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A mild light-induced cleavage of the S–O bond of aryl sulfonate esters enables efficient sulfonylation of vinylarenes†

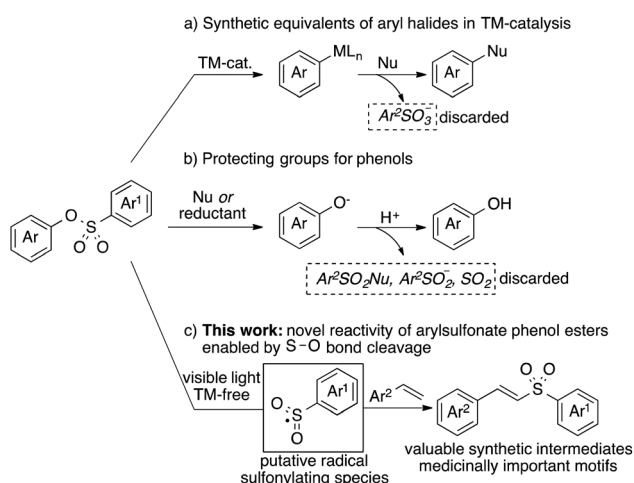
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A new mode of S–O bond activation has been discovered, which constitutes novel reactivity of easily available and bench-stable arylsulfonate phenol esters. This protocol enables access to putative sulfonyl radical intermediates, which enable straightforward 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 1a).¹ Meanwhile, the robustness of arylsulfonate groups under a variety of reaction conditions renders them useful protecting groups of phenols (Scheme 2b).² In both scenarios, different forms of organosulfur byproducts are discarded. The 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 the S–O bond⁴ 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 and -heteroarenes to furnish valuable vinyl sulfones (Scheme 1c).

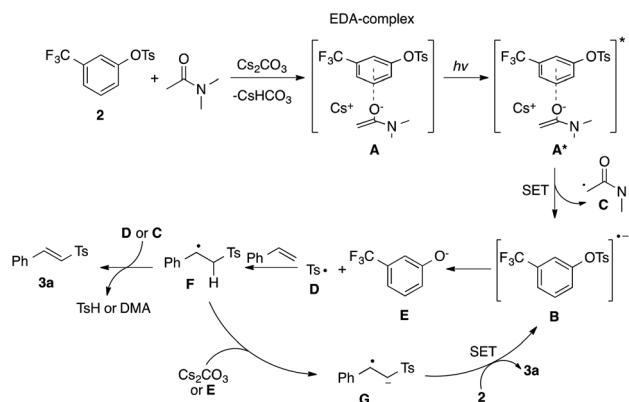
Within the framework of our ongoing studies on the development of light-induced synthetic methodologies,⁶ we unexpectedly discovered a sulfonylation of styrene **1a** with arylsulfonate phenol ester **2a** into vinyl sulfone **3a** (Table 1). Vinyl sulfones have received considerable attention in recent 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 excess amounts of oxidants.⁹ In contrast, the observed sulfonylation reaction takes advantage of mild light-induced activation of the S–O bond, thus potentially providing an 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 the tosylate of commercially available *meta*-CF₃ phenol is the best



Scheme 1 Diverse reactivity of arylsulfonate phenol esters.

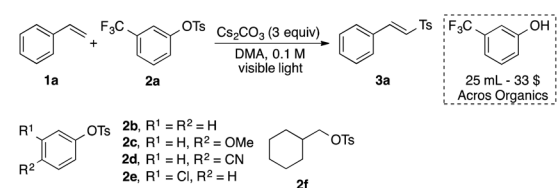
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Scheme 2 Proposed reaction mechanism.



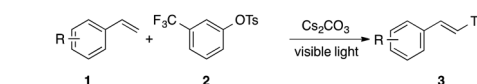
Table 1 Optimization of reaction parameters^a


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 ₂ CO ₃ (2 equiv.) instead of Cs ₂ CO 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), Cs₂CO₃ (0.3 mmol), DMA (0.1 M), and a 40 W 427 nm LED. ^b GC/MS yield.

source of tosyl groups. The reaction proceeds best by 427 nm visible light irradiation of 0.1 M DMA solution in the presence of 3 equiv. of Cs₂CO₃ (entry 1). Introducing other electron-rich or -deficient substituents across the phenolic aromatic ring led to diminished yields (entries 2–5). The 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 the amount of base played a detrimental role as well (entry 11), and 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).

