16

Seminar

13th-16th April 2026

Abstract's Book

Girona Seminar 2026, April 13th to April 16th 2026

Welcome Letter

Dear colleagues,

On behalf of the organizing committee, we are delighted to welcome you to the Girona Seminar and the corresponding Young Researchers Symposium, taking place in the city of Girona, Catalonia (Spain), from April 13th to April 16th at the "La Mercè" Auditorium.

Since 1993, the Institute of Computational Chemistry and Catalysis (IQCC) has been organizing this biennial conference. Early editions were focused on theoretical chemistry, which changed in 2006 when for every seminar a different research topic related to the IQCC interests was chosen. In the last two editions of the Girona Seminar (2022 and 2024) the subthemes were "Biocatalysis" and "Supramolecular Chemistry". For the next edition in 2026, the topic will be "*Synthesis and functionalization of cyclic compounds: experimental and theoretical perspectives*".

The Girona Seminar has an outstanding reputation for excellence and highly engaged discussion, and it has become a focal point for scientists at the forefront of chemistry to present and discuss their latest developments. The meeting also aims to promote new collaborations, bringing together young and senior scientists in a beautiful environment and in an informal and friendly setting. In order to put special emphasis on the research of young researchers, prior to the main meeting there will be a one-day Young Researchers Symposium. This symposium will be organized for, and by, PhD students in order to showcase their results, and we encourage all participants of the Girona Seminar to also attend this symposium.

We are very pleased to have you with us and hope you will find the meeting both enriching and enjoyable.

Best regards,

The Organizing Committee

Organizing and Scientific Committee

Arnau Call Quintana

Anna Pla-Quintana

Albert Poater Teixidor

Anna Roglans Ribas

Young Researchers Symposium

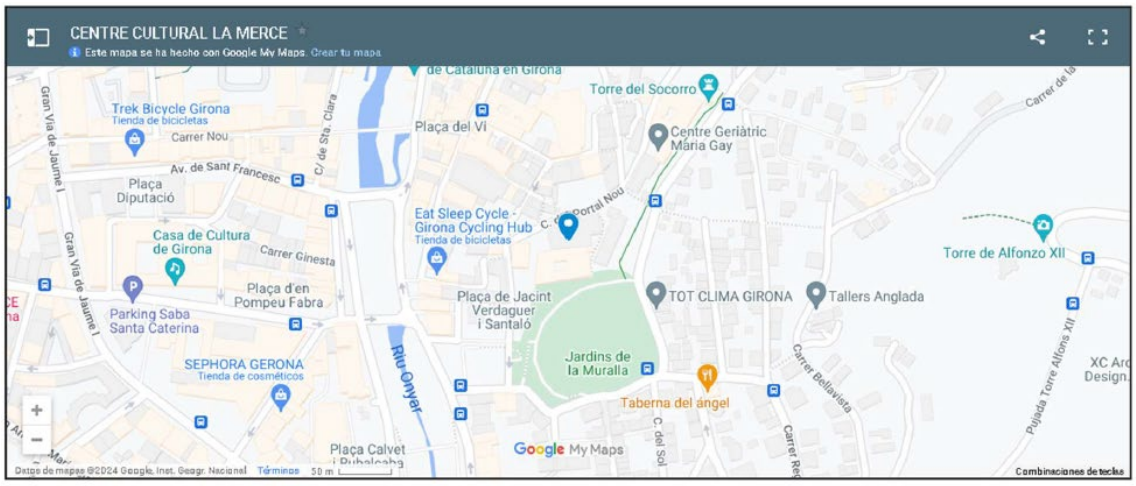
Albert Artigas

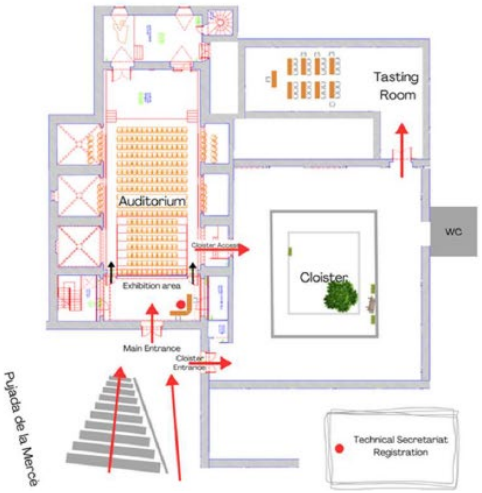
Sergio Fernández Martín

Venue

Girona Seminar 2026 will be held in Girona at the Auditori of Centre Cultural la Mercè, located in the city centre.

Address: Pujada de la Mercè, 12, 17004 Girona





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RSEQ Real Sociedad Española de Química

SCQ Societat Catalana de Química

GEQO RSEQ

RSEQ

STCAT RSEQ Sección Territorial de Cataluña Secció Territorial de Catalunya

Monday 13th

10:00 Photochemical BF_3-catalyzed oxo-Diels-Alder reactions: a mechanistic study - **Alice Genovese**

10:20 Rh-catalyzed cycloaddition cascade of allenynes and maleimides - **Elias A. Romero-Cavagnaro**

10:40 Exploring the intramolecular chemistry of iron(v)-oxo-carboxylato species - **Andrea Álvarez**

Coffee break

11:30 Mechanism-driven engineering of photoenzyme CvFAP towards new-to-nature decarboxylative radical cyclization - **Cristina Berga**

11.50 Skeletal rearrangement of biaryls via rhodium-azirine intermediate: a route to solid-state emissive polycyclic sulfamates - **Nil Insa-Carreras**

12:10 Computational study of the catalyzed cycloaddition reaction of CO_2 to propylene oxide in a biphasic media - **Thalia Ortiz-Garcia**

12:30 Synthesis and characterization of COF-metal nanoparticle hybrids for catalytic applications - **Adrián Navarro**

12:50 Inductive diastereoselective rationale for a catalytic strategy to build densely chiral five-membered carbocycles - **Carmen María Arenas-Baeza**

13:10 Desymmetrization of malonic monoesters and malonic acids via enantioselective catalytic C(sp^3)-H oxidation - **Nikos Siakavaras**

Lunch

15:00 Aryl halides reactivity via ferrioxalate photocatalysis - **Carles Bernabeu**

15:20 Synthesis of allyl-functionalized cyclic dilactones for biocomposite applications - **Mahrou Moshfeghnia**

15:40 Predicting stereoselectivity in γ-lactonization through a simple computational model of the reactant complex - **Muhammad Ehtisham**

16:00 Mechanistic and kinetic study of the electrochemical CO_2 reduction with a manganese(I) catalyst - **Guillem Pey**

Coffee break

16:50 **Round table –** Science Beyond Academia: Careers in Industry (**Jordi Mestres**, **Francesco Zaccaria** and **Laia Vicens**)

Tuesday 14th

9:45	Regioselective pyridine C-H-functionalization and skeletal editing - **Armido Studer** (Plenary Speaker)
10:30	Axially chiral macrocycles for precision molecular recognition - **M. Magdalena Cid** (Keynote Speaker)
	Coffee break
11:30	Aryne atropisomers: and yet they rotate! - **Yoann Coquerel** (Keynote Speaker)
12:00	Electrostatic and conformational control of aromatic O- vs. N-methylation in SAM-dependent methyltransferases - **Helena Girame**
12:05	Axial-to-point chirality transfer in cyclopropanation reaction - **Nerea Iragorri**
12:10	Supramolecular mask assisted regio and chemo-selective synthesis of fullerene derivatives via radical anion mechanism - **Piyush Piyush**
12:15	Computational evidence on a modular family of chiral cavitand receptors: tuning the chirotopical response of achiral fullerene guests - **Fiza Fariha**
12:20	Chiral self-folding cavitand receptors based on calixarene macrocycles - **Agustí Lledó**
12:35	Molecular complexity from simple building blocks: (asymmetric) C-H activation or rare hypervalent compounds? - **Joanna Wencel-Delord** (Plenary Speaker)
	Lunch
15:00	Carboxylic acid directed lactonization of aliphatic C-H bonds - **Miquel Costas** (Keynote Speaker)
15:30	From molecular cooperation to metal oxides in the synthesis of cyclic carbonates - **Sergio Posada-Pérez**
15:45	Inverse pyridine rhodium(I) carbonyls for metalligand cooperative cyclisation - **Nil Roig**
16:00	New opportunities in catalysis using sulfoximines - **Vincent Gandon** (Keynote Speaker)
16:30	Enantioselective nitrene transfer reactions enabled by dirhodium(II) catalysis - **Michael Andresini**
16.45	Scale-up of enantioselective catalytic lactonization at nonactivated γ-C-H bonds using affordable manganese catalysts - **Francesco Zaccaria**
17.00	From peptides to drugs: enabling technologies for non-canonical amino acids synthesis - **Quentin Lefebvre** (Plenary Speaker)

Wednesday 15th

9:30	DFT characterization of mechanisms in cyclization and functionalization reactions - **Feliu Maseras** (Plenary Speaker)
10:15	The iridium-catalyzed benzene-methane dehydrogenative coupling - **Pedro J. Pérez** (Keynote Speaker)
10:45	Hypervalent bromine dimerization: a streamlined approach to biphenylene-embedded helicoidal structures - **Àlex Díaz-Jiménez**
	**Coffee break**
11:30	High concentration ring closing metathesis for efficient synthesis of macrocyclic musk compounds - **Anna Kajetanowicz** (Keynote Speaker)
12:00	Amino-acid donor promiscuity of LBCA TrpB reveals distinct reactivity in the tryptophan synthase complex - **Eduard Masferrer-Rius**
12:05	Photocatalytic C-H functionalization and ring opening of saturated aza-heterocyles - **Sophia Lecellier**
12:10	Controlling abiological cyclization pathways in heme-dependent enzymes - **Hande Abes**
12:15	Catalytic carbocyclization of 1,5-bisallenes for rapid assembly of molecular complexity - **Mou Mandal**
12:30	C–H bonds oxidation of cyclic hydrocarbons via radical and cationic paths - **Marco Galeotti**
12:45	Digital approaches in reactions involving cyclic compounds - **Juan V. Alegre-Requena** (Keynote Speaker)
13:15	CROMLAB, S.L.
	**Lunch**
15:00	Boron-mediated remote carbon migration for ring-closing transformations - **Elena Fernández** (Keynote Speaker)
15:30	DFT insights into the mechanism of γ-lactonization and enantioselective ether desymmetrization mediated by bioinspired Mn and Fe complexes - **Josep M. Luis**
15:45	Modelling cyclization reactions inside nanocavities - **Gregori Ujaque**
16:00	Beyond planar aromaticity: defining 3d-aromaticity with illustrative examples - **Miquel Solà** (Keynote Speaker)
16:30	Computational investigation of anion-induced allosteric regulation in a cationic capsule for cation recognition - **Zanira Mushtaq**
16.35	Functional role of cyclic π-conjugated molecules in hybrid interfaces: a theoretical study of fullereneperovskite electron transfer - **Gibu George**
16.40	Palladium-catalyzed apex-type reaction for the synthesis of polycyclic aromatic hydrocarbons - **Adrià Montal**
16.45	Fluorination control of the stability of the PD_8I_{16} square antiprism - **Arslan Ahmad**

Thursday 16th

9:30	Shaping molecular reactivity with light – from spin states to selective synthesis - **Rene M. Koenigs** (Plenary Speaker)
10:15	Cycloaddition reactions of arynes and alkynes in the synthesis of nanographenes and unconventional polycyclic conjugated systems - **Dolores Pérez** (Keynote Speaker)
10:45	General access to chiral piperidines via enantioselective HAT-initiated C(sp^3)-H oxidation - **Muthuramalingam Sethuraman**
	Coffee break
11:30	Integrated computational frameworks for exploring free energy landscapes in the light of synthesis and functionalization of cyclic compounds - **Maren Podewitz** (Keynote Speaker)
12:00	Regioselective acylation of resorcinol derivatives via an engineered biocatalyst - **Alexander Swoboda**
12:05	A computational quest for controlled antiaromatic reactivity of pentalene dimerization - **Carles Alcaide**
12:10	Functionalized ruthenium catalysts for sustainable synthesis of cyclic compounds - **Rabab Maqsood**
12:15	Aromatics with a twist: synthesis, structure and properties - **Irena G. Stará** (Plenary Speaker)

Social Program

Tuesday, 14th

Centro Cultural de la Mercè

Included in registration

Time: 18:00 h. - Traditional Music & Welcome Cocktail

Venue: Centro Cultural de la Mercè

Enjoy a warm welcome with traditional music and a cocktail reception in a unique cultural setting.

Wednesday, 15th

Guided Tour to Girona

Included in registration

Time: 18:00 h.

Meeting Point: Centro Cultural de la Mercè (Event Venue)

Discover the charm of Girona through a guided walking tour of its historic streets. Admire the city's stunning architecture, picturesque views, and rich history. This immersive experience offers a perfect blend of cultural exploration in one of Catalonia's most beautiful destinations.

Gala Dinner | Restaurant La Miranda

Included in registration

Address: Carrer dels Ciutadans, 14, 17004 Girona

Time: 20:00 h.

The gala dinner will take place at La Miranda, located in a truly unique building on one of Girona's most historic and lively streets—recognized as Architectural Heritage of Catalonia. The venue has been carefully restored, preserving its original architectural elements while offering a chic, warm, and welcoming atmosphere.

