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A visible-light-catalyzed sulfonylation reaction of an aryl selenonium salt *via* an electron donor–acceptor complex†

Yuqing Wang, Liang Zhao, Xinyu Hao, Kun Jin, Rong Zhang, Chunying Duan and Yaming Li *

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An efficient synthesis of sulfone structures through selenonium salts and sodium sulfinates was developed. Under the irradiation of a blue LED lamp, the two substrates generate aryl and sulfonyl radicals through the activation of the intermediate electron donor acceptor (EDA) complex, thereby synthesizing aromatic, heteroaromatic and aliphatic sulfones in medium to good yields. The advantages of this strategy are metal-free, mild conditions and the leaving group is recycled to construct new selenonium salts.

Introduction

The sulfone structure (R–SO_2–R) is an important building blocks and is widely used as a synthetic intermediate in fine and bulk chemical fields.[1–5] Molecules containing sulfone units play prominent roles in agricultural chemicals, pharmaceutical formulations, and polymers.[6–10] Many bioactive molecules and herbicide safety agents also contain this functional group,[11–16] including bicalutamide, used for the treatment of prostate cancer; the preferred drug for treating leprosy, dapsone; the migraine drug eletriptan; and the excellent pre-vaccine soil treatment agent pyroxasulfone (Fig. 1).

There are several methods to synthesize sulfones, and the oxidation of sulfides remains a widely applied strategy,[17–19] which achieves the conversion of intermediate sulfoxide to hydrocarbons with sulfonyl halides catalyzed by a Lewis or Brønsted acid and offers an alternative approach to sulfone synthesis.[20]

However, these classic reactions typically exhibit limitations such as harsh reaction conditions and low regioselectivity,[21–23] prompting the development of diverse efficient catalyst systems. In 2014, Rao reported the one-step synthesis of symmetric diarylsulfones using $K_2S_2O_8$ as a sulfonation reagent.[24] Furthermore, sulfone is prepared using DABSO [DABCO $(SO_2)_2$], potassium pyrosulfite, and thiourea dioxide[25–32] as alternative sources of sulfur dioxide. Over the last decades, the synthetic routes to sodium aryl sulfites have been through cross-coupling with various electrophilic reagents, either under transition metal-catalyzed or metal-free conditions. In 2023, Nevado reported a tripartite enantioselective carbo-sulfonylation process of olefins, sodium arenesulfinates, and aryl halides, integrating photoredox and nickel catalysis.[33] In 2020, Tang devised a copper-mediated decarboxylative sulfonation reaction between aryl acetic acid and sodium sulfite, offering a novel way of decarboxylative coupling to produce sulfones.[34]

In 2019, Ritter reported sulfonium salts which allowed for direct access to a vast selection of intricate small-molecule derivatives since there was no requirement for a guiding group to achieve selectivity.[35] Subsequently, Ritter broadened the use of sulfonium salts as precursors to include C–O, C–N, and C–CF_3 coupling with a variety of functional groups,[36–38] which laid a strong foundation for the research of subsequent researchers. In the last few years, the use of electron donor–acceptor (EDA) complex (Scheme 1a) initiation to construct C–S bonds has become increasingly popular[39,40] due to the ability of EDA complexes to generate radical ion pairs and take part in a variety of reactions without the need for external

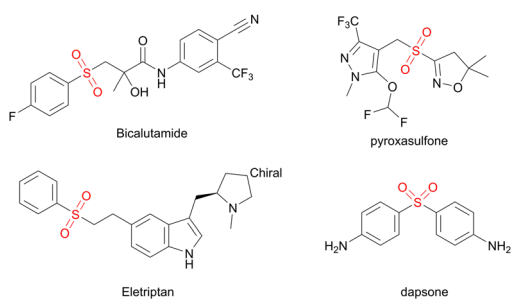

Fig. 1 Examples of –SO_2-containing drugs.

