

| GROUP

## ORGANOMETALLIC CATALYSIS, ORGANIC SYNTHESIS AND METHODOLOGY (COSMO)

ICBMS - UMR 5246, UNIVERSITÉ CLAUDE BERNARD LYON 1 - CNRS - INSA LYON - CPE LYON

OLIVIER  
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Professor



### TRANSITION METAL-CATALYZED FUNCTIONALIZATION OF UNACTIVATED C(SP<sup>3</sup>)-H BONDS



**COSMO is a research group focusing on several aspects of transition-metal catalysis, with a particular emphasis on C(sp<sup>3</sup>)-H bond functionalization.**

**Our team is part of ICBMS, a synthetic chemistry and biochemistry research and teaching unit, working under the authorities of University Lyon 1, CNRS, INSA Lyon and CPE-Lyon ([www.icbms.fr](http://www.icbms.fr)). It belongs to the Department of Chemistry and Biochemistry of the Faculty of Sciences and Technology, located on the La Doua Campus of the University of Lyon, in Villeurbanne.**

### C-H BOND FUNCTIONALIZATION

The transition-metal-catalyzed direct functionalization of C-H bonds of (hetero)arenes and alkanes is of great interest, because it allows a more direct access to original organic molecules, which are potentially useful for the discovery of new drugs, agrochemicals or materials.

The functionalization of unactivated C(sp<sup>3</sup>)-H bonds is a current major research focus in our group. These seemingly inert C-H bonds raise issues of reactivity, chemo-, regio- and stereoselectivity which we seek to address.

Our research approach ranges from method development (including catalyst design and screening) to mechanistic studies (experimental and DFT) and applications to the multi-step synthesis of bioactive molecules and natural products.

### PALLADIUM-CATALYZED INTRAMOLECULAR C(SP<sup>3</sup>)-H ACTIVATION

We have recently investigated a selective intramolecular C(sp<sup>3</sup>)-H activation approach, starting from (hetero)aryl bromides or chlorides and giving rise to olefins or polycyclic molecules depending on the nature of the activated alkyl group and of the palladium catalyst. Our research efforts focused on the development of new catalytic systems and cascade reactions, mechanistic studies, as well as applications to the synthesis of biologically active molecules. For example verapamil, an anti-hypertensive drug, and coralydine (see structure), a tetrahydroprotoberberine alkaloid, were synthesized using this approach.



### PALLADIUM-CATALYZED INTERMOLECULAR C(SP<sup>3</sup>)-H FUNCTIONALIZATION

We are currently developing a new intermolecular C(sp<sup>3</sup>)-H functionalization strategy which allows to achieve the  $\beta$ - and longer-range arylation of carboxylic esters and Boc-amines, via Pd-catalyzed migrative cross-coupling. Useful (hetero)arylated products were synthesized, including phenylalanine analogues and homologues and 3-arylpiperidines (see structures).

#### | Key references

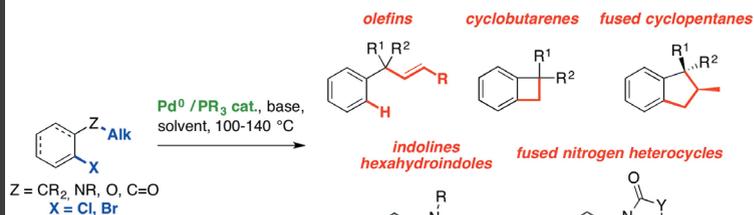
*Angew. Chem. Int. Ed.* 2003, 5736; *Chem. Eur. J.* 2007, 792; *J. Am. Chem. Soc.* 2008, 15157; *Angew. Chem. Int. Ed.* 2009, 179; *J. Am. Chem. Soc.* 2010, 10706; *Org. Lett.* 2011, 1816; *Org. Lett.* 2012, 398; *Chem. Eur. J.* 2012, 4480; *Angew. Chem. Int. Ed.* 2012, 10399.

## EQUIPMENT

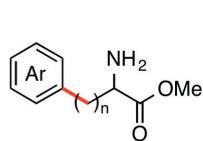
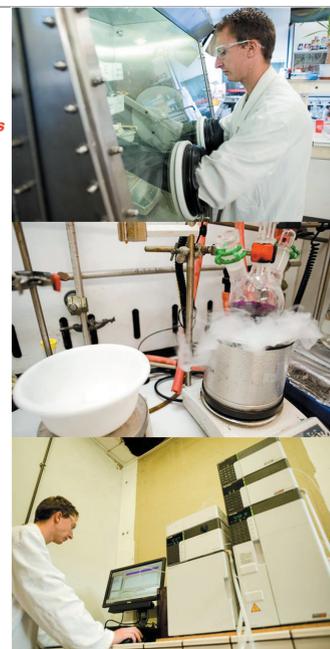
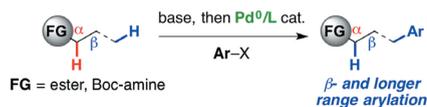
- > GC/MS system,
- > HPLC system with chiral phase columns, glove-box,
- > Schlenk tubes.



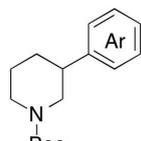
## INTRAMOLECULAR C(sp<sup>3</sup>)-H FUNCTIONALIZATION



## INTERMOLECULAR C(sp<sup>3</sup>)-H FUNCTIONALIZATION: MIGRATIVE CROSS-COUPPLINGS



arylalanines and homologues



3-arylpiperidines

## Key references

*Angew. Chem. Int. Ed.* 2010, 7261; *Chem. Eur. J.* 2012, 1932; *Angew. Chem. Int. Ed.* 2012, 10808; *Chem. Sci.* 2013, 2241.

## COMPETENCES

Organic synthesis, organometallic catalysis and synthesis (ligands, metal complexes, reactive intermediates), DFT calculations.

## COLLABORATIONS

Several academic collaborations including Dr. Eric Clot, Institut Charles Gerhardt, Montpellier for DFT calculations. Current or former industrial partnerships with Servier, Bayer CropScience.

## STAFF

**Olivier Baudoin**, Professor  
**Rodolphe Jazzar**, CNRS Fellow  
**Paolo Larini**, Lecturer  
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1-3 Post-Docs  
4-5 PhD Students  
3-4 Master's Students

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