PHARMACIE
Santé
Université Paris Cité

XXII RCO

Paris, May, 29th 2026

BOOK OF ABSTRACTS

TABLE OF CONTENTS

ORGANIZING COMITTEE

Dr Marie-Isabelle Lannou
President

Dr Mathieu Berthelot
Secretary

Dr Diana Lamaa
treasurer

Dr Etienne Brachet
treasurer

Pr Philippe Belmont
Communication manager

Dr Claire Cuyamendous
Communication manager

WELCOME, A FEW WORDS

On behalf on the organizing committee, I am very pleased to welcome you all at the faculty of Pharmacy of the University of Paris Cité for the 22nd Rencontres de Chimie Organique. This one-day conference, organized every year by the Universities of Île-de-France region, offers the opportunity to attend two plenary lectures by world renowned speakers, two invited lectures by young french researchers as well as fourteen oral presentations by young researchers PhD students or post-doctoral fellows and over 50 posters. Communications will deal with a wide range of fields such as catalysis, new methods in organic synthesis, total synthesis of natural products, medicinal chemistry, organometallic chemistry and new NMR methods. Two poster presentation sessions will also take place. Typically, 150 to 200 participants coming from universities across the Île-de-France region attend this event.

We would like to express our sincere gratitude to the Faculty of Pharmacy of Paris for hosting this event. We also extend our warm thanks to all our academic and industrial sponsors for their generous support, which makes this event possible.

We hope that you will enjoy the program and that this conference will be rich in scientific exchanges, leading to future collaborations.

Marie-Isabelle Lannou
President of the Organizing Committee

OUR SPONSORS

huber
Inspired by **temperature**

mtci
Ecole Doctorale
Médicament - Toxicologie
Chimie - Imageries

BUCHI

CDD VAULT
Complexity Simplified

METTLER TOLEDO

vwr™
part of avantor

PorphyChem
Porphyrin Chemicals & Engineering

MDPI

AIS
Advion Interchim
scientific

TCI

JACOMEX

SCF IdF
Société Chimique de France
Bureau Île-de-France

Fondation de la Maison de la Chimie

fluorochem.

PROGRAM

8h – 8h45	Registration and Welcome of Participants
8h45 – 9h00	Welcome Address by the President
9h00 – 9h50	**Plenary lecture: Prof. Dr. M. Christmann** Title: Scrutinization of Natural Products and Reaction Intermediates Using Chemical Synthesis and Data Science
9h50-10h05	« Flash » communication Sponsors
10h05-10h20	**OC-01 Koffi Assa**: Access to inter-nucleoside C-C links by metal catalyzed cross-coupling reactions on glycal type nucleosides
10h20-10h35	**OC-02 Jiasheng Feng:** Sustainable access to 1,3-diamine precursors via iron-catalyzed c(sp^3)–H amination of sulfamate derivatives
	Coffee break/ Poster Session
11h20-11h35	**OC-03 Théo Durand:** Synthesis and reactivity of N-aminopyridinium salts as novel photochemical tools for peptide functionalization
11h35-11h50	**OC-04 Arthur Baudement**: Enantioselective Total Synthesis of Exotine A and B
11h50-12h05	**OC-05 Jun Fang**: Cobalt-catalyzed [2+2+2] cycloadditions of alkynyl yndiamides with nitriles
12h05-12h20	**OC-06 Mélanie Sébastien**: Synthesis and optimization of novel peptidomimetics derivatives inhibiting the efflux pumps of Pseudomonas aeruginosa
12h20-12h45	**Invited lecture: Dr. A. Godard** Title: From PhD Research to DeepTech Venture: Translating Organic Chemistry into Surgical Innovation
	Lunch break/Poster Session
14h00-14h50	**Plenary lecture: Dr. L. Marzo** Title: From photons to carbonyls: sustainable approaches for the synthesis of ketones
14h50-15h05	« Flash » communication Sponsors
15h05-15h20	**OC-07 Batoul Karim**: Bis(iminophosphorane)phosphine NPN Co ^{II} complex for hydrosilylation reactions
15h20-15h35	**OC-08 Camil Benbouziyane:** Total synthesis of (±)-piperhancin b and efforts towards the synthesis of polycyclic neolignans
15h35-15h50	**OC-09 Carla Dubois**: New access to spiroketal enol ether derivatives *via* gold(I)- catalyzed relay catalysis
	Coffee break/ Poster Session
16h30-16h45	**OC-10 Romain Triaud**: Synthesis of novel copper complexes for potential use in the diagnosis of Alzheimer's disease
16h45-17h00	**OC-11 Jospin Le Blanc Lele Losso**: Electrochemical enantioselective nickel-catalyzed cross-coupling of aldimines with aryl iodides.
17h00-17h15	**OC-12 Gabriel Goujon**: A new sulfoximine scaffold for the generation of fluorinated and deuterated radicals.
17h15-17h30	**OC-13 Xavier Xancho**: Diastereo- and enantioselective palladium-catalyzed cycloadditions of 5-vinyloxazolidine-2,4-diones
17h30-17h45	**OC-14 Joan Pereira**: Bio-inspired total synthesis of daphnepapytone A
17h45 – 18h10	**Invited lecture: Dr. C. Chauvier** Title: Organoalkali-catalyzed C–Si cross-couplings with *N*-*tert*-Butyl-*N*'-silyldiazenes
18h10-18h30	Awards Ceremony for Oral Communications and Posters + Closing remarks

PLENARY LECTURES

Prof. Dr. Matthias Christmann
Freie Universität, Berlin

Scrutinization of Natural Products and Reaction Intermediates Using Chemical Synthesis and Data Science

Dr. Leyre Marzo Puerta
Universidad Autonoma de Madrid

From Photons to Carbonyls: Sustainable Approaches for the Synthesis of Ketones

Dr. Leyre Marzo Puerta
Universidad Autónoma de Madrid

Scrutinization of Natural Products and Reaction Intermediates Using Chemical Synthesis and Data Science

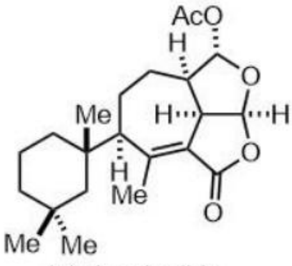
Mathias Christmann

Freie Universität Berlin, Institute of Chemistry and Biochemistry, Takustr. 3,
14195 Berlin, Germany
mathias.christmann@fu-berlin.de

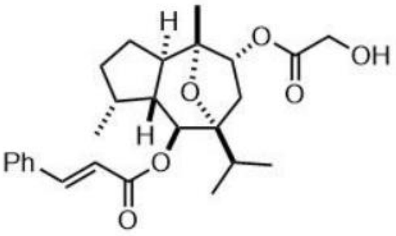
Organic synthesis constitutes *the* enabling science for the creation of new compositions of matter with ramifications for material's science, medicine and biology. Our research program is dedicated to the understanding and modulation of biologically relevant pathways with small molecules[1-3] (Fig. 1). A fundamental challenge in synthesis planning of these target molecules lies in the identification of larger building blocks in order to minimize the number of carbon-carbon bond forming reactions. To this end, we develop catalytic transformations of readily available terpene feedstock. Herein, we demonstrate the utility of catalytically transformed small terpene building blocks in the synthesis of larger terpenes such as sesqui-, tri- and homoterpenoids.

These synthetic studies are complemented by data science approaches that support the extraction, organization, and analysis of chemical information from the literature. By linking molecular structures, reaction data, and bibliographic information, such methods enable the systematic comparison of natural products, synthetic intermediates, and plausible biosynthetic or reaction pathways.

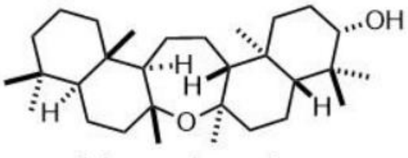
Together, chemical synthesis and data science provide complementary tools for the scrutinization of complex molecular systems. While synthesis offers experimental validation through the preparation and interrogation of defined compounds, data driven methods facilitate the recognition of patterns, relationships, and inconsistencies across large bodies of chemical knowledge.



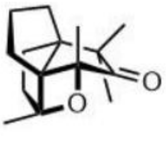
(+)-darwinolide



(+)-englerin A



(+)-cupacinoxepin



dichrocephone B

References :

[1] Siemon, T.; Wang, Z.; Bian, G.; Seitz, T.; Ye, Z.; Lu, Y; Cheng, S.; Ding, Y.; Deng, Z.; Liu, T.; Christmann, M. *J. Am. Chem. Soc.* **2020**, *142*, 2760.

[2] Wiese, L.; Kolbe, S. M.; Weber, M.; Ludlow, M.; Christmann, M. *Chem. Sci.* **2024**, *15*, 10121.

[3] Christmann, M. *Org. Lett.* **2025**, *27*, 4

From Photons to Carbonyls: Sustainable Approaches for the Synthesis of Ketones.

Leyre MARZO

[1] Organic Chemistry Department (Módulo 1), and Institute for Advanced Research in Chemical Sciences (IAdChem)
Universidad Autónoma de Madrid, 28049 Madrid, Spain.
e-mail: leyre.marzo@uam.es

Ketones are highly versatile building blocks found in countless natural products. Although thousands of methods exist for their synthesis, there remains a strong need for more sustainable and environmentally friendly approaches. This talk will explore diverse photochemical approaches to prepare complex ketones form simple building blocks.

Cycloalkanols proved to be excellent precursors for the synthesis of highly complex ketones. Herein we exploit the photochemical ring opening of unstrained cycloalkanols followed by a Giese reaction to obtain highly functionalized ketones in a racemic and enantioselective manner. We have demonstrated that the reaction can be performed either under photocatalytic conditions, or photochemical ones through the formation of an EDA complex. Moreover, this method enables the decarboxylative synthesis of C-4 substituted chroman-2-ones under very mild conditions.[1]

In addition, in recent years, the photochemical activation of NHC-derived acyl azolium salts has enabled the development of sustainable acylation reactions. In this regard, herein we present a photochemical study of the reactivity of acyl azolium salts that comprises the detection and characterization of the triplet excited state and of the decisive ketyl radical intermediate. Moreover, this mechanistic insight allowed us the development of an alternative method based on a silane-mediated tandem HAT/XAT activation strategy that enables not only the acylation of alkyl bromides, but also the acylation of the more challenging alkyl chlorides. The method has proven to be efficient regardless of the electronic properties of the acyl azolium or the substituents present in the alkyl halide. Furthermore, its robustness has been proven through the functionalization of natural product derivatives either as acyl azolium or alkyl bromide derivatives.[2]

Acknowledgments: We thank the Spanish Government (PID2023-146050NA-I00; RYC2021-031590-I; RTI2018-095038–B-I00, PID2019-110091GBI00), CAM (PIPF-2023/ECO-30898; SI1/PJI/2019-00237), DFG (TRR 325-444632635) and the Alexander von Humboldt foundation.

References:

[1] a) N. Salaverri, B. Carli, S. Diaz-Tendero, L. Marzo*, J. Alemán*, *Org. Lett*. **2022**, *24*, 3123; b) N. Salaverri, B. Carli, P. Gratal, L. Marzo*, J. Alemán*, *Adv. Synth. Catal*. **2022**, *364*, 1689; c) B. Carli, N. Salaverri, L. Martínez-Fernández, M. Goicuría, J. Alemán*, L. Marzo* *Org. Lett*. **2024**, *26*, 4542; d) E. Kowalska, B. Carli, J. Alemán,* L. Marzo,* Anna Albrecht* *Adv. Synth. Cat*. **2025**, *367*, e70174

[2] I. MacLean, D. J. Grenda, E. Echávarri, S. Muth, P. Nuernberger, L. Marzo*, *J. Am. Chem. Soc*. **2025**, *147*, 31324.

INVITED LECTURES

Dr. Amélie Godard
Fluornil

From PhD Research to DeepTech Venture: Translating Organic Chemistry into Surgical Innovation

Dr. Clément Chauvier
Institut Parisien de Chimie Moléculaire

Organoalkali-Catalyzed C–Si Cross-Couplings with *N-tert*-Butyl-*N*’-Silyldiazenes

IL-01

From PhD Research to DeepTech Venture: Translating Organic Chemistry into Surgical Innovation

Amélie Godard[1]
[1] *FLUONIR, Université Bourgogne Europe, 9 Avenue Alain Savary, 21 000 Dijon,*
France
Amelie.godard@fluonir.fr

Scientific entrepreneurship is often perceived as a departure from research, but in reality, it is a demanding extension of it. For a PhD student in organic chemistry, the path from the round-bottom flask to a clinical startup is rarely a straight line; it is a complex process of translating chemical properties into medical solutions. In this presentation, I will share the journey that led to the creation of **FLUONIR**, a deeptech company specializing in fluorescence-guided surgery (FGS), and discuss how we transformed a doctoral research project into a structured innovation strategy.

The scientific core of this work lies in the development of targeted fluorescent probes emitting in the second near-infrared window (NIR-II, 1000–1700 nm). During my PhD, the objective was to overcome the physical limitations of traditional imaging. By working in the NIR-II window, we could significantly reduce photon scattering and tissue autofluorescence, allowing deeper and more precise *in vivo* detection of tumors such as glioblastomas and ovarian cancers [1,2]. At that stage, our success was measured by high image resolution, probe photostability, and the specificity of our targeting ligands. However, the filing of a patent [3] and the support of SATT Grenoble Alpes forced us to look beyond the bench. We had to ask a question that academic training rarely addresses: “Is this a great molecule, or is it a great product?”

A major turning point occurred when we moved out of the chemistry lab to meet the end-users. Through discussions with head and neck surgeons, we realized that the unmet need was not simply a higher signal-to-noise ratio. Clinicians needed a tool capable of clearly delineating tumor margins in real time during complex invasive procedures, without disrupting the surgical workflow. This immersion reshaped the entire project. It was no longer only about molecular performance, but about clinical integration. This feedback loop between chemists and clinicians is what transformed our academic research into a targeted innovation strategy.

Building a startup such as FLUONIR also means navigating a completely different ecosystem. For a young researcher, this transition involves a steep learning curve in intellectual property, regulatory strategy, financing, and business development. It also requires building interdisciplinary teams where organic chemists, clinicians, engineers, and business developers learn to work toward a common objective. I will discuss how the regional ecosystem, including hospitals, incubators, academic laboratories, technopoles, and industrial equipment manufacturers, acts as a catalyst to bridge the gap between proof-of-concept and market-ready solutions.

Today, FLUONIR’s roadmap is structured around two complementary horizons. In the short term, we leverage our expertise in fluorescent chemistry to provide custom molecular design and preclinical imaging services. In the longer term, our ambition is to bring our own targeted imaging agents into the operating room by combining fluorescent probes with therapeutic antibodies to improve surgical precision and patient outcomes. Through this experience, I aim to show PhD students that a background in organic chemistry, characterized by resilience and analytical rigor, can become a powerful foundation for entrepreneurship. It is possible to build a career that does not choose between science and impact, but instead uses one to fuel the other.

References:

[1] Godard A. *et al. Bioconjugate Chemistry* (2020), DOI: 10.1021/acs.bioconjchem.0c00175.
[2] Godard A. *et al. Journal of Medicinal Chemistry* (2023), DOI: 10.1021/acs.jmedchem.3c00100.
[3] Patent US2022322945A1.

IL-02

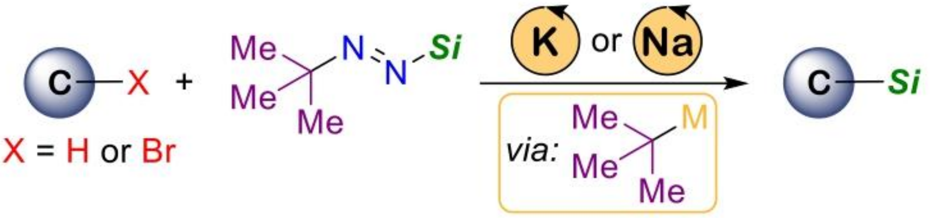
Organoalkali-Catalyzed C–Si Cross-Couplings with *N*-*tert*-Butyl-*N*'-Silyldiazenes

Clément CHAUVIER

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

Organosilicon compounds have become indispensable tools in the chemical sciences, as evidenced by their growing applications in organic synthesis, drug discovery, and materials science. Among the conventional methods for C–Si bond formation, cross-coupling reactions provide a particularly versatile route to organosilicon compounds due to the broad range of organic substrates and silylating reagents that can be used.[1] However, many of these methods are limited by the specific nature and/or the amount of promoters required to facilitate the key C–Si bond formation.

This communication will describe the invention and development of a novel C–Si cross-coupling strategy through the design of a new class of silylating reagents, namely silylated *tert*-butyl diazenes (*t*Bu–N═N–SiR_3). The synthetic utility of these reagents will be demonstrated in their ability to rapidly assemble diverse organosilicon compounds *via* silylation of C–H[2] and C–Br[3] bonds upon simple treatment with catalytic amounts of alkali metal alkoxides. Mechanistic considerations highlighting the involvement of alkali metal-stabilized *tert*-butyl carbanion intermediates will be discussed along with their conceptual implications, notably for transposing the stoichiometric metalation chemistry of group 1 polar organometallic reagents (e.g. organolithium compounds) into a catalytic framework.



• General • Catalytic • Transition metal-free • Ambient conditions

---

[1] For recent reviews on C–Si cross-couplings by C–H functionalization, see: a) I. F. Yu, J. W. Wilson, J. F. Hartwig, *Chem. Rev.* **2023**, *123*, 11619–11663; b) C. Cheng, J. F. Hartwig, *Chem. Rev.* **2015**, *115*, 8946–8975; c) S. C. Richter, M. Oestreich, *Trends Chem.* **2020**, *2*, 13–27.

[2] a) X. Zhang, L. Fensterbank, C. Chauvier, *ACS Catal.* **2023**, *13*, 16207–16214; b) B. Neil, L. Saadi, L. Fensterbank, C. Chauvier, *Angew. Chem. Int. Ed.* **2023**, *62*, e202306115; c) B. Neil, F. Lucien, L. Fensterbank, C. Chauvier, *ACS Catal.* **2021**, *11*, 13085–13090; d) Y. Zeng, L. Fensterbank, C. Chauvier, *ChemCatChem* **2025**, *17*, e202500121; e) L. Saadi, L. Valade, C. Chauvier, *Chem. Sci.* **2025**, *16*, 9794–9801.

[3] B. Neil, T. Deis, L. Fensterbank, C. Chauvier, *Angew. Chem. Int. Ed.* **2025**, *64*, e202419496.

Oral Communications

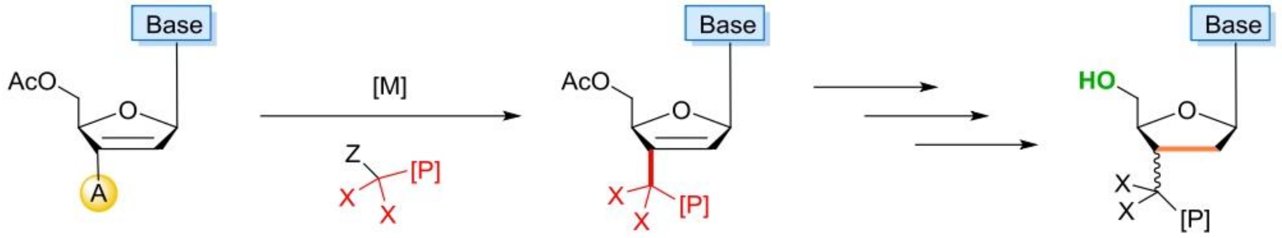
OC-01

Access to inter-nucleoside C-C links by metal catalyzed cross-coupling reactions on glycal type nucleosides.

Koffi ASSA,[1] Latifa ILLIA MAGAGI,[1] Victor MONNOT,[1] Jacques UZIEL,[1] Morgane DE ROBICHON,[1] Marc LECOUVEY,[2] Evelyne MIGIANU-GRIFFONI,[2] and Angélique FERRY,[1]

[1] BioCIS, CY Cergy Paris Université, 5 Mail gay Lussac 95000 Neuville sur-Oise
[2] CB3S, Université Sorbonne Paris Nord, 1 Rue de Chablis 93000 Bobigny
Koffi.assa@cyu.fr

Nucleosides and nucleotides represent a ubiquitous family of biomolecules involved in many key processes in biology. Given their importance, it is not surprising that this class of molecules is emerging as prototypes for the discovery of bioactive compounds. In particular, the development of unnatural mimicry is an important area of research.[1] The modification on the 3' position of the furanoside ring is particularly interesting because it is the location of the phosphate bond in DNA/RNA polymers. The AZT drug bearing an azido group at this position attests to the importance of such derivatives. However, modulation at the 3' position is synthetically difficult according to current methods. We therefore propose to develop a new method to insert at the 3' position of the nucleoside a phosphorylated function bonded to the nucleoside by an unnatural carbon-carbon bond (C-C). This synthesis is carried out by metal-catalyzed coupling reaction between an unsaturated 3'-iodonucleoside and a metallic phosphonates reagents. The synthesis of small oligomers is planned in order to obtain mimics of oligonucleotides. This method provides a new pathway to access non-natural oligonucleotide analogues.



[M] = Metals (Zn, Cu, Pd) Z = Metal (Zn or Cu) A = Halide (I) X = H or F

[1] A. Salihovic, A. Taladriz-Sender and G. A. Burley, *Chem. Sci.* **2025**, 16, 11700.

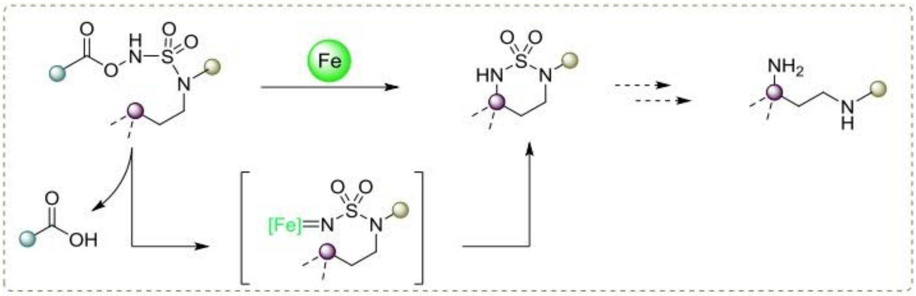
OC-02

Sustainable Access to 1,3-Diamine Precursors via Iron-Catalyzed C(sp³)–H Amination of Sulfamate Derivatives

Jiasheng FENG, Guillaume PRESTAT, Farouk BERHAL

Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques, Université Paris Cité, 45 Rue des Saints-Pères,
75006, Paris, France
jiasheng.feng@etu.u-paris.fr

Nitrogen-based scaffolds are ubiquitous in pharmaceuticals, forming the backbone of a wide range of bioactive molecules. Among these, diamines represent an important subcategory. While the synthesis of 1,2-diamines is well established, their isomeric counterparts—1,3-diamines—remain relatively underexplored, offering both a synthetic challenge and an opportunity for innovation. Current methods for 1,3-diamine synthesis often rely on metal catalysis under harsh conditions, frequently requiring external oxidants or environmentally harmful heavy metals such as rhodium or iridium.[1] For several years, our group has been developing more sustainable processes for nitrene insertion into C=C and C(sp³)–H bonds via iron-catalyzed activation of hydroxylamine, providing a versatile route to C–N bond formation.[2] Hydroxylamine has gained recently considerable as a clean, readily available nitrene precursor. Its intrinsic oxidizing properties eliminate the need for external oxidants, offering a more sustainable and environmentally benign alternative.



In this context, the group of Eric Meggers demonstrated the efficiency of benzoylated urea-based substrates in iron-catalyzed C(sp³)–H amination, yielding five-membered imidazolidinone heterocycles as precursors to 1,2-diamines.[3] Building on this concept, our strategy involves the use of acylated sulfamate substrates to enable the selective formation of analogous six-membered sulfamate products. This approach offers a green, efficient, and operationally straightforward route to access 1,3-diamine frameworks. In this communication, we will present and discuss the optimization of the reaction conditions, along with a comprehensive analysis of the reaction's scope and limitations.

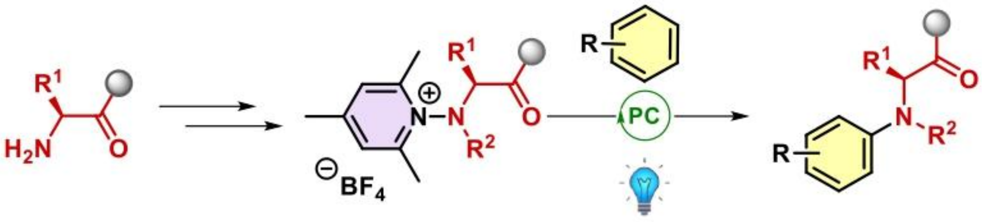
References :
[1] (a) H. Lebel, K. Huard, S. Lectard, *J. Am. Chem. Soc.* **2005**, *127*, 14198; (b) H. Lebel, S. Lectard, M. Parmentier, *Org. Lett.* **2007**, *9*, 4797; (c) S. D. Griggs, A. Martin-Roncero, A. Nelson, S. P. Marsden, *Chem. Commun.* **2021**, *57*, 919.
[2] (a) G. Kirby, L. Grimaud, M. R. Vitale, G. Prestat, F. Berhal, *J. Org. Chem.* **2021**, *23*, 9428; (b) H. Esteves, T. Xavier, S. Lajnef, F. Peyrot, G. Lefèvre, G. Prestat, F. Berhal, *ACS. Catal.* **2024**, *14*, 4329.
[3] L. Jarrige, Z. Zhou, E. Meggers, *Angew. Chem. Int. Ed.* **2021**, *60*, 6314.

Synthesis and Reactivity of N-Aminopyridinium Salts as Novel Photochemical Tools for Peptide Functionalization

Théo DURAND,[1] Benoît CROUSSE[1], Sandrine ONGERI[1], Guillaume DAGOUSSET[1]
[1] FluoPEPIT - BioCIS, Uiversité Paris-Saclay, 91400 France
theo.durand@universite-paris-saclay.fr

Photoredox catalysis has recently emerged as a powerful tool for carrying out radical reactions under particularly mild and eco-friendly conditions (ambient temperature, numerous compatible solvents including water, catalytic amount of photocatalyst, etc.), using visible light as the sole energy source.[1] These conditions help to explain why photoredox catalysis is increasingly used to functionalize highly complex substrates at a late stage of synthesis.[2] Photocatalysis therefore appears to be a method of choice for functionalizing very complex molecules such as peptides of interest.

N-aminopyridiniums are becoming highly attractive new tools for the formation of amidyl radicals.[3] Due to their *N-N* bond being photoreducible using an electron transfer from the excited state of an appropriate photocatalyst under very mild conditions, these salts are ideal suppliers of nitrogen-centered radicals to perform amination of aromatic/unsaturated molecules. However, substrates incorporating amino acids have never been synthesized nor used. Our first objective, achieved during the first half of my PhD, was to synthesize new amino acids containing aminopyridinium groups and to develop a metal-free, photocatalyzed coupling of the pyridinium groups derived from these amino acids with aromatic molecules. The second objective, currently under development, is to extend this strategy to short peptides, and then to peptides of therapeutic interest.



R^1 = amino acid lateral chain
R^2 = withdrawing group

Scheme 1. *N*-Aminopyridinium synthesis and reactivity

References :
[1] T. P. Yoon, M. A. Ischay, J. DU; *Nat. Chem*. **2010**, *2*, 527
[2] P. Bellotti, H.-M. Huang, T. Faber, F; *Chem. Rev*. **2023**, *123*, 4237.
[3] P. Roychowdhury, S. Samanta, H. Tan, D. C. Powers; *Org. Chem. Front*. **2023**, *10.*, 2563-2580.

OC-04

Enantioselective Total Synthesis of Exotine A and B

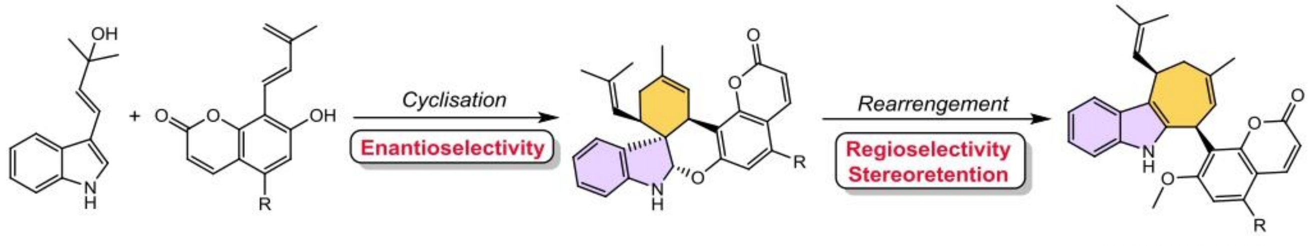
Arthur Baudement,[1] Radosław Suchanek,[2] Luc Neuville,[1] Geraldine Masson[1]

[1] ICSN, CNRS UPR 2301, *1, av. de la Terrasse, Université Paris-Saclay, Gif-sur-Yvette 91198 Cedex, France*
[2] Department of Organic Chemistry, Wroclaw University of Science, Poland
Arthur.baudement@cnrs.fr

Exotines are two natural products isolated from *Murraya exotica*, a plant native to Southeast Asia.[1] These compounds exhibit promising biological activity and feature a unique chiral cyclohepta[b]indole core, making them appealing targets for total synthesis. To date, two total syntheses have been reported, but none of them is enantioselective. [2,3]

Guided by the biosynthetic hypothesis involving a spirocyclisation–rearrangement sequence, we developed an enantioselective Chiral phosphoric acid (CPA) catalyzed spirocyclisation of indole derivative with phenolic dienes to access enantioenriched chromenoindole intermediates. Comprehensive experimental and DFT studies reveal the factors governing the diastereo and enantioselectivity.

A subsequent methylation and a stereoretentive 1,2-alkyl shift of the 3,3′-spiroindoleinine intermediate enable formation of the cyclohepta[b]indole core. This strategy provides Exotine A and Exotine B in good yields and excellent enantiopurity.



Exotine A and B

References :

[1] Liu, B.-Y.; Zhang, C.; Zeng, K.-W.; Li, J.; Guo, X.-Y.; Zhao, M.-B.; Tu, P.-F.; Jiang, Y. *Org. Lett.* **2015**, *17* (17), 4380–4383.
[2] Cheng, B.; Volpin, G.; Morstein, J.; Trauner, D. *Org. Lett.* **2018**, *20* (14), 4358–4361.
[3] Lepovitz, L. T.; Martin, S. F. *J. Org. Chem.* **2021**, *86* (16), 10946–10953.

OC-05

Cobalt-Catalyzed [2+2+2] Cycloadditions of Alkynyl Yndiamides with Nitriles

Jun FANG,[1] William PARISOT,[1,2] Phannarath PHANSAVATH,[1] and Virginie VIDAL[1]

[1] PSL University, Chimie ParisTech, Institute of Chemistry for Life and Health Sciences,
CNRS 8060, CSB2D Team, 75005 Paris, France
[2] Max-Planck-Institut für Kohlenforschung, 45470 Mülheim an der Ruhr, Germany
phannarath.phansavath@chimieparistech.psl.eu; virginie.vidal@chimieparistech.psl.eu

The pyridine skeleton is the second most common type of ring found in medicinal compounds that exhibit biologically relevant activity.[1] In that context, heteroaromatic rings synthesis via [2+2+2] cycloadditions[2] is a particularly appealing synthetic tool because it allows access to an important variety of organic compounds in a single, atom-economical step.

R^1 = *n*-Bu, Bn; R^2 = Ts
or R^1,R^2 = Cz; n = 1,2
R^3 = aryl, alkyl, heteroaryl

39 examples
up to 95% yield
>99:1 r.r.

- New [2+2+2] pyridine-based cycloadducts
- Broad scope
- High regioselectivity
- Green solvent
- Post-functionalization reactions
- Gram scale

As part of our ongoing work on transition metal-catalyzed cycloaddition reactions,[3] we present here a novel user-friendly [2+2+2] cycloaddition of alkynyl yndiamides[4] with nitriles, providing access to 39 new 2,3-dihydro-1H-pyrrolo[2,3-c]pyridin-7-amine and 1,2,3,4-tetrahydro-1,7-naphthyridin-8-yl)-9H-carbazole derivatives under sustainable catalytic conditions. The in situ catalytic system uses a simple, inexpensive, and commercially available cobalt salt with a diphosphine ligand and 2-MeTHF as a green bio-based solvent. This versatile catalytic system shows appreciable functional tolerance and affords complex pyridine scaffolds with high regioselectivity, producing a single regioisomer in up to 95% yield.[5]

References :
[1] Taylor, R. D.; MacCoss, M.; Lawson, A. D. G. *J. Med. Chem.* **2014**, 57, 5845-5859.
[2] a) Vollhardt, K. P. C. *Angew. Chem. Int. Ed.* **1984**, 23, 539- 556. b) Gandon, V.; Aubert, C.; Malacria, M. *Chem. Commun.* **2006**, 2209-2217. c) D'Souza, B. R.; Lane, T. K.; Louie, J. *Org. Lett.* **2011**, 13, 2936-2939. d) Wang, C.-S.; Sun, Q.; García, F.; Wang, C.; Yoshikai, N. *Angew. Chem. Int. Ed.* **2021**, 60, 9627-9634. e) Cai, J.; Cen, K.; Zhai, Z.; Wei, J.; Liu, Y.; Feng, Y.; Yu, J.; Liu, H.; Zhao, F.; Wang, Q. *Adv. Synth. Catal.* **2024**, 366, 3913-3919.
[3] a) Ye, F.; Haddad, M.; Ratovelomanana-Vidal, V.; Michelet, V. *Org. Lett.* **2017**, 19, 1104-1107. b) Huvelle, S.; Matton, P.; Tran, C.; Rager, M.-N.; Haddad, M.; Ratovelomanana-Vidal, V. *Org. Lett.* **2022**, 24, 5126-5131. c) Parisot, W.; Huvelle, S.; Haddad, M.; Lefèvre, G.; Phansavath, P.; Ratovelomanana-Vidal, V. *Org. Chem. Front.* **2023**, 10, 1309-1315. d) Parisot, W.; Haddad, M.; Phansavath, P.; Lefèvre, G.; Ratovelomanana-Vidal, V. *Chem. Eur. J.* **2024**, 30, e202400096.
[4] Mansfield, S. J.; Christensen, K. E.; Thompson, A. L.; Ma, K.; Jones, M. W.; Mekareeya, A.; Anderson, E. A. *Angew. Chem. Int. Ed.* **2017**, 56, 14428-14432.
[5] Fang, J.; Parisot, W.; Phansavath, P.; Ratovelomanana-Vidal, V. *Org. Lett.* **2026**, 28, 4240−4245.

