PhD position in supramolecular chemistry

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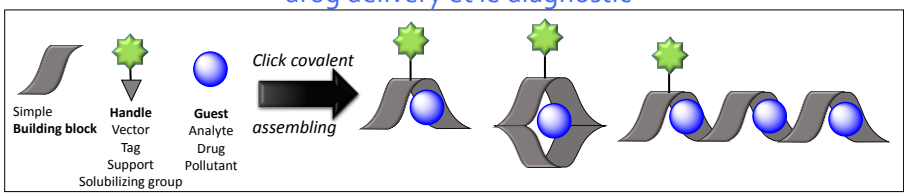
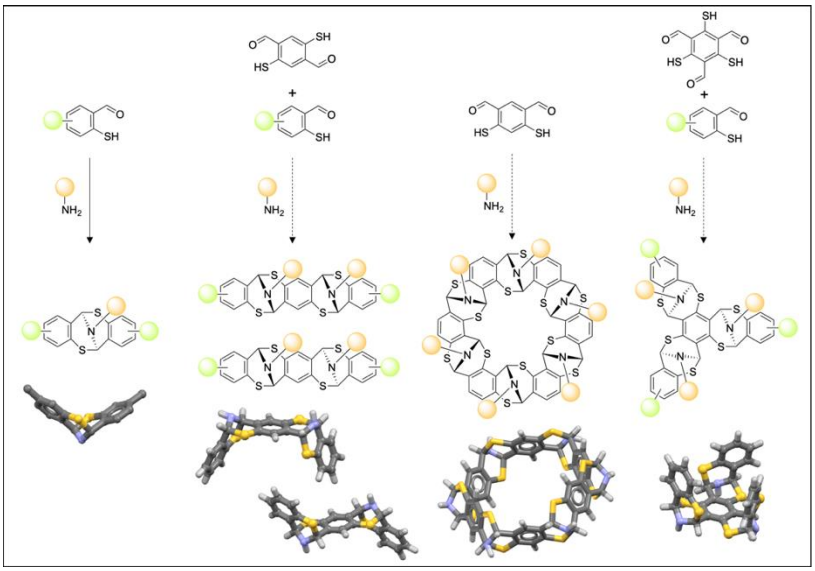
(Poly)dithiocins for drug delivery and sensing – Les polydithiocines : nouveaux cavitands pour le drug delivery et le diagnostic



*This research project aims to produce new self-assembled organic architectures toward the recognition of biologically relevant molecules sur as **antiviral agents or sensing of biological markers of neurodegenerative diseases**.*



THE PROJECT: During investigations on the dynamic combinatorial chemistry of functionalized thiophenols, we recently re-discovered by serendipity the condensation reaction of 2-mercaptobenzaldehydes with amines to give 1,5-dithiocins. Such a reaction was only reported a couple of times in the literature and poorly investigated.[1-2] As preliminary results, we already synthetized a range of 1,5-dithiocins with good yields in mild conditions on a wide range of thiosalicyladehydes and biogenic amines. These V-shaped 1,5-dithiocins are readily accessible in gram-scale and will serve, like Tröger bases, as binders toward therapeutic and sensing applications.

At present, the true challenge resides in synthesizing and assembling by simple condensation bis- or tris(thiolsalycilaldehydes) to yield **a new family of extended poly-dithiocins** of various topologies (i.e., cleft shaped, macrocyclic, bowl shaped). The primary amines clicked with these monomers will be chosen in order to confer to the resulting new cavitand with **some binding features toward guests (antiviral agent such as amantadine or reporting dye)** inside their concave side and to bear **a biochemical tag (epitope or vectorizing agent)** on their convex side for the selective binding of target proteins.
One should note that the 1,5-dithiocin motif is **chiral** with two bridgehead stereogenic atoms of interdependent configuration. Stereochemical information transfer can be expected to take place during the formation of one or both of these two remarkable regions through non-covalent (template, concave) or covalent (epitope, convex) effect.

THE CANDIDATE: the candidate recruited will have a strong background in organic chemistry and a sound knowledge of organic physical chemistry. Since molecular dynamics simulations will be a tool of choice for understanding the driving forces in the formation of host/guest complexes, we also expect the candidate to be willing to invest in acquiring new skills. Scientific curiosity and the ability to work in a team are essential. Collaboration with the ENS Lyon will be included for *in silico* structural studies of the architectures (E. Dumont), and with the Aix-Marseille University (N. Vanthuyne) for their stereochemical/dynamic features.

THE LAB: The Applied Supramolecular Group (*http://www.icbms.fr/csap*) develops families of complex architectures from simple building blocks for tailored molecular recognition and long-range propagation of molecular information. CSAp explores new fundamental concepts leading to disruptive technological applications. For selected recent publications, see: *Nat. Chem.* 2020, *12*, 202; *ACS Chem. Biol.* 2019, *14*, *2512; Chem. Sci.* 2019, *10*, 277; *Sci. Rep.* 2019, *9*, 1; *Org. Lett.* 2018, *20*, 2420; *Chem. Commun.* 2016, *52*, 14219; *J. Org. Chem.* 2016, *81*, 654.

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