The study on the generality of the 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 the 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

Table 2 Scope of vinyl arenes^a


3a , 89%	3b , 73%	3c , 60%
3d , 54%	3e , 62%	3f , 75%
3g , 72%	3h , 74%	3i , 55%
3j , 80%	3k , 50%	3l , 93% 1 mmol, 81%
3m , 77%	3n , 83%	3o , 69% ^b
3p , 81%	3q , 51% 8:1 E/Z	3r , 42%
3s , 53%		

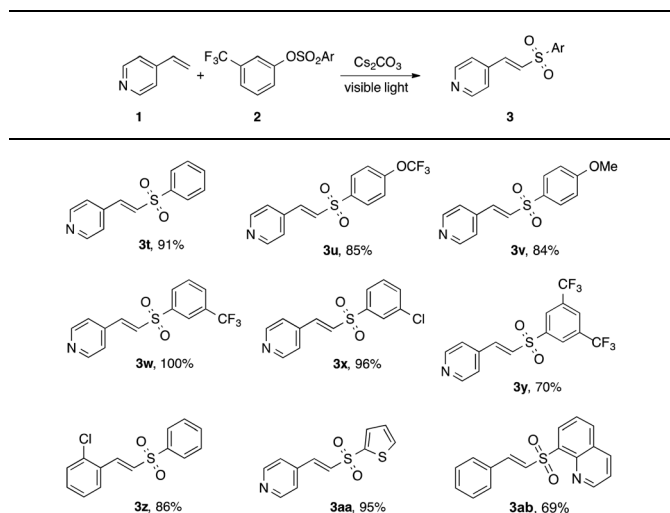
^a Reaction conditions: **1** (0.1 mmol), **2** (0.3 mmol), Cs₂CO₃ (0.3 mmol), DMA (0.1 M), and a 40 W 427 nm LED. ^b 450 nm LED.

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 a vinyl sulfone derivative of estrone (**3s**).

Next, the scope of the sulfone moiety was examined (Table 3). Gratifyingly, diverse substitution patterns of arylsulfonate phenol esters posed no problem for the developed protocol providing excellent yields of the respective vinyl sulfones **3t–3x**. Importantly, this protocol may successfully be applied toward sulfone **3y** featuring a 3,5-bis(trifluoromethyl)phenylsulfone fragment, a very useful synthon, for 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** and **3ab** in 95 and 69% yields, respectively.

The proposed mechanism of this sulfonylation reaction is depicted in Scheme 2. The base-assisted¹³ formation of electron donor–acceptor (EDA) complex¹⁴ **A** between arylsulfonate phenol ester **2** and a 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



Table 3 Scope of aryl sulfonate esters^a

^a Reaction conditions: **1** (0.1 mmol), **2** (0.3 mmol), Cs₂CO₃ (0.3 mmol), DMA (0.1 M), and a 40 W 427 nm LED.

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, 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**, closing the catalytic cycle.¹⁹

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 the phenylsulfone group with the 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.^{21–24}

Conclusions

In summary, we have uncovered a novel reactivity of arylsulfonate phenol esters, featuring mild visible light-induced cleavage of the 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

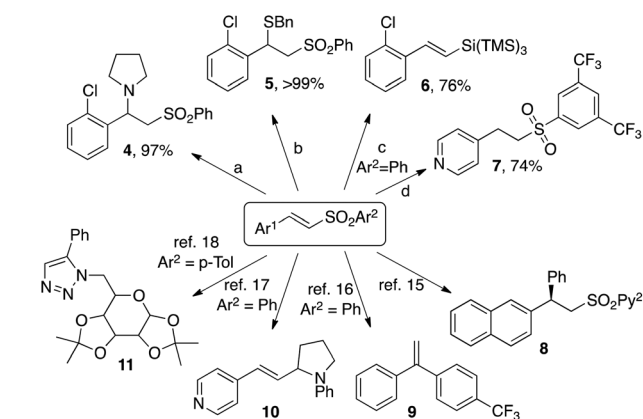
The authors declare no conflict of interest.

