C.I.R.P
Centro interuniversitario di ricerca sulle reazioni pericicliche e sintesi di sistemi etero e carbociclici

UNIVERSITÀ DEGLI STUDI DI MILANO

Società Chimica Italiana

4th International Workshop on Pericyclic Reactions and Synthesis of Hetero- and Carbocyclic Systems

University of Milan
Palazzo Greppi, Sala Napoleonica
Via S. Antonio 12, Milano

Abstract Book

28 - 30th of June, 2017

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DIPARTIMENTO DI SCIENZE FARMACEUTICHE

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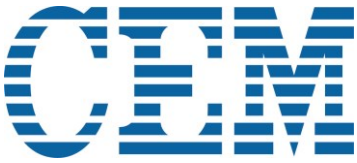

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Organizing Committee

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Paola Conti

Emanuela Erba

Maria Luisa Gelmi

Concetta La Rosa

Sara Pellegrino

Paolo Quadrelli

Organizing Secretariat

Sabrina Pavan

sabrina.pavan@unimi.it

Tel. +390250314471

Fax +390250314476

Welcome

Welcome to the 4th INTERNATIONAL WORKSHOP ON PERICYCLIC REACTIONS AND SYNTHESIS OF HETERO- AND CARBOCYCLIC SYSTEMS hosted by the University of Milan.

The workshop is organized by the Centro Interuniversitario di Ricerca Sulle Reazioni Pericicliche e Sintesi di Sistemi Etero e Carbociclici (CIRP, https://users.unimi.it/cirp/).

The Center was founded in 1992 by a group of researchers from ten Italian Universities. It was aimed at creating a network based on their common scientific interest for pericyclic reactions. They are an old tool to obtain both heterocycles, carbocyclic systems and complex chemical structures and represent a pivotal step in many modern applications such as medicinal chemistry, in material chemistry, polymers, nano- and two-dimensional materials.

The Consortium organizes a national congress every two years, where researchers and, mostly, young scientists have the opportunity to present their research achievements on the above topics.

Every 10 years, an *international meeting* is organized, with the contribution of internationally qualified scientists, who support the sessions with plenary lectures.

Organizing this workshop, the University of Milan is offering an opportunity for all the participants, and mainly for young researchers, to disseminate and discuss the latest researches in this field, their applications and the theoretical and mechanistic aspects in using this old but modern tool.

This meeting will allow you to establish new collaborations between different research groups and lovers of the pericyclic reactions.

This event is also the occasion to celebrate 25 years of the Center.

Welcome to Milano

General Information

LOCATION

The event takes place at University of Milan, Palazzo Greppi, Sala Napoleonica, Via S. Antonio 12. It is located in the city center (five-minute walk from the underground stations of Missori (M3 yellow line) or Duomo (M1/M3, red and yellow).

ORAL/POSTER PRESENTATIONS

The lecture hall is equipped with a projector and Window or Mac computers. Microsoft Power Point facilities are available.

Memory key is preferred instead of a personal laptop computer. All speakers are kindly invited to contact the conference desk before their presentation.

All posters will be on view throughout the workshop.

SOCIAL EVENTS

- Welcome lunch will take place on 28th Wednesday from 12.00 to 14.30 at Palazzo Greppi, Via S. Antonio 12.

- The cruise on ”NAVIGLIO GRANDE” will take place on 28th Wednesday at 19.30.

- The Social Dinner will take place on Thursday 29th at 20.00 at ***Loggiato d'onore,*** first floor of the central courtyard of the University of Milan, via Festa del Perdono, 7.

CELEBRATION OF 25TH ANNIVERSARY OF CIRP

Thursday June 29th

h 17.50

"An excursus of the History of the PERICYCLIC REACTIONS AND SYNTHESIS OF HETERO- AND CARBOCYCLIC SYSTEMS CENTER: from the origins to nowaday applications"

A contribution of: Francesco De Sarlo

Paolo Grünanger

Sara Pellegrino

Donato Pocar

About the Center

CIRP: ***CENTRO INTERUNIVERSITARIO DI RICERCA SULLE REAZIONI PERICICLICHE E SINTESI DI SISTEMI ETERO E CARBOCICLICI***

The "Interuniversity Center on PERICYCLIC REACTIONS AND SYNTHESIS OF HETERO- AND CARBOCYCLIS SYSTEMS" was chartered in 1992, but since 1978 a group of University Researchers has been organizing every two years a National Meeting on Pericyclic Reactions. More than 80 scientists belonging to 10 Universities are members of the Center.

The aim of the Center is to create scientific links between research groups of different Universities who share interests in synthesis, mechanisms and applications involving pericyclic reactions.

Scientific meetings, organised every two years by the Center, give the opportunity for discussions on these subjects, and contacts between the different groups. These meetings are particularly addressed to young researchers allowing them to disseminate their activities and scientific results related to the title subjects.

Scientific programme . The synthesis of carbocyclic and heterocyclic compounds is a research field of historical significance for the Center and it is still of outstanding value for the present activities.

The aim of the Center is the development of pericyclic reactions both as a synthetic tool and as a theoretical investigation field. Pericyclic reactions are a powerful tool for the synthesis of new carbocyclic and heterocyclic systems characterized by a very rich substitution pattern. Enantio-, diastereo- and regio-selectivity can be easily controlled.

By this way, complex chemical structures of biological interest can be obtained. It has to be stressed that cyclic compounds are often valuable intermediates for the preparation of open chain products. Furthermore, pericyclic reactions represent a pivotal step in many modern applications such as medicinal chemistry, in material chemistry, polymers, nano- and two-dimensional materials.

Accordingly, the scientific programme of the Center encompasses all the themes that have been deeply studied for many years by the different research groups. At present the following main fields are actively developed: diene and heterodiene [4+2]-cycloadditions; [3+2]-cycloadditions, mainly 1,3-dipolar cycloadditions; [2+2]- and [6+4]-cycloadditions, electrocyclic reactions; sigmatropic rearrangements; ene syntheses. In recent years, many of these reactions have been revisited in "green" form and are used mostly as a synthetic tool for modern applications.

In line with modern trends, several research groups are active in the detection of new entries to heterocyclic systems by using catalytic processes.

SCIENTIFIC PROGRAMME

WEDNESDAY, JUNE 28th

12.30-14.30 Registration and light lunch

14.30-14.50 Welcome addresses

SESSION 1

Chairmen Andrea Goti, Giovanni Poli

14.50-15.40 PL1 **Oliver Reiser** - University of Regensburg (Germany)

Turning hay to gold: pericyclic reactions as key step for the catalytic conversion of renewable resources

15.40-16.00 OC1 **Valentina Pirovano** - University of Milano (Italy)

2- and 3-Vinylindoles as 4π components in cycloaddition reactions

16.00-16.20 OC2 **Franca M. Cordero** - University of Firenze (Italy)

Divergent reactivity of diastereomeric highly decorated spirocyclopropane isoxazolidines

16.20-16.40 OC3 **Carla Ormachea** - Universidad Nacional del Litoral (Argentina)

Nitropyrroles and nitroindoles: cycloaddition reactions assisted by microwave irradiation: solvent effect. An experimental-theoretical study

16.40-17.10 **Coffee break**

Chairmen Paola Conti, Giuseppe Faita

17.10-17.30 OC4 **Samantha E. Bodman** - University of Canterbury, Christchurch (New Zealand)

Investigating photochemical cyclisation on 1,10-phenanthroline derivatives and their metal complexes

17.30-17.50 OC5 **Irene De Silvestro** - University of Edinburgh (UK)

Biomimetic total synthesis of Thymarnicol

17.50-18.10 OC6 **Francesca Piazzolla** - University of Perugia (Italy)

Multicomponent high pressure promoted Diels-Alder reactions: metal-free access to biaryls and heterobiaryls

19.30 **Cruise on "Naviglio Grande"**

THURSDAY, JUNE 29th

SESSION 2

Chairmen Paolo Quadrelli, Oliver Reiser

9.00-9.50 PL2 **Andrew Whiting -** Durham University (UK)

In pursuit of selectivity, mechanism and utility in N=X cycloadditions

9.50-10.10 OC7 **Helena Macut -** University of Milano (Italy)

On resin cycloaddition of sulfonylazides with cyclopentanone enamines as a synthetic tool toward depsipeptide mimics

10.10-10.30 OC8 **Domenico Albanese -** University of Milano (Italy)

Solventless synthesis of quaterphenyls and terphenyls under phase transfer catalysis conditions

10.30-10.50 OC9 **Stefano Menichetti** – University of Firenze (Italy)

Synthesis of [4], [5] and [6]azahelicenes through the Povarov reaction

10.50-11.20 **Coffee break**

Chairmen Giorgio Abbiati, Andrew Whiting

11.20-11.40 FS1 **Flash Communications** (P2, P3, P4)

11.40-12.00 OC10 **Maria Laura Alfieri** - University of Napoli Federico II (Italy)

Synthesis and properties of new 1,4-benzothiazine based cyanines with a potential as functional dyes

12.00-12.20 OC11 **Jacopo Ceccarelli -** University of Firenze (Italy)

A facile approach to polycyclic nitrogen heterocycles from 1-(2-pyridyl)- and 1-(2-quinolyl)-2-propen-1-ol

12.20-12.40 OC12 **Luca Messaggi -** Anton Paar srl (Italy)

A green, catalyst-free, solvent-free, high yielding one step synthesis of functionalized benzo[f]furo[3,2-c]chromen-4-(5*H*)-ones and furo[3,2-c]quinolin-4-(5*H*)-ones**.**

12.40-14.30 **Lunch**

SESSION 3

Chairmen Gianluigi Broggini, Stefano Menichetti

14.30-15.20 PL3 **Giovanni Poli** - University of Pierre et Marie Curie Paris 6 (France)

From core-shell nanogel catalysis to green applications of the Murai reaction

15.20-15.40 OC13 **Roberto Romeo -** University of Messina (Italy)

Synthesis of bicyclic piperazinones by Pd(II)/Cu(II)-catalyzed domino functionalization of carbon-carbon double bonds

15.40-16.00 OC14 **Marta Meazza -** University of Southampton (UK)

Recent advances in the synthesis of carbocycles and heterocycles by synergistic catalysis

16.00-16.20 OC15 **Sabrina Giofrè** - University of Milano (Italy)

Coupling of alkynyl- and alkenyl carbamates in oxidative conditions

16.20-16.50 **Coffee break**

Chairmen Anna Barattucci, Alberto Brandi

16.50-17.10 FS2 **Flash Communications** (P5, P8, P12)

17.10-17.30 OC16 **Aurora Mancuso** - University of Messina (Italy)

"Tuning" sugar functionalized OPEs with biological interest

17.30-17.50 OC17 **Camilla Parmeggiani** - University of Firenze (Italy)

Oxidation of hydroxylamines with hypervalent iodine reagents

17.50 -18.30 *Celebration of 25th anniversary of CIRP*

Francesco De Sarlo, Sara Pellegrino, Donato Pocar

From the past to the future of pericyclic reactions

18.30-19.30 Consortium meeting

20.00 **Gala Dinner on site**

FRIDAY, JUNE 30th

SESSION 4

Chairmen Egle Beccalli, Marco De Amici

9.00-9.50 PL4 **Gian Cesare Tron –** University of Piemonte Orientale "A. Avogadro" (Italy)

Toward an ideal synthesis of medicinally relevant compounds. The use of nitrile n-oxides and nitrile imines as electrophilic partners in novel isocyanide-mediated multicomponent reactions

9.50-10.10 OC18 **Stefano D'Errico** - University of Napoli Federico II (Italy)

An efficient synthetic strategy for the functionalization of 9-ribosyl purine (Nebularine)

10.10-10.30 OC19 **Laura Legnani** - University of Pavia (Italy)

Modeling studies of the triazoletropane-based compound Maraviroc and two synthetic analogues: a rationalization of their antiviral inhibitory activity

10.30-10.50 OC20 **Gregorio Cullia** - University of Milano (Italy)

1,3-Dipolar cycloaddition as a key step for the synthesis of 3-haloisoxazoline-based antiparasitic agents

10.50-11.20 **Coffee break**

Chairmen Francesca Clerici, Franca Cordero

11.20-11.40 OC21 **Tania M. G. Salerno** - University of Messina (Italy)

Curcumin: how much more is there to explore?

11.40-12.00 OC22 **Giovanni Di Mauro** - University of Napoli Federico II (Italy)

A modular synthesis of aminoimidazoles through amide activation

12.00-12.20 OC23 **Lucia Chiummiento** - University of Basilicata (Italy)

Synthesis and anti-hepatic cancer activity of permethylated anigopreissin A analogues

12.20-12.30 **Maria Luisa Gelmi** - Closing Remarks

PLENARY LECTURES

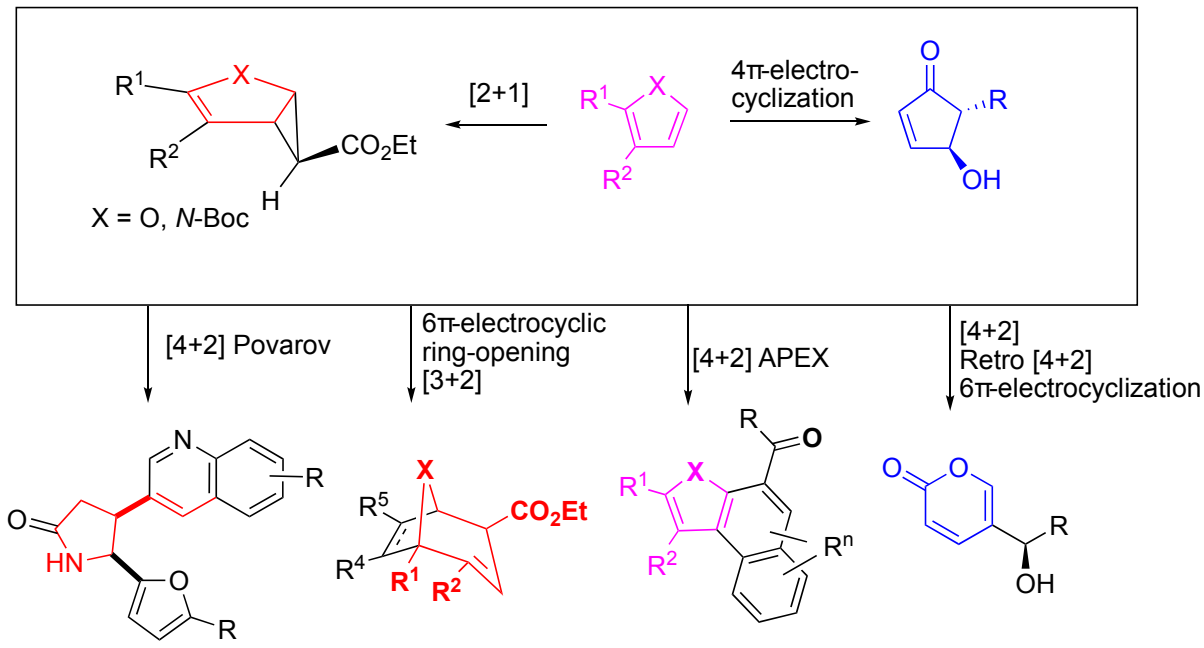
PL01

Turning Hay to Gold: Pericyclic Reactions as Key Step for the Catalytic Conversion of Renewable Resources

Oliver Reiser

Institute of Organic Chemistry, University of Regensburg, 93053 Regensburg, Germany
Oliver.Reiser@ur.de

The conversion of hay to gold was reported in 1812 by Jacob and Wilhelm Grimm[1] to proceed in quantitative yield, using simple spinning wheels. We have been unable to reproduce these results, but using microreactors, mag(net)ic catalysts and blue and green lightsabers, we were able to develop the synthesis of fine chemicals and drugs, often exceeding the value of gold, from renewable resources and other readily available starting materials. Pericyclic reactions have been the key step in many of these transformations.[2]



1. Jacob and Wilhelm Grimm, "Rumpelstilzchen," *Kinder- und Hausmärchen*, Vol. 1 (Göttingen: Verlag der Dieterichschen Buchhandlung, 1857) in *Children's and Household Tales -- Grimms' Fairy Tales*, No. 55, pp. 281-84.

2. Leading references: (a) O. Reiser, *Isr. J. Chem.* **2016**, *56*, 531-539; (b) O. Reiser, *Acc. Chem. Res.* **2016**, *49*, 1990-1996; (c) D. Dobler, O. Reiser, *J. Org. Chem.* **2016**, *81*, 10357-10365; (d) N. Arisetti, O. Reiser, *Org. Lett.* **2015**, *17*, 94-97

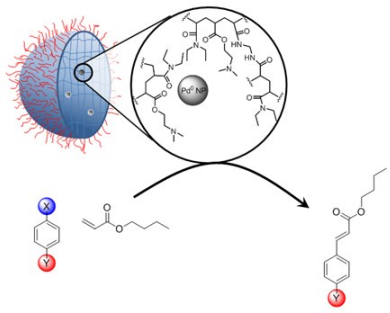
PL02

FROM CORE-SHELL NANOGEL CATALYSIS TO GREEN APPLICATIONS OF THE MURAI REACTION

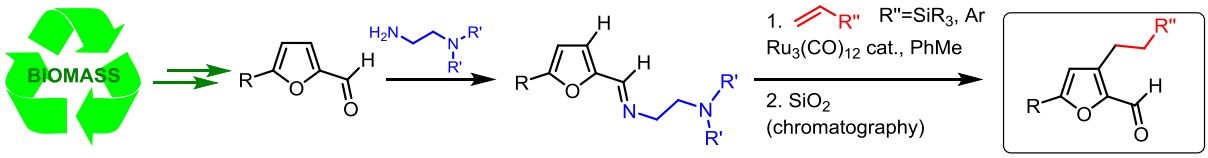
Giovanni Poli

Sorbonne Universités, UPMC Univ Paris 06, CNRS, Institut Parisien de Chimie Moléculaire (IPCM), UMR 8232, 4 place Jussieu, 75005 Paris, France

The presentation will cover two of the main projects we tackled recently in the team. I will initially present the development of a new nanostructured well-defined core-shell nanogel capable of stabilizing Pd0 nanoparticles in its core. This stable hybrid nanogel could be successfully exploited as a catalyst for the Mizoroki-Heck coupling. The performance of this new catalyst as well as the nature of this catalysis will be discussed.[1]



The second part of the talk will deal with our efforts in the development of new C-H activation based catalytic methods on biomass-derived building blocks. In particular, we have recently developed a Ru-catalyzed hydrofurylation of alkenes involving a directed C-H activation at C3 of the furan ring. This result was achieved through the involvement of an appropriate easily removable bidentate amino-imine directing group. The reaction optimization, scope as well as the mechanism of this new transformation will be described and commented.[2]



1. A. Pontes da Costa, D. Rosa Nunes, M. Tharaud, J. Oble, G. Poli, J. Rieger, *ChemCatChem*, in print, DOI: 10.1002/cctc.201601645.

2. C. Pezzetta, L. F. Veiros, J. Oble, G. Poli, *Chem. Eur*. in print DOI: 10.1002/chem.201701850

PL03

IN PURSUIT OF SELECTIVITY, MECHANISM AND UTILITY IN N=X CYCLOADDITIONS

Andy Whiting

Durham University, UK

The hetero Diels-Alder reaction between a nitroso hetero dienophile and a diene is a useful tool in organic chemistry. Since 1947 and the pioneering work of Wichterle,[1] this reaction has been widely studied and numerous nitroso and diene partners have been used to enlarge its scope and efficiency.[2] For a number of years, we have been interested in developing clean new methods for the control of the regio- and stereo-control in nitroso-cycloaddition reactions, particularly through probing the interactions of different nitroso species with metal complexes.[3] Indeed, we have been working see if we can develop metal complexes derived from low cost sustainable sources, that are capable of both forming nitroso species in situ by air-based oxidation, and then eliciting stereocontrol in subsequent Diels-Alder trapping reactions.[4] In most cases examined to date, it appears that oxidation of hydroxamic acids *in situ* occurs *via* a dissociative step from the metal catalyst, and results in such highly reactive acyl species that are rapidly trapped by dienes without the ability to control stereoselectivity using the metal complex. Interestingly, although such catalysts do not affect the acyl nitroso-Diels-Alder reactions in any detectable way, subsequent Diels-Alder reactions are influenced to some extent by solvent effects, and substantially by substituent effects.[4] In this presentation, we will examine recent developments in our understanding of some of the principles (practical and theoretical) which appear to exercise control over such reactions, and some surprising, yet useful applications for the synthesis of different heterocyclic products.[5] We also examine recent applications on related reactions involving hydrazine oxidation to access azo-compounds which can also be trapped by cycloaddition reactions.[6]

References

1. O. Wichterle, *Collect. Czech. Chem. Commun.*, **12**, 292-304 (1947)

2. For reviews on HDA reactions of nitroso reagents, see: (a) J. Streith, A. Defoin, *Synthesis*, 1107-1117 (1994); (b) H. Waldmann, *Synthesis***,** 535-551 (1994); (c) P. F. Vogt, M. J. Miller, *Tetrahedron,* **54**, 1317-1348 (1998); (d) Y. Yamamoto, H. Yamamoto, *Eur. J. Org. Chem.*, 2031-2043 (2006); (e) B. S. Bodnar, M. J. Miller, *Angew. Chem. Int. Ed.*, **50**, 5630-5647 (2011).

3. (a) K. R. Flower, A. P. Lightfoot, H. Wan, A. Whiting, *Chem. Commun.*, 1812-1813 (2001); (b) A. P. Lightfoot, R. G. Pritchard, H. Wan, J. E. Warren, A. Whiting, *Chem. Commun.*, 2072-2073 (2002); (c) K. R. Flower, A. P. Lightfoot, H. Wan, A. Whiting, *Perkin Trans. I*, 2058-2064 (2002).