RCO XXII
Paris, May 29th 2026
Rencontres de Chimie Organique
PHARMACIE
Santé
Université Paris Cité

Synthesis and optimization of novel peptidomimetics derivatives inhibiting the efflux pumps of Pseudomonas aeruginosa

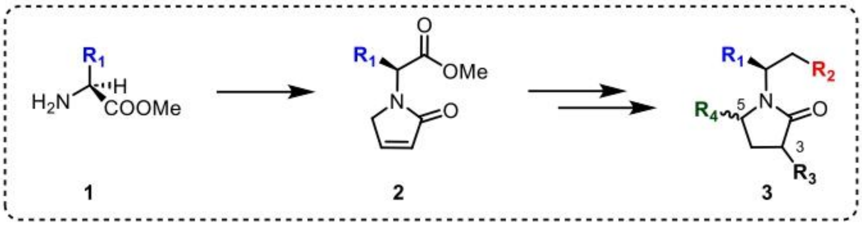
Mélanie SEBASTIEN,[1] Hilal WEHBI,[1] Florent BARBAULT,[2] Laurine VASSEUR,[2] Isabelle BROUTIN,[1] Marie-Isabelle Lannou,[1] Gilles PHAN,[1] Joëlle PERARD[1]

[1] CiTCoM UMR 8038, Université Paris Cité, Faculté de Pharmacie de Paris, 4 avenue de l'Observatoire, 75006.
[2] ITODYS UMR 7086, Université Paris Cité, UFR de Chimie, 15 rue Jean Antoine de Baïf, 75013.

Melanie.sebastien@etu.u-paris.fr

The rise of multidrug-resistant *Pseudomonas aeruginosa* (PA) is a critical challenge in the treatment of cystic fibrosis (CF), as this pathogen is a leading cause of morbidity and mortality in CF patients. PA's resistance is often attributed to its efficient efflux pumps, particularly the MexAB-OprM system, [1] which expels antibiotics before they can act. Addressing this mechanism is crucial to overcome treatment failures and to improve patient outcomes.

In this study, funded by the French association "Vaincre la Mucoviscidose," we present an innovative approach aimed at inhibiting PA's efflux pump system. We focus on the synthesis of novel peptidomimetics designed to block the MexB transporter, a key player in the recognition and expulsion of antibiotics. Unlike traditional inhibitors, our peptidomimetics are built on a newly developed scaffold[2] that could enhance their affinity and specificity for MexB, potentially leading to more effective inhibition of efflux activity. Docking analysis and initial biological test have shown promising results.



This strategy represents an encouraging new avenue in combating antibiotic resistance in CF patients. By targeting the efflux pump mechanism, we hope to restore the efficacy of existing antibiotics and offer a much-needed therapeutic solution for this vulnerable patient group.

References :
[1] Glavier, M.; *Nat*. Commun. 2020, 11, 4948.
[2] Souquet, F.; *Synthesis*. 2020, 2970–2978.

OC-07

Bis(iminophosphorane)phosphine NPN Co^{II} Complex for Hydrosilylation reactions

Batoul KARIM,[1] Ingrid POPOVICI,[1] Audrey AUFFRANT [1]

[1] Laboratoire de Chimie Moléculaire (LCM), CNRS, Ecole Polytechnique, Institut Polytechnique de Paris, Route de Saclay, 91120 Palaiseau, France
batoul.karim@polytechnique.edu

Among the methods allowing the reduction of unsaturated bonds, hydrosilylation has emerged as a particularly valuable methodology enabling the conversion of various derivatives into organosilicon intermediates under relatively mild conditions.[1] It presents the advantage to employ easy-to-handle and affordable silane reagents and to produce organosilicon compounds that can be further functionalized.

This reaction, which is used at the industrial level, mainly rely on platinum catalysts.[2] However, catalysts based on more abundant metals have increasingly been developed as an alternative.[3] Ligand engineering is generally required to develop complexes with these metals, with a performance comparable to those of noble ones.

For such reductive processes, electron-rich ligands lead in general to very reactive catalytic species. Given our interest for iminophosphoranes (P=N) which are ylide type electron rich N based ligands, we studied the potential of mixed ligands associating iminophosphoranes with other coordinating moiety (pyridine, phosphine…)[4,5] having complementary electronic properties to develop hydrosilylation catalysts.

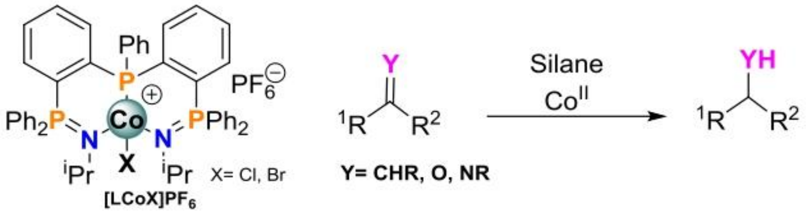


Figure 1. Co-catalyzed hydrosilylation reactions

In this work, we present the synthesis of an unprecedented bis(iminophosphorane)phosphine (NPN) ligand, as well as the synthesis and characterization of its Co^{II} complexes and discuss their catalytic activity in the hydrosilylation of olefins[6] and polar bonds.

References:

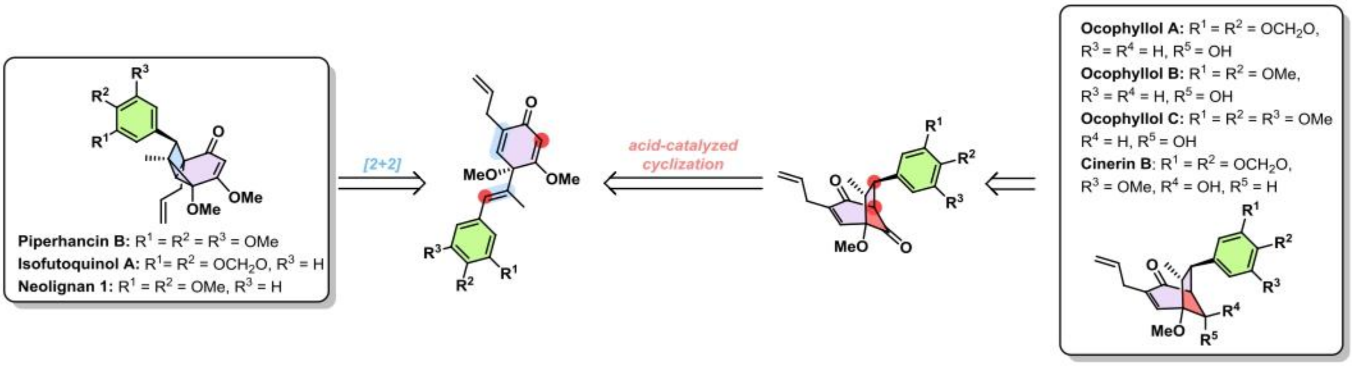
[1] Troegel, D.; Stohrer, J.; *Coord. Chem. Rev.* **2011**, 255, 1440–1459.
[2] Speier, J. L.; Webster, J. A.; Barnes, G. H.; *J. Am. Chem. Soc.* **1957**, 79, 974–979.
[3] de Almeida, L. D.; Wang, H.; Junge, K.; Cui, X.; Beller, M.; Angew. *Chem. Int. Ed.* **2021**, 60, 550–565.
[4] García-Garrido, S. E.; Presa Soto, A.; García-Álvarez, J.; *Adv. Organomet. Chem.* **2022**, 77, 105–168.
[5] Popovici, I.; Barthes, C.; Tannoux, T.; Duhayon, C.; Casaretto, N.; Monari, A.; Auffrant, A.; Canac, Y.; *Inorg. Chem.* **2023**, 62, 2376–2388.
[6] Popovici, I.; Chen, Y.; Bourcier, S.; Casaretto, N.; Auffrant, A.; *Dalton Trans.* **2025**, 54, 15705.

Total synthesis of (±)-piperhancin B and efforts towards the synthesis of polycyclic neolignans

Camil BENBOUZIYANE,[1] Cyrille KOUKLOVSKY[1] and Aurélien de la TORRE[1]

[1] Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO)
Équipe Méthodologie, Synthèse et Molécules thérapeutiques (MS&MT)
camil.benbouziyane@universite-paris-saclay.fr

Neolignans are a class of natural products produced by various plant families, including *Magnoliaceae*, *Piperaceae* and *Lauraceae*. They are composed of two propylbenzene units, but display a diversity of possible cyclization and oxidation patterns, making it a natural product class of ca. 200 members[1]. Piperhancins A and B[2], neolignan 1[3] and ocophillols A-C[4] have not succumbed to total synthesis to date, while cinerin B[5] and isofutoquinol A[6] were only synthesized in racemic form[7]. In this project, we propose to achieve the total synthesis of these intricated natural products.



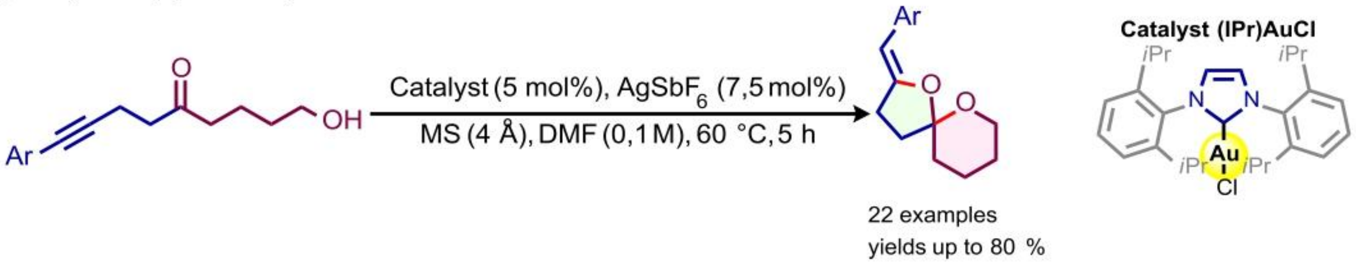
References :
[1] Teponno, R. B.; Kusari, S.; Spiteller, M. *Nat. Prod. Rep.* **2016**, *33*, 1044.
[2] Yang, F.; Su, B.-J.; Hu, Y.-J.; Liu, J.-L.; Li, H.; Wang, Y.-Q.; Liao, H.-B.; Liang, D. *J. Org. Chem.* **2021**, *86*, 5284
[3] Li, J.; Tanaka, M.; Kurasawa, K.; Ikeda, T.; Nohara, T. *Chem. Pharm. Bull.* **2005**, *53*, 235.
[4] Coy, E. D.; Cuca, L. E.; Sefkow, M. *J. Nat. Prod.* **2009**, *72*, 1245.
[5] Coy, E. D.; Cuca, L. E.; Sefkow, M. *Phytochem.* **2009**, *70*, 1309.
[6] Matsui, K.; Munakata, K. *Tetrahedron Lett.* **1976**, *17*, 4371.
[7] (a) Shizuri, Y.; Nakamura, K.; Yamamura, S.; Ohba, S.; Yamashita, H.; Saito, Y. *Tetrahedron Lett.* **1986**, *27*, 727. (b) Coy, E. D.; Cuca, L. E.; Sefkow, M. *Org. Biomol. Chem.* **2010**, *8*, 2003.

New Access to Spiroketal Enol Ether Derivatives via Gold(I)-Catalyzed Relay Catalysis

Carla DUBOIS[1,2], Stéphane WITTMANN[1], Mohammad KRAYANI[1], Chloée BOURNAUD[1], Martial TOFFANO[1], Jean-François BETZER[2], Giang VO-THANH[1].
[1] Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO), **Université Paris-Saclay**, 17 Avenue des sciences, 91400 Orsay, France
[2] Institut de Chimie des Substances Naturelles (ICSN), **CNRS, Université Paris-Saclay**, 1 Avenue de la Terrasse, 91190 Gif-sur-Yvette, France
carla.dubois@ens-paris-saclay.fr

Spiroketals are a prominent class of natural products exhibiting a wide range of biological activities, making them valuable scaffolds in medicinal chemistry. [1] Our research focuses specifically on the spiroketal enol ether motif. Despite its prevalence in bioactive molecules, a general and efficient synthetic methodology to access this specific architecture remains elusive. Existing synthetic strategies typically involve arduous multi-step sequences and extensive functional group manipulations. Furthermore, controlling the stereoselectivity of the double bond remains a significant challenge. To overcome these limitations, recent advancements in spiroketal synthesis have focused on the use of trifunctional substrates, which facilitate more direct and streamlined construction of these complex framework.[2,3]

In this communication we report a novel synthetic route toward spiroketal enol ethers via a cascade reaction sequence characterized by high functional group tolerance. This synthesis proceeds in two stages, the formation of a hemiketal intermediate through the addition of a hydroxyl group to a carbonyl, followed by a gold(1) (NHC)-catalyzed 5-*exo*-dig cyclization involving a pendant alkyne. Under optimized reaction conditions, a variety of spiroketal enol ether derivatives were isolated in moderate to good yields (up to 80%).



The details of this synthetic study, including substrate scope and mechanistic insights, will be presented and discussed in this communication.

References :

[1] Sperry, J.; Wilson, Z. E.; Rathwell, D. C. K.; Brimble, M. A. Isolation, Biological Activity and Synthesis of Benzannulated Spiroketal Natural Products. *Nat. Prod. Rep.* **2010**, *27* (8), 1117–1137. https://doi.org/10.1039/B911514P.
[2] Toshima, H.; Furumoto, Y.; Inamura, S.; Ichihara, A. Synthesis of Spiroacetal Enol Ethers *via* Intramolecular Conjugate Addition of Hemiacetal Alkoxides to Alkynoates. *Tetrahedron Letters* **1996**, *37* (32), 5707–5710. https://doi.org/10.1016/0040-4039(96)01206-3.
[3] Yoneda, N.; Fukata, Y.; Asano, K.; Matsubara, S. Asymmetric Synthesis of Spiroketals with Aminothiourea Catalysts. *Angew Chem Int Ed Engl* **2015**, *54* (51), 15497–15500. https://doi.org/10.1002/anie.201508405

OC-10

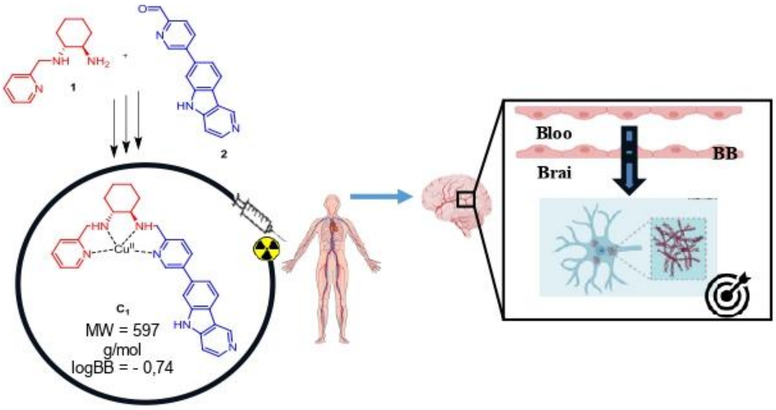
Synthesis of novel copper complexes for potential use in the diagnosis of Alzheimer's disease

Romain TRIAUD, Alban MOYEUX, Olivier GAGER, Milena SALERNO
Laboratoire Chimie Bioorganique, Biophysique et Biomatériaux pour la Santé (CB3S), UMR 7244
Université Sorbonne Paris Nord, 1 rue Chablis Bobigny 93000
Triaud.romain@gmail.com

Predicting Alzheimer's disease is the focus of many research projects. In the literature, the potential of PET-tau to predict cognitive decline and the development of brain atrophy in Alzheimer's patients has been proposed[1] . In our laboratory, we are developing new copper complexes for PET-tau imaging in the diagnosis of this disease. With a longer lifetime than radiotracers already in use, copper complexes appear to be an innovative solution.

Previous work in our laboratory led to the synthesis of new copper complexes targeting amyloid plaques, yielding promising results.[2] The aim of the present study is to synthesize a series of new copper complexes designed for tau protein aggregates. These complexes will be derived from [18F]-Flortaucipir and [18F]-RO948, two molecules able to recognise tau. The key step in this synthetic strategy is a reductive amination between a diamine and a molecule capable of targeting tau. The synthesis of the ligand that will allow the preparation of the first complex involves Suzuki couplings followed by reductive cyclisation.

Due to solubility problems, the ligand synthesis pathway had to be adapted by adding an indole ring protection/deprotection step. As a result, one of the ligands was successfully synthesized in 6 steps and then the complex was obtained. The other ligands are still being synthesized using the same strategy.
We have synthesized a new novel copper complex that may be able to specifically target tau protein aggregates and contribute to the development of new strategies in the diagnosis of Alzheimer's disease.



References :
[1] Ossenkoppele et al *Lancet Neurol.* **2022** 21, 726-34
[2] Dellal et al, *JBIC.* 2023 28, 777-790

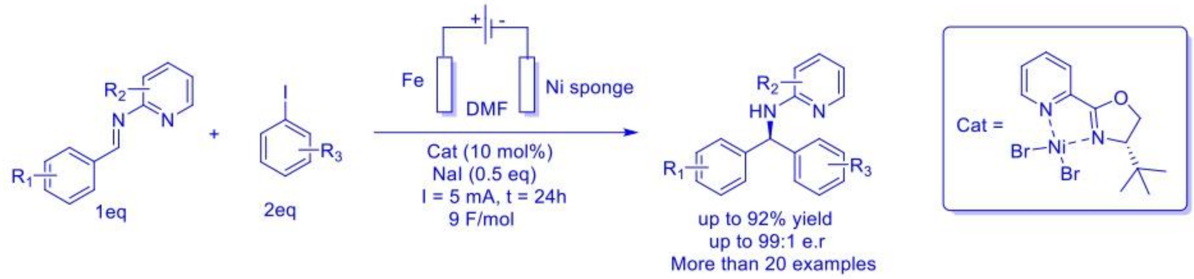
Electrochemical Enantioselective Nickel-Catalyzed Cross-Coupling of Aldimines with Aryl Iodides

Jospin Le Blanc LELE FOSSO,[1] Killian DA GRAÇA,[1] Mohamed MELLAH,[1] and Emmanuelle SCHULZ[1]

[1] Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO), Université Paris-Saclay, 17 Av. des Sciences, 91190 Orsay
Jospin-le-blanc.lele-fosso@universite-paris-saclay.fr

Benzylamines are key motifs in medicinal chemistry, modulating the physicochemical and pharmacological properties of bioactive molecules.[1] Conventional synthetic methods rely on the use of organometallic reagents or transition-metal-catalyzed (palladium, rhodium, and copper) processes, often requiring stoichiometric reducing agents.[2] Cobalt- or nickel-catalyzed reductive arylations have recently emerged as more sustainable alternatives.[3] For example, Zhou et al. developed a protocol using a chiral nickel complex and manganese as a co-reducing agent for the synthesis of chiral benzylamines.[3b] In 2022, Reisman's group described also a method using manganese as a co-reducing agent, as well as an electrochemical approach enabling the production of achiral benzylamines.[4] This strategy, which relies on the use of electrons as reducing agents, constitutes a sustainable approach, avoiding the use of stoichiometric metal reducing agents. However, the enantioselective synthesis of benzylamines via electrochemical processes remains largely unexplored.

In this context, we developed an enantioselective electrocatalytic coupling process of imines with halogenated derivatives, enabling the preparation of chiral benzylamines with good stereochemical control.



After optimizing the chemical and electrochemical parameters of the reaction, the electrochemical conditions developed enable the efficient synthesis of numerous highly enantioenriched benzylamines under mild conditions. This work ultimately opens up significant prospects for the development of more environmentally friendly synthetic methods, inline with sustainable development objectives.

References :

[1] a) D. Ghislieri, N. J. Turner, *Top. Catal.* **2014**, *57*, 284-300 ; b) C. K. Prier, R. K. Zhang, A. R. Buller, S. Brinkmann-Chen, F. H. Arnold, *Nat. Chem.* **2017**, *9*, 629-634

[2] a) E. Le Gall, M. Troupel, J.-Y. Nédélec, *Tetrahedron* **2006,** *62,* 9953-9965 ; b) N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2004**, *126*, 13584-13585 c) G.-N. Ma, T. Zhang, M. Shi, *Org. Lett.* **2009**, *11*, 875-878 ; d) C. Wu, X. Qin, A. M. P. Moeljadi, H. Hirao, J. S. Zhou, *Angew.Chem. Int.Ed.* **2019**, *131*, 2731-2735

[3] a) J. Xiao, M. Wang, X. Yin, S. Yang, P. Gu, X. Lv, Y. Zhao, Z. Shi, *Angew. Chem. Int. Ed.* **2023**, *62*, e202300743 ; b) L. Zhang, X. Wang, M. Pu, C. Chen, P. Yang, Y.-D. Wu, Y. R. Chi, J. S. Zhou, *J. Am. Chem. Soc.* **2023**, *145*, 8498-8509

[4] R. F. Turro, M. Brandstätter, S. E. Reisman, *Angew. Chem. Int. Ed.* **2022**, *61*, e202207597

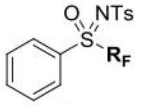
A New Sulfoximine Scaffold for the Generation of Fluorinated and Deuterated Radicals

Gabriel GOUJON,[1] Bruce PÉGOT,[1] Elsa ANSELMI,[1,2] Emmanuel MAGNIER[1]

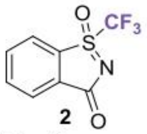
[1]Université Paris-Saclay, UVSQ, CNRS, UMR 8180, Institut Lavoisier de Versailles, 78000, Versailles, France
[2]Université de Tours, Faculté des Sciences et Techniques, 37200 Tours, France
gabriel.goujon-laisney@uvsq.fr

Fluoromethyl groups are of high interest for modifying electronic properties of molecules, and are especially relevant for improving drug efficacy. Insertion of -CF_3 group is well described in the literature, and a lot of FDA-approved drugs today contain this motif. Recognizing the importance of fluorine in medicinal chemistry but hampered by the recent controversy surrounding PFAS, reactions for the insertion of non-PFAS fluorinated motifs have emerged, such as the -CF_2H moiety. N-tosylated sulfoximines have demonstrated their effectiveness in these reactions **1**,[1-2] though little research has been conducted on monofluoromethylation, or on combining fluorine and deuterium chemistry in novel functional groups.

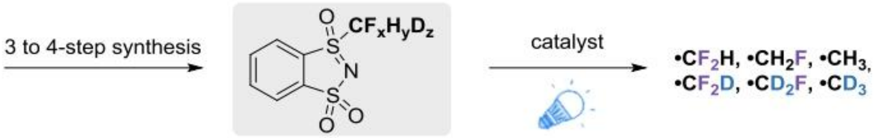
Inspired by the cyclic sulfoximine **2** described by Adachi and Ishihara,[3] we are presenting herein the multi-gram scale synthesis of a new cyclic sulfoximine scaffold **3** capable of generating in photoredox catalysis all of the fluorinated methyl radicals (from •CF_3 to •CH_2F) with an improved reactivity compared to acyclic sulfoximines. This scaffold also has the critical advantage to be able to generate the •CH_3 radical, to be usable in flow chemistry, and recyclable after use.[4-5] Moreover, easy deuteration of these benzodithiazoles enables them to react as •CF_xD_y donors, forming unique functional groups.



1
Acyclic sulfoximine



2
Adachi's reagent



3
fluorinated and/or deuterated benzodithiazoles

References :
[1] Zhang, W.; Wang, F.; Hu, J. *Org. Lett.* **2009**, *11*, 2109-2112.
[2] Noto, N.; Koike, T.; Akita, M. *ACS Catal.* **2019**, *9*, 4382-4387.
[3] Adachi, K., Ishihara, S. *Japan Tokkyo Kokai Patent*, **2005**, 145917.
[4] Wu, P., Goujon, G., Pan, S., Tuccio, B., Pégot, B., Dagousset, G., Anselmi, E., Magnier, E., Bolm, C. *Angew. Chem. Int. Ed.* **2024**, 63, e202412418.
[5] Goujon, G.; Briand, M.; Leclerc, N.; Pégot, B.; Dagousset, G.; Anselmi, E.; Magnier, E. *Org. Process Res. Dev.* **2025**, *7*, 1831-1836

OC-13

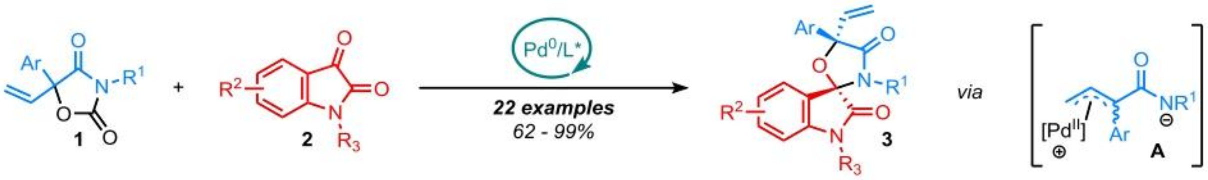
Diastereo- and Enantioselective Palladium-Catalyzed Cycloadditions of 5-Vinyloxazolidine-2,4-diones

Xavier XANCHO,[1] Pinar YILDIRIM,[1] Nicolas CASARETTO[2] and Alexis ARCHAMBEAU [1]

[1] Laboratoire de Synthèse Organique, UMR 7652, CNRS, Ecole Polytechnique, ENSTA,
Institut Polytechnique de Paris, 91128 Palaiseau CEDEX, France
[2]Laboratoire de Chimie Moléculaire, UMR 9168, CNRS, Ecole Polytechnique,
Institut Polytechnique de Paris, 91128 Palaiseau CEDEX, France
xavier.xancho@polytechnique.edu

Nitrogen-containing heterocycles are ubiquitous scaffolds in pharmaceutical compounds due to their ability to interact easily with biological targets, making them highly valuable in drug discovery.[1] Among available synthetic strategies, cycloadditions represent a powerful approach to rapidly construct complex heterocyclic frameworks.[2] In particular, dipolar cycloadditions of transient zwitterionic π-allylpalladium(II) complexes have emerged as a reliable strategy for the stereocontrolled formation of carbo- and heterocycles.[3] In this context, our research group have recently disclosed 5-vinyloxazolidine-2,4-diones **1** (VOxD) as a promising substrate.[4] Under palladium-catalyzed conditions, VOxD **1** undergo ring-opening by oxidative addition and decarboxylation, leading to a dipolar key intermediate **A** able to react with an electrophilic cycloaddition partner.

In this presentation, we describe a diastereo- and enantio-controlled palladium-catalyzed synthesis of various oxazolidinones **3** *via* a (3+2) cycloaddition between VOxD **1** and isatins **2**. A dynamic kinetic resolution process allowed to reach high diastereo- (up to 87:13) and enantioselectivity (up to 97:3). Moreover, the reaction exhibited broad functional group tolerance (22 examples) and post-functionalization reactions were performed to further highlight the synthetic value of this method.



dr up to 87:13
er up to 97:3

References :
[1] Marshall, C. M.; Federice, J. G.; Bell, C. N.; Cox, P. B.; Njardason J. T. *J. Med. Chem.* **2024**, *67*, 11622–11655.
[2] Jørgensen, K. A.; Kobayashi, S. *Cycloaddition Reactions in Organic Synthesis;* Wiley-VCH: Weinheim, **2001**.
[3] For a review: Niu, B.; Wei, Y.; Shi, M. *Org. Chem. Front.* **2021**, *8*, 3475–3501.
[4]For selected publications: a) Sculler, A.; Casaretto, N.; Archambeau, A. *J. Org. Chem.* **2023**, *88*, 9941–9945. b) Li, K.; Zhen, S.; Wang, W.; Du, J.; Yu, S.; Wi, Y.; Guo, H. *Chem. Sci.* **2023**, *14*, 3024–3029. c) Roblin, A.; Casaretto, N.; Archambeau, A. *Org. Lett.* **2023**, *25*, 6453–6458. d) Busicchia, M.; Roblin, A.; Dubois, C.; Mekranter, N.; Casaretto, N.; Archambeau, A. *J. Org. Chem.* **2024**, *89*, 12370–12377.

OC-14

Bio-Inspired Total Synthesis of Daphnepapytone A

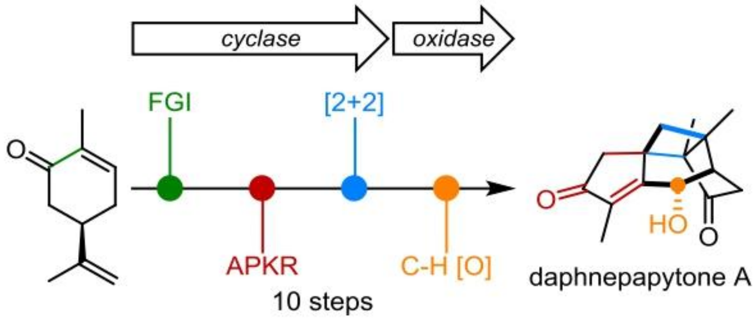
Joan PEREIRA,[1] Nicolas CASARETTO,[2] Gilles FRISON,[3] Bastien NAY[1]

[1]Laboratoire de Synthèse Organique, Ecole Polytechnique, CNRS, ENSTA, Institut Polytechnique de Paris, 91128 Palaiseau
[2]Laboratoire de Chimie Moléculaire, CNRS, Ecole Polytechnique, Institut Polytechnique de Paris, 91128 Palaiseau
[3]Sorbonne Université, CNRS, Laboratoire de Chimie Théorique, 75005 Paris
joan.pereira@polytechnique.edu

Daphnepapytones are sesquiterpene natural products isolated from the stems of Daphne papyracea in 2022, a plant utilized in traditional Chinese medicine against diabetes, rheumatic pain, and traumatic injury.[1],[2] This natural product features a highly congested tetracyclic architecture incorporating a unique, densely substituted cyclobutane ring. In 2025, several groups have reported total syntheses, highlighting the growing interest in daphnepapytone A.[3]

Our retrosynthetic approach is partly biomimetic and involves a two-phase sequence: skeleton construction followed by late-stage oxidation. The key steps to construct the guaiane core include an Eschenmoser–Tanabe fragmentation of (R)-carvone epoxide, an allenylation, and a regioselective distal allenic Pauson Khand reaction. Then, oleodaphnone intermediate was engaged in a [2+2] biomimetic photocycloaddition, affording the bridged cyclobutane core of the target molecule. Finally, a late-stage chemoselective C–H oxidation yielded a triketone intermediate, which was reduced in a remarkably chemo- and stereoselective manner to deliver the natural product.

In addition to the total synthesis of daphnepapytone A, we achieved the total syntheses of three other guaiane-type sesquiterpenes: oleodaphnone, diarthroncha C, and daphnenicillata W (including a structure revision). Moreover, we observed unexpected rearrangements due to the lability of the cyclobutane moety.



References :
[1] Huang, S.-Z.; Wang, Q.; Yuan, J.-Z.; Cai, C.-H.; Wang, H.; Mándi, A.; Kurtán, T.; Dai, H.-F.; Zhao, Y.-X. J. Nat. Prod. **2022**, 85 (1), 3–14.
[2] Hu et al. Shanghai Scientific & Technical Publishers **1999**, 1.
[3] For the total synthesis see, Pereira, J.; Casaretto, N.; Frison, G.; Nay, B. *Chem. Sci.* **2025**, 16 (25), 11375–11380. Stoltz, B. M. *et al. Chem. Sci.* **2025**, 16 (25), 11381–11385. She, X. *et al. Org. Lett.* **2025**, 27 (21), 5480–5484. Hanson, P. R. *et al. J. Org. Chem.* **2025**, 90 (42), 14977–14983. Christmann, M. *et al. ChemRxiv* **2025**; Breit, B. *et al. Org. Lett.* **2026**, 28 (10), 3255–3259. Banwell, M. G. *et al. Org. Lett.* **2026**.

Posters

Towards sustainable enantioselective electrocatalytic carboxylation of benzyl halides using CO_2 as C1-building block.

Killian DA GRACA,[1] Lianjian HU,[1] Emmanuelle SCHULZ [1] and Mohamed MELLAH [1]

[1] ICMMO, Université Paris-Saclay, 17 Av. des Sciences, 91190 Orsay
killian.da-graca@universite-paris-saclay.fr

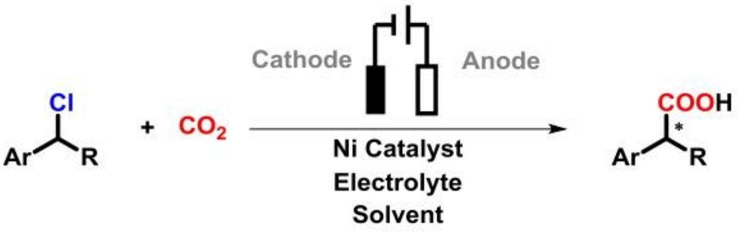
Carbon dioxide has a major impact on global warming; it is responsible for approximately 26% of the greenhouse effect occurring in the Earth's atmosphere. The increase in its concentration is the primary driver of climate change observed on a global scale since the last decades of the 20th century.

CO_2 can be used as a raw material and a "reagent" through various techniques. Its valorization allows the production of chemical compounds or even pharmaceuticals, such as ibuprofen, which contains a carboxylic acid function on a chiral benzylic position.

