

Cite this: *Chem. Sci.*, 2020, 11, 13071

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 25th May 2020
Accepted 13th October 2020

DOI: 10.1039/d0sc02947e

rsc.li/chemical-science

Silyloxymethanesulfinate as a sulfoxylate equivalent for the modular synthesis of sulfones and sulfonyl derivatives†

Dae-Kwon Kim,‡ Hyun-Suk Um,‡ Hoyoon Park, Seonwoo Kim, Jin Choi and Chulbom Lee *

An efficient protocol for the modular synthesis of sulfones and sulfonyl derivatives has been developed utilizing sodium *tert*-butyldimethylsilyloxymethanesulfinate (TBSOMS-Na) as a sulfoxylate (SO₂²⁻) equivalent. TBSOMS-Na, easily prepared from the commercial reagents Rongalite™ and TBSCl, serves as a potent nucleophile in *S*-alkylation and Cu-catalyzed *S*-arylation reactions with alkyl and aryl electrophiles. The sulfone products thus obtained can undergo the second bond formation at the sulfur center with various electrophiles without a separate unmasking step to afford sulfones and sulfonyl derivatives such as sulfonamides and sulfonyl fluorides.

Introduction

Synthesis of sulfonyl compounds by means of C–S bond formation is of high importance as sulfonyl linkages constitute mainstay structural motifs in a wide variety of pharmaceuticals, agrochemicals and organic materials.¹ The direct installation of the SO₂ unit, in particular, has long been practiced employing sulfur dioxide² and recently underwent notable advancement owing to the development of sulfur dioxide surrogates, such as DABSO³ and metal sulfite salts,⁴ that enabled facile SO₂ insertion in various processes. For the generation of the sulfonyl motif, the amphoteric reactivity of the sulfur atom has been mostly exploited, conjoining a nucleophile and an electrophile to give rise to sulfonyl compounds (Scheme 1A). Broader access to sulfonyl products may be feasible by engaging two electrophiles such as organohalides, which are more readily available than the corresponding nucleophiles. While this approach has been implemented in reductive settings, the scope is limited largely to substrate systems paired up by each of aryl and alkyl halides due to the requirement for distinctive reactivity toward transition metal activation or radical generation.⁵ The protocol providing more general access to a wider range of sulfonyl products including aliphatic as well as aromatic derivatives from large pools of electrophiles would be of high synthetic value, but remains unexplored.

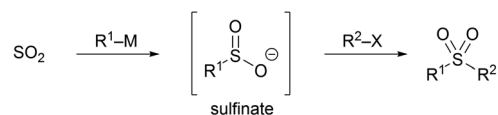
From the disconnection vantage point, central to various syntheses of sulfonyl compounds is the intermediacy of an organosulfinate capable of reacting with electrophiles. A variety of sulfonyl derivatives have indeed been shown to function as precursors that form the sulfinate intermediate upon removal of one sulfonyl substituent from the sulfur center.⁶ For the *de novo* synthesis enlisting two electrophiles, a sulfinate having a removable masking group already in place can serve as the starting point (Scheme 1B). This strategy based on a dianion equivalent of sulfur dioxide, sulfoxylate (SO₂²⁻), has been put into practice by making use of sodium salts of 3-methoxy-3-oxopropane-1-sulfinate (SMOPS),⁷ benzothiazole-2-sulfinate (BTS),⁸ hydroxymethanesulfinate (Rongalite™),⁹ and its acyl derivative (Rongacyl).¹⁰ Despite their utility in certain settings, however, a range of shortcomings are associated with the methods using these reagents. For example, SMOPS and BTS are prepared from mephitic thiol and sulfide compounds

Department of Chemistry, Seoul National University, Seoul 08826, Republic of Korea.
E-mail: chulbom@snu.ac.kr

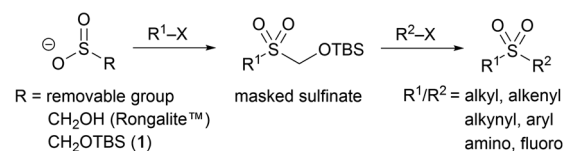
† Electronic supplementary information (ESI) available: Experimental procedures, characterization data for all new compounds and other experimental details. See DOI: 10.1039/d0sc02947e

‡ These authors equally contributed.

A. Sulfur dioxide (SO₂) approach



B. Sulfoxylate (SO₂²⁻) approach with TBSOMS-Na



Scheme 1 Synthetic strategies for installing sulfonyl units.



through rather laborious processes, and release of the sulfonates requires unmasking under strongly basic and nucleophilic conditions, which are unsuitable for sensitive molecules. Direct use of the commercial reagent Rongalite™ is advantageous in terms of accessibility and cost, but has been limited mostly to the formation of sulfonamides in the presence of a large excess of the reagent to avoid a side reaction producing undesired symmetrical sulfones due to the labile hydroxymethyl group. The Rongacyl reagent free from this problem has proven to be quite effective in the preparation of various sulfonyl derivatives, but its utility has been limited to aliphatic substrates.

