MULTI-CATALYTIC ENANTIOSELECTIVE METHODOLOGY AS ENTRY TO NEW SUPRAMOLECULAR TOOLS

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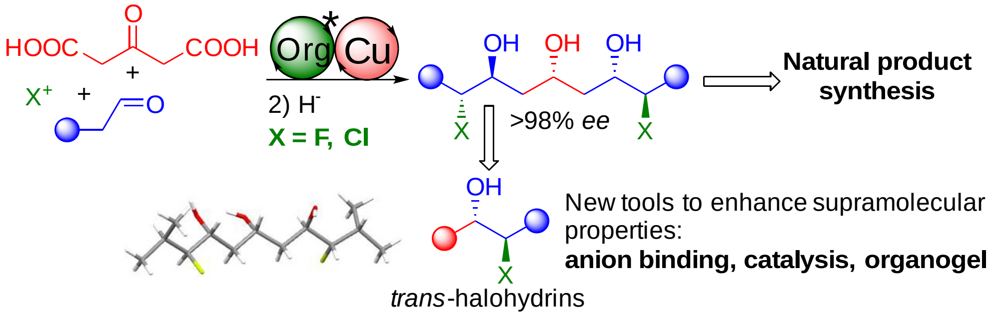
The development of innovative engineered molecular or supramolecular entities is crucial to selectively and efficiently create a required chemical, physical or biological function of interest. However, development of these new chemical tools strongly depends on our ability at rapidly and stereoselectively constructing the required complex molecular objects of interest.

In this context, we have been able to develop an original multi-catalytic process combining an enantioselective enamine catalyzed aldehyde halogenation and copper catalyzed diastereoselective aldolization directly providing valuable halohydrins (X = F, Cl). Notably, performing the reaction in a bidirectional fashion, ketodiols possessing four acyclic stereogenic centers are formed in >98% *ee*.[1] These ketodiols, accessed in one operation from commercial products are direct precursors of 1,3,5-polyols, a class of compounds present in numerous naturals products. As a result, this strategy provides a straightforward synthesis of natural 1,3,5-polyols after dehalogenation as well as halogenated natural products analogues.[2]

Cascade multi-catalytic halogeno-aldolization:



Moreover, at the fundamental level, the precedently undisclosed *trans*-halohydrins represent valuable tools to enhance crucial supramolecular polyols properties leading to considerably improved anion binding, H-bonding or organogelating molecules.[3]

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[1] A. Quintard, J. Rodriguez, *ACS Catal.* **2017**, *7*, 5513.

[2] A. Quintard, C. Sperandio, J. Rodriguez, *Org. Lett.* **2018**, *20*, 5274.

[3] C. Sperandio, G. Quintard, J-V. Naubron, M. Giorgi, M. Yemloul, J-L. Parrain, J. Rodriguez, A. Quintard, *Submitted manuscript*.