With its elegant design, natural greenery, and intimate spaces, La Miranda provides a distinctive setting where guests can enjoy a memorable evening. Each room and corner is thoughtfully designed to create a unique experience

Progamme

Plenary

Studer, Armido
Wencel-Delord, Joanna
Lefebvre, Quentin
Maseras, Feliu
Koenigs, Rene M.
G. Stará, Irena

Keynote

Cid, M. Magdalena
Coquerel, Yoann
Costas, Miquel
Gandon, Vincent
Pérez, Pedro J.
Kajetanowicz, Anna
Alegre-Requena, Juan V.
Fernández, Elena
Solà, Miquel
Pérez, Dolores
Podewitz, Maren

Contributed

Genovese, Alice
Romero-Cavagnaro, Elias A.
Álvarez, Andrea
Berga, Cristina
Insa-Carreras, Nil
Ortiz-Garcia, Thalia
Navarro, Adrián
Arenas-Baeza, Carmen Maria
Siakavaras, Nikos
Bernabeu, Carlos
Moshfeghnia, Mahrou
Ehtisham, Muhammad
Pey, Guillem
Lledó, Agustí
Posada-Pérez, Sergio
Roig, Nil
Andresini, Michael
Zaccaria, Francesco
Díaz-Jiménez, Àlex
Mandal, Mou
Galeotti, Marco
Luis, Josep M.
Ujaque, Gregori
Muthuramalingam, Sethuraman

Girona Seminar 2026, April 13th to April 16th 2026

Flash

Girame, Helena
Iragorri, Nerea
Piyush, Piyush
Fariha, Fiza
Masferrer-Rius, Eduard
Lecellier, Sophia
Abeş, Hande
Mushtaq, Zanira
George, Gibu
Montal, Adrià
Ahmad, Arslan
Swoboda, Alexander
Alcaide, Carles
Maqsood, Rabab

16 Girona Seminar

13th-16th April 2026

Synthesis and functionalization of cyclic compounds

Plenary speakers

16 Girona Seminar
13th-16th April 2026
Synthesis and functionalization of cyclic compounds

REGIOSELECTIVE PYRIDINE C-H-FUNCTIONALIZATION AND SKELETAL EDITING

Armido Studer*

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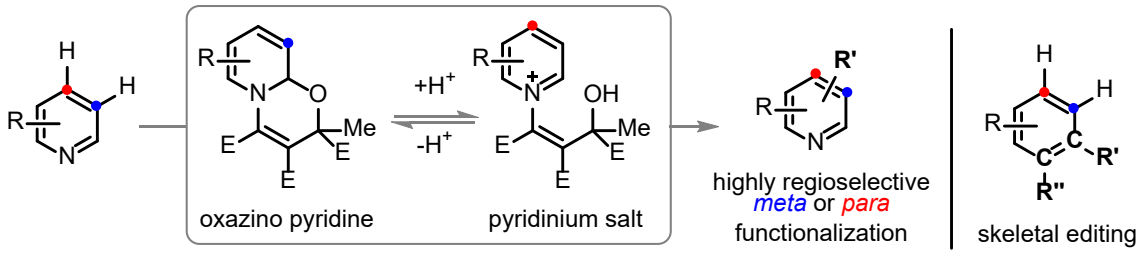
Pyridines belong to the most abundant heteroarenes in medicinal chemistry and in agrochemical industry. In the lecture, highly regioselective pyridine C-H functionalization through a dearomatization/rearomatization sequence will be discussed. The dearomatized oxazino pyridines can be easily prepared on a large scale, and *meta*-functionalization becomes achievable through light-initiated radical alkylation and ionic transformations.[1] As example, using such an approach *meta*-fluorinated pyridines are readily accessible.[2] The same intermediates upon protonation to give the corresponding pyridinium salts also allow the highly regioselective radical *Minisci para*-alkylation.[3,4] In addition, Cu-catalyzed *meta*-arylation[5] and switchable radical *para/meta*-difluoromethylation[6] through such intermediates will be presented. Radical *meta*-nitration[7] and ionic *meta*-hydroxylation[8] work equally well through such intermediates. Finally, it will be shown that this dearomatization concept is also applicable to pyridine skeletal editing.[9] Further, it will be discussed that an alternative radical dearomatization process can be used for C to N mutation in indoles and benzofurans.[10]



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2) Haring, M.; Balanna, K.; Cheng, Q.; Lammert, J.; Studer, A. *J. Am. Chem. Soc.* **2024**, *146*, 30758.
3) Cao, H.; Bhattacharya, D.; Cheng, Q., Studer, A. *J. Am. Chem. Soc.* **2023**, *145*, 15581.
4) Wang, Z.; Xu, P.; Studer, A. *Org. Chem. Front.* **2024**, *11*, 3849.
5) Guo, S.-M.; Xu, P.; Studer, A. *Angew. Chem. Int. Ed.* **2024**, *63*, e202405385.
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7) Balanna, K.; Studer, A. *J. Am. Chem. Soc.* **2025**, *147*, 7485.
8) Bhattacharya, D.; Studer, A. *Angew. Chem. Int. Ed.* **2025**, *64*, e202423512.
9) Cheng, Q.; Bhattacharya, D.; Haring, M.; Cao, H.; Mück-Lichtenfeld, C.; Studer, A. *Nat. Chem.* **2024**, *16*, 741.
10) Wang, Z.; Xu, P.; Guo, S.-M.; Daniliuc, C. G.; Studer, A. *Nature* **2025**, *642*, 92.

16 Girona Seminar
13th-16th April 2026
Synthesis and functionalization of cyclic compounds

MOLECULAR COMPLEXITY FROM SIMPLE BUILDING BLOCKS: (ASYMMETRIC) C-H ACTIVATION OR RARE HYPERVALENT COMPOUNDS?

Joanna Wencel-Delord*

Institute of Organic Chemistry, JMU Würzburg, Germany
e-mail: joanna.wencel-delord@uni-wuerzburg.de

The efficient synthesis of complex molecular scaffolds in a straightforward, cost- and resource-efficient manner is a key challenge in modern synthetic chemistry. Using simple building blocks to access molecular complexity quickly using abundant and non-toxic catalysts or metal-free conditions is a highly appealing approach for both academic and industrial sectors. During this presentation conceptually very different and complementary approaches towards molecular complexity will be discussed, focusing on 3d-metal-catalysed asymmetric C-H activation[1],[2] and light-promoted direct conversion of simple alkanes into valuable amines.[3] Finally, the use of hypervalent bromines[4] and chlorines[5] as emerging molecular bricks for a multitude of applications, including medicinal chemistry and material science, will be presented.

1) Brunard, E.; Huang, F.; Díaz-Jiménez, À.; Kostiukovska, S.; Wencel-Delord, J. *Angew Chem Int Ed* **2026**, 65 (7), e23241. https://doi.org/10.1002/anie.202523241.
2) a) Jacob, N.; Zaid, Y.; Oliveira, J. C. A.; Ackermann, L.; Wencel-Delord, J. *J. Am. Chem. Soc.* **2022**, *144* (2), 798–806. https://doi.org/10.1021/jacs.1c09889. b) Luc, A.; Oliveira, J. C. A.; Boos, P.; Jacob, N.; Ackermann, L.; Wencel-Delord, J. *Chem Catalysis* **2023**, *3* (10), 100765. https://doi.org/10.1016/j.checat.2023.100765.
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4) Lanzi, M.; Dherbassy, Q.; Wencel-Delord, J. *Angew. Chem. Int. Ed.* **2021**, *60* (27), 14852–14857. https://doi.org/10.1002/anie.202103625.
5) Lanzi, M.; Rogge, T.; Truong, T. S.; Houk, K. N.; Wencel-Delord, J. J. Am. Chem. Soc. 2023, 145 (1), 345–358. https://doi.org/10.1021/jacs.2c10090.

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Synthesis and functionalization of cyclic compounds

FROM PEPTIDES TO DRUGS: ENABLING TECHNOLOGIES FOR NON-CANONICAL AMINO ACIDS SYNTHESIS

Quentin Lefebvre*, David Pierrot, Gerhard Müller

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The field of medicinal chemistry is witnessing growing interest in peptides, peptidic, and semi-peptidic macrocycles as promising beyond rule-of-5 (bRo5) therapeutic modalities.[1] However, both linear and cyclic peptides present several limitations that hinder their broader therapeutic development, such as rapid metabolic degradation, fast clearance from the body, and high conformational flexibility. Replacement of natural amino acids by more complex, non-canonical amino acids could help tackle these challenges, but efficient methodologies to access these building blocks are scarce, even more so when considering enantiopurity. We will show how enabling technologies and methodologies such as photochemistry, electrochemistry, and enantioselective catalysis[2,3,4] can help streamline synthesis of non-canonical amino acids to support the systematic de-peptidization of lead compounds in medicinal chemistry programs.

References:
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2) C. N. Ungarean, E. M. Larin, D. T. Egger, P. Ziegler, Q. Lefebvre, T. C. Fessard, B. Morandi, Org. Lett. 2024, 26, 2784
3) M. Martinelli, C. Giorgiutti, T. Fessard, Q. Lefebvre, Org. Biomol. Chem. 2023, 21, 9230
4) S. Murthuramalingam, A. Call, Q. Lefebvre, M. S. Sigman, M. Costas, 10.26434/chemrxiv-2025-3l55k

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13th-16th April 2026
Synthesis and functionalization of cyclic compounds

DFT CHARACTERIZATION OF MECHANISMS IN CYCLIZATION AND FUNCTIONALIZATION REACTIONS

Feliu Maseras

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Computational chemistry has made a substantial contribution to the characterization of the mechanisms of reactions involving cyclic compounds. Here we present some some selected examples of applications to this field of the methods of computational homogeneous catalysis[1] , in particular density functional theory (DFT) and microkinetic modeling. Specifically, we will discuss the mechanism of a selective intramolecular synthesis of heterocycles involving single electron transfer (see Figure 1),[2] the divergent outcomes of fullerene reactivity in solution and ball-milling conditions,[3] and the regioselectivity of the functionalization of an aromatic ring in organic electrosynthesis.[4]

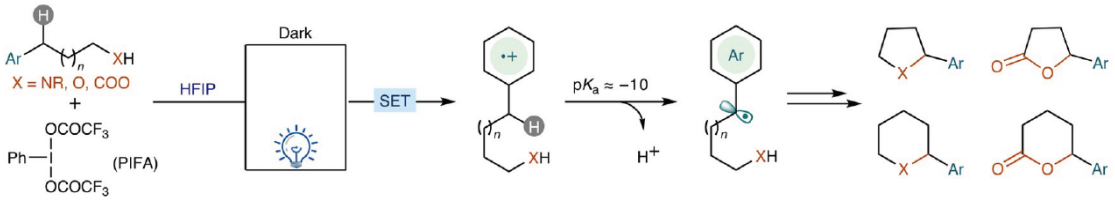

Figure 1. Intramolecular cyclization involving a C(sp_3)-H bond.

References
1) J. N. Harvey, F. Himo, F. Maseras, L. Perrin, ACS Catal., 2019, 9, 6803.
2) J. Xie, J. Zhang, S. Kasemthaveechok, S. López-Resano, E. Cots, F. Maseras, M. H. Pérez-Temprano, Nature Synthesis, 2024, 3, 1021.
3) E. Garca-Padilla, F. Maseras, íCell Reports Phys. Sci., 2025, 6, 102434.
4) M. Díaz-Ruiz, F. Maseras, ChemistryEurope, 2025, 3, 2500032.

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Synthesis and functionalization of cyclic compounds

SHAPING MOLECULAR REACTIVITY WITH LIGHT – FROM SPIN STATES TO SELECTIVE SYNTHESIS

Rene M. Koenigs*

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Photochemistry offers unique opportunities for reaction discovery by enabling the generation and control of highly reactive intermediates under mild conditions. Our research explores how visible-light activation can unlock novel reactivity modes of species such as carbenes, radicals and nitrenes, providing access to previously unattainable bond constructions and heterocyclic frameworks. This approach highlights photochemistry as a powerful platform for advancing modern synthetic methodology.

Herein, we present our recent advances in photochemical and photocatalytic carbene and nitrene transfer reactions. Emphasis will be placed on strategies to access either singlet or triplet states and how this electronic control enables distinct applications in synthetic methodology.[1,2] Approaches to modulate nitrene reactivity via single-electron transfer pathways or direct photoexcitation will be highlighted, supported by mechanistic and computational studies that have guided the discovery of advanced cycloaddition chemistry.[3]

We further outline an international, collaborative research program that integrates fundamental reactivity studies, reaction development, and mechanistic insight with translational applications in drug discovery. This work demonstrates how photochemical methods can unlock the potential of reactive intermediates and convert fundamental discoveries into new strategies for the synthesis of therapeutic candidates.[4-6] Together, these studies highlight photochemistry as a powerful driver of innovation at the interface of fundamental and applied research.

[1] (a) Empel, C.; Pham, Q. H.; Koenigs, R. M. Acc. Chem. Res., 2024, 57, 2717-2727. (b) Li, F.; Pei, C.; Koenigs, R. M.; Angew. Chem. Int. Ed. 2022, 61, e202111892.
[2] (a) Guo, Y.; Pei, C.; Koenigs, R. M. Nature Commun. 2022, 13, 86; (b) Guo, Y.; Pei, C.; Jana, S.; Koenigs, R. M. ACS Catal. 2021, 11, 337; (c) Empel, C.; Koenigs, R. M.; Chem Catalysis, 2022, 2, 2506.
[3] (a) I. Sliusarevskyi, J. Diaz, S. Senapati, B. J. Ebel, N. J. Linnartz, I. M. Oppel, C. Empel, P. W. H. Chan, R. M. Koenigs, Angew. Chem. Int. Ed. 2025, 64, e202509870. (b) Li, F.; Zhu, W. F.; Empel, C.; Datsenko, O.; Xu, Y.; Ehrler, J. M.; Atodiresei, I.; Knapp, S.; Mykhailiuk, P.; Proschak, E.; Koenigs, R. M. Science, 2024, 383, 498-503.
[4] (a) Hussain, Y.; Prasanna R.; Empel, C.; Proschak, E.; Koenigs, R. M.; Chauhan, P. Angew. Chem. Int. Ed. 2025, e202416956. (b) L. Yi, A. S. Makarov, B. Maity, D. Kong, R. Alshehri, L. Cavallo, R. M. Koenigs, M. Rueping, Angew. Chem. Int. Ed. 2026, e18508. (c) Senapati, S.; Hota, S. K.; Kloene, L.; Empel, C.; Murarka, S.; Koenigs, R. M. Angew. Chem. Int. Ed., 2025, 64, e202417107

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Synthesis and functionalization of cyclic compounds

AROMATICS WITH A TWIST:

SYNTHESIS, STRUCTURE AND PROPERTIES

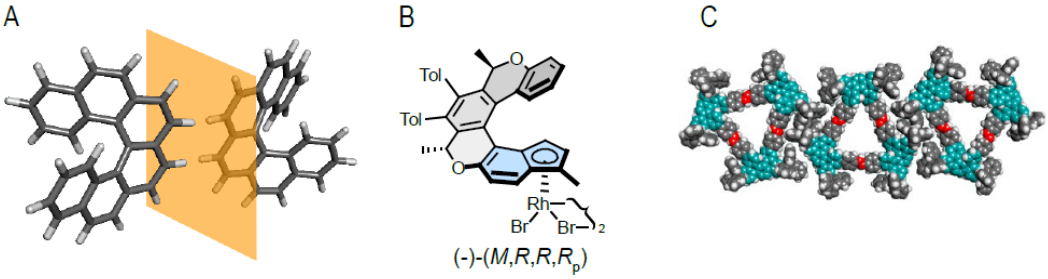
Tereza Edlová, Václav Ráliš, Jan Hanus, Katsiaryna Kutsenka, Václav Houska, Nikola Broftová, Jindřich Nejedlý, Michal Šámal, Jiří Rybáček, Jaroslav Vacek, Ivo Starý, Irena G. Stará

Institute of Organic Chemistry and Biochemistry, Czech Academy of Sciences, Flemingovo náměstí 2, 166 00 Prague 6, Czech Republic
e-mail: stara@uochb.cas.cz

With their twisted architecture and rigid 3D π-conjugated backbones, inherently chiral helicenes have received significant attention in recent years. Their unique helical structure gives rise to remarkable physicochemical properties, making them versatile building blocks for a wide range of applications — from enantioselective catalysis and molecular recognition to supramolecular self-assembly, surface modification, and the design of cutting-edge chiral materials.[1]

In this talk, I will present a versatile synthetic route to helicenes via intramolecular [2+2+2] cycloisomerization of aromatic triynes (Fig. 1A), show examples of successful structure-driven control in rhodium- and iridium-catalyzed reactions employing helicene-based metal complexes (Fig. 1B),[2] demonstrate the single-molecule conductance of helicenes measured by the STM break-junction method to understand charge transport through helical polyaromatic systems, explore helicenes as emitters of circularly polarized luminescence (CPL), and, last but not least, present evidence how the architecture of molecular building blocks (Fig. 1C) dictates the structure and properties of complex helicene-based macrocycles.[3]

