LABORATOIRE DE CHIMIE ENS DE LYON

ÉCOLE NORMALE SUPÉRIEURE DE LYON

PhD Position at ENS de Lyon (starting sept 2022) – ED 206

Synthesis of Enantiopure Cryptophanes with *Syn*-Configuration: Study of the Chiroptical Properties of these Derivatives and their Complexes.

Synthèse de cryptophanes énantiopurs de configuration *syn* : étude des propriétés chiroptiques de ces dérivés et de leurs complexes.

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Keywords: multistep organic synthesis, supramolecular chemistry, ^{129}Xe NMR, chiroptical properties, enantiopure compounds.

Cryptophanes are hollow molecular receptors that exhibit original complexation properties towards many substrates. Moreover, the vast majority of these compounds possess an inherent chirality. Thus, enantiopure cryptophanes and their complexes can be studied using a wide range of chiroptical techniques (ECD, ORD, VCD, ROA) to obtain structural information. Until now, most of these studies concerned the derivatives with the *anti*-configuration, the latter being the easiest to obtain. The *anti*-configuration originates from the helical arrangement of the three chains linking the two cyclotribenzylene (CTB) units (*anti*-**1** compound; figure 1). Very recently we reported the synthesis of new cryptophanes possessing the *syn* configuration. The inherent chirality of these derivatives is different since the two CTB units have different substituents and the helical arrangement of the chains is absent on these derivatives. We can therefore expect these new compounds to have different chiroptical properties than the *anti*-derivatives. To date, *syn*-cryptophanes have been very poorly described in the literature due to the difficulties in preparing them and very few studies regarding their chiroptical properties have been published. Interestingly, the recently prepared *syn* precursor (*syn*-**2** compound; Figure 1) offers the opportunity to develop the design of new optically active *syn* derivatives with novel properties. [1]

The primary goal of this PhD work will be to optimize the synthesis of compound *syn*-**2**, which have

[1] Brotin, T. ; Jeanneau, E. ; Berthault, P. ; Léonce, E. ; Pitrat, D. ; Mulatier, J. C. *J. Org. Chem.* **2018**, 83, 23, 14465-14471.

been obtained from a multi-steps synthesis with a low yield. Then, the applicant will develop the synthesis of new optically active cryptophane derivatives in order to study their binding properties with different guest molecules. Xenon will be the guest of choice because cryptophanes with small internal cavities have a high affinity for this noble gas. In addition, these supramolecular complexes offer the possibility of designing molecular tracers for medical imaging (MRI). Part of this work will be carried out in collaboration with University of Saclay-Paris Sud (Laser Polarized xenon-129).

Then, the search for efficient methods to obtain these compounds in their enantiopure form will also be addressed during this thesis. The applicant will study the properties of these new enantiopure derivatives by means of different chiroptical techniques. Part of this work will be carried out in collaboration with University of Bordeaux (Vibrational Circular Dichroism and Raman Optical Activity).

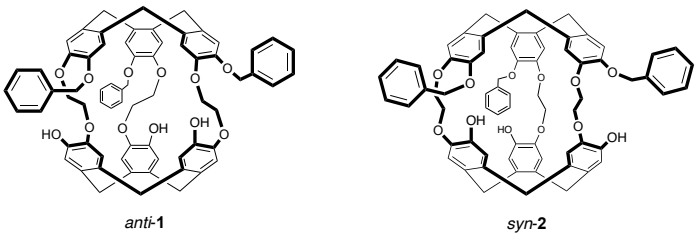

Figure 1: Chemical structures of dissymmetrical *anti*-**1**(left) and *syn*-**2** (right) cryptophanes. Both structures possess an inherent chiral structure.

Along this phD work, the candidate will get strong skills, knowledge and autonomy in several disciplinary fields such as organic synthesis, supramolecular chemistry, spectroscopic characterization and chiroptical techniques.

Profile of the candidate

We are looking for a highly motivated candidate with a master 2 diploma in organic chemistry. The applicant must have a strong background in organic chemistry and in spectroscopic techniques organic compounds (NMR, UV-visible, IR). A resume, cover letter and the transcript of records corresponding to the M2 diploma must be sent to Dr Thierry Brotin. E-mail: thierry.brotin@ens-lyon.fr