1st Bern Symposium on Radical Chemistry

University of Bern, Department of Chemistry, Biochemistry and Pharmaceutical Sciences
June 27-28, 2024


Prof. Hongli Bao
Fujian Institute of Research on the Structure of Matter


Prof. Shunsuke Chiba
Nanyang Technological University


Prof. Laurence Feray
Aix-Marseille Université


Prof. Dmitry Katayev
University of Bern


Prof. Bernd Giese
University of Fribourg


Dr. Emmanuel Lacôte
Université Claude Bernard Lyon 1


Prof. Yannick Landais
University of Bordeaux


Prof. Chaozhong Li
Shanghai Institute of Organic Chemistry


Prof. John A. Murphy
University of Strathclyde


Prof. Cristina Nevado
University of Zurich


Dr. Cyril Ollivier
Sorbonne-Université


Prof. Derek Pratt
University of Ottawa


Prof. David J. Procter
University of Manchester


Prof. Ilhyong Ryu
Osaka Metropolitan University and NWCU Hsinchu


Prof. Franziska Schönebeck
RWTH Aachen


Prof. Armido Studer
University of Münster


Prof. Hideki Yorimitsu
Kyoto University


Prof. Samir Zard
École Polytechnique Palaiseau


Prof. Jieping Zhu
École Polytechnique Fédérale de Lausanne

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The 1st Bern-SRC will have an exciting scientific programme that includes the Paracelsus Lecture 2024, 4 plenary lectures, 13 invited lectures and 2 poster sessions with world-leading speakers focused on modern aspects of synthetic organic chemistry using free radicals.

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Prof. Philippe Renaud, University of Bern
Prof. Dmitry Katayev, University of Bern

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Program

Thu, June 27, 2024

08.00	Registration / Welcome Coffee
08.45	Welcome Message by *Dr. Fabrice Dénès*, University of Bern
09.00	*Prof. Derek Pratt*, University of Ottawa «No HAT Required! Unusual Radical-Trapping Antioxidant Mechanisms of Metal Thiosemicarbazones and Organoboranes Provide New Strategies for Preventing Oxidative Cell Death»
09.45	*Dr. Cyril Ollivier*, Sorbonne-Université «Visible light-induced radical processes and organometallic catalysis»
10.10	*Prof. Chaozhong Li*, Shanghai Institute of Organic Chemistry «Phosphorylation of Alkyl Radicals»
10.35	Coffee Break & Poster Session
11.15	*Prof. Ilhyong Ryu*, Osaka Metropolitan University / NWCU Hsinchu «Radical Strategies for Functionalization of C=C Double Bonds»
11.40	*Prof. John Murphy*, University of Strathclyde «Alkali Metal Salts and Radicals»
12.05	*Prof. Laurence Feray*, Aix-Marseille Université «Radical Reactions Involving Ynamides»
12.30	Lunch Break
14.00	*Prof. Franziska Schönebeck*, RWTH Aachen «Dynamic Stereomutation with Metalloradicals»
14.45	*Prof. Dmitry Katayev*, University of Bern «Switchable Divergent Synthesis of Fluorinated Compounds Using Photoredox Catalysis»
15.10	*Dr. Emmanuel Lacôte*, Université Claude Bernard Lyon 1 «Free Radical Photochemistry in Dispersed Media»
15.35	Coffee Break & Poster Session
16.25	*Prof. Bernd Giese*, University of Fribourg «Serendipity in Radical Chemistry»
16.50	*Prof. Samir Zard*, École Polytechnique Palaiseau «Some Aspects of Radical Allylations»
17.15	Paracelsus Prize Winner 2024 *Prof. Armido Studer*, University of Münster «Radical Hydrogen Atom Transfer to pi-Systems»
18.00	End of Day 1

Program

Fri, June 28, 2024

08.45	*Prof. Jieping Zhu*, École Polytechnique Fédérale de Lausanne «A Bioinspired Non-Biomimetic Synthesis of Lignans enabled by Radical Cation Intermediates»
09.30	*Prof. Shunsuke Chiba,* Nanyang Technological University «Dearomative transformation via polysulfide anions photocatalysis»
09.55	*Prof. Yannick Landais*, University of Bordeaux «New Approaches to the synthesis of urethanes and polyurethanes through free-radical processes»
10.20	Coffee Break
10.50	*Prof. Hongli Bao*, Fujian Institute of Research on the Structure of Matter «Mechanistic Investigation of Copper-Catalyzed Asymmetric Esterification: Revealing A New NLEs Analysis Model»
11.15	*Prof. Hideki Yorimitsu*, Kyoto University «Reductive Dimetalation of Alkynes»
11.40	*Prof. Cristina Nevado*, University of Zurich «Metaloradical intermediates as a playground for structural complexity»
12.05	*Prof. David J. Procter*, University of Manchester «From sulfonium salts to samarium catalysis: new radical chemistry for synthesis»
12.50	Closing words and end of the symposium

TALKS

Mechanistic Investigation of Copper-Catalyzed Asymmetric Esterification: Revealing A New NLEs Analysis Model

Xiaotao Zhu+,[1] Meirong Huang+,[2] Hongli Bao*,[1] and Xinhao Zhang *,[2]

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Non-linear effects (NLEs), dealing with the relationship between ee values of ligand and product, classically serve as a widespread tool for investigating asymmetric reaction mechanisms. However, the NLEs analysis model only often provides intuitive information in simple systems, leaving the application in complex systems indirect and vague. Here, we report a new NLEs analysis model that directly connects the relationship between ee values of metal complexes and products, with the purpose of solving the challenges that occur in complex systems. Through an in-depth analysis of the mechanism of our previous copper-catalyzed asymmetric esterification reactions, we found an intrinsic linear relationship between the ee values of the key active metal complex (LLCuI) and product within this traditionally non-linear system. This new NLEs model holds promise as a powerful tool for the exploration of asymmetric catalysis mechanisms, heralding new avenues in the understanding and application of catalytic processes.

References:

[1] (a) Puchot, C.; Samuel, O.; Dunach, E.; Zhao, S.; Agami, C.; Kagan, H. B. *J. Am. Chem. Soc.* **1986**, *108*, 2353-2357; (b) Guillaneux, D.; Zhao, S.-H.; Samuel, O.; Rainford, D.; Kagan, H. B. *J. Am. Chem. Soc.* **1994**, *116*, 9430-9439; (c) Zhang, S. Y.; Girard, C.; Kagan, H. B. *Tetrahedron: Asymmetry* **1995**, *6*, 2637-2640; (d) Girard, C.; Kagan, H. B. *Angew. Chem. Int. Ed.* **1998**, *37*, 2922-2959; (e) Kagan, H. B. *Adv. Synth. Catal.* **2001**, 343, 227-233

[2] (a) Satyanarayana, T.; Abraham, S.; Kagan, H. B. *Angew. Chem. Int. Ed.* **2009**, *48*, 456-494. (b) Ahn, J. M.; Ratani, T. S.; Hannoun, K. I.; Fu, G. C.; Peters, J. C. *J. Am. Chem. Soc.* **2017**, *139*, 12716-12723. (c) Geiger, Y.; Achard, T.; Maisse‐François, A.; Bellemin‐Laponnaz, S. *Eur. J. Org. Chem.* **2021**, *2021*, 2916-2922. (d) Zhu, X.; Li, Y.; Bao, H. *Chin. J. Chem.* **2023**, *41*, 3097-3114.

Dearomative Transformation via Polysulfide Anions Photocatalysis

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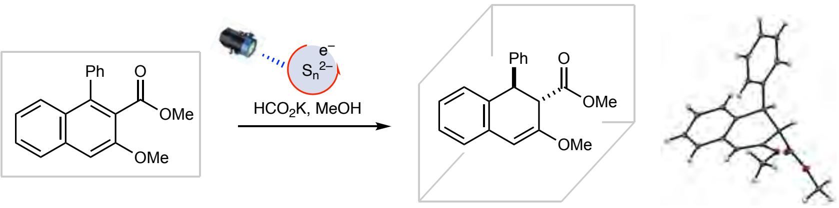
Sulfur forms catenated homoatomic polysulfide dianions S_n^{2-} (commonly, n = 2-8) and a persistent radical anion $S_3^{\bullet-}$ (which has been recognized as a chromophore in ultramarine blues).[1] The redox potentials of polysulfide anions have been elucidated mainly for the development of alkali metals-sulfur batteries. We recently revealed that these polysulfide anions function to mediate single-electron transfer and hydrogen atom transfer under irradiation with visible light.[2-5] This lecture will present recent efforts in our group for dearomative transformation under polysulfide anion photocatalysis.



[1] R. Steudel, T. Chivers, The role of polysulfide dianions and radical anions in the chemical, physical and biological sciences, including sulfur-based batteries. *Chem. Soc. Rev.* **2019**, *48*, 3279-3319.

[2] H. Li, X. Tang. J. H. Pang, X. Wu. E. K. L. Yeow, J. Wu, S. Chiba, Polysulfide anions as visible light photoredox catalysts for aryl cross-coupling. *J. Am. Chem. Soc*. **2021**, *143*, 481-487.

[3] H. Li, S. Chiba, Synthesis of α-tertiary amines by polysulfide anions photocatalysis via single-electron transfer and hydrogen atom transfer in relays. *Chem. Catal.* **2022**, *2*, 1128-1142.

[4] E. Y. K. Tan, A. S. Mat Lani, W. Sow, Y. Liu, H. Li, S. Chiba, Dearomatization of (hetero)arenes through photo-driven interplay between polysulfide anions and formate. *Angew. Chem. Int. Ed*. **2023**, *62*, e202309764.

[5] E. Y. K. Tan, A. Dehdari, A. S. Mat Lani, D. A. Pratt, S. Chiba, Dearomative dimerization of quinolines and their skeletal rearrangement to indoles triggered by single-electron transfer, *ChemRxiv* **2024**, https://doi.org/10.26434/chemrxiv-2024-4k222-v3

Radical Reactions Involving Ynamides

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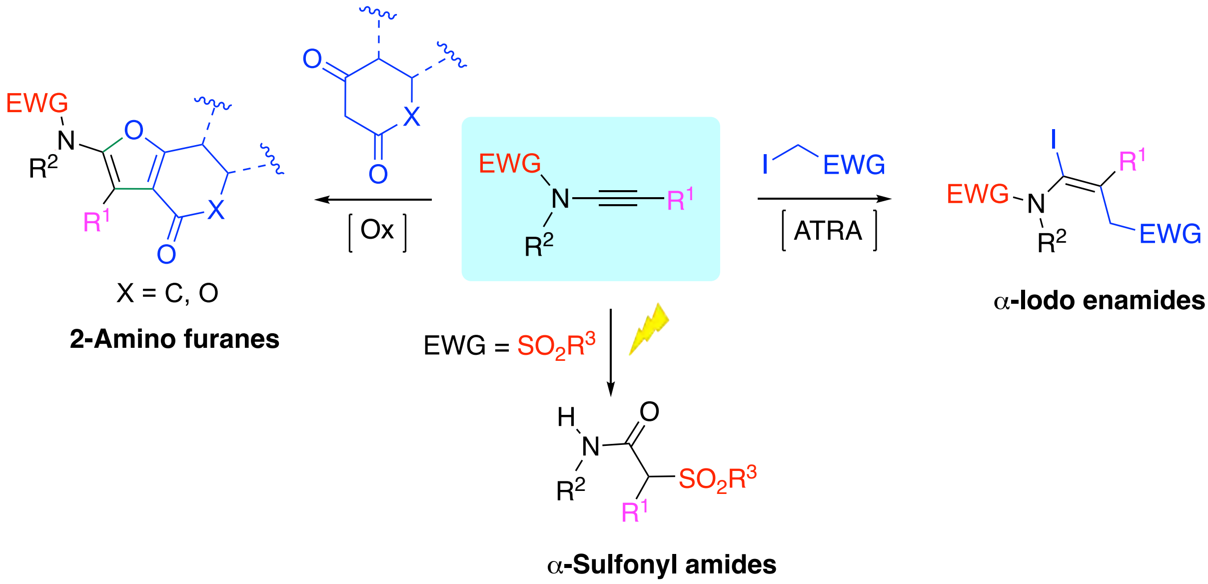
The interest in ynamides as building blocks for organic synthesis has been growing exponentially since the turn of the century. Due to the electron donating effect of the nitrogen atom, tempered by the nature of its electron withdrawing substituent, ynamides behave as activated polarized alkynes that have been extensively used to perform regioselective, rapid, and elegant constructions of versatile *N*-containing molecules. Regarding radical chemistry, ynamides act as electron rich radical acceptors.



We present here recent advances in reactivity of ynamides towards radical in intermolecular processes. Ynamides react with electrophilic carbon centered radicals through ATRA methodology [1] or in the presence of oxidant [2] to perform one-pot synthesis of α-iodo enamides [3] and 2-amino furanes, respectively. Under light activation *N*-sulfonyl ynamides can rearrange in α-sulfonyl amides.

[1] N. Dwadnia, H. Lingua, D. Mouysset, L. Mimoun, D. Siri, M. P. Bertrand, L. Feray, *J. Org. Chem.*, **2020**, *85*, 4114–4121.

[2] A. Galibert-Guijarro, D. Mouysset, L. Mimoun, M. P. Bertrand and L. Feray, *J. Org. Chem.*, **2023**, *88*, 2464–2473.

[3] L. Feray, M. P. Bertrand, A. Galibert-Guijarro *Synthesis*, **2023**, *55*, 27–44.

Serendipity in Radical Chemistry

Bernd Giese

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Unexpected experimental results are important eye-openers for the discovery of new scientific areas. I will discuss how serendipity boosted our research in synthetic chemistry, physical chemistry and biological chemistry.

The research of radical chemistry in biological systems has led to the question why radical reactions in living cells often differ from radical syntheses in the laboratory. One condition for life-sustaining reactions in cells is homeostasis. This means that both concentrations of important reaction intermediates, as well as rates of vital chemical reactions have to remain constant during biological processes. On the other hand, living cells have to adopt to changing environmental conditions. For many redox reactions it turned out to be typical that

1) the site of radical generation differs from the site of radical reactions with the substrate,

2) the generated radical is different from the radical that reacts with the substrate,

3) an electron transporting chain establishes the chemical communication between these different radicals, and

4) reactions of radicals with substrates occur at interfaces (water/protein).

This means that chemical reactions do not occur in homogeneous solutions but in very complex, compartmentalized systems. We have now shown that under these conditions 1) chemical reactions with substrates are often of zero order, and 2) that redox active molecules of the electron transporting chain posses enough flexibility to guarantee stable reaction rates. Thus, “survival of life” is the answer to the question why nature puts a large amount of energy in the synthesis of complex, compartmentalized systems.[1-3]

[1] V. Chaber, L. Babel, M. Füeg, M. Karamash, E. Madivoli, N. Herault, J. Dantas, C. Salgueiro, B. Giese, K. M. Fromm, *Angew. Chem.* **2020,** *59,* 12331.
[2] M. Karamash, M. Stumpe, J. Dengjel, C. Salgueiro, B. Giese, K. M. Fromm, *Front. Microbiol.* **2022**.
[3] B. Giese, M. Kharamash, K. M. Fromm, *FEBS Let*. **2023**, 166.