4. (a) J. A. K. Howard, G. Ilyashenko, H. Sparks, A. Whiting, *Dalton Trans.*, 2108-2111 (2007); (b) J. A. K. Howard, G. Ilyashenko, H. A. Sparkes, A. Whiting, A. R. Wright, *Adv. Synth. Catal.*, **350**, 869-882 (2008).

5. (a) D. Chaiyaveij, L. Cleary, A. S. Batsanov, T. B. Marder, K. J. Shea, A. Whiting, *Org. Lett.,* **13**, 3442-3445 (2011); (b) F. Tripoteau, L. Eberlin, M. A. Fox, B. Carboni and A. Whiting, *Chem. Commun.*, **49**, 5414-5416 (2013); (c) L. Eberlin, B. Carboni, A. Whiting, *J. Org. Chem.*, **80**, 6574–6583 (2015); (d) D. Chaiyaveij, A. S. Batsanov, M. A. Fox, T. B. Marder, A. Whiting, *J. Org. Chem.*, **80**, 9518-9543 (2015).

6. D. Chaiyaveij, A. Whiting, unpublished results.

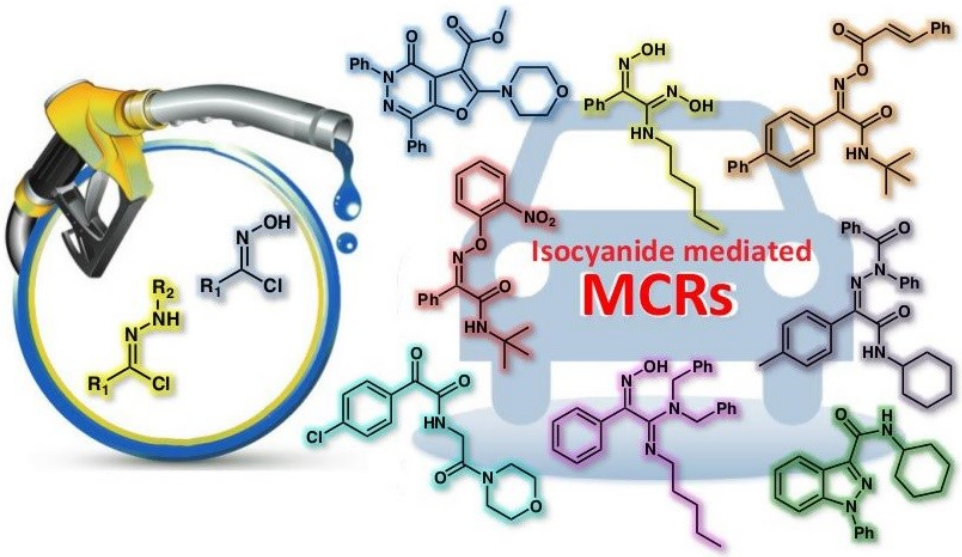
PL04

TOWARD AN IDEAL SYNTHESIS OF MEDICINALLY RELEVANT COMPOUNDS. THE USE OF NITRILE N-OXIDES AND NITRILE IMINES AS ELECTROPHILIC PARTNERS IN NOVEL ISOCYANIDE-MEDIATED MULTICOMPONENT REACTIONS

Gian Cesare Tron
(giancesare.tron@uniupo.it)

Università del Piemonte Orientale – Dipartimento di Scienze del Farmaco – Largo Donegani 2- 28100 Novara

Over the last decades, multicomponent reactions (MCRs) have demonstrated to be a viable short-cut for the rapid assembly of medium-complexity molecular skeletons, usually accessible via a multistep approach through two-component chemistry. Mixing three or four components in the same vessel may alter the typical course of an unproductive two-component reaction, an often neglected advantage of MCRs. Indeed, the third and the fourth components may be able to intercept unstable and untamed intermediates, suppressing undesired reactive pathways and channeling the reaction toward the formation of a single product. In this lecture, our recent works based on the multicomponent reactions between the 1,3-dipolar species nitrile *N*-oxides or nitrile imines, isocyanides and a third nucleophilic component will be discussed. In particular, their mechanism of reaction and the potential of these transformations in organic and medicinal chemistry will be highlighted.



ORAL COMMUNICATIONS

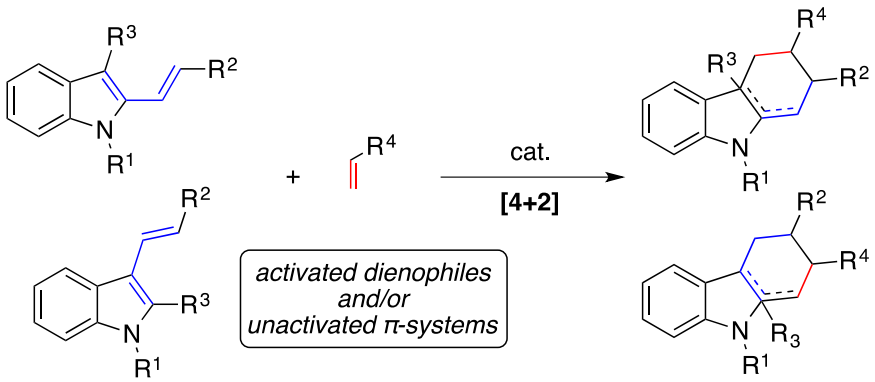
OC1

2- AND 3-VINYLINDOLES AS 4Π COMPONENTS IN CYCLOADDITION REACTIONS

Valentina Pirovano, Elisabetta Rossi, Giorgio Abbiati

DISFARM, Sez. di Chimica Generale e Organica "A. Marchesini", Università degli Studi di Milano
Via Venezian 21, 20133, Milano (Italy)

[4+2]-Cycloaddition reactions are among the most useful transformations in synthetic organic chemistry. They are a widely used method for the assembly of simple and complex six membered carbo- and heterocyclic compounds. The reaction is modulated by the substituents on both the diene and the dienophile partners and by the design of different catalytic species. In particular, among dienes, internal-external ring dienes represent a class of very useful and versatile molecules and their participation as 4π-components in cycloaddition reactions allows for the construction of complex polycyclic compounds. Taking a peak to the structure of 2- and 3-vinylindoles, it is easy to claim that they pertain to this class of molecules and, during the last ten years we developed several strategies to access carbazole derivatives through [4+2] cycloaddition reactions of vinylindoles with a plethora of unsaturated compounds. In particular, starting from Lewis acids catalyzed reactions with cyclic and acyclic dienophiles,[1] we explored the possibility of using cationic gold(I) species to promote the reaction of vinylindoles with unactivated π-systems as dienophiles. (e.g. *N*-allenamides, propargylic esters). In this way we were able to construct complex and intriguing architectures in a stereocontrolled fashion.[2] In addition, considering the importance of asymmetric syntheses of carbazole derivatives, we investigated the reactivity of 3/2-substituted-2/3-vinylindoles with *N*-allenamides under chiral gold(I) catalysis for the synthesis of a new series of dearomatized indoles bearing a quaternary C4a/C9a stereocenter.[3] The results obtained in our last studies on [4+2] cycloaddition reaction with vinylindoles will be discussed with particular focus on the choice of catalysts and on the reaction mechanisms.



1. a) G. Abbiati, V. Canevari, D. Facoetti, E. Rossi, *Eur. J. Org. Chem.*,517 (2007); b) V. Pirovano, G. Abbiati, M. Dell'Acqua, D. Facoetti, M. Giordano, E. Rossi, *Synlett*, **23**, 2913, (2012); c) V. Pirovano, M. Dell'Acqua, D. Facoetti, S. Rizzato, G. Abbiati, E. Rossi, *Eur. J. Org. Chem.,* 6267 (2013); d) E. Rossi, V. Pirovano, M. Negrato, G. Abbiati, M. Dell'Acqua, *Beilstein J. Org. Chem.,* **11***,* 1997, (2015).

2. a) V. Pirovano, L. Decataldo, E. Rossi, R. Vicente, *Chem. Commun.,* **49**, 3594, (2013); b) V. Pirovano, E. Arpini, M. Dell'Acqua, R. Vicente, G. Abbiati, E. Rossi, *Adv. Synth. Catal*., ***358***, 403 (2016).

3. V. Pirovano, M. Borri, G. Abbiati, S. Rizzato, E. Rossi, *Adv. Synth. Catal., DOI: 10.1002/adsc.201700280*, (2017).

OC2

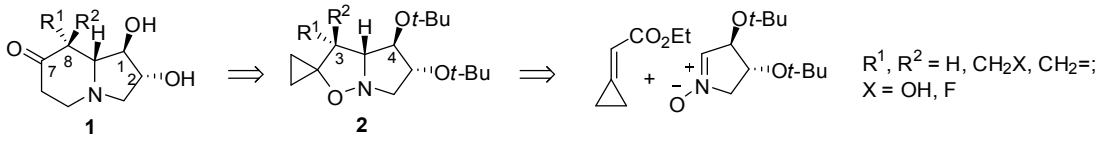
DIVERGENT REACTIVITY OF DIASTEREOMERIC HIGHLY DECORATED SPIROCYCLOPROPANE ISOXAZOLIDINES.

Carolina Vurchio, Franca M. Cordero, Alberto Brandi.

Department of Chemistry "Ugo Schiff", University of Florence, via della Lastruccia 13, 50019 Sesto Fiorentino (FI).

(+)-Lentiginosine, a natural 1,2-dihydroxyindolizidine, is an inhibitor of fungal amyloglucosidases, and chaperone activity of Heat shock protein 90 (Hsp 90).[1] The non-natural enantiomer (−)-lentiginosine is a potent proapoptotic agent against tumor cells of different origin with low toxicity toward normal cells.[2]

In the search for novel lentiginosine analogues endowed with proapoptotic properties,[3] the synthesis of 7,8-disubstituted 1,2-dihydroxyindolizidines **1** was attempted through the convenient strategy involving 1,3-dipolar cycloaddition/thermal rearrangement (Brandi–Guarna rearrangement) (Scheme 1). Unexpectedly, a marked reactivity difference of diastereomers featuring a 3-hydroxymethyl group on the convex face or on the more crowded concave face of the spiro-fused bicyclic system **2** was found. In particular, one diastereomer smoothly undergoes the Brandi–Guarna rearrangement to indolizidinone and fluorination of the primary alcohol. The other diastereomer behaves in a rather different way, as the thermal rearrangement is less efficient and by treatment with fluorinating agents selectively affords an unexpected highly strained tetracyclic spirocyclopropane isoxazolidine or the corresponding 3-methylene cycloadduct. Both new spiro-fused isoxazolidines rearrange to the corresponding indolizidinones under heating, shedding light on an unprecedented different aspect of the Brandi–Guarna rearrangement.



Scheme 1. Retrosynthetic pathway to 7,8-disubstituted 1,2-dihydroxyindolizidines **1**.

In this presentation the results of cycloaddition, fluorination and rearrangement reactions will be presented and discussed along with a study on the reactivity of enone (**1**, $R^1 = R^2 = CH_2$) with different alkenes.

[1] F. Dal Piaz, A. Vassallo, M. G. Chini, F. M. Cordero, F. Cardona, C. Pisano, G. Bifulco, N. De Tommasi, A. Brandi, *PLoS One*, **7**, e43316 (2012).
[2] A. Minutolo, S. Grelli, F. Marino-Merlo, F. M. Cordero, A. Brandi, B. Macchi, A. Mastino, *Cell Death Dis*., **3**, e358 (2012).
[3] (a) C. Vurchio, F. M. Cordero, C. Faggi, B. Macchi, C. Frezza, S. Grelli, A. Brandi, *Tetrahedron,* **71**, 5806-5813 (2014); (b) F. M. Cordero, C. Vurchio, C. Faggi, A. Brandi *Org. Chem. Front.*, **3**, 1651-1660, (2016).

OC3

NITROPYRROLES AND NITROINDOLES: CYCLOADDITION REACTIONS ASSISTED BY MICROWAVE IRRADIATION: SOLVENT EFFECT. AN EXPERIMENTAL-THEORETICAL STUDY.

Carla Ormachea, María Kneeteman, Pedro Mancini

Universidad Nacional del Litoral (UNL) – Facultad de Ingeniería Química
IQAL (Instituto de Química del Litoral) (UNL-CONICET). Santa Fe, Argentina

The Diels-Alder (DA) reaction is one of the more important reactions in organic synthesis. With its property to form carbon-carbon, carbon-heteroatom, and heteroatom-heteroatom bonds, the reaction allows the construction of six membered rings in one step with regioselectivity and stereospecificity. The substituents groups of both dienes and dienophiles, properly selected, can be transformed into other functional groups after the cycloaddition to obtain a large variety of compounds. For this reason, this reaction is used for the preparation of diverse carbocyclic and heterocyclic compounds with biological activity. Over the years, it has been proved that heterocycles could act as dienophiles in this kind of cycloaddition reactions when these compounds are properly activated with electron-withdrawing groups (EWGs).

Specific *polar* Diels-Alder (P-DA) reactions using aromatic carbo- and heterocyclic nitro-substituted dienophiles and different dienes were developed in last years. In general, these cited polar cycloaddition are a domino process initialized by a P-DA reaction to give the formally [4+2] cycloadduct followed for the subsequent irreversible elimination of nitrous acid which is the responsible factor for the feasibility of the overall process.

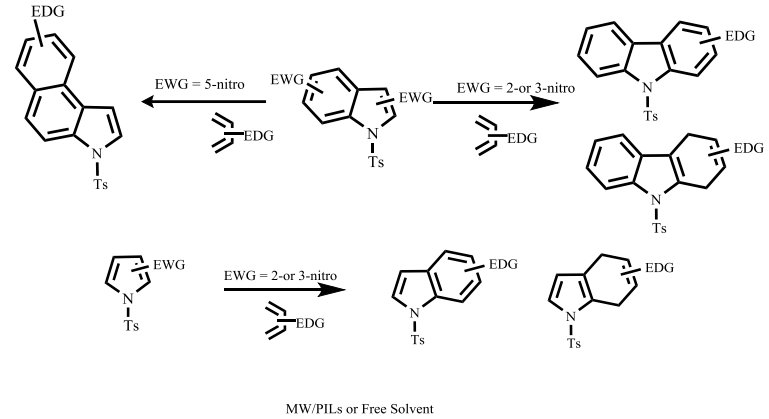
Considering the potential influence of the solvents and its specific effect, the reactions were developed under conventional thermal conditions using toluene or protic ionic liquids (PILs) as reaction media. The experimental results showed that using neoteric solvents the reactions were faster that those developed in traditional organic solvent.

On the other hand, the microwave-assisted controlled heating has become a powerful tool in organic synthesis. This condition is being used to accelerate organic reactions and generally increases the yield. In the MW region, the electromagnetic energy affects the molecular rotation without changes in the molecular structure. Knowing the influence of MW irradiation to improve organic reaction, we carry out some experiences on P-DA process using this methodology.

Then, the principal aim of this work is to study the P-DA reactions of electrophilic nitro substituted pyrroles and indoles with different dienes using MW irradiation, instead of conventional heating, in two experimental situations, in presence of PILs as solvent and, complementary, in free solvent conditions. Specially the last one could be important due to the low impact on the environment. Moreover, we discuss the behavior of the reaction between the dienophiles and elecron-rich dienes in a theoretical way within the Molecular Electron Density Theory (MEDT). For this purpose, we choose the reactions between *N*-mesylnitropyrroles and isoprene as an example of these type of processes.

The tosyl-nitropyrroles and tosyl-nitroindoles explored showed that they can react as electrophilic ethylenes with dienes of different nucleophilicity under microwave heat in P-DA reactions. The presence of the nitro substituent induces the electrophilic activation of the heteroatomic ring, in which this strong electron-drawing group is present. This group is also responsible of the reaction orientation and the selectivity observed. Although the reactions with different pairs diene/dienophile offer similar

behavior when are develop under conventional heating or with microwave irradiation, in the last experimental conditions we observe times of reaction significantly short to get comparable yields when the solvents are PILs or in free solvent conditions. In the last two situations, the yields obtained are similar. This result explain why the free solvent conditions is frequently used as a tool in microwave systems due to more simple manipulations, low cost, guarantee of good products separation, and commitment with the environment.



The computationally studied mechanism shows that the TSs, in the presence of PIL clearly evidences the presence of a hydrogen bond between one oxygen atom of the nitro group and the acidic hydrogen atom of the methylimidazolium cation, which accounts for the acceleration found in these P-DA reactions in PILs respect to the use of classical molecular solvent in thermal condition. Finally, an analysis of the global and local CDFT reactivity indices at the ground state of the reagents allows explaining the reactivity and selectivity in these P-DA reactions. The nucleophilic character of dienes together with the high electrophilic character of dienophiles account for the polar character of these DA reactions. Inclusion of one PIL molecule hydrogen bonded to these electrophiles markedly increases the corresponding electrophilicity index. This behavior accounts for the catalytic role of PILs to allow the reaction to take place through a more polar process. On the order hand, analysis of the electrophilic and nucleophilic Parr functions account for the regioselectivity found experimentally in some cases.

It is noteworthy that in spite of the high polar character of these DA reactions involving strongly electrophilically activated dienophiles, the aromatic character of these heterocyclic compounds, which is loss along the cycloaddition reactions, accounts for the high activation energy found in these P-DA reactions.

- F. Friguelli, A. Tatichi, *The Diels-Alder reaction. Selected practical methods*, Wiley (2002)
- E. Corey, *Angew. Chem. Int. Ed.*, **41**, 1650-1667 (2002)
- B.Biolatto, M. Kneeteman, E. Paredes, P. M. E. Mancini, *J. Org. Chem.*, **66**, 3906-3912 (2001)
- L.R. Domingo, M.J. Aurell, M.N. Kneeteman, P.M. E. Mancini, *J. Molecular Structure*, **853**, 68-76 (2008)
- C. Della Rosa, P. M. Mancini, M. Kneeteman,; A. F. López Baena; M. A. Suligoy, L. R. Domingo, *Journal of Molecular Structure*, **1079**, 47–53 (2015)
- P. M. E. Mancini, M. N. Kneeteman, C. D. Della Rosa, C. M. Ormachea, A. Suarez, L. R. Domingo, *Tetrahedron Lett* , **53**, 6508-6511 (2012)
- Gaussian09, 2009; Vol. Gaussian, Inc., Wallingford CT.
- A. D. Becke, *J. Chem. Phys.*, **98**, 5648-5652 (1993)
- C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B*, **37**, 785-789 (1988)
- C. M. Ormachea, P. M. E. Mancini, M. N. Kneeteman, L. R. Domingo, *Theor. Chem.*, **1072**, 37-42 (2015)

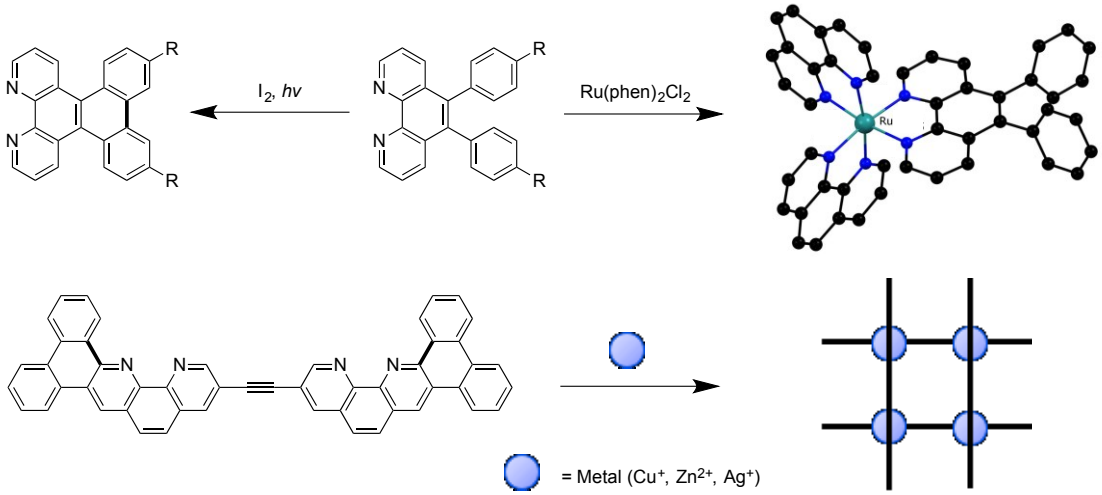
OC4

INVESTIGATING PHOTOCHEMICAL CYCLISATION ON 1,10-PHENANTHROLINE DERIVATIVES AND THEIR METAL COMPLEXES

Bodman, Samantha E., Fitchett, Christopher M.

Department of Chemistry, University of Canterbury, Christchurch, New Zealand, 8041

Over the past twenty years, remarkable progress has been made in the design and construction of organic electronic devices. Small molecules with large aromatic surfaces, such as polycyclic aromatic hydrocarbons (PAHs), have been successfully used in the construction of a range of organic semiconductors. Currently there are two approaches to obtain PAHs, the top-down and the bottom-up methods. The bottom-up approach uses controlled organic synthesis, obtaining molecules of specific size and shape. The design and development of new and innovative procedures for the preparation of heteroaromatic analogues of graphene, where the peripheral sites contain nitrogen atoms is the target of this research. We have been investigating the potential of photochemical cyclisation as a synthetic tool to augment the current chemical methods used for the preparation of these large aromatic ligands. The metal complexes of these molecules display novel chemical and physical properties due to the high degree of electronic delocalization across the planar ligand. The resultant heteroatom-containing molecules have been complexed with a variety of metals. The results presented will include a series of mononuclear ruthenium (II) complexes with ligands that have the potential to undergo photochemical and chemical cyclisation. The photochemical route for the preparation of larger planar molecules is currently being investigated, and a series of novel supramolecular molecules will also be discussed.