Figure 1



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Keynote speakers

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AXIALLY CHIRAL MACROCYCLES FOR PRECISION MOLECULAR RECOGNITION

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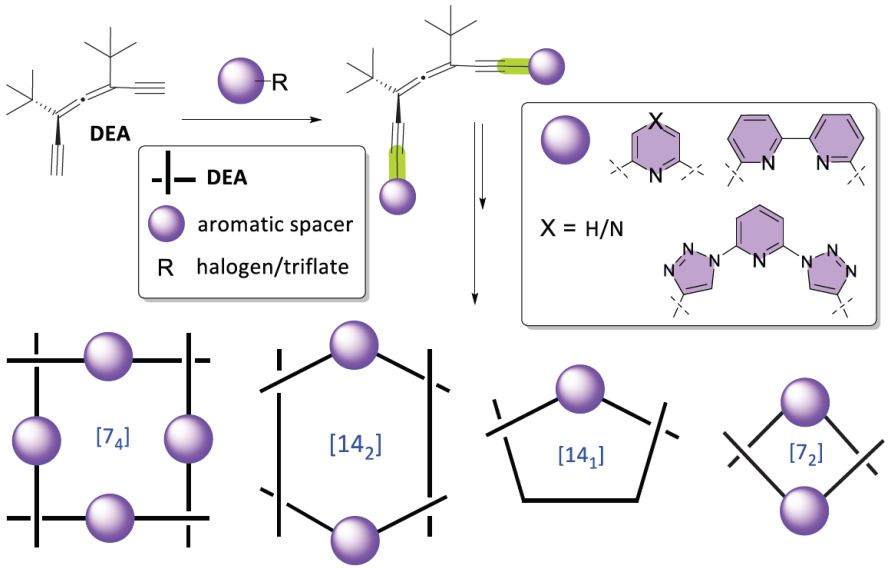
Chiral macrocycles are key structural motifs in modern chemistry due to their relevance in supramolecular recognition, functional materials, and harmaceutical applications.[1] Their welldefined cavities and conformational rigidity enable selective host–guest interactions and the formation of highly organized supramolecular architectures. In this context, our group focuses on the synthesis of allenophanes, axially chiral, shape-persistent macrocycles ontaining diethynylallene (DEA) units and aromatic spacers, in order to obtain systems with enhanced sensing capabilities. The resulting macrocycles Scheme 1) behave as chiral hosts possessing well-defined three-dimensional cavities. Host–guest studies demonstrate guest-induced conformational switching, accompanied by characteristic electronic circular dichroism (ECD) spectral changes, which serve as diagnostic signatures of molecular recognition and chiral induction.[2][3]



Scheme 1. General structure of the allenophanes

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ARYNE ATROPISOMERS: AND YET THEY ROTATE!

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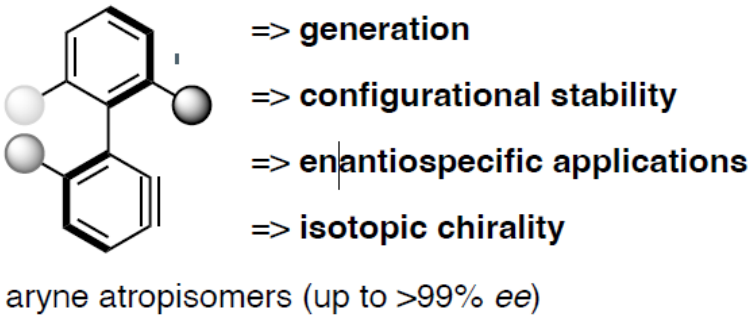
And yet they rotate! Highly enantioenriched aryne atropisomers having a biaryl stereogenic axis vicinal to the reactive triple bond are demonstrated to exist.[1] These reaction intermediates are easily produced in situ and can undergo the standard aryne cycloaddition chemistry in a highly enantiospecific manner.[2] Notably, some enantiopure aryne atropisomers (with ≥99% ee) have allowed the practical syntheses of small nanographenes, triptycene and anthracene derivatives that embed stereogenic axes of controlled absolute configurations with >99% preservation of the stereogenic information. Using this approach, the (low!) barrier to reaction between arynes and furan could be experimentally determined.[3] Ultimately, bis(aryne) atropisomers derived from BINOL can produce enantioisotopomers of atropisotopomers, some isotopically 'minimally' chiral compounds, with equally high retention of the stereogenic information. Chirality analysis is then the challenge.[4]



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CARBOXYLIC ACID DIRECTED LACTONIZATION OF ALIPHATIC C-H BONDS

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Reactions that enable selective functionalization of strong aliphatic C–H bonds open new synthetic paths to rapidly increase molecular complexity and expand chemical space.[1] Particularly valuable are reactions where site-selectivity can be directed toward a specific C–H bond by catalyst control.[2] In this talk we will discuss the development of manganese catalysts for the site- and stereoselective lactonization of unactivated C–H bonds in carboxylic acid substrates to deliver lactones.[3] Novel families of chiral Mn catalysts have been developed that activate aqueous hydrogen peroxide to promote intramolecular lactonization under mild conditions, via carboxylate binding to the metal center. This class of catalysts exhibits high site-selectivity and enables the oxidation of unactivated C–H bonds even in the presence of a priori more reactive secondary and tertiary ones. The factors governing site-selectivity have been uncovered. Most remarkably, by manipulating the absolute chirality of the catalyst, lactonization of prochiral substrates can proceed with excellent levels of diastereo and enantioselectivity. Such control has been successfully exploited in the late-stage lactonization of natural products such as camphoric, camphanic, ketopinic, and isoketopinic acids and intermediates in the path towards terpenoid natural products. Mechanistic analysis assisted by computational analyses provide models to predict site and enantioselectivity.

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NEW OPPORTUNITIES IN CATALYSIS USING SULFOXIMINES

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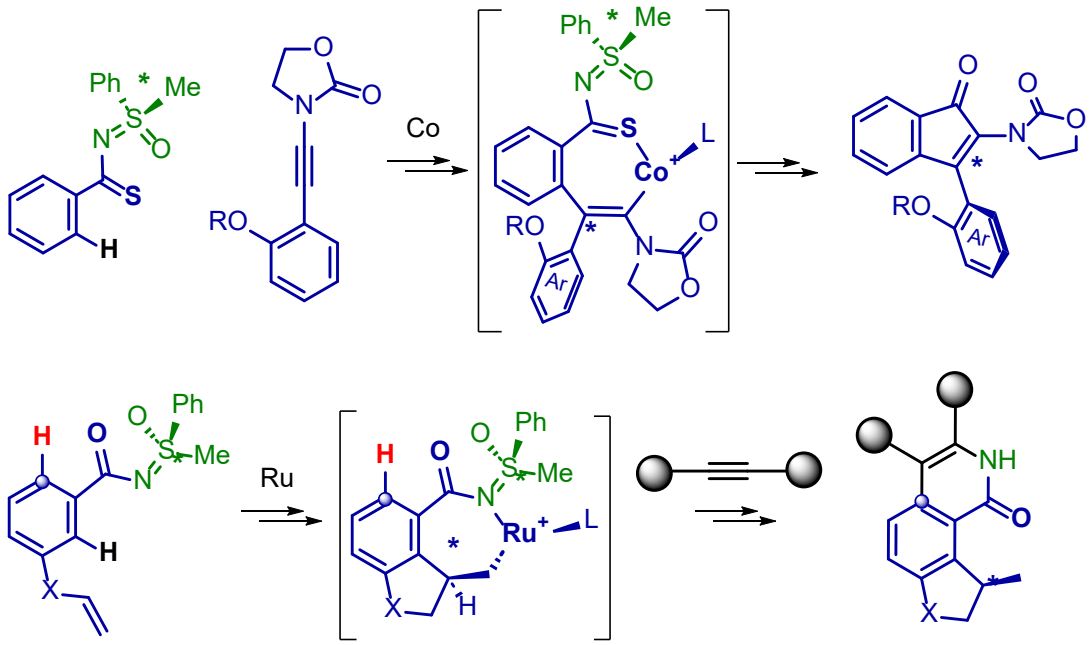
Mechanistic switches in sulfoximine-directed, transition metal-catalyzed C–H activation reactions enable the formation of distinct polycyclic compounds from readily available precursors.[1] This presentation will summarize the key factors that govern these unique cyclizations, where sulfoximines function not only as chiral directing groups but also as reactive moieties that spontaneously detach from the product once their role is fulfilled.



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THE IRIDIUM-CATALYZED BENZENE-METHANE DEHYDROGENATIVE COUPLING

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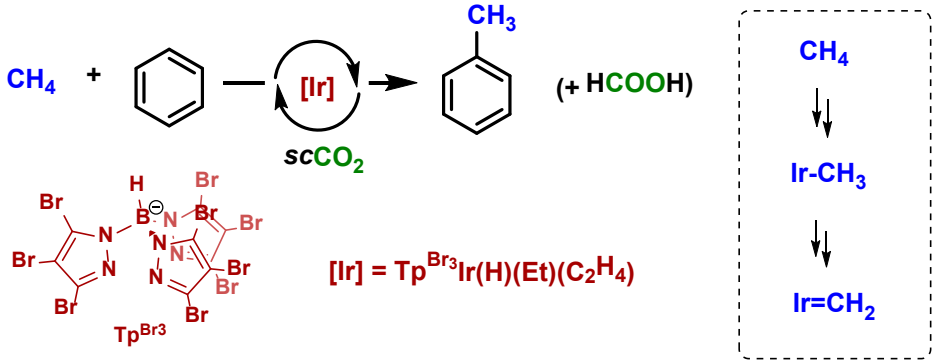
In the development of homogeneous catalysts for methane functionalization, methane was found to undergo dehydrogenation to Ir=CH_2 units, which further react with benzene to form toluene.[1] Such transformation represents a significant addition to the limited range of metal-catalyzed methane functionalizations. This method was similarly applied to ethane to produce ethylbenzene. These reactions proceed through methylidene or ethylidene intermediates (Ir=CHR, R = H, Me) resulting from double dehydrogenation. The mechanism is corroborated by experimental results, DFT calculations, and microkinetic modeling.



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HIGH CONCENTRATION RING CLOSING METATHESIS FOR EFFICIENT SYNTHESIS OF MACROCYCLIC MUSK COMPOUNDS

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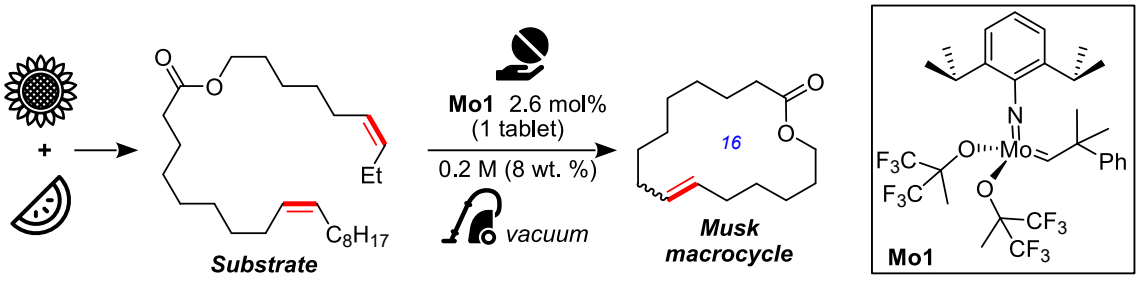
Macrocyclic musk compounds are valuable raw materials for the flavor and fragrance industry, and olefin metathesis reaction, since Fürstner's pioneering research,[1] has been a convenient method for their synthesis.[2] For many years, macroRCM was carried out at high dilutions to avoid the formation of undesired side products, but recently there has been increasing attention to designing catalysts that allow to increase the reaction concentration to 0.02-0.1 M.[3] The employment of reactive distillation, which allows the preparation of musk-scented compounds in the presence of both ruthenium and molybdenum catalysts at concentration of 0.2 M or higher, makes us prominent participants in this general trend.[4] During the presentation I will highlighted our key findings.



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DIGITAL APPROACHES IN REACTIONS INVOLVING CYCLIC COMPOUNDS

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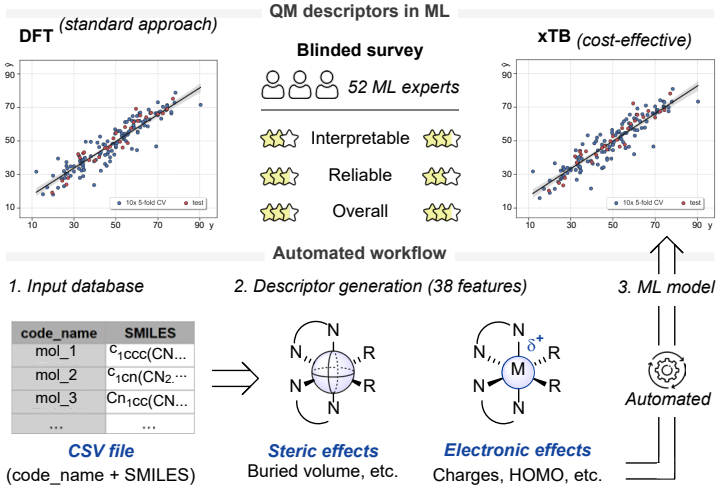
Cyclic compounds are often observed as intermediates in reaction mechanisms. Driven by the growing demand for digitalization, techniques such as Density Functional Theory (DFT) and machine learning are gaining increasing popularity in mechanistic studies. In this work, we first present computational mechanistic studies of a P-based coupling reaction designed to achieve hydroxylation and amination using H_2O and ammonia.[1] The DFT calculations revealed an unexpected cyclic intermediate as the driving force of the reaction, representing an important difference compared to its preceding couplings.[2],[3]

Then, machine learning strategies to predict the reactivity of cyclic compounds will be introduced, using a C–C homologation as an example.[4] We first present our initial approaches based on DFT calculations and then introduce our newest automated workflows,[1] aiming to democratize and popularize the use of machine learning within the broader chemistry community (Figure 1).



