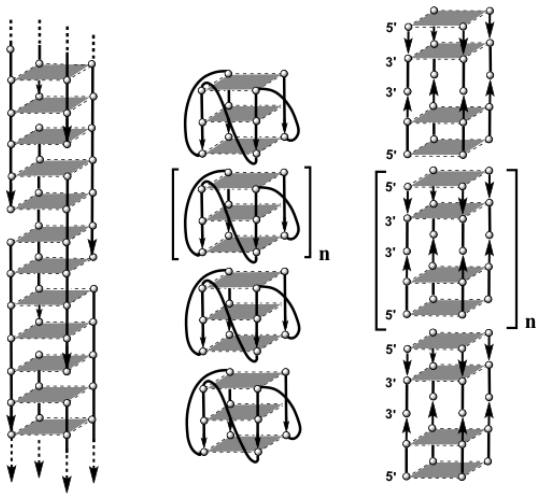
[2]*Institute for Microelectronics and Microsystems, National Council Research of Italy, Via P. Castellino 111, 80131 Napoli, Italy*

[3]*Institute of Protein Biochemistry, National Council Research of Italy, Via P. Castellino 111, 80131 Napoli, Italy*

e-mail: nicola.borbone@unina.it

Supramolecular DNA G-quadruplex structures are among the most promising biomaterials in the fields of medical and nanotechnological applications.[1] G-quadruplexes are non-canonical secondary structures of DNA that form when guanines or suitable G-rich oligodeoxynucleotide (ODN) strands are annealed in the presence of monovalent coordinating cations. Depending on the annealing conditions and on the ODN sequence, some G-rich ODNs have the ability to form very long rod-shaped G-quadruplex aggregates known as G-wires (Figure). Because of the interesting optical[2] and conductive[3] properties of G-wires, much effort is being devoted to the setting up of reproducible synthetic protocols for the obtainment of G-wires having specific structure and length.

In this communication we report the preliminary results of our study aimed at the obtainment of a new type of G-wires by annealing G-rich ODNs incorporating a 3'-3' inversion of polarity site and having the 5'-CGG-3' 3-mer at both 5'-ends, which in our previous studies induced the formation of quadruplex multimers by end-to-end stacking[4,5].



[1] Davis, J. T. *Angew. Chem. Int. Ed.* **2004**, *43* (6), 668-698.
[2] Changenet-Barret, P.; Emanuele, E.; Gustavsson, T. et al. *J. Phys. Chem. C* **2010**, *114* (34), 14339-14346.
[3] Liu, S.-P.; Weisbrod, S. H.; Tang, Z. et al. *Angew. Chem. Int. Ed.* **2010**, *49* (19), 3313-3316.
[4] Borbone, N.; Amato, J.; Oliviero, G. et al. *Nucleic Acids Res* **2011**, *39* (17), 7848-7857.
[5] D'Atri, V.; Borbone, N.; Amato, J. et al. *Biochimie* **2014**, *99*, 119-128.

Poster-8

Synthesis of blue organic dyes and their application as sensitizers Dye-Sensitized Solar Cells

Matteo Bartolini,[c], Alessio Dessì[a] Alessandro Mordini,[a,c] Adalgisa Sinicropi,[b] Maurizio Peruzzini,[a]. Riccardo Basosi,[b], Maurizio Taddei,[b] Lorenzo Zani,[a] Gianna Reginato.[a] and Massimo Calamante,[a,c]

[a]*Istituto di Chimica dei composti organometallici (CNR-ICCOM), via Madonna del Piano 10, 50019 Sesto Fiorentino, Italy.*

[b]*Dipartimento di Biotecnologie Chimica e Farmacia, Università degli Studi di Siena, via A. Moro 2, 53100 Siena, Italy.*

[c]*Dipartimento di Chimica "U. Shiff" Università degli Studi di Firenze, via della Lastruccia 13, 50019 Sesto Fiorentino, Italy.*

e-mail: mcalamante@iccom.cnr.it

Dye-sensitizer solar cells (DSSC) are currently considered one of the most promising alternatives to traditional silicon solar cells[1]. The research activity in this field is mostly focused on the design and synthesis of new organic dyes with potential application in this kind of devices.[2] The synthesis of new dyes with high molar extinction coefficient and specific color (blue in particular) in order to increase the aesthetic properties and ease their integration in buildings and objects are the main focus in the research in the field of DSSC.
Aiming to this goal, we selected as new auxiliary acceptor group the (*E*)-3,3'-bifuranylidene-2,2'-dione (Figure 1)[3], a strong electron-withdrawing system which was firstly prepared in 1882.[4] The synthesis of this dye has been optimized and its derivatization using Pd-catalysed cross-coupling reactions has been firstly accomplished. Then, two new D-A-π-A dyes containing the (*E*)-3,3'-bifuranylidene-2,2'-dione as auxiliary acceptor group have been designed, synthesized and characterized: the two new dyes showed an intense blue color in solution and, when adsorbed on a TiO_2 electrode, both a broad absorption of the red/near-infrared light between 500 and 800 nm and right electrochemical potentials for a proper use in DSSCs.

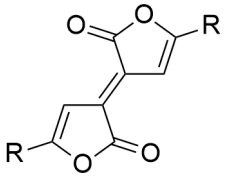


Figure 1

1. O'Reagan, B.; Grätzel, M. *Nature* **1991**, *353*, 737.
2. *Dye-sensitized solar cells* (Ed.: K. Kalyanasundaram), EPFL Press, Lausanne **2010**.
3. Kingsberg, E. *Chem. Rev.* **1954**, *54*, 59.
4. Von Pechmann, H. *Ber.* **1882**, *15*, 885.

Poster-9

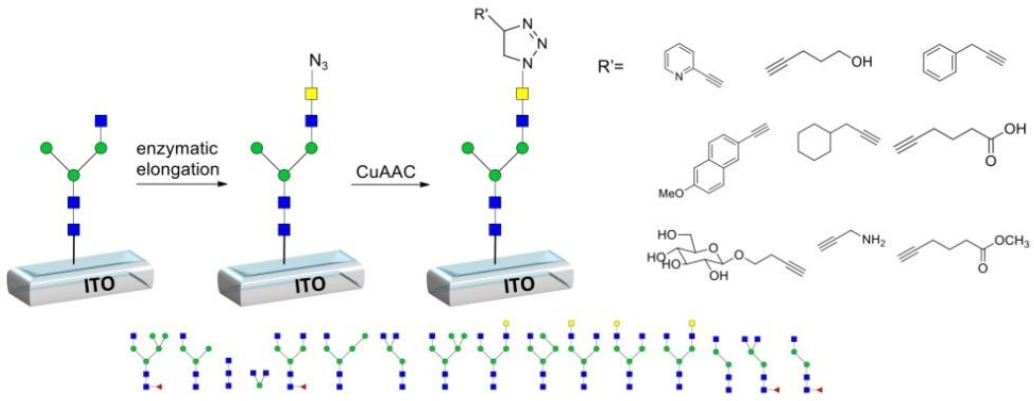
On chip development of N-glycan mimetics for improving CLRs targeting

Anna Cioce[a], Sonia Serna[a], Álvaro Hernández[a], Giulio Goti[b], Anna Bernardi[b], Niels C. Reichardt[a]

a) Glycotechnology unit,CICbiomaGUNE, Paseo Miramon 182,20009 San Sebastian(Spain)
b) Department of chemistry,Università degli studi di Milano,via Golgi 19,20133 Milano(Italy)
e-mail: acioce@cicbiomagune.es

Carbohydrate-lectin interactions play an important role in the immune system with functions including cell adhesion, glycoprotein turnover and recognition and neutralization of pathogen e.g. by triggering immune responses. Although carbohydrate-lectin interactions are highly specific, their binding strength is relatively weak; binding affinity can be increased by a multivalent ligand presentation or chemically optimizing ligands to the lectin binding site.
Carbohydrate microarray have recently emerged as high-throughput tools for studying carbohydrate-protein interactions and for screening the specificity of carbohydrate processing enzymes.
Here, we present a combination of enzymatic synthesis on printed glycan scaffolds with subsequent chemical diversification for the on-chip preparation of a large collection of glycomimetics for screening of C-type lectin ligands with increased affinity.

Our glycan array platform with glycans hydrophobically attached to a transparent and conductive indium tin-oxide coated glass slide allows the *in situ* analysis of chemical and enzymatic transformations by mass spectrometry while interactions with labeled proteins can be observed with a fluorescence scanner.[1]
Initially a number of N-glycan scaffolds with varying antennae number are immobilized on the surface; subsequently, by enzymatic elongation with a mutant galactosyl transferase and non-natural azido-*N*-acetyl-D-galactosamine nucleotide donor, one or more azides were introduced on all substrates on the chip. The azide functions were then reacted with a panel of structurally and electronically varied alkynes by copper(I)-catalyzed azido alkyne cycloaddition (CuAAC) to arrive at a library of N- glycan mimetics with novel binding properties compared to the natural homologues.



General strategy for the on-chip preparation of N-glycan mimetics

[1] Beloqui, A.; Calvo, J.; Serna, S.;Wilson, Iain, B., H.; Martin-Lomas, M.; Reichardt, N., C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7477-7481

Poster-10

Functionalization of graphene-based material with arynes under non-conventional conditions

Manuel Vázquez Sulleiro[1], Sabela Quiroga,[2] Diego Peña,[2] Dolores Pérez,[2] Enrique Guitián,[2] Alejandro Criado[1,3], Maurizio Prato[1,3]

[1] *Department of Chemical and Pharmaceutical Sciences, University of Trieste, P.le Europa 1, 34127 Trieste, Italy.*

[2] *Centro Singular de Investigación en Química Biológica y Materiales Moleculares (CIQUS), C/Jenaro de la Fuente s/n, 15782, Santiago de Compostela, Spain.*

[3] *Carbon Nanobiotechnology Group, CICbiomaGUNE, Ed. Pº Miramón 182, 20009 Guipúzcoa, Spain.*

e-mail: acriado@cicbiomagune.es

Graphene is a promising next-generation material with a unique set of electronic, mechanical, and thermal properties. Consequently, graphene-based materials (GBMs) exhibit a wide variety of potential applications in sensing, energy storage, catalyst support, supercapacitors, and optoelectronic devices.[1]

Cycloaddition reactions are a versatile chemical functionalization as they enable a controllable site modification and the introduction of a variety of substitution, creating the possibility of increasing polarity and solubility.[2] However, chemical transformations frequently require tedious and long procedures, which, sometimes, can be avoided using alternative approaches. The use of these non-conventional condition reactions is able to save time, to avoid unstable suspensions and improve reaction efficiency.[3]

This work is based on the developing of non-conventional approaches to efficiently and mildly functionalized GBMs. We focused on relatively unexplored cycloaddition reactions of arynes with GBMs. In particular, we generated different arynes by thermal decomposition of corresponding aryl anhydrides (**1**) at high temperatures (**Figure 1**). Due to the good absorption of microwave irradiation (MW) of carbon-based materials, GBMs play two roles in the reaction process: as reagent and, at the same time, as MW absorbing matrix which allows high temperatures to be reached in short times under solvent-free conditions. The functionalized GBMs were characterized by several techniques such as Thermo Gravimetrical Analysis (TGA); Raman, UV-Vis and IR spectroscopies; Transmission Electron Microscopy (TEM) and X-Ray Photoelectron Spectroscopy (XPS) analysis, confirming a clear functionalization.

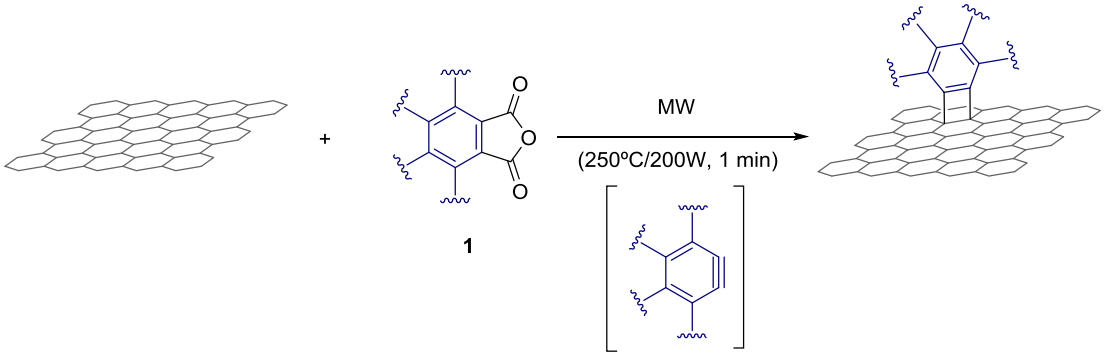


Figure 1

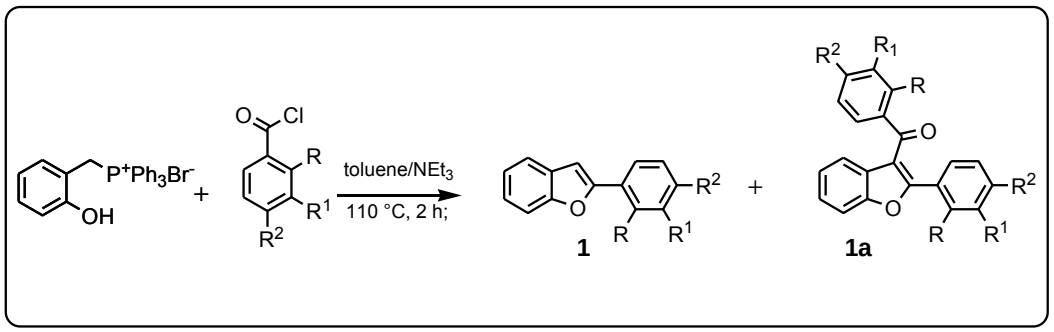
[1] Geim, A. K. *Science* **2009**, *324*, 5934. b) Ferrari, A. C. *et al. Nanoscale*, **2015**, *7*, 4598.
[2] Marchesan, S.; Melchionna, M.; Prato, M. *ACS Nano*, **2015**, *9*, 9441.
[3] Vázquez, E.; Giacalone, F.; Prato, M. *Chem.Soc.Rev*., **2014**, *43*, 58.

Poster-11

Unexpected Synthesis of 2-Phenyl-3-benzoylbenzofurans under Wittig Conditions

Giovanna L. Delogu and Michela Begala
Department of Life and Environmental Science, Unit of Drug Sciences, University of Cagliari, Via Ospedale 72, 09124 Cagliari, Italy
e-mail: delogug@unica.it, michelabegala@unica.it

In the course of our program directed at the synthesis of novel MAO inhibitors,[1] we planned to synthesize 2-phenylbenzofuranes using the intramolecular Wittig procedure due to its ease and simplicity.[2]
However, while developing our project using this procedure, we found that the GC/MS analysis of the crude reaction mixture revealed, together with the desired product of cyclization **1**, the unexpected side product **1a**, which, after extensive analysis by NMR and mass spectrometry, turned out to be the 2-phenyl-3-benzoyl benzofurane.



3-Benzoyl[*b*]benzofurans are structural cores to a host of bioactive molecules in pharmaceutical use or development. Representative examples include amiodarone, a clinically used drug for controlling intractable cardiac arrhythmias, LY 320135, a potent cannabinoid CB_1 receptor antagonist, and benzbromarone, an uricosuric agent.
From a synthetic viewpoint, 2-aryl-3-benzoyl benzofuran derivatives bearing strongly deactivating groups on both phenyl rings such as NO_2 and CN, could provide convenient intermediates in the preparation of more complicated pharmacologically valuable compounds. As a result, numerous approaches to the benzofurane scaffold have been disclosed in the literature. Most synthetic approaches to 2,3-disubstituted benzofurans introduce the C3-substituent on the preformed benzo[*b*]furan ring at the end of the synthesis. Traditionally, the simple and straightforward method for the C3 acylation of benzofurans appeared to be the Fridel-Craft reaction using acylchlorides.[3] However this method suffer from some limitations *e.g.* the poor regioselectivity, especially when strongly deactivated acyl chloride are used.[4] Here in we report a simple, regioselective, one-pot route for the preparation of new deactivated 2-aryl 3-benzoyl benzo[*b*]furans via ilide acylation under Wittig condition.

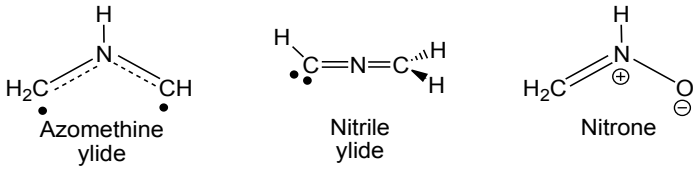
1. Ferino, G.; Cadoni, E.; Matos, M. J.; Quezada, E.; Uriarte, E.; Santana, L.; Yáñez, M.; Viña, D.; Picciau, C.; Serra, S.; Delogu, G. *Chem. Med. Chem.* **2013**, *8*, 956-966.
2. Hercouet, A.; Le Corre, M. *Tetrahedron Lett.* **1979**, *23*, 2145-2148.
3. Twyman, L. J. *Tetrahedron Lett.* **1999**, *40*, 9383-9384.
4. Thévenin, M.; Thoret, S.; Grellier, P., Dubois, J. *Bioorg. Med. Chem.*, **2013**, *21*(17), 4885-4892.

Poster-12

Understanding the mechanisms of [3+2] cycloaddition reactions within the Molecular Electron Density Theory

Luis R. Domingo and Mar Ríos-Gutiérrez
Department of Organic Chemistry, University of Valencia, Dr. Moliner 50, 46100 Burjassot, Valencia, Spain
e-mail: domingo@utopia.uv.es

The molecular mechanism of Three-Atom-Components (TACs) participating in [3+2] cycloaddition (32CA) reactions has remained an enigma since 1965, when Huisgen proposed a concerted mechanism for these important organic reactions.[1] Numerous *Molecular Electron Density Theory*[2] (MEDT) studies devoted to understand the relationship between TAC structures, *i.e. pseudodiradical*, carbenoid or zwitterionic structures, and their reactivity in 32CA reactions have allowed establishing a useful classification of 32CA reactions based on their molecular mechanism into *pseudodiradical*-type (*pr-type*), carbenoid-type (*cb-type*) and zwitterionic-type (*zw-type*) reactions[3,4] (see Scheme). TACs with a *pseudodiradical* character participate in *pr-type* 32CA reactions taking place easily through earlier transition state structures (TSs) with a non-polar character;[3] TACs with a carbenoid character participate in *cb-type* 32CA reactions whose feasibility depends on the polar character of the reaction, *i.e.* the nucleophilic character of the carbenoid TAC and the electrophilic character of the ethylene derivative;[4] likewise, TACs with a zwitterionic character participate in *zw-type* 32CA reactions controlled by nucleophilic/electrophilic interactions taking place at the TSs, similar to *cb-type* reactions.[3] This useful classification permits the understanding of the reactivity of TACs in 32CA reactions depending on their electronic structure and that of the ethylene derivative.



	Structure	
pseudodiradical	carbenoid	zwitterioinic
	Reactivity	
pr-type	*cb-type*	*zw-type*

Scheme. Electronic structure of TACs and the proposed reactivity types in 32CAs.

1. Huisgen, R. *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 633–645
2. Ríos-Gutiérrez, M.; Domingo, L. R.; Pérez, P. *RSC Adv.* **2015**, *5*, 84797–84809
3. Domingo, L. R.; Emamian. S. R. *Tetrahedron*, **2014**, *70*, 1267–1273
4. Domingo, L. R.; Ríos-Gutiérrez, M.; Pérez, P. *Tetrahedron* **2016**, *72*, 1524–1532

Poster-13

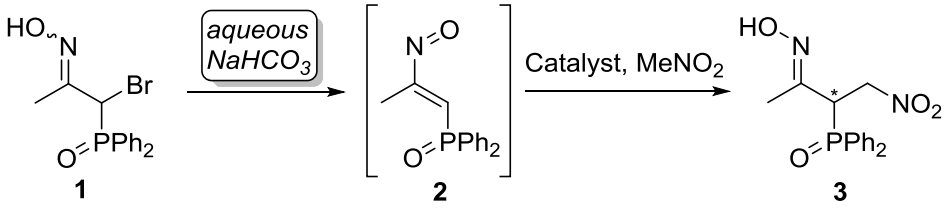
Catalytic Asymmetric Conjugate Addition of Nitrocompounds to Phosphorylated Nitrosoalkenes

Jesús M. de los Santos, Ana M. Ochoa de Retana, Francisco Palacios and Zouhair Es Sbai
Department of Organic Chemistry I, Faculty of Pharmacy, University of the Basque Country (UPV-EHU), Paseo de la Universidad 7. 01006 Vitoria-Gasteiz (Spain)
e-mail: zouhairessbai@yahoo.fr

The α-functionalization of ketones in an umpolung sense, in which nucleophilic species add to an electrophilic α-carbon, affords an attractive alternative to enolate/azaenolate-based methods and is suitable to catalysis. Recently, we have been involved in exploring ways to achieve this through the use of nitrosoalkenes.[1] These latter have received a great deal of attention especially due to their efficiency as heterodienes in [4+2]-cycloaddition processes.

