University of Granada

VI REQOMED

BOOK OF ABSTRACTS

GRANADA, SPAIN

JUNE 19-21th, 2013

University of Granada

VI Mediterranean Organic Chemistry Meeting,

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VI Mediterranean Organic Chemistry Meeting. VI REQOMED.

Libro de Resúmenes.

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Dear Colleagues,

In the name of the Organizing Committee it is our great pleasure to welcome you to the VI Mediterranean Organic Chemistry Meeting, "VI REQOMED" to be held in Granada, Spain, 19-21 June, 2013. This scientific congress will be focus on the presentation and discussion of research works concerning any theoretical, practical and industrial-applied aspects in the Organic Chemistry. The congress will feature 12 lecturers of recognized prestige coming from universities and research centers located in every Mediterranean country, which will present the last results on the synthesis of new catalysers in organic chemistry, new advances in nanotechnology and nanochemistry, the rational design of natural product derivatives with antifungal activity, antiviral activity, etc. and on the development of original strategies for synthesizing of bioactive molecules. The programm is rounded off by 22 oral communications, which are a representation of so many research groups, and around 80 posters. If considered together, all the communications establish novelty chemistry processes, cleaner and more efficient, and the preparation of chemicals with applications in the pharmaceutical, cosmetic, parfum, agri-food and insecticide industries.

The Madrasah of Granada was founded as mosque school in 1349 by the Nasrid monarch Yusuf I. The Madrasah functioned as a university until late 1499. In 1531, the University of Granada was founded by Holy Roman Emperor Charles V, which is located in the *Hospital Real*, a historic building in the city of Granada designed by order of the Catholic Monarchs in 1504. Granada has an ancient history, inhabited by Iberians (Ilturur), Romans (Ilíberis), Ziríes (Madinat Garnata), Almoravids and Almohads , Nasrids , before the Spanish Catholic Monarchs reconquered the city. Nowadays Granada offers the attractive visits to unique enclaves such as the complex of the *Alhambra* and the *Generalife* (World Heritage Site), the Cathedral and the Royal Chapel, Monastery of *La Cartuja* or the historical Moorish *Albaicín* quarter (World Heritage Site), all of them accessible on foot. In addition there is a possibility of trying a wide range of "tapeo granadino" in taverns and bars and tasting the traditional dishes from Granada. We hope to see you in Granada.

Prof. Alejandro Fernández Barrero

President of the Organizing Committee

PROGRAMM

Wednesday June 19th, 2013

12,00-16,30 Welcoming and Registration

Opening Session Aula Magna "Pascual Rivas" Facultad de Ciencias (UGR)

16,30-17,00 Excmo Sr. Rector UGR, Ilmo Sr Decano Facultad de Ciencias, Presidente del Grupo Especializado Química Orgánica de la Real Sociedad Española de Química.

Session I Chairman: Prof. Joan Bosch Cartes

17,00-17,30 Invited Lecture 1 **"Catalysis by Lewis superacids: Olefin activation and applications to fragrance chemistry"** Prof. Elisabet Duñach (Nice,France)

17,30-18,00 Invited Lecture 3 " **Cucurbiturils - Nanocontainers for Supramolecular Chemistry in Water"** Dr. Uwe Pischel (University of Huelva)

18,00-18,45 Poster Session

19,00 **Guided visit to the city: Granada-Albayzín**

20,45 **Cocktail & Welcome reception**

Thursday June 20th, 2013

Session II Chairman: Prof. Carmen Nájera

9,00-9,30 Invited Lecture 6 **"Enantioselective synthesis of intermediate products in the generation of hepatitis C virus inhibitors".** Prof. José Miguel Sansano (University of Alicante).

9,30-10,00 Invited Lecture 4 **"Halogen Bonding Receptors for Anion Recognition and Sensing".** Dr Antonio Caballero (University of Murcia).

10,00-10,40 Oral Communications (1-4)

Elena Ghirardi	*Highly Stereoselective Cyclocondensation Reactions. Enantioselective Synthesis of Substituted cis-Decahydroquinolines*
Eva Belmonte Sánchez	*Gold nanoparticles as effective catalyst of the three-component coupling between aldehydes, amines and alkynes*
Gonzalo Durán Sampedro	*New energy transfer cassettes based on Coumarin-BODIPY dyads*
Esteban Urriolabeitia Arrondo	*Ru-catalyzed oxidative coupling of (hetero)aryl derivatives with internal alkynes using primary amines as directing groups*

10,40-11,15 Poster Session

11,15-11,30 Coffee Break

Session III Chairman: Prof. Fernando López Ortiz

11,30-12,00 Invited Lecture 2 **"Síntesis y Funcionalización de Dendrímeros para Aplicaciones Biomédicas."** Prof. Ezequiel Pérez-Inestrosa Villatoro (University of Málaga).

12,00-12,30 Invited Lecture 8 **"Neoglycoconjugates based on β-cyclodextrin, dendrimers and nanoparticles for sensing and drug delivery**". Dr. Juan Manuel Casas (University of Almería).

12,30-13,20 Oral Communications (5-9)

Alberto Martínez Cuezva	*Versatile Access to Chiral Indolines by Catalytic Asymmetric Fischer Indolization*
M Araceli González Campaña	*Water as Efficient Hydrogen-Atom Donor by Coordination to Metal Comple*
Ángeles Farran Morales	*New Macrocycles with Naphthyridine and Carboxamide Units*
Eduardo Laga Lazaro	*Funcionalización de aminoácidos catalizada por paladio*
Raúl Gotor Candel	*Colorimetric sensing of HCN (g) and cyanide in solution and gas phase*

13,20-15,30 Lunch at Faculty of Science

Session IV Chairman: Prof. José Ramón Pedro Llinares

15,30-16,00 Invited Lecture 5 **"Reacciones de adición conjugada de alquinos enantioselectivas"** Prof. Gonzalo Blay (University of Valencia).

16,00-17,10 Oral Communications 10-16

Ignacio Fdez de las Nieves	*Application of matrix assisted pulse gradient diffusion NMR on Persea caerulea fractions*
José Antonio González Delgado	*Aproximación biomimética hacia Apocarotenoides: Síntesis de Apotrisporina E y Apotrientrioles A-B*
Juan Manuel López Romero	*Synthesis of DMABI Non-Planar Chromophores*
Víctor Rojas	*Synthesis, conformational studies and activity of new S-linked GalNAc peptides*
Fernando Reyes Benítez	*MDN-0010, a siamycin-like peptide that potentiates the antifungal activity of caspofungin*
Azucena González Coloma	*Biotechnological production of biopesticides of botanical origin*
Sonia Abás Prades	*Cyclic α-iminophosphonates by the first diastereoselective [3+2]cycloadditon reaction of diethyl isocyanomethylphosphonate and maleimides*

17,10-17,30 Coffee Break

Session V Chairman: Prof. Ángel Gutiérrez Ravelo

17,30-18,00 Invited Lecture 10 **"Transition metal-catalyzed reactions: paving the way for enantioselective syntheses of natural products".** Dra. Yolanda Díaz (University Rovira-Virgili of Tarragona)

18,00-18,30 Oral Communications 17-19

Alicia Monleón Ventura	*Synthesis of densely functionalized 5-halogen-1,3-oxazin-2-ones by halogen-mediated regioselective cyclization of N-Cbz-protected propargylic amines: A combined experimental and theoretical study*

María de Gracia Retamosa Hernández	*Reactivity and scope of synthetic unnatural prolines as organocatalysts*
Emmanuel Vrancken	*Versatile Transition Metal-Catalyzed Uninterrupted Multi-Step Sequences To Di- And Trisubstituted Isoxazole Derivatives from Propargylic Alcohols.*

18,30-19,00 Poster Session

21,00- Symposium dinner "Palacio de los Córdova"

Friday June 21th, 2013

Session VI Chairman: Prof. Miguel Yus Astiz

9,30-10,00 Invited Lecture 11 "**The use of phenyliodine bis(trifluoroacetate) as both a reactant and a building block in oxidative C-C coupling"** Dr. Alexandr Shafir (UAB-ICIQ)

10,00-10,30 Invited Lecture 9 **"Aproximación a la Química de Cariofileno orientada a la diversidad estructural"** Dr. Antonio José Macías (University of Cádiz).

10,30-11,00 Poster Session

11,00-11,30 Coffee Break

Session VII Chairman: Prof. Isidro González Collado

11,30-12,00 Invited Lecture 7 **"A journety through Rh(I)-catalyzed [2+2+2] cycloaddition reactions: from mechanistic studies to the search of new catalysts"** Dra. Anna Pla Quintana (University of Gerona).

12,00-12,30 Oral Communications (20-22)

Félix Busqué Sánchez	*New Molecular Switches for Photoinduced Control of Neuronal Signaling with NIR Light*
Ana Sousa-Herves	*Multifunctional dendritic polyglycerol as a novel platform for paclitaxel delivery*
Vicente Blas Ferrando	*Synthesis of perylenediimide-phthalocyanine arrays*

12,30-13,00 Invited Lecture 12 "**Del laboratorio a la industria: ¿Misión imposible?** Prof. Andrés Garcia-Granados (University of Granada)

13,00 Meeting Closure and **"Aldrich Chemistry" best poster awards**.

13,30 **Lunch Closure**

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INVITED LECTURES

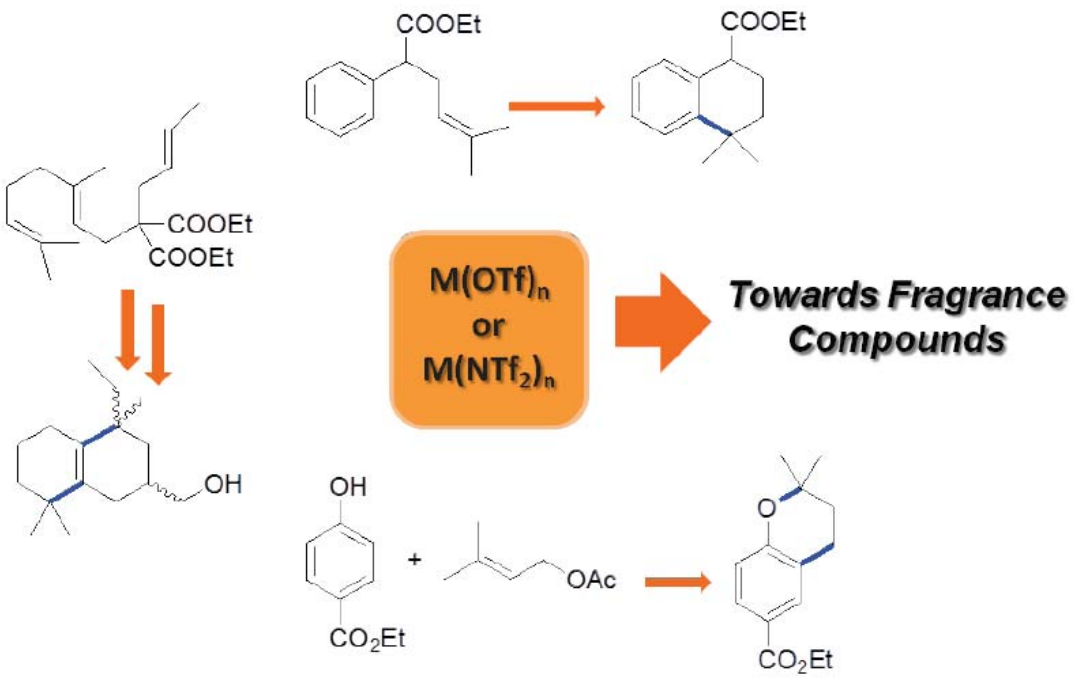
(IL-1) Catalytic activation of olefins by Lewis superacids: applications to fragrance chemistry

Elisabet Duñach

Institut de Chimie de Nice, Université de NiceSophia-Antipolis, CNRS, UMR 7272, 06108 NICE CEDEX 2, FRANCE dunach@unice.fr http://www.unice.fr/icn

The selective functionalisation of isolated C-C double bonds by nucleophiles using catalytic methods is still a challenge in organic synthesis.[1] We developed the catalysis by Lewis superacids derived from metallic triflates and triflimides[2] for the regiocontrolled additions and cyclisations to non-activated olefins.[3]

These catalysts are highly efficient for the cycloisomerisation of dienes[4] and polyenes,[5] as well as for hydroarylation processes.[6]



Applications of the Lewis acid catalytic methodology to the synthesis of target compounds of interest in the field of favours and fragrances with their olfactory evaluation will be presented.[7]

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(IL-2) Síntesis y Funcionalización de Dendrímeros para Aplicaciones Biomédicas

Ezequiel Pérez-Inestrosa,[1] Antonio Jesús Ruiz-Sanchez,[1] Pablo Mesa,[1] Isabel Morato,[1] Francisco Najera,[1] Daniel Collado[1] and Yolanda Vida[1]

1Departmento de Química Orgánica, Facultad de Ciencias, Universidad de Málaga, Campus de Teatinos, 29071 Málaga, España, y Centro Andaluz de Nanomedicina y Biotecnología-BIONAND, Parque Tecnológico de Andalucía, 29590-Málaga, España, e-mail: inestrosa@uma.es

Basándose en las innovaciones de la nanotecnología, se están investigando y desarrollando con éxito, nuevos métodos y materiales con propiedades innovadoras para aplicar en las principales áreas de investigación biomédica, como los nanosistemas terapéuticos, nanomateriales médicos, sistemas de diagnóstico, medicina regenerativa y biomateriales de implante, que en la actualidad están generando resultados favorables y prometedores.

Probablemente, los Dendrimeros representan las estructuras a escala nanométrica que están demostrando más y mejores expectativas para las aplicaciones biomédicas. Frente a los tres tipos de arquitecturas macromoleculares tradicionales (lineal, entrecruzada y ramificada), que generalmente conforman productos poli-dispersos de diferentes pesos moleculares, los Dendrímeros ofrecen la oportunidad de generar macromoléculas mono-dispersas, de arquitecturas controladas y similares a aquéllos observados en los sistemas de interés biológico.

Las posibles aplicaciones biomédicas de los Dendrímeros derivan de los tres dominios estructurales críticos que lo configuran: a) la multivalencia de la superficie, que contiene un número definido de sitios de interacción potencialmente reactivos o de reconocimiento, b) los espacios internos entre los brazos que rodean el centro y c) el centro al que se fijan las ramificaciones. Sobre estos tres dominios se desarrolla la potencialidad de los Dendrímeros en las aplicaciones biomédicas.

En esta comunicación se presenta la síntesis y la funcionalización de un nuevo tipo de sistemas dendriméricos (Dendrímeros y Dendrones) y su estudio en procesos de reconocimiento molecular, incluyendo las interacciones con el sistema inmunológico.[1]

Este nuevo tipo de Dendrimeros (***BAPAD***: ***B****is****A****minoalkyl****P****olyA****A****mide****D****endrimers)*,[2] se obtiene por el acoplamiento iterativo de di(beta-amino)ácidos preparados por reducción de los correspondientes grupos azido o nitro.

La versatilidad de estos Dendrímeros deriva de la aproximación sintética empleando los dinitro derivados, de acuerdo con la estrategia que se aplica en la construcción del Dendrímero.

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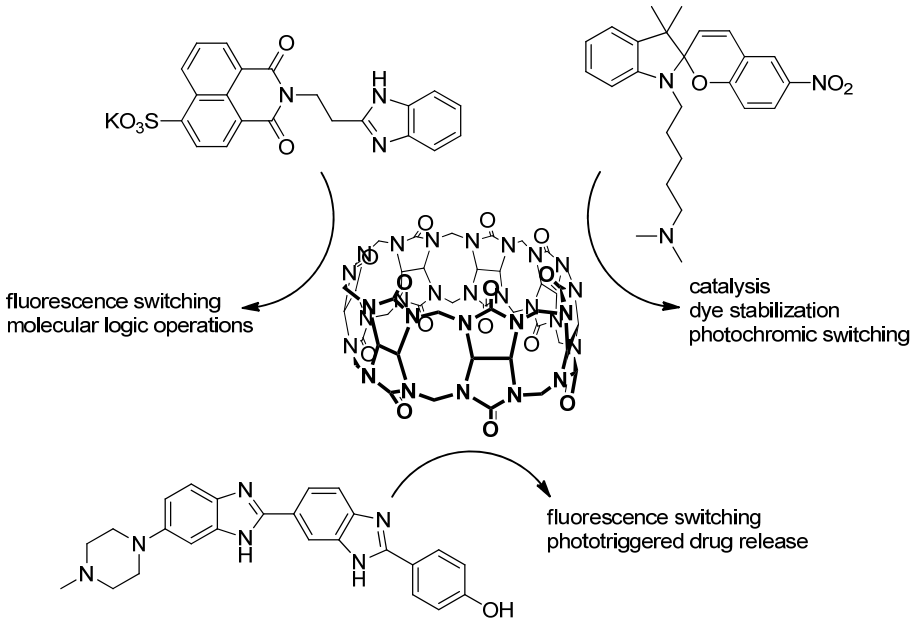
(IL-3) Cucurbiturils - nanocontainers for supramolecular chemistry in water

Uwe Pischel
CIQSO – Center for Research in Sustainable Chemistry and Department of Chemical Engineering, Physical Chemistry, and Organic Chemistry, University of Huelva, Campus de El Carmen, E-21071 Huelva, Spain

Cucurbiturils are water-soluble macrocycles that are composed of *n* glycoluril units (*n* = 5-8, 10) linked by methylene bridges. These container-type host molecules have two portals with electron-rich carbonyl groups and a hydrophobic cavity. Guests interact through hydrophobic effects exerted by the inner cavity and cation-π interactions at the portal. This identifies protonated polyamines or organic cations as preferred cargo. Currently the enormous potential of cucurbiturils in supramolecular chemistry and nanochemistry is unfolding, which is witnessed by applications in sensing, drug delivery, chemistry in confined spaces, *etc*.[1] This presentation will highlight our contributions to these developments and focuses on fluorescent and photochromic guests that provide an additional layer of functionality to supramolecular host-guest complexes.[2] In concrete I will discuss the applications of the resulting assemblies for molecular information processing,[3] phototriggered guest release,[4] and the stabilization of photochromic switches.[5]



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Acknowledgments
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(IL-4) Halogen Bonding Receptors for Anion Recognition and Sensing

Antonio Caballero,[1,2] Fabiola Zapata,[1,2] Sam Bennett[2], Lydia C. Gilday[2], Paul D. Beer[2]

1 Departamento de Química Orgánica, Universidad de Murcia, Campus de Espinardo, 30100, Murcia, Spain, e-mail: antocaba@um.es

2 Inorganic Chemistry Laboratory, Department of Chemistry University of Oxford South Parks Road, Oxford OX1 3QR (UK)

The term halogen bonding (XB) is used in analogy with the well known hydrogen bonding (HB) and is the noncovalent bonding interaction between halogen atoms that function as electrophilic centres (Lewis acids) and neutral or anionic Lewis bases. The origin of the attraction is attributed to a positive region on the halogen that corresponds to the electronically-depleted outer lobe of the R-X σ bond. The intermolecular force known as halogen bonding arises from the interaction of the positively charged σ-*hole* with electron donating species, resulting in a strongly linear geometry which maximises the interface of opposite charges.[1] To date, almost all the investigations into halogen bonding have been conducted in the solid state, crystal engineering of magnetic, conducting and liquid crystalline materials. Halogen bonding in solution is still in its infancy.

We report in this lecture our advances in the construction of new interlocked structures, pseudorotaxanes[2] and catenanes,[3] as well as anion receptor[4] and sensors[5] (Figure 1) using the halogen bonding as a driving force or as a binding site.

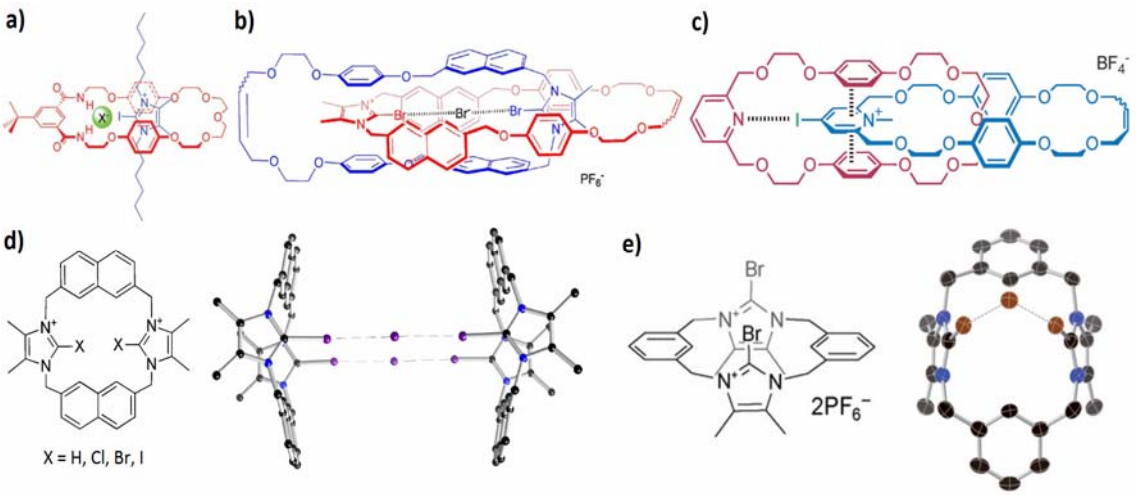

Figure 1: Structures of the different halogen bonding pseudorotaxane a) and imidazolium b) and piridinium c) catenanes. d) and e) Structures of the halogen bonding receptor and their corresponding X-ray of the iodide and bromide complexes.

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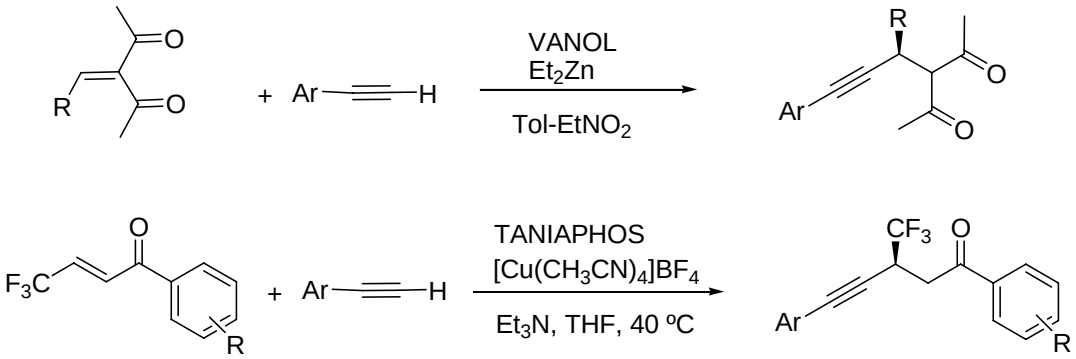
(IL-5) Development of catalytic asymmetric procedures for conjugate alkynylation of enones and related compounds

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

The conjugate addition of carbanionic species to electrophilic double bonds, i.e. unsaturated carbonyl compounds, is one of the most attractive methods for constructing a new C-C bond. Among the different kinds of carbon nucleophiles, terminal alkynes are of interest to create functionalized internal alkynes, which are versatile building blocks. An interesting case of these reactions results with unsaturated carbonyl and related compounds bearing β-substituents, where a new stereogenic center is formed, control of the enantioselectivity being crucial.

Enantioselective procedures for the conjugate alkynylation of enones and related compounds have been carried out by using pre-formed alkynyl organometallic reagents and different catalysts or chiral auxiliaries.[1] A more convenient approach from the environmental and atom-economy point of view is the generation of the reactive alkynyl-metal species from terminal alkynes and a catalytic amount of a chiral metal complex. Several successful examples of this approach have been reported by using Cu, Rh, or Co catalysts.[2] Despite these advances, there are still some matter of improvement related with low enantioselectivity, and substrate or alkyne scope.

In this lecture we will disclose our recent developments on the enantioselective conjugate alkynylation of enones and unsaturated esters, including the alkynylation of Knoevenagel adducts and 3-alkoxycarbonyl coumarins using zinc complexes[3] as well as the alkynylation of fluorinated enones under copper catalysis.



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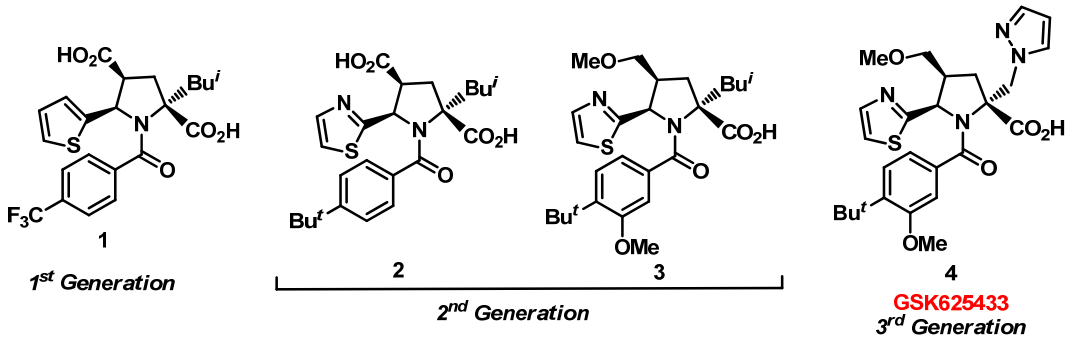
(IL-6) Enantioselective synthesis of intermediate products in the generation of hepatitis C virus inhibitors

José Miguel Sansano

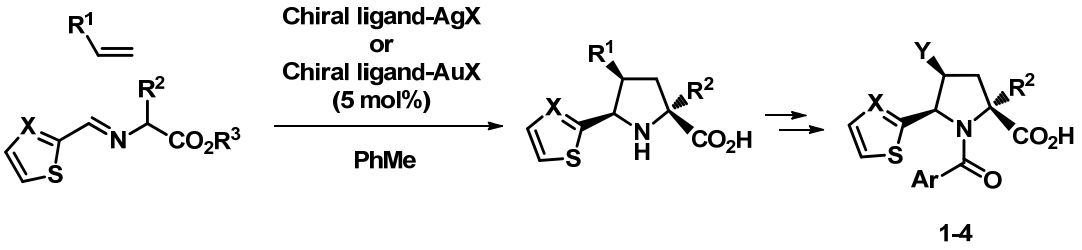
Departamento de Química Orgánica e Instituto de Síntesis Orgánica, Universidad de Alciante, 03080-Alicante (Spain), e-mail: jmsansano@ua.es

Hepatitis C virus (HCV)[1] attacks cells in the liver, where it multiplies (replicates) and causes liver inflammation and kills liver cells. HCV is the leading reason for liver transplants in the world and various treatments are designed to eradicate the virus and/or help slow or stop disease progression.[2] In this sense, promising *in vivo* results of proline-core GSK-antiviral agents (1st, 2nd and 3rd generations) were obtained several years ago.[3]



GlaxoSmithKline (GSK) hepatitis C virus inhibitors

These polysubstituted pyrrolidine-based precursors of molecules **1**-**4** can be easily obtained, in enantiomerically pure form, employing a chiral silver(I) or a chiral gold(I)-catalyzed 1,3-dipolar cycloaddition between stabilized azomethine ylides and acrylates. This key reaction step occurred under very mild conditions in very good yields and high enantioselections. Chiral phosphoramidites and (*R*)- or (*S*)-binap were the most appropriate and versatile ligands together with non-coordinating anions of silver(I) or gold(I) salts. The high enantiodiscriminations observed were carefully studied and supported by DFT/ONIOM calculations.[4,5] Additional steps to conclude the synthesis are well known conventional chemical processes.[6]



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(IL-7) A journey through Rh(I)-catalyzed [2+2+2] cycloaddition reactions: from mechanistic studies to the search for new catalysts

Magdalena Parera, Anna Dachs, Lídia Garcia, Anna Roglans, Anna Pla-Quintana

Departament de Química i Institut de Química Computacional i Catàlisi (IQCC), Universitat de Girona, Campus de Montilivi s/n, 17071 Girona, Spain, e-mail:anna.plaq@udg.edu.

One of the main goals of modern organic synthesis is to develop new reactions in which molecular complexity is rapidly increased. The transition metal-catalyzed [2+2+2] cycloaddition reaction of three unsaturated partners,[1] which allows for the formation of three new bonds in a single reaction step, is a nice example of such a reaction type. The transformation runs with total atom economy, facilitates a rapid increase in molecular complexity and is capable of effectively constructing a variety of polysubstituted hetero- and carbo-cycles. Therefore, it offers significant advantages in the development of economical, more ecological syntheses of complex synthetic targets.

Of the different metals that are able to catalyze the [2+2+2] cycloaddition reaction, our group at the University of Girona has focused on the use of rhodium. After a first block of studies devoted to the application of this cycloaddition reaction to polyunsaturated macrocycles[2] and to the preparation of value-added compounds such as non-proteinogenic aminoacids[3] and pyridines[4], our interest has now moved on to new aspects of the reaction. The search for new effective and recoverable catalysts for this transformation has led to the use of dendritic phosphoramidite ligands for the Rh-catalyzed [2+2+2] cycloaddition reactions allowing for an unprecedented enhancement of the enantiodiscrimination.[5] We have also applied the transformation to substrates with complex topologies and discovered a new reaction mechanism which explains the formation of isomers of the expected [2+2+2] cycloadducts.[6] Finally, given the great interest in understanding the reaction mechanisms so as to be able to improve these processes, we have undertaken a detailed study of the mechanism of the [2+2+2] cycloadition reaction by means both of ESI-MS and DFT calculations.[7]

This presentation will cover the most recent contributions of our group in these areas.

Acknowledgements.

We would like to thank the MINECO (CTQ2011–23121/BQU) and the AGAUR (2009SGR637) for financial support.

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(IL-8) Neoglycoconjugates based on β-cyclodextrin, dendrimers and nanoparticles for sensing and drug delivery

Juan M. Casas-Solvas, Manuel C. Martos-Maldonado, Ahmet Aykaç, Antonio Vargas-Berenguel

Department of Chemistry and Physics, University of Almería, Crta. Sacramento, La Cañada de San Urbano, 04120 Almería, Spain, e-mail: jmcasas@ual.es

Carbohydrates are the most abundant type of organic molecule on Earth. The ability of these molecules to act as energy reservoirs and building blocks was quickly established since their discovery in the mid XIX century. However, their capability to transfer biological information and take part in many biological recognition and adhesion events remained uncharted for years until the fact became evident that the outer surface of cells are coated with abundant sugars in the form of polysaccharides, glycolipids and glycopeptides (the *glycocalyx* "sweet husk"). Nature uses a special class of proteins named "lectins" (from the Latin "legere", to pick out or choose) to recognise and bind these sugars. Lectins have been demonstrated to be ubiquitous and, most importantly, able to discriminate among very similar oligosaccharides where structural differences are very subtle.[1] Such feature has been exploited for several applications which take advantage of the lectin-carbohydrate recognition and binding process. For example, an increasing number of biosensors which give a macroscopic response upon such interaction has been designed and constructed in the last decade.[2] These devices not only allow a deeper study of the mechanism of the molecular recognition but also have industrial and clinical uses. Furthermore, carbohydrates can also be used as bioreconocible vectors in site-specific drug delivery strategies. For instance, labeling drugs or drug carriers with carbohydrates which specifically interact with receptors that are over-expressed in cancer cells leads to their selective accumulation on these cells, which minimizes drugs toxicity toward healthy tissues.[3]

In the last few years our research group has been involved in the development of carbohydrate-containing derivatives, dendrimers and nanoparticles useful for lectins sensing. We chose ferrocene as a sensing moiety for these sugar-based biosensors since electrochemical methods demonstrate some advantages such as low cost and high sensitivity with relatively simple instrumentation. More importantly, they are well suited for operating in turbid and physiological media. In addition, we have designed site-specific drug delivery systems based on gold nanoparticles coated with β-cyclodextrins as macrocyclic drug carrier moieties and lactose as biological vectors for PNA and galectin-3 lectins.

Acknowledgments

The authors acknowledge the financial support from the Spanish Ministry of Economy and Competitiveness (Grant CTQ2010-17848), the Andalusian Government (Grant FQM06903), the EU Regional Development Fund and the EU through a Marie Curie ITN program (CYCLON 237962).

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(IL-9) Aproximación a la química de cariofileno orientada a la diversidad estructural

Antonio José Macías Sánchez

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Cádiz, Campus Universitario de Puerto Real, 11510 Puerto Real, Cádiz, e-mail: antoniojose.macias@uca.es

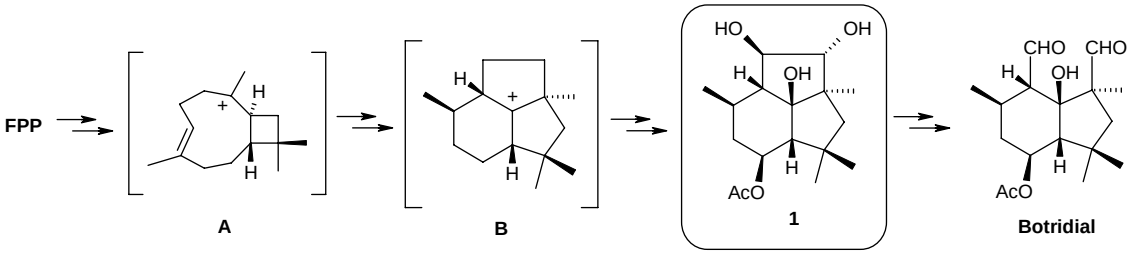
La denominada síntesis orientada a la diversidad ("diversity oriented synthesis" –DOS)[1] se ha desarrollado en la última década como una herramienta alternativa a la síntesis orientada al objetivo para la obtención de nuevas moléculas de interés en estudios de química genética y en el descubrimiento de nuevos fármacos. Este tipo de estudios pretenden explorar el denominado espacio químico, con el fin de buscar compuestos que interaccionen con las enzimas o los receptores adecuados.

Durante varios años, nuestro grupo ha abordado el control del hongo fitopatógeno *Botrytis cinerea*, mediante el estudio de metabolitos de bajo peso molecular implicados en procesos de infección. Uno de los metabolitos mejor estudiados es botridial, un factor de virulencia,[2] que promueve la muerte celular y posterior invasión del hongo.[3]

La biosíntesis de botridial y metabolitos relacionados implica la ciclación de pirofosfato de farnesilo (FPP) para originar un catión cariofilenilo (A), que evoluciona para dar lugar a intermedios de tipo presilfiperfolano (como por ejemplo **1**), a partir de los que se originan botridial y derivados.[4] La alteración de la biosíntesis de botridial puede conducir al control del hongo al eliminar uno de los factores de virulencia del mismo.[3]

El sesquiterpeno cariofileno proporciona la base para una amplia variedad de transformaciones que conducen a sesquiterpenos tricíclicos.[5] Aprovechando esta capacidad para la diversidad estructural, nuestro grupo de investigación ha abordado la preparación de un cierto número de sesquiterpenos tricíclicos como punto de partida de un método de control de *B. cinerea*.[6]

En esta presentación se discutirán las distintas aproximaciones abordadas, incluyendo reagrupamientos de los esqueletos de clovano e isocariolano que conducen a una destacada diversidad estructural y la obtención de nuevos esqueletos sesquiterpénicos.



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(IL-10) Transition metal-catalyzed reactions: paving the way for the enantioselective syntheses of natural products

Yolanda Díaz, Sébastien Soriano, Josep Llaveria, Mariam Azzouz, M. Isabel Matheu, Sergio Castillón

Departament de Química Analítica i Química Orgànica, Universitat Rovira i Virgili, C/ Marcel·lí Domingo s/n, Tarragona 43007, Spain, e-mail: yolanda.diaz@urv.cat

In the achievement of the synthesis of natural products, such as glycolipids, iminosugars, nucleosides, etc, and synthetic analogues thereof, our group has always been interested in the development of efficient methods for the enantioselective preparation of chiral synthons. In this regard, transition-metal catalyzed processes have boosted the construction of complex architectures, with high atom economy and, in an enantioselective manner, using chiral metal complexes.

This presentation will illustrate the contributions of our group to this field though enantioselective syntheses of a series of active molecules.[1] The talk will highlight the Pd-catalyzed allylic amination reaction[2] as one of the most powerful, versatile methods for the construction of carbon-nitrogen bonds for its easy manipulation, high activity and high enantioselectivity. We will describe our progress on the asymmetric Pd-catalyzed allylic amination reactions of linear allylic carbonates with different N-nucleophiles for the preparation of chiral branched allyl amine derivatives, showing that regioselectivity can be tuned by interplay of steric and hydrogen bonding interactions. Ruthenium-catalysed cross-metathesis of alkenes and stereoselective osmium-mediated dihydroxylation reactions will complete the repetoire of the metal catalyzed processes involved in the synthetic strategies presented.

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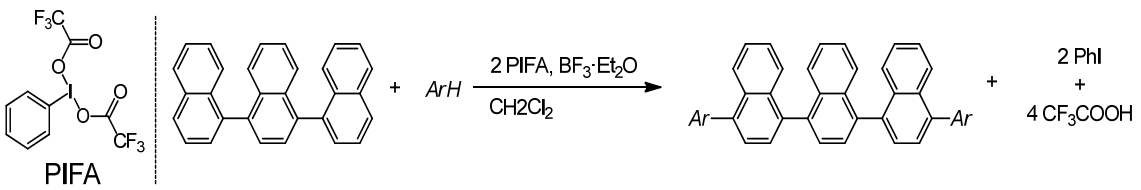
(IL-11) Phenyliodine bis(trifluoroacetate) as both a reactant and a building block in oxidative C-C coupling

Alexandr Shafir,[1,2] Wusheng Guo,[1] Zhiyu Jia,[1] Enrico Faggi,[1] Erik Gálvez, Rosa María Sebastián,[1] Adelina Vallribera[1], Roser Pleixats[1]

[1]*Department of Chemistry, Universitat Autònoma de Barcelona, Cerdanyola del Vallès (Barcelona) 08193 Spain*

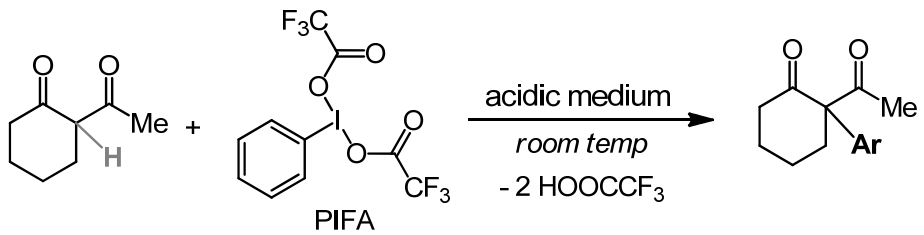
[2]*Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans 16, 43007, Tarragona, Spain, e-mail: ashafir@iciq.es*

Hypervalent iodine reagents, such as λ^3-iodanes, have found widespread use in oxidative reactions. The reactivity of the iodine center in such system is quite unique, resembling in some cases that associated with transition metals.[1] For this reason, in addition to being used as terminal oxidants in metal-catalyzed processes, hypervalent iodine has been found to promote interesting metal-free oxidative transformation, including direct C-C coupling. In this talk, recent progress in our laboratories[2] on the use of phenyliodine bis(trifluoroacetate) (**PIFA**) in constructing polyarenes *via* direct C-C coupling will be presented (Scheme 1).



Scheme 1. Direct arylation of the linear ter-naphthalene using PIFA-BF_3.

In addition to their role as oxidants, hypervalent iodine reagents also serve as building blocks in organic synthesis, as exemplified by the delivery of an aryl fragment by the diaryl λ^3-iodanes (e.g. Ph_2IX) under basic conditions.[3] Our results on the ability of PIFA to promote an alternative arylation pathway under acidic conditions will be presented here (Scheme 2).



Scheme 2. Arylation of a β-diketones under acidic conditions using PIFA.

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(IL-12) Del laboratorio a la industria: ¿Misión imposible?

Andrés García-Granados
Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Granada, Fuentenueva s/n, 18071 Granada, Spain. aparra@ugr.es

Cuando se realiza investigación en la Universidad española el paso del laboratorio a la industria es complejo si bien las circunstancias de cada especialidad y el planteamiento de este tránsito es, de hecho, muy variado.

En un extremo del abanico podemos considerar una investigación aplicada "bajo demanda", en la que el paso hacia la industria es iniciativa y responsabilidad de otros. En el otro extremo del mismo nos encontramos con la situación en la que, a partir de sus conocimientos y experiencias previas, el investigador decide iniciar la complicadísima labor de lo que ahora, a la fuerza, se ha puesto tan de moda como es la de ser "emprendedor".

Mi vocación y experiencia personal, y de la que por tanto puedo hablar con conocimiento de causa, es de esta faceta de iniciativa emprendedora y en un campo muy concreto como es el de la Química Orgánica y dentro de ella el sector o especialidad de Productos Naturales.

La realidad española es que desarrollar una investigación aplicada cuyos resultados puedan plasmarse en un período inferior a 5 años sólo está al alcance del que, además de tener esa vocación, no necesite currículum, porque es evidente que ni los resultados reales son publicables e incluso es dicutible (y discutiremos) que pueda y deba darse suficiente información en una patente que teóricamente "proteja" el fruto de esa investigación. Hasta hace muy poco los resultados en transferencia de tecnología no contaban ni como mérito ante la ANEP e incluso ahora cuentan de una forma un tanto discutible.

Otro problema intríseco para la transferencia de tecnología es el hecho de que cuanto más novedosa sea una idea, tanto más trecho le queda para ser llevada a la práctica. En su camino se producirán condicionamientos legales y de gestión por parte de tu Institución, condicionamientos económico-empresariales (aspectos que ya empiezan a quedar más lejos de nuestra profesión), y condicionamientos legales por parte de la Administración que constituyen un campo de minas en la que el enemigo, se diga lo que se diga, es el "emprededor", ensalzado en teoría pero obstaculizado en la realidad.

Desde una perspectiva, evidentemente sectorial y particular, pero con elementos comunes en muchos casos, intentaré desgranar las experiencias de mi Grupo de Investigación esperando que nuestro testimonio pueda ser de utilidad a los investigadores jóvenes que sientan la vocación de intentar recorrer este camino.