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BORON-MEDIATED REMOTE CARBON MIGRATION FOR RING-CLOSING TRANSFORMATIONS

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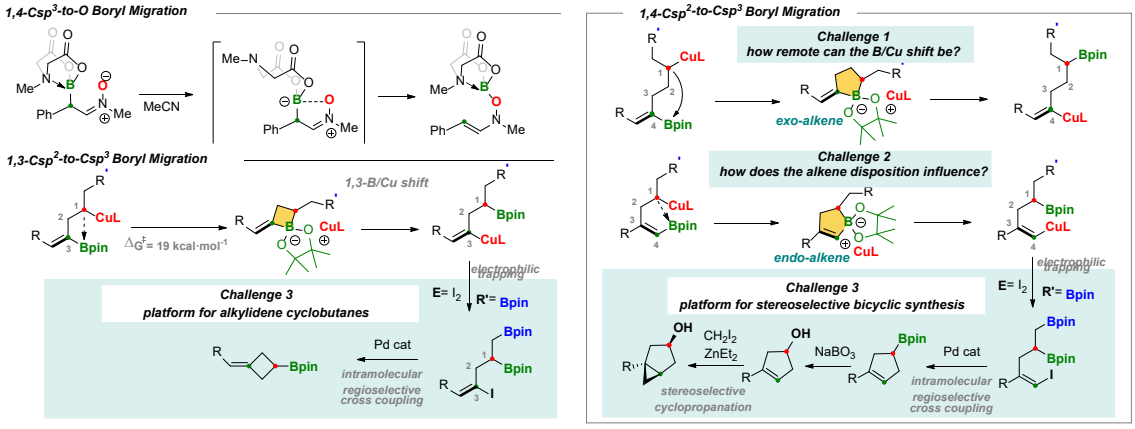
Migration reactions provide ingenious strategies to translocate reactive sites to positions that are otherwise difficult or inaccessible, enabling synthetic transformations that would be challenging through conventional approaches. While single-site migration has been extensively explored, often with excellent regio- and stereocontrol, the simultaneous migration of two remote sites along a carbon chain remains largely underdeveloped. This is primarily due to the exponentially increased complexity in controlling chemo-, regio-, and stereoselectivity. In this context, boron-mediated transformations have emerged as a powerful solution: the ability of boron to form stable yet reactive boronate complexes allows the concerted migration of distant carbon centers, enabling the construction of complex cyclic architectures with high stereochemical fidelity.[1,2] Such reactions are particularly useful for the assembly of small-sized rings, spirocycles, and fused polycyclic scaffolds, which are challenging to construct via conventional strategies.[3,4]



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BEYOND PLANAR AROMATICITY: DEFINING 3D-AROMATICITY WITH ILLUSTRATIVE EXAMPLES

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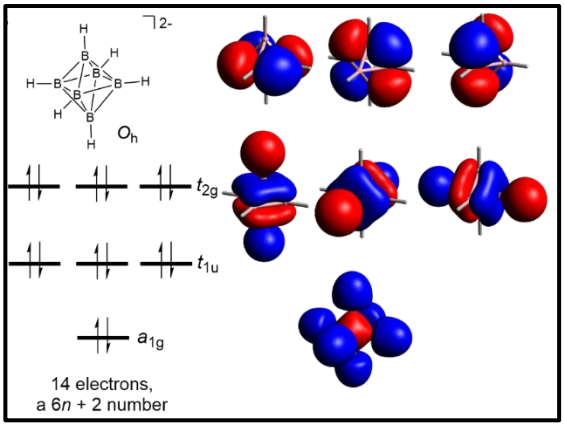
A number of π-conjugated macrocycles with puckered or cage-like structures exhibiting aromatic character according to both experiments and calculations have been recently reported. We look at their electronic structures and compare them to 2D-aromatic polycyclic aromatic hydrocarbons and three-dimensional (3D) aromatic compounds (such as closo boranes). We discover that the macrocycles investigated up to this point should be classified as 2D-aromatic with three-dimensional molecular structure (2D-aromatic-in-3D) and not as really 3D-aromatic using qualitative theory paired with quantum chemical calculations.[1] We discuss the requirements for a molecule to be consider 3D-aromatic. Among them, we conclude that they should have highly symmetric structures (or nearly so), leading to (at least) triply degenerate molecular orbitals, and for tetrahedral or octahedral molecules an aromatic closed-shell electronic structure with 6n + 2 electrons. Then, the aromaticity of *closo* and *nido* boranes and carboranes[2,3] as well as that of some inorganic cages[4,5] is discussed.



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CYCLOADDITION REACTIONS OF ARYNES AND ALKYNES IN THE SYNTHESIS OF NANOGRAPHENES AND UNCONVENTIONAL POLYCYCLIC CONJUGATED SYSTEMS

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The discovery of graphene and other carbon-based materials has marked the beginning of a new paradigm in materials science, where synthetic organic chemistry plays a key enabling role. In this context, the controlled bottom-up preparation of nanoscale graphene fragments (nanographenes) and other polycyclic conjugated hydrocarbons (PCHs) with defined geometries and tunable electronic properties continues to attract considerable attention. Among the available strategies, aryne intermediates have proven to be exceptionally powerful synthetic tools, offering efficient and often convergent routes to complex aromatic polycycles.[1,2]

In this lecture, some recent contributions from our group to this field will be presented, with particular emphasis on the use of polycyclic arynes and bisaryne precursors for the straightforward access to extended and/or structurally complex aromatic architectures. Our efforts towards the synthesis of singular aromatics and relevant π-functional materials will be showcased, including selected examples resulting from the successful combination of solution-phase chemistry based on [4+2] or metal-catalyzed [2+2+2] aryne cycloaddition reactions with the on-surface transformation of the thus-prepared polycyclic precursors.[3] Furthermore, examples of the onsurface reactivity of unconventional polycyclic conjugated systems such as [N]phenylene derivatives and cyclobutadiene-containing oligoacenes will be also presented.[4,5]

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INTEGRATED COMPUTATIONAL FRAMEWORKS FOR EXPLORING FREE ENERGY LANDSCAPES IN THE LIGHT OF SYNTHESIS AND FUNCTIONALIZATION OF CYCLIC COMPOUNDS

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Computational chemistry has evolved into a cornerstone for accelerating experimental discovery, yet its predictive power remains tethered to the quality of the underlying chemical and computational models. As we seek to guide experimental design with higher precision, the field is undergoing a paradigm shift: moving away from static, single-structure calculations in implicit media toward ensemble-based, dynamic explorations that incorporate explicit solvation. While this transition offers a more realistic representation of the chemical environment, it introduces significant hurdles in computational scaling, data interpretation, and model reliability. [1]

In this presentation, I will discuss recent methodological developments aimed at navigating these complexities across various systems. I will begin by discussing a static exploration of a catalytic mechanism,[3,4] highlighting the necessity of moving beyond simplified chemical models to ensure mechanistic reliability. This foundation is then further refined at the computational level through microsolvation strategies that identify and incorporate the most critical solvent-solute interactions.[5, 6]

Combined, these advancements provide a more robust framework for mapping the free energy landscapes of complex systems, ultimately moving us closer to a truly predictive understanding of reactivity in solution.

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PHOTOCHEMICAL BF_3-CATALYZED OXO-DIELS-ALDER REACTIONS: A MECHANISTIC STUDY

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Understanding the mechanistic details of chemical reactions is essential for controlling reactivity, improving selectivity and designing more efficient synthetic protocols. In this study, we explore the mechanism of an oxo-Diels-Alder reaction[1] promoted by BF_3. Using a thiazolonic substrate bearing a phenyl ring as a model system, competing pathways were studied with Density Functional Theory (Figure 1). Spectroscopic evidence, including transient absorption and emission lifetime measurements, supports the involvement of excited reactive species. Under blue light irradiation, the starting thiazolone is excited and undergoes a rapid radical recombination with styrene. The resulting diradical intermediate undergoes IC to a closed-shell singlet zwitterion, which cyclizes intramolecularly to form the dihydropyranothiazole core. The corresponding thermal reaction proceeds with the same product but lower conversion, attributed to a higher barrier.

In line with other recent studies,[2] this work underscores the value of integrating computational modeling with experimental analysis to uncover mechanistic pathways and rationalize observed reactivity trends.

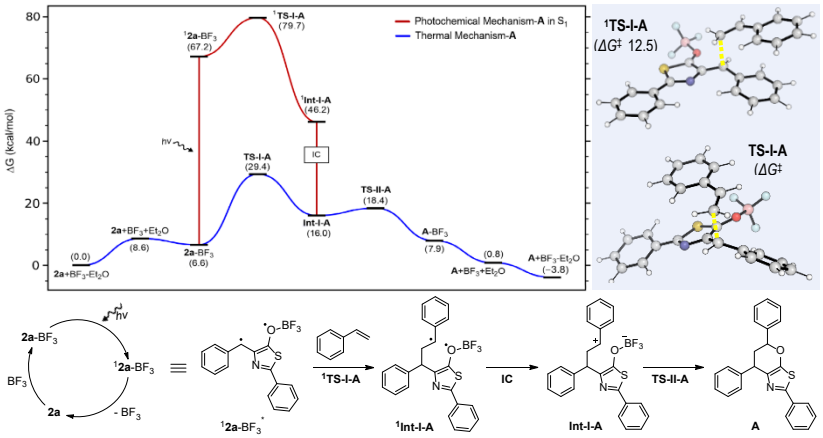

Figure 1. Pathways of the oxo-Diels-Alder reaction studied.

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RH-CATALYZED CYCLOADDITION CASCADE OF ALLENYNES AND MALEIMIDES

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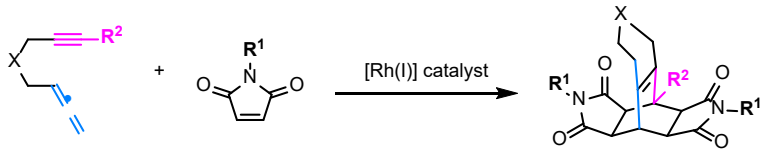
Transition-metal-catalyzed cyclization reactions are powerful tools in modern synthetic organic chemistry, enabling the formation of multiple bonds and/or stereogenic centers from nonactivated C–C unsaturated substrates such as alkynes, allenes, and alkenes with high atom economy.[1] Allenes, in particular, offer unique unsaturation patterns for the construction of novel cyclic structures, although controlling selectivity remains challenging.[2] Fine-tuning the catalytic system and reaction medium is a key strategy to address this issue.[3]

In this work, we present our latest advancements in the development of a novel cyclization process that involves allenynes and maleimide derivatives using a rhodium catalyst, enabling the efficient synthesis of bicyclo[2.2.2]oct-7-ene derivatives (Scheme 1). Experimental and theoretical studies indicate that the reaction described herein proceeds via a tandem cycloaddition/Diels–Alder sequence, in which a noncanonical [2 + 2 + 2] cycloaddition with one maleimide generates a conjugated diene that subsequently reacts with a second maleimide in a thermal Diels–Alder reaction. Such behavior contrasts with prior reports where the process follows the formation of a non reported, vinylallene intermediate.[4]

Our findings highlight the versatility and efficiency of this transition metal-catalyzed cascade reaction allowing precise control over chemo- and diastereoselectivity. This approach not only simplifies the synthesis of complex polycyclic structures but also enhances our understanding of selectivity in cyclization reactions.



Scheme 1. General reaction between 1,6-allenyne and maleimide derivatives

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EXPLORING THE INTRAMOLECULAR CHEMISTRY OF IRON(V)-OXO-CARBOXYLATO SPECIES

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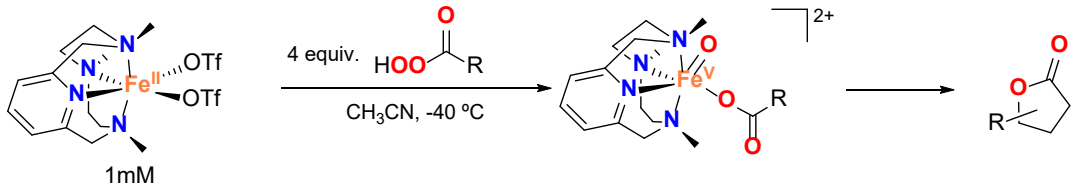
The development of iron(V)-oxo synthetic models that can mimic the reactivity of the iron-oxygenases that are found in nature is an important challenge. Their characterization though, has been hampered due to their high reactivity. It is important to highlight that iron(V)-oxo-carboxylato species have been postulated as the key compounds in the catalytic oxidation of carboxylic acids that leads to the formation of γ-lactones[1]. In this work, the intramolecular reactivity of an iron(V)-oxo-carboxylato species, $[Fe^{V}(O)(OC(O)R)(PyNMe_3)]^{2+}$, reported in the QBIS-CAT research group has been studied[2].It has been observed that both the accumulation of the iron(V)-oxo-carboxylato compound and the formation of the corresponding γ-lactone are affected by the strength of the γ-C-H bond. Moreover, it could be observed that the iron(V)-oxo-carboxylato species is directly related to the formation of the corresponding γ-lactones by following the formation of the lactone along the formation and the decay of the high-valent species. Also, through intra and intermolecular reactivity competition studies, it has been confirmed that the iron(V)-oxo-carboxylato species is directly related to the formation of the γ-lactones. Finally, mechanistic studies are being carried out to gain more insight into the mechanism for the formation of the γ-lactones.



Generation of $[Fe^{V}(O)(OC(O)R)(PyNMe_3)]^{2+}$ species by reaction of $[Fe^{II}(PyNMe_3)(OTf)_2]$ with different peracids at -40 ºC in acetonitrile followed by the γ-lactone formation.

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MECHANISM-DRIVEN ENGINEERING OF PHOTOENZYME CvFAP TOWARDS NEW-TO-NATURE DECARBOXYLATIVE RADICAL CYCLIZATION

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The fatty acid photodecarboxylase from *Chlorella variabilis* (CvFAP) decarboxylates fatty acids via light-driven catalysis, using the flavin adenine dinucleotide (FAD) cofactor to generate carbon-centered radical intermediates.[1] While these highly reactive, short-lived radical intermediates are difficult to control, this work repurposed CvFAP's natural reactivity towards intramolecular C-C bond formation, using carboxylic acid substrates to perform decarboxylative radical cyclization reactions. Mechanistic studies between the native decarboxylation reaction and the novel cyclization pathway demonstrated that CvFAP can promote 5-*exo*-trig radical cyclization (Figure 1).[2]

To optimize the experimentally characterized process, we employed a rational design of enzyme variants supported by density functional theory calculations and molecular dynamics simulations. These analyses elucidated the mechanistic requirements governing the transient radicals, revealing how synergistic mutations remodel the active site to favor substrate folding and productive pre-organization for cyclization, also by disfavoring binding modes that lead to the native proton-coupled electron transfer pathway. Our computational modelling guided next rounds of protein engineering, leading to a more efficient and selective enzyme: M4 variant achieved an 80% selectivity, a significant increase from the 1% yield observed in the original enzyme. This study demonstrates CvFAP's malleability and the power of computationally guided engineering in redirecting radical intermediates toward high-value synthetic reactivities.

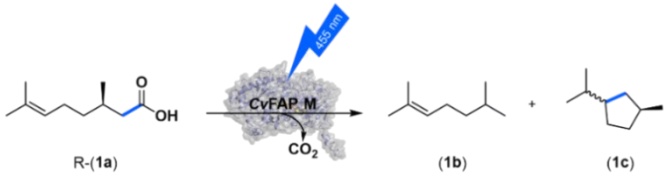

Figure 1. Biocatalytic decarboxylation of R-(1a) to the linear alkene (1b), and intramolecular cyclization to the cyclic product (1c).

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SKELETAL REARRANGEMENT OF BIARYLS VIA RHODIUM-AZIRINE INTERMEDIATE: A ROUTE TO SOLID-STATE EMISSIVE POLYCYCLIC SULFAMATES

Nil Insa-Carreras[a], Àlex Díaz-Jiménez[a], Andrea Pinto[b], Laura Rodríguez[b], Albert Poater[a], Anna Roglans[a], and Anna Pla-Quintana[a].

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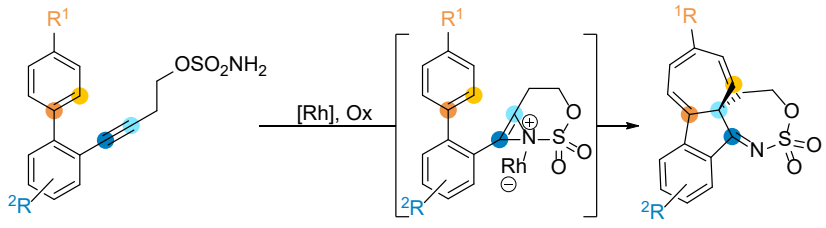
Metal nitrene species play an important role in nitrene-transfer reactions, enabling the formation of C-N bonds and allowing nitrogen-containing building blocks to be introduced into organic molecules.[1] Remarkably, nitrene reaction with alkynes[2] have emerged as a straightforward way to construct fused polycyclic molecules.

