Subject

Titre : **ENANTIOSELECTIVE ALLYLBORATION OF ISATINES CATALYZED BY CHIRAL BINOL-DERIVED PHOSPHORIC ACIDS. APPLICATION TO THE SYNTHESIS OF BIOACTIVE MOLECULES.**

Keywords : ORGANOCATALYSIS, ALLYLBORATION, HYDROXYOXINDOLES, PROTEASOME

Description :
The heterocyclic oxindole core is present in a lot of natural products with strong biological activities and also in pharmaceuticals. Because of these applications, the catalytic building of its quaternary chiral center is currently a challenge in organic chemistry. In organic chemistry, the allylboration reaction is an efficient tool to create a C-C bond. Because of this reaction transition state, it is possible to efficiently control the diastereoselectivity when aldehydes are reacted. Starting from Antilla's study [*J. Am. Chem. Soc*., 2010, 11884], enantioselective allylboration of aldehydes catalyzed by chiral binol-derived phosphoric acids led to very good results. However, ketone substrates have been less studied because of their weaker reactivity with allylboranes and the harder control of the new quaternary center configuration. Only five examples of enantioselective allylboration reaction have been currently described using as catalysts either organometallic phosphine based complexes, BINOL or an amino-alcohol derived from an amino-acid. To the best of our knowledge, no process using bifunctional organocatalysts such as binol-derived phosphoric acids able to activate both the nucleophile and the electrophile has been yet developed.
The project is based on the expertise of the CORINT team in organocatalysis with the use of phosphoric acid in catalytic enantioselective reactions [*Org. Lett.* **2011**, 94; *J. Am. Chem. Soc.* **2012**, 10389; *Chem. Commun.* **2014**, 7495; *Chem. Eur. J.* **2015**, 1704; *Chem. Commun.* **2015**, 5383], in boron chemistry and especially the synthesis of new allylboranes and their application in multi-step synthesis [*Eur. J. Org. Chem*. **2015**, 2470], and in the chemistry of 3-hydroxyoxindoles that are potent proteasome inhibitors [*J Med Chem*, **2014**, 9211*, J Org Chem* **2014**, 10945].
The goal is to check catalysts already prepared in the laboratory in the enantioselective allylboration of isatines, in order to form enantio-enriched 3-hydroxyoxindoles that could be further transformed. The optimized method will be applied to different substrates in order to prepare high added value synthesis intermediates that can lead to natural products such as convolutamydines.

Applicant.

Applicants should have a master degree in molecular chemistry, with a strong background in organic synthesis, and skills with bench work. Candidates with a preliminary practical experience with multi-steps synthesis, catalysis or organometallic synthesis will be welcome.

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