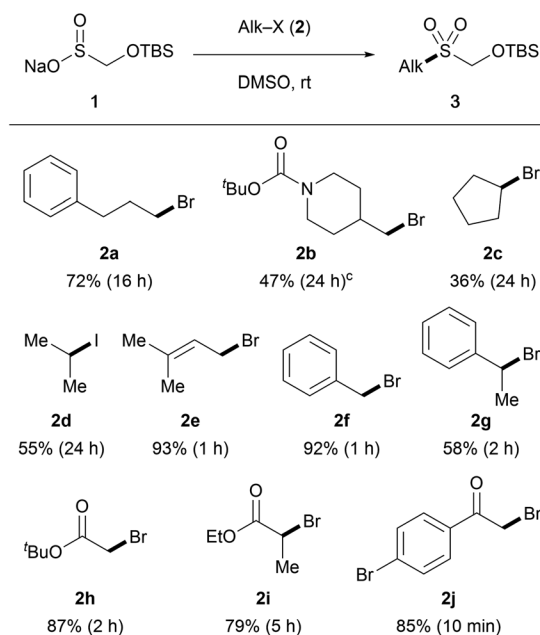
With the goal of developing an efficient method enabling modular access to a diverse range of sulfonyl products including alkyl, alkenyl, alkynyl, and aryl derivatives, we sought to probe sodium *tert*-butyldimethylsilyloxymethanesulfinate (TBSOMS-Na, **1**) for its potential to work as an effective sulfonylating reagent.¹¹ We envisaged that the potent reactivity of **1** toward π -allylpalladium species could be translated into C–S bond formation with other types of electrophiles. Of particular interest was the prospect of subjecting the resulting TBSOCH₂ sulfone directly to the second reaction without a separate unmasking step. It was anticipated that the mildness and mechanistic orthogonality of the fluoride-induced desilylation event would allow for a wide swath of reactions to be viable with a broad range of functional groups being tolerated. Thus, the synthetic sequence from TBSOMS-Na to sulfonyl products may be performed through operationally simple, all-in-one-pot procedures. We report here our studies on the novel sulfinate TBSOMS-Na for use as a versatile sulfoxylate equivalent in the modular and efficient synthesis of sulfones, sulfonamides and sulfonyl fluorides.

Results and discussion

Our studies started with examining the reactivity of TBSOMS-Na (**1**), readily prepared as a shelf-stable solid from Rongalite™ and TBSCl in 97% yield, in *S*-alkylation with alkyl electrophiles (Table 1). Gratifyingly, the reaction of **1** (1.5 equiv.) with an assortment of alkyl halides proceeded smoothly to afford the corresponding *S*-alkylated products in moderate to good yield (in DMSO at ambient temperature, unoptimized). The primary bromide **2a** participated well in the reaction to afford the TBSOCH₂ sulfone while the β -branched primary bromide **2b** produced a 4 : 1 mixture of sulfone and sulfinate ester products. As expected, secondary halides displayed diminished reactivity (**2c** and **2d**), and excellent yields of sulfone products were obtained from the reactions of activated systems such as allylic (**2e**), benzylic (**2f** and **2g**) and α -carbonyl halides (**2h–2j**). It should be noted that sulfinate esters arising from *O*-alkylation were formed as minor products in most cases (*S* : *O* = 4 : 1–6 : 1), whereas *S*-alkylation took place predominantly with activated substrates (>10 : 1).

We next probed the feasibility of using TBSOMS-Na as a nucleophile in the *S*-arylation reactions. For our initial survey, we chose diaryliodonium salts as the arylating agent because of their ability to undergo arylation as well as their accessibility, nontoxic nature, and air and moisture stable properties. The

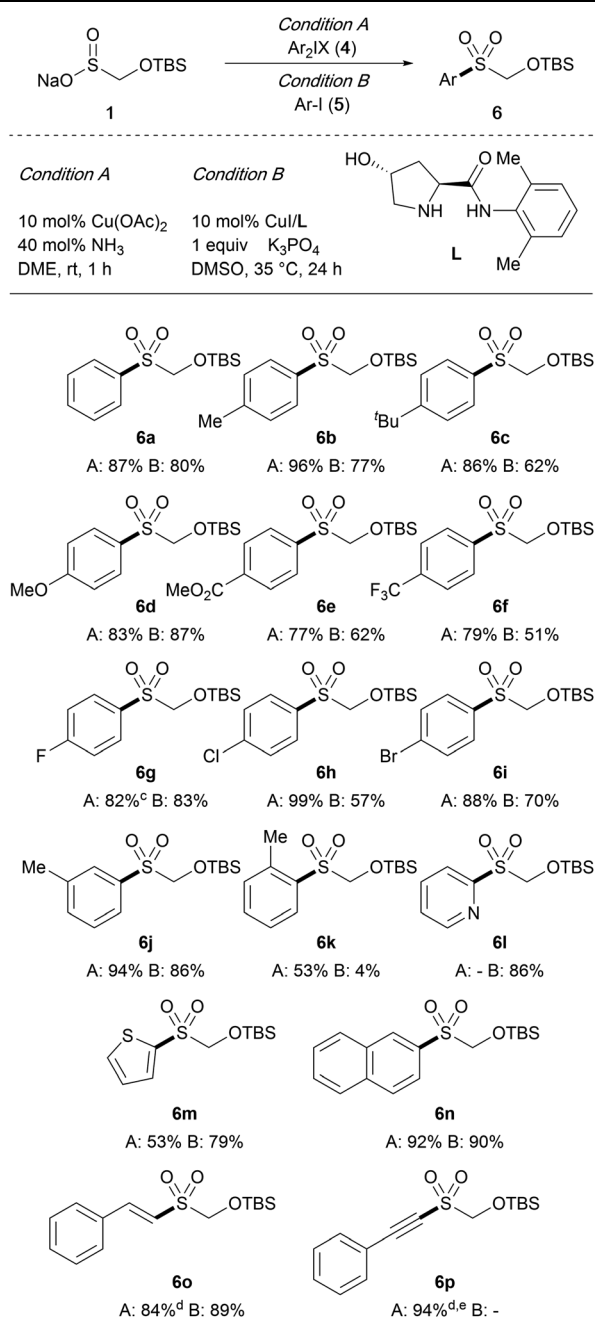
Table 1 *S*-Alkylation of TBSOMS-Na with alkyl halides^{a,b}



^a Reaction conditions: TBSOMS-Na (0.6 mmol) and alkyl halide (0.4 mmol) in DMSO (1.6 mL). ^b Isolated yields. ^c Inseparable mixtures of sulfone and sulfinate ester (*S* : *O* = 4 : 1).

