Ecole Doctorale des Sciences Fondamentales

Title of the thesis: Exploration of aldolases substrate specificity for applications in organic synthesis.

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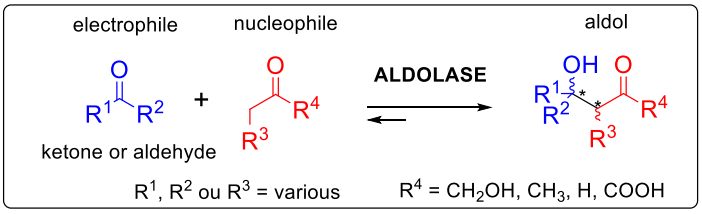
Summary:

In the field of green chemistry, isolated enzymes are well-established as useful tools for the development of new processes in organic synthesis. Biocatalysts facilitate the stereo-, regio- and enantioselectively production of a large variety of organic compounds in exceptionally soft and mild conditions. **The discovery and study of new enzymes with amazing properties, is an international major aim in order to widen the chemist's toolbox for applications in sustainable organic synthesis.** Our research group is particularly focused on aldolases, enzymes catalyzing stereoselectively C-C bond formation. **The main objective of this project is to explore new aldolases, isolated from the biodiversity, and discovered by high throughput screening. This innovating multi-disciplinary project, at the interface of chemistry and biology, is part of a partnership established several years ago with the CEA-Génoscope** (Evry).
These biocatalysts will be screened for original catalytic activities, never described before, as exemplified in the scheme below. Our experience has already been illustrated by the publication of the screening of several aldolase families with different properties. By structure modulation of the electrophiles and nucleophiles, their substrate specificity will be fully studied, for the best hits, in the preparation of attractive aldols as such or as synthons of more complex molecules of biological interest. Their stereochemistry will be determined by running small scale syntheses. This substrate specificity study will be extended to enzymes from our library, for the research of new and particularly original reactions.



Skills targeted:
Biocatalysis (enzyme production and purification, mutant construction (error-prone PCR or semi-rational approach) enzymatic reaction implementation), analysis (HPLC, UV spectroscopy), classical organic synthesis and purifications (silica gel or ion exchange chromatography), NMR, Mass spectrometry analysis.

No pre-requisite in biocatalysis and/or in enzymology is required.

References from our group:
D. Chambre, et al *Chem Commun*. **2019**, *55*, 7498-7501. V. Laurent, et al *Angew. Chem., Int. Ed. Engl.*, **2018**, *57*, 5467-5471. A. Uzel et al *ACS Catal*. **2020**, *10*, 2538-2543. V. Laurent et al *Adv. Synth. Catal.* **2019**, *361*, 2713-2717.