Several studies on the carboxylation of benzylic positions have been published, but they rely on the use of excessive amounts of reducing metals, raising environmental concerns.

The group of R. Martin [1] investigated a carboxylation reaction of benzyl halides with CO_2, catalyzed by an achiral Ni complex; however, this reaction requires a large excess of zinc as a reducing agent. The same reactivity was explored by the group of P. Li [2], using a chiral Ni complex, which enables the formation of enantioenriched products. Nonetheless, an excess of manganese as a reducing agent is still necessary. An electrocatalytic system for the carboxylation of chlorinated derivatives was developed by the group of G. Silvestri [3] in 1984. This system allows the synthesis of carboxylic acids using CO_2, but several challenges remain, particularly regarding enantioselectivity. In 2014, the group of J.-X. Lu [4] demonstrated the possibility of synthesizing a chiral carboxylic acid at the benzylic position from CO_2 using an electro-catalytic system catalyzed by an enantiopure Co-Salen complex, a reaction limited to only one substrate, a low yield and an enantioselectivity value that can be improved.

We thus aim to develop an electro-catalytic system for the synthesis of enantioenriched benzylic carboxylic acids from CO_2, without the use of reducing metals.



A detailed overview of the optimizations performed on the electrocatalytic system, including electrode materials, applied potential, current intensity, and supporting electrolyte, as well as on the reaction conditions such as substrate scope, ligands, concentration, temperature, and reaction time, will be here presented.

References :
[1] León, T., Correa, A. & Martín, R. *J. Am. Chem. Soc.* **2013**, 135, 4, 1221–1224
[2] Wang, L., Li, T., Perveen, S., Zhang, S., Wang, X., Ouyang, Y. & Li, P. *Angew. Chem. Int.* **2022**., *134*, 51.
[3] Silvestri, G., Gambino, S., Filardo, G. and Gulotta, A. *Angew. Chem. Int.* **1984**, 23, 979-980.
[4] Chen, B., Zhu, H., Yan, X., Sun, Q., Wang, H. & Lu, J. *Electrochem. Commun.* **2014** *42, 55–59*.

PO-02

A Metal-Free route to trifluoromethylated indolizines: harnessing light and EDA complexes

Corinne COUTANT,[1] Jean-Fabrice KOFFI, [1] Lielou LANTIGNER,[1] Christine TRAN[1], Abdallah HAMZE,[1] Sandrine PIGUEL[1]
[1] BioCIS, UMR-CNRS-8076, Paris-Saclay University, 17 Avenue des Sciences, 91400 Orsay, France
corinne.coutant@universite-paris-saclay.fr

Indolizines (pyrrole[1,2-*a*]pyridines) are privileged bicyclic scaffolds composed of fused 5- and 6-membered aromatic rings. Owing to their planar 10 π-electrons system, they display attractive photophysical and (electro)chemical characteristics, and have found applications in materials science (dyes, fluorescent materials, OLEDs, pH probes). In parallel, numerous indolizine derivatives have demonstrated promising biological activity, including anticancer, antibacterial, antifungal, anti-inflammatory, antiviral, and anti-neurodegenerative effects.[1] Despite this broad potential, the indolizine core remains relatively underexplored in medicinal chemistry. Incorporation of the trifluoromethyl group is a powerful strategy in drug design, as fluorinated motifs can dramatically influence metabolic stability, lipophilicity, and bioavailability. However, most trifluoroalkylation methods rely on metal catalysis or photocatalysts, often requiring expensive reagents, harsh conditions, or generating undesirable by-products.[2,3] Herein, we report a photocatalyst-free, light-mediated three-component strategy for the selective C-3 trifluoromethylation of indolizines. The transformation proceeds under mild conditions and does not require any external photoredox catalyst. Mechanistic investigations support the in-situ formation of an electron-donor–acceptor (EDA) complex, thereby enabling direct photoactivation and radical generation. The successful incorporation of a wide range of substituents at the C-3 position demonstrates the versatility and robustness of the developed protocol, enabling the synthesis of 20 trifluoromethylindolizine derivatives in yields of up to 82%. This work offers a sustainable and practical alternative to conventional perfluoroalkylation strategies and opens new perspectives for the development of fluorinated indolizine derivatives of potential biological interest.

Figure 1: Novel strategy for the perfluoroalkylation of indolizine derivatives through an EDA complex.

References:
[1] Botezatu A. V., Furdui B., Busuioc A., Dinică R. M., *Eur J Med Chem*, **2025**, *297*, 117908.
[2] Abula A., Xu Z., Zhu Z., Peng C., Chen Z., Zhu W., Aisa H. A., *J. Chem. Inf. Model*. **2020**, *60*, 6242–6250.
[3] Liu X., Zhong S., Liu J., Fu H., Cao H., *Chem. Commun*. **2026**, *62*, 1479–1496.

PO-03

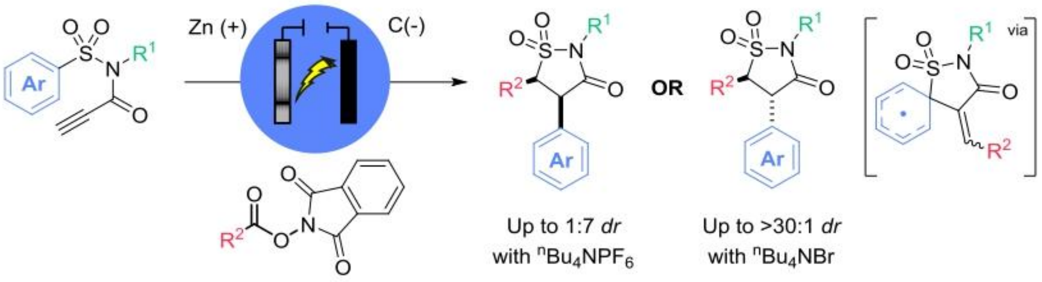
Electrochemical Truce-Smiles rearrangement for the diastereodivergent access to functionalized isothiazolidinones

Sébastien MEYER and Aurélie CLARAZ

Institut de Chimie des Substances Naturelles, CNRS, Université Paris-Saclay, 91198 Gif-sur-Yvette, France.
sebastien.meyer@cnrs.fr

Radical Truce–Smiles rearrangements have emerged as a powerful strategy for regioselective arylation, enabling the rapid assembly of complex molecular frameworks.[1] Electrochemical variants, which use electrons as traceless reagents and allow fine control over reaction conditions,[2] represent attractive alternatives to conventional redox methods and hold considerable promise for the synthesis of original compounds under mild conditions; yet electrochemical Truce-Smiles rearrangements remain underdeveloped.[3]

Herein, we report an electricity-induced reductive radical coupling between redox-active esters and *N*-arylsulfonylpropiolamides, affording novel 4-aryl-5-alkyl isothiazolidinones dioxides in a user-friendly undivided cell. This method proceeds through a cascade sequence featuring a non-desulfonylative Truce-Smiles rearrangement[4] as a key step. The diastereoselectivity can be switched by careful selection of the electrolyte anion, enabling access to either kinetic or thermodynamic isomers with moderate and high selectivities, respectively. Control experiments probing isomerization clarified the roles of both the electrolyte anion and anodically generated Zn salts in governing the observed selectivity.[5]



References :

[1] a) Holden, C. M.; Greaney, M. F. *Chem.–Eur. J.* **2017**, *23*, 8992-9008. b) Snape, T. J. *Chem. Soc. Rev.* **2008**, *37*, 2452-2458.
[2] Kingston, C.; Palkowitz, M. D.; Takahira, Y.; Vantourout, J. C.; Peters, B. K.; Kawamata, Y.; Baran, P. S. *Acc. Chem. Res.* **2020**, *53*, 72-83.
[3] For examples from our group: a) Derat, E.; Masson, G.; Claraz, A. *Angew. Chem., Int. Ed.* **2024**, *63*, e202406017. b) Meyer, S.; Neuhut, A.; Claraz, A. *Org. Biomol. Chem.* **2024**, *22*, 8102-8108.
[4] For a photochemical approach: Yan, J.; Cheo, H. W.; Teo, W. K.; Shi, X.; Wu, H.; Idres, S. B.; Deng, L.-W.; Wu, J. *J. Am. Chem. Soc.* **2020**, *142*, 11357-11362.
[5] Meyer, S.; Claraz, A. *Org. Lett.* **2025**, *27*, 13756-13761.

PO-04

Green Chemistry and ultra-high frequency heating

Baptiste LAFON[1,2], Christophe LEN[1], Amélie AUVIGNE[2]

[1] Chimie ParisTech, 11 rue Pierre et Marie Curie, F-75005 Paris
[2]Thales AVS MIS, 2 rue Marcel Dassault, 78140 Vélizy-Villacoublay
baptiste.lafon@chimieparistech.psl.eu

Sustainable chemistry has become a key area of research and development for the chemical, pharmaceutical, and cosmetic industries. It involves the design, development, and implementation of chemical products and processes that aim to reduce or eliminate the use and generation of hazardous substances for human health and the environment, integrating current industrial practices into the broader framework of sustainable development.

Microwave technology has seen unprecedented industrial development in various fields such as agri-food (drying, cooking...) and polymers (vulcanization...). Research in inorganic and organic chemistry, and more specifically in molecular chemistry, has embraced this technology, highlighting unmatched purities and yields of target products through a different heating mechanism (Joule effect and dielectric hysteresis heating) compared to conventional heating (thermal conduction). Current commercially available equipment (CEM, Milestone, Anton Paar, Biotage, Sairem...) is widely used in academic research, particularly in biomass chemistry and its derivatives. These systems are mainly designed for small-volume batch reactors due to the limited penetration depth of electromagnetic waves. Continuous flow chemistry, as an alternative technology, offers significant processing advantages, including improved thermal management, better mixing control, applicability to a wider range of reaction conditions, scalability, energy efficiency, waste reduction, enhanced safety, the possibility of using heterogeneous catalysis, and the ability to perform multi-step synthesis. The combination of microwaves and continuous flow is rarely used in academic and industrial research. However, this approach can be highly advantageous for scale-up purposes. Nonetheless, a major obstacle has emerged during industrial implementation, requiring the use of high-power electromagnetic systems operating at suitable frequencies.

Thales and Chimie ParisTech are following up a previous collaboration that resulted in the design of innovative equipment combining microwaves and continuous flow for synthetic chemistry.

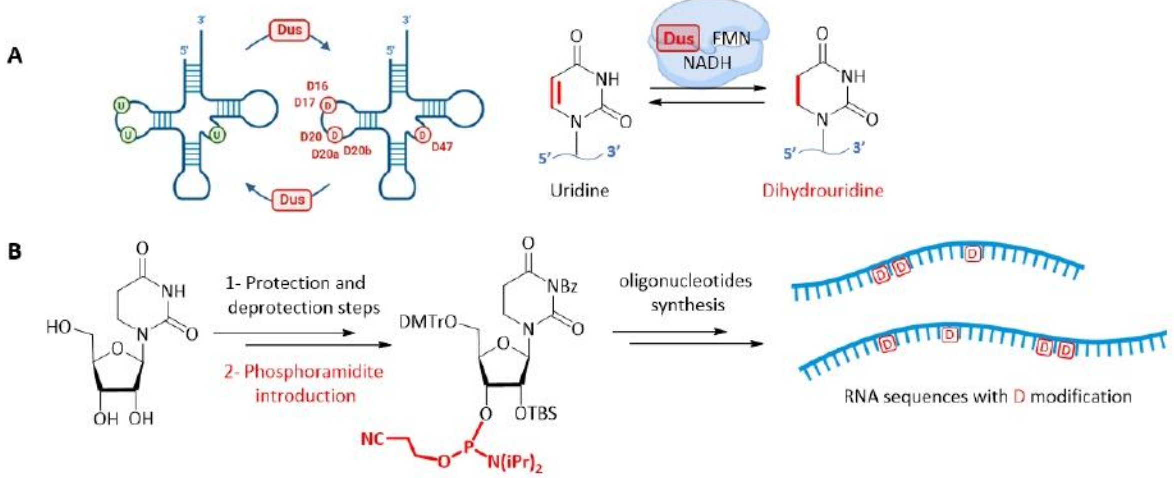
Dihydrouridine as a redox sensor : synthesis of specific oligonucleotides to study the reversibility of Dus catalysis

Marine CHARTIER,[1,2] Laura IANNAZZO,[1] Mélanie ETHEVE-QUELQUEJEU,[1] Damien BREGEON,[2]
Djemel HAMDANE [2]

[1] LCBPT, Paris Cité University, 45 rue des Saints-Pères, 75 270 PARIS CEDEX
[2] Dev2a, IBPS, Sorbonne University, 7 quai Saint Bernard, 75 252 PARIS CEDEX
marine.chartier@sorbonne-universite.fr

Chemical modifications in RNAs influence regulation of protein production in cells. One such modification, knows as dihydrouridine (D),[1] plays a crucial role in this process. D is the second most abundant RNA modification after pseudouridine which convert uridine into dihydrouridine by flavin-dependant enzymes (FMN) know as Dus (Dihydrouridine synthase), (Schema 1.A). This RNA modification, principally present in tRNA, is the only one directly relying on NADPH and represents a promising redox sensor model for studying the impact of redox stress on RNA function and translational adaptation in redox metabolism, and consequently, protein synthesis. Recently, Dev2a laboratory has demonstrated the reversibility in Dus catalysis to convert uridine into dihydrouridine and dihydrouridine into uridine. To study this reversible property, the chemical synthesis of specific RNA sequences will be carried out by a chemical approach based on solid phase synthesis (SPS). It requires the synthesis of D phosphoramidite to introduce D at specific sites (Schema 1.B). Experiments to determine kinetics properties and the impact of chemicals environments on this reversibility will be carried.

In addition, to establish D as a redox sensor mark, we aim to develop new chemicals tools to identify all D across the transcriptome to explore how cells adapt to stress. Selective and sensitive D labelling will be developed by functionalizing the D with fluorescent group.[2]



Schema 1 : A. tRNA dihydrouridylation by Dus enzymes and chemical structure of uridine reduction. B. Simplified synthetic route of dihydrouridine phosphoramidite for their introduction into oligonucleotides.

References :
[1] Brégeon, D. *et al; ACS Chem. Biol.* **2022**, 17, 1638–1657.
[2] Kaur, J., Raj, M. & Cooperman; *RNA,* ***2011***, 17, 1393–1400.

Functionalization of strained olefins in bicyclic lactones

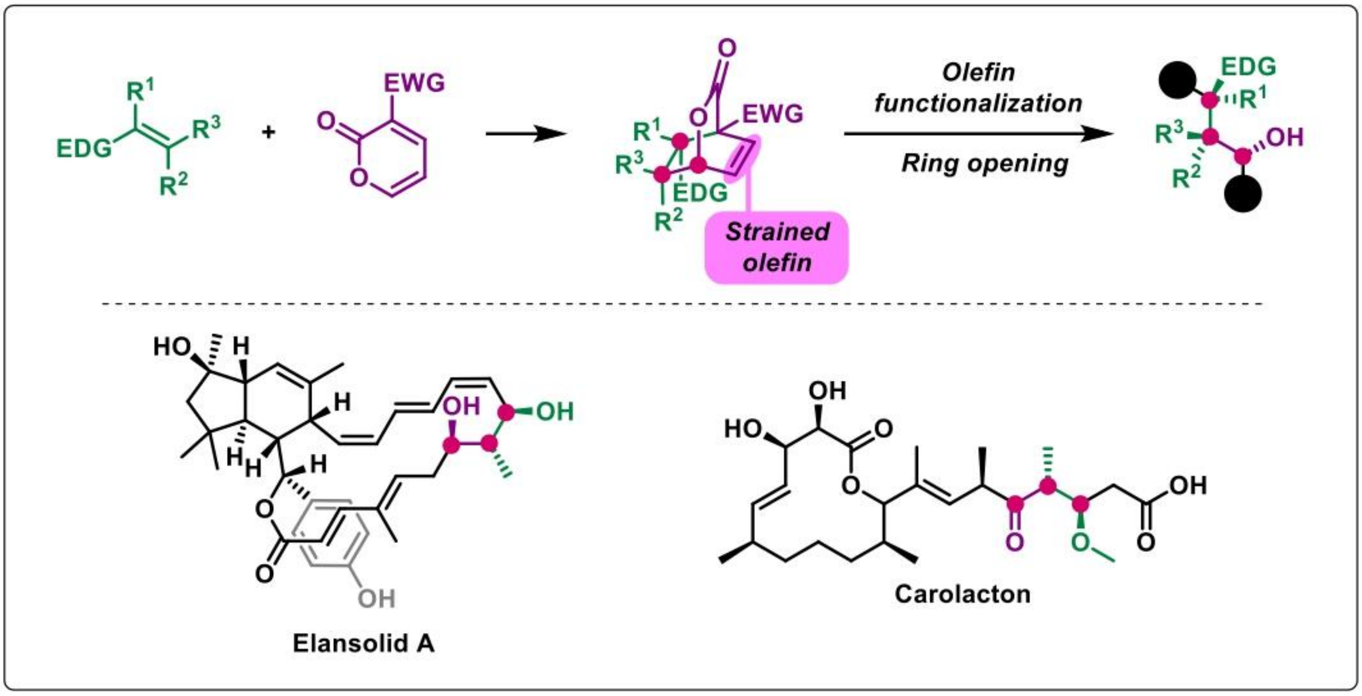
Céline BOUCHEL,[1] Cyrille KOUKLOVSKY,[1] Valérie ALEZRA,[1] Aurélien DE LA TORRE.[1]

[1] Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO), Université Paris-Saclay,
17-19 Avenue des Sciences, 91400 Orsay.
celine.bouchel@universite-paris-saclay.fr

Enantioselective synthesis of acyclic molecules remains a major challenge due to conformational flexibility, especially when building quaternary stereocenters. These motifs are key features in many natural products and pharmaceuticals, yet their controlled construction is still difficult.

Our approach uses Inverse Electron Demand Diels–Alder (IEDDA) reactions to generate bicyclic lactones as versatile intermediates.[1] While previous studies mainly exploited the lactone functionalization,[2-3] we focus on the underexplored strained alkene reactivity in the bicyclic scaffold.

This reactivity opens new strategies for the stereocontrolled synthesis of complex acyclic targets, such as natural compounds including polypropionates units.[4]



References:
[1] de la Torre, A; *Angew. Chem. Int. Ed.* **2022**, *61,* e202208185.
[2] Cho, C.-G.; *Org. Lett.* **2013**, *15,* 132–135.
[3] Jiang, X.; *Org. Lett.* **2017**, *19*, 3167–3170.
[4] Zhang, W.; *Mar. Drugs* **2020**, *18*, 569.

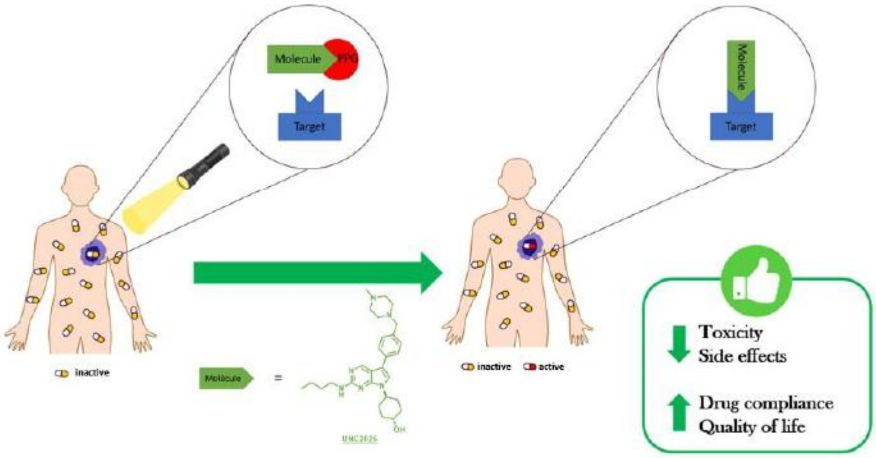
PO-07

Photopharmacological tools with π-extended coumarins based on TAM kinase inhibitor UNC2025

Sébastien BILLOTTE,[1] Gaëlle FONTAINE,[2] Frédéric BOLZE,[3] Alexandre SPECHT,[3] Sophie BOMBARD,[2] Sandrine PIGUEL[1]

[1] BioCIS UMR 8076 CNRS, Université Paris-Saclay, Faculté de Pharmacie, Bâtiment Henri Moissan, 17 avenue des Science, 91400 Orsay, France
[2] CMBC UMR 9187 CNRS U 1196 Inserm, Institut Curie, 110 Avenue de Bures, 91440 Bures-sur-Yvette, France
[3] CBST UMR 7199 CNRS, Université de Strasbourg, Faculté de Pharmacie, 74 route du Rhin, 67401 Illkirch-Graffenstaden, France
sebastien.billotte@universite-paris-saclay.fr

Photopharmacology is an emerging therapeutic field that aims to control spatiotemporally drugs activity using light. Various strategies have been developed, including the photoremovable protecting groups (PPGs). This approach entails covalently attaching a photoremovable moiety to an active drug, which inactivates it. During light exposure, the PPG is cleaved, restoring the drug's initial activity. By triggering drug release through external stimuli, such processes enhance selectivity.[1] This study aims to synthesize photocleavable tyrosine kinase inhibitors as a therapeutic tool against cancer. These inhibitors target the TAM kinase family (Tyro3, Axl, and Mer), known to be overexpressed in several types of cancers. [2,3] They are based on the structure of a well-known inhibitor of this family, UNC2025.[4] To develop effective photocleavable inhibitors suitable for clinical use, the nature of PPG is crucial. Indeed, PPGs should absorb at the highest possible wavelength closest to the therapeutic window to ensure good penetration and low phototoxicity.[5] In this work, we describe the use of π-extended coumarins to afford photocleavable versions of UNC2025, which absorb in the visible light.



References :
[1] M. Welleman, I.; et al. *Chem. Sci.*, **2020**, *11 (43)*, 11672–11691.
[2] Le Bescont, J.; et al. *ChemPhotoChem*, **2021**, *5 (11)*, 989–994.
[3] Breton-Patient, C.; et al. *ChemBioChem*, **2024**, *25 (8)*, e202300855.
[4] Zhang, W.; et al. *J. Med. Chem.*, **2014**, *57 (16)*, 7031–7041.
[5] Weinstain, R.; et al. *Chem. Rev.*, **2020**, *120 (24)*, 13135–13272.

PO-08

Aminocyclobutanes as precursors of endoperoxides

Théo GUITTET[1,2], Yvan SIX[2] and Laurent FERRIÉ[1*]

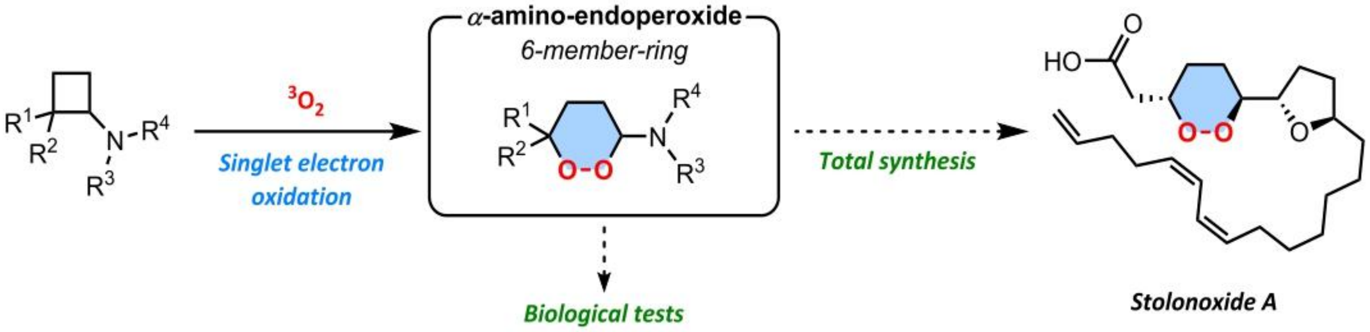
[1]Equipe Substances Naturelles - BioCIS (UMR 8076), Université Paris-Saclay, 91400 Orsay, France
[2] Laboratoire de Synthèse Organique (LSO, UMR 7652), École Polytechnique,
Institut Polytechnique de Paris, CNRS, 91128 Palaiseau, France

theo.guittet@universite-paris-saclay.fr theo.guittet@polytechnique.edu

Endoperoxides are natural or unnatural products containing a peroxide moiety embedded in a ring. They can be found in different types of living organisms (plants, fungi, sponges, bacteria…). The roles of these molecules vary depending on the species, but are often related to defense mechanisms. Indeed, endoperoxides can exhibit different biological activities, potent biological activities, with antibacterial, anticancer or anti-parasitic effects. For instances, artemisinin,[1] a natural endoperoxide, is currently one of the most active drugs against malaria.

Several studies have been reported on the preparation of endoperoxides, but few describe the preparation of α-aminoendoperoxides.[2] We now wish to present our results of a study being conducted on the use of aminocyclobutane precursors for the synthesis of α-aminoendoperoxides. To improve this transformation, various parameters have been investigated, such as the choice of the solvent, the nature of the oxidant or the substrate structure.

Aside the chemical studies, further biological activity studies will be designed to improve our understanding of the structural motifs that are responsible for antiparasitic activity. Furthermore, α-aminoendoperoxides could serve as interesting synthons in the total synthesis of natural endoperoxides,[3] such as stolonoxides,[4,5] for which no total synthesis has been reported so far.



References:
[1] You-you, T.; Mu-Yun, N.; Yu-rong, Z.; Lan-na, L.; Shu-lain, C.; Mu-qun, Z.; Xiu-zhen, W.; Zheng, L.; Xiao-tian, L. *Planta Med.* **1982**, *44*, 143–145.
[2] Fontana, A.; Gonzàlez, M. C.; Gavagnin, M.; Templado, J.; Cimino, G. *Tetrahedron Lett*. **2000**, *41*, 429–432.
[3] Dembitsky, V. M.; *Eur. J. Med. Chem.* **2008**, *43*, 223-251.
[4] Jamey, N.; Ferrié, L.; *Org. Lett.* **2024**, *26*, 5741–5745.
[5] Madeleine, C.; Six, Y.; Buriez, O. *Angew. Chem.* **2007**, *119*, 8192–8195.

PO-09

Novel prodrug strategy for the chemical decaging of oligonucleotides in RNA-based therapy

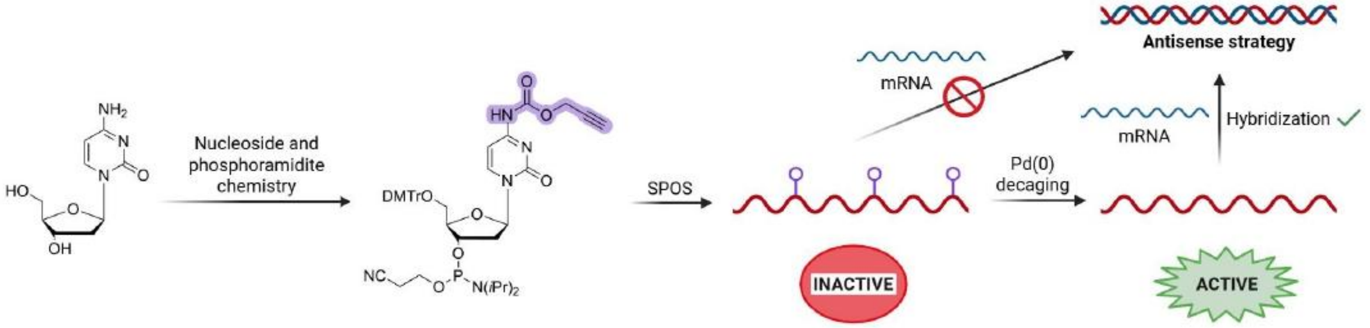
Célia MORISSET, [1] Clara TESTARD, [1] Dylan COELHO, [1] Chea Julie ING, [1] Mélanie ETHEVE-QUELQUEJEU[1] and Laura IANNAZZO[1]

[1] UMR 8601 – LCBPT, Université Paris Cité, CNRS, 45-47 rue des Saints-Pères 75006 Paris
celia.morisset@etu.chimieparistech.psl.eu

Interest in antisense therapy, involving siRNA or ASO (antisense oligonucleotide) has soared in recent years, as illustrated by the clinical approval of thirteen ASOs by the Food and Drug Administration (FDA).[1] The delivery of oligonucleotides is a major challenge that remains to be tackled. This hurdle may be overcome by converting the ASO into a prodrug, in which caged nucleobases obstruct its hybridization to the target mRNA sequence.

Several stimuli-responsive strategies have been developed to selectively restore the caged oligonucleotide's base-pairing ability, of which photocaging has been the most extensively explored. However, its applicability suffers from light cytotoxicity and poor tissue penetration,[2] urging for the development of alternative strategies.

Bioorthogonal organometallic (BOOM) chemistry constitutes a novel approach for the decaging of oligonucleotides.[3] Here, we propose the chemical modification of a nucleobase, with a functional group sensitive to Pd(0) in non-cytotoxic concentrations.[4] Caged oligonucleotides obtained by solid-phase oligonucleotide synthesis (SPOS) from a phosphoramidite bearing the modified unit will serve as a model ASO. The synthesis of a modified phosphoramidite containing a Pd-cleavable moiety and the development of compatible SPOS reaction conditions will be presented, to provide a robust and reproducible methodology. Hybridization experiments should in turn validate that our prodrug system may selectively be activated upon the addition of a chemical stimulus.



Graphical abstract

References :
[1] Collota, D., Bertocchi, I., Chiapello, E., Collino, M.; *Front. Pharmacol.* **2023**, *14*, 1304342
[2] Debart, F., Dupouy, C., Vasseur, J.-J.; *Beilstein J. Org. Chem.* **2018**, *14.*, 436-469
[3] Weiss, J., Dawson, J., Fraser, C., Rybski, W., Torres-Sánchez, C., Bradley, M., Patton, E., Carragher, N., Unciti-Broceta, A.; *J. Med. Chem.* **2014**, *57*, 5395-5404
[4] Li, J., Yu, J., Zhao, J., Wang, J., Zheng, S., Lin, S., Chen, L., Yang, M., Jia, S., Zhang, X., Chen, P.; *Nat. Chem.* **2014**, *6*, 352-361

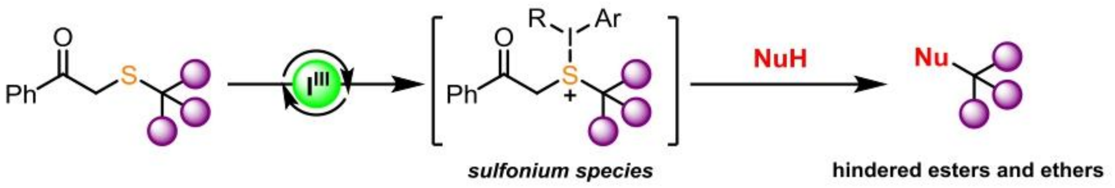
Hypervalent Iodine mediated Pummerer fragmentation reaction toward hindered ester and ether.

Lingchao CHENG and Thomas BODDAERT

CP^3A, ICMMO, 17 Avenue des Sciences, Orsay, France
lingchao.cheng@universite-paris-saclay.fr

The facile synthesis of ethers and esters has long been a task in drug design, as the incorporation of the ether and ester group enhances the solubility and bioavailability, thereby improving the druggability.[1] Hindered dialkyl ethers can aid in the escape-from-flatland of bioactive molecules and improve the drug-target interaction to promote the drug efficacy and selectivity.[2] Moreover, the ester moiety is not only a common functional group in polymers, drugs and biologically relevant compounds, but also serves as a protecting group for alcohols.

Although reliable alternatives to classical synthetic methods, such as metal-catalyzed metathesis, photochemical and electrochemical approaches,[3-5] have recently emerged to prepare hindered esters and ethers, the development of convenient, green and efficient synthetic strategies is still being sought. To address this challenge, our group developed a hypervalent iodine mediated-Pummerer fragmentation reaction[6] to convert phenacyl sulfide derivatives into a large diversity of hindered ester and ether compounds under mild conditions.



sulfonium species

hindered esters and ethers

27 examples
up to 96% yield

References :
[1] Zheng, L.; Aimaiti, Z.; Long, L.; Xia, C. Wang, W., Zhou, Z. Z. *J. Med. Chem*. **2024**, *67*, 728–753.
[2] Lin, A. J.; Lee, M.; Klayman, D. L. *J. Med. Chem*. **1989**, *32*, 1249–1252.
[3] Empel, C.; Pei, C.; He, F.; Jana, S.; Koenigs, R. M. *Chem. Eur. J.* **2022**, *28*, e202104397.
[4] Zhang, Y. ; Han, X. ; Li, D. ; Wang, J. ; Luan, X. ; Ni, S.-F., Das, S. ; Zhang, W.-D. *ACS Cent. Sci.* **2025**, *11*, 742–752.
[5] Köckinger, M.; Hanselmann, P.; Roberge, D. M.; Geotti-Bianchini, P.; Kappe, C. O.; Cantillo, D. *Green Chem*. **2021**, *23*, 2382-2390.
[6] Kaiser, D.; Klose, I.; Oost, R.; Neuhaus, J.; Maulide, N. *Chem. Rev*. **2019**, *119*, 8701-8780.