reaction with diphenyliodonium triflate under the reported catalyst-free conditions (DMF, 90 °C, 24 h),¹² however, led to decomposition of **1**, forming only a trace amount of the *S*-phenylation product. In light of the infeasibility of the thermal conditions, we elected to explore the possibility of catalysis. To this end, a series of copper catalysts known to be capable of effecting arylation with diaryliodonium salts were screened. Surprisingly, it was found that the *S*-arylation could be carried out most efficiently with the Cu(II) catalyst system developed for the oxidative cross-coupling of arylboronic acids.¹³ In the event, in the presence of 10 mol% Cu(OAc)₂ and 40 mol% NH₃ (7 N in MeOH), the reaction of TBSOMS-Na (**1**) with diphenyliodonium triflate took place at ambient temperature to furnish the *S*-phenylation product **6a** in 87% yield (Condition A). As illustrated in Table 2, the air and moisture tolerant reaction conditions proved to be efficient with substrates that incorporated a wide range of functional groups at the aryl ring, such as alkyl, ether, ester, trifluoromethyl, and halide groups. In most cases, the reaction was completed within 1 h to generate the TBSOCH₂ sulfone products while tolerating significant electronic variation in the aryl ring. On the other hand, *ortho*-substitution was inimical to this Cu-catalyzed reaction as shown by the relatively lower yield of **6k**, forming a contrast to the thermal process,¹² in which the sulfone product arose typically from transfer of the sterically more demanding aryl group of a mixed diaryliodonium reagent. In addition to the aryl substrates, heteroaryl iodonium salts were also found to be viable participants of the reaction giving rise to the 2-pyridyl (**6l**) and thiophenyl (**6m**) sulfones. Finally, the protocol could be



Table 2 S-Arylation of TBSOMS-Na^{a,b}

^a Condition A: TBSOMS-Na (0.22 mmol), iodonium salt (0.2 mmol), Cu(OAc)₂ (0.02 mmol) and NH₃ (0.08 mmol) in DME (1.0 mL). Condition B: TBSOMS-Na (0.5 mmol), aryl iodide (1.0 mmol), CuI (0.05 mmol), L (0.05 mmol) and K₃PO₄ (0.5 mmol) in DMSO (3.2 mL). ^b Isolated yields. ^c TBSOMS-Na (0.2 mmol) and iodonium salt (0.4 mmol). ^d Unsymmetrical iodonium salts were incorporated. ^e Cu(OAc)₂ and NH₃ were absent in the reaction conditions.

extended to promote *S*-alkenylation (**6o**) and *S*-alkynylation (**6p**) by using alkenylaryl and alkynylaryl iodonium salts, respectively, the latter of which reacted in the absence of a copper catalyst.¹⁴

Having established a mild catalytic protocol for *S*-arylation using iodonium reagents, we next explored the possibility of obtaining the same products from aryl halides. Among various C(sp²)-S coupling methods for aryl sulfone synthesis,^{15–20} the copper catalyst supported by the proline-derived ligand L was deemed suitable due to its known ability to promote *S*-arylation of sulfonates with aryl iodides under mild conditions.^{15f} Indeed, using 10 mol% CuI and ligand L in the presence of K₃PO₄, the reaction of TBSOMS-Na (**1**) with aryl iodides **5** in DMSO at 35 °C was completed in 24 h to furnish the corresponding aryl and heteroaryl sulfones in moderate to good yield (Condition B). In general, the same level of the reaction scope was maintained, but the sulfone products were formed in relatively lower yields in comparison to the reaction with iodonium reagents. However electron-rich substrates gave higher yields, mirroring the trends found in this catalyst system, and a more pronounced steric effect was noted in the reaction of the *ortho*-substituted substrate (**6k**). The copper-catalyzed reaction was also viable for the *S*-alkenylation (**6o**). These results, taken together with those of the reaction with iodonium salts, establish the feasibility of converting TBSOMS-Na (**1**) to aryl, alkenyl and alkynyl sulfones under the mild conditions we were targeting at the outset.

With the observation of the efficient *S*-arylation of **1** with iodonium salts under remarkably mild reaction conditions, we examined the applicability of the protocol to aryl sulfone synthesis with other sulfonates (Table 3). In stark contrast to **1**, sulfonates bearing other removable masking groups did not fare well in the Cu-catalyzed *S*-arylation, and only BTS provided the phenylated product in low yield (entries 1 vs. 2–4). In addition, both methanesulfonate and *p*-toluenesulfonate failed to couple with diphenyliodonium triflate under the standard conditions

Table 3 Cu-Catalyzed *S*-arylation of organosulfonates with diphenyliodonium salt^{a,b}

Entry	R	Additive	Yield (%)
1	CH ₂ OTBS (1)	—	87
2	2-Benzothiazole (BTS)	—	35
3	CH ₂ CH ₂ CO ₂ Me (SMOPS)	—	0
4	2-Pyridyl	—	0
5	Me	—	0
6	<i>p</i> -Tol	—	0
7	<i>p</i> -Tol	10 mol% 1	46
8	<i>p</i> -Tol	20 mol% 3a'	21
9	<i>p</i> -Tol	20 mol% 6a	10

Structure of **1**: NaO-S(=O)-CH₂-OTBS

Structure of **3a'**: Ph-CH₂-CH₂-CH₂-CH₂-O-S(=O)-CH₂-OTBS

Structure of **6a**: Ph-S(=O)-CH₂-OTBS

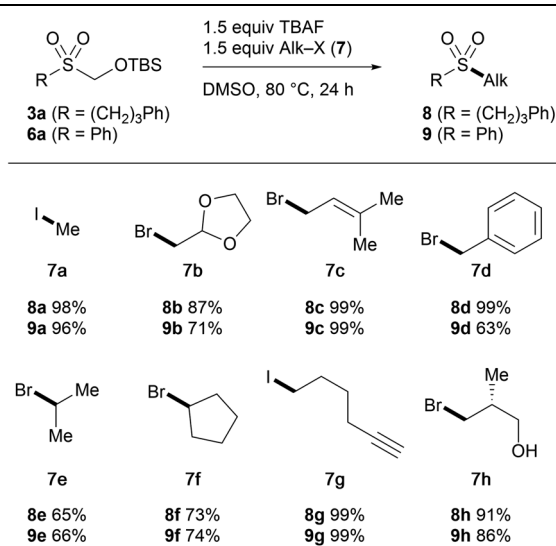
^a Reaction conditions: sodium *p*-toluenesulfonate (0.22 mmol), diphenyliodonium triflate (0.2 mmol), Cu(OAc)₂ (0.02 mmol) and NH₃ (0.08 mmol, 7 N in MeOH) in DME (1.0 mL). ^b Isolated yields.