ORAL COMMUNICATIONS

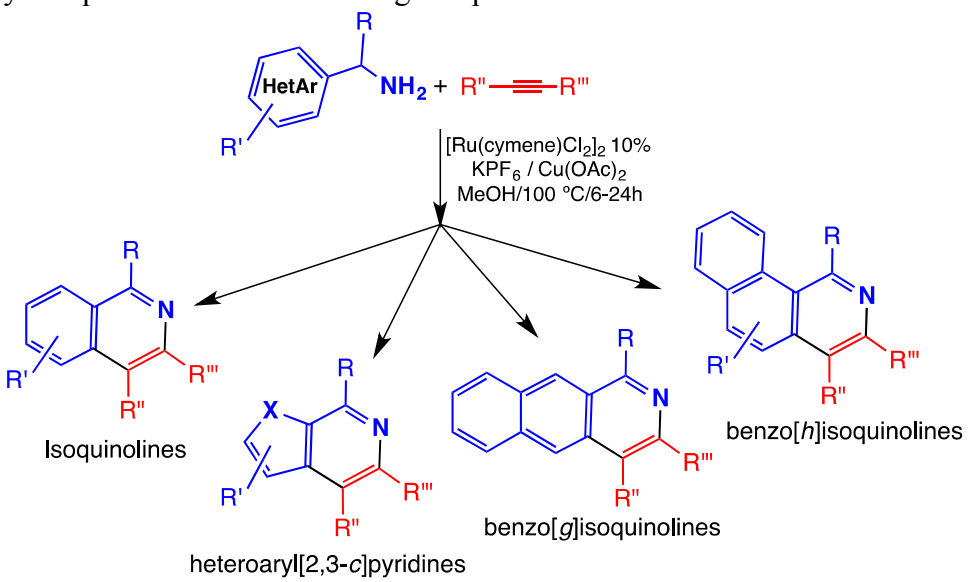
(OR-22) Ru-catalyzed oxidative coupling of (hetero)aryl derivatives with internal alkynes using primary amines as directing groups

Pedro Villuendas[1], Sara Ruiz[1], Esteban P. Urriolabeitia[1]

1 Instituto de Síntesis Química y Catálisis Homogénea, CSIC-Universidad de Zaragoza, Pedro Cerbuna 12, 50009 Zaragoza, Spain, e-mail: esteban@unizar.es

The isoquinoline core and related motifs containing heterocycle-fused pyridines are ubiquitous scaffolds among natural products or compounds with pharmaceutical and biological activity.[1] In spite of the existence of well established methods for their synthesis, isoquinolines, thienopyridines and other heterocycle-fused pyridines still are difficult to prepare in specific cases. The development of alternative pathways using conceptually different routes is still of high interest. In this respect, the use of transition metals to catalyse C-H functionalizations is a well-known synthetic strategy.[2]

One of the most successful metal-mediated methods for the synthesis of *N*-heterocycles is the directed oxidative coupling of internal alkynes with (hetero)aryl-based substrates, where the directing group in the (hetero)aryl moiety carries the N atom which is finally incorporated to the *N*-heterocycle. While imines and oximes were known to undergo this reaction,[3] the use of readily available unprotected primary amines as directing groups (see the Scheme) has not been reported before. In this communication we describe the Ru-catalysed oxidative coupling of primary amines with internal alkynes which affords a wide variety of isoquinolines, benzoisoquinolines and fused heteroaryl-pyridines. In addition of the broad range of targeted compounds achievable, different isomers of each one are accesible, and the presence of a large number of electron-attracting and -releasing substituents in different positions is tolerated. The method is actually competitive with standard organic procedures.



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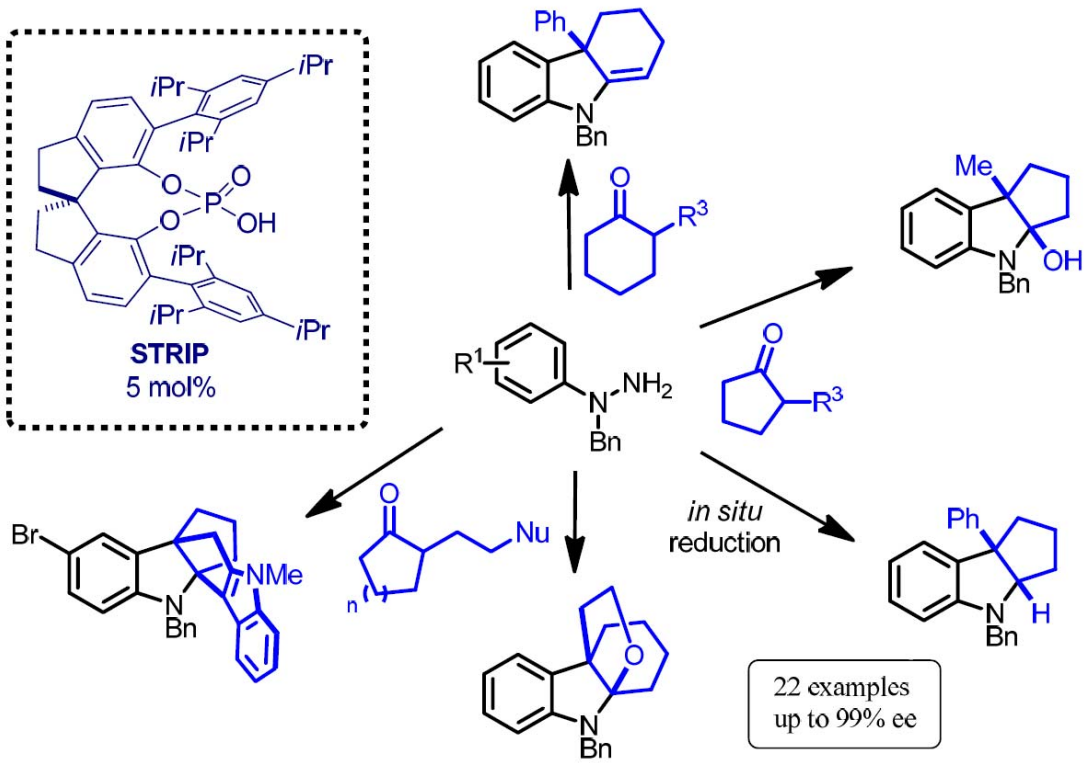
(OR-26) Versatile Access to Chiral Indolines by Catalytic Asymmetric Fischer Indolization

Alberto Martínez, Matthew J. Webber, Benjamin List
Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, D-45470 Mülheim an der Ruhr, Germany

Indoles are heterocyclic compounds widely distributed in nature, and their synthesis has attracted massive attention. The acid-mediated Fischer indolization of phenylhydrazones,[1] first reported over 120 years ago, remains one of the most widely used procedures for the construction of indoles. In 2011 our group reported the first catalytic asymmetric Fischer indolization promoted by a novel spirocyclic chiral phosphoric acid.[2] We speculated that this procedure, originally designed for the synthesis of chiral 3-substituted tetrahydrocarbazoles, could potentially have further-reaching applications in organic synthesis, just as the non-asymmetric version. Here we present that the chiral Brønsted acid (*R*)-STRIP is able to catalyze the asymmetric Fischer indolization of a range of monosubstituted cyclopentanones and cyclohexanones to give chiral fused indolines bearing a quaternary stereogenic center at the 3-position. The method has been extended to include substrates bearing a tethered nucleophile, thus allowing for enantioselective indolization/ring-closing cascades to complex propellanes featuring two vicinal quaternary stereocenters.[3]



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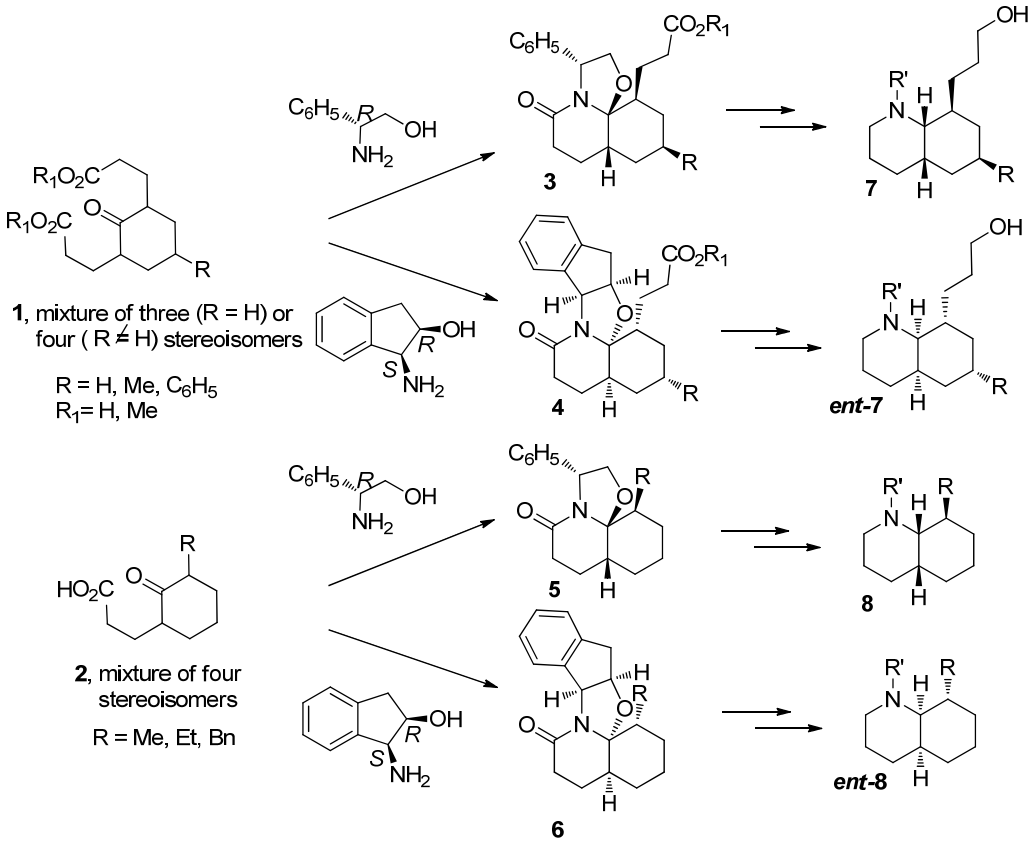
(OR-28) Highly Stereoselective Cyclocondensation Reactions. Enantioselective Synthesis of Substituted *cis*-Decahydroquinolines

Mercedes Amat, Elena Ghirardi, Rosa Griera, Laura Navío, Núria Llor, Joan Bosch
Laboratory of Organic Chemistry, Faculty of Pharmacy, and Institute of Biomedicine (IBUB), University of Barcelona, Av. Joan XXIII, s/n, 08028-Barcelona. e-mail: elena.ghirardi@ub.edu

Cyclocondensation reactions of (*R*)-phenylglycinol and (1*S*, 2*R*)-*cis*-1-amino-2-indanol with 2-oxocyclohexanepropionate derivatives **1** and **2** (racemates or mixtures of stereoisomers) stereoselectively lead to enantiopure lactams **3-6** in processes that involve the generation of up to four stereocenters in a single synthetic step via desymmetrization with differentiation of enantiotopic chains and/or dynamic kinetic resolution processes. A rationale for the stereochemical outcome of these highly stereoselective transformations will be presented.



Lactams **3-6** have proven to be useful precursors of a variety of diversely substituted enantiopure *cis*-decahydroquinolines **7** and **8** (R'= H, Boc).

Acknowledgements: Financial support from the MICINN, Spain (project CTQ2012-35250/BQU), and the DURSI, Generalitat de Catalunya (grant 2009-SGR-1111).

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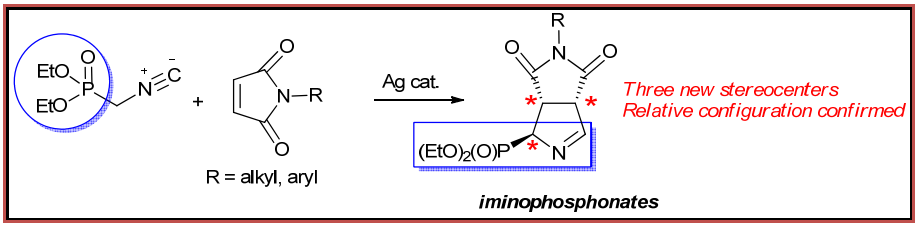
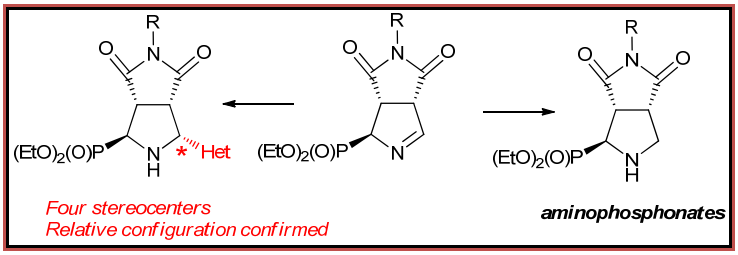
(OR-31A) Cyclic α-iminophosphonates by the first diastereoselective [3+2]cycloadditon reaction of diethyl isocyanomethylphosphonate and maleimides

Sonia Abás, Juan Molina, Carlos Arróniz, Judith Palà and Carmen Escolano
Department of Organic Chemistry, Faculty of Pharmacy, and Institute of Biomedicine (IBUB),University of Barcelona, Spain, e-mail: cescolano@ub.edu

The distinctive reactivity of isocyanoacetates has been recognised as an advantageous characteristic for the entrance to heterocyclic compounds. Amongst the synthetic possibilities that isocyanoacetates offer, [3+2] cycloaddition reactions with electron-deficient alkenes have been conceived as one of the most convergent approaches to the preparation of pyrrolines. Seeking new applications of isocyano derivatives and new strategies for accessing 1-pyrroline compounds, we envisaged the possibility of performing a [3+2] cycloaddition reaction between diethyl isocyanomethylphosphonate and maleimides. This original reaction gave direct access to cyclic iminophosphonates in good yields and with exclusive diastereoselectivity. In this reaction three stereocenters are generated in one synthetic step. The relative configuration of the new bicyclic compounds is determined unambiguously by X-Ray crystallography. Based on the stereochemistry of the final products a putative mechanism is proposed for this new reaction.[1]



The obtained new compounds are highly functionalised and two transformation possibilities are considered. In this sense, reduction of the imine double bond was easily performed to prepare cyclic aminophosphonates. α-Aminophosphonates, the phosphonic analogues of α-aminoesters, are interesting as chiral building blocks for constructing peptidomimetic structures. Moreover, the addition of nucleophiles to the imine bond has occurred diastereoselectively generating a new stereocenter which relative configuration has been determined.



Acknowledments
Finnancial support from the Ministerio de Ciencia e Innovación (MICINN), Spain (Project CTQ2009-07021/BQU), and AGAUR, Generalitat de Catalunya (2009-SGR-1111).

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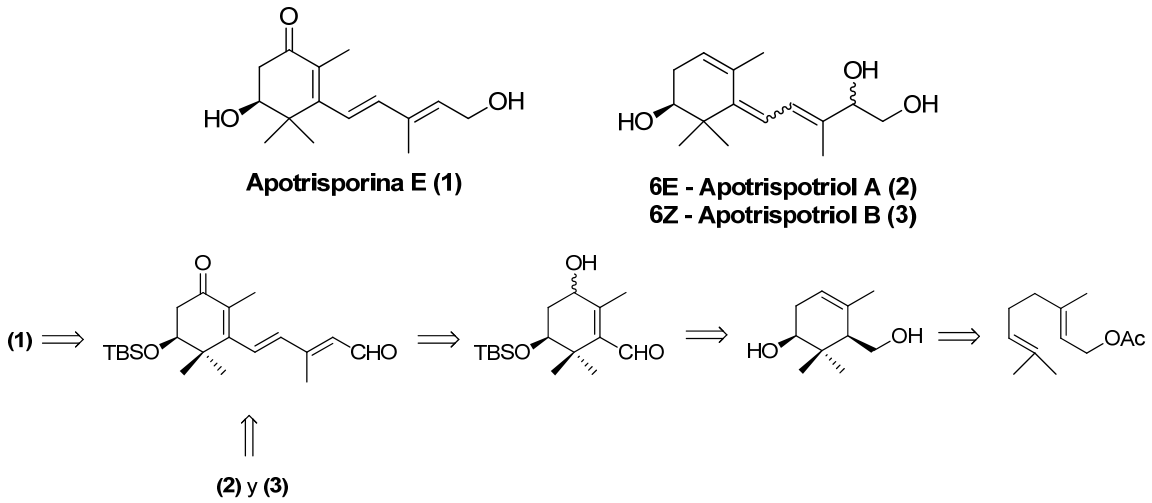
(OR-34) Aproximación biomimética hacia Apocarotenoides: Síntesis de Apotrisporina E y Apotrientrioles A-B

José Antonio González Delgado,[1,2] Jesús F. Arteaga,[2] M. Mar Herrador del Pino[1], Alejandro Fernández Barrero[1]

[1]*Department of Organic Chemistry, Institute of Biotechnology, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: afbarre@ugr.es*

[2]*CIQSO-Centre for Research in Sustainable Chemistry and Dept. of Chemical Engineering, Physical Chemistry and Organic Chemistry, University of Huelva, Campus el Carmen, 21071 Huelva, Spain*

Los compuestos Apotrisporina E **(1),** Apotrientriol A **(2)** y Apotrientriol B **(3)** son apocarotenoides identificados por primera vez en 1986 y 2012 respectivamente en cultivos de hongos mucorales como *B. trispora* y *P. blakesleeanus*.[1] En esta comunicación se describe por primera vez la puesta a punto de una aproximación sintética hacia apocarotenoides del tipo de los trisporoides (C18) y monociclofarnesanos (C15) basada en una etapa clave de ciclación biomimética regioselectiva catalizada/mediada por Cloruro de Titanoceno[2] (proceso radicalario) y por ácido de Lewis ($ZrCl_4$)[3] (proceso carbocatiónico). Como ejemplo de la viabilidad de esta estrategia se describe la síntesis **1-3,** donde también se aplicará un acoplamiento HWE para introducir la cadena lateral triénica.



Los compuestos obtenidos han servido para confirmar las estructuras y estereoquímicas propuestas por vía espectroscópica y para la realización de ensayos de actividad carotenogénica e inductora de la sexualidad en *Phycomyces blakesleeanus*.

Agradecimientos

Se agradece al Ministerio de Economía y Competividad la ayuda recibida, Proyecto CTQ2010-16818-BQU.

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(P-038) Synthesis of DMABI Non-Planar Chromophores

Juan Manuel López–Romero,[1] Manuel Doña–Flores,[1] Jesús Hierrezuelo,[1] Rodrigo Rico,[1] Martins Rutkis[2]

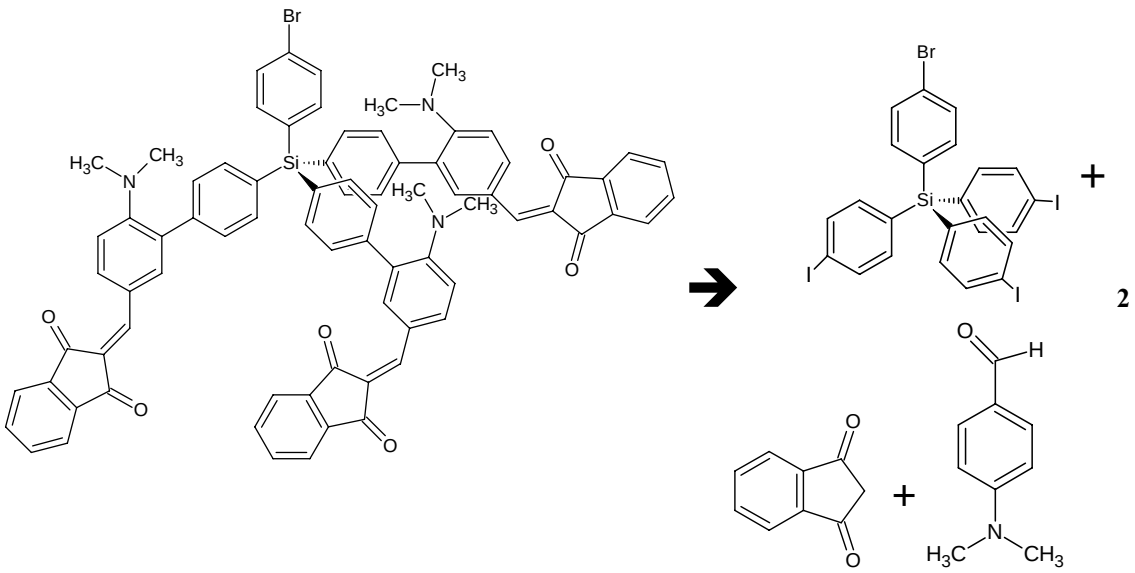
[1] *Dept. of Organic Chemistry, Faculty of Sciences, University of Málaga, 29071 Málaga, Spain.*

[2] *Institute of Solid State Physics, University of Latvia, 8 Kengaraga st., Riga, LV-1063, Latvia.*

e-mail: jmromero@uma.es

A group of molecules that are being investigated for their use as chromophores, having optical and induced electrical properties, are indanedione derivatives having an electron-donor and electron-acceptor group in the same molecule structure.[1] Among them, 2-(*N*, *N*–Dimethylaminobenzyliden)indan-1,3-dione (DMABI) derivatives possess excellent optical properties since they have a high dipolar photoinduced electron transfer, occurring in an intramolecular and reversible way in the molecule.[2]

The objective in this work is the synthesis and structural characterization of the DMABI derivative **1**. The synthesis has been carried out in five steps starting from *p*–(*N*,*N*–dimethylamino)benzaldehyde, indanodione and the triphenyl silicon derivative **2**.[3] Synthetic details will be reported in the poster presentation.



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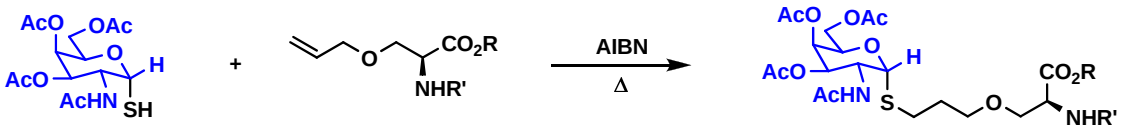
NOTE: this communication was finally presented as poster.

(OR-39) Synthesis, conformational studies and activity of new *S*-linked GalNAc peptides

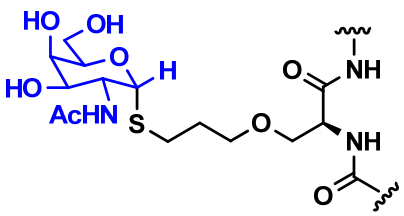
Víctor Rojas, Francisco Corzana, Alberto Avenoza, Jesús H. Busto, Jesús M. Peregrina
Department of Chemistry, Centro de Investigación en Síntesis Química (CISQ), University of La Rioja, C/Madre de Dios, 51, 26006 Logroño, La Rioja, Spain. e-mail: victor.rojas@unirioja.es

In the last years, our group developed a research line that involved the design of new glycopeptides with well-defined conformational preferences, which is based on the incorporation of non-natural amino acids in the glycopeptidic sequence.[1] These studies showed that the presentation of the carbohydrate moiety had a marked influence on the activity.[2] Using cross metathesis reactions, we also carried out structural modifications of the length of the side chain that connect the carbohydrate and the peptide backbone, with the aim of discovering new forms of orientation of the carbohydrate respect to the backbone.[3]

In this work we have carried out the chain elongation of the specific Tn-residue (GalNAc-α-O-Ser/Thr), which is a human specific tumor-associated carbohydrate antigen. In this case, we used the efficient hydrothiolation reaction between 3,4,6-tri-*O*-acetyl-2-acetamido-2-deoxy-1-thio-α-D-galactopyranose and allyl-serine derivatives to generate *S*-linked glycopeptides.



Moreover, we have obtained valuable intermediates using orthogonal deprotection reactions, to finally gain a Tn mimic, with ends in form of diamides. This class of compounds has been studied from their conformational viewpoint using Nuclear Magnetic Resonance and Molecular Dynamics, and their biological activities are under evaluation.



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(OR-41) Water as Efficient Hydrogen-Atom Donor by Coordination to Metal Complexes

Araceli G. Campaña,[1] Miguel Paradas,[1] Tania Jiménez,[1] Irene Rodríguez-Márquez,[1] Elena Buñuel,[2] Diego J. Cárdenas,[2] Juan M. Cuerva.[1]

[1]*Department of Organic Chemistry, Faculty of Science, University of Granada, Campus Fuentenueva, Avda. Severo Ochoa, s/n, E-18071, Granada, Spain, e-mail: araceligc@ugr.es*

[2]*Department of Organic Chemistry, Universidad Autónoma de Madrid, Campus de Cantoblanco, 28049, Madrid, Spain.*

Efficient proton and electron transfer lies at the heart of the remarkable success of energy conversions in photosynthesis and respiration. In many biological systems proton transfer (PT) is coupled to electron transfer (ET) allowing the assembly of thermodynamically favoured reaction pathways, and avoiding high-energy intermediates.

Here we show theoretical evidences of an unprecedented water mediated long-range PCET process between metal complexes (Figure 1).[1] Water mediates the long-range proton-coupled electron transfer between two Cu complexes separated by 11 Å in the peptidylglycine α-hydroxylating monooxygenase (PHM) cofactor. The proposed mechanism, which involves three H-atom exchanges, accounts for long-range electron transfer in metalloenzymes, and may be ubiquitous in nature.

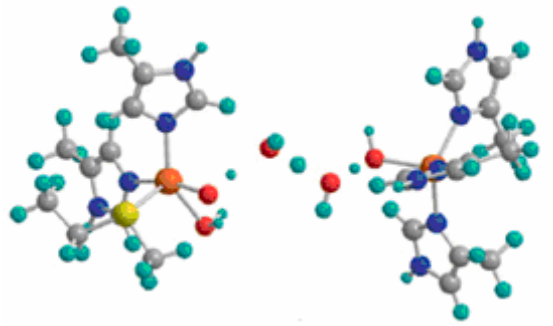

Fig 1.: Structure of the transition state for the proton-coupled electron transfer between Cu complexes.

Taking into account that aquo or hydroxo complexes of other transition metals are generally present in vital processes in nature, those complexes could also play an essential role in many organic synthetic reactions. In this sense, water would be an extraordinary safe and cheap hydrogen atom transfer (HAT) reagent in the reduction of carbon-based radicals. Therefore in recent years, solid evidence of HAT reductions involving water as hydrogen atom source have been presented.

Water becomes an excellent hydrogen atom donor in the presence of bis(cyclopentadienyl)titanium(III) chloride (Cp_2TiCl) towards carbon radicals. In this work we also show that the efficiency of Ti(III) aqua complexes as an unique class of HAT reagents is based on two key features: (a) excellent binding capabilities of water towards titanocene(III) complexes and (b) a low activation energy for the HAT step.[2]

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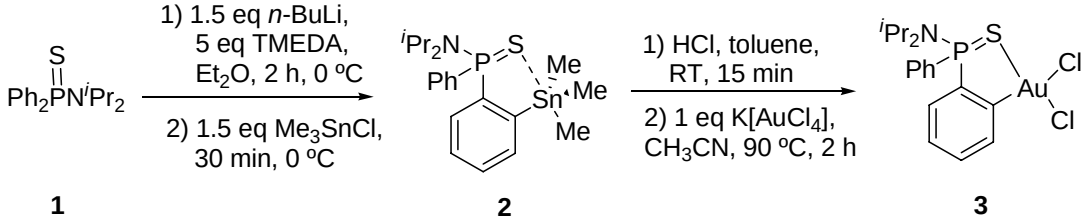
(OR-43) GOLD NANOPARTICLES AS EFFECTIVE CATALYST OF THE THREE-COMPONENT COUPLING BETWEEN ALDEHYDES, AMINES AND ALKYNES

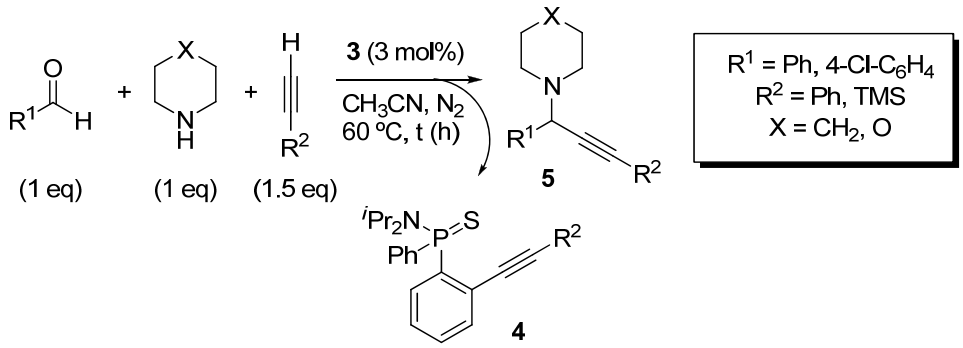
Belmonte, E.; Hajjouji, H.; García-López, J.; Fernández, I.; Iglesias, M. J.; El Laghdach, A.; López Ortiz, F.
Universidad de Almería, Almería, 04120, España. email: evebs89@hotmail.com

Gold(III) complexes are nowadays the focus of great attention due to their applications as catalyst in organic synthesis[1]. We have developed a method of synthesizing cycloaurated gold(III) phosphinothioic amide-based molecules starting from their *ortho*-tin derivatives in excellent yields[2]. The gold(III) phosphinothioic complex **3** was prepared according to Scheme 1.



Scheme 1. Procedure for the preparation of the Au(III) complex **3**.

The new Au(III) complex has been applied in a three-component coupling process (A^3) of aldehydes, alkynes and amines (Scheme 2). In this way, a variety of propargylamines **5** were obtained in good yield under very mild reaction conditions.



Scheme 2. Three-component coupling reaction mediated by complex **3**.

Structural studies of the reaction showed that complex **3** decomposes into *o*-alkynylphosphinothioic amide **4** and gold nanoparticles. The latter proved to be the real catalyst. These nanoparticles were characterized through TEM and XPS analysis. The results obtained indicate that the catalytic species consist of Au(I) nanoparticles of a diameter of 2-3 nm. Further applications of complex **3** are under investigation.

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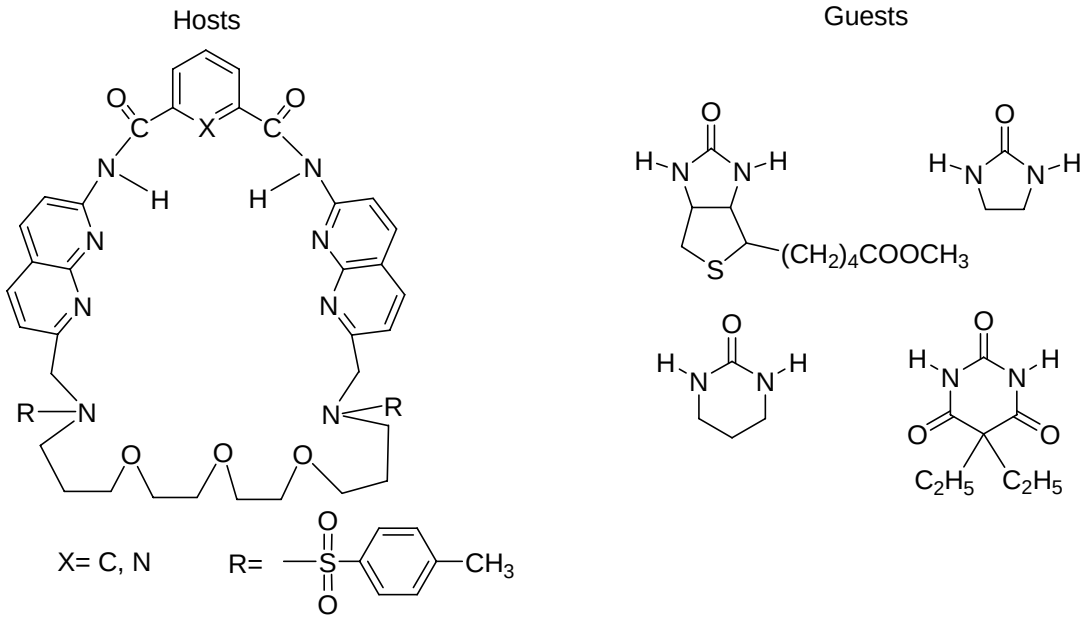
(OR-45) New Macrocycles with Naphthyridine and Carboxamide Units

M.A. Farrán[1], D. Santa María [1], M.A. García[1], R.M. Claramunt[1], G.J. Clarkson [2]
1 *Departamento de Química Orgánica y Bio-Orgánica, UNED, Paseo Senda del Rey 9, 28040 Madrid, Spain, e-mail: afarran@ccia.uned.es*
2 *Department of Chemistry, University of Warwick, University Library Rd. CV4 7AL Coventry UK.*

We present here a series of new macrocylic hosts designed to interact with biotin and other ureas through multiple hydrogen bonds giving rise to improved binding constants.[1] They are symmetrical macrocycles containing benzenedicarboxamide or pyridinedicarboxamide moities, and two naphthyridine units bonded by a chain of 17 atoms, whose structures are depicted in the Scheme below.



All complexes were modeled by Molecular Mechanics calculations (Monte Carlo Conformational Search, AMBER force field) and minimum energies associated to the most stable structures were calculated.[2] Experimental binding constants were measured by ^{1}H NMR titrations in non polar solvents monitoring the changes in N-H carboxamide group chemical shifts. In most cases a good correlation with the predicted minimum energies for the complexes.was found.

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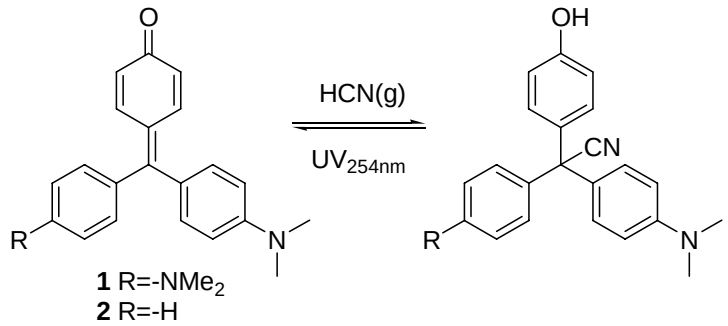
(OR-55A) Colorimetric sensing of HCN (g) and cyanide in solution and gas phase

Raúl Gotor[1], Ana M. Costero[1], Salvador Gil[1], Margarita Parra[1], Ramon Martínez-Mánez[2], Félix Sancenón[2], Pablo Gavina[1]

Centro de Reconocimiento Molecular y Desarrollo Tecnológico (IDM),Unidad mixta Universidad Politécnica de Valencia-Universidad de Valencia, Spain. [1]Departamento de Química Orgánica, Universitat de València, Dr. Moliner 50, 46100, Burjassot, Valencia., e-mail: raul.gotor@uv.es
[2]Departamento de Química, Universidad Politécnica deValencia, Camino de Vera s/n, 46022, Valencia.

Cyanide anion is considered an extremely hazardous chemical for physiological systems[1]. However, cyanide is commonly used in different industrial activities. On the other hand, the gaseous form of cyanide (hydrogen cyanide) is also of concern. In fact, HCN is categorized as a chemical warfare under the class of blood agents. Detection of cyanide in liquid samples has been achieved by means of several methods and colorimetric chemosensors are of special interest because of their relative low cost, selectivity and the possibility of "naked-eye" detection, without the use of expensive non portable devices[2]. Nevertheless, it is apparent from the literature that many reported chromogenic chemosensors for cyanide anion also display sensing features for HS- which is one of the most important interferents in the design of probes for cyanide. Besides, the number of probes for the selective detection of hydrogen cyanide in gas phase is scarce[3]. In the present communications we report the synthesis, characterization and behaviour as colorimetric probes for cyanide in aqueous solution and HCN in gas phase of two new triarylcarbocation derivatives. One of the prepared probes shows kinetic selectivity between CN- and HS- and besides differentiation between these two anions could easily be achieved by the known photo-dissociation of leucocyanides after UV irradiation[4]. In addition, remarkable limits for the detection of CN- in water were achieved. Moreover, probe 1 adsorbed on aminated silica was successfully used for selective detection of HCN in gas phase with a limit of detection of 2 ppm.



Scheme 1. Reaction scheme for probes **1** and **2** in the presence of HCN (g), and its reversible reaction under UV light

This outstanding results, both in selectivity and in sensitivity for detection of CN- in aqueous solution and HCN in gas phase make the prepared chemosensors useful for a wide range of applications.

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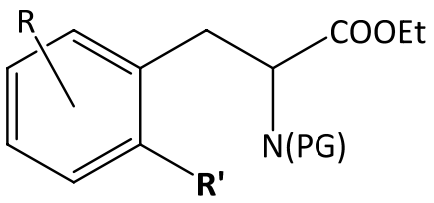
(OR-58) Funcionalización de aminoácidos catalizada por paladio

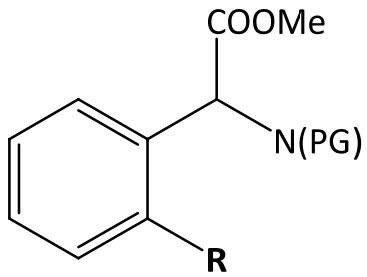
E. Laga[†*], A. García-Rubia[‡], E. P. Urriolabeitia[†], C. Cativiela[†], J. C. Carretero[‡]
‡Dept. Química Orgánica, Univ. Autónoma de Madrid, c/Francisco Tomás y Valiente, 7, 28049, Madrid.
†Instituto de Síntesis Química y Catálisis Homogénea (CSIC-Univ. de Zaragoza), c/Pedro Cerbuna, 12, 50009, Zaragoza. Tfno.: 876553525; e-mail: elaga@unizar.es

La funcionalización de un aminoácido puede llevar a la modificación de la actividad de la macromolécula donde se integra, permitiendo regular controladamente la actividad de esta última. Una herramienta muy útil de funcionalización es la activación dirigida de enlaces C-H por metales de transición, aunque hasta ahora se han descrito muy pocos ejemplos de funcionalización catalítica de aminoácidos.[1] La introducción de grupos directores auxiliares coordinantes, como el grupo 2-piridilsulfonilo, ha demostrado ser muy eficaz en la funcionalización de sustratos poco reactivos, como la arilación de aminoácidos en posición Csp^3-H,[2a] o la reacción de alquenilación de tipo Fujiwara-Moritani.[2b]

En este trabajo se presenta la funcionalización de derivados de fenilalanina, catalizada por paladio y utilizando el grupo 2-piridilsulfonilo como auxiliar director. Se ha llevado a cabo de forma eficaz la alquenilación de fenilalaninas con un amplio rango de olefinas. La reacción ocurre con retención de la configuración en la posición □ y es compatible con una gran variedad de grupos funcionales en el anillo aromático. Una pequeña modificación de este método permite la funcionalización catalítica de fenilglicinas dando lugar a la obtención de sustratos halogenados, por acoplamiento C-X, alcoxilados (C-O) y alquenilados (C-C).



R = -H, p-OMe, p-I, p-Me
R' = -CH=CH-EWG



R = -Cl, -Br, -I, -O-,
-CH=CH-EWG

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(OR-60B) Application of matrix assisted pulse gradient diffusion NMR on *Persea caerulea* fractions

Ignacio Fernández[1], Juan Manuel Álvarez Caballero[2,3], Álvaro Raya Barón[1], Alegría Carrasco[4], Luis Enrique Cuca Suárez[2] and Alberto Fernández Gutiérrez[4]

[1] *Department of Chemistry and Physics, University of Almeria, Ctra. Sacramento s/n, 04120 Almeria, Spain, e-mail: ifernan@ual.es*

[2] *National University of Colombia, Cr 30 No 45-03, Bogotá, Colombia*

[3] *University of Magdalena, Cr 32 No 22-08, Santa Marta, Colombia*

[4] *Department of Analytical Chemistry, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain.*

Polyphenols, including flavonoids, are well-known antioxidants, present in a large number of plant origin matters, and have a wide range of recognized biological activities including anticancer, antimalarial, anti-inflammatory, and antiviral. Analysis of mixtures of natural products commonly employs HPLC that can be time-consuming and surely expensive. NMR is one of the most powerful tools in the elucidation of structures, where diffusion NMR methods has become an important approach for many chemists interested on unravelling problems in complex mixtures, molecular volumes estimation, hydrogen-bonding interactions, or aggregation states issues. However, the application of this kind of method becomes more difficult when diffusion coefficients are very similar or spectra are highly overlapped. Very recently, it has been shown that performing DOSY in a matrix which can interact differentially with the analytes can resolve signals from similar compounds that would otherwise show the same diffusion behaviour.[1] Several matrixes have been used for these purposes, which include SDS micelles, soluble polymers such as polyvinylpyrrolidone or polyethyleneglycol, and regular or revered silica.

We report herein: 1) the isolation and structural elucidation of two flavonoids glycosides from *Persea caerulea*, a specimen mainly located in Colombia, Ecuador and Venezuela; 2) resolution of this mixture by means of matrix assisted PFG (Pulse Field Gradient) diffusion NMR measurements in SDS micelles, and 3) understanding of the interactions produced between the different flavonoids glycosides and the SDS-micelles.

The gross structures of these two flavonoids were elucidated by analyses of NMR, ESI-TOF and ESI-IT MS/MS spectra which were all in agreement with literature data. The stereochemistry of the sugar moieties were deduced from analyses of DQF-COSY and NOESY spectra together with their ^{1}H-^{1}H coupling constants.

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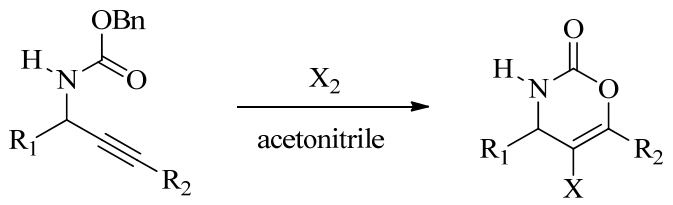
(OR-61) Synthesis of densely functionalized 5-halogen-1,3-oxazin-2-ones by halogen-mediated regioselective cyclization of *N*-Cbz-protected propargylic amines: A combined experimental and theoretical study

Gonzalo Blay, Luis R. Domingo*, Alicia Monleón and José R. Pedro*
Department of Organic Chemistry, University of Valencia, C/ Dr. Moliner, 50, 46014 Burjassot, Valencia, Spain, e-mail: alicia.monleon@uv.es

Typically the activation of the carbon-carbon triple bond against nucleophilic attack is based on the formation of a cationic metal complex[1] or an incipient halonium ion.[2] The electrophilic cyclization of functionalized alkynes possessing a nucleophilic group in close proximity to the triple bond constitutes an important strategy in the construction of a great variety of heterocycles and carbocycles.[3]

Very recently we have reported a convenient method for the synthesis of chiral nonracemic *N*-benzyloxycarbonyl-protected propargylic amines (*N*-Cbz) by the addition of terminal alkynes to imines generated in situ from α–amido sulfones in the presence of diethylzinc and BINOL-type ligands as catalyst.[4] We envisioned that the *N*-Cbz-protected propargylic amines must be suitable substrates to prepare densely functionalized 1,3-oxazin-2-ones or oxazolidin-2-ones (cyclic carbamates) through an *O*-halocyclization process. Cyclic carbamates represent an important class of compounds that show interesting properties in pharmaceutical or agrochemical areas.[5]

In this communication, we report a very efficient synthesis of 5-halogen-1,3-oxazin-2-ones by regioselective halocyclization reaction of chiral non-racemic *N*-Cbz-protected propargylic amines using I_2, Br_2 and Cl_2 as electrophile sources. In order to support the observed results, the mechanism for this reaction was investigated using DFT methods at the B3LYP/6-311G* level.



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2 (X = I)
3 (X = Br)
4 (X = Cl)

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(OR-62) MDN-0010, a siamycin-like peptide that potentiates the antifungal activity of caspofungin

Noureddine El Aouad, Maria Cândida Monteiro, Jesús Martín, Ignacio González, Sara Palomo, José R. Tormo, Ignacio Pérez-Victoria, Olga Genilloud, Francisca Vicente, Fernando Reyes

Fundación MEDINA, Centro de Excelencia en Investigación de Medicamentos Innovadores en Andalucía, Parque Tecnológico de Ciencias de la Salud, Avda. del Conocimiento 3, 18016-Granada, Spain, e-mail: fernando.reyes@medinaandalucia.es

Invasive fungal infections (IFI) along with the increase in the immunocompromised patient population are characterized by diagnostic difficulties and extreme mortality with fatality rates ranging from 30% to 80% in neutropenic patients.[1] To combat these life-threatening infections, only a limited number of antifungal agents are available. Among them, the most frequently used are amphotericin B and triazole drugs, targeting the fungal cell membrane, a structure common to all eukaryotic cells.[2] The echinocandins are the most recent class of antifungal agents and inhibit the synthesis of β-D-glucan in fungal cell wall, a selective target. However, in spite of significant efforts made over the last years, IFI are still a major cause of morbidity and mortality in immunocompromised patients.[3] The alarming numbers and the lack of effective medicines have driven the search for new, broad-spectrum fungicidal agents which include reformulating existing antifungals as well as the search for synergistic compounds or compounds able to potentiate the effect of known antifungal drugs that can be used for treatment and prophylaxis.[4] Examples reported previously of a synergistic effect among known antifungals and natural products include punicalagin with fluconazole,[5] and natural phenolics with amphotericin B, fluconazole and itraconazole.[6] It has also been demonstrated that the combination of echinocandins with a range of structurally diverse antimicrobial peptides results in potent synergistic killing of *Candida* spp. *in vitro*.[7]

As part of our program focused on the discovery of new natural products potentiating the antifungal effect of caspofungin, we observed that extracts of the actinomycete *Streptomyces* sp. were able to inhibit the growth of *Candida albicans* when combined with a sublethal dose of the fungicide. Bioassay-guided fractionation of these extracts led to the isolation of MDN-0010, a new peptide structurally related to the antiviral siamycins I and II, as the molecule responsible for the detected biological activity. Data on the rational followed during the screening campaign, the structural elucidation of the new molecule and its biological activity will be presented.