PO-11

Functionalization of Imines with DHPs under visible light

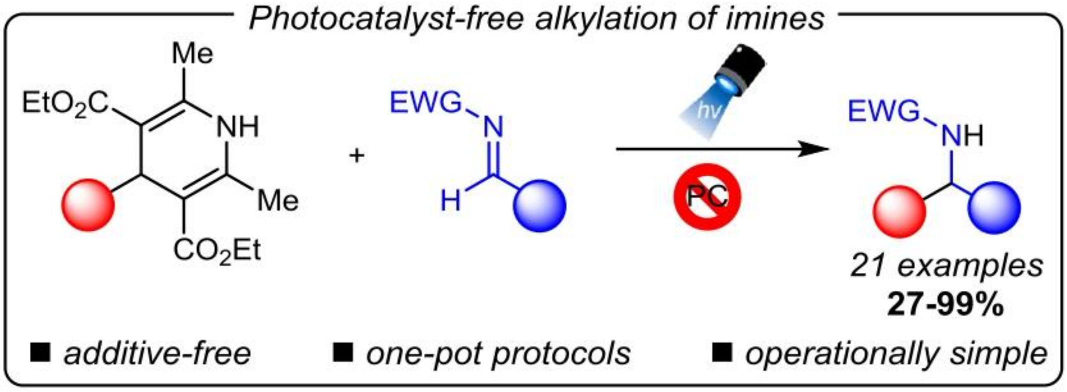
Damien GIRAL, Maxime BOUQUIN, Erwan LE GALL, Marc PRESSET

Groupe Electrosynthèse, Catalyse et Chimie Organique, ICMPE (UMR 7182), CNRS - UPEC
2-8 rue Henri Dunant, F-94320 Thiais, France
damien.giral@u-pec.fr

Mannich-type reactions between imines and nucleophilic radicals, generated using light, have emerged as a powerful tool in organic chemistry thanks to the development of photocatalytic processes. These reactions combine the operational simplicity of the Mannich reaction with the high reactivity of photogenerated radicals, allowing the synthesis of highly substituted scaffolds under mild conditions. This approach thus represents an attractive strategy for the eco-compatible synthesis of α-disubstituted secondary amines.

Among common radical precursors, functionalized-dihydropyridines (DHPs) play a significant role. Whereas they were initially used as hydride donors in photochemical reaction[1], they have been more recently used as alkyl donors. Very recently DHPs were found to be efficient reaction partners in a Mannich type reaction with N-aryl imines[2]. However, their use relies on the combined utilisation of both a photocatalyst and a Lewis-acid catalyst under blue LED irradiation.

In this communication, we report a novel photocatalyst-free reaction between 4-functionalized-DHPs and imines. Interestingly, this transformation is built on the use of N-sulfonyl imines and provides an efficient and straightforward entry to diverse α-disubstituted sulfonamides in good yields. This methodology significantly improves the eco-compatibility of such syntheses while simplifying the experimental procedure. This approach is also extended to multicomponent versions with *in situ* generated imines and DHPs. Mechanistic studies were conducted showing that DHPs serve both as radical precursor and terminal reductant.



---

[1] Chen Y., Generation of Alkoxyl Radicals by Photoredox Catalysis Enables Selective C(sp3)-H Functionalization under Mild Reaction Conditions; *Angew. Chem. Int. Ed.* **2016**, *55*, 1872-1875

[2] Feng-X; Liu-X., Visible-Light-Promoted Enantioselective Acylation and Alkylation of Aldimines Enabled by 9-Fluorenone Electron-Shuttle Catalysis; *J. Am. Chem. Soc*. **2024**, *146*, 20401–20413

Synthesis and Characterization of Novel Bismuth Cationic Complexes

Fabio BECCUCCI,[1] Djamila AZROU,[2] Regis GUILLOT,[2] Christophe BOUR,[2] Marie VAYER [1]

[1] BioCIS, UMR CNRS 8076, Université Paris-Saclay, 91400 Orsay, France
[2] ICMMO, UMR CNRS 8182, Université Paris-Saclay, 91400 Orsay, France
fabio.beccucci@universite-paris-saclay.fr

A large number of catalytic homogeneous transformations rely on the use of complexes of rare late transition metals of the 2nd and 3rd rows (Pd, Ru, Rh, Ir, Pd, Pt, Au). One way to reduce the cost of these processes is to use surrogates of precious metal catalysts based on abundant main group elements (Ca, Ga, In, Bi …) or 1st row transition metals.

Organobismuth compounds are particularly attractive because they can be readily obtained from inexpensive and low-toxicity inorganic bismuth salts, and hold significant appeal in synthesis owing to their distinctive properties and reactivity. In fact, organobismuth compounds exhibit an extensive diversity of geometries, influenced by factors such as the oxidation state of bismuth, its charge, and the number of coordinated elements. Its most common oxidation state + III possess a soft Lewis acidic behavior due to the weak shielding of its 4f electrons.[1] Hence, its synthetic applications are mainly based on Lewis acidic catalysis. In particular, bismuth triflate ($Bi(OTf)_3$) has been extensively studied in that application.[2]

On the other hand, the team of Pr Christophe Bour has been studying weakly coordinating anions (WCA).[3] These species, typically aluminate or teflate anions, exhibit high electronic delocalization, which reduces electrostatic interactions. As a result, their corresponding cations display enhanced electrophilicity and improved Lewis acidity.[3]

In the aim of improving the Lewis acidity of bismuth(III) complexes, we present here the synthesis and characterization of novel bismuth cationic complexes, and the study of their Lewis acidity. We used two radically different ligand geometry, a planar N,C,N pincer ligand that allowed the generation of monomeric bismuth(I) complexes,[4] and a tridentate C,N,C ligand that was recently used in a bismuth Lewis acid catalysis.[5]

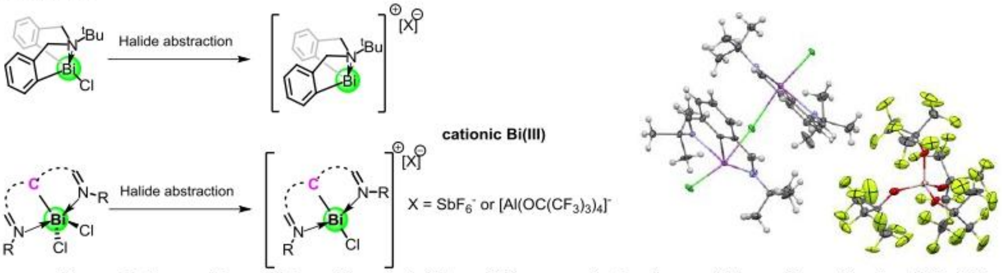


Figure 1. Formation of bismuth salt (left) and X-ray analysis of one of the salt synthesized (right).

References :

[1] Berger, R. J. F.; Rettenwander, D.; Spirk, S.; Wolf, C.; Patzschke, M.; Ertl, M.; Monkowius, U.; Mitzel, N. W.; *Phys. Chem. Chem. Phys.* **2012**, *14*, 15520-15524.

[2] Antoniotti, S.; Dalla, V.; Duñach, E.; *Angew. Chem. Int. Ed.* **2010**, *49*, 7860-7888.

[3] Li, Z.; Thiery, G.; Lichtenthaler, M. R.; Guillot, R.; Krossing, I.; Gandon, V.; Bour, C.; *Adv. Synth. Catal.* **2018**, *360*, 544-549.

[4] Šimon, P.; de Proft, F.; Jambor, R.; Růžička, A.; Dostál, L.; *Angew. Chem. Int. Ed.* **2010**, *49*, 5468-5471.

[5] Yang, X.; Kuziola, J.; Béland, V. A.; Busch, J.; Leutzsch, M.; Burés, J.; Cornella, J.; *Angew. Chem. Int. Ed.* **2023**, *62*, e202306447.

PO-13

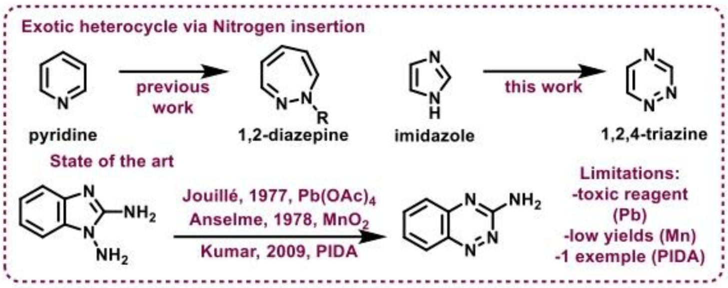
Skeletal editing of 2-aminobenzimidazole to benzo[*e*][1,2,4]triazin-3-amine via nitrogen insertion

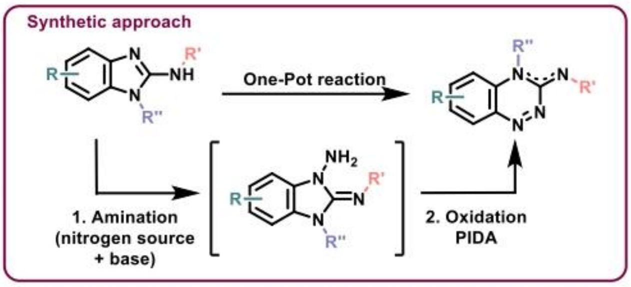
Alexis LEBLAIS,[1] Xavier MOREAU,[1] Clément GHIAZZA[1]

[1] *Université Paris-Saclay, UVSQ, CNRS, UMR 8180 Institut Lavoisier de Versailles, 78035 Versailles Cedex, France*
alexis.leblais@uvsq.fr

The modulation of molecules of interest is generally carried out by peripheral modifications of aromatic rings, which are often seen as 'immutable' structures and incorporated in early stages. However skeletal editing methods have grown in popularity in recent years, because they enable the direct modification of the nature of aromatic/heteroaromatic rings without the need to resynthesize a similar molecule from a different starting substrate.
Such transformation is realized by inserting, deleting or substituting one or more of the atoms within the aromatic ring. In 2022, two teams demonstrated the insertion of a nitrogen atom into cyclopentadiene and pyrrole rings in order to expand the ring and obtain pyridines and pyrimidines, respectively. [1],[2] In line with this, a recent report of our laboratory has focused on the insertion of a nitrogen atom into pyridine motifs in order to form 1,2-diazepines.[3]

Following our interest in the synthesis of exotic heterocycle via skeletal editing technics, we herein report the conversion of 2-aminobenzimidazole to benzo[*e*][1,2,4]triazin-3-amine via nitrogen insertion. The insertion of nitrogen into 1*H*-benzo[*d*]imidazole-1,2-diamine as already being described in the past but the different strategies showed some limitation such as: the use of toxic reagent (Pb), obtained as a by-product in low yields (Mn), or only 1 example described (PIDA).[4],[5],[6]
Our synthetic approach consists in the development of a one-pot reaction involving an electrophilic amination to obtained the intermediate which is then oxidized to obtained the final product. We have optimized the reaction conditions and succeed in obtaining 20 examples of substituted benzo[*e*][1,2,4]triazin-3-amines.


Exotic heterocycle via Nitrogen insertion


Synthetic approach

[1] Levin, M. D. et al. *Angew. Chem. Int. Ed.* **2022**, *61* (46), e202213041.
[2] Morandi, B. et al. *Science.* **2022**, *377* (6610), 1104-1109.
[3] Ghiazza, C. et al. *J. Am. Chem. Soc.* **2024,** *146* (4), 2845-2854.
[4] Joullié, M. M. et al. *J. Org. Chem.* **1977**, *42* (3), 542-545.
[5] Anselme, J. P. et al. *J. Org. Chem.* **1978**, *43* (13), 2693-2696.
[6] Kumar, D. et al. *Synthesis.* **2009**, *2009* (10), 1663-1666.

PO-14

Sm(II)-catalyzed selective azidation of phthalamides Direct access to triazole-fused tetraheterocycles

Bin WU, Qian HE, Emmanuelle SCHULZ, Mohamed MELLAH.

MSCO, groupe Catalyse Moléculaire, ICMMO, 17 Avenue des Sciences 91400 Orsay
bin.wu@universite-paris-saclay.fr

Samarium diiodide (SmI_2), often called the Kagan reagent,[1] is one of the most powerful and versatile single-electron transfer (SET) reducing agent in organic chemistry. Since its introduction by Henri Kagan in the late 1970s, it has evolved from a niche laboratory reagent into a key tool for synthesizing complex natural products and pharmaceuticals. Today, more than 99% of SmI_2 reactions use a stoichiometric excess, with fewer than 1% operating catalytically.[2] Developing efficient regeneration methods is therefore crucial. For over a decade, our group has developed samarium-based catalytic procedures that use electrochemistry to regenerate the active divalent species. Under mild conditions, this electrocatalytic approach enables C–C bond formation, [3] selective reduction of aromatic nitro compounds to anilines[4] or azobenzenes,[5] and CO_2 reduction to carboxylic acids.[6]

Building on this work, we are now investigating the selective reduction of phthalimides. We have developed a Sm(II)-electrocatalyzed method for the selective reductive azidation of phthalimides, achieving in situ regeneration of SmI_2 and yields of 72–93% using $TMSN_3$ as the nucleophile in the presence of H_2O.

During the study of reaction scope, we found that the introduction of a long-chain alkyne moiety at the nitrogen position enables the one-pot construction of cyclic compounds through a thermal Huisgen cycloaddition. The triazole-fused products obtained through this method were obtained in moderate to excellent yields.

References:
[1] Namy J. L., Girard P., Kagan H. B., *New J. Chem.*, **1977**, *1*, 5.
[2] David J. Procter, et al. *Angew. Chem. Int. Ed.* **2025**, *64*, e202519678.
[3] Sun, L.; Sahloul, K.; Mellah, M. *ACS Catal.*, **2013**, *3*, 2568.
[4] Y.-F. Zhang, E. Schulz, M. Mellah, *ChemCatChem*, **2024,** 9, e202400303
[5] Zhang, Y. -F.; Mellah, M. *ACS Catal.* **2017,** *7,* 8480
[6] Bazzi, S.; Schulz, E.; Mellah, M. *Org. Lett*. **2019**, 21, 24, 10033 ; S. Bazzi, L. Hu, E. Schulz, M. Mellah, *Organometallics*, **2023**, *42*, 1425

PO-15

Host Directed Therapy: Design and Synthesis of RED-SMU1 Disruptors as New Antiviral Agents Against Influenza A Virus

Aurélie GERNET[1], Alessandra CORIO[1], Laurent LE CORRE[1], Nicolas PIETRANCOSTA[2], Thibaut CREPIN[3], Pierre-Olivier VIDALAIN[4], Nadia NAFFAKH[5], Tania XAVIER[1], Christine GRAVIER-PELLETIER[1], Patricia BUSCA[1]

[1]LCBPT, Equipe Synthèse Organique pour la Recherche Biomédicale, Université Paris-cité, CNRS UMR8601, 75006 Paris.
[2]Centre de Neuroscience Sorbonne Université, CNRS UMR8265 - Inserm U1341 - UMPC UMCR18, Laboratoire des Biomolécules CNRS UMR 7203, 75005 Paris.
[3]Institut de Biologie Structurale, UMR 5075 CEA-CNRS-UGA, 38042 Grenoble.
[4]Centre International de Recherche en Infectiologie, Université Lyon 1, CNRS UMR5308 - INSERM U1111, ENS Lyon, 69342 Lyon.
[5]Unité de Génétique Moléculaire des Virus à ARN, Département de Virologie, Institut Pasteur, Sorbonne Paris Cité, Université Paris Diderot EA302, CNRS UMR 3569, 75015 Paris.
aurelie.gernet@u-paris.fr

Influenza-A virus (IAV) is an infectious respiratory disease affecting annually billions of people across the globe and causing more than 300,000 deaths. Various therapies are currently being used for the treatment of IAV, but resistant strains have already been found against most of them. Host Directed Therapy, an emerging therapeutic strategy consisting in targeting a host protein complex instead of the virus itself, represents a promising avenue for the development of broad-spectrum antiviral drugs and an innovative approach to face the ongoing challenge posed by IAV.[1]

In this context, our team focused on the RED-SMU1 complex, a human protein complex involved in splicing of pre-mRNA, which appeared to be essential for the replication of the virus and therefore representing a valuable target.[2] Indeed, by disrupting this complex, the replication of Influenza-A can be reduced, thereby limiting its pathogenicity.[3] *In silico* screening of more than 4,000 compounds followed by biological evaluation of the best candidates, allowed the identification of the compound ALG61 (Figure 1), a “hit” capable of inhibiting not only the formation of the Red-SMU1 complex but also the replication of the virus *in cellulo*. Starting from this compound, our aim is to design and synthesize RED-SMU1 disruptors. Several analogues were synthesized with different variations including scaffold hopping. This work presents our latest results regarding the synthesis and the biological activity of these RED-SMU1 disruptors.

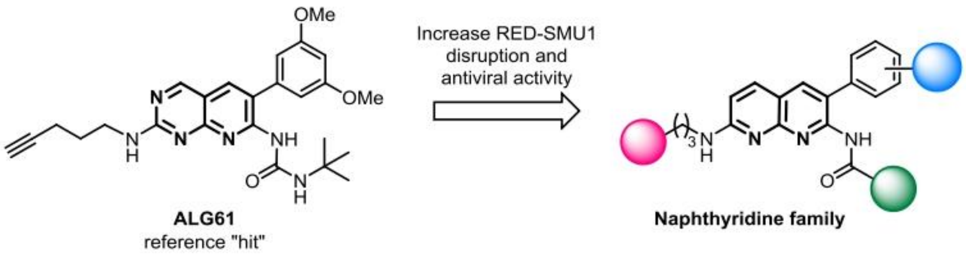


Figure 1. Structure of ALG61 and targeted compounds

[1] Kaufmann, S. H. E.; Dorhoi, A.; Hotchkiss, R. S.; Bartenschlager, R. *Nat. Rev. Drug. Discov*. **2018**, *17* (1), 35–56.
[2] a) Spartz, A. K.; Herman, R. K.; Shaw, J. E. *Mol. Cell. Biol.* **2004**, *24* (15), 6811–6823; b) Chung, T.; Wang, D.; Kim, C.-S.; Yadegari, R.; Larkins, B. A. *Plant Physiol.* **2009**, *151* (3), 1498–1512.
[3] a) Fournier, G.; Chiang, C.; Munier, S.; Tomoiu, A.; Demeret, C.; Vidalain, P.-O.; Jacob, Y.; Naffakh, N. *PLOS Pathogens* **2014**, *10* (6), e1004164; b) Ashraf, U.; Tengo, L.; Le Corre, L.; Fournier, G.; Busca, P.; McCarthy, A. A.; Rameix-Welti, M.-A.; Gravier-Pelletier, C.; Ruigrok, R. W. H.; Jacob, Y.; Vidalain, P.-O.; Pietrancosta, N.; Crépin, T.; Naffakh, N. *Proc. Natl. Acad. Sci. U.S.A* **2019**, *116* (22), 10968–10977.

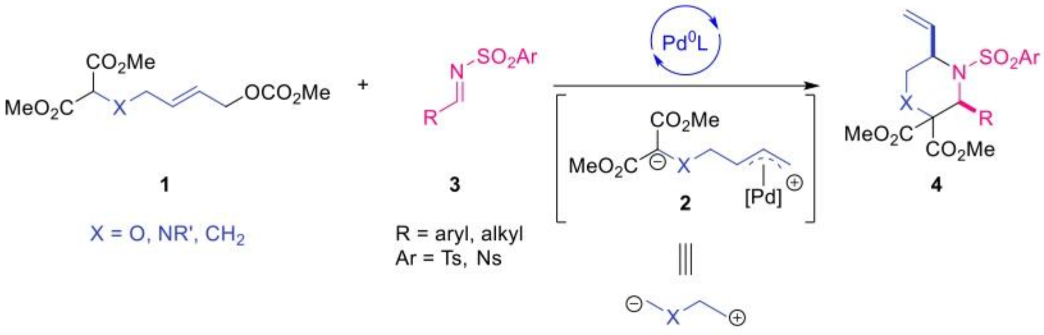
Pallado-Catalysed Cycloadditions of a New 1,4-Dipole: Access to Six-Membered *N*-Heterocycles

Marc BUSICCHIA,[1] Nicolas CASARRETTO,[2] Alexis ARCHAMBEAU

[1] Laboratoire de Synthèse Organique (LSO, UMR 7652), CNRS, Ecole Polytechnique, ENSTA, Institut Polytechnique de Paris, Route de Saclay, 91120, Palaiseau, France
[2] Laboratoire de Chimie Moléculaire (LCM, UMR 9168), CNRS, Ecole Polytechnique, ENSTA, Institut Polytechnique de Paris, Route de Saclay, 91120, Palaiseau, France
marc.busicchia@polytechnique.edu

Six-membered *N*-heterocycles are ubiquitous in bioactive and natural products among FDA-approved drugs. Among the most described ones can be found different saturated heterocycles such as piperidine, piperazine or morpholine.[1] Among all the strategies to reach such heterocycles, cycloaddition appears as an attractive strategy, as it allows to form two sigma bonds in one step. In our group, we are interested in the cycloaddition of transient zwitterionic π-allylpalladium^{II} complexes.[2] It allows to control stereoselectively the formation of cycloadducts by the use of a palladium catalysis, which we recently applied to the formation of various heterocycles.[3]

Among all the different precursors reported in the literature, none of them grant access to the formal cycloaddition of a C-C-X-C (X = heteroatom) synthon. A synthetic equivalent of this synthon could be allyl carbonates **1**, easily accessible from 1,4-butenediol. In the presence of a palladium catalyst, an oxidative addition of allyl carbonate **1** occurs, followed by a decarboxylation and a deprotonation by the released base, leading to the 1,4-zwitterionic π-allylpalladium^{II} complex **2**, now able to react with an electrophilic cycloaddition partner. In the presence of an electrophilic 1,2-dipole, new strategies can be developed to form important six-membered heterocycles. Herein, we describe a palladium-catalyzed cycloaddition between allyl carbonate **1** and sulfonimine **3** as electrophilic partner, unlocking access to various heterocycles **4** in good yields and diastereoselectivities.



References :
[1] Marshall, C. M.; Federice, J. G.; Bell, C. N.; Cox, P. B.; Njardarson, J. T.; *J. Med. Chem.* **2024**, *67*, 11622.
[2] (a) Niu, B.; Wei, Y.; Shi, M.; *Org. Chem. Front.* **2021**, *8*, 3475. (b) Trost, B. M.; Mata, G.; *Acc. Chem. Res.* **2020**, *53*, 1293. (c) Allen, B. D. W.; Lakeland, C. P.; Harrity, J. P. A.; *Chem. Eur. J.* **2017**, *23*, 13830.
[3] For selected publications: (a) Scuiller, A.; Karnat, A.; Casaretto, N.; Archambeau, A.; *Org. Lett.* **2021**, *23,* 2332. (b) Roblin, A.; Casaretto, N.; Archambeau, A.; *Org. Lett.* **2023**, *25*, 6453. (c) Busicchia, M.; Roblin, A.; Dubois, C.; Mekranter, N.; Casaretto, N.; Archambeau, A.; *J. Org. Chem.* **2024**, *89*, 12370.

Mannich reactions with alkylzinc halides

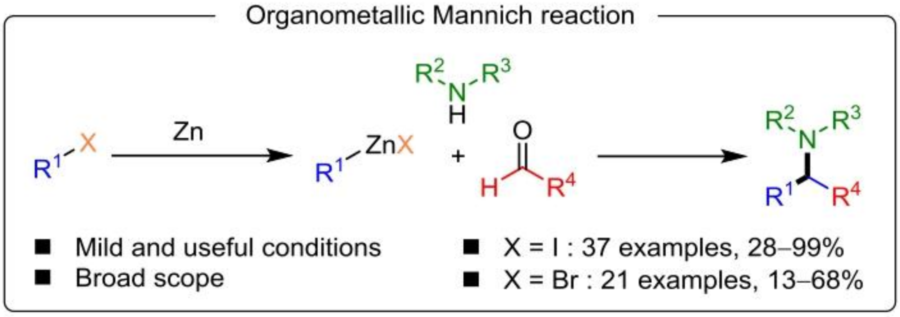
Marwane ASKOUR, Marine PINAUD, Alexis BEAUFILS, Erwan LE GALL and Marc PRESSET

Institut de Chimie de et des Matériaux Paris-Est, Université Paris Est Créteil, CNRS, UMR 7182
2 rue Henri Dunant, 94320 Thiais, France
marwane.askour@u-pec.fr

The Mannich reaction is a benchmark in multicomponent chemistry, enabling rapid access to α-branched amines through simultaneous C–C and C–N bond formation. While the use of organometallic nucleophiles has expanded its scope,[1] applications with nonstabilized sp³-hybridized reagents remain rare and challenging.[2]

We report that mixed (heteroleptic) organozinc reagents can efficiently engage in the three-component Mannich reaction.[3,4] These species, readily generated from alkyl iodides or bromides by direct zinc insertion, provide straightforward access to highly substituted α-branched amines. The method tolerates a wide range of organozinc reagents, secondary amines, and both aromatic and aliphatic aldehydes. Remarkably, the observed reactivity trends are strongly influenced by the nature of the alkyl halide precursor and reaction conditions.

This work demonstrates a cost-effective and broadly applicable strategy that significantly expands the scope of the organometallic Mannich reaction, opening new perspectives for the streamlined construction of complex amine architectures.



- Mild and useful conditions
- Broad scope
- X = I : 37 examples, 28–99%
- X = Br : 21 examples, 13–68%

References :
[1] J. Paul, M. Presset, E. Le Gall, *Eur. J. Org. Chem.* **2017**, 23862406.
[2] J. Esquivias, R. Gómez Arrayás, J. C. Carretero, *Angew. Chem. Int. Ed.* **2007**, *46*, 92579260.
[3] M. Pinaud, E. Le Gall, M. Presset, *J. Org. Chem.* **2022**, *87*, 49614964.
[4] B. Leroux, A. Beaufils, F. Banchini, O. Jackowski, A. Perez-Luna, F. Chemla, M. Presset, E. Le Gall, *Beilstein J. Org. Chem.* **2024**, *20*, 28342839.

PBLG-based orienting systems for spectral enantiodifferentiation of of chiral pharmaceutical compounds using ^{19}F 1D NMR

Vincent CHIAPOLINO,[1] François-Marie MOUSSALLIEH,[1] Philippe LESOT [1,2] and Boris GOUILLEUX[1]

[1] *Université Paris-Saclay, ICMMO (UMR 8182), CB2MR, 17-19, Avenue des Sciences, F-94100 Orsay, France.*
[2] *Centre National de la Recherche Scientifique (CNRS), 3, Rue Michel Ange, F-75016 Paris, France.*
vincent.chiapolino@universite-paris-saclay.fr

Molecular chirality is a major concern in organic and pharmaceutical chemistry as enantiomers may have different bioactivities with potential toxic side-effects. There is, therefore, a continuous need for innovative analytical methods to determine the enantiopurity of active pharmaceutical principles (API).
Chiral HPLC/GC, X-ray crystallography, chiroptical or NMR tools are well-known methods for chiral analysis.[1] Among them, NMR in isotropic solutions is a popular and widespread approach for enantiomeric discrimination that relies on the use of chiral auxiliaries in interaction with the enantiomers, thus forming temporary or permanent diastereomeric clusters.[2]

An alternative based on the use of lyotropic chiral liquid crystals (CLC) can be proposed to solve stereochemistry problems arising from stereogenic centers. Indeed, in CLCs, enantiomers exhibit a difference of averaged molecular orientation with respect to the NMR magnetic field. This may lead to a variation of residual anisotropic NMR interactions, such as chemical shift anisotropy (RCSA), dipolar coupling (RDC) and quadrupolar coupling (RQC), thus inducing spectral enantio-separations.[3]
Recently, the analytical potential of ^{19}F-{^{1}H} NMR in CLCs has recently been highlighted to discriminate mono- or trifluorinated APIs while ^{19}F-RCSAs and (^{19}F-^{19}F)-RDCs have enabled efficient enantiomeric discriminations and reliable determination of ee's.[4],[5]

Here, we present our latest developments with routine NMR equipments (including low-field benchtop spectometers) showing the versatility of this methodology to analyze severals APIs with specific chemical and therapeutic properties. The possibility to optimize the resulting enantio-resolution along with the influence of the magnetic field strength on the suitability of this approach will be reported.

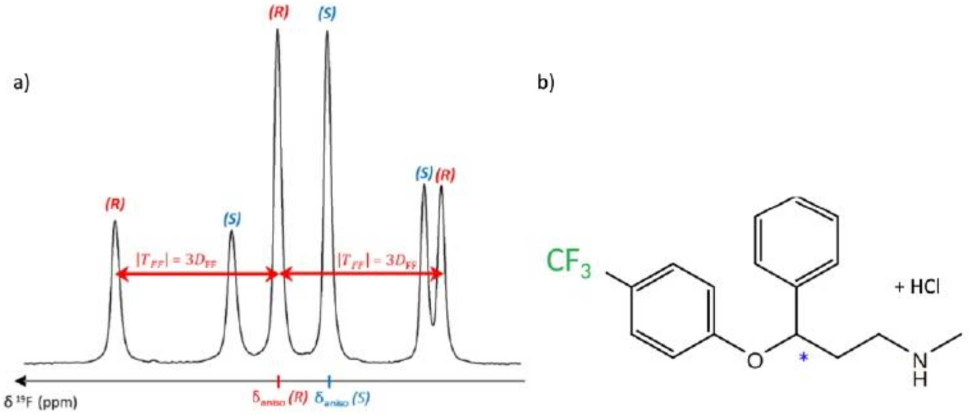


Figure 1. Enantiomeric discrimination observed on the 282 MHz ^{19}F spectrum of Fluoxetine hydrochloride dissolved in a PBLG-based CLC.

[1] Calcaterra et al, *J. Pharm. Biomed. Anal. 2018.* **2018**, *147*, 323–340.
[2] Wenzel et al, *Chirality*. **2003**, *15*, 256–270.
[3] Lesot et al, *Prog.in Nucl. Magn. Reson*. **2020,** *116,* 85–154.
[4] Gouilleux et al, *Analyst*. **2024**, *149*, 3204–3213.
[5] Chiapolino et al, *J. Pharm. Anal*. **2026,** online, DOI: 10.1016/j.jpha.2025.101469.

New reactivities in multicatalysis merging photocatalysis and organocatalysis

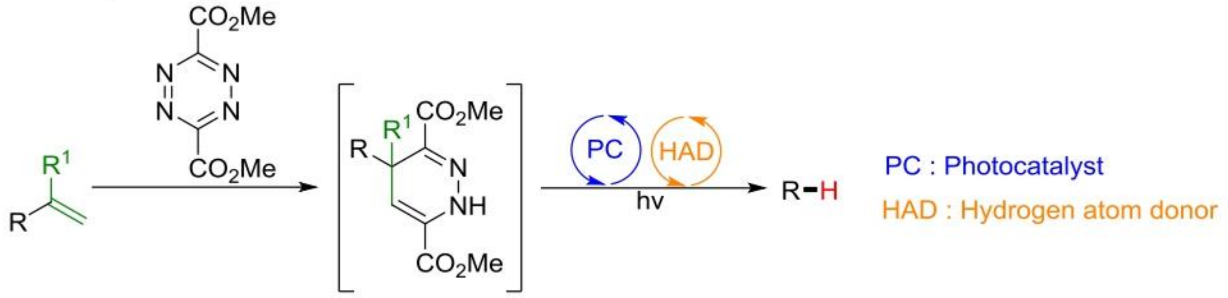
Thomas AUCOUTURIER,[1] Guillaume DAGOUSSET,[1]

[1] BioCIS (Biomolécules : Conception, Isolement, Synthèse) (UMR 8076), 10 Av. des Sciences 91190 Gif-sur-Yvette.
Thomas.aucouturier@universite-paris-saclay.fr

Over the past 15 years, photocatalysis has undeniably established itself as the method of choice for developing new radical transformations under particularly mild conditions. One of the reasons for this success lies in the fact that many substrates can be effective sources of radicals, through photocatalyzed oxidative or reductive single electron transfert (SET). For example, carbon radicals are readily available from the reduction of haloalkanes or the oxidation of carboxylates. Other substrates, such as amines (via the formation of a pyridinium salt) or aldehydes (via the formation of a 1,4-dihydropyridine), require pre-activation to become alkylating agents by photochemistry. On the other hand, no general photoredox catalysis method has yet made it possible to use alkenes as alkylating agents via a dealkenylation process, despite their wide availability and natural abundance.

This work builds on the radical dealkenylation strategies previously reported by O. Kwon[1] and T. Luo[2] [3], combined with our group's established expertise[4] in photocatalytic methodologies. Herein, we present the development of a novel photocatalytic approach enabling radical hydrodealkenylation, offering new safer and better controlled reactivity.

Our strategy relies on the initial activation of the alkene through its transformation into a pro-aromatic 1,4-dihydropyridazine via an inverse electron-demand Diels–Alder (IEDDA) reaction. This intermediate is subsequently subjected to mild photocatalytic conditions, enabling efficient conversion into the desired hydrodealkenylation product.



This methodology has proven effective across a range of differently substituted alkenes, proceeding under mild conditions and delivering the corresponding products in moderate to high yields.