Switchable Divergent Synthesis of Fluorinated Molecules Using Photoredox Catalysis

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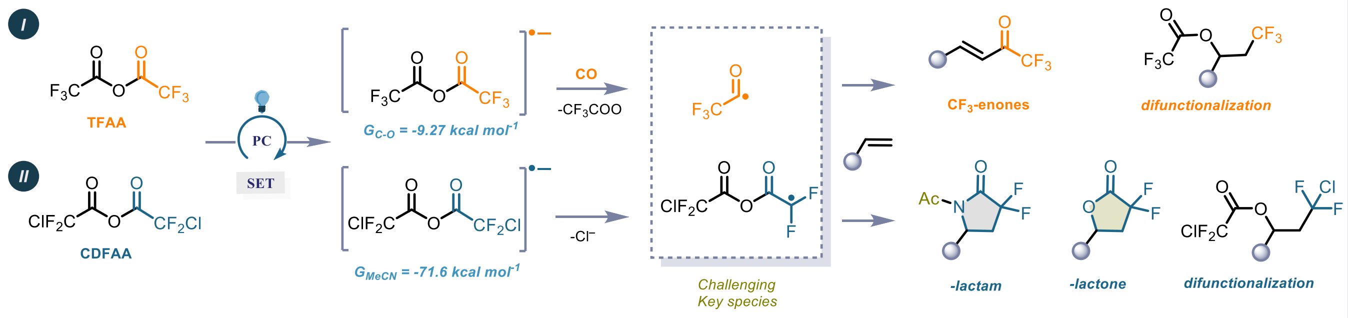
The introduction of fluorine atoms into molecules significantly alters their chemical, physical, and biological properties. Therefore, it is a very attractive method to elaborate innovative materials, agrochemicals, and pharmaceuticals.[1]

Recent progress in the design of redox active reagents, capable to transfer nucleophilic, ambiphilic, and electrophilic type of fluorinated radicals significantly broadened the field of fluorine chemistry.[2] Yet, the synthetic complexity to access such scaffolds is often associated with multi-step processes and hinders the practicability of utilising these reagents for the synthesis of vital molecules.



- Inexpesive starting material
- With or without CO pressure
- One step simple protocol
- Scalable in batch and in flow
- Bifunctional activation
- Chemo- and regioselective
- Synthesized >110 examples
- Late-stage functionalization
- Solvent controlled
- Mechanistic studies

In this presentation, I will discuss some of the latest works from my group on the strategies of using structurally simple, inexpensive, and readily available fluorinated acetic anhydrides and carboxylic acids as redox active reagents to access various fluoroalkyl radicals. The reactivity of these species can be further adjusted using the principal of switchable divergent synthesis in photocatalysis, allowing to synthesize a wide range of fluorinated molecules.[3-5]

[1] (a) Purser S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2007**, *37*, 320-330; (b) Berger, R.; Resnati, G.; Metrangolo, P.; Wever, E.; Hilliger, J. *Chem. Soc. Rev.* **2011**, *40*, 3496.

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[3] K. Zhang, D. Rombach, N. Y. Nötel, G. Jeschke, D. Katayev, *Angew. Chem. Int. Ed.* **2021**, *60*, 22487

[4] R. Giri, I. Mosiagin, I. Franzoni, N. Y. Nötel, S. Patra, D. Katayev, *Angew. Chem. Int. Ed.* **2022**, *61*, e2022091.

[5] R. Giri, E. Zhilin, D. Katayev, *Chem. Sci.* **2024**, in press.

Low energy-photon radical photopolymerizations in dispersed media

Emmanuel Lacôte

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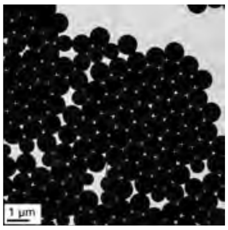
In this talk we will first present how NHC-Boryl or sulfur-based radicals can be formed via visible (blue) light irradiation, and how this can be used to initiate efficient photopolymerizations in emulsion[1] and dispersion,[2] overcoming the scattering of the photons by the particles formed. The latexes generated are made of monodisperse particles with sizes up to the micrometer-scale.



We will then examine how one can transition toward the red[3] and how the organic surfactant can be replaced by inorganic CeO$_2$ nanoparticles toward the photochemical formation of latexes of Pickering-stabilized filmogenic CeO$_2$-armed polymer particles.

[1] "Visible-light Emulsion Photopolymerization of Styrene" Le Quéméner, F.; Subervie, D.; Morlet-Savary, F.; Lalevée, J.; Lansalot, M.; Bourgeat-Lami, E.; Lacôte, E. *Angew. Chem. Int. Ed.* **2018**, *57*, 957-961; DOI: 10.1002/anie.20171048.

[2] "Visible-Light Initiated Dispersion Photopolymerization of Styrene" Canterel, R.; Lalevée, J.; Bourgeat-Lami, E.; Lacôte, E.; Lansalot, M. *Angew. Chem. Int. Ed.*, **2023**, e202309674; doi.org/10.1002/anie.202309674.

[3] "A Methylene Blue/Sodium sulfinate Photo-Initiating System for the Red-Light Emulsion Photopolymerization of Methyl Methacrylate" Kalout, H.; Lansalot, M.; Bourgeat-Lami, E.; Morlet-Savary, F.; Lacôte, E.; Lalevée, J. *Adv. Funct. Mater*. **2024**, accepted for publication.

New Approaches to the synthesis of urethanes and polyurethanes through free-radical processes

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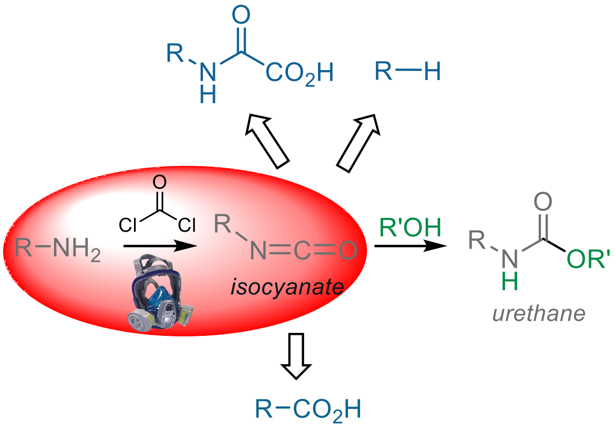
Urethanes display attractive biological activities and constitute key structural motifs in many targets having clinical potential.[1] Urethanes exhibit excellent proteolytic stabilities, and are thus often used as peptide bond surrogates. They are also widely used as amine protecting groups, showing orthogonality and stability towards acids, bases or hydrogenation. The urethane linkage is also found in polyurethanes (PUs), an important class of polymers with a wide range of applications in furniture and interiors, automotive industry, electronics and appliances, packaging and footwear industries.[2] The addition of alcohols (polyols) to (poly)isocyanates is probably the most reliable method to access urethanes and PUs. However, the use of isocyanates in industrial applications is increasingly subjected to international regulations, as they are known to be powerful irritants and are classified as carcinogenic to animals and potentially to humans. Their synthesis also relies on the use of poisonous phosgene. This presentation will describe recent efforts in our laboratory to develop methods to access isocyanates and also directly urethanes without phosgene. Strategies relying on the use of amines,[3] alkanes[4] or carboxylic acids[5] based in particular on photocatalysis and metal catalysis, will be described.



[1] A. K. Ghosh, M. Brindisi, *J. Med. Chem.* **2015**, *58*, 2895 and references therein.
[2] H.-W. Engels, H.-G. Pirkl, R. Albers, R. W. Albach, J. Krause, A. Hoffmann, H. Casselmann, J. Dormish, *Angew. Chem. Int. Ed.* **2013**, *52*, 9422.
[3] (a) G. G. Pawar, F. Robert, E. Grau, H. Cramail, Y. Landais, *ChemComm.* **2018**, *54*, 9337. (b) I. M. Ogbu, G. Kurtay, F. Robert, Y. Landais, *ChemComm.* **2022**, *58*, 7593. (c) I. M. Ogbu, G. Kurtay, M. Badufle, F. Robert, C. Silva Lopez, Y. Landais, *Chem. Eur. J.* **2023**, *29*, e2022029. (d) Q. Jaussaud, I. M. Ogbu, G. G. Pawar, E. Grau, F. Robert, T. Vidil, Y. Landais, H. Cramail, *ChemRixv* **2024**. DOI: 10.24820/ark.5550190.p012.092.
[4] J. Lusseau, F. Robert, Y. Landais, *ACS Cat.* **2023**, *21*, 14257.
[5] J. Lusseau, D. Uduagwu, F. Robert, Y. Landais, *Adv. Synth. Cat.* **2024**, *366*, 2209.

Phosphorylation of Alkyl Radicals

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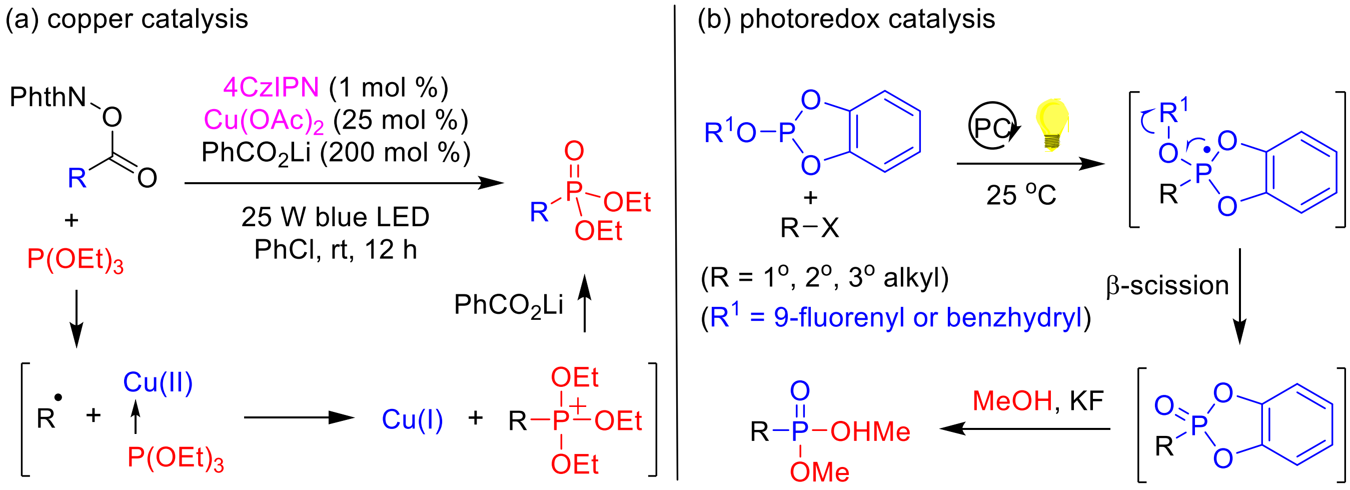
Organophosphorus compounds have found widespread applications in various areas ranging from biochemistry to ecology, medicine, agriculture, and materials science. A variety of methods have been developed for C(sp^3)–phosphorylation, including nucleophilic and electrophilic phosphorylation and phosphoryl radical addition onto unsaturated bonds. However, methods based on the phosphorylation of alkyl radicals remain elusive. Studies on the formations and properties of phosphoranyl radicals by Bentrude and others in the 1970s led to the conclusion that radicals such as methyl radical add to trivalent phosphorus reversibly while radicals such as isopropyl radical do not react at all.[1]



Our investigation on copper-catalyzed radical reactions led to the hypothesis of “copper-assisted phosphite transfer”, based on which the copper-catalyzed decarboxylative phosphonylation of *N*-acyloxyphthalimides with trialkyl phosphites was successfully accomplished under mild conditions (Fig. 1a).[2a] Furthermore, our extensive study on alkyl radical addition to phosphites revealed that primary, secondary and even tertiary alkyl radicals add efficiently to 9-fluorenyl (or benzhydryl) *o*-phenylene phosphite. Thus, a radical variant to the Arbuzov reaction was successfully developed under photoredox-catalyzed conditions via radical addition–β-scission sequence (Fig. 1b).[2b] The extension of the above strategies to alkyl radical phosphinylation reactions will also be discussed.[3]

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[3] (a) Y. Cheng, J. Zhen, L. Chai, J. Wang, J. Yin, L. Zhu, C. Li, *Angew. Chem. Int. Ed.* **2024**, *63*, e202316764. (b) J. Wang, Y. Zhang, L. Zhu, X.-S. Xue, C. Li, *Angew. Chem. Int. Ed.* **2024**, *63*, e202400856. (c) L. Chai, Y. Cheng, L. Zhu, C. Li, *CCS Chem.* **2024**, accepted.

Alkali Metal Salts and Radicals

John A. Murphy, Kenneth F. Clark, Alexander J. Stewart, SebTyerman, Kristian Kolodziejczak,

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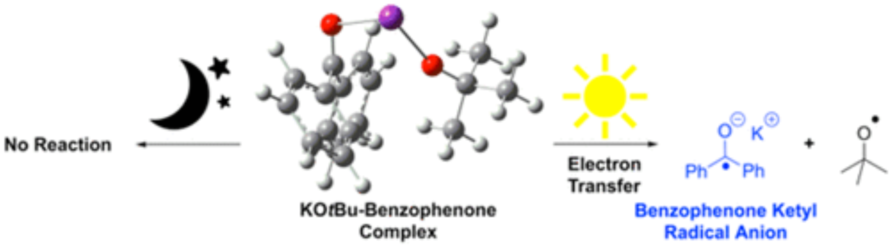

Recently, we reported that KO*t*Bu undergoes a photo-mediated electron transfer reaction to benzophenone.[1] This presentation will update our studies on the reactions of alkali metal salts with organic substrates.

[1] G. Nocera, A. Young, F. Palumbo, K. J. Emery, G. Coulthard, T. McGuire, T. Tuttle and J. A. Murphy, *J. Am. Chem. Soc.* **2018**, *140*, 9751–9757.

Metaloradical intermediates as a playground for structural complexity

Prof. Dr. Cristina Nevado Blazquez, Xia Hu, Xiaoyoung Du, Sergio Cuesta-Galisteo, Johannes Schörgenhumer, Cedric Hervieu, Mariia Kirillova

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Our group has recently explored the reactivity of C and N centered radicals, in combination with transition metals, to streamline the functionalization of π-systems.

Here, we will present our efforts to generate and harvest these valuable intermediates in synthetically relevant contexts, including recent results towards their application in asymmetric transformations.[1] Further, examples of Nickel catalyzed dicarbofunctionalizations of alkenes and alkynes in a chemo-, regio- and stereoselective manner utilizing radicals as well as studies on the mechanistic features underlying these transformations will be presented in this lecture.[2]

[1] a) C. Hervieu, M. Kirillova, T. Suárez, M. Müller, E. Merino, C. Nevado, *Nat. Chem*., **2021**, *13*, 327.
b) C. Hervieu, M. Kirillova, S. Cuesta-Galisteo, Y. Hu, E. Merino, C. Nevado, *Nat. Chem*., **2024**, *16*, 607–614.

[2] a) S. Cuesta-Galisteo, J. Schörgenhumer, X. Wei, E. Merino, C. Nevado, *Angew. Chem. Int. Ed.,* **2021**, *60*, 1605.
b) X. Wei, W. Shu, A. García-Domínguez, E. Merino, C. Nevado, *J. Am. Chem. Soc.* **2020**, *142*, 13515.
c) X. Hu, I. Cheng-Sánchez, S. Cuesta-Galisteo, C. Nevado, *J. Am. Chem. Soc.* **2023**, *145, 6270*.
d) X. Du, I. Cheng-Sánchez, C. Nevado *J. Am. Chem. Soc.* **2023**, *145*, 12532.
e) S. Cuesta-Galisteo, J. Schoergenhumer, C. Hervieu, C. Nevado*,*Angew. Chem. Int. Ed*., **2024**, e202313717.
f) X. Hu, I. Cheng-Sánchez, W. Kong, G. A. Molander, C. Nevado**doi.org/10.1038/s41929-024-01153-0*

Visible Light-Induced Radical Processes and Organometallic Catalysis

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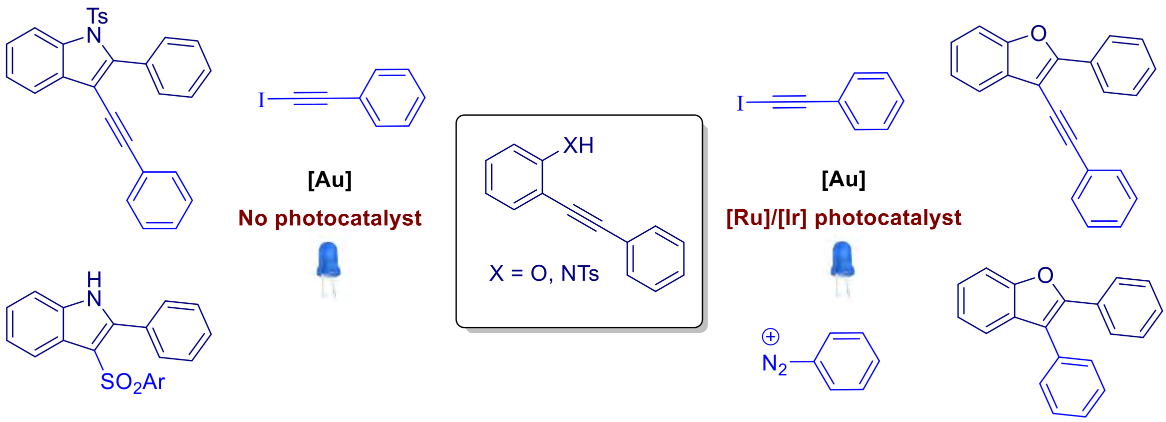
Visible light-assisted transformations are playing an increasingly important role in synthetic chemistry and have attracted considerable attention, particularly in metal-catalyzed homogeneous reactions.[1] The merging of organometallic catalysis and photocatalysis is a rapidly expanding field of great interest to the chemical research and industrial communities. It overcomes the limitations of both strategies and opens up new possibilities for cross-coupling reactions. In this context, the use of visible light activation to facilitate oxidative addition on gold intermediates, *via* photoredox catalysis or photosensitization, has proven to be an effective way to circumvent the lack of reactivity in gold chemistry.[2-4] This presentation will demonstrate the power and potential of these dual catalytic processes under light activation to promote efficient cross-coupling reactions with this metal.



