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Axe Hétérocycles et Matériaux Fonctionnels

PhD project: Study and development of polar organometallic tools: towards the preparation and selective functionalization of heterocycles

The synthesis of (hetero)aromatic compounds is an omnipresent challenge for the organic chemist due to their multiple and varied applications. Indeed aromatic and heterocycle moieties are everywhere in day life, either in materials science, optics, electronics or biology. Thus, researches in organic synthesis methodologies are continually in progress for the preparation of heterocycles and their functionalization.

That is why, the aim of this PhD project is to develop original organometallic reagents to allow the development of innovative synthetic sequences for the preparation of highly functionalized (hetero)aromatic derivatives. In particular, we will focus our attention on bimetallic ate complexes as metalating reagents for metal-halogen exchange (MHE) or deprotonation. Their design, preparation and reactivity will be studied at first on heterocycle model and then exemplify to various heterocycles. Bimetallic ate complexes result in combining a polar organometallic (*e.g.* an organolithium) with a "soft" organometallic (organomagnesium for example), which the behaviour is different from those of the precursor. The principle is a synergy created by mixing two different organometallic reagents allowing increased selectivity and reactivity as well as use under non-cryogenic conditions compared to the monometallic reagent.

To this purpose, particular interest will be incline toward the modification of the external metal M' (Li, Na, K), while keeping magnesium as the central metal (M), to modulate the basicity/nucleophilicity ratio of the ate complex. Therefore, their efficiency and chemoselectivity to either deprotonate or promote MHE on (hetero)aromatics will be studied. Moreover, combination of ate complexes with an appropriate chiral ligand will be examined to perform chirality transfer from the reagent to the final heterocycles.

Next part of this PhD project will deal with the use of the ate complexes for the preparation and the regioselective functionalization of heterocycles as (aza)lactone, (aza)lactame, pyridine, pyrimidine…, involving metalation steps followed by electrophilic trapping. A particular interest will be focused on the metalation steps, with important methodological work to optimize the reaction conditions for the preparation and functionalization of such heterocycles with highly selectivities (chemo- and regioselectivities). After a step-by-step process development, original one-pot strategies will be investigated.

Complementary to the synthetic part of the project, the study of those polar organometallics species seems important to obtain useful informations about the reactivity, regio- and enantioselectivity of the reaction. To this purpose, advanced NMR and X-rays diffraction experiments will be performed in collaboration. The biological properties of the synthesized heterocycles will be studied as well in collaboration with the biological platform of L2CM (antibacterial and antiviral activities).

The PhD contract is *financially supported* by a French government grant (MESR).

Key-words: organometallic chemistry / synthetic methodology / heterocycles.

Research profile: The student should have a background in organic chemistry, knowledge of organometallic chemistry is recommended. The candidate should have good handling skills, especially in cryogenic conditions, and be able to work independently for literature searches.

Submission of applications: applications should be sent to S. Touchet (sabrina.touchet@univ-lorraine.fr) and C. Comoy (corinne.comoy@univ-lorraine.fr) including a cover letter, a detailed CV showing the cursus and previous completed internships, exam marks, and the email address of an internship referent.

References: (1) S. Touchet, S. S. Reddy Kommidi, P. Gros *Chemistry Select* **2018**, *3*, 3939-3942. (2) (a) A. Chartoire, C. Comoy, Y. Fort *Org. Biomol. Chem.* **2011**, *9*, 1839-1845. (b) A. Jasselin-Hinschberger, C. Comoy, A. Chartoire, Y. Fort *J. Org. Chem.* **2013**, *78(11)*, 5618-5626. (c) A. Jasselin-Hinschberger, C. Comoy, Y. Fort *Eur. J. Org. Chem.* **2014**, *(32)*, 7226-7231.

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