Radical-based Transformations through Reductive Carbon–Sulfonyl Bond Activation

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Keywords: Sulfone; Radical; C–SO_2 bond activation; Photoredox catalysis; Alkylation

Organosulfones are versatile intermediates in organic synthesis because of the ease with which they permit facile structural modification through α-functionalization or conjugate addition.[1] Due to the inherent stability of sulfonyl groups, strong reducing agents such as Na amalgam and Mg are generally required for their removal. Recently, organosulfones have attracted considerable attention in cross-coupling reactions as a new class of electrophiles.[2] Our group and others have developed several transition-metal catalyzed cross-coupling reactions of functionalized aromatic and benzylic sulfones via carbon–sulfonyl (C–SO_2) bond activation.[2c] Substituents on the sulfonyl group were found to provide a powerful new avenue for controlling reactivity. Building on these reports, next we envisioned that a controlled single electron reduction of sulfones would have the potential to establish a new method for the generation of carbon radicals in organic synthesis and expand the utility of sulfones. In this presentation, we will present a radical-based transformations through reductive C–SO_2 bond activation of sulfones.

1. Giese reaction via reductive desulfonylation of alkylsulfones

We have developed a simple method for the conversion of tertiary alkylsulfones to tertiary alkyl radicals, and their alkylation to generate quaternary carbon centers.[3] The Giese reaction proceeds efficiently using readily available Zn powder with 1,10-phenanthroline (phen) as a new single electron reducing agent. The tetrazolyl group on the sulfonyl group was found to be an effective substituent for radical generation. A variety of quaternary products could be synthesized from tertiary alkylsulfones and electron-deficient olefins. And substrates in which the olefin moieties were introduced by α-alkylation of secondary sulfones can be employed in an intramolecular Giese reaction, giving interesting spiro compounds. The radical generation process involving a single electron transfer and subsequent fragmentation of sulfone radical was investigated by control experiments and theoretical calculations.

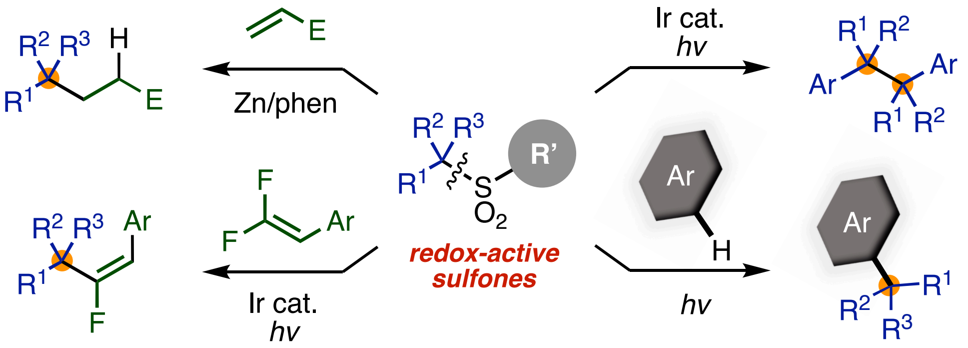
2. Desulfonylative transformations by visible-light photoredox catalysis

Building on our previous work with regards to the application of sulfones in catalysis, we found that visible-light photoredox catalysts can be employed to promote the reductive desulfonylation of tertiary alkylsulfones and their reaction with *gem*-difluoroalkenes.[4] Notably, this method produces thermodynamically unfavorable *E*-fluoroalkenes as the major products in one-pot, compounds that are difficult to synthesize by traditional routes. Investigation of the origin of stereoselectivity indicates that the Ir catalyst also promotes photocatalytic *Z/E* isomerization of initially generated *Z*-isomers to give the observed *E*-isomers.

When benzylic sulfones were used instead of alkyl sulfones, the desulfonylative homocoupling proceeded smoothly.[5] This method enables the facile synthesis of a variety of multiply-arylated ethanes, including those functionalized with deuterium or fluorine at the benzylic position prior to cross-coupling, which provides interesting motifs in medicinal chemistry.

3. Visible-light-induced direct C–H alkylation of polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) are fragments of graphene that have attracted considerable attention as a new class of carbon-based materials. The functionalization of edge positions in PAHs is important to enable the modulation of physical and chemical properties essential for various applications. However, straightforward methods that combine functional group tolerance and regioselectivity remain sought after. We have developed a photochemical approach for the direct alkylation of carbon–hydrogen bonds in PAHs that takes place in a regiospecific manner, an outcome that has never been achieved in the related thermal reactions.[6] A reaction mechanism involving a single electron transfer process from photo-excited PAHs to sulfones, and a rationale for the origin of regioselectivity are proposed on the basis of spectroscopic analyses and theoretical calculations.



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