Copper-Catalyzed Hydroboration and Hydroallylation of 1-Trifluoromethylthioalkenes

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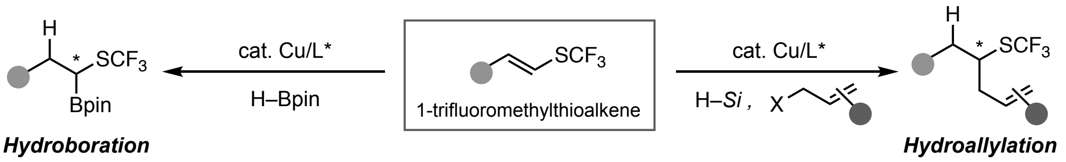
Since their enhanced lipophilicity, metabolic stability, and bioavailability, organofluorine derivatives are an important class of compounds in medicinal chemistry. In particular, trifluoromethylthio (SCF_3) group has received significant attention in the design and synthesis of pharmaceuticals and agrochemicals because of its strong electron-withdrawing nature and high lipophilicity.[1] Although various methods for the synthesis of SCF_3-containing compounds have been reported,[2] it is still difficult to obtain optically active SCF_3 derivatives with high enantiopurity. Therefore, the development of efficient synthetic methods for chiral SCF_3 molecules is highly desired.

Herein, we report a copper-catalyzed regio- and enantioselective hydroboration of 1-trifluoromethylthioalkenes with pinacolborane (H–Bpin). 1-Trifluoromethylthioalkenes can be easily prepared from the corresponding alkenyl halides according to the literature methods.[3] Using the 1-trifluoromethylthioalkene as a starting platform, the in-situ generated copper hydride species undergoes the regio- and enantioselective insertion to form an optically active α-SCF_3 alkylcopper intermediate. Subsequent σ-bond metathesis with H–Bpin provides the boron-substituted SCF_3 compound in an enantioenriched form. Moreover, the copper hydride-based strategy can also be expanded to the three-component coupling reaction of 1-trifluoromethylthioalkenes, hydrosilanes, and allylic electrophiles. Also in this reaction, the judicious choice of chiral ligand induces the high regio- and enantioselectivity. These approaches can provide the chiral SCF_3 compounds, which are difficult to prepare by other means.



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