State Key Laboratory of Fine Chemicals, School of Chemical Engineering, Dalian University of Technology, Dalian 116024, Liaoning, P.R. China.
E-mail: ymli@dlut.edu.cn

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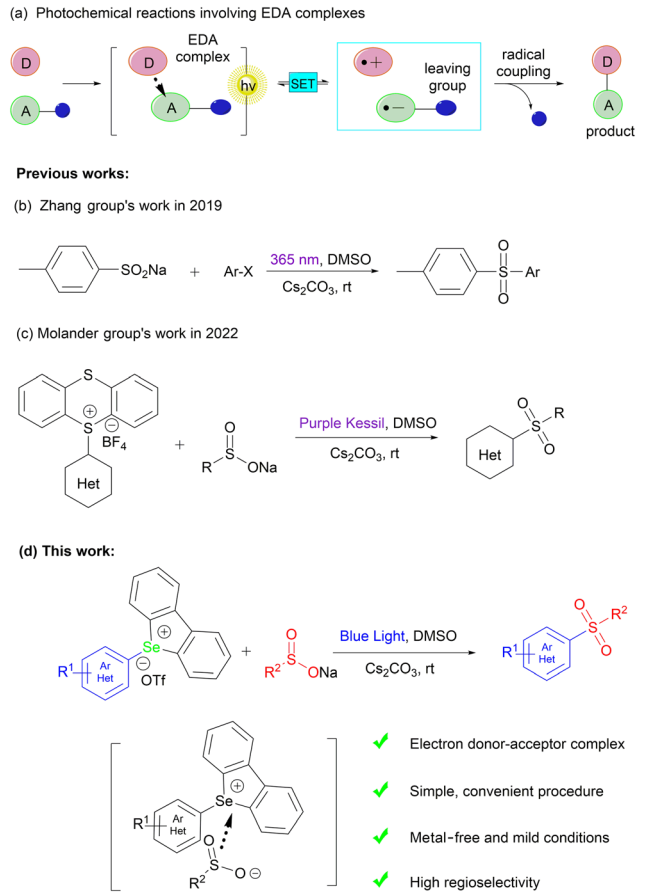


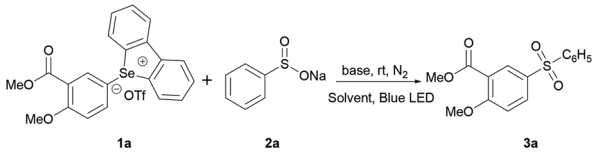
Scheme 1 Method for synthesizing sulfone and the mechanism of the EDA complex.

photocatalysts. Zhang presented a novel approach in 2019 for sulfone synthesis, involving the formation of EDA complexes between sodium sulfites and aryl halides under a 365 nm wavelength light source (Scheme 1b).[41] In 2022, Molander documented the photoactivated sulfonylation of sulfonium salts through an EDA complex approach that employed sulfonium salts as electron-deficient acceptors and sodium sulfite salts as electron-rich donors (Scheme 1c).[42] Considering that an EDA complex is a weak noncovalent bonding interaction, the C–Se bond is more active than the C–S bond and less is known about aryl selenonium salts.[43] In this paper we report an aryl selenonium salt as an aryl source and a sodium sulfite salt as a sulfur dioxide source to generate sulfones without the involvement of a photosensitizer (Scheme 1d).

Results and discussion

Initially, an aryl selenonium salt (**1a**) and sodium benzenesulfinate (**2a**) were chosen as the model substrates for condition optimization of the visible light-induced C–Se sulfonylation reaction. As shown in Table 1, the base was screened first. The reaction can take place without an additive or catalyst, and the

Table 1 Optimization of the reaction conditions



Entry	Base	Solvent	Time (h)	Yield[a] (%)
1	None	DMSO	18	27
2	K_2CO_3	DMSO	18	39
3	Cs_2CO_3	DMSO	18	49
4	$CaCO_3$	DMSO	18	30
5	Cs_2CO_3	DMF	18	42
6	Cs_2CO_3	Acetone	18	31
7	Cs_2CO_3	DCM	18	38
8	Cs_2CO_3	MeCN	18	32
9[b,]	Cs_2CO_3	DMSO	18	59
10[b,c]	Cs_2CO_3	DMSO	18	58
11[b,e]	Cs_2CO_3	DMSO	18	68
12[b,f]	Cs_2CO_3	DMSO	18	60
13[d]	Cs_2CO_3	DMSO	18	nd
14[b,e]	Cs_2CO_3	DMSO	12	43
15[b,e]	Cs_2CO_3	DMSO	36	71
16[b,g]	Cs_2CO_3	DMSO	18	38

Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), additive (0.4 mmol), and DMSO (0.15 M) at room temperature under blue light irradiation for 18 h. [a] Isolated yield. [b] 6 eq. of **2a**. [c] $[Ru(bpy)_3]Cl_2$ (5 mol%). [d] No light or in an O_2 environment. [e] 3 eq. of Cs_2CO_3. [f] 4 eq. of Cs_2CO_3. [g] Open to air.

results obtained by using Cs_2CO_3 are the best (Table 1, entries 1–4). When increasing the amount of Cs_2CO_3 to 3 or 4 equivalents (Table 1, entries 9 *vs.* 11 and 12), the yields of the corresponding sulfone increased to 68% or 60%, respectively. Subsequently, various solvents commonly employed in photocatalysis were experimented with, all of which successfully propelled the reaction, and DMSO showed better performance in terms of yields (Table 1, entries 3 *vs.* 5–8). Adjusting the reaction stoichiometry to six equivalents of sodium benzenesulfinate and one equivalent of selenonium salts, the reaction furnished **3a** in 59% yield (Table 1, entries 3 and 9). Control experiments showed that the yield was found to be almost unchanged when $[Ru(bpy)_3]Cl_2$ was added (Table 1, entry 10), while no product formation was observed when there was no light irradiation, proving that light was necessary (Table 1, entry 13). Notably, open-to-air or in O_2 atmosphere experiments afforded different results to those found under an inert atmosphere, indicating that oxygen affects the transformation (Table 1, entries 13 and 16). Finally, shortening the reaction time to 12 hours led to a low yield of 43%, whereas prolongation of the reaction time to 36 hours resulted in a mere 3% increase in yield (Table 1, entries 14 and 15). Therefore, the optimized conditions were defined as the use of a sodium sulfite salt (6 eq.) and 3 equivalents of Cs_2CO_3 in DMSO at room temperature under an inert gas atmosphere under blue LED irradiation for 18 hours (Table 2).

With the optimized reaction conditions in hand, we investigated the scope of this transformation. Various sodium aryl sulfites were first evaluated, and substrates with electron-

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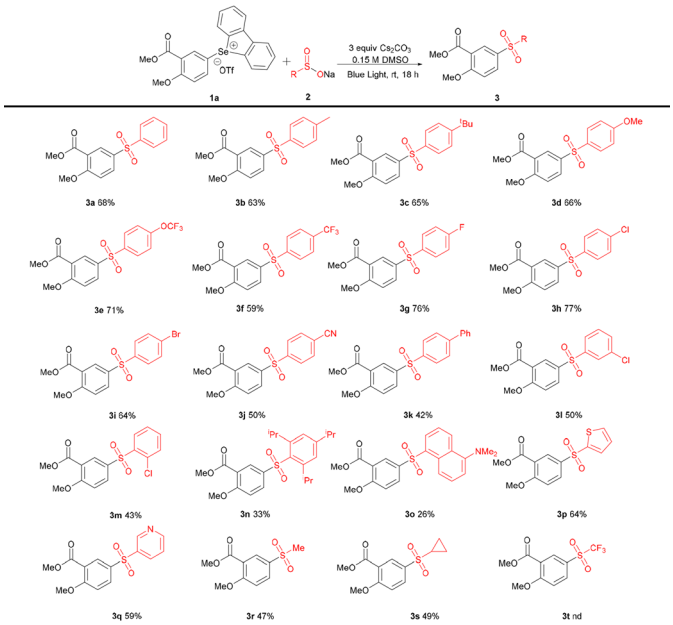
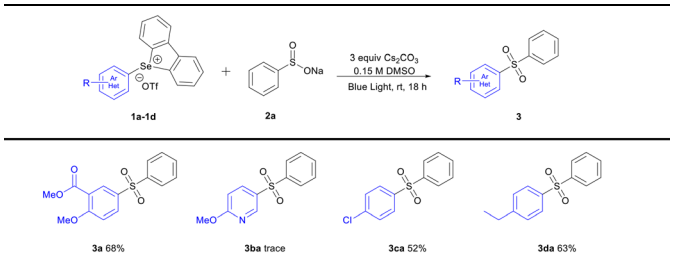
Table 2 Substrate scope of C–S sulfonylation with **1a**[a]