We have previously described the generation of phosphorus substituted nitrosoalkenes and their use in conjugate addition of some nucleophilic reagents,[2a] formal [3+2] cycloaddition reactions for the preparation of *N*-hydroxypyrroles,[2b] and hetero-Diels–Alder cycloaddition processes.[2c,2d]

In this preliminary study, the asymmetric organocatalytic conjugate addition of nitrocompounds to phosphorylated nitrosoalkenes **2**, previously prepared through base-promoted dehydrohalogenation of bromooximes **1**, leading to chiral functionalized oximes **3** is reported. The outcome of this conversion proceeds *via* an umpolung reaction, relative to enolate/azaenolate methods. As potential organocatalysts for this transformation, we have used chiral amines including cinchona alkaloids, as well as chiral amino (thio)ureas, bifunctional catalysts broadly employed in a variety of transformations.



Acknowledgements. The authors thank the *Universidad del País Vasco/Departamento de Educación, Universidades e Investigación del Gobierno Vasco* (UPV-EHU, GIU/09/57; IT–992-16) and *Dirección General de Investigación del Ministerio de Ciencia e Innovación* (MCINN, Madrid DGI, CTQ2015–67871-R) for supporting this work. UPV/EHU–SGIker technical support for NMR spectra (MCINN, GV/EJ, and European Social Found) is also gratefully acknowledged.

1. For an excellent review see: Gilchrist, T. L. *Chem. Soc. Rev*. **1983**, *12*, 53–73.
2. (a) de los Santos, J. M.; Ignacio, R.; Aparicio, D.; Palacios, F. *J. Org. Chem*. **2007**, *72*, 5202–5206. (b) de los Santos, J. M.; Ignacio, R.; Aparicio, D.; Palacios, F.; Ezpeleta, J. M. *J. Org. Chem*. **2009**, *74*, 3444–3448. (c) de los Santos, J. M.; Ignacio, R.; Rubiales, G.; Aparicio, D.; Palacios, F. *J. Org. Chem*. **2011**, *76*, 6715–6725. (d) de los Santos, J. M.; Ignacio, R.; Es Sbai, Z.; Aparicio, D.; Palacios, F. *J. Org. Chem*. **2014**, *79*, 7607–7615.

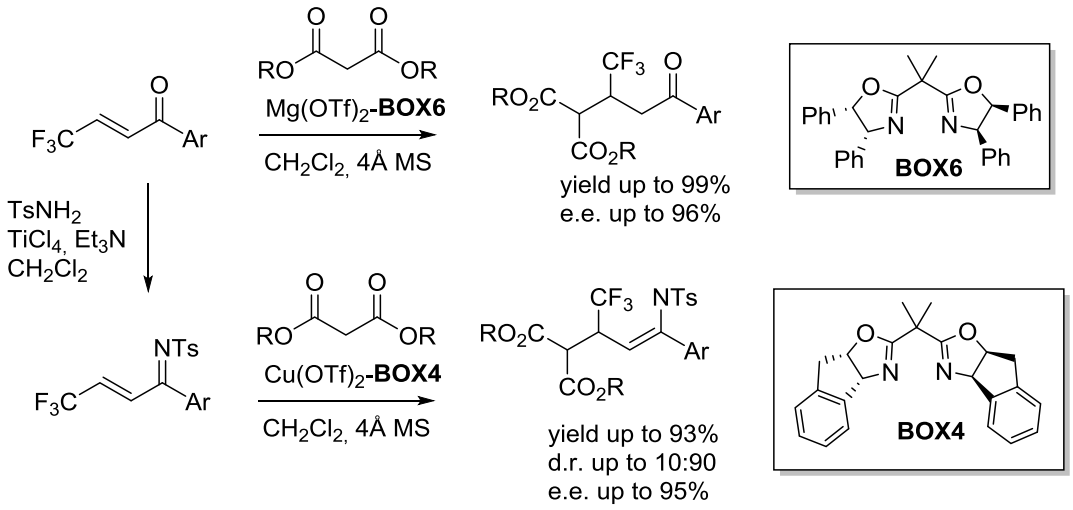
Poster-14

Asymmetric Conjugate Addition of Malonic Esters to β-Trifluoromethyl Enones and β-Trifluoromethyl Enimines

Miguel Espinosa, Jorge Herrera, Toni Iborra, Gonzalo Blay,* Luz Cardona, José R. Pedro*
Departament de Química Orgànica, Facultat de Química, Universitat de València, C/ Dr. Moliner 50, 46100-Burjassot (Valencia), Spain
e-mail: miguel.espinosa@uv.es

Chiral fluorinated compounds have found wide application in different fields including medicinal, agricultural and material sciences.[1] In particular, molecules bearing a chiral center attached to a trifluoromethyl substituent have a special interest due to the occurrence of this motif in biologically active compounds.[2] Accordingly, considerable efforts have been addressed to the catalytic asymmetric synthesis of molecules with a CF_3-containing stereocenter. Among the reported methodologies, the functionalization of trifluoromethylated prochiral carbons is one of the most straightforward for this purpose.[3]

As a part of our current research on enantioselective Michael-type reactions,[4] we report in this communication the asymmetric conjugate addition of malonic esters to β-trifluoromethyl α,β-*N*-tosylimines using catalysis by Mg(II) and Cu(II), respectively.



Acknowledgements: Financial support by MINECO (CTQ2013-47494-P) is gratefully acknowledged. M.E. thanks the Generalitat Valenciana for a predoctoral grant.

1. (a) Hiyama, T. in *Organofluorine Compounds: Chemistry and Applications*; Yamamoto, H. Ed.; Springer: New York, 2000. (b) Uneyama, K. *Organofluorine Chemistry*; Blackwell: Oxford, 2006.
2. Nie, J.; Guo, H.-C.; Cahard, D.; Ma, J.-A. *Chem. Rev.* **2011**, *111*, 455-529.
3. (a) Zhao, M.-X.; Zhu, H.-K.; Dai, T.-L.; Shi, M. *J. Org. Chem.* **2015**, *80*, 11330-11338. (b) Sanz-Marco, A.; Garcia-Ortiz, A.; Blay, G.; Pedro, J. R. *Chem. Commun.* **2014**, *50*, 2275-2278. (c) Blay, G.; Fernandez, I.; Muñoz, M. C.; Pedro, J. R.; Vila, C. *Chem. Eur. J.* **2010**, *16*, 9117-9122.
4. (a) Espinosa, M.; Blay, G.; Cardona L.; Pedro, J. R. *Chem. Eur. J.* **2013**, *19*, 14861-14866. (b) Espinosa, M.; Garcia-Ortiz, A.; Blay, G.; Cardona L.; Muñoz, M. C.; Pedro, J. R. *RSC Adv.* **2016**, *6*, 15655-15659.

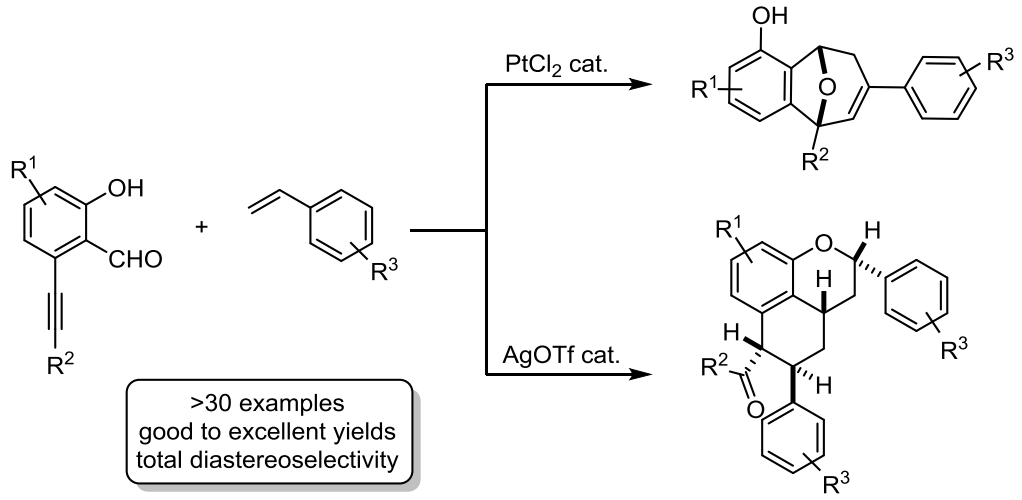
Poster-15

Divergent Catalyst-Dependent Reactivity of *O*-Alkynylsalicylaldehydes and Alkenes

Tamara Arto, Francisco J. Fañanás, Félix Rodríguez and Patricia Fernández
Departamento de Química Orgánica e Inorgánica de la Universidad de Oviedo
Julián Clavería, 8, 33006, Oviedo
patri_sy@hotmail.com

ortho-Alkynylbenzaldehydes are very useful reagents that have been widely used to generate isochromenylium derivatives through metal-catalysed cycloisomerization reactions. The subsequent reaction of these intermediates with the appropiate coupling partners has become a valuable strategy to access a wide range of interesting molecules.[1]

In this context, we have observed that *ortho*-alkynylsalicylaldehydes, a particular type of *ortho*-alkynylaldehydes show a different reactivity pattern. Thus, herein we present a new switchable synthesis of 5,9-epoxybenzo[7]annulenes or benzo[*de*]chromenyl ketones from *ortho*-alkynylsalicylaldehydes and styrenes. An appropiate selection of the catalyst ($PtCl_2$ or AgOTf) is the key to get one or the other final product.



1. Asao, N.; *Synlett*, **2006**, 1645-1656.

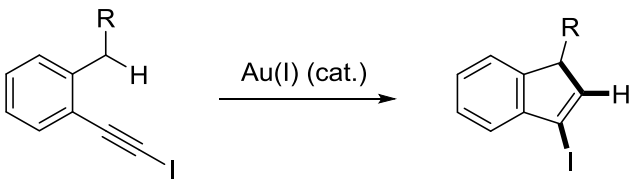
Poster-16

Activación C-H mediante vinilidenos de oro(I)

Pablo Morán-Poladura, Eduardo Rubio, José M. González and Paula Fernández-Canelas
Departamento de Química Orgánica e Inorgánica e Instituto Universitario de Química.
e-mail: fernandezcpaula@uniovi.es

Los yodoalquinos son una clase de acetilenos dotados de notables características estructurales y elevada reactividad.[1] Se han propuesto como precursores para formar vinilidenos de Au(I), especies intermedias elusivas, que poseen potencial interés sintético.[2]

En esta comunicación se presentan los resultados correspondientes a la reacción de yodoalquinos con catalizadores de oro(I) para lograr la activación de enlaces C(sp3)-H, a través de la generación previa de yodovinilidenos, que se muestra en el siguiente esquema.



Se discutirán también otro tipo de transformaciones relacionadas con la reactividad de haloalquinos en presencia de catalizadores carbofílicos.

1. This is an example of a footnote. Please, adhere to ACS style: (a) Sun, A.; Lauher, J.W.; Goroff, N. S.; *Science* **2006**, *312*, 30–34; (b) Barluenga, J.; González J. M.; Llorente, I.; Campos, P. J.; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 893–894; *Angew. Chem.* **1993**, *105*, 928–929; c) Fürstner, A.; Schlecker, A.; Lehmann, C.W.; *Chem. Commun*. **2007**, 4277–4279.

2. This is an example of a footnote. Please, adhere to ACS style: (a) Morán-Poladura, P.; Suárez-Pantiga, S.; Piedrafita, M.; Rubio, E.; González, J. M.; *J. Organomet. Chem*. **2011**, *696*, 12–15; (b) Morán-Poladura, P.; Rubio, E.; González, J. M.; *Angew. Chem. Int. Ed.* **2015**, *54*, 3052 3055.

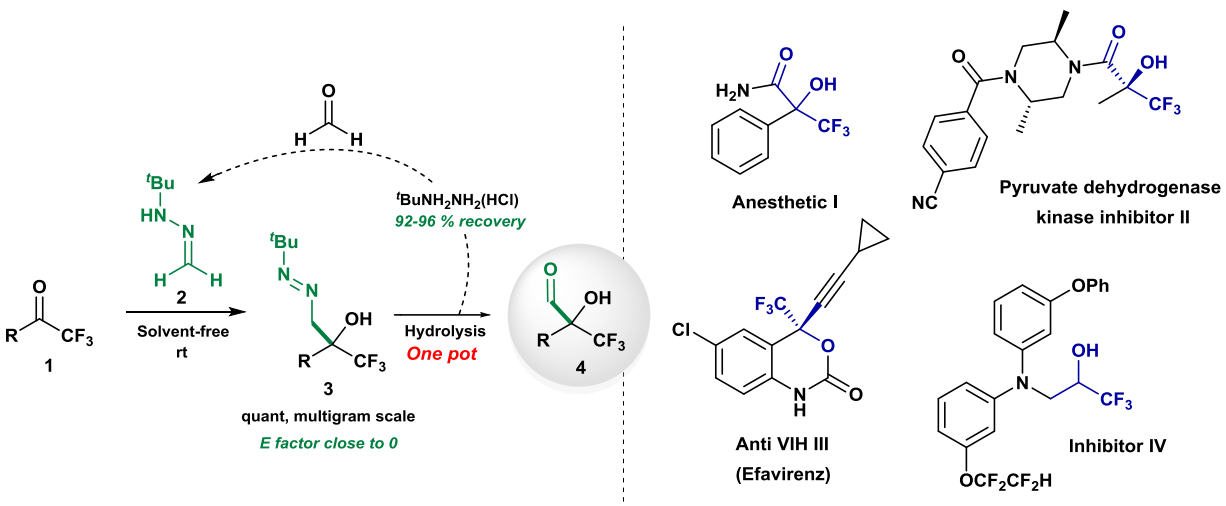
Poster-17

Green nucleophilic formylation strategy for the functionalization of trifluoromethyl ketones

Esteban Matador, David Monge, José M. Lassaletta and Rosario Fernández
[a]*Departamento de Química Orgánica, Universidad de Sevilla, Sevilla, Spain*
[b]*Instituto de Investigaciones Químicas, Sevilla, Spain*
e-mail: ffernan@us.es

An efficient, scalable and operationally simple one-pot, 2-step strategy for the formylation of trifluoromethyl ketones is presented. The key step is a diaza-carbonyl-ene reaction of formaldehyde *tert*-butyl hydrazone **2**[1] and trifluoromethyl ketones **1** under solvent-free conditions. This reaction proved to be fast, clean and high-yielding, affording densely functionalised α-hydroxy α-trifluoromethyl diazenes **3**.[2]

Ensuing diazene-to-aldehyde transformation, avoiding protection/deprotection reactions and chromatographic purifications, and subsequent derivatizations in one-pot fashion, provide a direct entry to a variety of useful trifluoromethylated building blocks for target-oriented synthesis. The selected examples shown in *Scheme **1*** include α-hydroxy amides **I** and **II**, the marketed anti-HIV agent Efavirenz **III** and β-aminoalcohol **IV**. The organocatalytic enantioselective version of this reaction is currently under development.



*Scheme **1***. α-Hydroxy aldehydes **4** as bulding blocks in target-oriented synthesis.

[1] Revision articles: a) Crespo-Peña, A.; Monge, D.; Martín-Zamora, E.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 12912–12915. b) Monge, D.; Crespo-Peña, A. M.; Martín-Zamora, E.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. Chem. Eur. J. **2013**, *19*, 8421. c) Serrano, I.; Monge, D.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *Chem. Commun.* **2015**, *51*, 4077.
[2] Matador, E.; Monge, D.; Fernández, R. Lassaletta, J. M. *Green Chem*. **2016** DOI: 10.1039/c6gc00408c.

Poster-18

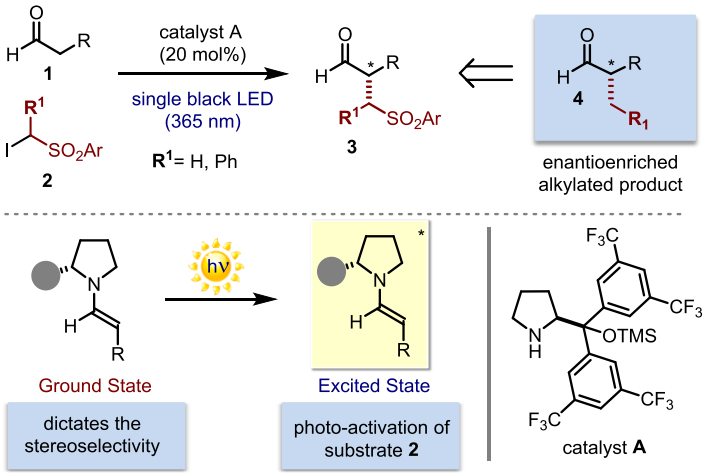
Photochemical Enantioselective Alkylation of Aldehydes with α-Iodo Sulfones

Giacomo Filippini[†], Mattia Silvi[†] and Paolo Melchiorre[†‡]

[†] *ICIQ - Institute of Chemical Research of Catalonia, Av. Països Catalans 16, 43007 (Tarragona, Spain),* [‡]*ICREA - Catalan Institution for Research and Advanced Studies, Pg. Lluís Companys 23, 08010 (Barcelona, Spain)*

gfilippini@iciq.es

Visible light photo-organocatalysis has recently emerged as a powerful activation strategy for the implementation of enantioselective chemical transformations. Our research group has demonstrated that key transient intermediates of organocatalytic processes, in the ground state or in the excited state, can actively participate in the photo-excitation of organic substrates without the need for an external photosensitizer.[1] This reactivity enabled the development of light-driven stereoselective α-alkylations of carbonyl compounds which could not be realized under thermal activation. We are interested in further expanding this light-mediated activation strategy to develop the enantioselective coupling of aldehydes (**1**) and α-iodo sulfones (**2**, Scheme 1). Chiral enamines, generated by condensation of aldehyde **1** with the commercially available chiral secondary amine catalyst **A**, can directly reach an electronically excited state upon light absorption triggering the formation of reactive radical species from the organic halide **2**. Simultaneously, the ground state chiral enamine provides effective stereochemical induction for the enantioselective alkylation process. Product **3** bears a stereogenic centre decorated with a sulfone moiety that can subsequently be converted into a methyl or a benzyl group allowing for the development of a stereoselective formal alkylation of aldehydes.



Scheme 1. Formal photo-organocatalytic enantioselective methylation of aldehydes.

Acknowledgements: This work was supported by the ICIQ Foundation, MINECO (project CTQ2013-45938-P and Severo Ochoa Excellence Accreditation 2014-2018, SEV-2013-0319), and by the European Research Council (ERC 278541 - ORGA-NAUT).

[1] (a) Arceo, E.; Jurberg, I. D.; Álvarez-Fernández, A.; Melchiorre, P. *Nature Chem.* **2013**, *5*, 750. (b) Woźniak, Ł; Murphy, J. J.; Melchiorre, P. *J. Am. Chem. Soc.* **2015**, *137*, 5678-5681. (c) Silvi, M.; Arceo, E.; Jurberg, I. D.; Cassani, C.; Melchiorre, P. *J. Am. Chem. Soc.* **2015**, *137*, 6120-6123.

Poster-19

A highly active catalyst system for the aerobic oxidation of alcohols and methylene compounds

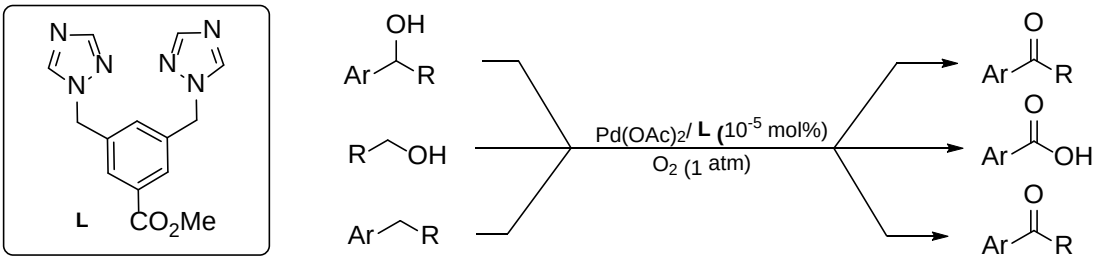
Garazi Urgoitia, Ainhoa Maiztegi, Raul SanMartin, María Teresa Herrero, Esther Domínguez, Iratxe Astarloa and Aimar García

Department of Organic Chemistry II, Faculty of Science and Technology, University of the Basque Country (UPV/EHU). Sarriena auzoa, z/g 48940 Leioa, Spain.

e-mail: raul.sanmartin@ehu.eus

Aryl ketones and arenecarboxylic acids are versatile intermediates in the preparation of functional materials.[1] Classical synthesis of ketones and carboxylic acids by oxidation of alcohols is a well established transformation performed by a wide range of oxidizers.[2] In this context, oxygen is an interesting alternative since it is cheap, readily available and water is the only by-product. A number of metal catalysts have been reported to promote such oxidations but relatively high catalyst amounts are required and, sometimes, pressures above 5 atm.[3]

We wish to present a very active catalyst system based on the use of air stable and relatively inexpensive palladium acetate and a readily available bis-(1,2,4)-triazolyl ligand **L** that allows the efficient oxidation of benzyl alcohols and non-functionalized benzylic positions into the corresponding carbonyl and carboxylic compounds at atmospheric pressure using catalyst loadings as low as 10^{-5} mol%.



