Visible-Light-Induced Chemoselective Synthesis of α-Chloro and Vinyl Sulfones by Sulfonylation of Alkenes

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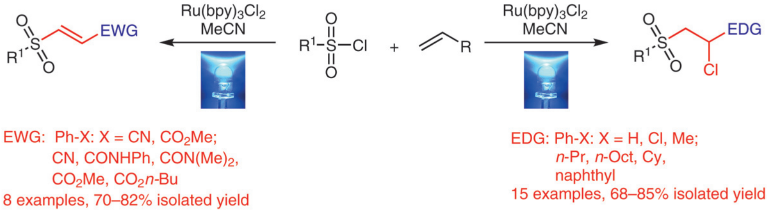

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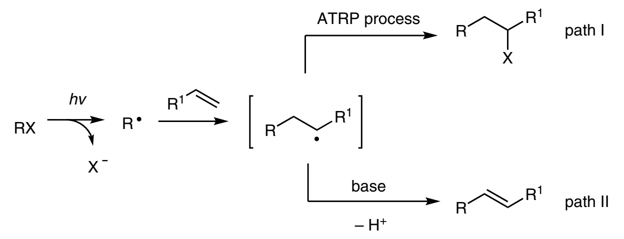
Abstract Direct sulfonylation between alkenes and sulfonyl chloride was achieved at room temperature by a visible-light-induced photoredox process. This method allows the chemoselective synthesis of α-chloro and vinyl sulfone derivatives with moderate to high yields. The selectivity of the reaction was fully controlled by the electronic properties of the alkenes.

Key words visible-light-induced reaction, atom-transfer radical addition, sulfonylation of alkenes, chemoselectivity, α-Chloro sulfones, vinyl sulfones

Over the past decade, atom-transfer radical addition (ATRA) has attracted much attention as a versatile tool in organic synthesis.[1] Typically, ATRA represents a practical synthetic path for difunctionalization of alkenes or alkynes with activated halides in a highly atom-economic way, providing the corresponding alkyl or vinyl halides as important intermediates for further transformation.[2] With the combined efforts of several research groups, various modes of catalytic processes have been reported and applied in academic research laboratories and even in industry.[3] Despite great progress, the development of more efficient, environment-friendly and sustainable methods for ATRA reactions are still highly desirable.

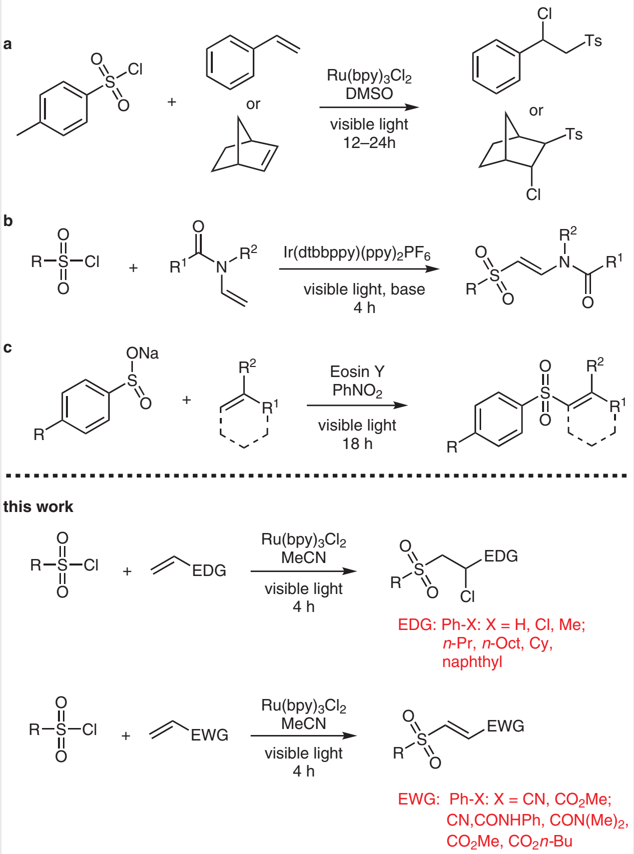
Recently, visible-light-induced processes have become a powerful tool for the ATRA reaction due to their mild conditions, high efficiency, and convenient workup.[4] In principle, the addition of a halide ion to the radical intermediate is the key step to generate the desired radical addition product (Scheme 1, path I).[4a,d,f,i,j,5] However, these radical cations are excellent hydrogen atom donors that can give rise to dehalogenated products especially under basic conditions (Scheme 1, path II).[6] Thus, achieving control of the selectivity of visible-light-activated ATRA seems attractive.



