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Postdoctoral position

Project title : CRYSTALBALL - Artificial enzymes as heterogeneous catalysts

Keywords : organic and inorganic synthesis – protein crystallography – catalysis - mechanism

Duration : 18 months

Location : Laboratoire de Chimie et Biologie des Métaux, Grenoble, France.

Salary : ~ 2000 Euros net income per month

Candidate profile : We are offering a post-doctoral position to realize the catalytic part of the *Crystalball* project. The candidate will be asked to synthesize organic ligands and substrates plus inorganic complexes as well as to explore the catalytic field of oxidation reactivity. Some knowledge or interest in biochemistry and/or in spectroscopy will be appreciated.

Apply before end of October to start in February using: cv, *brief description of research experience, list of publications and reference contacts.*

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CRYSTALBALL

Artificial enzymes as heterogeneous catalysts

Keywords: organic and inorganic synthesis – protein crystallography – catalysis - mechanism

The project «*crystalball*» represents a major asset for the design of a sustainable chemistry, with an original combination of biocatalysis and chemical metal based catalysis. Our original strategy relies on the conception of a heterogeneous crystal/solution version of the already demonstrated artificial enzymes technology coupled to an infinite declension of catalyzed reactions.[1, 2, 3]

The project will be based on the setting up of oxidation reactions catalyzed «*in cristallo*», thanks to the gain in mechanical and chemical stability of protein crystals by Cross Linking methods (CLEC).[4] This mature methodology comprises the introduction of chemical connections between the protein molecules into the lattice of the protein crystal. Up to now, the CLEC technology has been benchmarked for the biocatalysis implicating reductases but the field of oxidation remains to be explored. We will increase the stability of our hybrid family based on NikA, a Ni transport protein in *E. coli*, in order to scan more reactions conditions (solvent, temperature, pH), that will permit infinite oxidation reactions.

The project will focus on two catalytic oxidation reactions (i) the controlled hydroxylation of polycyclic aromatic hydrocarbons, pollutant compounds, (ii) the transformation of sulfide into sulfoxides, ultimate enantioselective step for the synthesis of sulfoxide based drugs in the pharmaceutical industry. The selection of these reactions results of the oxidative capacity of our already demonstrated NikA hybrids, in which the inorganic complex drives the nature of the reaction.[1]

Working program

The biohybrids will be structured by the insertion of iron catalysts into NikA as a protein platform, already in hand in the laboratory.[1, 5, 6, 7] The CLEC method will represent the cornerstone of the project. Subsequent comparison of the solid hybrid catalytic properties with the ones of the hybrid in solution will validate our strategy.

The project plan for the catalytic part is declined with three principal tasks:

(i) Synthesis of crystalline FeL⊂NikA hybrids.

This task deals with the optimization of our different FeL⊂NikA. The synthesis of the inorganic complexes FeL will be performed with two series of ligands. The first series will give iron complexes with N4O coordination on a skeleton of bis-(2-methylpyridine)diamine known to be efficient catalysts for oxygen transfer reactions on sulfide and alkenes. The second series will give iron complexes with N2O3 coordination with ligands containing one phenolate moiety. The latter series needs to be extended to more members by slights modifications of their backbone to provide higher activity. The group will optimize the production of hybrid crystals.

(ii) Stabilization of the hybrid crystals by cross linking method.

Such a method implicates the reaction *in cristallo* of difunctionnal organic molecules such as dialdehyde. Here, mechanical and chemical stability of the crystals will be targeted.

(iii) Search for a reductive activation of dioxygen.

Here stands the challenging task. The goal substrates are polyaromatic α, β substituted alkenes, since they represent analogs of the building blocks of lignin, a well-known frame for drugs synthesis and substrate for iron dioxygenases. We so plan (a) to first test heterogeneous catalysis for oxygen transfer reaction from sulfides to sulfoxides using NaOCl as oxidant in order to compare the reactivity of the stabilized hybrids with the one of our Fe(N2py2)⊂NikA hybrids in solution previously studied.[5] We hope to gain in terms of stability, TON and enantioselectivity. A special focus on synthesis of drugs, such as omeprazole, is planned. (b) To oxidize either polyaromatic hydrocarbons or small sized aromatic alkenes using dioxygen as the oxidant.[7] Best substrates will be selected according to our docking method. Expected products will range from hydroxylation of phenyl rings to phenol or further to catechols, diols, or products issued from double bond cleavage.

The final goal is to optimize the solid catalytic system designed in terms of selectivity and stability.

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