Acknowledgments This research was supported by the Basque Government (IT-774-13), the Spanish Ministry of Economy and Competitiveness (CTQ2013-46970-P) and the University of the Basque Country (UFI QOSYC 11/12). A.G and G.U. thank the Spanish Ministry and the University of the Basque Country for a predoctoral and postdoctoral scholarship respectively. Technical and human support provided by SGIker of UPV/EHU is gratefully acknowledged.

[1] See for example: a) Deng, Y.; Chin, Y.-W.; Chai, H.; Keller, W. J.; Kinghorn, A. D. *J. Nat. Prod.* **2007**, *70*, 2049-2052; b) Jia, X.; Zhang, S.; Wang, W.; Luo, F. Cheng, J. *Org. Lett.* **2009**, *11*, 3120.

[2]: a) Azizian, S.; Eftekhari- Bafrooei, A; Bashiri, . *Kinet. Catal*. **2010**, *51*, 24; b) Yusubov, M. S.; Zagulyaeva, A. A.; Zhadankin, V. V. *Chem.–Eur. J*., **2009**, *15*, 11091; c) Hinzen, B.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1*, **1997**, 1907.

[3] See for example: a) Costa, V. V.; Jacinto, M. J.; Rossi, L. M.; Lander, R.; Gusevskaya, E. V. *J. Catal.*, **2011**, *282*, 209; b) Liu, G.; Tang, R.;. Wang,, Z. *Catal. Lett*., **2014**, *144*, 717; c) Wang, J.; Lang, X.; Zhaorigetu, B.; Jia, M.; Wang, J.; Guo, X.; Zhao, J. *ChemCatChem*, **2014**, *6*, 1737.

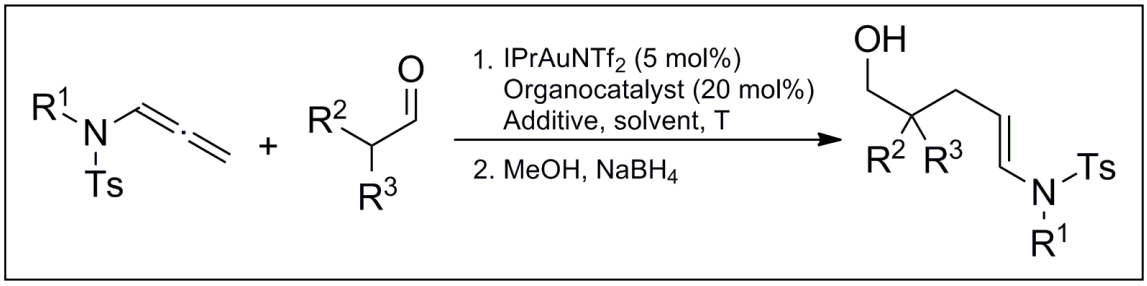
Poster-20

GOLD(I) OPERATIONAL IN SYNERGISTIC CATALYSIS FOR THE INTERMOLECULAR α-ADDITION REACTION OF ALDEHYDES ACROSS ALLENAMIDES

Silvia González-Pelayo, Alberto Ballesteros, Pablo Morán-Poladura, José M. González
Departamento de Quiímica Orgánica e Inorgánica, Instituto Universitario de Química Organometálica ''Enrique Moles'', Universidad de Oviedo. C/ Julián Clavería 8, 33006 Oviedo, Spain
gonzalezpelayos@gmail.com

Asymmetric organocatalysis is well stablished as a powerful tool to promote chemical transformations with good yield and enantioselectivity.[1] For years, gold(I) has been extensively used for the activation of unsaturated compounds toward different nucleophiles.[2] These two strategies can be combined in a synergistic manner to afford new chemical transformations.[3]

Herein we report the synergistic combination of gold(I) catalysis with L-proline and L-proline-derived organocatalysts to activate both aldehydes and allenamides respectively.[4] With this strategy we were able to build all-carbon quaternary stereocenters with moderate yield and enantioselectivity. In some cases certain additives were necessary to modulate the selectivity.



[1] Melchiorre, P.; Marigo, M.; Carlone, A.; Bartoli, G.; *Agew. Chem. Int. Ed.* **2008**, *47*, 6138.

[2] Hashmi, A. S. K.; *Chem. Rev.* **2007**, *107*, 3180.

[3] Loh, C. C. J.; Enders, D.; *Chem.- Eur. Jour.* **2012**, *18*, 10212.

[4] Ballesteros, A.; Morán-Poladura, P.; González, J. M.; *Chemm. Commun.* **2016**, *52*, 2905

Poster-21

Natural and Mimetics of *Neisseria meningitidis* A Capsular Polysaccharide fragments: Conformational Study

Luca Unione,[a] Ana Ardá,[a] Francisco Corzana,[b] Luigi Lay,[c]
Roberto Adamo,[d] Jesús Jimenéz-Barbero[a] and Calloni Ilaria,[a]

a. *CIC bioGUNE, Parque Tecnológico de Bizkaia, 48160 Derio, Spain*
b. *Departamento de Química, Universidad de La Rioja, Madre de Dios, 51,E-26006 Logroño (La Rioja), Spain;*
c. *Department of Chemistry and CRC ''Materiali Polimerici'' (LaMPo), University of Milan, Via Golgi 19, 20133 Milan, Italy;*
d. *Novartis Vaccines and Diagnostics, Via Fiorentina 10, 53100 Siena, Italy;*

e-mail:icalloni@cicbiogune.es

Neisseria meningitidis serogroup A (MenA) is an aerobic diplococcal Gram-negative bacterium responsible for epidemic meningitis disease, especially in the Sub-Saharian region of Africa[1]. The carbohydrate capsule (capsular polysaccharide, CPS), which covers the bacteria cell surface, has been identified as the primary virulence factor of Men A. Consequently, there is an increasing interest in making use of the CPS or mimetics thereof as potential vaccines against meningitis disease. Structurally, CPS consists of (1→6)-linked 2-acetamido-2-deoxy-α-D-mannopyranosyl phosphate repeating units, predominantly O-acetylated at 3-OH (80%)[2]. This polysaccharide suffers from chemical liability in water[3], and therefore it is only preserved at low temperatures or lyophilized formulations. Thus, the design and synthesis of novel and hydrolytically stable structural analogues of MenA CPS is of paramount importance. The hydrolysis of the glycosidic linkage can be prevented by chemical modification of the glycosyl 1-O-phosphates moiety using sugar mimicry, where a methylene group replaces either the endo-cyclic oxygen atom at the pyranose ring[4] or the interglycosidic oxygen[5]. Since structure and function are intrinsically correlated in biomolecules, in order to identify the best candidate able to mimic the molecular behaviour of the natural counterpart, both in free solution and in the protein bound state, structural studies are required. The aim of this study has been to determine the three-dimensional structure of MenA capsular polysaccharide and its carba and C-glycosyl analogues using Molecular Modelling and NMR spectroscopic techniques[6,7]. We believe that the expected results will provide fundamental information in order to determine which analogue could better mimic the natural structural features and to achieve the stimulation of immune response in host-pathogen interactions.

---

[1]Rouphael, N. G.; and Stephens, D. S. *Method Mol. Biol.* **2012**, *799*, 1-20.
[2] Bundle, D. R.; Smith, I. C. and Jennings, H. J. Biol. Chem. 1974, 249, 2275-2281.
[3] Berti, F.; Romano, M. R.; Micoli, F.; Pinto, V.; Cappelletti, E.; Gavini, M.; Proietti, D.; Pluschke, G.; MacLennan, C. A.; and Costantino, P. *Vaccine* **2012**, *30*, 6409-6415.
[4] Gao, Q.; Tontini, M.; Brogioni, G.; Nilo, A.; Filippini, S.; Harfouche, C.; Polito, L.; Romano, M. R.; *ASC Chem. Biol.* **2013**, *8*, 2561-2567.
[5] Fallarini, S.; Buzzi, B.; Giovarruscio, S.; Polito, L.; Brogioni, G.; Tontini, M.; Berti, F.; Adamo, R.; Lay, L. and Lombardi G. *ASC Infect*. Dis. **2015**, *1*, 487-496.
[6] Asensio, J. L.; Cañada, F. J.; Cheng, K.; Khan, N.; Mootoo, D. R. and Jiménez-Barbero J. *Chem. Eur. J.* **2000**, *6*, 6.
[7] Wormald, M. R.; Petrescu, A. J.; Pao, Y. L.; Glithero, A.; Elliot, T. and Dwek R. A. *Chem. Rev.* 2002, 102, 371-386.

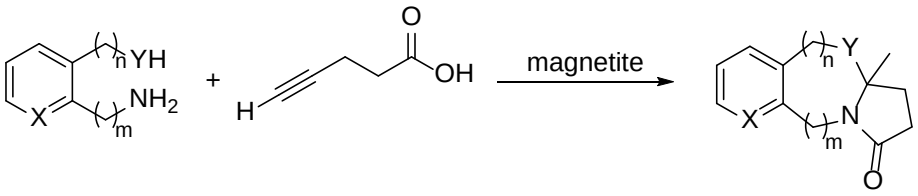
Poster-22

Catalytic activity of magnetic iron species in tandem reactions between pentynoic acid and dinucleophiles

María Teresa Herrero, Raul SanMartin, Esther Dominguez and Iker Jauregibeitia
Department of Organic Chemistry II, Faculty of Science and Technology, University of the Basque Country (UPV/EHU). Sarriena auzoa, z/g 48940 Leioa, Spain.
e-mail: raul.sanmartin@ehu.eus

The development of efficient catalyst systems is a priority in synthetic chemistry. In this regard, over the last years catalysts based on metals of the first row of periodic table have proven to be a valuable alternative to precious metals.[1] Among then, iron species are particularly attractive owing to their availability, price and low toxicity.[2]

In this context, we have recently discovered that Fe (II) and Fe (III) halides catalyze efficiently the formation of complex polyheterocycles *via* a cascade process from alkynoic acids and *ortho*-functionalized amides.[3] We decided to evaluate the activity of iron magnetic species as catalyst in aforementioned process and the possibility of their recycling by magnetic decantation. In this communication, we wish to report our most remarkable results on this matter.



Acknowledgments This research was supported by the Basque Government (IT-774-13), the Spanish Ministry of Economy and Competitiveness (CTQ2013-46970-P) and the University of the Basque Country (UFI QOSYC 11/12). Technical and human support provided by SGIker of UPV/EHU is gratefully acknowledged.

[1] See for example: a) Chakraborty, S.; Guan, H. *Dalton Trans.* **2010**, *39*, 7427; b) Lipschutz, M. I.; Tilley, T. D. Ang. Chem., Int. Ed. 2014, 53, 7290; b) Miao, J.; Ge, H. *Eur. J. Org. Chem.* **2015**, *36*, 7859; c) Sun, Y.; Tang, H.; Chen, K.; Hu, L.; Yao, J.; Shaik, S.; Chen, H. *J. Am. Chem. Soc.* **2016**, *138*, 3715.
[2] a) Bauer, E.B. *Curr. Org. Chem.* **2008**, *12*, 1341; b) Liu, L. X. *Curr. Org. Chem.* **2010**, *14*, 1099; c) Bolm, C. *Nat. Chem*. **2009**, *1*, 420.
[3] Díaz de Sarralde, J.; Herrero, M. T.; SanMartin, R.; Domínguez, E. *Patent Appl.* P201430635ES, *April 30, 2014.*

Poster-23

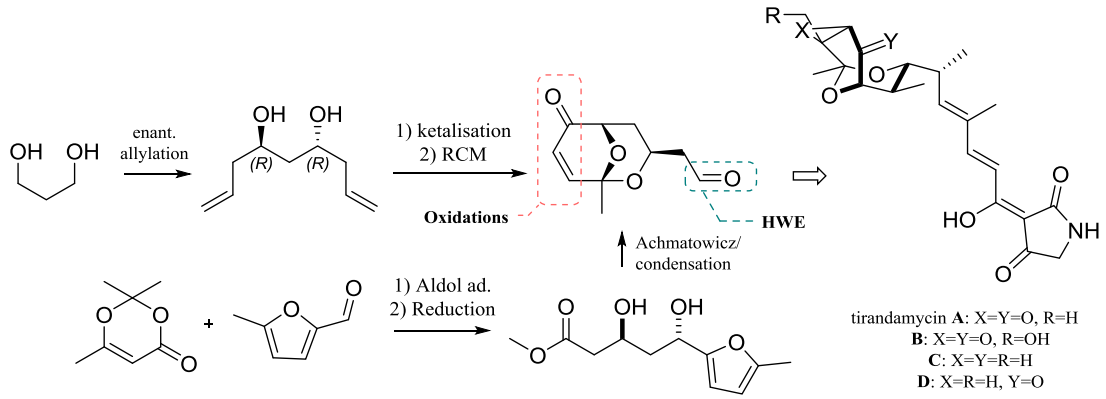
Synthesis of Truncated Tirandamycin A-D Derivatives as new Antihelminthic Agents

Tania Jiménez, Morten Grøtli and Carl J. Wallentin
Department of Chemistry and Molecular Biology, University of Göteborg
SE-412 96, Sweden
e-mail: tania.jimenez@chem.gu.se

Lymphatic filariasis (LF) caused by the parasitic nematodes *B. malayi*, represents a worldwide health crisis with over 200 million people infected and another 20% of the global population at risk for infection.[1] Thus, a top priority of the WHO is to search for new antihelminthic drugs that kill adult parasites, have new mechanisms of action and exhibit fewer side effects than the current medications available

Tirandamycins A-D (TAMs A-D) derivatives have attracted much attention as potential antihelminthic agents for the treatment of LF,[2] as they inhibit asparagyl-tRNA synthase (AsnRS), an excellent filarial target for *B. malayi*.[3] Due to their pharmacological properties and their intriguing molecular architectures, a handful of total syntheses have been documented in the literature.[4] However, common for all these achievements are lengthy synthetic routs not amenable late stage derivatization and thus, they are not applicable to drug development programs.

Two different synthetic protocols that are able to produce advanced intermediates in 2–3 steps have been pursued, providing a short, robust and scalable route to access key intermediates suitable for library synthesis.



[1] WHO: Lymphatic Filariasis: Reasons for Hope, ed. J. Dzenowagis, World Health Organization, Geneva, 1997.
[2] (a) Z. Yu, S. Vodanovic-Jankovic, N. Ledeboer, S.-X. Huang, S. R. Rajski, M. Kron and B. Shen, *Org. Lett.*, **2011**, *13*, 2034; (b) M. E. Rateb, Z. Yu, Y. Yan, D. Yang, T. Huang, S. Vodanovic- Jankovic, M. A. Kron and B. Shen, *J. Antibiot.*, **2014**, *67*, 127.
[3] M. Kron, K. Marquard, M. Härtlein, S. Price, R. Leberman. *FEBS Lett.* **1995**, *374*, 122.
[4] (a) R. H. Schlessinger, G. R. Bebernitz, P. Lin and A. J. Poss, *J. Am. Chem. Soc*., **1985**, *107*, 1777; (b) P. DeShong, S. Ramesh, V. Elango and J. Perez, *J. Am. Chem. Soc*., **1985**, *107*, 5219; (c) S. Danishefsky and D. F. Harvey, *J. Am. Chem. Soc*., **1985**, *107*, 6647; (d) S. J. Shimshock, R. E.Waltermire and P. DeShong, *J. Am. Chem. Soc*., **1991**, *113*, 8791; (e) M. Chen and W. R. Roush, *Org. Lett.*, **2012**, *14*, 426; (f) H. Yoshimura, K. Takahashi, J. Ishiharaa and S. Hatakeyama, *Chem. Commun.*, **2015**, *51*, 17004.

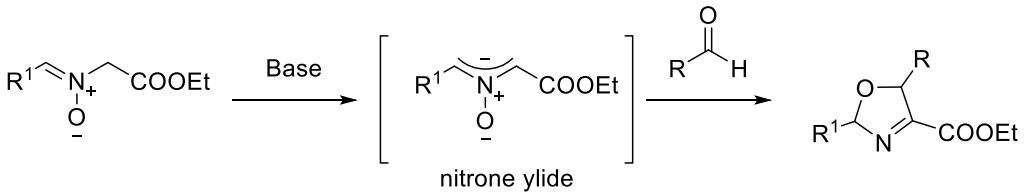
Poster-24

Lithium-Catalyzed Totally Stereoselective Synthesis of 2-Alkyl-3-Oxazolines

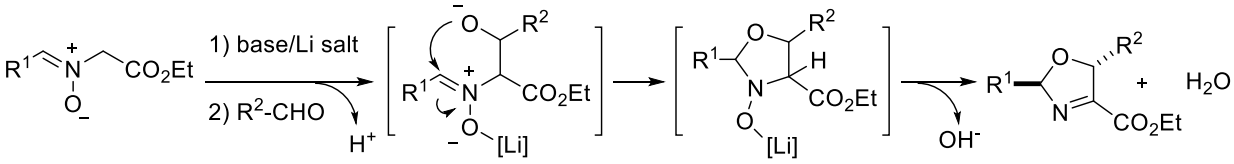
I. Delso, T. Tejero, P. Merino and V. Juste-Navarro
Departamento de Síntesis y Estructura de Biomoléculas, Instituto de Síntesis Química y Catálisis Homogénea (CSIC- Universidad de Zaragoza), C/ Pedro Cerbuna 12, 50009, Zaragoza.
e-mail: vjuste@unizar.es

In contrast to the well-established methods for accessing 2-oxazolines, the preparation of isomeric 3-oxazolines (2,5-dihydrooxazoles) have received far less attention.[1] The scarce methods reported for the synthesis of 3-oxazolines include ring-opening of 2H-aziridines followed by trapping with aldehydes, oxidation of 1,3-oxazolidines and Boyer reaction between aliphatic aldehydes and azido- or aminoalcohols.

In continuation with our work on the reactions of nitrone ylides with electrophiles[2] we have investigated the reaction with aldehydes which provides 3-oxazolines in a stereoselective way.



The process involves an initial nucleophilic attack to the aldehyde followed by intramolecular oxygen addiction to the nitrone moiety and lithium-assisted elimination of water regenerating the lithium ion which actually is the catalytic specie.



Various Li-based catalytic systems are possible and the self-regenerated water is required for continuing the catalytic cycle. Experimental, spectroscopic and computational mechanistic studies have provided evidences of the lithium ion catalysis and allowed rationalizing the several competing catalytic processes.

[1] Yeh, V.; Iyengar, R. *Oxazoles, Vol. 4* Eds.: A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor, Elsevier, Oxford, **2008**, pp. 487-543.

[2] (a) Merino, P.; Tejero, T.; Diez-Martinez, A.; Gultekin, Z. *Eur. J. Org. Chem.* **2011**, 6567-6573. (b) Merino, P.; Tejero, T.; Diez Martinez, A. *J. Org. Chem.* **2014**, *79*, 2189-2202.

Poster-25

Enantioselective synthesis of polysubstituted conformationally restricted spiro-nitroprolinates mediated by a (*R*,*R*)-Me-DuPhos·AgF-catalyzed 1,3-dipolar cycloaddition

Alberto Cayuelas,† Carmen Nájera,† Ricardo Ortiz,† José M. Sansano,† Abel de Cózar,‡◊ Fernando P. Cossío‡ and Olatz Larrañaga‡

‡*Department of Organic Chemistry I, University of the Basque Country, 20018 San Sebastián-Donostia (Spain),* †*Department of Organic Chemistry, University of Alicante, 03080 Alicante (Spain),* ◊*IKERBASQUE, Basque Foundation for Science, 48013 Bilbao (Spain).*
e-mail: olatz.larranaga@ehu.es

The importance of having a wide number of enantiomerically enriched sterically congested polysubstituted organic compounds is continuously increasing. In this communication, the origins of the enantioselective synthesis of constrained spirocycles stemming from 1,3-dipolar cycloaddition between α–imino γ–lactones **7** and nitroalkenes **8** catalyzed by (R,R)-Me-DuPhos **18** and AgF will be discussed (Figure 1A).[1] For this purpose, we have performed DFT calculations at M06(PCM)/6-31G*&LanL2DZ//B3LYP(PCM)/6-31G*&LanL2DZ level of theory in order to shed light on the high diastereo- and enantioselections (Figure 1B).