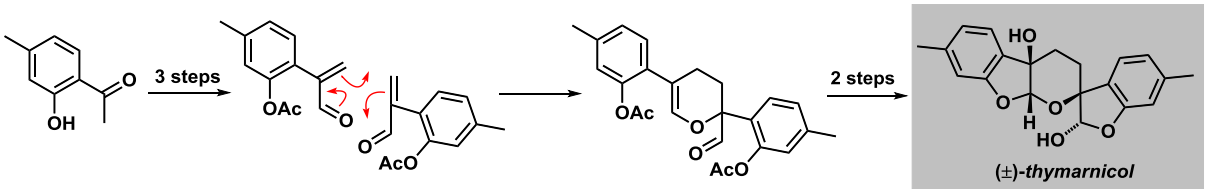
OC5

BIOMIMETIC TOTAL SYNTHESIS OF THYMARNICOL

Irene De Silvestro and Andrew L. Lawrence

The University of Edinburgh

The first total synthesis of a naturally occurring dimeric thymol-derivative isolated from *Arnica sachalinensis*[1,2] (named here thymarnicol) has been accomplished in 6 steps. A detailed discussion of the successful synthesis and several failed approaches will be presented. Key to the success of the synthesis was a biomimetic *hetero*-Diels-Alder dimerization, which provides compelling evidence in support of the biosynthetic dimerization pathway proposed by Passreiter and co-workers.[1] The origin of the remarkable regioselectivity observed in the *hetero*-Diels–Alder cycloaddition have been investigated. DFT calculations showed that this transformation proceeds through a rare example of C_2-symmetric bis-pericyclic transition state. Finally, it has been discovered that the subsequent oxidation occurs spontaneously when the substrate is exposed to visible light in air.



1. C. M. Passreiter, G. Willuhn, H. Weber, K-J. Schleifer, *Tetrahedron*, **55**, 2997-3006 (1999).
2. C. M Passreiter, H. Weber, D. Bläser, R. Boese, *Tetrahedron*, **58**, 279-282 (2002).

OC6

MULTICOMPONENT HIGH PRESSURE PROMOTED DIELS-ALDER REACTIONS: METAL-FREE ACCESS TO BIARYLS AND HETEROBIARYLS

Andrea Temperini[*], *Francesca Piazzolla*[*], *Lucio Minuti*[**]

[*] Dipartimento di Chimica e Tecnologia del Farmaco, Università degli Studi di Perugia, Via del Liceo 1, 06123 Perugia, Italy

[**] Dipartimento di Chimica, Università degli Studi di Perugia, Via di Elce di Sotto 8, 06123 Perugia, Italy

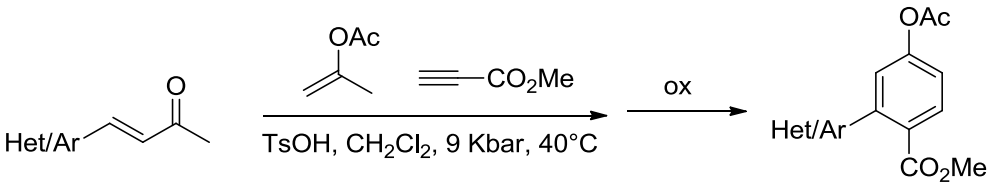
Biaryl and heterobiaryl compounds play an important role in several fields of science, acting as pharmacologically active molecules[1], host material for light emitting diodes[2], chiral auxiliaries and liquid crystals[3].

The most common approaches to the synthesis of these scaffolds involve metal catalyzed cross-couplings[4], organocatalyzed reactions, photochemical reactions[5] and sequential cyclization-aromatization processes, among which Diels-Alder cycloadditions are widely represented.

High pressure (7-11 Kbar) has already been used as activating factor to improve regio- and stereoselectivity in Diels-Alder cycloadditions[6].

Herein, we report a novel multicomponent high pressure promoted synthesis of biaryls and heterobiaryls consisting of an acid catalyzed enolacetylation of variously substituted (hetero)benziliden-acetones in the presence of isopropenyl acetate, followed by [4+2]π cycloaddition with methyl propiolate. The resulting cycloadducts are then oxidized to give the desired products.

In contrast with the previously reported synthetic strategies, the presented method tolerates a wide range of substituents and allows the synthesis of polyfunctionalized products under metal-free conditions and mild reaction temperature.



1. L. Costantino, D. Barlocco, *Current Medicinal Chemistry,* **13**, 65–85 (2006)

2. J. Seo, S. K. Jeon, J. Y. Lee, *Organic Electronics,* **34**, 33-37 (2016)

3. G. W. Gray, *Liquid Crystals,* **24**, 5-14 (1998)

4. S. P. Stanforth, *Tetrahedron,* **54**, 263-303 (1998)

5. T. L. Chan, Y. Wu, P. Y. Choy, F. Y. Kwong, *Chemistry – A European Journal,* **19**, 15802-15814 (2013)

6. L. Minuti, A. Temperini, E. Ballerini, *Journal of Organic Chemistry*, **77**, 7923-7931 (2012)

OC7

ON RESIN CYCLOADDITION OF SULFONYLAZIDES WITH CYCLOPENTANONE ENAMINES AS A SYNTHETIC TOOL TOWARD DEPSIPEPTIDE MIMICS

Helena Macut, Emanuela Erba, Maria-Luisa Gelmi, Sara Pellegrino

DISFARM Sezione di Chimica Generale e Organica "A. Marchesini", Università degli Studi, Milano Italy

The cycloaddition reaction between enamines and sulfonyl azides is a well known and explored click reaction.[1] In our group, we recently observed that tosylazide–cyclopentanonenamine cycloadducts are not stable but directly rearrange yielding to highly reactive diazoalkane compounds.[2] (Figure 1) Here we present the application of this reaction in the synthesis of cyclic depsipeptide mimics. The insertion of the C4 alkyl chain, deriving from cyclopentanone, followed by intramolecular cyclization, allowed to stabilize the secondary structure of the cyclic peptide. In particular, we were able to obtain a cyclic model of a δ-turn and of an α-helix.[3] Since it is known that stapled helices have an improved pharmacological profile and are more resistant to proteases,[4] this procedure might be of a significant importance in the synthesis of peptides with potential therapeutic value.

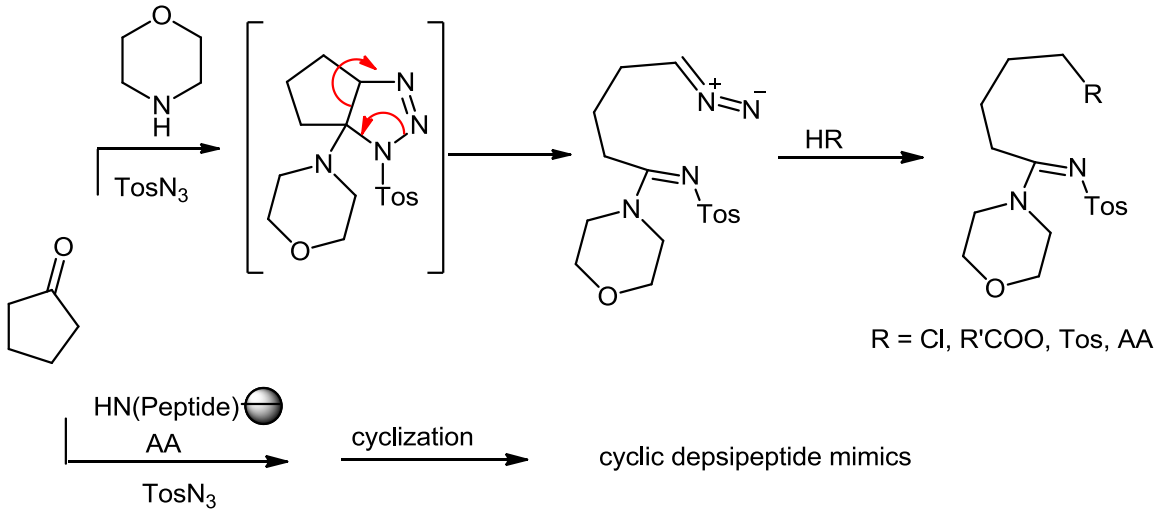


Figure 1. Schematic presentation of the synthesis of cyclic depsipeptide mimics.

1. a) R. Fusco, G. Bianchetti, D. Pocar *Gazz. Chim. Ital.*, 1961, **91**, 933–957; b) S. Xie et al *JACS* 2015, **137**, 2958-2966
2. Erba et al., *Synlett*, 2012, **23**, 1523-1525.
3. Y. Zhang et.al. *J. Biol. Chem*. 2014; **289**: 942-955.
4. G. L. Verdine et al.,*Methods Enzymol*. 2012, **503**, 3-33.

OC8

SOLVENTLESS SYNTHESIS OF QUATERPHENYLS AND TERPHENYLS UNDER PHASE TRANSFER CATALYSIS CONDITIONS

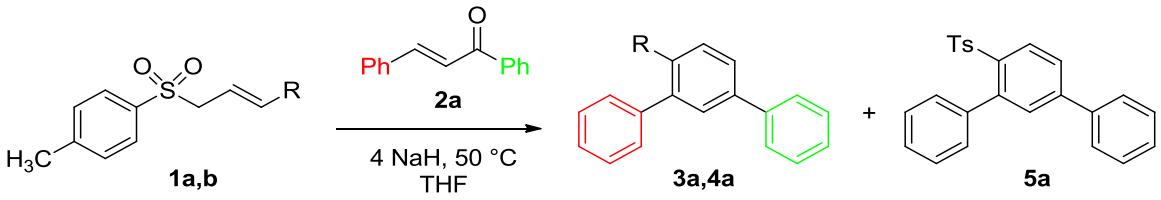
Domenico Albanese, Dario Destro, Selene Brunialti

Department of Chemistry, Università degli Studi di Milano

The synthesis of polysubstituted aromatic compounds relies on various strategies involving multistep approaches using organometallic species or cycloadditions, or under acid or basic reaction conditions. The synthesis of terphenyls has recently aroused a great deal of interest since this skeleton has been found in many bioactive compounds. Moreover, *meta*-terphenyls have been used as intermediates for the synthesis of covalent nanostructures and as electron transporting material to develop new highly efficient organic light emitting diodes (OLED).

Although several procedures allow the synthesis of the terphenyl skeleton, the development of alternative methods is still an issue since the regioselective construction of carbon–carbon bonds is a target not always easy to be achieved.

A more practical approach to terphenyls has been realized by a few direct procedures capable of generating the central benzene ring with a single reaction involving easily available reagents. For example, a mixture of *meta*-terphenyl **3a** (50% yield) along with sulfonyl-*meta*-terphenyl **5a** (36% yield) has been obtained by reacting allylsulfone **1a** with chalcone **2a** in the presence of excess of NaH in THF at 50 °C (Scheme 1).[1] By the same approach, 1,2,4-quaterphenyls **4a** can also be obtained by using an aryl substituted allyl sulfone **1b**.[2]



1a,3a R = H; **1b,4a** R = Ar

Scheme 1

In order to develop a more practical approach and increase the selectivity, we planned to carry out this reaction under phase transfer catalysis (PTC) conditions. In fact, PTC represents a powerful tool to replace hazardous and relatively expensive reactants such as NaH with cheap and practical bases such as alkaline carbonates and hydroxides. In addition, mild reaction conditions, safety, operational simplicity, and high selectivity are widely accepted typical features of PTC processes that allow an easy scale-up of reactions.

The best results have been obtained by heating at 70 °C for 1 h equimolar amounts of allylsulfones **1** and chalcones **2** in the presence of solid NaOH (4 eq) and PEG 1000 (0.4 eq) as phase transfer catalyst. No additional solvent is required to ensure fast conversion of the reactants in a short time.[3]

Under these reaction conditions the desired terphenyls and quaterphenyls have been obtained with complete selectivity. In particular, a variety of substituted chalcones **2a–h** afforded the corresponding 1,2,4-triphenylbenzenes **4a–h** in 51–71% yield (Chart 1).

meta-Terphenyls **3a-c** have also been prepared with complete regioselectivity, although with 22-39% yields (Chart 1).

This new fast and chemoselective method for the assembly of *meta*-terphenyl and 1,2,4-tetraphenyl skeleton under PTC conditions proved to be efficient and environmentally friendly.

The method uses allyl sulfones **1** and chalcones **2** as easily available starting materials along with cheap, solid NaOH and PEG 1000. Moreover, no organometallic species or inert atmosphere are required. In particular, the use of PEG 1000 as a PTC catalyst enables to avoid the use of any organic solvent thus adding value to the procedure. The choice of PEG 1000 was found to be crucial in order to develop a completely chemoselective method generating the desired compounds **3** and **4** without formation of the corresponding sulfonylated byproducts.

Good yields were obtained with electron–withdrawing or electron–releasing groups on the benzene ring of chalcones, whereas heteroaromatic chalcones were also shown to be good substrates for the reaction. (*E*)-4-Phenylbut-3-en-2-one (**2d**), bearing a methyl group instead of a benzene ring also provided good yield of the terphenyl **4d**.

Further work is in progress in order to increase the yield of *meta*-terphenyls involving the use of allylsulfone **1a** and to ascertain the role of PTC in the chemoselective reaction.

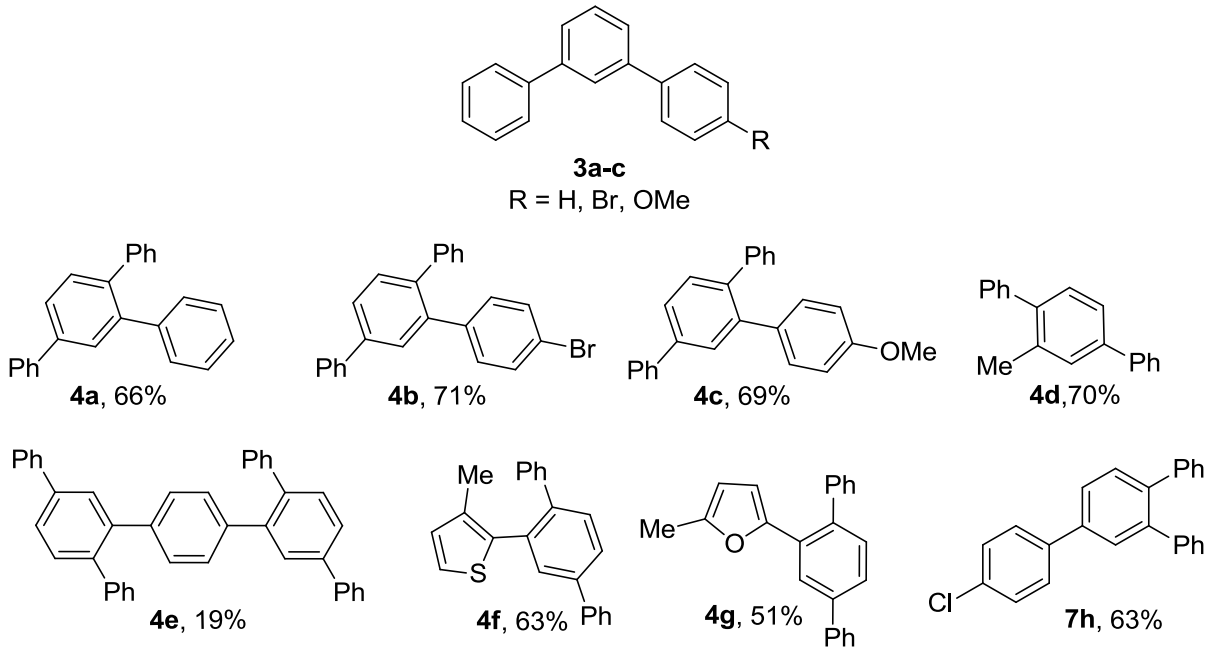


Chart 1

1. Chang, M.Y.; Chan, C.K.; Lin, S.Y.; Wu, M.H. *Tetrahedron* **2013**, 69, 9616–9624.
2. Chang, M.Y.; Chan, C.K.; Lin, S.Y.; Wu, M.H. *Tetrahedron* **2013**, *69*, 10036–10044.
3. Albanese, D.; Destro, D.; Brunialti, S. *Catalysts* **2016**, 6, 142; doi:10.3390/catal6090142.

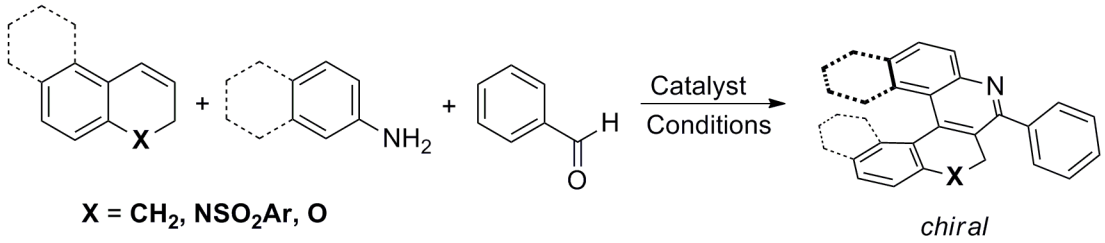
OC9

SYNTHESIS OF [4], [5] AND [6]AZAHELICENES THROUGH THE POVAROV REACTION

Stefano Menichetti,[a] *Martina Lippi,*[a] *Roberta Franzini,*[b] *Claudio Villani,*[b] *Caterina Viglianisi*[a]

[a]Department of Chemistry 'Ugo Schiff' University of Florence, Via Della Lastruccia 3-13 - 50019, Sesto Fiorentino (FI), Italy. [b] [b]Department of Chemistry and Technology of Drugs, University 'La Sapienza' Roma, P.le A. Moro 5 - 00185 Roma (Italy). stefano.menichetti@unifi.it

Helicenes and heterohelicenes are challenging chiral structures that continuously stimulate new interest and find new applications. From just a chemical curiosity with inherent chirality, these compounds are now commonly used in asymmetric synthesis, materials science and medicinal chemistry.[1] On the other hand, among imino cycloadditions, the Povarov reaction, *i.e*. the reaction of electron-rich olefins with *N*-aryl imines, provides a straightforward and modular entry to tetrahydroquinolines and, after oxidation, quinolines, in turn very useful heterocyclic systems.[2]
In this communication, we report how, with the proper choice of electron-rich olefins and N-aryl imines, the Povarov reaction can be exploited for the synthesis of [4], [5] and [6]azahelicenes. Scope and limitation of the procedure as well as preliminary attempts of resolution of final helical shaped quinolines will be discussed.



1. a) Y. Shen, C-F. Chen *Chem. Rev*. **112**, 1463–1535 (2012); b) M. Gingras *Chem. Soc. Rev.* 2013, **42**, 968-1006 (2013).
2. a) X. Jiang, R. Wang *Chem. Rev*. **113**, 5515-5546 (2013); b) G. Masson, C. Lalli, M. Benohoud, G. Dagousset *Chem. Soc. Rev.* **42**, 902-923 (2013); c) M. Fochi, L. Caruana, L. Bernardi *Synthesis*, **46**, 135-157 (2014).

OC10

SYNTHESIS AND PROPERTIES OF NEW 1,4-BENZOTHIAZINE BASED CYANINES WITH A POTENTIAL AS FUNCTIONAL DYES

Maria Laura Alfieri, Lucia Panzella, Alessandra Napolitano

Department of Chemical Sciences, University of Naples Federico II, Naples, Italy

In recent years cyanine dyes have largely been exploited, because of their peculiar chromophoric and fluorescence properties, as biological reporters and in other technological applications[1]. This class of compounds typically features organic nitrogen centers, one of the imine (acceptor) and the other of the enamine (donor) type to form a push-pull system. In this frame, benzothiazine cyanines represent an interesting yet poorly explored class of chromophore systems. Structurally related to the $\Delta^{2,2'}$-bi-(2*H*-1,4-benzothiazine), the structural core of trichochromes, a group of aminoacidic pigments with a peculiar pH dependent chromophore occurring in red human hair[2-3], they show an extension of the cyanine type system a characteristic that should expectedly result in a larger bathochromic shift in acid. The novel cyanine-type dyes, designated trichocyanines, are built upon a modular D-π-A architecture which incorporates a 2H-1,4-benzothiazine ring as the imine-containing A component (Me/Ph substituent), a substituted phenyl ring as the electron-donating D component and an exocyclic double bond with a further conjugation option. These compounds could be easily prepared in good yields by a facile condensation of 3-phenyl- or 3-methyl-2*H*-1,4-benzothiazines with *N*-dimethyl- or o-methoxyhydroxy-substituted benzaldehyde or cinnamaldehyde derivatives (Figure 1). With all compounds, a significant bathochromic shift (ca. 100 nm) was observed upon protonation, which resulted in a marked modification and intensification of the visible color.[4]

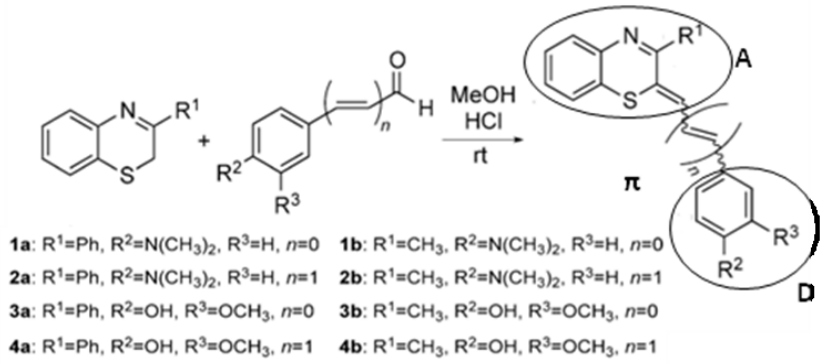


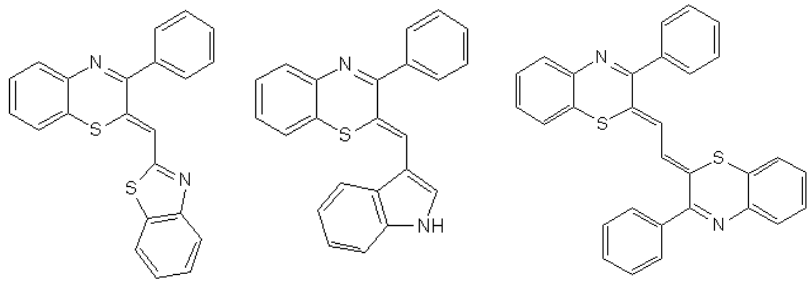
Figure 1. *Trichocyanines, a new class of benzothiazine cyanines*

The peculiar nucleophilic character of 1,4-benzothiazine moiety in the 4*H*-enamine tautomeric form would suggest that extended chromophores could be also obtained by reaction with bifunctional dialdehydes in order to build up a conjugated bridge between the two benzothiazine units.

