

Research Topic for the ParisTech/CSC PhD Program

Field: Chemistry, Physical Chemistry and Chemical Engineering

Subfield: Organic chemistry

Title: Collective total synthesis of quinazoline alkaloids

ParisTech School: Ecole Polytechnique

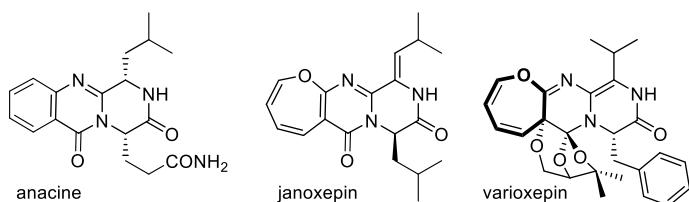
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Lab, website: Laboratoire de Synthèse Organique, <https://naygroup.wordpress.com/>

Short description of possible research topics for a PhD:

Natural products are an important source of chemical leads for biological purposes. Owing to their limited availability, it is important to design efficient synthetic routes amenable to scale-up for applied perspectives. Among natural products, quinazoline alkaloids are a large class of peptide-derived compounds from fungal origin, possessing a wide variety of biological activities (for example antibiotic, anticancer, phytotoxic). On the structural point of view, their diversity results from various oxidative functionalizations, leading to the hydroxylation or the dehydrogenation of the diketopiperazine ring, or to the conversion of the aromatic part into an oxepin (examples below). All these structural features render the total synthesis of these natural products particularly challenging. This project aims to apply synthetic methodologies already developed in our laboratory to the synthesis of representative natural products of this series, using C-H oxidation and cycloaddition strategies. Collective approaches will allow us to synthesize several quinazoline products in a single divergent synthetic process.



Required background of the student: (Which should be the main field of study of the applicant before applying) The applicant should have a Master degree in organic chemistry and a strong interest in organic synthesis, synthetic methodologies and the biological interface. A good level of spoken and written English is expected.

A list of 5(max.) representative publications of the group: (Related to the research topic)

- M. Zaghouani et al.: Multifaceted study on a cytochalasin scaffold: lessons on reactivity, multidentate catalysis and anticancer properties, *Chem. Eur. J.* **2018**, doi: 10.1002/chem.201804023
- D.-Y. Sun et al.: Asymmetric Total Synthesis of Distaminolyne A and Revision of its Absolute Configuration, *Org. Lett.* **2017**, *19*, 714–717.
- M. Zaghouani et al.: First Total Synthesis, Structure Revision and Natural History of the Smallest Cytochalasin: (+) Periconiasin G, *Chem. Eur. J.* **2016**, *22*, 15257–15260.
- B. Laroche et al.: Ring-closing enyne metathesis of terminal alkynes with propargylic hindrance, *J. Org. Chem.* **2015**, *80*, 5359–5363.
- X.-W. Li et al.: Bio-inspired formal synthesis of hirsutellones A-C featuring an electrophilic cyclization triggered by remote Lewis acid-activation, *Chem. Eur. J.* **2013**, *19*, 16389–16393.