Acknowledgements

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Notes and references

- (a) A. Littke, in *Modern Arylation Methods*, Ed. L. Ackermann, Wiley-VCH, Weinheim, 2009, p. 25; (b) H. Zeng, Z. Qiu, A. Dominguez-Huerta, Z. Haerne, Z. Chen and C.-J. Li, *ACS Catal.*, 2017, **7**, 510; (c) D. Kalyani, *Pure Appl. Chem.*, 2014, **86**, 315; (d) B.-J. Li, D.-G. Yu, C.-L. Sun and Z.-J. Shi, *Chem.-Eur. J.*, 2011, **17**, 1728.
- P. G. M. Wuts, T. W. Greene, in *Greene's Protective Groups in Organic Synthesis*, Wiley-Interscience, 4th edn, 2007, p. 421.
- (a) A. Wimmer and B. König, *Beilstein J. Org. Chem.*, 2018, **14**, 54; (b) C. Shen, P. Zhang, Q. Sun, S. Bai, T. S. A. Hor and X. Liu, *Chem. Soc. Rev.*, 2015, **44**, 291; (c) K. L. Dunbar, D. H. Scharf, A. Litomska and C. Hertweck, *Chem. Rev.*, 2017, **117**, 5521; (d) P. Chauhan, S. Mahajan and D. Enders, *Chem. Rev.*, 2014, **114**, 8807; (e) T. Kondo and T. Mitsudo, *Chem. Rev.*, 2000, **100**, 3205; (f) I. Beletskaya and V. P. Ananikov, *Chem. Rev.*, 2011, **111**, 1596; (g) C. C. Eichman and J. P. Stambuli, *Molecules*, 2011, **16**, 590.
- For examples of S–O bond cleavage leading to reactive organosulfur species, see: (a) G. L'Hermine and D. J. Pasto, *J. Org. Chem.*, 1990, **55**, 5815; (b) F. Cottard and D. J. Pasto, *J. Org. Chem.*, 1994, **59**, 4642; (c) T. Kawamura, P. J. Crusie and J. K. Kochi, *Tetrahedron Lett.*, 1972, **40**, 4075; (d) I. W. Still and M. T. Thomas, *Tetrahedron Lett.*, 1970, **48**, 4225; (e) D. D. Gregory and W. S. Jenks, *J. Org. Chem.*, 1998, **63**, 3859; (f) A. P. Darmanyan, D. D. Gregory, Y. Guo and W. S. Jenks, *J. Phys. Chem. A*, 1997, **101**, 6855; (g) Y. Guo, W. S. Jenks, *J. Org. Chem.* 1995, **60**, 5480.



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), Et₃N (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).