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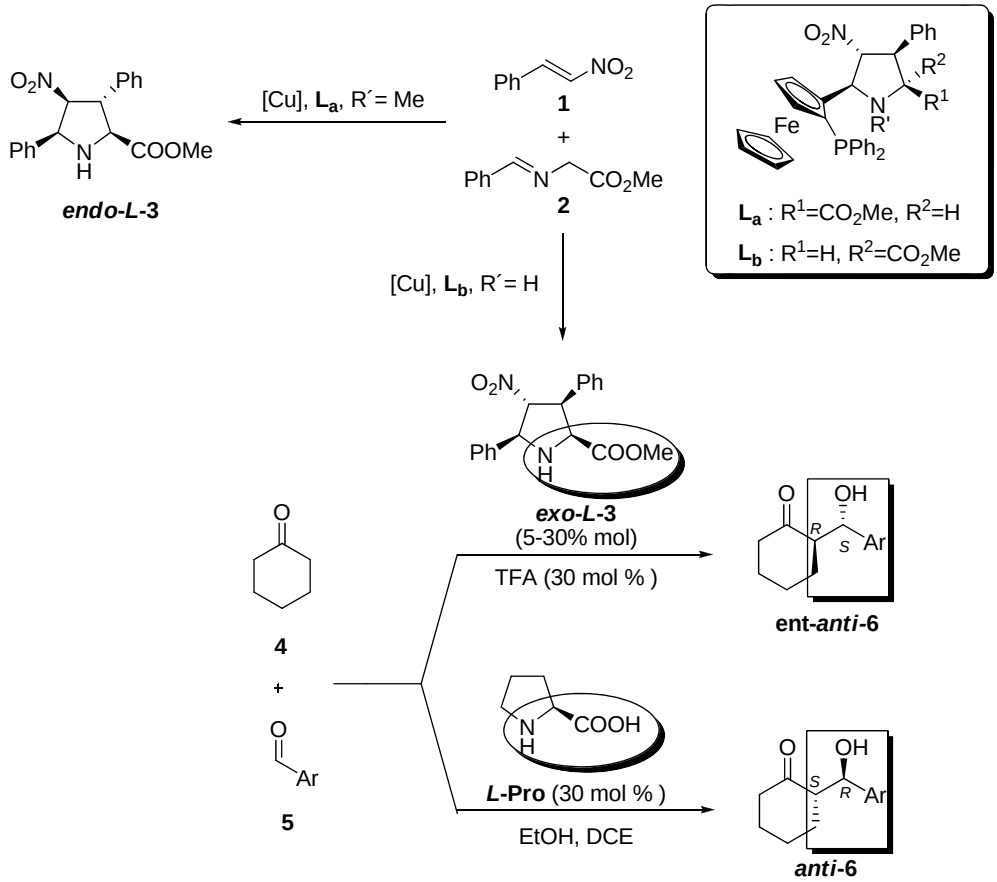
(OR-64) Reactivity and scope of synthetic unnatural prolines as organocatalysts

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

Departamento de Química Orgánica I, Universidad del País Vasco-Euskal Herriko Unibersitatea, 20018 San Sebastián-Donostia, Spain, P. Manuel de Lardizabal 3.

(mariadegracia.retamosa@ehu.es)

Recently, the synthesis of hybrid ferrocene-pyrrolidine ligands $\mathbf{L_a}$ and $\mathbf{L_b}$ via (3+2) cycloadditions has been described by our group[1]. These novel ligands, in the presence of copper (I) salts, successfully provided densely substituted unnatural proline derivatives **3** with excellent regio- and enantiocontrol. In turn, these densely substituted pyrrolidines **3** have been used as organocatalysts in aldol reactions[2] yielding adducts **6**. These latter compounds possess the opposite stereochemistry obtained when natural L-Proline is used as organocatalyst. Other variables such as organocatalyst structure, catalyst load, reaction rate, additives and temperature have also been studied.



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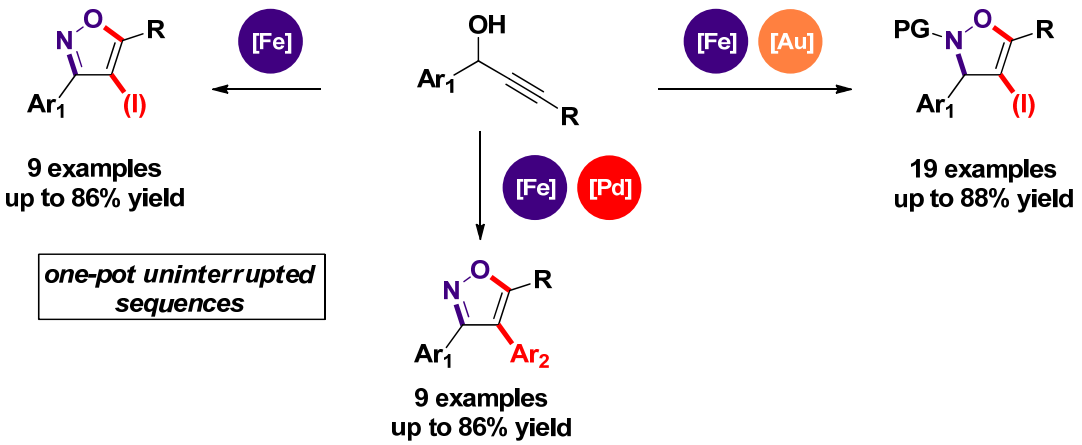
(OR-77) Versatile Transition Metal-Catalyzed Uninterrupted Multi-Step Sequences To Di- And Trisubstituted Isoxazole Derivatives from Propargylic Alcohols.

Eric Gayon,[1] Emmanuel Vrancken[1] and Jean-Marc Campagne[1]
Institut Charles Gerhardt, UMR 5253 UM2, CNRS, ENSCM, UMI; AM2N, 8 Rue de l'Ecole Normale - 34296 Montpellier Cedex 5 emmanuel.vrancken@enscm.fr

Increasing research efforts are directed toward the development of new methodologies with high synthetic efficiency and atom economy. To achieve this goal, synthetic chemists have shown great interest for one-pot, multi-step sequences of reactions. These are inherently more efficient since they avoid the isolation and purification of intermediates required for traditional iterative synthetic methods.[1] Isoxazole derivatives exert interesting biological activities and are core components of many pharmaceutically valuable compounds.[2] In this communication, our efforts to build up uninterrupted multi-step one-pot sequences to obtain fully various isoxazoles and isoxazolines derivatives from readily available propargylic alcohols using Fe, Au and Pd catalysts will be presented.[3]



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(OR-79) New Molecular Switches for Photoinduced Control of Neuronal Signaling with NIR Light

Marta Gascón[1], Mercè Izquierdo[2], Pau Gorostiza[2,3], Rafael Yuste[4], Ramon Alibés[1], Félix Busqué[1] and Jordi Hernando[1]

[1]*Departament de Química, Universitat Autònoma de Barcelona, 08193 Campus de Bellaterra, Barcelona, Spain, felix.busque@uab.es*

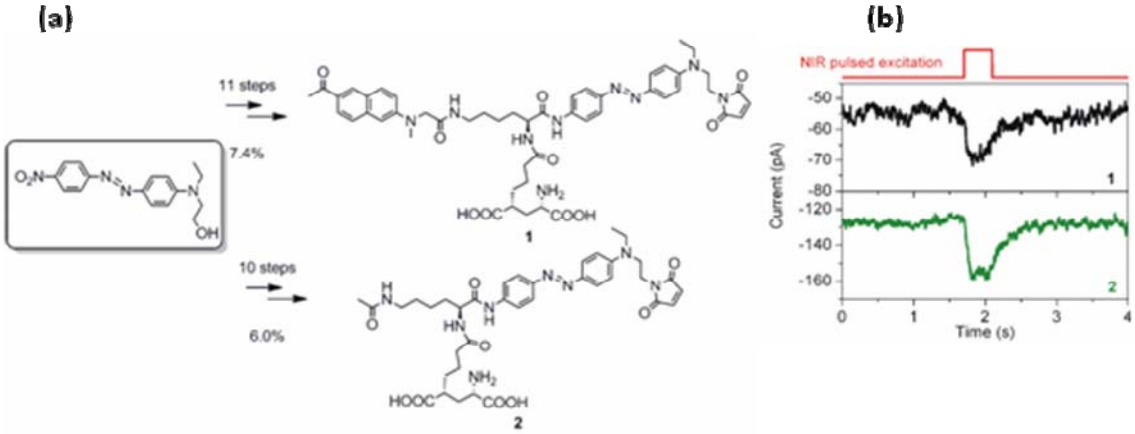
[2] *Institute for Bioengineering of Catalonia (IBEC), Spain*

[3]*Institució Catalana de Recerca i Estudis Avançats (ICREA), Spain*

[4]*Department of Biological Sciences, Kavli Institute for Brain Science, Columbia University New York, USA*

The development of optical methods and molecular photoswitches for remote control of biological functions is a emerging area of research.[1] Gorostiza et al. have showed that photoinduced *trans-cis* isomerization of azobenzene derivatives using UV-vis light allows the ion channels in neurons to be gated on demand.[2] Despite their successful performance, operation of these systems under irradiation with NIR light would be desired, since it has more penetration depth, with less damage, in biological tissues than UV-vis light.

Herein we report a novel strategy to develop molecular photoswitches driven by NIR light to allow light-induced control of the neuronal ion channels regulated by ionotropic glutamate receptors (iGluR). An additional unit has been incorporated to the original photoswitch structure reported. This new fragment should act as a sensitizer, absorbing NIR light via a non-linear optical process and then transferring its excitation energy to the azobenzene group, which should undergo photoisomerization. Thus, target compound **1** and reference compound **2** have been synthesized (Scheme 1) and upon NIR irradiation of cells conjugated with these compounds, reversible photoinduced currents were measured, validating our strategy to develop NIR-responsive switches for biological applications.



Scheme 1: (a) Syntheses of molecular photoswitches **1** and **2**. (b) Changes in current measured for neuronal cells incubated with compounds **1** and **2** upon irradiation with NIR light.

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(OR-87) New energy transfer cassettes based on Coumarin-BODIPY dyads

Gonzalo Durán-Sampedro,[1] Lorena López-Martínez,[1] Antonia R. Agarrabeitia,[1] Inmaculada García-Moreno,[2] Angel Costela,[2] Eduardo Peña Cabrera[3], María J. Ortiz[1]

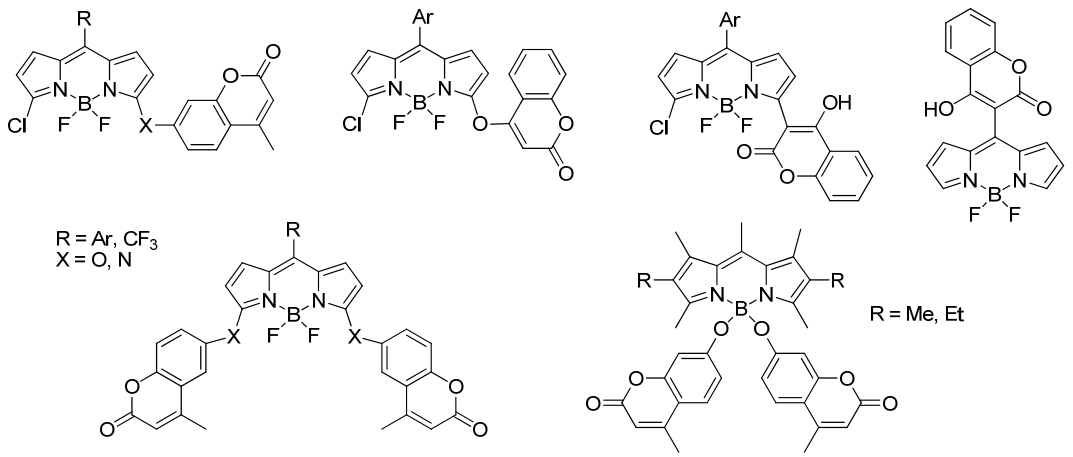
1Department of Organic Chemistry I, Complutense University of Madrid, Avda. Complutense s/n, 28040 Madrid, Spain, e-mail: mjortiz@ucm.es

2Department of Physical Chemistry, Institute Quimica-Fisica "Rocasolano", C.S.I.C., Serrano 119, 28006 Madrid, Spain.

3Department of Chemistry, University of Guanajuato, Col. Noria Alta S/N Guanajuato, Gto. 36050 México

Highly luminescent material have attracted considerable attention over the past decades due to their outstanding optical properties and they have found widespread applications such as laser dyes, biomolecular markers, photonic devices, chemical sensors and sensitizers for photodynamic therapy.[1] Since it is still difficult to design single organic dyes with desirable photophysical properties for certain applications, has recently been paid to exploring architectures multifluorophores donor-acceptor energy. In this regard, energy-donor-acceptor systems have been constructed, including rhodamine, fluorescein, coumarin, boron dipyrromethane (BODIPY) and cyanine derivatives.[2] Specifically, there are only two examples of coumarin-BODIPY dyads. Thus, Lin *et al.*[3] have prepared ratiometric sensing of fluoride anions and Guo *et al.*[4] have synthesized through-bond energy transfer cassettes based on these fluorophores.

Herein, we present a new series of systems where we have connected the coumarin donor to the BODIPY acceptor through C-C, C-O or C-N bonds in different positions.



Through-bond energy transfer processes induced in the new dyes allow recording high efficient and stable laser emission in the red spectra region pumping the solutions at 355 nm.

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(OR-94) Multifunctional dendritic polyglycerol as a novel platform for paclitaxel delivery

Ana Sousa-Herves,[1] Pia Welker,[2] Patrick Würfel,[2] Kai Licha,[2] Jayant Khandare,[1] Marcelo Calderón[1], Rainer Haag[1]

1Institut für Chemie und Biochemie, Freie Universität Berlin, Takustrasse 3, 14195 Berlin, Germany, e-mail: ana.sousa@fu-berlin.de

2 mivenion GmbH, Robert-Koch-Platz 4, 10115 Berlin, Germany

In the last years, polymer-drug conjugates have emerged as promising platforms to improve the therapeutic value of many low molecular weight drug candidates by increasing their water solubility, bioavailability, and their blood circulation time.[1]

Recently, increased attention has been paid to dendrimers as drug carriers because of their monodispersity, multiple sites of attachment and controllable, well-defined size and structure.[2] Thus, the covalent attachment of drugs to dendritic scaffolds is a promising route for controlling the loading and release of the active species. In addition, the inherent multivalency of dendrimers allows the simultaneous incorporation of different molecules of interest, such as imaging agents, targeting ligands, or biocompatible molecules.

In this presentation we will report the synthesis and in vitro studies of cleavable polymer–drug conjugates derived from biocompatible dendritic polyglycerol [3] (dPG) and ester-bearing paclitaxel. More specifically, we have prepared macromolecular conjugates based on neutral dPG and anionic dendritic polyglycerol sulfate [4] (dPGS) that can be cleaved both by esterases and by the acidic pH typically found in solid tumors and in the intracellular compartments endosome/lysosome. The cleavage properties and cytotoxicity values obtained for the new conjugates will be presented. Furthermore, the cellular uptake of dPG and dPGS-paclitaxel conjugates labelled with a fluorescent dye has been evaluated and will be discussed.

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(OR-103) Synthesis of perylenediimide-phthalocyanine arrays

Vicente M. Blas-Ferrando,[1] Javier Ortiz,[1] Fernando Fernadez-Lazaro[1], Ángela Sastre-Santos[1,*]

1 División de Química Orgánica Instituto de Bioingeniería, Universidad Miguel Hernández, Elche 03202, Spain. e-mail: asastre@umh.es

Molecular and supramolecular architectures composed of arrays of photoactive moieties ordered in a suitable disposition are of interest because upon selective light excitation of a given chromophore they can undergo directional multi-step electron and/or energy transfer processes. In this direction, phthalocyanines (Pcs) have attracted much attention because their singular electronic properties, and have been combined with a large number of electron-poor systems. On the other hand, perylenediimides (PDIs) have demonstrated exceptional photochemical stability, strong absorption of visible light, and high fluorescence quantum yields. Due to these features, PBI derivatives have been used as active components in organic field-effect transistors and photovoltaic cells. In the last few years, an increasing number of PDIs covalently linked to additional electro-active moieties have been reported, thus broadening the scope of their potential applications.
During the last few years we have been involved in the synthesis and characterization of interesting molecular and supramolecular eletroactive systems based mainly on Pcs and PDIs as building blocks [1]. Herein, we will report the more recent results obtained in our group related with the synthesis of the phthalocyanine-perylenedimides arrays [2] (Figure 1) mainly focussed in the synthesis of electron transfer systems, together with the photoinduced electron transfer properties for their application as artificial photosynthetic systems and in organic photovoltaics.

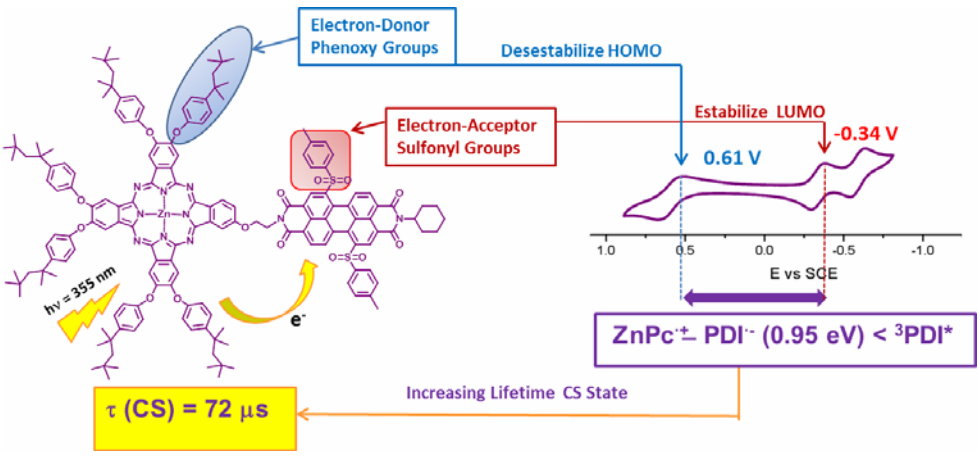

Figure 1. Phthalocyanine-Perylenediimide system with a long-live charge separated state

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(OR-120) Biotechnological production of biopesticides of botanical origin

A. González-Coloma[1], C. E. Díaz[2], A. F. Barrero[3], M. M. Herrador del Pino[3], A. González Portero[2], P. Arteaga Burón[3], J. F. Arteaga[4], J.Burillo[5]

.[1]*Instituto de Ciencias Agrarias, CSIC, Spain.* [2]*Instituto de Productos Naturales y Agrobiología, CSIC, Spain.* [3]*Dpt. Química Orgánica, Instituto de Biotecnología, U. de Granada, Spain.* [4]*Dpt. Ingeniería Química, Fisíco Química y Química Orgánica, U. de Huelva, Spain.* [5]*CITA, Zaragoza, Spain*

Endangered-rare plant species have been selected as being good sources of bioactive and valuable compounds. *Artemisia granatensis* Boiss. (Royal chamomile) (Asteraceae) is a small aromatic perennial bush endemic to Sierra Nevada and its presence has been reduced to scree deposits and rocky areas at high altitude (2400-3220 m). At present it is seriously endangered and protected by the EU Habitats Directive. Despite the medicinal and ecological interest of this plant there is only one report on the presence of eudesmanolides in the aerial part[1].We have successfully cultivated *A. granatensis* in artificial systems (plants in artificial soil and transformed *in vitro* roots) to generate enough plant biomass (aerial and root) for its chemical and biological study [2]. A new eudesmanolide (**17**) along with six sesquiterpenes (**11-16**), nine monoterpenes (**2-10**), one nor-monoterpene (**1**), three acetylenic spiroacetal enolethers (**18-20**) and one coumarin (**21**) have been identified from the aerial plant ethanolic extract. Acetylenic spiroacetal enolethers **18-19** and coumarins **21-23** have been isolated from the transformed root ethanolic extract. Significant insect antifeedant properties were determined for the aerial plant extract, spiroacetals **19-20** and secoguaianolides **13**+**14** and **16**.

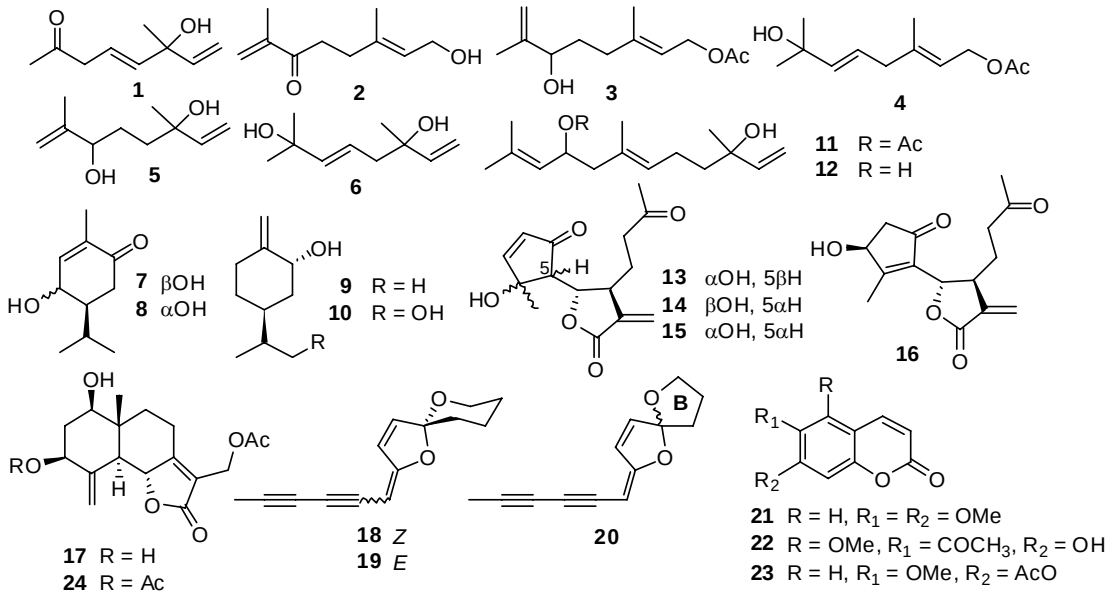

Fig. 1. Compounds isolated from aerial parts (**1-21**) and transformed roots (**18**, **19**, **21-23**) of *Artemisia granatensis*.

This work has been supported by Junta de Andalucía (Excellence Project P08-FQM-3596) and a JAE-CSIC predoctoral Fellowship to A.G. Portero.

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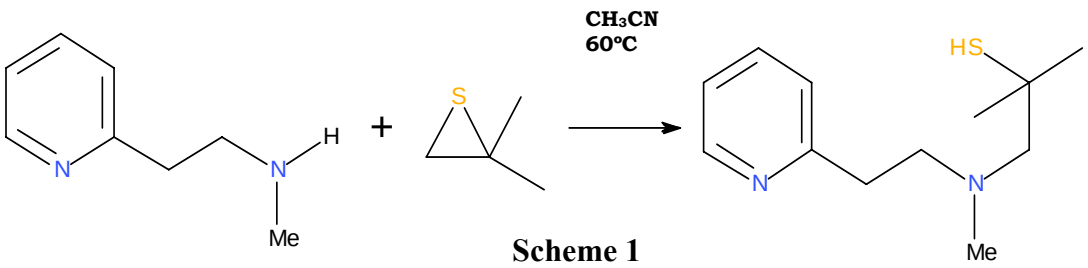
POSTERS

(P-021) Synthesis and study of bimetallic complexes of Ni(II) with ligands type N_2S as analogs of active sites of metalloenzymes

Alejandro Cabrera García[1], David Benjamín Guzmán Ríos[1], Pedro Martín Zarza[2], Pedro Esparza Ferrera[2], Ángel Gutiérrez Ravelo[3], Javier González Platas[4]

[1]Máster Universitario en Investigación en Química, Intensificación en Química Orgánica, [2]Dpto. Química Inorgánica, [3]Dpto. Química Orgánica, [4]Dpto. Física Fundamental II. Universidad de La Laguna

The study of modeling compounds, which reproduce the nature spectroscopic properties and reactivity of the active sites of metalloenzymes, has been a topic of great interest in which representing the knowledge of the behavior of these systems[1,2]. We propose here the preparation of the PATH ligand [3,4] (Scheme 1) and two of its complexes with Ni(II),



Scheme 1

[Ni(PATH)](ClO_4) and [Ni(PATH)](SCN). X-ray diffraction crystallography studies have shown bimetallic nature of the both complexes, with peculiar coordination environments to Ni(II).

Besides these structural studies, both complexes have been studied by UV-vis electronic spectroscopy, ^{1}H and ^{13}C Nuclear Magnetic Resonance spectroscopy, thermogravimetric analysis and by electrochemical techniques.

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(P-023) New advances in Titanocene(III) chemoselectivity: Barbier-type reaction vs homolytic epoxyde opening.

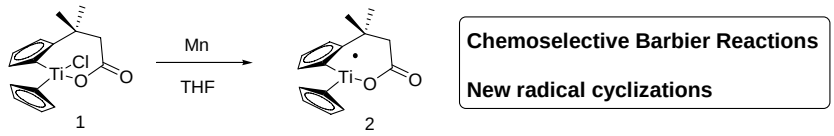
Sara P. Morcillo,[1] Ángela Martínez-Peragón,[1] Verena Jakoby,[2] Andreas Gansäuer,[2] José Justicia,[1] and Juan M. Cuerva[1]

[a] *Department of Organic Chemistry, Faculty of Sciences, University of Granada, C. U. Fuentenueva s/n, 18071 Granada, Spain*

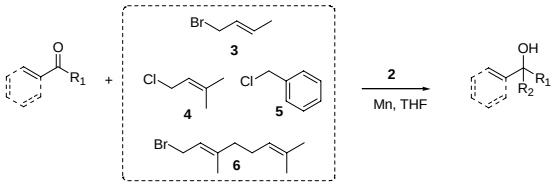
[b] *Kekulé-Institut für Organische Chemie und Biochemie Universität Bonn Gerhard-Domagk-Strasse 1, 53121 Bonn, Germany. e-mail: samorcillo@gmail.com*

Titanocene(III) complexes are nowadays useful tools in organic synthesis, thus promoting different kind of reactions (pinacolizations, Barbier's type reactions, epoxide opening, etc.) under smooth reaction conditions depending on the nature of the starting material.[1] However, the lack of chemoselectivity towards certain functional groups is a weakness of these titanium(III)-based reactions. In this sense, we hypothesized that a fine tuning of the electronic and/or steric properties of a tailor-made titanocene(III) complex could solve these drawbacks.

In the present communication, we describe that titanium carboxylate **1** in the presence of Mn dust yield a chemoselective titanocene(III) complex **2** able to promote Barbier-type reactions,[2] being compatible with the presence of activated carbonyl groups and/or epoxides. This reactivity is unprecedented in Ti(III)-chemistry, showing the potential versatility of these complexes in organic synthesis.



It is also remarkable that the Barbier reaction using prenylic halides as pronucleophiles takes place exclusively with α-selectivity,[2] which is difficult to obtain using other methodologies.



In these studies we were mainly interested in to build efficiently epoxypolyprene structures for subsequent uses in terpene synthesis.

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(P-024) Synthesis and photophysics of a new family of fluorescent 9-alkyl substituted xanthenones

Ángela Martínez-Peragón,[1] Delia Miguel,[1] Luis Crovetto,[2] José M. Álvarez-Pez,[2] Rocío Jurado,[1] José Justicia[1] and Juan M. Cuerva.[1]

[1] *Department of Organic Chemistry, Faculty of Sciences, University of Granada*

[b] *Department of Physical Chemistry, Faculty of Pharmacy, University of Granada*

Fluorescein and its derivatives are extensively used for visualization and diagnostic in biological and medical applications due to their high fluorescence quantum yield in aqueous media and easy conjugation with biomolecules.[1]

Until now, it was considered that the aryl group at C-9 is essential to preserve the strong fluorescence that characterizes fluorescein and some its derivatives.

In the present communication, we have demonstrated that the requirement of an aryl group at C-9 is no longer needed, and 9-alkyl xanthenones with different aliphatic pedant groups can be prepared and purified, without loss of the fluorescence properties (Figure 1). These compounds represent a breakthrough in the comprehension of the optical properties of fluorescein taking into account the similarities between the properties of the new derivatives and such parent compound. Therefore, new fluorescent sensors can be easily developed.

The use of new derivatives as sensors entails a full understanding of the complex photophysics of the dyes. Therefore, we have also studied the excited-state proton-transfer reactions promoted by phosphate buffer that interconvert the two prototropic forms existing at the physiological pH, as it happens in fluorescein[2] or other xanthene derivatives[3] (Figure 2).

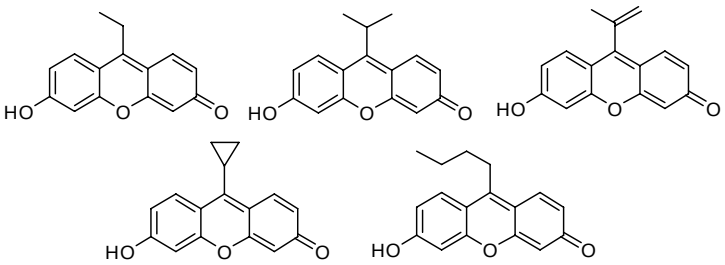

Figure 1

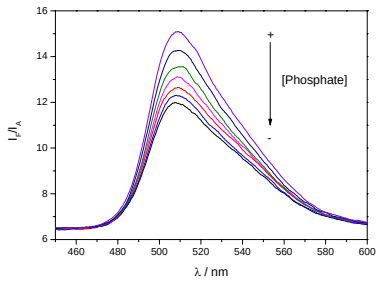

Figure 2

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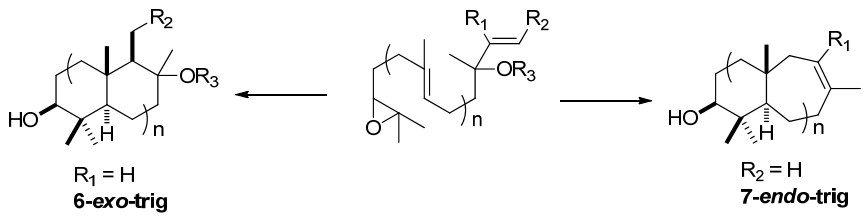
(P-025) Titanocene(III)-catalyzed 6-*exo* versus 7-*endo* cyclizations of epoxypolyprenes

Jose Justicia,[1] Tania Jiménez,[1] Delia Miguel,[1] Rafael Contreras-Montoya, [1] Rachid Chahboun, [1] Enrique Álvarez-Manzaneda,[1] Daniel Collado-Sanz,[2] Diego J. Cárdenas,[2] Juan M. Cuerva[1]

[1]*Department of Organic Chemistry, Faculty of Sciences, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: dmalvarez@ugr.es*

[2]*Department of Organic Chemistry, Faculty of Sciences, Universidad Autónoma de Madrid, Tres Cantos, Madrid.*

Natural terpenes are attractive goals in organic synthesis because of their structural complexities and relevant biological activities. In this context, bioinspired cationic cyclizations of the corresponding starting polyprenes have been extensively studied.[1] Nevertheless, cationic cyclizations of simple unfunctionalized polyprenes present some drawbacks, such as low yields, poor regio- and stereoselectivities and/or the access to cyclic products presenting a thermodynamically unfavorable exocyclic double bond or a tertiary oxygenated function instead of the corresponding alkene. These limitations would be easily overcome using other propagating species such as carbon-centered radicals. In this sense, our group has developed an efficient and highly stereoselective methodology for radical cyclization of epoxypolyprenes catalyzed by Cp_2TiCl.[3]
In this work, we have determined the substitution pattern required to control the 6-*exo*-trig *versus* 7-*endo*-trig cyclization mode using Cp_2TiCl, and how the use of suitable substituents in the polyenic chain of the starting epoxypolyenes drives in a controller manner for the synthesis of a wide range of 6-membered rings carbocycles with a trisubstituted oxygenated substitution pattern.



Scheme 1. Selective formation of 6-membered or 7-membered carbocycles

The success of our approach resides in the high regioselectivity in the addition of the transient radicals to the corresponding double bonds. Thus, we demonstrated that geranyl, farnesyl, and geranylgeranyl derived epoxypolyprenes exclusively undergo a sequence of 6-*endo*-trig cyclizations. On the other hand, the final cyclization of linalyl, nerolidyl and geranyllinalyl derived epoxypolyprenes takes place with an unusual 7-*endo*-trig regiochemistry.

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(P-027) Enantiopure *cis*-decahydroquinolines towards the enantioselective synthesis of lepadin alkaloids

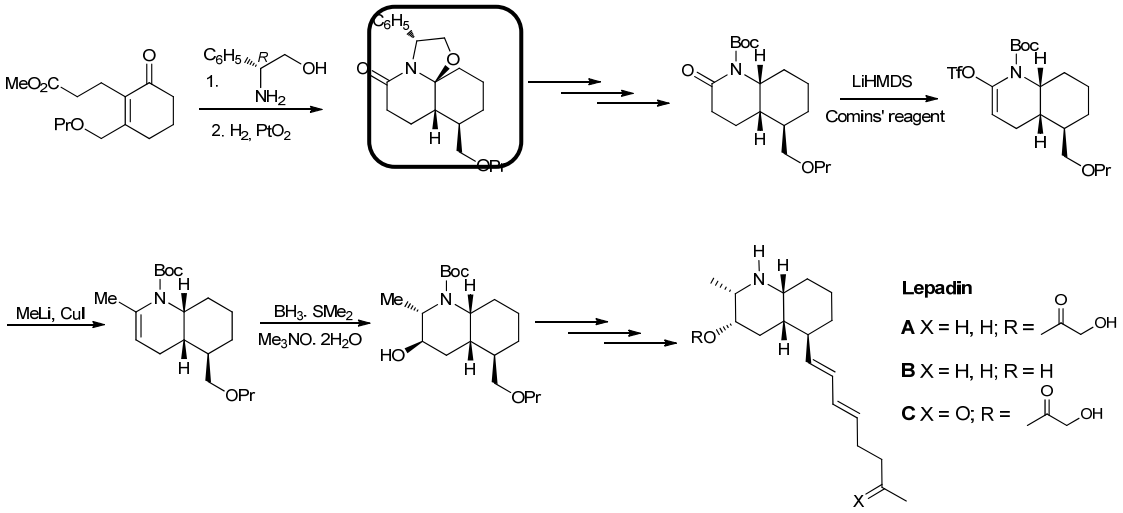
Mercedes Amat, Alexandre Pinto, Rosa Griera and Joan Bosch

Laboratory of Organic Chemistry, Faculty of Pharmacy, and Institute of Biomedicine (IBUB), University of Barcelona, Av. Joan XXIII, s/n 08028-Barcelona, email: alexgregorio@ub.edu

The lepadin alkaloids are a small group of *cis*-decahydroquinoline alkaloids first isolated from different marine sources during the period 1991-2002. Structurally, all of them incorporate a methyl substituent at the C-2 position of the decahydroquinoline nucleus, a functionalized eight-carbon chain at C-5, and a free or acylated hydroxy group at C-3. However, they display a diversified array of relative stereochemical relationships.

Lepadins exhibit a variety of important biological properties such as *in vitro* cytotoxicity against several human cancer cell lines, neuronal nicotinic acetylcholine receptor antagonism, and antiplasmodial and antitrypanosomal activity. Further pharmaceutical research on these alkaloids is hampered by the low quantities of available samples, so the development of facile enantioselective routes to lepadins or synthetic analogs is required.

In the context of our studies on the enantioselective synthesis of *cis*-decahydroquinolines from phenylglycinol-derived tricyclic lactams,[1] we will present our studies on the synthesis of A-C lepadin alkaloids.



Acknowledgements: Financial support from the MICINN, Spain (project CTQ2012-35250/BQU), and the DURSI, Generalitat de Catalunya (grant 2009-SGR-1111).

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(P-029) Synthesis of Fluorinated and Phosphorated γ-Lactams

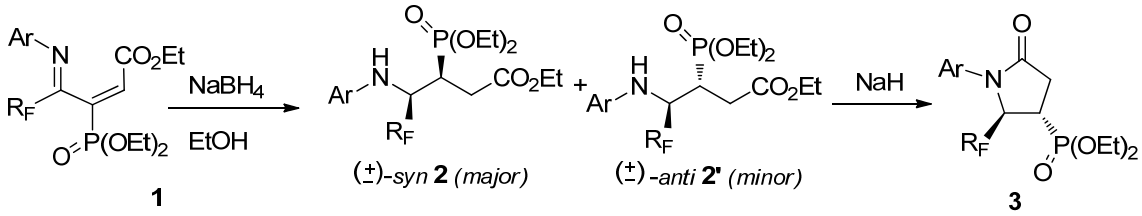
María González, Concepción Alonso, María Fuertes, Gloria Rubiales and Francisco Palacios*

Departamento de Química Orgánica I and Centro de Investigación Lucio Lascaray (Lucio Lascaray Research Center) Facultad de Farmacia. Universidad del País Vasco/Euskal Herriko Unibertsitatea. Paseo de la Universidad 7, 01006 Vitoria-Gasteiz, Spain. e-mail: maria.gonzalezs@.ehu.es

Fluoroalkyl β-aminophosphonates and polyfluorophosphorylated-γ-lactams could be interesting compounds because these new compounds containing phosphorus[1] and fluorine substituents[2] may be useful substrates for the preparation of biologically active compounds of interest in medicinal chemistry.[3]

We report here the synthesis of a new type of functionalized *trans*-γ-lactams **3** in a diastereoselective way (Scheme 1). Functionalized polyfluorophosphorylated 1-azadienes **1** have been prepared by Wittig reaction of ethyl glyoxalate and perfluorophosphorylated conjugated phosphoranes.[4] Subsequent reduction of both carbon-carbon and carbon-nitrogen double bonds of these 1-azadienes **1** constitutes a convenient synthetic route leading to novel fluoroalkyl β-aminophosphonates **2**/**2'** as a diastereomeric mixture, with the *syn* β-aminophosphonate **2** being obtained as major diastereoisomer. We have also shown that based mediated cyclocondensation of diastereomeric mixture of aminophosphonates leads exclusively to a new type of functionalized *trans*-γ-lactams **3** in a diastereoselective fashion.

A computational study has also been used to explain observed diastereoselectivity of these reactions.



Scheme 1

Acknowledgements

This work was financially supported by the *Universidad del País Vasco/Departamento de Educación, Universidades e Investigación del Gobierno Vasco* (UPV/EHU-UFI 11/22; IT-422-10) and *Dirección General de Investigación del Ministerio de Ciencia e Innovación* (DGI, CTQ2012-34323). M. González thanks the *Departamento de Educación, Universidades e Investigación del Gobierno Vasco for a predoctoral fellowship*. We also thank SGIker technical support for computational resources, and NMR spectra (MCINN, GV/EJ, and European Social Found).

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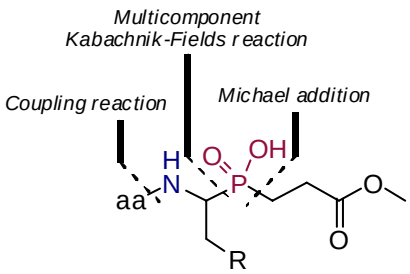
(P-030) Synthesis of novel phosphinopeptides derived from leucine and homophenylalanine as inhibitors of cathepsin C.

Jesús M. de los Santos, Zouhair Es Sbai, Anna Tomczak, Francisco Palacios

Department of Organic Chemistry I, Faculty of Pharmacy, Lucio Lascaray Research Center, University of the Basque Country, Paseo de la Universidad 7, 01006 Vitoria-Gasteiz, Spain, e-mail: jesus.delossantos@ehu.es

Cathepsin C (dipeptidyl peptidase I) plays a key role in the activation of several degradative enzymes linked to tissue destruction in inflammatory diseases. Loss of function mutations in the cathepsin C gene result in periodontal disease and palmoplantar keratosis. Thus, cathepsin C inhibitors could potentially be effective therapeutics for the treatment of such diseases as chronic obstructive pulmonary disease and cystic fibrosis.[1] The application of phosphonic analogues of peptides as protease inhibitors is based on the concept of the resemblance of the phosphonic moiety to the high-energy tetrahedral transition state of the amide bond hydrolysis. This, however, seems not to apply to cathepsin C, although introduction of phosphonic acid moiety to short peptides afforded from weak to strong inhibitors of this enzyme.[2,3]
Based on substrate specificity profiling of cathepsin C and by use of molecular modeling, we have designed a new class of phosphinopeptidic inhibitors of this enzyme.



1 R = ^{i}Pr, Bn

Figure 1

In this study we will describe the synthesis of these novel phosphinopeptides derived from leucine (**1**, R = ^{i}Pr) and homophenylalanine (**1**, R = Bn) as potential cathepsin C inhibitors (Fig. 1). This synthetic strategy involves the multicomponent Kabachnik-Fields reaction for the construction of the *N-C-P* moiety. After formation of the corresponding *α*-aminophosphinate, the Michael addition of acrylic esters to the phosphinate group followed by coupling reaction of the *N*-terminal amino group with different amino acids leads to phosphinopeptides **1**.

Acknowledgements

This work was financially supported by the *Universidad del País Vasco/Departamento de Educación, Universidades e Investigación del Gobierno Vasco* (UPV/EHU-UFI 11/22; IT-422-10) and *Dirección General de Investigación del Ministerio de Ciencia e Innovación* (DGI, CTQ2012-34323). We also thank SGIker technical support for NMR spectra (MCINN, GV/EJ, and European Social Found).