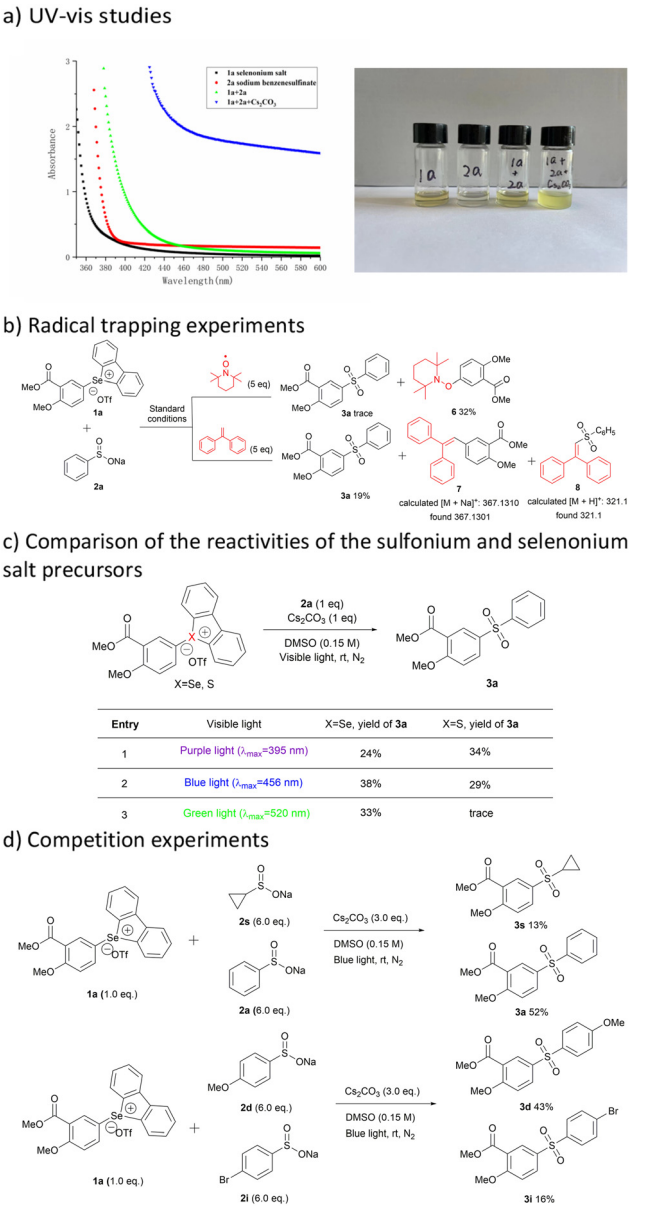


[a] All reactions were performed in a Schlenk tube with **1** (1.0 eq., 0.2 mmol), sodium sulfite (6 eq.), and Cs_2CO_3 (3 eq.) in DMSO (1.34 mL) at room temperature under an inert gas atmosphere under blue LED irradiation for 18 h.

donating (**3b–3e**) or electron-withdrawing groups (**3f–3j**) at the *para* position of the benzene ring exhibited favourable reactions with yields ranging from 50% to 77%. The chlorine group at the *ortho*- or *meta*-position could also exhibit reactivity to give the sulfone products (**3l** and **3m**). The yields of the corresponding sulfones obtained from biphenyl and polycyclic aromatic hydrocarbon were 42% (**3k**) and 26% (**3o**), respectively. Medically relevant heterocyclic sodium sulfites are also suitable electron donors, providing the corresponding pyridyl (**3q**) and thiophenyl (**3p**) derivatives in moderate yields. The sulfonation technique was expanded to include alkyl sulfinic acids in order to achieve the desired methyl sulfone **3r** and cyclopropyl sulfone **3s**. Ultimately, as anticipated, the presence of the steric effect restricted the accessibility of **3n** in a slightly diminished yield (33%). We also attempted trifluoromethyl sulfone, but no target product (**3t**) was detected. In addition, the sulfonylation of 4-chlorophenyl, 4-ethylphenyl and 2-methoxypyridyl selenonium salts was carried out, respectively (Table 3), and the corresponding sulfones **3ca** and **3da** were obtained in 52% and 63% yields. Unfortunately, the performance of the electron-deficient pyridine heterocycle selenonium salt **1b** was poor. In order to elucidate the mechanism of this sulfonylation reaction, UV-vis and radical trapping studies were performed (Scheme 2). The UV-vis spectra of each component and the reaction mixture were measured in DMSO to investigate the formation of the intermediate EDA complex, with the selenonium salt (Scheme 2a, black square) exhibiting absorption bands in the visible region alongside **2a** (Scheme 2a, red circle), and a combination of **1a** and **2a** (Scheme 2a, green triangle) demonstrated the formation of new molecular aggregates in the basal state along with the deepening of the color. When Cs_2CO_3 was added to the mixture (Scheme 2a, blue triangle), significant color changes and red