We report a new rhodium-catalyzed cascade reaction of alkyne-tethered biaryl sulfamates, that enables the construction of spirocyclic cycloheptatrienes with a high solid-state fluorescence.[3] Detailed mechanistic studies, supported by density functional theory (DFT) calculations, reveal a key rhodium-bound azirine intermediate that undergoes a dearomative single-carbon insertion into the biaryl framework. This reaction proceeds via a distinct, noncarbene-based pathway, expanding the scope of nitrene-mediated rearrangements beyond classical Büchner-type mechanisms. The method provides a modular route to structurally complex and photoactive scaffolds through rationally designed cascade processes.



- Rh-catalyzed nitrene-alkyne spirocyclization.
- Azirine-mediated dearomative C-insertion.
- Solid-state fluorescence tunable by substituents.
- Up to 71% quantum yield.

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COMPUTATIONAL STUDY OF THE CATALYZED CYCLOADDITION REACTION OF CO_2 TO PROPYLENE OXIDE IN A BIPHASIC MEDIA

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[b] *Department of General Chemistry: Algemene Chemie (ALGC), Vrije Universiteit Brussel, Belgium*
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The reaction of carbon dioxide with epoxides to form cyclic carbonates converts a greenhouse gas into valuable chemicals, supporting carbon utilization and greener, more sustainable chemical production. This work investigates the catalyzed cycloaddition reaction of propylene oxide to carbon dioxide (CO_2) in a biphasic media using computational chemistry methods. The system is defined in a box with periodic boundary conditions in which there is an explicit water layer and an implicit organic (epoxide) layer. The catalyst for the reaction is a compound formed by an iodine anion and an organic amphoteric cation that is lodged in the interphase,[1] and the reaction is thought to follow the epoxide activation mechanism, consisting of the epoxide activation, a nucleophilic attack that causes the opening of the epoxide, the insertion of the CO_2 molecule and the closing of the corresponding cyclic carbonate ring.[2]

Molecular dynamics calculations are performed in VASP to better understand the evolution of this reaction, and to allow for the exploration of various types of interactions without the need for pre-defined force fields, since they are calculated directly from the electronic density, which is useful in systems with complex bonding environments such as this one.

This study highlights the importance of solvent polarity and hydrogen bonding interactions in facilitating the reaction. Key findings indicate that the reaction proceeds through a concerted mechanism, with significant barriers that can be lowered by optimizing reaction conditions. Furthermore, the occurrence of the reaction in the interphase region has a key role on the feasibility of the mechanism, since it allows a point of easy contact between the organic-soluble epoxide and the hydrogen bond donor groups of the catalyst, which are needed for the activation step.

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SYNTHESIS AND CHARACTERIZATION OF COF-METAL NANOPARTICLE HYBRIDS FOR CATALYTIC APPLICATIONS

Adrián Navarro, Roser Pleixats, Albert Granados, Jordi García-Antón, Adelina Vallribera, Laia Francàs, Carolina Gimbert-Suriñach, Xavier Sala

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The European Union (EU) has set an ambitious goal: to achieve net-zero CO_2 emissions by 2050, as outlined in the EU Green Deal approved in 2020.[1] A key component of this transition is the development of new, efficient, and robust materials capable of driving key electrochemical transformations such as the hydrogen evolution (HER) and oxygen evolution (OER) reactions.[2] Covalent Organic Frameworks (COFs) provide high crystallinity, ordered porosity, and well-defined organic linkages, enabling the precise control of chemical environments at the nanoscale. Their catalytic performance can be significantly enhanced through the incorporation of active metal nanoparticles (MNPs).[3] In this work, we develop COF@MNP hybrids using two complementary synthetic approaches. In the first route, MNPs are generated *in situ* within pre-formed COFs, and in the second strategy, pre-synthesized MNPs are used as nucleation centers for framework growth, leading to core-shell-like hybrid architectures. Together, these methods enable systematic control over metal dispersion and particle size. Characterization of the obtained porous hybrid materials confirms the effective integration of the MNPs while preserving the crystallinity and structural integrity of the COF. HRTEM (Figure 1a), SEM, and STEM-HAADF (Figure 1b) reveal the crystalline lattice planes of the MNPs, the framework morphology, and the dispersion of the incorporated nanoparticles. In addition, electrochemical studies (Figure 1c) demonstrate the successful application of these hybrid materials in water splitting reactions. Comparative benchmarking against MNPs in the absence of COF support indicates that the hybrid materials improve catalytic activity and long-term stability.

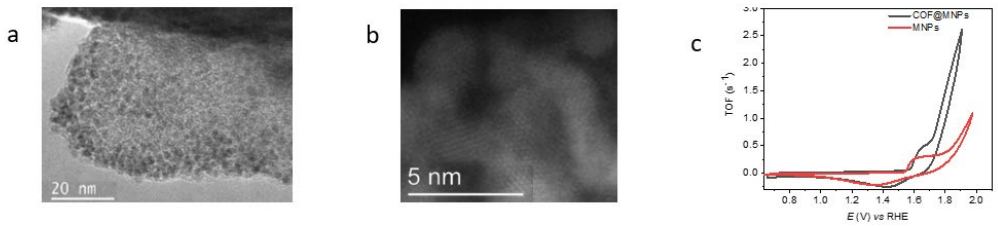

Figure 1. (a) HRTEM image of the COF@MNPs; (b) STEM-HAADF image showing lattice fringes of the MNPs; (c) TOF-normalized cyclic voltammograms for OER (borate buffer, pH 9) comparing MNPs (in red) and the COF@MNP hybrid (in black).

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INDUCTIVE DIASTEREOSELECTIVE RATIONALE FOR A CATALYTIC STRATEGY TO BUILD DENSELY CHIRAL FIVE-MEMBERED CARBOCYCLES

Carmen María Arenas-Baeza*[a], Eva Rivera-Chao[b], Paula Dominguez-Molano[a], Andrea Chaves-Pouso[b], Jorge J. Carbó[a], Martín Fañanás-Mastral[b,c], Elena Fernández[a]

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The access to highly-substituted cyclopentanes and cyclopentenes, bearing congested arrays of stereocenters within the cyclic frameworks, is an incentive in modern synthetic chemistry due to its presence in a wide range of bioactive molecules.[1-3] Here, we report a streamlined synthetic strategy for accessing stereocongested five membered carbocycles from enantioenriched branched borylated 1,4 dienes,[4,5] providing access to complex multi-stereogenic cyclopentane architectures. The method enables precise control over diastereoselectivity and enantiospecificity in the construction of adjacent stereocenters within the newly formed cyclic frameworks. DFT calculations provide understanding of the origin of diastereoselection along the Cu-catalyzed borylcupration step, allowing to establish a stereochemical model that rationalizes the key ligand-substrate and intrasubstrate interactions governing selectivity (**Figure 1**).

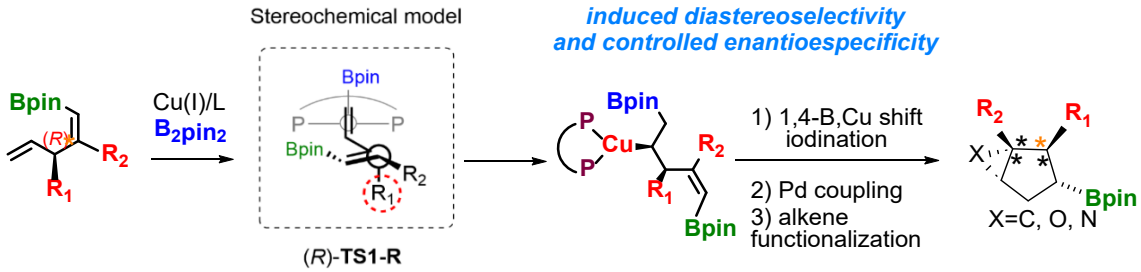

Figure 1. Catalytic sequential protocol to prepare stereocongested five-membered carbocycles from enantioenriched branched borylated 1,4-dienes

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DESYMMETRIZATION OF MALONIC MONOESTERS AND MALONIC ACIDS VIA ENANTIOSELECTIVE CATALYTIC C(SP^3) —H OXIDATION

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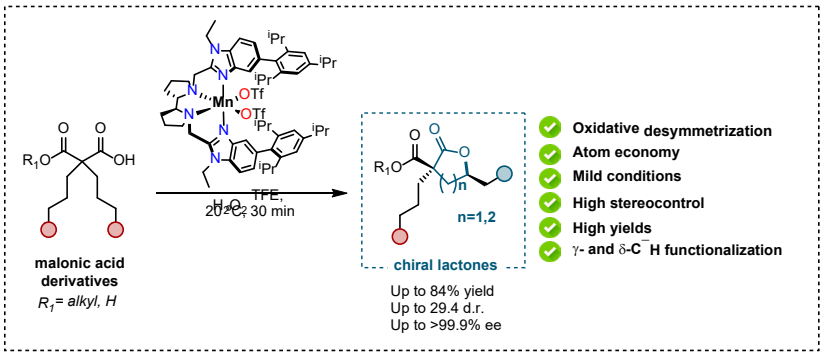
All-carbon quaternary chiral centers are present in a *plethora* of pharmaceutical and biologically active molecules. Due to this, there is an increasing interest in the development of new and efficient catalytic methodologies for the enantioselective construction of these motifs.[1] Malonates and their derivatives rank among the best candidates as they are highly accessible starting materials with low cost. Over the last years, different approaches based on hydrolysis, reduction and addition reactions have been developed to construct chiral malonates from simple substrates.[2-4] Although the desymmetrization of malonates based on C—H bond functionalization has not been reported previously.

Leveraging asymmetric *γ*-lactonization can provide high stereo control in the oxidation of non-activated C-H bonds, [5] herein we proved that this reaction can be applied in the desymmetrization of homo-disubstituted malonates and diacids. The reaction provides outstanding levels of regio- and enantiodiscrimination when using sterically encumbered Mn catalysts and H_2O_2 as the oxidant. Our approach enables straightforward and general access to quaternary chiral centered scaffolds that can be valuable intermediates for the synthesis of pharmaceutical and bio-active products.



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ARYL HALIDES REACTIVITY VIA FERRIOXALATE PHOTOCATALYSIS

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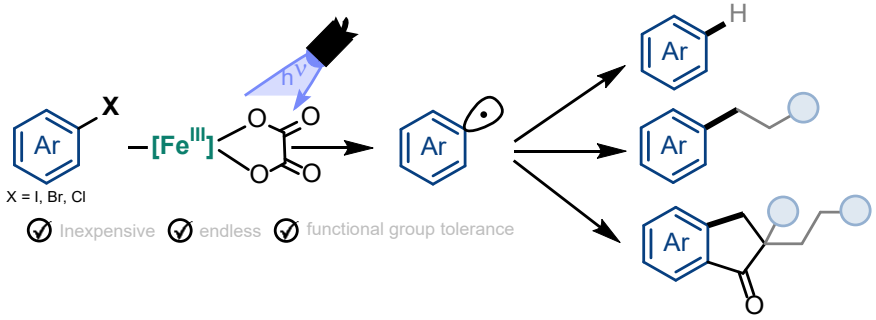
The development of new pharmaceuticals, agrochemicals and materials hinges on the use of palladium-catalysed cross-coupling reactions. This type of reactivity has made of aryl halides highly valuable building blocks for organic synthesis. However, although the use of palladium as a catalyst has a great importance in academic and industrial settings,[1] the high cost and the volatile availability of this metal represents a concern which is driving chemists to face the challenge of replacing reactions catalysed by this precious metal with more abundant and sustainable ones.[2] Among the various existing alternatives, iron has emerged as one of the most attractive and promising ones in view of its low toxicity and large abundance, among other desirable properties.[3] Despite recent advances in iron-catalysed methods, current methodologies still limit their applicability in organic synthesis.

In this work, we present the use of light as an unprecedented approach to overcome these limitations. To achieve this, we have made use of ferrioxalate photocatalysis[4] to access highly reducing low-valent iron species that enable the reduction of aryl halides to aryl radicals. Using this catalytic system we have carried out various reactions with aryl halides such as hydrodehalogenation, reductive Heck reaction and indanone synthesis, which demonstrate the versatility of this new system and the development of a new synthetic methodology.



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SYNTHESIS OF ALLYL-FUNCTIONALIZED CYCLIC DILACTONES FOR BIOCOMPOSITE APPLICATIONS

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Natural fibers-reinforced polymer composites represent sustainable and recyclable alternatives to conventional plastics and synthetic fiber-reinforced composites with competitive performance.[1] However, the intrinsic hydrophilicity and high polarity of natural fibers limit their compatibility with comparatively less polar polymer matrices, resulting in poor interfacial adhesion and suboptimal composite performance. Accordingly, the incorporation of a third component as a coupling agent can improve the interfacial compatibility between the fiber and the polymer matrix by promoting chemical interactions.[1,2] To achieve fully biocomposite materials, polylactide (PLA) and poly(butylene succinate) (PBS) are widely recognized among biopolymers, while various natural fibers serve as reinforcement due to their lignin, hemicellulose, and cellulose content.[2,3,4]

The development of fully bio-based reactive coupling agents constitutes an effective strategy to enhance fiber-matrix interfacial interactions in PLA-based biocomposites. In this work, an allyl-functionalized dilactone was synthesized through a multi-step procedure and employed as a monomer in ring-opening polymerization (ROP). The resulting polymer was subsequently chemically modified to generate a reactive coupling agent suitable for PLA/natural fiber composite systems.[5,6] The successful incorporation of functional groups along the polyester backbone provides a versatile platform for further chemical modification and interfacial engineering. This approach offers a promising route toward the design of fully bio-based reactive compatibilizers aimed at improving the performance and sustainability of PLA-based biocomposites.

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PREDICTING STEREOSELECTIVITY IN γ-LACTONIZATION THROUGH A SIMPLE COMPUTATIONAL MODEL OF THE REACTANT COMPLEX

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The stereoselective oxidation of non-activated C(sp^3)–H bonds is one of the most challenging yet powerful transformations in organic synthesis, as it enables direct access to stereochemically rich oxygenated scaffolds. However, because C(sp^3)–H bonds are ubiquitous in organic molecules, controlling site, diastereo, and enantioselectivity remains highly challenging. Recently, Costas and co-workers reported the site- and stereoselective γ-lactonization of non-activated primary and secondary C(sp^3)–H bonds by Mn complexes using H_2O_2 as the oxidant.[1][2] To fully exploit the potential of such bioinspired C(sp^3)–H oxygenation reactions, identifying the factors controlling selectivity, together with the development of predictive models, is of critical importance.

Herein, we present a simple, predictive, and robust computational methodology that, based on the analysis of the most stable reactant species, predicts the site of C(sp^3)–H oxidation. The predictive power of the model is consistent with the experimentally observed stereoselectivities and is further supported by the calculation of the reaction Gibbs free energy barriers. The methodology was evaluated on a series of chiral and prochiral carboxylic acids. Collectively, our results show that the site of oxidation can be rationalized by the relative orientation of the accessible γ- C(sp^3)–H bonds with respect to the reactive Mn-oxo unit.