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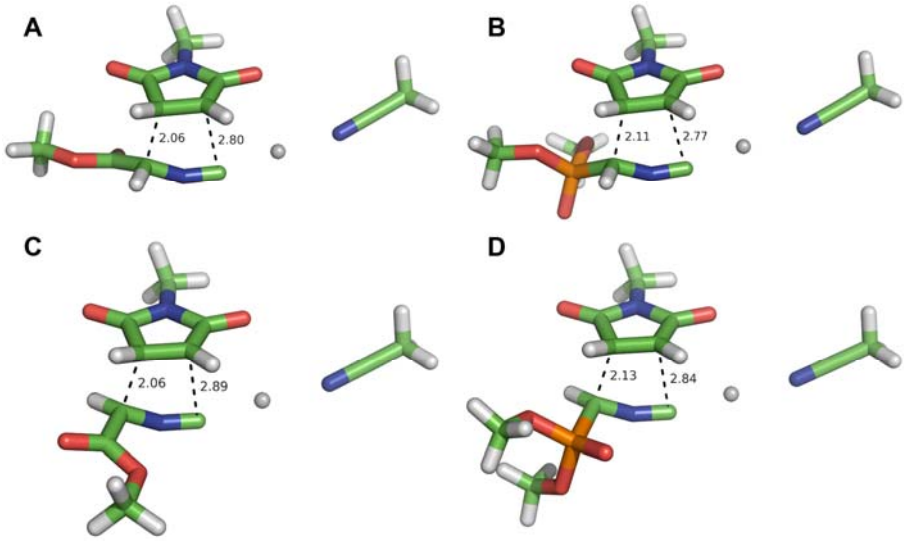
(P-031B) Theoretical studies and transition states to compare the stereoselectivity in the formation of cyclic iminoesters vs. iminophosphonates

J. Maria Campanera,[2] F. Javier Luque,[2] Sonia Abas,[1] and Carmen Escolano[1]
[1]*Department of Organic Chemistry,* [1]*Department of Physics and Chemistry, Faculty of Pharmacy, and Institute of Biomedicine (IBUB), University of Barcelona, Spain, e-mail: cescolano@ub.edu*

An interesting feature of the cycloadditions reported in our group between Phosmic and maleimides is their high diastereoselectivity in sharp contrast with the low diastereoselectivity previously observed by Grigg in his pioneering work with isocyanoacetates.[1] In order to gain insight into these differences, theoretical calculations were carried out. Full geometry optimization of obtained diastereoisomeric iminoesters was performed at the B3LYP/6-31+G(d) level. Both compounds proved to be energetically comparable, with only 0.4 Kcal mol^{-1} difference. In the phosphonate series the energetic difference between the obtained diastereoisomer and the putative one was 4 kcal mol^{-1}. This fact might be enough to justify the excellent diastereoselectivity of the reaction described. To further confirm the preceding trends, the transition states for the [3+2] cycloaddition reactions of the two reactions with the methyl isocyanoacetate and Phosmic were identified at the B3LYP/6-31+G(d) level. The effect of the catalyst was taken into account by adding a silver cation coordinated to acetonitrile. The geometries of the transition states reveal an asynchronous concerted process, where the length of the bond that involves the carbon atom 6a is around 0.7 Å shorter than the bond with carbon atom 3a.



In order to determine the relative stability between the transitions states for *endo* and *exo* cycloadditions, single-point calculations were performed using both M06L and PB+ZORA density functional. The results consistently show a distinctive trend for the addition of compounds bearing ester and phosphonate moieties.

Acknowledments
Finnancial support from the Ministerio de Ciencia e Innovación (MICINN), Spain (Project CTQ2009-07021/BQU), and the Agència de Gestió d'Ajuts Universitaris i Recerca (AGAUR), Generalitat de Catalunya (2009-SGR-1111).

(P-032) Electrochemical reduction of iodoalkenes

Héctor Felipe González-Cruz,[1] Pedro J. Campos,[1] Gonzalo Guirado,[2] Miguel Á. Rodríguez[1]

1Departamento de Química, Centro de Investigaciones en Síntesis Química, Universidad de La Rioja, Avda. Madre de Dios, 51, 26006 Logroño, España, e-mail: hector-felipe.gonzalez@unirioja.es

2Unitat de Química Física, Departament de Química, Universitat Autònoma de Barcelona, Campus de Bellaterra, 08193 Barcelona, España

In the context of our studies on photochemical reactions, we have described the use of iodoalkenes in the photochemical cyclizations with formation of six-membered rings by direct photolysis.[1] In order to gain further insights into the behavior of iodoalkenes, we decided to carry out electrochemical studies.[2]

The use altogether of Cyclic Voltammetry and Controlled Potential Electrolysis allows disclosing the electrochemical reduction mechanism for those compounds. Cyclic voltammetry studies show a two-electron irreversible reduction wave c.a. -2 V vs. SCE, depending on the vinyl iodide derivative (Figure 1). Controlled-potential electrolysis, at the first reduction wave level, yields selectively to the corresponding vinyl derivative after the passage of 2 F. These results are consistent with an ECE mechanism; where the first one-electron reduction process leads its corresponding anion radical (E, electrochemical step). Later, this intermediate evolves, by the departure of iodide anion, to a vinyl radical (C, chemical step). Finally, a second-electron transfer should give a vinyl anion (E, electrochemical step); from which a protonation reaction can take place to obtain the final reduced derivative **B** (Scheme 1).

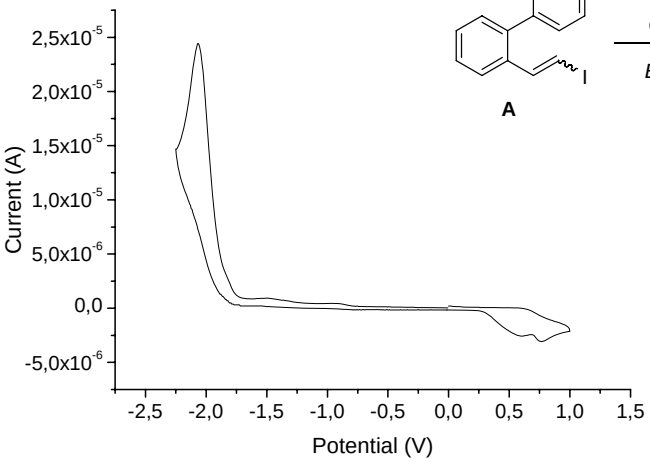
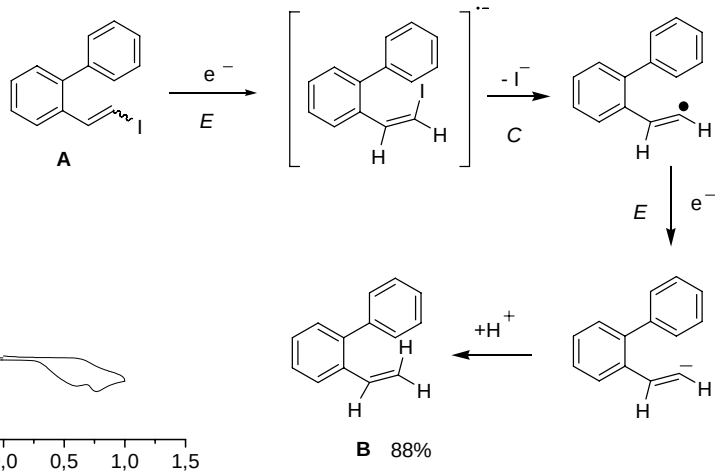


Figure 1.- Scan rate 0.5 Vs^{-1}



Scheme 1

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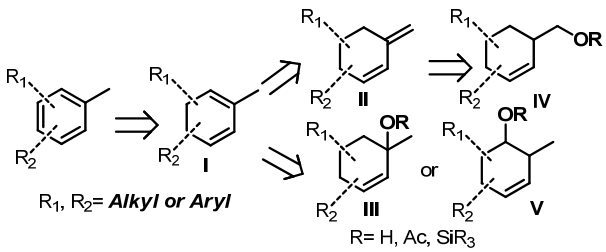
(P-033) Metal-Free Aromatization Promoted by Iodine

Victoriano Domingo, [1] Consuelo Prieto,[1] Rocío Garrido,[1] Lucia Silva, [2] Jesús M. L. Rodilla,[2] Jose F. Quilez[1], Alejandro F. Barrero*[1]

[1]*Department of Organic Chemistry, Institute of Biotechnology, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: afbarre@ugr.es*

[2] *Department of Chemistry, University of Beira Interior, Rua Marquês d'Ávila e Bolama, 6200-Covilhã, Portugal.*

Aromatics are "privileged structures"[1] that occur widely in different forms in such areas as the pharmaceutical industry, natural products and ligands in catalysis. A tremendous range of tools for aromatization exist, although typical procedures require the use of metals. In a similar way, typical methods for the synthesis of biaryls, such as the Scholl reaction, Gomberg-Bachmann reaction or Ullmann coupling or Suzuki coupling are carried out different quantities of metals[2]. Having in consideration the rising costs of these and the waste generated require that new methods be found for the production of aromatics and the synthesis of biaryls. Thus we have though that molecular iodine would be an adequate reactive for aromatization and we reasoned that a 4 π system in a cyclohexane framework is needed to displace the reaction to the corresponding aromatics and we were intrigued to discover whether this transformation could be more generally applied from the corresponding dienes (I-II) or their corresponding precursors, homo-, allylic alcohols and derivatives with different leaving groups (III-V).



Here we describe a novel, easy process for the aromatization promoted by molecular iodine. To show the versatility of this environment-friendly procedure we have applied the aromatization conditions to a series of complex terpenes and biaryl precursors.

Akwnoledgements:

We thank to Ministerio de Economía y Competitividad (Spain) the grant, Project CTQ2010-16818-BQU.

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(P-035) Estudio de la interacción sexual en Mucorales: Análisis de apocarotenoides mediante HPLC-Masas

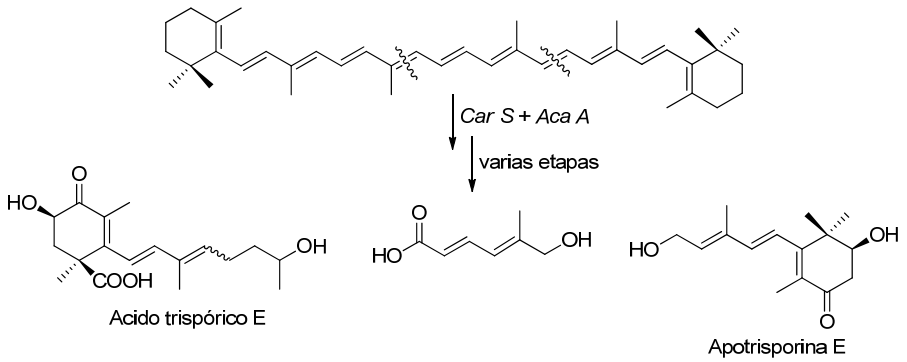
Alejandro F. Barrero*,[1] M. Mar Herrador,[1] Pilar Arteaga,[1] José-Antonio González-Delgado[1,2] , Eugenio Alcalde[3] y Enrique Cerdá-Olmedo*[3]

[1]*Departamento de Química Orgánica. Facultad de Ciencias. Universidad de Granada. Campus de Fuente Nueva, s/n, 18003 Granada, España.* afbarre@ugr.es

[2]*CIQSO-Centro para la Investigación en Química Sostenible y Departamento de Ingeniería Química, Química Fisíca y Químíca Orgánica. Facultad de Ciencias Experimentales. Universidad de Huelva. Campus el Carmen, s/n, 21071, Huelva, España*

[3]*Departamento de Genética. Facultad de Biología. Universidad de Sevilla. Reina Mercedes, s/n, 41071, Sevilla, España*

Phycomyces blakesleeanus (Mucoromycotina, Mucorales, Choanephoraceae) es uno de los hongos que se usa para la obtención industrial de β-caroteno, un pigmento natural con actividad antioxidante y pro-vitamínica A, con aplicaciones industriales farmacéuticas, agroalimentarias y cosméticas.[1] Se ha observado que cultivos mixtos de los sexos (+) y (–) de este hongo provocan un aumento notable de la producción de β-caroteno y se ha postulado que esta carotenogenesis está mediada por señales químicas de tipo apocarotenoide. Recientemente hemos demostrado que durante la interacción sexual β-caroteno se oxida degradativamente mediante las carotenooxidasas*CarS* y *AcaA* en fragmentos de 18, 15 y 7 carbonos originando tres familias de apocarotenoides: trisporoides, ciclofarnesoides y metilhexanoides respectivamente.[2] Con el objetivo de establecer la ruta biosintética hacia los apocarotenoides bioactivos estamos llevando a cabo cultivos individuales y mixtos y estudiando la distribución de apocarotenoides a distintos tiempos de su crecimiento. Con este objetivo se han puesto a punto métodos analíticos de HPLC-Masas para optimizar la detección de los distintos metabolitos de naturaleza apocarotenoide que se generan en *Phycomyces blakesleeanus*. En esta comunicación presentamos una discusión sobre los resultados y sus implicaciones biosintéticas.



Agradecimientos: Se agradece al Ministerio de Ciencia e Innovación (Proyecto CTQ 2010-16818, subprograma BQ) la subvención de esta investigación.

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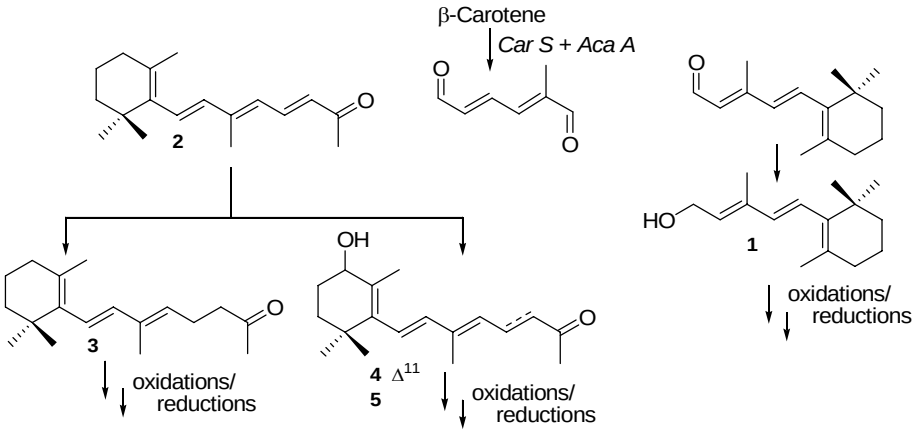
(P-036) Síntesis química de precursores biosintéticos de apocarotenoides: Biotransformaciones mediante *Phycomyces blakesleeanus*

Alejandro F. Barrero*,[1] M. Mar Herrador,[1] Pilar Arteaga,[1] Emilio Mirassou,[1] Eugenio Alcalde[2] y Enrique Cerdá-Olmedo*[2]

[1]*Departamento de Química Orgánica. Facultad de Ciencias. Universidad de Granada. Campus de Fuente Nueva, s/n, 18003 Granada, España.* afbarre@ugr.es

[2]*Departamento de Genética. Facultad de Biología. Universidad de Sevilla. Reina Mercedes, s/n, 41071, Sevilla, España*

Para el hombre y el ganado, β-caroteno es la principal fuente natural de vitamina A aunque tiene otros efectos beneficiosos debido a sus propiedades antioxidantes y colorantes.. Actualmente la producción industrial de β-caroteno se realiza por síntesis química y además biotecnológicamente usando hongos mucorales como por ejemplo *Phycomyces blakesleeanus*.[1] La interacción sexual entre los sexos (+) y (–) de este hongo provoca un aumento notable de la cantidad de β-caroteno y desencadena una ruta biosintética hacia apocarotenoides que origina tres familias de apocarotenoides: trisporoides, ciclofarnesoides y metilhexanoides respectivamente.[2] La ruta comienza con los productos directos de la degradación pero los pasos posteriores no se conocen.



En esta comunicación presentamos la síntesis química de los apocarotenoides C15, **1** y C18, **2-5** a partir de α- y β-ionona. **1-5** son intermedios tempranos en esta ruta y se ha estudiado su biotransformación mediante mutantes no productoras de β-caroteno de *Phycomyces blakesleeanus*. El empleo de ese tipo de mutantes es muy interesante pues evita la necesidad de marcaje isotópico y está conduciendo a aportaciones relevantes en la ruta.

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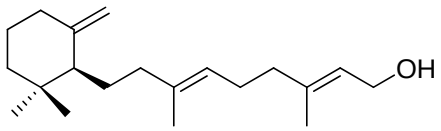
(P-037) Producción biotecnológica de terpenoides olorosos e insecticidas a partir de *Bellardia trixago* L.

Alejandro F. Barrero,[1] M. Mar Herrador del Pino,[1] Pilar Arteaga Burón,[1], Alejandro F. Arteaga,[2] Jesús Burillo Alquézar,[3] Rubén Muñoz,[4] Azucena González Coloma[4]

[1]*Departamento de Química Orgánica, Instituto de Biotecnología, Universidad de Granada, Campus de Fuente Nueva, s/n, 18071 Granada, España. afbarre@ugr.es*
[2]*CIQSO-Centro para la Investigación en Química Sostenible y Departamento de Ingeniería Química, Química Física y Química Orgánica, Facultad de Ciencias Experimentales, Universidad de Huelva, Campus el Carmen, 21071 Huelva, España.*
[3]*Departamento de Ciencia, Tecnología y Universidad, Centro de Investigación y Tecnología Agroalimentaria de Aragón, Gobierno de Aragón, Avda Montañana, 930, Zaragoza, España.*
[4]*Instituto de Ciencias Agrarias. Consejo Superior de Investigaciones Científicas. Serrano 115-bis, 28006 Madrid, España.*

Las plantas aromáticas proporcionan abundantes productos de partida para las industrias alimentaria, farmacéutica, de perfumería y cosmética, etc. Una de ellas es *Bellardia trixago* L., también denominada *Trixago apula* Steven y *Bartsia trixago* L. (*Scrofulariaceae*) que se encuentra ampliamente distribuida por la Región Mediterránea. La composición química de su resina revela una alta concentración de diterpenos.[1] En Andalucía se encuentran tres quimiotipos diferentes, uno ellos contiene altas proporciones de monomalonato de trixagol.[2] Trixagol (**1**) posee un esqueleto monocíclico que constituye un bloque de construcción quiral adecuado para los productos de aplicación en Perfumería dihidro-γ-ionona (**2**) y α-ambrinol (**3**)[3]. Otro quimiotipo contiene mayoritariamente monomalonato de geranil-geraniol. Ge-GeOH (**4**) un compuesto de alto interés por sus propiedades farmacológicas y como materia prima para la síntesis de diterpenos, a través de ciclaciones biomiméticas. En esta comunicación se presentarán los resultados de un estudio para la puesta a punto de cultivos que faciliten la producción de estos diterpenos, paralelamente se ha llevado a cabo un test preliminar de búsqueda de compuestos insecticidas sobre diferentes extractos, fracciones y compuestos puros, mostrando varios una interesante actividad repelente contra pulgones.



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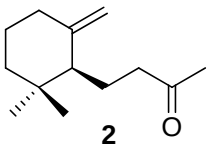

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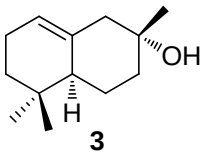

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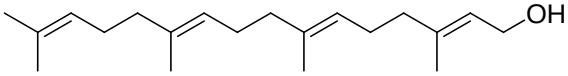

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Agradecimientos
Se agradece a la Junta de Andalucía (Proyecto de Excelencia P08-FQM-3596) la subvención de esta investigación.

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(P-040) Determination of the absolute configuration in epimeric amino acids from natural peptides: a new approach combining Marfey´s method with HPLC-SPE-NMR

Ignacio Pérez-Victoria, Gloria Crespo, Fernando Reyes
Fundación MEDINA, Centro de Excelencia en Investigación de Medicamentos Innovadores en Andalucía, Parque Tecnológico de Ciencias de la Salud, Avda. del Conocimiento, 3. 18016 Granada, Spain, e-mail: ignacio.perez-victoria@medinaandalucia.es

Natural non-ribosomal peptides may be comprised of both proteinogenic and non-proteinogenic amino acids with L- or D- configuration. Regarding the structural elucidation of these compounds, once the sequence and planar structure of a natural peptide has been established, determination of its amino acid chirality is typically carried out by application of Marfey's method.[1] This consists in a complete acid hydrolysis of the peptide and a subsequent derivatization of the resulting amino acid pool with a chiral reagent [1-fluoro-2,4-dinitrophenyl-5-L-alanine amide (FDAA, Marfey's reagent) or similar] which incorporates in its structure a strong chromophore. Derivatization of enantiomeric L- and D- amino acids with the chiral reagent converts them into diastereomeric pairs that can be separated by conventional reversed-phase HPLC. Comparison of retention times with those of the corresponding derivatized amino acid standards allows unambiguous establishment of chirality at C_α. The use of LC-MS and ion extraction processing greatly facilitate such analyses especially for those cases where peak overlap among different amino acid derivatives occurs. Nevertheless, amino acids carrying a second chiral center may be problematic. Marfey's derivatives of epimeric amino acids at the second chiral center are very difficult or impossible to resolve by reversed-phase HPLC in some cases and thus the establishment of absolute configuration at this second chiral center is not trivial. Such is the case of isoleucine (Ile) and threonine (Thr) which can be found in many natural peptides also as their *allo*-forms, or 3- and 4-hydroxyproline (Hyp) which may occur in nature with both *cis* or *trans* configurations. We propose a new approach based on the use of Marfey's method combined with HPLC-SPE-NMR to sort out this problem. This approach is based on the fact that Marfey's derivatives of epimeric amino acids display different chemical shifts. Thus, simple comparison of trapped HPLC peak ^{1}H NMR spectra with the corresponding spectra of standards allows unambiguous assignment of the absolute configuration at the second chiral center in such cases. The use of a low volume microcryoprobe facilitates the analysis of the very minor amounts of Marfey´s derivatives usually obtained after the hydrolysis of a peptide at a sub-milligram scale. This novel approach will be illustrated for the pair L-Ile/L-*allo*-Ile and applied to a family of natural cyclopeptides recently isolated from the fungus *Onychocola sclerotica*.[2]

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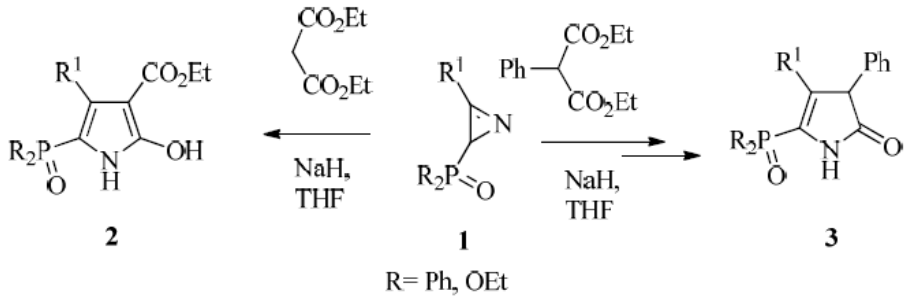
(P-042) Selective synthesis of phosphorylated pyrrole derivatives from 2H-azirines

F. Palacios*, A. M. Ochoa de Retana, A. Vélez del Burgo, G. Fernández de Trocóniz.
Departamento de Química Orgánica I, Facultad de Farmacia, "Centro de Investigaciones Lascaray", Universidad del País Vasco, Paseo de la Universidad nº 7, 01006 Vitoria-Gasteiz, Spain.
e-mail:ander.velez@ehu.es

2*H*-Azirine ring systems represent an important class of compounds because of their high reactivity. They can be used as key intermediates in organic synthesis in the preparation of heterocycles and acyclic functionalized amino derivatives. On the other hand, pyrroles are important heterocycles broadly used in material science and as important intermediates in the synthesis of natural products. The preparation of 2*H*azirine- phosphine oxides and -phosphonates through base mediated Neber reaction of β- ketoxime tosylates and their use for the synthesis of aminophosphorus derivatives, oxazoles or aziridines has been reported.[1]

Continuing with our interest in the chemistry of small strained nitrogen heterocycles, we report here a new strategy for the preparation of functionalized pyrroles **2, 3** containing phosphorus substituents such as a phosphine oxide (R = Ph) or a phosphonate group (R = OEt) by the selective addition of enolates derived from malonates to phosphorylated azirines **1** in presence of in THF[2] (Scheme).



Acknowledgments.

The authors thank the Dirección General de Investigación del Ministerio de Ciencia e Innovación (MCINN, Madrid DGI, CTQ2012-34323BQU) and the Universidad del País Vasco - Departamento de Educación Universidades e Investigación of Gobierno Vasco (UPV/EHU-UFI 11/22; IT-422-10) 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).

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(P-044) Synthesis and structure of fluorinated benzodiazepinones

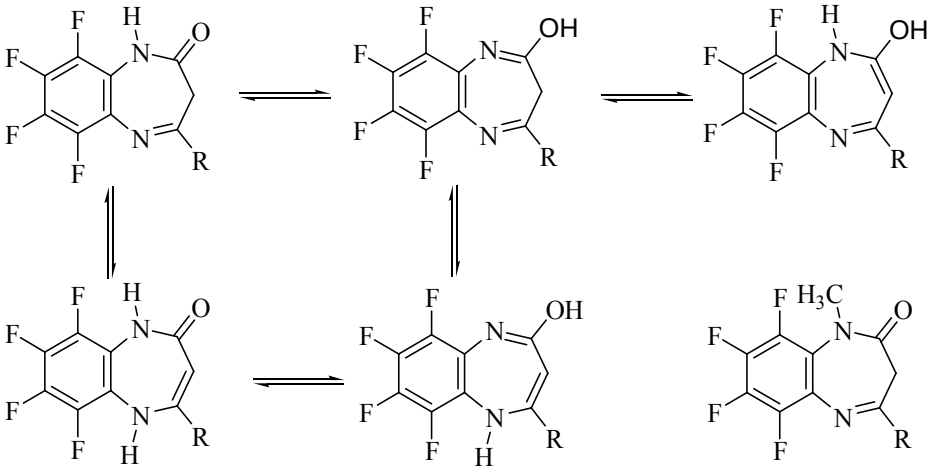
Rosa M. Claramunt,[1] Concepción López,[1] M. Carmen Torralba,[2] M. Rosario Torres,[2] Ibón Alkorta,[3] José Elguero[3] and Marta Pérez-Torralba[1]

1Departamento de Química Orgánica y Bio-Orgánica, Facultad de Ciencias, UNED, Senda del Rey 9, 28040-Madrid, Spain, e-mail: mtaperez@ccia.uned.es.

2Departamento de Química Inorgánica I and CAI de Difracción de Rayos-X, Facultad de Ciencias Químicas, UCM, 28040- Madrid, Spain

3Instituto de Química Médica, Centro de Química Orgánica Manuel Lora-Tamayo, CSIC Juan de la Cierva 3, 28006-Madrid, Spain.

In order to find lead compounds to act as Nitric Oxide Synthase (NOS) inhibitors,[1,2] we have synthesised and characterised the 1,5-benzodiazepinones (**1**,**2**).



Tautomers of **1**, R= CH_3 **2**, R= CH_3

6,7,8,9-Tetrafluoro-4-methyl-2,3-dihydro-1*H*-1,5-benzodiazepin-2-one (**1**) was prepared by reaction of 1,2-diamino-3,4,5,6-tetrafluorobenzene with ethyl acetoacetate,[3] and its further treatment with iodomethane in basic conditions yielded 6,7,8,9-tetrafluoro-1,4-dimethyl-2,3-dihydro-1*H*-1,5-benzodiazepin-2-one (**2**).We report here their complete structural study by multinuclear NMR (^{1}H, ^{13}C, ^{15}N, ^{19}F), as well as X-ray diffraction analysis.

In the case of 1,5-benzodiazepinone **1** all possible tautomeric forms and the seven-membered ring inversion barriers have been theoretically calculated (B3LYP/6-311++G(d,p) for the non fluorinated model compound.[3] The transition states are planar or nearly planar and the invertomers are either identical or they correspond to enantiomers. Experimental determination using Dynamic NMR of the inversion barriers will also be achieved.

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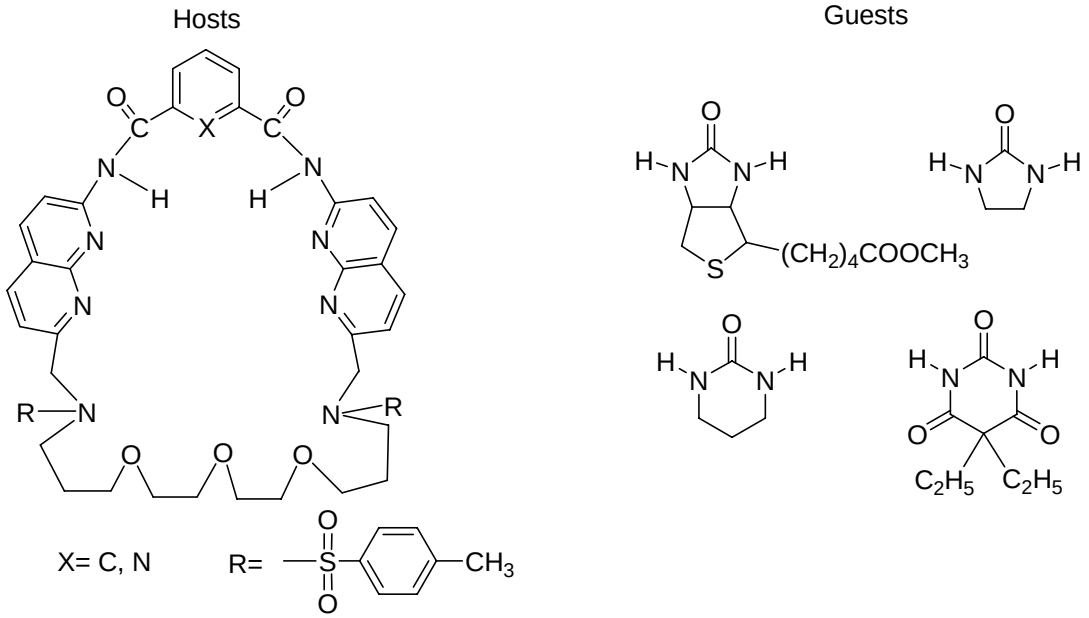
(P-045) New Macrocycles with Naphthyridine and Carboxamide Units

M.A. Farrán[1], D. Santa María [1], M.A. García[1], R.M. Claramunt[1], G.J. Clarkson [2]
[1]*Departamento de Química Orgánica y Bio-Orgánica, UNED, Paseo Senda del Rey 9, 28040 Madrid, Spain, e-mail: afarran@ccia.uned.es*
[2]*Department of Chemistry, University of Warwick, University Library Rd. CV4 7AL Coventry UK.*

We present here a series of new macrocylic hosts designed to interact with biotin and other ureas through multiple hydrogen bonds giving rise to improved binding constants.[1] They are symmetrical macrocycles containing benzenedicarboxamide or pyridinedicarboxamide moities, and two naphthyridine units bonded by a chain of 17 atoms, whose structures are depicted in the Scheme below.



All complexes were modeled by Molecular Mechanics calculations (Monte Carlo Conformational Search, AMBER force field) and minimum energies associated to the most stable structures were calculated.[2] Experimental binding constants were measured by ^{1}H NMR titrations in non polar solvents monitoring the changes in N-H carboxamide group chemical shifts. In most cases a good correlation with the predicted minimum energies for the complexes.was found.

Acknowledgements:

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(P-046) *Geranium macrorrhizum* boiss cultivado como fuente de terpenoides bioactivos

Barrero, A. F.*;[1] Herrador del Pino, M. M.;[1] Arteaga Burón, P.;[1] González Coloma, A.;[2] Navarro Rocha, J.;[3] Burillo Alquézar, J.[3]

[1]*Departamento de Química Orgánica, Instituto de Biotecnología, Universidad de Granada, Granada, Campus de Fuente Nueva, s/n, 18071 Granada. España.*

[2]*Departamento de Protección Vegetal. Instituto de Ciencias Agrarias-CCMA. Consejo Superior de Investigaciones Científicas. Serrano 115-bis, 28006 Madrid, España.* [3]*Departamento de Industria e Innovación, Ciencia, Tecnología y Universidad, Centro de Investigación y Tecnología Agroalimentaria de Aragón, Gobierno de Aragón, Avda Montañana, 930, Zaragoza, España.*

afbarre@ugr.es

Geranium macrorrhizum (Geraniaceae) es una especie que se está presente en forma silvestre en el Centro-Sur de Europa. El estudio químico del aceite esencial de sus partes aéreas revela como componente mayoritario el sesquiterpeno germacrona (cerca del 50% del total).[1]

Germacrona contiene una estructura y funciones que se han revelado como fuente de una gran diversidad estructural mediante pocas etapas de síntesis, se ha utilizado en la preparación del antitumoral β-elemeno[2] y se han descrito interesantes propiedades antitumorales.

Por todo ello se ha pensado que un cultivo apropiado, seleccionando una variedad productora de germacrona y condiciones que den lugar a buenos rendimientos, podría constituir una fuente sostenible de esta molécula.

En esta comunicación se presentan los resultados de un estudio comparativo de la composición química de dos variedades seleccionadas provenientes de Inglaterra y Hungria. Para cada una de ellas se ha determinado el rendimiento en germacrona y un conjunto de poliprenoides acíclicos entre los que es mayoritario solanesol, según el año, tipo de cultivo y parte de la planta. Los resultados indican que la variedad proveniente de Hungría presenta un contenido en germacrona como mínimo 5 veces mayor.

Para complementar este estudio, se están evaluando sus extractos frente a plagas importantes en la agricultura, de igual manera que en agricultura convencional o ecológica, y con diferentes modos de alimentación.

Agradecimientos

Se agradece a la Junta de Andalucía (Proyecto de Excelencia P08-FQM-3596) la subvención de esta investigación.

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(P-047) BODIPY-silica nanoparticles as a colorimetric and fluorescent turn-on chemosensor for trivalent cations.

Andrea Barba-Bon, [1,2] Ana M. Costero, [1] Salvador Gil[1], Margarita Parra[1] and Juan Soto[1]
1Instituto de Reconocimiento Molecular y Desarrollo Tecnológico (IDM) Unidad Mixta Universidad Politécnica de Valencia-Universidad de Valencia, Spain, e-mail: anbarbon@alumni.uv.es
2CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Barcelona, Spain.

Metal ions can pose severe risks to human health and environment; Cr^{3+} deficiency has been reported to disturb glucose levels and lipid metabolism.[1] Fe^{3+} is indispensable for most organisms, and both its deficiency and overload can induce various disorders[2]. Finally, Al^{3+} also plays very important roles in cells and environmental food chains.[3] Due to these facts, it is important to develop safe and effective procedures to detect trivalent cations[4], especially for realizing naked-eye detection with simple and low-cost operations

Two BODIPY derivatives were successfully synthesized, characterized and used for the fabrication of BODIPY-immobilized silica nanoparticles These probes shows a "turn-on" response with trivalent cations whereas the probe remained silent in the presence of competitive cations .Compound **1** can be only used in fluorescence studies whereas compound **2** gives sensing response through two different channels (UV-vis and fluorescence). The observed color change or enhanced fluorescence emission might be attributed to the binding of M^{3+} to the 2-aminoethanol moiety which reduces the electron-donating ability of the nitrogen atom conjugates to the BDP core. This fact can suppress the ICT or the PET quenching process. On the other hand, compound **2** can be used as a sensor for Cu^{2+} due to its unique behaviour in the UV-vis spectrum. Finally, the sensing experiments can be carried out in solutions containing up to 80% what means practically aqueous solution. The limits of detection are between 10^{-7}-10^{-8} M.

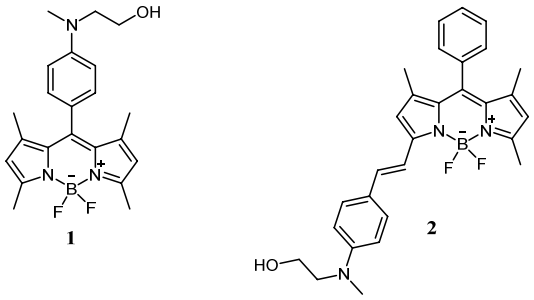

Chart 1. BODIPY dyes

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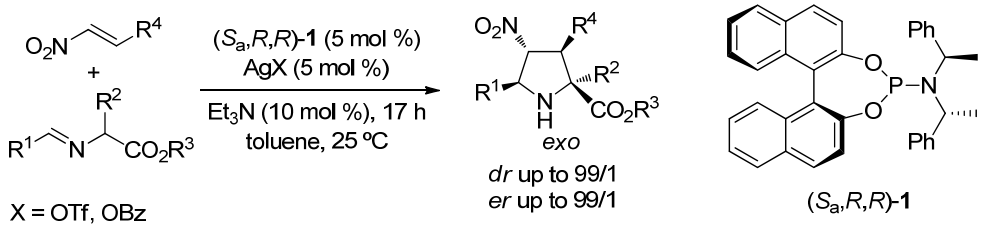
(P-048) Phosphoramidite-AgX Complexes as Chiral Catalysts for 1,3-Dipolar Cycloaddition of α-Amino Acids derived Iminoesters and Nitroalkenes

Luis M. Castelló, Juan Mancebo-Aracil, Carmen Nájera* and José M. Sansano*

Departamento de Química Orgánica e Instituto de Síntesis Orgánica, Universidad de Alciante, 03080-Alicante (Spain), e-mail: cnajera@ua.es, jmsansano@ua.es

The enantioselective silver-catalyzed 1,3-dipolar cycloaddition (1,3-DC) of azomethine ylides, derived from α-amino acids, with nitroalkenes can be carried out with copper(I) complexes formed from ferrocenyl-type phosphanes to afford the corresponding *exo*-cycloadducts. We have recently discovered that chiral phosphoramidite **1** and its enantiomer,[1] as monodentate privileged ligands, in combination with copper(II) triflate are general catalysts for this type of cycloaddition giving the corresponding enantioenriched tetrasubstituted prolines.[2] These kind of prolines are important inhibitor of $\alpha_4\beta_1$–integrin-mediated hepatitis melanoma metastasis[3] and can be used as chiral organocatalysts in the general asymmetric direct aldol reaction.[4] However, the asymmetric 1,3-D of azomethine ylides and nitroalkenes with chiral silver complexes has not been reported to date.

We communicate here the first example of the enantioselective 1,3-DC of azomethine ylides and nitroalkenes catalyzed by phosphoramidite **1** and silver salts[5] such as AgOTf and AgOBz derived complexes. Different α-amino acids derived imino esters such as methyl benzylideneneaminoglycinate and α-substituted imino esters from leucine and phenylalanine have been used as azomethine ylide precursors. Electron-deficient, and electron-rich β-nitrostyrenes reacted smoothly at room temperature in toluene. This methodology allows the preparation of a variety of prolines, useful candidates for organocatalyzed asymmetric aldol reactions.[4] The preparation of the key enantiomerially enriched intermediate in the route furnishing farnesyl transferase inhibitors is envisaged.[6]



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(P-049) Understanding the local reactivity in polar organic reactions through electrophilic and nucleophilic Parr functions.

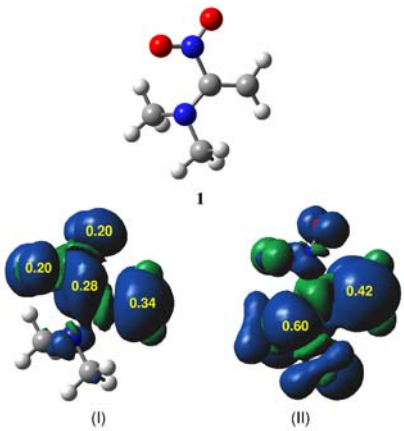
Luis R. Domingo[1], Patricia Pérez[2] and José A. Sáez[3]

1 Universidad de Valencia, Departamento de Química Orgánica, Dr. Moliner 50, E-46100 Burjassot, Valencia, Spain. e-mail: domingo@utopia.uv.es. web: www.luisrdomingo.com

2 Universidad Andrés Bello, Facultad de Ciencias Exactas, Departamento de Ciencias Químicas, Laboratorio de Química Teórica, Av. República 275, 8370146 Santiago, Chile.

3 Instituto de Tecnología Química UPV-CSIC, Camino de Vera s/n, 46022 Valencia, Spain.

Building upon our recent studies devoted to the bonding changes in polar reactions,[1-3] we have proposed two new electrophilic, P_k^+, and nucleophilic, P_k^-, Parr functions to study the regio- and chemoselectivity in polar reactions.[4] These local functions are based on the study of the C-C bond formation step along polar reactions, which take place by a *centre-to-centre* coupling of two *zwitterionic pseudoradical* species.[1-3] These studies suggested that the bonding changes demanded by the σ bond formation are favoured by the global charge transfer from the nucleophile to the electrophile that takes place in polar reactions, and not by HOMO-LUMO interactions as proposes the Frontier Molecular Orbital theory. In our reactivity model, the atomic spin density (ASD) analysis at the radical anion and at the radical cation of the reagents provides the characterization of the most electrophilic and nucleophilic centres of the molecules, and makes it possible to establish the local reactivity in polar reactions. Although the proposed Parr functions give a similar local reactivity as the Fukui functions,[5] the latter are conceptually wrong because they are based on frontier molecular orbitals.



Maps (I) of ASD of the radical anion and the local electrophilic Parr function values, and (II) of ASD of the radical cation and the local nucleophilic Parr function values of the ambiphilic captodative ethylene **1**.

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(P-050) Cyclizations of Natural Germacrone and its Epoxyderivatives Catalyzed by Superacids

M. Carmen Pérez Morales,[1] M. Mar Herrador,[1] José F. Quílez del Moral,[1] Gilles Lemière,[2] Elisabet Duñach[2] and Alejandro Fernández Barrero[1]

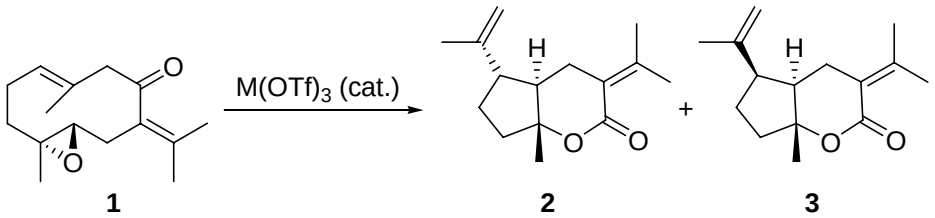
[1]*Department of Organic Chemistry, Institute of Biotechnology, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: afbarre@ugr.es*

[2]*Institut de Chimie de Nice, UMR7272, Université de Nice-Sophia Antipolis, CNRS, Parc Valrose, 06108 Nice Cedex 2, France, e-mail: dunach@unice.fr*

Germacrone is a natural sesquiterpene isolated in multigram scale from the essential oil of *Geranium macrorrhizum* or *Baccharis latifolia*.[1] Since germacradienes are postulated to be biosynthetic intermediates of an extensive group of different sesquiterpenic structures[2] we conceived that natural germacrone could well be used in a reagent-based approach to efficiently generate many structurally diverse compounds. In this regard, we have recently reported the first results showing a new type of transannular cyclization of germacrone mediated by HSO_3Cl at low temperature.[3]

This presentation will deal with the results obtained after treating germacrone, its epoxyderivatives germacrone-4,5-epoxide, germacrone-1,10-epoxide and isogermacrone-4,5-epoxide with catalytic amounts of superacids and Lewis superacids. The outcome of these reactions will be compared with the results produced when these compounds were treated with other acid media.

As an example, epoxide **1** in the presence of a catalytic amount of bismuth (III) triflate or aluminium (III) triflate ($M^+ {}^-O_3SCF_3$) led the preparation of the bicyclic structures **2** and **3**.



The structure of lactone **2** was determined by NMR analysis and was confirmed by X-Ray christallography.

Acknowledgements:

We thank the grants to Junta de Andalucía, Spain (Proyecto de Excelencia P08-FQM-3596) and Ministerio de Ciencia e Innovación (Spain) (Proyecto CTQ2010-16818).