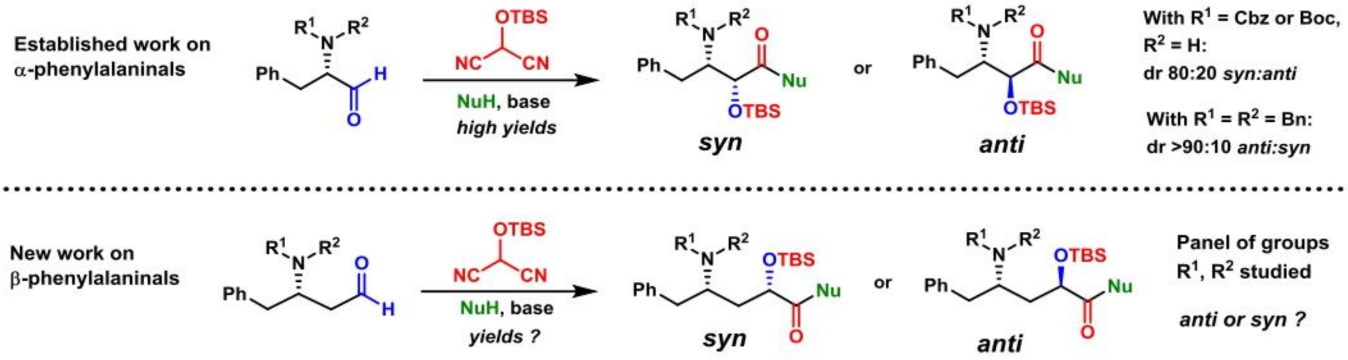
References :
[1] Kwon, O et al; *Science*. **2019**, *364*, 681-685.
[2] Luo, T et al; *J. Am. Chem. Soc.* **2021**, *143*., 14046–14052.
[3] Luo, T et al; *Chem. Eur. J.* **2023**, 29, e202203425.
[4] Dagousset et al, G; *Angew. Chem.* **2025**, 137, e202424459

MAC Oxyhomologation Reactions of *N*-protected α-Phenylalaninals and β-Phenylalaninals: a Comparative Study

Yuqiao ZHAO, Xuefeng HE, Sandrine DELOISY, David J. AITKEN
ICMMO, CNRS, Université Paris-Saclay, 91405 Orsay, France
yuqiao.zhao@universite-paris-saclay.fr

The one-pot three-component MAC (Masked Acyl Cyanide) reaction can be used to combine an aldehyde, a nucleophile and a masked acyl cyanide reagent (typically *tert*-butyldimethylsilyloxymalononitrile) to give products that are formally oxyhomologated derivatives of the starting aldehyde.[1] In principle, when the electrophilic substrate is an *N*-protected α-aminoaldehyde or β-aminoaldehyde, the expected oxyhomologation products are ester or amide derivatives of α-hydroxy-β-aminoacids or α-hydroxy-γ-aminoacids, respectively. Over the years, only the former of these substrate types has been studied and our group has applied the methodology to access a variety of α-hydroxy-β-aminoacid derivatives.[2-6]

A key issue in a MAC reaction employing a chiral non-racemic substrate is diastereoselectivity. By studying selected *N*-protected α-phenylalaninals, we have deduced that the protecting group suite has a decisive role in controlling the diastereoselectivity. With a single carbamate protecting group (Cbz or Boc), the reaction is selective for the formation of *syn* products, whereas with dibenzyl protection a high *anti* selectivity is observed.



To further probe the significance of the *N*-protecting group, we have undertaken a study of the oxyhomologation reaction of *N*-protected β-phenylalaninals. Such substrates have not been described before as electrophilic partners for MAC reactions. In this presentation, we will describe these results and compare them with those obtained for the analogous *N*-protected α-phenylalaninals.

References :
[1] Nemoto, H.; Ma, R.; Suzuki, I.; Shibuya, M. *Org. Lett.* **2000**, *2*, 4245-4247.
[2] Esgulian, M.; Belot, V.; Guillot, R.; Deloisy, S.; Aitken, D. J. *Org. Biomol. Chem.* **2017**, *15*, 1453-1462.
[3] Esgulian, M.; Buchotte, M.; Guillot, R.; Deloisy, S.; Aitken, D. J. *Org. Lett.* **2019**, *21*, 2378-2382.
[4] He, X.; Buchotte, M.; Guillot, R.; Deloisy, S.; Aitken, D. J. *Org. Biomol. Chem.* **2022**, *20*, 1769-1781.
[5] He, X.; Guillot, R.; Deloisy, S.; Aitken, D. J. *Org. Lett.* **2024**, *26*, 2207-2211.
[6] Cabua, M. C.; He, X.; Secci, F.; Deloisy, S.; Aitken, D. J. *ChemistryOpen* **2025**, *14*, e202400279.

PO-21

Scalable methods for the preparation of functionalised *N*-Acetyl-D-glucosamine

Justine BARAKAT,[1] Inès MOHAMED;[1,2] Silvère BONNET,[2] Benoit DARBLADE,[2] Yoann PASCAL,[2] Sébastien VIDAL,[1] Stéphanie NORSIKIAN[1].

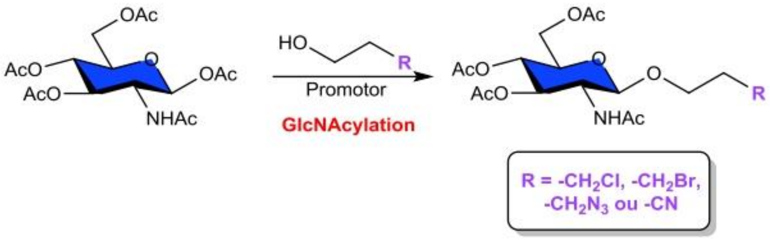
[1]Institut de Chimie des Substances Naturelles, CNRS, Avenue de la Terrasse, 91190 Gif-sur-Yvette
[2]Elicityl, Avenue Ambroise Croizat, 38920, Crolles
justine.barakat@cnrs.fr, ines.mohamed@cnrs.fr

N-Acetyl-D-glucosamine (GlcNAc) or 2-(acetylamino)-2-deoxy-D-glucose is a monosaccharide widely found in nature.[1] It constitutes a fundamental building block of structural biopolymers such as chitin and is present in a wide variety of natural oligosaccharides usually linked through 1,2-*trans* glycosidic bonds.[2] These carbohydrate motifs play a central role in a variety of essential biological systems, including blood group antigens, human milk oligosaccharides, complex glycoproteins, and several tumor-associated biomarkers. Despite their significant importance in carbohydrate chemistry and chemical biology, access to functionalized GlcNAc derivatives remains limited. This is due both to the challenges associated with their extraction from natural sources and to the cost and complexity of their chemical synthesis.

Previous studies have explored the direct use of *N*-Acetyl-D-glucosamine as donor in glycosylation to improve atom economy and avoid amine protection and deprotection steps,[3] in opposition to 2-amino-glycosides with specific protecting groups on the amine moiety (e.g. carbamates, amides, azide, nitro). However, this approach is often limited by the formation of a stable oxazolinium intermediate, which significantly decreases the glycosylation efficiency. The present project aims to overcome these limitations by developing improved methodologies for GlcNAc glycosylation, enabling the production of functionalised *N*-Acetyl-D-glucosamine in significant quantities – on the multigram scale.

In this context, our laboratory has previously established a straightforward and efficient glycosylation protocol employing peracetylated GlcNAc as the glycosyl donor in the presence of a catalytic amount of metal triflates as promoter.[4] This microwave-optimized synthesis enabled the preparation of various functionalized saccharides using a wide range of glycosyl acceptors although this was limited by large-scale production.

In this work, we further optimized the existing synthetic pathway to improve reaction yield, stereoselectivity, and reproducibility (*Scheme 1*). Particular attention was devoted to the scalability of the process, and the conditions were successfully optimized on large scale resulting in significantly increased quantities of the target compounds while preserving efficiency and reliability of the glycosylation protocol.



Scheme 1 : Direct use of N-Acetyl-D-glucosamine peracetylated as donor in glycosylation

References :

[1] Varki A, Cummings RD, Esko JD, Freeze HH, Stanley P, Bertozzi CR, Hart GW, Etzler ME, editors. Essentials of Glycobiology. 2nd ed. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory Press; **2009**.

[2] Shivatare, S. S.; Shivatare, V. S.; Wong, C.-H., *Chem. Rev.* **2022**, *122*, 15603.

[3] Beau, J.-M.; Boyer, F.-D.; Norsikian, S.; Urban, D.; Vauzeilles, B.; Xolin, A. *Eur. J. Org. Chem.* **2018**, 5795.

[4] Xolin, A.; Stevenin, A.; Pucheault, M.; Norsikian, S.; Boyer, F.-D.; Beau, J.-M. *Org. Chem. Front.* **2014**, *1*, 992.

Synthesis and Evaluation of β-Lactam Prodrugs to Combat Bacterial Resistance

Maëva DE MOURA PERALTA,[1] Katie BURKE,[1] Quentin HERAIL,[2] Michel ARTHUR,[2] Mélanie ETHEVE-QUELQUEJEU,[1] Laura IANNAZZO[1]

(1) LCBPT, UPC, Chemistry of RNA, nucleosides, peptides and heterocycles, 45 rue des Saints-Pères, 75006, Paris
(2) Cordeliers Research Centre, Bacterial structures involved in modulating antibiotic resistance, 15 rue de l'Ecole de Médecine, 75006, Paris
maeva.de-moura-peralta@etu.u-paris.fr

Modern medicine relies on the availability and effectiveness of antibiotics. Unfortunately, we are facing a major public health crisis: antibiotic resistance. This is due to overuse and a lack of innovation in the field.

In 2015, a Global Action Plan on Antimicrobial Resistance was launched. Indeed, the World Health Organization (WHO) announced that, by 2050, this crisis could lead to a catastrophic situation, also known as a "therapeutic impasse." The WHO has therefore called for the development of new antibiotics to combat bacterial resistance.

Among the various classes of antibiotics used today to treat bacterial infections, β-lactams are the most used. They inhibit the synthesis of the bacterial cell wall by binding to the proteins involved in its formation.

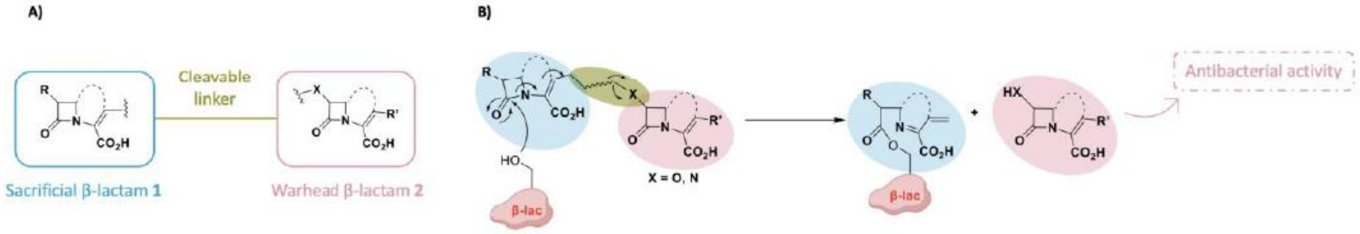
Over the past decade, our team has developed synthetic methodologies to produce carbapenem analogs, a subclass of β-lactams and demonstrated their activity as transpeptidase inhibitor. [1-2]

In response to antibiotic treatment, bacteria developed resistance by producing degradation enzymes called β-lactamases.

The objective of the project proposed here is to develop a new family of narrow-spectrum antibiotics, based on β-lactam scaffold specifically targeting resistant Gram-negative bacteria. The strategy involves synthesizing innovative prodrugs, as illustrated in Scheme 1A.

The synthesized prodrugs contain two β-lactam structures linked together by a cleavable linker. β-lactam 1 constitutes the sacrificial moiety of the prodrug: it is intentionally targeted and degraded by β-lactamases, as illustrated in the mechanism in Scheme 1B.

This process leads to the release of the second warhead β-lactam 2 which can then exert its antibacterial activity.



Scheme 1. A) Structure of prodrugs. B) Envisaged mecanism of action of the synthesized prodrugs.

References:

[1] S. Saidjalolov, E. Braud, Z. Edoo, L. Iannazzo, F. Rusconi, M. Riomet, A. Sallustrau, F.Taran, M. Arthur, M. Fonvielle, M. Etheve-Quelquejeu, *Chem. Eur. J.* **2021,** *27*, 7687-7695

[2] K. Burke, Q. Herail, I. Zerguine, C. Bougault, M. Arthur, M. Etheve-Quelquejeu, L. Iannazzo, *Chem. Eur. J.*, **2025**, 31

PO-23

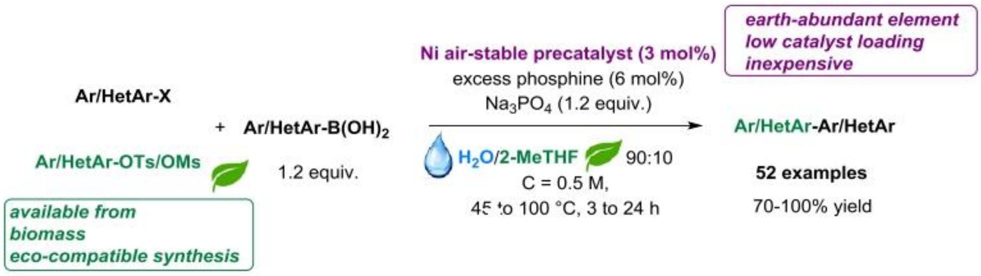
Green Suzuki-Miyaura cross-couplings in aqueous media mediated by air-stable nickel precatalysts

Yunbo ZHAO, Aïssa Id BOUALIM, Parvine TRAN, Marie-Isabelle LANNOU
Laboratoire CiTCoM, UMR 8038, Equipe PNAS
Université Paris Cité, Faculté de Pharmacie, 4 Avenue de l'Observatoire, 75006 Paris
yunbo.zhao@etu.u-paris.fr

In the context of the sustainability-focused development plan outlined by the United Nations in 2015, the need for green and sustainable chemistry and engineering has been clearly identified as a major challenge. However, the lack of "green" manufacturing processes is an unsolved problem in major areas especially in organometallic catalysis. Hence, despite their exponential development, cross-coupling (C-C) reactions remain highly polluting due to the use of over-exploited low-abundant palladium (0.015 mg/kg earth crust) and organic solvents, which represent over 80% of the chemical waste of the chemical industry.[1] Although significant advances have been made in the field thanks to micellar systems, these works only focus on organic halides and none of them concern eco-compatible *O*-based electrophiles.[2]

For this reason, we have developed an eco-compatible Suzuki-Miyaura cross-coupling which allows access to biaryl as well as heteroaryl compounds. The process combines a non-noble metal complex and sustainable *O*-based electrophiles, as well as more conventional heteroaryl/aryl halides in a green media composed of 90% water. In details, the association we have targeted gathers the use of:

- Aryl/heteroaryl halides, as well as their corresponding tosylates and mesylates, which are valuable electrophilic partners in cross-coupling reactions. Notably, tosylates and mesylates can be readily synthesized from biomass-derived phenols, offering a chemically stable and eco-compatible alternative that aligns with the principles of sustainable chemistry.[3]
- An air-stable catalyst issued from "non-noble" abundant and inexpensive nickel (84 mg/kg earth crust). A catalyst loading as low as 3 mol% was employed, and further reduction to 1 mol% was feasible by extending the reaction time, without significant loss in yield. The protocol was also amenable to gram-scale synthesis, delivering the coupling product in consistently high yield.
- Aqueous reaction media composed of 90% water and 10% of a bio-sourced organic solvent (methyl tetrahydrofuran) for solubility issues, allowing a significant reduction of chemical wastes (Scheme 1).



Scheme 1

References :
[1] Shaughnessy, K. H.; De Vasher, R. B. *Curr. Org. Chem.* **2005**, *9*, 585–604.
[2] a) Handa, S.; Slack, E. D.; Lipshutz, B. H. *Angew. Chem. Int. Ed.* **2015**, *54*, 11994-11998.; b) Guo, X. ; Dang, H.; Wisniewski, R. Simmons, E. M. *Organometallics*, **2022**, *41*, 1269-1274.
[3] Lei, X.; Jalla, A.; Shama, M. A. A.; Stafford, J. M.; Cao, B. *Synthesis*, **2015**, 2578–2585.

PO-24

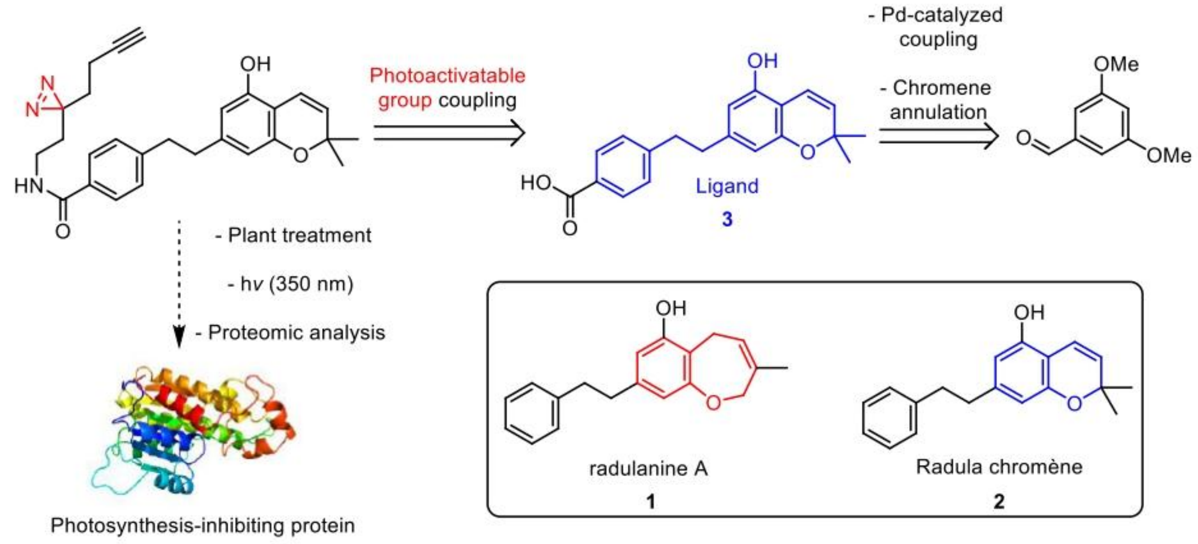
Synthesis of a photoaffinity probe derived from Radula chromene for target identification in photosynthesis inhibition

Léa LAURENT [1], Nicolas FAY [1], Emmanuel BAUDOUIN [2], Bastien NAY [1*]
[1] Laboratoire de Synthèse Organique (LSO, UMR 7652), Ecole Polytechnique,
Institut Polytechnique de Paris, CNRS, 91128 Palaiseau, France
[2] Laboratoire de Biologie du Développement (UMR 7622), Institut de Biologie Paris-Seine,
Sorbonne Université, CNRS, 75005 Paris, France
Lea.laurent@polytechnique.edu

Radula-derived natural products, such as radulanine A **1** and Radula chromene **2**,[1] have been shown to exhibit herbicidal activity in model plants such as *Arabidopsis thaliana*.[2] Preliminary biological studies indicate that these compounds inhibit photosynthesis by targeting the QB site of photosystem II.[2],[3] However, to date, their complete mechanism of action, as well as their uptake and translocation in plants, remain poorly understood. In this context, this project aims to develop chemical tools to identify ligand–protein interactions and uncover new biological targets.

To address this challenge, we developed a photoaffinity probe based on the Radula chromene scaffold for proteomic "target fishing" experiments. [4] Our design relies on the incorporation of three key elements: a bioactive chromene-based ligand to ensure binding to the target protein, a diazirine moiety as a photoactivatable group enabling covalent capture upon UV irradiation, and a terminal alkyne handle for subsequent biotin conjugation via copper-catalyzed azide–alkyne cycloaddition (CuAAC).[5]

A synthetic route toward a functionalized chromene acid **3** was developed, enabling the introduction of the photoactivatable moiety. The targeted probe was successfully synthesized and has been submitted for biological evaluation.



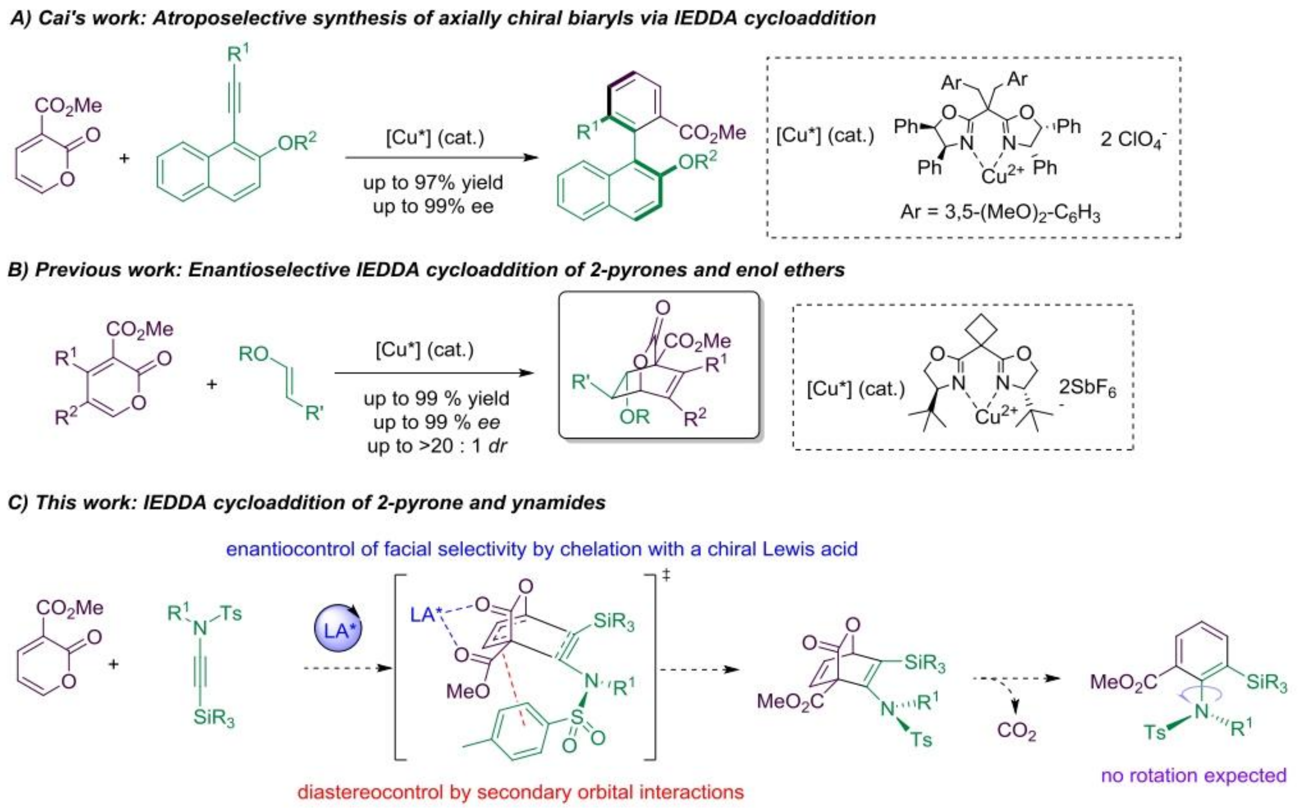
References :
[1] Asakawa, Y ; *Phytochemistry* **1978**, 17, 2005–2010.
[2] Thuillier, S ; *Pest Management Science* **2024**, *80*, 156–165.
[3] Nay, B ; Thuillier, S ; FR 3132613 A1. **2022**.
[4] James R. Hill ; *J. Med. Chem*. **2018**, 61, 16, 6945–6963.
[5] Smith, E ; *Future Med Chem* **2015**, *7*, 159–183.

Towards Atroposelective Synthesis of Axially Chiral Compounds

Dang Khoi DUONG,[1] Valérie ALEZRA,[1] Aurélien DE LA TORRE,[1] Cyrille KOUKLOVSKY[1]

[1]Université Paris-Saclay, CNRS, Institut de Chimie Moléculaire et des Matériaux d'Orsay, UMR 8182, 91400, Orsay, France
dang-khoi.duong@universite-paris-saclay.fr

Axial chirality is widely encountered in natural products and bioactive molecules, as well as chiral catalysts and ligands with high demand of enantioselective synthesis methodologies. Inverse-electron-demand Diels–Alder (IEDDA) reactions of 2-pyrones have emerged as a promising strategy for the construction of complex molecular frameworks,[1] especially those bearing stereogenic axes. In 2021, Cai *et al.* reported the first atroposelective synthesis of axially chiral biaryls via a Cu(II)-catalyzed IEDDA cycloaddition of 2-pyrones with naphthyl alkynes.[2] Subsequently, our group disclosed an enantioselective cycloaddition of 2-pyrones with acyclic enol ethers following a similar fashion.[3] In this work, we aim to develop a new enantioselective cycloaddition of 2-pyrones with ynamides, enabling the access to new classes of C-N atropisomers. Herein, we will discuss our preliminary results obtained in this domain.



A) Cai's work: Atroposelective synthesis of axially chiral biaryls via IEDDA cycloaddition

B) Previous work: Enantioselective IEDDA cycloaddition of 2-pyrones and enol ethers

C) This work: IEDDA cycloaddition of 2-pyrone and ynamides

enantiocontrol of facial selectivity by chelation with a chiral Lewis acid

diastereocontrol by secondary orbital interactions

References :
[1] Huang, G.; Kouklovsky, C.; de la Torre, A.; *Chem. Eur. J.* **2021**, *27*, 4760 – 4788.
[2] Xu, M.-M.; You, X.-Y.; Zhang, Y.-Z.; Lu, Y.; Tan, Kui.; Yang, L.; Cai, Q.; *J. Am. Chem. Soc.* **2021**, *143*, 8993–9001.
[3] Huang, G.; Guillot, R.; Kouklovsky, C.; Maryasin, B.; de la Torre, A.; *Angew. Chem. Int. Ed.* **2022**, *61*, e202208185.

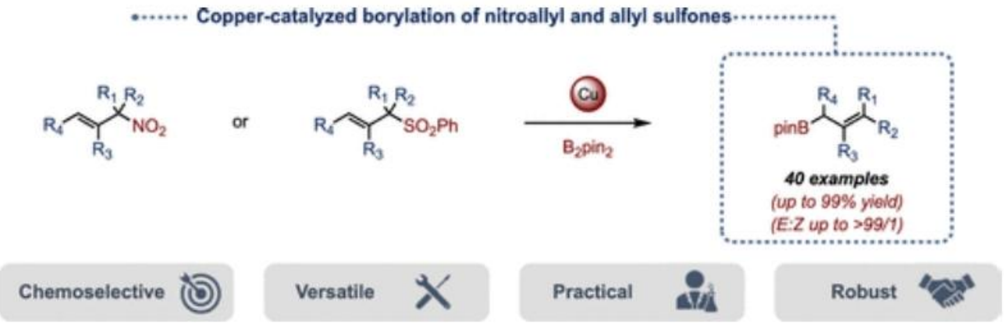
PO-26

Copper-catalyzed synthesis of diversely functionalized allyl boranes, starting from nitro allyl and allyl sulfones derivatives

Nicolas FINCIAS,[1] Louis CLAVIER,[1] Cora ESCANDE DE MESSIERES,[1] Marianne GUILLARD,[1] Mansour DOLE KERIM,[1] Nicolas CASARETTO,[1] Julian GARREC,[1] Stellios ARSENIYADIS,[2] Laurent EL KAIM[1]

[1] Laboratoire de Synthèse Organique (LSO UMR 7652) CNRS, Ecole Polytechnique, ENSTA-Paris, Institut Polytechnique de Paris, 91128 Palaiseau Cedex, France
[2] Queen Mary University of London, Department of Chemistry, London E1 4NS, U.K.
cora.escande@ensta-paris.fr

We report[1] a new transition-metal-catalyzed borylation of allyl derivatives using nitroallyls and allylsulfones for the first time. The pioneering work of Miyaura[2] and Ito[3] prompted the study of numerous catalysts and allyl derivatives, however the scope of accessible functions remains limited. The precursors described provide straightforward access to a wide variety of functional groups (esters, cyanides, sulfones, silyl-protected alcohols) due to the acidic α-position of the nitro or sulfone group. The allylboranes are obtained in excellent yields regardless of the functional group. For example, the method enables the synthesis of γ-fluoroallyl boronic esters, which are useful building blocks, as well as tri- and tetrasubstituted allylboranes. Moreover, copper represents one of the most environmentally friendly alternatives to palladium. The synthetic utility of allylboranes was demonstrated through various post-functionalizations. The results were rationalized through DFT calculations, which reveal a mechanism different from what observed with conventional leaving groups.

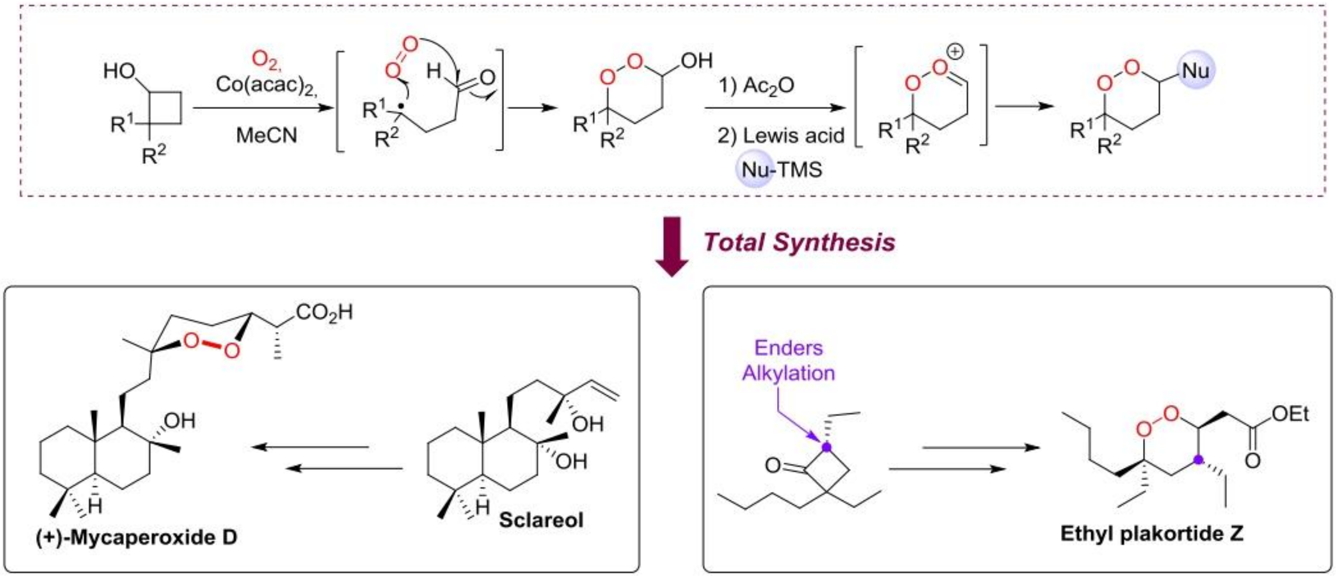


References:
[1] Fincias, N; Clavier, L; Escande de Messières, C; Guillard, M; Dole Kerim, M; Casaretto, N; Garrec, J; Arseniyadis, S; El Kaïm, L; *JACS Au* **2025**, *5* (1), 99-110.
[2] Ishiyama, T; Ahiko, T; Miyaura, N; *Tetrahedron Lett*. **1996**, *37*, 6889–6892.
[3] Ito, H; Kawakami, C; Sawamura, M; *J. Am. Chem. Soc.* **2005**, *127*, 16034–16035.

Total Synthesis of Marine Endoperoxides: Mycaperoxides B, C, D and G, and Ethyl Plakortide Z

Nicolas JAMEY,[1] Mansour DOLE KERIM,[1] Bastien CHAMPCIAUX,[1] Laurent EVANNO,[1] Bruno FIGADERE,[1] Laurent FERRIE,[1]
[1] BioCIS, Université Paris-Saclay, CNRS, Bâtiment H. Moissan, 6 rue d'Arsonval, 91400 Orsay, France
laurent.ferrie@universite-paris-saclay.fr

Marine endoperoxides are compounds produced mainly by sponges or tunicates, and likely play a role as anti-fouling agents, enabling these organisms to remain clean. Their biological activity is diverse, with properties that are mainly cytotoxic, antiviral, antibacterial, or antiparasitic.[1] In recent years, our team has developed methods for accessing endoperoxides based on the insertion of molecular oxygen into constrained cycloalkanols, followed by activation of the endoperoxyacetal function to introduce various silylated nucleophiles.[2–4] Here we illustrate the application of these different methods to the total synthesis of several marine endoperoxides. Mycaperoxides B, C, D, and G were synthesized from sclareol, allowing the introduction of decalin via a divergent strategy.[5] We also focused on the total synthesis of ethyl plakortide Z, an endoperoxide with the distinctive feature of having an ethyl group on the 1,2-dioxane motif, which was introduced by an Enders alkylation[3,6]



References :

[1] Ferrié, L., in *Adv Heterocycl Chem* (Eds.: E.F.V. Scriven, C.A. Ramsden), Academic Press, **2021**, pp. 57–146.

[2] López, M. M., N. Jamey, A. Pinet, B. Figadère, L. Ferrié, *Org. Lett.* **2021**, *23*, 1626–1631.

[3] Champciaux, B., N. Jamey, B. Figadère, L. Ferrié, *J. Am. Chem. Soc.* **2025**, *147*, 3353–3359.

[4] Pinet, A., B. Figadère, L. Ferrié, *Adv. Synth. Catal.* **2020**, *362*, 1190–1194.

[5] Kerim, M. D., L. Evanno, L. Ferrié, *Chem. – Eur. J.* **2023**, *29*, e202203004.

[6] Jamey, N., L. Ferrié, *Org. Lett.* **2024**, *26*, 5741–5745.

