17èmes Rencontres de Chimie Organique

19 avril 2019

Gif-sur-Yvette

Book of Abstracts

Le mot du comité d'organisation

C'est avec un très grand plaisir que nous vous accueillons sur le campus CNRS de Gif-sur-Yvette pour la 17ème édition des Rencontres de Chimie Organique. Cette édition des RCO est organisée par l'ICSN (CNRS-Université Paris-Saclay) et rassemble environ 160 personnes.

Les RCO, créées en 2003 avec le soutien de la Section Ile de France de la Société Chimique de France (SCF), sont un événement annuel rassemblant les jeunes chercheurs de la région Ile-de-France. Cet évènement a été créé par Gérard Cahiez qui nous a malheureusement quitté récemment et auquel nous rendrons hommage cette année.

Pour cette édition, les conférences plénières seront données par le Prof. Berit Olofsson (Stockholm University, Suède) et le Prof. Tobias Ritter (Max-Planck-Institut für Kohlenforschung, Allemagne).

Les doctorants et post-doctorants franciliens présenteront leurs travaux de recherche sous forme de douze communications orales et d'une cinquantaine de posters.

Nous remercions les sponsors pour avoir rendu possible cette manifestation et bien entendu vous, chers participants, pour votre présence. Nous sommes certains que vous saurez profiter de cette journée pour partager votre recherche et découvrir celle des autres.

Le comité d'organisation :

Dr Kevin Cariou, Président
Dr Xavier Guinchard, membre du bureau
Dr Arnaud Voituriez, membre du bureau
Nawel Goual, doctorante
Capucine Mahe, doctorante
Vincent Delattre, doctorant

We thank our generous sponsors

Labex Charmmmat : Un projet articulé autour des sciences des matériaux et la catalyse homogène bio-inspirée. Le laboratoire d'excellence (LabEx) CHARMMMAT a été créé autour de deux domaines de la communauté sud-francilienne à forte visibilité internationale : les sciences des matériaux et la catalyse homogène bio-inspirée. CHARMMMAT réunit ainsi chimistes, informaticiens et physiciens, provenant de l'Université Paris-Sud, l'Université Versailles St-Quentin, l'École Polytechnique, le CNRS, l'ENS Cachan, le CEA, l'École Centrale de Paris et l'Université d'Évry Val d'Essonne. CHARMMMAT rassemble la Chimie, la Physique et l'Informatique au service des attentes de la société en matière d'énergie, de santé, d'environnement et d'information.

Avec un effectif de près de 200 personnes, l'**ICSN** constitue le pôle chimie du campus CNRS de Gif sur Yvette. L'Institut est situé en bordure du futur campus Paris-Saclay, qui regroupera près de 10% de la recherche française, et fait partie intégrante de cette nouvelle Université. L'ICSN développe des activités à l'interface chimie-biologie, avec les substances naturelles comme objet d'étude et source principale d'inspiration.

Créée en 1857, la **Société Chimique de France** a pour vocation de rassembler toutes les personnes physiques et morales quels que soient leurs secteurs d'activité (organismes publics ou privés) concernées par les sciences de la chimie et leurs applications, de représenter les intérêts des chimistes et de promouvoir le rôle des sciences chimiques. En particulier les RCO bénéficient du soutien de la Section Ile-de-France de la SCF.

TCI est un fabricant de produits chimiques qui fournit des réactifs organiques de qualité supérieure depuis plus d'un demi-siècle avec pour devise de « Participer à l'évolution de la société au travers des réactifs ». Les produits TCI sont utilisés aux quatre coins du monde, tous domaines confondus, et apportent une différence significative dans la vie des scientifiques du monde entier.

L'**Université Paris-Saclay** propose une large gamme de formations de la licence au doctorat au sein de schools et d'écoles doctorales, de haut niveau international, dans les domaines des sciences de la nature et des sciences humaines et sociales. 8 000 étudiants en masters, 5 000 doctorants, autant d'élèves ingénieurs et un large cycle en licence rassemblent quelque 65 000 étudiants au sein des établissements fondateurs et associés.

Le 19 octobre 2019, le **CNRS** fêtera ses 80 ans d'existence. Pas encore un siècle, mais un âge vénérable qui nous donnera tout au long de cette année l'occasion de célébrer dans l'Hexagone et à l'étranger les valeurs qui sont au fondement de notre institution : la liberté de la recherche, l'avancée des connaissances, le travail en équipe, l'excellence scientifique, l'innovation et le transfert, le progrès social, la diffusion de la culture scientifique comme antidote aux contre-vérités et à l'obscurantisme.

RCO 2019 Program

8h45-9h15	**Registration of Participants**
9h15-9h45	**Opening of the RCO 2019 - Honoring Pr Cahiez Memory**
9h45-10h45	**CHARMMMAT Plenary Lecture: Prof. Tobias Ritter** Max-Planck-Institut für Kohlenforschung, Allemagne
10h45-11h30	**Coffee Break and Poster Session**
11h30-11h45	**Aurélien ADENOT** – NIMBE, CEA, CNRS, Université Paris-Saclay *Sulfonylative Hiyama Cross-Coupling: Development and Mechanistic Insights*
11h45-12h00	**Anne-Laure BARTHELEMY** – Institut Lavoisier de Versailles *Divergent synthesis of 1,2-benzothiazine or benzoisothiazole analogs containing a S-trifluoromethyl sulfoximine group.*
12h00-12h15	**Sokna BAZZI** – Molecular catalysis laboratory, ICMMO, Université Paris-Saclay *$SmCl_2$ catalyzed site-selective hydrocarboxylation of alkenes and alkynes via CO_2 activation*
12h15-12h30	**Maxime DE ABREU** – CiTCoM, Faculté de Pharmacie de Paris, Université Paris Descartes *New Photochemical Generation of Nitrogen-Centered Radical: an Application to Phthalazine Synthesis.*
12h30-12h45	**Karen DE LA VEGA-HERNANDEZ** – IPCM, Sorbonne Université *A Radically Different Approach to Vinylgermanes: Germylzincation of α-Heteroatom-Substituted Alkynes*
12h45-14h15	**Lunch**
14h15-14h30	**Céline DORVAL** – Laboratoire de Chimie Moléculaire, Ecole Polytechnique *Unusual bonds activation and cobalt-catalyzed cross-coupling*
14h30-14h45	**Jade DUSSART** – Laboratoire CSPBAT, Université Paris 13 *Convenient one-pot reaction for the synthesis of α hydroxyphosphinates and 1-hydroxymethylene-1,1-bisphosphinates*
14h45-15h00	**Glwadys GAGNOT** – Unité de Chimie et Biocatalyse, Institut Pasteur *Highly modified imidazo[1,2-α]pyrazin-3(7H)-one luciferin analogues: synthesis of exotics heterocyclic cores and chemiluminescence properties*
15h00-15h15	**Guillaume LEVITRE** – ICSN, CNRS, Université Paris-Saclay *Asymmetric Organocatalysis – Synthesis of Cyclohepta[b]indoles by [4+3] Cycloaddition*
15h15-15h30	**Jacopo LESMA** – FLUOPEPIT, BioCIS, CNRS, Université Paris Saclay *Synthesis of novel fluorinated peptidomimetics as potential protein aggregation inhibitors in amyloidoses*
15h30-16h30	**Coffee Break and Poster Session**
16h30-16h45	**Aymane SELMANI** – i-CLeHS, PSL Université Paris, Chimie ParisTech *Regioselective Control of Alkyne Insertion in Rhodium-Catalyzed Asymmetric Arylative Cyclization*
16h45-17h00	**Ju WU** – MSMT, ICMMO, Université Paris-Saclay) *Electrochemical dearomative 2,3-difunctionalization of indoles*
17h00-18h00	**ICSN Plenary Lecture: Prof. Berit Olofsson** Stockholm University, Suède
18h00-18h15	**Concluding Remarks**

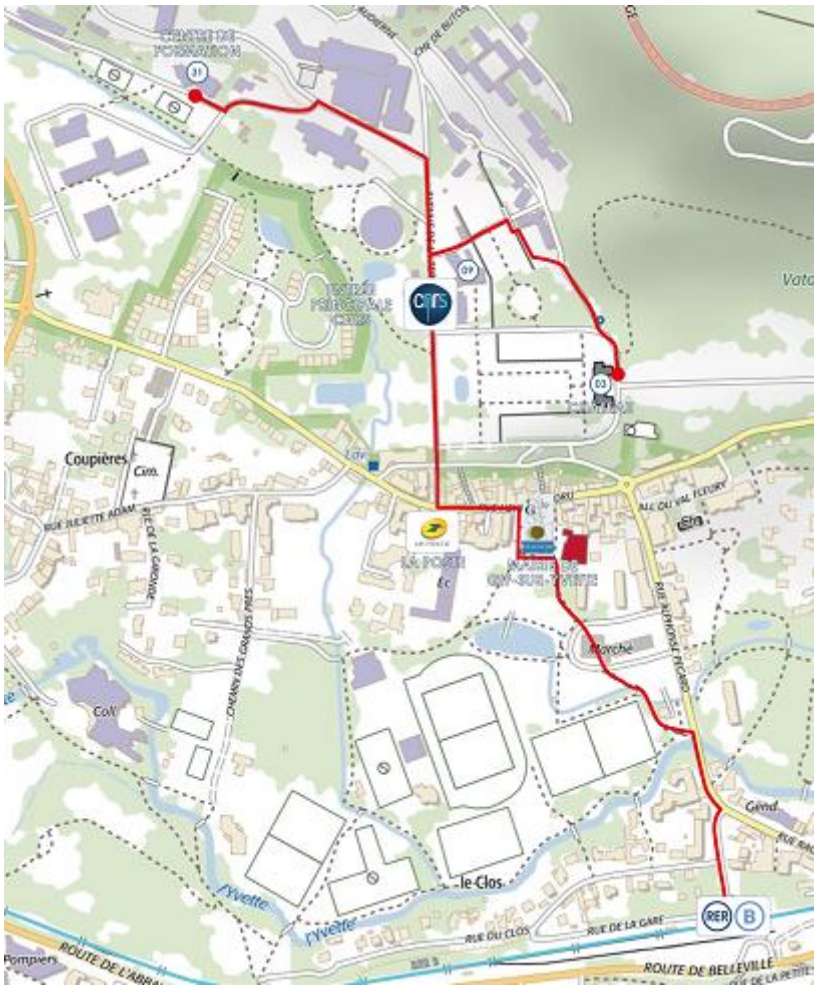
Historique

Depuis sa création, la journée s'est déroulée dans différentes universités et centres de recherche franciliens :

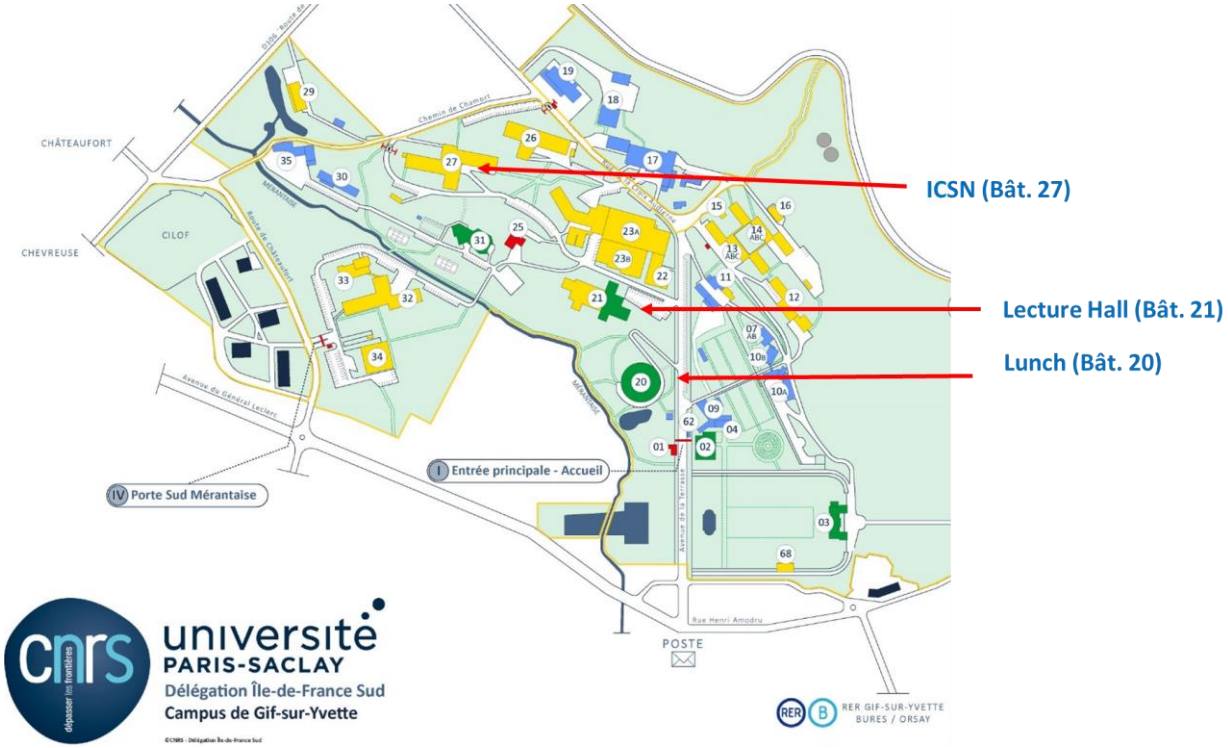
2018	Sorbonne Université	C. Bolm, C. Mazet
2017	Thiais	T. Gaich, J. Zhu
2016	Bobigny	A. Minaard, S. Lemaire
2015	Cergy	A. Spivey, J. Waser
2014	Paris Descartes	M. Niggemann, D.J. Dixon
2013	ENS Cachan	P. H. Seeberger, M. J. Gaunt
2012	Paris Sud	M. Sanford, I. Markó
2011	Versailles	V. Aggarwal, M. Movassaghi
2010	UPMC	G. Bertrand, B. List
2009	Paris Descartes	I. Marek, V. Gouverneur
2008	ICSN	S. Clark, V. Snieckus
2007	Paris Sud	J. Clayden, P. Kundig
2006	Chimie ParisTech	A. Fürstner, C. Mioskowski
2005	Polytechnique	E. Carreira, J.M. Campagne, J. Barluenga
2004	Versailles	A. Wessel, P. Vogel
2003	Cergy	P. Knochel, A. Commerçon

Coming to the RCO 2019

From the RER B, Gif-sur-Yvette Station, 10 min walk:



Getting to the Lecture Hall :



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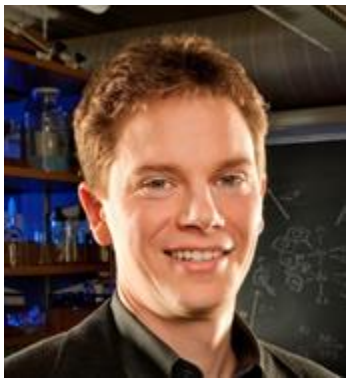
Campus de Gif-sur-Yvette

Plenary Lectures

Prof. Dr. Tobias Ritter



Vita

since 2018	Managing Director, Max-Planck-Institut für Kohlenforschung
since 2015	Director at the Max-Planck-Institut für Kohlenforschung, Mülheim / Ruhr, Germany
2015-2017	Visiting Professor, Harvard University, Cambridge, USA
2012-2015	Professor of Chemistry and Chemical Biology, Harvard University, Cambridge, USA
since 2011	Founder and Scientific Advisor, SciFluor, USA
since 2010	Chemist at the Massachusetts General Hospital, Boston, USA
2010-2012	Associate Professor for Chemistry and Chemical Biology, Harvard University, Cambridge, USA
2006-2010	Assistant Professor of Chemistry and Chemical Biology, Harvard University, Cambridge, USA
2004-2006	Post-Doctoral Fellow, California Institute of Technology, Pasadena, USA
2004	Ph.D. Organic Chemistry, ETH Zürich, Schweiz
1999	Master of Science, Technische Universität Braunschweig
1975	born in Lübeck, Germany

Late-Stage Functionalizations

Prof. Tobias Ritter, PhD
Max Planck Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
45470 Mülheim, Germany
ritter@mpi-muelheim.mpg.de

RWTH Aachen University University
Department for Chemistry
Landoltweg 1
52074 Aachen, Germany

Massachusetts General Hospital
Department of Radiology
55 Fruit Street
Boston, MA 02114 USA

The unnatural isotope fluorine–18 (^{18}F) is used as a positron emitter in molecular imaging. Currently, many potentially useful ^{18}F-labeled probe molecules are inaccessible for imaging, because no fluorination chemistry is available to make them. Syntheses must be rapid on account of the 110-minute half-life of ^{18}F, and fluorination should ideally be executed as the ultimate synthetic step. I will describe the development of novel, modern reactions directed at the synthesis of ^{18}F and ^{19}F containing complex small molecules. In particular, I will describe the approach to functionalize complex small molecules at a late stage, and the challenges associated with it, as well as the applications for late-stage C-H functionalization reactions to create molecular complexity for applications in catalysis, drug discovery, and medicine.

Nature **2011**, *473*, 470
Science **2011**, *334*, 639
Nature **2016**, *534*, 369
Nature **2018**, *554*, 551

Prof. Dr. Berit Olofsson

Academic background and career

Berit Olofsson was born in Sundsvall, Sweden, in 1972. She studied Chemical Engineering at LuTH (Luleå) and LTH (Lund), and got her MSc in 1998 after a project work at Akzo Nobel Central Research in Arnhem, The Netherlands.

She performed her PhD studies 1998-2002 at Stockholm University (SU) and later at KTH (Stockholm) under the guidance of Prof. Peter Somfai. The PhD project dealt with asymmetric, divergent synthesis of vicinal amino alcohols via vinylepoxides and vinylaziridines.

She subsequently went to Bristol University, UK for a post doc with Prof. Varinder K. Aggarwal in 2003-2004. The project started out as a total synthesis of (-)-Epibatidine, and was later widened to include methodology development on alfa-arylation of ketones. Returning to Sweden, she became assistant supervisor in the group of Prof. J.-E. Bäckvall at SU.

Berit started her independent career with a position as Assistant Professor at SU in 2006. She became "Docent" in March 2008, and got a permanent position as Associate Professor (Lektor) in 2010. She was promoted to Professor in 2013, and spent 3 months in Stellenbosch, South Africa as a STIAS Fellow 2014/2015. She became the Deputy Dean for the Chemistry Section in August 2017, and was elected as a ChemPubSoc Europe Fellow in 2018. Since January 2019, she is the **Dean of Chemistry**.

Metal-Free Functionalization of Heteroatom Nucleophiles with Iodine(III) Reagents

Berit Olofsson

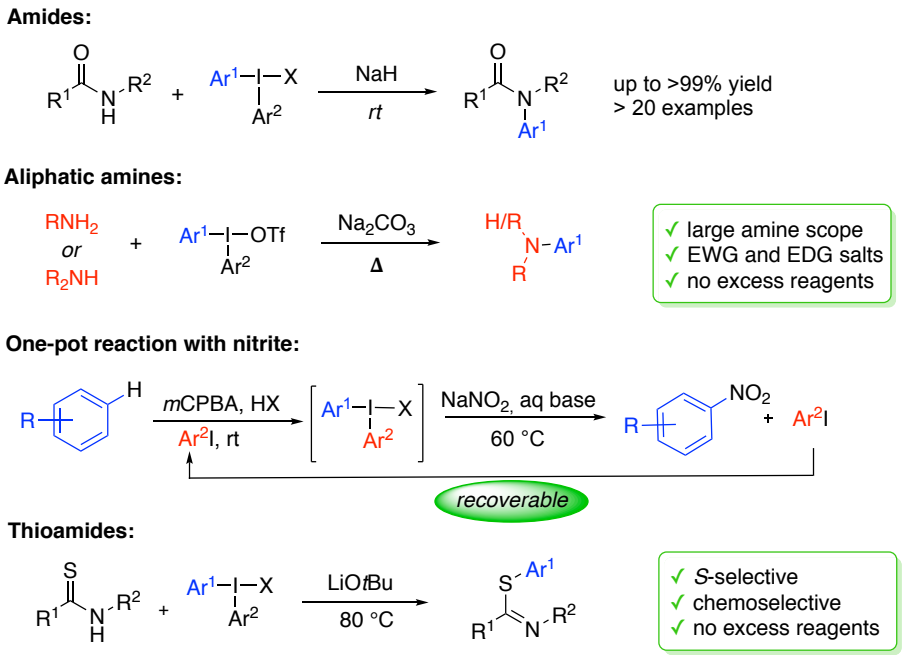
Department of Organic Chemistry, Stockholm University, Sweden; berit.olofsson@su.se

Aniline and amide derivatives are ubiquitous in Nature, in medicinal applications and material science. Consequently, the research focus on development of efficient synthetic methodology for *N*-arylation of nitrogen nucleophiles remains intense. While transition metal-catalyzed cross couplings have been successful with a wide variety of nitrogen nucleophiles, the drawbacks associated with transition metal catalysis, including toxicity, cost, need for substrate-dependent designer ligands, and risk of product contamination has led to an increased focus on development of metal-free methodology for C-N bond formation.[1]

Diaryliodonium salts are sustainable, reactive and selective electrophilic arylation reagents.[2] We have developed several one-pot syntheses of diaryliodonium salts and other iodine(III) reagents, making these reagents easily available. We have also demonstrated their efficiency in arylation of various heteroatom and carbon nucleophiles under mild and metal-free conditions.

In the lecture, our recent results on the *N*-arylation of amides,[3] aliphatic amines[4] and nitrite[5] will be presented. The first one-pot reaction, where diaryliodonium reagents are formed from iodine(I), and subsequently trapped by *in situ* addition of *N*-centered nucleophiles, will also be described.[5]

In contrast to amides, the arylation of thioamides proceeds with high *S*-selectivity to provide aryl thioimidates.[6] Mechanistic studies of nucleophiles with several nucleophilic sites (enolates, amides, thioamides, nitrite) will be discussed, and our recent findings of tetracoordinated intermediates in *O*-arylations will be presented.[7]



(1) Sun, C.-L.; Shi, Z.-J. *Chem. Rev.* **2014**, *114*, 9219-9280.
(2) Merritt, E. A.; Olofsson, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 9052-9070.
(3) Tinnis, F.; Stridfeldt, E.; Lundberg, H.; Adolfsson, H.; Olofsson, B. *Org. Lett.* **2015**, *17*, 2688-2691.
(4) Purkait, N.; Kervefors, G.; Linde, E.; Olofsson, B. *Angew. Chem. Int. Ed.* **2018**, *57*, 11427-11431.
(5) Reitti, M.; Villo, P.; Olofsson, B. *Angew. Chem. Int. Ed.* **2016**, *55*, 8928-8932.
(6) Villo, P.; Kervefors, G.; Olofsson, B. *Chem. Commun.* **2018**, *54*, 8810-8813.
(7) Stridfeldt, E.; Lindstedt, E.; Reitti, M.; Blid, J.; Norrby, P.-O.; Olofsson, B. *Chem. Eur. J.* **2017**, 13249-13258.

Oral Communications

Oral Communication n°1

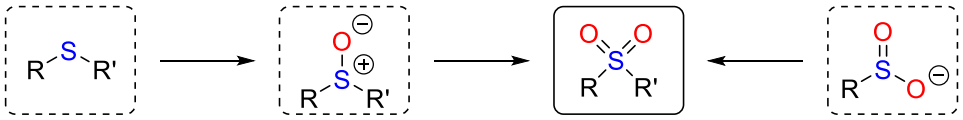
Sulfonylative Hiyama Cross-Coupling: Development and Mechanistic Insights

Aurélien ADENOT,[1] Joëlle CHAR,[1] Niklas VON WOLFF,[1] Guillaume LEFEVRE[1] and Thibault CANTAT[1,*]

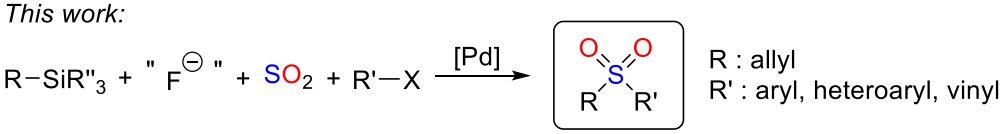
[1] NIMBE, CEA, CNRS, Université Paris-Saclay, CEA Saclay, 91191 Gif-sur-Yvette cedex, France
aurelien.adenot@cea.fr

Due to distinctive structural and electronic features, sulfones have attracted a particular attention over the past few decades, making it a widespread functional group.[1] Present in many contemporary pharmaceuticals and agrochemicals (*e.g.* the antibiotic Thiamphenicol or the herbicide Pyroxasulfone), they are also used as essential intermediates in organic synthesis (*e.g.* the Julia olefination or the Ramberg-Backlund rearrangement). Given this combination of a prominent biological activity and an appealing synthetic utility, numerous methodologies have been developed for their preparation.[1] However, the most common methods (see Scheme below) suffer from significant limitations with harsh reaction conditions or regioselectivity issues. Recently, the insertion of a molecule of sulfur dioxide between two partners was investigated and reactions involving organomagnesium,[2] organozinc[3] and organoboron[4] compounds were reported. Herein we report a direct single-step palladium-catalyzed synthesis of sulfones involving organosilanes, sulfur dioxide and organohalides. Experimental trends were rationalized through mechanistic experiments and DFT-calculations.

Traditional routes for sulfone synthesis:



This work:



References :
[1] Liu, N-W; Liang, S; Manolikakes, G; *Synthesis* **2016**, *48*, 1939.
[2] Deeming, A S; Russel, C J; Hennessy, A J; Willis, M C; *Org. Lett.* **2014**, *16*, 150.
[3] Rocke, B N; Bahnck, K B; Herr, M; Lavergne, S; Mascitti, V; Perreault, C; Polivkova, J; Shavnya, A; *Org. Lett.* **2014**, *16*, 154.
[4] Chen, Y; Willis, M C; *Chem. Sci.* **2017**, *8*, 3249.
[5] von Wolff, N; Char, J; Frogneux, X; Cantat, T; *Angew. Chem. Int. Ed.* **2017**, *56*, 5616.

Oral Communication n°2

Divergent synthesis of 1,2-benzothiazine or benzoisothiazole analogs containing a *S*-trifluoromethyl sulfoximine group.