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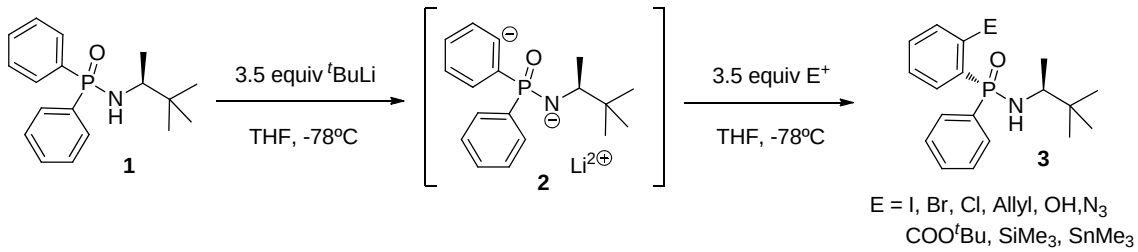
(P-051) Diastereoselective synthesis of *P*-quiral *ortho*-funcionalizated phosphinic amides

Miguel Ángel del Águila Sánchez and Fernando López Ortiz
Department of Physic and Chemistry, University of Almería, Carretera Sacramento s/n,04120 Almería, Spain, e-mail: mds147@ual.es

P-quiral compounds are important ligands in asymmetric catalytic transformations. A well-established method for synthesizing this class of compounds consists of the enantioselective deprotonation of prochiral PMe_2 moieties of phosphine-boranes and sulfides.[1] In recent years, we have developed a complementary approach for accessing to *P*-stereogenic ligands based on the desymmetrization of Ph_2P moieties via directed *ortho*-lithiathion (D*o*Li) and subsequent electrophilic trapping reactions. We have shown the feasibility of achieving enantioselective *ortho*-deprotonation of diphenylphosphinic amides using the chiral base [^{n}BuLi·(-)-sparteine] and diastereo-selective *ortho*-lithiations of chiral (*S*)-*P*,*P*-diphenyl-*N*-(1-phenylethyl)phosphinic amides. However, the stereoselectivities obtained were low (ee = 60%[2], dr ≤ 80:20,[3]).
In this report, we describe a highly efficient diastereoselective synthesis of *P*-chiral phosphinic amides by applying the D*o*Li methodology to (*S*)-*N*-(3-methylbutan-2-yl)-*P*,*P*-diphenylphosphinic amide (**1**) (Scheme 1). After some experimentation, we found that the treatment of phosphinic amide (**1**) with 3.5 equivalents of ^{t}BuLi in THF at -78 ºC affords an orange solution indicating the formation of the *N*- and *ortho*-dianion (**2**). Addition of a variety of electrophiles to (**2**) at -78 ºC produces the rapid discoloration of the solution leading to the *P*-chiral *ortho*-functionalized derivatives (**3**) showing large structural diversity in good yields (up to 82%) and excellent diastereoselectivity (up to 97:3).



Scheme 1

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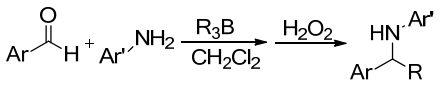
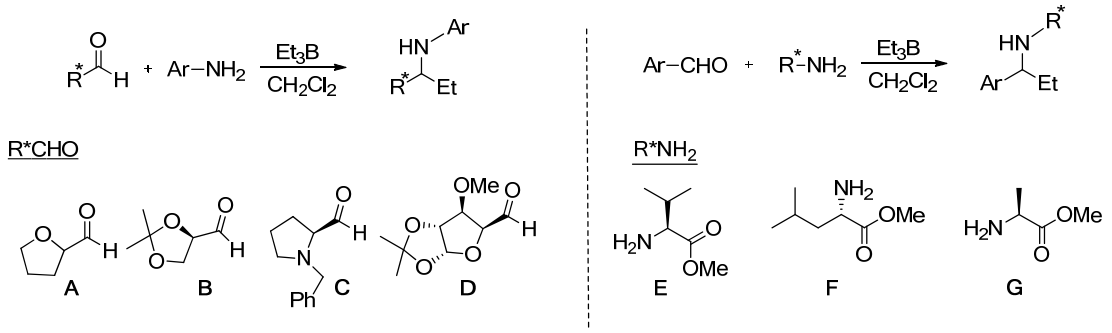
(P-052) Diastereoselective synthesis of chiral amines by imines alkylation

Amelia Díaz , Carmen Muñoz, María Sánchez and María Valpuesta
Department of Organic Chemistry, Science Faculty, University of Málaga, Campus de Teatinos s/n, 29071 Málaga, Spain, e-mail: amelia@uma.es

Chiral amines are important chemical building blocks, which are most well recognized in the pharmaceutical industries for imparting desirable biological activity to chemical entities.[1] The 1,2-addition of alkyl groups to the C=N bond is a basic widely spread methodology for the preparation of alkylamines. However most of the alkylating procedures are mediated by ionic species and require therefore highly basic reagents, which limit severely the choice of suitable substrates. Free radical additions to activated imino compounds offer increased synthetic accessibility of chiral amines, but lack of general methods for stereocontrol has hindered their development.[2]
We have recently described a one-pot alkylative amination reaction for arylaldehyde derivatives that involves three components with trialkylborane as the alkylating agent. Our methodology is the first example of these processes for non–activated imines using a wide variety of trialkylboranes. The broad applicability of the procedure was ascertained by extending this reaction to enolizable aldehydes and aliphatic amines.[3]



We describe herein the one-pot procedure for the alkylation of non activated chiral imines, based on the use of triethylborane as the alkylating agent and enantiomerically pure aldehydes. We have studied the effect of the temperature and the influence of the heteroatom located at the position vicinal to the carbonyl on reaction efficiency and stereoselectivity.



At present we are studying the same alkylation reaction using chiral imines derivated of aminoacids, valuing the influence of the amine nature as well.

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(P-053) Ti/Ni-promoted inter- and intramolecular Michael-type addition of aryl halides and triflates to activated alkenes

Irene Rodríguez-Márquez, Alba Millán, Ángela Martínez-Peragón, Luis Álvarez de Cienfuegos, Delia Miguel, Araceli G. Campaña and Juan M. Cuerva
Department of Organic Chemistry, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: irenerm@ugr.es

The combination of radical and late transition metal chemistry has emerged as a very efficient approach for the formation of C-C bonds.
In this context, our group has recently reported that the combination of a smooth single electron transfer (SET) reagent, such as Cp_2TiCl, and a late transition metal, like Pd or Ni, can promote efficient Barbier-type allylation and propargylation reactions of carbonyl compounds as well as new cyclization reactions using stable and easily handled allylic and propargylic carboxylates as pronucleophiles[1]. The success of our strategy was based on the two following facts: (a) the *in situ* Cp_2TiCl-mediated reduction of the transient Pd or Ni organometallic species, and (b) the trapping of the radical intermediates by homogeneous Cp_2TiCl.
Herein, following the excellent results of our previous findings, we wish to report a new Michael-type addition to activated alkenes catalyzed by the multimetallic system Ti/Ni/Mn. This method uses haloarenes instead of nucleophilic aryl reagents. Nickel couples an α,β-unsaturated ester with aryl and vinyl halides with moderate to good yields. The success of the catalytic process is based on the excellent cooperation between the transition metal (Ni) and the radical reagent (Cp_2TiCl).
In addition, the intramolecular protocol allows the synthesis of different carbo- and heterocycles of five and six-membered rings with high yields from easily accessible aryl iodides, bromides, chlorides and triflates (Fig.1).

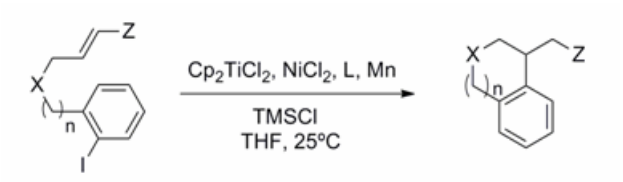

Figure 1

References

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(P-054) Estudio fitoquímico y actividad antifúngica de especies del género *Baccharis* frente al hongo *Botrytis cinérea*

Ana Andreina Pinto,[1] Antonio Ruano,[1] Juan Amaro-Luis,[2] Isidro González Collado, [1]
[1]*Universidad de Cádiz, Facultad de Ciencias, 11510, Puerto Real, España.*
[2]*Universidad de Los Andes, Departamento de Química, 5101, Mérida, Venezuela.*

El género *Baccharis,* perteneciente a la familia Asteraceae, comprende aproximadamente 500 especies y está ampliamente distribuida en América y Europa. Los estudios fitoquímicos realizados hasta ahora muestran que las especies de este género biosintetizan un elevado número de flavonoides y terpenoides, en especial diterpenos de la serie de los labdanos y clerodanos[1]. Los metabolitos aislados de estas especies han mostrado una amplia variedad de actividades biológicas, entre las que destaca la actividad antifúngica.[2]

En esta comunicación se presentarán los resultados obtenidos en el estudio bio-dirigido, que se está llevando a cabo en colaboración entre los departamentos de química y de química orgánica de las Universidades de Mérida, Venezuela, y Cádiz, España, respectivamente, de las especies *B. zumbadorensis, B. trinervis, B. prunifolia, B.latifolia y B. erectifolia;* y que están orientados a la obtención de extractos naturales que puedan ser utilizados para el control de la podredumbre gris, en cultivos comerciales, dentro de lo que se conoce como agricultura ecológica.

La selección de las fracciones cromatográficas sometidas a estudio, se seleccionaron atendiendo a la actividad antifúngica mostrada por dichas fracciones frente al hongo fitopatógenos *Botrytis cinerea.* Actualmente se ha encontrado que los extractos en diclorometano de *B. zumbadorensis* y *B. trinervis* muestran una fuerte inhibición de crecimiento del hongo con un porcentaje de inhibición de 92% y 82%, a una concentración de 125 ppm. De estos extractos se han aislado compuestos que han presentado actividad fungistática frente a este fitopatógeno y cuyas estructuras están siendo elucidadas por técnicas de RMN mono y bidimensionales (^{1}H-RMN, ^{13}C-RMN, COSY, HMQC, HMBC).

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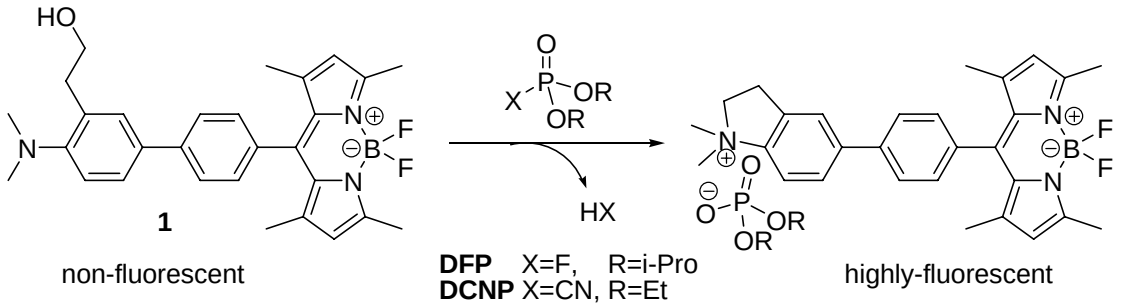
(P-055B) Synthesis and evaluation of borondipyrromethene (BODIPY) chemosensors for the sensitive nervous agent sensing

Raúl Gotor*, Katherine Chulvi, Ana M. Costero, Salvador Gil, Margarita Parra, Pablo Gavina, Alejandro Lorente

Centro de Reconocimiento Molecular y Desarrollo Tecnológico (IDM),Unidad mixta Universidad Politécnica de Valencia-Universidad de Valencia, Spain.[1]Departamento de Química Orgánica, Universitat de València, Dr. Moliner 50, 46100, Burjassot, Valencia., e-mail: raul.gotor@uv.es

The use of chemical-warfare (CW) agents has proven the need for development of reliable and accurate methods to detect these lethal compounds. Among CW, nerve agents are especially dangerous, being classified as weapons of mass destruction. Nerve agents inhibit the acetylcholinesterase, resulting in acetylcholine accumulation in the synaptic junctions; this hinders muscles from relaxing[1]. From a chemical viewpoint, nerve agents are organophosphonates with good leaving groups. Current nerve-agents-monitoring methods are mainly based on biosensors, ion mobility spectroscopy, photonic crystals, electrochemistry, microcantilevers, and optical-fiber arrays and show certain limitations, such as low portability and complexity.[2] The development of chemosensors has proven to be a good alternative to these methods, as the needed instrumentation for detection is widely available, even being analyzable by the naked eye. We present here a small library of fluorescent chemosensors for nervous agents based on a highly fluorescent BODIPY core. BODIPY fluorophore has remarkable photophysical properties, such as high quantum yields, non solvent dependent fluorescence and outstanding photostability. Fluorophore is connected to a 2-(2-dimethylamino)phenyl)ethanol sensing unit which will cyzclizate in the presence of organophosphorous agents[3] (scheme 1), yielding an ammonium quaternary salt. The synthesized chemosensors shows fluorescence quenching due to photoelectron transfer (PET) or internal charge transfer (ICT), but upon cyclization of the sensing unit, fluorescence is restored indicating the presence of these toxic agents.



Scheme 1. Reaction scheme of probe 1 with a generic nervous agent mimic

With these methodology, fast, sensitive and selective detection of nervous agents di-isopropylfluorophosphate (DFP) and diethylcyanophosphonate(DCNP) has been achieved.

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(P-056A) Polyphenols in cork processing wastewater, antioxidant activity and potential uses.

Diana Santos, Carla Gaiolas, Lúcia Silva, Arlindo Gomes

Chemistry Department, Unity of Textile & Paper Materials, University of Beira Interior, 6201-001-Covilhã, Portugal

Cork is a natural, renewable and biodegradable material produced from the bark of the cork oak (*Quercus suber L.*). The production of cork is an environmental sustainable activity and contributes to the preservation of the more than 2.2 million hectares of natural forest ecosystem that is typical in Mediterranean countries.[1] The composition of the effluent from boiling process, the first stage of cork industrial processing, includes corkwood extracts, namely polyphenols, and their depuration is difficult to accomplish by biological treatment due to limited biodegradability and high toxicity.[1] Phenolic compounds have a wide variety of relevant properties, namely, their antioxidant, anti-inflammatory, radical scavenger and antimicrobial properties.[2] The interest in natural polyphenols compounds for nutraceutical and cosmetic applications has increased considerably in recent years because of its properties and because they do not show adverse effects as it is frequently the case of their synthetic counterparts.[3]

Therefore, the recovery of useful organics from cork boiling wastewater (CBW) may contribute to improve the environmental and economic outcome of cork industry. In this study a sample of CBW was studied in terms of total phenolic and flavonoid contents, antioxidant activity and detailed chemical analysis by HPLC–DAD-ESI-MS^n.

The results reported in table 1 showed that CBW has high phenolic and flavonoids concentration and a very strong antioxidant activity. Besides these features the chromatographic analysis allowed us the identification of 18 compounds: gallic acid, protocatechuic acid, p-Hydroxyphenyllactic acid, protocatechuic aldehyde, conyferaldehyde esculetin, caffeic acid, siringic acid, vanillin, ferrulic acid, eriodictyol, naringenin, ellagic acid-hexoxe, ellagic acid-pentose, di-hexahydroxydiphenoyl-glucose, ellagic acid, vescalagin and tannic acid. Consequently, it is possible to anticipate an enormous potential for the use of CBW as source of valuable polyphenols compounds.

Table 1 – Values for IC_{50}, antioxidant activity index (AAI), total phenolic and flavonoid contends in CBW (mean and standard deviation for more than 3 analysis).

Total phenol (mg tannic acid/g dry weight)	Total flavonoids (mg quercetine/g dry weight)	IC_{50} (µg /mL)	AAI	Antioxidant activity
96,00 ± 1.22	8.66 ± 0.08	10.68 ± 1.02	2.30 ± 0.09	Very strong

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(P-056B) Antioxidant activity and total phenolic compounds of *Lavandula luisieri*

João Araújo,[1] Fernanda Delgado,[2] Jesus Rodilla,[1] Arlindo Gomes,[1] Lúcia Silva[1]

[1]*Chemistry Department, Unity of Textile & Paper Materials, University of Beira Interior*, 6201-001-Covilhã, Portugal

[2] *CERNAS/IPCB*, *Centro de Estudos de Recursos Naturais, Ambiente e Sociedade*, Quinta da Sra. de Mércules 6001-909 Castelo Branco, Portugal

Lavandula luisieri (Rozeira) Riv.-Mart. is an aromatic *Labiatae* endemic to the Iberian Peninsula, common in the South of Portugal and in the Southwest of Spain[1]. This plant is characteristic of the syntaxon *Cisto-Lavanduletae*, a class which includes thermo- to supra-Mediterranean dry and semi-arid, sub-humid secondary scrub communities producing aromatic compounds[2]. The extraction of natural substances with antioxidant activity, to replace synthetic food preservatives has gained great importance. Extensive research has been dedicated to identification of antioxidant compounds of natural sources, and the antioxidant activity of many plants has been investigated.

This work consists in the evaluation of antioxidant activity using the DPPH method[3], in different parts of *Lavandula luisieri* using ethanol extraction. In this study, flowers, leaves and stems of the *Lavandula luisieri*, were subdued to extractions with ethanol. The results of DPPH assay were expressed in IC_{50}, defined as the amount of antioxidant required to reduce 50% of the initial concentration of DPPH. The ability of compounds to remove the organic radical DPPH, can be expressed as its antioxidant activity. The antioxidant activity index (AAI) was calculated by:

$$AAI = \frac{[DPPH]_{final}}{IC_{50}}$$

With the this test, the extracts of *Lavandula luisieri* showed very strong antioxidant activity (AAI >2) in all parts of the plant (table 1).

Table 1 – Values for IC_{50} (µg /mL), antioxidant activity index (AAI) and total phenolic content (expressed as mg gallic acid/g of dry weight).

Part of the plant	IC_{50}	AAI	Antioxidant activity	Phenol Content
Flowers	8.36 ± 1.65	3.18 ± 0.08	Very strong	132,61 ± 1.56
Leaves	10.43 ± 1.78	3.35 ± 0.06	Very strong	177,83 ± 3.82
Stems	16.00 ± 1.92	2.74 ± 0.09	Very strong	130,20 ± 2.53

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(P-057) Discrimination of nerve gases mimics and other organo phosphorous derivatives in gas phase using a colorimetric probe array

Katherine Chulvi,[1,2] Pablo Gaviña,[1,2] Ana M. Costero,[1,2] Salvador Gil,[1,2] Margarita Parra,[1,2] Raúl Gotor,[1,2] Santiago Royo,[1,3,4] Ramón Martínez-Máñez,[1,3,4] Félix Sancenón,[1,3,4] and José-L. Vivancos[1,4,5]

[1]Centro de Reconocimiento Molecular y Desarrollo Tecnologico (IDM), Unidad Mixta Universidad Politecnica deValencia Universidad de Valencia. [2]Departamento de Quımica Organica, Universitat de Valencia, Dr Moliner, 50, 46100 Burjassot, Valencia, Spain. E-mail: ana.costero@uv.es; Fax: +34 963543151; Tel: +34 963544410. [3]Departamento de Quımica, Universitat Politecnica de Valencia Camino de Vera s/n, 46022, Valencia, Spain. [4]CIBER de Bioingeniera Biomateriales y Nanomedicina (CIBER-BBN), Spain. [5]Departamento de Proyectos de Ingenierı Universitat Politecnica deValencia, Camino de Vera s/n, 46022, Valencia, Spain

Nerve agents, used as chemical warfare weapons, are some of the most toxic known chemical agents. They are hazardous as liquid and vapour and can cause death within minutes after exposure.[1] Are highly toxic to mammals due to their capacity to interfere with the action of the nervous system through the inhibition of acetylcholinesterase as a result, a dysfunction in the nerve system appears. Many organophosphates and organo phosphonates, sometimes used as pesticides, act as a "nerve agents" and they are one of the most common causes of poisoning worldwide via intoxication through inhalation, ingestion and dermal absorption.

Some analytical procedures based on biosensing assays and physical techniques have been used to detect these compounds.[2] However, they show certain limitations in their use typically involving difficult portability and low selectivity. So the use of chromogenic chemosensors is one of the most promising since they are versatile, printable and colour modulations can be easily measured using image capturing systems or allow the detection of colour changes by the naked eye.[3]

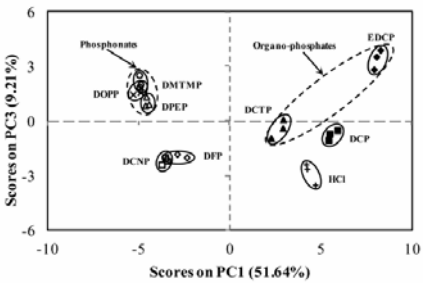

Fig2. PCA score plot of PC1 and PC3 for some simulants and HCl and the trial clustering.

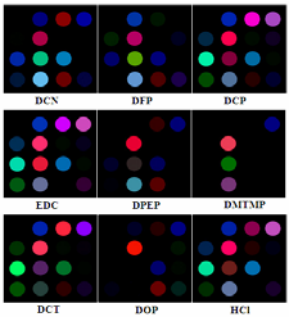

Fig1. Colour difference maps for 8 nerve agent simulants and HCl.

Our lab group been developed a colorimetric array for chromogenic discrimination of organophosphorous derivatives in gas phase. It is composed by a total of 16 dyes such alcohol, amine, pyridine groups and also push-pull chromophoros. Initial colours of the dyes change after the exposure to the simulant of nerve agents in vapour phase. The mathematical probabilistic treatment of the value obtained in the colour differenced map Fig 1, for the R, G, and B coordenates, bring us a clear PCA capable to discriminate the different nerve agent simulants, Fig 2.

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(P-059) Synthesis and evaluation of 8-di-(2-picolyl)aminoBODIPY as a zinc cation sensor

María de Lourdes Betancourt Mendiola,[1] Eduardo Peña Cabrera,[1] and Ana María Costero[2]

[1]*Department of Chemistry, University of Guanajuato. Noria Alta S/N, 36050 Guanajuato; Gto., 36050 México e-mail: eduardop@ugto.mx*

[2]*Centro de Reconocimiento Molecular y Desarrollo Tecnológico University of Valencia, Dr. Moliner, 50, 46100-Burjassot, Valencia, Spain*

Zinc is one of the most important metals is the human body, it is present in every cell, is an essential part in the structure of many enzymes and has an important role in transcription processes. Zinc is found as a part of complexes structures and also as a free ion. As a free chelatable cation, zinc is present in the brain and pancreas tissue. Zinc possess importance because it is present in many physiological processes, nevertheless its mechanism of action is not well understood.[1]

There are many methods for zinc detection; one of the most outstanding is based in fluorescence phenomenon. Usually, fluorescent cation sensors have in their structure a coordinative part that is responsible of the metal coordination and a fluorophore as responsive structure. There are a huge of possible combinations between the ligand and the fluorophore, therefore in the present work we restrict the use of di-(2-picolyl)amine as an acceptor for zinc (II) and the BODIPY core as a fluorescent unit. In the past years, many studies show the extraordinary capability of di-(2-picolyl)amine to sense zinc cations[2] and it is well known the advantages of the use of BODIPY core as a chromophore.[3]

Our group has developed a non-emissive molecule capable of changing its photochemical properties in the presence of zinc (II). In the absence of metal cations, its fluorescence intensity should be weak because of fluorescence quenching by PET process, and the interaction of zinc (II) should interrupt this process and the BODIPY fluorescence emission is recovered.

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(P-060) Diffatonce: a new software package for analyzing diffusion NMR data

Francisco Manuel Arrabal Campos and Ignacio Fernández

Department of Chemistry and Physics, University of Almeria, Ctra. Sacramento s/n, 04120 Almeria, Spain, e-mail: ifernan@ual.es

DiffAtOnce is a new program for processing PFG NMR diffusion data distributed under www.diffatonce.com. NMR data from major manufacturers can be imported and all processing is done in a user-friendly graphical user interface. The program is written in Visual Basic.NET in a free-standing compiled version for PC-platforms.

Pulsed field gradient diffusion NMR is now an important tool for many chemists interested on unraveling problems in complex mixtures, molecular volumes estimation, hydrogen-bonding interactions, or aggregation states issues. Many major manufacturers of spectrometers offer different hardware and software implementations to acquire and process such data, but in such software's the processing of the data is hardly manageable and need to use additional programs in order to obtain *D*-values and/or hydrodynamic radii.

We present herein a new software package able to obtain quantitative self-diffusion data in a very simple manner allowing the calculation of radii including different molecular models such as sphere, cylinder or ellipsoid. The program works with any conventional or "home-made" sequence, and allows the introduction of different standards, viscosities, gradient-pulse shapes, sequences, etc. permitting the exportation of the data as postcript, pdf or excels formats.

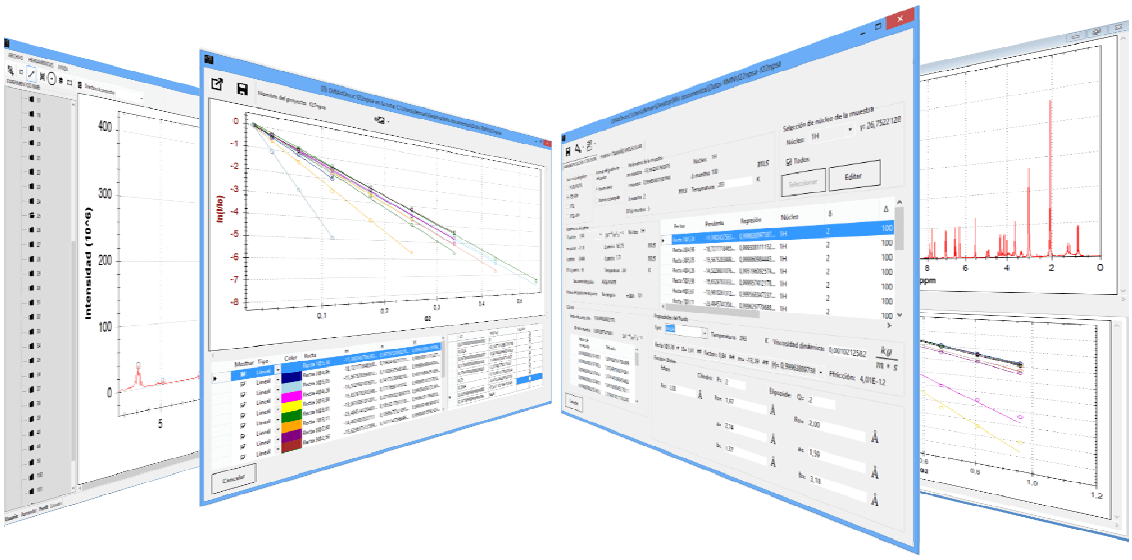

Figure 1. Some windows of the graphical user interface of the DiffAtOnce program. Most of the functionality is easily accessible from here.

The software has been tested in several applications ranging from organometallics, coordination compounds, supramolecular host-guest systems, natural products mixtures, and purely organic species.

(P-063) Design of colorimetric sensors based on NO_2 propierties for oxidative deprotection of benzylic silyl ethers

L. Alberto Juárez Díaz,[1,2] Ana Mª. Costero Nieto,[1,2] Margarita Parra,[1,2] Salvador Gil[1,2]
[1] *Centro de reconocimiento molecular y desarrollo tecnologico (IDM), Valencia, Spain.*
[2] *Department of Organic Chemistry, Universitat de Valencia, Doctor Moliner 50, 46100 Burjassot, Valencia, Spain.*

The reactivity and physical properties of nitrogen dioxide have been areas of interest for the scientific community1,2. The adverse effects of NO2 in the environment and human health are well known and different organizations already warn of the dangers of exposure3. This fact and the possibility of high concentration of NO2 due to the combustion of fuels, as well as the oxidation of NO to NO2 in the air makes the develop of new detection systems an important research subject.
Bearing in mind that the oxidative deprotection of the silyl ether derivative by NO2 will result in the corresponding cetones carbonil compound. We propose the synthesis of different diazo derivates presenting an off-on sensor mechanism in the presence of NO2.

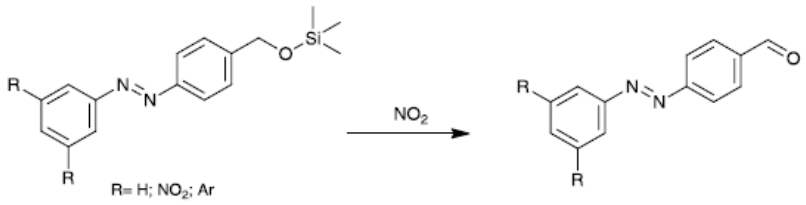

Figure1. Sensing system based on deprotection of benzylic trimethyl silyl ethers with gaseous NO_2

The reaction of figure 1 has been well established4 and it presents some advantages regard to other deprotection procedures. In the case of silyl ether, yields are quantitative and the reaction conditions are soft (room temperature, solvent free process and ambient pressure)5. The direct oxidation of silyl ethers to yield the corresponding carbonyl derivates (Figure 1) results in the corresponding chromogenic change induced by the variation in the electronic properties of the compounds. Colour variations can be modulated by changes in R- substituent.

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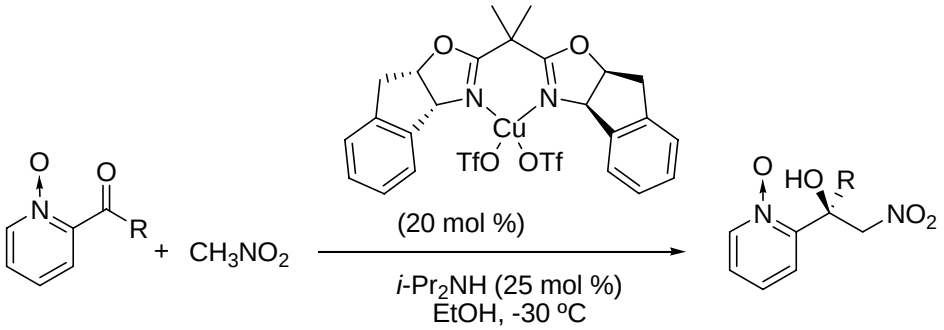
(P-065) The construction of quaternary stereocenters via the Henry reaction: Enantioselective addition of nitromethane to 2-acylpyridine *N*-oxides catalyzed by BOX-Cu(II) complexes

Gonzalo Blay,* Melireth Holmquist and José R. Pedro*

Departament de Química Orgànica, Facultat de Química, Universitat de València, C/ Dr. Moliner 50, 46100-Burjassot, Spain, e-mail: melireth.holmquist@uv.es

The enantioselective construction of quaternary stereocenters is a challenging goal that has attracted much attention during the last years.[1] Asymmetric nucleophilic addition to prochiral ketones provides one of the most attractive approaches toward chiral building blocks containing oxygenated quaternary stereocenters. On the other hand, enantiomerically enriched nitroalkanols which can be obtained by condensation of nitroalkanes with carbonyl compounds (Henry or nitro-aldol reaction) have a high scientific and commercial value as building blocks for pharmaceuticals and agrochemicals. During the past years, considerable progress on the development of catalytic enantioselective procedures for the Henry reaction using aldehydes and aldimines as electrophiles has been achieved.[2] However, the most challenging enantioselective Henry reaction with prochiral ketones still has to be developed. So far, the direct asymmetric addition of nitromethane to ketones has been only achieved with highly electrophilic compounds such as trifluoroacetophenones and α-ketoesters.

As part of our continuous research on the Henry reaction our group has described the enantioselective copper-catalyzed addition of nitromethane to α-ketoesters[3] and substituted glyoxals.[4] In this communication we will report the enantioselective addition of nitromethane to 2-acylpyridine *N*-oxides catalyzed by BOX-Cu(II) complexes[5] to give the corresponding nitroaldols bearing a pyridine ring attached to a tertiary alcohol, with enantiomeric excesses above 80%.



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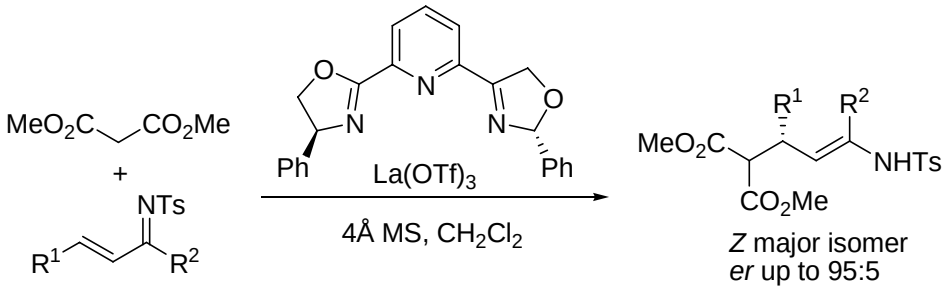
(P-066) La(III)-catalyzed asymmetric conjugate addition of malonate esters to α,β-unsaturated *N*-sulfonyl imines

Gonzalo Blay,* Luz Cardona, Miguel Espinosa and José R. Pedro*
Departament de Química Orgànica, Facultat de Química, Universitat de València, C/ Dr. Moliner 50, 46100-Burjassot, Spain, e-mail: mieslo@alumni.uv.es

Conjugate addition reactions have played a crucial role in organic synthesis. The importance of this transformation is boosted by the wide diversity of compounds that can serve as nucleophiles and electrophiles to generate a varied array of products.[1] Such reactions often result in the generation of a new stereocenter, and consequently considerable efforts have been devoted to the development of asymmetric catalytic versions of 1,4-addition reactions. Unsaturated carbonyl compounds and nitroalkenes have been often used as electrophilic partners in asymmetric conjugate additions of easily enolizable nucleophiles such as 1,3-dicarbonyl and related compounds. In this context, α,β-unsaturated imines, readily prepared via condensation of *N*-substituted amines with the parent unsaturated ketones, have emerged as an interesting family of compounds with important applications in the synthesis of nitrogen-containing molecules. However, in contrast to carbonyl substrates and nitroalkenes, the asymmetric conjugate addition of carbon nucleophiles to α,β-unsaturated imines has been scarcely studied.[2]

In this communication we report the asymmetric conjugate addition of malonate esters to α,β-unsaturated *N*-sulfonyl imines catalyzed by PyBOX-La(OTf)$_3$ complexes in the presence of 4Å MS.[3] The reaction gives the corresponding *Z*-enamines bearing a steregoenic center at the allylic position with good yields and enantiomeric ratios up to 95:5.



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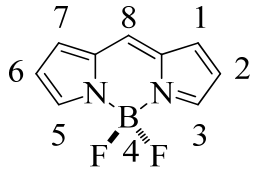
(P-067) The Biellmann BODIPY; a privileged building block for the preparation of *meso*-substituted BODIPY dyes.

Eduardo Peña-Cabrera,[1] Ismael Valois-Escamilla,[1] Juan. O. Flores-Rizo,[1] C. F.Azael Gómez-Durán,[1] José L. Belmonte-Vázquez,[1] Mayra R. Martínez-González,[1] Ismael J. Arroyo,[1] Carlos A. Osorio-Martínez,[1] Lourdes Betancourt-Mendiola,[1] Enrique Alvarado-Martínez,[1] Arlette Urías-Benavides,[1] Brenda D. Gutiérrez-Ramos,[1] Jorge Bañuelos,2 Teresa Arbeloa López,[2] Iñigo López Arbeloa[2]

[1]*Department of Chemistry, University of Guanajuato, Col. Noria Alta S/N Guanajuato, Gto. 36050 México.*

[2]*Departamento de Química Física. Universidad del País Vasco/EHU. Aptdo. 644, 48080 Bilbao, Spain.*

Truly remarkable applications of dipyrromethene-BF_2 fluorophores **1** (BODIPY®)[1] continue to appear in the literature. These fluorescent compounds were first reported by Treibs and Kreuzer in 1968.[2] Little did they know about the great impact these analogues were to have in so many disciplines. The properties of this family of compounds are reported in excellent reviews.[3]



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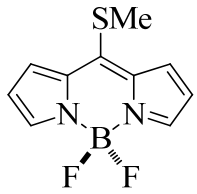

Biellmann BODIPY 2

The ability to introduce a substituent at the 8-position in a highly convergent manner is of paramount importance. The typical Lindsey method[4] involves the acid-catalyzed condensation of an aryl aldehyde with excess pyrrole, followed by DDQ oxidation and coordination with BF_3. Herein, we wish to report a much improved method that is based upon the use of the Biellmann BODIPY **2**[5] in a Pd-catalyzed Cu(I)-mediated cross-coupling reaction (the Liebeskind-Srogl cross-coupling reaction)[6] with boronic acids and organostannanes to obtain *meso*-substituted BODIPY dyes.

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(P-068) Aproximación epigenética a la activación de la producción de metabolitos crípticos por especies del fitopatógeno *Colletotrichum* spp.

Wesley Faria Gomes[1], Carlos Garrido[2], María Carbú,[2] Maria Fátima das Graças Fernandes da Silva[3], Isidro González Collado[1].

[1] *Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Cádiz, 11510, Puerto Real, España.*

[2]*Universidad de Cádiz. Dpto. de Biomedicina y Biotecnología, Laboratorio de Microbiología Facultad de Ciencias de Mar y Ambientales, Universidad de Cádiz, 11510, Puerto Real, España*

[3] *Departamento de Química, Universidad Federal de São Carlos, 13565905, São Paulo, Brasil.*

Colletotrichum es un género de hongos filamentosos que engloba a más de un centenar de especies, muchas de las cuales son capaces de infectar a un único hospedador, pero otras pueden afectar a más de un centenar de plantas diferentes, incluyendo cultivos hortícolas, frutales, plantas ornamentales, y especies forestales.[1] En España, son tres las especies que poseen mayor importancia debido a las enfermedades que causan y a las enormes pérdidas económicas que ocasionan a los agricultores, como son *Colletotrichum acutatum*, *C. gloeosporioides* y *C. graminicola*. Las dos primeras especies (*C. acutatum* y *C. gloeosporioides*) son causantes de la antracnosis en numerosos cultivos frutales, teniendo especial incidencia en la fresa y en los cítricos, mientras que *C. graminicola* es el agente causante de la antracnosis del maíz y el sorgo. Estas especies se encuentran ampliamente extendidas a nivel mundial, ocasionando grandes pérdidas económicas en países como Estados Unidos, Brasil, Israel, España, Portugal, Italia o Francia, entre otros.

Durante los últimos años se han llevado a cabo estudios químicos orientados al conocimiento del metabolismo secundarios de estas especies de hongos, lográndose caracterizar algunos nuevos metabolitos, aunque la producción de estos, en las condiciones ensayadas, ha sido minoritaria.[2]

Actualmente, con el fin de mejorar el rendimiento y el perfil metabólico, referido a las cantidades y tipos de metabolitos secundarios producidos por las especies del género *Colletotrichum*, se están llevando a cabo estudios epigenéticos mediante la utilización de diferentes medios de cultivo vegetales y, el uso de modificadores epigenéticos.

En esta comunicación se presentarán los resultados obtenidos a partir de dos cepas de *C. acutatum* (aisladas de fresa y de flor de naranja), una cepa de *C. gloeosporioides* (aislada de fresa) y una cepa de *C. graminicola* (aislada de maíz), siendo estas cultivadas en medios pobres, alimentados con extractos de fresa, tomate, naranja y cereales. Al mismo tiempo, se están estudiando los metabolitos producidos tras la adicción de diferentes modificadores epigenéticos, como son el 1,3-diaminopropano y SAHA.

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(P-069) New benzopolycyclic cage amines with NMDA receptor antagonist activity

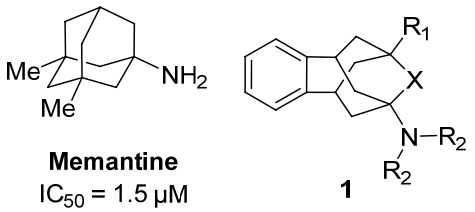
Santiago Vázquez*,[1] María D. Duque,[1] Eva Torres,[1] Elena Valverde,[1] María Lafuente,[1] and Francesc X. Sureda[2]

[1]*Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, and Institute of Biomedicine (IBUB), Universitat de Barcelona, Av. Joan XXIII s/n, 08028 Barcelona, SPAIN, e-mail: svazquez@ub.edu*

[2]*Unitat de Farmacologia, Facultat de Medicina i Ciències de la Salut, Universitat Rovira i Virgili, C/ St. Llorenç 21, 43201 Reus, SPAIN*

N-Methyl-D-aspartate (NMDA) receptor antagonists act by protecting neurons from excessive pathological calcium influx, which leads to neuronal damage and finally to neuronal cell death, common features in neurodegenerative disorders such as Alzheimer's disease. So far, memantine is the only NMDA receptor antagonist that has been introduced for the treatment of this disease (Figure 1)[1].

In the last few years our research group has synthesized and carried out the pharmacological evaluation of a large variety of new memantine analogues. We found that amines of general structures **1** were active as NMDA receptor antagonist, some of them with IC_{50} values similar to that of memantine (Figure 1)[2].



Compound	X	R_1	R_2	IC_{50} (μM)
1a	O	Me	Me	3.9 ± 0.4
1b	O	H	Me	3.8 ± 0.3
1c	CH_2	Me	Me	11.8 ± 3.1

Figure 1. Memantine and general structures of polycycles **1** and their activity values.

We present here the design and synthesis of new derivatives of general structure **3** along with their evaluation as NMDA receptor antagonists (Figure 2). The synthesis of these compounds revolves around a Prins-Ritter reaction of a non-conjugated enone with chloroacetonitrile to give the chloroacetamide **2** that was further elaborated to **3**.

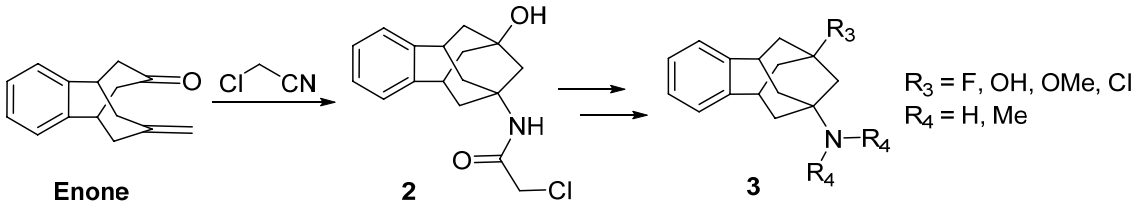


Figure 2. New benzopolycyclic amines.

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(P-070) Ciclopropanaciones mediadas por especies de baja valencia de Ti y Zr derivadas de dicloruros de metalocenos.

Mª Jesús Durán-Peña, José Manuel Botubol Ares, Rosario Hernández-Galán e Isidro G. Collado

Departmento de Química Orgánica, Universidad de Cádiz, Campus Universitario Río San Pedro s/n, 11510, Puerto Real, Cádiz, España, e-mail: mari.duranpena@alum.uca.es

Los cicloalcanos se encuentran en la naturaleza formando parte de un amplio número de compuestos orgánicos, incluyendo el ciclopropano, el cicloalcano más pequeño de la serie y el de mayor tensión de anillo. A pesar de ello, la unidad ciclopropano se encuentra como elemento estructural base en un amplio rango de Productos Naturales que poseen una amplia variedad de actividades biológicas.[1] Todo ello ha provocado un gran interés por el desarrollo de nuevas metodologías sintéticas para obtener ciclopropanos.

Las ciclopropanaciones mediante complejos de zirconio son un área de investigación reciente.[2] Es bien conocido que los dicloruros de zirconoceno y titanonoceno pueden ser reducidos hasta los correspondientes complejos de baja valencia por especies tales como la amalgama Na/Hg, naftalenuros o por metales como Mn o Mg.[3] En esta comunicación presentaremos los resultados obtenidos al tratar alcoholes alílicos con las especies resultantes de la reducción de estos dicloruros en presencia de dihaloalcanos, así como los mecanismos de reacción propuestos para la obtención de ciclopropanos y *gem*-dimetilciclopropanos (*Figura 1.*)

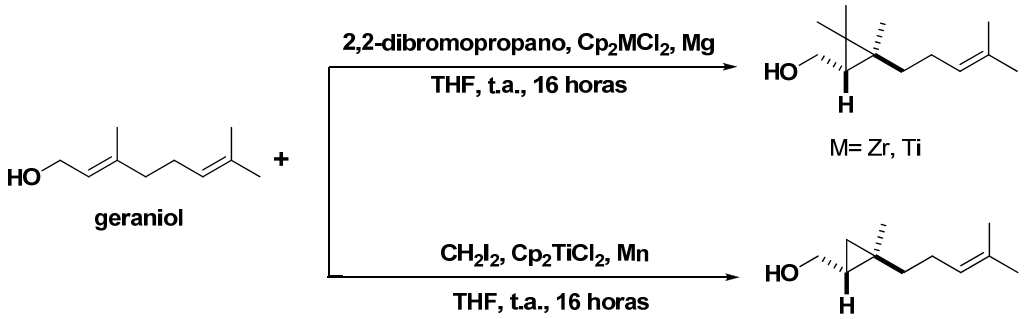

Figura 1. Ciclopropanación regio y estereoselectiva mediante especies de Ti y Zr de baja valencia.