Scheme 1 General sequences for ATRA and dehalogenated process

Sulfone groups are prevalent structural motifs in natural products, pharmaceuticals, agrochemicals, and materials.[7] Despite some examples of transition-metal-catalyzed ATRA processes,[8] the manipulation of these valuable structures under visible-light conditions in a chemoselective ATRA manner remains elusive.

In 2012, the Stephenson group reported a visible-light-induced ATRA of 4-toluenesulfonyl chloride (TsCl) to styrene and norbornene, however, the substrate scopes of the sulfonyl chlorides and the alkenes are limited (Scheme 2, a).[4b] On the other hand, Yu and co-workers described the direct coupling of sulfonyl chlorides with enamides in the presence of 1.5 equivalents of Na_2HPO_4(Scheme 2, b).[9] Alternatively, the König group demonstrated a visible-light-induced coupling of alkynes and aryl sulfinates with one equivalent of nitrobenzene as the additive (Scheme 2, c).[10] Although these methods provided the desired products in attractive routes, the chemoselective synthesis of α-chloro and vinyl sulfone derivatives without additives still has

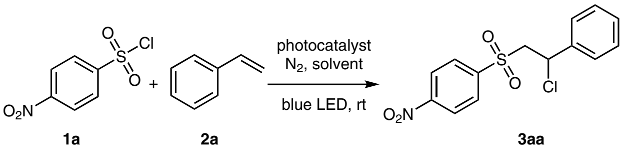


Scheme 2 Visible-light-induced methods for the synthesis of α-chloro and vinyl sulfone derivatives

been elusive. Herein, we report an electronic-property-controlled visible-light-induced chemoselective sulfonylation of alkenes to access these valuable structures.

Initially, 4-nitrobenzenesulfonyl chloride **1a** and styrene **2a** were chosen as the model substrates. The model reaction was performed with **1a** (0.5 mmol), **2a** (0.5 mmol), and a catalytic amount of Ru(bpy)$_3$Cl$_2$ (2 mol%) in MeCN (2 mL; Table 1, entry 1). The reaction mixture was stirred at room temperature and irradiated using a blue LED (5 W) under N$_2$ atmosphere. After 4 h, the desired product **3a** was generated in 86% yield. Subsequently, various photocatalysts such as Ir(ppy)$_3$, Ir(dtbbppy)(ppy)$_2$PF$_6$, Eosin Y, Eosin B, Rhodamine B, and methylene blue hydrate were examined (Table 1, entries 2–7). Ru(bpy)$_3$Cl$_2$ was the most effective catalyst. Decreasing the amount of Ru(bpy)$_3$Cl$_2$to 1 mol% still led to a yield of 81% (Table 1, entry 8). Thus, 1 mol% of Ru(bpy)$_3$Cl$_2$ was used as the photocatalyst. In the solvent screening, MeCN provided the highest yield among all (Table 1, entries 8–13). It is noteworthy that the reaction was completely inhibited when a base (such as Et$_3$N, K$_2$CO$_3$, or Na$_2$HPO$_4$) was added to the reaction mixture. Furthermore, no desired product was achieved when the reaction was carried out in the absence of a photocatalyst and visible light (Table 1, entries 14 and 15).