PO-28

RCO XXII
Paris, May 29th 2026
Rencontres de Chimie Organique
PHARMACIE
Santé
Université Paris Cité

From natural products to reactive metabolites: combined Bio-electrochemical prediction of furanic compounds' toxicity

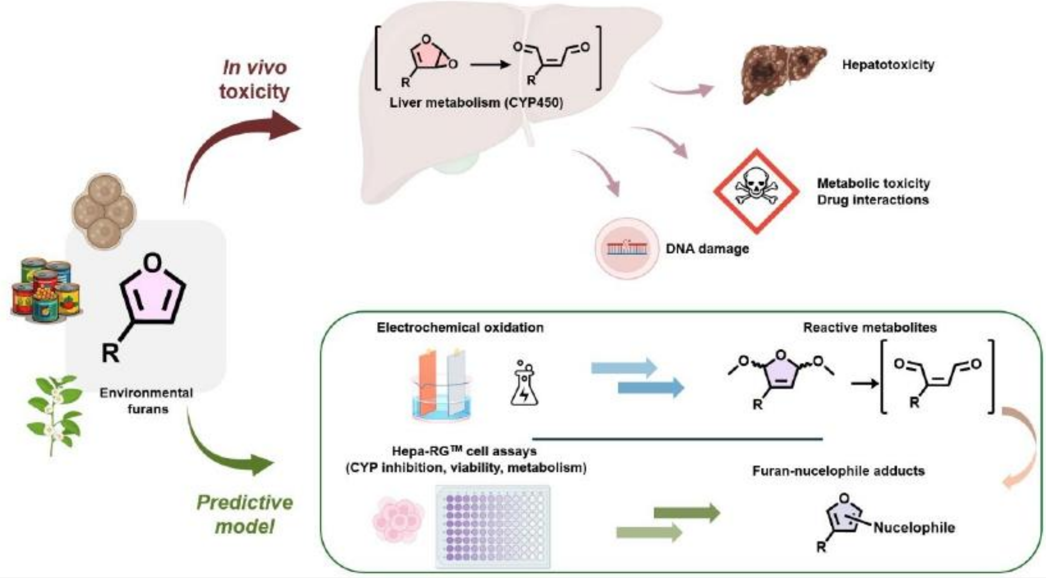
Imène AYADEN[1], Chouaha Bouzidi[1], Thomas Gaslonde[1], Joelle Viret-Perard[1], Céline Hoffmann[2], Xavier Cachet[1]
[1] *Equipe Produits Naturels, Analyses et Synthèses, Laboratoire CiTCoM UMR 8038 CNRS-Université Paris Cité, Faculté de Pharmacie de Paris, F-75006 Paris, France*
[2] *Université Paris Cité, CNRS, INSERM, UTCBS, F-75006 Paris, France*
xavier.cachet@u-paris.fr

Furanic compounds, characterized by furan or dihydrofuran rings, are widespread natural products found in plants, fungi, and various botanical extracts, as well as in food and environmental matrices. While some of them are suspected to be toxic, their mechanisms of action remain insufficiently understood, particularly regarding metabolic bioactivation. Furanic natural products generally undergo oxidation by cytochrome P450 enzymes into electrophilic 1,4-enedial intermediates, which can react with nucleophilic cellular targets, leading to oxidative stress, enzyme inhibition, and organ injury. To better characterize these mechanisms and develop predictive tools adapted to natural compound mixtures, we combined an electrochemical mimicry of CYP450-mediated oxidation with a human hepatic cell model based on HepaRG™ cells.

Electrochemical oxidation enabled the generation of reactive intermediates, used as predictors of reactivity. These intermediates were trapped using glutathione, allowing the formation, isolation, and characterization of stable adducts, and the establishment of kinetic reactivity profiles. This approach provides a rapid means to identify natural compounds prone to bioactivation into toxic metabolites.

To assess biological relevance, selected furanic compounds were further evaluated in HepaRG cells, where CYP3A4 activity was monitored using bioluminescence assays. Several compounds exhibited strong CYP inhibition, consistent with intracellular formation of reactive metabolites. Importantly, mass spectrometry analysis confirmed the formation of predicted adducts in a cellular system, underlying their relevance as biomarkers of exposure.

This research highlights the value of combining electrochemical and cellular approaches to investigate the safety of natural products and provides a framework for the rapid screening of naturally occurring furans in toxicological risk assessment.



References:
Li H., Peng Y., Zheng J. (2016) Adv. Mol. Toxicol. 10:55-97.
Tian M., Peng Y., Zheng J. (2022) Drug Metab. Dispos. 50:655-670.
Ning J., Tian Z., Wang J., Wang B., Tian X., Yu Z., Huo X., Feng L., Cui J., James T.D., Ma X. (2021) Angew. Chem. Int. Ed. 61, e202113191
L. Peterson, Chem. Res. Toxicol. 2013, 26, 6–25

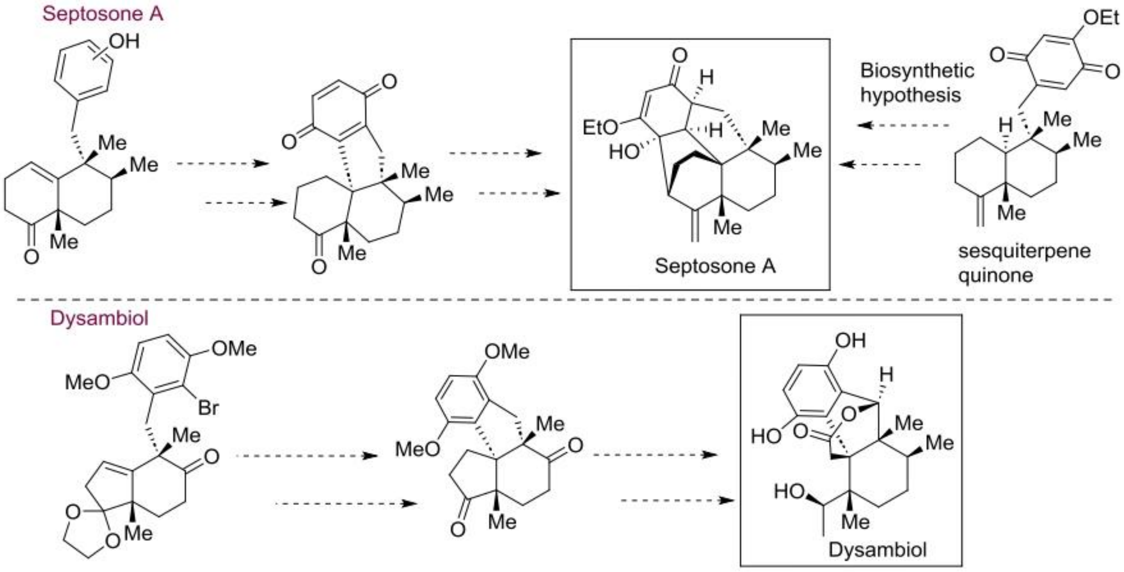
PO-29

Synthetic Studies towards Total Synthesis of Septosone A and Dysambiol

Jie LI,[1] Cyrille KOUKLOVSKY[1] and Guillaume VINCENT[1]

[1] Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO)
Unviversité Paris-Saclay, Bâtiment Henri Moissan 1 (HM1)
17, Avenue des Sciences, 91400 Orsay, France
jie.li@universite-paris-saclay.fr

Septosone A and dysambiol are structurally complex, marine-derived terpene natural products that exhibit significant anti-inflammatory potential.[1-3] Septosone A is characterized by a distinctive pentacyclic skeleton, hypothesized to arise biosynthetically via the cyclization of a sesquiterpene quinone. Inspired by this pathway, our retrosynthetic design targets a similar precursor, proposing a key intramolecular cyclization between an internal trisubstituted alkene and a phenol through a metal-hydride hydrogen atom transfer (MHAT) process to construct the requisite five-membered ring.[4] In parallel, our efforts toward the synthesis of dysambiol—which features an unprecedented secomeroterpene framework with a rare lactone bridge and six contiguous stereocenters—are currently underway. Our synthetic strategy relies on an intramolecular Heck reaction between an internal trisubstituted alkene and an aryl bromide to establish the core five-membered ring.



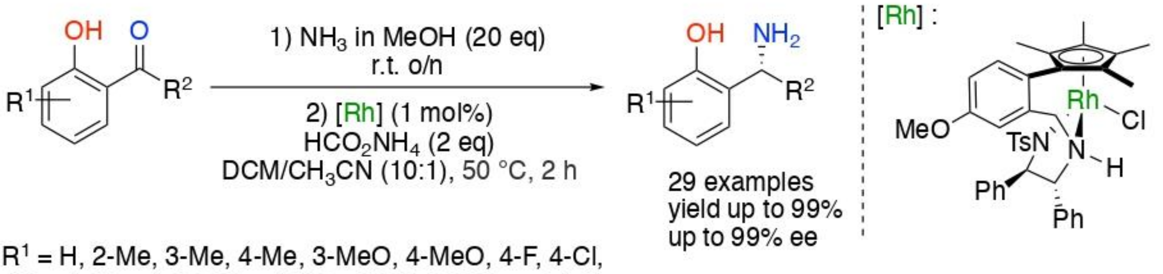
References :
[1] Gui, Y.-H.; Jiao, W.-H.; Zhou, M.; Zhang, Y.; Zeng, D.-Q.; Zhu, H.-R.; Liu, K.-C.; Sun, F.; Chen, H.-F.; Lin, H.-W. *Org. Lett*. **2019**, *21*, 767–770.
[2] Robert A, H.; Andrew, S. *Nat. Prod. Rep*. **2023**, *40*, 1590-1594.
[3] Jiao, W.-H.; Li, J.-X.; Liu, H.-Y.; Luo, X.-C.; Hu, T.-Y.; Shi, G.-H.; Xie, D.-D.; Chen, H.-F.; Cheng, B.-H. Lin, H.-W. *Org. Lett*. **2023**, *25*, 6391–6395.
[4] Schoenn, G.; Kouklovsky, C.; Guillot, R.; Magauer, T.; Vincent, G. *Angew. Chem. Int. Ed*. **2025**, *64*, e202505270.

Synthesis of α-Substituted Primary Amines through Asymmetric Transfer Hydrogenation

Chonghuo LIU,[1] Phannarath PHANSAVATH,[1] and Virginie VIDAL[1]

[1]PSL University, Chimie ParisTech, Institute of Chemistry for Life & Health Sciences
CNRS UMR 8060, CSB2D Team, 75005 Paris, France
phannarath.phansavath@chimieparistech.psl.eu, virginie.vidal@chimieparistech.psl.eu

α-Chiral primary amines, where the NH_2 group is preserved, play crucial roles in drug design and synthesis.[1] These motifs are not only present in many drug molecules but also serve as versatile building blocks for rapid library diversification through NH_2 functionalization, accelerating the development of amine-based therapeutics.[2] Among them, the chiral 2-(1-aminoethyl) phenol unit is a privileged pharmacophore in bioactive compounds. Despite their significance, only few examples of direct catalytic enantioselective synthesis of these structures are reported.[3,4] A key challenge in asymmetric transfer hydrogenation of NH imines is the instability and inaccessibility of NH imine substrates. In our continuous interest for transition metal catalyzed asymmetric reductions,[5] we address this issue by developing a Rh(III)[6]-catalyzed asymmetric transfer hydrogenation (ATH) of stable NH imines, prepared via condensation of readily available ortho-hydroxyaryl alkyl ketones with NH_3 in methanol. The ATH with other transition metals is also underway.



29 examples
yield up to 99%
up to 99% ee

R^1 = H, 2-Me, 3-Me, 4-Me, 3-MeO, 4-MeO, 4-F, 4-Cl, 4-Br, 4-CF_3, 4-CO_2Me, 4-NO_2, 4-CN, 2,3-Me_2, 2,4-Me_2, 3,5-Me_2, 2,3,5-Me_3, 4-C_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 2-thienyl, 2-furyl, 2-naphthyl

R^2 = Me, Et, Ph

References :

[1] A. Ricci, L. Bernardi, Methodologies in Amine Synthesis: Challenges and Applications, Wiley-VCH, Weinheim, 2021.

[2] (a) T. C. Nugent, S. M. Marinova, *Synthesis*, **2013**, *45*, 153. (b) Q. Yin,Y. Shi, J. Wang, X. Zhang, *Chem. Soc. Rev.* **2020**, *49*, 6141.

[3] (a) M. Zhang, H. Li, K. Wu, N. Rong, S. Lin, H. Yang, Q. Yin, *Chin. J. Chem.* **2024**, *42*, 2211. (b) I. K. Mangion, C.-y. Chen *et al.*, *Org. Lett.* **2014**, *16*, 2310. c) Y. Zheng, G. J. Clarkson, M. Wills, *Org. Lett.* **2020**, *22*, 3717.

[4] T. B. Nguyen, H. Bousserouel, Q. Wang, F. Guéritte, *Org. Lett.* **2010**, *12*, 4705.

[5] (a) L. Bacheley, R. Ravindra, G. Guillamot, P. Phansavath, V. Ratovelomanana-Vidal, *Adv. Synth. Catal.* **2024**, *366*, 1019. (b) L. Bacheley, R. Molina Betancourt, R. Ravindra, G. Guillamot, P. Phansavath, V. Ratovelomanana-Vidal, *Eur. J. Org. Chem*. **2023**, *26*, e202300383. (c) R. Molina-Betancourt, L. Bacheley, A. Karapetyan, G. Guillamot, P. Phansavath, V. Ratovelomanana-Vidal, *ChemCatChem* **2022**, *14*, e202200595.

[6] (a) L-S. Zheng, Q. Llopis, P.G. Echeverria, C. Férard, G. Guillamot, P. Phansavath, V. Ratovelomanana-Vidal, *J. Org. Chem.* **2017**, *82*, 5607. (b) P. G. Echeverria, L-S. Zheng, Q. Llopis, P. Phansavath, V. Ratovelomanana-Vidal, *SynOpen* **2022**, *6*, 75.

Fate of ^{14}C-Radiolabeled Polyethylene Terephthalate Nanoplastics in mice after oral administration

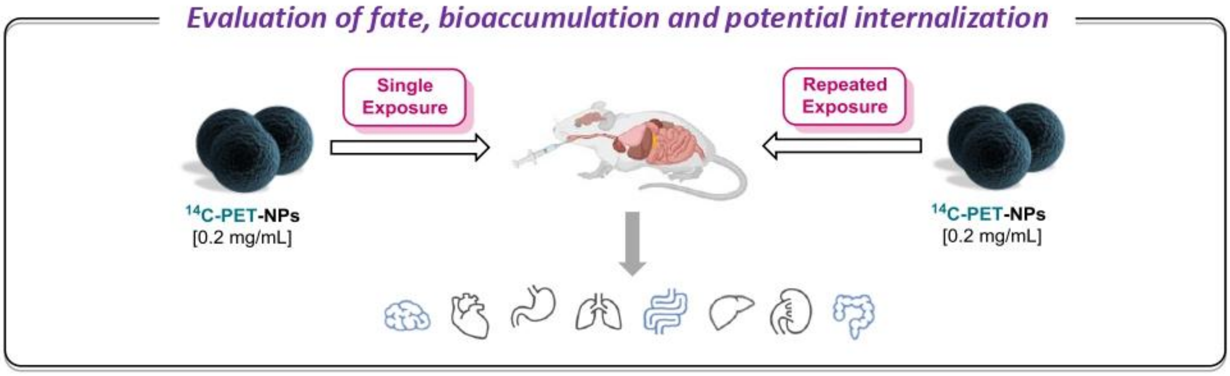
Clara FAURE,[1] Alberto PALAZZOLO,[1] Justyne VETEL,[2] Vérane BARD,[2] Amélie DELTHEIL,[1] Timothée D'ANFRAY,[1] Sebastien BRUYERE,[1] Etienne GRAU,[3] Mathilde KECK,[2] Frédéric TARAN,[1] Marie CARRIERE,[2] Antoine SALLUSTRAU*[1]

[1] Service de Chimie Bio-organique et Marquage (SCBM), DMTS, CEA-Saclay, F-91191, Gif-sur-Yvette, France
[2] Systèmes Moléculaires et nanoMatériaux pour l'Energie et la Santé (SyMMES), DIESE, CEA-Grenoble, 38000 Grenoble, France
[3] LCPO, Université de Bordeaux, 16 Avenue Pey-Berland, 33600, Pessac, France
clara.faure@cea.fr

Annual plastics production has considerably increased during the last century because of their uses in many sectors such as industry, health, research or food.[1] Among these plastics, PET (polyethylene terephthalate) is found in our daily life. It contributes to environmental pollution and represent a significant source of contamination by ingestion of micro and nano-plastics (NPLs).

More particularly, investigations on NPLs in complex biological environments are usually challenging due to the difficulty to monitor them, especially in environmentally relevant exposure concentrations.[2] Among these investigations, most of them are focused on marine organisms (oysters for example[3]) and uses fluorescence that already showed limitations. Thus, using radioactivity structurally incorporated in NPLs would circumvent these limitations and allow a more representative and quantitative assessment of their biodistribution in environmentally realistic scenarios.

This work aims to provide an evaluation of nano-plastics fate in mice after oral administration. It focuses on their fate, bioaccumulation and potential internalization. These issues will be addressed by coupling *in vitro* and *in vivo* approaches with methods for plastics synthesis, radiolabeling and highly sensitive detection and quantification, including technics.



References:

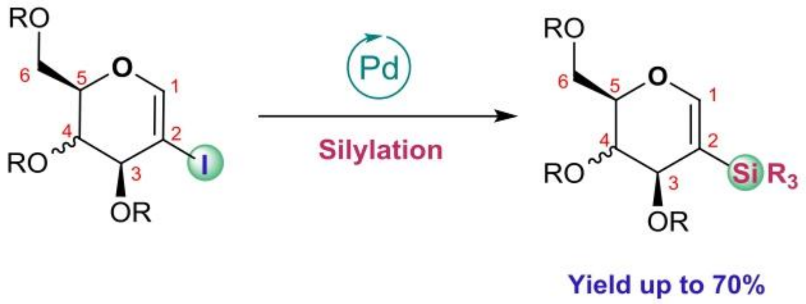
[1] Plastics Europe: Plastics - the facts 2024, an analysis of European plastics production, demand and waste data, **2024.**
[2] Lenz R.; Enders K.; Nielsen T.G.; *Proc. Natl. Acad. Sci. USA*, **2016**, *113*, E4121-E4122.
[3] Ward, J. E.; Kach, D. J.; *Mar. Environ. Res.,* **2009**, *68*, 137.

Development of a palladium-catalyzed silylation of glycals

Abir JERTILA,[1] Morgane DE ROBICHON,[1] Jacques UZIEL,[1] and Angelique FERRY[1]

[1] BioCIS, CY Cergy Paris Université, 5 Mail Gay Lussac, 95000 Neuville-sur-Oise, France
abir.jertila@cyu.fr

Glycomimetics are ideal compounds to leverage new diagnostic and therapeutic target opportunities. They are gaining increased interest as they offer the possibility of emulating carbohydrate activities while circumventing their drawbacks as drug candidates. One of the current challenges associated with glycomimetics is the development of innovative and efficient methods to extend their structural diversity to accelerate the discovery of therapeutically relevant molecules. While the literature focuses predominantly on the anomeric position (C1), the synthetic toolbox for the functionalization of the C2 position was largely enriched in the last decade by the use of the bench-stable 2-iodoglycals. These compounds, readily obtained in a single step from commercially available starting materials, proved to be powerful substrates in metal catalyzed cross-coupling reactions, as illustrated by the several C-C and C-heteroatom bond formation reported in the literature.[1] The objective of this project is to explore new reactivity through the development of a silylation reaction at the C2 position of 2-iodoglycals via cross-coupling reactivity. Although C–Si bond formation through metal-catalyzed reactions already exists in the literature, it has been less studied in the context of cross-coupling reactions. The introduction of a silylated function is of great interest due to the versatility offered by the multiple post-functionalization possibilities. Indeed, a silylated function constitutes a strategic intermediate allowing easy access to the corresponding hydroxylated, deuterated, halogenated, or even borylated group. A palladium-catalyzed cross-coupling methodology allowing the efficient introduction of a silyl group at the C2 position of 2-iodoglycals has been successfully developed. Various C2-modified glycosides from the glucal series, bearing different silyl groups, have been successfully obtained in good yields (up to 70%).



References :

[1] (a) Dharuman, S.; Vankar, Y.-D. *Org. Lett.* **2014**, *16*, 1172. (b) Bordessa, A.; Ferry, A.; Lubin-Germain, N. *J. Org. Chem.* **2016**, *81*, 12459-12465. (c) de Robichon, M.; Bordessa, A.; Lubin Germain, N.; Ferry, A. *J. Org. Chem.* **2019**, *84*, 3328-3339. (d) Monasson, O.; Malinowski, M.; Lubin-Germain, N.; Ferry, A. *Synthesis.* **2022**, *54*, 3414-3420. (e) Malinowski, M.; Banoun, C.; de Robichon, M.; Lubin-Germain, N.; Ferry, A. *Eur. J. Org. Chem.* **2021**, *12*, 1521-1524.

Wavelength-dependent formation of cycloreversion products from thietanes

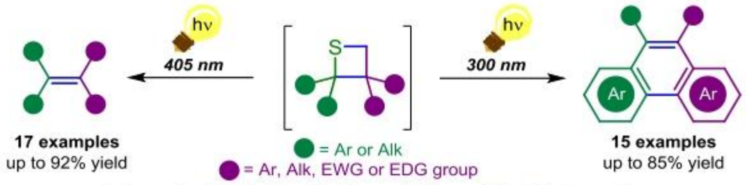
Matthias Georges[1], Gabriel Cormier[1], Manuel Pedrón[2], Antoine Laurens[2], Timothé Ferrasse[1], Ilaria Ciofini[2], Thomas Boddaert[1]

[1] ICMMO, Université Paris-Saclay, 17 Avenue des sciences, Orsay
[2]Chimie ParisTech, PSL University, CNRS, i-CLeHS, 75005 Paris, France
matthias.georges@universite-paris-saclay.fr

Because of their ubiquitous nature, alkenes have been the subject of extensive research and the olefin metathesis reaction rapidly supplanted the Wittig olefination to become the method of choice for preparing them. More recently, metal-catalyzed and photochemical carbonyl-olefin metathesis reactions, including the formation of the oxetane ring followed by the cycloreversion of the strained ring, emerged as reliable alternative strategies.[1-2] A Mallory electrocyclization reaction could also be included in the process to achieve functionalized phenanthrene derivatives.[3]

In contrast to oxetanes, fragmentation of thietanes,[4] which are their sulfur analogs, has been way less explored to date due to their synthetic access, which remained challenging until recently. Indeed, our group newly reported a domino photochemical synthesis of a wide variety of thietanes, where unstable thiocarbonyls are generated *in situ* via a Norrish-type II fragmentation of phenacyl[5] or pyrenacyl[6] sulfide precursors, which then participate in a thia-Paternò-Büchi reaction with diverse alkene partners.

Taking advantage of the straightforward access to functionalized thietanes, we investigated the cycloreversion of these four-membered ring sulfur-containing heterocycles and developed a selective general synthesis of sterically-hindered alkenes or phenanthrenes by a simple adjustment of the wavelength of irradiation of thietane substrates.



Scheme 1: Photochemical reactivities of the thietane ring

References :
[1] Ludwig, J. R.; Zimmerman, P. M.; Gianino, J. B.; Schindler, C. S. *Nature*, **2016**, 533, 374–379.
[2] Harvey, F. M.; Bochet, C. G. *Org. Biomol. Chem.* **2020**, 18, 8034–8057.
[3] Zhang, Y.; Wang, J.; Guo, Y.; Liu, S.; Shen, X. *Angew. Chem. Int. Ed.* **2024**, 136, e202315269.
[4] Gotthardt, H.; Nieberl, S. *Liebigs Ann. Chem.* **1979**, 866–869.
[5] Lapuh, M. I.; Cormier, G.; Chergui, S.; Aitken, D. J.; Boddaert, T. *Org. Lett.* **2022**, *24*, 8375–80.
[6] Cormier, G.; Allain, C.; Boddaert, T. *Angew. Chem. Int. Ed.* **2024**, 63, e202412602.

PO-34

New γ-Functionalizations of Enals via Photochemistry

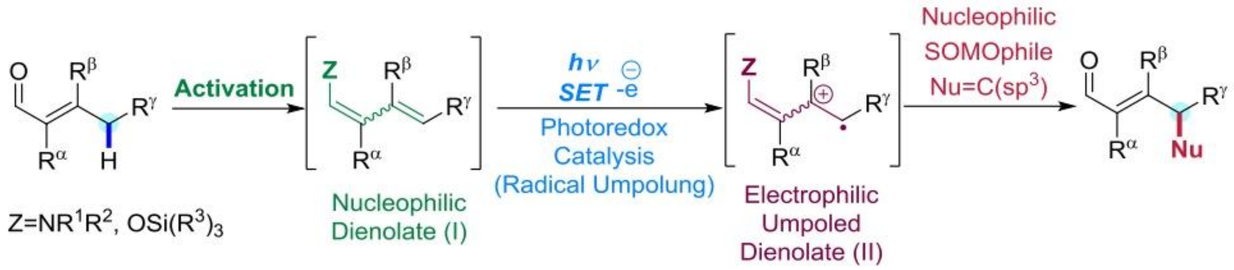
Soumaya JEMAIL,[1] Guillaume DAGOUSSET,[1]

[1] BioCIS, University of Paris-Saclay, 17 Av. des Sciences, 91190, Orsay, France
Soumaya.jemail@univeriste-paris-saclay.fr

A conventional approach to the γ-alkylation of α,β-unsaturated aldehydes, also known as enals, involves the generation of a nucleophilic dienolate derivative (I), which can react with a suitable polar electrophile, or in radical chemistry, with a carbon-centered radical.[1] However, the number of effective electrophiles remains limited, and in the radical approach, C–C bond formation at the γ-position is generally restricted to the inclusion of an activated C(sp³).

We aim to address these challenges by developing innovative regio- and stereoselective γ-alkylation methods in enals. Our central strategy involves single-electron oxidation (SET) of the nucleophilic dienolate derivative via photocatalysis, thereby reversing its polarity (radical umpolung) and generating an electrophilic radical cation (II).[2] This intermediate could react with a variety of nucleophilic SOMOphiles, enabling regioselective incorporation of inactivated C(sp^3) groups at the γ-position.

In this work, we present a new photocatalytic approach involving SET of silylated dienol ethers, an activated form of enals, to enable intramolecular γ-C–C bond formation. Initial tests with intramolecular γ-alkylations of silylated dienol ethers, provided the desired γ-alkylated product in a good yield, confirming the viability of the strategy. Yields were shown to depend on the nature of the solvent, photocatalyst, the substrate, and the hydrogen atom donor.



References:

[1] (a) Balletti, M; Marcantonio, E; Melchiorre, P; *Chem. Commun.* **2022**, *58*, 6072–6075. (b) Briand, M; Thai, L. D; Bourdreux, F; Vanthuyne, N; Moreau, X; Magnier, E; Anselmi, E; Dagousset, G. *Org. Lett*. **2022**, *24*, 9375–9380. (c) Banoun, C; Bourdreux, F; Dagousset, G. *Chem. Commun*. **2023**, *59*, 760–763.

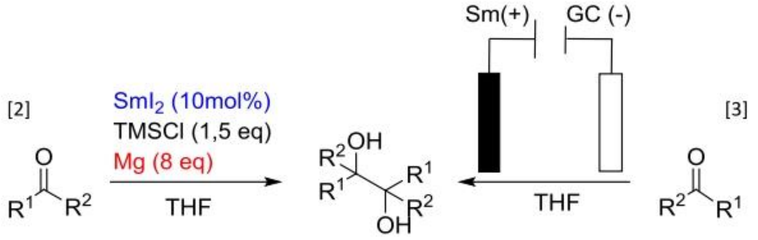
[2] (a) Seebach, D. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 239–258. (b) Chen, J.-J; Zhang, Y; Huang, H.-M. *Catal. Sci. Technol*. **2022**, *12*, 5241–5251.

Toward new methods for enantioselective samarium diiodide catalysis

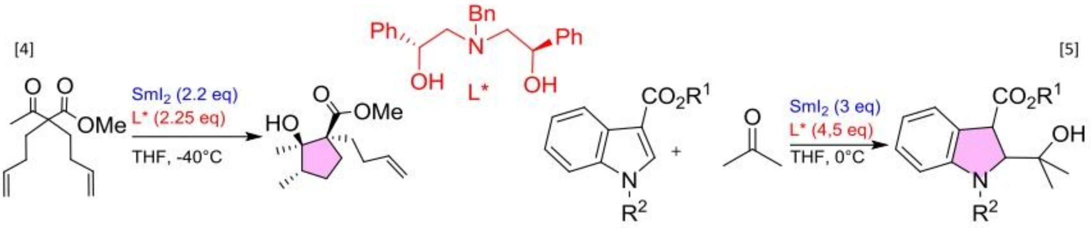
Nathan VIALAR, Emmanuelle SCHULZ, Mohamed MELLAH.

MSCO-ECM, ICMMO, 17 Avenue des Sciences 91400 Orsay
Nathan.vialar@universite-paris-saclay.fr

Samarium diiodide, coined as “Kagan’s reagent” who described its easy synthesis in 1977,[1] is a great versatile reductive reactant in organic chemistry. It is known as a highly regio-, chemo- and stereoselective single electron transfer (SET) reagent. However, this reagent faces several drawbacks notably its use in excess, which rules out any industrial adaptation. Although SmI_2 as a catalytic reagent is very attractive, it remains underdeveloped in satisfying ways. Endo and coworkers developed a Sm catalytic pinacol coupling reaction but used a great amount of magnesium as a co-reductant to regenerate the active Sm(II) species.[2] Therefore, our group has provided results in support of more environmentally friendly chemistry through the electrogeneration of the Sm^{II}/Sm^{III} pair and its use in electrocatalysis.[3]



Furthermore, the radical intermediate resulting from the SET is planar and it results in the loss of chiral information. Nevertheless, recent progress has been made in the field of enantioselective reactions involving the use of SmI_2.[4,5] These methods show great promise, but they require large quantities of chiral ligands and SmI_2 which, once again, makes them difficult and costly to apply to large-scale production.



We are therefore working on the development of samarium-promoted enantioselective electrocatalytic reactions using catalytic amounts of various chiral ligands from the bisoxazoline, binol, salen, amidinate families or from the Evans tridentate chiral aminodiol ligand.[6] To conduct this research, we will study the enantioselectivity in (sub)stoichiometric conditions, characterize different chiral samarium complexes and then develop the electrocatalytic version by modifying current, ligands and quantity of electrogenerated SmI_2 in order to perform pinacol coupling and Barbier type reactions.

References:
[1] Namy J. L., Girard P., Kagan H. B., *New J. Chem.*, **1977**, *1*, 5.
[2] Nomura R., Matsuno T., Endo T. *J. Am. Chem. Soc.*, **1996**, *118*,11666.
[3] Sun L., Sahlou, K., Mellah M. *ACS Catal*. **2013**, *3*, 2568.
[4] Kern N., Plesniak M. P., McDouall J. J. W., Procter D. J. *Nat. Chem.* **2017**, *9*, 1198.
[5] W.-Y. Zhang, U.-C. Wang, Y. Wang, C. Zheng, S.-L. You. *J. Am. Chem. Soc.* **2023,** *145*, 10314.
[6] Evans D. A., Nelson S. G., Gagne M. R., Muci A. R. *J. Am. Chem. Soc.*, **1993**, *115*, 9800.

Synthesis and RNA Binding Properties of Novel Azaspirocycles

Jiayi ZHU,[1] C. Fleurisson,[1] Y. Foricher,[2] A. Braun,[2] E. Benedetti,[1] L. Micouin[1]
[1] Université Paris Cité, CNRS, Laboratoire de Chimie et de Biochimie Pharmacologiques et Toxicologiques, F-75006 Paris, France
[2] Sanofi R&D, Integrated Drug Discovery, F-94400 Vitry-sur-Seine, France

jiayi.zhu@etu.u-paris.fr

Spirocycles, found in natural and synthetic products,[1] have recently gained attention in medicinal chemistry due to their unique 3D structure and favorable physicochemical properties, such as enhanced solubility, reduced lipophilicity, and improved metabolic stability.[2] Their rigidity also facilitates better binding element orientation, boosting efficacy and selectivity, making them valuable compounds for drug development.[3]

In this study, we present diverse synthetic pathways for the preparation of novel azaspirocycles, starting from bicyclic hydrazines functionalized at their bridgehead carbon atoms. Key reactions leading to the desired spirocyclic cores include double reductive amination, intramolecular cyclization, and N–N bond cleavage.[4]

As stated above, the resulting molecules show promise in medicinal chemistry. With increasing interest in nucleic acid targeting as a complementary strategy to protein-directed approaches for developing new bioactive compounds, we explored the applicability of the different azaspirocycles as RNA binders. As a proof of concept, select compounds demonstrated strong affinity for HIV-1 TAR RNA and effectively inhibited Tat/TAR interactions, suggesting their potential relevance for therapeutic development.[5]

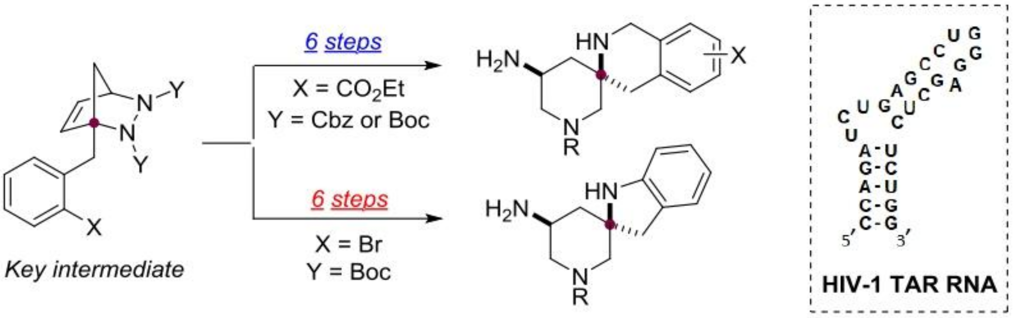


Figure 1. Access to novel azaspirocycles

References :
[1] Moss, G. P. *Pure Appl. Chem.* **1999**, *71*, 531.
[2] Benedetti, E. Micouin, L. *Expert Opin. Drug Discov.* **2024**,
[3] Talele, T. T. *J. Med. Chem.* **2020**, *63*, 13291.
[4] Fleurisson, C. Graidia, N. Foricher, Y. Benedetti, E. Micouin, L. *Org. Biomol. Chem.* **2023**, *21*, 3542.
[5] Fleurisson, C. Graidia, N. Azzouz, J. Di Giorgio, A. Gaysinski, M. Foricher, Y. Duca, M. Benedetti, E. Micouin, L. *Chem. Eur. J.* **2024**, e202403518.