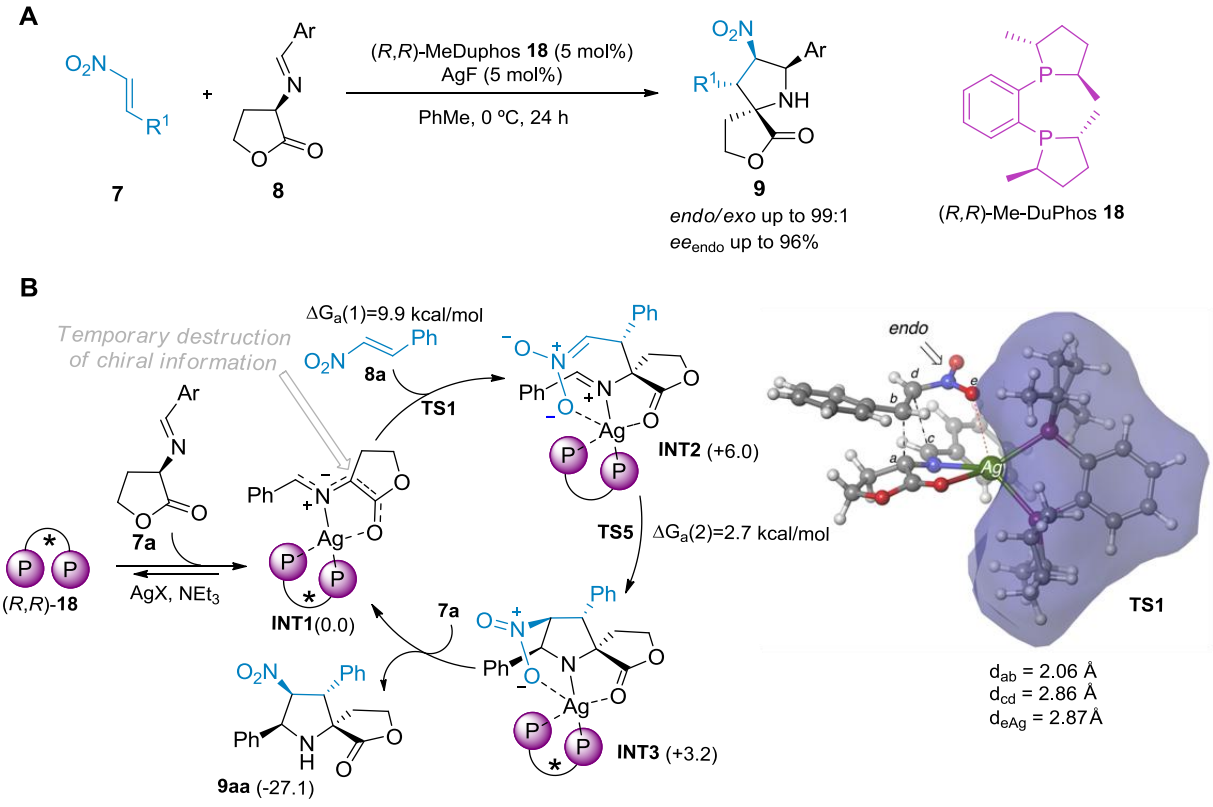


Figure 1. (A) General scheme of the reaction under study. (B) Relative energies (in kcal/mol) of the profile associated with the reaction between nitroalkene **8a** and ylide **INT1** to yield **9aa** and the geometrical feature of the least energetic transition structure **TS1**.

[1]Cayuelas, A.; Nájera, C.; Ortiz, R.; Sansano, J. M.; Larrañaga, O.; de Cózar, A.; Cossío, F. P. *Org. Lett.* **2016** (DOI: 10.1021/acs.orglett.6b01273).

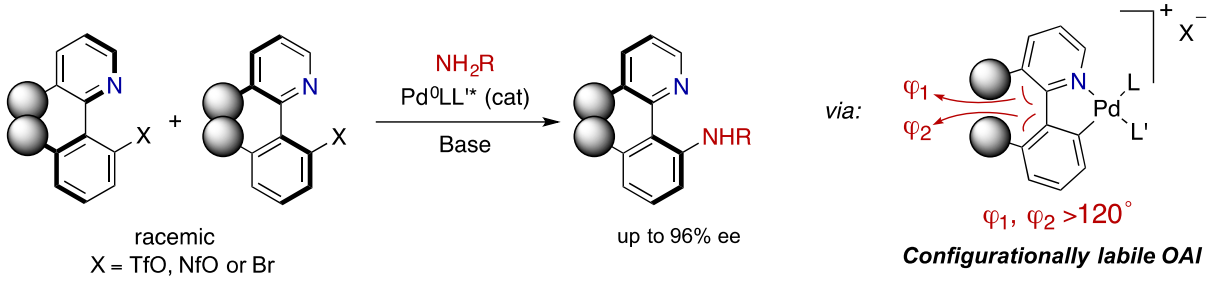
Poster-26

Dynamic Kinetic Asymmetric Buchwald–Hartwig Approach for the Synthesis of Heterobiaryl Amines

Antonio Romero-Arenas, Pedro Ramírez-López, Abel Ros, Javier Iglesias-Sigüenza, Rosario Fernández and José M. Lassaletta
Instituto Investigaciones Químicas (CSIC-US)
e-mail: jmlassa@iiq.csic.es

IAN-amines (amines derived from ***I***soquinoline and 2-***A***mino ***N***aphthalene), are a family of axially chiral heterobiaryls with a great potencial in catalyst design (N-ligands and bifunctional organocatalysts). However, their applications have not been developed significantly due to the lack of a general, reliable procedure for their asymmetric synthesis.[1]

In this communication, we wish to report on the development of a dynamic kinetic asymmetric (DYKAT) Buchwald-Hartwig methodology for the enantioselective synthesis of IAN- and related heterobiaryl amines from racemic heterobiaryl electrophiles. The strategy, previous developed in our research group for the synthesis of axially chiral heterobiaryls *via* C–C (Suzuki)[2] and C–P bonb forming reactions,[3] relies on the formation of cationic, cyclic oxidative addition intermediate which allows the labilization of the chiral axis due to a widening of the angles φ_1 and φ_2 involved in its configurational stability. In this way, we have accomplished the synthesis of several families of IAN-type amines with high yields and excellent enantioselectivities (up to 96%).



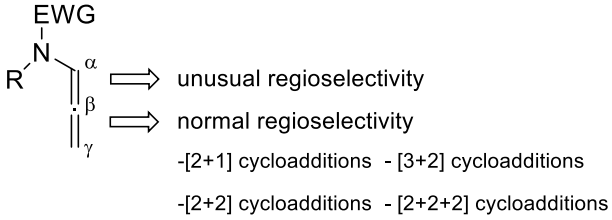
1. Luesse, S. B.; Counceller, C. M.; Wilt, J. C.; Perkins, B. R.; Johnston, J. N. *Org. Lett.* **2008**, *12*, 2445.
2. Ros, A.; Estepa, B.; Ramírez-López, P.; Álvarez, E.; Fernández, R.; Lassaletta, J.M. *J. Am. Chem. Soc.* **2013**, 135, 15730
3. Ramírez-López, P.; Ros, A.; Estepa, B.; Fernández, R.; Fiser, B.; Gómez-Bengoa, E.; Lassaletta, J.M. *ACS Catal.* **2016**, *6*, 3955.

Poster-27

Gold Catalyzed [3+2] Cycloaddition Reaction of Vinyldiazo Compounds and N-Allenamides

Enol López and Luis A. López
Departamento de Química Orgánica e Inorgánica, Universidad de Oviedo, c/ Julián Clavería, 8, 33006, Oviedo, Spain.
E-mail: uo215264@uniovi.es

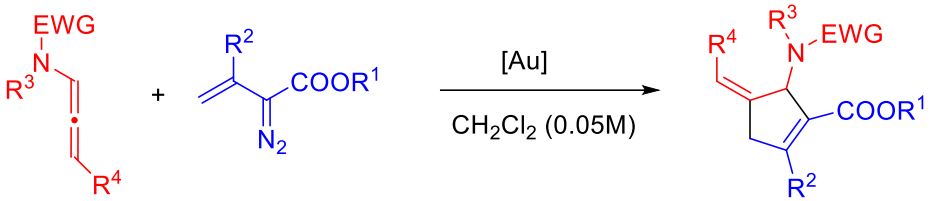
Many selective transition metal-catalyzed cycloaddition reactions of N-allenamides have been reported in the last decades.[1] However, gold complexes have only recently been recognized as useful catalysts in this type of transformations. Whereas the participation of the terminal bond represents the most common regioselectivity pattern,[2] the involvement of the C_α=C_β bond is extremely unusual in gold-catalyzed cycloaddition reactions of this type of allenic scaffolds (Scheme 1).



Scheme 1. Regioselectivity patterns in Gold Catalyzed [n+2] cycloadditions.

On the other hand, metal catalyzed transformations of stabilized vinyldiazo derivatives have received in the last years great attention. However, to the best of our knowledge, the cycloaddition reaction between vinyldiazo compounds and allene derivatives remains unexplored. In this regard, we thought that the recent introduction of gold-catalysts as efficient catalysts in transformations involving vinyldiazo compounds could pave the way for a successful coupling with N-allenamides.

In this communication, we report the gold-catalyzed [3+2] cycloaddition of vinyldiazo compounds and allenamides (Scheme 2).[3]



Scheme 2.Gold catalyzed [3+2] cicloaddition of vinyl diazo derivatives and allenamides.

$_\alpha$=C_β bond represents, as stated before, an infrequent regioselectivity pattern in gold-catalyzed cycloadditions involving allenamides. From a mechanistic point of view, these results are consistent with the initial activation of the diazo reagent. This hypothesis has been supported by a computational study.

[1] Yu. S., Ma, S., *Angew. Chem. Int. Ed*. **2012**, 51, 3074.
[2] See for example, Suárez-Pantiga, S., Hernández-Díaz, C., Rubio, E., González, J. M., *Angew. Chem. Int. Ed.*, **2012**, 51, 11552.
[3] López, E., González, J., López, L.A. *Adv. Synth. Cat.*, **2016**, *358*, 1428.

Poster-28

Spiroisoxazolidines: Promising Scaffolds for Anticancer Agents through Protein/non-Peptide Small-Molecule Interactions

Antonio De Nino,[a] Vincenzo Algieri,[a] Beatrice Russo,[a] Monica Nardi,[a] Pedro Merino,[b] Ignacio Delso[b] and Loredana Maiuolo[a]

[a] *LabOrSy - Department of Chemistry and chemical technologies, University of Calabria, Cubo 12C, Via P. Bucci - 87036 Rende (CS) - Italy*

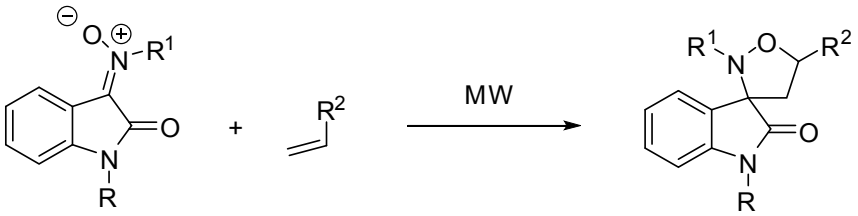
[b] *Laboratorio de Síntesis Asimétrica, Departamento de Química Orgánica, Facultad de Ciencias. Edificio D. Planta 3, Universidad de Zaragoza, Campus San Francisco - 50009 Zaragoza, Aragon - Spain*

e-mail: maiuolo@unical.it

Spiro compounds have always been prevalent in organic synthesis due to the pronounced biological activities. In particular, the spirooxindoles have emerged as attractive synthetic targets. These spirooxindoles seem to be promising candidates for drug discovery, since they incorporate simultaneously oxindoles and other heterocyclic moieties.[1] p53 is the tumor suppressor protein that has been the most intensively studied for nearly 30 years. Infact, the p53 is a transcriptional factor that plays a key role in regulation of several cellular processes, including the cell cycle, apoptosis, DNA repair, and angiogenesis. The murine double minute 2 (MDM2) protein is the primary cellular inhibitor of p53, functioning through direct interaction with p53.[2] Design of non-peptide, small-molecule inhibitors that block the MDM2-p53 interaction has been sought as an attractive strategy to activate p53 for the treatment of cancer and other human diseases.

The 1,3-dipolar cycloaddition reactions represent the favorite method for the construction of five-membered heterocycles, important frameworks of various natural products. In particular, the 1,3-dipolar cycloadditions of nitrones with alkenes afforded isoxazolidines, which are interesting intermediates for the synthesis of β-amino alcohols and alkaloids or, more recently, of cyclic and bicyclic 4'-aza-analogues of 2',3'-dideoxynucleosides, isoxazolidinyl nucleosides with antiviral or anticancer activity.[3]

In the present work, the synthesis of spiro-compounds containing both indole and isoxazolidine rings will be illustrated. The synthesis was realized by microwave-assisted 1,3 dipolar cycloaddition between opportune nitrones of indole derivatives and vinyl-substrates. The choice of the substrates and substituents and the study of trend of reactions were supported by docking and computational calculations.



1. Yu, B.; Yu, D-Q; Liu, H-M. *European Journal of Medicinal Chemistry*, **2015**, *97*, 673−698.

2. Wang, S.; Zhao, Y.; Bernard, D.; Aguilar, A.; Kumar, S. *Top Med Chem*, **2012**, *8*, 57–80.

3. a) Bortolini, O.; De Nino, A.; Eliseo, T.; Gavioli, R.; Maiuolo, L.; Russo, B.; Sforza, F. *Bioorg. Med. Chem.*, **2010**, 18, 6970-6976; b) Maiuolo, L.; Bortolini, O.; De Nino, A.; Russo, B.; Gavioli, R.; Sforza, F. *Australian Journal of Chemistry*, **2014**, 67, 670-674

Poster-29

Iron(III) catalyzed synthesis of Δ^4 2,7-disubstituted oxepenes

Daniel A. Cruz,[1] Juan I. Padrón[1,2] and Víctor S. Martín[1]

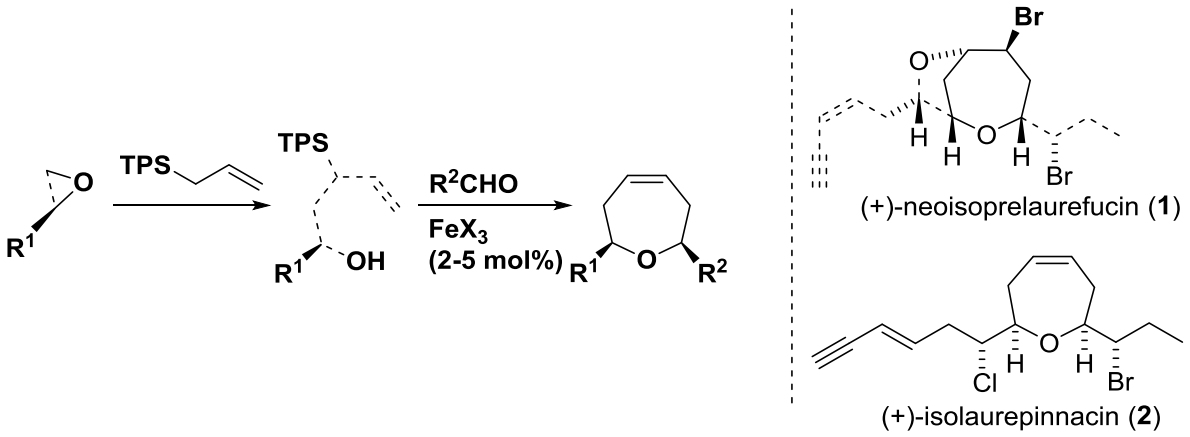
[1] *Instituto Universitario de Bio-Orgánica "Antonio González" (CIBICAN), Departamento de Química Orgánica, Universidad de La Laguna, Francisco Sánchez 2, 38206 La Laguna, Tenerife, Spain*

[2] *Instituto de Productos Naturales y Agrobiología, Consejo Superior de Investigaciones Científicas, La Laguna, Avda. Astrofísico Francisco Sánchez 3, 38206 La Laguna, Tenerife, Spain.*

vmartin@ull.es

Medium size oxacycles are structural motifs present in a wide range of marine natural products.[1] Unsaturated seven member oxacycles (oxepenes) represent a main goal due to their biological relevance, as well as important synthetic targets.

Oxepenes have been synthesized using different methodologies but none of them through direct Prins cyclization.[2]



Scheme 1. Synthesis of Δ^4 2,7-disubstituted oxepenes.

In this work, we will present the syntheses of 2,7-disubstituted oxepenes in one step, with good diastereomeric ratio, through direct Prins cyclization with Fe(III) salts as a sustainable metal catalyst. This methodology is the key step in our approach to the total synthesis of (1) and (2) (Scheme 1).

Acknowledgments: We thank the Spanish MINECO, co-financed by the European Regional Development Fund (ERDF), CTQ2014-56362-C2-1-P for financial support. D. A. C. thanks MINECO for a FPI fellowship.

[1] Kadota, I.; Yamamoto, Y. *Acc. Chem. Res.* **2005**, *38*, 423-432.
[2] Berger, D.; Overman, L. E.; Renhowe, P. A. *J. Am. Chem. Soc*. **1997**, *119*, 2446-2452.

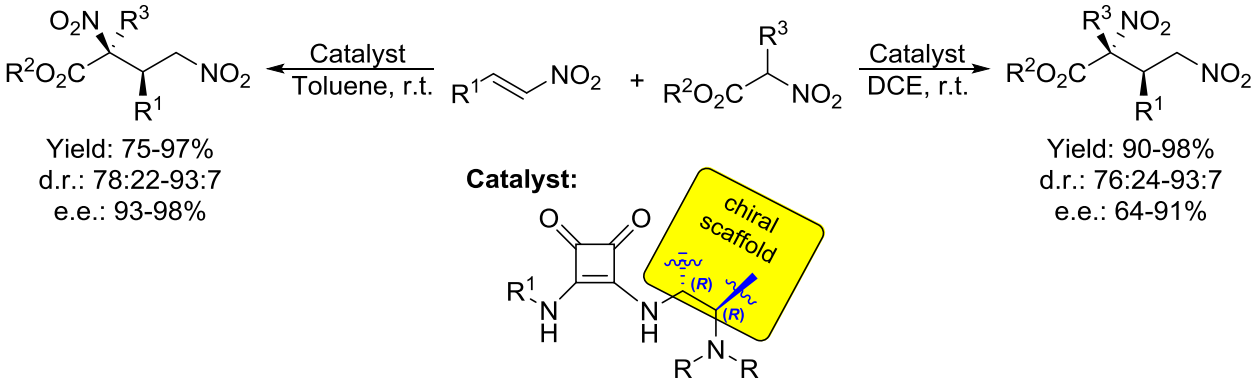
Poster-30

Organocatalytic Diastereodivergent Enantioselective Michael Additions Using Stereodirecting Elements with the Same Absolute Chirality.

Jose I. Martínez, María Muñiz Uxue Uria, Efraím Reyes, Luisa Carrillo and Jose L. Vicario.
Química Orgánica II, UPV / EHU, Bº Sarriena s/n
e-mail: joseignacio.martinezf@ehu.eus

The consecution of enantioenriched molecules is an issue of great interest for synthetic chemists and in this field asymmetric catalysis has shown a excellent efficiency. Generally, to accomplish the separate synthesis of opposite enantiomers of a molecule mirror images of the catalytic species are employed. However, the generation of multiple stereocentres in one reaction step shows up as a big challenge to selectively modulate not only the enantioselectivity but also the diastereoselectivity along the reaction process.

In this context, we have recently reported a catalytic and enantioselective diastereodivergent synthesis of densely functionalized cycloalkanes via Michael/Henry cascade reaction. It was demonstrated that the stereoselectivity was induced in the first Michael step under catalyst control whereas the second Hernry step occurred under substrate control. Noteworthy, the diastereoselectivity could be inverted using organocatalysts with the same absolute stereochemistry. [1] Herein we report a thorough study of the first Michael key step applying this methodology towards the promotion of the diasterodivergent and enantioselective addition of α-nitroesters to β-nitrostyrenes using the same catalytic system (Figure 1).[2]



Acknowledgements: Authors thank the Spanish MINECO (FEDER CTQ2014-52107-P), the Basque Government (IT328-10 and postdoctoral fellowship to J. I. M) and UPV/EHU (UFI QOSYC 11/22 and EHUA1524) for financial support. Membership in the COST action CM1407 (NatChemDrugs) is also acknowledged.

[1] Martínez, J. I.; Villar L.; Uria, U.; Carrillo, L.; Reyes, E.; Vicario J. L. *Adv. Synth. Catal.*, **2014**, *356*, 3627.
[2] Martínez, J. I.; Uria, U.; Muñiz, M.; Carrillo, L.; Reyes, E.; Vicario J. L. *Beilstein J. Org. Chem.*, **2015**, 2577.