- 5 (a) D. Zheng, J. Yu and J. Wu, *Angew. Chem. Int. Ed.*, 2016, **55**, 11925; *Angew. Chem.*, 2016, **128**, 12104; (b) M. P. Bertrand, C. Ferreri, in *Radicals in Organic Synthesis*, Ed. P. Renaud, M. Sibi, Wiley-VCH, Weinheim, 2001, vol. 2, p. 485; (c) X.-Q. Pan, J.-P. Zou, W.-B. Yi and W. Zhang, *Tetrahedron*, 2015, **71**, 7481; (d) O. Mozziconacci, M. Tamba, K. Bobrowski, G. Kciuk, M. P. Bertrand, S. Gastaldi, V. I. Timokhin and C. Chatgililoglu, *J. Phys. Chem. A*, 2012, **116**, 7623; (e) K. Gilmore, B. Gold, R. J. Clark and I. V. Alabugin, *Aust. J. Chem.*, 2013, **66**, 336.
- 6 (a) M. Ratushnyy, M. Parasram, Y. Wang and V. Gevorgyan, *Angew. Chem. Int. Ed.*, 2018, **57**, 2712; *Angew. Chem.*, 2018, **130**, 2742; (b) P. Chuentragool, M. Parasram, Y. Shi and V. Gevorgyan, *J. Am. Chem. Soc.*, 2018, **140**, 2465; (c) D. Kurandina, M. Rivas, M. Radzhabov and V. Gevorgyan, *Org. Lett.*, 2018, **20**, 357; (d) M. Parasram, P. Chuentragool, Y. Wang, Y. Shi and V. Gevorgyan, *J. Am. Chem. Soc.*, 2017, **139**, 14857; (e) D. Kurandina, M. Parasram and V. Gevorgyan, *Angew. Chem. Int. Ed.*, 2017, **56**, 14212; *Angew. Chem.*, 2017, **129**, 14400; (f) M. Parasram, P. Chuentragool, D. Sarkar and V. Gevorgyan, *J. Am. Chem. Soc.*, 2016, **138**, 6340.
- 7 (a) S. Y. Woo, J. H. Kim, M. K. Moon, S.-H. Han, S. K. Yeon, J. W. Choi, B. K. Jang, H. J. Song, Y. G. Kang, J. W. Kim, J. Lee, D. J. Kim, O. Hwang and K. D. Park, *J. Med. Chem.*, 2014, **57**, 1473; (b) B. A. Frankel, M. Bentley, R. G. Kryger and D. G. McCafferty, *J. Am. Chem. Soc.*, 2004, **126**, 3404; (c) S. Liu, B. Zhou, H. Yang, Y. He, Z.-X. Jiang, S. Kumar, L. Wu and Z.-Y. Zhang, *J. Am. Chem. Soc.*, 2008, **130**, 8251; (d) L. Ni, X. S. Zheng, P. K. Somers, L. K. Hoong, R. R. Hill, E. M. Marino, K.-L. Suen, U. Saxena and C. Q. Meng, *Bioorg. Med. Chem. Lett.*, 2003, **13**, 745; (e) D. C. Meadows and J. Gervay-Hague, *Med. Res. Rev.*, 2006, **26**, 793; (f) J. Morales-Sanfrutos, J. Lopez-Jamarillo, M. Ortega-Munoz, A. Megia-Fernandez, F. Perez-Balderas, F. Hernandez-Mateo and F. Santoyo-Gonzalez, *Org. Biomol. Chem.*, 2010, **8**, 667; (g) A. F. Kisselev, W. A. van der Linden and H. S. Overkleeft, *Chem. Biol.*, 2012, **19**, 99.
- 8 (a) N. S. Simpkins, *Tetrahedron*, 1990, **46**, 6951; (b) D. C. Meadows and J. Gervay-Hague, *Med. Res. Rev.*, 2006, **26**, 793; (c) A. L. Krasovskiy, E. S. Balenkova and V. G. Nenajdenko, *Tetrahedron*, 2007, **63**, 12481; (d) M. G. Braun, B. Quiclet-Sire and S. Z. Zard, *J. Am. Chem. Soc.*, 2011, **133**, 15954; (e) Q. Shu and Y. Lu, *Angew. Chem. Int. Ed.*, 2010, **49**, 7753; *Angew. Chem.*, 2010, **122**, 7919; (f) J.-N. Desroisiers and A. B. Charette, *Angew. Chem. Int. Ed.*, 2007, **46**, 5955; *Angew. Chem.*, 2007, **119**, 6059; (g) J.-N. Desroisiers, W. S. Bechara and A. B. Charette, *Org. Lett.*, 2008, **10**, 2315; (h) X. Liu, X. Chen and J. T. Mohr, *Org. Lett.*, 2015, **17**, 3572; (i) J. Fritz and D. J. Wardrop, *Org. Lett.*, 2006, **8**, 3659; (j) F. Hof, A. Schutz, C. Fah, S. Meyer, D. Bur, J. Liu, D. E. Goldberg and F. Diederich, *Angew. Chem. Int. Ed.*, 2006, **45**, 2138; *Angew. Chem.*, 2006, **118**, 2193; (k) M. N. Noshi, A. El-awa, E. Torres and P. L. Fuchs, *J. Am. Chem. Soc.*, 2007, **129**, 11242; (l) B. Fisher, R. J. Lepage, J. M. White, Y. Ye, E. H. Krenske and M. A. Rizzacasa, *Org. Biomol. Chem.*, 2017, **15**, 5529; (m) E. Rodrigo, I. Alonso, J. L. Garcia Ruano and M. B. Cid, *J. Org. Chem.*, 2016, **81**, 10887; (n) Z. Li, R. Yazaki and T. Ohshima, *Org. Lett.*, 2016, **18**, 3350; (o) U. Sankar, C. V. S. Kumar, V. Subramanian, K. K. Balasubramanian and S. Mahalakshimi, *J. Org. Chem.*, 2016, **81**, 2340.