In this work the investigation was focused on the preparation of new benzothiazine-based systems, by reaction of the easy accessible 3-phenyl-(*2H*)1,4-benzothiazine[5] with aromatic and heteroaromatic aldehydes and dialdehydes.

Reaction of 3-phenyl-(*2H*)1,4-benzothiazine with benzothiazole-2-carboxyaldehyde at 1:1 molar ratio in acetonitrile/hydrochloric acid at 70°C afforded a major product yellow in color that was obtained in pure form in moderate yields following column chromatography. This was subjected to complete structural analysis that confirmed the expected structure **1** (Figure 2). The chromophoric properties were systematically investigated over the whole pH range; the intense absorption at 432

nm of the cyanine at neutral pH was shifted bathochromically to 467 nm and then to 518 nm under acidic conditions indicating the formation of two protonated forms, that were tentatively identified by parallel experiments on model compounds. Under the same conditions, reaction of the 3-phenyl-(*2H*)1,4-benzothiazine with indole-3-carboxyaldehyde afforded in moderate yields after PLC purification a major product identified as **2** (Figure 2). The product showed an absorption maximum in neutral media at 444 nm, with a bathochromic shift at 545 nm in acid.



Glyoxal was initially explored as model dialdehyde affording under the same reaction conditions a major product that was isolated in 55% yield after chromatographic purification.

Figure 2. *Products 1-2-3*

This was formulated as the symmetric 2Z,2Z'-(1,2-etandiilidene)bis(3-phenyl-*2H*-1,4-benzothiazine) (**3**) based on complete structural characterization. The intense absorption maximum at 474 nm at neutral pH underwent shifts to 643 nm on acidification attributed to the protonation of the benzothiazine nitrogen.

High molar extinction coefficients (around 10000 $M^{-1}cm^{-1}$) were associated to the all phenyl-substituted benzothiazine cyanines.

In conclusion, the ease of the synthetic procedures and the peculiar acidichromic behavior of these compounds would hint to their exploitation as pH sensors or related applications.

1. W. Sun, S. Guo, C. Hu, J. Fan, X. Peng, *Chem Rev,* **116**, 7768−7817 (2016).
2. A. Napolitano, L. Panzella, L. Leone, M. d'Ischia, *Acc. Chem. Res*., **46**, 519-528 (2013).
3. L. Leone, O. Crescenzi, A. Napolitano, V. Barone, M. d'Ischia, *Eur. J. Org. Chem.,* **27**, 5136-5140 (2012).
4. L.Leone, A. Pezzella, O. Crescenzi, A. Napolitano, V. Barone, M. d'Ischia, *ChemistryOpen.,* **4**, 370-377 (2015).
5. C. Santacroce, D. Sica, R:A: Nicolaus, *Gazz. Chim. Ital.,* **98**, 85-96 (1968)

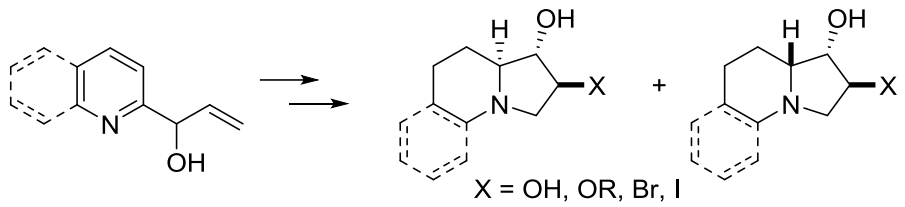
OC11

A FACILE APPROACH TO POLYCYCLIC NITROGEN HETEROCYCLES FROM 1-(2-PYRIDYL)- AND 1-(2-QUINOLYL)-2-PROPEN-1-OL

Jacopo Ceccarelli, Donatella Giomi, Alberto Brandi

Dipartimento di Chimica"Ugo Schiff", Università di Firenze, 50019 Sesto Fiorentino (FI), Italy

Nitrogen heterocycles are well established as privileged scaffolds commonly present in many biologically active molecules and, in particular, polyhydroxylated indolizidine alkaloids have received considerable attention because of their remarkable biological activities and applications as pharmaceutical tools. Natural (+)-lentiginosine [(1S,2S,8aS)-octahydroindolizine-1,2-diol] is a potent and selective inhibitor of fungal amyloglucosidases as well as Heat shock protein 90 (Hsp90), while the non-natural enantiomer acts as an apoptosis inducer on tumor cells of different origin.[1]



In this context, 1-(2-pyridyl)- and 1-(2-quinolyl)-2-propen-1-ol, obtained by vinylation of commercially available 2-pyridine- and 2-quinoline-carboxaldehyde, behaved as useful reagents for the synthesis of indolizidine and benzo[e]indolizidine systems through a simple process involving bromination, reduction, and nucleophilic substitution (via elimination/addition). 1-(2-Pyridyl)-2-propen-1-ol afforded (±)–lentiginosine, in ca. 27% overall yield, as well as the non-natural diastereomer with inverted configuration at C-8a.[2]

Synthetic applications and mechanistic aspects of this new methodology will be presented.

1. F. M. Cordero, D. Giomi, A. Brandi, *Curr. Top. Med. Chem*., **14**, 1294-1307 (2014).

2. D. Giomi, R. Alfini, A. Micoli, E. Calamai, C. Faggi, A. Brandi, *J. Org. Chem*., **76**, 9536-9541 (2011).

OC12

A GREEN, CATALYST-FREE, SOLVENT-FREE, HIGH YIELDING ONE STEP SYNTHESIS OF FUNCTIONALIZED BENZO[F]FURO[3,2-c] CHROMEN-4-(5*H*)-ONES AND FURO[3,2-c]QUINOLIN-4-(5*H*)-ONES

Luca Messaggi

Anton Paar Italia srl.

A green, three-component reaction of 1-hydroxy-3H-benzo[f]chromen-3-ones and 4-hydroxyquinolin-2(1H)-ones, aromatic aldehyde, and isonitrile was developed, for the first time, which resulted in a variety of substituted functionalized benzo[f]furo[3,2-c]chromen-4-(5H)-ones and furo[3,2-c]quinolin-4-(5H)-ones in excellent yields. The merits of the present protocol include use of microwave irradiation, catalyst-free, solvent free, atom-efficient, no work up or column purification. The present method is milder yet advanced than the previous reports for the synthesis of related structures, furo-chromen-4-ones, furopyrimidines, furopyranones etc. The synthesized compounds have been virtually screened against a series of therapeutic targets and have shown promising binding with some of them.

OC13

SYNTHESIS OF BICYCLIC PIPERAZINONES BY Pd(II)/Cu(II) CATALYZED DOMINO FUNCTIONALIZATION OF CARBON-CARBON DOUBLE BONDS

R. Romeo,[1] *M. A. Chiacchio,*[2] *S. V. Giofrè,*[1] *G. Broggini*[3]

[1]Dept of Chemical, Biological, Pharmaceutical and Environmental Sciences, Univ. of Messina, S.S. Annunziata, 98168 Messina, Italy

[2]Dept. of Drug Science, Univ. of Catania, V.le A. Doria 6, 95125, Catania, Italy

[3]Dept of Chemical and Environmental Sciences, Univ. of Insubria, via Valleggio 11, 22100, Como, Italy

Palladium-catalyzed domino processes offer an easy entry to the formation of complex molecular scaffolds in a single transformation. Many valuable synthetic routes have been designed and developed towards the construction of several functionalized heterocyclic systems, based on various combination of new bonds (i.e. carboamination, diamination, carbooxygenation, dioxygenation and aminooxygenation reactions).[1] In this context, reactions performed in a doubly intramolecular manner have proven to be useful tools to convert acyclic alkenes and alkynes that contain two nucleophiles into heteropolycyclic products.

Alkenylureas **1** arising from glycine allylamides were proven to be suitable substrates for the synthesis of bicyclic five-membered ring-fused piperazinones. The intramolecular domino processes, performed under oxidative conditions with bis(acetonitrile)palladium dichloride as catalyst and copper(II) chloride in a stoichiometric amount by microwave activation, were completely selective, involving either diamination **2** or aminooxygenation **3** (Fig. 1).[2] The oxazolo-fused piperazinones **3** have shown to be endowed of an interesting antitumoral activity, at μM level, against two human thyroid cancer cell lines.[3]

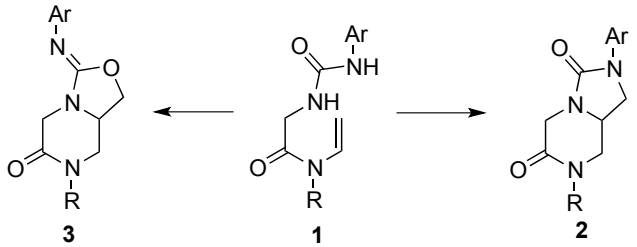


Figure 1

The extension of Pd-catalyzed diamination domino process to alkenyl sulfamates **4** led to the formation of [1,2,5]thiadiazolo-fused piperazinones **5** or **6**.[4] This bicyclic system has been exploited for the synthesis of new histone deacetylases (HDAC) inhibitors **7** and **8** (Fig, 2).

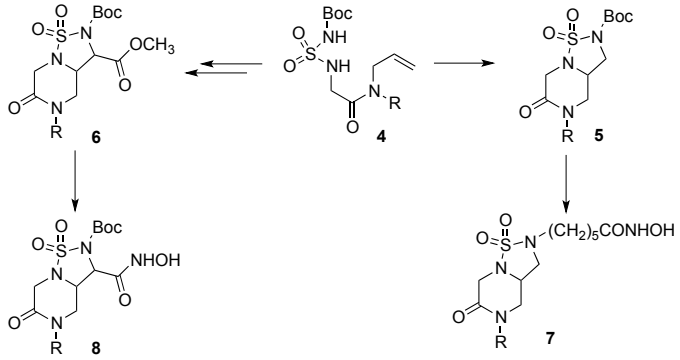


Figure 2.

Biological tests indicate that **7** and **8** show a good antiproliferative effect over breast and colon cancer cells, with IC_{50} values in the low μM range, and good activity as HDAC inhibitors.

References.

1. E. Beccalli, G. Broggini, S. Gazzola, A. Mazza Org. Biomol. Chem., 2014, 12, 6767–6789¸ P. Chavez, J. Kirsch, J. Streuff, . Mu iz *J. Org. Chem*., **2012**, 77, 1922−1930.

2. G. Broggini, V. Barbera, E. M. Beccalli, U. Chiacchio, A. Fasana, S. Galli, S. Gazzola Advanced Synthesis &Catalysis, 2013, 355, 1640–1648.

3. U. Chiacchio, V. Barbera, R. Bonfanti, G. Broggini, A. Campisi, S. Gazzola, R. Parenti, G. Romeo. *Bioorg. Med.Chem*., **2013**, 21, 5748–5753.

4. U. Chiacchio, G. Broggini, R. Romeo, S. Gazzola, M. A. Chiacchio. *RSC Advances*, **2016**, 6, 57521-5752.

OC14

RECENT ADVANCES IN THE SYNTHESIS OF CARBOCYCLES AND HETEROCYCLES BY SYNERGISTIC CATALYSIS

Marta Meazza

University of Southampton, Department of Chemistry, Southampton, UK
Aarhus University, Center for Catalysis, Aarhus, DK

Synergistic catalysis has recently emerged as an important tool in Organic Chemistry.[1] The use of two independent catalytic cycles that work in concert to form a single carbon-carbon bond presents several advantages, such as the concurrent activation of nucleophiles and electrophiles allowing to find new avenues and untrodden paths in asymmetric synthesis (Figure 1).

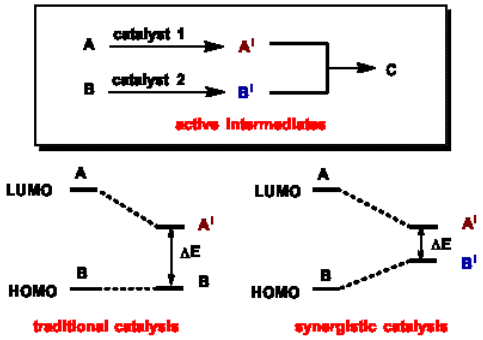


Figure 1: Synergistic catalysis vs traditional catalysis

Based on this concept we have developed new methodologies merging metal Lewis acid activation of alkyl-azaarenes and aminocatalysis. Concretely, we first developed a diastereoselective addition of alkyl-benzoxazoles to MBH carbonates, catalyzed by Ag salt and an organic base.[2] Then, we expanded the concept to an enantioselective addition of alkyl-azaarenes to enals, synergistically catalyzed by $Pd(OAc)_2$ and a secondary amine catalyst.[3]

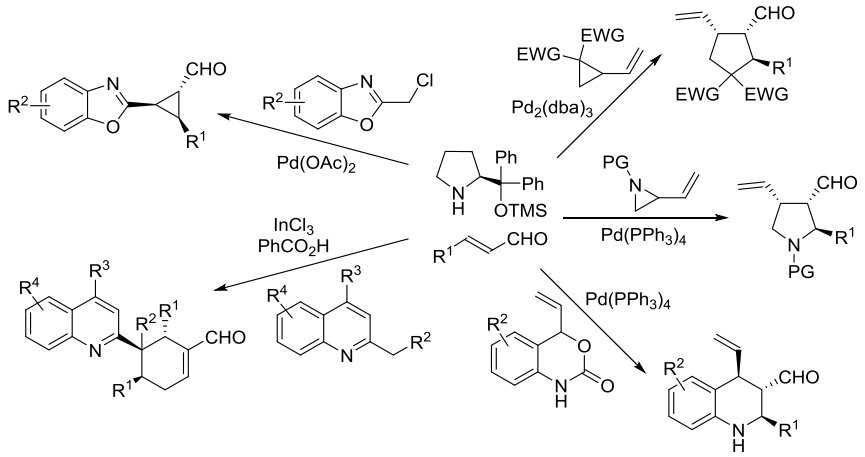
Despite the challenges that this approach faces such as autoquench of the catalysts, metal Lewis catalysis and iminium catalysis work in concert to achieve the Michael addition of azaarenes to enals in good yields and stereoselectivities.

Based on these grounds, we applied the concept to the synthesis of carbocycles and heterocycles. First, we expanded the scope of the present methodology studying the compatibility with cascade reactions.[4] We therefore developed a new cyclopropanation of alkyl-benzoxazoles, joining three consecutive catalytic cycles: metal Lewis acid, iminium and enamine catalysis. This approach allows the access to a new cyclopropane motif, decorated with benzoxazoles, in excellent yields and enantioselectivities. Subsequently, the reaction concept was broadened to include two subsequent synergistic catalytic cycles (Lewis acid- and iminium-ion catalyzed), followed by a cascade reaction.[5]

A highly diastereo- and enantioselective double addition of unactivated alkyl-quinolines to enals was developed, combining the organocatalytic activation of α,β-unsaturated aldehydes, with the $InCl_3$ activation of the alkyl-quinoline aided by benzoic acid in a Brønsted acid-assisted Lewis acid catalysis.

Pushing the boundaries of synergistic catalysis, we developed a domino reaction for the synthesis of highly substituted cyclopentanes *via* a ring expansion of vinyl cyclopropanes.[6,7,8] This methodology combines four catalytic cycles, breaking one C-C bond and forming 2 C-C bonds. The first synergistic step consists in the Pd-catalyzed opening of vinyl cyclopropanes, coupled with an organocatalyzed Michael addition. Next, the enamine intermediate generated, reacts with the allyl intermediate through a Tsuji-Trost reaction. The products were obtained in good yields and excellent diastereo- and enantioselectivities (up to 19:1 dr and 99% *ee*). Later, we reported an asymmetric [3+2] cycloaddition of vinyl aziridines with α,β-unsaturated aldehydes, based on synergistic catalysis.[9] This methodology allows the formation of attractive pyrrolidine structures in good yields (up to 84%), moderate diastereoselectivities and enantioselectivities up to >99%.

Finally, this synergistic concept was applied to a decarboxylative [4+2] cycloaddition between Pd-activated vinyl benzoxazinanones and iminium-ion activated α,β-unsaturated aldehydes, providing highly substituted vinyl tetrahydroquinolines in good to high yields, and excellent enantio- and diastereoselectivities (>98% ee and >20:1 d.r.).[10]



Scheme 1: General scheme of the reacions for the synthesis heterocycles and carbacycles through synergistic approaches.

1. M. Meazza, R. Rios, *Synthesis*, **48**, 960-973 (2016).

2. V. Ceban, P. Putaj, M. Meazza, M. B. Pitak, S. J. Coles, J. Vesely, R. Rios, *Chem. Commun.*, **50**, 7447-7450 (2014).

3. M. Meazza, V. Ceban, M. B. Pitak, S. J. Coles, R. Rios, *Chem. Eur. J.*, **20**, 16853-16857 (2014); **Highlighted in Synfacts 2015, 11(01), 0066.**

4. M. Meazza, M. E. Light, A. Mazzanti, R. Rios, *Chem. Sci.*, **7**, 984-988 (2016).

5. M. Meazza, F. Tur, N. Hammer, K. A. Jorgensen, *Angew. Chem. Int. Ed*., **56**, 1634-1638 (2017).

6. M. Meazza, H. Guo, R. Rios, *Org. Biomol. Chem.*, **15**, 2479-2490 (2017).

7. M. Meazza, R. Rios, *Chem. Eur. J.*, **22**, 9923-9928 (2016).

8. K. Zhang, M. Meazza, A. Izaga, C. Contamine, M. C. Gimeno, R. P. Herrera, R. Rios, *Synthesis*, **49**, 167-174 (2017).

9. L. Næsborg, F. Tur, M. Meazza, J. Blom, K. S. Halskov, K. A. Jørgensen, *Chem. Eur. J.*, **23**, 268-272 (2017).

10. L. A. Leth, F. Glaus, M. Meazza, L. Fu, M. K. Thøgersen, E. A. Bitsch, K. A. Jørgensen, *Angew. Chem. Int. Ed.*, **55**, 15272-15276 (2016); **Highlighted in Synfacts 2017, 13(02), 0176.**

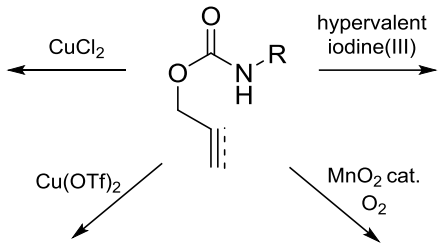
OC15

COUPLING OF ALKYNYL- AND ALKENYL CARBAMATES IN OXIDATIVE CONDITIONS

S. Giofrè[a], *G. Broggini*[b], *E. M. Beccalli*[a]

[a]DISFARM, Sezione di Chimica Generale e Organica "A. Marchesini", Università degli Studi di Milano [b]Dipartimento di Scienza e Alta Tecnologia, Università dell'Insubria

Intramolecular hydroamination reactions of unactivated alkenes and alkynes constitute an attractive process for the formation of nitrogen-containing heterocycles with 100% atom-economical result.[1] In addition, the possibility of the concomitant functionalitation of the heterocycle represents the major challenge of the synthetic pathway. Our studies have been focused on the reactivity of unsaturated carbamates under oxidative conditions, performing the reaction both in the presence and in the absence of a copper catalyst. The will to achieve a functionalized heterocycle and the aim to work in step economy have encouraged us to investigate a domino process[2] in the presence of nucleophilic species. Besides, working with copper salts and aromatic solvents, a particular reactivity involving the solvents has been reported.



1. a) K. Hii, *Pure Appl. Chem.*, **78**, 341-349 (2006); b) P. W. Roesky, T. E. Müller, *Angew. Chem. Int. Ed*., **42**, 2708-2710 (2003).

2. a) L. Tietze, *Chem. Rev.,* **96**, 115-136 (1996); b) F. Felpin, E. Fouquet, *ChemSusChem*, **1**, 718-724 (2008).

OC16

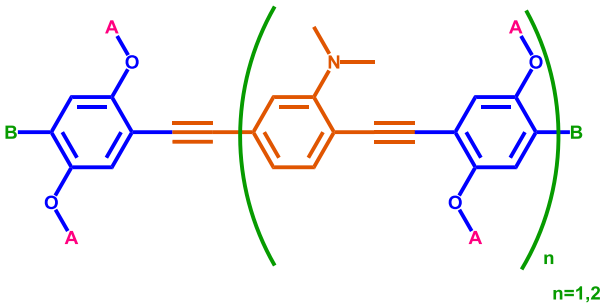
"TUNING" SUGAR FUNCTIONALIZED OPES WITH BIOLOGICAL INTEREST

Aurora Mancuso, Paola Bonaccorsi, Tania M. G. Salerno, Anna Barattucci

Dipartimento di Scienze Chimche, Biologiche; Farmaceutiche ed Ambientali (ChiBioFarAm), Università degli Studi di Messina, Viale F. Stagno d'Alcontres 31, 98166, Vill. S. Agata – Messina

mancusoaurora@gmail.com

Oligo phenylene ethynylenes (OPEs) are conjugated molecules that have found a wide range of applications in electrically conducting materials, bio-chemical sensors, and supramolecular assemblies. Their photophysical properties, connected to their extensive conjugation, can be tuned by modulating their structure and substituents.[1]
Recently, we reported the synthesis of end-only glucose functionalized OPEs where the synergy of the amino substituent at the central core, the chain length and the carbohydrate decoration, is the keystone for their use in the biological field. In fact, the balanced contribution of the hydrophilic (sugar) and hydrophobic (aryl conjugated system) moieties gives rise to the permeation of some of these OPEs to the cellular membrane, showing their potential uses as dyes in fluorescent imaging microscopy. Furthermore, the presence of the dimethylamino group is responsible of the generation of singlet oxygen, opening the way in their use as Photosensitizers in Photodynamic therapy.



