

Sujet de Thèse – ADR Ecole doctorale chimie 2023

## CO<sub>2</sub> as a transient directing group for remote C-H functionalizations of alcohols.

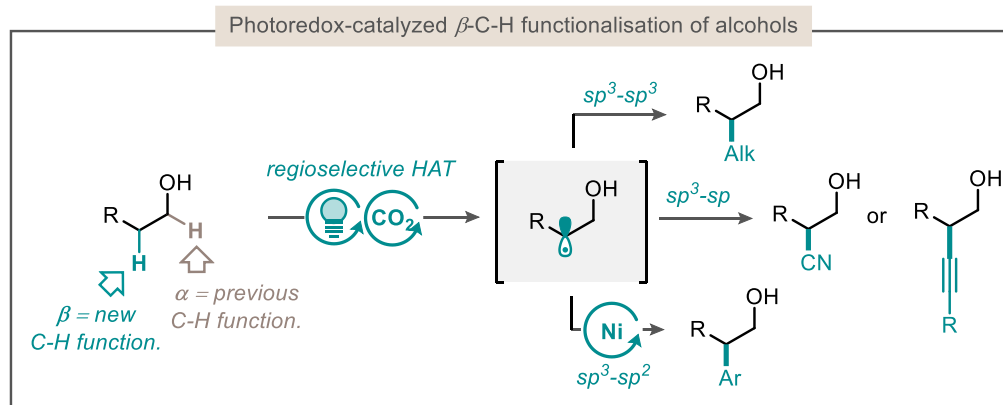
### Le CO<sub>2</sub> comme groupement directeur transitoire pour la fonctionnalisation C-H des alcools.

[Laboratory SCORE \(Synthèse et Catalyses Organique, Organométallique et Rédox\)](#)

**Key-words:** photoredox catalysis, hydrogen atom transfers, nickel catalysis, remote C-H functionalisation, CO<sub>2</sub>.

**Context:** The catalytic formation of C-C bonds directly from the corresponding C(sp<sup>3</sup>)-H bonds is a powerful method to quickly improve molecular complexity. The recent advent of photoredox catalysis has opened new opportunities in C-H activation by allowing the generation of free radicals from C(sp<sup>3</sup>)-H bonds through catalytic hydrogen atom transfers (HAT).<sup>1</sup> In such reactions, the regioselectivity is determined by kinetic and thermodynamic factors such as the polarity of the targeted C-H bond and the stability of the resulting radical. Consequently, these transformations are limited to the functionalisation of C-H bond in  $\alpha$ -position of arenes, alkenes or heteroatoms. Our group has recently contributed to this field with the development of a photoredox-catalyzed method to achieve the  $\alpha$ -C-H alkylation of unprotected alcohols and polyols by using CO<sub>2</sub> as a traceless activating group.<sup>2</sup> However, the activation of remote and less reactive C-H bonds remains highly challenging and constitutes an attractive area of investigations.

**PhD project:** The project aims to design and explore an unprecedented methodology to selectively forge C-C bonds in  $\beta$ -position of hydroxyl groups. This strategy would provide a new way to think the retrosynthesis of complex molecules.<sup>3</sup> To achieve this goal, CO<sub>2</sub> will be used as a transient, non-toxic and abundant directing group to guide the photoredox-catalyzed HAT to the desired C-H bond. The whole process will be orchestrated by a dual organocatalytic system. The resulting C-centred radical will provide a versatile platform to build new  $\beta$ -C(sp<sup>3</sup>)-C(sp<sup>3</sup>) bonds (Giese-type alkylations) or  $\beta$ -C(sp<sup>3</sup>)-C(sp) (cyanation, alkynylation). The combination of the photoredox-catalyzed HAT process with nickel-catalyzed C-C bond formation will be deeply investigated to perform enabling challenging (enantioselective)  $\beta$ -arylations/alkylations of alcohols ( $\beta$ -C(sp<sup>3</sup>)-C(sp<sup>2</sup>)). Methodology developments in dual photoredox/transition metal catalysis and extensive mechanistic investigations (NMR, cyclic voltammetry, luminescence experiments...) will constitute the core of this exploratory and multidisciplinary project.



**Candidate profile:** we are looking for a dynamic and highly self-motivated candidate demonstrating solid competences in organic synthesis and appreciating to work as a team. An experience in molecular catalysis and radical chemistry will be appreciated. For Further information, contact Jérémy Merad ([jeremy.merad@univ-lyon1.fr](mailto:jeremy.merad@univ-lyon1.fr)), Abderrahmane Amgoune ([abderrahmane.amgoune@univ-lyon1.fr](mailto:abderrahmane.amgoune@univ-lyon1.fr))

<sup>1</sup> L. Capaldo, D. Ravelli, M. Fagnoni, *Chem. Rev.* **2022**, *122*, 1875-1924; b) L. Capaldo, L. Lafayette Quadri, D. Ravelli, *Green Chem.* **2020**, *22*, 3376-3396; c) L. Capaldo, D. Ravelli, *Eur. J. Org. Chem.* **2017**, 2056-2071.

<sup>2</sup> G. Archer, R. Meyrelles, B. Maryasin, M. Médebielle, J. Merad\*, manuscript in preparation

<sup>3</sup> S. K. Sinha, S. Guin, S. Maiti, J. P. Biswas, S. Porey, D. Maiti, *Chem. Rev.* **2022**, *122*, 5682-5841.