Table 1 Screening of the Reaction Conditions[a]



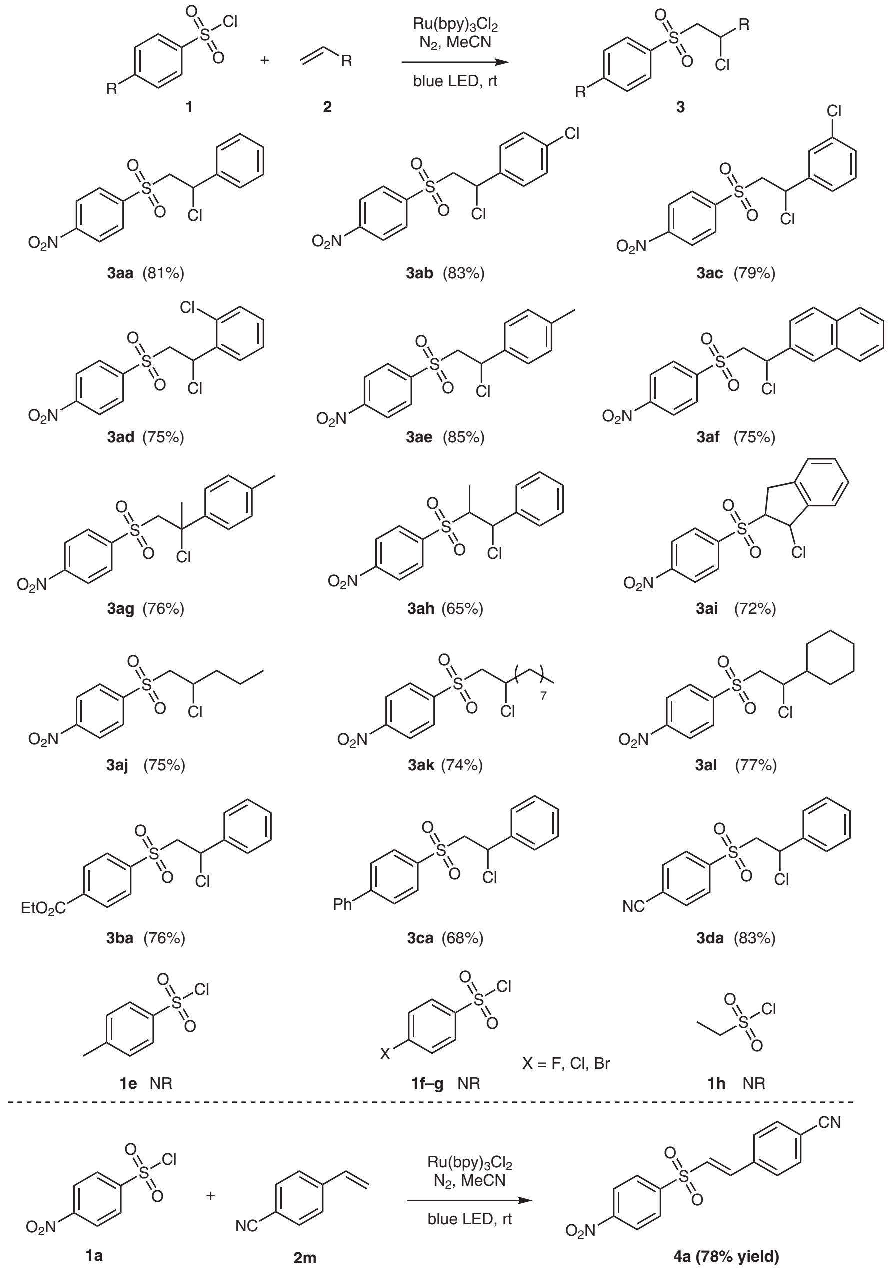
Entry	Photocatalyst (mol%)	Solvent	Yield (%)[b]
1	Ru(bpy)$_3$Cl$_2$ (2)	MeCN	86
2	Ir(ppy)$_3$(2)	MeCN	63
3	Ir(dtbbppy)(ppy)$_2$PF$_6$ (2)	MeCN	80
4	Eosin Y (2)	MeCN	trace
5	Eosin B(2	MeCN	trace
6	Rhodamine B (2)	MeCN	trace
7	Methylene blue hydrate (2)	MeCN	trace
8	Ru(bpy)$_3$Cl$_2$ (1)	MeCN	81
9	Ru(bpy)$_3$Cl$_2$ (1)	DMF	trace
10	Ru(bpy)$_3$Cl$_2$ (1)	DMSO	trace
11	Ru(bpy)$_3$Cl$_2$ (1)	acetone	53
12	Ru(bpy)$_3$Cl$_2$ (1)	DCM	trace
13	Ru(bpy)$_3$Cl$_2$ (1)	MeOH	48
14[c]	Ru(bpy)$_3$Cl$_2$ (1)	MeCN	NR[d]
15		MeCN	NR
16[e]	Ru(bpy)$_3$Cl$_2$ (1)	MeCN	NR