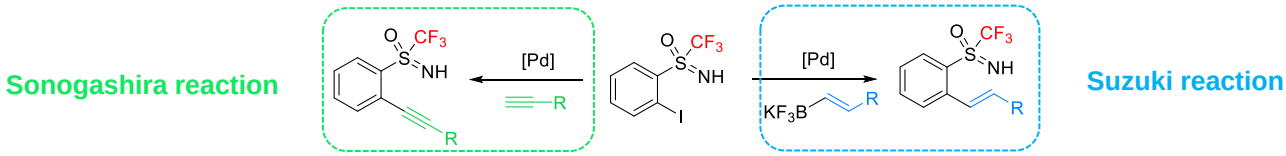
Anne-Laure BARTHELEMY,[1] Elsa ANSELMI,[1] Karinne MIQUEU[2] and Emmanuel MAGNIER[1]

[1] Institut Lavoisier de Versailles - UMR 8180, Université de Versailles Saint-Quentin en Yvelines, 45 avenue des Etats-Unis 78035 Versailles Cedex

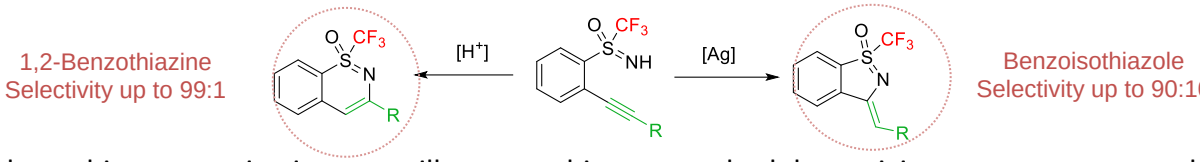
anne-laure.barthelemy@uvsq.fr ; emmanuel.magnier@uvsq.fr

[2] IPREM - UMR 5254, Université de Pau et des Pays de l'Adour, Technopole Héloiparc, 2 avenue du Président Pierre Angot 64053 Pau Cedex 09

The sulfoximine group is an emerging and very promising moiety for pharmaceuticals, agrochemicals and bioactive compounds.[1] In continuation of our research program dedicated to the preparation of highly functionalized *S*-perfluorinated sulfoximines,[2] we have developed efficient cross-coupling reaction such as Stille, Suzuki[3] and Sonogashira reactions starting from *o*-iodo phenylsulfoximine. These new compounds are bench stable, and even in the presence of the free *N*H sulfoximine, no cyclization was observed, paving the way to the control of this reaction in a second step.



In the case of the molecules obtained from the Sonogashira coupling reaction, we aimed to control the cyclization to selectively synthesize 1,2-benzothiazine or benzoisothiazole analogs. Indeed, benzothiazines represent an interesting framework for their structural diversity and application in life sciences. It is noteworthy that the construction of these heterocycles starting from sulfoximines is growing in interest for organic chemists[4].



Throughout this communication, we will present this new methodology, giving access to unprecedented *S*-perfluorinated 1,2-benzothiazine and benzoisothiazole analogs, in a regioselective manner. DFT studies were also performed to better understand the regioselectivity and the mechanism of the cyclisation.

References :

[1] a) Reggelin, M; Zur, C.; *Synthesis* **2000**, 1-64. b) Frings, M.; Thomé, I.; Schiffers, I.; Pan, F.; Runsink, J.; Raabe, G.; Bolm, C; *Chem. Eur. J.* **2014**, *20*, 1691-1700. c) Frings, M.; Thomé, I.; Bolm, C.; Beilstein *J. Org. Chem.* **2012**, *8*, 1443-1451. d) Sirvent, J. A.; Lücking, U.; *Chem. Med. Chem*. **2017**, *12*, 487-501

[2] Le, T. N.; Diter, P.; Pégot, B.; Bournaud, C.; Toffano, M.; Guillot, R.; Vo-Thanh, G.; Magnier, E.; *Org. Lett.* **2016**, *18*, 5102-5105

[3] A.-L. Barthelemy, A. Prieto, P. Diter, J. Hannedouche, M. Toffano, E. Anselmi, E. Magnier, *Eur. J. Org. Chem.* **2018**, 3764-3770

[4] a) Harmata, M.; Rayanil, K.; Gomes, M. G.; Zheng, P.; Calkins, N. L.; Kim, S.-Y.; Fan, Y.; Bumbu, V.; Lee, D. R.; Wacharasindhu, S.; Hong, X.; *Org. Lett.* **2005**, *7*, 143-145. b) Cheng, Y.; Bolm, C.; *Angew. Chem. Int. Ed.* **2015**, *54*, 12349-12352. c) Dong, W.; Wang, L.; Parthasarathy, K.; Pan, F.; Bolm, C.; *Angew. Chem. Int. Ed.* **2013**, *52*, 11573. c) Cheng, Y.; Dong, W.; Parthasarathy, K.; Bolm, C.; *Org. Lett.* **2017**, *19*, 726-729. d) Wen, J.; Tiwari, D. P.; Bolm, C.; *Org. Lett.* **2017**, *19*, 1706-1709

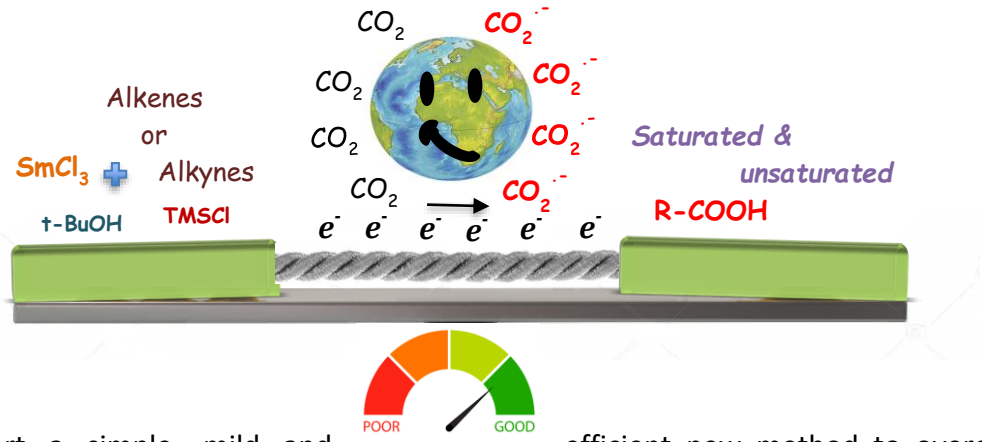
Oral Communication n°3

$SmCl_2$ catalyzed site-selective hydrocarboxylation of alkenes and alkynes via CO_2 activation

Sokna BAZZI,[1] Mohamed MELLAH[1]

[1] Molecular catalysis laboratory, ICMMO (UMR 8182), Paris Sud University 91405 Orsay, France
Sakna.bazzi@u-psud.fr

Nowadays, Carbon dioxide is one of the most discussed topics after the **IPCC**'S report on the impact of global warming related to increasing levels of this greenhouse gas **(GHG)** in the atmosphere.[1] On the good side, its unbeatable characteristics (cheap, available and inherently renewable gas) make the **CO_2** a very attractive option to be considered and the best candidate to be used in organic chemistry, especially for **C-C bond formation** reactions.[2] However, the thermodynamic stability and the kinetic intertie remain an immense obstacle in the way of its reduction. Particularly, the **hydrocarboxylation** reactions of unsaturated substrates (mainly alkenes and alkynes) via **CO_2 activation** to produce carboxylic acids are quite rare, notably those leading to the **anti-Markovnikov** products, challenging for the metal catalysis.[3]



Herein, we report a simple, mild and efficient new method to overcome these barriers. By using a **catalytic** amount of samarium dichloride (**$SmCl_2$**), generated *in situ* by electrochemistry, we were able to **reduce and activate** efficiently the CO_2 delivering the radical anion **$CO_2^{\cdot-}$**. This radical initiates then a selective **anti Markovnikov** mechanism with the unsaturated starting material in the presence of **tert-butanol** as a proton donor. Relaying on this new reactivity, we now have an excellent strategy to convert abundant feedstocks into a valuable carboxylic acids with no need for an expensive ligand or substoichiometric reductant.

References:
[1] https://www.carbonbrief.org/in-depth-qa-ipccs-special-report-on-climate-change-at-one-point-five-c
[2] Tortajada, A.; Juliá-Hernández, F.; Börjesson, M.; Moragas T.; Martin, R.; *ACIE* **2018**, *57*, 15948.
[3] Meng, Q.-Y.; Wang, S.; Huff, G.S.; Konig, B.; *JACS* **2018**, *140*, 3198.

Oral Communication n°4

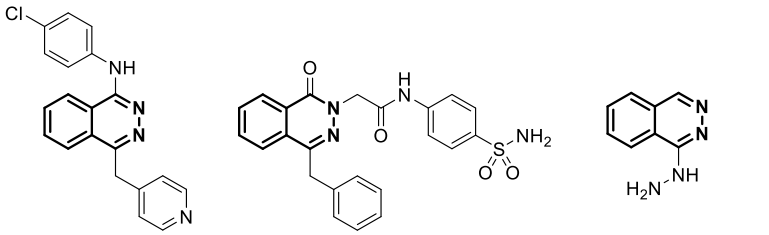
New Photochemical Generation of Nitrogen-Centered Radical: an Application to Phthalazine Synthesis.

Maxime DE ABREU, Philippe BELMONT, Etienne BRACHET

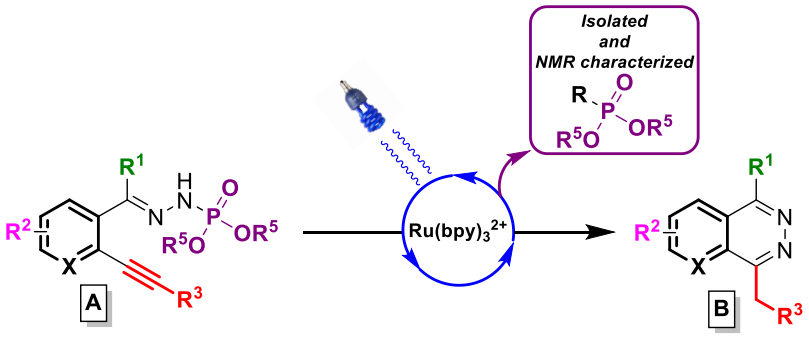
Université Sorbonne Paris Cité (USPC), Université Paris Descartes, Faculté de Pharmacie de Paris, UMR-CNRS 8038 (CiTCoM), 4 Avenue de l'Observatoire, 75006 Paris.

maxime.de-abreu@parisdescartes.fr

Therapeutic properties of nitrogen-containing heterocycles have been known for decades.[1] The phthalazine scaffold is no exception since it has been proved to have antitumor[2] and antibacterial[3] properties, in addition to its antihypertensive[4] properties for which it is already marketed in Europe and in the USA.



Our laboratory is involved in the development of new photochemical reactions[5] and has reported in 2016 the synthesis of the phthalazine scaffold *via* an innovative visible-light induced amination followed by a Smiles rearrangement.[6] Here we describe a new way to access the phthalazine B, starting from phosphonohydrazone derivatives A.



In this work, we will describe the reaction conditions' optimization, the scope and the mechanistic proposal for this reaction. [7]

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Oral Communication n°5

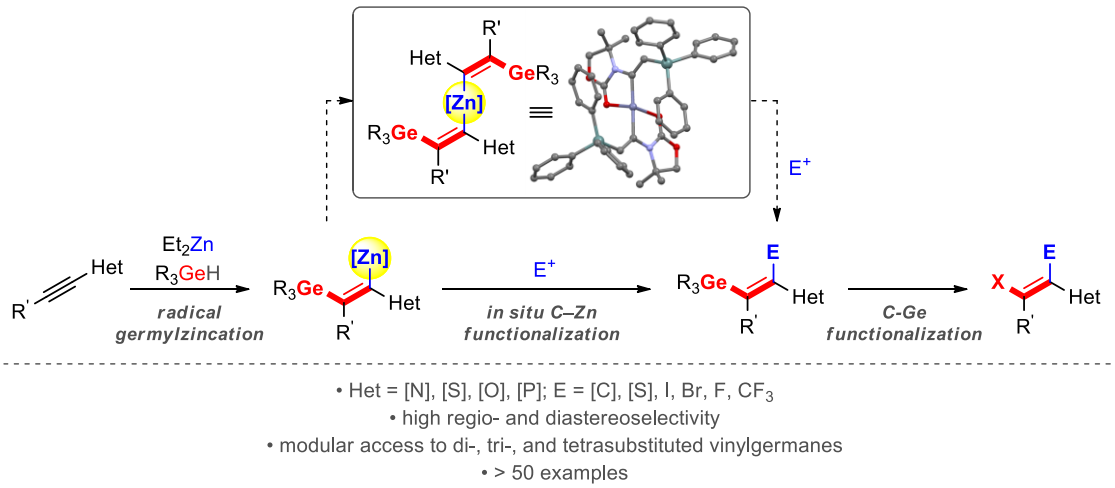
A Radically Different Approach to Vinylgermanes: Germylzincation of *α*-Heteroatom-Substituted Alkynes

Karen DE LA VEGA-HERNANDEZ,[1] Elise ROMAIN,[1] Anais COFFINET,[1] Kajetan BIJOUARD,[1] Geoffrey GONTARD,[1] Fabrice CHEMLA,[1] Franck FERREIRA,[1] Olivier JACKOWSKI[1] and Alejandro PEREZ-LUNA[1]

[1] Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire, 4 place Jussieu, 75005 Paris, France
karen.de_la_vega_hernandez@sorbonne-universite.fr

The synthetic appeal of vinylgermanes has recently increased in light of specific features that make them useful to overcome some limitations met with the more popular group 14 homologues vinylsilanes and vinylstannanes.[1] Despite the different approaches developed for accessing vinylgermanes with substituents distal to Ge,[2] no synthetic method for the direct preparation of derivatives having two substituents in that position has so far been reported.

To satisfy this demand, we disclosed here the first germylzincation reaction of triple bonds from the simple combination of a germane and Et_2Zn with an alkyne in a radical chain process.[3] The generality of the methodology is demonstrated for several heteroatom-substituted acceptors, including terminal and internal triple bonds. This protocol creates in a single synthetic operation a C(sp^2)-Ge bond and a C(sp^2)-Zn bond, and the *β*-zincated vinylgermanes that showed exceptional stability were isolated and characterized by NMR spectroscopy and X-ray crystallography. The unique feature of this new approach is that the C(sp^2)-metal bond formed remains available for further in situ Cu(I)- or Pd(0)-mediated functionalization, a fact that is in sharp contrast with other attempted germylmetalation reactions.[4] Thus, this protocol offers modular access to elaborated tri- and tetrasubstituted vinylgermanes that are useful for the preparation of stereodefined alkenes.



• Het = [N], [S], [O], [P]; E = [C], [S], I, Br, F, CF_3
• high regio- and diastereoselectivity
• modular access to di-, tri-, and tetrasubstituted vinylgermanes
• > 50 examples

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Oral Communication n°6

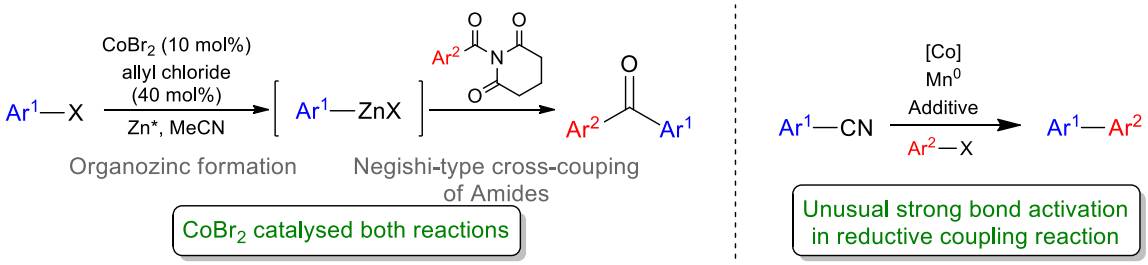
Unusual bonds activation and cobalt-catalyzed cross-coupling

Céline DORVAL,[1] Corinne GOSMINI.[1]

[1] Laboratoire de Chimie Moléculaire, Ecole Polytechnique, CNRS, Route de Saclay, 91128 Palaiseau cedex

celine.dorval@polytechnique.edu

Over the last forty years, the development of metal-catalyzed cross-coupling reactions revolutionized the formation of carbon-carbon and carbon-heteroatom bonds. Those reactions commonly involve an electrophile bearing a suitable leaving group, mainly halides, with an organometallic reagent to be coupled within the coordination sphere of the transition-metal catalyst. Quite recently, organic chemists expended significant research efforts in developing efficient and sustainable procedures under mild conditions, for instance by using non-precious metal catalysts, weakly nucleophilic organometallics or new coupling partners from renewable sources.[1] Among all the organic compounds extracted from biomass, carboxylic acids present several advantages: high availability, low or no toxicity and a broad structure diversity which make them ideal coupling partners. As a consequence, chemists have been developing new coupling reactions involving carboxylic acids[2] or their derivatives, such as amides, as coupling partners.[3] Organozinc compounds present mild nucleophilicity and offer an excellent functional group tolerance which make them an interesting nucleophilic partner in cross-coupling reactions. In 2003, we revealed an easy to handle cobalt-catalysed formation of aryl zinc compounds, necessitating no particular precautions,[4] and their reactivity in Negishi-type reactions with acid chloride or anhydride derivatives,[5a] among others.[5b] In the continuity of this work, we released a sequential organozinc formation and Negishi cross-coupling of amides catalysed by cobalt salt that will be presented.[6] Another approach focuses on reductive cross-coupling which allows to couple two electrophiles and avoids handling potentially hazardous organometallic reagents.[7] With this concern, our group, in particular, uses low-cost and insensitive cobalt catalytic systems to perform direct reductive cross-couplings.[8] In the continuity of the group work, some results will be shown concerning the activation of strong C-X bonds like C-CN bond to lead to various cross-coupling reactions.



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Oral Communication n°7

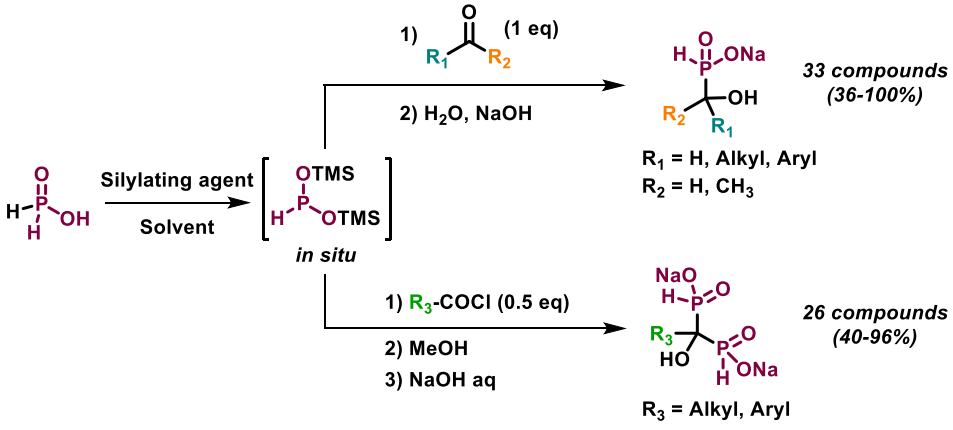
Convenient one-pot reaction for the synthesis of α-hydroxy-phosphinates and 1-hydroxymethylene-1,1-bisphosphinates

Jade DUSSART, Julia DESCHAMP, Evelyne MIGIANU-GRIFFONI and Marc LECOUVEY

Laboratoire CSPBAT, UMR 7244 CNRS, Equipe de Chimie Bioorganique et Synthèse asymétrique
Université Paris 13, 1 Rue de Chablis, F-93000 Bobigny, France
jade92.dussart@gmail.com

Phosphinates and bisphosphonates are an interesting class of compounds showing a high stability due to P-C bond and the ability to mimic phosphate esters and carboxylates. Phosphinates are reported in the literature to have potential biological activity for instance on brain disorders, cancer, malaria or leishmaniosis.[1] Among phosphorylated molecules used in clinic, 1-hydroxymethylene-1,1-bisphosphonates (HMBPs) occupy a prominent place. Because of their affinity for the calcium ions, they are currently the most widely used treatment of bone pathologies.[2] Moreover, these compounds have interesting antitumor effects on soft tissue primary tumor models (breast, prostate…). In contrast to bisphosphonates, limited number of studies has focused on the synthesis and chemical properties of bisphosphinates which should be less hydrophilic than HMBPs and thus should enhance biological properties.[3-4]

Several methodologies have been already described for the synthesis of phosphinates while only one method has been reported for the preparation of bisphosphinic acids.[1] For both, many drawbacks remain in terms of yields, reaction time and easy handling.[3] In this context, we developed a convenient and straightforward one-pot procedure for the synthesis of α-hydroxyphosphinates and bisphosphinates.[5-7] In this communication, we will disclose the various reaction parameter optimizations leading to a general efficient procedure and the method reproducibility.



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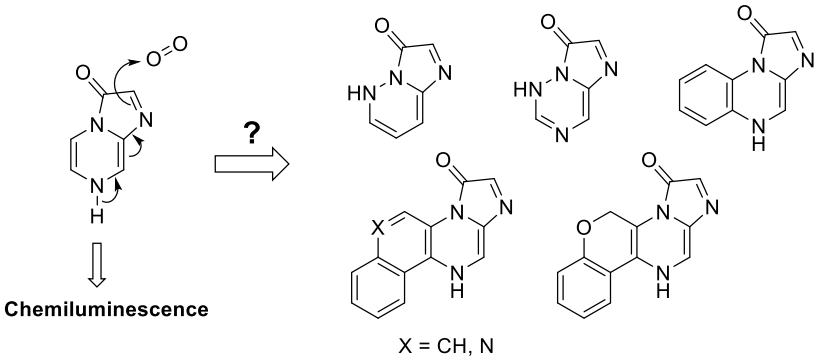
Oral Communication n°8

Highly modified imidazo[1,2-*a*]pyrazin-3(7*H*)-one luciferin analogues: synthesis of exotics heterocyclic cores and chemiluminescence properties

Glwadys GAGNOT,[1,2] Vincent HERVIN,[1] Eloi P. COUTANT,[1] Yves L. JANIN[1]

[1] Unité de Chimie et Biocatalyse, Institut Pasteur, UMR 3523, CNRS, 28 rue du Dr. Roux, 75724 Paris Cedex 15, France.
[2] Université Paris Descartes, Sorbonne Paris Cité, 12 rue de l'École de Médecine, 75006 Paris, France.
glwadys.gagnot@pasteur.fr



In the course of our work on the design and study of improved imidazo[1,2-*a*]pyrazin-3(7*H*)-one luciferins related to coelenterazine,[1]-[3] we undertook the synthesis of analogues featuring altered heterocyclic cores which could still undergo an oxidative process susceptible to produce a photon.

We wish to describe the synthesis of *O*-acetylated derivatives of imidazo[1,2-*b*]pyridazin-3(5*H*)-one, imidazo[2,1-*f*][1,2,4]triazin-7(1*H*)-one, imidazo[1,2-*a*]quinoxalin-1(5*H*)-one, benzo[*f*]imidazo[1,2-*a*]quinoxalin-3(11*H*)-one, imidazo[1',2':1,6]pyrazino[2,3-*c*]quinolin-3(11*H*)-one and 5,11-dihydro-3*H*-chromeno[4,3-*e*]imidazo[1,2-*a*]pyrazin-3-one. To achieve this, extensive uses of Buchwald-Hartwig N-arylations were made alongside old – and sometimes forgotten – heterocyclic chemistry. From these analogues of marine luciferins, the studies of their chemiluminescence properties were undertaken. This provided original insights regarding the influence of such alterations on the wavelength of the photon emitted by chemiluminescence means.

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Oral Communication n°9

ASYMMETRIC ORGANOCATALYSIS – SYNTHESIS OF CYCLOHEPTA[*B*]INDOLES BY (4+3) CYCLOADDITION

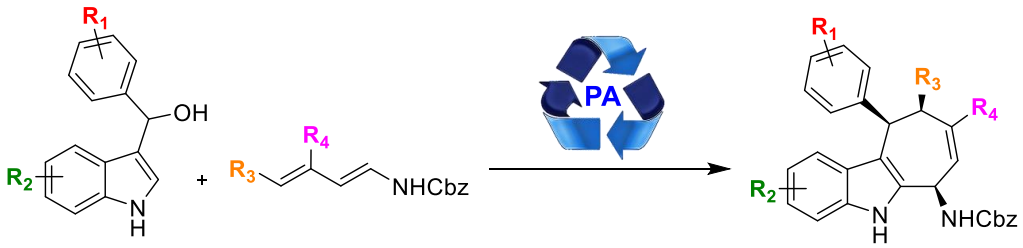
Guillaume LEVITRE,[1] Coralie GELIS,[1] Jérémy MERAD,[1] Luc NEUVILLE[1] and Géraldine MASSON [1]

[1] Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Université Paris-Sud, Université Paris-Saclay, 1 av. de la Terrasse, 91198 Gif-sur-Yvette Cedex, France

guillaumelevitre@yahoo.fr

A lot of pharmaceutical drugs and natural products have as their central motif the cyclohepta[*b*]indole.[1] Therefore a considerable interest in these units and their synthesis has developed. The stereoselective [4+3] cycloaddition is one of the most convergent strategies for the synthesis of chiral polysubstituted cyclohepta[*b*]indole derivatives. Although the utility of these reactions has been explored fruitfully over the past two decades, quite limited progress has been made in catalytic asymmetric variants.[2]

On the basis of these facts, we describe herein the first examples of phosphoric acid-catalyzed enantioselective (4+3) cycloaddition of 3-indolylmethanols and dienecarbamates (Scheme 1). Excellent enantioselectivities (up to 98% ee) were observed for a broad spectrum of substrates under mild conditions. Moreover, these functionalized cyclohepta[b]indole derivatives could be used as the key intermediates for further transformations to reach additional molecular diversity.[3]



>20 examples
up to 83% yield
up to 98% ee
rd>95:5

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Oral Communication n°10

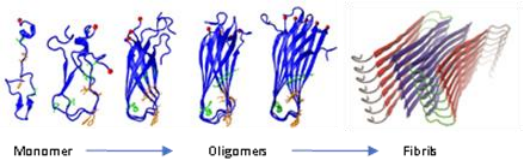
Synthesis of novel fluorinated peptidomimetics as potential protein aggregation inhibitors in amyloidoses

Jacopo LESMA,[1] Nicolò TONALI,[1] Faustine BIZET,[1]Jean-Louis SOULIER, [1] Julia KAFFY,[1] Sandrine ONGERI[1]

[1] *FLUOPEPIT, BioCIS, CNRS, Université Paris Sud, Université Paris Saclay, 5 rue Jean Baptiste Clément, 92290 Châtenay-Malabry*

Jacopo.lesma@u-psud.fr

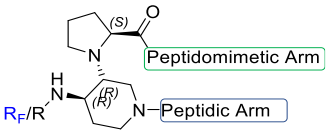
The self-assembly process of misfolded peptides or proteins has been reported to be the common process of more than twenty degenerative diseases, called amyloidoses. This aggregation process is triggered when the monomeric random coil and non-toxic peptide starts to adopt a β-sheet structure, which self-aggregate to form toxic oligomeric species and finally fibrils. The aggregation of hIAPP peptide in Type II diabetes (T2D) and of $A\beta_{1\text{-}42}$ peptide in Alzheimer's Disease (AD) is suspected to be one of the major causes of cellular death in both pathologies [1].



Our group has recently reported a novel class of acyclic β-hairpin peptidomimetics as efficient inhibitors of the $A\beta_{1\text{-}42}$ aggregation process. These molecules, built on a piperidino-pyrrolidine β-turn mimic, are bearing two recognition peptidic or peptidomimetic arms designed to interact with the target [2].