Poster-31

Zinc-catalyzed multicomponent reactions; Straightforward synthesis of functionalized furan derivatives

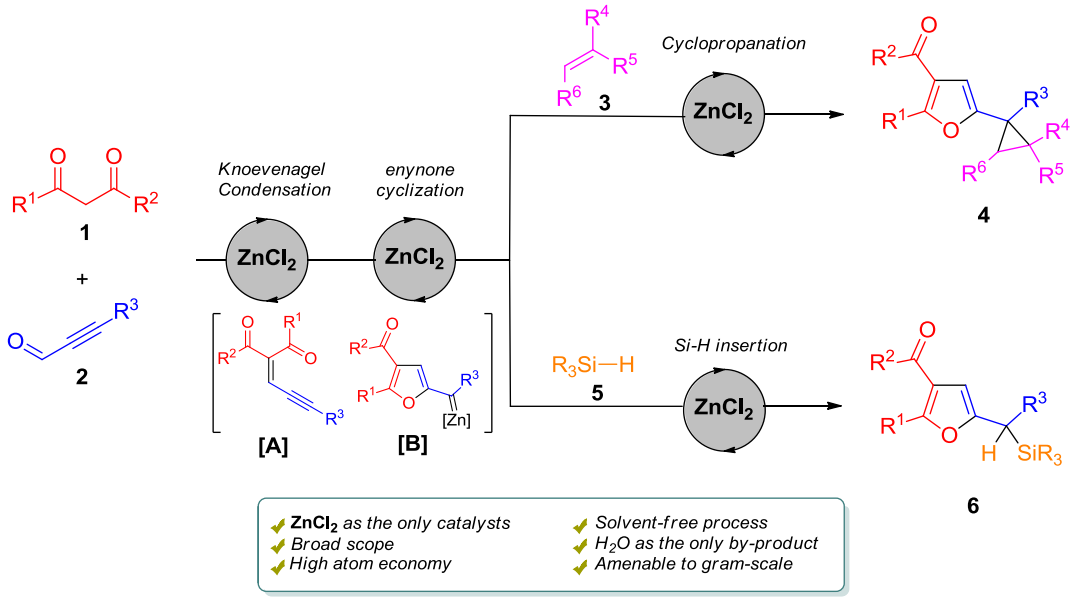
S. Mata, R. Vicente, L. A. López

Department of Organic and Inorganic Chemistry, University of Oviedo, c/ Julián Clavería 8, 33006-Oviedo

uo215315@uniovi.es

Nowadays, the replacement of noble transition metals (scarce, expensive and toxic) by abundant and low toxic first-row transition metals represents an active research field. Besides, multicomponent reactions have become very popular in recent years due to these protocols offer clear advantages over traditional stepwise methodologies.

In the last few years our group has pursued the development of sustainable synthetic methodologies based on the use of simple salts as catalysts. In this context, we reported the zinc-catalyzed three-component synthesis of functionalized furan derivatives. Thus, the reaction of 1,3-dicarbonylic compounds **1**, alkynals **2** and alkenes **3** represents a convenient methodology for the synthesis of cyclopropyl-substituted furan derivatives **4**.[1] On the other hand, the replacement of alkene components by silanes **5** led to the formation of silyl-substituted furan derivatives **6**.[2]



A sequence consisting of an initial Knoevenagel condensation of **1** and **2** forms intermediate enynone [**A**]. Then a 5-exo-dig cyclization takes place to give rise to 2-furyl-zinc (II)-carbene intermediate [**B**]. A final cyclopropanation or insertion into the Si_H bond would account for the formation of the products **4** and **6** respectively.

[1] S. Mata, J. González, R. Vicente, L. A. López, *Eur. J. Org. Chem.* **2016** (DOI: 10.1002/ejoc.201600393)
[2] S. Mata, L. A. López, R. Vicente, *Chem. Eur. J.* **2015**, *21*, 8998.

Poster-32

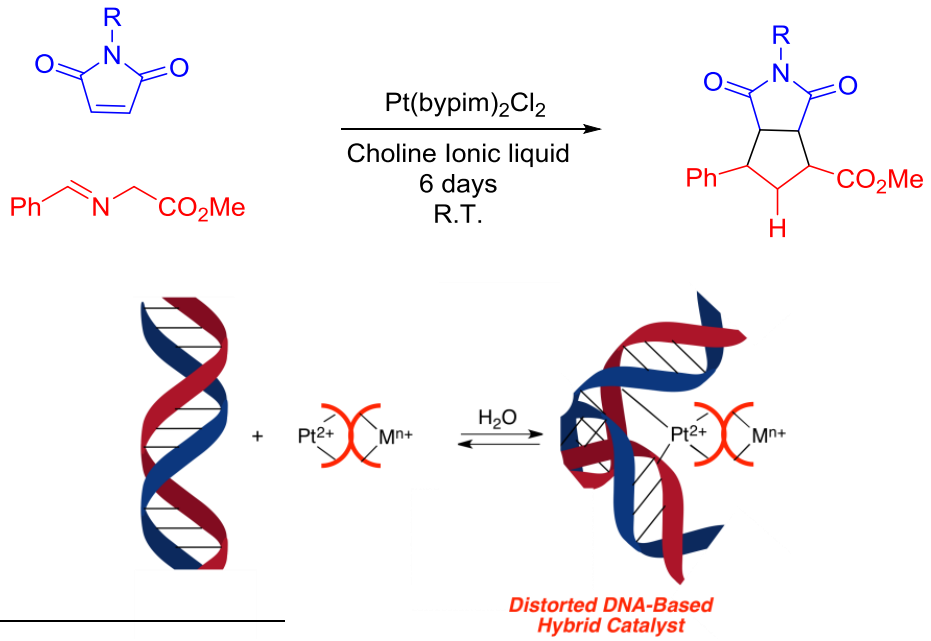
Evaluation of a DNA-Pt(II) complex as catalyst in [3+2] cycloadditions in ionic liquid media

Ivan Rivilla,[1] Thomas Schäfer,[2] Fernando P. Cossío,[1] and Sara Mchichou.[1]
[1]*Departamento de Química Orgánica, Facultad de Química, Universidad del País Vasco-Euskal Herriko Unibertsitatea, Pº Manuel Lardizabal 3, 20018, San Sebastián-Donostia and Donostia International Physics Center (DIPC) P.O. Box 1072, 20018 San Sebastián-Donostia*
[2]*POLYMAT, Universidad del País Vasco-Euskal Herriko Unibertsitatea, Centro Joxe Mari Korta, Av. Tolosa 72. 20018, San Sebastián-Donostia.*
smchichou001@ikasle.ehu.eus

DNA has emerged as a versatile scaffold for synthesis and catalysis being the inspiration for a new class of bio-organometallic catalysts possessing an organometallic moiety.[1] These compounds should combine the catalytic activity of transition metals with the well-defined architecture of DNA.

Platinum(II) complexes can interact with DNA, thus distorting the helical structure. We thought the Pt(II) complex containing heterocycles could tie Guanosine(G) residues present in the DNA resulting in a concave/convex shape.[2]

In the last years, our group has tested the catalytic activity of Pt(II)-DNA complex in [3+2] cycloadditions reactions in aqueous media. In order to explore new reactivity we performed previous experiment in ionic liquid. The hybrid catalysis aims to combine the catalytic power of transition metal catalysis with the chiral architectures of DNA, with the ultimate goal of creating new catalysts.



[1] Boersma, A.J.; Megens, R.P.; Feringa, B.L.; Roelfes, G.; *Chem. Soc. Rev.*, **2010**, *39*, 2083-2092.
[2] Fichtinger-Schepman, A. M.J.; van der Veer, J.L.; den Hartog, J.H.J.; Lohman, P.H.M.; Reedijk, J.; *Biochemistry*, **1985**, *24*, 707-713.

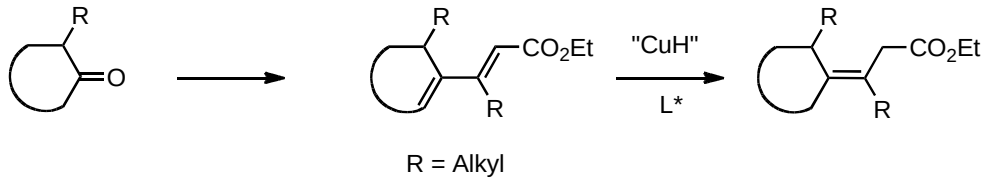
Poster-33

Studies on the Catalytic and Stereoselective Reduction of α,β,γ,δ-Unsaturated Esters to Tetrasubstituted Olefins

Silvia Vinhas,[2] Rita Sigüeiro,[1] Patricia González, [1]J. Enrique Borges,[2]Antonio Mouriño[1]
[1]*Department of Organic Chemistry, University of Santiago, Avda Ciencias s/n, 15782 Santiago de Compostela, Spain and* [2]*Department of Chemistry and Biochemistry, UCIBIO/ REQUIMTE, Rua do Campo Alegre 687, 4169-007 Porto, Portugal*
e-mail: antoniol.mourino@usc.es; jrborges@fc.up.pt

The tetrasubstituted olefin moieties can be found in a wide range of biologically active natural products and pharmaceutical drugs and have also been used as building block precursors of other functionalities. Interestingly, the congested nature of the double bond has made the synthesis of tetrasubstituted olefins a formidable challenge over the last decades. While the classical Wittig reaction and variants have found important applications in the stereoselective formation of mono- and disubstituted alkenes from aldehydes, these reactions offer poor stereoselectivity or low reactivity when applied to the synthesis of tetrasubstituted alkenes from ketones. Despite the recent developments of promising synthetic strategies to tetrasubstituted olefins such as carbometallation of alkynes and palladium-catalyzed cross coupling processes, new stereoselective and efficient strategies are still needed. [1]

We describe here our initial results on the development of stereoselective synthetic strategies to (*Z*)-tetrasubstituted functionalized olefins from ketones, where the key step is a catalytic reduction of an α,β,γ,δ-unsaturated ester.[1,2]



R = Alkyl

References and Notes

1. For a review, see: Flynn, A. B.; Ogilvie, W. W. *Chem. Rev*. **2007**, *107*, 4698-4745.

Poster-34

Synthesis of nitrostyrenes and benzonitriles from styrenes: oxidative cleavage of the double bond in ionic liquids

Michele Casiello,[1] Angelo Notarangelo,[1] Wojtek Sikorsky,[3] Caterina Fusco,[2] Leonarda Bellebuono,[1] Pietro Cotugno,[1] Antonio Monopoli,[1] Francesco Ciminale[1] and Angelo Nacci[1,2]

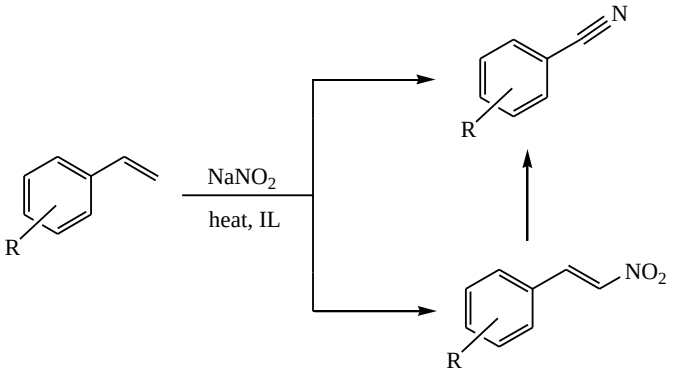
[1] *Dept. of Chemistry, University of Bari "Aldo Moro", Via Orabona, 4, 70126 Bari, Italy, michele.casiello@uniba.it*
[2] *CNR – ICCOM, Dept of Chemistry, University of Bari "Aldo Moro", Via Orabona, 4, 70126 Bari – Italy*
[3] *University of Wrocław, Faculty of Chemistry, 14 F. Joliot-Curie, 50-383 Wrocław, Poland*
e-mail: angelo.nacci@uniba.it

Nitrile functional group occurs in natural products of diverse plants and animals and is found in many useful compounds such as dyes, pharmaceuticals, agrochemicals and polymers (i.e. methyl cyanoacrylate – used in super glue – and nitrile rubber).[1] Particularly, benzonitriles are key synthetic intermediates useful for generating many other functional groups on the aromatic ring such as amines, amides, aldehydes and heterocyclic compounds.[2]

Many methodologies have been reported to prepare these compounds such as Sandmeyer and Rosenmund reactions,[3] as well as dehydration of amines, alcohols or oximes.[4]

Recently, the oxidative cleavage of double bond of styrenes is gaining interest as an alternative route of access to aromatic nitriles. However, this latter strategy suffers from the drawbacks of requiring harsh reaction conditions, multiple steps, metal oxidants and/or large stoichiometric excess of reactants.[5]

In our continuing efforts aimed at developing sustainable chemical processes, we discovered a simple method for converting directly styrenes into benzonitriles under metal free and mild conditions. The oxidative cleavage can be simply accomplished by heating styrenes with sodium nitrite in molten tetraalkylammonium salts as ionic liquid media.
Protocol proves to be flexible allowing also the preparation of β-nitrostyrenes, intermediates of the oxidative cleavage, by modulating reaction conditions.[6]



1 M. B. Smith and J. March, March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Wiley, Hoboken, NJ, 6th edn, 2007.
2 Zong, X.; Zheng, Q-Z; Jiao, N. *Org. Biomol. Chem.*, **2014**, *12*, 1198.
3 A. J. Fatiadi, Preparation and synthetic applications of cyano compounds, Wiley, New York, 1983
4. Oischi, T.; Yamaguchi, K.; Mizuno, N.; *Angew. Chem., Int. Ed.*, **2009**, *48*, 6286.
5. a) Gong, T.-J.; Xiao, B.; Cheng, W.-M.; Su, W.; Xu, J.; Liu, Z.-J.; Liu L.; Fu, Y. *J. Am. Chem. Soc.*, **2013**, *135*, 10630; b) Xu, J. H., Jiang, Q.; Guo, C. C. *J. Org. Chem.*, **2013**, *78*, 11881.
6. Bui, T.; Syed, S.; Barbas, C. F. *J. Am. Chem. Soc.*, **2009**, *131*, 8758.

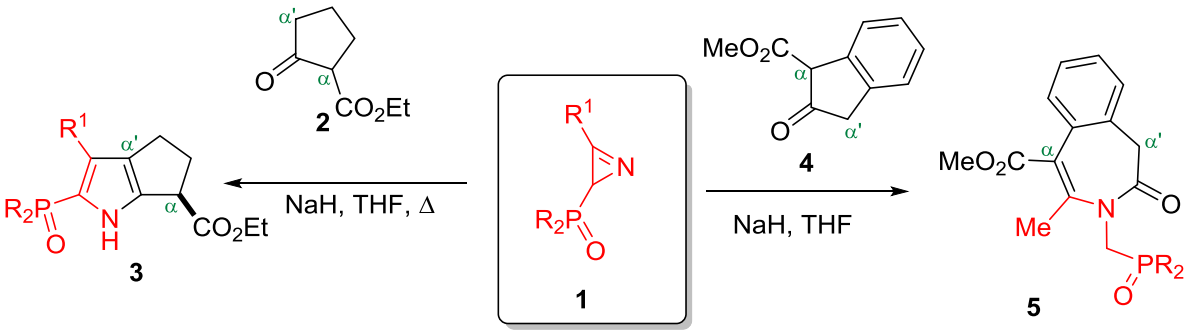
Poster-35

Reaction of 2*H*-Azirine-Phosphine Oxides and-Phosphonates with Cyclic Enolates Derived from Alkyl 2-oxo-cyclopentanecarboxylate

Francisco Palacios, Ander Velez del Burgo, Jesús M. de los Santos,
Edorta Martinez de Marigorta, Ana M. Ochoa de Retana
Department of Organic Chemistry I, Faculty of Pharmacy, Center for Research and Advanced Studies "Lucio Lascaray", University of the Basque Country, Paseo de la Universidad nº 7, 01006, Vitoria-Gasteiz, Spain.
e-mail: anamaria.ochoaderetana@ehu.es

2*H*-Azirine ring systems represent an important class of compounds because of their high reactivity and because they can be used as key intermediates in organic synthesis in the preparation of heterocycles and acyclic functionalized amino derivatives.

Following our studies on the synthetic applications of this heterocycles, here we disclose a simple convenient strategy for the selective synthesis of bicyclic cyclopenta[*b*]-pyrroles **3** containing a phosphine oxide or a phosphonate group in 2-position by addition of enolates derived from a cyclic *β*-keto ester **2** to 2*H*-azirine-phosphine oxide **1a** or -phosphonate **1b,** in the presence of NaH in refluxing THF. Also, the addition of enolates derived from indenone-carboxylate **4** to azirines **1** with base (NaH) leds to the formation of functionalized 1*H*-benzo[*d*]azepines **5**.[1]



Acknowledgements: The authors thank the Dirección General de Investigación del Ministerio de Ciencia e Innovación (MCINN, Madrid DGI, CTQ2015-67871-R) and the Universidad del País Vasco - Departamento de Educación Universidades e Investigación of Gobierno Vasco (GV, IT 992-16; UPV/EHU UFI QOSYC 11/12) for supporting this work. A. Vélez del Burgo thanks the Ministerio de Educación (Madrid) for a predoctoral fellowship. We also thank SGIker technical support for NMR spectra (MICINN, GV/EJ, and European Social Found).

1. (a) Palacios F., Ochoa de Retana A. M. and Velez del Burgo A. *J. Org. Chem*. **2011**, *76 (22), 9472–* .(b) Velez del Burgo A, Ochoa de Retana A. M., de los Santos Jesús M. and Palacios F. *J. Org. Chem*. **2016**, *81, 100–108.*

Poster-36

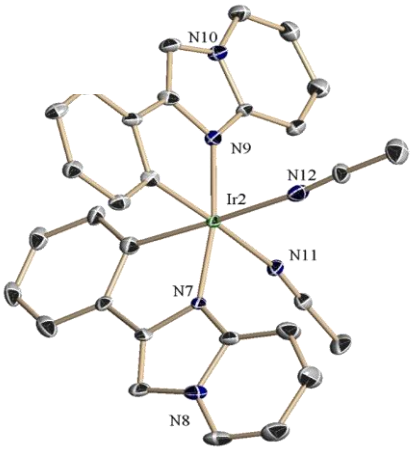
New Iridium complexes: a new scope of thermal and photoredox reactions

Odriozola-Gimeno, M.,[*] Rivilla, I.,[*] Torrent-Sucarrat, M,[*,#] Cossio, F. P.[*]

[*]*Departamento de Química Orgánica I, University of the Basque Country (UPV/EHU), Centro de Innovación en Química Avanzada (ORFEO−CINQA) and Donostia International Physics Center (DIPC),* [#] *Ikerbasque, Basque Foundation for Science, Mª Díaz de Haro 3, E-48013 Bilbao, Spain*
mikel.odriozola@ehu.es

In the last decades, transition metal catalysts have caused a revolutionary change in organic synthesis. Additionally, iridium and ruthenium complexes have emerged as a powerful photocatalysts, due to the possibility of being excited by visible light and to promote single electron transfer processes generating radicals. This novel approach allows the access to currently unknown or inaccessible mechanistic pathways.[1]

In our group, we have experiences in the synthesis of imidazo[1,2-a]pyridines and imidazo[1,2-a]pyrimidines, which can be used to synthesize new iridium complexes.[2] In this work, we present a new set of thermal and photocatalytic reactions in presence of our novel complex and fac-Ir(ppy)$_3$. Furthermore, computational calculations were performed so as to bring some insight to the reaction mechanism.



[1] (a) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C.; *Chem. Rev*. **2013**, *113*, 5322; (b) Zuo, Z.; Ahneman, T. D.; Chu, L.; Terret, J. A.; Doyle, A. G.; MacMillan, D. W. C. *Science* **2014**, *345*, 437; (c) Jin, J.; MacMillan, D. W. C. *Nature* **2015**, *525*, 87; (d) Terrett, J. A.; Cuthbertson, J. D.; Shurtleff, V. W.; MacMillan, D. W. C. *Nature* **2015**, *524*, 330; (e) Wang, C.; Qin, J.; Shen, X.; Riedel, R.; Harms, K.; Meggers, E. *Angew. Chem. Int. Ed*. **2016**, *55*, 685.
[2] Aginagalde, M.; Vara, Y.; Arrieta, A.; Zangi, R.; Cebolla, V.L.; Delgado-Camon, A.; Cossío, F.P.; *J. Org. Chem*. **2010**, *75*, 2776.

