Institut de Chimie de Clermont-Ferrand

ÉCOLE DOCTORALE DES SCIENCES FONDAMENTALES
Université Clermont Auvergne

cnrs

Allocation doctorale

Thesis Title	**PEPTOID FOLDAMERS FOR ASYMMETRIC ORGANOCATALYSIS**
University	Université Clermont Auvergne
Doctoral School	Sciences Fondamentales
Laboratory	Institut de Chimie de Clermont-Ferrand (UMR CNRS 6296)
Team / research group	Chimie Organique et Médicinale / Peptoid
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Keywords	Peptidomimetic; Foldamer; Peptoid; Catalysis; Asymmetric synthesis

Summary

Non-natural oligomers with defined sequences, known as 'foldamers', have the ability to adopt well-defined and stable three-dimensional structures in both organic and biological media. Various aliphatic and aromatic foldamers have been developed. Among these, peptoids (oligomers of *N*-substituted glycines) are peptide mimetics that are the result of the displacement of side chains from the α-carbons to the adjacent nitrogen atoms, resulting in tertiary amide bonds. Peptoids have several advantages. Their iterative synthesis is perfectly controlled in solution and on support. Peptoid sequence diversity, based on the use of primary amines, far exceeds that of peptides, and secondary structures may arise from the formation of *cis*- or *trans*-amides, or a combination of both.

Research conducted by our group and others, have demonstrated that it is possible to selectively obtain either the *cis* or *trans* conformation of amides by strategically designing the side chains attached to the amide nitrogen. In particular, our research has enabled the development of highly stable peptoids that adopt the helical Polyproline I (PPI) conformation. These folded peptoids can now serve as platforms for a predictable spatial arrangement of functional group(s). The chirality of the helices provides a basis for asymmetric catalysis, paving the way for organocatalysis. Furthermore, in the field of organocatalysis, N-Heterocyclic Carbenes (NHC) play a crucial role by enabling a diverse array of reactions, including cross- or intramolecular benzoin condensations, Stetter reactions, hetero-Diels-Alder reactions, and transesterification.

The proposed thesis will draw on the team's combined expertise in peptoids and NHC [4,5]. The aim of this study is to develop catalysts derived from peptoids with axial chirality onto which stable carbene precursors have been grafted. (imidazolium, triazolium or thiazolium). Secondly, the activity of the organocatalysts will be carefully evaluated by screening a series of chosen C-C bond forming reactions. This approach represents a promising alternative to conventional strategies using small molecules or peptides.

References

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2- Roy, O. et al. Homogeneous and Robust Polyproline Type I Helices from Peptoids with Nonaromatic alpha-Chiral Side Chains. J. Am. Chem. Soc. **2017**, 139 (38), 13533-13540. https://doi.org/10.1021/jacs.7b07475

3- Flanigan, M.D. et al. Organocatalytic Reactions Enabled by N-Heterocyclic Carbenes. *Chem. Rev.* **2015**, *115*, 17, 9307.

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5- Akhdar, A. et al.Cage-like structures based on constrained cyclic arylopeptoids. Chem. Commun. **2023**, 59 (52), 8087-8090. https://doi.org/10.1039/D3CC01956J

Profile and skills. Profile and skills. The candidate must hold a Master 2 or equivalent degree (or be in the process of obtaining one) in Organic Chemistry, Bioorganic Chemistry or any other Master's degree with a focus on the organic discipline. Scientific rigor and strong motivation are required. Initial experience in one of the following areas would be an advantage: multi-step synthesis, catalysis, peptide/peptidomimetic chemistry, etc.

How to apply. Please submit a detailed curriculum vitae and cover letter, transcripts of grades and rankings, and any other relevant documents to help us evaluate your application.