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A Mild Light-Induced Cleavage of S—O Bond of Aryl Sulfonate Esters Enables Efficient Sulfonylation of Vinylarenes

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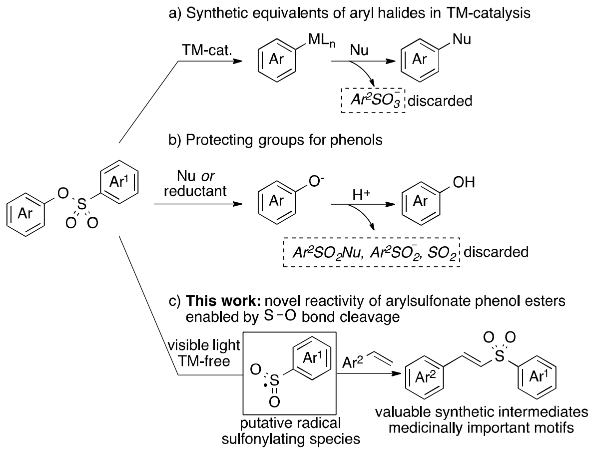
Abstract: A new mode of S—O bond activation has been discovered, which constitutes novel reactivity of easily available and bench stable arylsulfonate phenol esters. This novel protocol enables access to putative sulfonyl radical intermediates, which empower straightforward access to valuable vinyl sulfones.

Aryl sulfonate phenol esters are versatile synthetic intermediates in organic chemistry. A facile C—O bond cleavage under transition metal (TM)-catalyzed conditions makes them valuable alternatives to aryl halides in cross-coupling reactions (Scheme 1, a)[1]. Meanwhile, the robustness of arylsulfonate groups under variety of reaction conditions renders them useful protecting groups of phenols (Scheme 2, b).[2] In both scenarios, different forms of organosulfur byproducts are discarded. Ability to utilize these intermediates as sulfonylating reagents, on another hand, would offer an attractive alternative strategy toward incorporation of organosulfur motifs into organic molecules.[3] Herein we report mild, light-induced TM-free activation of S—O bond[4] of aryl sulfonate phenol esters leading to the formation of putative sulfonyl radicals.[5,9] Thus the generated reactive sulfone species add across the double bond of vinyl arenes an -heteroarenes to furnish valuable vinyl sulfones (Scheme 1c).

Within the framework of our ongoing studies on the development of light-induced synthetic methodologies,[6] we unexpectedly discovered a sulfonylation of styrene **1a** with arylsulfonate phenol ester **2a** into vinyl sulfone **3a** (Table 1). Vinyl sulfones have received considerable attention in recent years, as these motifs are featured in medicinally relevant structures,[7] and also serve as useful reactive intermediates.[8] Most of the established protocols toward synthesis of vinyl sulfones rely on employment of TM-catalysts and/or utilizing excessive amounts of oxidants.[9] In contrast, the observed sulfonylation reaction takes advantage of mild light-induced activation of S—O bond, thus potentially providing alternative route toward vinyl sulfones. Intrigued by the uncovered novel reactivity of arylsulfonate phenol esters and inspired by the importance of vinyl sulfones,[8,9] we performed an optimization of this interesting transformation.[10] It was found that tosylate of commercially available *meta*-CF_3 phenol is the best source of tosyl group. The reaction proceeds best under 427 nm visible light irradiation of 0.1 M DMA solution in the presence of 3 equiv. of Cs_2CO_3 (entry 1). Introducing other electron-rich or –deficient substituents across the phenolic aromatic ring led to diminished yields (entries 2-5). Derivative of aliphatic alcohol showed no reactivity, thus indicating the necessity of an aromatic ester for the successful transformation (entry 6). Employment of DMSO instead of DMA was equally efficient (entry 7). Switching to other solvents commonly used in radical chemistry was not productive (entries 8-10). Lowering amount of base played a detrimental role, as well (entry 11) Addition of radical scavengers such as TEMPO or galvinoxyl completely suppressed this sulfonylation reaction (entries 12-13). Finally, the test experiment indicated that this reaction does not proceed in the absence of light (entry 14).



Scheme 1 Diverse reactivity of arylsulfonate phenol esters.

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† Footnotes relating to the title and/or authors should appear here.

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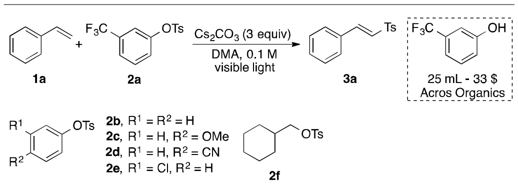
Table 1 Optimization of reaction parameters.^{a}



