PhD position available at the University of Rennes

Title : Möbius Artificial Enzymes
Keywords : hexaphyrin, topology, chirality, aromaticity, coordination, recognition, catalysis
General information: The thesis will be carried out in the team *Macrocycles Pyrroliques et Processus Bio-Inspirés*, under the supervision of Dr. Stéphane Le Gac, at the *Institut des Sciences Chimiques de Rennes* (UMR CNRS 6226; https://iscr.univ-rennes1.fr/pyrrolic-macrocycles-exotic-coordination-and-adaptative-systems). Period: Oct. 2023-Sept. 2026. Rough salary: ~2100 €/month (financial support from the ANR, MOBAZYM project).

Description:

Möbius rings are inherently chiral objects, mirror images being generated by twisting the Möbius band according to a right or a left screw sense (Fig. 1a).[1] Compared to other sources of chirality, Möbius chirality has been scarcely investigated at the molecular level and thus constitutes an innovative stereogenic element. Currently, a major obstacle remains the asymmetric preparation of Möbius compounds. Focusing on a [28]hexaphyrin scaffold,[2] our group has investigated an original approach for chirality induction taking advantage of the dynamic character of the twisted π-system (Fig. 1b).[3] Indeed, this conformationally flexible scaffold undergoes rapid *P* ↔ *M* equilibrium in solution, thus exhibiting a dynamic Möbius chirality. This feature enables transfer of chirality under thermodynamic control, useful to build up adaptative systems. Recently, we have investigated Möbius Zn(II)-hexaphyrins bearing various functionalities (Fig. 1c) and demonstrated efficient and tunable *P/M* twist stereoselectivities, controlled by achiral effectors, which is unprecedented.[3] The next challenge is to study the reverse process, *i.e.* chirality transfer from a Möbius ring to a substrate. More precisely, we aim at the achievement of a Möbius-hexaphyrin catalyst exhibiting stereoselective transformation/discrimination that, ultimately, will further be incorporated in a protein scaffold, leading to so-called Möbius Artificial Enzymes. This project will be tackled in strong collaboration with the team of Prof. Jean-Pierre Mahy at Paris-Saclay University.

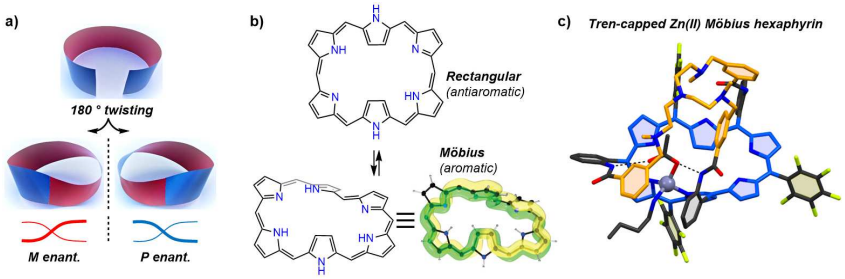

Figure 1. (a) The two enantiomers of a Möbius ring. (b) Rectangular and Möbius conformers of a [28]hexaphyrin. (c) Bio-inspired Möbius-type metallo-receptor.[3a]

The work of the PhD student in Rennes will thus consist in the design and synthesis of Möbius hexaphyrins functionalized with chiral coordinating arms, reactive groups for bio-conjugation as well as water solubilizing groups. The complexation of zinc in bio-compatible media, targeting *P/M* twist chirality induction, will then be studied by NMR, UV-vis absorption and circular dichroism analysis. Optimized systems will be transfer into the next steps of the project.

Profile of applicant:

The candidate, with a Master 2 degree in molecular chemistry, must have a solid knowledge in general chemistry and more particularly in organic synthesis and NMR spectroscopy. The synthesis and characterization in solution of dynamic macrocyclic ligands and zinc complexes will constitute an important part of this thesis. A strong practical aptitude as well as a significant personal investment will be necessary. People interested will kindly send a CV, a motivation letter, the contact details of two people who can recommend the candidate as well as their Master's transcript and diploma (stephane.legac@univ-rennes.fr).

References:

[1] R. Herges, *Chem. Rev.* **2006**, *106*, 4820-4842. [2] T. Tanaka, A. Osuka, *Chem. Rev.* **2017**, *117*, 2584-2640. [3] a) H. Ruffin, G. Nyame Mendendy Boussambe, T. Roisnel, V. Dorcet, B. Boitrel, S. Le Gac, *J. Am. Chem. Soc.* **2017**, *139*, 13847-13857; b) R. Benchouaia, N. Cissé, B. Boitrel, M. Sollogoub, S. Le Gac, M. Ménand, *J. Am. Chem. Soc.* **2019**, *141*, 11583-11593; c) B. Boitrel, S. Le Gac, *Chem. Commun.* **2020**, *56*, 9166-9169; d) B. Boitrel, S. Le Gac, *Chem. Commun.* **2021**, *57*, 3559-3562; e) H. Ruffin, A. Fihey, B. Boitrel, S. Le Gac, *Angew. Chem. Int. Ed.* **2022**, *61*, e202113844.