

Research Topic for the ParisTech/CSC PhD Program

***Field:** Chemistry, Physical Chemistry and Chemical Engineering

Subfield: Organic Chemistry

Title: Isocyanide Based Multicomponent Reactions and Transition Metal Catalysis

ParisTech School: ENSTA ParisTech

Advisor(s) Name: Laurent El Kaim (laurent.elkaim@ensta-paristech.fr)

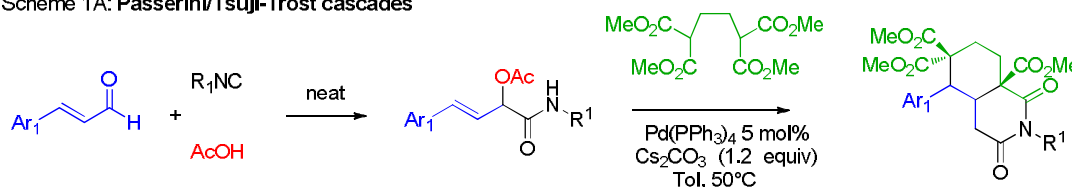
(Lab, website): <http://ucp.ensta-paristech.fr/sor.php>

Short description of possible research topics for a PhD: The purpose of the project is to bring new tools for the preparation of complex organic derivatives with potential interest for the pharma industry. Isocyanides are carbene type derivatives easily prepared from amines. They are best known for their use in Ugi coupling, a 4-component reaction which has been extensively used for the preparation of libraries of bioactive heterocycles. The ENSTA research group in organic chemistry has a strong expertise in the field of isocyanide based multicomponent reactions (MCRs). We have disclosed in 2005 an important extension of the Ugi reaction known as Ugi-Smiles couplings and have studied various reactions of isocyanides with electrophilic derivatives.¹ Our activities are now following two directions:

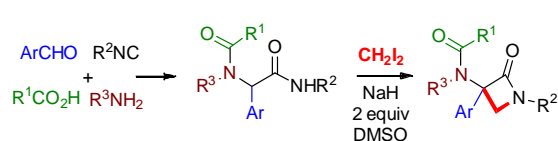
- Use of MCRs to afford fast access to starting material with suitable functionalities for original organometallic transformations (Scheme 1A).^{2a,b}
- Chemistry of amide dianions applied to the synthesis of heterocycles (Scheme 1B).^{3a,b}
- Nitro chemistry coupled with transition metal catalysis.⁴

This PhD project will focus on Tsuji-Trost reactions working with diamide anions and nitro compounds. IMCRs will be used as much as possible to prepare starting materials and reach libraries of biologically active compounds.

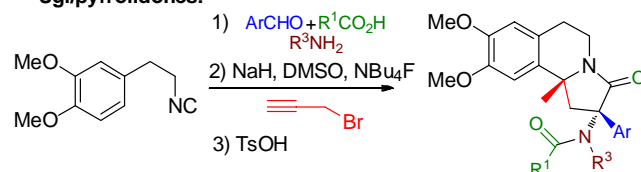
Scheme 1A: Passerini/Tsuji-Trost cascades



Scheme 1B: Ugi/ β -lactams:



Ugi/pyrrolidones:



Required background of the student: General Organic Chemistry

A list of representative publications of the group:

- 1)a) L. El Kaïm, L. Grimaud, J. Oble, *Angew. Chem., Int. Ed.*, **2005**, 44, 7961-7964. b)L. El Kaïm, L. Grimaud, *Eur. J. Org. Chem.* **2014**, 7749-7762.
- 2) a) M. Cordier, A. Dos Santos, L. El Kaïm, N. Narboni, *Chem. Commun.*, **2015**, 51, 6411-6414. b) E. H. El Mamouni, M. Cattoen, M. Cordier, J. Cossy, S. Arseniyadis, H. Iitki, L. El Kaïm, *Chem. Commun.*, **2016**, 52, 14490 - 14493.
- 3a) A. Zidan, L. El Kaim et al, *Angew. Chem Int. Ed.*, **2017**, 56, 12179-12183.3b) A. Zidan, L. El Kaim et al, *Org. Lett.*, **2018**, 20, 2568-2571.
- 4) M. Dolè Kerim, S. Jia, C. Theodorakidou, S. Prévost, L. El kaim, *Chem Commun.* **2018**, in press, 10.1039/C8CC06536E