Going on with our research, and in a way to explore the tuning of their photophysical and biological behaviour by modulating the sugar pattern, the elongation and the terminal substitution, we have synthesized new OPEs glycosides, whose general structure is reported in figure. The first results of our research will be reported in this communication.[2]

1. V. Kaliginedi, P. Moreno-García, H. Valkenier, W. Hong, V. M. García-Suárez, P.Buiter, J. L. H. Otten, J. C. Hummelen, C.J. Lambert, T. Wandlowski *J. Am. Chem. Soc*., **2012**, 134, 5262-5275
2. E. Deni, A. Zamarrón, P. Bonaccorsi, M. C. Carreño, Á. Juarranz, F. Puntoriero, M. T. Sciortino, M. Ribagorda, A. Barattucci *European J. Med. Chem.*, **2016**, 111, 58-71

OC17

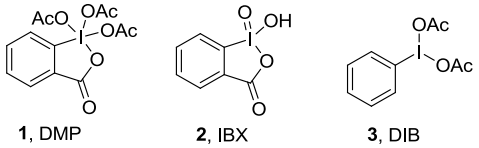
OXIDATION OF HYDROXYLAMINES WITH HYPERVALENT IODINE REAGENTS

Camilla Parmeggiani,[a,b] *Camilla Matassini,*[a] *Francesca Cardona,*[a] *Andrea Goti*[a]

[a] Dipartimento di Chimica "Ugo Schiff", Università degli Studi di Firenze, via della Lastruccia 3-13, 50019 Sesto Fiorentino, Italy.

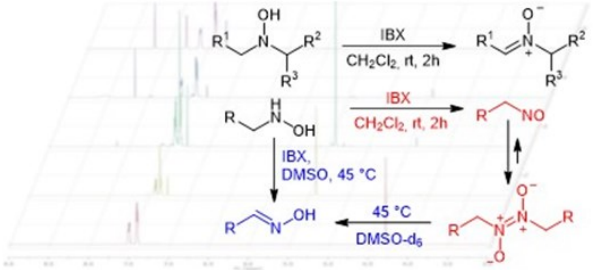
[b] CNR-INO @ European Laboratory for Non Linear Spectroscopy, Università degli Studi di Firenze, via Nello Carrara 1, 50019 Sesto Fiorentino, Italy .

For many years, we have been strongly involved in the use of nitrones as useful and versatile synthetic intermediates for the obtainment of alkaloids and other nitrogenated products.[1]
In the search for a novel and convenient metal-free synthesis of nitrones, our attention was turned to DMP (**1**, Dess-Martin periodinane) and the closely related IBX (**2**, *o*-iodoxybenzoic acid) and DIB (**3**, diacetoxyiodo benzene), which are known to oxidize alcohols to the corresponding aldehydes and ketones in mild reaction conditions. Moreover, IBX has been investigated by the Nicolau group as an oxidant for nitrogenated compounds.[2]



1, DMP **2**, IBX **3**, DIB

We describe herein our studies on the oxidation of *N*,*N*-disubstituted hydroxylamines to the corresponding nitrones. The substrate scope is quite satisfying, including cyclic, acyclic and functionalized hydroxylamines. The procedure is very simple and user-friendly and affords the target compounds with high efficiency and regioselectivity, highlighting IBX as the reagent of choice for the preparation of aldonitrones from nonsymmetric hydroxylamines. Evidence for a mechanism involving nitrogen to iodine coordination has been collected by ^{1}H-NMR studies.[3] Moreover, *N*-monosubstituted hydroxylamines revealed an interesting divergent behavior depending on the reaction conditions. While IBX oxidation in dimethylsulfoxide at 45 °C furnished oximes as reported, the oxidation in dichloromethane at rt afforded efficiently the unusual corresponding nitroso dimers, providing a novel straightforward and convenient access to these compounds.



Acknowledgements. The research leading to these results has received funding from the ERC under the European Union's Seventh Framework Programme (FP7/2007-2013) / ERC grant agreement n° [291349] on photonic micro robotics

1. A. Brandi, F. Cardona, S. Cicchi, F. M. Cordero, A. Goti, *Chem. Eur. J.* **2009**, *15*, 7808-7821.

2. a) K. C. Nicolaou, C. J. N. Mathison, T. Montagnon, *Angew. Chem., Int. Ed.* **2003**, *42*, 4077−4082. b) K. C. Nicolaou, C. J. N. Mathison, T. Montagnon, *J. Am. Chem. Soc.* **2004**, *126*, 5192−5201.

3. C. Matassini, C. Parmeggiani, F. Cardona, A. Goti, *Org. Lett.* **2015**, *17*, 4082-4085.

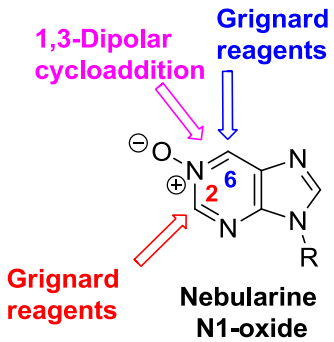
OC18

AN EFFICIENT SYNTHETIC STRATEGY FOR THE FUNCTIONALIZATION OF 9-RIBOSYL PURINE (NEBULARINE)

S. D'Errico,[a,b] *G. Oliviero,*[c] *N. Borbone,*[b] *G. Piccialli*[a,b]

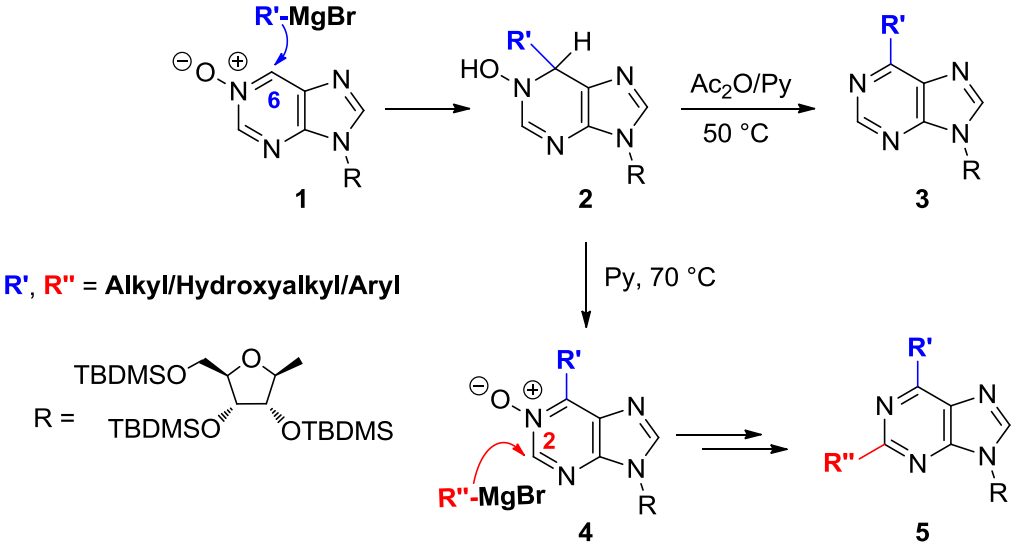
[a]*Centro di Servizio di Ateneo per le Scienze e Tecnologie per la Vita (CESTEV), Università di Napoli 'Federico II', via T. De Amicis 95, 80145 Napoli, Italy*
[b]*Dipartimento di Farmacia, Università di Napoli 'Federico II', via D. Montesano 49, 80131 Napoli, Italy* [c]*Dipartimento di Medicina Molecolare e Biotecnologie Mediche, Università di Napoli 'Federico II', via S. Pansini 5, 80145 Napoli, Italy*

In the last decades, many research groups have focused their attention to the preparation of new modified nucleosides and nucleotides to expand the pool of molecules with potential antineoplastic, antihypertensive and antiviral activities. In this context, efforts have been directed to the synthesis of sugar and/or base-modified nucleosides. Many nucleobase analogues exist and several nucleoside analogues have been employed against cancer and viral diseases. In addition, base modified nucleosides often show fluorescent properties, and can be used as fluorescent probes for the analysis of DNA and RNA structures as well as for analysing the interaction of DNA and RNA with binding proteins. Purine bases and nucleosides bearing a C or N-substituent at C2 and C6 positions represent an important class of compounds possessing a broad spectrum of biological effects including cytostatic, antiviral, antibacterial as well as receptor modulation activity. The reactivity imparted to purines and related nucleosides by halogenation at C6 and C2 positions has opened the way to the construction of new libraries of C6 and C2 modified nucleosides generally through direct aromatic nucleophilic substitution (S_NAr), or metal-mediated cross-coupling processes. We have recently reported on the reactivity of 9-ribosyl purine (nebularine) N1-oxide demonstrating that its C6(C2)-N1-O^- nitrone moiety can react with dipolarophiles and with Grignard reagents leading to their addition on the C6 or C2 carbons of the purine base.

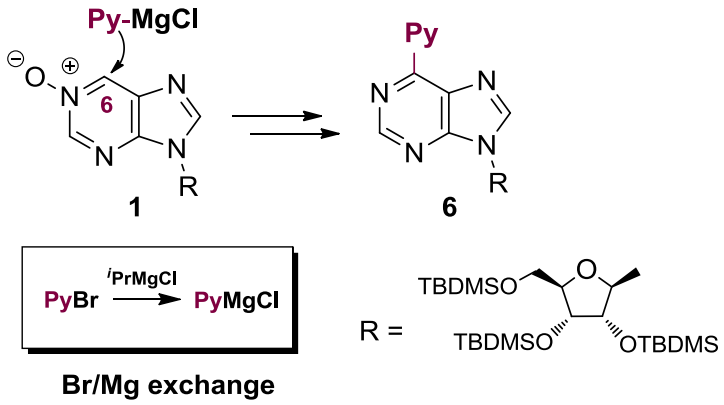


In particular, we observed that the sugar-protected nebularine N1-oxide **1** can regioselectively react with Grignard reagents at the more electrophilic C6 position leading to an adduct, which re-aromatized by treatment with Ac_2O/pyridine, furnishing the C6-substituted purine nucleoside **3** in high yields.[1] We have also shown that a second alkyl/aryl substituent can be introduced at C2 by a similar strategy, that is, by the addition of a Grignard reagent to the C6- substituted nebularine N1-oxides through the opening/reclosing of the pyrimidine ring induced by the Grignard reagent itself.

Through this approach, we have synthesized new collections of 2,6-dialkyl(aryl)purine nucleosides **5**.[2]



A slightly modified synthetic procedure allowed us also to insert pyridinyl residues at the C6 purine position to obtain the few explored C6-pyridinyl nucleosides **6**.[3] The last are appealing nucleoside analogues because the presence of a nitrogen atom in the C6 residue can potentially alter the hydrogen-bonding capabilities of the nucleoside as well as promote its coordination to biologically important metals, such as platinum and ruthenium. We have discovered that they can be easily accessed after bromine-magnesium exchange between bromopyridines and ^{i}PrMgCl.



References:

1. D'Errico, S.; Piccialli, V.; Oliviero, G.; Borbone, N.; Amato, J.; D'Atri, V.; Piccialli, G. *Tetrahedron* **2011**, *67*, 6138–6144.
2. D'Errico, S.; Oliviero, G.; Borbone, N.; Piccialli, V.; D'Atri, V.; Mayol, L.; Piccialli, G. *Eur. J. Org. Chem.* **2013**, 6948–6954.
3. D'Errico, S.; Oliviero, G.; Borbone, N.; Nici, F.; Piccialli, V.; Pinto, B.; D'Alonzo, D.; Mayol, L.; Piccialli, G. *Eur. J. Org. Chem.* **2015**, *2015*, 2244–2249.

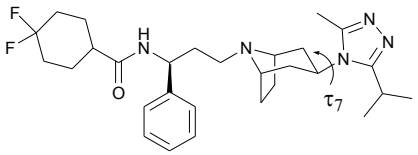
OC19

MODELING STUDIES OF THE TRIAZOLETROPANE-BASED COMPOUND MARAVIROC AND TWO SYNTHETIC ANALOGUES: A RATIONALIZATION OF THEIR ANTIVIRAL INHIBITORY ACTIVITY

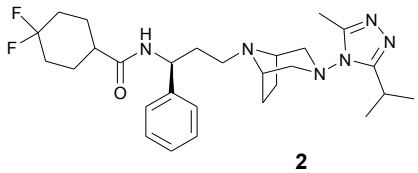
Laura Legnani,[a] Lucio Toma,[a] Stefania Villa,[b] Giovanni Grazioso,[b] Diego Colombo[c]

[a]Dipartimento di Chimica, Università di Pavia, Via Taramelli 12, 27100 Pavia, Italy
[b]Dipartimento di Scienze Farmaceutiche, Università di Milano, Via Mangiagalli 25, 20133 Milano, Italy
[c]Dipartimento di Biotecnologie Mediche e Medicina Traslazionale, Università di Milano, Via Saldini 50, 20133 Milano, Italy.

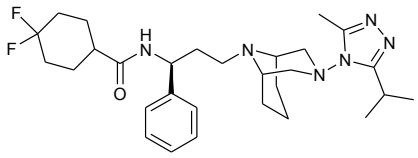
Maraviroc **1**, a triazoletropane-based compound synthesized by Pfizer,[1] is the only CCR5 inhibitor approved by both US FDA and the European Medicines Agency for the treatment of antiretroviral drug-experienced and naive patients.[2]
Two structural analogues of **1**, in which the azabicyclooctane moiety is replaced by a diazabicyclooctane **2** or diazabicyclononane **3**, were synthesized and their infectivity reduction power determined through a viral neutralization assay. The diazabicycloctane derivative maintained a significant infectivity reduction power, whereas the diazabicyclononane was less effective.



1



2



3

Biological data were rationalized through a computational study that allowed to determine the conformational preferences of the compounds and hypothesize a correlation between the inhibitory activity, the bridge length of the bicycle, and the rotational barrier around dihedral angle τ_7 (C4-C3-N1"'-C5"').[3] A high-field NMR analysis supported the modeling results, confirming the high flexibility of the studied molecules and the existence in solution of the calculated conformers, as evidenced by specific NOESY contacts.

1. D. A. Price, S. Gayton, M. D. Selby, J. Ahman, S. Haycock-Lewandowski, B. L. Stammen, A. Warren, *Tetrahedron Lett.*, **46**, 5005-5007 (2005).

2. G. G. Xu, J. Guo, Y. Wu, *Curr. Top. Med. Chem.*, **13**, 1504-1514 (2014).

3. L. Legnani, D. Colombo, A. Venuti, C. Pastori, L. Lopalco, L. Toma, M. Mori, G. Grazioso, S. Villa, *Med. Chem. Commun.*, **8**, 422-433 (2017).

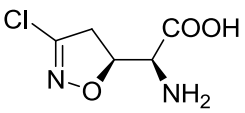
OC20

1,3-DIPOLAR CYCLOADDITION AS A KEY STEP FOR THE SYNTHESIS OF 3-HALOISOXAZOLINE-BASED ANTIPARASITIC AGENTS

G. Cullia, M. Carlomagno, A. Pinto, L. Tamborini, C. De Micheli, P. Conti

Department of Pharmaceutical Sciences (DISFARM), University of Milan

Dihydroisoxazole-containing compounds occupy an important place in the medicinal chemistry field. Among the variety of active compounds characterized by this group, the natural antibiotic acivicin [(*S*,*S*)-**1**, fig. 1], isolated from *Streptomyces sviceus*, drew much attention because of its interesting biological properties.[1] This compound acts as an antimetabolite inhibiting the activity of a series of glutamine-requiring enzymes, resulting in antibiotic and antitumor activity.

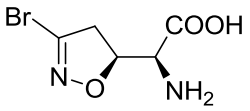


(*S*,*S*)-**1**

Figure 1

A number of total syntheses of (*S*,*S*)-**1** have appeared in literature.[2] Most of these approaches involve a 1,3-dipolar cycloaddition (1,3-DPCA) reaction to construct the isoxazolinic ring. Our group proposed a simplified synthesis of (*S*,*S*)-**1** , which allowed to obtain it in only 5 steps with a 34% overall yield and which could be performed in gram scale.[3]

Based on (*S*,*S*)-**1**, we described a new set of inhibitors of the enzyme cytidine 3-phosphate synthetase, a glutamine-dependent amidotransferase, of *Trypanosoma brucei* (*Tb*CTPS). While the amino acid group showed to be optimal for mimicking the L-glutamine structure, the substitution of the chlorine atom with a better leaving group, such as bromine [bromoacivicin, compound (*S*,*S*)-**2**, fig. 2], led to an increase in potency.[4] Because of the interesting properties of this electrophile, which displays an optimally balanced reactivity, our group is currently active in the design of targeted covalent inhibitors characterized by the presence of the 3-bromoisoxazoline as warhead.



(*S*,*S*)-**2**

Figure 2

In the recent years, we dedicated our activity to the design and synthesis of inhibitors of *Plasmodium falciparum* glyceraldehyde 3-phosphate dehydrogenase (*Pf*GAPDH) as new potential antimalarial agents.[5] This enzyme possesses a catalytic cysteine residue that is susceptible to alkylation in presence of 3-bromoisoxazolinic inhibitors resulting in irreversible inhibition. Interestingly, the affinity towards the target enzyme can be modulated by varying the nature of the side chain at the 5-position of the isoxazoline (general structures are shown in fig. 3). Moreover, this part of the molecule can be suitably modified to properly tune properties such as solubility/lipophilicity, which may significantly affect the cell penetration capability of the tested derivatives.

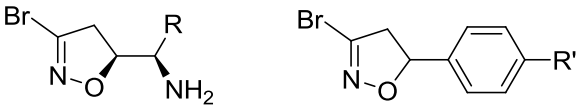


Figure 3

Notably, the new derivatives also showed a preferential inhibition of the plasmodial enzyme over the human orthologue,[6] as reflected by the large difference between the observed *in vitro* activities toward parasite and human cells (selectivity index in the order of 10^4).

Despite 1,3-DPCA belongs to the old group of pericyclic reactions, it is still precious in the medicinal chemistry field. Considering the growing consideration that covalent inhibitors have reached in the last years, in conjunction with the unique properties of the 3-halo-4,5-dihydroisoxazole warhead, this reactions might soon live a new golden age.

1. L. J. Hanka, D. G. Martin, G. L. Neil, *Cancer Chemother. Rep.*, **57**, 141-148 (1973)

2. a. D. M. Vyas, Y. Chiang, T. W. Doyle, *Tetrahedron Lett.*, **25**, 487-490 (1984); b. J. E. Baldwin, J. K. Cha, L. I. Kruse, *Tetrahedron*, **41**, 5241-5260 (1985); c. S. Hanessian, B. Vanasse, *Can. J. Chem.*, **65**, 195-199 (1987); d. S. Mzengeza, C. M. Yang, R. A. Whitney, *J. Am. Chem. Soc.*, **109**, 276-277 (1987).

3. A. Pinto, P. Conti, L. Tamborini, C. De Micheli, *Tetrahedron: Asymmetry*, **20**, 508-511 (2009)

4. a) P. Conti, A. Pinto, P. E. Wong, L. L. Major, L. Tamborini, M. C. Iannuzzi, C. De Micheli, M. P. Barrett, T. K. Smith, *ChemMedChem*, **6**, 329-333 (2011); b) L. Tamborini, A. Pinto, T. K. Smith, L. L. Major, M. C. Iannuzzi, S. Cosconati, L. Marinelli, E. Novellino, L. Lo Presti, P. E. Wong, M. P. Barrett, C. De Micheli, P. Conti, *ChemMedChem*, **7**, 1623-1634 (2012)

5. S. Bruno, A. Pinto, G. Paredi, L. Tamborini, C. De Micheli, V. La Pietra, L. Marinelli, E. Novelino, P. Conti, A. Mozzarelli, *J. Med. Chem.*, **57**, 7465-7471 (2014)

6. S. Bruno, M. Margiotta, A. Pinto, G. Cullia, P. Conti, C. De Micheli, A. Mozzarelli, *Bioorg. Med. Chem.*, **24**, 2654-2659 (2016)

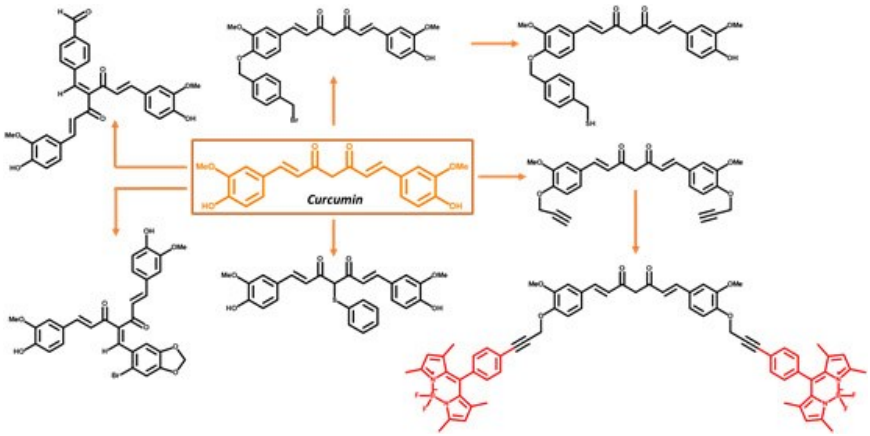
OC21

CURCUMIN: HOW MUCH MORE IS THERE TO EXPLORE?