as well (entries 5 and 6). Intriguingly, upon addition of 10 mol% **1**, a rapid reaction took place to furnish diarylsulfone **12d** (46%) along with sulfone **6a** (9%) (entry 7). Furthermore, sulfinate ester **3a'** and sulfone **6a** additives (20 mol%) also induced phenylation, albeit with low conversions in these cases (entries 8 and 9). Although the mechanism of the reaction remains unclear, these results indicate involvement of the TBSOCH₂ moiety derived from the Rongalite™ architecture in the coordination of copper, playing a critical role for successful *S*-arylation.

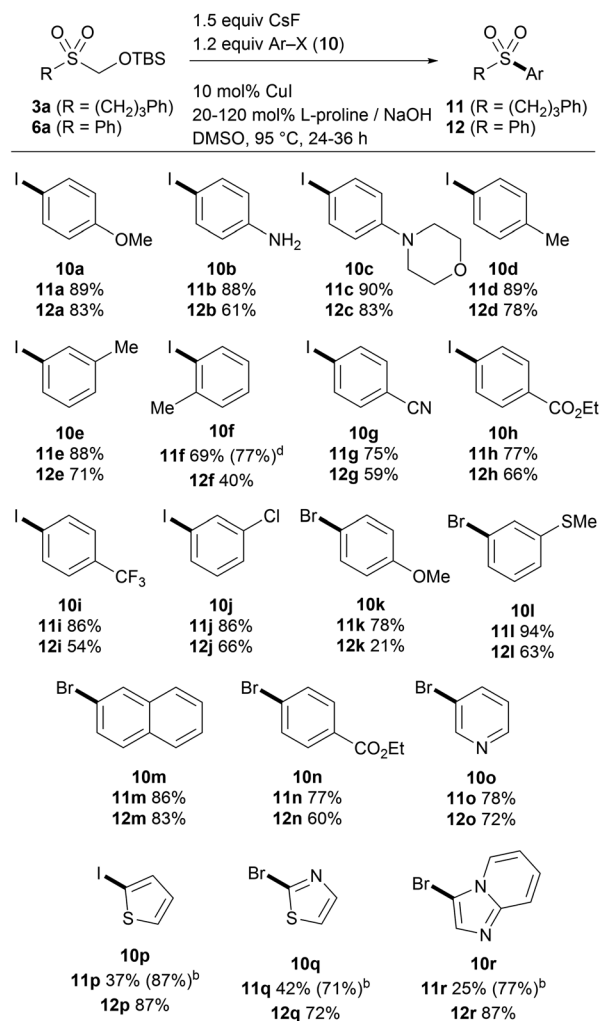
In order to demonstrate the utility of TBSOMS-Na as a novel sulfoxylate equivalent in the modular synthesis of sulfones, the TBSOCH₂ sulfone was probed for its ability to react with second electrophiles. After a set of screening experiments, it was found that the TBSOCH₂ group could be replaced directly with various alkyl and aryl groups through the reactions performed in the presence of TBAF or CsF, which likely revealed *in situ* the requisite sulfinate for C–S bond formation at the sulfur center. We first examined the *S*-alkylation of alkyl (**3a**, R = CH₂CH₂-CH₂Ph) and aryl (**6a**, R = Ph) sulfones in their reactions with alkyl electrophiles (Table 4). Treatment of **3a** and **6a** with alkyl halides at 80 °C in the presence of TBAF gave the dialkyl (**8**) and alkyl aryl (**9**) sulfones in good to excellent yield. An array of alkyl halides containing acetal (**7b**), alkene (**7c**), aryl (**7d**), alkyne (**7g**), and hydroxy (**7h**) groups all participated well in the reaction. Similar to the alkylation of **1** (cf. Table 1), the reaction with secondary halides was less efficient, and high yields were uniformly obtained from reactive substrates with the exception of the reaction of **6a** with benzyl bromide which gave a lower yield of **9d** due to the *O*-alkylation forming the sulfinate ester (25%).

Table 4 Modular synthesis of unsymmetrical sulfones via direct *S*-alkylation^{a,b}



^a Reaction conditions: TBSOCH₂ sulfone **3a** or **6a** (0.4 mmol), alkyl halide (0.6 mmol) and TBAF (0.6 mmol) in DMSO (1.6 mL). ^b Isolated yields.

Table 5 Modular synthesis of unsymmetrical sulfones via direct *S*-arylation^{a,b,c}



^a Reaction conditions for **11**: TBSOCH₂ sulfone **3a** (0.4 mmol), aryl halide (0.48 mmol), CuI (0.04 mmol), L-proline (0.08 mmol), NaOH (0.08 mmol) and CsF (0.6 mmol) in DMSO (0.4 mL), 24 h. ^b Reaction conditions for **12**: TBSOCH₂ sulfone **6a** (0.4 mmol), aryl halide (0.48 mmol), CuI (0.04 mmol), L-proline (0.48 mmol), NaOH (0.08 mmol) and CsF (0.6 mmol) in DMSO (0.4 mL), 36 h. ^c Isolated yields. ^d 36 h.