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No HAT Required! Unusual Radical-Trapping Antioxidant Mechanisms Provide New Strategies for Preventing Oxidative Cell Death

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The radical-mediated autoxidation of the phospholipids of cell membranes drives ferroptosis, the cell death process that is believed to underlie neurodegeneration and the damage that occurs upon reperfusion of ischemic tissue following stroke or organ transplant. Radical-trapping antioxidants (RTAs) are small molecules which inhibit lipid autoxidation by intercepting chain-propagating peroxyl radicals and have emerged as the most promising therapeutic candidates for pathologies wherein ferroptosis has been implicated. The vast majority of potent anti-ferroptotic RTAs are aromatic amines, which react with peroxyl radicals via H-atom transfer (HAT) from their labile N-H bonds. We recently characterized and/or designed scaffolds that do not rely on HAT for inhibition of (phospho)lipid peroxidation and associated cell death. The first are metal thiosemicarbazones, which undergo ligand-based radical addition and subsequent radical combination reactions that occur largely independently of the metal centre, enabling the paradoxical design of potent platinum-based cytoprotective agents. The second are boronic esters and amides derived from catechols and diaminonapthalenes. The former have previously been developed by Renaud as powerful radical precursors for use in elegant radical chain processes, but which we show can be engineered to undergo interrupted homolytic substitution to trap radicals instead. Both of these new radical-trapping scaffolds suppress ferroptotic cell death in multiple cell lines and can be optimized to achieve potent cytoprotective activities that are on par with some of the most promising pre-clinical and clinical candidates to treat ferroptosis-related conditions. These results underscore the central role of radical reactions in a key pathological cell death process and highlight how radical chemists' mechanistic understanding can be exploited for the design and/or development of seemingly absurd bioactive compounds.

From sulfonium salts to samarium catalysis: new radical chemistry for synthesis

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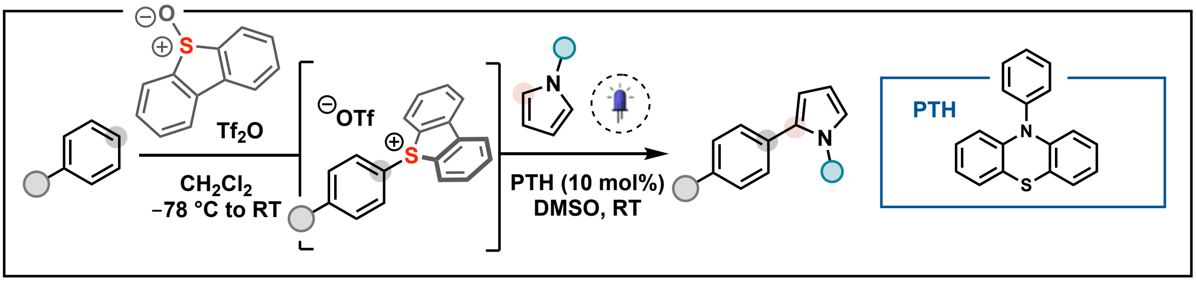
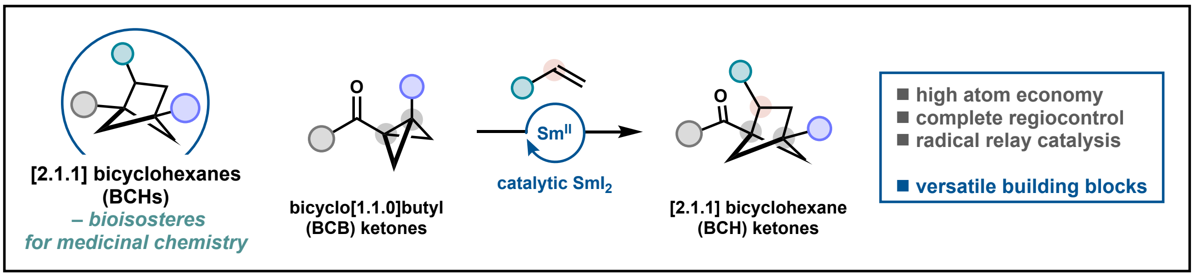
Part I – Our approach to transition metal-free cross-coupling uses sulfur to replace metals in activating substrates and generating reactive intermediates for exploitation in C–C bond-formation. In particular, we will describe the exploitation of *in situ* generated aryl sulfonium salts in photocatalytic[1] and photochemical[2] coupling processes involving aryl radicals.



Part II – Samarium(II) iodide is one of the most widely-used single electron transfer reductants in chemistry. We will describe our recent studies on catalysis with SmI$_2$[3] and the application of Sm(III)-ketyl radicals in a catalytic approach to bioisostere synthesis.[4]



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Radical Strategies for Functionalization of C-H and C=C Bonds

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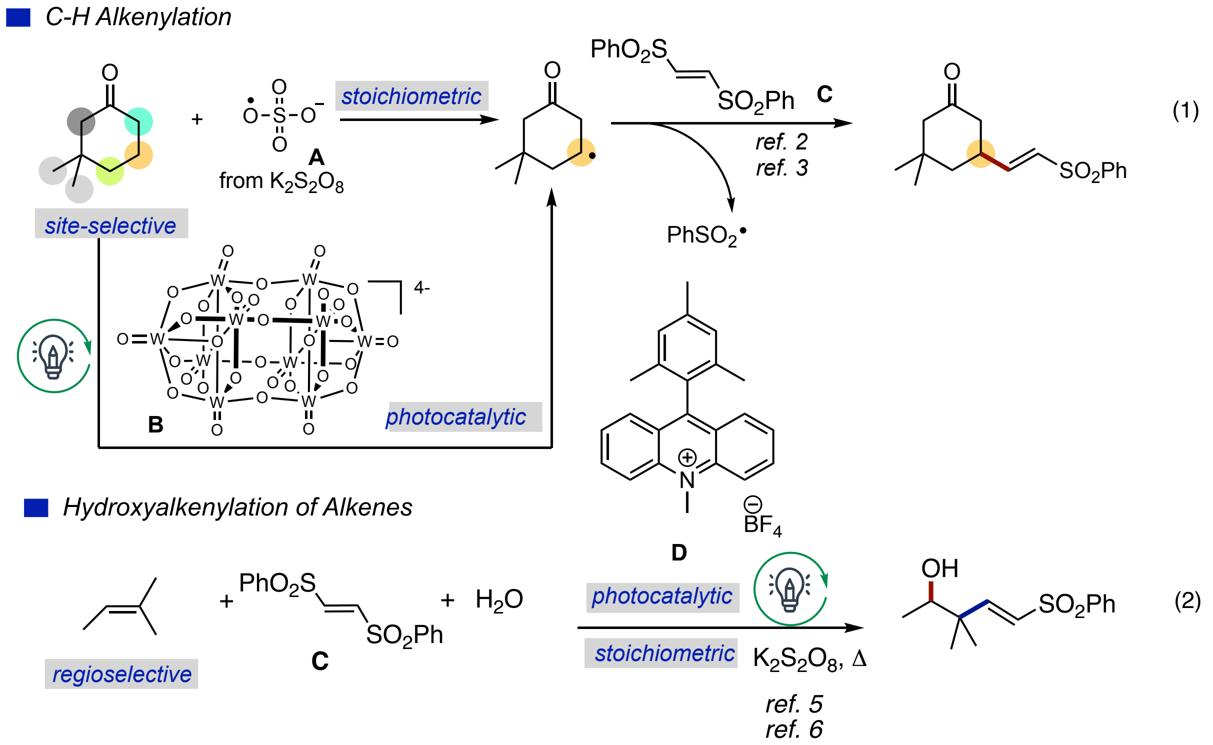
Developing new strategies to functionalize basic organic molecules such as alkanes and alkenes is at the forefront of synthetic organic chemistry. We have been involved in this challenge, capitalizing on the potential of radical-based strategies involving photocatalyst **B** for alkane functionalization.[1] Our recent efforts involve C(sp^3)-H alkenylation using 1,2-bis(phenylsulfonyl)ethylene **C**, [2,3] and the related allylation, alkynylation, and imination, [4] in which the site-selectivity was ensured by an S_H2 process caused by oxygen-centered radical species such as **A** (stoichiometric) and **B** (photocatalytic) (eq 1). This Lecture focuses on the regioselective hydroxyalkenylation of alkenes using **C** (eq 2), for which either a stoichiometric protocol using **A**[5] or a photocatalytic protocol using Fukuzumi catalyst **D**[6] works well.



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Dynamic Stereomutation with Metalloradicals

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The prevalence of odd oxidation states in less precious metals bears significant untapped potential for the discovery and exploration of fundamentally distinct reactivity modes *via* metalloradical catalysis. This presentation will discuss the distinct reactivity of a $Ni^{(I)}$-metalloradical complex, which contrasts organic free radical reactivity as well as closed shell metal reactivity. Mechanistic details will be presented along with applications in synthesis, including reactivity modes which were previously inaccessible.

Intermolecular Hydrogen Atom Transfer Reactions to π-Systems

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Water activation, which allows this earth-abundant resource to be transferred into value added compounds, is a key topic in the field of small molecule activation. We demonstrate a unique water activation strategy enabled by a photocatalytic phosphine-mediated radical process under mild conditions, generating a metal-free PR_3-H_2O radical cation intermediate, where both hydrogen atoms are used in the following chemical transformation through sequential heterolytic (H+) and homolytic (H•) cleavage of the two O-H bonds.[1]

In the second part of the lecture, 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.[2] The same intermediates also allow the highly regioselective *Minisci para*-alkylation[3,4], Cu-catalyzed *meta*-arylation,[5] and switchable *para/meta*-difluoromethylation.[6] Furthermore, it will be shown that the concept is also applicable to pyridine skeletal editing.[7]

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Reductive Dimetalation of Alkynes

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Electron injection into alkynes is a well-known process that ends up with providing *trans*-alkenes via protonations of vinylic carbanions. However, applications of such reactions for *nonprotonative* transformations have been limited due to the inherent instability of radical anion intermediates. Here we will discuss recent developments in the generation of *vic*-dimetalated alkenes by reductive metalation of alkynes in the presence of reduction-resistant metal electrophiles: (1) *syn*-diboration with trialkoxyboranes as reduction-resistant electrophiles (Figure 1a),[1] (2) *anti*-dimagnesiation and -dialumination with Mg- and Al-based electrophiles (Figure 1b),[2] (3) *syn*-borylmetalation using flow microreactors (Figure 2).[3]

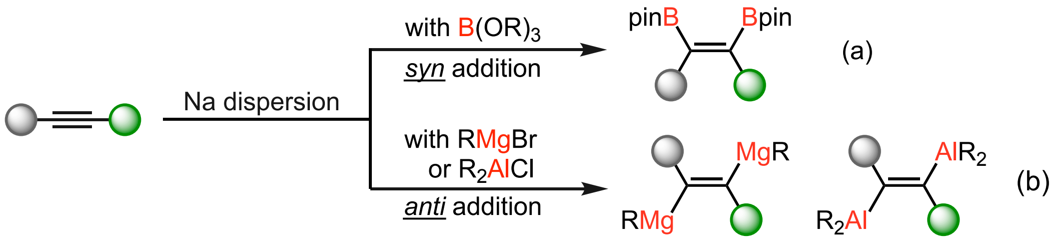

Figure 1. Reductive *syn*-diboration and *anti*-dimagnesiation and -dialumination of alkynes.

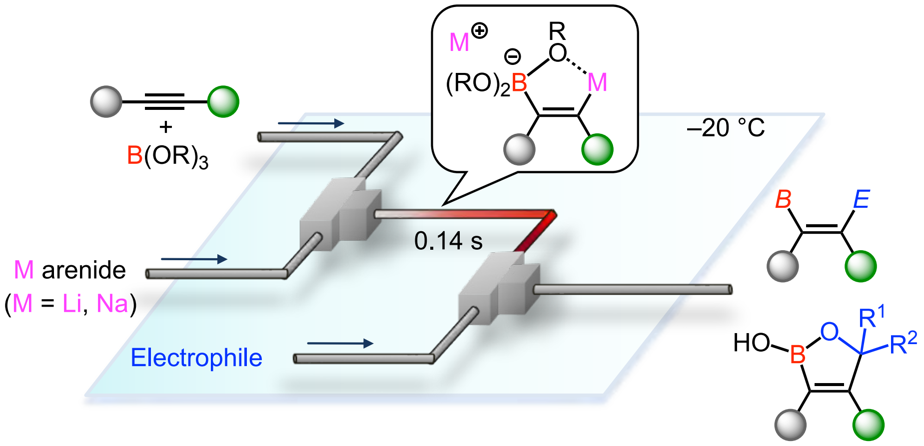

Figure 2. Unsymmetrical borylmetalation of alkynes using flow microreactors.

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Some Aspects of Radical Allylations

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Radical reactions offer many of the properties desired by synthetic organic chemists, in terms of variety, mildness of conditions, and a selectivity that is often complementary to that of ionic chemistry, making many protection steps superfluous. There is however one major difficulty, which derives from the propensity of radicals to interact with themselves (dimerisation, disproportionation) with extremely fast rates that are close to diffusion. In order to overcome this complication, it is essential to keep the steady-state concentration of radical species very low. This can be accomplished for example by contriving a chain reaction where the propagating steps are themselves quite fast, as for example in the typical, and now extremely popular, stannane based processes. While various *unimolecular* cyclisation and fragmentation steps can be efficiently incorporated into the radical sequence, kinetically slower *bimolecular* transformations, and in particular *intermolecular* additions to un-activated alkenes, have proven more difficult to implement. In the case of stannanes, the relatively slow addition to the alkene has to compete with premature hydrogen atom abstraction from the organotin hydride, a step that is usually thousands of times faster.

Over the years, we have shown that xanthates and related thiocarbonylthio derivatives allow the generation of radicals under conditions where the radicals possess a considerably increased effective lifetime, even in a concentrated medium. Intermolecular additions to un-activated alkenes, as well as a variety of reputedly difficult radical transformations can now be easily accomplished. No metals, heavy or otherwise, are required, and the starting materials and reagents are cheap and readily available. Complex, densely functionalized structures can be constructed in a convergent, modular fashion. In the course of our study, we have developed several radical allylation reactions, the most powerful relying on the unusual scission of a carbon-oxygen bond. Recent results and mechanistic aspects will be presented and briefly discussed.