Being encouraged by the promising results obtained with this new strategy, we decided to further investigate how modifications on the structure of both arms could modulate the activity as well as allow the inhibition of hIAPP aggregation. In this work we will present the synthesis of fluorinated analogues derived from our most active compounds. Indeed, to the best of our knowledge, only few examples of fluorinated peptides and peptidomimetics having anti-amyloid aggregation properties, have been yet reported, although the presence of fluorine can have drastic effect on the ligand-protein interactions and on the peptide stability [3]. The objective of introducing fluorine atoms is double:

i) elucidate how the unique electronic and structural characteristic can enhance both the β-hairpin stability and its anti-aggregation activity., ii) use these fluorinated derivatives as probes for ligand-protein interaction studies (^{19}F NMR experiments) [4] or for *in vivo* imaging (^{19}F MRI [5] or ^{18}F PET [6])



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Oral Communication n°11

Regioselective Control of Alkyne Insertion in Rhodium-Catalyzed Asymmetric Arylative Cyclization

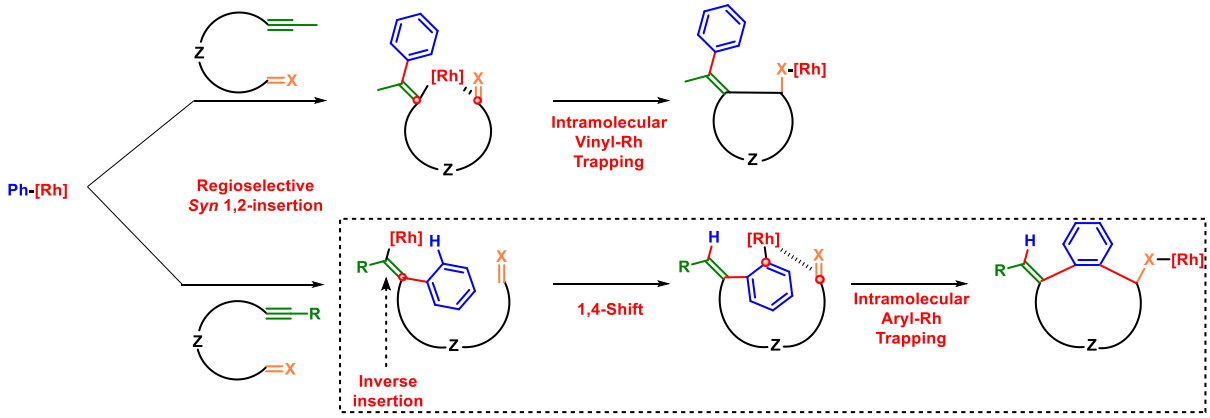
Aymane SELMANI, and Sylvain DARSES

Institute of Chemistry for Life and Health Sciences (i-CLeHS), PSL Université Paris, Chimie ParisTech - CNRS,
11 rue Pierre et Marie Curie 75005 Paris
aymane.selmani@chimie-paristech.fr

Transition-metal-catalyzed cascade reactions are powerful methods for the construction of structurally complex skeletons from simple acyclic building blocks in an atom-economical way.[1] Among them, the Rh-catalyzed arylative cyclization, initiated by nontoxic, stable and commercially available organoboron compounds, affords an efficient strategy for the synthesis of complex molecules via multiple C-C bond formations.[2]

Considering the importance of these scaffolds from biological and industrial interests,[3] our group has recently developed new enantioselective Rh-catalyzed cascade reactions of *N*- and *O*-tethered alkyne-enoates with arylboronic acids providing access to chiral pyrrolidines[4] and tetrahydrofurans. This process is ensured by a regioselective insertion of the alkyne into the aryl-Rh species, formed by transmetalation between Rh-catalyst and arylboronic acid.

In our continuous interest in the construction of chiral cyclic molecules, we investigated the role of the alkyne substituent. Pleasantly, we found that it has a dramatic effect on the regioselectivity of the alkyne insertion into the aryl-Rh species.[5] By judiciously modifying this alkyne substituent, the regioselectivity was completely reversed allowing to access to other families of cyclic scaffolds. Thanks to the inverse regioselective insertion, this vinyl-Rh reacts totally differently and undergoes a 1,4-shift to provide an aryl-Rh intermediate which can be intramolecularely trapped by an electrophile.



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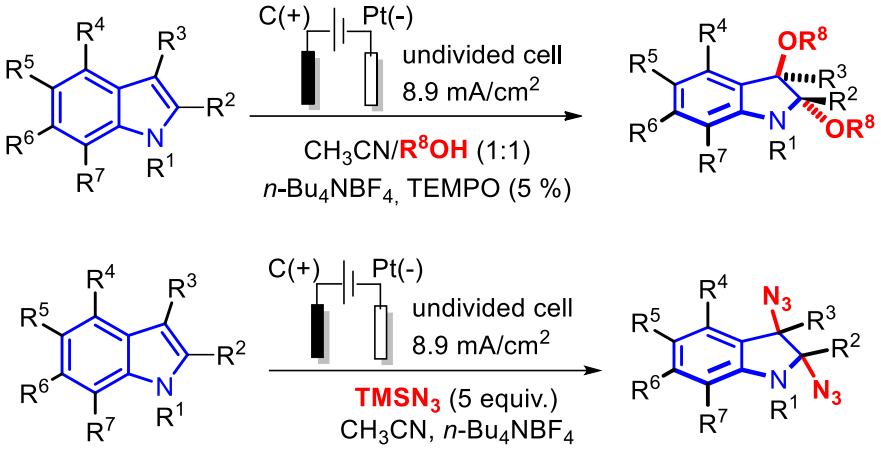
Oral Communication n°12

Electrochemical dearomative 2,3-difunctionalization of indoles

Ju WU,[1] Yingchao DOU, Cyrille KOUKLOVSKY, Guillaume VINCENT*.

[1] Institut de Chimie Moléculaire et des Matériaux d'Orsay
Université Paris-Sud, Université Paris-Saclay
guillaume.vincent@u-psud.fr

Electrosynthesis has enable the highly efficient and selective difunctionalization of alkenes which usually involves the generation of a radical intermediate which adds to the alkene.[1] In contrast, electrochemistry has been scarcely explored in dearomatization reactions.[2] In line with our interest in dearomatization reactions of indoles,[3] it inspired us to explore the electrochemical oxidation of indoles in presence of nucleophiles through, presumably, the oxidation of the indole nucleus into a radical cation which is, mechanistically, in contrast to most of the electrochemical difunctionalization of alkenes.



We report the use of electrochemistry to perform a direct oxidative dearomatization of indoles leading to 2,3-dialkoxy or 2,3-diazido indolines under undivided conditions at a constant current.[4] It avoids the use of an external oxidant and displays an excellent functional group compatibility. The formation of the two C-O or C-N bonds is believed to arise from the oxidation of the indoles into radical cation intermediates.

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Posters

Poster n°1

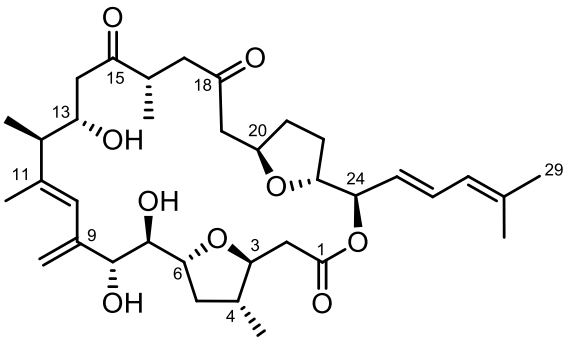
Total Synthesis of the Amphidinolide F

Laurent FERRIE,[1] Johan FENNETEAU, [1] Bruno FIGADERE,[1]

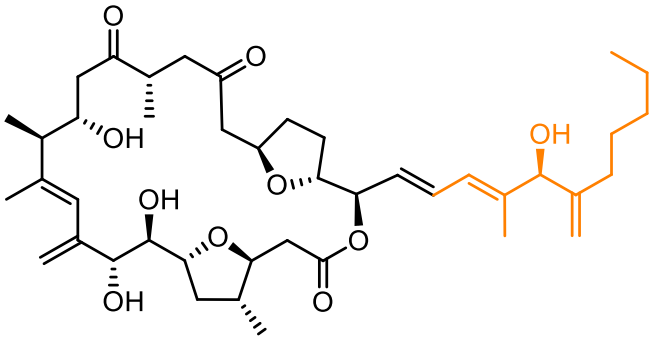
[1] Laboratoire de pharmacognosie, BioCIS, Faculté de Pharmacie, Université Paris-Saclay/CNRS, Chatenay-Malabry, 92290
Laurent.ferrie@u-psud.fr

Nature is an outstanding source of inspiration for organic chemists. In particular oceans are a pool of original and biologicaly active natural products. Despite their complex structure, their high level of activity makes them very valuable, illustrated by some recent examples of marketed anti-cancer drugs which possess a marine natural product origin (trabectedin, epothilones, halichondrin B). Accordingly, amphidinolides[1] are a promising source of potent anti-cancer agents.

Among of all its congeners, Amphidinolide C and related brother Amphidinolide F retained specially our attention by their structures containing two tetrahydrofurans in a macrolactone core. Due to the difficult availability from their natural source, total synthesis of amphidinolides C and F are necessary to explore further the biological activities of these compounds. After some synthetic studies towards these two natural products,[2],[3] we finally attained the total synthesis of amphidinolide F recently, through 23 steps considering the longest linear steps and 43 total steps.[4] The details of this major accomplishment will be discussed in the presented poster.



Amphidinolide F



Amphidinolide C

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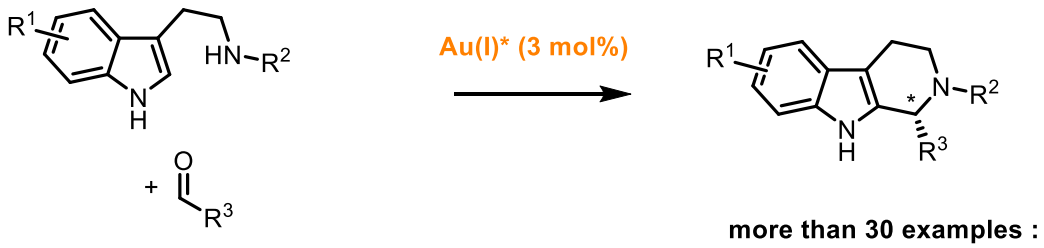
Poster n°2

The First Enantioselective Gold-Catalysed Pictet-Spengler Reaction

Nicolas GLINSKY-OLIVIER[1] ,Shengwen YANG[2] ,Vincent GANDON[2] and Xavier GUINCHARD[1]
[1] ICSN, CNRS, 1 Avenue de la Terrasse, 91190 Gif-sur-Yvette
[2] Université Paris Sud, 15 Rue Georges Clemenceau, 91400 Orsay
Nicolas.glinsky@cnrs.fr

The enantioselective Pictet-Spengler reaction is a key method for the synthesis of chiral tetrahydro-β-carbolines,[1] that are often biologically active compounds or intermediate for the synthesis of many drugs. Their synthesis is hence particularly important. [2] With the advent of organocatalysis, both chiral thioureas[3] and chiral phosphoric acids[4] gave access to good yields and enantiomeric excesses. However, there are no organometallic method to catalyze enantioselective Pictet-Spengler reactions. Following our previous observation that Au(I) complexes catalyze Pictet-Spengler reactions,[5] we developed an asymmetric version of this reaction using chiral Au(I) complexes.

During our optimization we investigated many parameters including the nature of the protection group of the tryptamine, the gold catalyst, the silver salts, the solvent … Numerous aldehydes can be used with the method but aromatic aldehydes gave the best results. More than 30 examples have been obtained with yields up to 99 % and enantiomeric excesses up to 96%.



more than 30 examples :
yields up to 99 %
ee's up to 96 %

References :
[1] Glinsky-Olivier, N.; Guinchard, X. *Synthesis* **2017**, *49*, 2605.
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Poster n°3

"CO" as a carbon bridge to build complex C2-branched glycosides using a palladium-catalyzed carbonylative Suzuki-Miyaura reaction from 2-iodoglycals

Morgane DE ROBICHON,[1] Andrea BORDESSA,[1] Nadège LUBIN-GERMAIN[1] and Angélique FERRY[1]

[1] Laboratoire de Chimie Biologique (LCB), Université de Cergy-Pontoise, EA 4505, 5 Mail Gay-Lussac, 95031 Cergy-Pontoise Cedex, France

morgane.de-robichon@u-cergy.fr

The involvement of glycoconjugates in numerous biological processes (cell adhesion, cell recognition or immunity) promotes the development of new access to these compounds. Analogues possessing an unnatural C-C bond (*C*-branched sugars) are largely studied due to their enzymatic and chemical stabilities and their conformational similarity towards C-O and C-N natural links. Metal-catalyzed processes revealed to be popular powerful tools to build C-C bond on the sugar backbone. Nevertheless, these types of transformation on sugars remain limited.[1,2] We already showed that carbonylative processes are efficient tools to build C2-glycoconjugates. Indeed, we described new access to C2-amidoglycals *via* an aminocarbonylation between 2-iodoglycals and amines. Diverse amines could be successfully linked on glycals leading to original glycolipid and glycopeptide mimics.[3] Herein, we present a carbonylative palladium-catalyzed Suzuki-Miyaura coupling reaction between 2-iodoglycal partners and diverse aryl- and alkenyl-boronic acids. The newly formed carbonyl link could be exploited to access to 2-aryl/alkenyl-methylene-α-glucopyranoside scaffolds *via* a three steps sequence including an indium-mediated Ferrier-type reaction.[4]

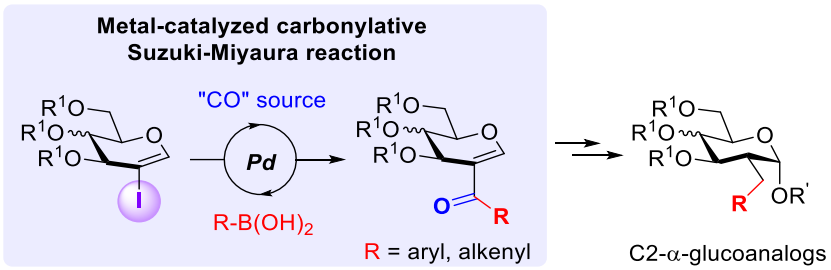

Figure 1 : Access to 2-keto-glycosides and C2-*α*-glucoanalogs

References :

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Poster n°4

Synthesis of Simplified Analogs of Marine Metabolites for Aurora B Kinase Inhibition

Charlotte JUILLET,[1] Dina BOYARSKAYA,[1] Ludmila ERMOLENKO,[1] Blandine BARATTE,[2] Stéphane BACH,[2] Sandrine RUCHAUD,[2] Ali AL-MOURABIT[1]

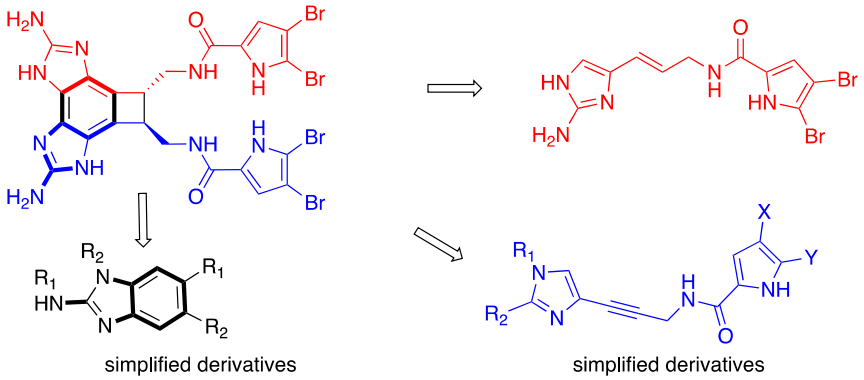
[1] Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Univ. Paris-Sud, Université Paris-Saclay, 1, av. de la Terrasse, 91198 Gif-sur-Yvette (France)
Charlotte.juillet@cnrs.fr
[2] Station Biologique de Roscoff, USR-3151, Place Georges Teissier, 29680 Roscoff
Sandrine.ruchaud@sb-roscoff.fr

Natural products chemistry is crucial for drug discovery. Indeed many successful drugs are bio-inspired from natural metabolites.

The pyrrole-2-aminoimidazole (P-2-AI) natural alkaloids are exclusively isolated from marine sponges and well known for their high structural diversity, high nitrogen-to-carbon ratio and interesting biological activities.[1] We focused our efforts to the syntheses of benzosceptrins[2] and oroidin[3] analogs for their biological activities.

A part of the numerous isolated P-2AI and their synthetic analogs have been found to inhibit various kinases including Aurora B kinase, CK1 or RIPK1 kinases.

Here we present new inhibitors derived from P-2-AI metabolites of the Aurora B kinase. The target Aurora B is essential for cell division via mitosis regulation, thus it plays a crucial role in tumorigenesis and represents a pertinent target against cancer. The objective of the study is to find potent and specific inhibitor for the characterization of the mechanism of action leading to the induction of cancer cells death.



References:

[1] A. Al-Mourabit, M. A. Zancanella, S. Tilvi, and. Romo, *Nat. Prod. Rep.*, **2011**, *28*, 1229-1260

[2] a) J. Appenzeller, S. Tilvi, M.-T. Martin, J.-F. Gallard, H. El-bitar, E.-T. Huu Dau, C. Debitus, D. Laurent, C. Moriou, A. Al-Mourabit, *Org. Lett.*, **2009**, *11*, 4874-4877

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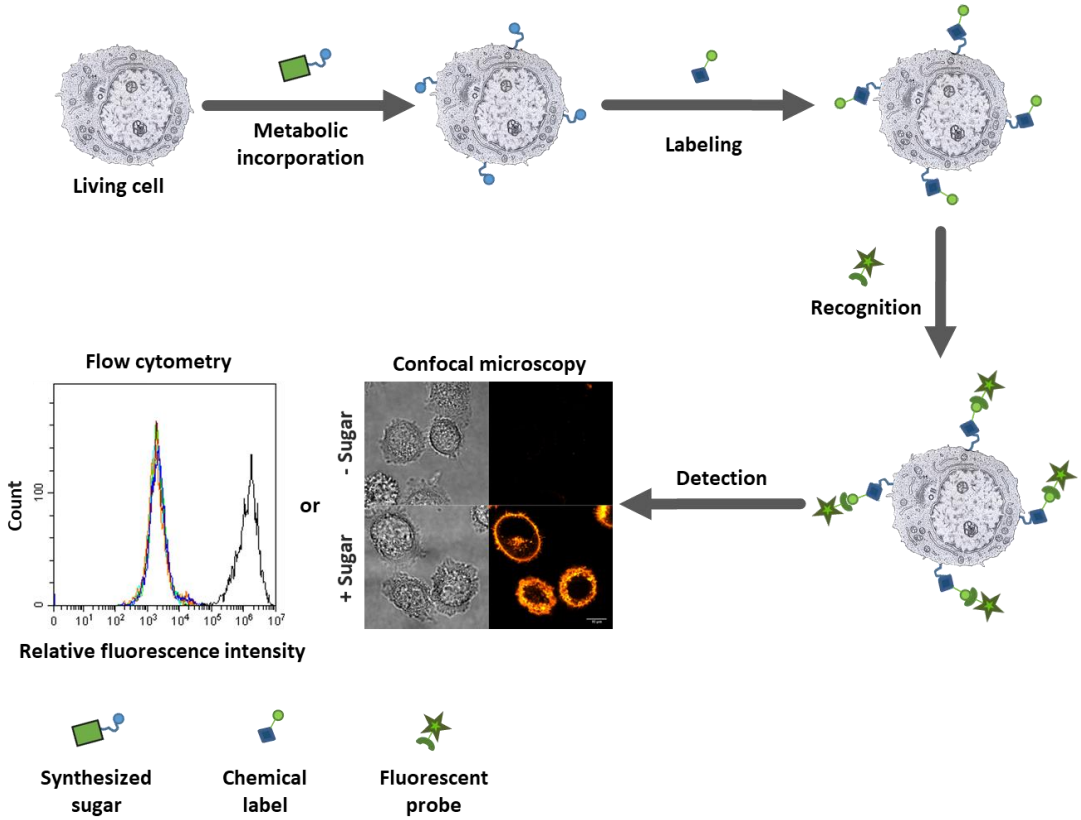
Poster n°5

Various unnatural saccharides for cell labeling by glycan metabolic engineering

Mathieu CARLIER,[1] Laura FOURMOIS,[1] Aurélie BARON,[1] Marie-Ange BADET-DENISOT,[1] Boris VAUZEILLES.[1,2]

[1]*ICSN, UPR-CNRS 2301, 91198, Gif-sur-Yvette Cedex, France, U. Paris-Saclay*
[2]*ICMMO, UMR-CNRS 8182, U. Paris-Sud, 91405 Orsay Cedex, France, U. Paris-Saclay*
mathieu.carlier@cnrs.fr

Glycan metabolic engineering is a powerful tool for cell labeling. This method uses a synthesized unnatural saccharide bearing a chemical reporter. This sugar is metabolically incorporated into glycans of living cells and may be labeled by fluorescent probes.[1],[2] The fluorescent probes can be detected by flow cytometry or visualized by confocal microscopy to validate the labeling of modified glycans *in cellulo*.



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Poster n°6

Stereoselective preparation and reactivity of 4-hydroxy-1-allenylboranes

Islem Ishak,[1] Pr. Franck FERREIRA[1], Dr. Olivier JACKOWSKI[1]

[1]Institut Parisien de Chimie Moléculaire (IPMC), Équipe Réactivité Organométallique et Catalyse pour la Synthèse (ROCS), 4 Place Jussieu, 75252 Paris cedex 5, Couloir 32-42 4ème étage

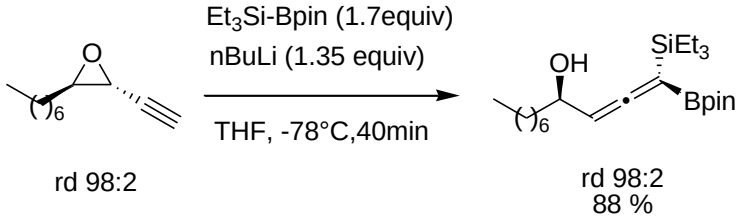
islem.ishak@sorbonne-universite.fr

Allenylmetals are important reagents in organic synthesis. In particular, allenylsilanes allow the stereoselective preparation of homopropargyl alcohols and amines, [1] frequently used in the asymmetric synthesis of many natural products. [2]

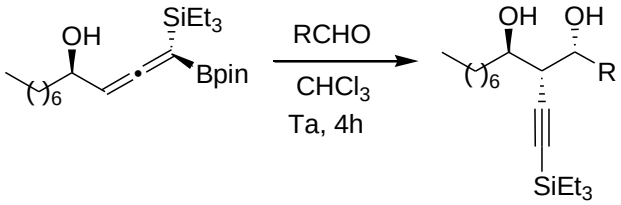
Among the reliable procedures for the preparation of multisubstituted allenylmetals, the SNi-type reactions between alkynyl oxiranes and organometallic reagents have earned increasing attention during the last years.[3]

During my first PhD year in France, we have studied the synthesis and reactivity of allenylborane. First the stereoselective synthesis of 4-hydroxy-allenylborane has been developed by a SNi-type reaction from a silyl borane with acetylenic epoxide in the presence of base.

Therefore, the study of borylation of acetylenic epoxides led to encouraging results and paved the way for a new stereoselective synthesis of allenylboranes.



Subsequently, the addition of this 4-hydroxy-1-allenylboranes on aldehyde has been investigated. Optimization of this reaction will be disclosed.



References:

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Poster n°7

Novel broad spectrum ß-lactamases inhibitors *via* [3+2]-cycloaddition of ynamide

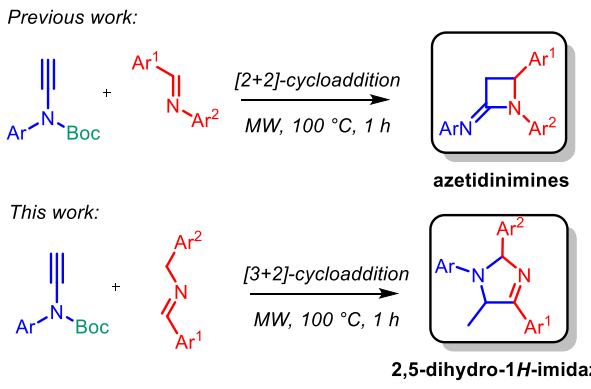
Agathe C. A. D'HOLLANDER,[1] Eugénie Romero,[1] Saoussen Oueslati,[2] Kamsana Vijayakumar,[1] Pascal Retailleau,[1] Thierry Naas,[2] Bogdan I. Iorga,[1] Robert H. Dodd,[1] Kevin Cariou.[1]

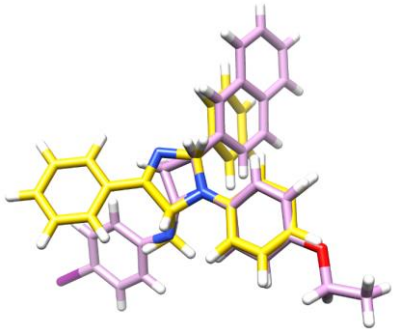
[1] Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Université Paris-Sud, Université Paris-Saclay, 1 Avenue de la Terrasse, 91198 Gif-Sur-Yvette, France

[2] Bacteriology-Hygiene Unit, Assistance Publique/Hôpitaux de Paris, Bicêtre Hospital, Le Kremlin-Bicêtre, France. EA7361 "Structure, dynamic, function and expression of broad spectrum β-lactamases", Université Paris-Sud, Université Paris-Saclay, LabEx Lermit, Faculty of Medicine, Le Kremlin-Bicêtre, France. Associated French National Reference Center for Antibiotic Resistance: Carbapenemase-producing Enterobacteriaceae, Le Kremlin-Bicêtre, France.

agathe.dhollander@cnrs.fr

β-Lactams are the most widely prescribed antibiotics. However, they are subject to ever increasing bacterial resistance that poses a major health threat worldwide. [1] One resistance mechanism involves β-lactamase enzymes that hydrolyze β-lactam rings. Augmentin, a common prescribed drug, proves that the combination of a β-lactam antibiotic (amoxicillin) with a β-lactamase inhibitor (clavulanic acid) can be highly successful.[2] Unfortunately, current treatments are not efficient against all β-lactamases and novel inhibitors are required, especially to fight the extremely threatening resistances caused by carbapenemases. We previously reported the synthesis of azetidinimine-based broad spectrum β-lactamases inhibitors *via* a [2+2]-cycloaddition of ynamides and imines (Scheme 1).[3] Based on the overall shape similarity observed on a 3D model of an azetidinimine superposed with an imidazoline, we envisaged the synthesis of imidazoline-based potential β-lactamases inhibitors by switching the imine substrate with a benzyl-imine substrate (Scheme 1). Optimisation of this reaction, a study of its scope along with its limitations will be presented here. Biological assessment of several analogues proving their broad spectrum β-lactamases inhibitor activity will also be shown.





