Ecole Doctorale de Chimie Moléculaire Paris Centre ED 406

Concours ED 406 – 2026 : Projet de thèse

Titre du projet de thèse	**Biocatalytic *vs* transition metal-catalyzed route to access high value-added building blocks**	
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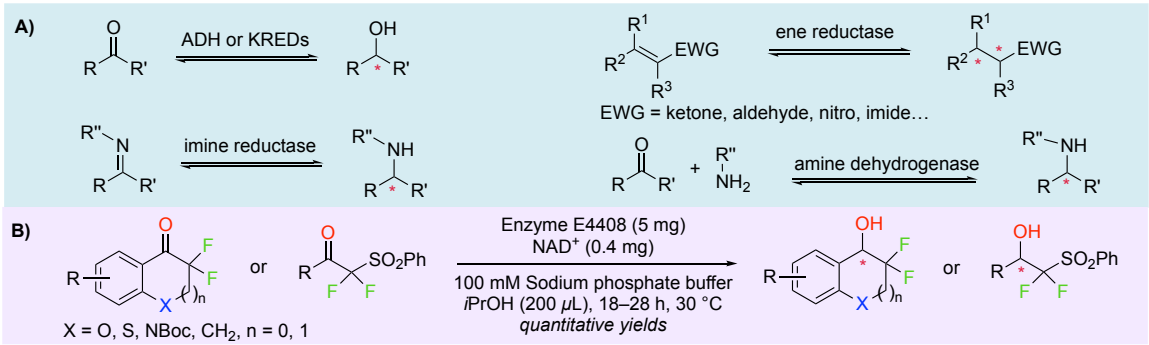
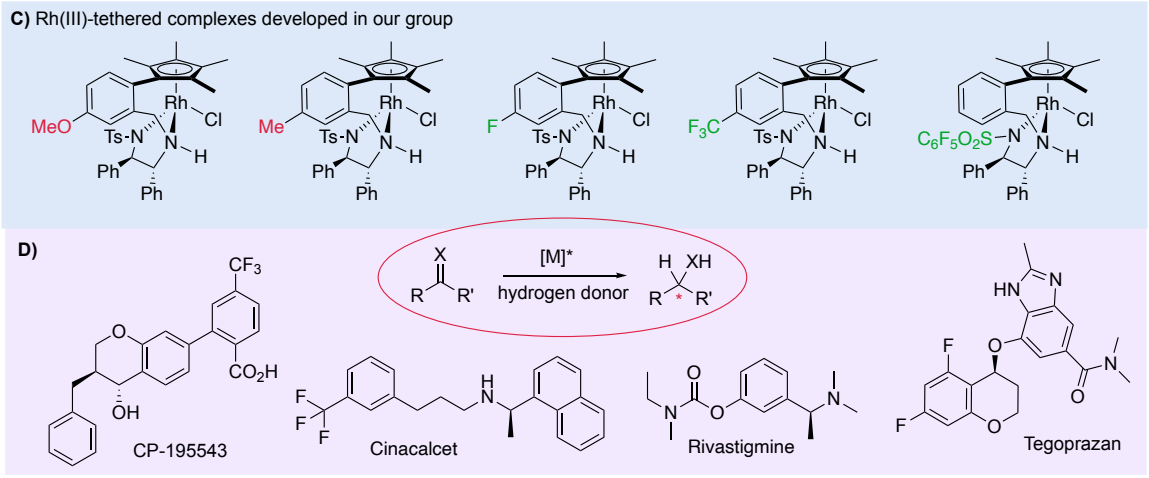
Societal concerns regarding economics, environment, and social well-being continue to emphasize the necessity for chemistry to enhance synthetic pathways to be more efficient, scalable, and economically viable. In this context and facilitated by the developments of microbiology, molecular biology, advances in DNA sequencing and gene synthesis,[1] biocatalysis has emerged as an essential tool used in academic and industrial domains, providing synthetic approaches with the exceptional specificity of enzymes to reach desired molecules.[2] In recent decades, enzyme and whole cell biocatalysis have been utilized for the synthesis of a diverse range of chemicals, primarily focusing on optically active intermediates such as fine chemicals and pharmaceutical precursors.[3] Since the early 2000s, numerous biocatalytic transformations applied in both academia and on industrial scale have been developed. On the other hand, the use of transition metal catalysts is particularly interesting in the context of green chemistry, especially for waste prevention, atom economy, energy efficiency, with generally high chemo-, regio- and enantioselectivity achieved.

