3-Position-selective Trifluoromethylation of Pyridine Rings Using Nucleophilic Activation based on 1,4-Reduction

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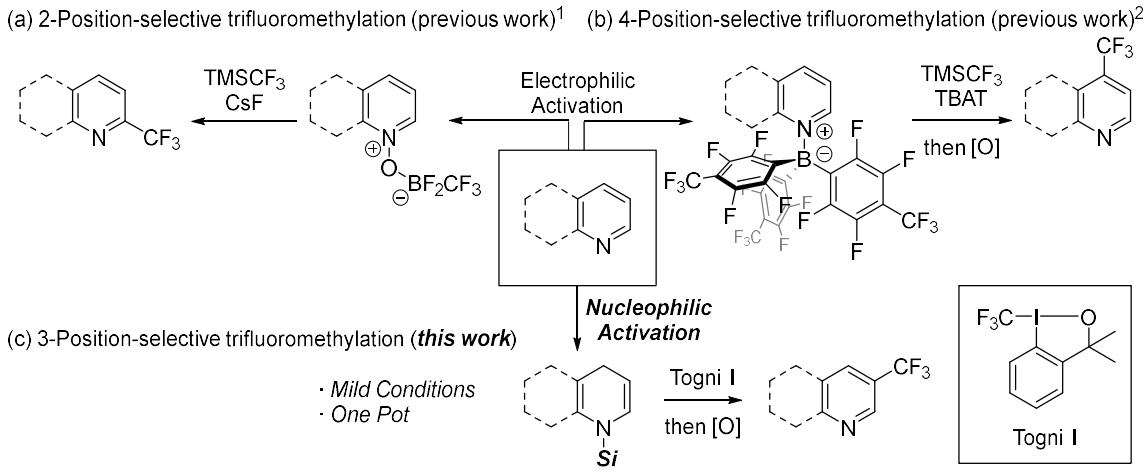
Trifluoromethyl group plays an important role in drugs, agrochemicals, and organic functional materials. Therefore, the development of regioselective C(sp^2)-H trifluoromethylation is one of the most important research subjects in synthetic organic chemistry. In the case of pyridine derivatives, regioselective C(sp^2)-H trifluoromethylation at the electrophilic 2- and 4-positions has been developed.[1,2] On the other hand, the example of trifluoromethylation at the 3-position is still rare, and a new methodology to achieve 3-position-selective C(sp^2)-H trifluoromethylation of pyridines is highly desirable. We report herein an efficient method for 3-position-selective introduction of a trifluoromethyl group into pyridine rings via the conversion of the C(sp^2)-H bonds.

To achieve 3-position-selective trifluoromethylation, we focused on the reaction of electron-rich *N*-silyl enamine intermediates, which can be derived from pyridine rings and a hydrosilane, with Togni reagent and subsequent oxidation. As a result, 3-position-selective trifluoromethylated pyridine derivatives were obtained in good yields.



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