PhD position in Organic and Supramolecular Chemistry at the Chemistry Laboratory of ENS Lyon, France

Synthesis of Chiral Receptors for the Selective Recognition, Detection and Extraction of Cesium and Thallium(I) in Aqueous Media

Supervisors: Dr. Nicolas De Rycke: nicolas.de-rycke@ens-lyon.fr – 04 72 72 88 63, Dr. Thierry Brotin: thierry.brotin@ens-lyon.fr – 04 72 72 89 11.

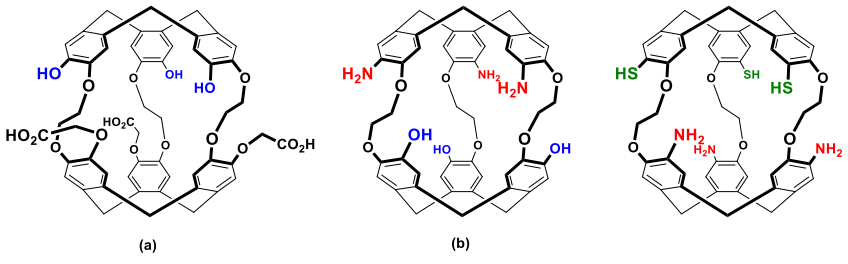
Laboratory of Chemistry (UMR 5182), Supramolecular Chemistry and Chemical Biology Team, University of Lyon – Ecole Normale Supérieure de Lyon.

Key words: *Environmental and health issues; depollution of contaminated waters; sensors; multi-steps organic synthesis, enantiopure compounds; host-guest chemistry; chiroptical properties.*

Thallium and cesium are two toxic elements that pose a major threat to living systems. Cesium-137 is a radioactive byproduct generated by nuclear fission processes in nuclear reactors and nuclear weapons testing. In 2011, the accident at the Fukushima nuclear power plant released significant amounts of radiocesium-137, resulting in long-term contamination of soils and oceans.[1] On the other hand, human activities have released large amounts of thallium(I) into nature, resulting in soil and groundwater contamination in several regions of the world. This is a major threat because thallium is known to be a very toxic metal, even at low concentrations.[2]

Among the various options proposed, synthetic molecular receptors can be prepared specifically to extract these two toxic elements from groundwater, although the synthesis of these compounds is difficult. Interestingly, the structure of these artificial compounds can be tuned to optimize the interactions between the host molecule and the metal cations. For example, our group has prepared several cryptophanes, a class of hollow macrocyclic compounds, which exhibit very high association constants with cesium and thallium in water.[3] So far, the affinity of these hosts for these two cationic species is very high in basic solution. To date, only one cryptophane being able to encapsulate cesium and thallium in water have been reported in the literature by our group (Scheme 1a). However, its moderate binding constant value toward cesium encapsulation (Ka = 650 M^{-1}) prevents its use for further sensor applications. [4]

The objective of this thesis will be to design new water-soluble cryptophane derivatives capable of efficiently encapsulating cesium and thallium at neutral pH. To do so, new functionalities will be introduced on the cryptophane backbone (Scheme 1b). This thesis project focuses on the synthesis and study of a new family of cryptophane derivatives in their racemic and enantiopure forms. Their supramolecular properties will be exclusively studied in aqueous medium, with a preference for soluble systems at neutral pH. In a second step, we will study the possibility of grafting these molecules on solid surfaces (gold surface, superparamagnetic nanoparticles).



Scheme 1. (a) Known C_3-symmetric cryptophane with good affinity for thallium at neutral pH; (b) new cryptophane candidates for selective complexation of thallium and cesium in aqueous solution at neutral pH.

These supramolecular systems will be studied using different techniques. For example, NMR of ^{133}Cs and ^{205}Tl will be used to characterize the formation of these host-guest complexes. Isothermal

titration calorimetry (ITC) is also a useful method to access the thermodynamic parameters of the binding process. Finally, since the overwhelming majority of cryptophanes are chiral, chiroptical techniques such as Electronic Circular Dichoism (ECD) and Vibrational Circular Dichroism (VCD) will be used to obtain information about these complexes. This, project will lead to a promising tool for effective cesium and thallium removal from groundwater and open up interesting perspectives for designing material for cesium and thallium extraction and detection. The PhD candidate will take the full advantage of the stimulating environment of the Chemistry Laboratory of ENS Lyon and strong experience of this research team in cryptophane design.[5]

Profile: We look for a highly motivated and talented synthetic organic PhD candidate. The applicant shall hold a master degree or equivalent that grants access to doctoral studies. An interest (or experience) in the synthesis of artificial receptors, supramolecular chemistry and chiroptical property studies would be appreciated.

Starting date: September 2023 – Duration: 3 years.

Emails: nicolas.de-rycke@ens-lyon.fr – thierry.brotin@ens-lyon.fr

Bibliographical references:

1) P. Li, Y. Gong, M. Komatsuzaki Sci. Total Environ. **2019**, *697*, 134060. DOI: 10.1016/j.scitotenv.2019.134060.
2) Kazantzis, G. *Environ. Geo. Health* **2000**, *22*, 275-280. DOI: 10.1023/A:1006791514080.
3) Brotin, T.; Montserret, R.; Bouchet, A.; Cavagnat, D.; Linares, M.; Buffeteau *J. Org. Chem.* **2012**, *77*, 1198–1201. DOI: 10.1021/jo202259r.
4) T. Brotin, P. Berthault, D. Pitrat, J.-C. Mulatier *J. Org. Chem.* **2020**, *85*, 9622 – 9630. DOI: 10.1021/acs.joc.0c00950.
5) Two other recent articles from the supervisors on cryptophane topic: M. Doll, P. Berthault, E. Léonce, C. Boutin, E. Jeanneau, T. Brotin, N. De Rycke *J. Org. Chem.* **2022**, *87*, 2912 – 2920. DOI: 10.1021/acs.joc.1c02774; (b) M. Doll, P. Berthault, E. Léonce, C. Boutin, T. Buffeteau, N. Daugey, N. Vanthuyne, M. Jean, T. Brotin, N. De Rycke *J. Org. Chem.* **2021**, *86*, 11, 7648–7658 DOI: 10.1021/acs.joc.1c00701.