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), and photocatalyst in indicated solvent (2 mL) were irradiated with a 5 W blue LED at rt for 4 h.
[b] Isolated yield.
[c] 1.5 equiv of base such as Et$_3$N, K$_2$CO$_3$, and Na$_2$HPO$_4$was added.
[d] No reaction.
[e] In the dark.

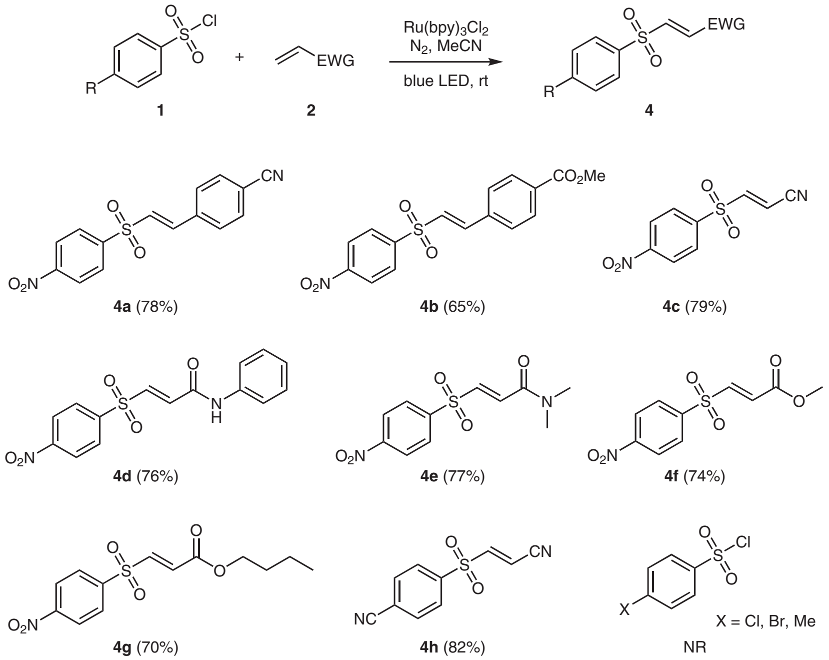
Having determined the optimal reaction conditions, we examined the scope and generality of the present method (Scheme 3).[11] To our delight, both aryl and aliphatic alkenes reacted well with 4-nitrobenzenesulfonyl chloride **1a**, affording the corresponding products **3aa–al** in good to excellent yield. The effects from steric hindrance for alkenes were not significant, and *para*-, *meta*- or *ortho*-chlorinated alkenes were converted into the corresponding products in 83%, 79% and 75% yield, respectively (**3ab–ad**). The internal alkenes, such as β-methylstyrene and indene, afforded the corresponding products in 65% and 72% yield, respectively (Scheme 3, **3ah** and **3ai**). Different aromatic sulfonyl chlorides containing functional groups such as NO$_2$, Ph, CN, and an ester were also well tolerated under the optimal conditions, affording the desired products **3ba–da** in moderate to high yields. However, the aryl sulfinic chloride, bearing an electron-donating group such as Me, is unsuitable for the present reaction conditions. The halo substituents including