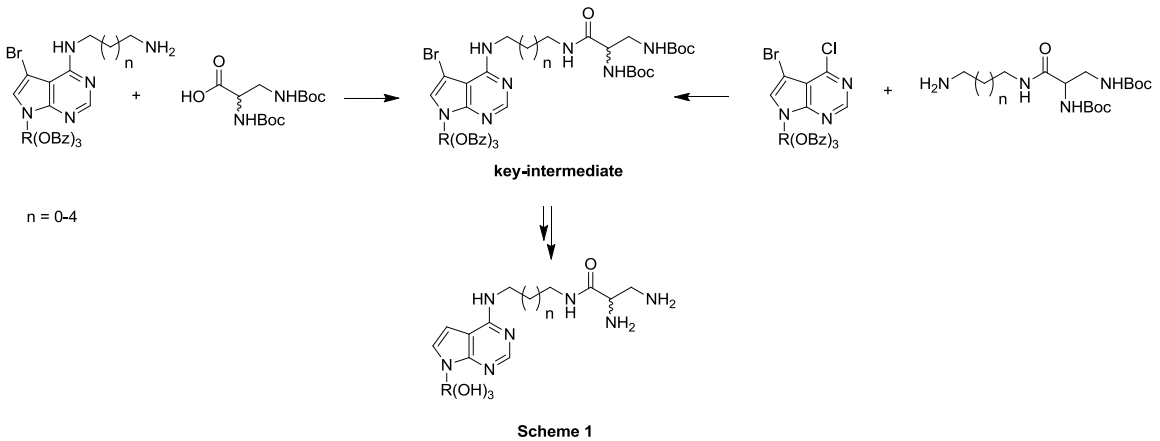
Poster-37

Synthesis and biological evaluation of a new collection of tubercidin-like nucleosides

Stefano D'Errico,[a] Nicola Borbone,[a] Elena Di Gennaro,[b] Andrea Zotti,[b] Alfredo Budillon,[b] Valeria Costantino,[a] Vincenzo Piccialli,[c] Luciano Mayol,[a] Gennaro Piccialli[a] and Giorgia Oliviero[a]

a Dipartimento di Farmacia, Università degli Studi di Napoli Federico II, Via D. Montesano 49, Napoli, Italy
b Experimental Pharmacology, Istituto Nazionale Tumori Fondazione G. Pascale - IRCCS, Via M. Semmola 52, Napoli, Italy
c Dipartimento di Scienze Chimiche, Università degli Studi di Napoli Federico II, Via Cinthia 4, Napoli, Italy
golivier@unina.it

It is well known that cells overexpress special transport systems involved in the uptake of exogenous polyamines, important cellular growth factors, which are present in a very high concentration in cancer cells. In the light of these considerations one can selectively deliver polyamine-drug conjugates to particular cell types. In one of our recent papers we have synthesized and evaluated the antitumor activity of a novel nucleoside analogue carrying a flexible chiral diamine on the C6 purine position of tubercidin, a very potent antitumor and antiviral agent.[1] Due to its toxicity, tubercidin was not approved by the FDA as a drug and efforts have been directed to the preparation of derivatives with an ameliorated toxicity profile. Herein, we present the synthesis of a collection of ten tubercidin analogues and the preliminary biological evaluation of their effects on the PC3, D145 and CAL27 cell lines. The tubercidin analogues are characterized by a linker (n = 2-6, scheme 1) separating the diamine from the nucleoside core. The key intermediates have been efficiently prepared both by divergent and convergent approaches using enantiomerically pure acids.



Scheme 1

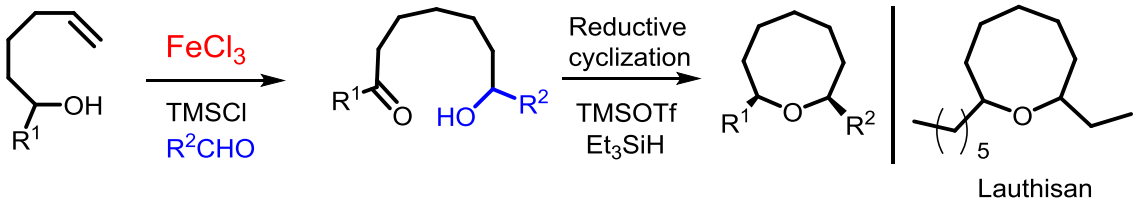
[1] D'Errico, S., Oliviero, G., Piccialli, G., et al. *Eur. J. Org. Chem.* **2015**, 7550-7556.

Poster-38

Two-steps synthesis of eight membered ring oxacycles

Juan M. López-Soria,[1,2] Víctor S. Martín[1] and Juan I. Padrón[1,2]
1 Instituto de Productos Naturales y Agrobiología, Consejo Superior de Investigaciones Científicas, La Laguna, Avda. Astrofísico Francisco Sánchez 3, 38206 La Laguna, Tenerife, Spain.
2 Instituto Universitario de Bio-Orgánica "Antonio González" (CIBICAN), Departamento de Química Orgánica, Universidad de La Laguna, Francisco Sánchez 2, 38206 La Laguna, Tenerife, Spain
jipadron@ipna.csic.es

In the last years, the presence of green and sustainable chemistry in organic synthesis community has increased significantly. Iron is one of the most important sustainable metal catalysts in organic chemistry because it is biological relevant, environmentally friendly, can adopt different oxidation states, and it is one of the most abundant and inexpensive in the earth´s crust.[1]



Scheme 1. Synthesis of Δ^4 2,7-disubstituted oxepenes.

In this work, we use iron(III) salts to catalyze a tandem reaction of three chemical events; Prins reaction, 1,5-hydride shift and the final oxidation. The resulting 1,7-hydroxy ketones are known precursors for eight membered ring oxacycles synthesis (Scheme 1).[2] With suitable substituents we can obtain natural products derivatives like *cis*-lauthisan in few steps and soft conditions.

Acknowledgments: We thank the Spanish MINECO, co-financed by the European Regional Development Fund (ERDF), CTQ2014-56362-C2-1-P for financial support. J. M. L. S. thanks Canary Government (ACIISI) for a Predoctoral fellowship.

[1] Holzwarth, M. S.; Plietker, B.; *ChemCatChem*, **2013**, *5*, 1650-1679.
[2] Carreño, M. C.; Des Mazery, R.; Urbano A.; Colobert, F.; Solladié, G.; *Organic Letters*, **2005**, *7* 2039-2042

Poster-39

Novel Supported Bifunctional Squaramide as Recoverable Organocatalysts for Enantioselective Nitro-Michael Addition

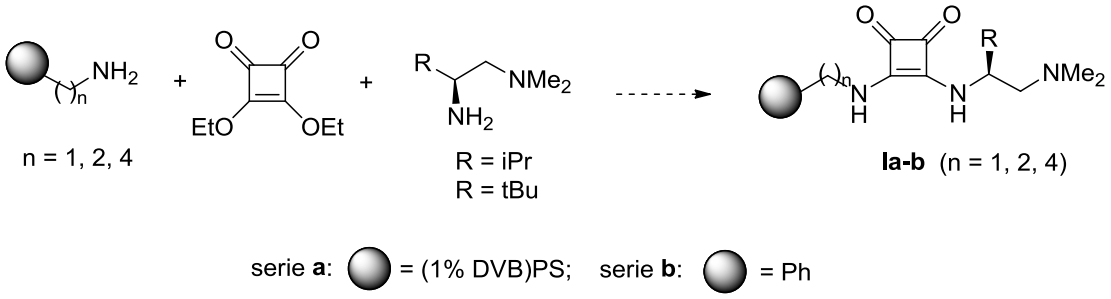
José M. Andrés*, Jorge Losada, Rafael Pedrosa*

Instituto CINQUIMA and Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid. Paseo de Belén 7, 47011-Valladolid. Spain

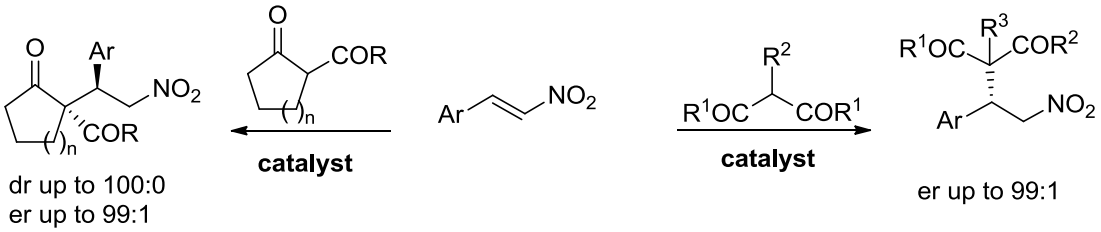
pedrosa@qo.uva.es

Together with ureas and thioureas, squaramides are privileged members of an important group of molecules widely used for organocatalysts based on non-covalent interactions. In general, all the bifunctional squaramides described until now are highly active catalysts, but methods leading to improvement of the recovering and reuse of the catalysts are desirable, and one possible solution consists on their immobilization onto a polymeric material.[1]

Because their interest as organocatalysts, we will present the synthesis of highly efficient, easily accessible, chiral supported bifunctional squaramide prepared from commercially available aminoalkyl polystyrene resins and 1,2-diamines derived from (*L*)-valine or (*L*)-tert-leucine (Scheme 1), and their use in enantio- and diastereoselective nitro-Michael addition reactions (Scheme 2). The catalysts can be used in only 2 mol% loading, and reused for at least five cycles in neat conditions. It has been also demonstrated that the supported catalysts are as effective as the homologous soluble catalysts.



Scheme 1. Synthesis of supported squaramides



Scheme 2. Stereoselective nitro-Michael additions catalized by squaramides **Ia-b**.

Acknowledgements: Authors thank MINECO (Project CTQ2014-59870-P) and JC y L (Project VA 064U13) for financial support.

[1] (a) Kasaplar, P.; Riente, P.; Hartmann, C.; Pericàs, M.A. *Adv. Synth. Catal.* **2012**, *354*, 2905-2910. (b) Kardos, G.; Soós, T. *Eur. J. Org. Chem.* **2013**, 4490-4494. *ACS Catal.* **2014**, *4*, 2137−2142.

Poster-40

Self-immolative Pro-drugs based on Vitamin C

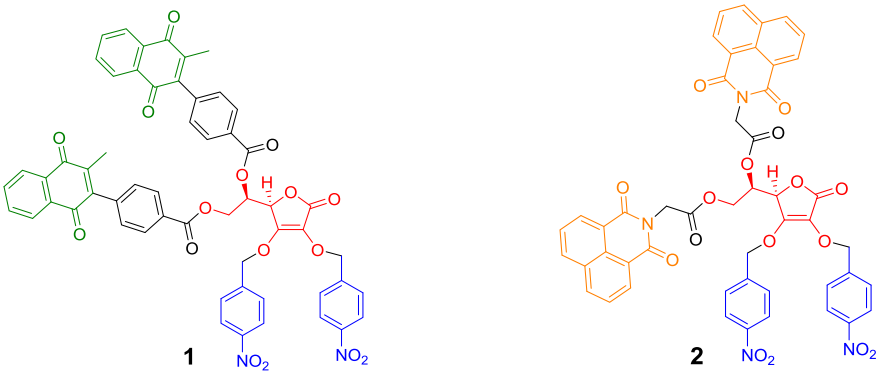
Diego M. Monzón, Belén González – Marrero, Víctor S. Martín, Romen Carrillo and Marcelle D. Perretti

Departamento de Química Orgánica, Instituto Universitario de Bio-Orgánica "Antonio González" (IUBO), Centro de Investigaciones Biomédicas de Canarias (CIBICAN), Universidad de La Laguna, Avda. Astrofísico Francisco Sánchez 2, Apdo. Correos 456, 38206-La Laguna, Santa Cruz de Tenerife, Spain.

e-mail: mperrett@ull.es

The development of novel therapies based on drugs which only act on the diseased tissue sparing the healthy one has always been the long sought aim of drug delivery. In this regard, we have designed and synthesized pro-drugs based on vitamin C (Figure 1) that can be activated in the presence of nitroreductases, which are known to be over-expressed in solid tumors.[1]

Once activated, the drugs act in a synergistic manner: on one hand reactive oxygen species (ROS) are generated due to single electron reduction of the quinones or the naphthylimides by ascorbate;[2] on the other hand, ROS buffering systems are depleted by reducing intra-cellular glutathione levels. Pro-drug **2** could also act as DNA intercalant considering other reported naphthylimide-bearing drugs. Additionally, both prodrugs have been also tested against parasites, as it is known that parasitic nitroreductases are very potent.



Acknowledgements: We thank the Spanish MINECO, co-financed by the European Regional Development Fund (ERDF), CTQ2014-56362-C2-1-P for financial support; and the Consejería de Economía, Industria, Comercio y Conocimiento, co-financed by the European Social Fund with 85%, for supporting the ULL.

[1] Johansson, E.; Parkinson, G. N.; Denny, W. A.; Neidle, S.; *Journal of Medicinal Chemistry* **2003**, *46*, 4009

[2] Silveira-Dorta, G.; Monzón, D. M.; Crisóstomo, F. P.; Martín, T.; Martín, V. S.; Carrillo, R.; *Chem. Commun.* **2015**, *51*, 7027.

Poster-41

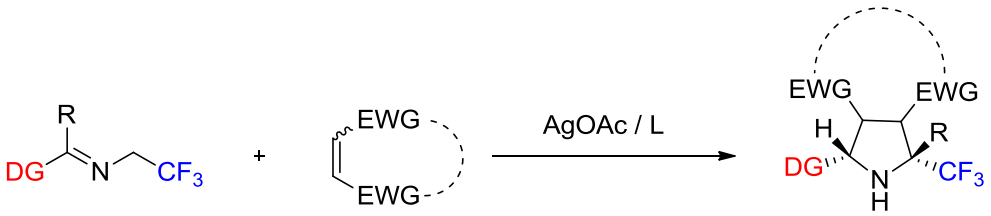
Stereoselective Ag-Catalyzed 1,3-Dipolar Cycloaddition of Activated Trifluoromethyl-Substituted Azomethine Ylides

Alberto Ponce, Javier Corpas, Inés Alonso, Javier Adrio*, Juan Carlos Carretero*

Dpto. de Química Orgánica, Universidad Autónoma de Madrid, Madrid, tfno. : +34914974709; e-mail: alberto.ponce@estudiante.uam.es

The pyrrolidine ring is ubiquitous in natural products and biologically active compounds[1]. In particular, modified proline derivatives have been extensively used to control the conformation of peptides for structure-activity relationship studies[2]. On the other hand, it is well documented that the replacement of hydrogen atoms with fluorine atoms in organic compounds may result in a clear improvement of their biological properties[3]. For instance, the introduction of one or several fluorine atoms proximal to an amine moiety decreases its basicity, which can result in an improvement in the metabolic stability and a reduction in the toxicity of the compound[4].

Herein we report an efficient method for the preparation of 2-trifluoromethyl pyrrolidines by a silver-catalyzed 1,3-dipolar cycloaddition of fluorinated azomethine ylides and activated olefins. Broad scope and high levels of diastereoselectivity have been achieved by using AgOAc/PPh_3 as the catalyst system. The high efficiency of the cycloaddition relies on the presence of a metal-coordinating group on the imine moiety, such as an ester or heteroaryl group. Examples of the catalytic asymmetric version of this cycloaddition has been developed by using (*R*)-Taniaphos as a chiral ligand.



DG = CO_2R or heteroaryl; 60-95% yield

L = PPh_3, 35 examples
(typically *endo* selective)
L = (*R*)-Taniaphos, 86-92% *ee*

1. (a) Kuhnert, M.; Blum A.;Steuber, H.; Diederich, W.E. *J. Med. Chem.* **2015**, *58*, 4845; (b) Roughley, S.D.; Jordan, A.M. *J. Med. Chem.* **2011**, *54*, 3451.
2. (a) Song, B.; Bomar, M.G.; Kibler, P.; Kodukula, K.; Galande, A.K. *Org. Lett.* **2012**, *14*, 732; (b) Whitby, L.R.; Ando, Y.; Setola, V.; Vogt, P.K.; Roth, B.L.; Boger, D.L. *J. Am. Chem. Soc.* **2011**, *133*, 10184.
3. (a) Gouverneur, V.; Muller, K. *Fluorine in Pharmaceutical and Medicinal Chemistry: From Biophysical aspects to Clinical Applications*, Imperial College Press, London, UK, **2012**; (b) Ojima, I. *Fluorine in Medicinal Chemistry and Chemical Biology*, Blackwell Publishing, West Sussex, **2009**; (c) Begue, J.P.; Bonnet- Delpon, D. *Bioorganic and Medicinal Chemistry of Fluorine*, Wiley, Hoboken, **2008**.
4. (a) Chaume, G.; Bebeau, O.; Lesot, P.; Brigaud, T. *J. Org. Chem.* **2010**, *75*, 4135.; (b) Schlosser, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 1496; (c) Schlosser, M. *Angew. Chem. Int. Ed.* **1998**, *110*, 1538.

Poster-42

Nucleophilic and electrophilic double aroylation of chalcones with benzils promoted by the dimsyl anion as a route to all carbon tetrasubstituted olefins

Alessandro Massi, Olga Bortolini, Pier Paolo Giovannini, and Daniele Ragno

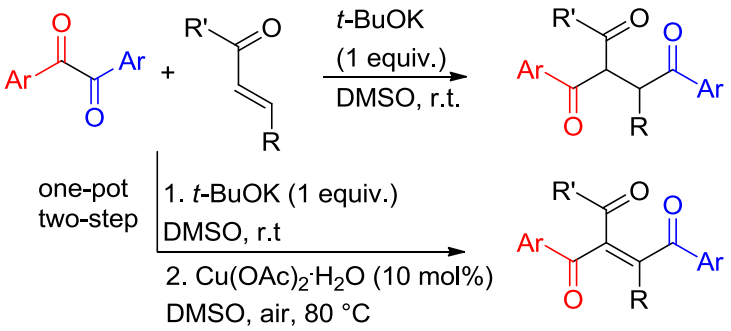
Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Ferrara, Via Fossato di Mortara 17-27, I-44121, Ferrara, Italy

e-mail: daniele.ragno@unife.it

In a previous contribution, we have demonstrated that methylsulfinyl (dimsyl) carbanion, generated by deprotonation of the DMSO solvent, served as surrogate of hazardous cyanide ion promoting the formation of benzoylated benzoins in an atom-economic fashion through sequential nucleophilic *C*- and electrophilic *O*-aroylations.[1]

As a logical extension of the study on the benzoin reaction, we reasoned that utility of dimsyl anion catalysis could be further enhanced by conducting a double *C*-aroylation process on activated alkenes, thus providing a novel variant of the parent Stetter reaction (hydroacylation process).

Indeed, Dimsyl anion promoted the polarity reversal of benzils in a Stetter-like reaction with chalcones to give 2-benzoyl-1,4-diones (double aroylation products), which in turn were converted into the corresponding tetrasubstituted olefins via aerobic oxidative dehydrogenation catalyzed by $Cu(OAc)_2$.[2]



[1] Bortolini, O.; Fantin, G.; Ferretti, V.; Fogagnolo, M.; Giovannini, P.P.; Massi, A.; Pacifico, S.; Ragno, D., *Adv. Synth. Catal.*, , *355*, 3244-3252.

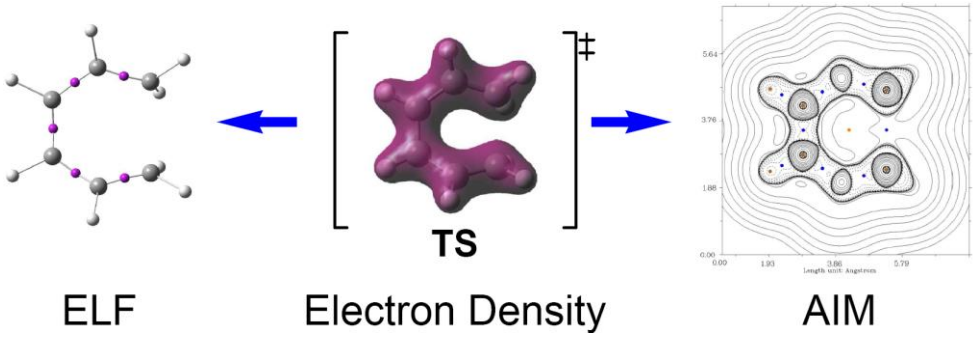
[2] Ragno, D.; Bortolini, O.; Fantin, G.; Fogagnolo, M.; Giovannini, P.P.; Massi, A., *J. Org. Chem.*, **2015**, 80, 1937-1945.

Poster-43

Aromaticity in Pericyclic Transition State Structures? A Critical Rationalisation based on the Topological Analysis of the Electron Localisation Function

Luis R. Domingo,[1] Mar Ríos-Gutiérrez,[1] Eduardo Chamorro[2] and Patricia Pérez[2]
[1]*Department of Organic Chemistry, University of Valencia, Dr. Moliner 50, 46100 Burjassot, Valencia, Spain*
[2]*Departamento de Ciencias Químicas, Millenium Nucleus Processes and Catalysis (CPC), Facultad de Ciencias Exactas, Universidad Andrés Bello, Av. República 230, 8370146 Santiago, Chile.*
e-mail: rios@utopia.uv.es

The nature of the electron delocalisation pattern within a cyclic structure, *i.e.* the aromatic character, is examined for six-membered cyclic transition state structures (TSs) involved in five representative examples of so-called pericyclic reactions, namely, (i) the Diels-Alder reaction between butadiene and ethylene, (ii) the electrocyclic reaction of hexatriene, (iii) the [3,3] sigmatropic rearrangement of 1,5-hexadiene, (iv) the [1,5] sigmatropic rearrangement of 1,3-pentadiene and (v) the ene reaction between propene and ethylene.[1] Topological analysis of the electron localisation function (ELF) of the electron density of the TSs evidences that in four of the five cases, at least one pair of atoms is not bound at the TS configuration, thus precluding a possible cyclic conjugation. This finding makes it possible to rule out the aromatic character of these TSs. High values of the synchronicity Sy index at the TSs contrast with the bonding changes evidenced by the topological analysis of the ELF. Although the atoms in molecules (AIM) topological analysis of the electron density of these TSs affords some bonding critical points (bcps) that suggest a bound TS structure, a comparative analysis of the bonding pattern given by the topological analysis of the ELF indicates that these bcps cannot be associated with a bonding region.



