

PhD offer (starting date November 2022)

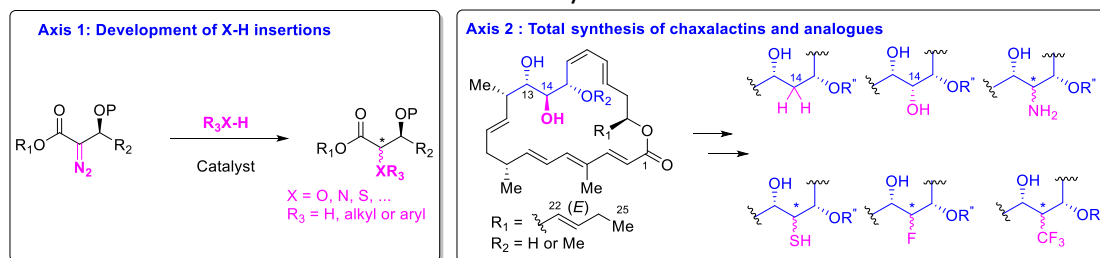
Development of X-H insertions on *O*-protected α -diazo- β -hydroxyesters Application to the first diverted total synthesis of chaxalactins

IMMM, UMR CNRS 6283 – Equipe Méthodologies et Synthèse Organique

Supervisors : Anne-Sophie Castanet, Anne-Caroline Chany

Funding : ANR, 36 months

In the context of diverted total synthesis (DTS), the development of new methods allowing the synthesis of a variety of natural products analogues from a common advanced precursor is of high value. The CHAXATAC project, funded by the ANR, aims first to develop **new stereoselective X-H insertions on *O*-protected α -diazo- β -hydroxy-esters**, used as synthetic platforms, towards the formation of various enantiopure α,β -diheterofunctional esters (**Axis 1, Scheme 1**). We aim to take advantage of the unique broad reactivity profile of the diazo functionality (C-H insertion, X-H insertion, migration, cyclopropanation, ...) ¹ to introduce structural diversity on the skeleton of natural products. **No X-H insertions have been reported so far on such diazocarbonyl compounds**. The challenge of this methodological task is to develop reaction conditions which favour the insertion reaction over competitive reactions. The usefulness of this new methodology for DTS will then be demonstrated in the **total synthesis** of antimicrobial chaxalactins and their analogues in C14 position, which is assumed to have an influence on the biological activity (**Axis 2, Scheme 1**). ² For this purpose, a synthetic strategy has been designed, implementing a diazo functionality in the C14 position on which a wide range of transformations could introduce structural diversity in the chaxalactins skeleton.



Scheme 1

Expected skills: Holder of a Master 2 degree or an engineering degree (or an international equivalent), the candidate must have a good theoretical and practical knowledge of organic synthesis as well as of the methods of analysis and characterization of organic compounds. Candidates are expected to be self-driven, have good communication skills and to be interested at the same time in development of new methodologies and in total synthesis of bioactive natural products.

Persons to contact: Anne-Caroline Chany (CR), anne-caroline.chany@univ-lemans.fr
Anne-Sophie Castanet (Pr), anne-sophie.castanet@univ-lemans.fr

Please send a detailed CV and a cover letter – Application online: <https://emploi.cnrs.fr>

¹ **Review on diazocarbonyl compounds:** (a) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKerverey, M. A. *Chem. Rev.* **2015**, *115*, 9981. (b) Zhang, Z.; Wang, J. *Tetrahedron* **2008**, *64*, 6577; (c) Zhang, Y.; Wang, J. *Chem. Commun.* **2009**, 5350; (d) **X-H Insertions** : Gillingham, D.; Fei, N. *Chem. Soc. Rev.* **2013**, *42*, 4918.

² Rateb, M. E.; Houssen, W. E.; Harrison, W. T. A.; Deng, H.; Okoro, C. K.; Asejo, J. A.; Andrews, B. A.; Bull, A. T.; Goodfellow, M.; Ebel, R.; Jaspar, M. *J. Nat. Prod.* **2011**, *74*, 1965.