F, Cl, and Br also did not survive the reaction conditions. Besides, aliphatic sulfonyl chloride **1h** was inert toward this transformation. It is worth noting that substrate **2m** with a strong electron-withdrawing group (CN) provided a vinyl product **4a** (78%) under the standard conditions. We assumed that the electronic property of the alkenes played a vital role in the transformation, thereby providing a route for the chemoselective synthesis of vinyl sulfone derivatives using electron-poor alkenes.

The above results in Scheme 3 prompted us to explore the applicability of this method for the preparation of vinyl sulfone derivatives.[12] Aryl alkenes containing strong electron-withdrawing groups such as CN and ester were tolerated, affording the corresponding products in high yields (Scheme 4, **4a** and **4b**). Other electron-poor alkenes such as acrylonitrile, α,β-unsaturated amide and α,β-unsaturated ester also showed good compatibilities, affording the corresponding products **4c–h** in moderate to excellent yields.

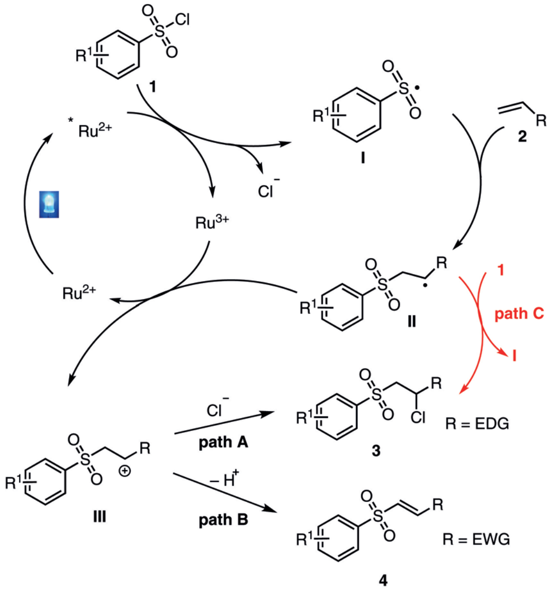


Scheme 3 Reaction scope for ATRA. *Reagents and conditions*: **1** (0.5 mmol), **2** (0.5 mmol), $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (1 mol%), and MeCN (2 mL), irradiated with a 5 W blue LED at rt for 4 h under N_2 atmosphere; isolated yield.



Scheme 4 Photocatalyzed synthesis of vinyl sulfone derivatives. *Reagents and conditions*: **1** (0.5 mmol), **2** (0.5 mmol), $Ru(bpy)_3Cl_2{\cdot}6H_2O$ (1 mol%) and MeCN (2 mL), irradiated with a 5 W blue LED at rt for 4 h under N_2 atmosphere; isolated yield.

Again, aryl sulfonyl chloride with halo and electron-donating group were still inert under the present reaction conditions.



Scheme 5 The proposed mechanism

According to our results and previous reports[4b,9,10,13] a plausible mechanism is depicted in Scheme 5. Initially, excitement of the photoredox catalyst $[Ru(bpy)_3]^{2+}$ under visible light irradiation generates the strongly reducing excited state $^*[Ru(bpy)_3]^{2+}$, and subsequent single-electron transfer (SET) between this species with sulfonyl chlorides **1** generates $[Ru(bpy)_3]^{3+}$ and sulfonyl radical **I**. Next, addition of sulfonyl radical **I** to alkene **2** affords the radical intermediate **II**, which further undergoes SET with $[Ru(bpy)_3]^{3+}$ complex to deliver intermediate **III**. Finally, intermediate **III** with an electron-donating group may undergo nucleophilic trapping by Cl^- to afford the corresponding product **3** (path A), while intermediate **III** containing an electron-withdrawing group tends to generate product **4** via deprotonation (path B). The direct formation of **3** through the Cl-atom transfer from sulfonyl chloride **1** to radical intermediate **II** is also the possible pathway (path C). In addition, due to the electronic effect of the substituents, sulfinic chloride with electron-donating groups such as *p*-TsCl and halo substituents cannot be easily activated at the initial SET process to generate the sulfonyl radical in this system.