Tania M.G. Salerno, Anna Barattucci, Aurora Mancuso, Paola Bonaccorsi

University of Messina, Department of Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, Viale F. Stagno d'Alcontres 31, 98166, Messina, Italy

In recent years, Curcumin, a natural pigment extract from *Curcuma longa*, has gained much attention due to its characteristics, such as low cost, no toxicity, good photochemical properties and good biological activity. It has been claimed that Curcumin acts as an anti-inflammatory, antiproliferative and antimetastatic agent that inhibits carcinogenesis and limits tumor growth. However, use of Curcumin, is limited by its chemical instability and poor bioavailability, due to the low water solubility. Another problem is that Turmeric extracts contain dozens of compounds, besides Curcumin, that is itself used as a mixture of three related molecules (Curcumin, bis-demethoxy and demethoxy Curcumin), and in some cases, researchers may observe promising biological effects but ascribe activity to the wrong molecule.[1] Recent investigations established approaches to improve the bioavailability and its therapeutic effects, such as the encapsulation of Curcumin with metal, non-metal and polymeric nanoparticles.[2]
Another important aspect of the Curcumin are its absorption and emission properties; in particular, it is a dye with an absorption band around 410−430 nm and a fluorescence band within 460−560 nm. The emission properties depend on the polarity of its environment, and modification of the structure could enhance fluorescence properties. Several Curcumin metal complexes have been synthesized and experimented for cellular imaging by fluorescence microscopy.[3]
The structure of curcumine, allows different chemical modification, such as modification of the β-diketo group and at the methylene carbon atom. It is also possible to alter the substitution pattern on the aromatic rings, and vary the unit between the two aromatic rings, in order to obtain several Curcumin analogues.



In this communication we will report the synthesis of new Curcumin derivatives some of which show luminescent properties that have been opportunely compared to the Curcumin ones,[4] and, some others that have been involved in a study to discover new active molecules for the estrogen receptor GPER in the treatment of Estrogen-Sensitive Tumors.[5]

1. T. Esatbeyoglu, P. Huebbe, I.M.A. Ernst, D. Chin, A. E. Wagner, G. Rimbach, *Angew. Chem. Int. Ed*., **51**, 5308 – 5332 (2012); K.M. Nelson, J.L. Dahlin, J. Bisson, J. Graham, G.F. Pauli, M.A. Walters, *J. Med. Chem*., **60**,1620-1637 (2017)
2. B. Hu, D. Sun, C. Sun, Y-F. Sun, H-X. Sun, Q-F. Zhu, X-R. Yang, Y-B. Gao, W-G. Tang, J. Fan, A. Maitra, R. A. Anders, Y. Xu, *Biochemical and Biophysical Res. Comm.,* **468**, 525-532 (2015)
3. G. Xu, J. Wang, G. Si, M. Wang, B. Wu, S. Zhou, *Dyes and Pigments,* **123**, 267-273 (2015)
4. P. Bonaccorsi, M.C. Aversa, A. Barattucci, T. Papalia, F. Puntoriero, S. Campagna, *Chem Commun*. **48**, 10550-10552 (2012); T. Papalia, G. Siracusano, I. Colao, A. Barattucci, M.C. Aversa, S. Serroni, G. Zappalà, S. Campagna, M.T. Sciortino, F. Puntoriero, P. Bonaccorsi, *Dyes and Pigments,* **110**, 67-71 (2014)
5. T. Papalia, R. Lappano, A. Barattucci, A. Pisano, G. Bruno, M.F. Santolla, S. Campagna, P. De Marco, F. Puntoriero, E.M. De Francesco, C. Rosano, M. Maggiolini, P. Bonaccorsi, *Org. Biomol. Chem.* **13**, 10437-10441 (2015).

OC22

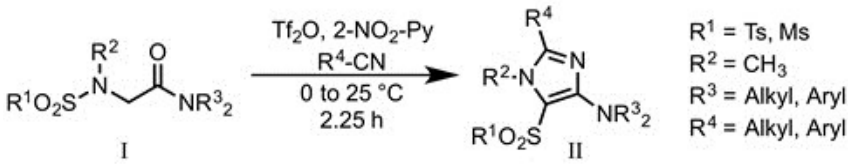
A MODULAR SYNTHESIS OF AMINOIMIDAZOLES THROUGH AMIDE ACTIVATION

G. Di Mauro,[1] *D. Kaiser,*[2] *N. Maulide*[2,*]

1 Department of Chemical Sciences, University of Naples Federico II, Italy
2 Institute of Organic Chemistry, University of Vienna, Austria

Substituted imidazoles are a highly important class of heterocyclic compounds, most valuable for their wide range of biological activity. Imidazoles play important therapeutic roles as antifungals,[1] proton pump inhibitors,[2] angiotensin inhibitors,[3] and kinase inhibitors.[4] Despite a vast amount of attention since 1858, only few unified approaches for the synthesis of imidazole-derivatives are known in the literature. To date, most syntheses rely on variations of Debus' classical condensation reaction to form the imidazole-core.[5] In addition, mechanistically more challenging transformations have been extensively studied in recent years.

Building upon the Maulide group's interest in the activation of amides,[6] and related work of others,[7] which have shown how the activation of amides leads to the formation of a key keteniminium intermediate, we became interested in the interception of this species with a nitrile nucleophile. We observed that the treatment of a tosyl-protected glycinamide derivative (**I**) with triflic anhydride and a nitrile led to the formation of an imidazole (**II**) with concomitant and unusual N-to-C tosyl migration.[8] Optimization of the conditions (solvent, base and temperature) allowed us to point out a simple approach to the formation of 4-aminoimidazoles from simple amides and nitriles.



The mechanistic and synthetic aspects of this new methodology will be discussed.

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[1] Karitzky, A.R. et al. *Comprehensive Heterocyclic Chemistry III,* **4,** 143-364 (1984).
[2] D. C. Metz, M. Vakily, T. Dixit, D. Mulford, *Aliment. Pharmacol. Ther.* **29**, 928–937 (2009).
[3] (a) P. M. Abadir et. al *PNAS* **108**,14849-14854 (2011); (b) G. K. Aulakh, R. K. Sodhi, M. Singh *Life Science* **81**, 615-639 (2007).

[4] J. C. Lee *Nature* **372**, 739–746 (1994).

[5] H. Debus, *Ann. Chem. Pharm*. **107**, 199-208 (1858).
[6] D. Kaiser, N. Maulide, *J. Org. Chem.* **81**, 4421-4428 (2016). And references therein.
[7] (a) K. L. White, M. Mewald, M. J. Movassaghi, *J. Org. Chem*. **80**, 7403 (2015). (b) K. J. Xiao, J. M. Luo, K. Y. Ye, Y. Wang, P. Q. Huang, *Angew. Chem. Int. Ed*. **49**, 3037 (2010). (c) A. B. Charette, M. Grenon, *Can. J. Chem*. **79**, 1694 (2001).
[8] For an imidazole synthesis involving the elimination of a tosylate (as *p*-toluenesulfinic acid), see the van Leusen imidazole synthesis: A. M. Van Leusen, J. Wildeman, O. H. Oldenziel *J. Org. Chem.* **42**, 1153-1159 (1977).

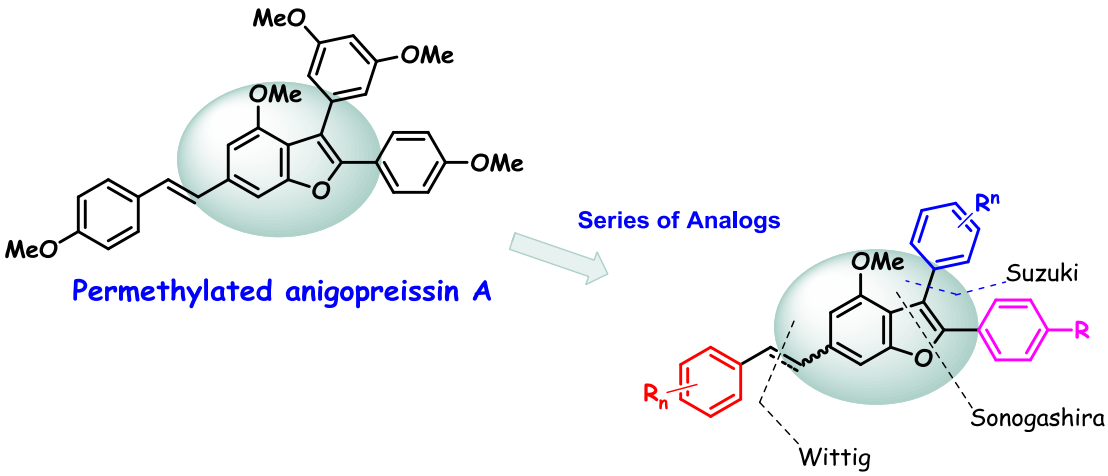
OC23

SYNTHESIS AND ANTI-HEPATIC CANCER ACTIVITY OF PERMETHYLATED ANIGOPREISSIN A ANALOGUES

Ilaria Caivano, Paolo Convertino, Lucia Chiummiento, Maria Funicello, Vittoria Infantino, Paolo Lupattelli, Anna Santarsiero

Department of Science, University of Basilicata, Via dell'Ateneo lucano, 10, 85100 Potenza, Italy

Resveratrol and its oligomers are natural stilbenoids with relevant biological activities[1] ranging from anti-cancer to antibiotic and anti-neurodegenerative. Anigopreissin A, a natural resveratrol dimer, extracts from *Anigozanthos preiissi* and *Musa Cavendish*[2] and very recently from *Macropidia fuliginosa*[3], presents an unusual benzofuryl *core* and its biological activity is not completely investigated. Permethylated Anigopreissin A (PAA),[4] the completely protected form of the natural compound, kills several human cancer cell, showing the highest activity against HepG2 (IC_{50}=0.24 μM)[5]. Biological activity of PPA and its pharmacological potential has generated extensive efforts toward the syntheses of its analogues. Herein we report the strategy used to modulate the introduction of the two aryl rings and the styryl moiety respectively on C2, C3 and C6 positions of the benzofuryl ring. Pd-catalyzed reactions (Sonogashira and Suzuki cross-couplings) and the Wittig olefination have been employed as the synthetic key steps. Regio- and chemo-selective procedures have been also carried out. Preliminary studies of structure-activity relationship and stability will be also showed.[6]



1. Y.-Q. Xue, J.M.Di, Y. Luo, K.-J. Cheng, X. Wei, Z. Shi**,** *Oxidative Medicine and Cellular Longevity,* **765832**, (2014).
2. a) D. Holscher, B. Schneider, *Phytochemistry* **44,** 471– 473 (1996); b) B. Schneider, *Phytochemistry* **64,** 459– 462, (2003).
3. R. Brkljača, J. M. White, S. Urban, *J. Nat. Prod.*, **78**, 1600-1608 (2015**)**.
4. L. Chiummiento, M. Funicello, M.T. Lopardo, P. Lupattelli, S. Choppin, F. Colobert, F., *Eur. J. Org. Chem.* 188-192, (2012).
5. P. Convertini, F. Tramutola, V. Iacobazzi, P. Lupattelli, L. Chiummiento, V. Infantino*, Chem.-Biol. Interactions,* **237**, 1–8, (2015).
6. I. Caivano, P. Convertini, E. D'Amato, M.Funicello, V. Infantino, P. Lupattelli, P. Nigro, A. Santarsiero, L. Chiummiento, *manuscript in preparation.*

FLASH and POSTER COMMUNICATIONS

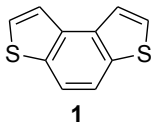
P1

NEW SYNTHESIS OF 1-BROMO BENZO[1,2-*b*:4,3-*b*']DITHIOPHENE THROUGH PHOTOCHEMICAL CYCLIZATION

Clara Baldoli,[a] *Silvia Cauteruccio,*[b] *Davide Dova, Emanuela Licandro.*[b]

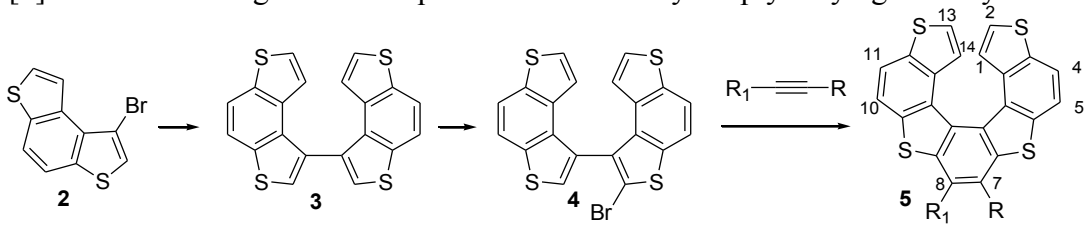
[a] CNR- Istituto di Scienze e Tecnologie Molecolari (ISTM). Dipartimento di Chimica dell'Università di Milano. Via C. Golgi 19, 20133 Milano

Thiophene-containing polycondensed aromatic compounds are important source of functional organic materials for different applications.[1] Some of them like benzo[1,2-*b*:4,3-*b*']dithiophene (BDT) (**1**) are also key intermediates in the synthesis of inherently chiral helical systems such as tetrathia[7]helicenes (7-TH).[2]



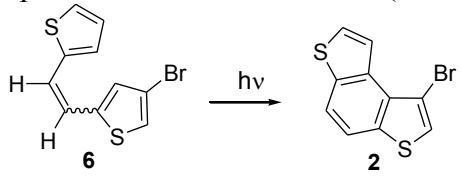
1

These molecules, that are object of extensively research in our group,[3] are extremely interesting conjugated systems with unique physicochemical properties provided by their helix-like structure. The search for new general and versatile synthetic strategies for the preparation of heterohelicenes is still a relevant target and recently a new synthesis of 7-TH systems has been carried out in our laboratories. The key step of this new approach is the final ring closure to form the helical structure through a Pd-catalyzed coupling with alkynes. (Scheme 1) This reaction gives the significant advantage of preparing a series of 7,8 substituted tetrathia[7]helicenes starting from a unique intermediate **4** by simply varying the alkyne counterpart.



Scheme 1

In this synthetic scheme the β-Br-BDT **2** (not reported in the literature) is a key starting compound, but its preparation is not trivial as the direct bromination of the parent BDT **1** gives the corresponding α-isomer. We have setup alternative synthesis for bromo BDT **2** and one of these involves the oxidative photocyclization of the parent brominated alkene **6**. (Scheme 2)



Scheme 2

As the carbon-halogen bond is not very stable in photochemical conditions, a systematic study of this reaction has been carried out to select the best conditions allowing the easy preparation of the target bromo BDT **2**.

1. C. Wang, W. Hu, D. Zhu et al., *Chem. Rev*., **112**, 2208-2267 (2012) .

2. Y. Shen, C-F Chen, *Chem. Rev.*, **112**, 1463-1535 (2012)

3. E. Licandro, S. Cauteruccio, D. Dova, *Advances in Heterocyclic Chemistry*, **118**, 2016.

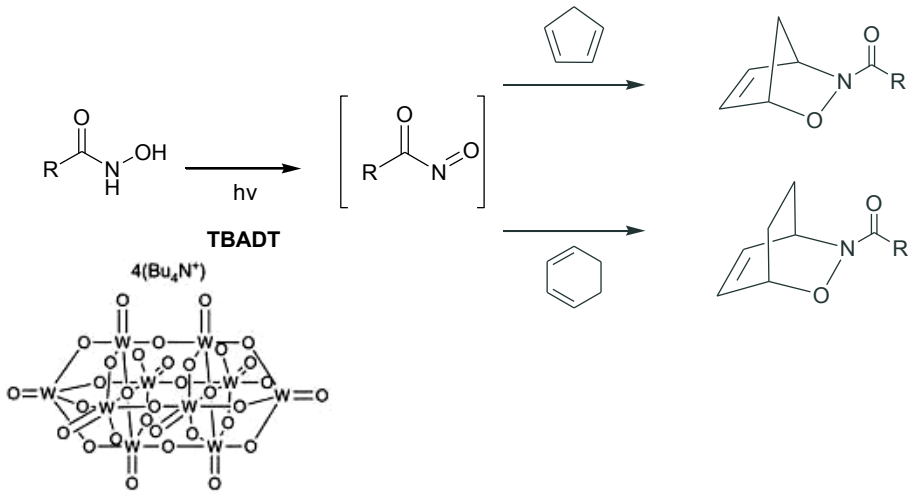
P2

TETRABUTYLAMMONIUM DECATUNGSTATE PHOTOCATALYZED SYNTHESIS OF NITROSOCARBONYLS

Teresa Basile, Luca Capaldo, Davide Ravelli, Paolo Quadrelli

University of Pavia, Department of Chemistry
Viale Taramelli 12, 27100 - Pavia, Italy

The tetrabutylammonium decatungstate (TBADT) is an efficient and robust photocatalyst able to promote photoredox reactions, as well as hydrogen atom transfer processes, starting from different classes of organic substrates. TBADT is also active upon solar light irradiation, allowing for the realization of the so-called "window ledge chemistry".
The [4+2] cycloaddition of dienes with nitrosocompounds, namely the nitroso-Diels-Alder (NDA) reaction, is a versatile method to generate highly reactive acylnitroso species from hydroxamic acid derivatives.



Because nitrosocarbonyl intermediates participate in a variety of organic reactions, the *in situ* formation of this highly reactive species using photoredox conditions would furnish a general procedure for patterning surfaces bearing a range of properties. Moreover, because nitrosocarbonyls serve as HNO donors, it could also provide a means to generate HNO in situ using visible-light to control its release. Mixing a solution of hydroxamic acid derivatives or their salts with conjugated dienes in the presence of catalytic amount of TBADT, acylnitroso HDA derivatives were afforded in good yields. Scope and limitations will be discussed in the light of the experimental conditions.

1. T. Yamase, T. Usami *J. Chem. Soc., Dalton Trans.* 183-190, (1988).
2. M. G. Memeo, P. Quadrelli *Chem. Rev.* **117**, 2108-2200, (2017).
3. C. P. Frazier, L. I. Palmer, A. V. Samoshin, J. Read de Alaniz *Tetrahedron Lett.* **56**, 3353-3357, (2015).
4. L. Capaldo, L. Buzzetti, D. Merli, M. Fagnoni, D. Ravelli *J. Org. Chem*. **81,** 7102-7109, (2016).
5. V. Santacroce, R. Duboc, M. Malacria, G. Maestri, G. Masson *Eur. J. Org. Chem.* 2095-2098, (2017).

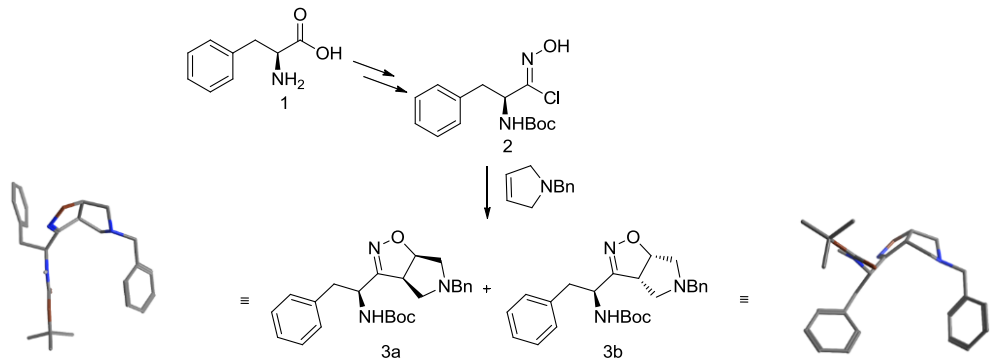
P3

NOVEL BICYCLIC Δ^2-ISOXAZOLINE DERIVATIVES AS POTENTIAL TURN INDUCERS IN PEPTIDOMIMETIC SYNTHESES

R. Bucci, S. Giofrè, A. Pinto, E. Erba, S. Pellegrino, M. L. Gelmi

[a]*DISFARM, Università degli Studi di Milano, Milan, Italy*

The preparation of hybrid peptides containing natural amino acids and non-natural molecular architecture mimicking secondary structure elements (such as turn mimics) is of great interest in different applications, ranging from catalysis to electrochemistry, biology and nanomedicine [1]. Furthermore, peptide mimics are attractive tools for the synthesis and development of drugs or peptides capable of withstanding the peptidase degradation.
The preparation of molecular scaffolds able to induce specific secondary structures is the main research field of our group[2].
The aim of this work is the preparation of diastereoisomeric Δ^2-isoxazoline compounds fused with a nitrogen containing ring (**3a** and **3b** in Scheme 1).
Due to their roles as medicinal scaffolds, the isoxazole ring is present in a large number of pharmaceutically active compounds[3] as selective modulators of the multidrug resistance protein, as activators of neuronal nicotinic acetylcholine receptors and as antipicornavirus agents.
To obtain compounds **3a** and **3b**, we used a synthetic protocol, which allows to avoid the known limitations of the traditional synthesis of nitrile oxides (Huisgen's *in situ* method or Mukaiyama's method[4]). The key synthetic step for their preparation is the [1,3]-cycloaddition reaction. Reaction conditions, able to control the diastereoselection, have been studied.



Scheme 1: Synthesis of compounds **3a** and **3b**

Studies on the use of both diastereoisomers **3** for the preparation of peptidomimetics are in progress.

