Recent Advances in Difluorocyclopropanation of alkenes using Ruppert–Prakash reagent.

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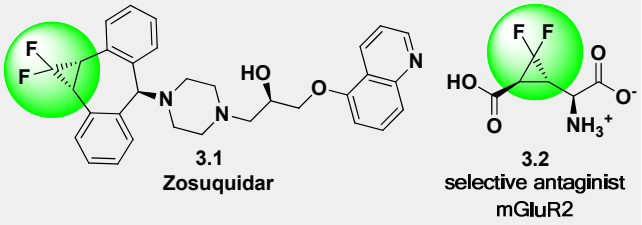
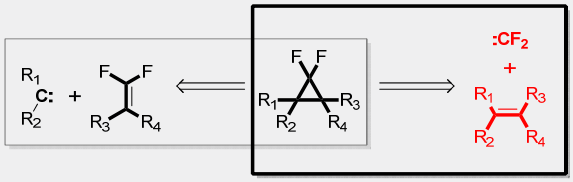
Introduction and Aim

Modern medicinal chemistry widely exploits two structural motifs to improve physico-chemical characteristics of the compounds: fluorine atoms and small rings.

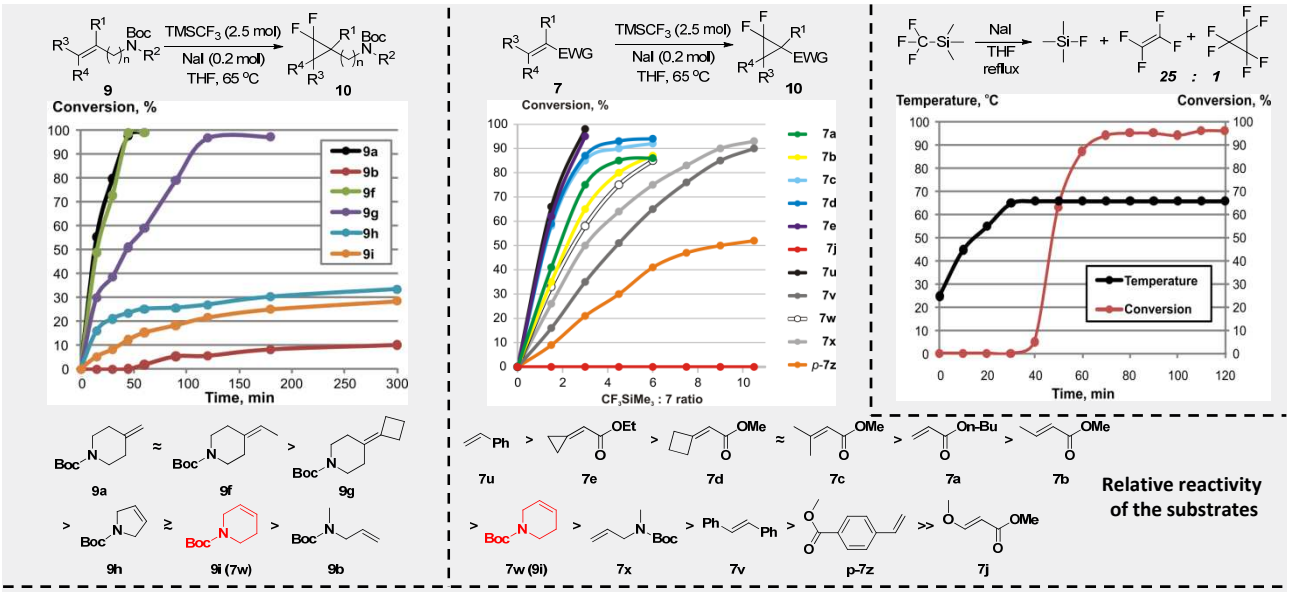
The best way for generating the smallest one example of them, difluorocyclopropane, is difluorocyclopropanation of alkenes by difluorocarbene or its synthetic analogues. The Ruppert – Prakash reagent (CF_3SiMe_3) is one of the most convenient difluorocarbene equivalent to achieve that transformation. Nevertheless, it was studied a bit to date, mostly with non-functionalized substrates.

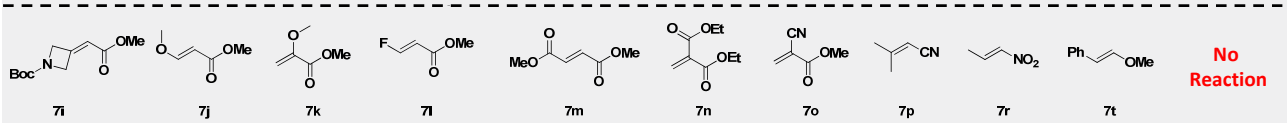
We optimized the reaction conditions and elaborated the methodology for using this reagent for a wide set of substrates called “slow addition protocol”. In a series of works, we described the synthesis of various functionalized difluorocyclopropanes – valuable building blocks for medicinal chemistry in a multigram scale by the evaluation of this protocol. The scope and limitations was significantly enlarged to electron-deficient substrates, the yields were extremely increased and the conditions was strongly optimized.



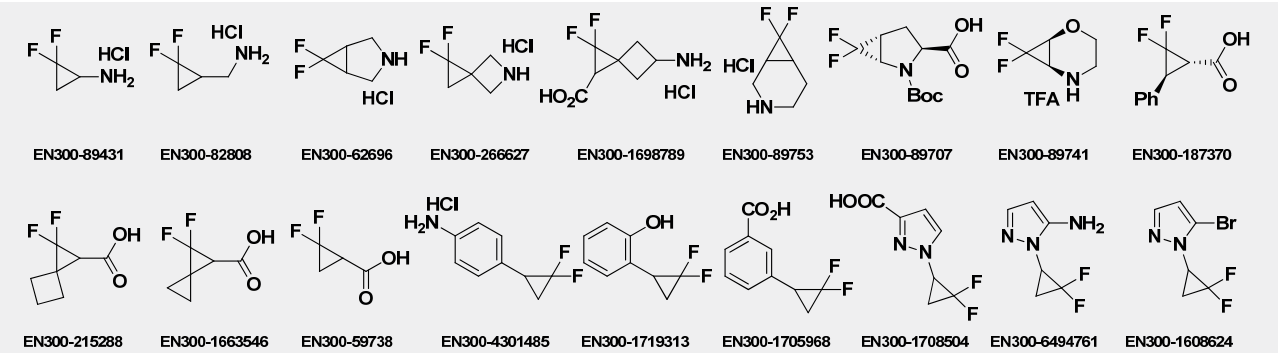


Process Optimization & Scope





Results



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