Palladium-catalyzed C8-H fonctionnalization of Naphthalenes: new methodologies and synthetic applications

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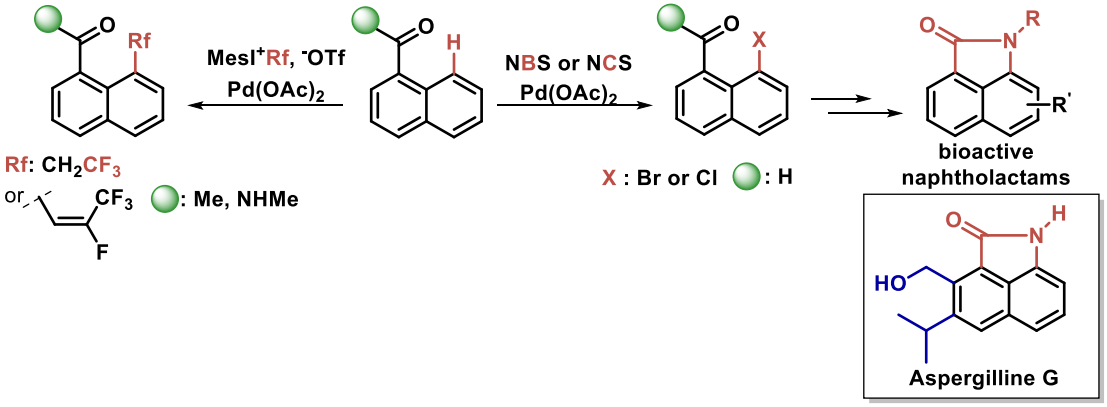
Over the past few decades, research into C-H bond activation has led to the discovery of new methods for synthesizing organic compounds.[1] One of the primary challenges associated with C-H activation is achieving selectivity due to the prevalence of C-H bonds in organic molecules. Our research group has focused on the naphthalene skeleton, employing carbonyls as directing group, and application in synthesis.[2]

In this work, we have successfully developed two regioselective functionalization techniques. Firstly, we achieved halogenation at the C-8 position of 1-naphthaldehyde utilizing an aldehyde as a weak directing group and palladium as a catalyst (Scheme 1.). This method has been applied to the synthesis of natural product skeletons as well as a library of naphtholactams.[3]

Secondly, we have investigated C8-fluoroalkylation and -fluoroalkenylation reactions. Various directing groups were explored. Good results have been showed with methyl-amide and methyl-ketone. Ultimately, we synthesized twenty-eight fluoroalkylated compounds and sixteen fluoroalkenylations, both demonstrating tolerance to multiple chemical functionalities with yields reaching up to 89% (Scheme 1.).[4]



Scheme 1. C8-functionnalisation of 1-carbonylnapthalenes via C-H activation

References

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[4] Manuscript submitted