[1] (a)Yao W., Yan Y., Xue L., Zhang C., Li G., Zheng Q., Zhao Y.S., Jiang H., Yao J., *Angewante Chemie*, **125**, 8875−8879, (2013); (b)Torabi S.F., Lu Y., *Current Opinion in Biotechnology*, **28**, 88−95, (2014).
[2] (a) Bonetti A., Pellegrino S., Das P., Yuran S., Bucci R., Ferri N., Meneghetti F., Castellano C., Reches M., Gelmi M.L., *Organic Letters*, **17**, 4468-4471 (2016); (b) Bucci R., Bonetti A., Clerici F., Nava D., Pellegrino S. Tessaro D., Gelmi M. L., *Chemistry- A European Journal,* DOI: 10.1002/chem.201701045
[3] Norman, B. H., Gruber, J. M., Hollinshead, S. P., Wilson, J. W., Starling, J. J., Law, K. L., Dantzig, A. H., *Bioorganic and Medicinal Chemistry Letters,* **12**, 883–886 (2002).
[4] (a) Huisgen, R., *Angew. Chem. Int. Ed.*, **2**, 633–645 (1963); Mukaiyama, T.; (b) Hoshino, T. J. *Am. Chem. Soc*. **82**, 5339 (1960).

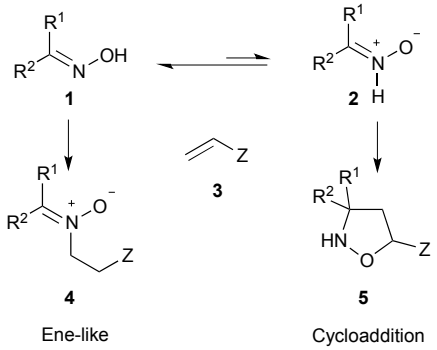
P4

COMPUTATIONAL STUDIES OF DUAL REACTIVITY OF OXIMES WITH ALKENES

Maria A. Chiacchio,[a] *Laura Legnani,*[b] *Tomas Tejero,*[c] *Pedro Merino,*[c]

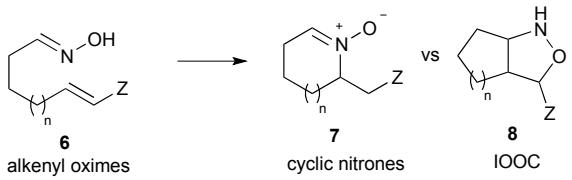
[a] Dipartimento di Scienze del Farmaco, Università di Catania, V.le A. Doria 6, 95125, Catania, Italy
[b] Dipartimento di Chimica, Università di Pavia, Via Taramelli 12, 27100 Pavia, Italy
[c] Laboratorio de Síntesis Asimétrica, Instituto de Sintesis Quimica y Catalisis Homogenea (ISQCH), Universidad de Zaragoza-CSIC, Zaragoza, 50009, Spain

Oximes can react with alkenes to yield isoxazolidines, key intermediates for the synthesis of a variety of nitrogen-containing compounds.[1] The intermolecular cycloaddition reaction of oximes, useful to prepare N-unsubstituted isoxazolidines like **5** (Scheme 1), takes place thanks to the existing tautomeric equilibrium oxime (**1**)-nitrone (**2**).
If tautomerizaton from an oxime to an NH-nitrone doesn't occur, competitive N-alkylation leading to nitrones **4** takes place (ene-type reaction). In general, depending on the substituents of the alkene, electron-deficient alkenes favor the formation of nitrones **4** and neutral or electron-rich alkenes lead to the formation of isoxazolidines **5**.[2]



Scheme 1

Hydrogen transfer process had been suggested to occur through a bimolecular process, as confirmed computationally very recently[3], and being a thermodynamically unfavorable process has more chance to be detected in an intramolecular course.
Consequently, although intermolecular reactions have been described, intramolecular processes have received more attention.[4]
In particular, the so-called intramolecular oxime-olefin cycloaddition reaction (IOOC) of alkenyl oximes,[5] has demonstrated to be a highly efficient approach to the synthesis of fused *N*-unsubstituted isoxazolidines precursors of various heterocyclic systems.
In the case of intramolecular processes with alkenyl oximes **6**, cyclic nitrones **7** or fused isoxazolidines **8,** after 1,2 prototropy**,** can be obtained (Scheme 2).
When the reactions are performed with γ-alkenyl oximes (n=0) the formation of [4,5]-fused systems is sterically disfavored and the only formation of stable five-membered cyclic nitrones **7** should be favored.
For δ- (n=1) and ε-alkenyl oximes (n=2) electronic effects due to the alkene substituent Z predominate. Consequently, cyclic nitrones **7** are obtained with electron-withdrawing substituents and isoxazolidines **8** in the rest of cases.[6]



Scheme 2

In order to determine the factors governing the selectivity of intramolecular reactions of alkenyl oximes and to predict the substrates to be obtained depending on the substitution pattern of the alkene, we have carried out an exhaustive computational study over several representative substrates. The study include DFT calculations of cycloaddition reactions and detailed analyses (quantum and topological) of the hitherto unraveled mechanism of the ene-type reaction between oximes and alkenes.

1. M.A. Chiacchio, S.V. Giofrè, R. Romeo, G. Romeo, and U. Chiacchio, *Curr. Org. Synth*, **13**, 726-749 (2016).

2. Isoxazolidine: A Privileged Scaffold for Organic and Medicinal Chemistry Mathéo Berthet, Thomas Cheviet, Gilles Dujardin, Isabelle Parrot, and Jean Martinez, *Chem. Rev*., **116**, 15235-15283 (2016).

3. Roca-López, D.; Darù, A.; Tejero, T.; Merino, P. *RSC Adv.*, **6**, 22161-22173 (2016).

4. Frank, E.; Mucsi, Z.; Szecsi, M.; Zupko, I.; Woelfling, J.; Schneider, G. *New J. Chem.*, **34**, 2671-26815 (2016).

5. Hassner, A.; Murthy, K. S. K.; Padwa, A.; Chiacchio, U.; Dean, D. C.; Schoffstall, A. M. *J. Org. Chem.*, **54**, 5277-5286 (1989).

6. Blackwell, M.; Dunn, P. J.; Graham, A. B.; Grigg, R.; Higginson, P.; Saba, I. S.; Thornton-Pett, M. *Tetrahedron*, **58**, 7715-7725 (2002).

P5

POVAROV REACTION FOR THE SYNTHESIS OF CYCLOPENTA[*C*]QUINOLINE DERIVATIVES AS ALLOSTERIC MODULATORS OF THE CDK2 PROTEIN

*Michael S. Christodoulou,[a, b]§ Fabiana Caporuscio,[a] Valentina Restelli,[c] Luca Carlino,[a] Giuseppe Cannazza,[a] Elisa Costanzi,[d] Cinzia Citti,[e] Leonardo Lo Presti,[b] Pasquale Pisani,[a] Roberto Battistutta,[d] Massimo Broggini,[c] Daniele Passarella,[b] Giulio Rastelli[a]**

[a] Dipartimento di Scienze della Vita, Università degli Studi di Modena e Reggio Emilia, Modena (Italy)
[b] Dipartimento di Chimica, Università degli Studi di Milano, Milano (Italy)
[c] Istituto di Ricerche Farmacologiche Mario Negri, Milano (Italy)
[d] Dipartimento di Scienze Chimiche, Università degli Studi di Padova, Padova (Italy)
[e] Dipartimento di Scienze e Tecnologie Biologiche e Ambientali, Università del Salento, Lecce (Italy)
§ Actual address: Dipartimento di Scienze Farmaceutiche, Università degli Studi di Milano, Milano (Italy)

CDK2 is an member of the CDK family, playing a significant role in controlling the G_1-to-S-phase checkpoint and in DNA replication.[1] Therefore, represents an important pharmacological target for arresting or recovering control of the cell cycle in dividing cells.[2] Unfortunately, the ATP-competitive CDK2 inhibitors identified to date are characterized by a pan-CDK activity spectrum (e.g., flavopiridol) or even a lack of specificity toward other PKs (e.g., indirubin), thus resulting in serious side effects that, combined with a high toxicity, have prevented their approval for clinical use. Recently, an inactive conformation of CDK2 with an open allosteric pocket was identified in a series of complexes with 8-anilino-1-naphthalene sulfonate (ANS).[3] Previous structure-based approaches allowed the identification of a hit compound expected to bind to this pocket.[4] Herein, we present the stereoselective synthesis of the hit compound, the revealment of the correct regiochemistry through X-Ray analysis and the biological activity of the pure stereoisomers. Modeling studies were performed to unveil the details of the interaction with CDK2.[5]

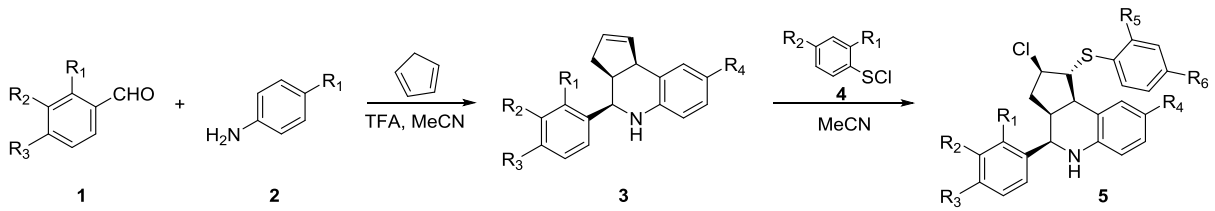


Figure 1. Synthesis of the target molecules.

1. S. Ortega, M. Malumbres M, M. Barbacid, *Biochim Biophys Acta*, **1602**, 73-87 (2002)

2. S. Lapenna, A. Giordano, *Nat Rev Drug Discov*, **8**,547-66 (2009)

3. S. Betzi, R. Alam, M. Martin, D. J. Lubbers, H. Han, S. R. Jakkaraj, G. I. Georg, E. Schçnbrunn, *ACS Chem. Biol.*, **6**, 492–501 (2011)

4. G. Rastelli, A. Anighoro, M. Chripkova, L. Carrassa, M. Broggini, *Cell Cycle*, **13**, 2296–2305 (2014)

5. M. S. Christodoulou, F. Caporuscio, V. Restelli, L. Carlino, G. Cannazza, E. Costanzi, C. Citti, L. Lo Presti, P. Pisani, R. Battistutta, M. Broggini, D. Passarella, Giulio Rastelli, *ChemMedChem*, **12**, 33 – 41 (2017)

P6

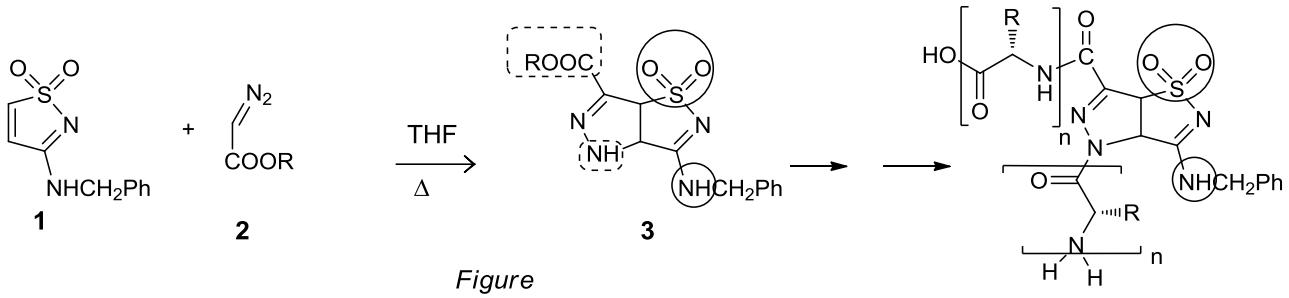
PYRAZOLO-ISOTHIAZOLE DIOXIDE: AN INTERESTING SCAFFOLD FOR THE PREPARATION OF PEPTIDOMIMETICS

D. Garanzini, S. Locarno, F. Clerici

Department of Pharmaceutical Sciences, University of Milan, Via Venezian 21, Milan -20133

There are many examples in literature of peptidomimetics that incorporate a heterocycle scaffold into a peptide, or a peptide-like sequence. The pre-organization of peptide shape, *via* the introduction of a structural heterocyclic motif that imparts conformational restriction, can enhance binding and hence therapeutic potential.[1]
Hitherto the standard approach to combine heterocycles and peptides has been to functionalize the side chain or the N/C termini of an amino acid building block with the heterocyclic moiety.[2] A few examples have been accomplished in which the heterocycles are part of the peptide backbone itself.[3]

By the way of a 1,3-dipolar cycloaddition reaction between diazoacetates **2** and the high reactive double bond of the 3-amino isothiazole dioxide partner **1**, the adducts **3** are obtained in high yield and complete regioselectivity.



Figure

The presence in compounds **3** of the carboxylic substituent and the pyrazole NH group can be exploited for coupling reaction with amino acids. By this way a peptide sequence can be generated characterized by the rigid planar geometry of the heterocyclic system favoring a particular orientation of the growing peptide chain (Figure).
Moreover the presence of the sulfonyl group as well as the NH group at C-3 is of interest. They can behave as hydrogen bond acceptor and donor, respectively, giving raise to interactions with proteins or other potential targets.

The synthesis of model peptidomimetics containing the heterocyclic scaffold, NMR analyses and computational studies are reported.

1. Cerminara, I.; Chiummiento, L.; Funicello, M.; Guarnaccio, A.; Lupattelli, P.; *Pharmaceuticals* 2012, **5**, 297-316.
2. Abell, A. D.; *Letters in Peptide Science,* 2002, **8**, 267-272.
3. El-Dahshan, A.; Nazir, S.; Ahsanullah, Latif Ansari, F.; Rademann, J.; *Eur. J. Org. Chem.* 2011, 730–739
4. Clerici; F.; Ferrario, T.; Gelmi, M. L.; Marelli, R. J.; *Chem. Soc. Perkin Trans. 1*, 1994, 2533.

P7

A "CLICK" CHEMISTRY APPROACH TO SYNTHESIZE NOVEL POTENTIAL ANTIMALARIAL AGENTS TARGETING ATG8-ATG3 PROTEIN-PROTEIN INTERACTION

Arianna Gelain[a], *Stefania Villa*[a], *Laura Legnani*[b], *Diego Colombo*[c], *Jürgen Bosch*[d,e], *Giovanni Grazioso*[a]

[a]Dipartimento di Scienze Farmaceutiche, Università degli Studi di Milano, Via L. Mangiagalli 25, 20133 Milan, Italy.
[b]Dipartimento di Chimica, Università degli Studi di Pavia, Via Taramelli 12, 27100 Pavia, Italy.
[c]Dipartimento di Biotecnologie Mediche e Medicina Traslazionale, Università degli Studi di Milano, Via Saldini 50, 20133 Milan, Italy
[d]Pediatric Pulmonology Division, Department of Pediatrics, Case Western Reserve University School of Medicine, Cleveland, Ohio
[e]Department of Biochemistry and Molecular Biology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

With the aim to identify inhibitors of the proteins involved in autophagy (Atg) of *P. falciparum*[1], we designed by computational techniques and synthesized by "click" chemistry a new class of peptidomimetics targeting Atg3 and Atg8 interaction[2]. The novel compounds (Figure 1), mimicking the Atg3 interaction motif, were tested showing an interesting protein-protein interaction inhibitory activity and the inhibition of *P. falciparum* growth.

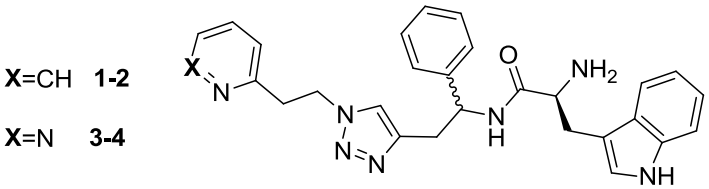


Figure 1. Structures of novel Atg8-Atg3 inhibitors

1. M, Duszenko, M. L. Ginger, A. Brennand, M. Gualdrón-López, M. I. Colombo, G. H. Coombs, I. Coppens, B. Jayabalasingham, G. Langsley, S. Lisboa de Castro, R. Menna-Barreto, J. C. Mottram, M. Navarro, D. J. Rigden, P. S. Romano, V. Stoka, B.Turk and P. A. M. Michels,. *Autophagy*, **7**, 127-158 (2011).
2. A. U. P. Hain, R. R. Weltzer, H. Hammond, B. Jayabalasingham, R. R. Dinglasan, D. R. M. Graham, D. R. Colquhoun, I. Coppens, and J. Bosch, *Journal of Structural Biology*, **180**, 551-562 (2012).

P8

IONIC LIQUIDS/ZnO NANOPARTICLES AS RECYCLABLE CATALYST FOR POLYCARBONATE DEPOLYMERIZATION

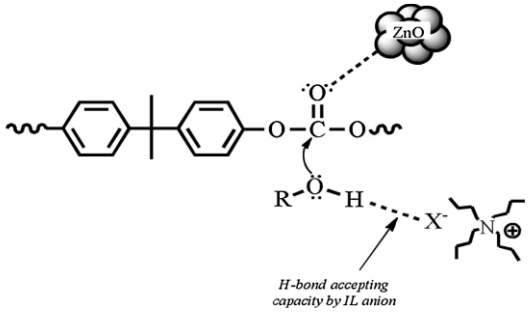
Francesco Iannone,[a] *Michele Casiello,*[b] *Antonio Monopoli,*[b] *Pietro Cotugno,*[b] *Maria Chiara Sportelli,*[b] *Rosaria Anna Picca,*[b] *Nicola Cioffi,*[b] *Maria M. Dell'Anna,*[c] *Angelo Nacci*[b]

a. University of Pavia, Department of Chemistry, Viale Tamarelli 12, 27100-Pavia (Italy)
b. University of Bari, Department of Chemistry, Via Orabona 4, 70126-Bari (Italy)
c. DICATECH, Politecnico di Bari, Via Orabona 4, 70126-Bari (Italy)

A useful protocol for waste bis-phenol A-polycarbonates (BPA-PC) chemical recycling is proposed based on a bifunctional acid/basic catalyst composed by nanostructured zinc oxide and tetrabutylammonium chloride (ZnO-NPs/NBu4Cl) in quality of Lewis acid and base, respectively.

X	β
AcO-	1.16
Cl-	1.00
Br-	0.67
BF_4-	0.37
I-	0.30
PF_6-	0.21

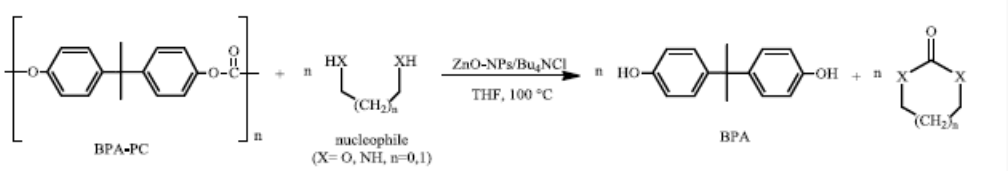
IL anions Kamlet–Taft parameters



IL	Yield
NBu_4OAc	99%
NBu_4Cl	98%
NBu_4Br	95%
NBu_4I	80%
[Bmim]OAc	90%
[Bmim]Cl	40%
[Bmim]Br	30%

PC depolymerization

Retro-polymerization reaction proved to be of general application for several nucleophiles, including water, alcohols, amines, polyols, aminols and polyamines, leading to the complete recovery of BPA monomer and enabling the PC poly-mer to function as a green carbonylating agent (green phosgene alternative) for preparing carbonates, urethanes and ureas. A complete depolymerization can be obtained in seven hours at 100 ◦C and ZnO nanocatalyst can be recycled several times without sensible loss of activity. Remarkably, when polycar-bonate is reacted with glycerol, it is possible to realize in a single process the conversion of two industrial wastes (BPA-PC and glycerol) into two valuable chemicals like BPA monomer and glycerol carbonate (the latter being a useful industrial solvent and fuel additive).



1. T. Yoshioka, K. Sugawara, T. Mizoguchi, A. Okuwara *Chem. Lett.* **34**, 282-283 (2005).
2. R. Zevenhoven, S. Eloneva, S. Teir *Catal. Today* **115**, 73-79 (2006).
3. Z. Y. Pan, Z. Bao, Y. X. Chen, *Chin. Chem. Lett.* **17**, 545-548 (2006).
4. a) Buysch H. J. (1995) *DE Patent* 4,324,778; b) M. Suzuki, K. Matsumoto (1995) *JP Patent* 07,207,059; c) A. Oku, S. Tanaka, S. Hata *Polymer* **41**, 6749-6753 (2000); d) L.C. Hu, A. Oku, E. Yamada *Polymer* **39**, 3841-3485 (1998); e) H. Tagaya, K. Katoh, J. Kadokawa *Polym. Degrad. Stab.* **64**, 289 (1999); f) M. Kitahara, A. Oda, T. Ban *Polym. Prepr. Jpn.* **54**, 1956-1959 (2005).
5. S. Vijaykumar, R.P. Mayank, J.-V. Petal *J. Polym. Environ*. **18**, 8-25 (2010).

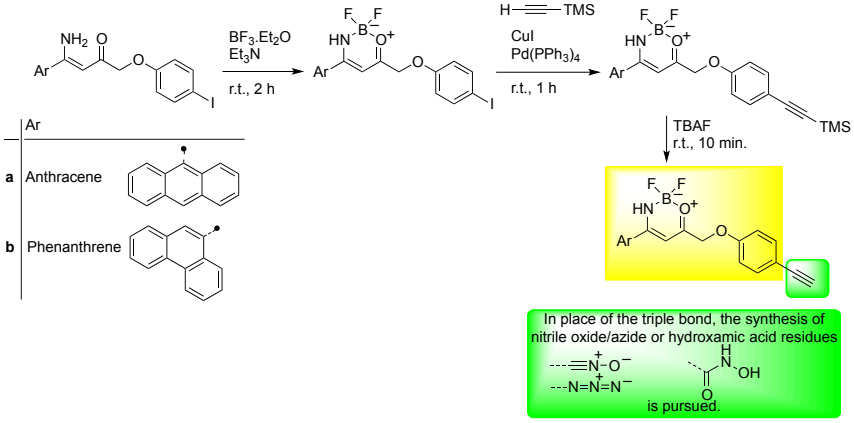
P9

FLUORESCENT PROBES FROM STABLE NITRILE OXIDES

Mattia Moiola,[a] *Misal Giuseppe Memeo*,[a]
Herman Overkleeft,[b] *Paolo Quadrelli*[a]

a. University of Pavia, Department of Chemistry, Viale Taramelli 12, 27100 - Pavia (Italy)
b. University of Leiden, Institute of Chemistry, Einsteinweg 55, 2333 CC - Leiden (The Netherlands)

Stable aromatic nitrile oxides undergo 1,3-dipolar cycloaddition reactions with 1-iodo-4-(prop-2-yn-1-yloxy)benzene affording the expected isoxazoles in very good yields and as single regioisomers. Reductive cleavage of the N-O bond and complexation with BF_3 afforded the corresponding boron complexes, further derivatized with a triple bond for click-chemistry applications.



