REGIO-, DIASTEREOSELECTIVE HALOGENATION AT QUATERNARY CARBON STEREOCENTER OF CF_3-CYCLOPROPYL CARBINOLS

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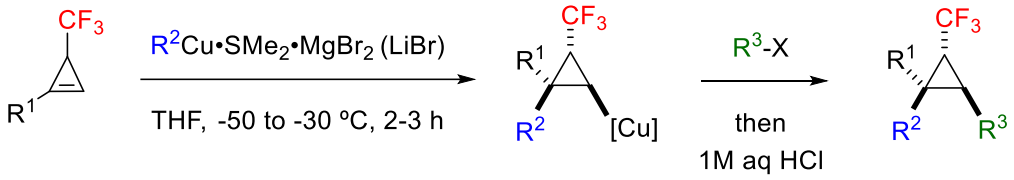
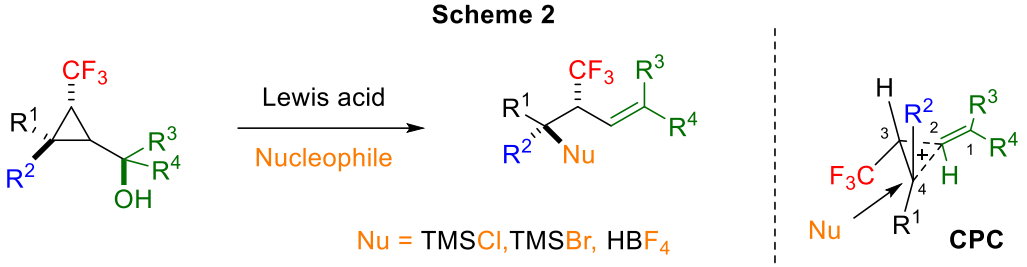
Scheme 1



The construction of molecules featuring adjacent stereocenters, including fluorinated motifs, is a challenging task in organic chemistry. To address this issue, we performed the copper-mediated carbometalation of CF_3-containing cyclopropenes to provide highly substituted cyclopropanes with excellent regio- and diastereoselectivity.[1] The carbometalation proceeds with *anti* diastereofacial preference towards the CF_3 group (Scheme 1). The relative configurations were assigned by analysis of the coupling constants and by single crystal X-ray diffraction.

Scheme 2



We further demonstrated that CF_3-cyclopropyl carbinol derivatives[1] undergo regio- and diastereoselective nucleophilic substitution at the quaternary carbon center to provide acyclic products as a single diastereomer (Scheme 2). The selectivity of the substitution is rationalized by the formation of a cyclopropylcarbinyl cation **CPC**, which reacts at the most substituted C4 carbon center.[2] The products are tertiary alkyl chlorides, bromides, and fluorides that are diastereomerically pure, and can be obtained in just four catalytic steps from commercially available alkynes. This approach provides access to acyclic products that bear two adjacent stereocenters decorated with halogens and the trifluoromethyl motif.

References:

[1] Myronova, V.; Cahard, D.; Marek, I. Stereoselective Preparation of CF_3-Containing Cyclopropanes. *Org. Lett.* **2022**, *24*, 9076-9080.

[2] Chen, X.; Patel, K.; Marek, I. Stereospecific nucleophilic substitution at quaternary carbon stereocenters of cyclopropyl carbinols. *Chem*, **2023**, *9*, *2*, 266−279.

[3] Lanke, V.; Marek, I. Nucleophilic Substitution at Quaternary Carbon Stereocenters. *J. Am. Chem. Soc*., **2020,** *142, 12*, 5543−5548.