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A Bioinspired but Non-Biomimetic Synthesis of Lignans Enabled by Radical Cation Intermediate

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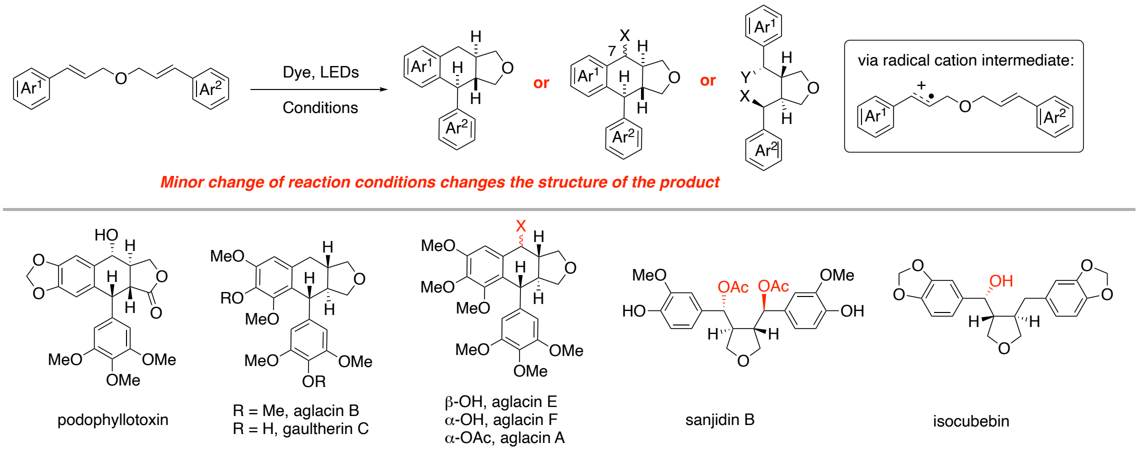
Lignans, displaying broad structural diversity and varying oxidation levels, are widely distributed in the plant kingdom. They possess significant pharmacological properties including anticancer, antimicrobial, anti-inflammatory, antiviral, immunosuppressive, cardiovascular and antioxidant activities.[1] Etoposide, an anticancer drug prepared from podophyllotoxin (which is isolated from the rhizome of podophyllum), is on the WHO's list of essential medicines.[2] Despite considerable progress in synthesizing this family of natural products, a sustainable, general and cost-effective chemical synthesis is still highly sought after in order to fully exploit their potential. We will present our divergent synthesis of aryltetralin cyclic ethers, dibenzyltetrahydrofurans and aryltetrahydronaphthalene lignans from dicinnamyl ethers under photoredox catalytic conditions.[3]



Minor change of reaction conditions changes the structure of the product

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POSTERS

Photocatalytic Generation of *N*-Centered Sulfamidyl Radical for Selective Functionalization of Si-H/Ge-H Bond

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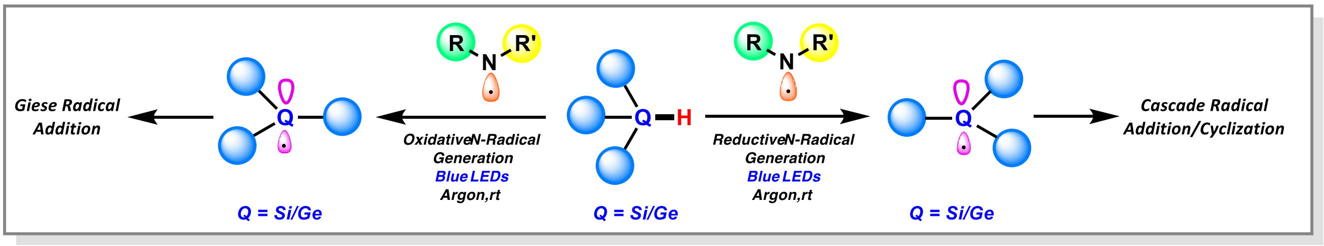
Abstract:

Organosilanes are versatile intermediates in organic synthesis, and they have prevailing applications in material science, agrochemicals, polymer science, and the pharmaceutical industry.[1a-b] Due to the high lipophilic nature of silicon, organosilanes, and silyl analogs of bioactive compounds have appreciable physiochemical properties which makes them an ideal candidate for drug discovery.[1c-e] To access organosilane, hydrosilylation of alkenes *via* direct activation of Si-H bond in hydrosilanes is vastly significant because of the high atom economy of the approach.[1f]



In the past two decades, visible light photoredox catalysis has made a significant impact in the field of synthetic organic chemistry. In addition to single electron transfer (SET) and energy transfer process, hydrogen atom transfer is more frequently encountered in photoredox catalysis. Recent reports on selective Si-H bond functionalization of hydrosilanes under photolytic conditions suffered from poor site-selectivity[2] likely due to the similar BDEs (Si-H vs C-H)[3].

In this presentation, the synthetic utility of newly designed hydrogen atom transfer catalyst/reagents induced *N*-centered radical assisted selective functionalization of Si-H/Ge-H bond (from hydrosilanes and hydrogermanes) for the hydro(silylation) and hydro(Germylation) followed by the Giese radical addition[4] as well as cascade radical addition/cyclization[5], under visible light-mediated metal free condition will be discussed.

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Base-induced formation of nitrobenzene radical

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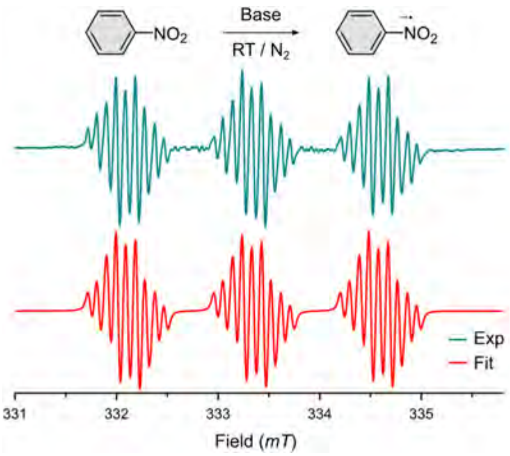
Radical-containing nitroarenes afford non-conventional reaction pathways with a broad scope of applications. For instance, in synthesis, they have been inventively exploited for olefin dihydroxylation,[1] hydrogen atom transfer[2] or transannulation[3] processes, while in biology they play a key role in the metabolic cycle of aerobic nitroreductases.[4] Radical formation in nitroarene compounds occurs either electrochemically,[5] by photoexcitation[6] or via reaction with bases,[7] but direct characterisation of the radical by means of electron paramagnetic resonance (EPR) is usually only possible in the former case, since the other procedures result in intermediate species. Thus, in our view, the method that yields structural and electronic information imposes conditions that are not the most suitable for more general syntheses. As such, we believe that studying whether nitroarenes radicals can be formed and characterized in simple conditions holds the potential to expand their transformative chemistry.

Here, building on previous studies,[7] we report our first attempts to address this possibility. We study the simplest nitroarene, *i.e.*, nitrobenzene, in presence of different nucleophilic bases (*tert*-butyllithium, sodium *tert*-butoxide, sodium bis(trimethylsilyl)amide, sodium isopropyl cyclopentadiene) and solvents (tetrahydrofuran, benzene) in inert atmosphere. Room temperature X-band measurements confirm the formation of a nitro-based radical for all cases, which is stable until exposed to air. Density functional theory calculations indicate that the process is driven by a single electron transfer from the base to the nitrobenzene, but the oxidised base was not detected. To the best of our knowledge, this is the first-time nitrobenzene radical is generated by simple bases and characterised by EPR. Current efforts in the group focus on exploiting these stable radicals for novel synthetic procedures.



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Organophotocatalytic Dyads Tame Transient Radical Couplings

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Molecular organic dyads consisting of linked Donor-Acceptor (D-A) moieties find numerous applications as optical and light-harvesting devices.[1] Upon photoexcitation, charge transfer or formal charge separation (CT) can be advantageous or parasitic depending on the target application. Building on previous learnings on pre-assembling electrogenerated radical cationic and anionic photocatalysts,[2,3] this talk exemplifies how CT or CS states can be leveraged to pre-assemble electronically-complementary reaction partners. Upon photoexcitation of the resulting CT or CS states, transient radicals – that would otherwise undergo synthetically useless defunctionalizations / polymerizations – are generated and react in close proximity for synthetically useful couplings.[4] This demonstrates a conceptual metal-free alternative to transition metal catalysis for intercepting transient radical intermediates, and demonstrates the key importance of aggregation effects in photochemistry often overlooked by synthetic chemists.[5]

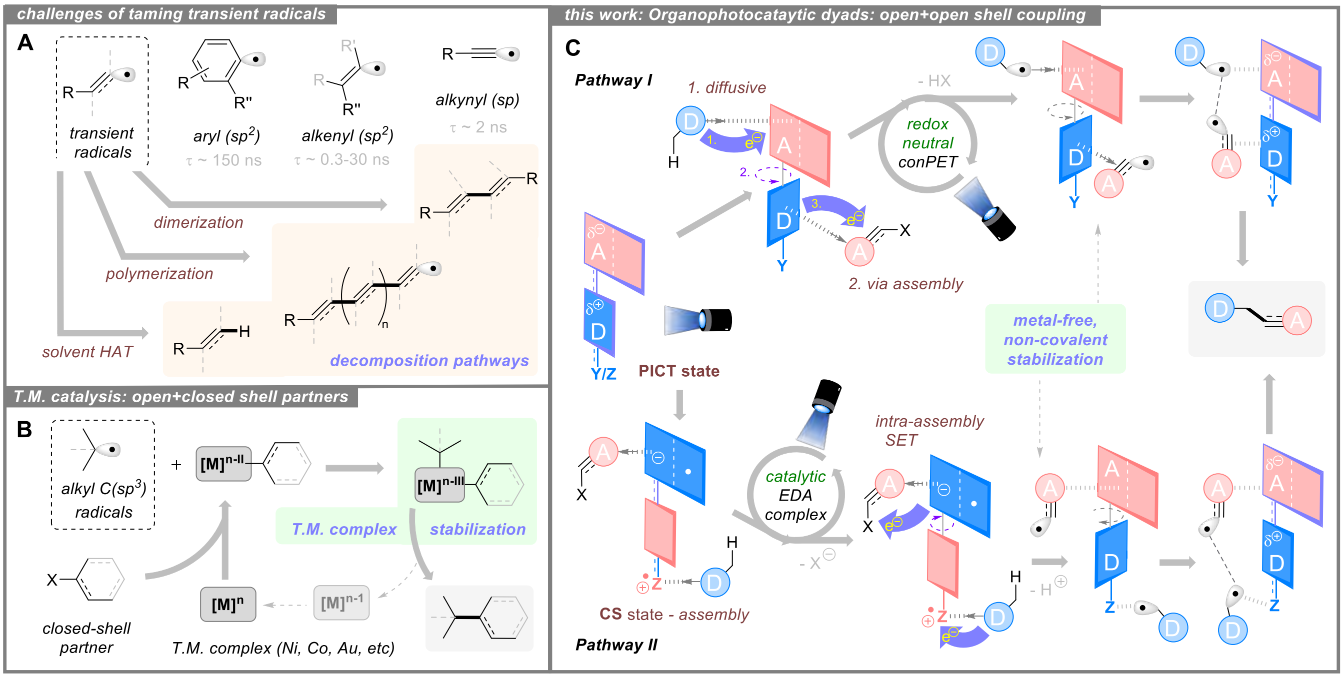

Figure 1. A. Properties and fates of transient radicals. **B.** Transition metal interception of transient radicals for couplings. **C:** Photocatalytic dyads - modes for generation / interception of radicals for couplings.

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Photochemical Iodine Atom Transfer Radical Addition & Cyclization for the Synthesis of Organoboron Derivatives, Cyclopropanes and Cyclopentanes

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The last 20 years, organic synthetic photochemistry, an alternative green and sustainable approach, has experienced a renaissance paving the way for the discovery of novel reactivities[1]. Atom Transfer Radical Addition (ATRA), is one of the most common photochemical reactions, pioneered by Kharasch developing numerous examples in the literature, either using thermal initiation, photochemical conditions, or alternative methods[2,3]. Alkylboronic esters such as boronic esters are highly advantageous and appealing synthetic intermediates for various transformations due to their stability and convenient handling and they can be easily modified[4]. Herein, we present a novel photochemical ATRA protocol where the iodo-reagent ICH_2Bpin, is activated using cheap ascorbic acid and Kessil LED 370 nm (2nd GEN) irradiation which enables its homolytic scission. The protocol was applied for the addition of ICH_2Bpin onto double bonds forming 1,3-iodoboronates which were converted one-pot to cyclopropanes although the unstable boronic intermediates has also been isolated[5]. Furthermore, the photochemical ATRA protocol has also been utilized to a cyclization reaction which led to the synthesis of cyclopetanes via α-boryl radicals which can be further modified. In all cases,the desired products were obtained in good to high yields. The reaction mechanism was extensively examined, revealing the formation of a halogen-bonded complex which initiates the process.

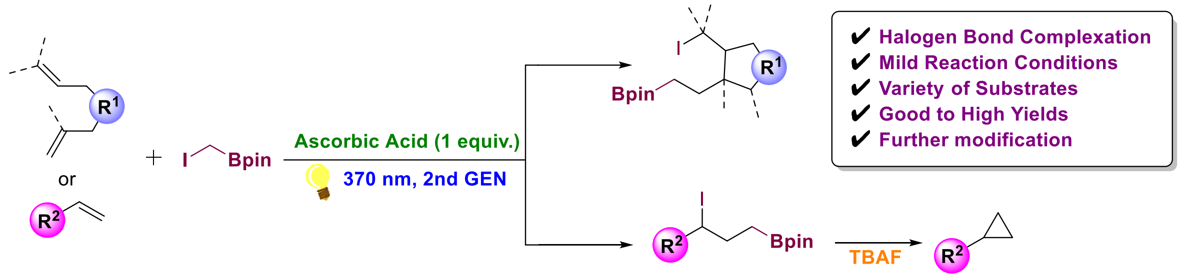

Figure 1. Photochemical ATRA reaction between alkenes and ICH_2Bpin using ascorbic acid

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Generation of 1-thioalkyl radicals from pinacol boronic ester precursors

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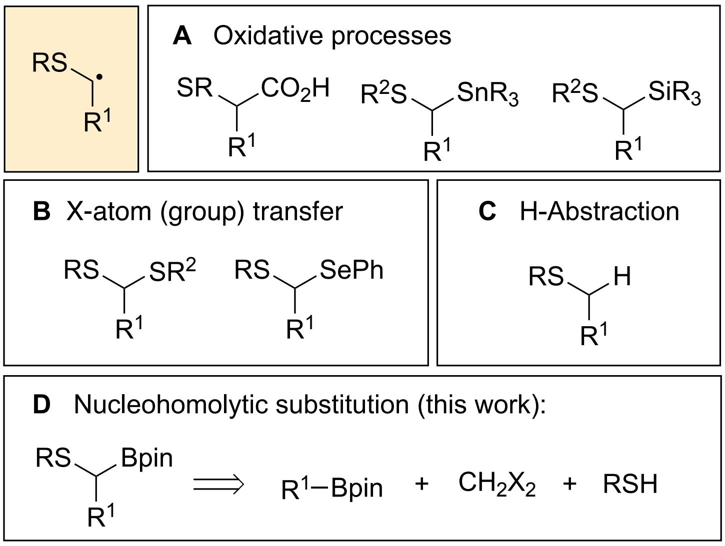
Over the last decades, the generation of 1-thioalkyl radicals has emerged as a powerful strategy for functionalization of thioethers, which represent important structural components of natural and biologically active compounds.[1] For example, the generation of 1-thioalkyl radicals by oxidative processes,[2] X-atom transfer[3] and H-abstraction[4] has been well established.



Scheme 1. Generation of 1-thioalkyl radicals.

Organoboron derivatives have proven over the years to be an efficient source of alkyl radicals.[5] Herein, we report a novel protocol for the generation of 1-thioalkyl radicals starting from 1-thioalkyl pinacol boronic ester precursors, readily prepared by Matteson homologation of commercially available boronic esters and subsequent 1,2-metalate shift with diverse sodium thiolates.