Topological analyses of the electron density of the TS associated with the electrocyclic reaction of hexatriene

1. Domingo, L. R.; Ríos-Gutiérrez, M.; Chamorro, E; Pérez, P. *Sent to publish*, **2016**.

Poster-44

Employment of a CTPR protein as catalyst in [3+2] Cycloaddition between Azomethine Ylides and Nitrostyrenes

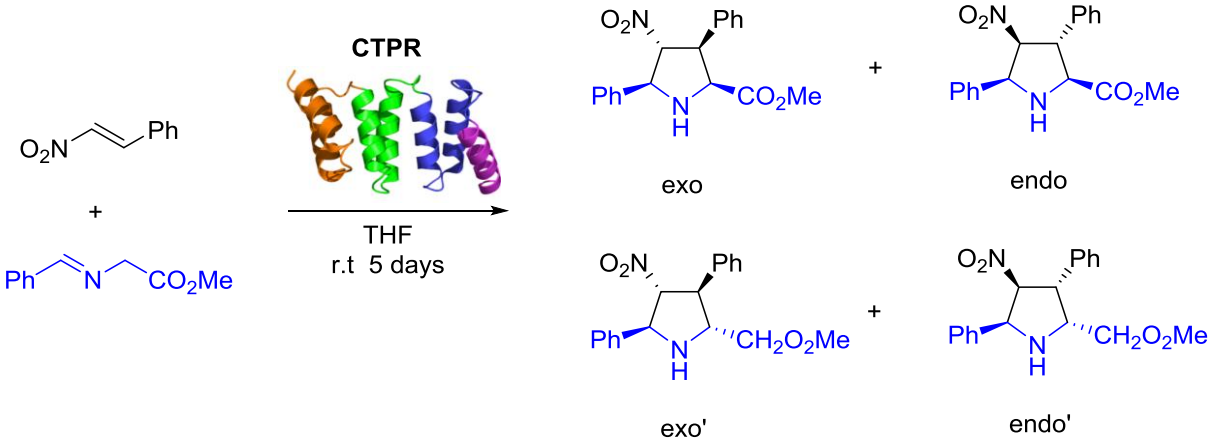
Mikel Odriozola-Gimeno,[†] Antonio Aires,[‡] Miquel Torrent-Sucarrat,[†#] Aitziber Lopez Cortajarena,[‡#] Fernando .P. Cossío,[†] and Ivan Rivilla,[†]

[†]*Departamento de Química Orgánica I, Universidad del País Vasco – Euskal Herriko Unibertsitatea and Donostia International Physics Center (DIPC), Pº Manuel Lardizabal 3, 20018, San Sebastián-Donostia, Gipuzkoa, (Spain).*
[‡]*Biomolecular Nanotecnology, CICbiomaGUNE, Parque tecnológico de San Sebastián Ed.PºMiramón 182, 20009, San Sebastián-Donostia, Gipuzkoa (Spain).*
[#] *Ikerbasque, Basque Foundation for Science, Mª Díaz de Haro 3, E-48013 Bilbao, (Spain).*
e-mail: ivan.rivilla@ehu.es

Substituted prolines constitute a privileged group of organic molecules in the design of new catalysts or in the chemical synthesis of biologically and pharmacologically interesting molecules. In our group, we have studied [3+2] cycloaddition between stabilized azomethine ylides and nitrostyrenes for the design of substituted prolines.[1]

During the last years, protein design has gained relevance for the development of new scaffolds that bind a variety of ligands. Ones of those targets on the protein design are the repeated proteins, the group of Prof. Kortajarena has been working in the design of new scaffolds introducing novel binding specifities onto existing structure or creating new scaffolds grafting known binding sites.[2]

As far as we know, it has not been reported a natural enzyme that catalyzes this kind of reaction, so we perform a [3+2] cycloaddition study (experimental and theoretical) between an imine and nitroestyrene using the designed CTPR protein. Our work has shown the enzymatic activity of the protein CTPR obtaining the four (exo, endo, exo', and endo') abducts.



[1] Arrieta, A.; Otaegui, D.; Zubia, A.; Cossío, F.P.; Díaz-Ortiz, A.; De la Hoz, A.; Herrero, M.A.; Prieto, P.; Foces-Foces, C.; Pizarro, J.L.; Arriortua, M.I. *J.Org.Chem.* **2007**, *72*, 4313-22.
[2] Grove, T.Z.; Cortajarena, A.L.; Regan, L. *Curr. Opin. Struc. Biol*. **2008,** *18*, 507-15.

Poster-45

Stereoselective Synthesis of (*Z*)-Halovinyl Carbohydrate Derivatives

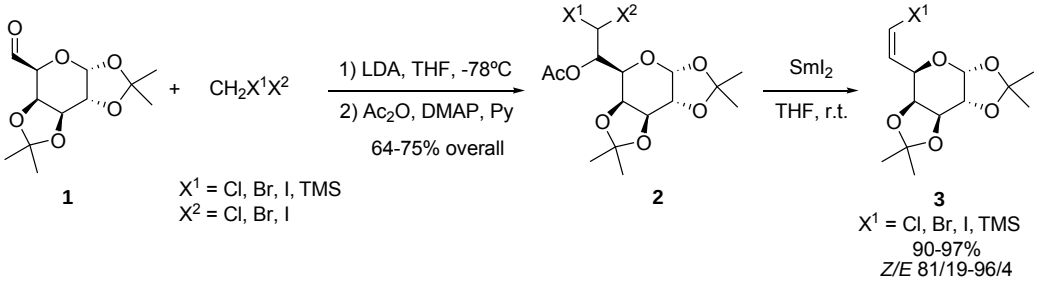
Raquel G. Soengas,[a] Artur M. S. Silva,[a] Martín Soto[b] and Humberto Rodríguez-Solla[b]
[a]*Departament of Chemistry & QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal*
[b]*Departamento de Química Orgánica e Inorgánica, Universidad de Oviedo, Julián Clavería 8, 33071 Oviedo, Spain*

e-mail: hrsolla@uniovi.es

Halovinyl carbohydrate derivatives are of great interest, on account of their usefulness as synthetic intermediates. The presence of the haloalkenyl moiety makes sugar halovinyls ideal precursors for palladium catalyzed coupling reactions, which could be exploited for the introduction of new substituents, the elongation of the sugar chain and the formation of C-glycosides. Accordingly, these derivatives have been used as intermediates in the preparation of natural products,[1] *C*-glycosides,[2] polyols[3] and nucleosides.[4]

We have recently described a novel, efficient and general methodology for the indium-promoted reduction of *gem*-dibromides to the corresponding (*E*)-vinyl bromides in ionic liquid media and under ohmic heating.[5] The procedure is very effective for the preparation of sugar (*E*)-bromoalkenes, which on Pd-catalyzed cross-coupling reactions (Heck, Stille, Suzuki, Kumada and Sonogashira) afforded sugar alkenes, dienes and enynes. Herein we describe a complementary methodology, consisting on an efficient, simple, and rapid process for the formation of sugar (*Z*)-haloalkenes by samarium diiodide-mediated 1,2-elimination[6] of α-polyhalomethylcarbinols.

Starting products were prepared by reaction of dihalomethyllithium with the corresponding sugar-aldehyde **1** at -78 °C. Acetylation of the isolated alcohols with Ac_2O in the presence of pyridine and DMAP, afforded the sugar-derived *O*-acetylated dihalo alcohols **2** in yields ranging between 64-75% and as a mixture of stereoisomers. The sugar-derived *O*-acetylated dihaloalcohols **2** were treated with 2.0 equiv. of SmI_2 in THF at room temperature for a clean conversion to the (*Z*)-vinyl halides **3** in excellent yields and selectivities.



[1] (a) Dixon, D. J.; Ley, S. V.; Gracza, T.; Szolcsany, P. *J. Chem. Soc., Perkin Trans. 1*, **1999**, 839-841. (b) Y. Krishna Reddy, J. R. Falck, *Org. Lett.* **2002**, *4*, 962-971.
[2] Goekjian, P. G.; Wu, T.; Kang, H; Kishi, Y. *J. Org. Chem.* **1991**, *56*, 6422-6434.
[3] Norsikian, S.; Soulé, J.-F.; Cannillo, A.; Guillot, R.; Tran Huu Dau, M.-E.; Beau, J.-M. *Org. Lett.* **2012**, *14*, 544-547.
[4] (a) Wnuk, S. F.; Sacasa, P. R.; Lewandowska, E.; Andrei, D.; Cai, S.; Borchardt, R. T. *Bioorg. & Med. Chem.* **2008**, *16*, 5424-5433. (b) Wnuk, S. F.; Yuan, C.; Borchardt, R. T.; Balzarini, J.; De Clercq, E.; Robins, M. J. *J. Med. Chem.* **1994,** *37*, 3579-3587. (c) S. F. Wnuk, M. J. Robins *Can. J. Chem*. **1993**, *71*, 192-198
[5] Soengas, R. G.; Silva, V. L. M.; Pinto,J.; Rodríguez-Solla, H.; Silva, A. M. S. *Eur. J. Org. Chem.* **2016**, 99-107.
[6] Concellón, J. M.; Rodríguez-Solla, H. *Chem. Soc. Rev.* **2004**, *33*, 599-609

Poster-46

ALKYNYLSILANES AS ALKYNYLATING AGENTS IN THE PRESENCE OF GOLD(I) CATALYSTS

José Manuel González, Alfredo Ballesteros and Belén Rubial
Dpto. de Química Orgánica e Inorgánica e Instituto Universitario de Química Organometálica "Enrique Moles", Universidad de Oviedo, C/ Julián Clavería 8, 33006
e-mail: rubialbelen@uniovi.es

The carbophilic nature of gold(I) complexes[1] makes them suitable agents to activate the **C-Si** bond in alkynylsilanes,[1,2] affording a gold(I) acetylide and a TMSX species in which X is the counteranion in the gold complex. When X is a non-coordinating counteranion, this species is highly electrophilic. Due to the affinity of silicon to form bonds with oxygen atoms,[3] this species could be used to activate or increase the electrophilicity of some oxygenated groups, allowing the corresponding alkynylation reaction.

This strategy has being succesfully applied to a variety of substrates to afford the corresponding alkynylated compounds.[4] A good scope of substituents and functional group tolerance has being observed. Further achievements in order to obtain enantioselective transformations have also being made.

[1] Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed.* **2007**, *46*, 3410-3449
[2] Cicak, H.; Vancik, H.; Mihalic, Z. *J. Org. Chem.* **2010**, *75*, 6969-6972.
[3] Weinhold, F.; West, R. *Organometallics* **2011**, *30*, 5815-5824.
[4] Rubial, B.; Ballesteros, A.; González, J. M. *Adv. Synth. Catal.* **2013**, *355*, 3337-3343.

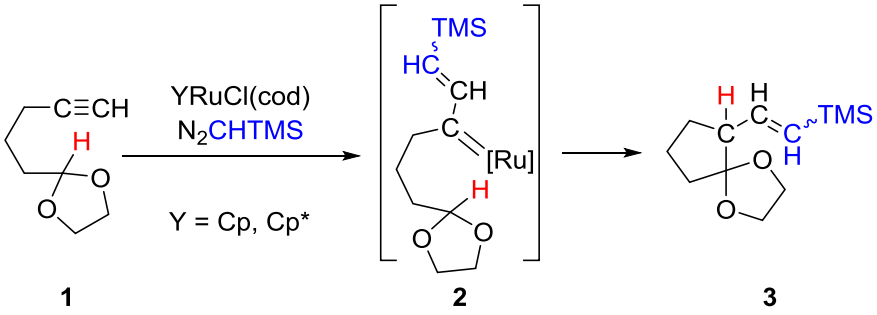
Poster-47

DFT and Kinetic Monte Carlo Study of TMS-Substituted Ruthenium Vinyl Carbenes:

Damián Padín, Jesús A. Varela and Carlos Saá
Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares (CIQUS) e Dpto. de Química Orgánica, Universidade de Santiago de Compostela, 15782, Santiago de Compostela, Spain
e-mail: carlos.saa@usc.es

Metal carbene complexes have proven their value in organic synthesis due to the number of catalytic organometallic transformations in which they are involved.[1] Conjugated vinyl ruthenium carbenes, smoothly prepared under mild conditions by treatment of Ru(II) complex Cp*RuCl(cod) in the presence of functionalized alkynes and diazoalkanes, have been recently proposed as intermediates in catalytic transformations that involve the formation of carbon-carbon[2] and carbon-heteroatom bonds.[3]

Herein we report a theoretical mechanistic study of the intramolecular redox, neutral process involving the cascade [1,n]-hydrogen transfer/cyclization[2b] of alkynyl acetal **1** with N_2CHTMS in the presence of Cp- and Cp*RuCl(cod) to afford (*Z*) and (*E*)-(trimethylsilyl)vinyl spiroacetal **3** through the conjugated vinyl ruthenium carbene intermediate **2**.[4] Kinetic Monte Carlo (KMC) simulations with rate coefficients, including tunneling probabilities for the hydride transfer step, were used to model the evolution of reactants, intermediates, and products for all calculated pathways.



Acknowledgment: This work was supported by the Spanish MINECO (project CTQ2014-59015R), the Xunta de Galicia (project GRC2014/032) and the European Regional Development Fund (projects CTQ2014-59015R and GRC2014/032). We also thank the ORFEO-CINQA network (CTQ2014-51912REDC). D. P. thanks XUGA for a predoctoral contract.

[1] *Contemporary Carbene Chemistry*; Moss, R. A.; Doyle, M. P. Eds.; John Wiley & Sons, Inc., Hoboken, New Jersey, U.S.A., 2014.
[2] (a) Vovard-Le Bray, C.; Derien, S.; Dixneuf, P. H. *C. R. Chim.* **2010**, *13*, 292-303. (b) Cambeiro, F.; López, S.; Varela, J. A.; Saá, C. *Angew. Chem. Int. Ed.* **2012**, *51*, 723-727.
[3] (a) Cambeiro, F.; López, S.; Varela, J. A.; Saá, C. *Chem. Int. Ed.* **2014**, *53*, 5959-5963. (b) González-Rodríguez, C.; Suárez, J. R.; Varela, J. A.; Saá, C. *Angew. Chem. Int. Ed.* **2015**, *54*, 2724-2728.
[4] Cambeiro, F.; Martínez-Núñez, E.; Varela, J. A.; Saá, C. *ACS Catal.* **2015**, *5*, 6255-6262.

Poster-48

Synthesis of new nanostructured chiral catalyst

Paolo Bovicelli,[a] Donatella Capitani,[b] Noemi Proietti,[b] Giuliana Righi,[a] Lorenza Suber[c] and Carla Sappino[d]

[a]*IBPM, CNR, Chem. Dept., Sapienza Università di Roma, P.le A. Moro 5, 00185, Roma*
[b]*IMC, CNR, Via Salaria km 29,300, 00015 Monterotondo Scalo*
[c]*ISM, CNR, Via Salaria km 29,300, 00015 Monterotondo Scalo*
[d]*Chem. Dept., Sapienza Università di Roma, P.le A. Moro 5, 00185, Roma*
e-mail: carla.sappino@uniroma1.it

Asymmetric catalysis represents a powerful method for the synthesis of enantiopure molecules, but its practical applications are extremely limited by high costs and severe ecological impact. Then the opportunity to recover and reuse the catalysts become a very important factor. Recently, the use of nanostructured materials led to the development of new catalysts combining advantages of both heterogeneous and homogeneous catalysis: nanoparticles are easily separated from the reaction mixture and, at the same time, their dispersibility in organic solvents makes their catalytic activity close to the homogeneous one.[1]

With the aim of the development of a novel versatile, magnetically recoverable and recyclable 'nanocatalyst', we focused on the design and synthesis of ligands bearing, in addition to a fine-tunable catalytic site (a β-amino alcohol motif),[2] a functionality for their covalent anchoring to magnetite nanoparticles (an alkoxysilane group). First, after a long optimization study, we selected structure 1 that, as shown in figure 1, led to excellent results, both in enantioselectivity and chemical yields, in the addition of diethyl zinc to a variety of aromatic aldehydes in homogeneous phase.

Together, we dealt with the choice of the best nanosized support and with the optimization of the immobilization conditions. We selected silica and magnetite-silica core shell nanoparticles.[3] The latter show a superparamagnetic behaviour, allowing a quick recovery by magnetic decantation. Regarding the immobilization step, we followed two different strategies that involved a condensation or a click chemistry reaction (Fig 2).

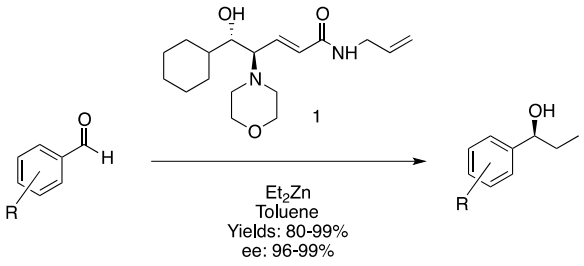


Fig 1

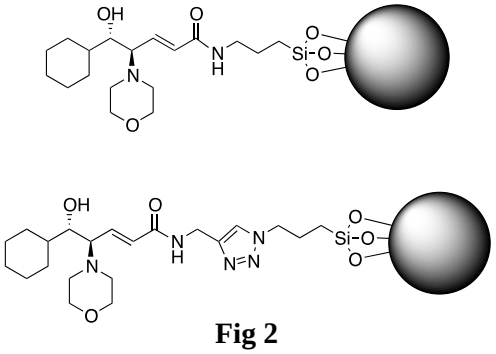


Fig 2

1 Shylesh, S.; Schuneman, V.; Thiel, W.R. *Angew. Chem., Int. Ed.* **2010**, *49*, 3428-3459.
2 Vicario, J.; Badia, D.; Carrillo, L.; Reyes, E.; Etxebarria, J. *Curr. Org. Chem.*, **2005**, 9, 219-235.
3 Rossi LM, Costa NJS, Silva FP, Wojcieszak R. *Green Chem.*, **2014**, *16*, 2906-2933.

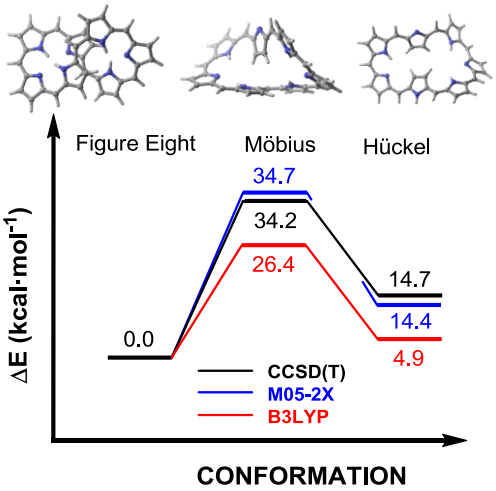
Poster-49

Relevance of the DFT Method to study expanded porphyrins with different topologies

Miquel Torrent-Sucarrat

Department of Organic Chemistry I, Universidad del País Vasco - Euskal Herriko Unibertsitatea (UPV/EHU) and Ikerbasque, Basque Foundation for Science, María Díaz de Haro, 3, 6º, 48013 Bilbao, Spain.
e-mail: miqueltorrentsucarrat@gmail.com

Meso-aryl expanded porphyrins present a structural versatility that allows them to achieve different topologies with distinct aromaticities and magnetic and electric properties.[1] In the last decade, several studies appeared in the literature studying these topological switches from an experimental and theoretical point of view, which most of them include density functional theory calculations, being the B3LYP the most used methodology. In this work, we show that the selection of the functional has a critical role on the geometric, energetic, and magnetic results of these expanded porphyrins, even the use of an inadequate methodology can generate the appearance of spurious stationary points in the potential energy surface. To illustrate these points, we study different molecular distortions of two expanded porphyrins, [32]-heptaphyrin and [26]-hexaphyrin, using eleven DFT functionals and single-point CCSD(T) calculations for benchmarking purposes. Our results conclude that the best performance is obtained with the M05-2X and M06-2X methods, while other functionals (among them it is important to remark B3LYP) show a lacking description of these topological switches.[2]



1. a) Shin, J. Y.; Kim, K. S.; Yoon, M. C.; Lim, J. M.; Yoon, Z. S.; Osuka, A.; Kim, D. **2010**, *39*, 2751-2761; b) Saito, S.; Osuka, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 4342-4373; c) Stepień, M.; Sprutta, N.; Latos-Grażyński, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 4288-4340.
2. a) Marcos, E.; Anglada, J. M.; Torrent-Sucarrat, M. *J. Phys. Chem. C.* **2012**, *116*, 24358–24366; b) Marcos, E.; Anglada, J. M.; Torrent-Sucarrat, M. *J. Org. Chem.* **2014**, *79*, 5036-5046; c) Torrent-Sucarrat, M.; Navarro, S.; Cossío, F. P.; Anglada, J. M.; Luis, J. M. *submitted*.