Modeling of the 3D shape of an imidazoline (yellow backbone) superposed with an azetidinimine (pink backbone)

Scheme 1: Design of imidazoline-based broad spectrum ß-lactamases inhibitors.

References :

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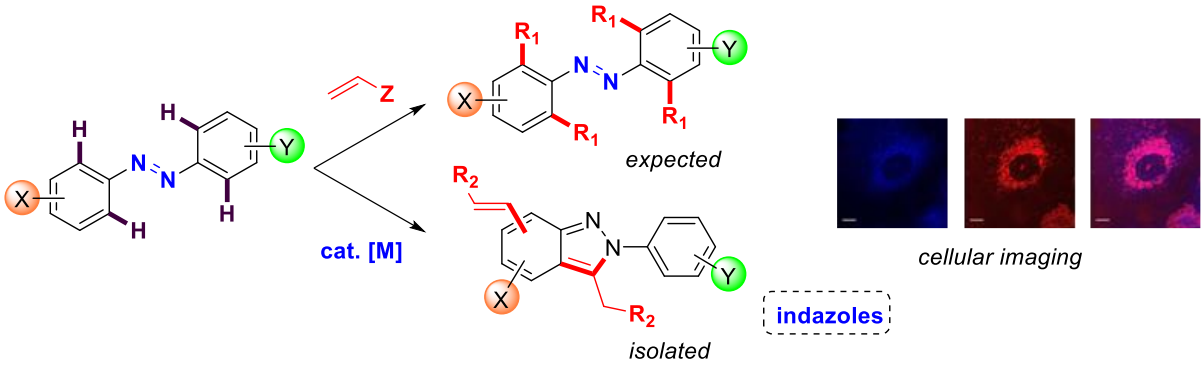
Poster n°8

Access to indazole fluorophores from azobenzenes via tandem double C-H activation and Michael addition: developments and applications

Nicolas Gigant,[1] Minh Thuong Khong,[1] Laura Fourmois,[2,3] Florence Mahuteau-Betzer,[2,3] Delphine Joseph[1]

[1] BioCIS, Université Paris-Sud, CNRS, Université Paris-Saclay, F-92296 Châtenay-Malabry, France.
[2] Institut Curie, PSL Research University CNRS, INSERM, Université Paris-Sud, Université Paris-Saclay, 91400 Orsay, France.
[3] Université Paris-Sud, Université Paris-Saclay, CNRS, UMR 187-U1196, 91405 Orsay, France.
nicolas.gigant@u-psud.fr

Azobenzenes have attracted considerable attention due to their unique photochromic properties and quite recently, our group started a diversity-oriented program for their synthesis.[1] If the preparation of simple azo units is efficiently reported, the synthesis of densely-substituted azo compounds remains a perpetual challenge for the organic chemist.[2] In our quest to generate original photo-switches, we speculated that the use of azobenzenes in the presence of alkenes could generate the targeted highly functionalized azos. However, after preliminary experiments, it rapidly turned out that this strategy provides various poly-substituted indazoles exhibiting interesting fluorescence after excitation at 365 nm under a UV lamp. This finding stimulated us to design a new eco-friendly process for the synthesis of 2*H*-indazoles via tandem oxidative dehydrogenative cross coupling – Michael addition at room temperature and to explore their photophysical properties. Several compounds exhibit high fluorescence quantum yield in water and allow a vesicles labeling in live cells upon one-photon and two-photon excitation.



References :
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Poster n°9

Pd-catalyzed Ring Opening of Bicyclic Aziridines Prepared by Flow Assisted Photochemical Transformation of Pyridinium Salts

João OLIVEIRA,[1,2] Filipa SIOPA,[1,2] Gredy KIALA,[2] Carlos AFONSO,[1] Julie OBLE,[2] Giovanni POLI,[2]

[1] Sorbonne Université, Faculté des Sciences et Ingénierie, CNRS, Institut Parisien de Chimie Moléculaire (IPCM), 4 place Jussieu 75252 Paris Cedex 05 France.

[2] Research Institute for Medicines (iMed.ULisboa), Faculty of Pharmacy, Universidade de Lisboa, Av. Prof. Gama Pinto,1649-003 Lisbon, Portugal.

joao96andre@gmail.com

Aziridines are highly reactive three-membered heterocycles. They are well known to organic chemists for their great potential as building blocks for the synthesis of carbocycles with significant biological activity, such as aminocyclopentitols and beta-lactams.

A short route for the synthesis of these structures is the photochemical transformation of pyridinium salts to bicyclic-aziridines. The photochemical rearrangement forms a cis-fused cyclopenteno-aziridine allylic cation which reacts stereospecifically with poor nucleophiles/solvent devising a stable bicyclic-aziridine containing a new C-Nu bond in trans-position (Figure 1).[1] Recently, Afonso's group reported the ring opening of these aziridines structures by performing a S_N2 reaction with nucleophiles such as azides, anilines, and thiols, forming new carbon-heteroatom bonds (Figure 1).[2] However, carbon-based nucleophiles were totally inert under these conditions.

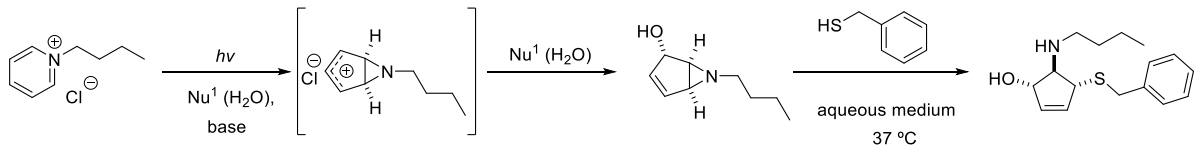

Figure 2. Photochemical transformation of pyridinium salt and an example of ring opening

By taking advantage of the skill in the synthesis and ring-opening of these aziridines of the Lisbon group, and of experience in palladium chemistry of the Paris team, recently we developed a palladium-catalyzed ring opening of vinyl aziridines. This process proceeds takes place through η^3-allylpalladium complex formation via aziridine cleavage, and γ-reactivity of carbon-based nucleophiles leading to new carbon-carbon bonds.

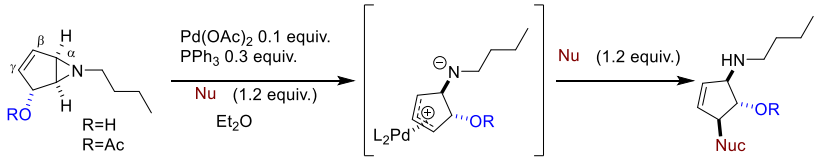

Figure 3. Palladium catalysis followed by nucleophilic attack

References :

[1] a) Kaplan, L.; Pavlik, J. W.; Wilzbach, K. E. *J. Am. Chem. Soc.* **1972**, 94, 3283. b) Ling, R.; Yoshida, M.; Mariano, P. S.; *J. Org. Chem* **1996,** *61*, 4439-4449.

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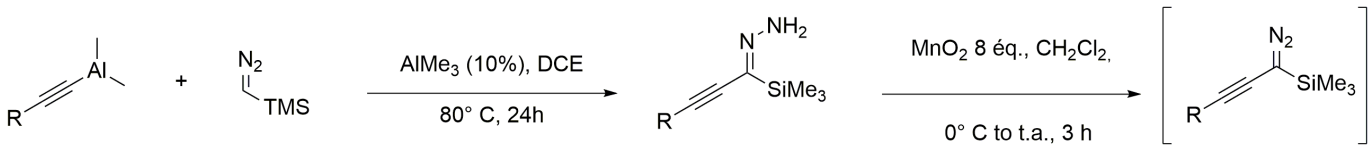
Poster n°10

Rapid and Effective Synthesis of α-Acyloxy-α-alkynyltrimethylsilanes

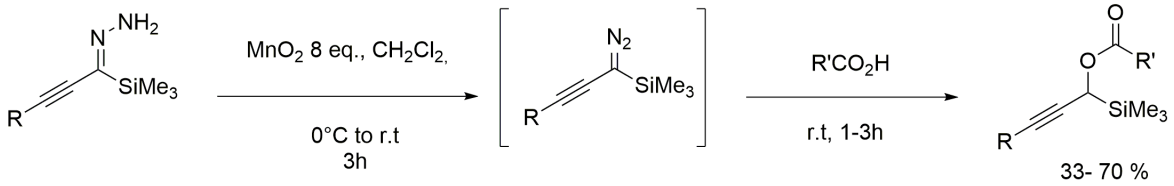
Tuan ZHAO,[1] Riccardo PICCARDI, [1] Laurent MICOUIN[1]

[1]Laboratoire de Chimie et Biochimie Pharmacologique et Toxicologique, UMR 8601 CNRS-Université Paris-Descartes, Faculté des Sciences Fondamentales et Biomédicales, 45 rue des Saints-Pères, 75006
tuan.zhao@etu.parisdescartes.fr

Our group is interested in investigating the reactivity of dimethylalkynyl aluminum reagents. In this context, we have recently showed that trimethylsilyl (TMS) diazomethane can react with alkynylaluminum reagents in an unreported manner to form unusual α-silylated alkynyl hydrazones. Such compounds can be easily oxidized into the corresponding α-silylated diazoalkynes under mild conditions.[1,2] The α-silylated diazoalkynes have never been described so far and show an intriguing reactivity.



We report here the reaction of these stable diazo species with different carboxylic acid derivatives to generate valuable α-acyloxy- α-alkynyl-trimethylsilanes.[3] This procedure avoids the delicate preparation and manipulation of unstable α-hydroxy propargyltrimethylsilanes. [4,5]



The isolated products can be employed as useful synthetic intermediates in a variety of transformations. We describe here their use as precursors in the synthesis of allenes.

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Poster n°11

Formation of low-valent Fe^0 and Fe^I species in Fe-catalyzed cross-coupling chemistry : key role of ate-Fe^{II} intermediates

Lidie ROUSSEAU[1,2], Christian HERRERO[3], Martin CLEMANCEY[4], Arnaud IMBERDIS[1], Geneviève BLONDIN[4], Jean-Marc LATOUR[4] and Guillaume LEFEVRE*[1,2]

[1] LCMCE, NIMBE, CEA, CNRS, Univ. Paris-Saclay, 91191 Gif, France
lidie.rousseau@cea.fr ;
[2] CSB2D, Institute of Chemistry for Life and Health Sciences, Chimie ParisTech, PSL University, CNRS, 75005 Paris, France ;
[3] ICMMO, Univ. Paris-Saclay, 91405 Orsay, France ;
[4] LCBM, pmb, Univ. Grenoble Alpes, CEA, CNRS, 38000 Grenoble, France

Ate-iron(II) species such as $[Ar_3Fe^{II}]^-$ (Ar = aryl) are key intermediates in Fe-catalyzed cross-coupling reactions between aryl Grignard reagents (ArMgX) and organic electrophiles.[1] They can be active species in the catalytic cycle,[2] or lead to Fe^0 and Fe^I oxidation states. These low oxidation states were shown to be catalytically active in some cases, but they mostly lead to unwished organic byproducts.[3,4]
This works relates a study of the evolution of $[Ar_3Fe^{II}]^-$ complexes towards Fe^0 and Fe^I oxidation states, through ^1H NMR, EPR and ^{57}Fe-Mössbauer spectroscopies, as well as DFT calculations, so as to discuss the role of both steric parameters and spin states in the reduction processes. Such mechanistic insights give a better understanding of iron-catalyzed C-C bond formation reactions, and can be exploited in the design of new ligands in order to selectively obtain a sole iron oxidation state in a catalytic process.

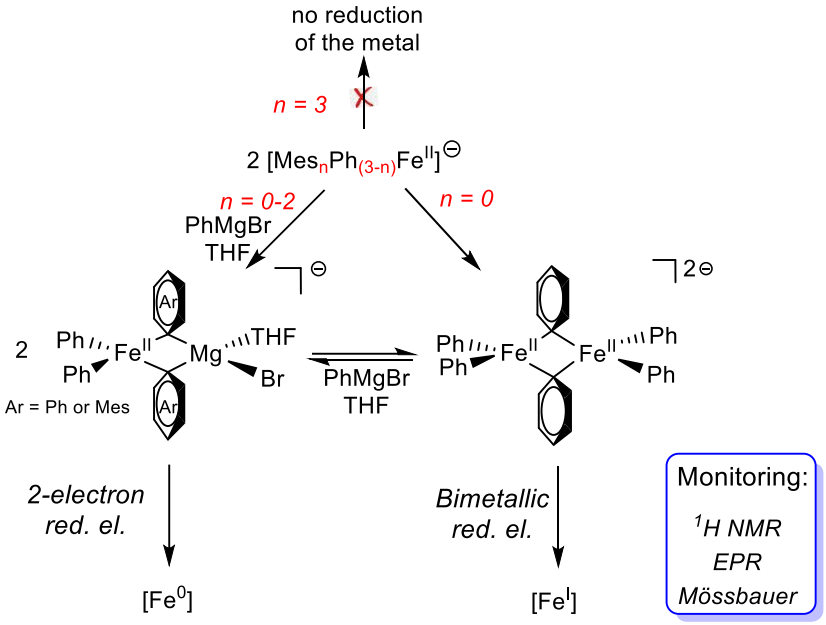

Figure: Pathways connecting ate-Fe^{II} (Mes = 2,4,6-trimethylphenyl) species with Fe^0 and Fe^I oxidation states

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Poster n°12

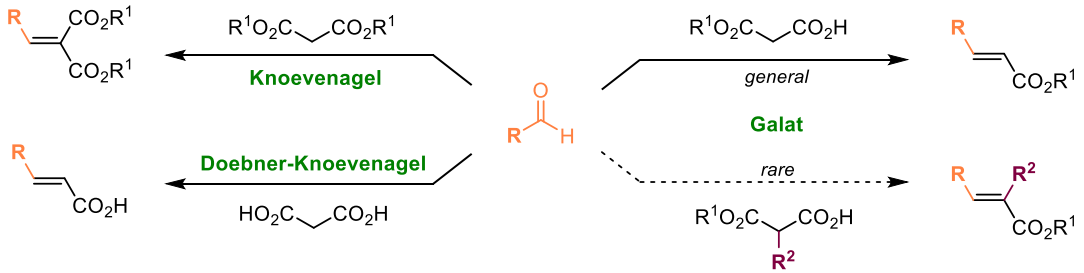
Eco-compatible synthesis of trisubstituted olefins via Galat reaction

Tania XAVIER, [1] Sylvie CONDON, *[1] Christophe PICHON, [1] Erwan LE GALL, [1] and Marc PRESSET*[1]

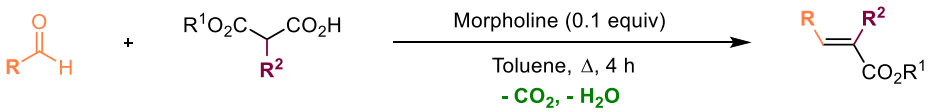
[1] Electrochimie et Synthèse Organique, ICMPE (UMR 7182), CNRS, UPEC, 2-8 rue Henri Dunant, F-94320 Thiais, France
xavier@icmpe.cnrs.fr

The olefination of aldehydes is one of the most fundamental reactions in organic synthesis. Indeed, it allows the preparation of an important motif found in various natural products and building blocks. Many methods have been elaborated for the stereoselective synthesis of disubstituted olefins, the most common relying on the use of the Wittig reaction and its derivatives and,[1] in a lesser extent, the Julia reaction.[2] Despite their efficiencies, all these reactions lead to the formation of stoichiometric amounts of useless byproducts.

Alternatively, the use of Knoevenagel-type reactions is a greener and powerful method for the construction of substituted acrylate derivatives.[3],[4] One of them was reported by Alexander Galat in 1946.[5] In his work, he described the direct synthesis of substituted acrylates by condensation of aldehydes and malonic acids half oxyester (MAHO). This reaction constitutes an attractive alternative to the classical Wittig reaction in terms of eco-compatibility, as the sole byproducts are H_2O and CO_2. However, the preparation of trisubstituted carbon-carbon double bonds using this method remains more challenging, as only isolated examples have been reported.



Herein, we present a general procedure for the olefination of aldehydes by substituted MAHO by means of a Galat reaction. This transformation, catalyzed by morpholine, is easy to set up, tolerates a broad range of substrates and affords an eco-compatible access to trisubstituted olefins.



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Poster n°13

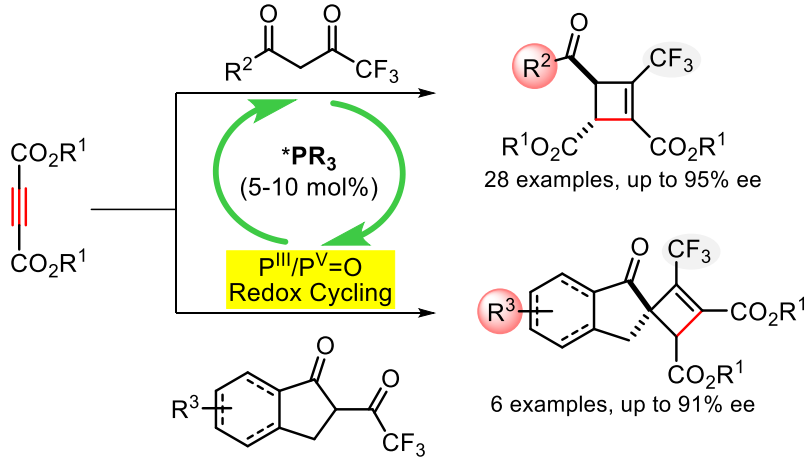
Catalytic and asymmetric process via P^{III}/P^{V}=O redox cycling: Access to (trifluoromethyl)cyclobutenes with a γ–Michael addition/Wittig olefination reaction

Charlotte Lorton, Thomas Castanheiro and Arnaud Voituriez

ICSN, CNRS UPR 2301, Université Paris-Sud, Université Paris-Saclay, 1 av. de la Terrasse, 91198 Gif-sur-Yvette, France
charlotte.lorton@cnrs.fr

Phosphines play a crucial role as stoichiometric reagents in a variety of reactions, daily used in organic synthesis (*e.g.* Wittig, Staudinger and Mitsunobu transformations). Despite their usefulness, these venerable reactions suffer from several drawbacks; in particular the concomitant formation of a stoichiometric quantity of phosphine oxide and the limitation to the formation of achiral or racemic compounds.[1] In an effort to address these concerns, the first Wittig reaction, catalytic in phosphine, has been investigated by O' Brien *et al.* in 2009. [2] Five years later Werner *et al.* developed a desymmetrisation of prochiral ketone, using a Wittig reaction, with moderate results in terms of yield and/or enantiomeric excess.[3]

In the present study, we report an efficient and highly enantioselective phosphine-catalyzed process via in situ phosphine oxide reduction, for the synthesis of chiral (trifluoromethyl)cyclobutenes (28 examples, up to 95% ee). Using the same methodology, CF_3-spirocyclic derivatives were also synthesized (6 examples, up to 91% ee).[4]



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[4]. Lorton, C.; Castanheiro, T. Voituriez, A. *Submitted.*

Poster n°14

Synthesis and peptide coupling studies of cyclic analogues of *S*-methyl-*L*-cysteine

Zeynab Imani,[1] Sylvie Robin,[1,2] David J. Aitken[1]

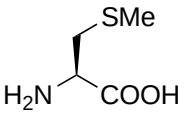
[1] ICMMO, Université Paris–Sud, Université Paris Saclay, Orsay, France ; [2] Université Paris- Descartes, UFR Sciences Pharmaceutiques et Biologiques, Paris, France

zeynab.imani@u-psud.fr

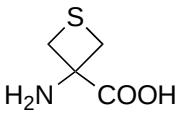
Nature makes use of a number of low-molecular weight sulfur-containing compounds including biotin, lipoic acid, S-methyl-methionine, glutathione and of course the proteinogenic α-amino acids methionine and cysteine.[1] A closely-related sulfur-containing α-amino acid is *S*-methyl-*L*-cysteine.[2] This metabolite is found in a number of plants including garlic, and it has been suggested that such organosulfur compounds may contribute to the antioxidant properties and health benefits of garlic as a foodstuff.[3]

As part of a program of studies focused on the behavior of conformationally-restricted analogues of sulfur-containing α-amino acids, we required a viable synthetic access to N- and C-capped derivatives of three cyclic analogues of *S*-methyl-*L*-cysteine: 3-aminothietane-3-carboxylic acid (Attc), 3-aminothiolane-3-carboxylic acid (Atlc) and 3-aminothiane-3-carboxylic acid (Atc).

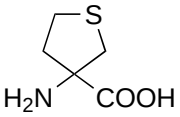
Taking the lead from some literature precedent,[4] we have investigated and optimized a synthetic approach based on a Bucherer-Bergs reaction conducted on the corresponding cyclic ketone precursors. In this presentation we will describe the details of this synthetic method and its application to the target N- and C-capped derivatives. We will also present our observations on peptide coupling reactions of Attc with a view to obtain short oligomers of this challenging α-amino acid.[4]



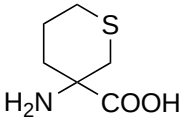
S-methyl-L-cysteine



Attc



Atlc



Atc

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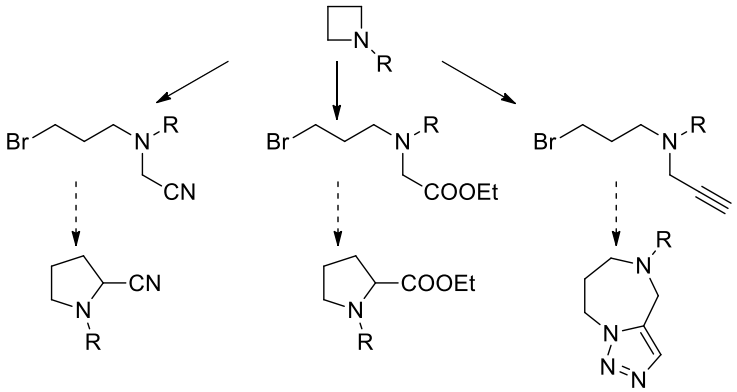
Poster n°15

Azetidine ring opening by electrophiles

Melvin RAULIN,[1] Karen WRIGHT,[1] Bruno DROUILLAT,[1] and François COUTY [1]

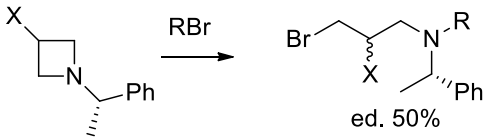
[1] Institut Lavoisier de Versailles, UMR 8180, Université de Versailles St-Quentin-en-Yvelines, Université Paris Saclay, 45 av. des Etats-Unis, 78035 Versailles Cedex, France
melvin.raulin@uvsq.fr

Azetidines are valuable substrates for the discovery of new reactions involving either ring-expansions or ring-cleavages due to their inherent ring-strain. We recently investigated the reaction of azetidines with cyanogen bromide, [1] and the conversion of the resulting cyanamides to guanidines.[2] During the course of this study, it was noted that benzyl bromide was also able to open the azetidine ring.[3] Screening of other electrophiles (eg bromoacetonitrile, bromoethyl acetate, allyl bromide, propargyl bromide) with a panel of substituted azetidines provided 3-halo-1-amino propane derivatives suitable for further derivatisation. Triazoloazepanes and α-substituted pyrrolidines could be obtained from these intermediates.



Ring opening of azetidines by electrophiles, and derivatisation of the resulting products

Moderate stereoselectivity in the ring opening of a 3-hydroxyl azetidine by cyanogen bromide was also observed. This selectivity could be improved by changing the 3-substituent of this derivative, to give enantio-enriched 3-bromo-2-substituted alkyl amines.



Stereoselectivity in the ring opening of 3-substituted azetidines

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Poster n°16

Synthesis of Planar-Chiral [2.2]Paracyclophane-based "3D Prodan"

Simon FELDER,[1] Marie-Leonie Delcourt,[1] Erica Benedetti,[1] and Laurent Micouin[1]

[1] Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques - UMR8601 CNRS, Université Paris Descartes, 45 rue des Saints Pères, 75006 Paris
ldsimon.felder@gmail.com

Since their discovery in 1949 by Brown and Farthing,[1] [2.2]paracyclophane (pCp) and its derivatives have attracted increasing attention due to their interesting three-dimensional architecture and peculiar reactivity. pCps present indeed a rather unique structure, which incorporates two benzene rings parallel in space and connected by two ethylene bridges in *para* position (Figure 1).[2] These geometrical constraints lead to transannular π–π ınteractions that confer on paracyclophanes intriguing spectroscopic properties.[3] As a result, these molecules can be employed to access new organic dyes and probes. In this context, our group become interested in the development of flexible strategies to prepare novel families of compact 3D fluorophores incorporating the paracyclophane scaffold.[4]

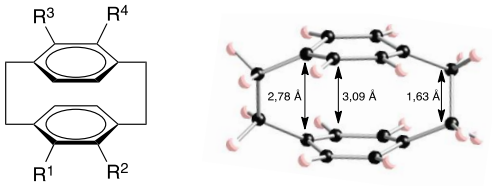
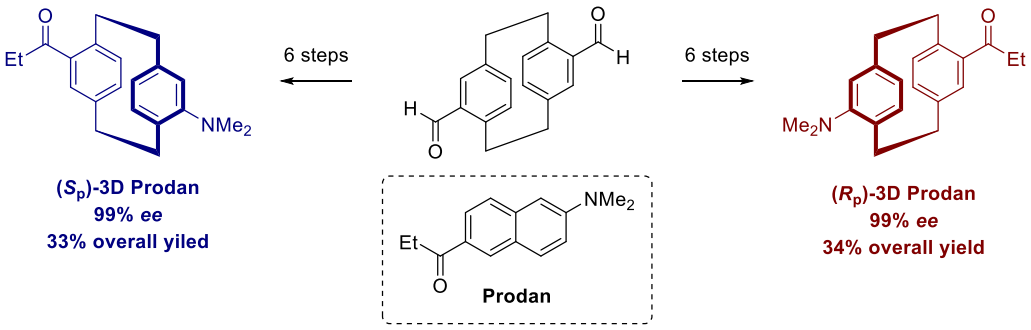


Figure 1. Structure of [2.2]paracyclophanes

Herein we present the synthesis of both enantiomers of a pCp-based analogue of Prodan, a well-known solvatochromic dye (Scheme 1).[5] The optimized synthetic procedure involves an asymmetric transfer hydrogenation (ATH) as the key step.[6] The new compounds show an enhanced solvatochromism in comparison with Prodan. Further studies on the chiroptical properties of the chiral "3D Prodan" derivatives (circular dichroism and circularly polarized luminescence) are on the way.



