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One year post-doctoral fellowship (LABEX SYNORG)

New asymmetric organocatalyzed methodologies for the nucleophilic dearomatization of pyridines : Application to the stereoselective synthesis of iminosugar *C*-glycosides

Heterocycles are abundant natural-occurring scaffolds and are involved in more than 90% of new drugs.[1] Among them, piperidine scaffold is of particular interest regarding its presence in numerous drugs such as Donepezil, Fentanyl or Raloxifene to cite a few.[2] This scaffold has also found applications as a sugar mimics where the oxygen atom of the sugar is replaced by a nitrogen to give rise to a so-called iminosugar. As a result of the presence of the basic function, which is protonated under physiological conditions, iminosugars have a high affinity for enzymes acting on carbohydrates, most prominently on glycosidases.[3] Whereas numerous methods have been developed for the synthesis of enantioenriched piperidines, organocatalytic approaches remain underexplored.[4] Through this project we intend to develop original organocatalytic methods for the synthesis of chiral polyfunctionalized piperidine derivatives by enantioselective nucleophilic dearomatization of *N*-alkyl or *N*-benzyl pyridiniums that have been reported only recently[5] in such reactions. The latter methodology will be applied to the synthesis of novel iminosugar-*C*-glycosides with the aim of increasing the structural diversity of the aglycones and thus their selectivity as enzyme inhibitors.
This project will be developed in collaboration between two teams of the LABEX SYNORG: the team of Dr V. Levacher and Dr S. Oudeyer (COBRA, Rouen) who have a long-standing expertise in enantioselective organocatalysis and the team of Pr O. Martin and Dr C. Nicolas at (ICOA, Orléans) who are interested in iminosugars chemistry.

Profile: Candidates must have obtained their PhD and possess a strong background in organic chemistry (synthesis, purification and analysis) and more particularly in asymmetric catalysis (methodology, chiral HPLC). Skills in organocatalysis and/or sugar chemistry will be appreciated.
CV, cover letter and at least 2 references should be sent by email to Sylvain Oudeyer.

Applications will be evaluated as soon as they will be received until the suitable candidate will be chosen.

The post doc is expected to start by the beginning of September 2017.

Website: Heterocycles team / Organocatalysis

[1] Dua, R.; Shrivastava, S.; Sonwane, S. K.; Srivastava, S. K. *Advan. Biol. Res.* **2011**, *5*, 120.
[2] Baumann, M.; Baxendale, I. R. *Beilstein J. Org. Chem.* **2013**, *9*, 2265.
[3] Stuetz, A.E.; Wrodnigg, T.M. *Adv. Carbohydr. Chem. Biochem.* **2011**, *66*, 187.
[4] Ding, Q.; Zhou, X.; Fan, R. *Org. Biomol. Chem.* **2014**, *12*, 4807.
[5] Garcia Mancheno, O.; Asmus, S.; Zurro, M.; Fischer, T. *Angew. Chem. Int. Ed.* **2015**, *54*, 8823. Bertuzzi, G.; Sinisi, A.; Caruana, L.; Mazzanti, A.; Fochi, M.; Bernardi, L. *ACS Catal.* **2016**, *6*, 6473. Bertuzzi, G.; Sinisi, A.; Pecorari, D.; Caruana, L.; Mazzanti, A.; Bernardi, L.; Fochi, M. *Org. Lett.* **2017**, *19*, 834.