PO-37

Synthesis of *N*-Trifluoroethyl and *N*-Difluoroethyl Azapeptides and Diazapeptides

Dimitra Kyrko,[1] Julia Kaffy,[1] Benoît Crousse[1,*]

[1]Université Paris-Saclay, CNRS, BioCIS UMR 8076, Orsay 91400, France; CY Cergy Paris Université, CNRS, BioCIS UMR 8076, Cergy-Pontoise 95000, France;
benoit.crousse@universite-paris-saclay.fr

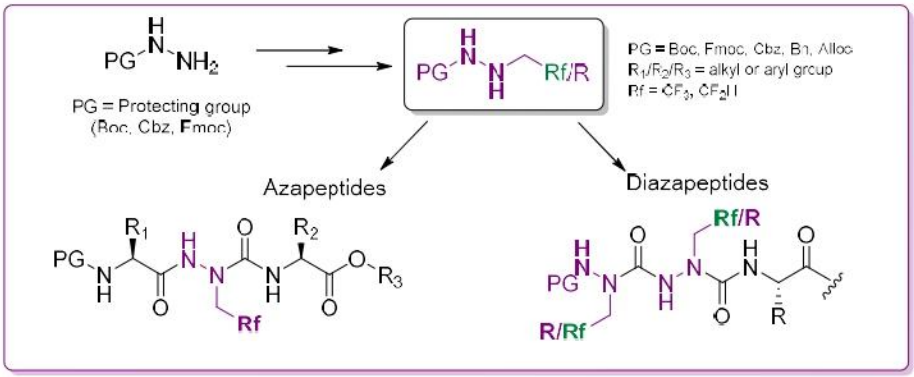
Fluorine is widely recognized for its ability to modulate the physicochemical and therapeutic properties of bioactive compounds, while also providing valuable ^{19}F NMR probes.

Accordingly, fluorinated peptidomimetics are particularly attractive in medicinal chemistry since peptide-based drugs combine high efficacy, potency, and selectivity. Yet their clinical application is often limited by rapid degradation, low membrane permeability, and poor solubility.

These limitations can be addressed through the synthesis of peptidomimetics such as azapeptides and diazapeptides, in which one or two α-carbons are replaced by nitrogen atoms, stabilizing specific secondary structures while preserving biological activity and proteolytic stability.[1-3]

Notably, the synthesis of $RfCH_2N$-substituted aza- and diaza-peptides remains unexplored.

Here we report the synthesis of novel peptidomimetics incorporating CF_3CH_2NH- and CF_2HCH_2NH- groups. Our approach relies on the coupling of fluorinated hydrazines with amino acids or hydrazines to access functionalized fluorinated scaffolds. The notably low nucleophilicity of the nitrogen bearing the $RfCH_2$-chain required optimization of the coupling conditions. The resulting motifs were further extended in solution or Solid Phase Peptide Synthesis (SPPS) using different synthetic approaches to obtain the desired fluorinated peptidomimetics with alkyl and aryl side chains (Scheme 1). NMR and X-ray crystallography analyses were performed to evaluate the influence of fluorinated groups on peptidomimetic conformation.



Scheme 1. Synthesis of CF_3CH_2NH- and CF_2HCH_2NH-substituted azapeptides and diazapeptides

References :

[1] Tarchoun, K., Yousef, M. & Bánóczi, Z. Azapeptides as an Efficient Tool to Improve the Activity of Biologically Effective Peptides. *Future Pharmacology*, **2022**, 2, 293–305.

[2] Shi, C. *et al.* Proteolytically Stable Diaza-Peptide Foldamers Mimic Helical Hot Spots of Protein Protein Interactions and Act as Natural Chaperones. *J. Med. Chem.*, **2023**, 66, 12005–12017.

[3] Kyrko, D., Cao, T., Retailleau, P., Kaffy, J. & Crousse, B. Access to *N* -Fluorinated Azapeptides and Azapeptoids as Peptidomimetic Scaffolds. *ACS Org. Inorg. Au*; **2025**, 5, 531–538.

Exploring the RNA-Binding Potential of Three-Dimensional Cyanines Derived From [2.2]Paracyclophane: A Structure–Property Relationship

Rongyu SUN, Cristian SIRETANU, Georgina ILIESKA, Simon FELDER,
Erica BENEDETTI* and Laurent MICOUIN*

Laboratoire de Chimie et de Biochimie Pharmacologiques et Toxicologiques, Université Paris Cité, CNRS, F-75006 Paris, France
Rongyu.sun@u-paris.fr

Targeting RNA with small molecules is considered the next frontier in drug discovery. Developing compounds that can bind to RNA structural motifs of low complexity with high affinity and selectivity could significantly expand the range of potential therapeutic targets.

Our group is currently investigating the potential of [2.2]paracyclophane (pCp)[1] as a building block for designing novel RNA ligands to enhance selectivity in nucleic acid binding.

In a previous study,[2] a pCp-based cyanine was synthesized using a scaffold-hopping approach inspired by established aromatic nucleic acid binders (Figure 1).[3] Shifting from a "flat" to a 3D molecular architecture led to the development of a fluorogenic ligand capable of differentiating between various nucleic acids (DNA, rRNA, tRNA). Notably, this cyanine derivative exhibited high selectivity for an RNA octa-loop over smaller loop sizes.

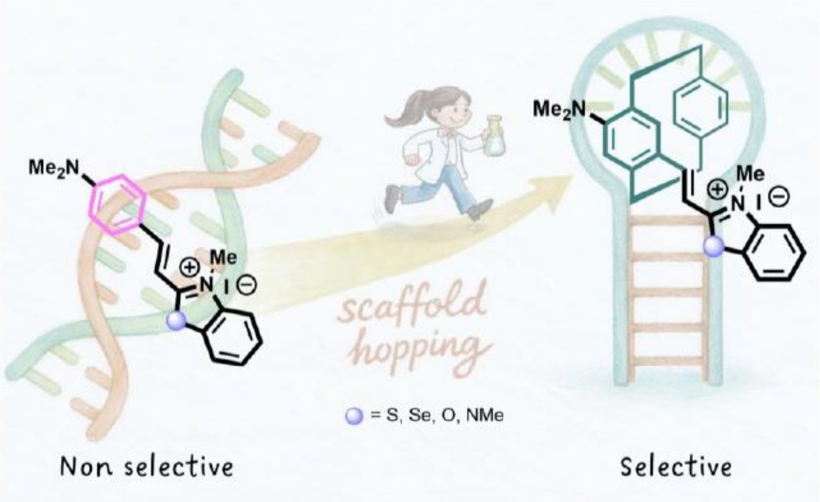


Figure 1: Novel 3D RNA binders

Building on this approach, we synthesized a series of cyanine dyes derived from pCp to establish structure–property relationships, offering valuable insights for designing more selective and effective RNA-targeting ligands. This study demonstrates the strength of the scaffold-hopping strategy in creating selective RNA binders by exploring new chemical spaces. It also emphasizes the potential of non-coplanar aromatic moieties as key motifs for targeting RNA secondary structures with improved selectivity.[4]

---

[1] Broadley, J. S; Robertson, J. M; *Nature* **1949**, *164*, 915.
[2] Felder, S; Sagné, C; Benedetti, E; Micouin, L; *ACS Chem. Biol.* **2022**, *17*, 3069.
[3] Sun, H; Tawa, G; Wallqvist, A; *Drug Discovery Today* **2012**, *17*, 310.
[4] Sun, R; Siretanu, C; Ilieska, G; Felder, S; Benedetti, E; Micouin, L; *ChemBioChem* **2026**, *27*, e202500835.

Merging organo- and organometallic catalysts for sequential asymmetric multicatalysis

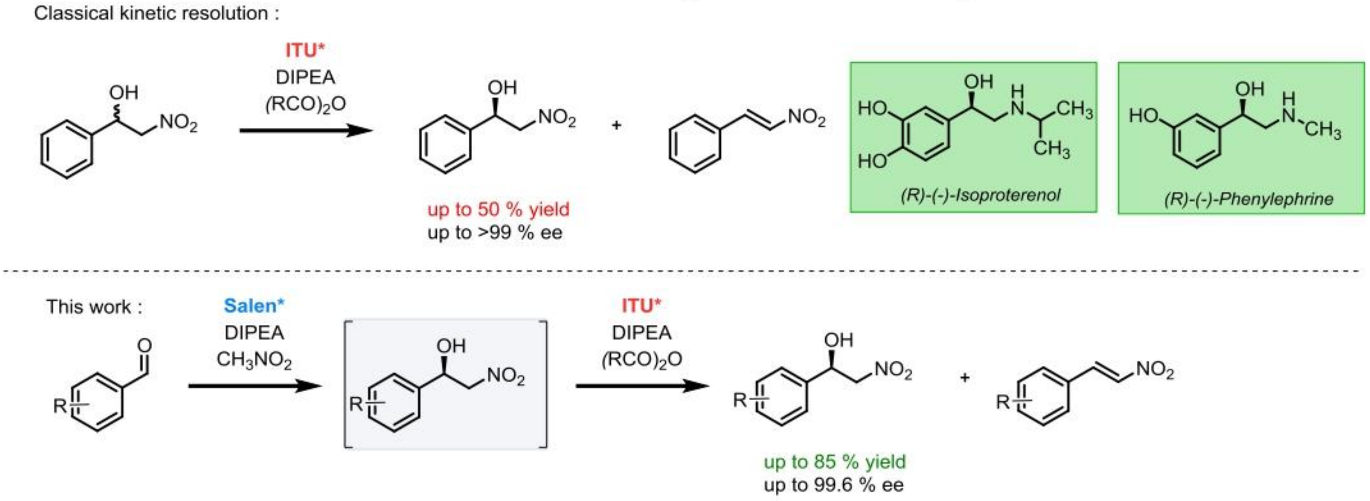
Veronika MYRONOVA,[1] Lea IBOS,[2] Mohamed MELLAH,[1] David KREHER,[2] Olivier DAVID,[2] Emmanuelle SCHULZ[1]

[1] Université Paris-Saclay, Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO)UMR 8182, ECM,
17 Avenue des Sciences, 91400 Orsay, France
[2] Institut Lavoisier de Versailles, SORG, 45 avenue des États-Unis, 78035 Versailles, France
veronika.myronova@universite-paris-saclay.fr

Asymmetric catalysis constitutes a powerful strategy for the synthesis of enantioenriched functionalized molecules. In recent years, asymmetric multicatalysis has emerged as an efficient approach for achieving highly selective transformations in one-pot processes, thereby enabling rapid access to molecular complexity. [1] Nevertheless, controlling catalyst cooperativity while minimizing mutual inhibition remains a significant challenge.[2]

Herein, we report a sequential asymmetric multicatalytic protocol that combines a metal–salen-catalyzed Henry reaction with an isothiourea-mediated acylative kinetic resolution (see Scheme). Building on the foundational developments in metal–salen chemistry first explored by Jacobsen[3] and the isothiourea-based kinetic resolution of secondary alcohols developed by Birman[4], we envisaged that the integration of these catalytic systems in a sequential manner would enhance both reactivity and selectivity. The nitro-aldol reaction of aryl aldehydes affords β-nitro alcohols, which are subsequently subjected to kinetic resolution to improve their enantiomeric purity. This approach provides access to valuable β-nitro alcohol derivatives in high yields and excellent enantiomeric excess.

Given the broad utility of β-hydroxy nitroalkanes as versatile intermediates in the synthesis of biologically active compounds, this work demonstrates the potential of sequential multicatalysis as an effective and selective alternative to conventional asymmetric methodologies.



References :

[1] J. Jao, C. Tan, Z. Li, Y. Liu, X. Han, Y. Cui. Design and Assembly of Chiral Coordination Cages for Asymmetric Sequential Reactions, *J. Am. Chem. Soc.* **2018**, *140*, 2251-2259.

[2] Y.-C. Yuan, M. Mellah, E. Schulz, O. R. P. David. Making Chiral Salen Complexes Work with Organocatalysts, *Chem. Rev.* **2022**, *122*, 8841-8883.

[3] a) B. D. Brandes, E. N. Jacobsen, *Tetrahedron: Asymm*. **1997**, *8*, 3927-3933.

[4] a) V. B. Birman, E. W. Uffman, H. Jiang, X. Li, C. J. Kibane. 2,3-Dihydroimidazo[1,2-a]pyridines: A New Class of Enantioselective Acyl Transfer Catalysts and Their Use in Kinetic Resolution of Alcohols, *J. Am. Chem. Soc.* **2004**, *126*, 12226–12227.

PO-40

Synthesis of non-natural bi- poly and heteroaryl amino-acids derivatives via Nickel-catalyzed Suzuki-Miyaura coupling

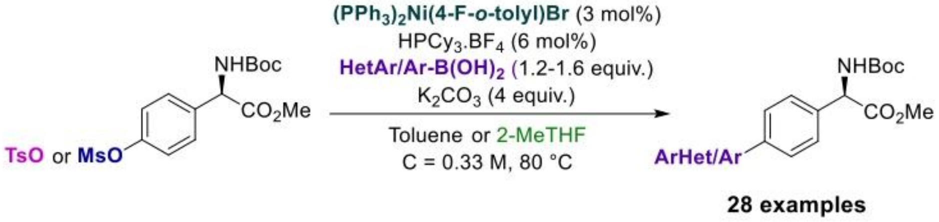
Jiaxiao Yang, Mamoudou Doucoure, Gustave Vilard, Ying Xu, Joëlle Pérard, Marie-Isabelle Lannou

Laboratoire CiTCoM, UMR 8038, Equipe PNAS, Faculté de Pharmacie,
Université de Paris Cité, 4 avenue de l'Observatoire 75006 Paris, France
ying.xu@etu.u-paris.fr

Enantiomerically active non-natural amino-acids derivatives are useful tools for the elaboration of peptidomimetics or as intermediates for the synthesis of pharmaceuticals. In this field, derivatives of phenyl glycine were recently proved to be potent dual inhibitors of Palsmodium Falcoparum M1 and M17 aminopeptidases[1] or a-mannosidase inhibitors.[2]

Despite interesting features, there are only a few examples of compounds that have been synthesized through Suzuki-Miyaura cross-coupling, classically using palladium catalysis and a substrate bearing a trifluoromethanesulfonyloxy group. Moreover, conducting this coupling in an enantioselective manner is very challenging due to the possible epimerization at the carbon a to the amino ester. Finally, even scarcer examples of this coupling involve nickel catalysts, and in this latter case, the catalytic charge remains high and the conditions require the use of a glovebox.[3]

Here we describe our methodology for the nickel catalyzed Suzuki-Miyaura cross-coupling of methyl 2-((tert-butoxycarbonyl)amino)-2-(4-((methylsulfonyl)oxy)phenyl)acetate for an easy access to enantiomerically active biaryl/polyaryl or heteroaryl derivatives using an air-stable nickel catalyst with a low catalyst loading.



The reaction is scalable up to 5 mmols and allows access to 28 unnatural amino acids with a good functional group tolerance and good enantiomeric excesses in most cases (25 examples > 81% ee). [4]

References:

[1] N. Drinkwater, N. B. Vinh c, 1, S. N. Mistry, R. S. Bamert, C. Ruggeri, J. P. Holleran, S.Loganathan, A. Paiardini, S. A.Charman, A. K. Powell, V. M. Avery, S. McGowan, P. J. Scammells, *Eur. J. Med. Chem*. **2016**, *110*, 43-64.
[2] C. Bello, Mi. Cea, G. Dal Bello, A. Garuti, I. Rocco, G. Cirmena, E. Moran, A. Nahimana, M. A. Duchosal, F. Fruscione, P. Pronzato, F. Grossi, F. Patrone, A. Ballestrero, M. Dupuis, B. Sordat, A. Nencioni, *Bioorg. Med. Chem*. **2010**, *18*, 3320-3334.
[3] H. Ueda, I. Kurimoto (**2003**), EP 1 481 967 A1, Process for the preparation of biaryl compounds EP Patent WO 2003/074478
[4] J. Yang, M. Doucoure, Y. Charifi, G. Villard, Y. Xu, J. Perard-Viret, M.-I. Lannou *J. Org. Chem.* 2025, 90, 30, 10927-10933.

PO-41

Impact of metal impurities on [^{18}F]fluoride metal capture for radiolabeling purpose: case study on a Gallium chelate

Noé LOCATELLI,[1] Lydia OUADFEL,[1] Axia MARLIN,[2] Benoit HOSTEN,[2] Marc PORT,[1] Fabienne DIOURY*[1]

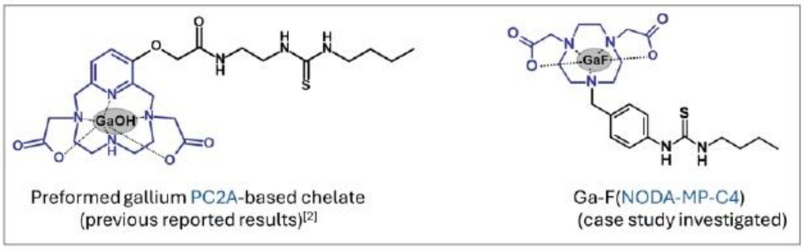
[1] Conservatoire national des arts et métiers, Laboratoire de Génomique Bioinformatique et Chimie Moléculaire (GBCM)
EA7528, Bâtiment Synergie, 8-10 rue de la Procession, 93210 Saint-Denis
[2] Hôpital Saint Louis, Unité Claude Kellershohn (UCK), Université Paris Cité INSERM UMR-S 1144, 1 Avenue Claude Vellefaux
75010 Paris
fabienne.dioury@lecnam.net

Positron Emission Tomography (PET) has emerged as a revolutionary medical imaging technique, to help diagnose and guide the treatment of cancer, as well as cardiac and neurological diseases. PET visualizes physiological and pathological processes by tracking a tracer labeled with a positron (β^+) emission nuclide. Among these, [^{18}F]fluoride is the most widely used nuclide for clinic applications due to its unique physical properties and wide availability (medical cyclotron production).

Conventional radiofluorination methods involve the formation of a C-F bond on the organic backbone of the tracer, which is almost the result of a nucleophilic substitution. This approach requires harsh reaction conditions, which limit its applicability to sensitive tracers such as biomolecules used as specific targeting agents.

To address the need for a milder ^{18}F-labeling method, strategies based on the capture of [^{18}F]fluoride by group13 metal (aluminum, gallium, indium) chelates have emerged as promising alternatives.[1] Our group recently reported the first chemical system based on a preformed gallium PC2A-based chelate (*Figure*) enabling radiofluorination by {Ga^{18}F} in water, at room temperature, in 86 % *radiochemical yield* (RCY).[2] However, the studies we have conducted using this system have occasionally revealed a lack of reproducibility in the RCY values determined by RP-HPLC. Some experimental observations have led us to examine the potential impact of metal contamination during the quality control process, especially since HPLC-column manufacturers had reported the effect of highly electronegative metal ions, such as trivalent aluminum, on ion-exchange capacity, leading to irreversible adsorption of certain analytes (Lewis bases, chelating agents).[3]

To investigate this phenomenon, the Ga-F(NODA-MP-C4) case study (*Figure*) was considered. We will discuss the impact of certain metal contaminants, such as the aluminum also used in this radiolabeling strategy that involves chelate chemistry and the coordination of fluoride anions to form a ternary species.



Preformed gallium PC2A-based chelate (previous reported results)[2]

Ga-F(NODA-MP-C4) (case study investigated)

Figure: Ternary gallium chelates discussed herein

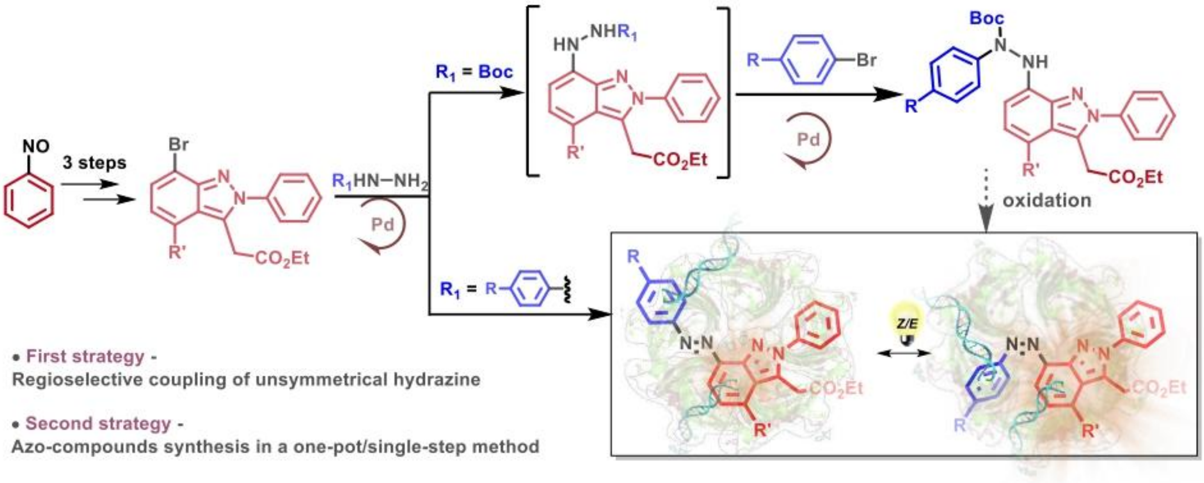
[1] Chansaenpak, K and al. *Chem. Rev.* **2016**, *45*, 954-971.
[2] Dioury, F and al. *Chem. Eur. J.* **2024**, *30*, e202403358.
[3] Ory, D et al. *J. Pharm. Biomed. Anal.* **2015**, *111*, 209-214.

One-Pot Synthetic Method to Access Photoswitchable and Fluorescent Azoheteroarenes

Xingyu Wang,[1] Sandrine Delarue-Cochin,[1] and Delphine Joseph[1]
[1] Université Paris-Saclay, CNRS, BioCIS, 91 400 Orsay, France
xingyu.wang@universite-paris-saclay.fr

As a part of a mechanistic study of pentameric ligand-gated ionic channels [1], we designed a model off-on fluorescent probe incorporating both a fluorescent indazole scaffold and photoswitchable azobenzene moiety. This compound exhibits promising photophysical behavior including reversible *E*↔Z photoisomerization at 406 nm, and fluorescence enhancement in the *Z*-isomer. To improve the photophysical properties of this lead compound and design new functional molecular switches with tailored optical and switching properties, we aim to develop a general, convergent, one-pot method for synthesizing dissymmetric azoheteroarenes. As traditional synthetic routes suffer from limited substituent compatibility and diversity [2], we therefore explored a sequential Pd-catalyzed Buchwald-Hartwig coupling strategy.

Here we report successful optimization of the first for the first coupling step, leading to 7-hydrazino-indazoles in excellent yields, and unexpected results obtained in the second coupling step revealing a competing oxidative pathway, yielding quinone-imine by-products. These findings highlight new synthetic challenges, including the stabilization of key intermediates and fine-tuning of catalytic conditions. Surprisingly, our results also reveal a novel one-step transformation from arylhydrazines to azo compounds, offering a potentially simplified route to access azoheteroarenes.



References : (Calibri, 10, flush left)

[1] Sauguet, L.; Shahsavar, A.; Poitevin, F.; Huon, C.; Menny, A.; Nemecz, À.; Haouz, A.; Changeux, J.-P.; Corringer, P.-J.; Delarue, M. Crystal structures of a pentameric ligand-gated ion channel provide a mechanism for activation. *Proc. Natl. Acad. Sci.* **2014**, *111*, 966-971.

[2] Crespi, S., Simeth, N. A. & König, B. Heteroaryl azo dyes as molecular photoswitches. *Nat. Rev. Chem.* **2019**, *3*, 133-146.

Cooperative Dual Catalysis for Asymmetric Ring Opening of Strained Cycles

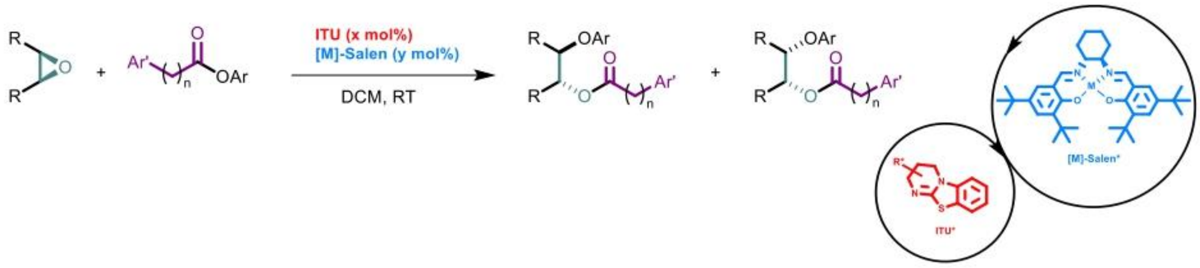
Sarah BOUERY,[1] Léa IBOS,[1] Mohamed MELLAH,[1] David KREHER,[2] Olivier DAVID,[2] Emmanuelle SCHULZ[1]

[1]ECM, MSCO-2, Institut de Chimie Moléculaire et des Matériaux d'Orsay, 17 Av. des Sciences, 91190 Orsay, France
[2] SORG, Institut Lavoisier de Versailles, 45 Av. des Etats Unis, 78000 Versailles, France
sara.el-bouery@universite-paris-saclay.fr

The fine chemicals sector dedicated to health applications increasingly requires new and sustainable methods to synthesize enantioenriched, functionalized molecules. Although asymmetric catalysis has already provided effective solutions, the growing demand for molecular complexity poses new challenges. In this context, the development of highly stereoselective reactions involving multiple catalysts promoting the same transformation, referred to dual asymmetric multicatalysis, emerges as a promising strategy.

A number of new organic transformations have been developed through cooperative/synergistic organo/organometallic catalysis.[1] The discovery of efficient isothiourea/transition metal (ITU/TM) cooperative catalytic systems to access chiral molecules continues to attract the attention of organic chemists, and many achievements have been accomplished. [2],[3],[4],[5]

Herein we propose cooperative multicatalysis for the opening of strained cycles, particularly epoxides, in a reaction with an activated ester. An interesting reactivity arises from the cooperative use of isothiourea and [M]-Salen complexes to promote the ring opening of epoxides, as described in the reaction below.



Ongoing efforts are aimed at optimizing reaction conditions, varying the scope of substrates, analyzing different double catalytic systems with particular reference to match and mismatch effects, and selecting the best conditions for controlling diastereo- and enantioselectivity to enable a mechanism to be proposed.

[1] N. T. Patil, V. S. Shinde, B. Gajula, *Org. Biomol. Chem.* **2012**, *10*, 211
[2] J. A. Kalow, A. G. Doyle, *J. Am. Chem. Soc.* **2010**, *132*, 3268-3269
[3] Schwarz, K. J., Amos, J. L., Klein, J. C., Do, D. T., Snaddon, T. N. *J. Am. Chem. Soc.* **2016**, *138*, 5214–5217
[4] Q. Wang, T. Fan, J. Song, *Org. Lett.* **2023**, *25*, 1246-1251
[5] T. Fan, Z. Shi, Q.-W. Gong, J. Song, L.-J. Gong, *Org. Lett.* **2024**, *26*, 1421-1425

Toward the Total Synthesis of *Daphniphyllum* Alkaloids: A fragment-based approach

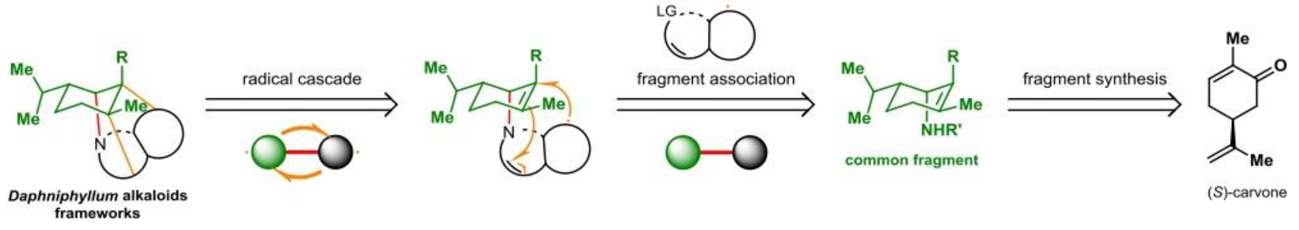
Maxime VIGOUREUX,[1] Zakaria MEFTAH[1] and Bastien NAY [2]

[1] Laboratoire de Synthèse Organique (LSO), Ecole Polytechnique, CNRS, Rte de Saclay, 91120 Palaiseau
maxime.vigoureux@polytechnique.edu

The *Daphniphyllum* alkaloids are a large and structurally complex family of natural products, with more than 300 compounds. They became a classical target for synthetic chemists due to their structural complexity and their biological activities, including anticancer and anti-HIV properties.[1] Since the pioneer biomimetic work of Heathcock in 1986, more than forty total syntheses, as well as many studies toward their skeletons, have been reported.[2]

In this project, we are developing a unified fragment-based synthesis strategy that could be applied to one-third of these alkaloids, covering nine subfamilies, using a key radical cascade step. The strategy is based on the association of a common fragment, shared among the subfamilies, with a second part specific to each subfamily. The association will be followed by a radical cascade to build the molecular complexity.[3]

The common fragment has been designed and synthesized. It serves as a platform to access different *Daphniphyllum* frameworks. A preliminary study on a model system was carried out to better understand the key radical cyclization. Based on these results, the structure of the common fragment and the reaction conditions were adapted, allowing us to achieve the first radical cyclization. Current work is focused on exploring different skeletons through various radical cyclizations and on reaching the alkaloids. The synthesis of the common fragment, the radical study on models, and the key radical cyclization will be discussed in this presentation.



References :

[1] S. Hanessian et al., *Chem. Rev.*, **2017**, *117*, 4104–4146 ; Zhong et al., *The Alkaloids*, **2021**, *85*, 113-176.

[2] C. H. Heathcock et al., *J. Am. Chem. Soc.* **1986**, *108*, 5650-5651 ; C. Heathcock et al., *Science*, **1990**, *248*, 1532–1534 ; K. Namba et al., *Angew. Chem.*, **2025**, *137*, e202517671 ; A. Li et al., *J. Am. Chem. Soc.* **2025**, *147*, 31, 27137-27142 ; T. Sato et al., *Angew. Chem. Int. Ed.*, **2025**, 64, e202508062 ; X. She et al., *Org. Lett.* **2025**, *27*, 27, 7423-7427 ; D. Dixon et al., *Org. Lett.* **2025**, *27*, 11485–11490.

[3] S. Herzon et al, *Angew. Chem. Int. Ed.*, **2021**, *60*, 1116–1150 ; K.C. Nicolaou et al., *Angew. Chem. Int. Ed.* **2006**, *45*, 7134 – 7186 ; T. J. Maimone et al., *Nat. Prod. Rep.*, **2018**, *35*, 174 ; P. S. Baran et al., *Angew. Chem. Novit*, **2026**, *2*, 1, e70017.

PO-45

WASTE2H2: Clean Hydrogen and Low-Carbon Chemicals from Plastic Waste via Catalytic Deconstruction Enabled by Novel Ionic Liquid Systems and Microwave-Assisted Heating

Romain TORLOTIN[1], Remi NGUYEN[1], Christophe LEN[1]

[1] Chimie ParisTech, PSL Research University, CNRS, Institute of Chemistry for Life and Health Sciences
romain.torlotin@chimieparistech.psl.eu

The accumulation of plastic waste constitutes one of the most urgent environmental challenges of the modern era. Global plastic production exceeds 300 million tons annually, yet less than 9% is effectively recycled, according to UNEP. Approximately 12% is incinerated, while the remaining 79% accumulates in landfills or disperses into natural ecosystems, resulting in pervasive and persistent environmental contamination. Although various chemical recycling strategies have been developed to convert plastic waste into value-added feedstocks or energy carriers, most approaches remain economically uncompetitive at industrial scale. Currently, the decarbonization of energy-intensive and hard-to-abate sectors has become a critical priority. Hydrogen (H_2) is widely regarded as a key energy vector for enabling this transition; however, its large-scale deployment depends on the development of production pathways that are both economically viable and genuinely low carbon.

Microwave (MW) irradiation has emerged as a promising alternative to conventional heating in synthetic chemistry, offering rapid and volumetric energy transfer, enhanced reaction rates, and improved selectivity. In parallel, ionic liquid (IL)-based catalytic systems have attracted significant attention owing to their tunable physicochemical properties, high thermal stability, and potential for efficient recovery and reuse. Despite these advantages, the synergistic integration of MW irradiation with IL-based catalysis remains largely unexplored for plastic waste valorization.

In this context, the WASTE2H2 project introduces an integrated strategy that combines IL-based catalytic systems with MW irradiation to enable the selective, single-step deconstruction of plastic waste into high-purity hydrogen and solid carbon. Operating under comparatively mild conditions and driven by renewable electricity, this approach circumvents the complexity of multistep processes while producing solid carbon as the sole co-product, which is readily recoverable and potentially valorisable. The IL-based catalytic system is designed for extended operational lifetimes with straightforward recycling, while MW irradiation contributes to improves energy efficiency relative to conventional thermal methods. Collectively, these attributes position WASTE2H2 as a promising and potentially scalable pathway for simultaneous plastic waste mitigation and low-carbon hydrogen production.

This project has received funding from the European Union's Horizon Europe research and innovation programme through the European Innovation Council under the grant agreement No. 101130249.