Scheme 1. Synthesis of enantiopure pCp-based 3D Prodan derivatives

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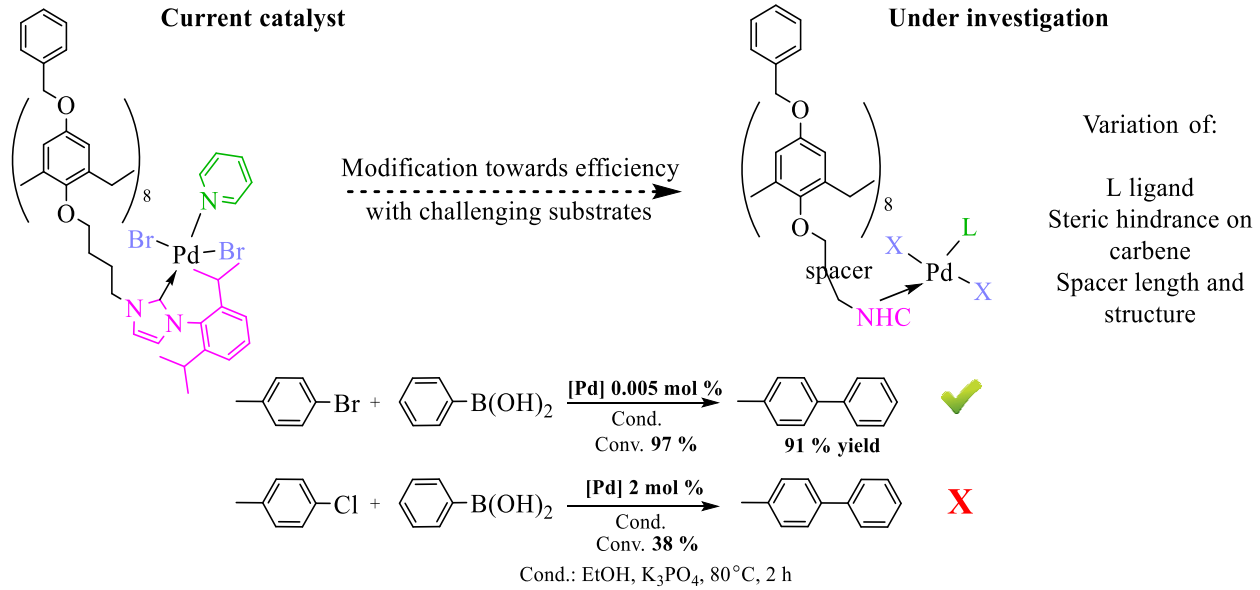
Poster n°17

Highly efficient NHC-Pd macrocyclic filterable catalysts

Sandra ABI FAYSSAL,[1,2] Ibrahim ABDELLAH,[3] Pauline KASONGO,[3] Axel LABATTUT,[3] Emmanuelle SCHULZ,[1] Cyril MARTINI[2,3] and Vincent HUC[3]

[1] LCM-ICMMO, Bât 420, Université Paris-Saclay, 15 rue G. Clémenceau, 91405 ORSAY CEDEX; [2] Novecal, Orsay;
[3] LCI-ICMMO, Bât 420, Université Paris-Saclay, 15 rue G. Clémenceau, 91405 ORSAY CEDEX
sandra.abifayssal@u-psud.fr

Catalysis is ubiquitous in fine chemistry. When organometallic complexes are used, one of the main challenges for industry is the metal removal in order to avoid the contamination of final products. This led to the development of filterable supported catalysts allowing for an efficient metal elimination. However, these catalysts suffer from a dramatically decrease in their activity as well as a lack of reproducibility, which is incompatible with the industrial applications. In this context, PEPPSI palladium complexes, as easily handled and very stable precatalysts,[1] were successfully attached on benzyloxycalix[8]arenes macromolecules[2] by our group. These NHC-Pd supported catalysts combine both heterogeneous (filterable) and homogeneous (high TON/TOF, reproducibility) catalysis features.[3] Their performances were mainly studied in Suzuki cross coupling, since it is a very powerful reaction widely used in both academic and industrial syntheses. Here, we describe our work in improving these catalysts to enhance their reactivity in the Suzuki reaction (especially with chlorinated substrates) but also test them in other important, widely used transformations. In this context, the substitution of the L ligand as well as the modification of the spacer length and the carbene steric hindrance are under investigation.[4]



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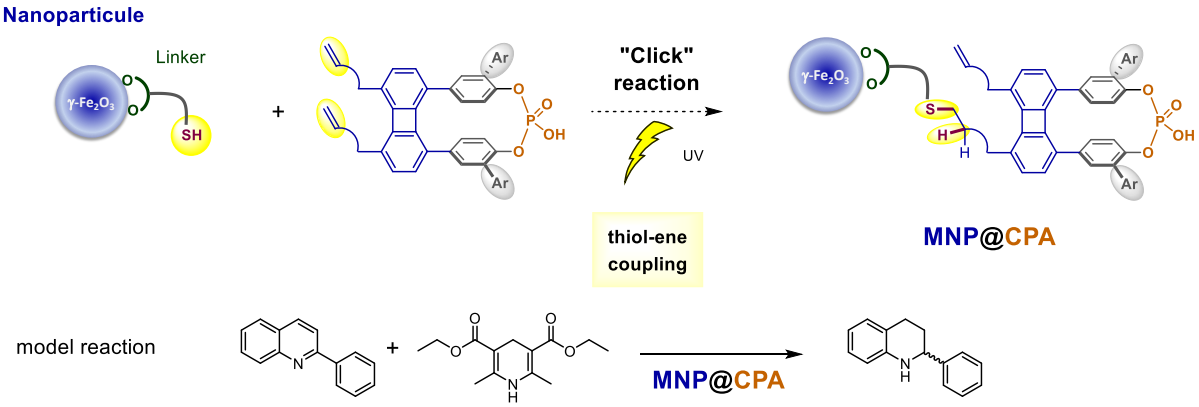
Poster n°18

Synthesis of Recyclable Asymmetric Organocatalysts with Brønsted Acid Function Linked on Magnetic Iron Nanoparticules

Sébastien THUEILLON[1,3], Erwann GUENIN[2], Jean-François BETZER[3], Angela MARINETTI[3], Joëlle PERARD[1]

[1]UMR 8038, CiTCoM, Faculté de pharmacie, CNRS, Université Paris Descartes, 4 avenue de l'observatoire, Paris
[2]TIMR, UTC, rue Roger Coutolenc, Compiègne
[3]ICSN, CNRS, 1 avenue de la terrasse, Gif-sur-Yvette
sebastien.thueillon@cnrs.fr

Asymmetric organocatalysis has proved to be an efficient way to obtain chiral multifunctional compounds rapidly and with good enantiomeric selectivity. Since the first work of Terada and Akiyama in 2004, using Chiral Phosphoric Acid (CPA), a wide range of methodologies and catalysts have been developed.[1]
Even so these CPA are strong tools used on a large variety of reactions, there is still room for improvement: these organocatalysts can only be obtained either with a large number of steps or a rather expensive price, and their catalytic loading is still pretty high (usually between 5 to 10 mol%). Recovery of the catalyst by chromatography purification led to the adventitious formation of the related sodium or calcium salts.[2]
In this work, we propose the use of magnetic iron nanoparticules, easy to obtain and with low toxicity, to be able to retrieve our catalyst, either BINOL-based (axial chirality) or 1,8-biphenylenediyl-based (planar chirality).[3] It has already be proved in the literature that due to this particules a catalyst can be reused up to 10 times and a simple magnet is needed in order to achieve that goal.[4]



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Poster n°19

NHC-Capped Cyclodextrins (ICyDs) for Copper-Catalyzed Carboboration Reactions

Zhonghang WEN,[1] Yongmin ZHANG,[1] Sylvain ROLAND,[1] Matthieu SOLLOGOUB[1]

[1] *Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire (UMR 8232), Paris, France.*
Zhonghang.wen@gmail.com

Association of a metal with a cavity is an efficient way to promote selectivity in catalytic processes. Our group was able to encapsulate a metal into the cavity of a cyclodextrin (CD) through capping of the cyclodextrin with a NHC ligand.[1] This capping induced a deformation of the cavity, and this new shape allowed to perform stereoselective gold-catalyzed cycloisomerisation reactions.[2] It also allowed regioselective copper-catalyzed hydroboration. Interestingly, the regioselectivity of this reaction was found to be governed by the size of the cavity. [3]

To further expand the scope of this new family of CD-NHC-based catalysts called ICyDs, we studied the copper-catalyzed carboboration reaction. We found that the cavity could enhance the regioselectivity of intermolecular alkylboration reactions. For intramolecular carboboration reactions, we accidentally found that CD-NHC or "classical" NHC ligands promote the formation of the unexpected six-membered ring together with the expected five-membered compound.[4]

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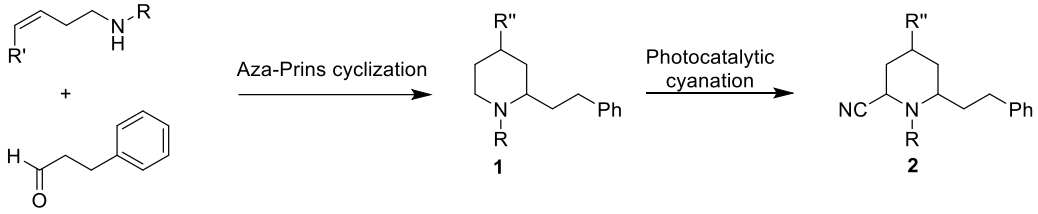
Poster n°20

PHOTOCATALYTIC CYANATION OF PIPERIDINE DERIVATIVES

Armando TALAVERA-ALEMAN, Guillaume DAGOUSSET, Christine THOMASSIGNY and Christine GRECK

Université de Versailles Saint-Quentin-en-Yvelines, ILV, UMR CNRS 8180, 45 avenue des Etats-Unis, 78035 Versailles Cedex, France.
Armando.talavera@uvsq.fr

The piperidine ring is very common in natural products, compounds that have this heterocycle display interesting biological activities as antioxidant, antibacterial, or anticancer.[1] In this context, different methodologies have been developed to synthetize piperidine derivatives.[2]
Photoredox catalysis has become an important approach in organic chemistry to modify small molecules, and it represents an economical and environmentally friendly methodology.[3]
In this work, we describe the synthesis of piperidines **1** by aza-Prins cyclization reaction, and their cyanation by photoredox catalysis, by the addition of the -CN group to the less substituted carbon in α of the nitrogen atom, to obtain **2**.



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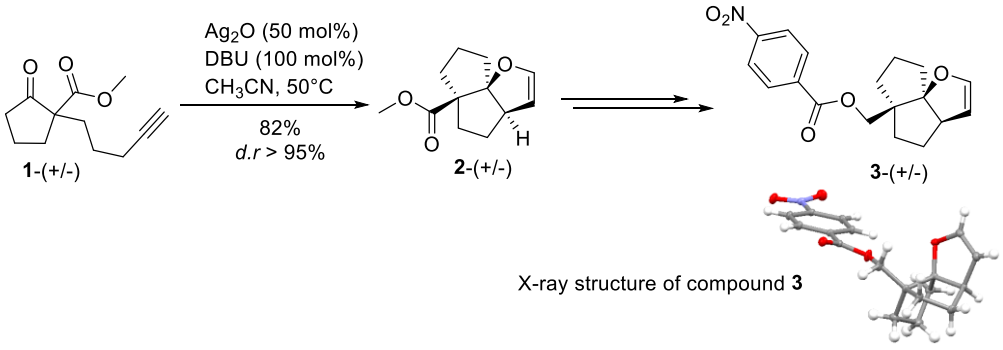
Poster n°21

Silver Oxide (I) promoted unique [3+2] carbocyclization

Bao YU,[1] Luca ALLIEVI,[1] Anna PERFETTO,[2] Ilaria CIOFINI,[2] Marie-Isabelle LANNOU,[1] Janick ARDISSON[1] and Geoffroy SORIN [1]

[1] Synthesis and Methods UMR 8038 CiTCoM, Faculty of Pharmacy, 4 Av. de l'Observatoire 75006 PARIS
[2] Theoretical Chemistry and Modelling UMR 8247 – Chimie ParisTech, PSL University, 11 rue Pierre et Marie Curie 75231 PARIS
yeb2017@hotmail.com

Intra- or intermolecular [3+2] cycloadditions are powerful tools for the efficient access to various 5-membered rings, which are widely represented in pharmaceuticals and natural products.
In this field, the vast majority of transformations, available in the chemist's toolbox, implies hetero 1,3-dipolar reagents or their synthetic equivalents, allowing access to a broad variety of heterocyclic compounds.[1] However, the synthesis of carbocycles, by this type of cycloaddition, is hampered by the difficulty to generate all carbon 1,3-dipoles rendering these reactions more challenging.[2]
To overcome this issue, the activation of alkenes or alkynes by transition metals appears a compelling alternative. In this field, "coinage metals" (Cu, Ag and Au), due to their strong alkynophilicity, have quite recently highlighted their efficiency in carrying out such cyclization.[3]
Herein, we present an unprecedented [3+2] cyclization promoted by silver oxide (I) leading to complex and congested molecules from readily available or easily synthesizable substrates (Scheme 2). The reaction is broad in scope and medium to good diastereoselectivities (up to 95/5) are obtained. [4]



Scheme 2

Finally, in order to shine light on the reaction mechanism, calculations based on Density Functional Theory were performed.

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Poster n°22

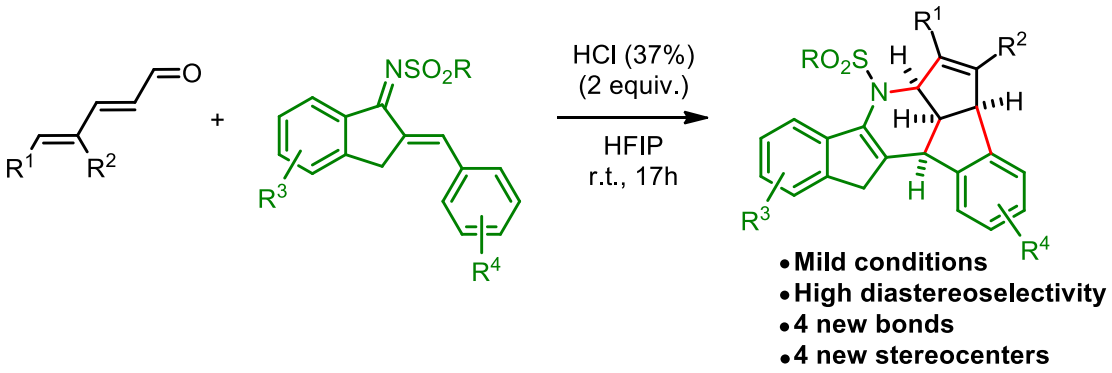
iso-Nazarov initiated diastereoselective cascade polycyclization

T.Duhail,[a] A.-S. Marques, [a] I. Chataigner,[b] V. Coeffard,[c] G. Vincent[d] and X. Moreau[a]

[a] ILV, UVSQ, Université Paris Saclay, UMR CNRS 8180, Versailles
[b] COBRA, UNIROUEN, Normandie Univ, UMR CNRS 6014, Rouen
[c] CEISAM, Université de Nantes, UMR CNRS 6230, Nantes
[d] ICMMO, Univ. Paris-Sud, Université Paris-Saclay, UMR CNRS 8182, Orsay

thibaut.duhail@uvsq.fr

Constructing molecular complexity and diversity from simple and readily available substrates is still pursued by the synthetic community. The development of domino polycyclizations[1] is one of the most appealing strategies to generate intricate polycyclic scaffolds in a single operation. In our continuous effort to explore efficient transformations of unsaturated aldehydes toward polycyclic architectures, we recently investigated this strategy by engaging 2,4-dienals[2] in the interrupted iso-Nazarov cyclization[3]. In this novel sequence, we envisioned that indanone-derived-α,β-unsaturated imines could react with a transient intermediate formed during the iso-Nazarov cyclization of 2,4-dienals. This approach affords fused hexacyclic ring systems bearing four contiguous stereogenic centers.



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Poster n°23

Heterogenization of chiral salen complexes used in asymmetric catalysis

M. Abd El Sater [a,b], I. Abdellah [b], N. Jaber [a] and E. Schulz [b]

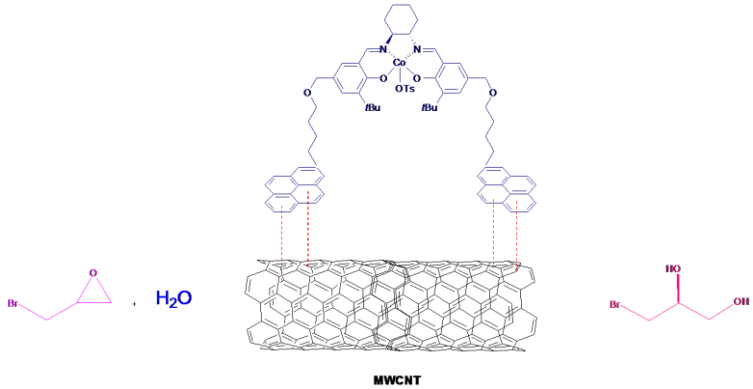
[a] Laboratoire de chimie médicinale et des produits naturels, Université Libanaise, Faculté des Sciences (I) et PRASE-EDST, Hadath, Beyrouth, Liban

[b] Equipe de Catalyse Moléculaire, Univ. Paris-Sud, ICMMO, UMR 8182, Orsay, F-91405, France

mariam.a.sater@outlook.com , emmanuelle.schulz@u-psud.fr

One of the challenges of asymmetric catalysis is to perform a sequence of several transformations in a single pot process to yield highly functionalized enantioenriched products. Furthermore, heterogenization of separate catalytic systems can induce, by their proximity, a desired cooperativeness or complementarity. [1]

Salen-type chiral complexes are widely known as versatile enantioselective catalysts in the field of asymmetric catalysis, according to combined metal, they catalyze various asymmetric reactions [2]. In this context and in accordance with the concept of green chemistry, the objective of this project is to perform structural modifications on these complexes to ensure their immobilization on carbon supports via non-covalent π-stacking interactions.



Thus, salen complexes of cobalt tagged with pyrene groups, providing non-covalent interaction with carbon based support [3], are synthesized and tested in the hydrolytic dynamic kinetic resolution reaction of epibromohydrin under homogeneous and heterogeneous conditions. The pyrsalen complex Co (III) -OTs immobilized on multiwall carbon nanotubes showed a good enantioselectivity associated with a high yield. Likewise, this catalyst, once recycled, has shown enhanced performance.

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Poster n°24

Catalyst-free cycloaddition of 1,3-diene-1-carbamates with azodicarboxylates: a rapid click reaction

Thomas VARLET,[+] Guillaume LEVITRE,[+] Pascal RETAILLEAU and Géraldine MASSON

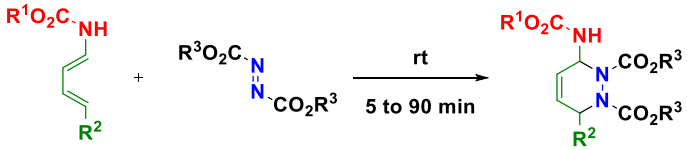
Institut de Chimie des Substances Naturelles CNRS, Universite Paris-Sud, Universite Paris-Saclay, 1 Avenue de la Terrasse, 91198 Gif-sur-Yvette Cedex, France

thomas.varlet@cnrs.fr

[+] *These authors contributed equally to this work*

Click chemistry has become a powerful chemical tool in various research areas such as organic chemistry,[1] drug discovery[2] or chemical biology.[3] As defined by Sharpless,[4] click chemistry encompasses *a chemical toolkit of simple, efficient and high yielding reactions that can be performed under mild conditions.* Click methods based on a Diels–Alder cycloaddition are gaining popularity since this reaction has the ability to form, modify and control the structure of materials on various length scales. However, the generation of a reactive diene–dienophile pair often requires either thermal activation or the use of catalysts for the activation of dienophiles.[5]

In this context, we have developed a catalyst-free [4+2] cycloaddition of 1,3-diene-1-carbamates with azodicarboxylates[6] that is tolerant of a variety of functional group. The reaction occurs in excellent yields and broad scope, and is complete on the minute time scale using easily accessible starting materials.



- Simple and efficient reaction
- Mild conditions
- High yields
- No byproducts
- Wide functional group tolerance
- Broad substrate scope

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Poster n°25

Photooxygenation of 2-Propargylfurans: a Path to Structural Diverse Nitrogen-Containing 5-Membered Rings

Guillaume FORCE,[1] Lucile MARIN,[1] Régis GUILLOT,[1] Vincent GANDON,[1] Emmanuelle SCHULZ,[1] and David LEBOEUF[1]

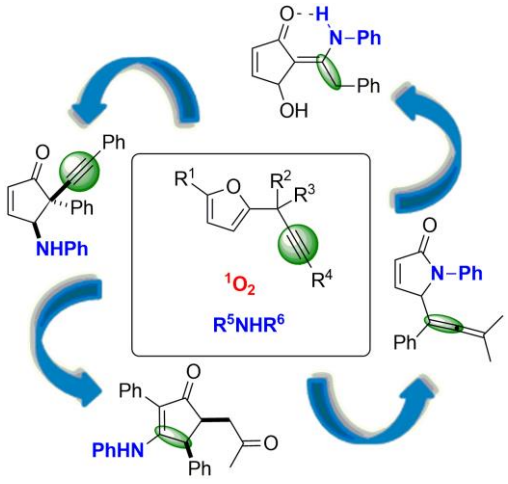
[1] Institut de Chimie Moléculaire et des Matérieux d'Orsay (ICMMO), CNRS UMR 8182, Université Paris-Sud, Université Paris-Saclay Bâtiment 420, 91405 Orsay cedex.

guillaume.force@u-psud.fr david.leboeuf@u-psud.fr

Furans are amongst the most versatile building blocks in organic synthesis. And, one of the major reasons is the ease with which the C-O bonds can be cleaved, creating an avenue for a bountiful variety of poly(hetero)cyclic scaffolds depending on the substrate pattern, the reactions conditions and the reaction partners employed. Moreover, the interest for furan derivatives lies in the fact that their usual precursors, furfural and 5-hydroxymethylfurfural, can be directly obtained from inexpensive biomass derived carbohydrates such as cellulose and hemicellulose. In that respect, the photooxygenation of furans is particularly appealing as this transformation relies on the simple utilization of singlet oxygen ($^1O_2$),[1] which can be generated from ground state triplet oxygen by visible light in the presence of trace amounts of a suitable photosensitizer (rose bengal, methylene blue, tetraphenylporphyrin, etc.).

As part of our interest in the reactivity of furans,[2] we reflected on the limits of this process, especially, whether it might be feasible to change the outcome of this reaction sequence to pave the way for a broader structural diversity.

To accomplish this goal, we turned our attention to 2-propargylfurans, which had never been explored with respect to photooxygenation. Herein, we demonstrate that a novel strategy for the synthesis of diverse nitrogen-containing cyclopentenones can be implemented through a subtle design of substrates.



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Poster n°26

Enantioselective Synthesis of *trans*-Cyclopentene Catalyzed by Bifunctional *N*-Heterocyclic Carbene/Thiourea Catalysts

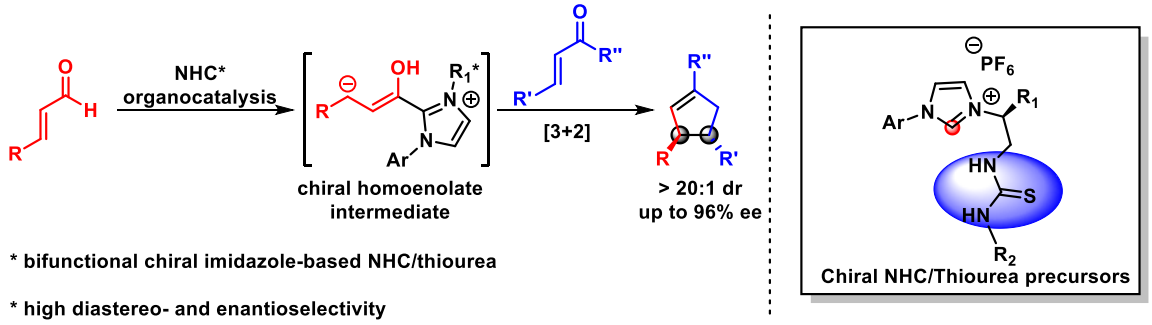
Zhiwei JIANG,[1] Chloée BOURNAUD,[1] Martial TOFFANO,[1] and Giang VO-THANH [1]

[1] Equipe de Catalyse Moléculaire, Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO), Université Paris-Sud, CNRS, Université Paris-Saclay, 91405 Orsay Cedex, France

Zhiwei.jiang@u-psud.fr

N-Heterocyclic Carbene (NHC)-based catalysis represent a very well documented field in asymmetric organocatalysis. In particular, the strong ability of NHCs to produce a variety of reactive intermediates, such as Breslow intermediates, acyl azoliums, α,β-unsaturated acyl azoliums, homoenolate equivalents, azolium enolates, and azolium dienolates, which facilitates the development of a variety of reaction modes. [1] Moreover, the design and synthesis of novel chiral NHC have been a challenging task in the field of asymmetric NHC-catalysis and receiving extensive attention. However, the type of chiral imidazole-based NHC still has limited attention, to the best of our knowledge, multifunctional carbene has been few reported so far.

Herein, we described an efficient strategy for the synthesis of a series of chiral imidazole-based bifunctional *N*-heterocyclic carbene/thiourea precursors. The corresponding NHCs were evaluated in asymmetric organocatalytic processes. *Trans*-1,3-(*S*),4-(*S*)-trisubstituted cyclopentenes were constructed from enals and chalcones via a homoenolate intermediate generated from addition of NHC to enal.[2] The presence of thiourea moiety and catechol improved notably the reactivity and enantioselectivity through hydrogen-bond interactions.



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Poster n°27

Understanding the catalytic carbonylation of epoxides for the valorization of carbon monoxide

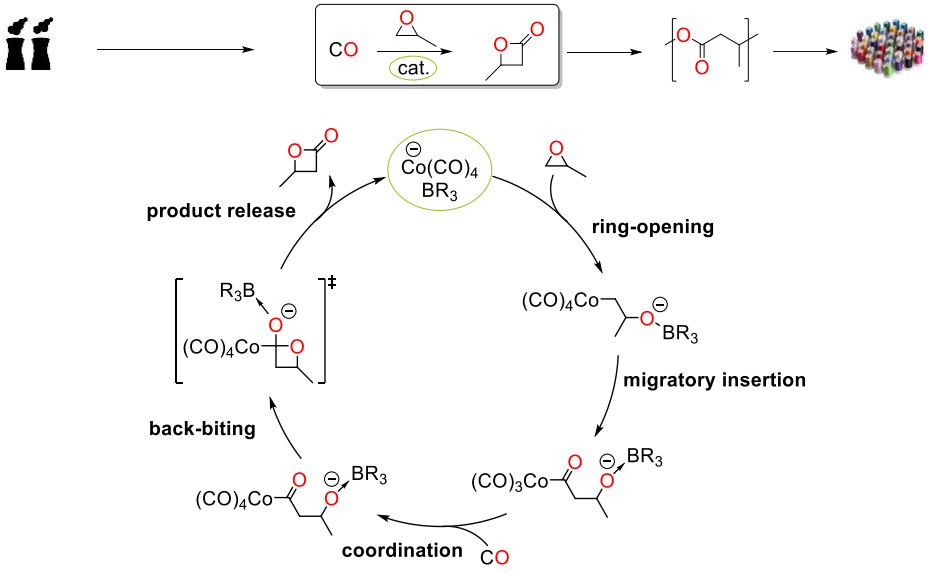
Louise PONSARD,[1] Emmanuel NICOLAS,[1] Thibault CANTAT[1,*]

[1] NIMBE, CEA, CNRS, Université Paris-Saclay, CEA Saclay, 91191 Gif-sur-Yvette cedex, France
louise.ponsard@cea.fr

Small molecules released as gaseous wastes by the industries, such as CO and CO_2, are attractive C_1 building blocks for the production of chemicals. They can indeed reduce our dependence on fossil feedstocks. The catalytic insertion of carbon dioxide into epoxides has been developed over the last decades for the production of cyclic and polymeric carbonates, with industrial success.[1] The same strategy can be used for the production of polyester from epoxides and carbon monoxide, possibly released from the production of steel.