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MECHANISTIC AND KINETIC STUDY OF THE ELECTROCHEMICAL CO_2 REDUCTION WITH A MANGANESE(I) CATALYST

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The atmospheric CO_2 concentration has been increasing since the 19th century due to the consumption of fossil fuels. CO_2 is notorious for absorbing IR radiation and re-emitting it back to Earth's surface, contributing to Global Warming. Despite that, CO_2 can be used for the synthesis of fuels and high-value products. The electrochemical reduction of CO_2 is an established framework that works under mild conditions, which allows the transformation of the latter into those products. Lloret-Fillol's group in 2018 developed a manganese(I) organometallic catalyst for the CO_2-to-CO reduction in anhydrous conditions that achieved maximum TOFs of 2100 s^{-1},[1] and when water ($[H_2O]$ ~ 0.5 M) was inserted into the reaction environment, it reached 39400 s^{-1}.[2]

The main goal of this study is to understand how the catalyst operates at low CO_2 concentrations, under dry conditions, and to determine the mechanism that explains the first-order dependency on $[CO_2]$ observed in kinetic experiments. To rationalize the experimental results, we have performed DFT calculations to determine different possible proton-assisted and anhydrous mechanisms and microkinetic simulations with COPASI.[3]

Our computational studies show that the previously proposed reductive dismutation mechanism[1] does not fulfill the kinetic conditions required to reproduce the experiments, since it does not show a first-order dependency in the experimental range. Furthermore, we revised the original proton-assisted mechanism[2] to comply with the dry experimental conditions and reformulated crucial steps for CO_2 insertions.

We found that the combined effect of CO_2 and H_2O in the rate-determining step leads to a first-order dependence with respect to $[CO_2]$ and an increase in the reaction order below $[CO_2]$ ~ 10^{-3} M, consistent with the experimental results.

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CHIRAL SELF-FOLDING CAVITAND RECEPTORS BASED ON CALIXARENE MACROCYCLES

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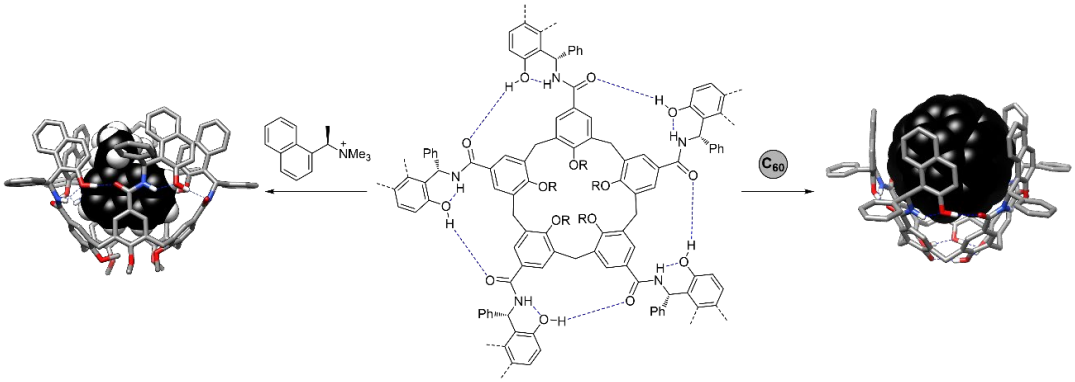
Self-folding cavitands are synthetic receptors that fold into hydrophobic concavities with the assistance of bio-inspired hydrogen bond networks.[1] These hosts have traditionally been built-up from resorcin[4]arenes, featuring relatively rigid structures and confined spaces of reduced volume that limit the emergence of meaningful applications. Recently, our lab has addressed these limitations by developing a new family of hosts based on calix[5]arene that display heightened dimensions and flexibility.[2-4] These receptors are stabilized in cone-shaped conformers by cooperative hydrogen bond networks, but benefit from the increased flexibility of the calix[5]arene scaffold thanks to a low degree of covalent restriction. The versatility of this approach is demonstrated with the development of a set of chiral and structurally diverse hosts with different shapes and molecular recognition properties. These hosts have been applied to the enantioselective molecular recognition of chiral guests,[3] and to the fine tuning of chiroptical response using achiral fullerene chromophores,[5] challenging the established notion that efficient chiral induction requires a rigid and highly preorganized confined space.



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FROM MOLECULAR COOPERATION TO METAL OXIDES IN THE SYNTHESIS OF CYCLIC CARBONATES

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The catalytic cycloaddition of CO_2 to epoxides constitutes a paradigmatic approach to the synthesis of five-membered cyclic carbonates, a class of cyclic compounds of high relevance as green solvents, electrolytes, and versatile intermediates for polymer and fine-chemical synthesis. In this talk we present a mechanistically evolution of catalytic systems for the efficient formation of cyclic carbonates under mild conditions progressing from molecular systems to heterogeneous materials. We initially developed cooperative homogeneous systems based on inexpensive alkali metal halides combined with highly nucleophilic aminopyridines. These systems enable selective carbonate formation at 60 °C and 1 bar CO_2. Experimental studies complemented by DFT calculations revealed a dual catalytic mechanism: aminopyridines promote epoxide ring-opening, while halide species facilitate CO_2 insertion and ring closure.[1] To enhance sustainability and recyclability, the nucleophilic component was subsequently immobilized onto polymeric resins, affording hybrid catalytic systems that preserve activity while enabling recovery and reuse.

Building upon the mechanistic understanding gained from molecular catalysis, we are currently extending this approach to fully heterogeneous metal oxide surfaces (SnO_2, ZnO, Al_2O_3). Periodic DFT investigations reveal how surface Lewis acid–base pairs and hydroxylation states modulate epoxide activation, CO_2 incorporation, and cyclic carbonate formation.[2]

Finally, we discuss emerging strategies to bridge homogeneous and heterogeneous catalysis, highlighting if single-atom catalytic sites on solid supports are a realistic alternative. The well-defined reactivity of molecular systems with the robustness of extended surfaces, may offer a promising platform for the next generation of CO_2-based cyclic compound synthesis.

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INVERSE PYRIDINE RHODIUM(I) CARBONYLS FOR METAL–LIGAND COOPERATIVE CYCLISATION

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Inverse pyridine pincer ligands[1] constitute a versatile platform for tuning the electronic properties of metal centres through functionalisation at the pendant nitrogen atom, while simultaneously enabling metal–ligand cooperative reactivity. In our recent work, metalation of a phosphine-based inverse pyridine ligand[2] yields a rhodium(I) chloride coordination polymer, from which two rhodium(I) carbonyl complexes were subsequently synthesised. These carbonyl complexes feature protonated and non-protonated pyridine backbones and were evaluated as catalysts for the cyclisation of 4-pentynoic acid (figure 1).[3] The inverse pyridine framework enables a cooperative interaction between the metal centre and the ligand. Our results suggest a mechanism in which protonation at the pendant nitrogen atom plays a key role in substrate activation, and also a substrate-mediated proton-shuttling step. Computational analyses provide further insight into the electronic structure of the complexes, and mechanistic studies support the proposed metal–ligand cooperative pathway.

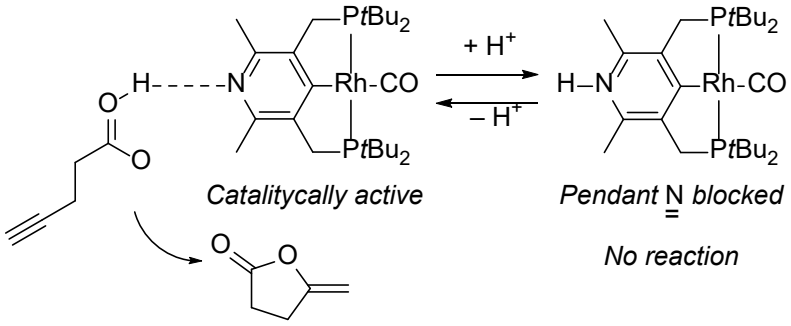

Figure 1. non-protonated and protonated inverse pyridine rhodium carbonyls, and the cyclisation of 4-pentynoic acid into the lactone product.

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ENANTIOSELECTIVE NITRENE TRANSFER REACTIONS ENABLED BY DIRHODIUM(II) CATALYSIS

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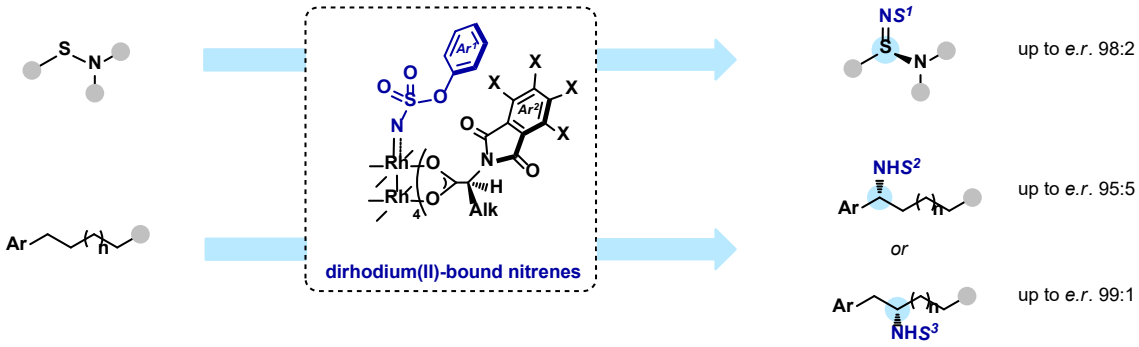
Nitrenes represent a powerful tool in organic synthesis for the formation of nitrogen-containing compounds. Recent developments in transition-metal-catalyzed transformations have further enhanced their synthetic utility by addressing chemo-, regio-, and enantioselectivity challenges.[1,2] This communication will focus on the use of electrophilic dirhodium(II)-bound nitrenes to achieve highly selective transformations.

1. The enantioselective synthesis of sulfinamidines via *S*-imidation, enabled by the combination of a suitable sulfamate as the nitrene source and a chiral dirhodium(II) tetracarboxylate catalyst, will be presented.[3,4]

2. The regio- and enantioselective amination of benzylic and homobenzylic sites, enabled by different combinations of reagents and catalysts, will be discussed.[5]



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SCALE-UP OF ENANTIOSELECTIVE CATALYTIC LACTONIZATION AT NONACTIVATED γ-C–H BONDS USING AFFORDABLE MANGANESE CATALYSTS

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Making added-value chiral molecules with high atom economy starting from readily available feedstocks is a routine task for Nature but a great challenge for synthetic chemists. Selective C(sp3)–H oxidation is a most interesting reaction in this respect, as it allows introduction of common oxygenated functionalities in a broad range of substrates without the need for preexisting functional groups. Unfortunately, in addition to the highly effective yet substrate specific oxygenases, only few examples of molecular catalysts are known to catalyze this kind of reaction. Most examples rely on noble metal complexes and/or functionalization of activated C–H bonds.
Over the last decade, our group has identified several manganese catalysts capable of effectively catalyzing selective oxidation of non-activated tertiary, secondary and primary C–H bonds under mild conditions.[1] A most notable example is the highly enantioselective γ-lactonization of carboxylic acids, providing chiral cyclic lactones in outstanding enantioselectivities (up to >99.9%) and yields (up to 96%) using H2O2 as a benign oxidant (Figure 1).[2] The applicability to a broad range of common substrates, the earth-abundant catalyst, the eco-friendly oxidant and the mild reactions conditions make this reaction particularly appealing with respect to sustainability and large-scale applications. However, scalability is limited by the need for complex, sterically encumbered ancillary ligands (Figure 1), making catalyst's cost prohibitive. This presentation will summarize our recent efforts to identify commercially available or easily synthesizable Mn catalysts for γ-lactonization of carboxylic acids. The synthesis of cyclic lactones on a multi-gram scale will be discussed.

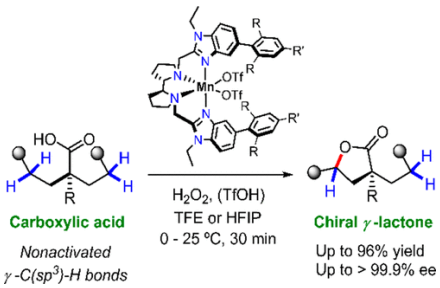

Figure 1. Mn-catalyzed, enantioselective γ-lactonization of carboxylic acids.[2]

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HYPERVALENT BROMINE DIMERIZATION: A STREAMLINED APPROACH TO BIPHENYLENE-EMBEDDED HELICOIDAL STRUCTURES

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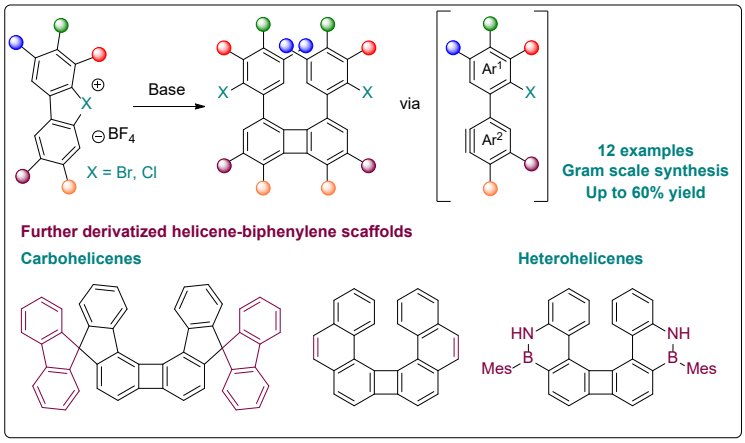
Biphenylene is regarded as a unique structure in organic chemistry due to the presence of an antiaromatic cyclobutadiene core embedded between two benzene rings. The strain and antiaromaticity associated with the four-membered ring give rise to intriguing electronic properties, such as small HOMO–LUMO gaps and high conductivity.[1],[2] However, current methodologies for the preparation of biphenylene scaffolds typically rely on high temperatures, transition-metal catalysis, or highly tailored starting materials. These requirements limit functional group tolerance and therefore restrict the array of accessible biphenylene derivatives. To address these challenges, we report herein the use of cyclic diaryl λ³-bromanes [3] as precursors for the synthesis of highly decorated biphenylenes, representing the first example of biradical reactivity of diaryl λ³-bromanes. Furthermore, subsequent chemical modifications provide access to a new approach for the construction of fluorescent carbo- and heteroatom-doped helicene-based biphenylene structures.



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CATALYTIC CARBOCYCLIZATION OF 1,5-BISALLENES FOR RAPID ASSEMBLY OF MOLECULAR COMPLEXITY

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Transition-metal-catalyzed cycloadditions provide powerful strategies for rapidly generating molecular complexity, although controlling regioselectivity in reactions of 1,5-bisallenes remains challenging.[1] We report two complementary catalytic platforms that address this limitation. First, a ligand-free Ni(0) catalyst enables highly selective head-to-tail [2+2+2] cycloadditions of bisallenes with acetylenes, delivering 6,6-fused hexahydroisoquinoline scaffolds which are privileged motifs in alkaloid and medicinal chemistry, under mild conditions with broad functional-group tolerance.[2] Computational studies reveal that selectivity arises from competing oxidative cyclization pathways in which the square-planar geometry of nickel metallacycles directs allene insertion towards the head-to-tail topology. In parallel, in-situ generated Pd(0) catalysis enables a regio- and stereocontrolled [2+2] carbocyclization-unsymmetrical difunctionalization cascades of 1,5-bisallenes, affording densely functionalized molecular frameworks. Together, these studies demonstrate how minimalist transition-metal systems can achieve precise selectivity while enabling rapid, atom-economical access to complex heterocyclic architectures.

