PhD proposal

"Functionalization of biosourced isohexides and polyols through borrowing hydrogen methodology"

Laboratory: Organic and Bio-organic Chemistry (COB), Institute for Molecular and Supramolecular Chemistry (ICBMS)

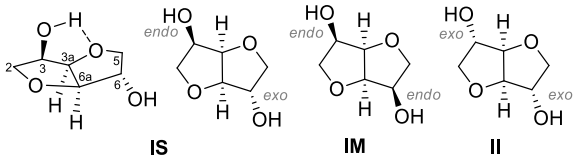
Supervisor: Pr. Florence Popowycz, Co-supervisor: Dr. Maïwenn Jacolot, ICBMS-INSA Lyon

Context of the proposal: The PhD position described below will be funded by the Chinese Scholarship Council and expected to start in October 2019 for 42 months. The candidate will be hosted in the COB laboratory (ICBMS-UDL-INSA-Lyon).

Scientific content:

Isosorbide, a major product of the starch industry,[1] is a renewable platform chemical able to significantly contribute to the future replacement of fossil resource-based products. This isohexide (**IS**) is a V-shaped chiral molecule of two *cis*-connected tetrahydrofuran rings with secondary hydroxyl groups in C-3 and C-6 positions with *endo* and *exo* configurations respectively. Isomannide (**IM** - *endo*/*endo*), produced from D-mannitol, and non-commercial isoidide (**II** - *exo*/*exo*) are two other diastereoisomers (figure 1).

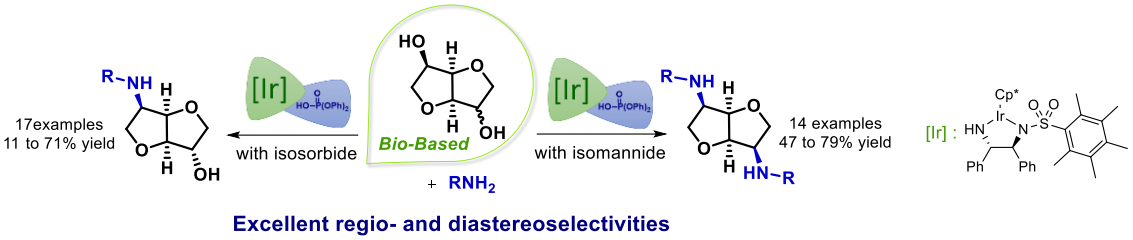
Figure 1. Chemical structure of bio-based isohexides



Functionalization of these chiral dianhydrohexitols into corresponding amines has attracted considerable interest for polymer applications and for asymmetric induction in organic synthesis (chiral auxiliaries, ligands and organocatalysts).[2]

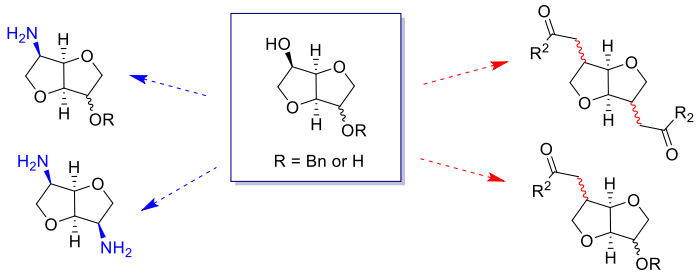
Very recently, our research group reported a direct and diastereoselective amination of these biosourced isohexides through a borrowing hydrogen (BH) methodology using a cooperative catalysis combining iridium metal and phosphoric acid.[3] This methodology is a sustainable alternative of the classic strategy of nucleophilic substitution after introduction of an appropriate leaving group.

Figure 2. Direct regio and diastereoselective amination of isohexide derivatives



Based on our methodology, the PhD proposal will first focus in developing the direct functionalization of isohexides *via* C-N and C-C bond formations (Figure 4).

Figure 3. PhD project: Direct functionalization of isohexide derivatives (C-N and C-C bond formation)



Nowadays, more sustainable alternatives has gained increasing attention such as the use of abundant first-row transition metals. In this regards, homogeneous catalysis using iron complexes should be further investigated due to its economic (0.109 €/kg) and ecological benefits (4th most common element in the earth's crust). A second aspect of the thesis will thus consist to develop the direct amination of mono-protected isosorbide as well as isosorbide and other polyols using iron metal species.

Required Background: We are looking for a highly motivated person with a strong background in organic chemistry (Master degree). Appropriate education profile should include experience in multi-step organic synthesis and associated analytical skills (NMR, MS, IR). Experience in organometallic chemistry and/or in asymmetric synthesis will be appreciated but are not mandatory. A good motivation to learn, communication skills, curiosity, and agreeable team spirit are also among important qualities. Proficient knowledge of English is also important.

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[1] Flèche, G.; Huchette, M. *Starch* **1986**, *38*, 26-30
[2] Janvier, M.; Moebs-Sanchez, S.; Popowycz, F. *Eur. J. Org. Chem.* **2016**, 2308; Janvier, M.; Moebs-Sanchez, S.; Popowycz, F. *Chimia.* **2016**, *70*, 77.
[3] Jacolot, M. ; Moebs-Sanchez, S.; Popowycz, F. *J. Org. Chem.* **2018**, *83*, 9456-9463 and *Eur. J. Org. Chem*. **2020**, 599-608.