Table 3 Substrate scope of selenonium salts





Scheme 2 Control experiments.

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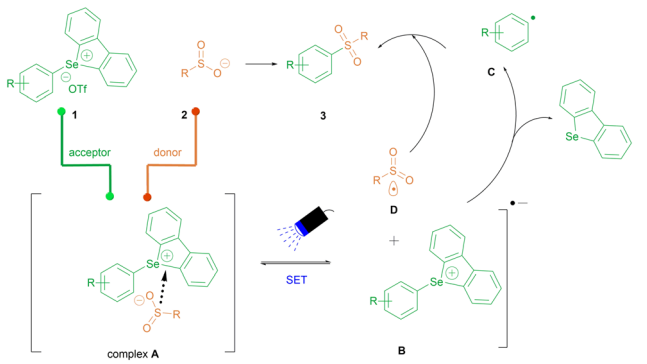
shifts in UV absorption were observed, indicating the formation of EDA complexes. Under the reaction conditions, radical trapping experiments were conducted utilizing TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxyl radical) and 1,1-diphenylethene. To our delight, both aryl and sulfonyl radicals were captured, affording **6** in 32% yield, while also the product **8** was detected by APCI Tof-MS. Free radical trapping agents inhibited their complete transformation into **3a**. It is shown that the sulfonylation reaction proceeds mainly *via* the radical pathway (see the ESI† for more experimental details) (Scheme 2b).

Subsequently, we compared the photoinduced sulfonation reactions of selenonium salts with those of sulfonium salts under different light sources. Under the irradiation of purple light, sulfonium salts exhibit greater reactivity than selenium salts (Scheme 2c, entry 1). However, under blue light irradiation, the reactivity of selenonium salts is slightly better (Scheme 2c, entry 2). When the maximum absorption wavelength is 520 nm (Scheme 2c, entry 3), the selenonium salts still exhibit good reactivity, suggesting a variance in the maximum absorption levels of selenonium and sulfonium salts. Finally, different competitive experiments were carried out (Scheme 2d). An evaluation of the reactivity of sulfinates **2a** and **2s** gave the corresponding products **3a** and **3s** in 52% and 13% yields, respectively. This suggested that activation by EDA complexes is more inclined to generate aryl sulfones. Moreover, the electron-rich product **3d** is more inclined to be generated than the electron-deficient product **3i**. This may be due to the sulfonyl radicals with electron-donating groups being more likely to collide with aryl radicals to form covalent bonds.

Based on our experiments, a possible mechanism was proposed as follows (Scheme 3). The electron-rich sulfinate anion **2** and the electron-deficient selenonium salt **1** form the EDA complex **A** in the ground state, which is then activated by blue-light irradiation and undergoes a single electron transfer (SET) within the complex to produce the sulfonyl radical **D**, affording the intermediate radical anion **B**. The dibenzoselenophenol, acting as a suitable leaving group, triggers an irreversible fragmentation event and generates aryl radical **C**. Subsequent selective coupling of the sulfonyl and aryl radicals generates the sulfone product **3**.



Scheme 3 A proposed reaction mechanism.

Conclusions

In conclusion, we have developed a new and efficient method of sulfone synthesis to generate aliphatic sulfones or aromatic sulfones in medium to good yields by a photocatalytic method using aryl selenonium salts and sodium sulfite as substrates in the absence of exogenous metal complexes or photosensitizers. As supported by mechanistic studies, the sulfonation reaction involves the formation of an EDA complex, followed by electron transfer within the complex under visible light irradiation, generating aryl radicals and sulfonyl radicals and selective coupling.

Conflicts of interest

There are no conflicts to declare.

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