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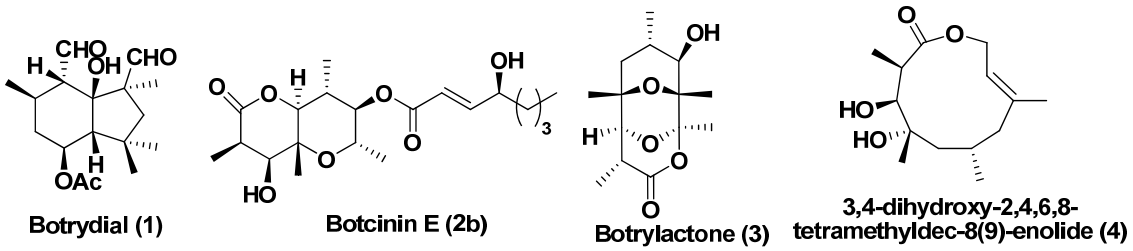
(P-071) A Shared Biosynthetic Pathway for Polyketide Produced by Botrytis *cinerea* Revealed through Mutasynthesis and Isotopic Labelling Experiments

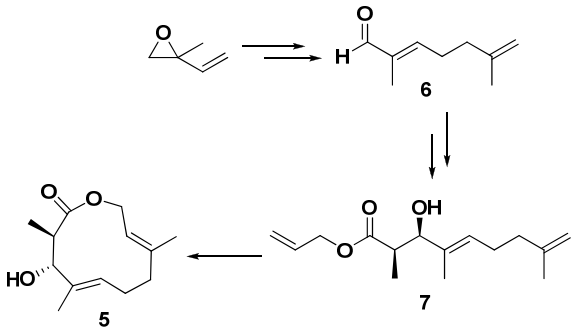
José Manuel Botubol Ares, Mª Jesús Durán-Peña, Antonio José Macías-Sánchez, Isidro G. Collado and Rosario Hernández-Galán

Department of Organic Chemistry, University of Cadiz, Campus Universitario Río San Pedro s/n, 11510, Cádiz, Puerto Real, Spain, e-mail: josemanuel.botubolares@alum.uca.es

Botrytis cinerea is a well-known phytopathogen that causes the grey mould disease, which affects a high number of commercial crops.[1] *B. cinerea* produces two major phytotoxic metabolites; a family of sesquiterpene metabolites with botryane skeleton, mainly botrydial (**1**), and two families of polyketide lactones: botcinins (**2**) and botrylactones (**3**). Recently, we have demonstrated by isotopic labelling experiments and the study of mutants with disrupted genes that botcinins and botrylactones share a biosynthetic pathway.[2] On the other hand, 3,4-dihydroxy-2,4,6,8-tetramethyldec-8-enolide (**4**) is a metabolite isolated too from a mutant strain of *B. cinerea*.[3]



In the context of our interest in metabolites produced by *B. cinerea* in general and in understanding how they are biosynthesized by the fungus, we decide to study the possible biosynthetic relationship of **4** with the other polyketides produced by this fungus: botcinins and botrylactones. In this communication, we describe the synthesis of **5**, an analogue compound of **4,** and based both in the mutasynthesis and feeding experiments with sodium [2-^{18}O]-acetate of mutant strains of *B. cinerea*, we propose a common biosynthetic route.



Synthetic route of **5**.

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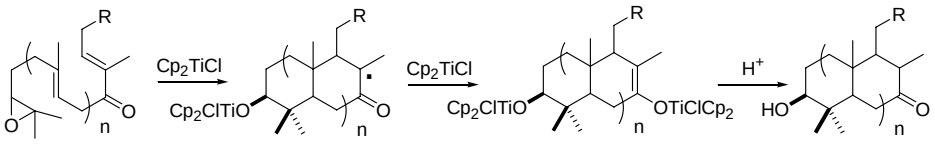
(P-072) Ti(III)-catalyzed cyclizations of ketoepoxypolyprenes: frustrated polycyclizations and unexpected stereoselectivities.

Sara P. Morcillo, Delia Miguel, Sandra Resa, Alba Millán, José Justicia, Juan M. Cuerva*

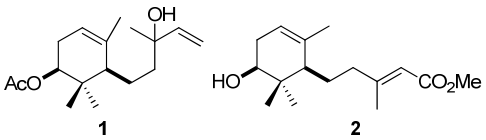
Department of Organic Chemistry, Faculty of Sciences, University of Granada, C. U. Fuentenueva s/n, 18071 Granada, Spain, e-mail: sandriw@correo.ugr.com

In recent years, the radical cyclisation of epoxypolyprenes catalyzed by titanocene(III) complex Cp_2TiCl[1] has emerged as a powerful tool for the synthesis of terpenic structures. This bioinspired protocol has been used for the cyclization, under smooth reaction conditions, of different polyprenes with high diastereoselectivity.[2] However, the preparation of compounds from incomplete cyclizations was not possible using this method.

In the present communication, we describe a new strategy for the control of Ti(III)-catalyzed bioinspired radical cyclizations using ketone groups allocated in appropriate positions in the starting epoxypolyenes. This method allowed us to truncate the cyclization in the desired stage, yielding the corresponding cyclization products with complete steroselectivity and high yields. The presence of ketone groups in the final cyclization products allowed us, apart of the excellent control in the cyclization process, generate alkenes in specific positions, as tri- and tetrasubstituted alkenes, present in natural terpenoids.



This strategy has been used in the synthesis of several natural terpenoids, as monocycles **1** and **2**, isolated from *Atermisia chamaemelifolia*[3] and *Celistopholis glauca*,[4] respectively, in a few steps and complete selectivity.



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(P-073) Identificación y caracterización de metabolitos crípticos en el hongo fitopatógeno *Botrytis cinerea* mediante el uso de técnicas epigenéticas.

Victoria E. González-Rodríguez,[2] Inmaculada Izquierdo-Bueno,[1] Javier Moraga,[1] Carlos Garrido,[2] María Carbú,[2] Jesús M. Cantoral,[2] Isidro González Collado.[1]

[1] Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Cádiz, 11510, Puerto Real, España. [2]Universidad de Cádiz. Departamento de Biomedicina y Biotecnología, Laboratorio de Microbiología Facultad de Ciencias de Mar y Ambientales, Universidad de Cádiz, 11510, Puerto Real, España

Botrytis cinerea es una de las especies de hongos fitopatógenos más importantes debido a que es capaz de afectar a cientos de cultivos, se encuentra ampliamente distribuido a nivel mundial y son muy elevadas las pérdidas económicas que ocasiona tanto en cultivos frutales, hortícolas, y ornamentales. La incidencia de este hongo lo ha convertido en un organismo modelo de investigación, siendo un patógeno de referencia para muchos grupos de investigación en todo el mundo. Muchos esfuerzos y recursos se emplean para: i) conocer a fondo los mecanismos metabólicos que este hongo emplea para causar infección y vencer las estrategias de resistencia desarrolladas por las plantas y, ii) buscar estrategias racionales y eficientes de control de este hongo para poder disminuir al mínimo su incidencia sobre los cultivos.

Hasta la fecha, se han identificado dos familias de toxinas que juegan un papel esencial en los mecanismos de infección de *B. cinerea*, botridial y botcininas,[1,2] cuyas rutas biosintéticas se han descrito recientemente. Además de estas tóxinas, se han detectado otros metabolitos secundarios producidos por *B. cinerea* que poseen actividad fitotóxica, y aunque se producen en muy pequeña cantidad en las condiciones de cultivo ensayadas, puede que jueguen un papel importante en el mecanismo de infección de *B. cinerea*.

Actualmente, se están llevando a cabo estudios epigenéticos para conseguir un mayor rendimiento en la producción de estas nuevas tóxinas y poder identificar nuevos metabolitos crípticos que no hayan sido producidos por el hongo en las condiciones ensayadas hasta el momento. Para conseguir este doble objetivo, se están utilizando medios de cultivos vegetales, que incluyen extractos de uva, calabacín y plantas ornamentales, así como modificadores epigenéticos. Los resultados, que se presentan en esta comunicación, muestran cambios tanto en el rendimiento, como en el perfil metabólico biosintetizado por el hongo.

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(P-074) Synthesis and evaluation of new π-conjugated systems based on heterocyclic oligophenylethynylene derivatives

Rocío Jurado,[1] Delia Miguel,[1] Luis Álvarez de Cienfuegos,[1] María Teresa González,[2] Juan M. Cuerva [1]

[1]*Department of Organic Chemistry, Faculty of Sciences, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: tiny@correo.ugr.es*

[2]*Instituto Madrileño de Estudios Avanzados en Nanociencia (IMDEA-Nanociencia), Ciudad Universitaria de Cantoblanco, E-28049 Madrid, Spain.*

Understanding of the charge transport characteristics of molecules in nanoscale metal-molecule-metal junctions is of fundamental interest and represents a key step toward the realization of molecule-based electronics.[1] Conventional methods to wire molecules rely on their self assembly on an electrode surface. Whenever two electrode tips are closer than the total length of a molecule, one or more of these molecules can self-assemble bridging the gap and forming a molecular junction. The most widely used techniques to achieve this are based on the break-junction (BJ) phenomena, mainly mechanically controllable break junction (MCBJ)[2] and scanning tunneling microscopy-based break junction (STMBJ)[3] (Figure 2).

π–Electron molecules, oligomers and polymers, are the subject of intense research since they can mediate charge transport along the π–conjugated pathway. In this sense, oligo(phenylene ehynylene) (OPE) compounds represent a particular unique family of molecular wires, due to they are fully π–conjugated rigid rod like molecules with an small HOMO-LUMO gap (~3eV).

Although many factors have been studied on OPE derivatives of different nature (like anchoring group, chemical structure, length, torsion angle, presence of groups with different electronic properties, molecular symmetry) it has not been analyzed how the replacing of the central benzene ring by a heterocyclic compound affects to the electron transport. In this way, our goal is to design, synthesize and evaluate a new family of OPE derivatives not only with π-deficient (pyridine, pyrimidine, pyrazine, pyridazine) but also π-excedent (thiophene) (Figure 1) with the STMBJ technique.

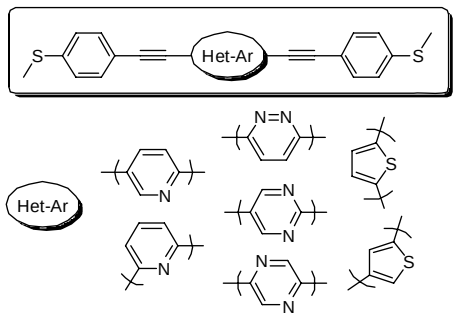

Figure 1. Proposed structures for OPE derivatives

Figure 2. Scanning tunneling microscope at IMDEA-Nanoscience

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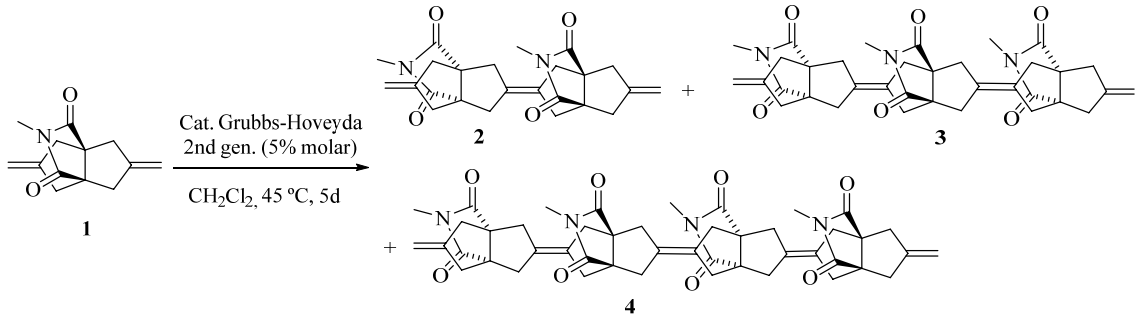
(P-075) Cross Metathesis of several Methylenecyclopentane Derivatives

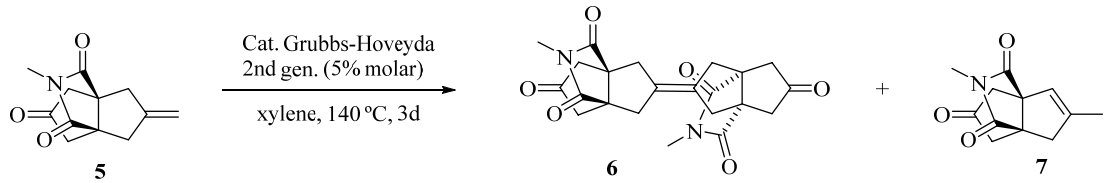
Ane Otermin, Tània Gómez, Eugenia Buden and Pelayo Camps

Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia and Institut de Biomedicina de la Universitat de Barcelona (IBUB), Universitat de Barcelona, Av. Joan XXIII, E-08028, Barcelona, Spain, e-mail: camps@ub.edu

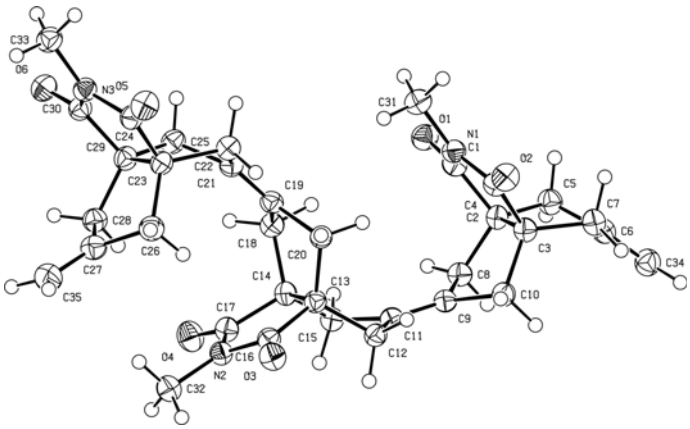
The cross metathesis (CM) of several methylenecyclopentane derivatives[1] like **1** and **5** using Grubbs-Hoveyda second generation catalyst has been studied. In these reactions, tetrasubstitued alkenes have been formed in good yields.
In the case of diene **1** products from single **2**, double **3** and triple **4** CM were formed.



With enone **5** a good yield of the CM product **6** was obtained working at 140 ºC in xylene for 3 d, showing the high thermal stability of this catalyst.



In general, high anti-stereoselectivity has been observed. The assignment of the stereochemistry of the single CM products has been performed through the analysis of the NMR data for the epoxide derivatives and in the case of the double CM product by X-ray diffraction analysis.



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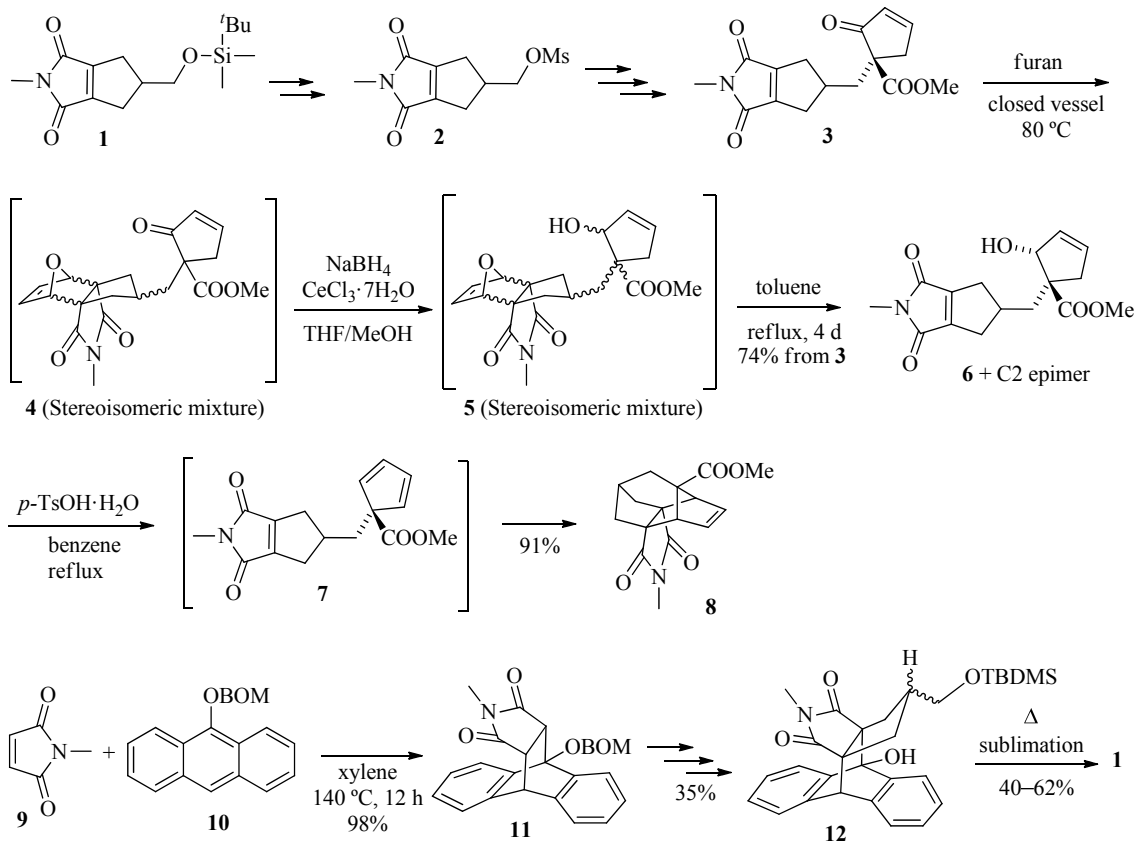
(P-076) A new entry to functionalized 2,8-ethanonoradamantane derivatives

Tània Gómez, Ane Otermin, Claudio Monasterolo and Pelayo Camps
Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia and Institut de Biomedicina de la Universitat de Barcelona (IBUB), Universitat de Barcelona, Av. Joan XXIII, E-08028, Barcelona, Spain, e-mail: camps@ub.edu

In connection with the preparation of polycyclic compounds as new scaffolds for the preparation of potentially active compounds, we have developed a synthetic sequence for the preparation of highly functionalized 2,8-ethanonoradamantane derivatives, whose key-step consists of an intramolecular Diels-Alder reaction. Chemoselective reduction of the intermediate enone **3** required protection of the maleimida function through their Diels-Alder adducts with furan. The maleimide function was recovered, after reduction of the enone, through a thermal retro-Diels-Alder reaction.[1] Dehydration of **6** gave polycycle **8**, probably through the intermediary of 1,1-disubstituted cyclopentadiene **7**.

Also, an alternative procedure to prepare the key intermediate, **1**, from *N*-methylmaleimide **9** with a yield five times higher than that previously described, have been developed. The C=C bond of *N*-methylmaleimida **9** was protected as a Diels-Alder adduct with 9-benzyloxymetoxyanthracene **10**. After annulation, hydroboration / oxidation and protection, **1** was obtained through a retro-Diels-Alder reaction.



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(P-078) $Sn(OTf)_2$ Catalysed Domino Synthesis of Clovamidines as antifungal Agents

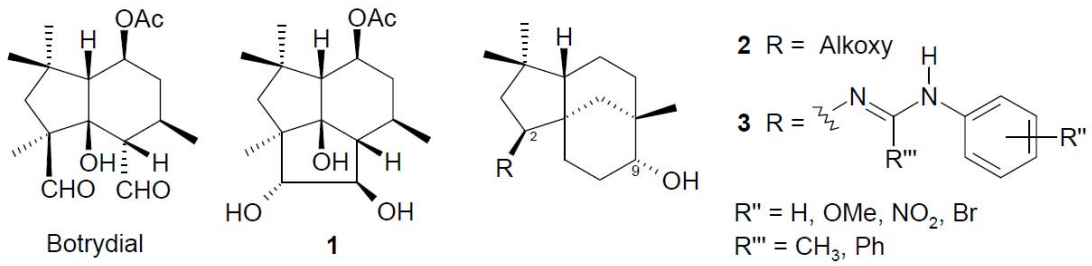
Adriana A. P. Bracarense, Dhionne C. Gomes, Antonio Ruano-González, Redouan Azarken, Beatriz O'Reilly, Jacqueline A. Takahashi, Rosario Hernández-Galán, Isidro G. Collado, Antonio J. Macías-Sánchez

Department of Organic Chemistry, Faculty of Science, University of Cádiz, Campus Universitario de Puerto Real, 11510 Puerto Real, Cádiz, Spain, e-mail: antoniojose.macias@uca.es

Plant pathogens such as *Botrytis cinerea* are responsible for serious economic losses.[1] Part of the interaction of *B. cinerea* with host plants involves the effect that botrydial, a nonspecific low molecular weight phytotoxin, has on the plant. Our research group has explored a method of fungal control using analogues of biosynthetic intermediates[3] (such as **1**) *en route* to botrydial. Sesquiterpene derivatives with several carbon skeletons have been prepared for this purpose.[2]

2β-Alkoxyclovane-9α-ol derivatives (such as **2**), present a structural similarity to key intermediates, such as **1**, in the biosynthesis of the phytotoxic botryane metabolites produced by *B. cinerea*, and they have been shown to inhibit the growth of *B. cinerea*.[4] Structure-activity studies on 2-alkoxyclovan-9-ols show a correlation between antifungal activity and the nature of the side chain at C-2, being the clovan-9-ol moiety an invariant.[5] In order to extend this methodology, we need to introduce side-chains with nitrogen atoms directly attached at C-2, as they have a greater binding potential with active centers from enzymes potentially involved in the biosynthetic pathway to botrydial. In order to accomplish this goal, we have explored a domino reaction involving the rearrangement of caryophyllene oxide, catalysed by Sn(II), and the capture of the resulting carbocation by a nitrile and an aromatic amine.

We present the preparation of *N*-(hydroxyclovanyl) amidines (**3**) via reaction of caryophyllene oxide with nitriles and arylamines, catalysed by $Sn(OTf)_2$. Competing reaction pathways and relevant biological activity is discussed.



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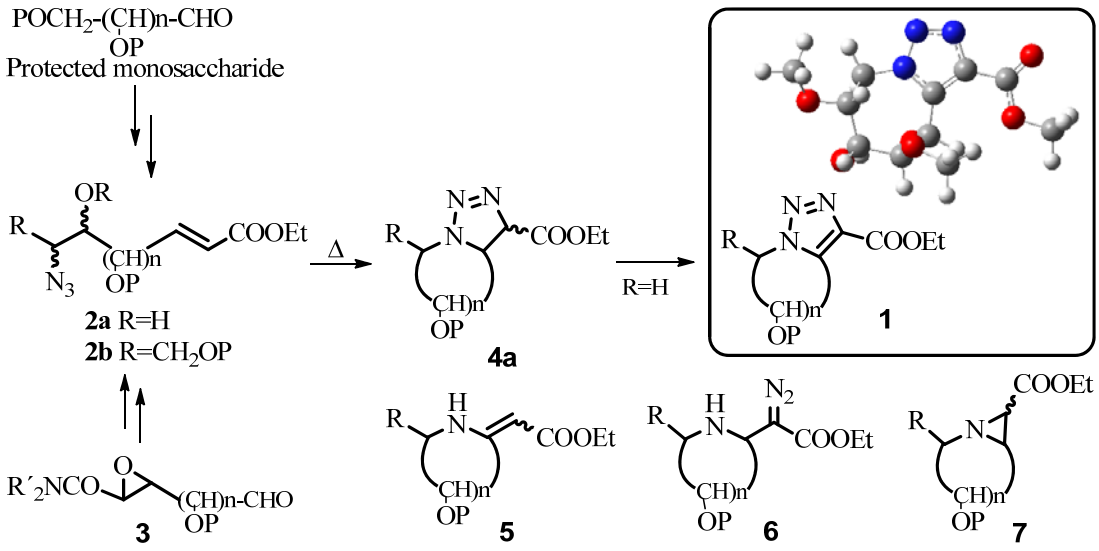
(P-080) Intramolecular [3+2] cycloaddition of azido-unsaturated esters derived of monosaccharides

M. Soledad Pino-González,[1] Antonio Romero-Carrasco,[1] Saturnino Calvo-Losada,[2] J. Joaquín Quirante[2]

[1] *Departamento de Química Orgánica and* [2]*: Departamento de Química Física. Facultad de Ciencias. Campus de Teatinos, s/n. Universidad de Málaga. 29071 Málaga (Spain)*

Iminosugars[1] have been shown to be very potent inhibitors of glycosidases and glycolsyltransferases. Due to their ability to resemble the transition states of the sugars involved in these processes, a variety of monocyclic and bicyclic iminosugars have been synthesized or isolated from natural sources over the years. As part of our ongoing work on the preparation of glycosidase inhibitors, we developed stereoselective methods for synthesizing iminosugars from 2,3-epoxyamides obtained from monosaccharides.[2]
Now, we are interested in the syntheses of novel bicyclic triazoles **1**, by intramolecular cycloaddition, due to the possibility of combining azido group and unsaturated esters in the same molecule. The triazole system is broadly considered in syntheses of bioactive products and the option of fused iminosugar with triazole has been evaluated.[3] Firstly, we started with a less complex azido derivative **2a** to continue with azido compounds **2b** obtained from our 2,3-epoxyamides **3**, by regioselective introduction of an azido group. The fused triazolines **4a** were formed by heating of **2a**. Aromatization of **4a** afforded byciclic triazoles **1**. There are several possibilities in the cyclization process depending on the reaction conditions and products **5, 6** and **7** can be formed. Moreover, we conducted a theoretical DFT based study of the cycloaddition to value the probability of formation of the triazoline **4a** and subsequent aromatization to triazole **1**, *versus* elimination to the unsaturated ester **5**.



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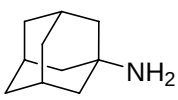
(P-081) Novel anti-influenza drugs: inhibitors of the V27A mutant M2 channel

Marta Barniol-Xicota,[1] Eva Torres,[1] Chunlong Ma,[2] Lawrence H. Pinto,[2] and Santiago Vázquez[1]

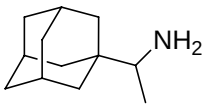
[1]*Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, and Institute of Biomedicine (IBUB), Universitat de Barcelona, Av. Diagonal 643, Barcelona, E-08028 Spain, e-mail: martabx@gmail.com*

[2]*Department of Neurobiology and Physiology, Northwestern University, Evanston, Illinois, USA*

Influenza virus, commonly known as *the flu*, has been a widespread pathogen agent among humans and animals since immemorial times. Normally its symptoms are mild even though new lethal outbreaks appear periodically, being able to evolve in a pandemia as happened with the "Spanish flu" (1917-1918, strain H1N1) which killed 20-50 million people worldwide. Recently, in April 2013, the strain H7N9 made the alarms ring in China, pointing out that the virus still is a real menace for public health.[1] Amantadine and rimantadine, which target M2 channel, have been the most effective anti-influenza drugs for decades, nevertheless trough several mutations of the M2 channel the virus has become resistant to them. As the main mutations of the channel consist in a change on its width, our main goal is to develop more voluminous M2 inhibitors since V27A mutants have a wider channel than wild type has.[2]

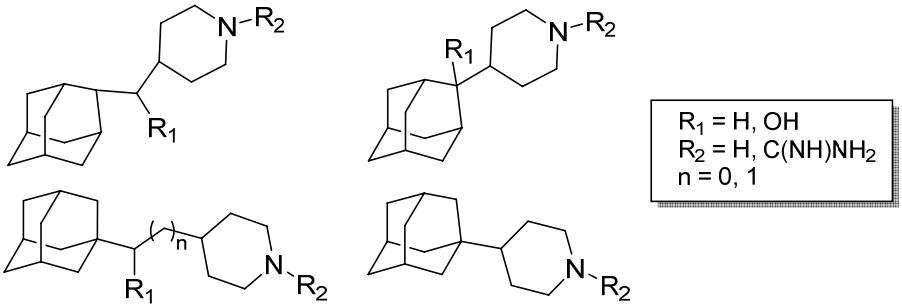


Amantadine



Rimantadine

According to that purpose we have synthesized a family of compounds in which the amino group, included in a piperidine ring, was moved further away from the adamantyl group. In order to figure out which is the optimum length for these compounds, we designed analogues changing the number of atoms which connected the adamantyl and the heterocyclic moiety. Moreover we found useful to include a guanidine functional group, in order to assess the effect of the basicity in the pharmacological activity. Finally the effect of introducing such a polar group as an alcohol was also evaluated.



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(P-082) Minor terpenes from *Pericallis echinata*

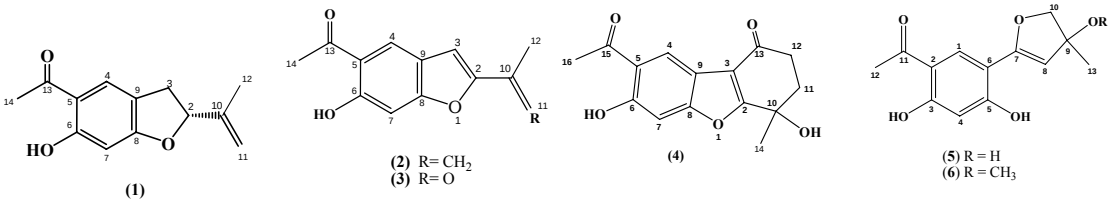
A. G. Portero[1], C. E. Díaz[1], M. Reina[1], A. González-Coloma[2], B. M. Fraga[1]

[1]*Instituto de Productos Naturales y Agrobiología, CSIC. Avda. Astrofísico F. Sánchez, nº 3, 38206. Tenerife, Spain.*
[2]*ICA-CCMA, CSIC, Serrano 115-dpdo, 28006 Madrid, Spain.*

Pericallis (*Asteraceae*) is an endemic genus of the Macaronesian region with 15 species, 13 of which grow in the Canary Islands. Phytochemically, these plants are characterized by their content in benzofuranes, sesquiterpenes and pyrrolizidine alkaloids.[1] These compounds have a great interest due to their broad range of activity including bactericidal,[2] antitumoral[3] and antifeedant.[4]

As part of our ongoing chemical and biotechnological research on the sustainable production of natural agrochemicals from Canary endemic species, we have selected *Pericallis echinata* (L. fil.) B. Nord., a plant endemic to the island of Tenerife with a restricted habitat.

We have reported the isolation of several benzofurane compounds from *P. echinata* and their activity against several insect species.[5] Here we describe the isolation of three new minor compounds from the aerial parts of *P. echinata*. Pericallona (**4**), pericanol (**5**) and methoxy-pericanol (**6**). The structures of these compounds were elucidated on the basis of their mono- and bi-dimensional NMR data. Pericallone (**4**) showed antifeedant activity against the generalist insect *Spodoptera littoralis*.



Acknowledgements:

This work has been supported by grant CTQ2009-14629-C02-01 and A.G. Portero by a JAE predoctoral fellowship.

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(P-083) *Persea indica* endophyte screening for the biotechnological production of biopesticides

P. Bolaños[1], C.E. Díaz[1], B.M. Fraga[1], C. Giménez[2], R. Cabrera[2], R. Muñoz[3], M.F. Andres[3], A. González-Coloma[3]

[1]*Instituto de Productos Naturales y Agrobiología, IPNA-CSIC. Avda. Astrofísico F. Sánchez, nº 3, 38206. Tenerife, Spain.*
[2]*UDI Fitopatología. Facultad de Biología. Universidad de La Laguna, Tenerife, Spain.*
[3]*Instituto de Ciencias Agrarias, ICA-CSIC, Serrano 115-bis, 28006 Madrid, Spain.*

Plants are a reservoir of microorganisms known as endophytes.[1] By definition, these microorganisms (mostly fungi and bacteria) live in the intercellular spaces of plant tissues. These endophytes produce bioactive substances that may be involved in the host-endophyte relationship. Therefore, these microorganisms represent a biotechnological source of bioactive metabolites.

We have isolated 34 different species of fungal endophytes from the tree *P. indica.* This plant is one of the dominant species of the Canarian laurel forest[2] and has been reported as a potential source of insect-control agents.[3] Endophytic fungi have been sampled during three different seasons and from different plant parts (leaf, stem and root) to check for differential distribution as a result of their adaptation to the physiological conditions in different plant parts.[4]

Molecular identification of each of the endophyte isolates was carried out by sequencing a rDNA region extracted from the mycelium followed by sequence comparison with previously identified fungal species (GenBank).[5] The distribution of endophyte species within the host plant and their seasonal frequency of isolation will be discussed.

These endophytes were cultured in liquid medium and the resulting extracts analyzed by HPLC-MS to compare their chemical profiles with that of the host plant. Moreover, we have also studied the biological activity of these fungal extracts against plant pests (insects, nematodes and fungal pathogens) to assess their potential as biotechnological biopesticides.

Acknowledgements

This work has been supported by grant CTQ2009-14629-C02-01 and P. Bolaños by a FPI predoctoral fellowship.

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(P-084) 5-Iodo-1,2,3-triazolium-based Fluorescent Halogen Bonding Sensors for Hydrogen Pyrophosphate Anion

Fabiola Zapata, Pedro Molina, Antonio Caballero

Departamento de Química Orgánica, Universidad de Murcia, Campus de Espinardo, 30100, Murcia, Spain, e-mail: fazafer@um.es

The field of anion recognition chemistry has expanded enormously during the past few decades, inspired in large part by the realization of the many fundamental roles negatively charged species play in a range of chemical, biological, medical and environmental processes[1]. Through the incorporation of complementary electrostatic, hydrogen bonding, Lewis acid-base and anion-π non-covalent interactions into acyclic and macrocyclic molecular framework design, numerous synthetic anion receptors and sensors have been developed[2].

One exciting alternative to the traditional non covalent interaction could be the utilization of the halogen bonding in the anion recognition.

We report in this communication the synthesis and the anion recognition studies of a new fluorescent halogen bonding receptor, using 5-Iodo-1,2,3-triazolium motif as a binding site and pyrene as a fluorescent signalling units.

The new halogen bonding shows an excellent selectivity for hydrogen pyrophosphate anion towards the rest of the anion tested, interestingly the formation of the complex results in a dramatic increase in the fluorescence emission intensity of the pyrene excimer.

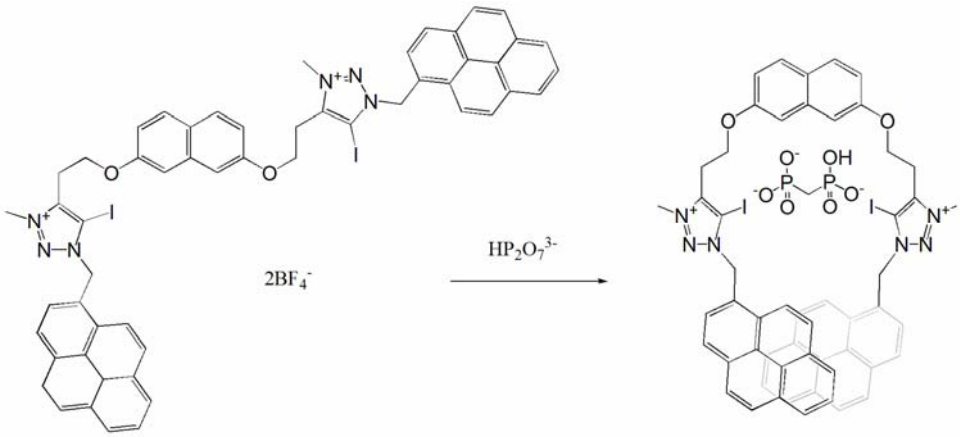

Figure 1: Schematic representation of the formation of the complex between the bidentate 5-Iodo-1,2,3-triazolium receptor and hydrogen pyrophosphate anions.

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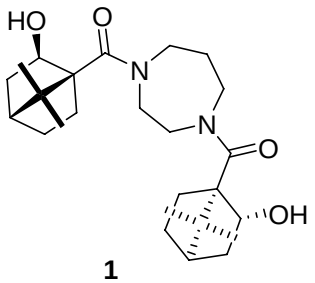
(P-085) New polymers functionalized with chiral bis(hydroxyamide) in asymmetric organozinc catalysis: Synthesis and catalytic properties

Rafael Sandoval, Esther M. Sánchez-Carnerero, Luis Cerezo, Beatriz Lora, Florencio Moreno and Santiago de la Moya*

Department of Organic Chemistry I, Complutense University of Madrid, Ciudad Universitaria s/n, 28040-Madrid, Spain, e-mail: santmoya@ucm.es

Our research group has demonstrated that certain chiral bis(hydroxyamides) derived from enantiopure ketoninic acid (CBHA, eg **1**) are able, not only to mimic the activity of other commonly used ligands in asymmetric organozinc catalysis (e.g. chiral amino alcohols),[1] but also to notably improve the chemical stability of both ligand and organozinc catalyst. These facts allowed us the development of a first family of polystyrene polymers decorated with such CBHA (**2**), which were easily recovered and reused in multiple successive applications (more than 20) of an organozinc-catalyzed asymmetric reaction (enantioselective ethylation of aldehyde) without loss of catalytic activity.[2]

In order to improve the catalytic activity of these interesting long-life reusable functional polymers, by minimizing adverse kinetic effects (when compared with the homogeneous parent ligand CBHA, due to the diffusion of reactants and products at the interface where the heterogeneous catalytic reaction occurs), we have designed and synthesized new families of CBHA-functionalized polymers, studying their asymmetric catalytic activity in comparison with both **1** and **2**. This communication presents the results obtained from this research.



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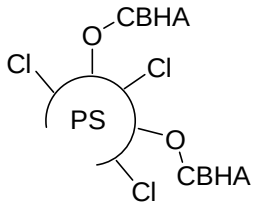

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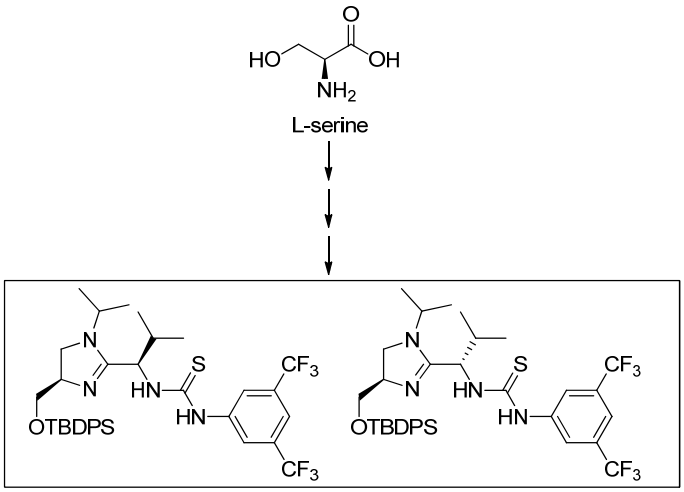
(P-086) Development of novel bifunctional chiral thiourea derivative as potential organocatalyst

Victor Blasco, Ana Escamilla, Ana C. Cuñat*, Nuria Roda, Juan F. Sanz*
Departamento de Química Orgánica , Facultad de Química, Universidad de Valencia, c/ Dr. Moliner 50, 46100-Burjassot, España, email: ana.escamilla@uv.es

In this communication, we are describing the design of a chiral bifunctional thiourea derivative bearing an imidazoline ring in expectation of its dual activation of both nucleophiles and electrophiles, which might cause it to promote a wide range of nucleophilic addition reactions.
There are two stereogenic carbons in the synthesized structure, and both come from enantiomerically pure L-aminoacids. The most important moiety of this structure is the imidazoline ring, which is prepared from an aldehyde and a chiral diamine. In turn, the diamine is obtained from the chiral aminoacid L-serine in several steps.
The rigidity of the chiral imidazoline scaffold and cooperative function of two N-H bonds in the compound are expected be crucial for its enantioselectivity.
The diastereosimomerical compounds will be will be tested as organocatalysts in several transformations, such as Henry or Aza-Henry,[1] Michael[2] and Mannich[3] reactions.



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(P-088) Synthesis of new *O*- and *C*- BODIPYs: Excellent laser dyes

Gonzalo Durán-Sampedro,[1] Antonia R. Agarrabeitia,[1] Luis Cerdán,[2] Angel Costela,[2] Inmaculada García-Moreno,[2] Ixone Esnal,[3] Jorge Bañuelos,[3] Iñigo López Arbeloa,[3] and María J. Ortiz [1]

1Department of Organic Chemistry I, Complutense University of Madrid, Avda. Complutense s/n, 28040 Madrid, Spain, e-mail: mjortiz@ucm.es

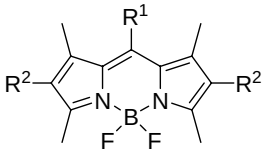
2Department of Physical Chemistry, Institute Quimica-Fisica "Rocasolano", C.S.I.C., Serrano 119, 28006 Madrid, Spain.

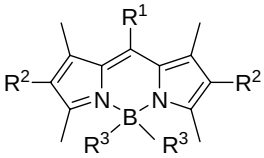
3Department of Physical Chemistry, UPV-EHU, 48080 Bilbao, Spain.

The 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene, so-called *F*-BODIPYs are a versatile family of dyes because they exhibit high fluorescence quantum yields, intense absorption, and tunable emission wavelength as well as high chemical versatility to be functionalized. Currently, these dyes have numerous applications such as fluorescent probes in biological systems, photosensitizers for photodynamic therapy, laser generators and as materials for incorporation into electroluminescent devices. [1]

Among the numerous modifications in the BODIPY core, the replacement of one or both of the fluorine atoms in *F*-BODIPYs has become an active area. Thus, a wide variety of *C*-BODIPYs, *E*-BODIPYs and *O*-BODIPYs via fluorine displacement by alkyl or aryl, ethynyl and alcoxy or aryloxy groups, respectively, have been synthesized. The introduction of these functionalizations has been employed to increase the Stoke's shift and chemical and photochemical stability of these fluorofores opening the way to a new class of highly luminescent dyes. [2]

In this comunication, we described the synthesis and emission properties characterization of a library of new *O*- and *C*-BODIPYs from commercially available BODIPYs. It is shown that these dyes are highly fluorescent and exhibit enhanced laser action with respect to their *F*-BODIPY analogues, both in liquid solution and solid phase.





Available BODIPYs

PM546: R^1 = Me; R^2 = H
PM567: R^1 = Me; R^2 = Et
PM597: R^1 = Me; R^2 = *t*Bu
PM605: R^1 = CH_2OCOMe; R^2 = Et
PM650: R^1 = CN; R^2 = Me

R^3 = CH_3COO, CF_3COO, CN, C≡CH

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(P-089) Versatile *meso*-functionalization of 8-methyl BODIPY dyes

Eduardo Palao,[1] Laura Montalvillo-Jiménez,[1] David Ortiz,[1] Antonia R. Agarrabeitia,[1] Jorge Bañuelos,[2] Teresa Arbeloa Lopez,[2] Iñigo Lopez-Arbeloa,[2] and Maria J. Ortiz[1]

[1]*Department of Organic Chemistry I, Complutense University of Madrid, Ciudad Universitaria s/n, 28040 Madrid, Spain, e-mail: mjortiz@ucm.es*

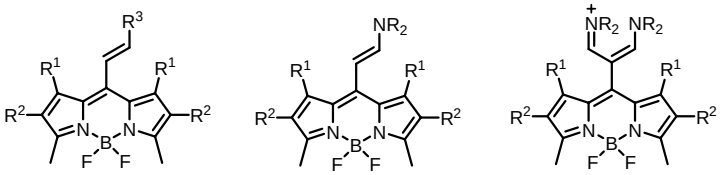
[2]*Department of Physical Chemistry, UPV-EHU, 48080 Bilbao, Spain.*

Among organic dyes, the 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacenes, commonly known as BODIPY, are a very interesting family of dyes that possess unique properties that have attracted increasing interest for their technological and/or biomedical applications.[1] Many of their applications require derivatization of the *meso*-position to obtain new BODIPY dyes with interesting photophysical properties.