Other differently substituted boron fluorescent probes were prepared with some functional groups employable in several biorthogonal reactions. The photochemical behaviour and the fluorescence properties were investigated and discussed, also in the light of theoretical calculations. The synthesis was clearly reliable and gave easily derivatizable boron complexes that demonstrated the use in further cycloaddition reaction, in particular via the click-chemistry methodology, typically employed in biochemistry.
Improvements on the fluorescent properties of enaminoketone-based boron complexes are actively pursued and preliminary tests on lysate to verify the presence of system interferences with bioorthogonal ligation have been performed in research laboratories in Leiden.

1. P. Caramella, P. Grünanger, *1,3-Dipolar Cycloaddition Chemistry*, Padwa Eds., New York: 1984; Vol. 1, pp. 291-392.
2. M. G. Memeo, P. Quadrelli *Chem. Rev.* **117**, 2108-2200, (2017).
3. L. F. Minuti, M. G. Memeo, S. Crespi, P. Quadrelli, *Eur. J. Org. Chem.* 821-829 (2016).

P10

1,3 DIPOLAR CYCLOADDITIONS OF AZIDES ON ENAMINES: MORE THAN 50 YEARS IN A "CLICK"

Emanuela Erba, Alessandro Contini, Sara Pellegrino, Donato Pocar

Dipartimento di Scienze Farmaceutiche, Sezione di Chimica Generale e Organica "A. Marchesini", Università degli Studi, Milano-Italy

Pioneering studies on "click" 1,3 dipolar cycloaddition of azides on enamines were reported in the early sixties[1], although the mechanism has been completely clarified only recently[2]. Depending on the nature of the azide reactant, the triazole cycloadduct can be isolated or can quickly decompose to other products. In this last case, the starting enamine drives the rearrangement to amidines (Paths A and B, Figure 1) or α-amino-imino compounds (Path C, Figure 1).
During the years, this synthetic approach led to different classes of compounds (e. g. nitrogen containing heterocycles, enantiopure carboxylic acids, diazoalkanes, chiral cyclic diamines)[3] used in a wide range of applications, from bioactive compounds to hybrid homogenous catalysts[4]. Here, the advances on this click reaction are presented.

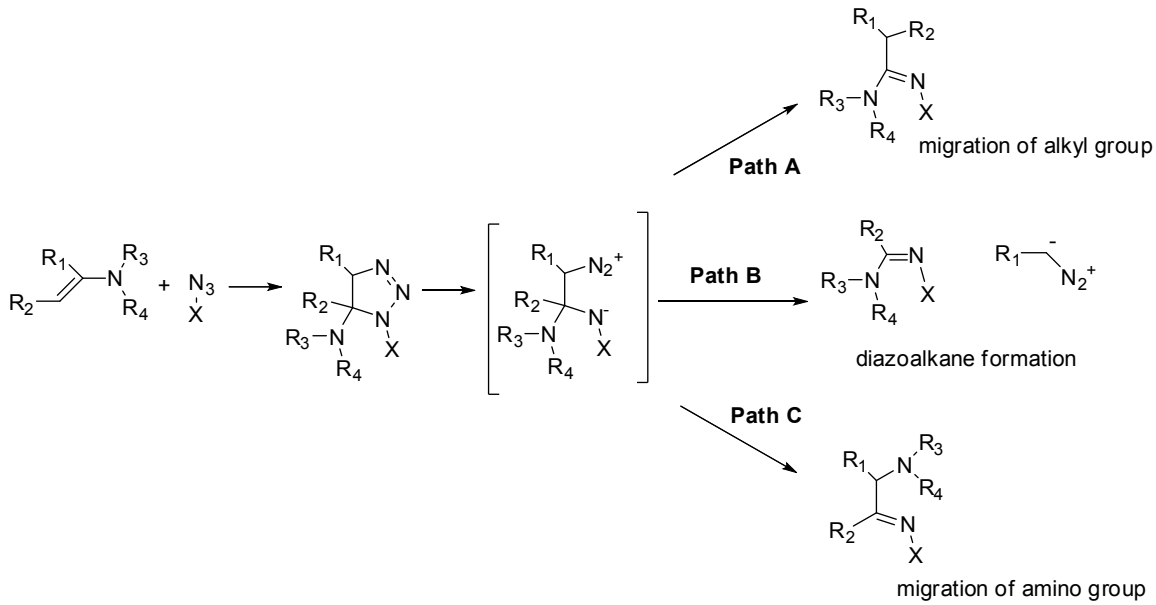


Figure 1

(1) R. Fusco, G. Bianchetti, D. Pocar *Gazz. Chim. Ital.*, **1961**, *91*, 933–957.
(2) a) S. Xie et al *JACS* **2015**, *137*, 2958-2966; b) A. Contini, E. Erba *RSC Advances* **2012**, *2*, 10652–10660.
(3) a) S. Pellegrino, A. Contini, M. L. Gelmi, L. Lo Presti, R. Soave, E. Erba *J. Org. Chem.* **2014**, *79*, 3094-3102; b) A. Contini, E. Erba, S. Pellegrino *Synlett* **2012**, *23*, 1523-1525, c) E. Erba, D. Pocar, P. Trimarco *Synthesis* **2006**, 2693-2696, d) F. Cassani, E. Erba, G. Celentano, D. Pocar *Synthesis* **2004**, 1041-1046 e) E. M. Beccalli, A. Contini, P. Trimarco *Eur. J. Org. Chem.* **2003**, 3976-3984.
(4) a) S. Pellegrino, N. Tonali, E. Erba, J. Kaffy, M. Taverna, A. Contini, M. Taylor,D. Allsop, M..L. Gelmi, S. Ongeri *Chem. Science* **2017**, *8*, 1295-1302; b) S. Pellegrino, G. Facchetti, A. Contini, M. L. Gelmi, E. Erba, R. Gandolfi, I. Rimoldi *RSC Advances* **2016**, *6*, 71529–71533.

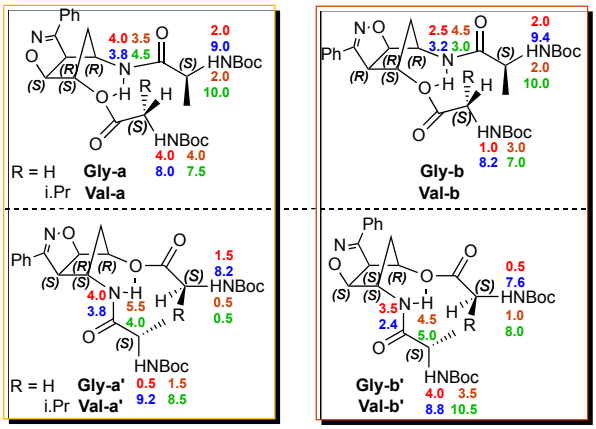
P11

CYCLOPENTA[*d*]ISOXAZOLINE β-TURN MIMICS: SYNTHETIC APPROACH, TURN DRIVING FORCE, SCOPE AND LIMITATIONS

Misal Giuseppe Memeo, Marco Bruschi, Luca Bergonzi, Paolo Quadrelli

University of Pavia, Department of Chemistry
Viale Taramelli 12, 27100 – Pavia, Italy

Turns are pivotal motifs that reverse the direction of peptide strands and helices. Turns are essential for protein structure and occur within protein binding sites, at protein-protein interfaces and in small bioactive peptides, playing a crucial role in recognition. The growing interest in these structures pushes many research groups to intensify the efforts in this area by designing and developing novel structures for specific applications and using classical scaffolds for promising new synthetic targets.



Model β□turn inducers were prepared from constrained oxazanorbornene aminols. Taking advantage of the starting materials geometry, new diastereoisomeric compounds were synthetized, introducing different aminoacidic residues. The products were spectroscopically characterized (VT- and NMR-titration, MD calculations). Temperature coefficients in DMSO are indicative for the existence of an intramolecular hydrogen bond. Chirooptical properties revealed a β-turn arrangement of all the synthesized compounds. The fused isoxazoline ring constraints the cyclopentane moiety, stabilizing a boat-like conformation that ensures the turn efficiency but limiting the accessibility to hindered amino acids.

1. T. A. Hill, N. E. Shepherd, F. Diness, D. P. Fairlie *Angew. Chem. Int. Ed.* **2014**, *53*, 13020-13041.
2. C. André, B. Legrand, C. Deng, C. Didierjean, G. Pickaert, J. Martinez, M. C. Averlant-Petit, M. Amblard, M. Calmes, *Org. Lett*. **14**, 960-963 (2012).
3. D. S. Kemp. *Trends Biotechnol.* **8**, 249-255 (1990).
4. Y. Shi, P. Teng, P. Sang, F. She, L. Wei, J. Cai, *Acc. Chem. Res.* **49**, 428-441 (2016).
5. R. F. Hirschmann, K. C. Nicolaou, A. R. Angeles, J. S. Chen, A. B. Smith III, *Acc. Chem. Res.* **42**, 1511-1520 (2009).
6. M. G. Memeo, M. Mella, V. Montagna, P. Quadrelli, *Chem. Eur. J.* **21**, 16374-16378 (2015).

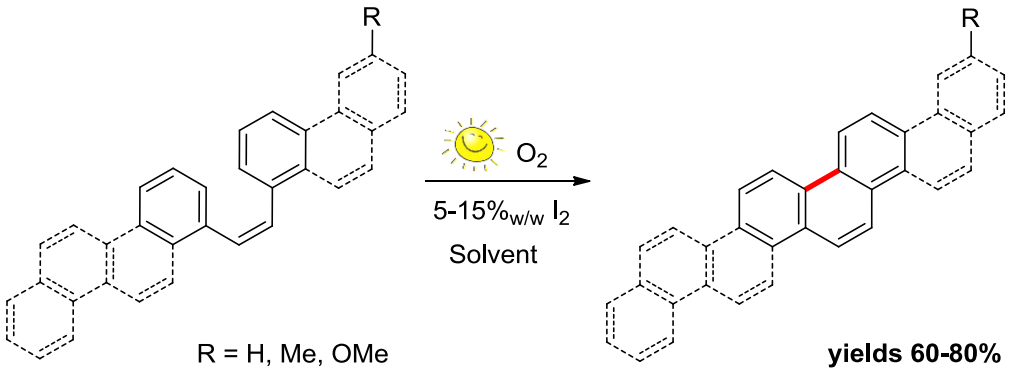
P12

SUNLIGHT INDUCED MALLORY PHOTOCYCLIZATION: AN ALTERNATIVE ROUTE TO SUBSTITUTED [*n*]PHENACENES

Carlotta Raviola, Silvia Garbarino, Luca Capaldo, Maurizio Fagnoni

PhotoGreen Lab, Department of Chemistry, University of Pavia, Viale Taramelli 12, 27100 Pavia, Italy
carlotta.raviola01@universitadipavia.it

Phenacenes have recently received much attention due to their potential application in organic electronic materials. Indeed, these polycyclic aromatic compounds have been exploited in organic field-effect-transistors (FETs)[1] as well as in the preparation of alkali metal doped phenacenes which exhibit superconductivity at low temperature.[2] Accordingly, different preparations of phenacenes[3] (either metal catalyzed or photochemical) have been reported, but their formation in a reasonable purity and in a large scale is still a challenge. We proposed herein the first sunlight driven metal-free synthesis of substituted [*n*]phenacenes based on the Mallory cyclization of stilbenes.[4] Thus, irradiation of an oxygen saturated solution of the chosen stilbene (**1**) and catalytic iodine in different organic solvents was found to afford phenacenes (**2**) in yield from discrete to excellent.



(1) J. H. Schön, C. Kloc and B. Batlogg, *Org. Electron*, **1**, 57-64 (2000).
(2) H. Okamoto, S. Hamao, H. Goto, Y. Sakai, M. Izumi,, S. Gohda, Y. Kubozono, R. Eguchi, *Nature*, **464**, 76-79 (2010).
(3) See for instance: (a) H. Mori, X.-C. Chen, N.-H. Chang, S. Hamao,Y. Kubozono, K. Nakajima,Y. Nishihara, *J. Org. Chem*.,**79**, 4973- 4983 (2014). (b) F. B. Mallory, C. W. Mallory, *Org. React.*, **30**, 1-456 (1984).
(4) S. Protti, G. A. Artioli, F. Capitani, C. Marini, P. Dore, P. Postorino, L. Malavasi, M. Fagnoni, *RSC Adv.*, **5**, 27470-27475 (2015).

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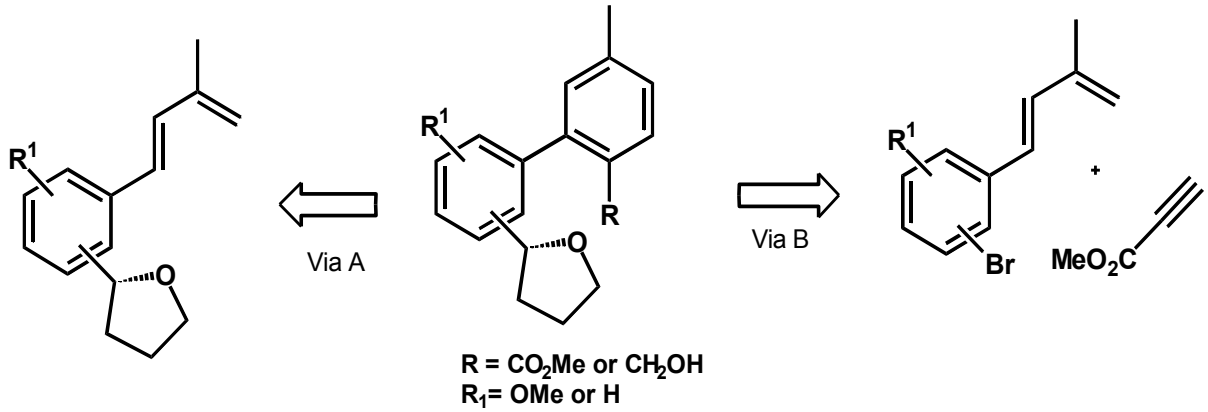
P13

EXPLORATION OF SYNTHETIC STRATEGIES FOR THE PREPARATION OF NOVEL TETRAHYDROFURAN-CONTAINING BIARYLS VIA DIELS-ALDER REACTION

Andrea Temperini,[a] *Lucio Minuti,*[b] *Francesca Piazzolla*[a]

[a] Dipartimento di Scienze Farmaceutiche, Università di Perugia, Via del Liceo 1, 06123 Perugia
[b] Dipartimento di Chimica, Biologia e Biotecnologie, Università di Perugia, Via Elce di Sotto 8, 06123 Perugia

The tetrahydrofuran ring and biaryl template represent privileged structures which occur in a variety of natural and unnatural products with significant biological activities. In continuation of our research directed toward the synthesis of heterocycles[1,2] and biaryls,[3,4] we herein provide two stereoselective synthetic routes for the preparation of a new scaffold as the tetrahydrofuran-containing biaryl.
Our approach involves an high-pressure and regioselective promoted Diels-Alder reaction of (*E*)-3-methyl-1-arylbuta-1,3-diene with methyl propiolate to give, after aromatization, the corresponding functionalized biaryl. The tetrahydrofuran moiety can be constructed starting from an aryl-Br or aryl-CO_2Me functional groups through the synthesis of a γ-phenylseleno ketone intermediate.



1. L. Minuti, A. Barattucci, P. M. Bonaccorsi, M. L. Di Gioia, A. Leggio, C. Siciliano, A Temperini, *Org. Lett*. **15**, 306-3909 (2013).

2) A. Temperini, A. Barattucci, P. M. Bonaccorsi, O. Rosati, L. Minuti, *J. Org. Chem*. **80**, 8102-8112 (2015). 3) L. Minuti, E. Ballerini, A. Temperini, *J. Org. Chem*. **77**, 7923-7931 (2012). 4) L. Minuti, E. Ballerini, A. Barattucci, P. M. Bonaccorsi, M. L. Di Gioia, A. Leggio, C. Siciliano, A Temperini, *Tetrahedron* **71**, 3253-3262 (2015).

List of Partecipants

ABBIATI	GIORGIO	*giorgio.abbiati@unimi.it*
ALBANESE	DOMENICO	*domenico.albanese@unimi.it*
ALFIERI	MARIA LAURA	*marialaura.alfieri@unina.it*
BALDOLI	CLARA	*clara.baldoli@istm.cnr.it*
BARATTUCCI	ANNA	*abarattucci@unime.it*
BASILE	TERESA	*teresabasile02@universitadipavia.it*
BECCALLI	EGLE	*egle.beccalli@unimi.it*
BODMAN	SAMANTHA	*samantha.bodman@pg.canterbury.ac.n*
BRANDI	ALBERTO	*alberto.brandi@unifi.it*
BROGGINI	GIANLUIGI	*gianluigi.broggini@uninsubria.it*
BRUSA	FILIPPO	*filippo.brusa@uninsubria.it*
BUCCI	RAFFAELLA	*raffaella.bucci@unimi.it*
CAUTERUCCIO	SILVIA	*silvia.cauteruccio@unimi.it*
CECCARELLI	JACOPO	*jacopo.ceccarelli@unifi.it*
CHIACCHIO	UGO MARIA	*uchiacchio@unict.it*
CHIACCHIO	ASSUNTA	*ma.chiacchio@unict.it*
CHIUMMIENTO	LUCIA	*lucia.chiummiento@unibas.it*
CHRISTODOULOU	MICHAIL	*michael.christodoulou@unimi.it*
CLERICI	FRANCESCA	*francesca.clerici@unimi.it*
CONTI	PAOLA	*paola.conti@unimi.it*
CORDERO	FRANCA MARIA	*franca.cordero@unifi.it*
CULLIA	GREGORIO	*gregorio.cullia@unimi.it*
DALLANOCE	CLELIA	*clelia.dalanoce@unimi.it*
DE AMICI	MARCO	*marco.deamici@unimi.it*
D'ERRICO	STEFANO	*stefano.derrico@unina.it*
DE SARLO	FRANCESCO	*fdesarlo1038@gmail.com*
DE SILVESTRO	IRENE	*irenedesilvestro@gmail.com*
DE SIMONI	GIOVANNI	*desimoni@unipv.it*

DI MAURO	GIOVANNI	*dm.giovanni91@gmail.com*
DI PALO	MARIA CONCETTA	*maricadipalo@gmail.com*
D'ORSI	ROSARITA	*rosarita.dorsi@gmail.com*
ERBA	EMANUELA	*emanuela.erba@unimi.it*
FAITA	GIUSEPPE	*faita@unipv.it*
FUNICELLO	MARIA	*maria.funicello@unibas.it*
GARANZINI	DAVIDE	*davide.garanzini@studenti.unimi.it*
GARBARINO	SILVIA	*silvia.garbarino87@gmail.com*
GELAIN	ARIANNA	*arianna.gelain@unimi.it*
GELMI	MARIALUISA	*marialuisa.gelmi@unimi.it*
GIOFRÈ	SABRINA	*sabrina.giofre@unimi.it*
GIOMI	DONATELLA	*donatella.giomi@unifi.it*
GOTI	ANDREA	*Andrea.goti@unifi.it*
GRAZIOSO	GIOVANNI	*Giovanni.grazioso@unimi.it*
GRÜNANGER	PAOLO	
IANNONE	FRANCESCO	*francesco.iannone@uniba.it*
IESCE	MARIA ROSARIA	*iesce@unina.it*
LA ROSA	CONCETTA	*concetta.larosa@unimi.it*
LEGNANI	LAURA	*laura.legnani@unipv.it*
LICANDRO	EMANUELA	*emanuela.licandro@unimi.it*
MACHETTI	FABRIZIO	*fabrizio.machetti@unifi.it*
MACUT	HELENA	*helena.macut@unimi.it*
MANCUSO	AURORA	*mancusoaurora@gmail.com*
MEAZZA	MARTA	*marta.meazza1@gmail.com*
MENICHETTI	STEFANO	*stefano.menichetti@unifi.it*
MINUTI	LUCIO	*lucio.minuti@unipg.it*
MOIOLA	MATTIA	*mattia.moiola01@ateneopv.it*
MOROZZI	CHIARA	*c.mori85@gmail.com*
ORMACHEA	CARLA	*cormachea@fiq.unl.edu.ar*
PARMEGGIANI	CAMILLA	*camilla.parmeggiani@unifi.it*
PELLEGRINO	SARA	*sara.pellegrino@unimi.it*

PIAZZOLLA	FRANCESCA	*francesca.piazzolla@studenti.unipg.it*
PIROVANO	VALENTINA	*valentina.pirovano@unimi.it*
POCAR	DONATO	*donato.pocar@unimi.it*
QUADRELLI	PAOLO	*paolo.quadrelli@unipv.it*
RAVIOLA	CARLOTTA	*carlotta.raviola01@universitdipavia.it*
ROMEO	ROBERTO	*robromeo@unime.it*
ROSSI	ELISABETTA	*elisabetta.rossi@unimi.it*
TAMBURINI	LUICIA	*lucia.tamborini@unimi.it*
SALERNO	TANIA	*tsalerno@unime.it*
TEMPERINI	ANDREA	*andrea.temperini@unipg.it*
WIYA MAYEMBA	YANNICK	*balondo36@gmail.com*

List of authors

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