Poster-50

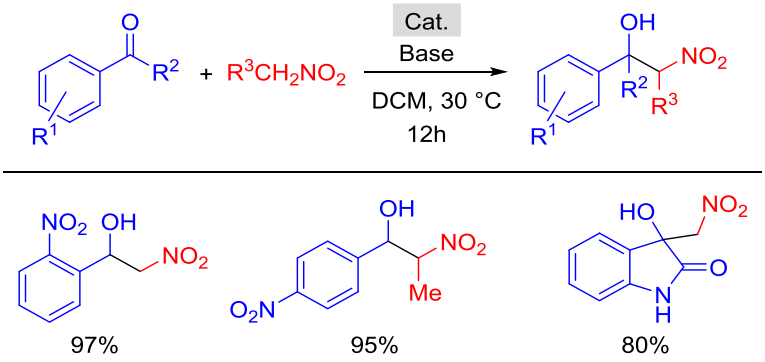
Well defined silver(I) macrocyclic complexes as catalyst for the Henry reaction

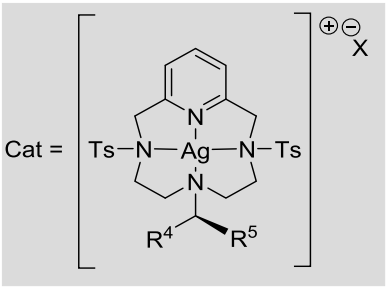
Alessandro Caselli[1], Daniele Valcarenghi[1], Giorgio Abbiati[2], Monica dall'Acqua[2] and Giorgio Tseberlidis[1]

[1] *Dipartimento di Chimica, Università degli Studi di Milano, via Golgi 19 – 20133 Milano – Italy, e-mail: giorgio.tseberlidis@unimi.it*

[2] *DISFARM, Sezione di Chimica Generale e Organica "A. Marchesini", Università degli Studi di Milano, Via Venezian, 21 – 20133 Milano – Italy*

Nitroalkanes are important reagents not only due to their propensity to undergo easy α-dealkylation but also for their facile interconversion to other organic functional groups. Even weak bases generate nitronate anions by abstraction of acidic α-hydrogens, which can attack carbonyl compounds to give valuable β-nitro alcohols, in the so-called Henry (or nitroaldol) reaction.





In the past few years, our attention has turned to the introduction of a pyridine moiety into the skeleton of tetraaza-macrocycles, with the aim to obtain ligands with increased conformational rigidity and different basicity. [1-3] Among different metals tested, we found that [Ag(I)(Pyridine-containing Ligand)] complexes can actually activate the aldehyde toward the nitronate nucleophilic attack, in the first example of a silver catalyzed Henry reaction. Moreover we have modified our ligands in order to attach in the proper position a suitable base to facilitate the reaction.

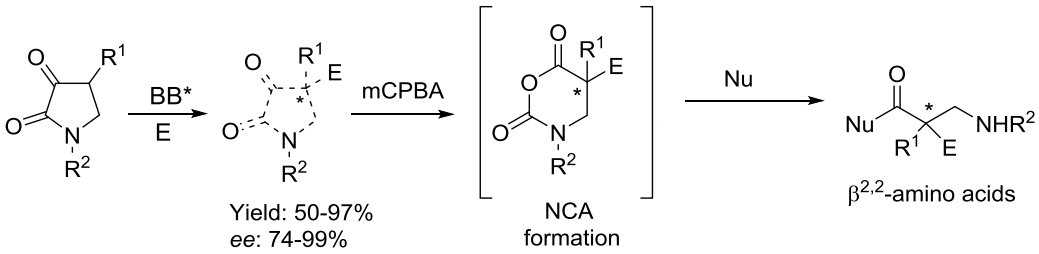
1. Castano, B. *et al. Green Chem.* **2014**, *16*, 3202.
2. Castano, B. *et al. Appl. Organomet. Chem.* **2011**, *25*, 824.
3. a) Pedrazzini, T. *et al. Eur. J. Inorg. Chem.* **2015**, *2015*, 5089; b) Dell'Acqua, M. *et al. J. Org. Chem.* **2014**, *79*, 3494; c) Trose, M. *et al. J. Org. Chem.* **2014**, *79*, 7311.

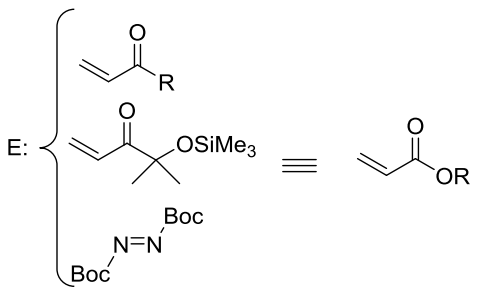
Poster-51

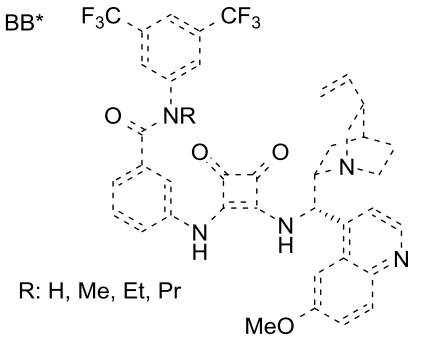
Bifunctional Bronsted Base Catalyzed C4-Functionalization of 2,3-Dioxopyrrolidines: An Entry to Quaternary α,α-Disubstituted β-Amino Acid ($\beta^{2,2}$-Amino Acid) Derivatives

Ana Vázquez, Eider Badiola, Silvia Vera, Antonia Mielgo and Claudio Palomo
Dpto. de Química Orgánica I, Facultad de Ciencias Químicas, EHU-UPV. c
e-mail: avazquezalbisu@hotmail.com

β–Amino acids are important building blocks for a wide variety of natural products, pharmaceutical agents and mimics of protein structural motifs. Unlike β^2-. β^3-, $\beta^{2,3}$, $\beta^{3,3}$-amino acids, stereoselective methods for the preparation of $\beta^{2,2}$-amino acids are less common. These are mainly focused on diastereoselective approaches while enantioselective entries to $\beta^{2,2}$-amino acids are very limited. Although these methods usually provide the corresponding $\beta^{2,2}$-amino acid derivatives in good yields, several protection, deprotection, activation steps are generally required for the incorporation of the resultant $\beta^{2,2}$-amino ester into a peptide segment and/or transformed into a more complex product, thus complicating the process. The present work describes a new catalytic enantioselective approach to $\beta^{2,2}$-amino acids. This approach is based on two unprecedented key elements, the Bronsted base catalysed region- and enantioselectice C4-functionalization of 2,3-dioxopyrrolidines and the regioselevtice Baeyer-Villiger rearrangement of the resultant adducts to afford β-amino acid *N*-carboxy anhydrides (β-NCAs). In spite of the presence of 2,3-dioxopyrrolidines in some natural products and drugs, their use in asymmetric catalysis has been scarcely investigated. In the present work, we describe the first application of these heterocycles as Michael donors in organocatalytic reactions.







Poster-52

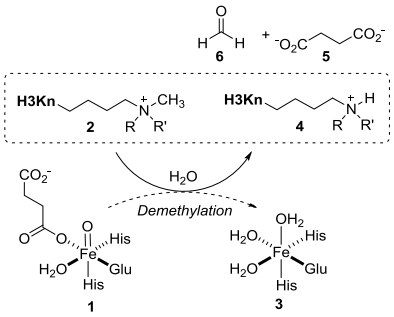
Spin states and reaction mechanisms for Jmj-C-Domain-Containing Histone Demethylases

N. Alberro,[1] M.Torrent-Sucarrat,[1,2,3] I. Arrastia,[1,2] A. Arrieta,[1] and F. P. Cossío*[,1,2]
[1]*Department of Organic Chemistry, University of the Basque Country, Manuel Lardizabal Etorbidea 3, 20018 Donostia, Spain* [2]*Donostia Internacional Physics Center, Pº Manuel Lardizabal 4 Etorbidea, 20018 Donostia, Spain* [3]*IKERBASQUE, Basque Foundation for Science, Maria Diaz de Haro 3, 48011 Bilbao, Spain*

nerea.alberro@ehu.es

Histone demethylases regulate the degree of methylation in lysine residues of histones. These enzymes play an essential role in epigenetics. This kind of DNA covalent changes are linked to cancer[1] and neurodegenerative diseases,[2] such us Alzheimer and Parkinson.

Although a general mechanism of the demethylation has been proposed for these α-ketoglutarate dependent non-heme iron (II) containing enzymes,[3] (see scheme 1) the details of the reaction have not been determined. In this work, we present our DFT results obtained for model systems that mimic the chief geometric and electronic features of the active site of JmjD domain-containing enzymes bound to model substrates. We have observed different mechanisms for the lysine demethylation according to the methylation degree of the lysine. It has been found that the *N*-demethylation reaction is stepwise and occurs on triplet and quintet potential energy hypersurfaces.[4]



Scheme 1

[1] Hojfeldt, J. W.; Agger, K.; Helin, K. *Nat. Rev. Drug Discov.* **2013**, *12*, 917-930.
[2] Abel, T.; Zukin, R. S.*Curr. Opin. Pharmacol.* **2008**, *8*, 57-64.
[3] Ng, S. S.; Kavanagh, K. L.; McDonough, M. A.; Butler, D.; Pilka, E. S.; Lienard, B. M. R.; Bray, J. E.; Savitsky, P.; Gileadi, O.; von Delft, F.; Rose, N. R.; Offer, J.; Scheinost, J. C.; Borowski, T.; Sundstrom, M.; Schofield, C. J.; Oppermann, U. *Nature* **2007**, *448*, 87-91.
[4] Alberro, N.; Torrent-Sucarrat, M.; Arrastia, I.; Arrieta, A.; Cossío, F.P., submitted.

LIST OF PARTICIPANTS

Agirre, Maddalen
Universidad del País Vasco-San Sebastián

Aizpurua, Jesús Mª
Universidad del País Vasco-San Sebastián

Alberro, Nerea
Universidad del País Vasco-San Sebastián

Algieri, Vincenzo
Università della Calabria

Alonso, Pedro
Universidad de Oviedo

Amat, Mercedes
Universidad de Barcelona

Andreu, Inmaculada
Universidad de Valencia

Aranzamendi, Eider
Universidad del País Vasco-Bilbao

Are, Celeste
Universidad de Barcelona

Arrastia, Iosune
Universidad del País Vasco-San Sebastián

Arrieta, Ana
Universidad del País Vasco-San Sebastián

Badiola, Eider
Universidad del País Vasco-San Sebastián

Ballesteros, Alfredo
Universidad de Oviedo

Ballini, Roberto
Università di Camerino

Barbolla, Iratxe
Universidad del País Vasco-Bilbao

Barolo, Claudia
Università degli Studi di Torino

Barroso, Raquel
Universidad de Oviedo

Bastida, Iñaki
Universidad del País Vasco-San Sebastián

Begala, Michela
Università degli Studi di Cagliari

Bello, Tamara
Universidad del País Vasco-San Sebastián

Bencivenni, Giorgio
Università di Bologna

Bernardi, Anna
Università degli Studi di Milano

Blay, Gonzalo
Universidad de Valencia

Bonjoch, Josep
Universidad de Barcelona

Borbone, Nicola
Università degli Studi di Napoli "Federico II"

Bortolini, Olga
Università degli Studi di Ferrara

Bosch, Joan
Universidad de Barcelona

Caballero, Javier
Universidad del País Vasco-San Sebastián

Calamante, Massimo
Università degli Studi di Firenze

Calloni, Ilaria
CIC BioGUNE, Bilbao

Campano, Teresa
Universidad del País Vasco-San Sebastián

Carral, Asier
Universidad del País Vasco-Bilbao

Carreño, M. Carmen
Universidad Autónoma de Madrid

Carrillo, Romen
Universidad de La Laguna

Cioce, Anna
CIC BiomaGUNE, San Sebastián

Cipolla, Laura
Università degli Studi di Milano-Bicocca

Conte, Valeria
Università degli Studi di Roma Tor Vergata

Correa, Arkaitz (UFI)
Universidad del País Vasco-San Sebastián

Corzana, Francisco
Universidad de La Rioja

Cossío, Fernando P.
Universidad del País Vasco-San Sebastián

Cozzi, Pier Giorgio
Università di Bologna

Criado, Alejandro
CIC BiomaGUNE, San Sebastián

De los Santos, Jesús
Universidad del País Vasco-Vitoria

De Napoli, Lorenzo
Università degli Studi di Napoli "Federico II"

Dell'Amico, Luca
ICIQ-Tarragona

Delogu, Giovanna
Università degli Studi di Cagliari

Delso, Ignacio
CSIC-Universidad de Zaragoza

Di Maio, Antonio
IIQ-CSIC-Universidad de Sevilla

Domingo, Luis Ramón
Universidad de Valencia

Eceiza, Maite
Universidad del País Vasco-San Sebastián

Echave, Haizea
Universidad del País Vasco-San Sebastián

Es Sbai, Zouhair
Universidad del País Vasco-Vitoria

Espinosa, Miguel
Universidad de Valencia

Etxabe, Julen
Universidad del País Vasco-San Sebastián

Fañanás, Francisco Javier
Universidad de Oviedo

Farinola, Gianluca M.
Università degli Studi di Bari

Fernández, Patricia
Universidad de Oviedo

Fernández, Paula
Universidad de Oviedo

Fernández, Rosario
Universidad de Sevilla

Filippini, Giacomo
ICIQ-Tarragona

Fisher, Béla
Universidad del País Vasco-San Sebastián

Freire, Félix
CICUS-Universidad de Santiago de Compostela

Gallego, Laura
Universidad de Sevilla

Ganboa, Iñaki
Universidad del País Vasco-San Sebastián

García, Aimar
Universidad del País Vasco-Bilbao

García, Ane
Universidad del País Vasco- San Sebastián

García, Lorena
Universidad del País Vasco-Bilbao

Giorgi, Simone
Università di Camerino

Goitia, Asier
Universidad del País Vasco-San Sebastián

Gómez-Bengoa, Enrique
Universidad del País Vasco-San Sebastián

González, José Manuel
Universidad de Oviedo

González, Silvia
Universidad de Oviedo

Goracci, Laura
Università degli Studi di Perugia

Guerrero, Itziar
Universidad del País Vasco-San Sebastián

Irastorza, Aitziber
Universidad del País Vasco-San Sebastián

Iriarte, Igor
Universidad del País Vasco-San Sebastián

Izquierdo, Joseba
Universidad del País Vasco-San Sebastián

Jauregibeitia, Iker
Universidad del País Vasco-Bilbao

Jiménez, Tania
University of Göteborg

Jiménez-Barbero, Jesús
CIC BioGUNE, Bilbao

Juste-Navarro, Verónica
CSIC-Universidad de Zaragoza

Landa, Aitor
Universidad del País Vasco-San Sebastián

Larrañaga, Olatz
Universidad del País Vasco-San Sebastián

Lassaletta, José María
IIQ-CSIC, Sevilla

Lepri, Susan
Università degli Studi di Perugia

Linares, Ana
Universidad del País Vasco-Bilbao

Liz-Marzán, Luis M.
CIC BiomaGUNE, San Sebastián

López, Enol
Universidad de Oviedo

López, Rosa
Universidad del País Vasco-San Sebastián

Maiuolo, Loredana
Università della Calabria

Marcantoni, Enrico
Università di Camerino

Martín, Rubén
ICIQ, Tarragona

Martín, Víctor S.
Universidad de La Laguna

Martínez, Ángel Manu
Universidad Autónoma de Madrid

Martínez, José I.
Universidad del País Vasco-Bilbao

Martínez , Montserrat M.
Universidade da Coruña

Martínez de Marigorta, Edorta
Universidad del País Vasco-Vitoria

Massaro, Marina
Università degli Studi di Palermo

Mata, Sergio
Universidad de Oviedo

Mauleón, Pablo
Universidad Autónoma de Madrid

Mayol, Luciano
Università degli Studi di Napoli "Federico II"

Mba, Miriam
Università di Padova

Mchichou, Sara
Universidad del País Vasco-San Sebastián

Medve, Laura
Università degli Studi di Milano

Mestre, Jordi
Universitat Rovira i Virgili, Tarragona

Mielgo, Antonia
Universidad del País Vasco-San Sebastián

Mirabella, Stefania
Università degli Studi di Firenze

Mouriño, Antonio
Universidad de Santiago de Compostela

Múgica, Odei
Universidad del País Vasco-San Sebastián

Muñoz, Lorena
Universidad del País Vasco-San Sebastián

Nacci, Angelo
Università degli Studi di Bari "Aldo Moro"

Nicasio, Mª Carmen
Universidad de Sevilla

Noto, Renato
Università degli Studi di Palermo

Ochoa de Retana, Ana Mª
Universidad del País Vasco-Vitoria

Odriozola, Amaiur
Universidad del País Vasco-San Sebastián

Odriozola, Mikel
Universidad del País Vasco-San Sebastián

Oiarbide, Mikel
Universidad del País Vasco-San Sebastián

Olaizola, Olatz
Universidad del País Vasco-San Sebastián

Olaizola, Yurre
Universidad del País Vasco-San Sebastián

Oliviero, Giorgia
Università degli Studi di Napoli "Federico II"

Ortega, Alexandere
Universidad del País Vasco-Bilbao

Pace, Andrea
Università degli Studi di Palermo

Padrón, Juan Ignacio
Universidad de La Laguna

Palomo, Claudio
Universidad del País Vasco-San Sebastián

Palumbo, Fabrizio
Universidad de Valencia

Passarella, Daniele
Università degli Studi di Milano

Pedrosa, Rafael
Universidad de Valladolid

Pérez-Saavedra, Borja
CICUS-Universidad de Santiago de Compostela

Pérez, Pedro J.
Universidad de Huelva

Perretti, Marcelle
Universidad de La Laguna

Piccialli, Gennaro
Università degli Studi di Napoli "Federico II"

Pinacho Crisóstomo, Fernando
Universidad de La Laguna

Pinto, Alexandre
Universidad de Barcelona

Pirovano, Valentina
Università degli Studi di Milano

Ponce, Alberto
Universidad Autónoma de Madrid

Poyatos, Macarena
Universitat Jaume I, Castellón

Pozo, Iago
CICUS-Universidad de Santiago de Compostela

Prandi, Cristina
Università degli Studi di Torino

Prato, Maurizio
Università degli Studi di Trieste
CIC BiomaGUNE, San Sebastián

Ragno, Daniele
Università degli Studi di Ferrara

Rebolledo, Ane
Universidad del País Vasco-Bilbao

Reyes, Efraím
Universidad del País Vasco-Bilbao

Riela, Serena
Università degli Studi di Palermo

Ríos, Mar
Universidad de Valencia

Rivilla, Iván
Universidad del País Vasco-San Sebastián

Rizzo, Simona
Istituto di Scienze e Tecnologie Molecolari
CNR-Milano

Rodríguez Solla, Humberto
Universidad de Oviedo

Rodríguez, Sandra
Universidad del País Vasco-San Sebastián

Rodríguez, Sandra
Universidad del País Vasco-Bilbao

Rubial, Belén
Universidad de Oviedo

Saá, Carlos
CICUS-Universidad de Santiago de Compostela

Sabuzi, Federica
Università degli Studi di Roma Tor Vergata

San Segundo, Marcos
Universidad del País Vasco-San Sebastián

Sánchez, Eduardo
Universidad del País Vasco-Bilbao

SanMartín, Raúl
Universidad del País Vasco-Bilbao

Sappino, Carla
Università di Roma Sapienza

Scrimin, Paolo
Università degli Studi di Padova

Sotomayor, Nuria
Universidad del País Vasco-Bilbao

Sotorríos, Lía
Universidad del País Vasco-San Sebastián

Tecilla, Paolo
Università degli Studi di Trieste

Tiecco, Matteo
Università degli Studi di Perugia

Torrent, Miquel
Universidad del País Vasco-San Sebastián

Tortosa, Mariola
Universidad Autónoma de Madrid

Tseberlidis, Giorgo
Università degli Studi di Milano

Unione, Luca
CIC BioGUNE, Bilbao

Urgoitia, Garazi
Universidad del País Vasco-Bilbao

Uria, Uxue
Universidad del País Vasco-Bilbao

Urriolabeitia, Esteban
CSIC-Universidad de Zaragoza

Urruzuno, Iñaki
Universidad del País Vasco-San Sebastián

Valdés, Carlos
Universidad de Oviedo

Valle, María
Universidad de Valladolid

Vazquez, Ana
Universidad del País Vasco-San Sebastián

Vera, Silvia
Universidad del País Vasco-San Sebastián

Zárate, Cayetana
ICIQ, Tarragona

LIST OF AUTHORS

D

N

O

P

Q

R

W

X

Z