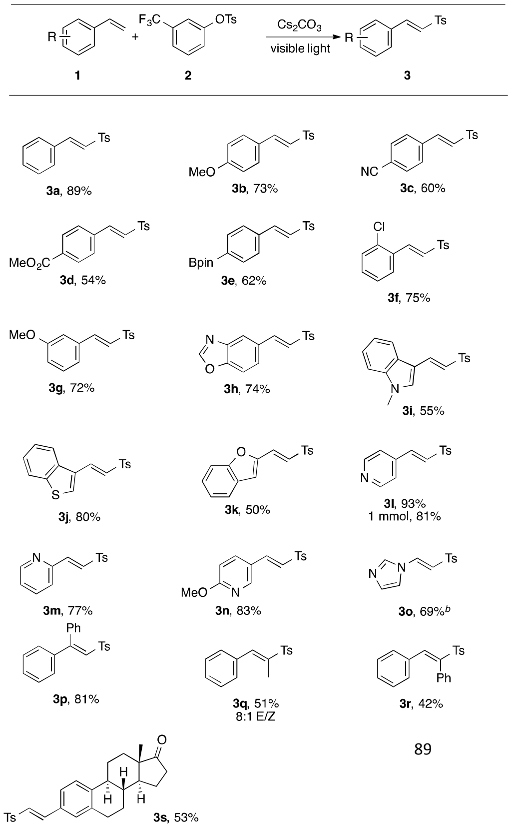
Entry	Deviation from standard conditions	Yield, %^{b}
1	none	90
2	**2b** instead of **2a**	40
3	**2c** instead of **2a**	16
4	**2d** instead of **2a**	78
5	**2e** instead of **2a**	10
6	**2f** instead of **2a**	0
7	DMSO instead of DMA	89
8	PhH instead of DMA	0
9	$PhCF_3$ instead of DMA	0
10	MeCN instead of DMA	15
11	Cs_2CO_3 (2 equiv.) instead of Cs_2CO_3 (3 equiv.)	64
12	galvinoxyl (2 equiv)	0
13	TEMPO (2 equiv)	0
14	no light, 60 to 100 °C	0

^{a} Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), Cs_2CO_3 (0.3 mmol), DMA (0.1 M), 40 W 427 nm LED. ^{b} GC/MS yield.

The study on the generality of this transformation of this sulfonylation reaction (Table 2) showed that styrenes possessing electron-releasing (**1b**) and –withdrawing (**1c**, **d**) substituents at the *para* position all reacted well to give the corresponding vinyl sulfones in good yields. Pleasingly, Bpin moiety-containing **1e** was compatible with the reaction conditions delivering vinyl sulfone **3e** in 62% yield. Substitution at the *ortho*- (**3f**), and *meta*- (**3g**) positions posed no problem, as well. Various vinyl heteroarenes were found to be capable partners in this sulfonylation reaction. Thus fused *N*-, *O*- and *S*-containing vinylarenes provided corresponding products **3h-3k** efficiently. This protocol also works with vinyl pyridines, producing **3l-3n** in excellent yields. The scale-up experiment proceeded smoothly to deliver vinyl sulfone **3l** in 81% yield. Notably, mild reaction conditions provided N-sulfonyl vinyl imidazole (**3o**) in good yield. Importantly, this reaction can also be carried out with disubstituted styrenes to produce various trisubstituted sulfones **3p-3r** in reasonable to good yields. Moreover, this reaction can be accomplished in a more complex setting to give access to vinyl sulfone derivative of estrone (**3s**).

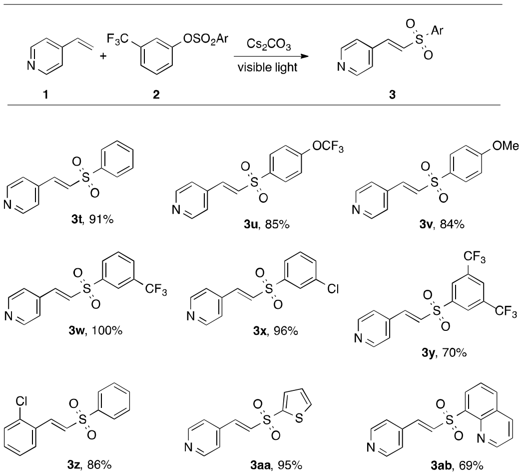
Next, the scope of the sulfone moiety was examined (Table 3). Gratifyingly, diverse substitution patterns on arylsulfonate phenol esters possessed no problem for the developed

Table 2 Scope of vinyl arenes.^{a}



^{a} Reaction conditions: **1** (0.1 mmol), **2** (0.3 mmol), Cs_2CO_3 (0.3 mmol), DMA (0.1 M), 40 W 427 nm LED. ^{b} 450 nm LED

Table 3 Scope of aryl sulfonate esters.^{a}



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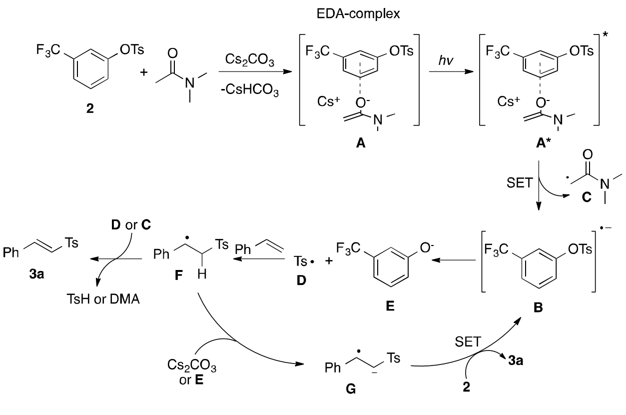
[a] Reaction conditions: **1** (0.1 mmol), **2** (0.3 mmol), Cs_2CO_3 (0.3 mmol), DMA (0.1 M), 40 W 427 nm LED.