The catalytic carbonylation of epoxides with gaseous CO leads to β-lactones and this reaction has attracted a particular attention over the past few years. Yet, only few catalytic systems have been developed, all containing a cobalt carbonyl complex assisted by a Lewis acid. [2][3][4][5]

Herein, we disclose the first theoretical study to understand the mechanism of carbonylation of epoxides using a cobalt catalyst with Lewis acids. The influence of the Lewis acidy on the activity was investigated through various boron compounds. The DFT calculations, linked with a Lewis acidity scale, can thus be used as a guide for the development of a novel catalytic system.



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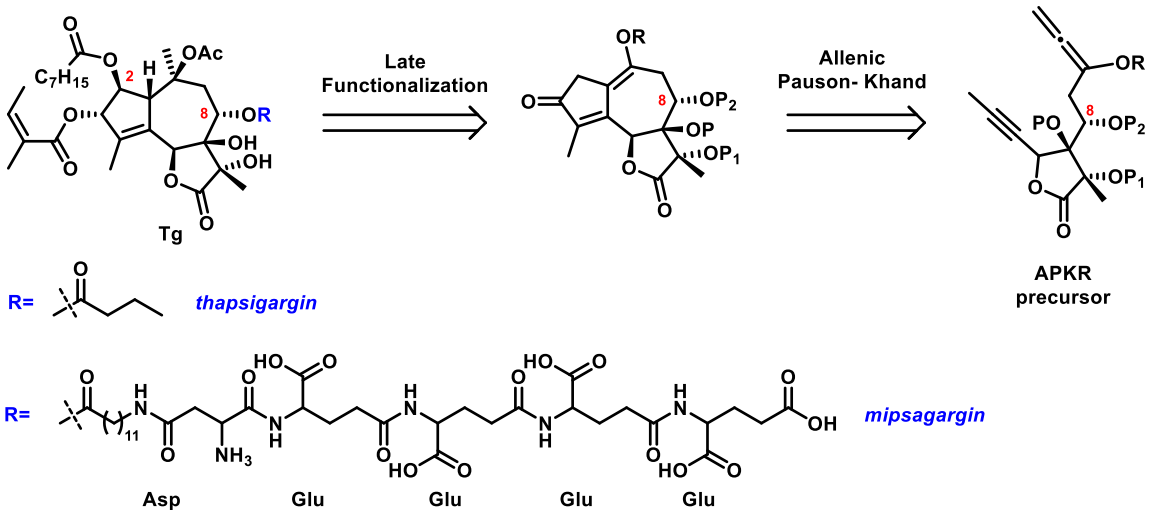
Poster n°28

Toward the Total Synthesis of Thapsigargin

Youssouf SANOGO,[1] Rajah BEN OTHMAN,[1] Florent BODINIER,[1] Marie-Isabelle LANNOU,[1] Geoffroy SORIN [1] and Janick ARDISSON [1]

[1] Synthesis and Methods UMR 8038 CiTCoM, Faculty of Pharmacy, 4 Av. de l'Observatoire 75006 PARIS
florent.bodinier@etu.parisdescartes.fr

Isolated from the mediterranean plant species *Thapsia garganica* (Apiaceae)[1], *thapsigargin* (*Tg*) is a highly oxygenated sesquiterpene lactone which belongs to the guaianolide family. Its interest towards treatment of prostate cancer is based on the potency of this compound as an inhibitor of the sarco/endoplasmic reticulum calcium ATPase (SERCA), which induces an increase in cytosolic calcium concentration and leads to apoptosis in almost all cells. *Tg* has been conjugated to peptides to produce suitable prodrugs which selectively kill prostate cancer cells. One of these prodrugs called *mipsagargin* is currently tested in clinical phase II.



We suggest that the *Tg* would be obtained through a key Allenic Pauson-Khand Reaction (APKR)[2,3] followed by a late functionalization to introduce the stereogenic center at C2 and the four esters. The synthesis of the APKR precursor will be discussed in due time.

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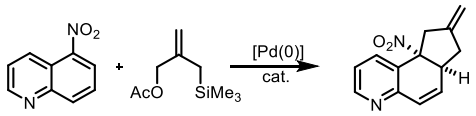
Poster n°29

Dearomatization of nitroindoles and nitrobenzofurans with vinylcyclopropanes by palladium(0)-catalyzed (3+2) cycloaddition

Johanne LING, Maxime LAUGEOIS, Véronique MICHELET, Virginie VIDAL and Maxime R. VITALE

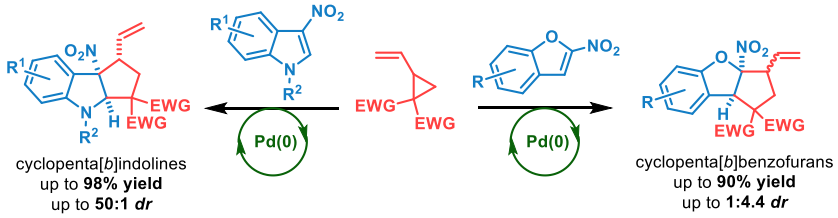
Institute of Chemistry for Life and Health Sciences (i-CLeHS) – Chimie ParisTech
11 Rue Pierre et Marie Curie, 75005 Paris
johanne.ling@chimie-paristech.fr

Dearomatization reactions represent powerful methods for building high molecular complexity and diversity starting from readily available feedstock materials such as arenes.[1-4] For this reason, tremendous efforts have been devoted to their development, notably by means of robust metal-based catalytic processes.[2] In this particular area of research, palladium catalysis has undeniably shown great potential.[3,4] Interestingly though, the vast majority of such catalytic transformations have so far capitalized on the nucleophilic character of electron-rich aromatic rings (phenols, anilines, indoles, etc.),[3] and the complementary palladium-catalyzed dearomatization of electron-deficient systems remained until very recently comparatively scarce.[4] In 2014, Trost *et al*. reached a significant milestone in this field by demonstrating that several nitroarenes including 5-nitroquinoline could undergo a formal (3+2) dearomative cycloaddition with a trimethylenemethane equivalent (Scheme 1).[4]



Scheme 1

In this area, in continuation of our interest for the use of vinylcyclopropanes (VCPs), we recently showed that electron poor nitroarenes could undergo a dearomative cycloaddition with this specific class of versatile all-carbon 1,3-dipole precursors. During the course of our studies, we could demonstrate that the desired reactivity could be reached when employing nitroindoles or nitrobenzofurans (Scheme 2).



Scheme 2

This efficient dearomative method could give access to a wide variety of cyclopenta[*b*]indolines and cyclopenta[*b*]benzofurans with good to excellent yields and variable levels of diastereoselectivity.[5]

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Poster n°30

Metal-free formylation of amines with CO_2 catalysed by NHC-capped cyclodextrines

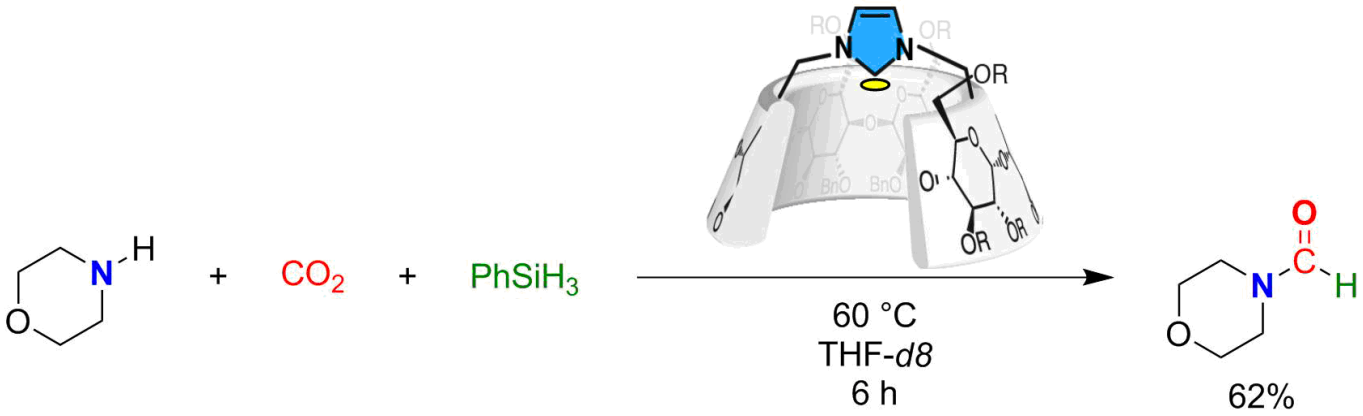
Clément HOARAU,[1] Kajetan BIJOUARD,[2] Lucile ANTHORE-DALION,[1] Matthieu SOLLOGOUB[2] and Thibault CANTAT[1]

[1] CEA, IRAMIS, LCMCE, UMR CNRS 3685, CEA/Saclay, 91191 Gif-sur-Yvette, France
[2] Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire, UMR 8232, 4 place Jussieu, 75005, Paris, France
clement.hoarau@cea.fr

The formylation of amines with CO_2 under mild pressure conditions has been extensively described employing a wide variety of transition-metal complexes as catalysts.[1a-e] The organocatalysis of this reaction has been described using Lewis bases such as nitrogen superbases,[2] ionic liquids,[3] organic salts[4] and *N*-heterocyclic carbenes.[5] The latter were described as being very efficient in this transformation, requiring only ambient temperature and pressure of CO_2.

New NHC based on α and β cyclodextrines were discovered[6] with the particularity of having a reactive site deep inside a cavity. This feature induces a steric hindrance further away from the reactive centre compared to regular NHCs, which makes them interesting objects of research in the field of catalysis.

Probing these unique catalysts on the formylation reaction promises new reactivity and selectivity owing to the different steric hindrance around the catalytic site of the carbene.



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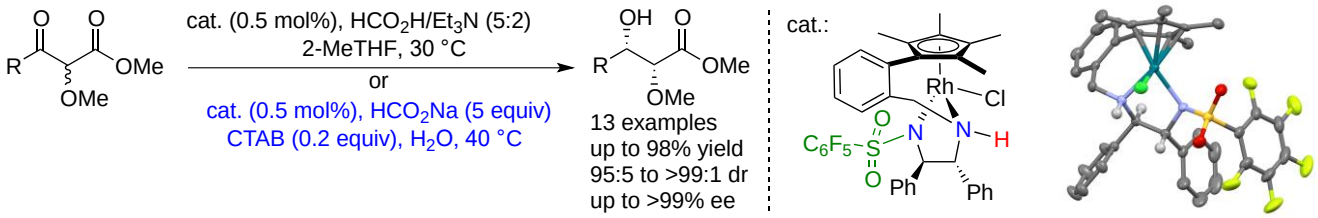
Poster n°31

Novel Rh(III)-Catalyzed Asymmetric Transfer Hydrogenation of α-Methoxy β-Ketoesters *via* DKR in Water: Toward a Greener Procedure

Bin HE, Longsheng ZHENG, Phannarath PHANSAVATH, and Virginie VIDAL

Institute of Chemistry for Health and Life Sciences (i-CLeHS) – Chimie ParisTech, 11 rue P. et M. Curie
75005 Paris
bin.he@chimie-paristech.fr

As part of our ongoing program aimed at developing efficient methods for the asymmetric reduction of functionalized ketones,[1] we recently developed the asymmetric transfer hydrogenation[2] of α-methoxy β-ketoesters using a new easy to-handle and air-stable *N*-pentafluorophenylsulfonyl-DPEN-based tethered rhodium(III) complex that operates under environmentally sound conditions. The reaction is efficient in 2-MeTHF with formic acid/triethylamine or in water with sodium formate. The corresponding *syn* α-methoxy β-hydroxyesters are obtained with high diastereoselectivities up to >99:1 dr and excellent levels of enantioselectivity up to >99:1 via a Dynamic Kinetic Resolution process.[3],[4]



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Poster n°32

Synthesis of Fluorescent Azafluorenones and Derivatives *via* a Ruthenium-Catalyzed [2 + 2 + 2] Cycloaddition

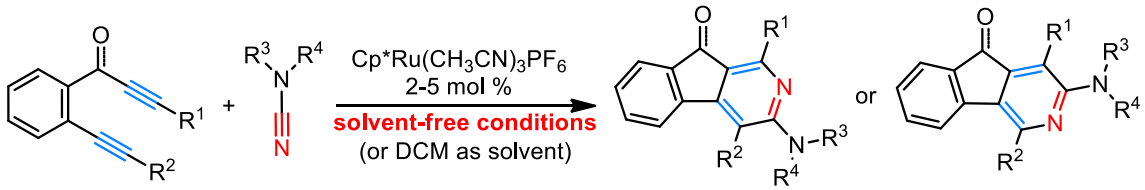
Christine TRAN,[1] Fei YE,[1] Ludovic JULLIEN,[2] Thomas LE SAUX,[2] Mansour HADDAD,[1] Véronique MICHELET[1,3] and Virginie VIDAL[1]

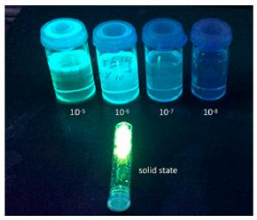
[1] PSL Research University, Chimie ParisTech, CNRS, Institute of Chemistry for Life and Health Sciences, 11 rue Pierre et Marie Curie, 75005 Paris, France
[2] PASTEUR, Chemistry Department, École Normale Supérieure, PSL University, Sorbonne University, CNRS, 75005 Paris, France
[3] Present address : University Côte d'Azur, Institut de Chimie de Nice, UMR 7272 CNRS, Parc Valrose, Faculté des Sciences, 06100 Nice, France

christine.tran@chimie-paristech.fr

Azafluorenones, azafluorenols and related compounds serve as privileged structures and constitute the central core of a variety of organic chemicals that have been found in natural products and biologically active molecules.[1]

As a continuation of our investigations on transition-metal-catalyzed [2 + 2 + 2] cyclisation,[2] an original and mild synthetic route for the preparation of novel azafluorenones and derivatives *via* a ruthenium mediated [2 + 2 + 2] cycloaddition of α,ω-diynes and cyanamides has been developed. This atom-economical catalytic process demonstrated remarkable regioselectivities to access fluorescent azafluorenone derivatives. The photophysical properties of azafluorenone derivatives have been evaluated, and photoluminescence phenomena at solid and liquid states have been highlighted.[3]





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Poster n°33

One pot Wittig reaction catalyzed by iron complexes from alcohols

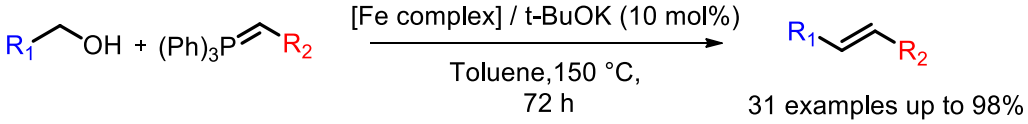
A. Djurovic [1], V. Gandon [2], C. Bour [3]

Équipe de Catalyse Moléculaire, ICMMO (UMR 8182), UPsud, Université-Paris-Saclay
Alexandre.djurovic@u-psud.fr

In 1979, the Wittig olefination was nobelized. It is widely used in organic synthesis for the preparation of alkenes from aldehydes or ketones and triphenylphosphonium ylides in stochiometric amount.[1] Wittig reactions and the exact nature of these species is commonly used to divide the Wittig reaction into three main groups, namely the ''classic'' Wittig reaction of phosphonium ylides, the Horner–Wadsworth–Emmons reaction of phosphonate anions, and the Horner–Wittig reaction of phosphine oxide anions. Each of these reaction types has its own distinct advantages and limitations. [2]

More recently, a domino reaction for C-C and C-H bonds formation was developed by Williams's team, where an iridium catalyst was used for dehydrogenation of alcohols, trapped with a phosphonium ylide then the corresponding alkenes were reduced into alkanes. [3] However, this domino process could not be interrupted for a simple access to the corresponding alkenes.

Recently in our team, an iron cyclopentadienone catalyst was used to promote ethylation of imines using ethanol as C_2 build-block. [4]
In this work, the same catalyst was used to oxidized various alcohols and directly trapped with triphenylphosphonium ylides in a one pot Wittig reaction.



One pot oxidation and Wittig reaction catalyzed by iron complex

References :
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Poster n°34

Synthesis and Functionalization of 3,5-Disubstituted 1,2-Dioxolanes: Toward the Total Synthesis of Mycangimycin

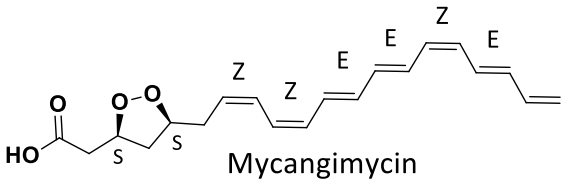
Alexis PINET,[1] Bruno FIGADERE[1] and Laurent FERRIE[1]

[1] BioCIS UMR 8076, CNRS, Université Paris-Saclay, 92290 Châtenay-Malabry, France
alexis.pinet@u-psud.fr bruno.figadere@u-psud.fr laurent.ferrie@u-psud.fr

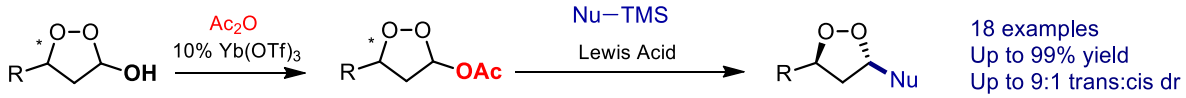
Among isolated and described natural products, endoperoxides species represent a small class of molecules. Assuredly, the most famous one is Artemisinin (Youyou Tu, 2015 Nobel Prize) which exhibits high therapeutic efficiency against paludism. This discovery allowed then endoperoxides to take its first steps as a therapeutic agent.

Mycangimycin have been isolated from *Streptomyces* by Clardy's team in 2009,[1],[2] revealing an uncommon mutualism and a very good antimalarial activity. This molecule is made of a long polyenic chain with seven conjugated double bonds and a rare 3,5-disubstituted 1,2-dioxolane ring, indeed, most of common endoperoxides (dioxolanes or dioxanes) exhibit tri- or tetra-substitution at their peroxide moiety.

Despite their potential in therapeutics as pharmacophores or as full-fledged molecules, the synthesis of endoperoxides have been scarcely studied. This is particularly the case for 3,5-disubstituted 1,2-dioxolanes, whose the synthesis and the mono-functionalization are hard to implement with actual methods.



Mycangimycin



R = alkyl, aryl, benzyl, Protected alcohols

Our strategy implies acetylation of a peroxyhemiacetal (from cyclopropanol ring expansion). The acetate is a good leaving group and allows in presence of a Lewis acid the generation of a peroxyoxocarbenium ion that can be attacked by various nucleophiles. This work constitutes the first steps for the total synthesis of mycangimycin[3], and/or therapeutically active synthetic endoperoxides.

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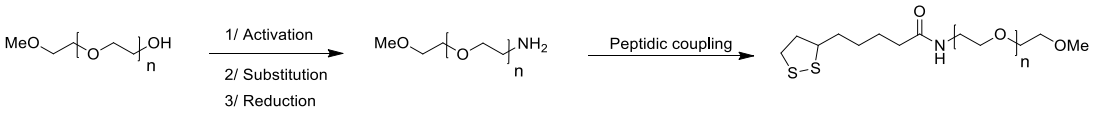
Poster n°35

Green Gold Nanoparticles by Flow Chemistry

Catherine GOMEZ,[1] Marion DEQUENNE,[1] Gauthier HALLOT,[1] Marc PORT[1]

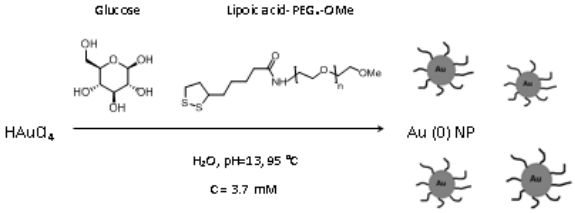
[1] Equipe de Chimie Moléculaire - Laboratoire GBCM - Conservatoire National des Arts et Métiers (Cnam)
2 Rue Conté, 75003, Paris
catherine.gomez@lecnam.net

Gold nanoparticles (GNPs) show a great interest for medical applications such as the theranostic.[1] Indeed GNPs combine a high atomic number and a good biocompatibility.[2] GNPs synthesis has been widely described[2] but our goal is to produce, in a large scale, stable, monodisperse and functionalized GNP by following a green process. Thiol groups are well known as efficient coating moiety for GNPs. Thus, functionalized lipoic acids were first synthesized and then introduced by the continuous flow process.
Lipoic acid, which is an excellent coating for GNPs, is monofunctionalized *via* the carboxylic acid with pegylated chains. To increase the solubility and stability of NPs, several polyethylene glycols (PEG) are synthesized.[3] Several procedures are described to obtain expected pegylated chains (n= 7, 11, 16, 22) in three steps. The final peptidic coupling is optimized according to the PEG size to obtain the amide lipoic acid-PEG$_n$-OMe.[4] The different steps are presented below.



Schema 1 : Synthesis of pegylated chains

These amides lipoic acid-PEG$_n$-OMe are then introduced on GNPs by the continuous flow process. Several techniques are described in the literature to obtain similar functionalized GNPs. For example, from GNPs coated with citrate, a ligand exchange is carried out to introduce lipoic acid-PEG$_n$-OMe *via* a batch reactor synthesis.[5] In this work, we tried to optimize the functionalized GNPs synthesis by continuous flow chemistry in one step.



Schema 2 : Production of GNPs by continuous flow process

To directly access to the functionalized GNPs, the synthesis from tetrachloroauric acid HAuCl$_4$ and amide lipoic acid-PEG$_n$-OMe was considered. We propose a new and attractive synthesis of functionalized GNPs to respect a maximum of green nanochemistry principles. To optimize the process, the amounts of reactants, reducing agent, time, flow rate, pressure and yield are studied.
Finally, the best pegylated coating to stabilize GNPs will be selected to vectorize GNPs towards several therapeutic targets.

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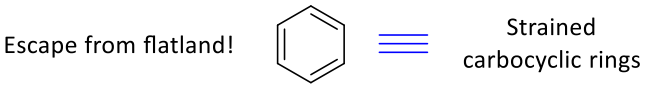
Poster n°36

Introduction of cyclopropyl and cyclobutyl ring on alkyl iodides through cobalt-catalyzed cross-coupling

Claire ANDERSEN,[1] Vincent FEREY,[2] Marc DAUMAS,[3] Patrick BERNARDELLI,[4] Amandine GUÉRINOT[1] and Janine COSSY[1]

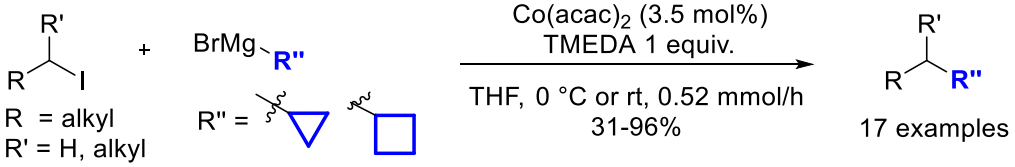
[1] Molecular, Macromolecular chemistry and materials, ESPCI Paris, CNRS, PSL University, 10 rue vauquelin, 75005 Paris, France. [2] Sanofi R&D, 371 rue du professeur Joseph Blayac, 34080 Montpellier, France. [3] Sanofi Chimie, Route d'Avignon, 30390 Aramon, France. 4 Sanofi R&D, 1 avenue Pierre Brossolette, 91380 Chilly-Mazarin, France.
claire.andersen@espci.fr

Benzene rings are ubiquitous frameworks in marketed drugs,[1] however, these rings have some disadvantages like poor solubility, toxicity as well as bioavailability problems.[2] Studies demonstrate that a compound increases its chance to become a marketed drug if it possesses an important numbers of saturated carbons, allowing a more complex 3D structure and escaping flatland.[3] A strategic way would be to replace a benzene ring by bioisosteres such as strained carbocyclic rings (Scheme 3).[4]



Scheme 3

The challenge rely on the incorporation of these bioisosteres on pharmaceutically relevant scaffolds in an easy fashion and at a late-stage. Metal-catalyzed cross-couplings have emerged as powerful tools for the formation of C-C bonds. Notably, Kumada-Corriu type reactions using cheap and abundant cobalt catalysis have already been developed in our laboratory for sp^2-sp^3 coupling reactions.[5] Based on this knowledge, we envisioned to use cobalt-catalyzed cross-coupling to introduce strained cycles on alkyl halides. Here, we report a coupling between various Grignard reagents including cyclopropylmagnesium bromide and cyclobutylmagnesium bromide with primary and secondary iodides using simple and cost-effective conditions. The reaction is efficient as well as chemoselective (Scheme 4).



Scheme 4

Acknowledgments: Sanofi is acknowledged for financial support.