Various approaches have been described in the literature for this purpose. Generally, this functionalization can be carried out by treatment of pyrrole and aromatic aldehydes or acid chloride,[1] although this route have limitations. Also, an important method for the introduction of the different functionalization in *meso*-position is the post-modification on some ready-made BODIPY, using 8-methylthio derivatives[2] or 8-halogenated BODIPYs.[3]

In addition, the methyl group in 8-position is not highly reactive; however, it is still able to participate in some condensation reactions. Recently, *meso*-polymethine substituted BODIPYs[4] and 8-aminoalkyl derivatives have been described.[5]

In this communication, we report the synthesis, photophysical and electrochemical properties of a new *meso*-styryl derivatives by regioselective Knoevenagel-type condensation with different aromatic and aliphatic aldehydes, as well as mono and diformylated products by Vilsmeier-type reaction.



These examples add further support to the proposal that methyl groups in *meso*-position of the BODIPY core are more prone to undergo these types of reactions that the methyl groups located at 3 and/or 5-positions.

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(P-090) Stereoselective Synthesis of a Marine Macrolide Side Chain

Janire Lamariano-Merketegi,[1,2] Adriana Lorente,[1,2] Fernando Albericio[1,2,3] and Mercedes Álvarez[1,2,4]

[1]*Institute for Research in Biomedicine, Barcelona Science Park-University of Barcelona, Baldiri Reixac 10, E-08028 Barcelona, Spain, email: janire.lamariano@irbbarcelona.org, mercedes.alvarez@irbbarcelona.org*

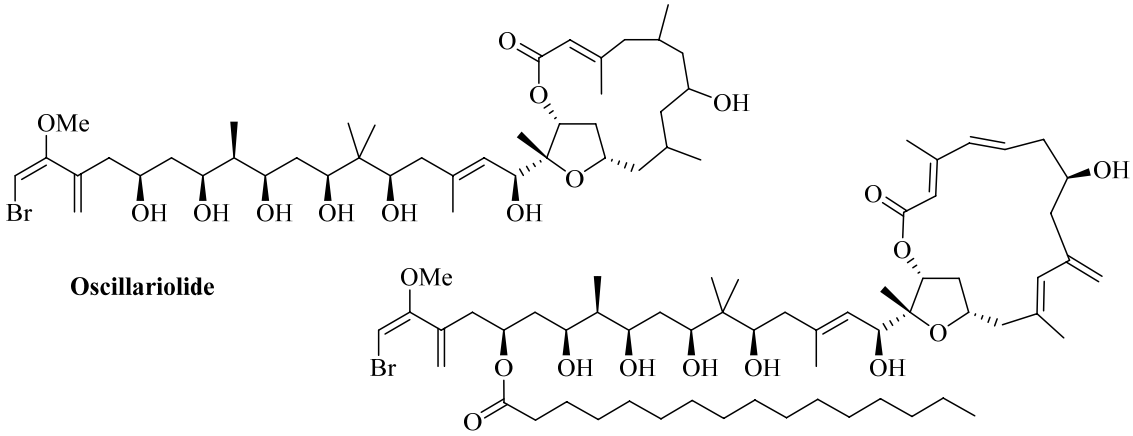
[2]*CIBER-BBN, Networking Centre on Bioengineering, Biomaterials and Nanomedicine, Barcelona Science Park;*

[3]*Department of Organic Chemistry, University of Barcelona, 08028 Barcelona, Spain;*

[4]*Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Barcelona, 08028 Barcelona, Spain*

Marine organisms are studied as a source of bioactive molecules against different diseases due to their promising in vitro activities. One important family of this type of drug molecules is marine polyketide macrolides.[1]

Oscillariolide and phormidolide are two examples of polyketide macrolides, with a common polyhidroxy chain linked to a THF ring. Osciallariolide was isolated from *Oscillatoria* sp. enabling the chemical structure elucidation. This compound showed activity against fertilized starfish eggs.[2] Nevertheless, the absolute configuration of the eight polyol stereocenters was unknown until the isolation of phormidolide.[3]



In this work we will describe our progress in a stereoselective synthetic strategy for the preparation of the polyhidroxylic side-chain present in oscillariolide and phormidolide.

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(P-091) Luminescent Metalosurfactants and Cassettes BODIPY-Bipyridines

Gloria Tardajos,[1] María J. Ortiz,[2] Antonia R. Agarrabeitia,[2] Laura Montalvillo-Jiménez,[2] Nerea Iza,[1] Teresa Montoro,[1] Andrés Guerrero-Martínez,[1] Eduardo Palao[1]

[1]*Department of Physical Chemistry, Complutense University of Madrid, Avda. Complutense s/n, 28040 Madrid, Spain.*

[2]*Department of Organic Chemistry I, Complutense University of Madrid, Avda. Complutense s/n, 28040 Madrid, Spain, e-mail: mjortiz@ucm.es*

The designs of molecular structures capable of responding to an external stimulus are the basis for building molecular devices. Molecular wires, diodes and transistors are some examples, with applications in fields such as medicine, biotechnology, electronics and optoelectronics. Of particular importance are supramolecular systems where processes of photoinduced charge and energy transfer can occur over long distances and in predetermined directions. Designing a supramoleclar structure with adequate space between electronic levels photoinduced processes, that enable load transfer with high efficiency, is the first step in realizing a true photochemical conversion of solar energy.1

Luminescent metalosurfactants, with one donor or acceptor groups capable of forming mixed and / or colloidal aggregates useful in charge transfer processes and / or energy and multichromophórics species have received much attention in recent years due to favorable photochemical and photophysical properties that have to be applied as synthetic systems conversion and storage of solar and optoelectronic devices. Among these systems are those formed by one or more chromophores BODIPYs (singlet emitter) polypyridine-metal complexes (triplet emitter).2

In this way we describe the synthesis of new metalosurfactants tris-bipyridine derivatives complexes and polypyridine-metal complexes covalently bonded to BODIPYs. An example of each type of system is shown in Figure 1.

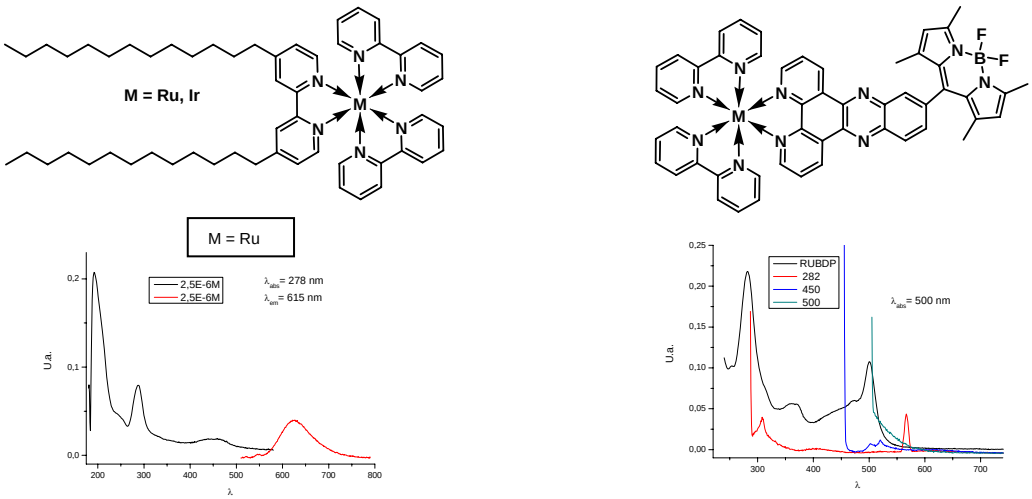

Figure 1

We are studying the photophysical properties of these systems, including the lengths of the half-lives of the various states involved. The results are being obtained show very promising.

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(P-092) Chiral 1,2-diamine-based *F*-BODIPYs: Synthesis and ground photophysical properties

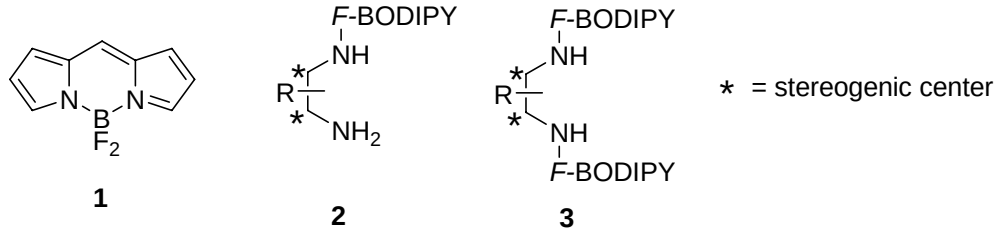
Esther M. Sánchez-Carnerero, Gonzalo Durán-Sampedro, Beatriz Lora, Florencio Moreno, Antonia R. Agarrabeitia, Santiago de la Moya* and María J. Ortiz*

Department of Organic Chemistry I, Complutense University of Madrid, Ciudad Universitaria s/n, 28040-Madrid, Spain, e-mail: mjortiz@ucm.es

Difluoroboradipyrromethene (*F*-BODIPY, **1**) derivatives constitute an important family of fluorescent dyes due to their outstanding photophysical properties that make them of special interest in the development of useful technological applications, such as dye lasers, biomolecular markers, photonic devices, chemical sensors, sensitizers for photodynamic therapy, etc.[1]

Chirality can play an important role in such applications, due to its influence on molecular recognition (chiral sensing), macro- and supramolecular organization (e.g. induction of morphologies with axial chirality, *helicity*, in polymeric materials), or optics (chirooptics). However, few examples of chiral *F*-BODIPYs have been described to date, being the studies on the possible modulation of the physicochemical properties by the stereochemical configuration inexistent.[2]

The facts above exposed, together with the importance that chiral 1,2-diamines have as privileged structures in several chiral-recognition phenomena (asymmetric catalysis, resolution of racemic mixtures, selective detection of diastereoisomers, etc.),[3] has prompted us to consider the synthetic development of two series of *F*-BODIPYs conveniently functionalized with a chiral 1,2-diamine moiety (*chiral 1,2-diamine-based F-BODIPYs*, **2** and **3**), as well as their study in order to know the role played by the (stereo)structure on their ground photophysical properties (absorption and fluorescence). The communication outlines the most important results of this research.



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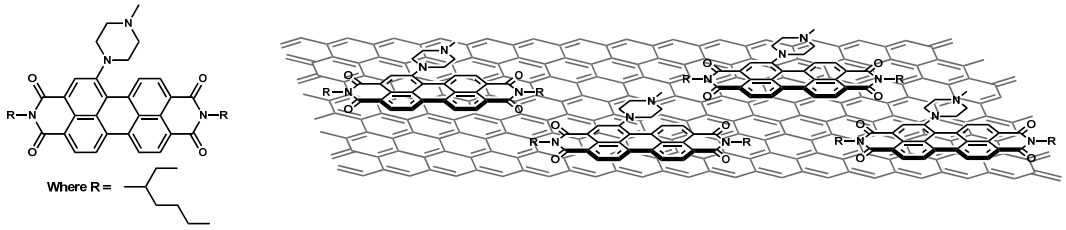
(P-093) Synthesis and characterization of supramolecular electron donor-acceptor perylenediimide-graphene hybrids

Luis Martín-Gomis,[1] Nikolaos Karousis,[2] Nikos Tagmatarchis,[2,*] Fernando-Fernández-Lázaro[1] and Ángela Sastre-Santos[1,*]

[1]*División de Química Orgánica, Instituto de Bioingeniería, Universidad Miguel Hernández, Elche 03202, Spain. e-mail: luis.martin@umh.es*

[2]*Theoretical and Physical Chemistry Institute, National Hellenic Research Foundation, 48 Vassileos Constantinou Avenue, Athens 116 35, Greece*

Perylenediimides (PDIs) represent a versatile family of aromatic planar organic compounds that have been extensively utilized for a wide range of high technological applications, light harvesting arrays or artificial photosynthetic systems.[1]
Nowadays, the interest of the scientific community on graphene and graphene-based materials is enormous, and the possibility to decorate them with different organic appends enlarge the window of possible technological applications. The acquisition of high quality few-layered graphene materials is an issue that must be circumvented and solvent assisted exfoliation using flat aromatic organic molecules as exfoliating assistants reveals as an extraordinary tool for that purpose.[2] Going a step further, the use of organic compounds facilitating the exfoliation of graphite without disrupting its novel electronic structure, while at the same time acting as electron donor components to the graphene layer, is a smart and convenient way to obtain graphene-based donor-acceptor hybrid materials.[3]
Here we present the synthesis and characterization of an electron-donor PDI derivative, bay-substituted with one piperazine append, and its successful use as exfoliating agent for graphite. Preliminary photophysic measurements show effective electronic communication between PDI and graphene flat surface and a potential application as active material in a new generation of graphene based photovoltaic devices.



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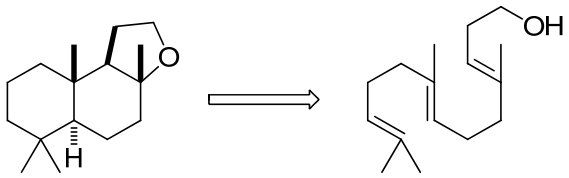
(P-095) Empleo de catalizadores de Ti(III) en la preparacion de ambrox

Juan Muñoz Bascón, Alejandro Rodríguez Foley, Esther Roldán Molina, Natalia Muñoz Padial, Nazaret Rivas Bascón, Antonio Rosales Martínez, Enrique Oltra Ferrero.
Dpto. de Química Orgánica, Universidad de Granada, Avda Fuentenueva s/n 18071 Granada, tfno: +34 958249371; e-mail: juaritu@correo.ugr.es

Ambrox es un compuesto natural, aislado del ámbar gris, que es usado ampliamente en perfumería por sus importantes propiedades fijativas.[1] Nuestro grupo de investigación ha contribuido al desarrollo de una nueva estrategia sintética para la obtención de terpenos basada en la apertura radicalaria de epoxipolienos catalizada por titanoceno (III).[2] Este nuevo procedimiento radicalario se caracteriza por su elevada regio y diastereoselectividad. El análisis retrosintético usado en la síntesis de ambrox se indica a continuación.



Ambrox

En esta comunicación se presentarán los resultados obtenidos en el proceso de ciclación empleando diferentes catalizadores de Ti(III).

Agradecimientos:

Ministerio de Economía y Competitividad (Proyecto CTQ2011-24443) y a la Junta de Andalucía (Proyecto P10-FQM-6050)

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(P-096A) Spatial scale patterns in seagrass defences: Phenolic compounds in *Zostera noltii*

Lauren Manck, Eva Zubía and María J. Ortega
Department of Organic Chemistry, Faculty of Marine and Environmental Sciences, University of Cadiz, 11510, Pto. Real, Cádiz, Spain, e-mail: mariajesus.ortega@uca.es

Plants are provided with a large arsenal of chemicals used as defensive mechanisms. Among these chemical compounds, secondary metabolites can also serve several ecological functions beyond defence, including protection against UV light, provision of lignin or nutrient storage, among others.

Seagrasses comprises a particular group of plants.[1] These plants are a paraphyletic group of marine hydrophilus angiosperms which evolved three to four times from land plants back to the sea. Due to their convergent evolution and origin, seagrasses share a number of analogous acquired metabolic adaptations that allow them to biosynthesize different secondary metabolites among which phenolic compounds are the most common. Despite the evidence of the widespread ocurrence of phenolic compounds in seagrasses, the role that they may play in seagrass systems has rarely been evaluated.[2]

Apart from this, seagrasses are also one of the most threatened ecosystems in the world, with a continuous and accelerating global loss rate that has led in the last decades to increase their protection.[3] In our study area, the Andalusian coasts, some ecological studies have shown changes in seagrass biomass over the years. Therefore, it would be interesting to establish if there is a correlation between the chemical content of natural products and the environmental and seasonal conditions.

In this context, we undertook the chemical study of the seagrass *Zostera noltii*, a marine plant widely distributed along the Andalusian area and living under different environmental conditions. In particular, we investigated the presence and abundance of phenolic metabolites in plants collected over a broad spatial scale pattern along the Andalusian coasts.

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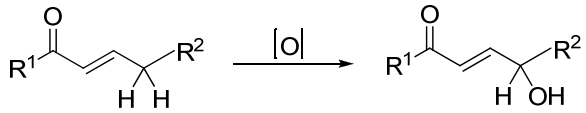
(P-096B) γ-Hydroxylation of enones: A new methodology promoted by a copper-aluminium mixed oxide

Ana Leticia García-Cabeza,[1] Rubén Marín-Barrios,[1] Francisco M. Guerra,[1] F. Javier Moreno-Dorado,[1] María J. Ortega,[2] Redouan Azarken,[1] Guillermo M. Massanet,[1] José M. Gatica[3] and Hilario Vidal[3]

[1] *Department of Organic Chemistry, Faculty of Sciences, University of Cadiz, 11510, Pto. Real, Cádiz, Spain.*

[2] *Department of Organic Chemistry, Faculty of Marine and Environmental Sciences, University of Cadiz, 11510, Pto. Real, Cádiz, Spain, e-mail: mariajesus.ortega@uca.es. 3 Department C.M.I.M. and Inorganic Chemistry, University of Cadiz, 11510, Pto. Real, Cádiz, Spain*

In the recent years, one of the main objectives in the synthetic organic chemistry field has been the transformation of C-H bonds into C-heteroatom bonds. Nowadays, because of the difficult functionalization of this type of bonds, a major challenge for the researchers involves the discovery of new methodologies to employ the C-H bond like any other functional group, which may open the way to the development of new reactions.



Allylic oxygenation is a clear example of C-H bond functionalization. Specifically, hydroxylation of enones in γ or δ position involves the allylic oxidation of an electronic deficient alkene.[1] Frequently, the formation of the desired hydroxyenone is accompanied by epoxides or overoxidation products, among others. Furthermore, the long reaction times, the poor yields and the difficult isolation of the hydroxylated product hamper an extensive use in organic synthesis.

For this reason, there is not a general method to perform this transformation and the approach of this type of reaction in the synthesis of complex molecules is still infrequent. Nevertheless, γ-hydroxyenones are interesting building blocks in the asymmetric synthesis of many organic molecules such as terpenes, which have usually a higly oxygenated functionalized backbone.[2]

In this way, we have developed an efficient chemical method for the introduction of a hydroxyl group at the γ position of enones, employing dioxygen (from the air) as the oxidizing agent in basic medium with the presence of a new prepared copper and aluminium mixed oxide as a promoter of the reaction. We have used a statical approach, the Design of Experiments, as an optimization tool, in order to reach the best reaction conditions for each substrate.[3,4,5]

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(P-097) Synthesis of complex Imidazol-naphthoquinone derivatives with antibiotic activity

Gema Guedes de la Cruz,[1] Félix Machín,[2] Ángel Gutiérrez Ravelo[1] and Ana Estévez-Braun[1]

[1] *Departamento de Química Orgánica, Instituto Universitario de Bio-Orgánica "Antonio González", Universidad de La Laguna, Avda. Astrofísico Francisco Sánchez 2, 38206 La Laguna, Tenerife, Spain, e-mail: gguedes@ull.es*

[2] *Hospital Universitario Nuestra Señora de Candelaria, Carretera del Rosario 145, 38010 Santa Cruz de Tenerife, Spain.*

Heterocyclic compounds offer a high degree of structural diversity and opportunities for the discovery of new drug candidates because of their ability to bind to multiple receptors with high affinity and favourable pharmacokinetic properties. In particular, nitrogen-containing polycyclic structures have been reported to be associated with a wide range of biological activities.[1] Furthermore, it is well known that quinones have various pharmacological properties[2], such as: antibacterial, antifungal, antiviral, antiinflammatory, antipyretic, antimalarial[2b] and anticancer activity.[2c]

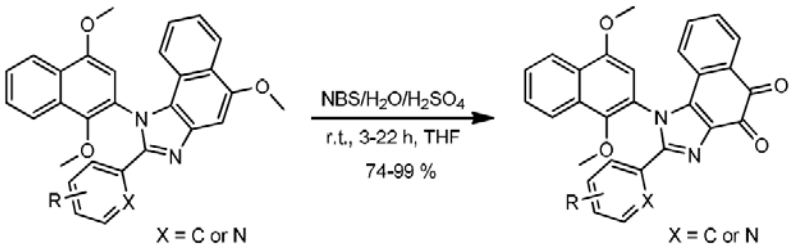

Figure 1: Preparation of 1*H*-naphtho[1,2-*d*]imidazole-4,5-dione

In this communication we report the preparation and antibiotic activity of a set of imidazol-naphthoquinone derivatives. These compounds were obtained through a regioselective and quimioselective oxidation of complex angular naphthoimidazoles previously synthesized in our research group.[3]

Acknowledgments

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(P-098) Multicomponent Synthesis of Novel Napthoquinone-Coumarin Conjugates and their effects on Topoisomerasa II.

Idaira Hueso Falcón,[1] Ángel Amesty Arrieta,[1,2] Ángel Gutiérrez Ravelo,[1] Félix Machín Concepción[3] and Ana Estévez Braun.[1]

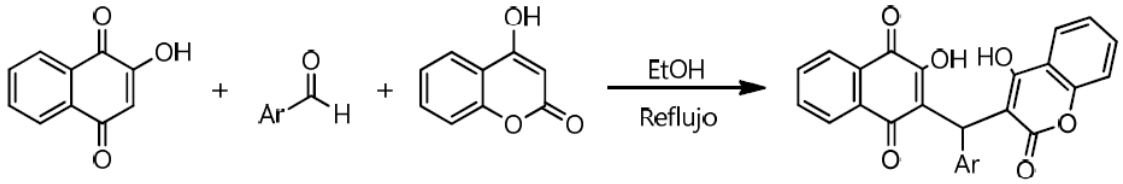
[1]*Departamento de Química Orgánica, Instituto Universitario de Bio-Orgánica "Antonio González", Universidad de La Laguna, Avda.Astrofísico Francisco Sánchez nº2, San Cristóbal de La Laguna, 38206 Tenerife, España.*

[2]*Facultad de Farmacia, Universidad Central de Venezuela, Apartado postal 40109, Caracas 1040-A, Venezuela.*

[3]*Unidad de Investigación del Hospital Universitario de La Candelaria, Ctra del Rosario, 145, 38010, Santa Cruz de Tenerife.*

Due to our interest in antitumoral quinonic compounds,[1] we studied the reaction of aldehydes with 2-hydroxy-1,4-naphthaquinones and 4-hydroxy-coumarin, to generate crossed adducts of biological relevance. In this communication we report the synthesis of a set of naphthoquinone-coumarin conjugates through a Multicomponent Reactions (MCR) combining Knoevenagel condensation and Michael addition.

The results obtained in the evaluation of these compounds as Topoisomerasa II inhibitors will be also discussed.



Acknowledgments

We thank the financial support from the Spanish MICINN (SAF2009-13296-C02-01) and MECC (SAF2012-37344-C03-01).

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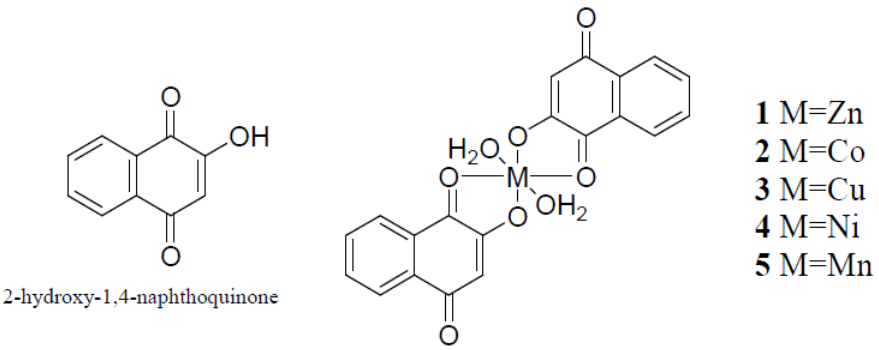
(P-099) Synthesis and cytotoxic activity of metallic complexes of 2-hydroxy-1,4-naphthoquinone

Sandra Oramas-Royo,[1] Concepción Torrejón,[2] Irene Cuadrado,[2] Sonsoles Hortelano,[3] Rita Hernández-Molina,[4] Beatriz de las Heras,[2] Ana Estévez-Braun,[1] and Ángel G. Ravelo[1]

[1]*Instituto Universitario de Bio-Orgánica "Antonio González", Department of Organic Chemistry, University of La Laguna, Avda. Astrofísico Fco. Sánchez 2, 38206, Tenerife, Spain.*
[2]*Department of Pharmacology, University Complutense, Plaza Ramón y Cajal, 28040 Madrid, Spain.*
[3]*Unidad de Inflamación y Cáncer. Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid, Spain.*
[4]*Department of Inorganic Chemistry, University of La Laguna, Tenerife, Spain*

The quinonic moiety is considered by the National Cancer Institute (NCI) as an important biologically validated scaffold for the development of new bioactive compounds with good levels of cytotoxicity.[1] On the other hand, transition metal-based drugs are increasing their importance in the therapy of cancer and other diseases and it is reported that metals can play an important role in modifying the pharmacological properties of known drugs.[2]

In this communication we describe the synthesis of a set of metallic complexes of 2-hydroxy-1,4-naphthoquinone (**1-5**) and their cytotoxicity in human cancer cells. The copper complex (**3**) was the most active compound of this series and the results presented here show that **3** significantly induced apoptosis in HepG2 human cancer cells by a mechanism that involves activation of caspases and modulation of apoptoticrelated proteins.[3]



Acknowledgments

We thank the financial support from the Spanish MICINN (SAF2009-13296-C02-01) and MECC (SAF2012-37344-C03-01). SOR thanks ACIISI and FSE for the predoctoral grant

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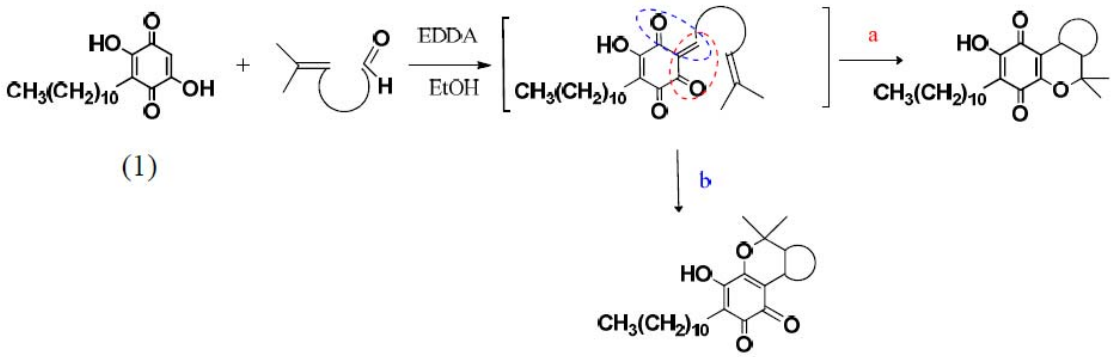
(P-100) Domino Synthesis of dihydropyran-embelin derivatives from unsaturated aldehydes

Rosalyn Peña Florez,[1,2] Ana Estévez-Braun,[1,2] and Ángel Gutiérrez Ravelo[1,2]
[1]*Departamento de Química Orgánica, Universidad de La Laguna, La Laguna, Spain, Avda Astrofísico Francisco Sánchez, s/n. Campus de Anchieta. 38206, La Laguna.*
[2]*Instituto Universitario de Bio-Orgánica "Antonio González", Avda Astrofísico Francisco Sánchez 2, 38206, La Laguna, Spain.*

Embelin (1) is isolated as the main secondary metabolite from *Embelia ribes.*[1] This benzoquinonic derivative showed antifertility, antitumor, anti-inflammatory, analgesic, antioxidant, hepatoprotective, wound healing and antibacterial activities.[2] These antecedents justify the interest in evolving newer synthetic methods for the construction of embelin derivatives.

In this communication, we report an efficient synthesis of new dihydropyran-embelin derivatives through one-pot organocatalytic tandem Knoevenagel condensation/hetero-6π-electrocyclization using a variety of unsaturated aldehydes.[3]



Acknowledgments

To MICINN (SAF 2009-13296-C02-01) and MECC (SAF 2012-37344-C03-01) for the financial support.

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(P-101) Synthesis, characterization and biological activity against *Leishmania infantum* of novel triazolo pyrimidine derivates

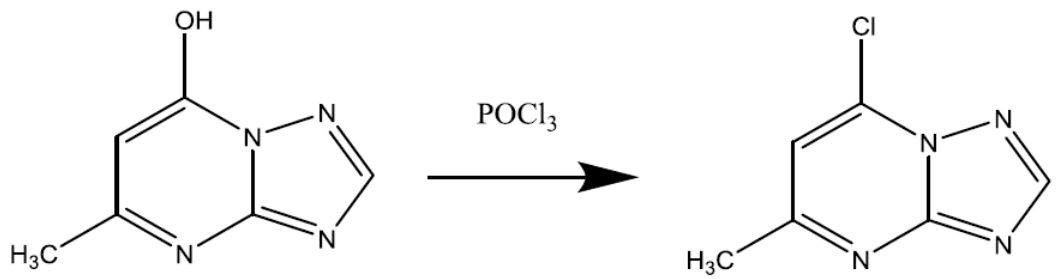
J. M. Méndez-Arriaga,[1,2,3] J. Isac-García,[1] José A. Dobado, [1] J. M. Salas,[2] M. Sánchez-Moreno,[3] Inmaculada Ramírez-Macías[3]

[1] *Grupo de Modelización y Diseño Molecular, Departamento de Química Orgánica, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain*

[2] *Departamento de Química Inorgánica, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain*

[3] *Departamento de Parasitología, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain,*

Leishmania infantum is one of the most common types of leishmania and one of the major pathogens of leishmaniasis infection. This disease affects around 12 million people in 88 countries, affecting mainly poor and remotes populations. Triazolopyrimidine derivates have shown effectiveness against the infect ion, so in this work we will study the synthesis[1] and the characterization of two of these compounds, and their biological activity.



The characterization of both compounds, has been performed by NMR, mass, UV and IR spectroscopy and elemental analysis. In the field of the bioassays, we study the cytotoxicity[2] of this derivates at different concentrations in 1% DMSO solution and his biological activity against *L. Infantum*.[3]

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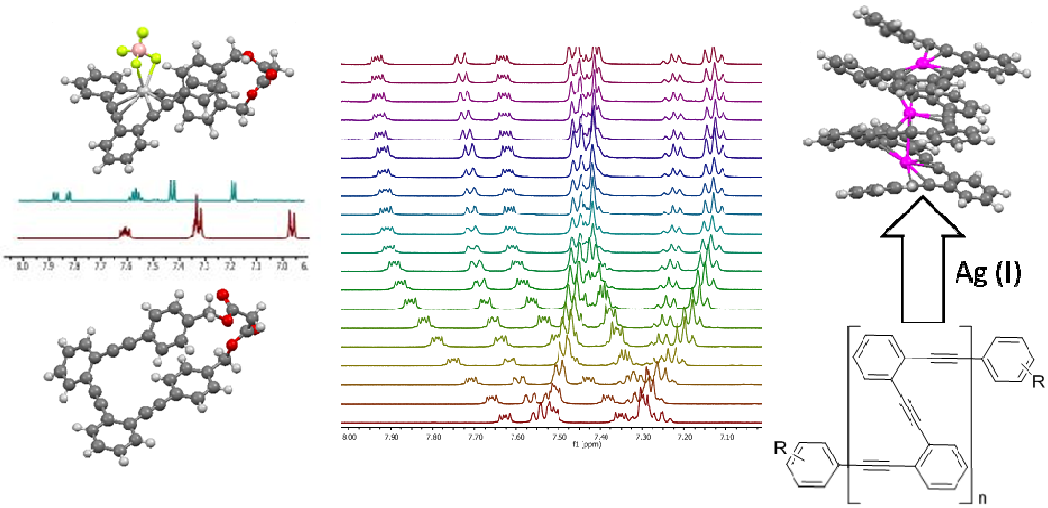
(P-102) Novel *o*-PEO-based helicates by Ag(I) templating

Ana Martín-Lasanta,[1] Alice Johnson,[2] Antonio J. Mota,[3]
Antonio M. Echavarren,[2] Juan M. Cuerva[1*]

[1]*Department of Organic Chemistry, University of Granada, Av. Fuentenueva, 18071 Granada, Spain.*
[2]*Institute of Chemical Research of Catalonia (ICIQ), Av. Países Catalans 16, 43007 Tarragona, Spain.*
[3]*Department of Inorganic Chemistry, University of Granada, Av. Fuentenueva, 18071 Granada,Spain.*

The synthesis of molecules that fold into well-defined secondary structures has attracted intense interest in recent years.[1] However, the existence of such arrangements is difficult to probe for unnatural oligomers in solution.[2] A strategy recently reported by our group in which covalent stapling is used to permanently fix conformationally flexible *o*PEOs into chiral nanocoils has provided further understanding.[3] Helical arrays can also be restricted by hydrogen bonding or metal ion coordination with organic bases. Helicates[4] take advantage of the superior coordination capabilities of pyridines or carboxylates to establish helical structures with Ag(I), Cu(I), Pd(II) among others.[5] However, the coordination capability of alkynes towards carbophilic metals to induce helical folding has not been explored to date. In this work, we report that simple Ag(I) salts can efficiently induce the helical folding of open *orto*-phenylethylene oligomers by coordination with the alkynes forming a molecular pocket. The binding properties of these oligomers were revealed by direct comparison of the NMR spectra for the open and stapled foldamers in the presence and absence of the metal. Quantitative binding affinities and stoichiometries have been determined by NMR and UV titrations for a wide range of compounds with different numbers of alkynes and synergistic interactions such as such as charge transfer and hydrogen bonding. Solid state studies and theoretical calculations also support our results.



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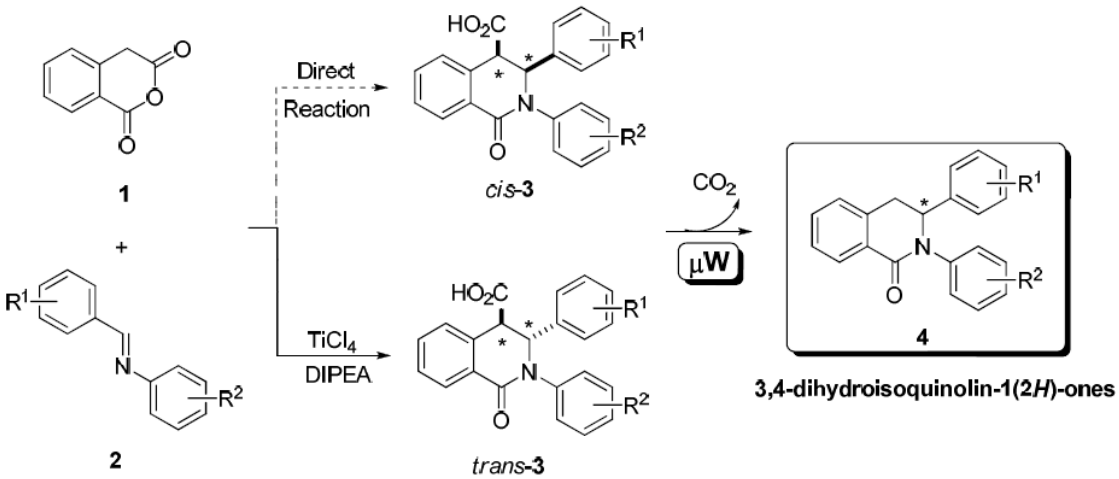
5. One example with Cu(I): Banno, M.; Yamaguchi, T.; Nagai, K.; Kaiser, C.; Hecht, S.; Yashida, E. *J. Am. Chem. Soc.* **2012**, *134*, 8718-8728.

(P-104) Experimental and Theoretical Studies on the Synthesis of 3,4-dihydroisoquinolin-1(2*H*)-ones

Tamara Bello,[1] Ana Arrieta,[1] Yosu Vara,[2] Fernando P. Cossío*,[1]
[1]*Departamento de Química Orgánica I, Universidad del País Vasco-Euskal Herriko Unibersitatea, 20018 San Sebastián-Donostia, Spain, P. Manuel de Lardizabal*
[2]*Ikerchem S. L., Donostia – San Sebastián, España* . (tamara.bello@ehu.es)

The reaction between cyclic anhydrides and imines provides a synthetic route to obtain many natural products and biologically active compounds.[1]
In a previous work carried out in our laboratory we described the *trans* selectivity in the reaction between homophtalic anhydride and different imines in the presence of $TiCl_4$/DIPEA. In contrast, the stereoselectivity of this reaction without further additives depends on the substituents of the imine, aryl substituents showing a high *cis* selectivity.[2]
In the present work we study the thermal and microwave-assisted decarboxylation reaction of *cis*- and *trans*- isoquinolonic acids obtained by means of these methdologies. DFT calculations predicted a mechanism which was tested using isotopic labelling experiments.



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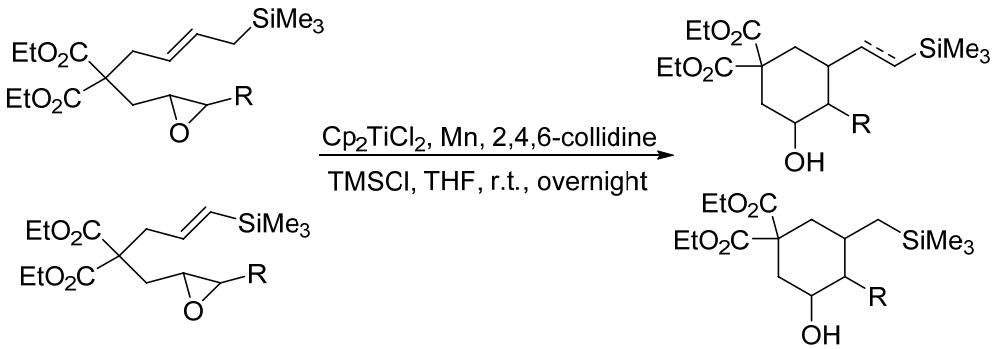
(P-105) Silicon stabilizes radical intermediates in the titanium (III) catalyzed cyclizations of allyl or vinyl silanes and epoxides

Hernández-Cervantes, C., Álvarez-Corral, M., Muñoz-Dorado, M., Rodríguez-García, I.
Organic Chemistry (University of Almeria) ceiA3, 04120-Almeria, Spain, e-mail: chc951@ual.es

It is well known that silicon has the ability to stabilize neighboring radicals due to the vacant *d*-orbitals, even when as remote as in the γ-position. Thus, silicon can direct, promote, or assist reactions that are, in its absence, difficult or messy or both, or even altogether impossible.[1] On the other hand, the addition of allylsilanes to epoxides is a well known reaction that has a great synthetic potential in the preparation of asymmetric alcohols. However, the compulsory stoichiometric quantities of strong Lewis acids needed, in addition to the low reproducibility of the results, make the process rather suitable. To the best of our knowledge, radical cyclization of allylsilanes or vinyl silanes and epoxides is still an unexplored field. It has been proved that Cp_2TiCl_2 promotes allylation and propargylation reactions of epoxides, aldehydes and ketones throw a radical process in which Ti(IV) is transformed into Ti(III).[2] Having previously studied the Cp_2TiCl_2 cyclization reaction of allylsilanes and epoxides for the formation of new carbocyclic alcohols, we are now studying for the first time the influence of the silicon atom in the stabilization of the radicals in its α or β carbons. Mechanistic studies show that the cyclization of allylsilanes leads to the formation of β silicon radicals, whereas α silicon radicals are obtained from vinylsilane derivatives. Comparison between both radical cyclization processes leads to the conclusion that the stabilizing effect is still more pronounced in α position, being the process more diastereo- and chemoselective.
This could be in agreement with the β-destabilizing effect of silicon in some electrochemical reactions.[3] In addition, when vinylsilanes are used, the carbocyclic alcohols are obtained in higher yields than with allylsilanes. By the use of chiral ligands, we are currently engaged in the optimization of this reaction in order to apply the methodology to the enantioselective synthesis of natural products.



Acknowledgments

Our acknowledgment to MEC for financial support (project CTQ2011-24443). C. H-C. acknowledges MECD for a FPU scholarship.

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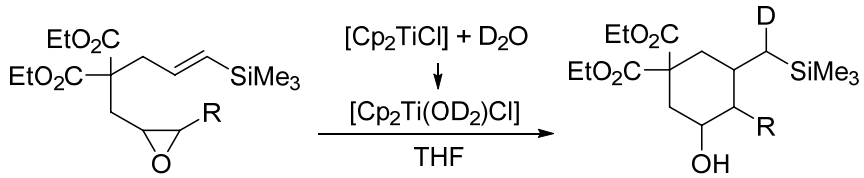
(P-106) Silicon effect in the Ti(III) catalyzed cyclization of vinyl silanes and oxiranes: a mechanistic study

García-Martínez, M., Hernández-Cervantes, C., Álvarez-Corral, M., Muñoz-Dorado, M., Rodríguez-García, I.

Organic Chemistry (University of Almeria) ceiA3, 04120-Almeria, Spain, e-mail: irodrigu@ual.es

Our research group has been able to use the electronic effect of silicon to control different types of reactions. In 2005 we described a silicon-directed synthesis of natural pterocarpans[1] through a Sakurai-metathesis route.[2] Silicon can also increase the reactivity of α radicals, formed in the homolytic opening of ozonides promoted and catalyzed by Ti(III), in Michael-type additions to ethyl acrylate.[3] We have also proved that the use of deuterium is effective in the study of the reaction mechanism for Ti (III) catalyzed reactions.[3] On the other hand, the addition of allylsilanes to epoxides is a well known reaction that has a great synthetic potential in the preparation of asymmetric alcohols due to the formation of a new stereogenic center. However, the use of stoichiometric quantities of strong Lewis acids combined with the low reproducibility of the results make the process unsuitable. To continue the study of silicon–directed, –induced, and –promoted reactions, we decided to explore the radical cyclization of allylsilanes or vinyl silanes and epoxides. It is known that radicals can be reduced by hydrogen atom transfer (HAT) from $[Cp_2Ti(OH_2)Cl]$.[4] With the aim of knowing the stage in which the radical is reduced, we treated vinylsilane derivatives with $[Cp_2Ti(OD_2)Cl]$ (deep blue) prepared in situ from $[Cp_2TiCl]$ (lime green) and D_2O. Deuterium incorporation took place in alpha silicon position which led us to conclude that alpha silicon radicals are obtained from vinylsilane derivatives. To the best of our knowledge this is the first evidence suggesting that alpha silicon radicals can be effectively reduced by HAT from water in a reaction promoted by $[Cp_2TiCl]$. These results are in contrast to those previously reported for allylic and benzylic radicals. We are currently engaged in the optimization of this reaction in order to apply the methodology to the enantioselective synthesis of natural products.



Acknowledgments

Our acknowledgment to MEC for financial support (project CTQ2011-24443). C. H-C. acknowledges MECD for a FPU scholarship and M G-M for an undergraduate scholarship.

