PhD Project (starting sept 2022)

# Synthesis and applications of a highly preorganised bifunctionalised chiral platform

*Under the co-supervision of*


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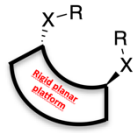
***keywords :*** *diols, axial chirality, enzymatic reactions, hélicoidal compounds, chiral ligands, material synthesis*

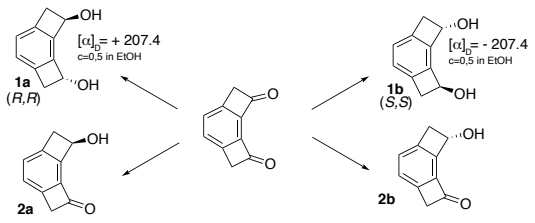


**Summary**: Synthesis / characterisation / applications of a new class of highly preorganised chiral compounds with chelating properties supported by a rigid planar platform for various applications (catalysis, materials). The project will include development / evaluation of the performances of derivatives with potential applications in domains such as

- New chiral catalysts
- « chiral building blocks » with axial chirality
- Access to helicoidal compounds with control of the helicity
- Templates for material synthesis


**Project:** This project is the continuation of a first series of results allowing access to enantiomerically pure (ee = 100%) families of chiral compounds from an unprecedented highly pre-organized planar rigid platform. Synthetic access to enantiomerically pure **1a** and to one of the keto-alcohols **2a**, **2b** have already been secured from corresponding diketone via different enzymatic reduction conditions carried out in water. To date, our studies have been limited to enzymatic reduction from raw fruits and vegetables in water that makes them low cost, green and very easy to implement reactions (raw carrots[1] led to pure **1a** with complete reduction of the diketone whereas horseraddish led to monoreduction product). One objective of this PhD will consist in the extensive screening of enzymatic conditions to identify access to all four enantiomerically pure compounds **1** and **2**. We will extend the study to the large family of isolated and commercially available Keto Reductases (KRED)[2] and to more conventional chiral hydride donors. Synthesis of amino chiral analogues will be also investigated through IRED (Iminoreductases)[3] reactions.




The originality of the project consists in the unprecedented rigid planar platform with very strong preorganisation (elbow shaped) and bearing one or two chiral centers with heteroatoms pointing in two different half-spaces. Those building blocks can have numerous applications in the conception of strongly preorganized compounds with potential applications in asymetric catalysis (chelating properties), materials for optic, chiral recognition and chiral helicoidal compounds or interactions. Securing access to the chiral keto-alcohols **2a**, **b** is also of great interest as they will induce dissymetrization of the two functional moieties, allowing further functionalization reactions such as introduction of two different functional groups (synthesis of amino alcohols for example). Evaluation of these enzymatic methods on cyclobutanone derivatives will also be assessed during this PhD.

This multidisciplinary project will allow the applicant to develop strong skills in enzymatic reaction, organic chemistry, spectroscopic characterization (NMR, HPLC, UV-Vis) and in chiroptical techniques (ECD, VCD and ROA).

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[1] Lacheretz R., Pardo D.G., Cossy J., *Org. Lett.*, **2009**, *11*, 1245-1248.
[2] a) Kambourakis, S. *et al.*, *Adv. Synth. Catal.* **2006**, *348*, 1958 – 1969 b) Wells, A., S. *et al Org. Process Res. Dev.* **2020**, 24, 6, 1131–1140
[3] Turner, N. J. *et al.*, *Curr Opin Chem Biol*, **2017**, *37*, 19-25