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3D-PRINTED EOSIN Y-BASED HETEROGENEOUS PHOTOCATALYST FOR ORGANIC REACTIONS

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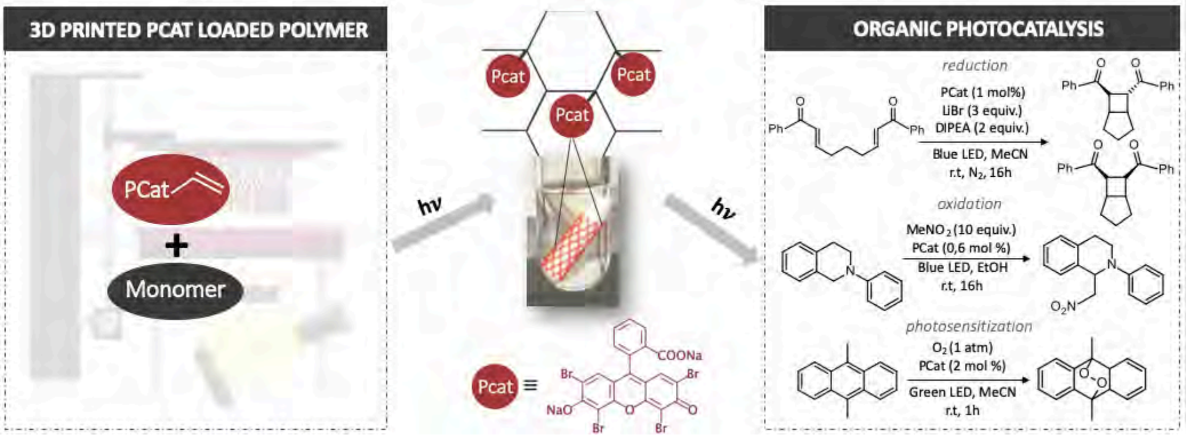
Photocatalysis for organic transformation has been considered as a powerful tool in organic synthesis since its revival in 2008 [1-2]. This innovative field of chemistry relies on the excitation of a photocatalyst (PCat) giving an excited state with unique properties, including the ability to transfer electrons or to transfer energy. However, most of the photocatalysts are prepared and used in homogeneous phase which limits the applications since the photocatalyst is not recovered at the end of the reaction. The solution is to switch from homogeneous to heterogeneous catalysis using a support with high accessibility to PCat [3-4]. The approach of this project is the fabrication and evaluation of new 3D printed polymer-based supported photocatalysts [5-6]. Polymeric supports are synthesized via free radical photopolymerization to yield a recyclable hierarchical polymeric network including a non-toxic PCat (eosin Y) covalently bounded. This 3D-printed object was then adapted to a stirring bar and its photocatalytic activity was evaluated through model organic reactions in oxidation, reduction, and photosensitization [7].



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Carboamidation of Olefins using Unactivated Hydrocarbons enabled by Photoelectrochemistry

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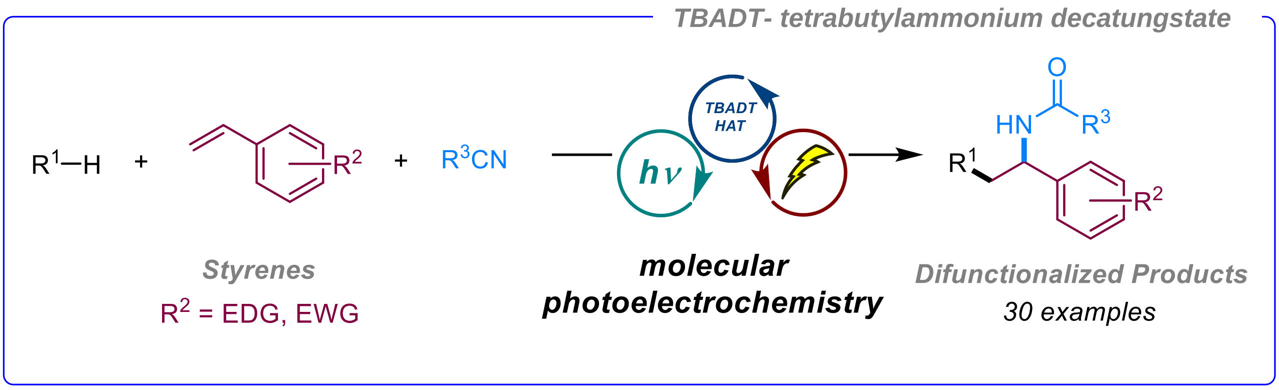
Alkenes are ubiquitous building blocks in organic synthesis and radical-mediated 1,2-difunctionalization of alkenes constitutes an elegant method to construct complex molecules from abundant alkene feedstock.[1] A new method has been developed for the carboamidation of styrenes with varying electronic properties using an array of hydrocarbons. This mild methodology integrates photoredox catalysis (**PRC**) and synthetic organic electrochemistry (**SOE**) unveiling a new pathway in photoelectrochemistry (**PEC**)[2]. The present reaction reveals a photocatalytic hydrogen atom transfer (**HAT**)[3] and an electrochemically mediated radical polar crossover (**RPCO**). The reaction culminates in a Ritter-type amidation in the presence of a nitrile molecule.[4] The reported methodology adeptly activates a diverse range of alkanes allowing the hetero-difunctionalization of styrenes. (**Figure 1**). Finally, our method also offered a greener approach towards the synthesis of pharmaceutically relevant cores such as 1,*n*-amino alcohols[5], and amino-substituted ketones.[6]



■ *Styrene difunctionalization* ■ *Photoelectrochemistry* ■ *Hydrogen atom transfer* ■ *Ritter amidation*

Figure 1: Photoelectrochemical styrene carboamidation *via* electro-recycled TBADT photocatalysis

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Theoretical analysis and reactivity of fluorinated radicals

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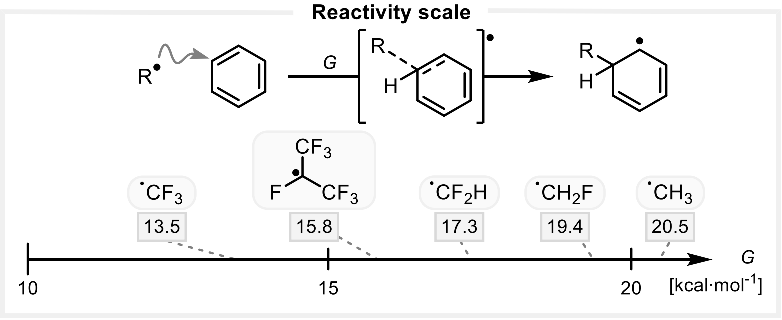
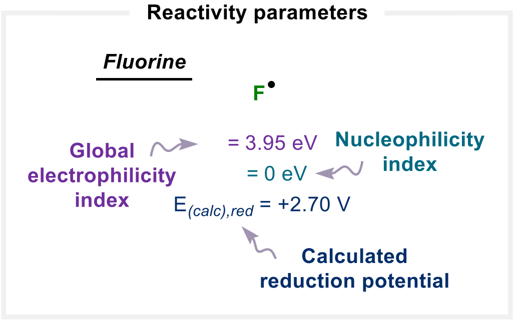
The ability of fluorine atom to alter the properties of a compound at the molecular or macromolecular level is overwhelming. Indeed, insertion of a single fluorine atom nearby a reactive center can have major impact on the chemical reactivity or the properties of a species. For this reason, installation of fluorine atoms and fluorinated motifs onto molecules has become an important synthetic endeavour. Nowadays, a powerful method to facilitate this challenge relies on the design of fluorinated Functional Group Transfer Reagents (FGTRs) which are capable of releasing the desired fluorinated radical upon activation with various stimuli (*e.g.* heat, light, electricity). The influence of the fluorine substitution on radical species was thoroughly investigated and documented by W. R. Dolbier.[1] To help in the design of new chemical transformations involving fluorinated radicals, we have developed a reactivity scale for over 40 radicals based on the calculated energy barriers for their addition to benzene.[2] Other relevant reactivity parameters have been obtained (*e.g.* electrophilicity, nucleophilicity, redox potential) to provide a broader picture of a radical's possible preference or incompatibilities vis-à-vis a given class of reaction partners. We hope that this analysis will stimulate the design of original FGTRs and novel transformations.





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Catalytic Demetallation of Dicobalt Hexacarbonyl Complexes using Near-Infrared Photocatalysis

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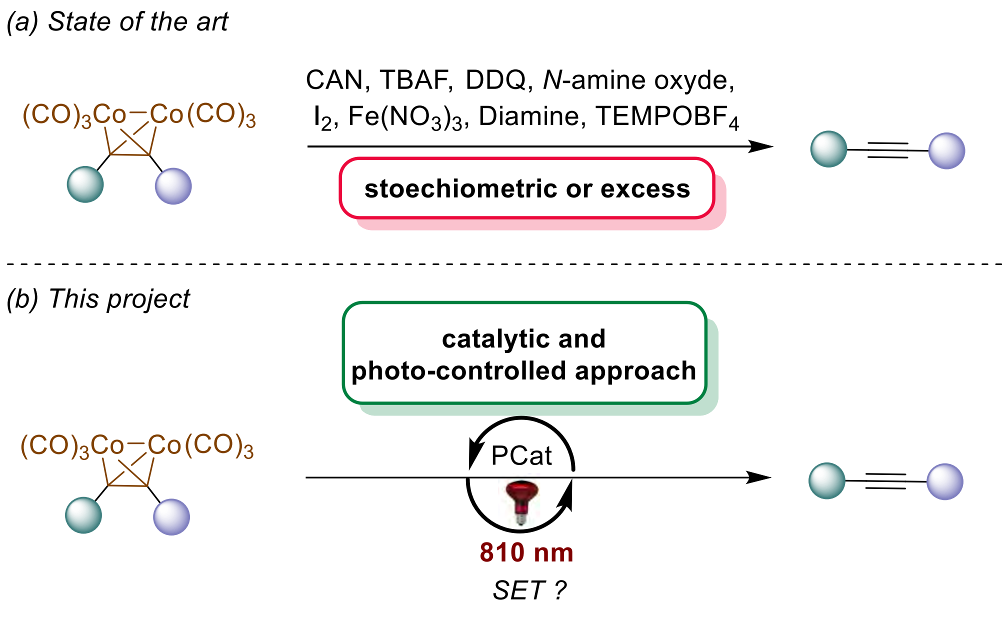
Dicobalt hexacarbonyl complexes are widely used in organic synthesis, both for Nicholas reactions and simply to protect a triple bond.[1] At the end, the alkyne moiety is recovered by the deprotection of these cobalt-complexed alkynes which requires the use of a stoichiometric amount of a one-electron oxidizing agent such as Ceric Ammonium Nitrate (CAN).[2] Our goal was to develop a catalytic method of demetallation using photocatalysis. After several optimization steps, the best results were obtained with near-infrared photocatalysis.[3] This method would allow photo-control of deprotection while limiting the quantity of oxidant required to a catalytic amount. This study includes a mechanistic discussion to understand if a Single Electron Transfer (SET) is involved in this reaction.



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Bifunctional Activation of Feedstock Chemicals for Solvent-Controlled Switchable Synthesis

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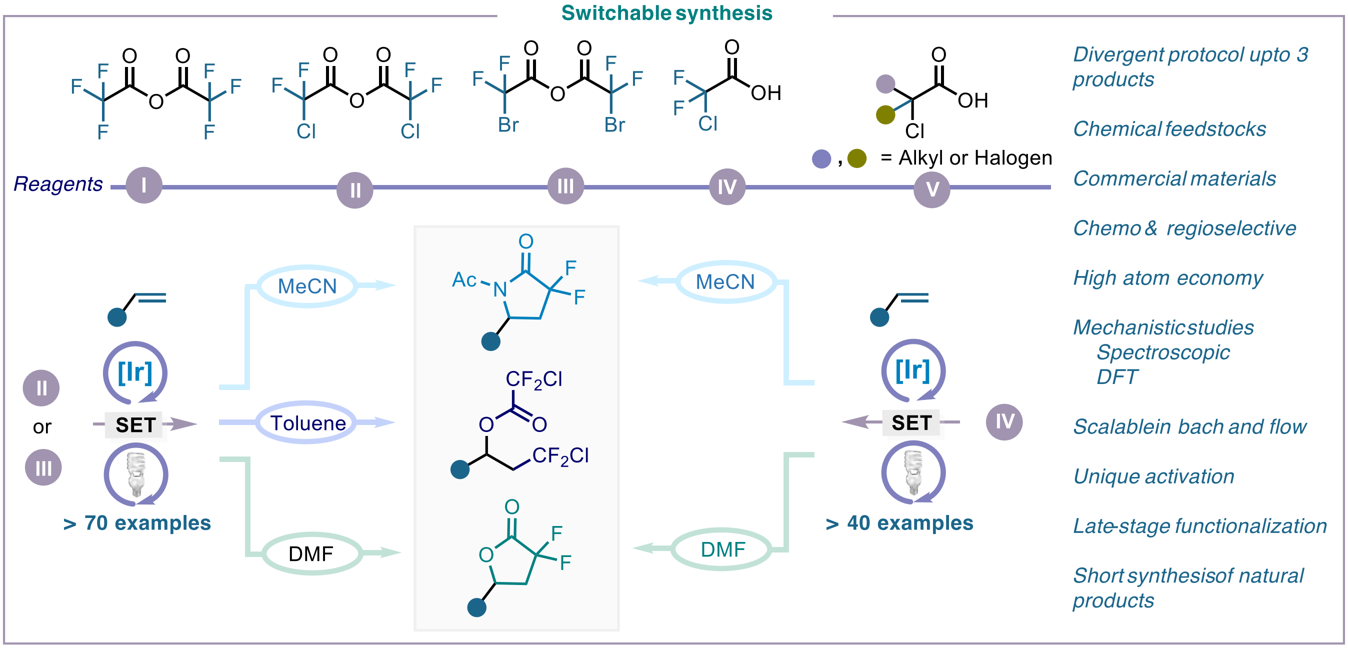
In the pharmaceutical industry, approximately 20-25% of drugs contain fluorine.[1] Synthetic chemists are currently engaged in active innovation to develop methods for the seamless integration of fluorine fragments into organic compounds. This branch of organofluorine chemistry is rapidly growing, focusing on generating fluorinated radicals from readily available functional group transfer reagents (FGTRs).[2] In this context, we found that fluorinated building blocks such as chlorodifloroacetic anhydride (CDFAA, II) as a promising precursor for bifunctional reagent and delivers a wide range of gem-difluorinated γ-lactams, γ-lactones, as well as promotes oxy-perfluoroalkylation under solvent-controlled reaction conditions.[3] Although most of anhydrides are prepared from the corresponding acids, developing a mild and operationally simple strategy to access gem-difluoro compounds using chlorodifloroacetic acid (CDFA, IV) can serve as beneficial entry for achieving step economic and practical synthesis of fluorinated cyclic scaffolds. These methodologies are flow and batch scalable, possess excellent chemo- and regioselectivity, and are useful for late-stage diversification of complex organic scaffolds as well as employed for concise synthesis of (±)-boivinianin A and epi-eupomatilone-6.[4]



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How Much Difference Makes a Methyl in Total Syntheses of Bridged Pyrazinoquinazolinone Alkaloids

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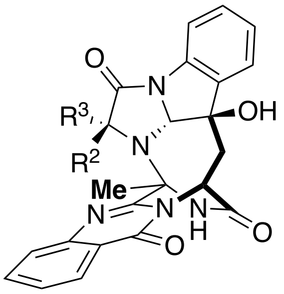
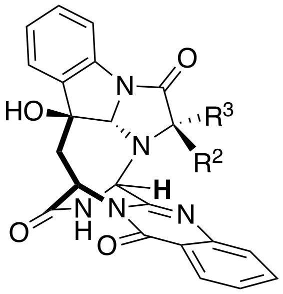
Pyrazinoquinazoline alkaloids, such as the fumiquinazolines and spiroquinazolinones or the pseudoenantiomeric cottoquinazolines or lapatins, are a diverse family of fungal metabolites that essentially differ in the amino acid precursors alanine for the former versus glycine for the latter.[1] They are produced in Nature by oxidative processes. However, their stereochemical features remain a matter of debate because of isolated amounts. Nonetheless, they display interesting bioactivities.