Encouraged by the results of alkylation, we then explored the direct arylation of the TBSOCH₂ sulfone **3a** (Table 5). We were pleased to find that the desired alkyl aryl sulfones **11** were generated from the reaction of **3a** with aryl halides under the conditions employing catalytic CuI and L-proline together with CsF (1.5 equiv).^{15b} A wide variety of aryl iodides (**10a–j** and **10p**) as well as bromides (**10k–o** and **10q–r**) proved to be competent participants in the coupling reaction, tolerating a range of functional groups in various positions of the aryl ring. The *ortho*-substituted iodide (**10f**) that exhibited poor efficiency in the reaction with **1** (cf. **6k**) gave a reasonable yield of the aryl sulfone product. Interestingly, a precipitous decrease in yield was observed in the reactions with some heteroaryl substrates



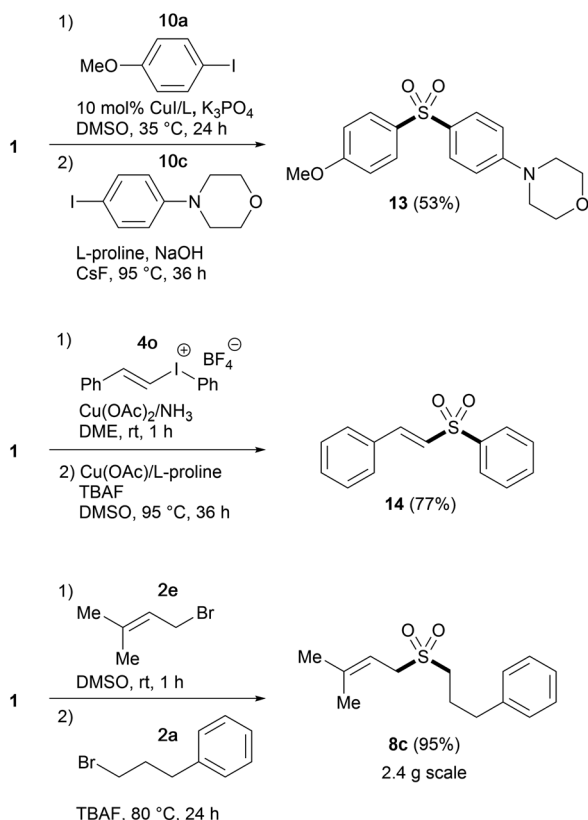
(**10p**, **10q** and **10r**). Noting the poor conversion and sluggishness of these reactions, we speculated that the copper catalyst might be rendered inactive by formaldehyde arising from the fluoride-induced desilylation.²¹ A control experiment carried out by running an otherwise efficient reaction in the presence of paraformaldehyde led to a significant decrease in the yield of the product (see the ESI†). In light of the effect of formaldehyde on the copper catalytic system, the reactions with heteroaryl halides were performed using an additional equivalent of *L*-proline, which was expected to trap formaldehyde while serving as the ligand. Gratifyingly, the reactions under these modified conditions gave the heteroaryl sulfone products in substantially increased yield.

Having established suitable conditions for arylation, we then examined the protocol for the synthesis of diaryl sulfones. As the reaction of phenyl sulfone **6a** proceeded more slowly than that of alkyl sulfone **3a**, susceptible to catalyst deactivation, the arylation was performed employing additional *L*-proline (Table 5). The copper-catalyzed direct arylation of **6a** under the modified conditions displayed broad substrate capacity, accommodating a range of aryl and heteroaryl halides. It is worthy of note that this consecutive *S*-arylation sequence with TBSOMS-Na constitutes an expeditious entry to unsymmetrical diaryl sulfones from two aryl electrophiles, a transformation that has never been demonstrated with a sulfoxylate synthon. We then further investigated the feasibility of the synthesis of unsymmetrical sulfones through single pot procedures without isolating the TBSOCH₂ sulfone intermediates (Scheme 2). When

TBSOMS-Na was subjected to the copper-catalyzed arylation with **10a** (35 °C, 24 h) and then with **10c** (95 °C, 36 h, 1 equiv *L*-proline), diaryl sulfone **13** was obtained in 53% yield. Moreover, the synthesis of an alkenyl aryl sulfone was also achieved in an atom-economical fashion by making use of both the alkenyl and aryl groups of the mixed iodonium reagent **4o**.²² Subsequent to the *S*-alkenylation of **1** with **4o**, the resulting TBSOCH₂ sulfone and the iodobenzene byproduct were treated with catalytic CuOAc (10 mol%) along with TBAF and *L*-proline in DMSO. This two-stage, one-pot procedure afforded the desired alkenyl aryl sulfone **14** in a yield of 77%. This one-pot strategy was also applicable to the synthesis of dialkyl sulfones as exemplified in the gram scale preparation of **8c**.

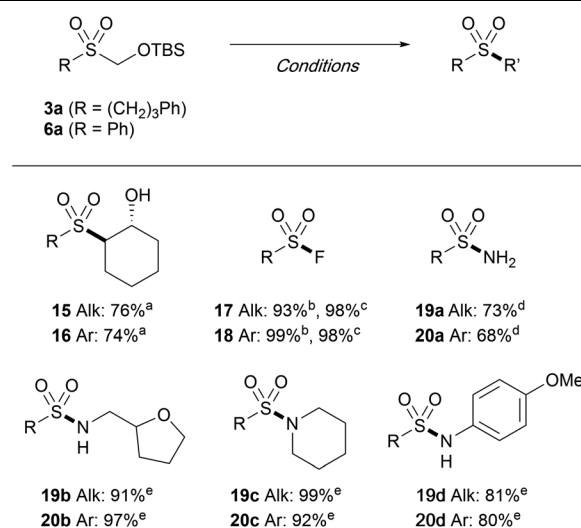
The versatility of the TBSOCH₂ sulfones as masked sulfinates was further demonstrated through the synthesis of a range of sulfonyl derivatives. As outlined in Table 6, sulfones **3a** and **6a** readily engaged in the reactions with various electrophiles in the presence of CsF or TBAF. The epoxide in cyclohexene was opened with exclusive *anti*-stereoselectivity upon treatment with sulfones **3a** and **6a** in water to furnish the *trans*-sulfonyl alcohols **15** and **16**. In addition to epoxides, the strategy of introducing substituents in place of the TBSOCH₂ group was amenable for the synthesis of sulfonyl fluorides as exemplified by the direct *S*-fluorination with NFSI or Selectfluor, both of which gave high yields. While the reaction with HOSA (hydroxylamine *O*-sulfonic acid) gave the primary sulfonamides (**19a** and **20a**), the secondary (**19b** and **20b**) and the tertiary (**19c** and **20c**) sulfonamides as well as the *N*-arylsulfonamides (**19d** and **20d**) were all prepared in good yields from the reactions carried out with the aid of NCS.