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C–H BONDS OXIDATION OF CYCLIC HYDROCARBONS VIA RADICAL AND CATIONIC PATHS

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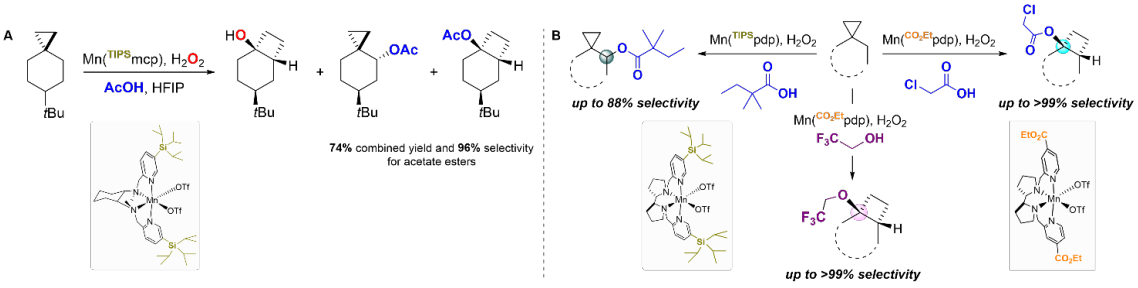
The conversion of C(sp^3)-H into C(sp^3)-O bonds constitutes a preferential modification in modern synthetic organic chemistry.[1] Among the numerous methodologies, C-H bond oxygenation executed by enzymes and bioinspired catalysts proceeds through a well-established HAT/OH rebound mechanism.[2] C-H functionalization products derived from competitive ligand transfer pathways are seldom observed and when they operate, the canonical hydroxylation reaction typically prevails.[3] Recently, we demonstrated that carboxylate transfer can be observed as main rebound pathway in manganese-catalyzed C-H oxidation of cyclopropane-containing hydrocarbons (Scheme 1A).[4]

Taking 6-tert-butylspiro[2.5]octane as model substrate, a new set of unrearranged and rearranged functionalized products has been obtained, by carefully modulating catalyst electronics and reaction conditions, with unprecedented control over chemoselectivity (Scheme 1B).[5] The scope of the reaction has been then extended to other cyclopropyl derivatives.



Scheme 1

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DFT INSIGHTS INTO THE MECHANISM OF γ-LACTONIZATION AND ENANTIOSELECTIVE ETHER DESYMMETRIZATION MEDIATED BY BIOINSPIRED Mn AND Fe COMPLEXES

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The selective functionalization of unactivated C(sp³)–H bonds is a major challenge in modern organic synthesis. Bioinspired high-valent transition metal complexes, particularly of manganese and iron, have emerged as powerful catalysts for these transformations.

First, we investigated the carboxylic acid-directed γ-lactonization of unactivated primary C–H bonds catalyzed by chiral Mn complexes [1]. DFT analysis reveals that the reaction proceeds via a rebound mechanism initiated by an unusual intramolecular 1,7-hydrogen atom transfer (1,7-HAT). This step occurs from a primary γ-C–H bond to a highly reactive Mn(V)-oxyl intermediate, generating a carbon radical that rapidly undergoes carboxylate transfer. Later, we extended the analysis to well-defined iron(V)-oxo-carboxylato species [2]. DFT calculations corroborate that the oxo moiety executes a selective C–H cleavage at the carboxylate's γ-position. Parallel to the Mn system, this involves the rare 1,7-HAT step, followed by a fast carboxylate rebound ensuring stereoretentive γ-lactone formation.

Finally, we studied the enantioselective C(sp³)–H bond oxidation of 1,3-meso diethers catalyzed by a sterically encumbered chiral Mn-oxo species [3]. Computational studies reveal the the initial HAT is followed by an electron transfer (ET) event and a rapid rebound. This sequential HAT-ET process leads to a chiral cationic intermediate, enabling the highly enantioselective desymmetrization of the cyclohexane derivatives.

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MODELLING CYCLIZATION REACTIONS INSIDE NANOCAVITIES

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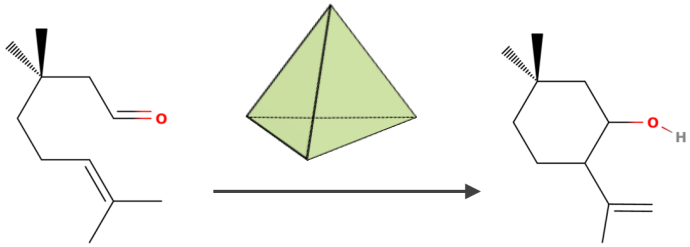
The synthesis of cyclic compounds through carbon-carbon bond-forming processes is a cornerstone of organic chemistry, often requiring harsh acidic conditions to proceed efficiently. Supramolecular coordination cages, such as the $[Ga_4L_6]^{12-}$ metallocage, have emerged as transformative catalysts capable of facilitating these cyclizations under neutral or even slightly basic conditions. [1]

This work employs multiscale modeling, combining molecular dynamics (MD), DFT, and QM/MM calculations to elucidate the molecular origins of catalysis[2] for two key processes: the Nazarov[3] cyclization of 1,4-pentadien-3-ols and the Prins cyclization of citronellal. [4] By comparing reactions in confinement versus bulk solution the results reveal that the metallocage acts as a source of acidic environment, significantly increasing the basicity of encapsulated alcohols. Preorganization, however, does note play the expected role. These insights provide a roadmap for the design of synthetic hosts that functionalize and cyclize small molecules with better performance.



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GENERAL ACCESS TO CHIRAL PIPERIDINES VIA ENANTIOSELECTIVE HAT-INITIATED C(sp^3)–H OXIDATION

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Enantioselective C(sp^3)–H functionalization reactions are appealing synthetic organic chemistry tools to streamline access to valuable chiral molecules from simple precursors.[1-2] Chiral piperidines are ubiquitous motifs in pharmaceuticals and natural products, yet methods for their preparation from simple non-chiral precursors remain limited.[3] We report a catalytic strategy for the preparation of chiral piperidines by site-selective α-C(sp^3)–H oxidation of achiral piperidines using hydrogen peroxide as oxidant and an evolved manganese catalyst in 2,2,2-trifluoroethanol. Piperidines are desymmetrized to afford chemically versatile chiral *N,O*-acetal products in good yields, with high enantio- and diastereoselectivity. The resulting products serve as key intermediates to access a diverse range of functionalized piperidines while retaining chirality. Mechanistic studies indicate that the reaction proceeds via a highly enantioselective hydrogen atom transfer followed by an electron transfer to generate a chiral iminium cation that is rapidly hydroxylated. Statistical models correlating reaction performance to molecular features provide a mechanistic basis for the stereoselective dictating elements and offer a tool for future reaction development.

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ELECTROSTATIC AND CONFORMATIONAL CONTROL OF AROMATIC O- VS. N-METHYLATION IN SAM-DEPENDENT METHYLTRANSFERASES

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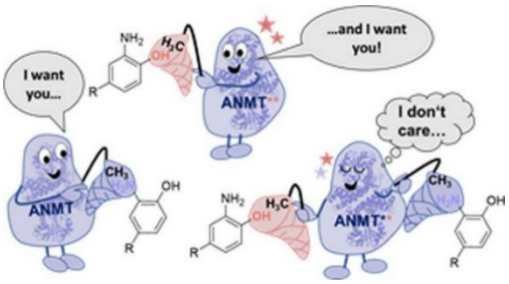
Traditional methylation methods in the chemical industry usually rely on toxic reagents, motivating the development of sustainable strategies like biocatalysts. *S*-Adenosyl-L-methionine (SAM)-dependent methyltransferases (MTs) catalyze most methyl transfer reactions in living organisms. They belong to a large family of enzymes that diversified over millions of years to chemoselectively functionalize oxygen, nitrogen, and carbon moieties of aromatic substrates.[1]

In this work, we combined molecular dynamics simulations, data analysis techniques, and electrostatic modeling to rationalize the difference in chemoselectivity among a set of evolutionarily related *N*- and *O*-MTs.[2] Our computational models reveal distinct open/closed conformational dynamics in the MTs' active site that modulate nucleophile preference, a finding confirmed by hydrogen/deuterium exchange mass spectrometry experiments. We finally demonstrate that non-conserved polar active site residues control the local electrostatic environment, which alters the conformational ensemble and ultimately determines which aromatic substituent is methylated. These findings provide insights for the rational design of improved SAM-dependent methyltransferases.



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AXIAL-TO-POINT CHIRALITY TRANSFER IN CYCLOPROPANATION REACTION

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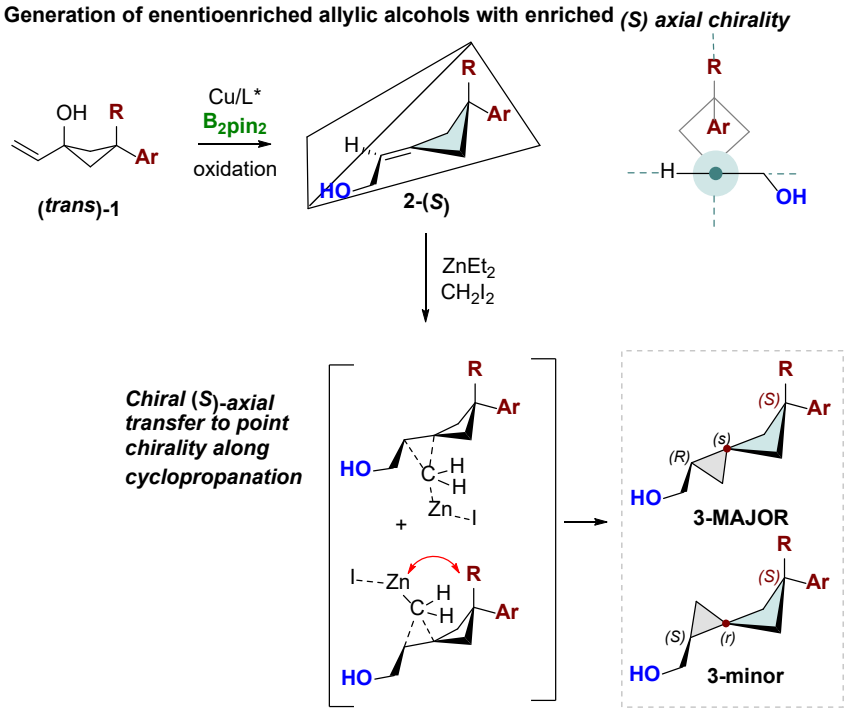
A robust method to generate cyclopropanes is the use of diiodomethane (CH_2I_2) with zinc complexes, which facilitates the addition to alkenes via a metal "carbenoid" species.[1] The desymmetrization of 1-vinylcyclobuta-1-ols (trans)-1 through an asymmetric Cu-catalyzed borylation, renders axially chiral allylborane systems 2-(S), with high asymmetric induction by precise selection of the chiral ligand.[2] The enantioenriched alkylidenecyclobutanes served as chiral platform to prove the conceptually challenging transference of the axial-to-point chirality through one new stereocenters and one pseudoasymmetric carbon generated via cyclopropanation, without enantioselective erosion (Figure).



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SUPRAMOLECULAR MASK–ASSISTED REGIO AND CHEMO-SELECTIVE SYNTHESIS OF FULLERENE DERIVATIVES VIA RADICAL ANION MECHANISM

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Fullerene derivatives exhibit enhanced properties compared to pristine fullerenes in various fields, including organic photovoltaics, perovskite solar cells, and biological applications. In recent years, researchers synthesized regioisomerically pure fullerene isomers via supramolecular mask strategy by utilizing Bingel-Hirsch reaction[1], Prato reaction[2] and Diels alder reaction[3]. A rapidly evolving approach is the radical anion pathway[4,5], which offers promising opportunities for fullerene functionalization.

In this work, we design heteroleptic supramolecular cages using bimetallic macrocycle based in Pd and H-TCPP (Tetrakis (4-carboxyphenyl) porphyrin), Zn-TCPP[6] and Pd-TCPP. The self-assembly reaction yields tetragonal prismatic cage capable of encapsulating large guests, such as fullerene. This supramolecular platform allows us to study the generation and stabilization of fullerene radicals within confined spaces provided by the cavities of the cages. Stability studies of the C_{60} radical anion within these cages revealed that the electronic and structural properties of the porphyrin cores significantly influence radical generation and stabilization. The long-lived C_{60} radical anions within confined spaces enable us to investigate the selectivity imposed by the cage towards the functionalization of C_{60} through radical-based pathways, coupled to the regioselectivity imposed by the supramolecular nanocage.

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COMPUTATIONAL EVIDENCE ON A MODULAR FAMILY OF CHIRAL CAVITAND RECEPTORS: TUNING THE CHIROTOPICAL RESPONSE OF ACHIRAL FULLERENE GUESTS

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Based on calix[5]arene,[1][2] a new family of self-folding cavitands[3][4] has been introduced by the Team Supra, which are capable of caging fullerene-like structures as well as tuning their chiroptical response. In parallel, the diverse structures, flexible conformations, and efficient guest binding have been investigated computationally by the Swart lab. DFT[5] studies and NCI analysis were carried out to understand and visualize the properties of this set of host-guest systems. The alignment of experimental and computational results was found with ECD.[6] Furthermore, MD[7][8] studies guided the trajectories as well as the interaction energy change. MD[7][8] studies are done in both implicit and explicit solvent modes to recognize the involvement of the solvent. The computational studies played an important role in unveiling the reason behind the conformational flexibility, interaction-repulsion forces, molecular stability, and fullerene binding efficiency. These are the modular nature of the cavitand scaffolds that provide a suitable environment to the fullerenes for tuning the chiroptical response across the visible spectrum.

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AMINO-ACID DONOR PROMISCUITY OF LBCA TRPB REVEALS DISTINCT REACTIVITY IN THE TRYPTOPHAN SYNTHASE COMPLEX

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Last Bacterial Common Ancestor (LBCA) tryptophan synthase β-subunit (TrpB) is a PLP-dependent enzyme that catalyzes L-tryptophan formation from indole and L-serine via a common aminoacrylate intermediate. Unlike many extant TrpBs, which are weakly active as isolated subunits and rely on allosteric activation by TrpA, LBCA TrpB has been reported to retain substantial stand-alone activity. [1-2]

In this study we quantify the amino-acid promiscuity of isolated LBCA TrpB and compare its reactivity profile to TrpB when in complex with TrpA, i.e. in the native tryptophan synthase assembly (TrpS; αββα), focusing on amino-acids that can access the same reactive intermediate through β-elimination. Under unified conditions, stand-alone LBCA TrpB rapidly converts L-serine to L-tryptophan, whereas the TrpS complex accumulates product more slowly. In contrast, with the non-canonical donor L-threonine (β-methyltryptophan formation), the preference reverses: TrpS outperforms stand-alone TrpB across the time course, reaching near-complete conversion while isolated TrpB remains comparatively sluggish.

Broadening the donor panel, stand-alone LBCA TrpB accepts multiple alternative amino-acids (D-serine, L-cysteine, O-phospho-L-serine, O-acetyl-L-serine), yielding L-tryptophan and supporting convergence to a shared intermediate. Overall, these results position LBCA TrpB as a promiscuous stand-alone catalyst for amino-acid donor variation, and show that complex assembly can reweight donor preference, favoring L-serine for isolated TrpB but L-threonine in the αββα complex.