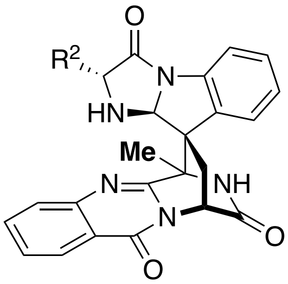


Fumiquinazoline K

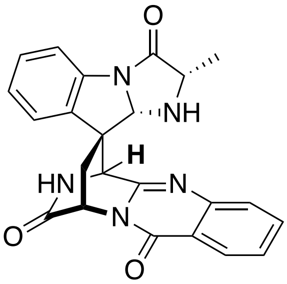
- Bioinspired approach
- Unified radical based
- Unambiguous elucidation of stereochemistry



Cottoquinazolines A-E



Spiroquinazolines



Lapatin A

Therefore, a short bioinspired unified approach to the fumiquinazolines and cottoquinazolines as well as to the spiroquinazolines is aimed for. Here we present results toward the total synthesis these natural products and demonstrate that the seemingly simple replacement of the proton for the methyl group may have significant consequences.

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C-N Bond Formation using Persistent Nitrogen-Centered Radicals

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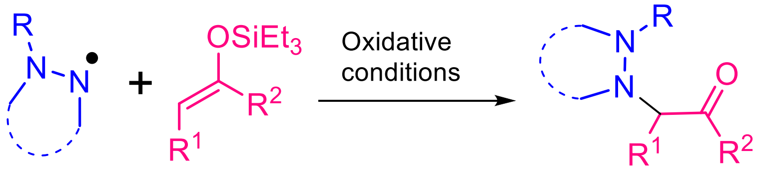
The formation of C-N bonds using radical reactions plays a prominent role in modern organic chemistry. There are diverse methods to generate transient nitrogen radicals *in situ* by reductive or oxidative conditions, proton-coupled electron transfer reactions or homolytic cleavage. [1] The resulting highly reactive N-radical will undergo cascade processes leading to the functionalization of Csp2, Csp1 [2] or Csp3 [3] carbon atoms by the formation of a new C-N bond.

We show here the other side of the picture, where a transient α-carbonyl radical generated *in situ* encounters a persistent N-centered radical, to afford α-functionalized ketones (Scheme). Late stage functionalizations will be demonstrated.



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Shuttle hydrogen atom transfer (HAT) for mild alkene transfer hydrofunctionalization

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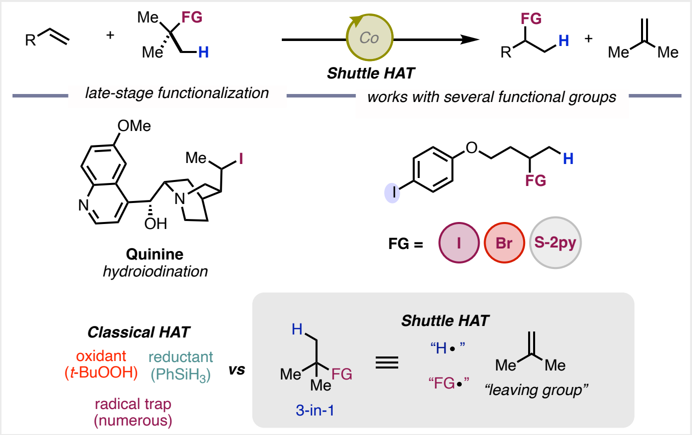
Hydrogen atom transfer (HAT) from a metal-hydride is a reliable and powerful method for functionalizing unsaturated C–C bonds in organic synthesis.[1, 2] Cobalt hydrides (Co–H) have garnered significant attention in this field, where the weak Co–H bonds are most commonly generated in a catalytic fashion through a mixture of stoichiometric amounts of peroxide oxidant and silane reductant. Here we show that the reverse process of HAT to an alkene, i.e. hydrogen atom abstraction of a C–H adjacent to a radical,[3, 4] can be leveraged to generate catalytically active Co–H species in a new application of shuttle catalysis coined shuttle HAT. This method obviates the need for stoichiometric reductant/oxidant mixtures thereby greatly simplifying the generation of Co–H under exceedingly mild reaction conditions. This approach opens the door for the introduction of functional handles (e.g., iodides) that were previously challenging through other catalytic approaches, and paves the way for new reagent design which incorporates this shuttle HAT platform. The shuttle HAT catalytic cycle can be interwoven with a reversible C–X bond forming cycle to shuttle a hydrogen atom and halogen atom between molecules. Unlike polar transfer reactions, the implementation of a radical pathway enables hydrofunctionalization to proceed with Markovnikov selectivity and prevents chain walking mechanisms.[5]



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Design and Synthesis of Efficient Initiator for Photoinduced Radical Polymerisation Utilizing the Anomeric Effect of Five-Membered Ring Molecules

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Abstract: Photochemical reactions are becoming essential tools both in academia and industry due to it's operational simplicity, environmentally friendly and economically sustainable nature in comparison to thermochemistry.[1] Particularly scientific community are attracted towards photoinduced radical polymerization (PRP) reaction due to it's various applications in the areas of dental restoration process, tissue engineering, artificial bone generation and 3D-Printing.[2] Herein we report the design of new initiator for PRP reaction via intramolecular hydrogen atom transfer reaction utilizing the inherent anomeric effect of five membered ring containing molecules. We have synthesized new efficient photoinitiator via barrierless sequential conjugate addition reaction.

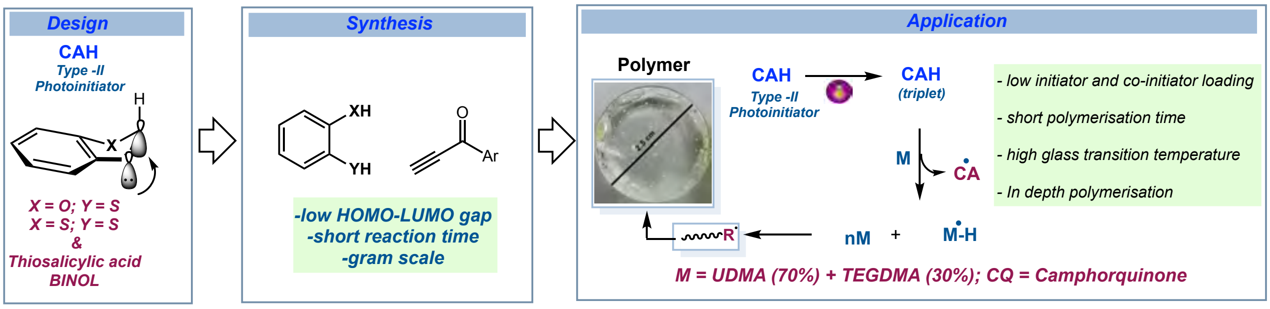

Figure: Design, synthesis of initiator and application in PRP reaction.

Polymerization of diurethane dimethacrylate (UDMA, 70%) and triethylene glycol dimethacrylate (TEGDMA, 30%) in presence of 450 nm LED (15 W) under the aerobic conditions turned out to be very efficient (71 seconds) using our newly synthesized 1,2-benzenedithiol (DTH) based initiator and the resultant polymeric material has excellent physical properties.[3, 4] Higher efficiency of this initiator is due to the low bond dissociation energy of C-H bond adjacent to the two heteroatoms and puckered ring structure of the five membered rings. This hypothesis was further supported by X-Crystal structure of the initiator, NMR and computational data.

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Access to Borylated Cyclopropanes via Homolytic Substitution

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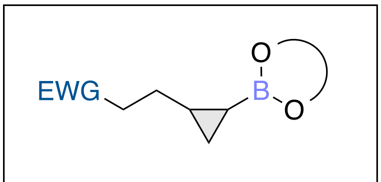
Cyclopropanes are prevalent in a variety of natural products, drugs and biologically active compounds. Due to their unique reactivity, they are valuable building blocks for synthetic chemistry, organocatalysis and medicinal chemistry. Traditional methods require highly reactive species, such as carbenes, ylids and carbanions.[1] Radical chemistry is emerging as a powerful technique, offering a robust approach to the formation of C(sp^3)-C(sp^3) bonds.[2]

Herein, we report a mild procedure for the cyclopropanation of boronic esters. This radical-mediated approach is particularly attractive, notably due to the procedure's convenience and ease of use, requiring no specific inert conditions. The developed method is diastereoselective and tolerates a wide range of functional groups. Insights into the reaction mechanism and the investigation of the stereochemistry will be discussed.



Borylated Cyclopropanes

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Highly Efficient Quantum Dots for Alkyl Radical Generation

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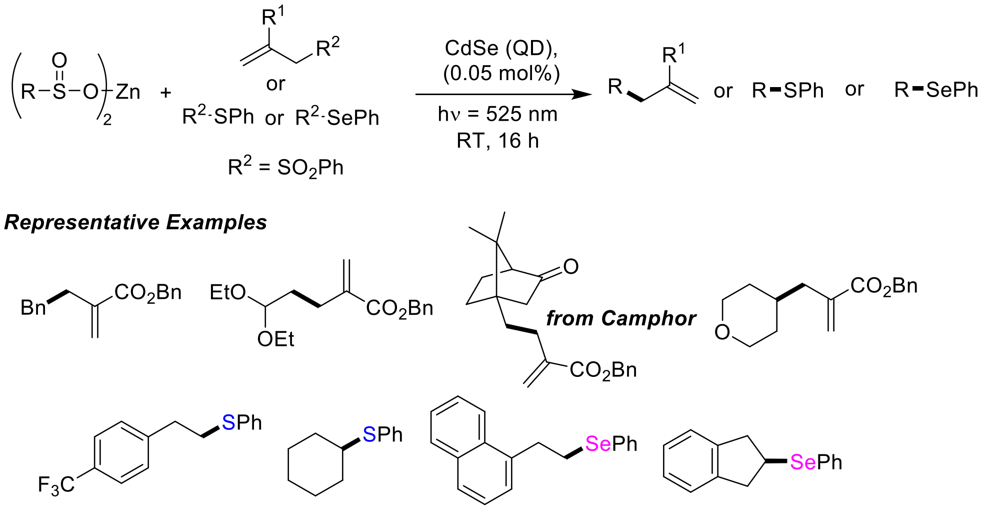
Quantum Dots (QD) are semiconducting materials in nanometer-sized with defined composition, shape, and size.[1] QD's are typically composed of inorganic core made up of hundreds to thousand atoms. In recent years photoredox catalysis[2] has emerged as powerful strategy for small molecules synthesis and late-stage functionalization under relatively mild reaction conditions. However, photocatalyst used are complexes of expensive and rare earth metals which operates under homogenous conditions and typically not ideal for large-scale industrial application.[3] Thus, other alternative for abundant material as photocatalyst has attract synthetic chemist to develop versatile materials to perform photoredox reactions with additional features of recyclability. In present study we have utilized CdSe QD as photocatalyst to oxidize wide range of zinc alkyl sulfinates[4] under photoredox condition generating alkyl radicals which subsequently forged into C-C, C-X (X = S, Se) bond forming reactions. The reaction is quite general and efficient for the generation of both primary and secondary radicals when trapped with allyl sulfone, furnished allylated products in moderate to good yields. Moreover, resultant radicals can further engage into sulfurization and selenylation products. The efficiency of CdSe is further demonstrated by recycling the QD by precipitation and filtration and used as such for next reaction which afforded the products with marginal loss.



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Introducing Cinchona Alkaloid Appended Thiol(s) in Gold Nanocluster Chemistry

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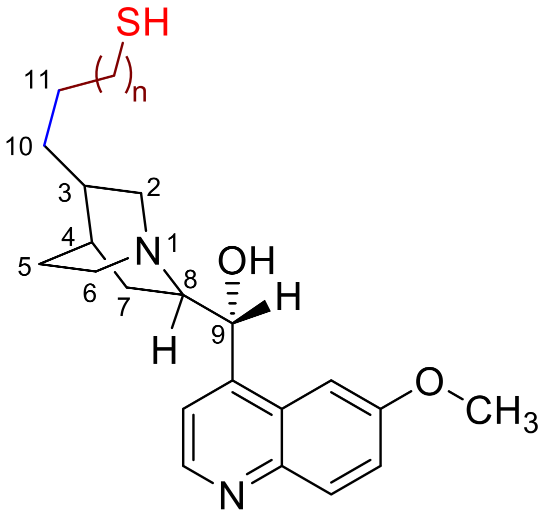
Cinchona alkaloids represent a diverse class of naturally occurring compounds that have been extensively studied and utilized in various fields of chemistry and biochemistry over the past two centuries.[1,2] These versatile molecules have demonstrated a wide range of applications, including their use as chiral organocatalysts, ligands, chromatographic selectors, antimalarial drugs, and NMR discriminating agents.

Our research aims to further explore the potential of cinchona alkaloid-appended thiols with varying chain lengths (n = 0, 2, 4, …) as chiral ligands in gold nanocluster chemistry, see figure. We plan to synthesize and incorporate these ligands into nanoclusters such as $Au_{25}(PET)_{18}$ through ligand exchange reactions (LER).[3] By introducing these chiral ligands, we aim to investigate their potential applications in enantioselective organocatalysis, NMR discrimination, and other related fields.[4]

In this poster presentation, we will showcase the synthesis of the alkaloid derivative and present its application as chiral ligand on atomically precise gold clusters.



L1 (n = 0, 2, 4, ….)

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Electrochemical Homo- and Cross- Annulation of Alkynes and Nitriles for the Regioselective Synthesis of 3,6-Diarylpyridines

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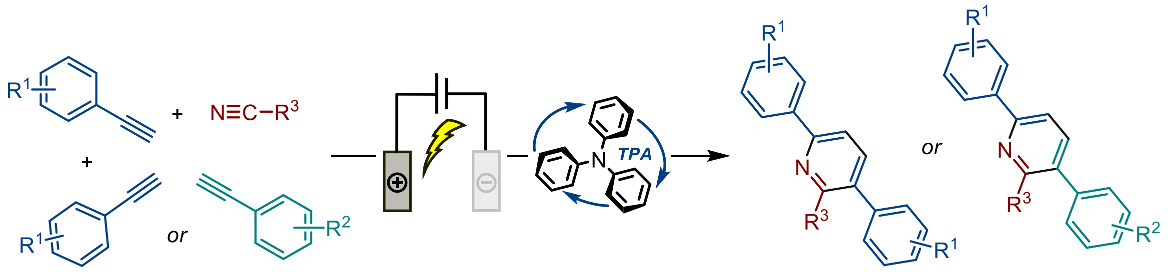
The pyridine moiety is among the most extensively used heterocycles in the field of drug design[1] as well as has agrochemical applications. [2] Given this importance and ubiquity, different pathways were developed for the synthesis of substituted pyridine-containing scaffolds. Besides classic strategies (*e.g.* Pd-catalyzed Suzuki cross coupling), one of the most promising approaches consists of a [2+2+2] intramolecular annulation of alkynes and nitriles. However, the methods reported so far relies on the use of transition metals or are mainly limited to the coupling of two identical alkynes.[3-4] Herein, we report an electrochemical strategy for a metal- and oxidant- free, green regioselective synthesis of 3,6-diarylpyridines (**Figure 1**).[5] Harvesting electrochemical energy and catalytic amounts of triphenylamine (**TPA**), two identical or two different alkynes can be coupled with a nitrile, resulting in a broad applicability in both homo- and cross- coupling to generate disubstituted pyridines. The method is also applicable for late-stage functionalization of pharmaceutical and bioactive molecules. Notably, the reaction demonstrated to be scalable up to gram scale in both batch and continuous flow, utilizing a cutting-edge electrochemical continuous flow reactor (FAVO^{TM} CreaFlow reactor).[6]



■ *metal and oxidant free* ■ *unprecedent [2+2+2] cross annulation* ■ *scalable in flow* ■ *green H_2 evolution*

Figure 1*: Electrochemical [2+2+2] annulation of alkynes and nitriles.*

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Radical-Type Reactivity of Novel 7-Coordinate Molybdenum Alkyl Complexes Supported by 1,3-Diketonates

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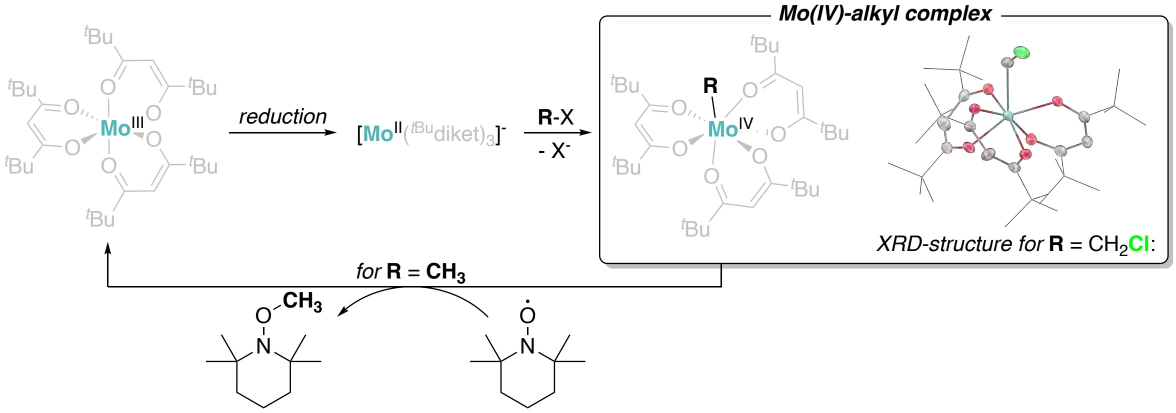
The selective C-X bond activation of simple organohalide substrates (*e.g.* dichloromethane) by low-valent transition metals is an attractive strategy for the preparation of (halogen-)alkyl complexes. The latter have been recognized as an important class of compounds, acting as precursors for the generation of methylene and methylene-bridged complexes, which represent proposed intermediates in a variety of important catalytic processes such as alkene metathesis, Fischer-Tropsch Synthesis or cyclopropanation.[1]

During the study of low-valent molybdenum complexes supported by 1,3-diketonates, we have found the selective reactivity of a homoleptic and anionic Mo(+II) complex with short-chain alkyl halides (R-X) such as dichloromethane. XRD solid state structure revealed the formation of a molybdenum-carbon bond as part of a novel 7-coordinate Mo(+IV) complex. Next to cyclopentadienyl supported complexes of the type [MoCp(NO)$_2$(CH$_2$X)],[2] this is the only second report of molybdenum halomethyl complexes.