Although a wide variety of sulfones and sulfonyl derivatives are accessed directly from the intermediate sulfone without a discrete unmasking step, isolation of the TBSOM sulfone may

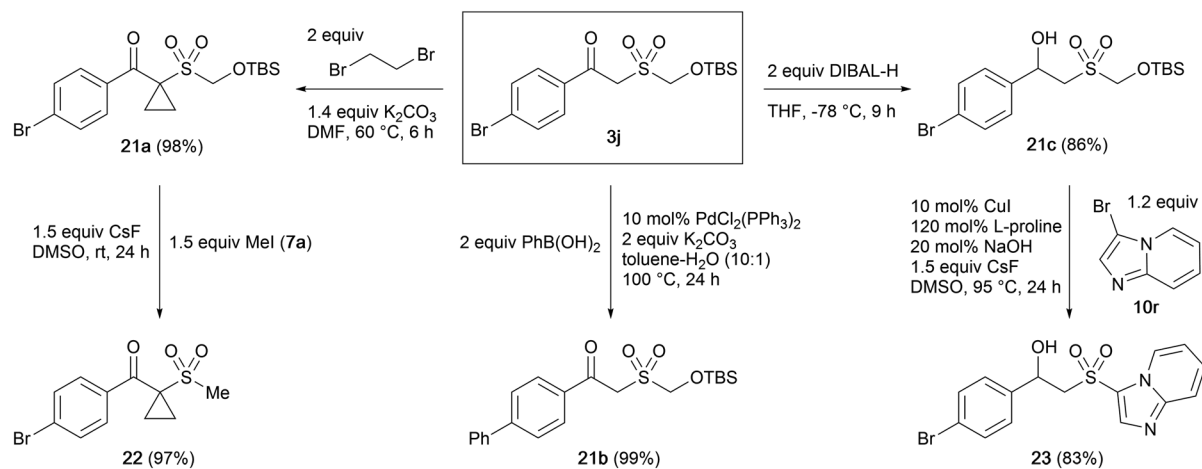


Scheme 2 One-pot synthesis of unsymmetrical sulfones.

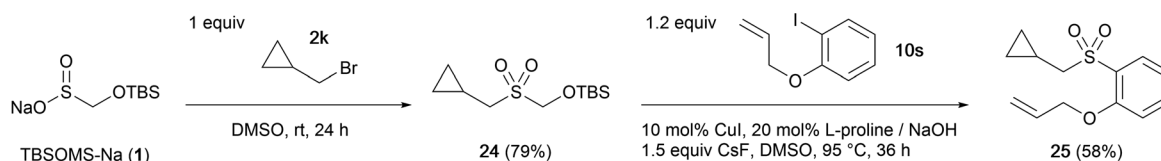
Table 6 Synthesis of sulfonyl derivatives^{a,b,c,d,e,f,g}



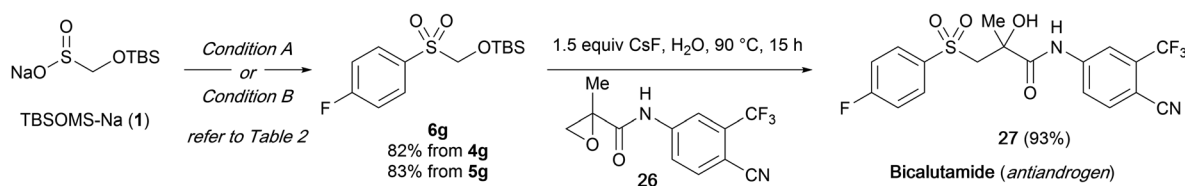
^a Cyclohexene oxide. ^b Selectfluor. ^c NFSI. ^d HOSA. ^e Amines with NCS. ^f Isolated yields. ^g For more experimental details, see the ESI.

A. Functionalization of TBSOCH₂ sulfone intermediates

B. Sulfone synthesis with halides prone to ring opening and ring closing



C. Synthesis of the pharmaceutically active compound



Scheme 3 Application of the sulfoxylate strategy for the modular synthesis of sulfonyl derivatives.

be beneficial in case structural elaborations are desired. We thus probed the robustness of the TBSOCH₂ moiety in the context of various functionalizations of β -ketosulfone **3j** (Scheme 3A).²³ When subjected to the alkylation with 1,2-dibromoethane, **3j** gave cyclopropane **21a** in high yield. Sulfone **3j** also sustained a palladium-catalyzed coupling with phenylboronic acid to give rise to biphenyl **21b** in nearly quantitative yield. Furthermore, we observed clean reduction of the ketone to β -hydroxysulfone **21c** using DIBAL-H, a reagent that might unmask the sulfones derived from SMOPS, BTS, and Rongacyl salts. Subsequently, the functionalized TBSOCH₂ sulfones **21a** and **21c** could be advanced to alkyl and aryl sulfones **22** and **23** via direct *S*-alkylation and -arylation, respectively, thus establishing the divergent synthetic strategy for unsymmetrical sulfones.

Next, we examined the viability of the sulfoxylate strategy with electrophiles whose incorporation in the sulfone synthesis might be complicated due to their sensitive structures (Scheme 3B). Starting from **1**, the sequence of *S*-alkylation with bromide **2k** followed by *S*-arylation with iodide **10s** under the standard conditions could be carried out uneventfully to form the alkyl aryl sulfone **25** with the cyclopropane and allyl moieties intact.²⁴

Lastly, the synthetic usefulness of the present sulfoxylate approach was demonstrated through an application in the synthesis of bicalutamide (**27**), an antiandrogen medication (Scheme 3C).²⁵ The TBSOCH₂ sulfone **6g** bearing a 4-fluorophenyl group was prepared efficiently from the reaction of **1** with diaryliodonium salt **4g** or aryl iodide **5g**. Subsequently, treatment of **6g** with an aqueous mixture of the known epoxide **26** and CsF afforded bicalutamide in a yield of 93%. The concise synthesis, avoiding the use of an expensive 4-fluorobenzenesulfinate salt or mephitic 4-fluorothiophenol, highlights the practical aspect of our sulfoxylate strategy.