European Innovation Council
Funded by the European Union

PO-46

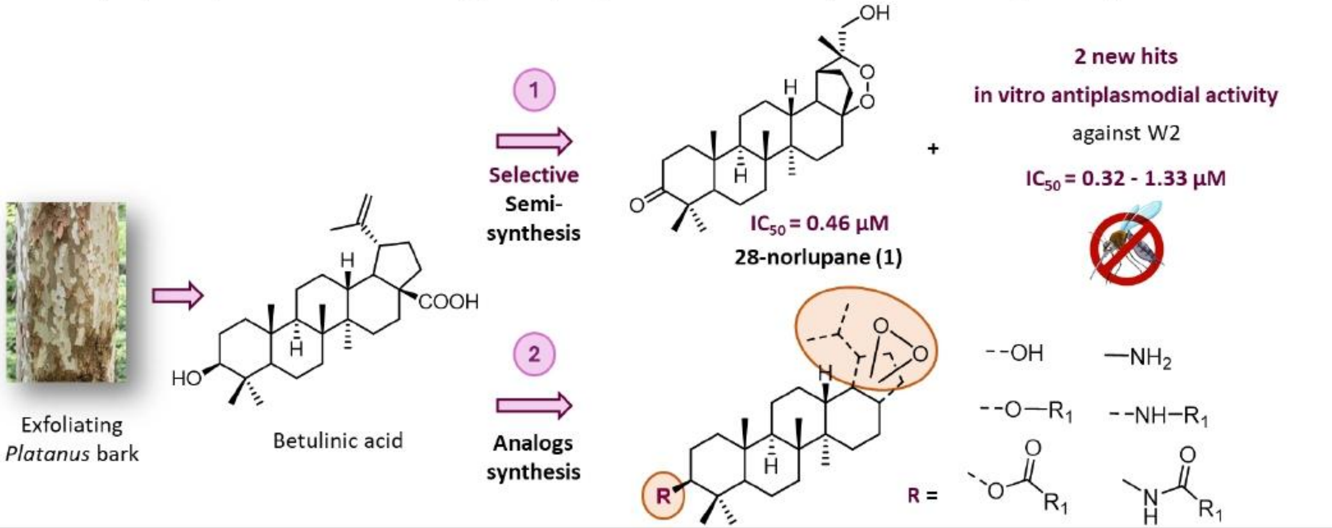
28-norlupane and its library: promising antiplasmodial compounds accessible from betulinic acid *via* selective semi-synthesis

Linh PHAN,[1] Chouaha BOUZIDI,[1] Claire CUYAMENDOUS,[1] Xavier CACHET[1]

[1] Cibles Thérapeutiques et conception de médicaments (CiTCoM), UMR CNRS 8038, Université Paris Cité, Faculté de Pharmacie, Paris, France
xavier.cachet@u-paris.fr

Malaria is one of the most dangerous and widespread tropical diseases in the world, particularly in developing countries. It is caused by protozoan parasites of the genus *Plasmodium*, and more specifically by *P. falciparum*. According to the WHO, in 2024, it caused approximately 610,000 deaths worldwide, with an estimated 282 million cases across 80 countries.[1] However, several challenges have emerged in relation to prevention and treatment, such as resistance, and toxicity.[2] The focus is therefore on developing new, more effective and non-toxic treatments derived from natural products.

Previous work in our laboratory has shown that a new "hit" compound, 28-norlupane endoperoxide **1**, originally isolated from *Dipterocarpus costatus*, exhibits good anti-plasmodial activity against *Plasmodium* sp. with lower toxicity in normal cells.[3] This compound **1** was successfully synthesized by a semi-synthetic route from betulinic acid, which was isolated from the exfoliating bark of *Platanus acerifolia*, a readily available source in the Paris region. However, this non-selective endoperoxidation approach afforded **1** in only 1.3% yield, along with a small library of other endoperoxide-oxidized analogs.[4] Two of these displays promising anti-plasmodial activity. The primary objective of this work is therefore to enhance the yield of **1** *via* a more selective pathway and to synthesize the? two new analogs with promising antiplasmodial activity. Secondly, we aim to expand our knowledge of structure-activity relationships (SARs) in the series through the preparation of a compound **1** analog library.



References:
[1] World malaria report 2025. Geneva: World Health Organization; 2025. Licence: CC BY-NC-SA 3.0 IGO.
[2] Okitwi, M.; *Nat. Comm.* **2025**, *16*, 7353.
[3] Malai, S.; *Phyto. Lett.* **2024**, *63*, 31-36.
[4] Zhonglian, M.; *J. Nat. Prod.* **2026**, *89*, 410-420.

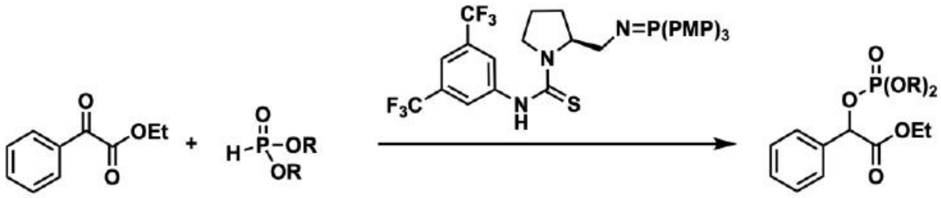
Chiral Bifunctional Iminophosphorane-Thiourea as Organocatalysts for Enantioselective Phospsha-Brook Rearrangement/Protonation Reactions

Emeric Garzi-Hiebel, Julie Kong, Martial Toffano, Chloée Bournaud and Giang Vo-Thanh

Université Paris-Saclay, Institut de Chimie Moléculaire et des Matériaux d'Orsay, 17 Avenue des sciences 91400 Orsay
emeric.garzi-hiebel@universite-paris-saclay.fr

Organocatalysis is a metal-free synthetic methodology, recognized as a highly attractive area in modern organic synthesis and green chemistry. It prevents metal pollution and relies on small organic molecules, often derived from the "chiral pool", which are relatively easy to access. The applications of organocatalysts have enabled numerous efficient enantioselective reactions, giving access to new synthetic routes for both natural and non-natural products.[1] Among them, chiral bifunctional organocatalysts featuring a hydrogen-bond donor function represent a particularly compelling class of catalysts.[2] They allow for better asymmetric induction by activating simultaneously nucleophiles and electrophiles while keeping the chiral scaffolds in close proximity to the transition state.

In this communication, we focus on bifunctional organocatalysts bearing an iminophosphorane and a thiourea moiety, that function as a Brønsted base and a hydrogen-bond donor, respectively.[3] Additionally, L-proline structure is used as a rigid chiral source for asymmetric induction. These organocatalysts were applied to the asymmetric phospha-Brook rearrangement, followed by a protonation step to afford tertiary phosphate derivatives in excellent yields (up to 98%) with promising enantioselectivity (up to 60%).



PMP = *p*-methoxyphenyl

yields up to 98%
ee up to 60%

The results of these studies will be presented and discussed in this communication.

References :
[1] Han, B; He, X; Liu, Y; He, G; Peng, C; Li, J; *Chem. Soc. Rev.* **2021**, *50.*, 1522.
[2] Formica, M; Rozsar, D; Su, G; Farley, A. J. M; Dixon, D. J; *Acc. Chem. Res.* **2020**, *53.*, 2235-2247.
[3] Kong, J; Lacroix, C; Bournaud, C; Yamashita, Y; Kobayashi, S; Vo-Thanh, G; *Adv. Synth. Catal.* **2024**, *366.*, 1101.

Development of chemical tools based on modified Arg-tRNA to study arginine cyclodipeptide synthase (RCDPS).

Lily LE THIESSE,[1] Emelyne GIRAUD,[2] Muriel GONDRY,[2] Laura IANNAZZO,[1] Mélanie ETHEVE-QUELQUEJEU[1]

[1] LCBPT, UPC, 45 rue des Saints-Pères 75006 Paris
[2] I2BC, CNRS, 12 Rue de la Croix Audierne, 91190 Gif-sur-Yvette
lily.le-thiesse@u-pariscite.fr

Aminoacyl-tRNA (aa-tRNA) are biomolecules containing a tRNA linked to an amino acid at the 2' or 3' position of the terminal ribose *via* an ester bond. They are crucial not only for ribosomal protein synthesis but also for non-ribosomal peptide synthesis (NRPS) including process for cyclopeptide synthesis. Recently, new core enzymes termed RCDPSs (Arginine cyclodipeptide synthases) have been identified. They catalyze the formation of cyclodipeptides using arginine-tRNA as substrates and produce highly diverse products such as 2,5-diketopiperazines notable for their biological activities.[1]

To understand the molecular basis of RCDPS specificity, it is crucial to have a relevant set of diverse arginine-tRNA analogs, as structural experiments with aa-tRNAs face two major challenges: 1) one concerns the intrinsic flexibility of tRNAs, which can hinder crystallization or affect crystal quality. To address this point, the use of aminoacylated analogs with shortened tRNAs, mimicking only their acceptor arms (known as microhelices) seems suitable; 2) the second challenge involves the intrinsic stability of aa-tRNAs, as the ester bond linking the aminoacyl group to the tRNA is highly susceptible to hydrolysis. This can be bypass by the replacement of the unstable ester bond with a triazole linkage.[2]
In this context, the work presented here will describe a chemoenzymatic approach to access stable aa-microhelices in which the ester bond will be replaced by a triazole linkage, thus making crystallographic studies possible. A second family of aa-tRNAs will be also presented using deoxy analogs to determine which regioisomer is preferred by the enzyme (Fig. 1).

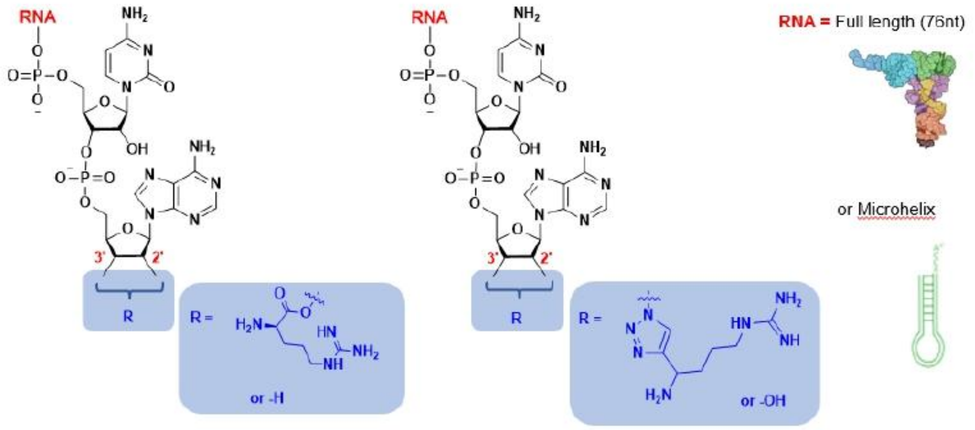


Figure 1: Targets Arg-tRNA molecules.

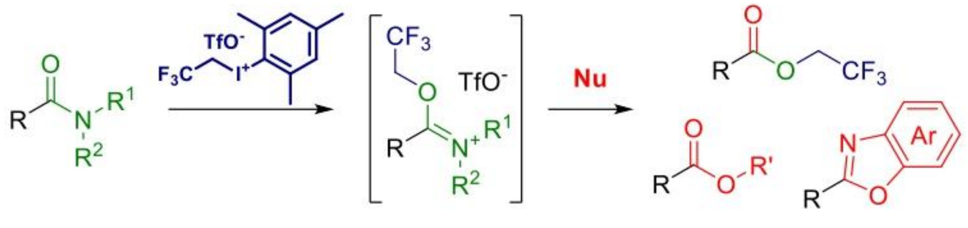
References:
[1] Canu, N; Moutiez, M; Belin, P; Gondry, M; *Nat. Prod. Rep.* **2020**, *37*, 312-321.
[2] Afandizada, Y; Abeywansha, T; Guerineau, V ; Zhang, Y ; Sargueil, B ; Ponchon, L ; Iannazzo, L ; Etheve-Quelquejeu, M; *Methods* **2024**, *229*, 94-107.

Electrophilic Amide Activation under Mild Conditions Using 2,2,2-Trifluoroethyl Iodonium Salt: Access to Esters and Benzoxazoles

ZHONG Tiancheng,[1] Amistadi-Revol Hugo,[1] Tremblais Julie [1] and Prévost Sébastien [1]

[1] Laboratoire de Synthèse Organique (LSO – UMR 7652), CNRS, Ecole Polytechnique, ENSTA, Institut Polytechnique de Paris,
828 boulevard des Maréchaux, 91120 Palaiseau (France)
tiancheng.zhong@ensta.fr

Amides are among the most common chemical moieties found in Nature, notably in amino acids.[1] Compared to other carbonyl groups, amides are generally more stable due to resonance stabilization, making their activation under mild conditions a significant synthetic challenge.[2] Recent efforts have focused on developing efficient methods for the transformation of amides, including transition-metal-catalyzed C–N activation, nucleophilic activation and electrophilic activation strategies.[3] In this study, we developed a novel, metal-free method for amide activation using 2,2,2-trifluoroethyl(mesityl)iodonium triflate as an electrophilic reagent.[4] Upon activation, aqueous acidic treatment enabled the formation of fluoroesters *via* hydrolysis of the imidate intermediate. Alternatively, alcohols and bis-nucleophiles such as 2-aminophenols could be incorporated to access esters and benzoxazoles, respectively. The method was further applied in a C–H functionalization sequence, demonstrating its synthetic utility in complex molecule derivatization. A plausible mechanism was proposed based on NMR studies. This method provides a versatile platform for further developments in amide functionalization, including selective activation and nucleophile incorporation.



- ***A mild, metal-free amide activation method***
- ***High selectivity and broad functional group tolerance***
- ***Application with C-H functionalization***
- ***48 examples, up to 99%***

Recently, we investigated the use of alternative alkyl iodonium salts, such as ((phenylsulfonyl)methyl)(p-tolyl)iodonium triflate, in palladium-catalyzed C–H functionalization to access complex aromatic scaffolds that serve as promising precursors to N-heterocycles.

References :

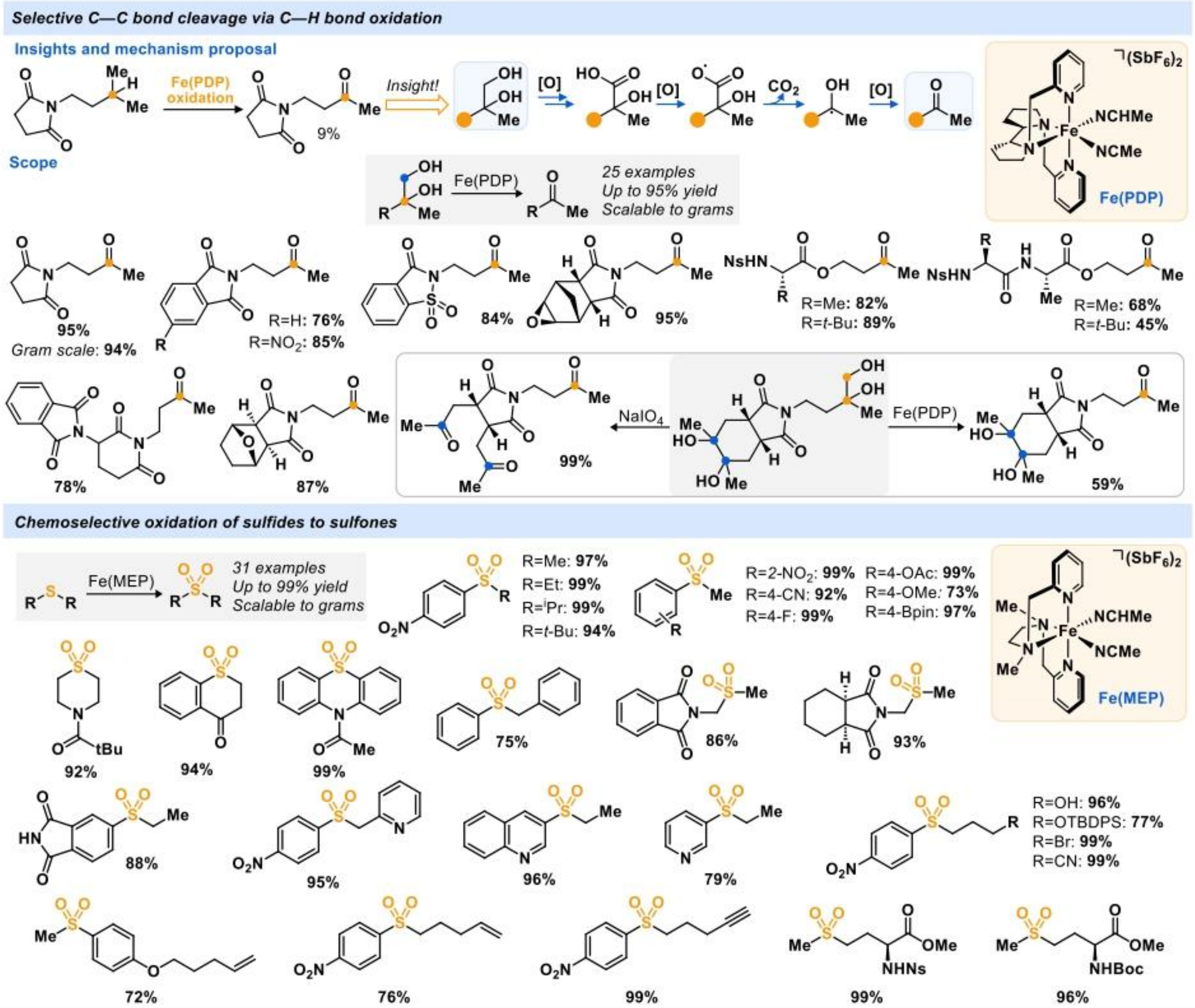
[1] Pitzer, J.; Steiner, K. *J. Biotech.* ***2016***, *235*, 32-46.
[2] Li, G.; Ma, S.; Szostak, M. *Trends in Chemistry* **2020,** *2* , 914-928.
[3] For reviews, see: (a) Pace, V.; Holzer, W.; Olofsson, B. *Adv. Synth. Catal.* **2014**, *356*, 3697-3736. (b) Kaiser, D.; Maulide, N. *J. Org. Chem.* **2016**, *81*, 4421-4428. (c) Kaiser, D.; Bauer, A.; Lemmerer, M.; Maulide, N. *Chem. Soc. Rev.* **2018**, *47*, 7899-7925. (d) Feng, M.; Zhang, H.; Maulide, N. *Angew. Chem. Int. Ed.* **2022**, *61*, e202212213.
[4] Zhong, T.; Amistadi-Revol, H.; Tremblais, J.; Prévost, S. *Org. Lett.* **2025**, *27,* 8858-8862.

Late-stage, C–H oxidation/decarboxylation and sulfur oxidation via non-heme iron catalysis diversion

Milena Cristina VIEIRA FERNANDES,[1] Felipe Akio SAITO,[1] Anna Beatriz FACUNDO E SILVA,[1] Kelita Angelo DE PAULA,[1] Emilio Carlos DE LUCCA Júnior[1]

[1] Instituto de Química, Universidade Estadual de Campinas, UNICAMP, C.P. 6154, CEP. 13083-970, Campinas, São Paulo, Brazil
m222555@dac.unicamp.br

Like cytochrome P450 enzymes,[1] iron catalysts that employ non-heme ligands exhibit the capability to generate iron-oxo species, which act as potent oxidizing agents capable of oxidizing C—H bonds as well as heteroatoms.[2,3] In light of the observation of an unanticipated byproduct, we developed a new methodology for the selective cleavage of C—C bonds through the oxidation of C—H bonds, utilizing FePDP in conjunction with H_2O_2. Additionally, by exploring a different catalyst, FeMEP, we developed a rapid, mild, and environmentally friendly approach for the oxidation of sulfides to sulfones.



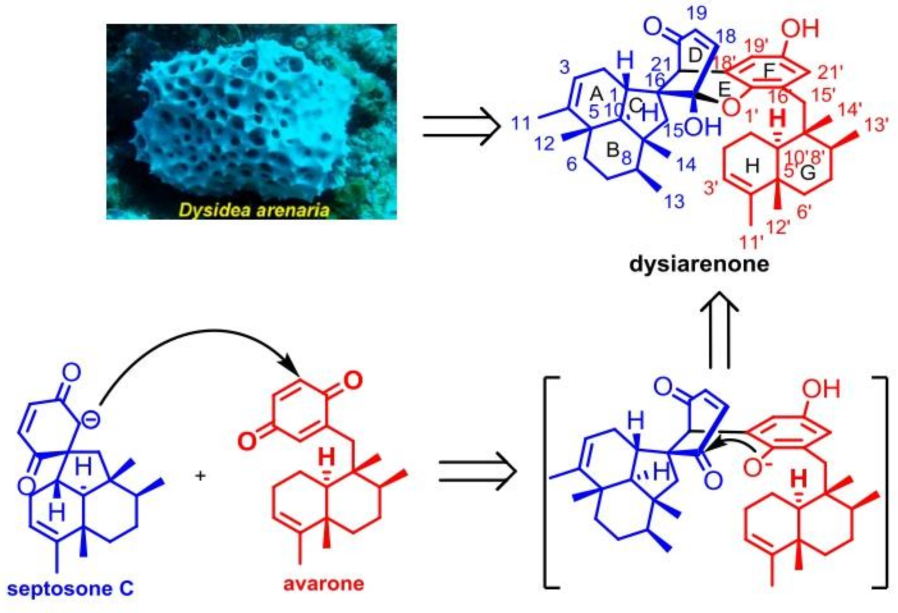
References :
[1] Guengerich, F. P.; *Chem. Res. Toxicol.* **2001**, 14, 6, 611–650;
[2] Niwa, T.; Nakada, M.; *JACS* **2012**, 134, 13538-13541;
[3] Chen, M. S.; White, M. C.; *Science* **2007**, 318, 783-787.

Toward the total synthesis of dysiarenone via an annulation between avarone and the septosone C skeleton

Zhijian ZHANG[1], Cyrille KOUKLOVSKY[1], Guillaume VINCENT[1]

1 Institut de Chimie Moléculaire et des Matériaux d'Orsay (ICMMO)
Universite-paris-saclay, Bâtiment Henri Moissan
17 Avenue des Sciences, 91400 Orsay, France
zhijian.zhang@universite-paris-saclay.fr

Sponges are significant multicellular organisms characterized by remarkable diversity and broad distribution.[1] Sponge-derived diterpenoids possess a broad spectrum of biological activities, including antibacterial, antifungal, antiviral, and antiparasitic effects.[2] Dysiarenone, a dimeric C_{21} meroterpenoid featuring potent inhibitory activity against COX-2 expression, was first isolated from the marine sponge Dysidea arenaria and reported by Lin's group in 2018.[3] Through retrosynthetic analysis, dysiarenone would be obtained from septosone C and avarone via a tandem cycloaddition aromatization reaction. To date, while the total synthesis of a diastereomer of septosone C has been documented.[4] The successful total synthesis of both the naturally occurring septosone C and dysiarenone remains an elusive challenge in organic synthesis.



References :

[1] Van Soest, R. W. M.; Boury-Esnault, N.; Vacelet, J.; Dohrmann, M.; Erpenbeck, D.; De Voogd, N. J.; Santodomingo, N.; Vanhoorne, B.; Kelly, M.; Hooper, J. N. A. *PloS one.* **2012**, *7* (4), e35105.

[2] Xia, J.; Chen, X.; Li, G.; Qiu, P.; Wang, W.; Shao, Z. *Mar. Drugs.* **2024**, *22* (10), 447–447.

[3] Jiao, W.-H.; Cheng, B.-H.; Chen, G.-D.; Shi, G.-H.; Li, J.; Hu, T.-Y.; Lin, H.-W. *Org. Lett.* **2018**, *20* (10), 3092–3095.

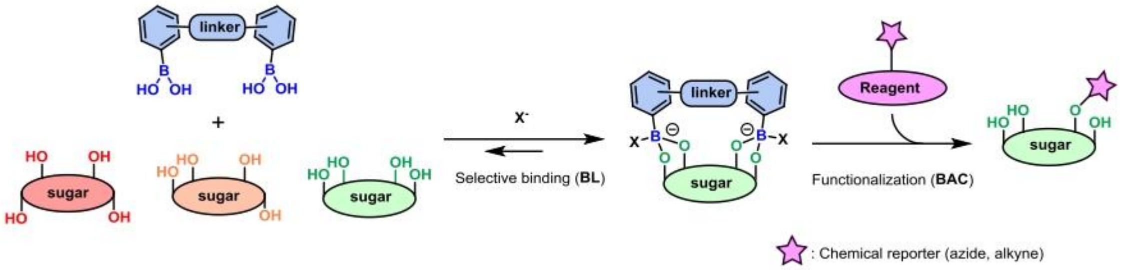
[4] G. Schoenn, C. Kouklovsky, R. Guillot, T. Magauer, G. Vincent, *Angew. Chem. Int. Ed.* **2025**, *64*, e202505270.

Mannose Recognition: Design, Synthesis and Reactivity of Mannose-Specific Boronolectins

Mathieu CHAOUAT,[1] Tania XAVIER,[1] Pascal BONNET [2] and Patricia BUSCA [1]

[1] Université Paris Cité, LCBPT – UMR 8601 CNRS, 45 rue des Saints-Pères, 75006 Paris, France
[2] Université d'Orléans, ICOA – UMR 7311 CNRS, rue de Chartres, 45100 Orléans, France
mathieu.chaouat@etu.u-paris.fr

Glycoproteins practically cover all eukaryotic cells and are responsible for numerous cellular communication and recognition events. Glycobiology underwent significant development at the end of the last century but remains hampered by the high structural complexity of glycans.[1] The need for new tools to study the structure and function of glycoproteins is therefore crucial, given that certain diseases result from glycosylation defects or are marked by specific surface oligosaccharides.[2] The recent development of Metabolic Oligosaccharide Engineering (MOE) by Carolyn Bertozzi and coworkers represents a significant breakthrough allowing the study of native glycans in living cells.[3] Our goal is to develop an alternative, chemical-based bioconjugation method. To specifically functionalize saccharides of interest, we aim to use boronolectins (BL) for their selectivity coupled with Boronic Acid Catalytic methods (BAC) to ensure reactivity.[4,5]



In this communication, we will disclose our latest results regarding the design, the synthesis and the complexation of several mannose-specific boronolectins.

References :
[1] Hart, G. W.; Varki, A. *Essentials of Glycobiology 4th edition*, Cold Spring Harbor (NY), **2022**.
[2] Smith, B. A. H.; Bertozzi, C.R. *Nat. Rev. Drug. Discov.* **2021**, *20*, 217.
[3] Palaniappan, K. K.; Bertozzi, C. R. *Chem. Rev.* **2016**, *116*, 14277.
[4] Bian, Z.; Liu, A.; Li, Y.; Fang, G.; Yao, Q.; Zhang, G.; Wu, Z. *Analyst* **2019**, *145*, 719.
[5] Graham, B. J.; Raines, R. T. *J. Org. Chem.* **2024**, *89*, 2069.

Acetoxy-Peroxyacetals: A Peroxycarbenium Precursor for the Synthesis of Hydroperoxides and Endoperoxides

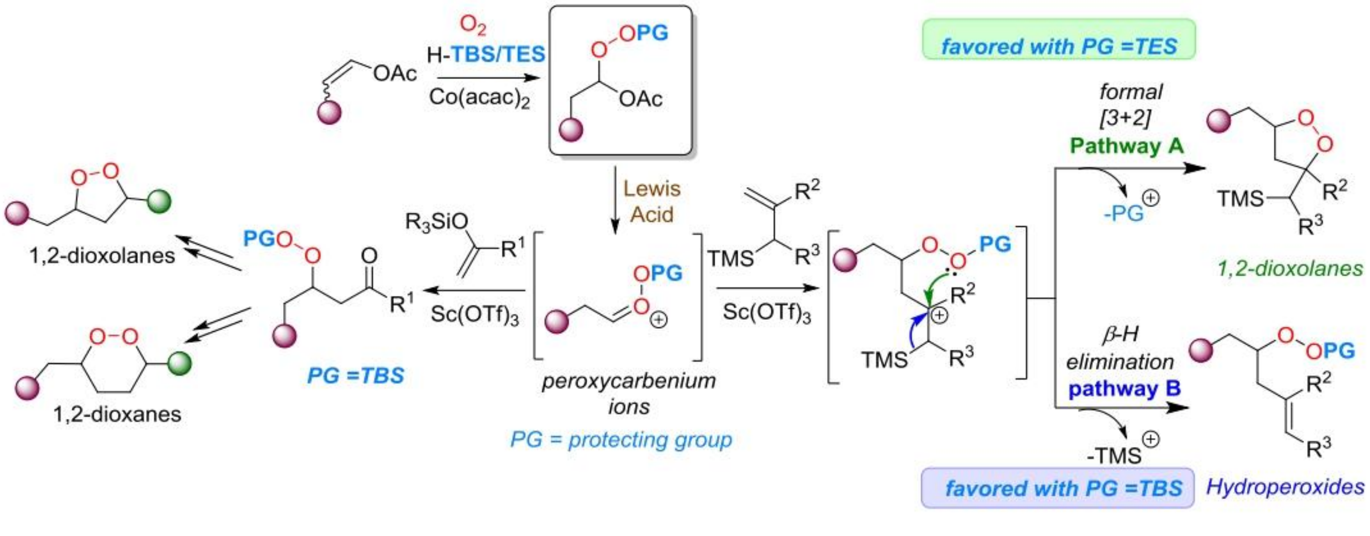
Yunxin XING,[1] and Laurent FERRIE[1]

[1] BioCIS, UMR 8076, Université Paris-Saclay, 91400, Orsay, France
yunxin.xing@universite-paris-saclay.fr

Peroxides are common motifs in natural products, valued for their diverse biological activities, including anti-inflammatory, antimalarial, and antitumor effects.[1] In synthetic chemistry, peroxy-ketals and -acetals provide promising opportunities through the formation of peroxycarbenium ions, enabling nucleophilic additions for the construction of oxygenated frameworks and functionalized endoperoxides.

While cyclic peroxyacetals are well-established intermediates,[2–4] acyclic counterparts remain less explored and are mostly limited to stabilized disubstituted systems. Pioneering studies by Dussault[5] and Woerpel[6] demonstrated that acyclic peroxyketals can undergo Sakurai or ene reactions to form 1,2-dioxolanes via formal [3+2] cycloaddition.

After intensive investigations, we developed primary acetoxy-peroxyacetals as efficient substrates for $Sc(OTf)_3$-catalyzed reactions with silylated nucleophiles, predominantly giving addition products, and the role of the protecting group was crucial. Bulky TBS protecting group improved selectivities and yields by suppressing desilylation or silyl migration, while allylsilyl nucleophiles generally favor addition over [3+2] cycloaddition depending on substituents and the peroxysilyl group. These compounds also served as versatile synthons for both hydroperoxides and endoperoxides (1,2-dioxolanes and 1,2-dioxanes). This approach has offered a new strategy based on sequential nucleophilic additions to peroxycarbenium species, analogous to iterative aldol or allylation processes.



References :
[1] Liu, D.-Z.; Liu, J.-K. Nat. Prod. *Bioprospect*. **2013**, *3*, 161–206.
[2] Pinet, A.; Figadère, B.; Ferrié, L. *Adv. Synth. Catal*. **2020**, *362*, 1190–1194.
[3] López, M. M.; Jamey, N.; Pinet, A.; Figadère, B.; Ferrié, L. *Org. Lett*. **2021**, *23*, 1626–1631.
[4] Champciaux, B., Jamey, N., Figadère, B. & Ferrié, L. *J. Am. Chem. Soc*. **2025**, *147*, 3353–3359
[5] Dussault, P.; Lee, I. Q.; Lee, H.-J.; Niu, Q. J.; Schultz, J. A.; Zope, U. R. *J. Org. Chem*. **2000**, *65*, 8407–8414.
[6] Ramirez, A.; Woerpel, K. A. *Org. Lett*. **2005**, *7*, 4617–4620.

PO-54

Three Component Reaction of *o*-Nitrobenzaldehydes, Cyanoacetates and Sulfur: Access to 3*H*-Benzo[1,2]dithioles

Zhiwei Xu[2], Thi Thanh Tam Nguyen [3], Chloée Bournaud [2], Martial Toffano [2], Vo-Thanh Giang[2], Pascal Retailleau [1], Thanh Binh Nguyen [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 France.

[2] Institut de Chimie Moléculaire et des Matériaux d'Orsay, CNRS, UMR 8182, Université Paris-Saclay, 17, avenue des Sciences, 91400 Orsay, France

[3] Université Paris-Est Créteil, CNRS, Institut de Chimie et des Matériaux Paris-Est, CNRS, UMR 7182, Thiais 94320, France

Supporting Information Placeholder

zhiwei.xu@universite-paris-saclay.fr

ABSTRACT:

A highly efficient, multicomponent protocol for the construction of 3*H*-benzo[1,2]dithioles[1] has been developed. Starting from readily available *o*-nitrobenzaldehydes, active acetonitriles, and elemental sulfur, this methodology provides a streamlined route to sulfur-containing heterocycles under mild, transition-metal-free conditions. The reaction exhibits significant synthetic versatility, accommodating *o*-halobenzaldehydes to allow for flexible substrate selection based on cost and commercial availability[2-5]. The synthetic utility of the resulting 3*H*-benzo[1,2]dithiole core was further demonstrated through its transformation into diverse derivatives via regioselective *S*-oxidation with HNO_3 and Michael addition with primary alkylamines.

DEMONSTRATION PLAN:

The poster presentation will be elaborated from several aspects, including background introduction, condition screening, substrate expansion, product application, and possible reaction mechanisms.

References :

[1] Rakitin, O. A. *Molecules.* **2021**, *26*, 3595.
[2] Song, Z.-L.; Bai, F.; Zhang, B.; Fang, J. *J. Agric. Food Chem.* **2020**, *68*, 2214.
[3] (a) Yang, S.; Guo, K.; Hu, H.; Liu, X.; Zhou, Y.; Jin, S. *J. Org. Chem.* **2026**, *91*, 258–265. (b) Liu, X.; Lv, W.; Dong, J.; Liu, Z.; Hu, F.; Zhou, C.; Zhou, Y. *Adv. Synth. Catal.* **2024**, *366*, 1978–1982. (c) Zhang, B.; He, S.; Dong, N.; Zhu, A.; Duan, H.; Wang, D.; Zhou, Y. *Org. Chem. Front.* **2024**, *11*, 3302.
[4] Liu, X.; Kong, X.; Zheng, J.; Zhou, J.; Wen, J.; Zhou, Y.; Jin, S.; Yin, G. *Chin. J. Chem.* **2026**, *44*, 251.
[5] Kang, J.; Ferrell, A. J.; Chen, W.; Wang, D.; Xian, M. *Org. Lett.* **2018**, *20*, 852.