PALLADIUM-CATALYSED SYNTHESIS OF MULTIFUNCTIONAL ALKENYL SULFONYL FLUORIDES

Terry Shing-Bong Lou and Michael C. Willis

Department of Chemistry, University of Oxford

Sulfonyl fluorides (SFs) – being a strong yet water-tolerant electrophile – are commonly used as covalent warheads in biological probes and irreversible protein inhibitors,[1] and as intermediate for the synthesis of sulfonyl-containing compounds.[2] SFs are typically synthesised from the corresponding sulfonyl chlorides, which have limited availability and stability, or from ethenesulfonyl fluoride (ESF), intrinsically limited to ethyl and ethylene linkers.[2a, 3]

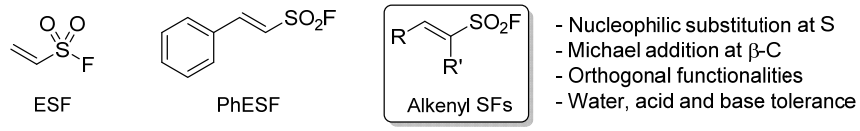
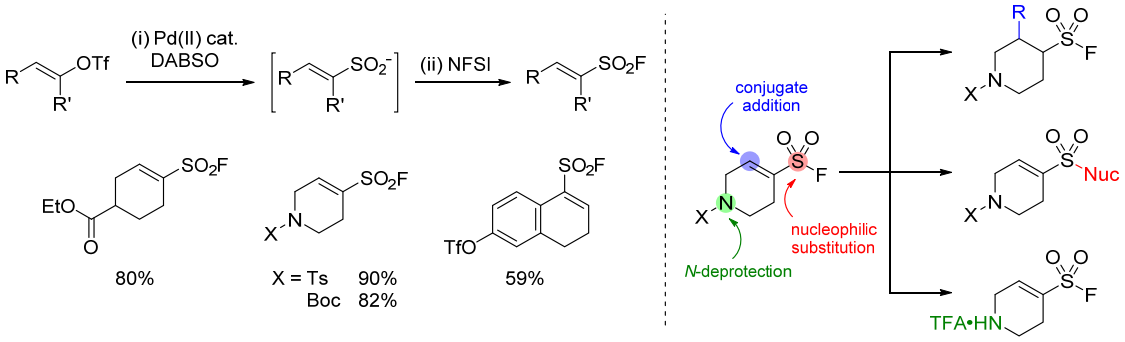


Figure 1. Ethenesulfonyl fluoride (ESF) as a common building block to access PhESF and other derivatives with ethylene linkers; alkenyl SFs with both α- and β-substituents are the focus of this work.

Building on previous results from our group,[4] we report a general catalytic synthesis of alkenyl SFs which contain multiple reaction sites for derivatisation and could therefore serve as multifunctional warheads. Various functional groups were well tolerated, with SFs prepared in good to excellent yields.

Derivatisation of the resulting alkenyl SFs was realised, including nucleophilic substitution at sulfur, conjugate addition at the *β*-carbon, hydrogenation, as well as amine functionalisation, demonstrating the versatility of this class of novel SFs.[5]



Scheme 1. Synthesis of alkenyl SFs with selected examples and the derivatisation of alkenyl SFs.

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[4] A. T. Davies, J. M. Curto, S. W. Bagley and M. C. Willis, *Chem. Sci.*, 2017, **8**, 1233-1237.

[5] T. S.-B. Lou and M. C. Willis, *unpublished results*.