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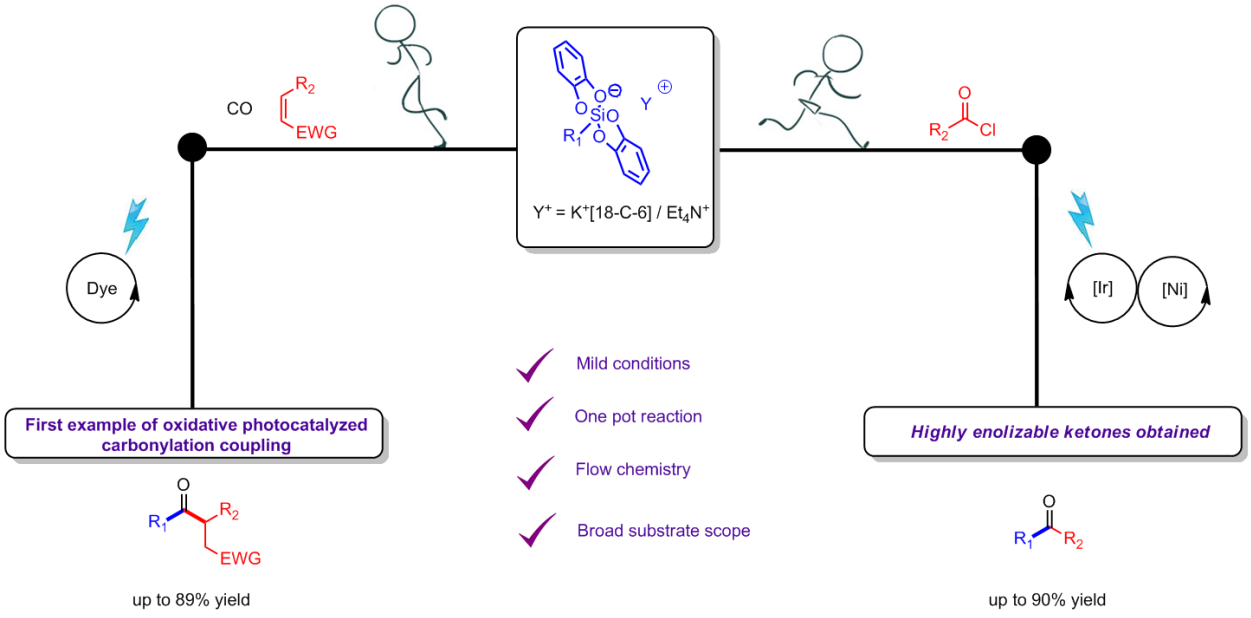
Poster n°37

Photocatalytic oxidation of bis-catecholato silicon compounds: A new way to envisage C-C bond

Etienne LEVERNIER, Cyril OLLIVIER, Louis FENSTERBANK

Institut Parisien de Chimie Moléculaire, Sorbonne Université, CNRS, 4 Place Jussieu, 75005 Paris, France
etienne.levernier@sorbonne-universite.fr

Photoredox catalysis now holds a privileged position in modern radical chemistry. Visible-light irradiation of several families of alkyl radical precursors, such as alkyl carboxylates[1] and alkyl trifluoroborates[2], is known to promote the efficient formation of alkyl radical species under photooxidation conditions. Recently, alkyl bis(catecholato)silicates were introduced to allow the smooth generation of a variety of alkyl radicals[3,4], including unstabilized primary ones. Our research focuses on exploring the range of possibilities that offer this new type of precursor. In addition of being able to achieve very interesting cross-coupling reactions we found that they can react with an acyl chloride forming ubiquitous ketones[5]. Their possible reaction in a multi-component way with a gas like CO has also also been evaluated[6] and the first example of oxidative photocatalyzed carbonylation coupling reported.



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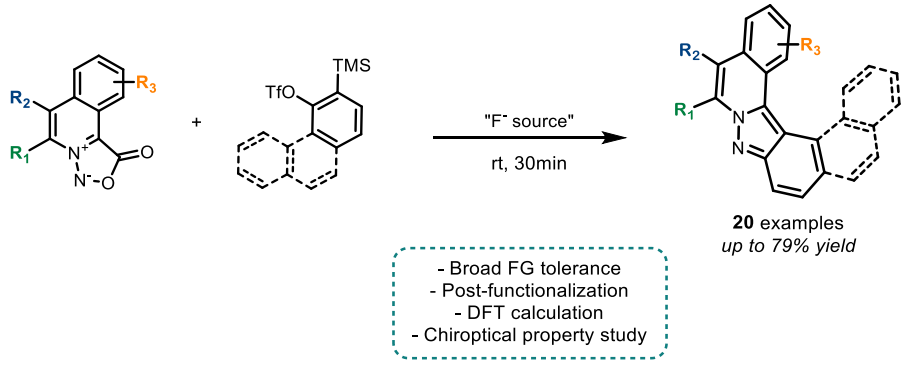
Poster n°38

Sydnone-Based Approach to Heterohelicenes through 1,3-Dipolar-Cycloadditions

Expédite YEN-PON,[1] Pier Alexandre CHAMPAGNE,[2] Lucie PLOUGASTEL,[1] Sandra GABILLET,[1] Pierre THUERY,[3] Mizuki JOHNSON,[4] Gilles MULLER,[4] Grégory PIETERS,[1] Frédéric TARAN,[1] K. N. HOUK,[2] Davide AUDISIO[1]

[1] SCBM, Institut Joliot, CEA, Université Paris Saclay, 91191 Gif-Sur-Yvette, France
[2] Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095, United States
[3] NIMBE, CEA, CNRS, Université Paris-Saclay, 91191 Gif-sur-Yvette, France
[4] Department of Chemistry, San José State University, San José, California 95192-0101, United States
expedite.yen-pon@cea.fr

Despite their fascinating structure and unique properties, the synthetic access to helicenes and heterohelicenes remains challenging and required multistep procedures. We reasoned that a late-stage formation of this helicoidal structure through sydnone/aryne 1,3-dipolar cycloadditions could allow a fast access to new Polycyclic Heteroaromatic Hydrocarbon (PHH).



Scheme 1. General scheme of heterohelicene synthesis

This strategy involved the design and synthesis of *ortho*-substituted polyaromatic sydnones. Over the process, an unprecedented regioselectivity in the cycloaddition step towards the more sterically constrained product was observed.[1] The origins of this phenomena were studied by DFT calculations in collaboration with group of Prof. K. N. Houk (UCLA). The study of the chiroptical properties of the [7]-azahelicenes separated enantiomers have been realized and revealed similar property to carbohelicene's.

This method allows the divergent access to [4], [5], [6], [7] and [8]-heterohelicenes and has been extended to substituted sydnones (EWG and EDG) and arynes with always the same observed regioselectivity (20 examples, *30-79%* yield) (Scheme 1). [2]

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Poster n°39

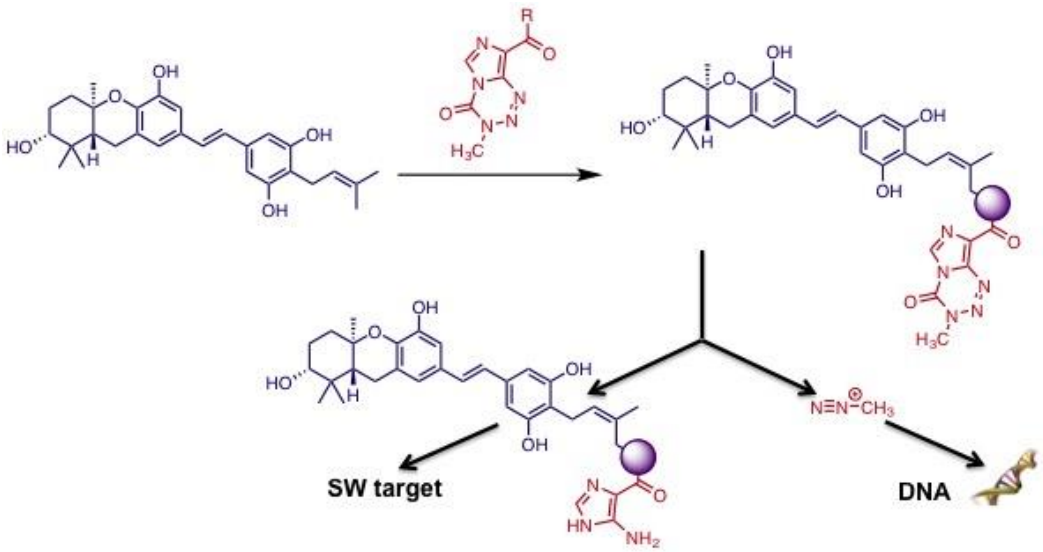
Innovative therapeutic strategy against glioblastoma: synthesis and biological evaluation of new dual molecules

Gwenaëlle JÉZÉQUEL,[1] Tiphaine PÉRESSE,[1] Sandy DESRAT,[1] Thierry VIROLLE[2], Jérôme BIGNON[1], and Fanny ROUSSI[1]

[1] Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Université Paris-Saclay, 1 Avenue de la Terrasse, 91198 Gif-sur-Yvette, France
[2] Université de Nice-Sophia Antipolis, Institut de Biologie Valrose, CNRS UMR7277, Inserm U1091, Nice, France
gwenaelle.jezequel@cnrs.fr

Glioblastoma multiforme (GBM) is by far the most malignant and common brain cancer, with a median length of survival of 15 to 18 months with treatment. The standard treatment consists in a combination of surgery, radiotherapy, and chemotherapy using temozolomide (TMZ), a DNA alkylating agent. However, this treatment only improves the median survival by three months, and some gliomas develop temozolomide resistance. Cho *et al.* have found that combining in a dual molecule TMZ and perillyl alcohol (POH), a natural compound that is active against glioblastoma, allows to increase the cytotoxicity against glioblastoma cells compared to POH alone, TMZ alone or the mixture of these two compounds.[1],[2] This conjugated compound is also cytotoxic against TMZ-resistant glioblastoma cells.

Our team has isolated new cytotoxic compounds from *Macaranga tanarius* and *Macaranga vedeliana,* schweinfurthins (SW), that are highly active against glioblastoma cells, and they seem to be active on an other target than DNA. [3],[4] Therefore, we synthesized new dual molecules combining schweinfurthin and temozolomide to study the activity of this new compound in the cell, and compared it with the schweinfurthin alone, the TMZ alone, and the mixture of SW and TMZ.



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Poster n°40

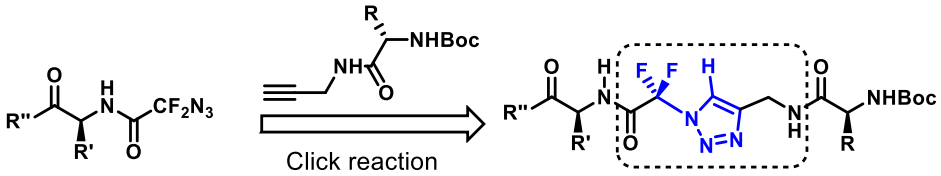
Fluorinated foldamers containing *N*-difluoromethyl-triazole scaffold.

José Laxio Arenas,[1] Thierry Milcent,[1] Julia Kaffy, [1] Benoit Crousse,[1] Sandrine Ongeri[1]

[1] FLUOPEPIT, BioCIS UMR-CNRS 8076, Université Paris-Sud, Université Paris Saclay, 5 rue Jean-Baptiste Clément, 92290 Châtenay-Malabry Cedex, France

jose.laxio-arenas@u-psud.fr

Introducing fluorine atom(s) into bioactive organic compounds has become a leading strategy for drug design.[1] Due to its unique properties, fluorine is frequently employed to modify biologically relevant properties such as metabolic stability, lipophilicity, and bioavailability. Regarding proteins, hydrophobicity is the main interaction to modulate peptide folding and therefore their biological activity.[2] Nevertheless, there is still no fluorinated peptide used as a drug. Moreover, since few years foldamers have emerged as useful secondary structure mimetics of proteins while only scarce examples of fluorinated foldamers have been reported.[3] We are currently focusing our research on the synthesis of fluorinated foldamers, using *N*-difluoromethyl triazolo-β-aza-ε-amino acid as a constrained scaffold, that can be used to design inhibitors of protein-protein interactions (PPIs).



Triazoles are known for their structural and electronic properties as peptide bond mimic exhibiting an increased *in vivo* stability.[4] *N*-difluoromethyl-triazole can be described as an analogue of the difluorogly-gly peptide that is challenging to prepare due to the instability of difluoroglycine. Furthermore, we have shown that the CH-F and NH-F interactions into *N*-difluoromethyl-triazole can induce extended structures to mimic β-strand-tetrapeptides.[5] Our present work is to incorporate triazolo-β-aza-ε-amino acids into the core of longer peptides to induce secondary structures. These foldamers could be of particular interest to meet the challenge of finding new classes of drugs targeting pathological PPIs such as those involved in Type 2 diabetes (T2D) or Alzheimer's disease (AD).

The synthesis *of N*-difluoromethyl-triazole containing peptidomimetics and preliminary biophysical evaluations of these fluorinated foldamers on the aggregation of amyloid proteins involved in T2D and AD will be presented.

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Poster n°41

Design, Synthesis and Biological Evaluation of Photoactivatable Inhibitors of the TAM Family

Julie LE BESCONT,[1,2] Liliane MOUAWAD,[2] and Sandrine PIGUEL [1,2]

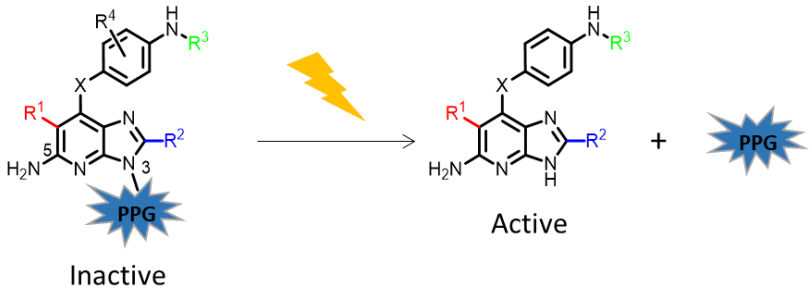
[1] Université Paris Sud, Université Paris-Saclay, CNRS, INSERM, UMR 9187-U 1196, 91405 Orsay Cedex, France ; [2] Institut Curie, PSL University, CNRS, INSERM, UMR 9187-U 1196, 91405

julie.le-bescont@curie.fr

The TAM family regroups three protein kinases : Tyro3, Axl and Mer. These proteins are involved in a lot of cellular pathways promoting survival and growth of cells in response to extracellular signals. The TAM family has been identified as a new and effective therapeutical target for cancer therapy, autoimmune and viral diseases[1]. Only a few molecules have been designed as TAM inhibitors, with a major interest for Axl and Mer. They are all targeting the highly conserved ATP binding site of the protein, like most of the kinase inhibitors. Although kinase inhibitors have been successful as therapeutic treatments against cancer, the lack of selectivity inducing side-effects is still one of the major drawbacks [2].

To bypass these selectivity issues, we will develop photo-controlled inhibitors, based on the photoactivatable protecting groups strategy[3]. Indeed, light offers majors advantages as a tool for biological applications, such as a high spatiotemporal precision, an accurate adjustment of wavelength and intensity, no contamination and low toxicity.

We first designed a serie of new imidazo[4,5-*b*]pyridines as potent inhibitors of the TAM family, performing docking studies on the X-ray structures of the three proteins of the family. We then performed structural modifications by introduction of a photoremovable protecting group (PPG) on the nitrogen N-3. This PPG will temporarily deactivate the molecule, providing spatial and temporal control over the release of the active molecule under light. The choice of the photoactivatable protecting group should meet some criteria such as easy to introduce groups, optimized photophysical properties, easy to cleave and biocompatible. We tested the photoactivatable properties of the synthesized compounds by following the kinetics of photocleavage. We are currently studying their *in vitro* activity.



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Poster n°42

Total synthesis of Tuberatolide B

Kelly MAURENT,[1] Andrei CORBU,[1] Stellios ARSENIYADIS [2]

[1] Institut de Chimie des Substances Naturelles, CNRS – UPR 2301
1 Avenue de la terrasse, 91190 Gif- sur- Yvette, France
[2] Queen Mary Unviversity of London, School of Biological and Chemical Sciences
Mile End Road, London E1 4NS, United Kingdom
kelly.maurent@cnrs.fr

Meroterpenoid Tuberatolide B, was isolated from Korean marine tunicate Botryllus tuberatus[1] and from Korean marine algae Sargassum Macrocarpum[2], respectively in 2011 and 2017.
Tuberatolide B shows interesting biological properties, among them, the inhibition of cancer growth. It induces, via generation of reactive oxygen species, apoptosis and an increase of DNA damage in cancer cells.
Tuberatolide B inhibits also STAT3 (Signaling Transducer and Activator of Transcription 3) signaling pathway. STAT3 plays an important role in cell development cycle, angiogenesis, inflammation and cancer metastasis. It is activated in 70% of different kind of cancers. Therefore inhibition of STAT3 is an interesting therapeutic target for the treatment of cancers.

Tuberatolide B is a natural compound of mixed biosynthesis: the lateral chain containing a terpenic lactone comes from the mevalonate pathway and the aromatic bicyclic fragment comes from polyketide biosynthesis. Having two structurally different fragments, we designed a convergent strategy to assemble not only Tuberatolide B, but also related meroterpenes of the same family.
The two sides were assembled using a powerful cross-metathesis reaction, generating the central tri-substituted double bond.
The 2*H*-chromene precursor was obtained by an intramolecular cyclisation of an alkyne intermediate in the presence of a gold catalyst.
The terpenic lactone was prepared by a palladium catalyzed enantioselective allylic alkylation (AAA).
This powerful and convergent approach as a proof-of-concept will allow the synthesis of a number of natural meroterpenes and their analogues for biological activity testing.

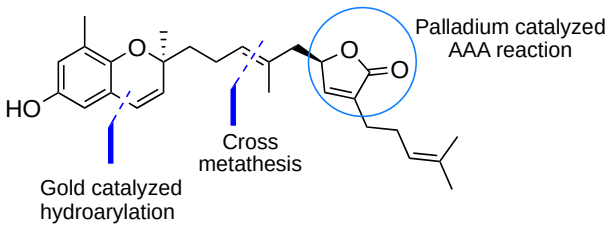

Figure 4. Tuberatolide B

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Poster n°43

NEW SYNTHETIC APPROACH TOWARDS AVIBACTAM ANALOGUES

Laure PEILLERON, Robert H. DODD and Kevin CARIOU[1]

[1] Institut de Chimie des Substances Naturelles, ICSN - CNRS UPR 2301, Université Paris-Sud,
1 Avenue de la Terrasse, 91190 Gif-sur-Yvette,
laure.peilleron@cnrs.fr

As resistant or multi-resistant bacteria are more and more common, there is an urgent need for new antibiotics and/or resistance suppressants.[1] Avibactam is a β-lactamases inhibitor (one of the major pathways of Gram-negative bacteria resistance) and its use in combination with ceftazidime was approved by the FDA in 2015.

The aim of this project is to design a new range of Avibactam analogues and to develop a new synthetic approach that will permit introduction of different structural features.

Our synthetic strategy is based on the cyclization of a tetrahydropyridine by electrophilic activation of the unsaturation. Previous work by our group on guanidine halo-cyclizations initiated by hypervalent iodine (III) will serve as a basis for this key step.[2] The monocyclic intermediate will arise from the ring closing metathesis of a di-allyl precursor. This latter will be obtained from a sequence of C- then N-allylation on a glycine derivative (Figure 1).

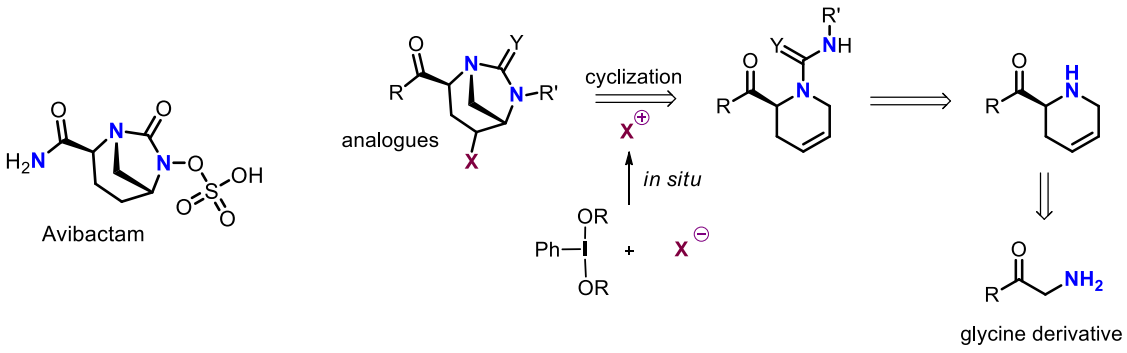

Figure 1: Retrosynthesis of Avibactam analogues

The asymmetric synthesis of the target monocyclic intermediate as well as a methodological study of the key hypervalent iodine (III)[3]-initiated cyclization step of hydroxy-urea derivatives will be presented.

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Poster n°44

Ugi azide MCR for the synthesis of new MraY inhibitors

Martin OLIVER,[1] Laurent LE CORRE[1], Sandrine CALVET-VITALE[1] and Christine GRAVIER-PELLETIER[1]

[1]Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques,
Université Paris Descartes, 45 rue des saints pères, 75006 Paris.
martin.oliver@etu.parisdescartes.fr
sandrine.calvet-vitale@parisdescartes.fr, christine.gravier-pelletier@parisdescartes.fr

Emergence of **Multidrug resistant (MDR)** bacteria becomes a major public health problem. Thus, the discovery and development of novel compounds, efficient against MDR strains, appears to be crucial for the future. In this context, our team is focused on the bacterial transferase MraY as a validated but still unexploited target for the discovery of new antibiotics. Recently, a crystal structure of the integral membrane enzyme $MraY_{AA}$ in complex with Muraymycin D2 has been solved[1] and shows the binding mode of this potent natural inhibitor into the MraY active site (Figure 1).

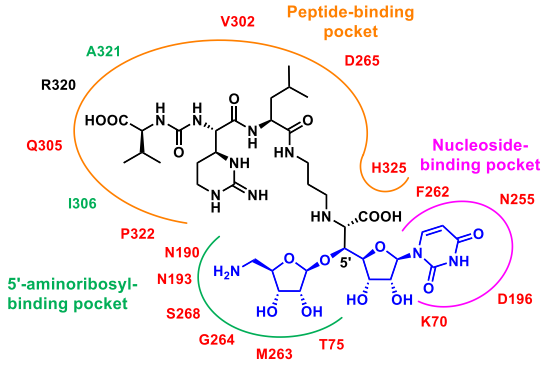

Figure 5 : Muraymycin D2 in $MraY_{AA}$ active site

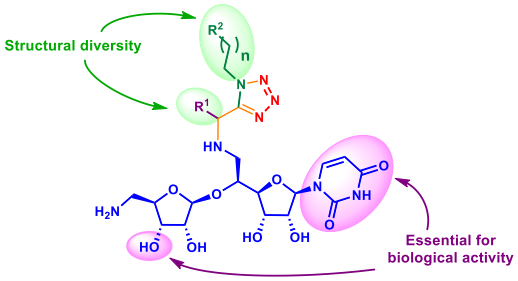

Figure 2 : 1,5-disubstituted tetrazole inhibitors

The aminoribosyl scaffold and the stereochemistry at C-5' in naturally occurring MraY inhibitors, have been proven to be crucial for their biological activity[2]. We intend to develop new simplified MraY inhibitors able to maintain strong interactions with the nucleoside and the 5'-aminoribosyl binding pockets and to provide an optimal filling of the peptide-binding pocket (Figure 1). We previously developed the synthesis of original inhibitors based on the aminoribosyl-*O*-uridine scaffold with a triazole linker[3].
In order to improve the inhibitory activity of such compounds, we envisaged the development of new inhibitors containing a 1,5-disubstituted tetrazole spacer, displaying the advantage of an additional functionalization point compared to the previous ones. The amino tetrazole scaffold is accessible through a Ugi Tetrazole four component reaction (UT-4CR). Recent results towards these inhibitors synthesis will be presented.

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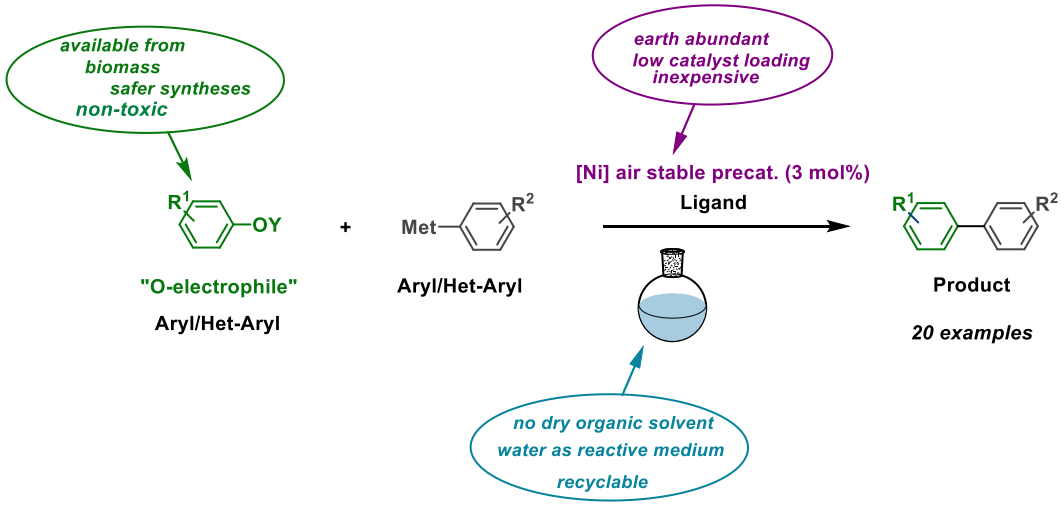
Poster n°45

organometallic catalysis in water involving oxygen-based electrophiles

Maximiliene SAAGUE TENEFO, Marie-Isabelle LANNOU[1], Geoffroy SORIN[1] and Janick ARDISSON[1]

x [1] Université de Paris Descartes, Faculté de Pharmacie de Paris
UMR CNRS 8038 CiTCoM , 4 avenue de l'observatoire 75270 paris cedex 06
maximiliene.saague_tenefo@etu.parisdescartes.fr

In the field of transition metal catalyzed cross-coupling reactions, the Suzuki–Miyaura reaction reveals of primary importance to build C-C, especially due to its wide application in pharmaceutical industry. In this context, homogeneous palladium catalyzed reactions involving aryl halides as electrophiles in organic media, have been widely employed both in academia and in industry[1-2]
. However, such transformations exhibit major drawbacks among these: synthesis and/or handling of organic halides, generation of large amount of organic waste (including about 70% for the solvent itself), high prices of palladium derivatives due to the depletion of the metal source. Consequently, there is an urgent need to set up less expensive and more eco-compatible systems.
This is the reason why we propose a powerful green system where we have been able to replace toxic aryl halides by oxygen-based electrophiles, easily available from phenols (biomass), organic solvent by water and palladium catalyst by an easily accessible air-stable nickel precatalyst at low catalytic loading.[3]
Moreover, contrary to pioneering works described by Lipshutz *et al.* no micellar medium is required.[4]



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Poster n°46

Glycan metabolic labeling: toward a new strategy for glycoconjugate vaccines preparation

Pauline AUBERT,[1] Aurélie BARON,[1] Annie LAMBERT,[2] Emilie CAMBERLAIN,[2] Cyrille GRANDJEAN,[2] Marie-Ange BADET-DENISOT,[1] and Boris VAUZEILLES [1,3]

[1] ICSN, UPR-CNRS 2301, Université Paris-Saclay, 91198, Gif-sur-Yvette Cedex
[2] UFIP, UMR-CNRS 6286, Faculté des Sciences et Techniques, Université de Nantes, 44322 Nantes Cedex 3
[3] ICMMO, UMR-CNRS 8182, Université Paris-Sud, Université Paris-Saclay, 91405 Orsay Cedex
pauline.aubert@cnrs.fr

