Coordination Chemistry Laboratory of the CNRS, Toulouse, France
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Team ALAMBIC
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PhD Position

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Design of bio-inspired lanthano-peptides catalysts

Keywords: peptide synthesis, lanthanide, luminescence, bio-inorganic chemistry

Project: Lanthanides (Ln) recently joined the family of elements essential to living organisms with the discovery of methylotrophic bacteria relying on Ln(III) for their metabolism [1]. The first Ln-enzyme, a methanol dehydrogenase, and the first Ln-trafficking protein have been identified. In addition to these native Ln-binding proteins, synthetic peptides have been designed using different types of scaffolds, such as lanthanide binding tags [2], lanthanide fingers [3], three stranded coiled coils [4], or short cyclic peptides containing unnatural amino acids [5]. Although small Ln(III) complexes have been used in catalysis,[6] the lanthano-peptides developed have never been used for this purpose.

Within the ALAMBIC team, one of the ongoing research projects is the design of lanthano-peptide catalysts. The use of synthetic peptide scaffolds combines the advantages of small molecule catalysts (synthetic, modularity of their structure) and enzymes (control of the 1st and 2nd coordination spheres, fine tuning of the reactivity) [7]. The main challenge of the project is to design an active site that accommodates the Ln(III) ion and provides positive interactions for the substrates of the catalysis, while preserving the peptide fold. The objectives are therefore to design and synthesise peptides with a well-defined structure, high affinity for Ln(III) and to implement positive interactions in the active site for substrate binding. This will be an important first step towards obtaining functional lanthano-peptides catalysts.

In order to achieve these objectives, this thesis will be divided into two parts. The first part will be devoted to the synthesis of peptide libraries (Fig. 1) in order to determine the parameters controlling the affinity for Ln(III) (number and type of binding amino acids, position in the sequence, pre-organisation of the binding site) and the peptide fold (hydrogen bonding, hydrophobic interactions, salt bridges). The use of non-natural amino acids to improve either of these parameters will be investigated.

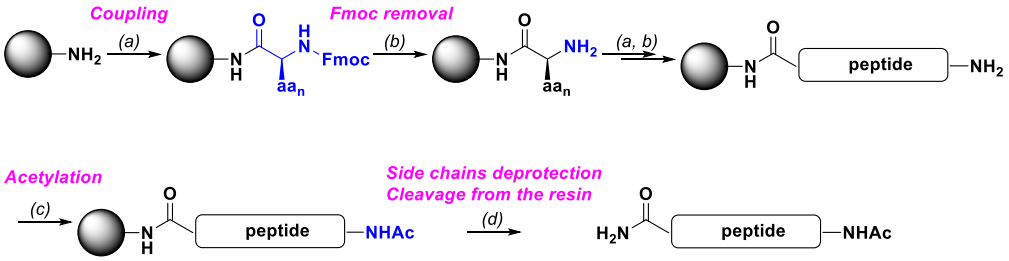

Figure 1 – Solid phase peptide synthesis.

The second part will be devoted to (i) the characterisation of the structure and stability of the peptide-Ln(III) complexes (NMR, circular dichroism, in silico modelling), (ii) the determination of the capacity of the peptides to bind Ln^{3+} ions (luminescence, UV-vis, NMR), (iii) the evaluation of the reactivity of the lanthano-peptides in model reactions. The different physical properties of Ln(III) will be an advantage to access complementary analytical techniques (Fig. 2).

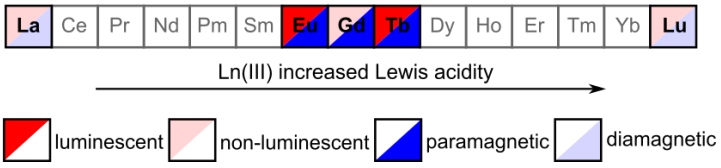

Figure 2 – Ln(III) used in the project and their physical properties.

Environment: The successful candidate will work in an exciting, dynamic and international environment at the Coordination Chemistry Laboratory of the CNRS in Toulouse, France. The technical and scientific environment in the laboratory and in the host team is of high quality and fully adequate for the realisation of the project. The successful candidate will be trained in advanced spectroscopic techniques such as (paramagnetic) NMR, steady-state and time-resolved emission spectroscopies, and circular dichroism.

Profile: We are looking for a highly motivated student with a background in molecular chemistry and excellent grades. Applicants should have a strong interest in multidisciplinary projects in the field of bio-inorganic chemistry. Experience in organic or peptide synthesis and in spectroscopy would be an added value. In addition, ability to write a scientific report, and strong teamwork skills are required.

Application: Please, send your resume and academic records as well as two references to emilie.mathieu@lcc-toulouse.fr.

References

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