SYNTHESIS OF FLUORINATED PYRAZOLO[1,5-*a*]PYRIDINES

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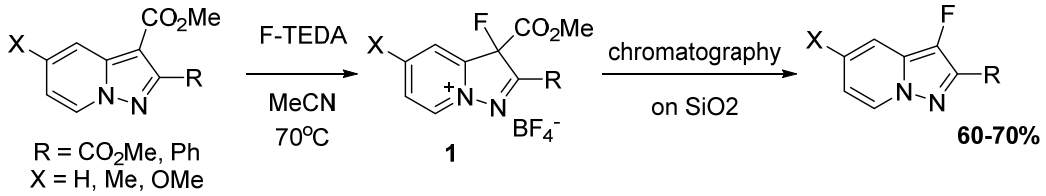
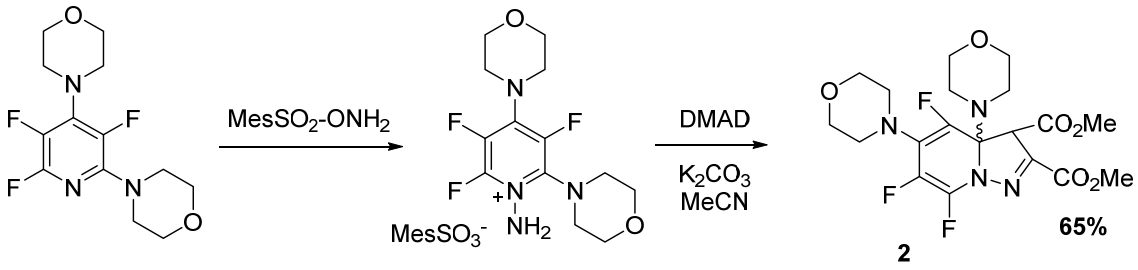
Pyrazolo[1,5-*a*]pyridines are interesting building blocks for medicinal chemistry. 2-Isopropyl-3-isobutyrylpyrazolo[1,5-*a*]pyridine (Ibudilast) is nonselective PDE3,4 inhibitor and has been marketed in Japan for over 20 years as anti-asthmatic and anti-inflammatory drug. Our preliminary modeling studies on ibudilast binding to PDEs shows that fluorinating analogs of ibudiast could possess stronger binding to PDEs.

In this work we tried two different ways to access fluorinated pyrazolo[1,5-*a*]pyridines. First, we studied electrophilic fluorination of pyrazolo[1,5-a]pyridine-3-carboxylates with F-TEDA. The fluorination readily proceeds with displacement of CO_2R-group by fluorine atom.



NMR studies of the reaction mixtures showed formation of the intermediate 1 which readily undergo decarboxylation upon chromatography on SiO_2. NMR kinetics studies was performed. Mechanism of this transformation will be discussed on the poster.

Another approach started from 2,4-dimorpholino-3,5,6-trifluoropyridine. *N*-amination and cycloaddition with DMAD gave product 2 which failed aromatization.



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