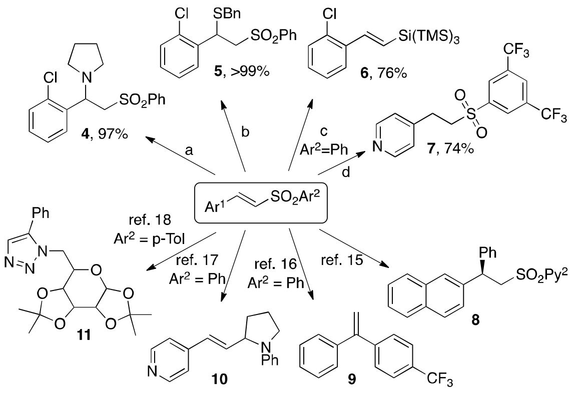
protocol providing excellent yields of the respective vinyl sulfones **3t-3x**. Importantly, this protocol may successfully be applied toward sulfone **3y** featuring 3,5-bis(trifluoromethyl)phenylsulfone fragment, a very useful synthon for the transition metal-catalyzed coupling reactions,[11] as well as for the modified Julia olefination reaction.[12] Heteroaryl sulfonates also participated well leading to products **3aa**, **3ab** in 95 and 69% yields, respectively.

The proposed mechanism of this sulfonylation reaction is depicted in the Scheme 2. The base-assisted[13] formation of an electron donor-acceptor (EDA) complex[14] **A** between arylsulfonate phenol ester **2** and molecule of DMA occurs first.[15] Upon excitation, this complex (**A***) undergoes a single electron transfer (SET)[16] leading to radical anion **B**, which fragments into sulfonyl radical **D** and phenoxide **E**. Addition of sulfonyl radical **D** to styrene[5d] produces benzyl radical **F**. In one scenario, the latter experiences intermolecular hydrogen atom transfer (HAT) with sulfonyl radical **D**, formed in parallel by cleavage of the S–O bond (**B**→**D**+**E**)[17] or, alternatively, with the radical **C**, formed during the first SET step (**A***→**B**), to produce the reaction product, vinyl sulfone **3a**. Alternatively, the electron catalysis may be operative.[18] In that case, deprotonation of **F** produces anion-radical **G**, which after intermolecular SET with **2** produces **3a** and radical-anion **B**, which closes the catalytic cycle.[19]



Scheme 2 Proposed reaction mechanism.

Further transformations of selected vinyl sulfones obtained highlight their synthetic usefulness (Scheme 3). Thus, conjugate Michael addition of pyrrolidine and benzenemethanethiol to vinyl sulfone **3z** delivered adducts **4** and **5** in virtually quantitative yields. Upon subjecting to free radical conditions, **3z** underwent substitution of phenylsulfone group with super silyl moiety giving rise to valuable vinyl silane **6**[20] in 76% yield. Hydrogenation of **3y** proceeded uneventfully producing alkylsulfone **7** in good yield. Versatility of the obtained vinyl sulfones may be further exemplified by transformations toward **8**-**11**, which have been featured in reported protocols.[21,22,23,24]



Scheme 3 Transformations of obtained vinyl sulfones. Conditions: a) **3z** (0.1 mmol), pyrrolidine (2.4 mmol), 70 °C. b) **3z** (0.1 mmol), BnSH (0.4 mmol), Et_3N (0.15 mmol), MeOH (0.25 M), rt c) **3z** (0.1 mmol), $(TMS)_3SiH$ (0.3 mmol), AIBN (0.25 mmol), benzene (0.05 M), reflux d) **3y** (0.1 mmol), Pd/C (0.005 mmol), hydrogen gas (balloon).

Conclusions

In summary, we have uncovered a novel reactivity of arylsulfonate phenol esters, featuring mild visible light-induced cleavage of S–O bond, which gives rise to putative sulfonyl radicals. The latter are capable of addition across various aromatic and heteroaromatic alkenes providing valuable vinyl sulfones. It is believed that this novel reactivity of arylsulfonate esters will find application in synthesis.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

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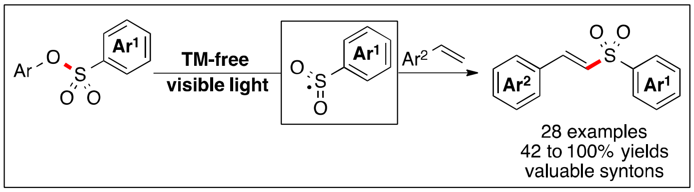

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