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NOM DU GROUPE DE RECHERCHE QUI ACCUEILLE L'ETUDIANT : MoNALISA (Modified Nucleic Acids, Lipids and Innovative Synthetic Approaches)
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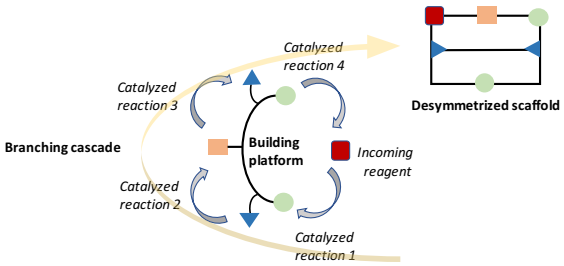
TITRE DU SUJET PROPOSE : MICADOS (MultICAtalysis for Diversity-Oriented Synthesis)

DESCRIPTIF DU SUJET PROPOSE (des références bibliographiques seront appréciées) :

Multicatalytic cascade transformations represents an integrated chemical approach reminiscent of the multi-step biosynthetic pathways developed by Nature.[1] The objective of the project is to apply this bio-inspired synthetic methodology to reagent-based diversity-oriented synthesis.[2] Implementation of this strategy intends to accelerate both exploration of chemical space and discovery of innovative synthetic transformations in an eco-responsible and sustainable way.

Versatile synthetic precursors will be designed to undergo an array of reactions pathways under different chemical environments. The folding of linear functionalized substrates into various cyclic scaffolds will be explored though multicatalytic cascade transformations.[3] Small aliphatic precursors will thus be prepared to be engaged in an approach combining two-directional synthesis and tandem reactions. Such a strategy was elegantly explored by R. A. Stockman and coll. who described the synthesis of a natural-like scaffold from a single precursor by means of a 12-fold branching pathway.[4]

C_2-symmetrical linear precursors will be considered as pluripotent building platforms. The versatile enal functionality will be exploited as a prototypical reacting terminus. Advantage will be taken of asymmetric multi-catalysis to enlarge the reactivity scope through the combination of different modes of activation.[5] From each precursor, arrays of reagents will be assessed in search for branching cascades leading to value-added desymmetrized scaffolds. Thanks to systematic analysis of the crude reaction mixture, the time- and energy-consuming limiting steps of purification and characterization will only be carried out after the scale-up of the sole reaction conditions resulting in the most productive transformations.



Beyond the facilitated exploration of chemical space with limited environmental impact, this diversity-oriented synthetic strategy bears a strong potential for the development of "activity-directed synthesis", a unique chemical approach mimicking the natural process of directed-evolution.[6]

1 Jurjens, G. *et al.* Lessons from the synthetic chemist nature. *Nat. Prod. Rep.* **2015,** *32,* 723.
2 O' Connor, C. J. *et al.* Diversity-oriented synthesis: producing chemical tools for dissecting biology. *Chem. Soc. Rev.* **2012,** *41,* 4444.
3 O'Connell, K. M. G. *et al.* Two-directional synthesis as a tool for diversity-oriented synthesis: Synthesis of alkaloid scaffolds. *Beilstein J. Org. Chem.* **2012,** *8,* 850.
4 Robbins, D. *et al.* Synthesis of natural-product-like scaffolds in unprecedented efficiency via a 12-fold branching pathway. *Chem. Sci.* **2011,** *2,* 2232.
5 Afewerki, S. *et al.* Combinations of aminocatalysts and metal catalysts: A powerful cooperative approach in selective organic synthesis. *Chem. Rev.* **2016,** *116,* 13512
6 a) Karageorgis, G. *et Al.* Efficient discovery of bioactive scaffolds by activity-directed synthesis. *Nat. Chem.* **2014,** *6,* 872