Conclusions

In summary, we have developed an efficient strategy for the modular synthesis of various sulfones and sulfonyl derivatives by using TBSOMS-Na (**1**) as a novel sulfoxylate equivalent. The TBSOMS-Na salt is shelf-stable and easily prepared in decagram scales from commercial reagents Rongalite™ and TBSCl, and has been shown to be a potent *S*-nucleophile to engage in various C–S bond formations effecting alkylation, alkenylation, alkynylation, and arylation at the sulfur center via the reaction with organohalides and iodonium salts. The



resulting TBSOCH₂ sulfones, which are robust to sustain a range of elaborations, can undergo the reaction with a second electrophile in the presence of a fluoride anion that directly replaces the TBSOCH₂ moiety with alkyl, aryl, fluoro, and amino groups to produce sulfones, sulfonyl fluorides and sulfonamides. This sequence of introducing two discrete electrophiles, which can be carried out in one-pot, will streamline synthetic strategies for the assembly of a wide variety of sulfonyl motifs. We anticipate that this sulfoxylate strategy, complementary to the approaches based on the use of sulfur dioxide, will provide a useful means for the construction of sulfonyl compounds.

Conflicts of interest

D.-K. Kim, H.-S. Um, H. Park, and C. Lee are inventors on patent application 10-2019-0126427 (Republic of Korea) submitted by Seoul National University that covers the modular synthesis of sulfones and sulfonyl derivatives using TBSOMS-Na.

Acknowledgements

Support for this research was provided by the National Research Foundation (NRF) funded by the Ministry of Science and ICT of Korea (2017R1A2B3002869 and 2020R1A2B5B03002271). H.-S. Um gratefully acknowledges Seoul National University for generous funding through the SNU Fellowship for Fundamental Academic Fields. This paper is dedicated to P. H. Dixneuf for his outstanding contribution to organometallic chemistry and catalysis.

Notes and references

- For reviews on the construction of C–S bonds, see: (a) T. Kondo and T.-A. Mitsudo, *Chem. Rev.*, 2000, **100**, 3205; (b) N.-W. Liu, S. Liang and G. Manolikakes, *Synthesis*, 2016, **48**, 1939; (c) J. Zhu, W.-C. Yang, X.-D. Wang and L. Wu, *Adv. Synth. Catal.*, 2018, **360**, 386. For reviews on the utility of sulfonyl motifs, see: (d) M. J. El-Hibri and S. A. Weinberg, *Encyclopedia of Polymer Science and Technology*, John Wiley & Sons, New York, 2002, vol. 4, pp. 1–26; (e) C. Dizman, M. A. Tasdelen and Y. Yagci, *Polym. Int.*, 2013, **62**, 991; (f) M. Feng, B. Tang, S. H. Liang and X. Jiang, *Curr. Top. Med. Chem.*, 2016, **16**, 1200; (g) P. Devendar and G.-F. Yang, *Top. Curr. Chem.*, 2017, **375**, 82; (h) K. A. Scott and J. T. Njardarson, *Top. Curr. Chem.*, 2018, **376**, 5; (i) B. M. Trost and C. A. Kalnals, *Chem.-Eur. J.*, 2019, **25**, 11193.
- (a) S. D. Burke, in *Encyclopedia of Reagents for Organic Synthesis*, ed. L. A. Paquette, John Wiley & Sons, Chichester, 1995, vol. 7, p. 4688; (b) P. Vogel, M. Turks, L. Bouchez, D. Marković, A. Varela-Álvarez and J. Á. Sordo, *Acc. Chem. Res.*, 2007, **40**, 931.
- For a seminal report, see: (a) H. Woolven, C. González-Rodríguez, I. Marco, A. L. Thomson and M. C. Willis, *Org. Lett.*, 2011, **13**, 4876. For reviews on DABSO, see: (b) E. J. Emmett and M. C. Willis, *Asian J. Org. Chem.*, 2015, **4**, 602; (c) M. C. Willis, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2019, **194**, 654.
- S. Ye, G. Qiu and J. Wu, *Chem. Commun.*, 2019, **55**, 1013.
- (a) J. Zhang, K. Zhou, G. Qiu and J. Wu, *Org. Chem. Front.*, 2019, **6**, 36; (b) Y. Li, T. Liu, G. Qiu and J. Wu, *Adv. Synth. Catal.*, 2019, **361**, 1154; (c) Y. Meng, M. Wang and X. Jiang, *Angew. Chem., Int. Ed.*, 2020, **59**, 1346.
- For reviews on sulfinates, see: (a) J. Aziz, S. Messaoudi, M. Alami and A. Hamze, *Org. Biomol. Chem.*, 2014, **12**, 9743; (b) D. Kaiser, I. Klose, R. Oost, J. Neuhaus and N. Maulide, *Chem. Rev.*, 2019, **119**, 8701. For examples of sulfinate precursors in the form of thiosulfonate, see: (c) D. H. R. Barton, B. Lacher, B. Misterkiewicz and S. Z. Zard, *Tetrahedron Lett.*, 1988, **44**, 1153; (d) P. K. Shyam and H.-Y. Jang, *J. Org. Chem.*, 2017, **82**, 1761; (e) P. K. Shyam, S. Son and H.-Y. Jang, *Eur. J. Org. Chem.*, 2017, 5025; (f) S. Son, P. K. Shyam, H. Park, I. Jeong and H.-Y. Jang, *Eur. J. Org. Chem.*, 2018, 3365. For examples of sulfinate precursors in the form of allyl sulfone, see: (g) G. Le Duc, E. Bernoud, G. Prestat, S. Cacchi, G. Fabrizi, A. Iazzetti, D. Madec and G. Poli, *Synlett*, 2011, 2943. For examples of sulfinate precursors in the form of 2-pyridyl sulfone, see: (h) Y. Zhao, W. Huang, L. Zhu and J. Hu, *Org. Lett.*, 2010, **12**, 1444; (i) Q. Zhou, A. Ruffoni, R. Gianatassio, Y. Fujiwara, E. Sella, D. Shabat and P. S. Baran, *Angew. Chem., Int. Ed.*, 2013, **52**, 3949; (j) Q. Zhou, J. Gui, C.-M. Pan, E. Albone, X. Cheng, E. M. Suh, L. Grasso, Y. Ishihara and P. S. Baran, *J. Am. Chem. Soc.*, 2013, **135**, 12994; (k) R. Gianatassio, S. Kawamura, C. L. Eprile, K. Foo, J. Ge, A. C. Burns, M. R. Collins and P. S. Baran, *Angew. Chem., Int. Ed.*, 2014, **53**, 9851. For examples of sulfinate precursors in the form of sulfonamide, see: (l) C. S. Richards-Taylor, D. C. Blackmore and M. C. Willis, *Chem. Sci.*, 2014, **5**, 222; (m) P. S. Fier and K. M. Maloney, *J. Am. Chem. Soc.*, 2019, **141**, 1441; (n) P. S. Fier, S. Kim and K. M. Maloney, *J. Am. Chem. Soc.*, 2019, **141**, 18416.
- J. M. Baskin and Z. Wang, *Tetrahedron Lett.*, 2002, **43**, 8479.
- J. J. Day, D. L. Neill, S. Xu and M. Xian, *Org. Lett.*, 2017, **19**, 3819.
- For reviews on Rongalite, see: (a) S. Kotha and P. Khedkar, *Chem. Rev.*, 2012, **112**, 1650; (b) S. Kotha, P. Khedkar and Y. Dommaraju, *Tetrahedron Lett.*, 2019, **60**, 631. For related examples, see: (c) W. Zhang and M. Luo, *Chem. Commun.*, 2016, **52**, 2980; (d) A. Shavnya, S. B. Coffey, K. D. Hesp, S. C. Ross and A. S. Tsai, *Org. Lett.*, 2016, **18**, 5848; (e) M. Wang, B.-C. Tang, J.-G. Wang, J.-C. Xiang, A.-Y. Guan, P.-P. Huang, W.-Y. Guo, Y.-D. Wu and A.-X. Wu, *Chem. Commun.*, 2018, **54**, 7641; (f) E. M. Alvarez, M. B. Plutschack, F. Berger and T. Ritter, *Org. Lett.*, 2020, **22**, 4593; (g) X.-L. Chen, B.-C. Tang, C. He, J.-T. Ma, S.-Y. Zhuang, Y.-D. Wu and A.-X. Wu, *Chem. Commun.*, 2020, DOI: 10.1039/D0CC05800A.
- A. Shavnya, K. D. Hesp and A. S. Tsai, *Adv. Synth. Catal.*, 2018, **360**, 1768.
- H.-S. Um, J. Min, T. An, J. Choi and C. Lee, *Org. Chem. Front.*, 2018, **5**, 2158.