While isolated as pure compounds in the solid state, we have observed fast decomposition in solution. To better understand the reactivity of these Mo(+IV) alkyl complexes, the use of deuterated alkyl halide substrate allowed for the preparation of deuterated analogues. ^{2}H NMR spectroscopy has been used as a selective probe to follow the alkyl ligand's reactivity. Its radical-type character favors hydrogen abstraction *e.g.* from THF and allows for facile and selective methyl radical transfer reactions to various acceptors such as TEMPO or diphenyl disulfide.



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Photoredox-catalyzed α-C-H alkylation of (poly)-hydroxylated substrates mediated by CO_2

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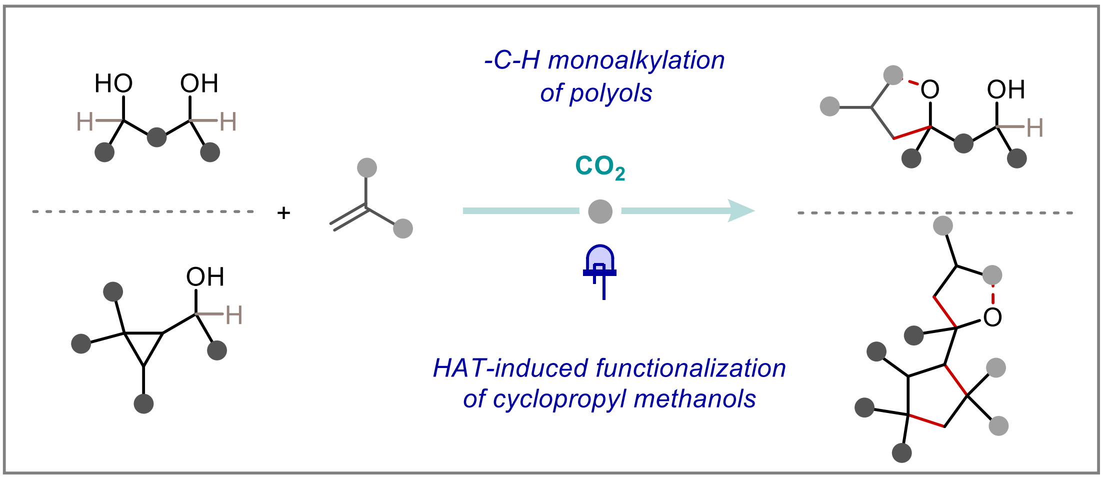
Carbon dioxide (CO_2) is an overproduced, inexpensive and non-toxic gas which can reversibly bind chemical functions with sufficient Lewis basicity. Consequently, it can be used to modify temporarily the reactivity of the corresponding molecules.[1] For instance, CO_2-promoted photoredox processes have been developed to achieve the α-C-H alkylation of aliphatic amines.[2] Our investigations in this area focuses on using CO_2 to transiently modulate the reactivity of hydroxylated molecules in order to develop original photoredox-catalyzed transformations. Recently, we have demonstrated that the catalytic and reversible carbonation of aliphatic polyols under CO_2 atmosphere constitutes a unique strategy to perform the α-C-H monoalkylation of these abundant feedstocks by photocatalytic hydrogen atom transfer (HAT).[3] Experimental and theoretical mechanistic studies have demonstrated an activation resulting from an intramolecular hydrogen bonding between the carbonate and the remaining alcohol.

In the meantime, we have discovered that CO_2 could be used to slow down keto-enol tautomerism in complex radical cascades.[4] This observation was applied to the design of an unprecedented cascade triggered by photocatalytic HAT and allowing the conversion of cyclopropyl methanol derivatives into elaborate building blocks in one step.



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N-Nitrosuccinimide: Versatile Organic Reagent for Radical Nitration

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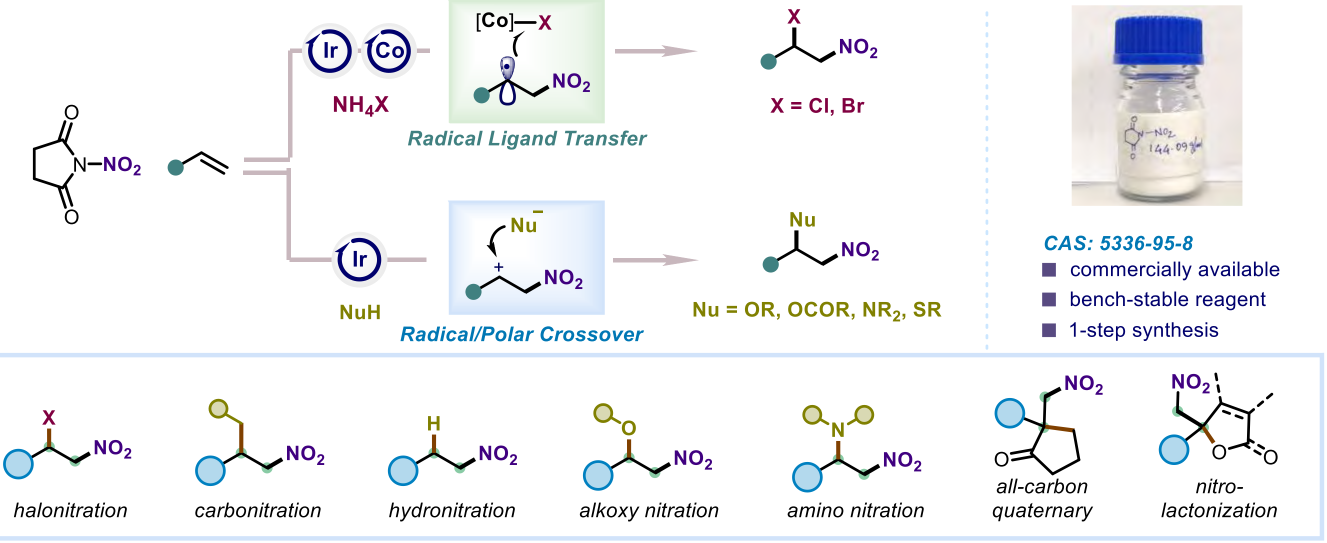
Nitrating reactions hold significant importance in organic synthesis and are foundational topics taught in schools. While the classical electrophilic nitration method using strong mineral acids prevailed for many years since its discovery in the 19th century, recent decades have seen a shift towards exploring new reactivity and reagents. Researchers now seek practical and mild reaction conditions for accessing nitro compounds. Organic nitrating reagents have emerged as key players in this endeavor, offering enhanced reactivity and enabling eco-friendly and sustainable nitration processes.[1]

Herein, we present a novel dual photoredox-mediated paradigm for difunctionalization of alkenes, yielding challenging 1,2-halonitroalkane molecules. We employ N-Nitrosuccinimide as a redox-active nitrating reagent to introduce a controlled amount of nitryl radicals into reaction mixture, while cobalt-mediated radical ligand transfer (RLT) facilitates the transfer of a secondary functionality into the organic scaffold. This synergistic process between photocatalyst and cobalt operates under mild conditions, enabling a one-pot synthesis of 1,2-chloronitro- and 1,2-bromonitroalkanes with excellent chemo- and regioselectivity, demonstrating exceptional functional group tolerance. Detailed mechanistic studies supported the role of cobalt as a radical halogen transfer catalyst. Furthermore, employing a net-neutral radical/polar crossover (RPC) approach under cobalt-free reaction conditions allowed to accommodate a variety of external protic nucleophiles, including thiols, alcohols, acids, and, notably, substituted amines.[2,3] Highly functionalized olefin scaffolds also successfully underwent nitrative difunctionalization, demonstrating the viability of these protocols for the late-stage functionalization of bioactive molecules.



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Revealing radical reactivity of BODIPY-based photocages

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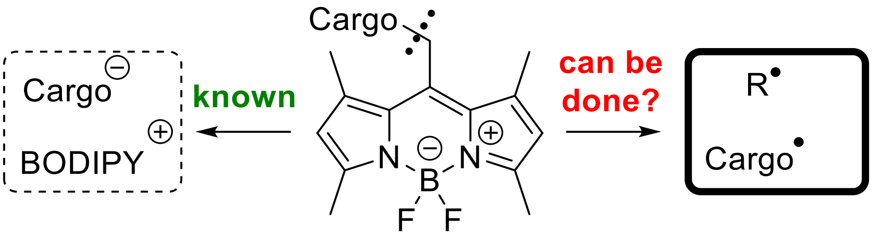
Photocages[1] are highly desirable compounds due to their potential applications in drug delivery systems. BODIPY-based photocages are promising candidates as the reactivity of the BODIPY scaffold enables a wide range of its modification.[2,3]

It has been previously shown that the photorelease of carboxylate from related BODIPY systems is a photoinduced S_N1 reaction. We have utilized this knowledge for the release of signaling lipids from π-extended BODIPYs.[4] Detailed mechanistic studies performed on these derivatives revealed possible parallel homolytic cargo cleavage.



Therefore, in the current study, we develop BODIPY-based systems, where a BODIPY-Cargo bond cleavage is a homolytic process, which enables a photoinduced release of organic radical species. Moreover, we will also present applications of this reactivity mode in polymerization.

This work was supported by the SNSF Swiss Postdoctoral Fellowships grant (217233)

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Silica Based Heterogeneous Photocatalyst for organic reactions

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(3) Institut des Sciences Moléculaires (ISM) UMR-5255, Université de Bordeaux, 33405, Talence, France
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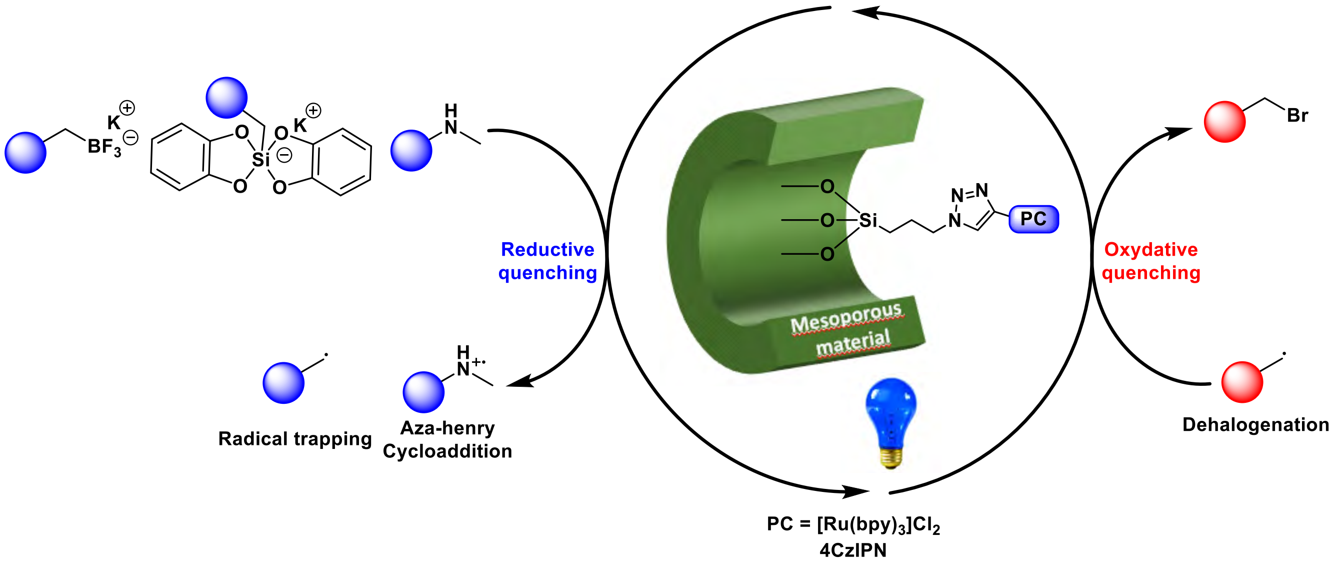
Radical chemistry offers a large synthetic potential due to its unique reactivity. Generation and control of this species in mild conditions remains a major challenge that could be handled by redox photocatalysis[1],[2]. This concept is based on radical species generation by the use of light into visible or near-infrared domains[3] via a photocatalyst (PCat) (organometallic complexes, organic dyes, semi-conductors) able to promote photoinduced electron transfert (PET). Elaborated PCat are now available, they play a key role in the transformation, but their recovery at the end the reaction is still challenging. Heterogenization of PCat appears to be a valuable solution to reach sustainable processes. Rapid and efficient synthesis of new supported photocatalyst is still a remaining challenge and the choice of the support is crucial. Thanks to their stability and versatility, silica-based porous material seems to be an interesting alternative to metal nanoparticles and polymers. The present project aims at preparing a new generation inorganic/organic photocatalysts and evaluate their performances in challenging radical reactions[4,5].



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Electrifying and (en)lightening aryl diazoesters

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Aryl diazoesters are an interesting class of reagent in organic synthesis that are converted into carbenes and metal carbenoids under light and metal catalysts under thermal conditions. These carbene/ carbenoids are then utilised in numerous organic transformations including, insertion, cycloaddition, cyclopropane formation etc. We have demonstrated that under photochemical and electro-photochemical condition aryl diazo esters are converted to carbenes and radical anions respectively and are harnessed in numerous ways to generate interesting heterocyclic scaffolds. Our presentation will be a vignette of this research.

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Photocatalytic generation of cyclopropenium cations

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We report photocatalytic decarboxylative functionalization of cyclopropenes (Scheme 1). Cyclopropenylphthalimides are obtained starting from a broad range of redox-active ester-substituted cyclopropenes in the absence of a nucleophile. Moreover, different carbon and heteroatom nucleophiles can be introduced when the acidic additive is present in the mixture. The mechanistic studies provide support for the radical-polar crossover mechanism proceeding through the formation of an aromatic cyclopropenium cation, followed by trapping with the nucleophiles.