The objectives of the project will be partly devoted to the development of enzymatic reductions. More particularly, the PhD student will investigate the interconversion between alcohols and aldehydes/ketones catalysed by alcohol dehydrogenases (ADH) or ketoreductases (KREDs), reduction of imines to amines by imine reductases, reduction of C=C bonds with ene reductases and reductive amination with amine dehydrogenases (Scheme, A). In this context, we have previously reported in collaboration with Seqens an efficient enzymatic reduction of α-*gem*-difluorinated heterocyclic and carbocyclic ketone derivatives by using a selection of new alcohol dehydrogenases (Scheme, B).[4] This mild biocatalytic process allowed the preparation of diversely functionalized enantioenriched β-*gem*-difluorinated (*S*)-alcohols in >99% yield and enantiomeric excesses ranging from 96% to >99%. A comparative study between enzymatic reduction and metal-catalyzed asymmetric transfer hydrogenation has demonstrated the efficiency of the enzymes collections but also the complementarity of the two methods. Given these encouraging results, the PhD project will focus on the use of new collections of enzymes to address the enzymatic reductions of C=O, C=N and C=C bonds to access a variety of high value-added building blocks of potential medicinal interest. This work will be carried out in collaboration with Seqens.



Another part of the project will involve the study of transition-metal catalyzed asymmetric reductions of new scaffolds bearing C=O and C=N bonds. This work will rely on the use of chiral Rh(III)-tethered complexes that were previously developed in our group[5] (Scheme, C) to install the oxygen- or nitrogen-bearing stereocenters by asymmetric transfer hydrogenation reaction. Other complexes involving both noble and non-noble metals will also be investigated.[6] A comparative study between enzymatic reduction and metal-catalyzed asymmetric transfer hydrogenation will be carried out as well. The PhD project will include application of these enzymatic and transition metal-catalyzed asymmetric reductions to the synthesis of various bioactive molecules such as rivastigmine (a cholinesterase inhibitor used to treat mild to moderate dementia in Alzheimer's and Parkinson's disease), cinacalcet (a calcium sensing receptor agonist used to treat secondary hyperparathyroidism in chronic kidney disease), CP-195,54 (treatment of Arthritis, Rheumatoid) or tegoprazan (treatment of acid-related gastrointestinal diseases) for example (Scheme, D).



Candidates must submit their application file before May 7, 2026 via the following link:

https://ed406.sorbonne-universite.fr/recrutement-et-financement/contrats-doctoraux-de-led406-concours

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[1] (a) Foley, A. M.; Maguire, A. R. *Eur. J. Org. Chem*. **2019**, *2019*, 3713. (b) Bornscheuer, U.; Huisman, G.; Kazlauskas, R. *Nature* **2012**, *485*, 185.

[2] Wolfenden, R.; Snider, M. J. *Acc. Chem. Res.* **2001**, *34*, 938.

[3] (a) Panke, S.; Held, M.; Wubbolts, M. *Curr. Opin. Biotechnol*. **2004**, *15*, 272. (b) Burns, M.; Martinez, C. A.; Vanderplas, B.; Wisdom, R.; Yu, S.; Singer, R. A. *Org. Process Res. Dev.* **2017**, *21*, 871. (c) Sheldon, R. A.; Woodley, J. M. *Chem. Rev.* **2018**, *118*, 801. (d) Wu, S.; Snajdrova, R.; Moore, J. C.; Baldenius, K.; Bornscheuer, U. T. *Angew. Chem. Int. Ed.* **2021**, *60*, 88.

[4] Bacheley, L.; Boutet, J.; Guillamot, G.; Gilles, P.; Martin, J.; Phansavath, P.; Ratovelomanana-Vidal, V. *Adv. Synth. Catal.* **2024**, *366*, 3511.

[5] (a) Zheng, L.-S.; Llopis, Q. ; Echeverria, P.-G.; Férard, C.; Guillamot, G.; Phansavath, P.; Ratovelomanana-Vidal, V. *J. Org. Chem*. **2017**, *82*, 5607. (b) He, B.; Zheng, L.-S.; Phansavath, P.; Ratovelomanana-Vidal, V. *ChemSusChem* **2019**, *12*, 3032.

[6] (a) Revue: Kosiuha, M.; Karapetyan, A.; Charron, O.; Meyer, C.; Phansavath, P.; Ratovelomanana-Vidal, V. *Synthesis* **2025**, *57*, 2909. (b) Bacheley, L.; Ravindra, R.; Guillamot, G.; Phansavath, P.; Ratovelomanana-Vidal, V. *Adv. Synth. Catal.* **2024**, *366*, 1019. (c) Molina-Betancourt, R.; Bacheley, L.; Karapetyan, A.; Guillamot, G.; Phansavath, P.; Ratovelomanana-Vidal, V. *ChemCatChem* **2022**, *14*, e202200595. (d) "Asymmetric Hydrogenation and Transfer Hydrogenation", Wiley-VCH Verlag GmbH, Weinheim, Germany, P. Phansavath, V. Ratovelomanana-Vidal, Eds, p 1-384, **2021**.