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PHOTOCATALYTIC C–H FUNCTIONALIZATION AND RING OPENING OF SATURATED AZA-HETEROCYLES

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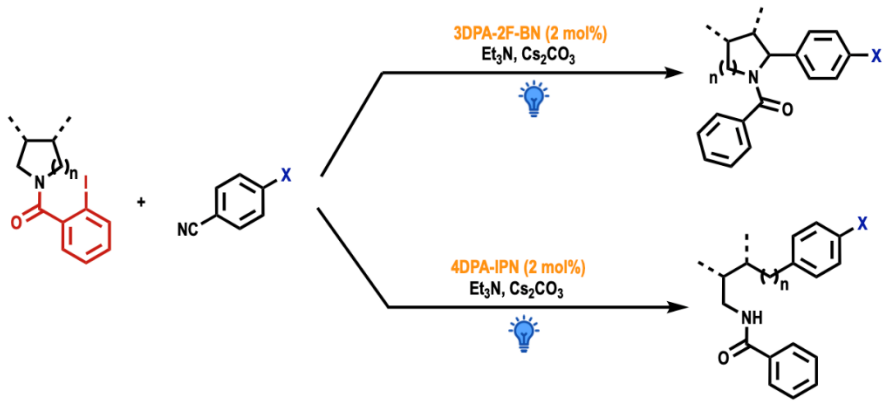
Saturated nitrogen-containing heterocycles are ubiquitous structural motifs in natural products and bioactive compounds, particularly piperidines, piperazines, and pyrrolidines.[1] Therefore, the development of catalytic strategies for the C–H functionalization of azaheterocycles remains a significant objective in synthetic chemistry.[2]

Herein, we report a photocatalytic strategy for the C–H functionalization of saturated aza-heterocycles under mild conditions. Our approach relies on a redox-active benzamide protecting group that is activated *via* a halogen-atom transfer (XAT) process to generate α-amino radicals. These intermediates readily engage in Giese additions and radical cross-coupling reactions, affording C–H alkylated and arylated products.[3] Furthermore, when a photocatalyst capable of undergoing a consecutive photoinduced electron transfer (conPET) mechanism is employed, the resulting products can further undergo ring-opening transformations.[4] Therefore, this strategy enables the deconstruction of cyclic amines through challenging C–N bond cleavage.



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CONTROLLING ABIOLOGICAL CYCLIZATION PATHWAYS IN HEME-DEPENDENT ENZYMES

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Selective ring construction through controlled cyclization pathways provides an effective way to access different cyclic products. Enzyme engineering has shown that Heme-dependent Myoglobin variants promote abiological nitrene-mediated C–H amidation of dioxazolones to form lactams with high selectivity.[1] In contrast, related heme enzymes with a different axial ligation favor lactone formation from the same substrate class as a striking example of enzyme-directed control over cyclic product outcome.

In this work, guided by previous studies characterizing the mechanisms of competing reaction pathways in metalloenzymes, which highlight enzymatic control over reactive intermediates[2], we present a comprehensive computational study of Myoglobin and CYP119 enzyme platforms to elucidate the mechanistic origins of lactam vs. lactone selectivity. Using Density Functional Theory (DFT) and Molecular Dynamics (MD) simulations, we investigate the electronic and geometric properties that govern the divergent lactam and lactone formation in these enzyme variants. In particular, we analyze the impact of axial ligand identity coordinating the heme center, as well as variations in surrounding active-site residues, on the electronic structure of key reactive intermediates and their geometric preorganization for ring closure. These results provide mechanistic insight into experimental observations showing how changes in metal coordination and enzyme environment can redirect a common abiological precursor toward distinct cyclic products.

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COMPUTATIONAL INVESTIGATION OF ANION-INDUCED ALLOSTERIC REGULATION IN A CATIONIC CAPSULE FOR CATION RECOGNITION

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Cation recognition by cationic receptors is generally difficult because of electrostatic repulsion between the positively charged host framework and incoming cations. In this study, the hexacationic receptor **3NDI^{6+}** was computationally examined to understand the structural changes that enable cation binding after anion recognition. Experimentally, the receptor adopts a sandwich-like conformation in its hexafluorophosphate salt form ([**3NDI^{6+}**@2PF_6^-]·4PF_6^-)where the internal cavity remains collapsed[1]. Upon the introduction of chloride ions, the first chloride ion acts as an allosteric modulator, inducing a conformational change that converts the structure into a more open capsule-like form. This rearrangement then allows the binding of a second chloride ion, forming the inclusion complex ([**3NDI^{6+}** ⊃2Cl^-]$^{4+}$). To investigate these structural changes, Density Functional Theory (DFT) calculations were carried out using the **ORCA** program with the **b97-3c** functional for the geometry optimization, and using **AMS** for the NMR calculations with the **KT2** functional and et-pvqz basis set, in both cases using **DMSO** as the solvent. In total, **different structures were optimized**, including the isolated **3NDI^{6+}**cage, the cage with two **PF_6^-** anions, the cage with one **Cl^-**, the cage with two **Cl^-** anions, and the chloride-bound cage interacting with a **K^+** ion. These structures allow a direct comparison of the geometrical changes and chemical shifts with the experimental NMR data as anions and cations interact with the host framework. The results provide insight into how chloride binding stabilizes the capsule-like conformation and creates an environment that enables cation recognition within the charged cage. This computational analysis helps explain the relationship between anion binding, structural rearrangement, and cation encapsulation in this supramolecular system.

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FUNCTIONAL ROLE OF CYCLIC π-CONJUGATED MOLECULES IN HYBRID INTERFACES: A THEORETICAL STUDY OF FULLERENE–PEROVSKITE ELECTRON TRANSFER

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Cyclic π-conjugated molecules represent an important class of functional materials due to their unique electronic structures and strong electron-accepting capabilities.[1] Among these systems, Buckminsterfullerene (C_{60}) has attracted considerable attention as a versatile molecular acceptor in organic and hybrid photovoltaic architectures.[2] Understanding how such cyclic frameworks interact electronically with semiconductor materials is crucial for rationally designing next-generation optoelectronic systems.

In this work, we present a theoretical investigation of the electronic interactions between C_{60} and the halide perovskite caesium lead iodide ($CsPbI_3$) at their hybrid interface. Using first-principles electronic-structure calculations combined with nonadiabatic molecular dynamics simulations, we analyse the orbital character, and dynamical evolution of electronic states across the interface. Our results reveal that structural fluctuations and orbital overlap between perovskite conduction states and fullerene orbitals create hybridized electronic states that facilitate efficient electron transfer.

The simulations provide a molecular-level description of how cyclic π-conjugated molecules operate as electron-accepting units in hybrid materials. These insights contribute to a deeper understanding of the functional behaviour of cyclic molecular systems and highlight key design principles for tailoring fullerene-based and related electron acceptors in emerging photovoltaic and optoelectronic applications.

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PALLADIUM-CATALYZED APEX-TYPE REACTION FOR THE SYNTHESIS OF POLYCYCLIC AROMATIC HYDROCARBONS

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Polycyclic aromatic hydrocarbons (PAHs) have attracted significant interest due to their potential use as organic semiconductors.[1] As a consequence, the synthesis of PAHs has become a significant challenge for organic chemists, who have developed a variety of methodologies to construct these compounds.[2] One of them are the annulative π-extension (APEX) reactions, which are a set of reactions that enable access to complex aromatic systems. from simple aromatic precursors in a single reaction step.[3] In our work, we report a new synthetic methodology of PAHs through an APEX-type reaction in which a C-X/C-H annulation reaction occurs between an aryne intermediate (**1**) and an aryl triflate (**2**) functionalized at the bay-region (a concave, armchair-like edge), catalysed by a palladium complex. The reaction has been used to synthesize a library of structurally diverse PAHs in a single, operationally simple step, most of which have never been reported before or are difficult to synthesize using alternative methods.

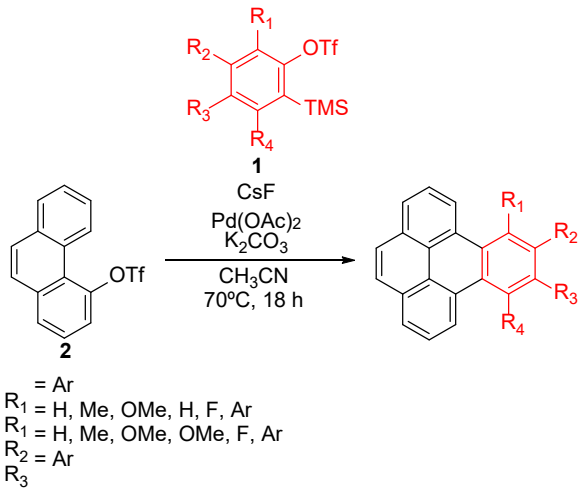

Figure 2. Pd-catalysed APEX reaction of aryl triflate with arynes.

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FLUORINATION CONTROL OF THE STABILITY OF THE PD_8L_{16} SQUARE ANTIPRISM

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Within the extensive family of Pd_nL_{2n} metal–organic cages, certain structures are significantly easier to access than others.[1] Small assemblies (Pd_2L_4 to Pd_6L_{12}) and large pseudospherical cages (≥$Pd_{12}L_{24}$) can be readily formed from planar aryl-based ligands. However, accessing intermediate-sized cages remains challenging because they require metal–ligand coordination vector angles in the range of 90–120°, which are difficult to achieve using conventional flat ligands. In this work, we present a comprehensive computational investigation aimed at understanding how fine-tuning the conformational preferences of ligands through perfluorination of the biphenyl backbone enables stabilization of the Pd_8L_{16} cage, which has been experimentally observed for the first time in both solution and the solid state.

To understand the effect of the dihedral twist angle, several electronic and steric parameters were calculated. The electronic descriptors include binding energy, Mayer bond order, natural bond orbital (NBO) charges, chemical potential, chemical hardness, and electrophilicity, while steric effects were analyzed using the percent buried volume ($\%V_{bur}$). Although these parameters provide valuable insights into the electronic and steric features of the system, our results indicate that they do not fully account for the enhanced stabilization of the Pd_8L_{16} cage upon perfluorination, suggesting that additional factors related to ligand conformational dynamics may play a key role in controlling the process.[1]

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REGIOSELECTIVE ACYLATION OF RESORCINOL DERIVATIVES VIA AN ENGINEERED BIOCATALYST

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Regioselective functionalization of phenols remains non-trivial because intrinsic ortho/para reactivity often leads to product mixtures, over-acylation, or competing *O*-functionalization. Achieving high site-selectivity typically requires strong acids, directing groups or carefully tuned reaction conditions rather than inherent catalyst-controlled selectivity.[1] The monoacetylphloroglucinol (MAPG) acyltransferase from *Pseudomonas protegens* (*Pp*ATase) is a versatile biocatalyst that performs highly regioselective C-C bond formation at ambient temperature in aqueous systems. It accepts a broad spectrum of non-natural substrates and acyl donors, without requiring costly cofactors, ultimately generating diverse polyketide scaffolds with multifaceted bioactivities.[2,3] The enzyme structure consists of three distinct subunits (denoted PhlA, PhlB, and PhlC), with four copies of each subunit assembling into a heterododecameric structure.[4] However, the catalytic machinery for the acyl transfer resides solely in the PhlC subunit.[5] When isolated from the other subunits, the catalytic subunit is both insoluble and inactive. By computationally analyzing the conformational dynamics of the multimeric complex we aim to rationally design a functional acyltransferase with a reduced oligomeric state that maintains catalytic activity while improving solubility and enabling further engineering.

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A COMPUTATIONAL QUEST FOR CONTROLLED ANTIAROMATIC REACTIVITY OF PENTALENE DIMERIZATION

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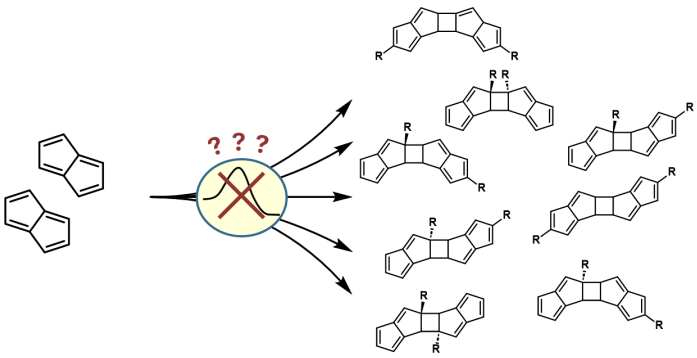
Antiaromatic systems like pentalene are key candidates for next-generation organic electronics due to their unique HOMO-LUMO gaps, yet their high reactivity and propensity toward dimerization limit their synthetic accessibility.[1] This work presents a systematic DFT investigation into the dimerization of pentalene and its substituted derivatives to elucidate how electronic and steric perturbations modulate this process.[2]

Our results reveal a complex mechanistic landscape highly sensitive to the substitution pattern. While most configurations follow an asynchronous concerted [2+2] cycloaddition, we identified specific pathways that diverge toward a stepwise process involving a remarkably stable reaction intermediate. Mapping the potential energy surfaces allows us to quantify how substituent effects dictate the nature of transition states and the depth of intermediate wells. The evolution of aromaticity indices correlates with this mechanistic bifurcation, confirming that the relief of antiaromatic strain stabilizes these transient species. Furthermore, global electronic descriptors rationalize this reactivity, showing that the transition to the dimer is driven by a significant gain in chemical stability. Notably, bulky substituents introduce substantial kinetic barriers, providing a "steric shielding" strategy to isolate persistent pentalenes. This study clarifies the chemical fate of pentalene and offers predictive guidelines for designing stable, functionalized antiaromatic frameworks.



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FUNCTIONALIZED RUTHENIUM CATALYSTS FOR SUSTAINABLE SYNTHESIS OF CYCLIC COMPOUNDS

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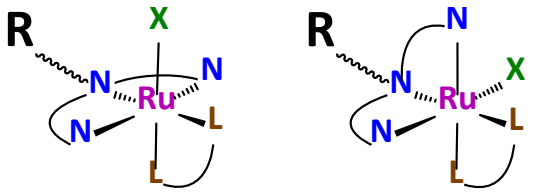
Chemical catalysis is fundamental to the transition towards green chemistry, requiring the optimization of reaction conditions to meet the global demand for renewable energy and environmental protection.[1] This work focuses on the development of functionalized ruthenium complexes specifically designed for the sustainable synthesis of cyclic compounds, primarily through the selective epoxidation of olefins.[2] We detail the synthesis of novel Ru catalysts featuring carboxylic acid (-COOH) functionalities within their ligand frameworks to evaluate their impact on catalytic efficiency and their potential to activate sustainable oxidants like hydrogen peroxide. Ru-complexes also exhibit photochemical properties that allow for photoactivated reaction schemes using visible light as a clean activator. To further enhance sustainability and system reusability, these catalysts are anchored onto mesoporous silica nanoparticles (MSN), which provide high surface area and stability while minimizing catalyst aggregation. This study evaluates the catalytic performance of Ru-complexes and their corresponding heterogeneous composites in the oxidation of alcohols and the formation of cyclic epoxides, investigating the effects of different solvents, green oxidants, and visible light activation on their activity and turnover numbers.



R = COOH or H
X = Cl or H_2O
L = C or N donor atom

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