- 9 (a) Y. Fang, Z. Luo and X. Xu, *RSC Adv.*, 2016, **6**, 59661; (b) N.-W. Liu, S. Liang and G. Manolikakes, *Synthesis*, 2016, 1939; (c) A. Garcia-Dominguez, S. Muller and C. Nevado, *Angew. Chem. Int. Ed.*, 2017, **56**, 9949; *Angew. Chem.*, 2017, **129**, 10081; (d) Y. Xi, B. Dong, E. J. McClain, Q. Wang, T. L. Gregg, N. G. Akhmedov, J. L. Peterson and X. Shi, *Angew. Chem. Int. Ed.*, 2014, **53**, 4657; *Angew. Chem.*, 2014, **126**, 4745; (e) H. Wang, Q. Lu, C.-W. Chiang, Y. Luo, J. Zhou, G. Wang and A. Lei, *Angew. Chem. Int. Ed.*, 2017, **56**, 595; *Angew. Chem.*, 2017, **129**, 610. For examples of photoredox synthesis of vinyl sulfones, see; (f) A. U. Meyer, S. Jager, D. P. Hari and B. Konig, *Adv. Synth. Catal.*, 2015, **357**, 2050; (g) S. Cai, Y. Xu, D. Chen, L. Li, Q. Chen, M. Huang and W. Weng, *Org. Lett.*, 2016, **18**, 2990.
- 10 See the ESI† for full optimization details.
- 11 (a) J. C.-H. Yim, M. Nambo and C. M. Crudden, *Org. Lett.*, 2017, **19**, 3715; (b) M. Nambo, E. C. Keske, J. P. G. Rygus, J. C.-H. Yim and C. M. Crudden, *ACS Catal.*, 2017, **7**, 1108.
- 12 (a) D. A. Alonso, M. Varea and C. Najera, *Tetrahedron Lett.*, 2004, **45**, 573; (b) D. A. Alonso, M. Fuensanta, E. Gomez-Bengoa and C. Najera, *Adv. Synth. Catal.*, 2008, **350**, 1823; (c) D. A. Alonso, M. Fuensanta, E. Gomez-Bengoa and C. Najera, *Eur. J. Org. Chem.*, 2008, 2915; (d) D. A. Alonso, M. Fuensanta, C. Najera and M. Varea, *J. Org. Chem.*, 2005, **70**, 6404.
- 13 R. P. Woodbury and M. W. Rathke, *J. Org. Chem.*, 1977, **42**, 1688.
- 14 (a) B. Liu, C.-H. Lim and G. M. Miyake, *J. Am. Chem. Soc.*, 2017, **139**, 13616; (b) E. Arceo, I. D. Jurberg, A. Alvarez-Fernandez and P. Melchiorre, *Nat. Chem.*, 2013, **5**, 750.
- 15 The UV-vis analysis of the reaction components indicated that the DMA solution of arylsulfonate phenol ester **2** and Cs_2CO_3 is capable of light absorption. For details, see the ESI†.
- 16 For examples of enolates as single electron donors, see: (a) K. J. Emery, T. Tuttle and J. A. Murphy, *Org. Biomol. Chem.*, 2017, **15**, 8810; (b) F. Cumine, S. Zhou, T. Tuttle and J. A. Murphy, *Org. Biomol. Chem.*, 2017, **15**, 3324; (c) E. Doni, S. Zhou and J. A. Murphy, *Molecules*, 2015, **20**, 1755 and references therein.
- 17 Monitoring the reaction by GC/MS showed that production of 1 equivalent of vinyl sulfone **3a** consumes 2 equivalents of arylsulfonate phenol ester **2a**.
- 18 A. Studer and D. P. Curran, *Nat. Chem.*, 2014, **6**, 765.
- 19 This pathway, however, does not account for the necessity of employment of 3 equivalents of arylsulfonate ester **2**. See the ESI† for details.
- 20 (a) J. M. Kanabus-Kaminska, J. A. Hawari, D. Griller and C. Chatgililoglu, *J. Am. Chem. Soc.*, 1987, **109**, 5268; (b) D. Griller, M. Lesage and C. Chatgililoglu, *J. Org. Chem.*, 1988, **53**, 3642; (c) A. Alberti and C. Chatgililoglu, *Tetrahedron*, 1990, **46**, 3963; (d) C. Chatgililoglu, *Acc.*



- Chem. Res.*, 1992, **25**, 188; (e) C. Chatgililoglu, *Chem.–Eur. J.*, 2008, **14**, 2310.
- 21 (a) P. Mauleon, I. Alonso, M. Rodriguez Rivero and J. C. Carretero, *J. Org. Chem.*, 2007, **72**, 9924; (b) T. Nishimura, Y. Takiguchi and T. Hayashi, *J. Am. Chem. Soc.*, 2012, **134**, 9086.
- 22 K. Yoshida and T. Hayashi, *J. Am. Chem. Soc.*, 2003, **125**, 2872.
- 23 (a) A. Noble and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 11602; (b) D. R. Heitz, K. Rizwan and G. A. Molander, *J. Org. Chem.*, 2016, **81**, 7308.
- 24 D. Sahu, S. Dey, T. Pathak and B. Ganguly, *Org. Lett.*, 2014, **16**, 2100.

