Experimental and Theoretical Investigations towards the (Het)-Aryne Route Using Heteroaryllithium as Key Reagents

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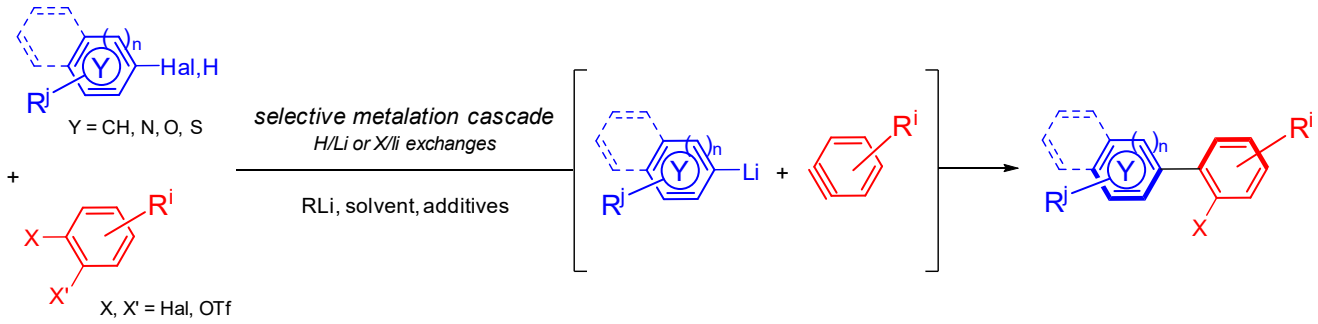
The biaryl pattern occupies an iconic role in chemistry, being a key structural feature of natural products, biologically active molecules, drugs, agrochemicals and other novel optical and mechanical materials. The access to complex target molecules is still challenging and the synthesis of aryl/hetaryl or hetaryl/hetaryl scaffolds, although highly important, is scarfely studied.

Because the most known (hetero)aryl-aryl bonding formations usually require Pd-catalyzed step, that induces a potentially toxic contamination of products, our main purpose has been to develop a reliable and generally applicable, transition-metal-free, hetero-aryl coupling using heteroaryllithiums as key reagents.

The reaction was meticulously studied by both experiment and computation (density functional theory) and comparison with phenyllithium was established. The results underlined the remarkable effect of additives, such as ligands and salts, on the coupling reaction and the potency of the method to construct expected heteroaryl-aryl backbones that open up a promising access to a wide range of heterobiaryl derivatives.



References :
[1] C. Demangeat, T. Saied, R. Ramozzi, F. Ingrosso, M. Ruiz-Lopez, A. Panossian, F. R. Leroux, Y. Fort, C. Comoy, *Eur. J. Org. Chem.* **2019**, 547-556, [doi.org/10.1002/ejoc.201801173]. [2] T. Saied, C. Demangeat, A. Panossian, F. R. Leroux, Y. Fort, C. Comoy, *Eur. J. Org. Chem.* **2019**, 5275-5284, doi.org/10.1002/ejoc.201900130]. [3] Project supported by the French Agence Nationale de la Recherche (ANR) (grant number ANR-14-CE06-0003-01, ChirNoCat).