Glycan metabolic labeling recently emerged as an efficient and popular strategy for *in vivo* modification of cellular glycans, including cell surface glycoproteins and glycolipids. This approach is based on the metabolic incorporation of a modified monosaccharide, bearing a bioorthogonal chemical handle or reporter group.[1] Following metabolic incorporation of this modified monosaccharide, resulting in the cell-surface presentation of the reporter group, bioorthogonal ligation can be used for direct visualization of surface glycans or other biologically relevant applications such as phenotypic screening on live cell.[2],[3] We have developed a pathogen detection method based on the metabolic engineering of bacterial surface carbohydrates.[4] We are currently exploring strategies for the preparation of glycoconjugate vaccines.[5]

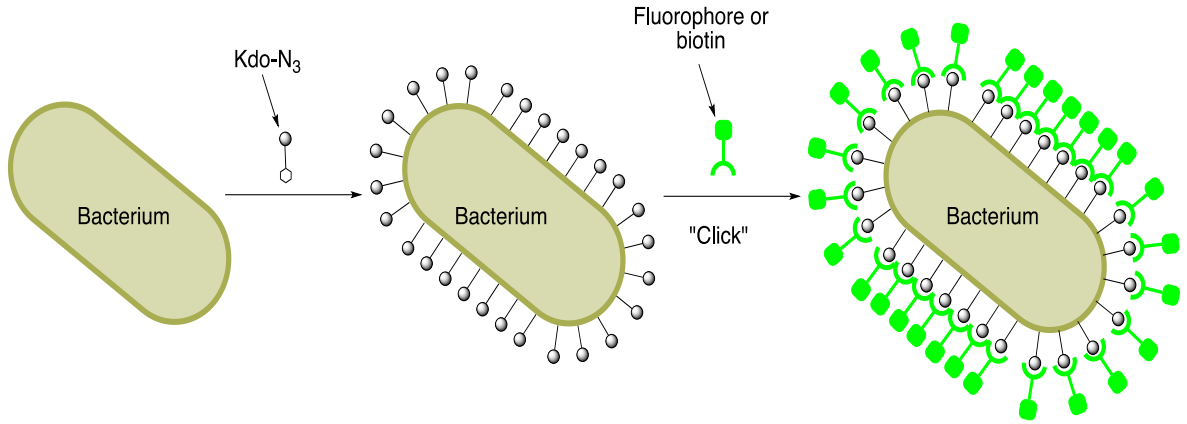

Figure 6. Metabolic labeling using Kdo-N_3

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Poster n°47

Ru-catalyzed carbonylative Murai reaction of *N*-containing aromatic systems

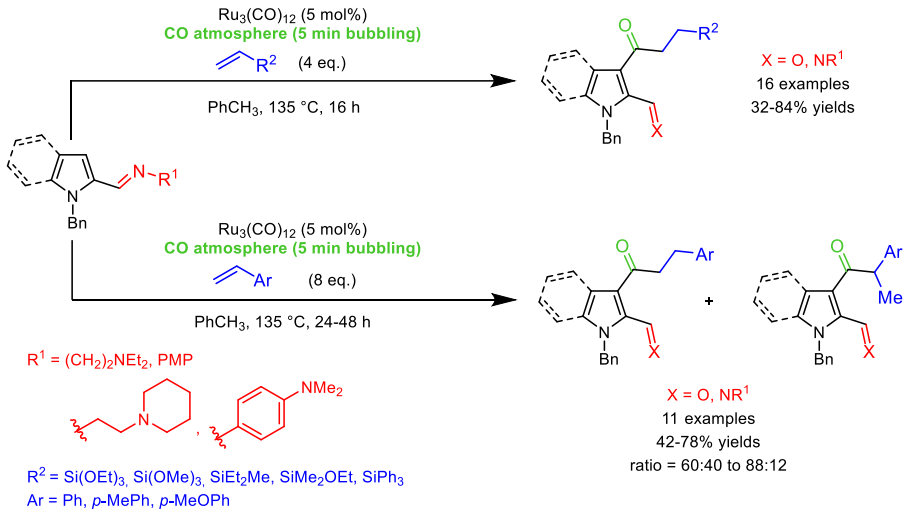
Roberto Sala,[1,2] Fares Roudesly,[2] Gianluigi Broggini,[1] Julie Oble,[2] Giovanni Poli [2]

[1] *Dipartimento di Scienza e Alta Tecnologia, Università dell'Insubria, Via Valleggio 9, Como, Italy*
[2]*Institut Parisien de Chimie Moléculaire (IPCM), 4 Place Jussieu, Sorbonne Université, 75252, Paris Cedex 05, France*
e-mail: r.sala@uninsubria.it

Nowadays, the direct and selective functionalization of non-acidic C-H bonds has emerged as a novel step-economical and eco-compatible strategy. It allows the use of simple and cheap starting materials for the construction of complex organic molecules by adding the C-H bonds to the most common directing and functionalizable groups, such as carbonyls, halides, alcohols, etc.

Furthermore, the direct functionalization of nitrogen containing heterocycles, moieties commonly present in many natural products, drugs and enzymes, remains an important topic.[1] In this context, we focused on a direct C3-H functionalization of nitrogen containing rings – such pyrrole or indole –, *via* a carbonylative version of the well-known Murai reaction.[2]

Basing on previous line research of our group,[3] we have recently developed a directed Ru(0)-catalyzed C3-acylation of *N*-heterocycle (pyrrole/indole) imines, which can be obtained by treatment with vinylsilanes or styrenes under carbon monoxide atmosphere. Various 3-carbonylated pyrrole- or indole-imines were obtained with moderate to good yields, as well as the corresponding aldehydes after hydrolysis, In the case of styrenes, a mixture of the linear (major) and branched (minor) isomers was obtained. In this communication, discovery, optimization and substrate scope of this new C-H activation based transformation will be disclosed.



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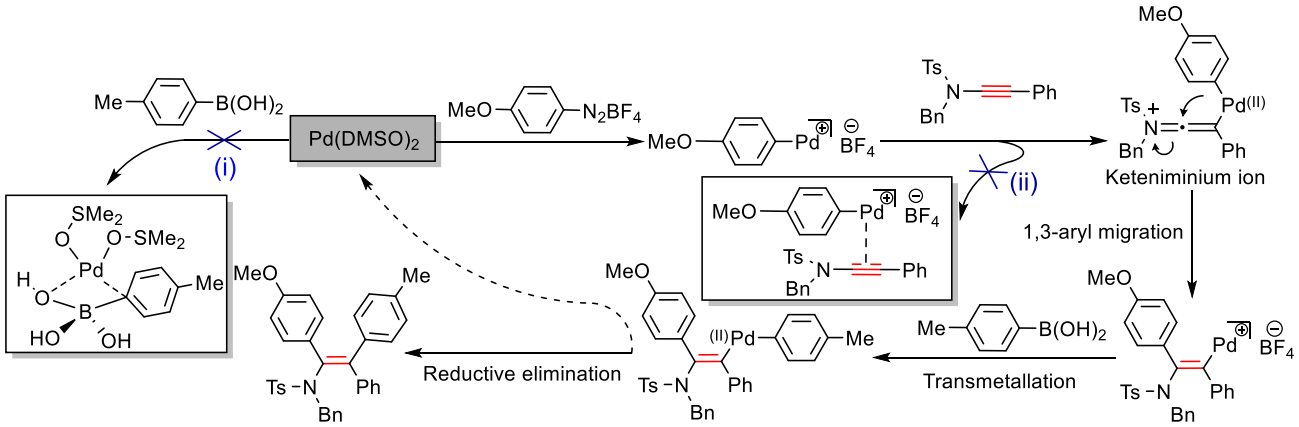
Poster n°48

Exploring the mechanism of the Pd (II)-catalyzed 1,2-diarylation of ynamide: a DFT study

Shengwen Yang,[1,2] Akhila K. Sahoo,[3] Vincent.Gandon[1,2,*]

[1]Institut de Chimie Moléculaire et des Matériaux d'Orsay, CNRS UMR 8182, Université Paris-Sud, Université Paris-Saclay, Bâtiment 420, 91405 Orsay cedex, France.
[2]Laboratoire de Chimie Moléculaire (LCM), CNRS UMR 9168, Ecole Polytechnique, Université Paris-Saclay, route de Saclay, 91128 Palaiseau cedex, France.
[3]School of Chemistry, University of Hyderabad (India)
shengwen.yang@u-psud.fr; vincent.gandon@u-psud.fr

Ynamides, a distinct class of N-substituted alkynes, have been used for various cyclization/cycloisomerization processes towards the construction of structurally diverse complex building blocks.[1] The group of Prof. Sahoo recently developed a strategy for Pd(II)-catalyzed 1,2-diarylation of ynamides.[2] We have performed a density functional theory study to clarify the mechanism of this new transformation. In this presentation, we will provide some insights into the origin of the chemo-, regio-, and stereoselectivity of the title reaction. In particular, the selectivity can be explained from the beginning of the mechanism and is likely due to two factors: (*i*) The activation of the aryldiazonium salt is favored over that of the arylborate; (*ii*) Coordination of the [(*p*-methoxyphenyl)$(DMSO)_2$Pd(II)]$^+$ fragment to the ynamide is a barrierless process which leads to a keteniminium complex, and no π-alkyne complex could be modeled.



DFT study of the *chemo- regio- and stereoselectivity*

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Poster n°49

Enantioselective gold(I)-catalysed reactions of 1,5-enynes and 1,6-enynes

Xu HAN,[1] Vincent GANDON[2] and Arnaud VOITURIEZ[1]

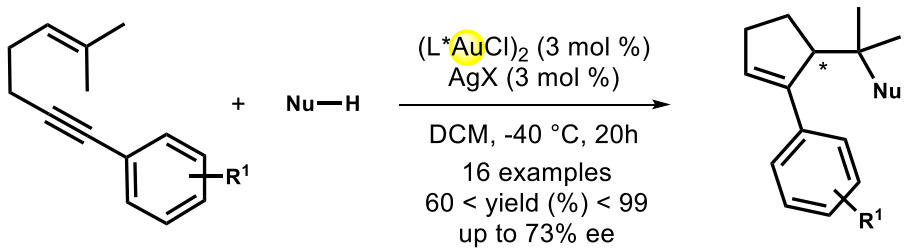
[1]*ICSN-CNRS, Université Paris-Saclay, 1 av. de la Terrasse, 91198 Gif-sur-Yvette (France)*

[2]*ICMMO, Université Paris-Saclay, bât. 420, 91405 Orsay (France)*

xu.han@cnrs.fr

Homogeneous gold catalysis has emerged as a powerful method in organic synthesis due to the unique ability of cationic gold(I) complexes to activate unsaturated bonds (mainly allenes, dienes and alkynes).[1] During the past decades, gold(I)-catalyzed reactions have been widely applied to access complex molecular frameworks. Particularly, cycloisomerization transformations of 1,n-enynes and other unsaturated substrates have provided simple, atom-economic and efficient approaches to cyclic and bicyclic compounds. In this presentation, we will summarize our work using chiral gold complexes and either 1,5-enyne and 1,6-enyne substrates, for an highly efficient access to complex carbocyclic and heterocyclic backbones.

In 2004, gold and platinum-catalyzed cycloisomerization reactions of **1,5-enynes** were reported by several teams,[2] which studied the skeletal rearrangement of this simple structure. Followed by this work, an alkoxycyclization[3a] and an enantioconvergent kinetic resolution[3c] of 1,5-enynes were developed. However, to the best of our knowledge, the simple enantioselective 1,5-enyne cyclization/nucleophilic addition has never been reported. In the present work, we developed this asymmetric transformation, using simple 1,5-enyne substrates. In reaction with different nucleophiles, and using chiral gold catalysts, a series of cyclopentene derivatives were synthesized in good yields and with enantioselectivities up to 73% ee (16 examples).



In this presentation, we will summarize also a new asymmetric transformation involving **1,6-enyne** substrates. The corresponding complex nitrogen-containing polycyclic structures were obtained in good yields and excellent enantioselectivities (up to 90% ee).

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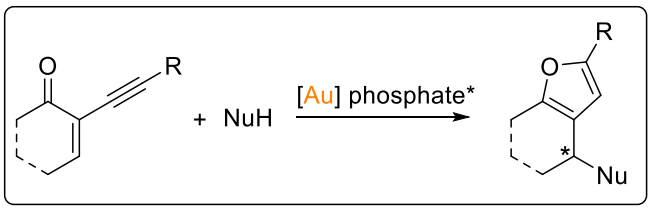
Poster n°50

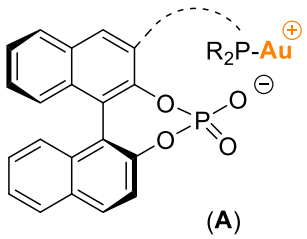
New Strategies for Enantioselective Gold (I) Catalysis

Zhenhao ZHANG,[1] Vitalii SMAL,[1] Arnaud VOITURIEZ, [1] Gilles FRISON,[2] Xavier GUINCHARD[1] and Angela MARINETTI[1]

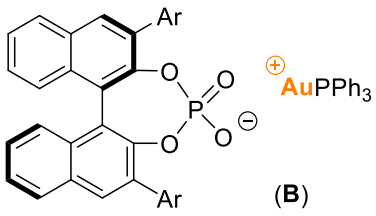
[1] Equipe 37, ICSN-CNRS, 1 avenue de la Terrasse, 91198 Gif-sur-Yvette
[2] LCM, École polytechnique, Route de Saclay, 91128 Palaiseau Cedex
zhenhao.zhang@cnrs.fr

In enantioselective organometallic catalysis, the mainstream approach relying on stereocontrol from the chiral ligand has been complemented recently by the chiral counterion strategy.[1] In this field, Binol-derived phosphates have demonstrated good efficiency as chiral anions in a limited range of catalytic reactions. In order to expand the scope of the method, its application to new reactions has been investigated, as typified here by the synthetically relevant tandem cyclization/nucleophilic addition reaction.[2] New chiral silver phosphates have been designed in the group for this purpose.[3] The gold(I) complexes (**A**)[4] with hybrid phosphine-phosphate ligands however illustrate a new working hypothesis and a possibly general strategy, that is the covalent tethering of the phosphate counterion to the metal catalyst. Tethering should afford increased geometrical constraints and molecular organization, with respect to the classical counteranions, thus enabling higher stereocontrol in targeted catalytic reactions. As a proof of concept, enantiomeric excesses up to 97% have been attained with (**A**) in the target reaction, while the same reaction performed from an analogous Ph_3PAu^+ with a chiral TRIP phosphate as the chiral counterion leads to a moderate 24% ee.





(**A**)



(**B**)

Ar = 2,4,6-(*i*-Pr)$_3$C$_6$H$_2$

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Poster n°51

Radical-Mediated Dearomatization of indoles with sulfinate reagents and phospithes for the synthesis of fluorinated and phosphonated spirocyclic indolines.

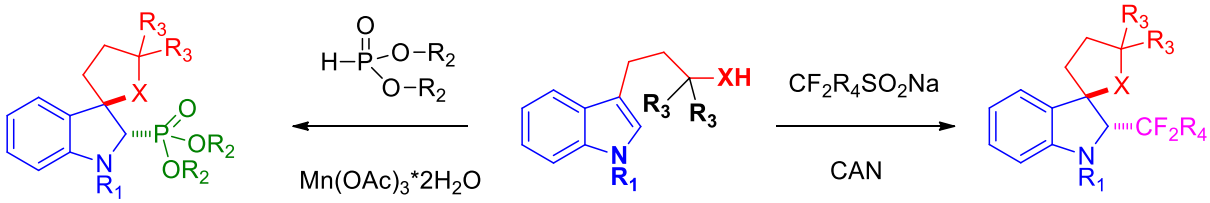
Ryzhakov D., Jarret M., Kouklovsky C., Vincent G.

Institute of Molecular Chemistry and the Materials of Orsay.
Buildings 410/420/430, Paris-South 11 University, UMR 8182

dmytro.ryzhakov@u-psud.fr

The spirooxindole scaffold is frequently found in natural products and biologically active compounds[1]. Some pharmaceuticals containing spirooxindole motif were also reported, stimulating a great interest in construction and modification of this skeleton[2]. However only few works were done to replace the carbonyl in position 2 by another valuable fonctional group[3].

Considering the importance of **CF3**, **CF2H** and **PO(OR)$_2$** groups in therapeutic and radical chemistry[4], we believe that the diastereoselective introduction of these functional groups into the structure of spiroindolines can lead to compounds of biological interest. Based on the recognized expertise of our group in the creation of spiroindoline compounds using the umpolung of indole[5], we developed a simple and efficient diastereoselective method for the synthesis of fluorinated and phosphonated spirocyclic indoline using respectively sulfinate reagents and CAN* as oxidant [6] or phospithes and $Mn(OAc)_3$.



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Poster n°52

Synthesis of Novel 4-chloro-tetrahydropyranated derivatives from kaurenoic and beyerenoic acid via Prins cyclization

Ana K. VILLAGÓMEZ-GUZMÁN[1, 2], Mario A. GÓMEZ-HURTADO[1], Gabriela RODRÍGUEZ-GARCÍA[1], Rosa E. DEL RÍO[1], Christine THOMASSIGNY[2], Christine GRECK[2].

[1]Instituto de Investigaciones Químico Biológicas, Edificio B-1, Universidad Michoacana de San Nicolás de Hidalgo, Ciudad Universitaria, Morelia, Michoacán, 58030, México.
[2]ILV-UMR CNRS 8180, Université de Versailles- St-Quentin-en-Yvelines, 45 avenue des Etats-Unis, 78035 Versailles Cedex, France.
villagomez.villagomez@uvsq.fr

Kaurenoic acid (**1**) is a bioactive tetracyclic diterpenoid involved in both primary and secondary metabolism of plants. It has been also employed as a precursor for the semisynthesis of novel kaurane-type diterpenoids with pharmacological activity. [1] The above mentioned is supported since several *ent*-kaurenes are active pharmaceutical ingredients from plants used as traditional medicines, highlighting those with anti-cancer activity, mediated by various biochemical pathways. [2]

With a similar pattern is the tetracyclic diterpene beyerenoic acid (**2**) isolated from the roots of *Viguiera hypargyrea*, whose spasmolytic effect and antibacterial activity against *Staphylococcus aureus*, *Enterococcus feacalis,* and *Candida albicans* were established by a bio-guided study. [3] Herein, kaurenoic (**1**) and beyerenoic acids (**2**) extracted from *Perymenium buphthalmoides* [4] were used as precursors for novel 4-chloro-tetrahydropyranated compounds **3** (Figure 1) via Prins reaction, a strategic method for carbon-carbon coupling reaction, and a useful tool for the tetrahydropyran moiety inclusion. [5] Such functional group depicts scientific interest due to their presence in a large number of natural products and biologically active therapeutic agents, therefore, the development of facile methodologies to access six-membered cyclic ethers becomes pertinent for organic synthesis. [6]

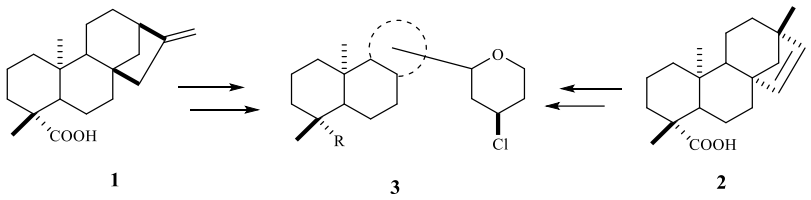

Figure 1. Prins products (**3**) from kaurenoic (**1**) and beyerenoic acid (**2**).

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Participants

Name	*Firstname*	*Affiliation*
Abdel Sater	Mariam	ICMMO
Abi Fayssal	Sandra	UPSud
Abou Hamdan	Hussein	Université de Paris-Sud
Adenot	Aurélien	CEA
Al-Mourabit	Ali	ICSN
Andersen	Claire	ESPCI
Anthore-Dalion	Lucile	CEA Paris Saclay
Archambeau	Alexis	Ecole Polytechnique
Ardisson	Janick	Université Paris Descartes
Aubert	Pauline	Université Paris-Saclay
Auvray	Marie	Institut Curie
Bachollet	Sylvestre	ENS
Barthelemy	Anne-Laure	Université de Versailles
Bayles	Thibault	ICSN
Bazzi	Sakna	ICMMO
Belmont	Philippe	Université Paris Descartes (Faculté de Pharmacie de Paris)
Benamara	Aziz	ESPCI
Benchekroun	Mohamed	ICSN
Betzer	Jean-Francois	ICSN
Bidjou-haiour	Shahra	Annaba
Boddaert	Thomas	Université Paris-Sud
Boudjadi	Narimane	Université Paris Descartes-faculté de pharmacie
Bournaud	Chloee	Université Paris Sud
Brachet	Etienne	Université Paris Descartes, Faculté de Pharmacie
Buendia	Julien	ICMMO
Cariou	Kevin	ICSN
Carlier	Mathieu	ICSN
Castanheiro	Thomas	ICSN
Chemla	Fabrice	Sorbonne Université
Chen	Yan	ICMMO
Cinquin	Olivier	ICSN
Condon	Sylvie	ICMPE-UPEC
Corbu	Andrei	ICSN
Curpanen	Sébastien	Sorbonne Université
Davi	Michael	ICMPE
De Abreu	Maxime	Faculté de Pharmacie de Paris - Université Paris Descartes
de la Vega Hernandez	Karen	Sorbonne Université
de Robichon	Morgane	Université de Cergy-Pontoise
Delattre	Vincent	ICSN
Deschamp	Julia	Université Paris 13
Desrat	Sandy	ICSN
Desvals	Arthur	ICMMO
Dhambri	Sabrina	Université Paris Descartes - Faculté de Pharmacie
D'hollander	Agathe	CNRS
Djurovic	Alexandre	ICMMO
Dorval	Céline	Ecole Polytechnique
Dou	Yingchao	ICMMO
Duhail	Thibaut	Université Versailles-St Quentin
Dussart	Jade	Université Paris 13
Ernouf	Guillaume	CEA Paris/Saclay - SCBM - Institut des sciences du vivant Frédéric Joliot
Escola	Antoine	Ecole Polytechnique

Fabrizio	Medici	ICSN
Febvay	Julie	ICSN
Felder	Simon	Université Paris Descartes
Ferreira	Franck	Sorbonne Université
Ferrié	Laurent	Université Paris-Sud/CNRS
Ferry	Angélique	Université de Cergy-Pontoise
Fodjo	Rachel	Faculté de Pharmacie de Châtenay-Malabry
Force	Guillaume	ICMMO
Fornarelli	Pauline	Institut Curie
Frites	Wahiba	Ecole Polytechnique
Gagnot	Glwadys	Université Paris Descartes
Gandon	Vincent	ICMMO
Gigant	Nicolas	PARIS SUD - Faculté de Pharmacie Châtenay-Malabry
Gillaizeau-Simonian	Nicolas	ESPCI Paris
Glinsky-Olivier	Nicolas	ICSN
Gomez	Catherine	CNAM
Goual	Nawel	ICSN
Guimard	Carole	ICSN
Guinchard	Xavier	ICSN
Habert	Loïc	ICSN
Han	Xu	ICSN
He	Bin	Chimie ParisTech
He	Xuefeng	ICMMO
Henry	Sylvain	TCI
HOARAU	Clément	CEA Paris-Saclay
Imani	Zeynab	Université Paris-Sud
Imberdis	Arnaud	CEA Saclay
Ishak	Islem	Sorbonne Université
Jackowski	Olivier	Sorbonne Université
Janin	Yves	CNRS
Jarret	Maxime	ICMMO
Jézéquel	Gwenaëlle	ICSN
Jiang	Zhiwei	Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO)
Juillet	Charlotte	ICSN
Keita	Antoinette	Université Paris Descartes
Kelly	Maurent	ICSN
Kjellberg	Marianne	CEA
Kool	Olivia	ESPCI Paris
Lannou	Marie-Isabelle	Université Paris Descartes
Laxio Arenas	José	Université Paris SUD
Le Bescont	Julie	Institut Curie
Le Gall	Erwan	UPEC
Lefebvre	Gauthier	ESPCI Paris
Lefèvre	Guillaume	Chimie ParisTech
Lesma	Jacopo	Universitè Paris Sud
Levernier	Etienne	Sorbonne Université
Levitre	Guillaume	ICSN
Ling	Johanne	Chimie ParisTech
Liu	Xueyang	Ecole Polytechnique
Liu	Yong-Peng	ICMMO
Lorton	Charlotte	ICSN
Mahe	Capucine	ICSN
Marinetti	Angela	CNRS

Masson	Thibaut	Institut Curie
Mellah	Mohamed	ICMMO
Monteil	Maëlle	Université paris 13
Morissette	Déborah	ICSN
Moyeux	Alban	Université Paris 13
Nawres	Bagannee	ICSN
Oliver	Martin	Université Paris Descartes
Olofsson	Berit	University of Stockholm
Peilleron	Laure	CNRS - Université Paris Sud
Perard Viret	Joëlle	CNRS, Université Paris Descartes
Perez Luna	Alejandro	Sorbonne Université
Picot	Ondine	ESPCI Paris
Pignier	Vincent	ICMMO
Pinet	Alexis	Université Paris Sud
Ponsard	Louise	CEA
Porée	Francois-Hugues	Université Paris Descartes - Faculté de Pharmacie
Pradal	Alexandre	Sorbonne Université
Qi	Chenxiao	ICMMO
Raulin	Melvin	Université de Versailles Saint-Quentin
Ritter	Tobias	Max-Plank Institut für Kohlenforschung
Roulland	Emmanuel	Université Paris Descartes
Rousseau	Lidie	CEA
Roussi	Fanny	CNRS
Roy	Myriam	Sorbonne Université
RR	Juales	ICSN
Ryzhakov	Dmytro	ICCMO
Saague Tenefo	Maximiliene	Université Paris descartes
Sabat	Nazarii	CNRS
Saiegh	Tomas	ESPCI Paris
Sala	Roberto	Sorbonne Université
Sanogo	Youssouf	ICSN
Scuiller	Anaïs	École Polytechnique
Selmani	Aymane	Chimie ParisTech
Sorin	Geoffroy	Faculté de Pharmacie, Université Paris Descartes
Sun	Rongyu	Université Paris Descartes
Talavera-Aleman	Armando	Université de Versailles Saint-Quentin
Thueillon	Sebastien	ICSN- Uuniversité Paris Descartes
Tian	Jiaxin	ICMMO
Tran	Christine	Chimie ParisTech
Varlet	Thomas	ICSN
Villagomez Guzman	Ana Karen	Université de Versailles Saint-Quentin
Voituriez	Arnaud	ICSN
Wen	Zhonghang	Sorbonne Université
Westermeyer	Anne	Chimie ParisTech
Wittman	Stéphane	ICMMO
Wu	Ju	ICMMO
Wu	Shiqi	Universite Paris Descartes
Xavier	Tania	UPE
Yamani	Khalil	Ecole superieure de physique et de Chimie industrielles de la ville de paris
Yang	Shengwen	ICMMO
Yen-Pon	Expédite	CEA Saclay
Yu	Yunliang	ICSN
Yu	Bao	Faculté de pharmacie, Université Paris Descartes

Zhao	Tuan	univerite paris descartes
Zhenhao	Zhang	ICSN
Zhou	Weiping	ICSN