Sulfonyl Pyrroles: Synthetic Linchpins for Late-Stage Functionalization of Primary Sulfonamides

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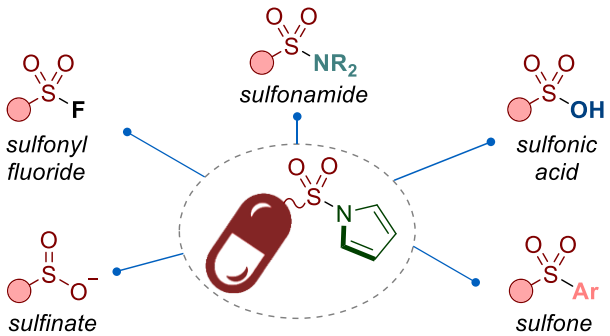
Late-stage functionalization is a useful strategy for the selective modification of complex molecules. Sulfonamides are prevalent in a variety of important compounds, most notably pharmaceuticals, however, ways to transform sulfonamides via S−N bond cleavage are rare. In particular, methods for the late-stage functionalization of complex sulfonamide-containing molecules are limited to a handful of recent reports.[1,2,3] Whereas the fields of C−N bond and amide activation have received much attention, the area of sulfonamide activation remains largely untouched. Thus, sulfonamide activation holds great potential in late-stage functionalization and the uncovering of new reactivities.

In this work, sulfonyl pyrroles are revealed as linchpins for primary sulfonamide functionalization.[4] These studies establish sulfonyl pyrroles, which were easily assembled from the corresponding primary sulfonamides via a Paal-Knorr/Clauson-Kaas-type reaction, as highly versatile reagents. This approach provides a variety of functional groups (e.g. sulfinates, sulfones, sulfonic acids, sulfonamides) using chemical, electrochemical or photochemical means. Furthermore, we demonstrate the utility of sulfonyl pyrroles for diversifying sulfonamide-containing drug molecules through late-stage functionalization. It is hoped these early findings highlight the untapped potential of sulfonyl pyrrole chemistry and encourage further investigations within the burgeoning field of sulfonamide activation.



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