Group Bio-Organic Chemistry
Project Click it! Exploring new possibilities with Si-free SuFEx reactions
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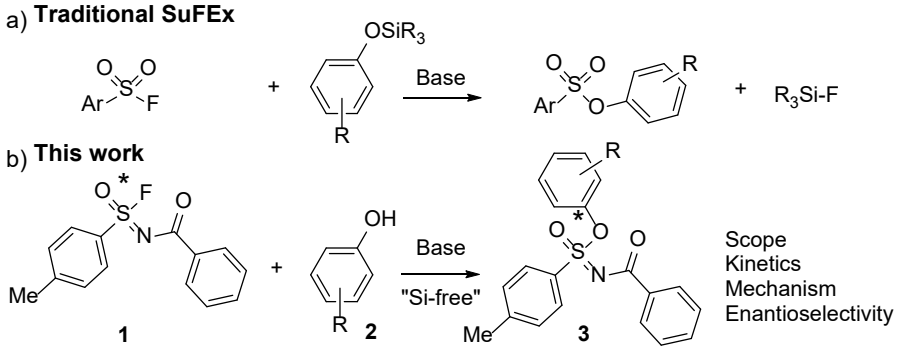
Introduction

Click reactions are likely one of THE developments in organic chemistry in the last decade. SuFEx reactions, in which an S-F moiety reacts with a silyl-protected phenol, have been developed as such powerful click reactions.[1] Important characteristics of click reactions are their high specificity and yield in benign conditions. Therefore, these reactions can be widely applied in the synthesis and modification of target molecules. For example, SuFEx has been used in modifications of peptides and proteins, syntheses of functional polymers, macrocycles, MOFs, functionalized surfaces, preparations of ionic liquids, and late-stage drug functionalization. Our interest lies in expanding this chemistry and exploring structural motifs which have not received the attention they deserve.



In our lab, we have recently developed fast, high-yielding Si-free and enantiospecific SuFEx reactions. The final sulfoximine products are interesting frameworks, as many can display biological activity.[2] We are currently looking into strategies to expand this chemistry, as the SuFEx methodology is an important reaction to access a variety of pharmaceutically highly relevant compounds.

Primarily, we want to know how broad the substrate scope and tolerance is for different reaction conditions, ultimately applying this reaction as bio-orthogonal click reactions. Moreover, we are interested in the variety of molecular skeletons we can create with this reaction. Therefore we are exploring routes using primary alcohols and other nucleophiles. Finally, we are interested in the synthesis of *chiral* sulfoximine products and their possible biological applications. Both enantioselective synthesis and chiral separation routes can be explored. Your work will contribute to the expansion of the current SuFEx toolbox, and you will be actively involved in papers resulting from this work.

Topics to be studied

Research projects regarding this topic are primarily focused on traditional organic 'small molecule' synthesis. Projects will include (a combination of) synthesis of starting materials, reaction optimization, mechanistic studies, and evaluation of the SuFEx reaction yielding chiral sulfoximine products.

Techniques to be used

Multistep organic synthesis, purification and characterization methods, such as chromatography (column, HPLC, chiral HPLC), NMR, mass spectrometry, IR.

More information

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Literature

(1) Dong, J.; Krasnova, L.; Finn, M. G.; Sharpless, K. B. *Angew. Chemie Int. Ed.* **2014**, *53* (36), 9430–9448.
(2) Frings, M.; Bolm, C.; Blum, A.; Gnamm, C. *Eur. J. Med. Chem.* **2017**, *126*, 225–245.