In conclusion, we have developed a visible-light-induced chemoselective process to access α-chloro and vinyl sulfone derivatives without any additives. The selectivity of the reaction is determined by the electronic properties of the alkenes. A series of substrates survived the reaction conditions to give the corresponding products in moderate to good yields. Notably, the prepared α-chloro and vinyl sulfone derivatives can be further modified to access other useful compounds.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1590925.

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(11) **1-[(2-Chloro-2-phenylethyl)sulfonyl]-4-nitrobenzene (3aa) – Typical Procedure**
A 10 mL reaction vessel with a magnetic stirring bar was equipped with 4-nitrobenzenesulfonyl chloride (100 mg, 0.5 mmol), styrene (52 mg, 0.5 mmol), $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (7.5 mg, 1 mol%), and MeCN (2 mL). The mixture was irradiated with a blue LED (5 W) and stirred at rt in an air atmosphere for 4 h. The distance of the reaction vial from the light source was about 2 cm. After the reaction, the solvent was removed under reduced pressure. Purification of the crude product was achieved by flash column chromatography using PE/EtOAc (6:1) as eluent; yield 132 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27–8.21 (m, 2 H), 7.92–7.86 (m, 2 H), 7.45 (m, 1 H), 7.35–7.27 (m, 2 H), 7.24 (d, *J* = 8.8 Hz, 1 H), 5.39 (t, *J* = 7.1 Hz, 1 H), 4.10–4.05 (m, 1 H), 4.00–3.94 (m, 1 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 150.7, 144.8, 137.8, 129.7,129.5, 129.1, 127.2, 124.1, 64.2, 54.9. ESI-MS: *m/z* = 326 [M+1]$^+$. Anal. Calcd for $C_{14}H_{12}ClNO_4S$: C, 51.62; H, 3.71; N, 4.30. Found: C, 51.75; H, 3.83; N, 4.17.

(12) **(*E*)-4-{2-[(4-Nitrophenyl)sulfonyl]vinyl}benzonitrile (4a) – Typical Procedure**
A 10 mL reaction vessel with a magnetic stirring bar was equipped with 4-nitrobenzenesulfonyl chloride (110 mg, 0.5 mmol), 4-vinylbenzonitrile (65 mg, 0.5 mmol), $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (7. 5 mg, 1 mol%), and MeCN (2 mL). The mixture was irradiated with a blue LED (5 W) and stirred at rt in an air atmosphere for 4 h. The distance of the reaction vial from the light source was about 2 cm. After the reaction, the solvent was removed under reduced pressure. Purification of the crude product was achieved by flash column chromatography using PE/EtOAc (6:1) as eluent; yield 123 mg (78%). ^{1}H NMR (400 MHz, DMSO): δ = 8.50–8.45 (m, 2 H), 8.24–8.19 (m, 2 H), 7.96 (m, 5 H), 7.87 (s, 1 H). ^{13}C NMR (101 MHz, DMSO): δ = 151.0, 146.0, 142.5, 137.1, 133.3, 130.7, 130.3, 129.5, 125.4, 118.8, 113.8. ESI-MS: *m/z* = 315 [M+1]$^+$. Anal. Calcd for $C_{15}H_{10}N_2O_4S$: C, 57.32; H, 3.21; N, 8.91. Found: C, 57.14; H, 3.36; N, 8.83.

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