Proposition de thèse 2019 – Equipe CSAp

Title: Synthèse éco-efficiente de nouveaux récepteurs artificiels pour la détection de biomolécules
Eco-efficient synthesis of new artificial receptors for biomolecules sensing

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Key words: host-guest chemistry, molecular recognition, self-assembling, biomolecule sensing, new click reaction.

Main context: Host guest chemistry is the core of sensing devices and extraction technologies. This central field of supramolecular chemistry, which was awarded two Nobel Prices in 1987 and 2017 relies on the use of synthetic objects displaying a well-defined and functionalized cavity to selectively bind some target guest molecules. The binding phenomenon may be accompanied by a characteristic optical signal (for detection) and by a change in the physical properties of the resulting complex, allowing its selective extraction from the starting medium. Following some solid proof of feasibility, we want to develop a new family (**Figure 1**) of synthetic receptors resembling the famous cucurbituril family, which has been successfully used for theranostic applications and as ingredients to produce smart materials. The added value of this new family relies in the efficiency and the modularity of the synthetic approach: assembling in mild conditions and in water is targeted in to deliver on demand, with high yields new architectures for tailored biological applications.

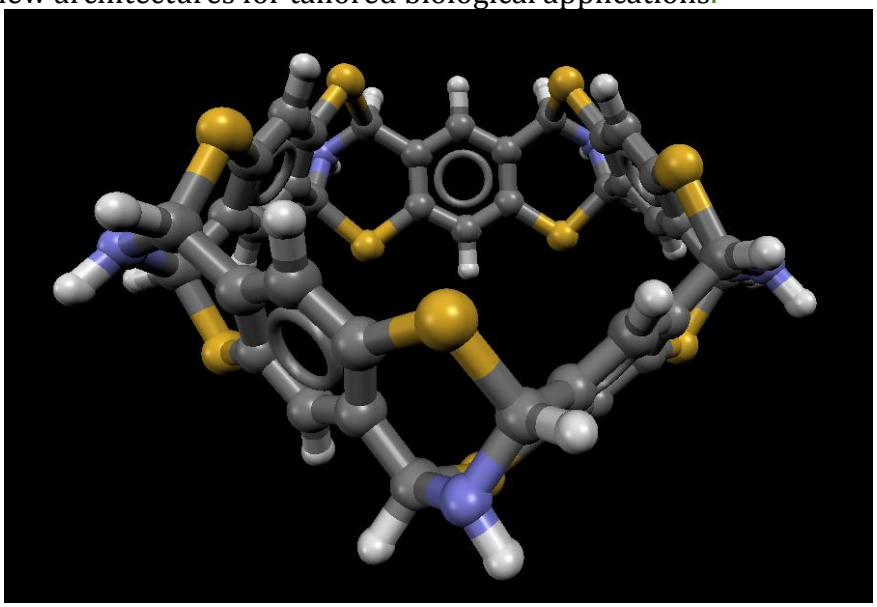

Figure 1. Simplified representation of polydithiocin cavitands

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Project: Centered on synthetic organic and supramolecular chemistry, the project aims at designing a new family of macrocyclic architecture by optimizing a new 2+1 click reaction. In our group, we have developed a strong expertise in the design and eco-efficient preparation (by self-assembling) of novel cavitands.[1],[2,] Our strategy consists in exploring the physico-chemical properties of these new objects in solution,[2] to optimize their applications in the field of health[3][4] and environmental sciences.[5]

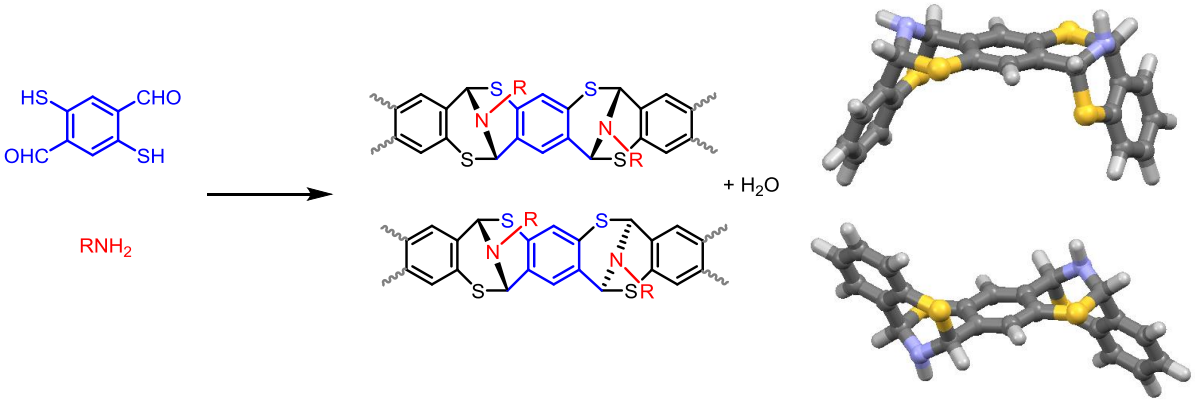

Figure 1 Eco-efficient 3-component click synthesis of diothiocins

A multi-disciplinary work-program extremely valuable for a Ph D training is targeted. The first phase will consist in optimizing the synthetic methodology for the production of polydithiocin cavitands based on the 2+1 click reaction. Kinetic and thermodynamic features will be monitored by various spectroscopic techniques in a perspective of optimization. The scope of the reaction, in terms of amine substrates (mono- and polyamines, synthetic and biogenic) will also be examined. A particular attention will be devoted to the experimental conditions affecting the stereoselectivity of the synthetic assembling process, preferentially affording either linear or closed species (figure 2)

The second phase of the project will consist in introducing specific functional groups born by the amine building block in order to deliver receptors with specific physical and biological properties. Solubilizing groups, chromophores, epitopes will be among the moieties introduced on the outer surface of the cavitand. Their binding and transportation properties, their biological activity will therefore be monitored by spectroscopic and microscopic techniques.

This PhD proposal requires a highly-motivated organic chemist willing to optimize the eco-efficient synthesis of new family of host molecules and explore their structural features and binding properties in order to develop applications at the interfaces with health sciences. Partnerships with laboratories specialized in antimicrobial agents, drug delivery/sensing and protein crystallization will also be part of the PhD.

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