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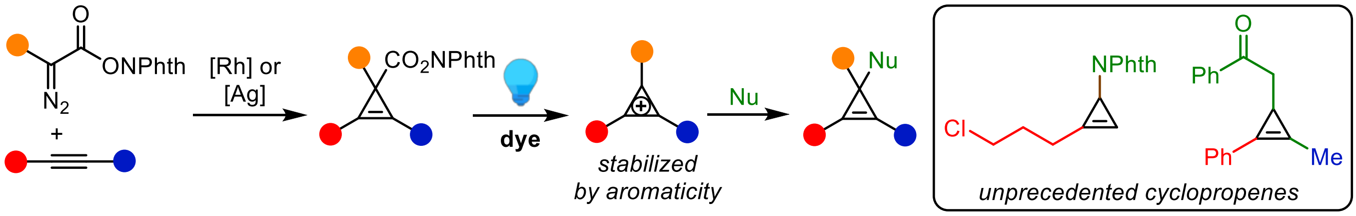

Scheme 1. Photocatalytic decarboxylative functionalization of cyclopropenes

Selective Hydrodemethylation of Methyl Alkylbenzenes with Carbon-Supported Potassium Hydride

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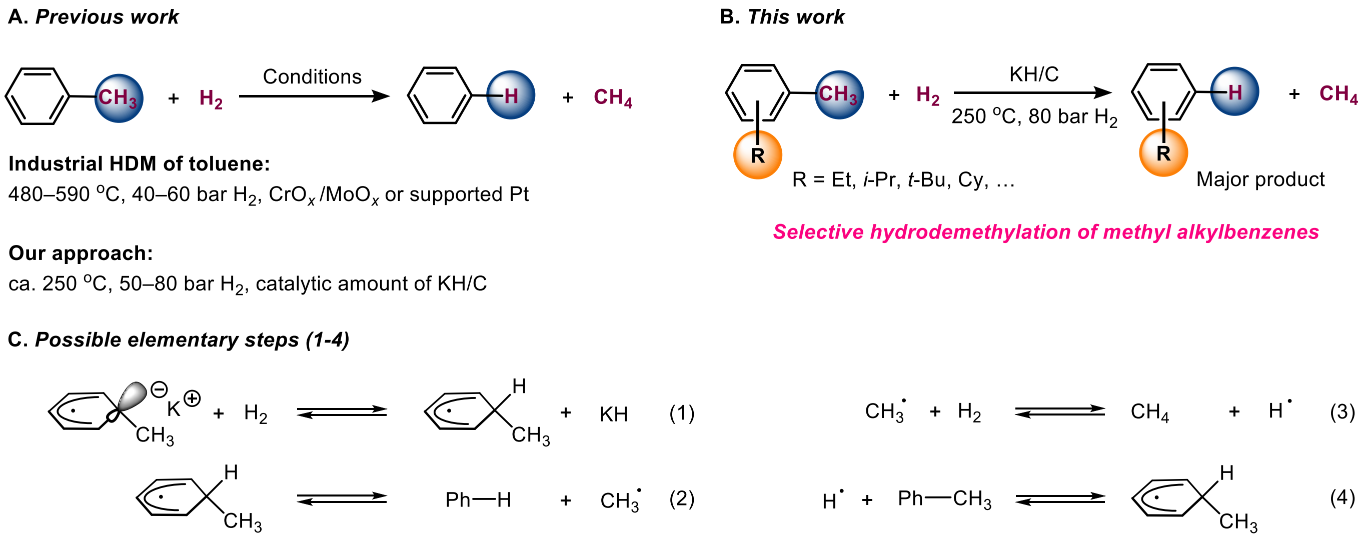
Benzene, toluene, xylenes (BTX) and higher alkylated aromatics are essential petrochemicals, and their production is balanced according to the demand using the hydrodemethylation (HDM) and, more generally, the hydrodealkylation (HDA) process, as well as the isomerization of xylenes and transalkylation processes. We have recently reported that the HDM of toluene to benzene proceeds when a catalytic amount of carbon-supported potassium hydride (KH/C) is heated in neat toluene to ca. 250 °C under 50-80 bar H_2 (for the industrial HDM process, a higher temperature of ca. 480-590 °C is used in combination with a transition metal catalyst, Scheme 1A).[1] In contrast, the transalkylation reaction relies on an acid catalyst and follows the Friedel-Crafts mechanism. The propensity to transalkylation of tertiary, secondary and primary alkyl groups is governed by the stability of the respective carbocations, i.e., 3° > 2° > 1° > CH_3.[2] Here, we studied HDA of various methyl alkylbenzenes with [KH/C + H_2] and found a selective HDM in preference to HDA for the removal of CH_3, C_2H_5, *i*-C_3H_7, *t*-C_4H_9, and *c*-C_6H_{11} substituents (Scheme 1B). That is, a [KH/C + H_2] reactive system provides the opposite reactivity trend to that observed in the Friedel-Crafts transalkylation, i.e., CH_3 > 1° > 2° > 3° alkyl substituent, suggesting a different mechanism, possibly involving radical species. We tentatively ascribe this HDM activity to result from the dissociation of H_2 on the potassium radical anion salts of the respective aromatic substrates. The formed hydrogen radical species then may serve as a chain transfer reagent (Scheme 1C).



Scheme 1. Industrial and emerging approaches to the HDM of toluene (A), selective HDM of methyl alkylbenzenes studied in this work (B), and conceivable steps involved in the developed HDM methodology with KH/C.

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Ball-milling-enabled Alkene Difunctionalization Through Radical Ligand Transfer and Electron Catalysis

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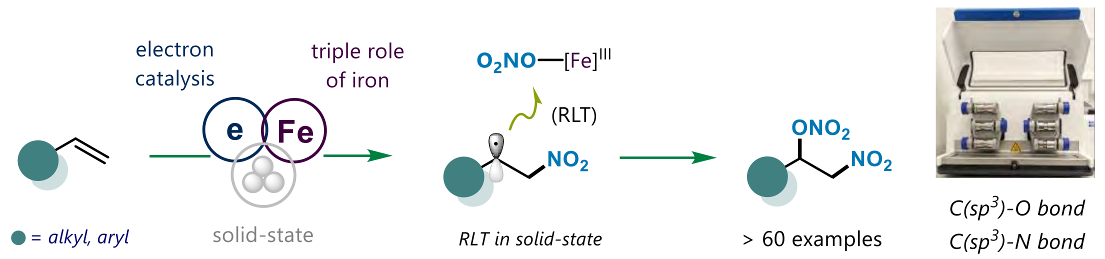
The nitro group (NO_2) plays a pivotal role in organic synthesis and finds extensive application across industry and academia. Despite significant advancements made in the field of nitration chemistry over past decades, nitration reactions of organic frameworks remain challenging from both experimental and practical standpoints.[1] Conventional methods for the direct functionalization of organic molecules involve the formation of the nitronium (NO_2^+) ion species in a highly corrosive acid mixture. However, this approach imposes various limitations, particularly for compounds containing acid-sensitive functional groups. Hence, there is a growing demand for protocols that ensure safety, as well as high level of chemo- and regioselectivity in nitration reactions, while operating under mild conditions.



- *Mild & selective*
- *Valuable products*
- *Cooperative catalysis*
- *Solvent-free conditions*
- *Excellent FG tolerance*
- *Operationally simple & scalable*

Herein, we report a general and modular protocol for olefin difunctionalization through mechanochemistry, facilitated by cooperative radical ligand transfer (RLT) and electron catalysis.[2] Utilizing mechanochemical force and catalytic amounts of TEMPO, ferric nitrate can leverage nitryl radicals, transfer nitrooxy-functional group via RLT, and mediate an electron catalysis cycle under room temperature. A diverse range of activated and unactivated alkenes exhibited chemo- and regioselective 1,2-nitronitrooxylation under solvent-free or solvent-less conditions, showcasing excellent functional group tolerance. It also demonstrated remarkable substrate compatibility, selectivity, and scalability. Mechanistic studies indicated a significant impact of mechanochemistry and highlighted the radical nature of this nitrative difunctionalization process. Additionally, the versatility of this catalytic concept is further highlighted by its ability to selectively introduce various other functional groups.

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Near-Infrared Photooxidation of Dihydrotetrazine for Applications in Bioconjugate Chemistry: a radical pathway?

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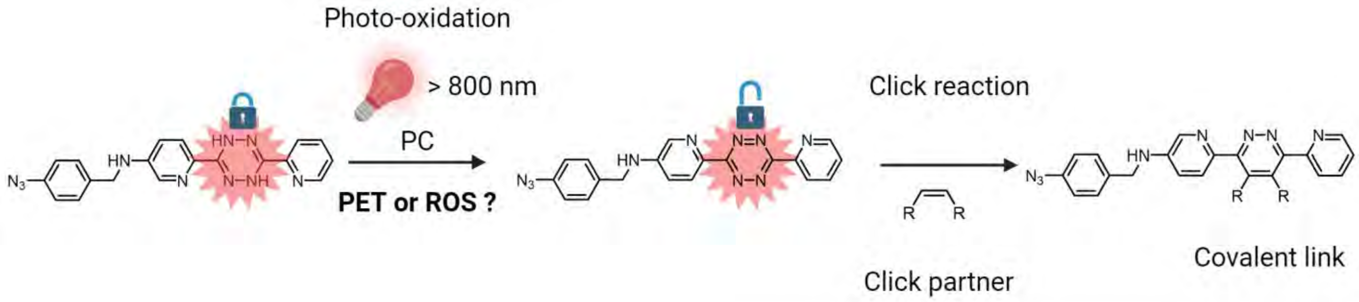
Synthetic chemists aspire to control each parameter involved in organic transformations, such as efficiency, selectivity (chemo-, regio-, enantio-selectivity), and kinetics. The next level of control needed for applications is the reaction's temporal and spatial trigger. This is particularly required for biological/pharmaceutical applications such as drug delivery or medical diagnostics.[1] Governing the reaction through a simple switcher is appealing, and the photo-click concept is a wonderful tool for achieving this goal.[1] In this case, the click reaction, which has many advantages (kinetic, selectivity…), is triggered by light. Until now, the photoclick concept has been developed from UV to visible light.[2] However, near-infrared light presents many advantages, such as light penetration, biocompatibility and low energy.[3]

Based on our previous works on NIR-photocatalysis driven by cyanines and squaraines[4,5], we tackle the challenge of NIR-Photoclick. Herein, the NIR-photooxidation of dihydrotetrazine to deliver the clickable tetrazine is presented. This study includes photocatalyst design, optimization, and mechanistic discussion. The last point is crucial to reach the best photocontrol. Does the reaction proceed through a photoinduced electron transfer, reactive species of O_2 or both?



Scheme 1 : Near-Infrared Light triggered click reaction

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MILD SYNTHESIS OF ARYLSULFONAMIDES USING N-SULFONYLAMINE

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Sulfonamides are pervasive in medicinal chemistry, but they draw a lot of attention from researchers in the field of organic chemistry, chemical biology or material sciences. Our group reported in 2020 that cell-permeable and fluorogenic rhodamine dyes can be generated by switching from lactone to lactam with sulfonamides as N source.[1] Recently, we reported the synthesis of a sulfonamide from BAPTA and constructed a calcium sensor based on this (Figure 1A).[2] However, as the classical method for introducing primary sulfonamide functionality requires harsh conditions, we would like to develop a novel method to facilitate the synthesis of arylsulfonamides.

We herein reported a mild and practical method for installing -SO2NH2 group to aniline derivatives. The key of this reaction relies on the in-situ generation of the active electrophile O2S=NR (Figure 1B).[3] We used this strategy to access a series of fluorescent sensors for metallic ions.

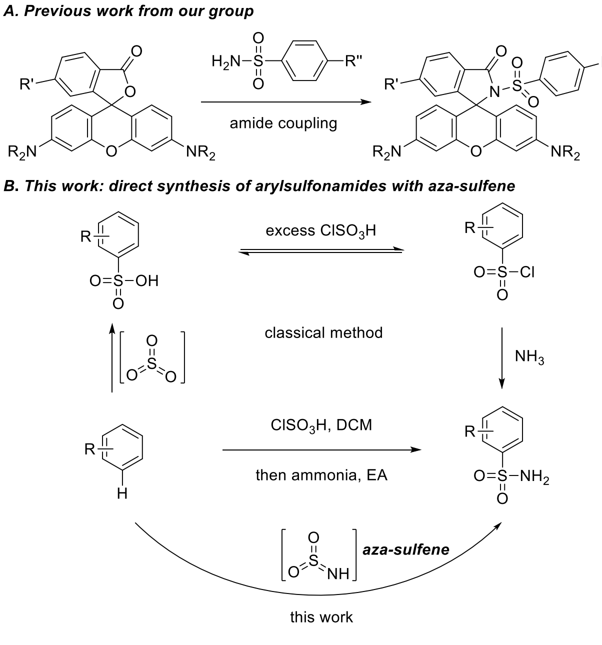

Figure 1. Our previous work using sulfonamide for fine-tuning Rhodamine (**A**). This work: a novel method for making sulfonamides (**B**).

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Unlocking Molecular Design via Dihalogenation of Unsaturated Hydrocarbons

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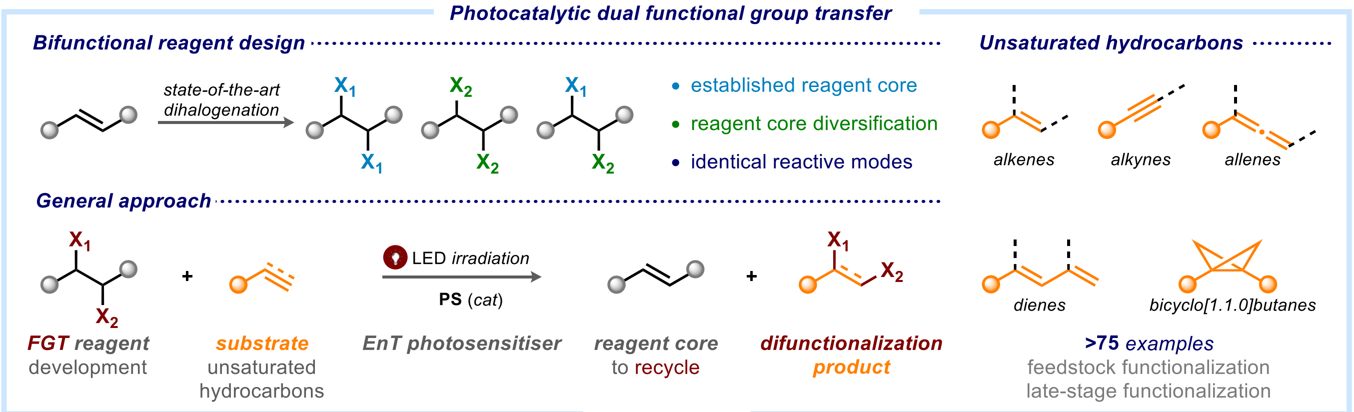
Functional group transfer (FGT) in organic chemistry is a fascinating research field of scientific discovery that provides opportunities for innovation in the area of advanced organic synthesis. These processes enable the creation of a wide range of complex molecules with diverse structures and functionalities in a straightforward and atom-economic fashion, which greatly facilitates the development of new chemical entities and materials. To date, the concept of monofunctional group transfer for installing singular transferrable functionality has been actively investigated by chemists and has already found widespread application in molecular design[1]. In contrast, dual functional group transfer is poorly examined and, as a relatively new concept in scientific exploration, has very promising applicability and significant fundamental advances. Given the strengths of photocatalytic methodologies that possess inexpensive, effective and wasteless protocols for efficient organization of chemical synthesis[2], we wish to report the unique fusion of energy transfer photocatalysis and dual functional group transfer that exhibits unprecedented atomic efficiency and overall low-cost of manipulation for dihalogenation of unsaturated compounds.

Initially, extensive research on reagent design was carried out to find key chemical frameworks suitable for sequential transfer of two halogens to unactivated olefins in a mild and selective manner and further reinstallation of desired functionalities to the reagent core for recycling purposes. Following investigations were conducted on optimization of the conditions for photocatalytic energy transfer, specifically targeting powerful photosensitizer possessing tolerance towards highly derivatized starting materials. Additionally, performed comprehensive mechanistic studies revealed the fundamentals of precisely controlled stepwise dihalogenations. Finally, the broad scope of unsaturated hydrocarbons (alkenes, alkynes, allenes, dienes and bicyclobutanes) was successively employed in the developed protocol of EnT-mediated dihalogen transfer, empowering methodology application and chemical diversification to advance late-stage functionalization in the fields of drug design and fine organic synthesis.



Key outputs

- Bench-stable reagent development
- Up to 50 gram scale synthesis
- EnT photocatalysis
- Mechanistic investigations
- Dual functional group transfer
- Transfer of mixed FGs
- Chemical diversification
- Broad FG tolerance

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