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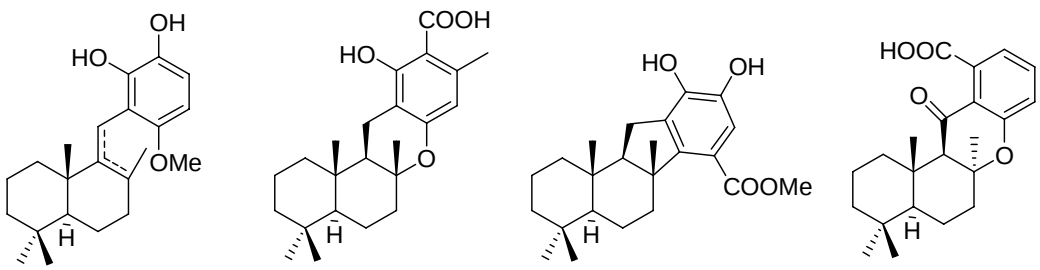
(P-107) A Diels-Alder strategy in the synthesis of bioactive merosesquiterpenes

Antonio Fernández,[1] Ettahir Boulifa,[2] Abdelaziz Dahdouh,[2] Ahmed I. Mansour,[2] Ali Haidöur,[1] Esteban Alvarez,[1] Rachid Chahboun[1] and Enrique Alvarez-Manzaneda[1]

[1]*Department of Organic Chemistry, Institute of Biotechnology, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: ajfvargas@ugr.es*

[2]*Laboratoire de Chimie Organique Appliquée, Département de Chimie, Faculté des Sciences, Université Abdelmalek Essaâdi, Tetouan, Morocco.*

Merosesquiterpene are an important group of biologically active natural products, including both marine and terrestrial fungi metabolites based on a sesquiterpene unit (a drimane-type terpene in most cases) joined to a phenolic moiety. Representative examples include the cholesteryl ester transfer protein (CETP) inhibitors wiedendiol A (**1**) and wiedendiol B (**2**),[1] the antibacterial hongoquercin A (**3**),[2] the antileukemic and antinflammatory pelorol (**4**)[3] and the recently isolated 15-oxopuupehenoic acid (**5**).[4]



1 Δ^{8}
2 $\Delta^{9,11}$
3
4
5

A new synthetic strategy to prepare this type of compounds starting from labdane diterpenes has been developed. The key step is the construction of the aromatic ring of target compounds *via* a Diels-Alder cycloaddition involving the diene system of diterpene.[5] Utilizing this, some of the above compounds were synthesized.

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(P-108) A contribution to the synthesis of adociaquinol

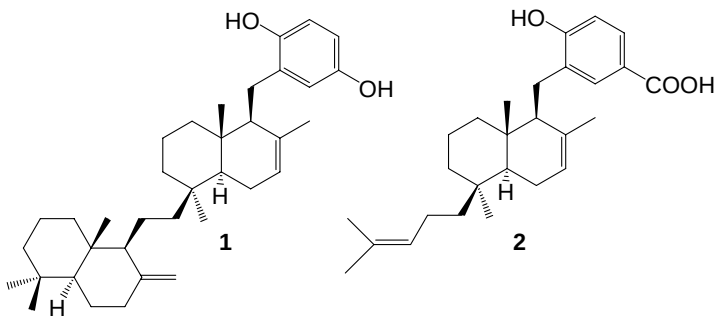
Fermín Jiménez[1], Ettahir Boulifa[2], Maria José Cano[1], Francisco Sánchez[1], Ahmed I. Mansour[2], Rachid Chahboun[1] and Enrique Álvarez-Manzaneda[1]

[1]*Department of Organic Chemistry, Institute of Biotechnology, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: fjr@ugr.es*

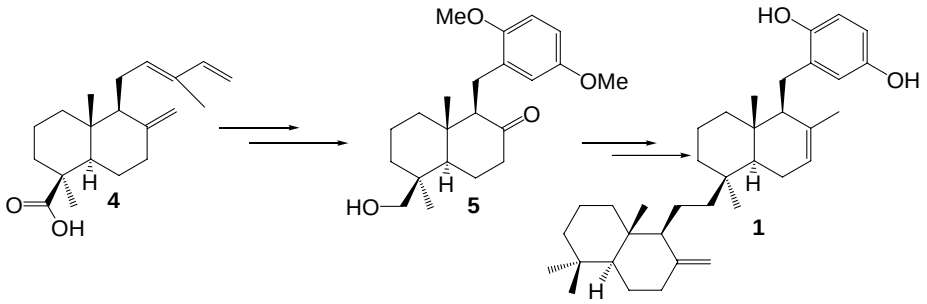
[2]*Laboratoire de Chimie Organique Appliquée, Département de Chimie, Faculté des Sciences, Université Abdelmalek Essaâdi, Tetouan, Morocco.*

Merotriterpenes are an unusual class of metabolites that show several important biological activities. Among these activities, should be highlighted the inhibition of HIV reverse transcriptase,[1-3] the inhibition of phosphatidylinositol-specific phospholipase C[4] or the H^+-ATPase protein pump activity.[5]

Recently, meroterpenoids with different functionalities on the C-4 of the drimane moiety have been reported. Adociaquinol (**1**), isolated from the marine sponge, *Haliclona (aka Adocia)* sp.[6] and (-)-jaspic acid (**2**) isolated from *Jaspis* cf. *Johnstoni* [7].



In order to explore its activity, a synthetic approach to adociaquinol (**1**) was developed, using as starting materials terpenoids easily accessible in nature, such as communic acid (**4**).



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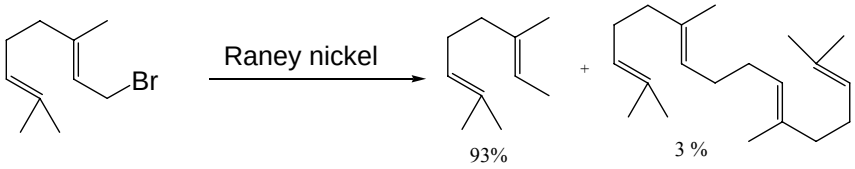
(P-109) Homocoupling reaction of allylic and bencylic halides mediated by a níckel reagent

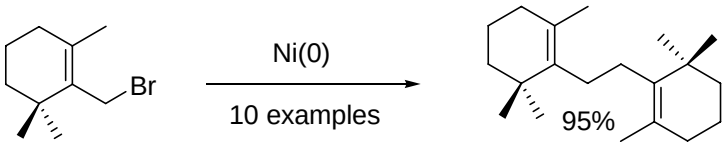
Rubén Tapia,[1] Ali Alkahouzan,[2] Antonio Fernández,[1] Kamal Chahboun,[2] Abdelaziz Dahdouh,[2] Ahmed I. Mansour,[2] Rachid Chahboun[1] and Enrique Álvarez-Manzaneda[1]
[1]*Departament of Organic Chemistry, Institute of Biotechnology, University of Granada, Avn.Fuentenueva 18071, Granada, Spain. e-mail: rubenes@correo.ugr.es*
[2]*Laboratoire de Chimie Organique Appliquée, Département de Chimie, Faculté des Sciences, Université Abdelmalek Essaâdi, Tetouan, Morocco.*

During our research into the use of Raney nickel as a chemoselective reductor[1] we have found that the reduction of allylic halides with this reagent, in some cases, afforded the expected product together with traces of the dimerization product.



Several conditions have already been used to perform the homocoupling of allylic halides; they include the use of Te reagents, [2] chlorotris(triphenylphosphine) cobalt (I)[3] or Cp_2TiCl.[4]

In this work we describe studies conducted to search for a new methodology to achieve the dimerization of allylic and benzylic halides, utilizing a nickel reagent.



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(P-110) Synthesis of new isoreticular porous mofs

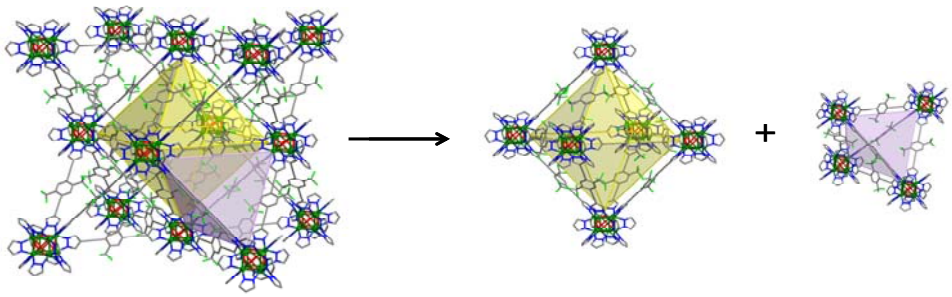
N. M. Padial[1], E. Quartapelle[2], C. Montoro[2], E. López[2], J. E. Oltra[1], V. Colombo[3], A. Maspero[3], N. Masciocchi[3], S. Galli[3], I. Senkovska[4], S. Kaskeld[4], E. Barea[2] and J. A. R.Navarro[2].

[1]*Department of Organic Chemistry,* [2]*Department of Inorganic Chemistry, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: nmpadial@ugr.es*

[3]*Dipartimento di Scienze Chimiche e Ambientali, Università dell'Insubria, Via Valleggio 11, 22100 Como, Italy*

[4]*Department of Inorganic Chemistry, Dresden University of Technology, Mommsenstrasse 6, 01069 Dresden, Germany*

We demonstrate here that it is possible to construct an isoreticular series of 3D, highly porous metal-organic frameworks of $[Ni_8(OH)4(H_2O)_2(L)_6]n$ formulation, based on octanuclear nickel(II) clusters acting as twelve-connected nodes, by employing bipyrazolate- and mixed pyrazolate/carboxylate-containing linkers of increasing extension. The length and functionalization of the ligands have a significant impact on pore size and polarity, on framework stability, and consequently, on the functional properties. Noteworthy, the incorporation of trifluoromethyl residues in the end members of the series gives rise to a remarkable increase of the hydrophobicity of the porous network without limiting its accessibility. The latter feature is highly beneficial for the capture of harmful volatile organic compounds under ambient humid conditions. The most hydrophobic materials of the series are able to capture efficiently and selectively diethylsulfide, employed as model of mustard gas chemical warfare agent, even under extremely moist conditions (80 % relative humidity).



$[Ni_8(OH)_4(H_2O)_2(L5\text{-}CF_3)_6]_n$ *n* *2n*

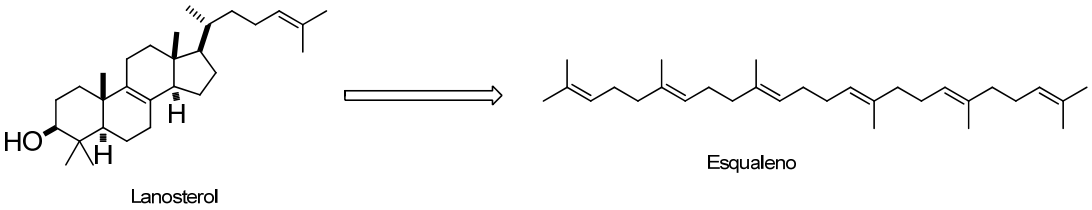
Acknowledgments:

To the Spanish Ministerio de Economía y Competitividad (CTQ2011-24443) and Junta de Andalucía (P10-FQM-6050).

(P-111) Empleo de complejos de titanoceno(III) en la sintesis de meroterpenos naturales

Nazaret Rivas Bascón, Alejandro Rodríguez Foley, Esther Roldán Molina, Juan Muñoz Bascón, Antonio Rosales Martínez, Enrique Oltra Ferrero.
Dpto. de Química Orgánica, Universidad de Granada, Avda Fuentenueva s/n 18071 Granada, tfno: +34 958249371; e-mail: juaritu@correo.ugr.es

La biosíntesis de lanosterol tiene lugar en dos pasos: epoxidación enantioselectiva de esqualeno, y su posterior ciclación estereoselectiva. La transformación global, logra la proeza extraordinaria de formar 4 anillos, 6 enlaces C-C y 7 centros quirales en una sola reacción, con pérdida de un único protón (ver figura). Este extraordinario proceso, respeta el principio de economía de átomos introducido por el Prof. B. Trost, con la finalidad de desarrollar procedimientos sintéticos sostenibles y altamente eficientes. Existe una sólida evidencia teórica y experimental de que esta ciclación es de naturaleza carbocatiónica. El interés por imitar esta ciclación natural ha hecho que prestigiosos grupos de investigación desarrollen ciclaciones en cascada de epoxipolienos inducidas por ácidos. El principal inconveniente de la ciclación en cascada de epoxipolienos vía carbocatiónica reside en la necesidad de introducir en la molécula grupos funcionales capaces de estabilizar el carbocatión generado, así como la baja diasteroselectividad observada en el proceso de ciclación.



Inspirados en la Naturaleza, nuestro grupo de investigación está realizando la síntesis de diversos meroterpenos naturales, siendo la etapa clave del proceso la ciclación radicalaria de epoxipolienos catalizadas por diferentes complejos de titanoceno(III). En esta comunicación se presentarán los últimos resultados obtenidos en nuestro laboratorio en este campo.

Agradecimientos

Al Ministerio de Economía y Competitividad (Proyecto CTQ2011-24443) y a la Junta de Andalucía (Proyecto P10-FQM-6050).

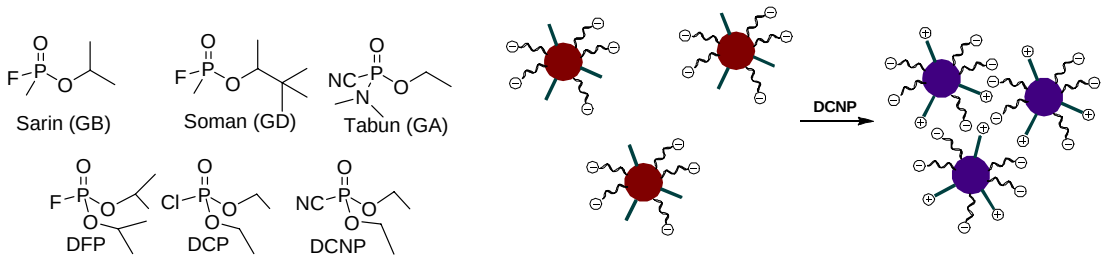
(P-112) Functionalized gold nanoparticles as a new approach for the direct colorimetric detection of DCNP nerve agent simulant

Almudena Martí,[1,2] Ana M. Costero,[1,2] Pablo Gaviña,[1,2] Salvador Gil,[1,2] Margarita Parra[1,2].

1. Centro de Reconocimiento Molecular y Desarrollo Tecnológico (IDM), Unidad Mixta Universidad de Valencia-Universidad Politécnica de Valencia, Spain., e-mail: almudena.marti@uv.es

2. Departamento de Química Orgánica, Universidad de Valencia, Dr. Moliner 50, 46100-Burjassot (Valencia), Spain.

Nerve agents are capable of interfering with the action of the nervous system. Their primary mode of action is the inhibition of acetylcholinesterase, resulting in an acetylcholine accumulation in the synaptic junctions that hinders muscles from relaxing.[1]



Our research group has developed a new family of reagents for the chromogenic detection of nerve agents simulants DFP, DCP and DCNP; based in the use of 2-(2-(N,N-dimethyl amino)phenyl ethanol reactive groups which are part of the conjugated π-system of donor-acceptor dyes.[2] On the other hand, the nucleophilic reactivity of the pyridine moiety of a push-pull azo dye towards nerve gases allowed us to develop off-on colorimetric sensors.[3]

In both cases, the reaction between the probe and the simulant generates a positive charge on the molecule. Based on this fact, we focused on the study of the behaviour of gold nanoparticles (AuNPs) functionalized with this type of moieties in front of nerve agents. Gold nanoparticles have unique optoelectronic properties, which can be easily tuned by changing their size, shape or their chemical environment.[4]

The sensing paradigm of the detection process, which is described below, consists in the generation of positive charges on the surface of the functionalized gold nanoparticles as a consequence of the reaction of the terminal nucleophilic ligands with the nerve agent simulant. These positive charges partially neutralize the original negative charge of the nanoparticles inducing their aggregation and thus a change in their surface plasmon resonance absorption and consequently a change in their color.[5]

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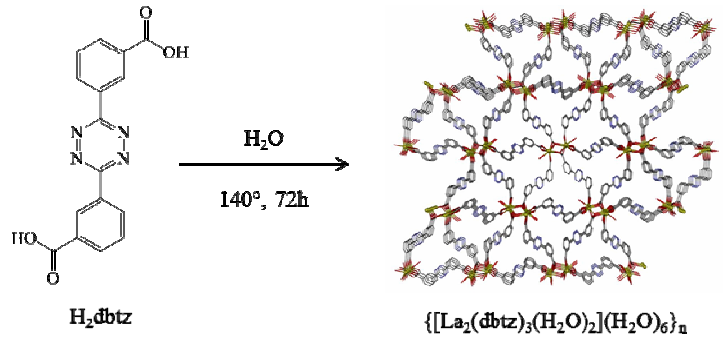
(P-113) A New Tetrazine-Based Linke forPreparation of MOF's

Antonio J. Calahorro,[1] Antonio Peñas-Sanjuan,[2] Manuel Melguizo,[2] David Fairen-Jimenez,[3] Guillermo Zaragoza,[4] Belén Fernández,[5] Alfonso Salinas-Castillo[6] and A. Rodríguez-Diéguez.[1]*

[1]*Departamento de Química Inorgánica, Universidad de Granada, Avda Fuentenueva s/n, 18071, Granada, Spain. email: antonio5@ugr.es.*
[2]*Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, Campus Las Lagunillas, 23071, Jaén, Spain.*
[3]*Department of Chemical & Biological Engineering, Northwestern University, 2145 Sheridan Road, Evanston, Illinois 60208-3120.*
[4]*Unidad de Rayos X; RIAIDT Edificio CACTUS, Universidad de Santiago de Compostela, 15782 Santiago de Compostela, Spain.*
[5]*Instituto de Parasitología y Biomedicina López-Neyra (CSIC), Avenida del Conocimiento S.N, Armilla (Granada).*
[6]*Departamento de Química Analítica, Universidad de Granada18071, Granada.*

Organic Chemistry is an essential ally in the design of Metal Organic Frameworks (MOFs) because, through it, we can synthetize new organic ligands that allow the construction of novel and fascinating materials. In this way, 3,6-disubstituted-1,2,4,5-tetrazine moieties have become popular as efficient electronic spacers in dinuclear and polynuclear systems[1] due to the fact that the tetrazine-based low-lying π^* orbital conveys strong p-accepting characteristics, leading to excellent electronic communication between the metal termini.

In this work, we report the design and synthesis of a new symmetrically multidentate bridging ligand, 3,3'-(1,2,4,5-tetrazine-3,6-diyl)dibenzoic acid (H_2dbtz), which contains two benzoic groups donors, bonding to the metals, and a central tetrazine π-acceptor function. In addition, we present the structural, luminescence and adsorption properties of the first examples of Metal-Organic Frameworks, $[Zn(dbtz)(H_2O)]_n$ and $\{[La_2(dbtz)_3(H_2O)_2](H_2O)_6\}_n$ with the new multidentate ligand H_2dbtz (scheme I) using solvothermal methods, demonstrating the potential of this new ligand to construct MOFs.



Scheme I. Synthesis of $\{[La_2(dbtz)_3(H_2O)_2](H_2O)_6\}_n$ using solvothermal methods.

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(P-114) Sintesis de furanoespongianos funcionalizados en el anillo a mediante ciclaciones radicalarias catalizadas por Ti(III)

Alejandro Rodríguez Foley, Antonio Rosales Martínez, Juan Muñoz Bascón, Natalia Muñoz Padial, Nazaret Rivas Bascón, J. Enrique Oltra Ferrero.

[1]*Departamento de Química Orgánica. Facultad de Ciencias, Campus de Fuentenueva. Universidad de Granada 18071. Granada.* joltra@ugr.es

Recientemente, en nuestro laboratorio hemos realizado la síntesis de spongia-13(16),14-dieno[1] (**1**), un furano-diterpeno natural aislado de *Spongia officinalis,*[2] que presenta actividad antiviral *in vitro*[3], mediante ciclaciones radicalarias catalizadas por Cp_2TiCl. En la actualidad, estamos realizando la síntesis de diferentes furanoespongianos funcionalizados en el anillo A, tal y como se puede observar en la figura 1.

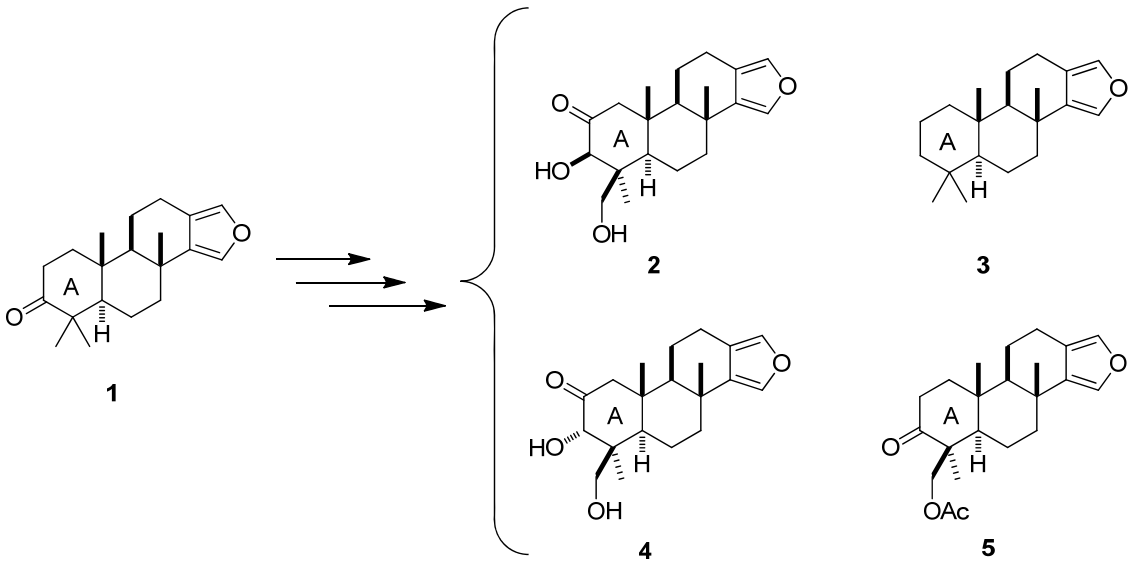

Figura 1.

En esta comunicación se describirán los avances obtenidos en la síntesis de furanoespongianos (**2-5**).

Agradecimientos

Al MICINN (CTQ2011-24443)) y la Junta de Andalucía (P07-FQM-3213 y P10-FQM-6050).

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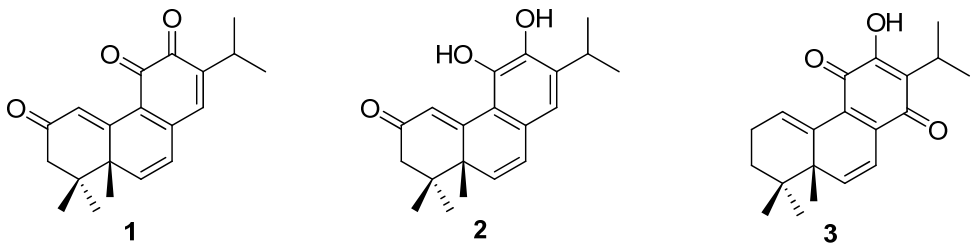
(P-115) Rearrangement of dehydroabietic acid derivatives skeleton: Synthetic approach to pygmaeocins B and C

Juan José Guardia,[1] Ibtissam Messouri,[1] Juan Antonio Gil,[1] José Miguel Ramos,[1] Ramón Álvarez-Manzaneda,[2] Rachid Chahboun[1] and Enrique Álvarez-Manzaneda[1]

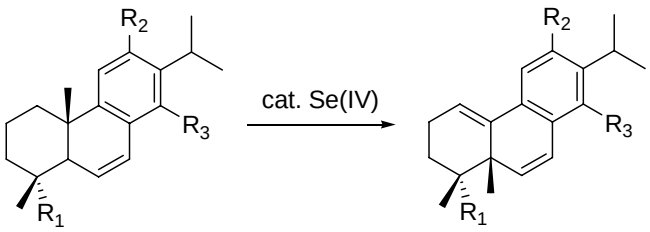
[1]*Department of Organic Chemistry, Institute of Biotechnology, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain. e-mail: pepo@correo.ugr.es*

[2]*Department of Chemistry and Physics, High Technical School and Faculty of Experimental Sciences, University of Almería, La Cañada, 04120 Almería, Spain.*

Rearranged abietane-type diterpenes such as pygmaeocins B **(1)** and C **(2)** have been isolated from the roots of *Pygmaeopremna herbacea* Moldenke by Meng and Hesse;[1a] this plant is used in Yunnan (China) as a folk medicine against inflammation and malaria. More recently salviakinone A **(3)** has been isolated from the roots of *Salvia przewalskii,*[1b] which is utilized in China for the treatment of various cardiovascular diseases.



Currently two total syntheses of pygmaeocins have been reported, in racemic form.[2] Salviakinone A **(3)** has not yet been synthesized. An efficient enantioselective route towards this type of compounds has been devised in order to confirm their absolute stereochemistry and evaluate their biological activity. We present a new methodology to achieve the rearrangement of the angular methyl group in dehydroabietic acid derivatives to the C-5 position, catalyzed by selenium (IV).



4: R_1 = CH_2OAc, R_2 = OMe, R_3 = H
5: R_1 = CHO, R_2 = OMe, R_3 = H
6: R_1 = COOMe, R_2 = OMe, R_3 = H
7: R_1 = COOMe, R_2 = H , R_3 = OMe

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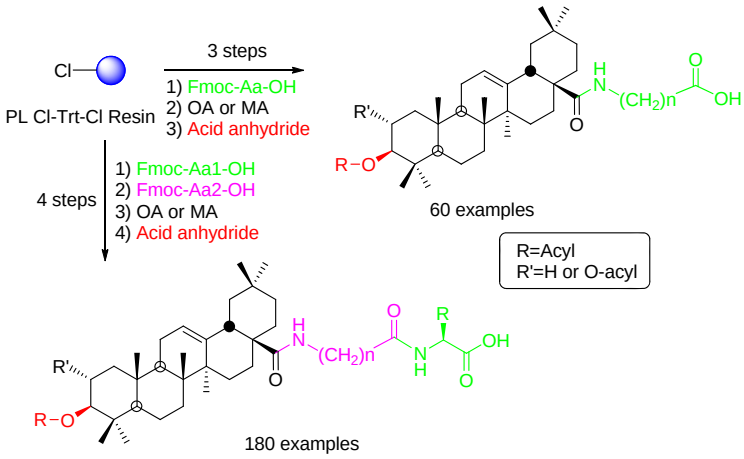
(P-116) Solid-phase synthesis of bioactive bifuctional derivatives of triterpene acids

Andrés Parra, Samuel Martín-Fonseca, Marta Medina-O'Donnell, Ignacio Fernández-Pastor, Francisco Rivas, Antonio Martínez and Andrés García-Granados
Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Granada, Fuentenueva s/n, 18071 Granada, Spain. aparra@ugr.es

Oleanolic acid (OA) and maslinic acid (MA) are triterpene compounds with a pentacyclic oleanene skeleton contained in the residues of olive milling.[1] These triterpene acids are shown to have some biological activities of interest, serving as hepatoprotective, antitumoral, antiviral, and antioxidant agents.[2] The combined use of Combinatorial Chemistry and Solid-Phase Organic Synthesis SPOS is a very useful tool to prepare wide libraries of Organic Natural Products.[3]



Through SPOS, we have optimized the appropriate methodology to generate several libraries of OA and MA derivatives using acylation and/or aminoacylation reactions. The above-mentioned oleanene triterpenes have two diversity areas in which we can join different substituents, namely the A-ring hydroxyl groups and the C-28 carboxylic group of the oleanene skeleton. On the C-28 carboxylic group several α- and ω-amino acid fragments have been linked, whereas, on the A-ring hydroxyl groups, several acyl fragments were coupled. Thus, we have compiled a broad library of 240 bifunctional derivative members which have been tested as anti-HIV and anti-cancer agents. The outcomes of the biological tests of these OA and MA bifunctional derivatives are unfinished but the early results are very promising in both tests. In this sense, especially notable is the potential anti-HIV activity of the derivatives that include in the hydroxyl groups one or two acyls that possess a terminal carboxylic fragment (phthaloyl, succinyl or glutaryl).

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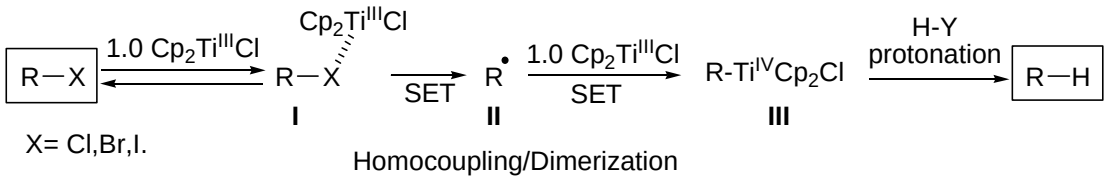
(P-117) Reductive Dehalogenation of Halogenides Mediated by Ti^{III}

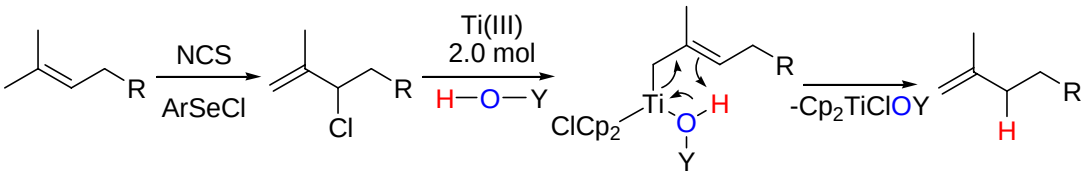
Consuelo Prieto[1], José A. González Delgado[2], Horacio Rodríguez[1], Jesús F. Arteaga[2], Alejandro F. Barrero[1*].

[1]*Department of Organic Chemistry, Institute of Biotechnology, University of Granada, Avda. Fuentenueva, 18071 Granada, Spain.* [2]*CIQSO-Center for Research in Sustainable Chemistry and Department of Chemical Engineering, Physical Chemistry and Organic Chemistry, University of Huelva, Campus el Carmen, 21071 Huelva, Spain. e-mail: jesus.fernandez@diq.uhu.es; afbarre@ugr.es*

Titanocene chloride (Nugent's reagent) is an excellent mediator in many reactions of synthetic interest. It behaves as a Lewis acid and forms complexes with halogenated derivatives (**I**). A monoelectronic transfer takes place from Ti(III) through these complexes leading to the homolytic cleavage of the X-Ti bond and subsequently to a C-centered radical. Various synthetic applications deriving from the reactivity of these radicals, including allylic and benzylic ones, are already known.[1] For example procedures for homocoupling/dimerization of halogenated derivatives.[2] Additionally we thought that the conditions that allow a rapid reduction of the radical intermediate (**II**) to the corresponding organotitanium (**III**) may well lead to its protonation in the presence of a suitable proton source (H-Y). This process would constitute a mild reductive dehalogenation method compatible with a number of functional groups that are unable to react with Ti^{III}. Here we communicate the results obtained in the development of a procedure for efficient reductive-dehalogenation of different types of halogenated derivatives.



Furthermore and bearing in mind the easy, selective and effective synthesis of the secondary chlorides using NCS/polymer-supported selenium bromide reagents on terpenoids with trisubstituted olefins,[3] together with the above reduction reaction, a two-step process represents the development of a new method for the isomerization of trisubstituted olefins to terminal positions.



Acknowledgement

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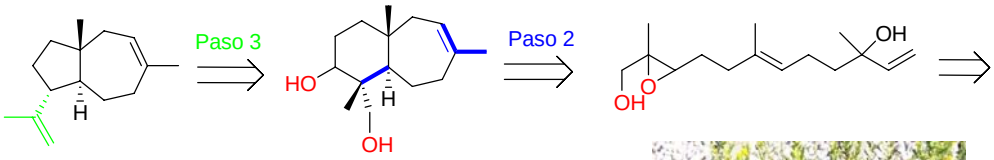
(P-118) Ti(III) en la síntesis biomimética de terpenos Daucanos, Valparanos y relacionados

M. Carmen Pérez Morales, José F. Quilez del Moral, Alejandro F. Barrero

Dpto. de Química Orgánica, Instituto de Biotecnología, Facultad de Ciencias Universidad de Granada, Avda de Fuentenueva s/n 18071 Granada Spain, e-mail: afbarre@ugr.es

Nuestro grupo viene desarrollando desde hace años una línea de investigación destinada a la síntesis total y estereoselectiva de sustancias bioactivas, que incluye la utilización de productos naturales renovables como material de partida y reacciones biomiméticas de ciclación o acoplamiento de tipo radicalario mediadas/catalizadas por Ti(III).[1] Los daucanos son sesquiterpenos bicíclicos que forman anillos de 5+7 miembros.[2] Estos compuestos tienen principalmente un papel de defensa frente a hongos, bacterias y diversos microorganismos. En esta comunicación se presenta la síntesis de estos compuestos a partir de (+)-nerolidol, compuesto natural accesible a escala de multigramos a partir de la abundante planta *Inula viscosa*. Los pasos clave para acceder a estos compuestos son tres, en primer lugar la funcionalización selectiva del isopropilideno terminal (+)-nerolidol, seguida de la ciclación radicalaria del correspondiente epoxialcohol y finalmente un contracción del anillo de seis miembros[3] para originar el esqueleto de daucano convenientemente funcionalizado.



Inula viscosa

Se comentará también el uso de esta estrategia en la preparación de valparanos, diterpenos tricíclicos de 5+6+7 miembros, así como otros compuestos relacionados

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Se agradece la financiación recibida, Junta de Andalucía (Proyecto de Excelencia P08-FQM-3596) y Ministerio de Ciencia e Innovación (Proyecto CTQ2010-16818).

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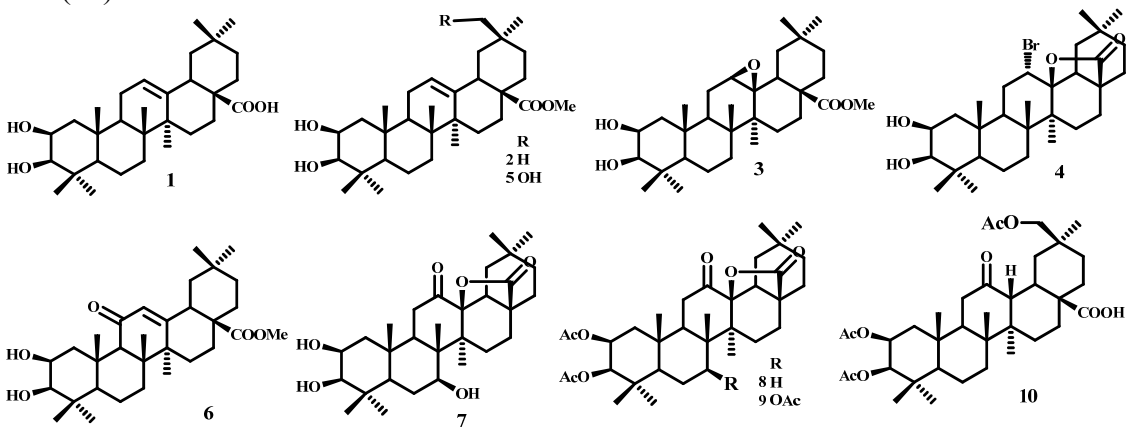
(P-119) Biotransformation of methyl maslinate and methyl 2α,3β-dihydroxy-12β,13β-epoxyolean-28-oate with *Rhizomucor miehei* CECT 2749

Antonio Martinez,[1] Andres Garcia-Granados,[1] Maria del Mar Diaz,[1] Alberto Perojil,[1] Andres Parra,[1] Francisco Rivas,[1] Antonia Fernandez-Vivas[2]

[1] *Departamento Quimica Organica.* [2] *Departamento de Microbiologia. Facultad de Ciencias, Universidad de Granada, Avda. Fuentenueva, 18071 Granada, Spain, e-mail: aramon@ugr.es*

Maslinic acid (**1**), a triterpenic acid that is very abundant in the olive-pressing wastes, displays biological activities of interest [1-3]. One target of our research group is to develop new derivatives of maslinic acid by biotransformation processes using filamentous fungi, to produce hydroxyl derivatives in non-active carbons of the substrates [4]. This communication concentrates on the biotransformation of methyl maslinate (**2**) and methyl 2α,3β-dihydroxy-12β,13β-epoxyolean-28-oate (**3**) by *R. miehei*. The first substrate was obtained by an esterification reaction of maslinic acid (**1**) to give methyl maslinate (**2**). The second substrate was produced by a bromination reaction of the same precursor (**1**), with Br_2 in CCl_4, to give 12α-bromo-28,13β-olide (**4**), after which this bromoderivative **4** was treated with sodium methoxide in methanol to give its methyl ester (**3**). The biotransformation of substrate **2** with *R. miehei* for 15 days gave the 30-hydroxyl (**5**) and the 11-oxo-olean-12-en (**6**) derivatives. The biotransformation of substrate **3** with *R. miehei* for 25 days gave 2α,3β,7β-trihydroxy-12-oxo-olean-28,13β-olide (**7**) together with a mixture of polar metabolites, which was acetylated isolating 2α,3β-diacetoxy-12-oxo-olean-28,13β-olide (**8**), 2α,3β,7β-triacetoxy-12-oxo-olean-28,13β-olide (**9**), and 2α,3β,30-triacetoxy-12-oxo-olean-28-oic acid (**10**).



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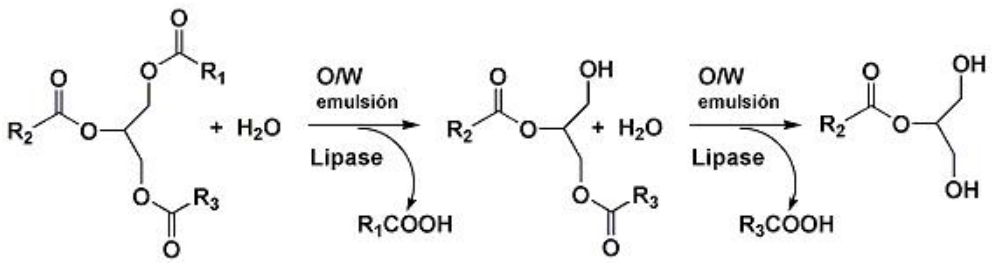
(P-121) Novel approach for monitoring lipase-catalysed hydrolysis of tryglicerides using H^1-NMR.

Alejandro F. Arteaga, Francisco J. Carmona, Manuela Lechuga, Deisi Altmajer, Miguel García-Román.
Chemical Engineering Department, University of Granada, Facultad de Ciencias, E-18071, Granada, Spain, jandro@ugr.es

The development of new strategies for the valorisation of oily residual biomass is very important for Spain. An interesting path for the valorisation of renewable oily substrates is the biosynthesis of glycerol esters, particularly monoglycerides (MAG), which are the most used emulsifiers in the food, cosmetic and pharmaceutical industries,[1] and which are considered as GRAS (Generally Recognized as Safe) by the FDA (Food and Drugs Administration).

Nowadays, the industrial production of MAG is carried out by glycerolysis with inorganic catalysts, at 220-250 ºC, which implies a high energy consumption and the appearance of undesired by-products in the reaction media.[2] For this reason the development of enzymatic processes, using lipases that act under mild conditions and show high selectivity and specificity, allows us to obtain high-quality products, which could not be obtained by conventional chemical procedures.[3]



In this work we have conducted the hydrolysis of triglycerides catalysed by lipases to yield MAG. To carry out the hydrolysis reaction the oily phase was previously emulsified in the aqueous phase using an emulsifier. Free commercial lipases are used. The oil phase consists of waste vegetable oil. Reactions are performed in a thermostated orbital shaker and appropriate reaction conditions were selected considering our previous results.[4,5] Progress of the reactions is monitored by H^1-NMR, surface tension and acidity index of the reaction products: MAG's, diglycerides (DAG's) and free fatty acids (FFA's). H^1-NMR has revealed as a good approach to a fast and easy way of monitoring the process.

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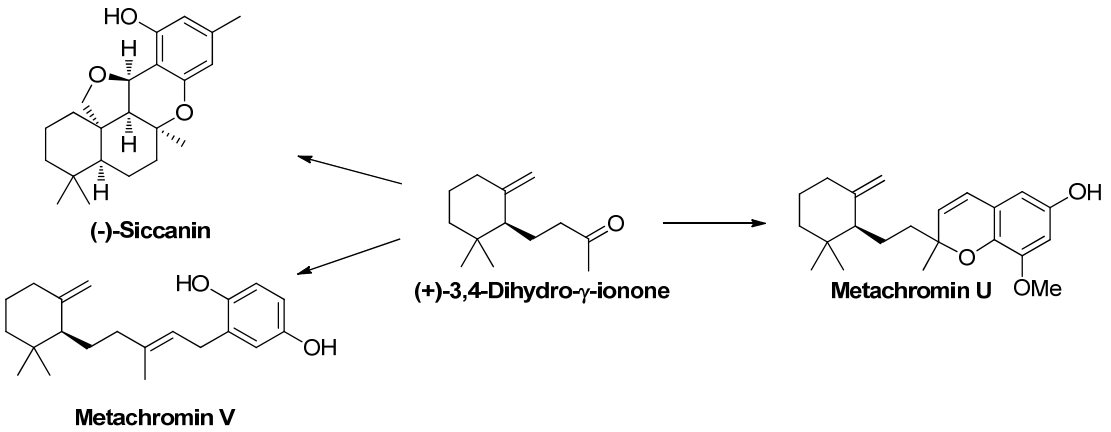
(P-122) A Short Enantiospecific Synthesis of Ambrein.

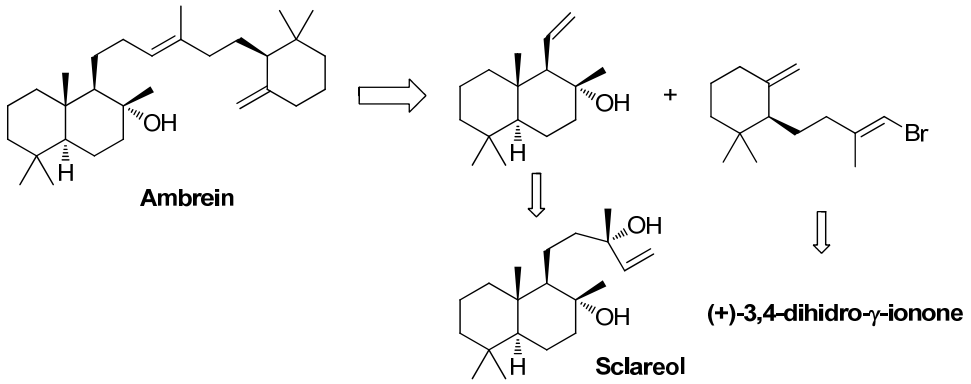
Alejandro F. Barrero, José F. Quílez del Moral, V. Domingo and Alexis Castillo R.

Organic Chemistry Department, Institute of Biotechnology, University of Granada, Campus de Fuente Nueva s/n, 18071 Granada, Spain. E-mail: afbarre@ugr.es

In the field of organic synthesis, the use of natural chiral synthons constitutes a strategy with many advantages over those implicating total synthesis. For example (+)-3,4-Dihydro-γ-ionone a natural versatile building block, obtained in multigrams scale after direct oxidative degradation of the ethereal extract from Bellardia trixago[1] has been effective in the synthesis of a wide variety of potent bioactive molecules such as (-)-siccanin, metachromins U and V.



Here, we present the formal synthesis of triterpene Ambrein[2], major constituent of ambergris an intestinal secretion from whale and formerly used in perfume industry. The rethrosynthetic planning is based in the use of (+)-3,4-Dihydro-γ-ionone and (-)-sclareol obtained from *Salvia sclarea L.* as starting chirons.



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