- 12 (a) N. Umierski and G. Manolikakes, *Org. Lett.*, 2013, **15**, 188; (b) N. Umierski and G. Manolikakes, *Org. Lett.*, 2013, **15**, 4972; (c) N. Margraf and G. Manolikakes, *J. Org. Chem.*, 2015, **80**, 2582.
- 13 H. Yang, Y. Li, M. Jiang, J. Wang and H. Fu, *Chem.–Eur. J.*, 2011, **17**, 5662.
- 14 A. Rodríguez and W. J. Moran, *J. Org. Chem.*, 2016, **81**, 2543.
- 15 For examples of coupling between sulfinates and aryl halides under copper catalysis, see: (a) J. M. Baskin and Z. Wang, *Org. Lett.*, 2002, **4**, 4423; (b) W. Zhu and D. Ma, *J. Org. Chem.*, 2005, **70**, 2696; (c) M. Bian, F. Xu and C. Ma, *Synthesis*, 2007, 2951; (d) Y.-Q. Yuan and S.-R. Guo, *Synlett*, 2011, 2750; (e) B. T. V. Srinivas, V. S. Rawat, K. Konda and B. Sreedhar, *Adv. Synth. Catal.*, 2014, **356**, 805; (f) M. Yang, H. Shen, Y. Li, C. Shen and P. Zhang, *RSC Adv.*, 2014, **4**, 26295; (g) J. Zhao, S. Niu, X. Jiang, Y. Jiang, X. Zhang, T. Sun and D. Ma, *J. Org. Chem.*, 2018, **83**, 6589.
- 16 For examples of coupling between sulfinates and aryl halides under palladium catalysis, see: (a) S. Cacchi, G. Fabrizi, A. Goggiamani and L. M. Parisi, *Org. Lett.*, 2002, **4**, 4719; (b) S. Cacchi, G. Fabrizi, A. Goggiamani and L. M. Parisi, *Synlett*, 2003, 361; (c) S. Cacchi, G. Fabrizi, A. Goggiamani, L. M. Parisi and R. Bernini, *J. Org. Chem.*, 2004, **69**, 5608; (d) L. A. Smyth, E. M. Phillips, V. S. Chan, J. G. Napolitano, R. Henry and S. Shekhar, *J. Org. Chem.*, 2016, **81**, 1285.
- 17 For examples of coupling between sulfinates and aryl halides under nickel catalysis, see: N.-W. Liu, S. Liang, N. Margraf, S. Shaaban, V. Luciano, M. Drost and G. Manolikakes, *Eur. J. Org. Chem.*, 2018, 1208.
- 18 For examples of coupling between sulfinates and aryl halides under metal-free conditions, see: (a) K. M. Maloney, J. T. Kuethe and K. Linn, *Org. Lett.*, 2011, **13**, 102; (b) S. Liang, R.-Y. Zhang, L.-Y. Xi, S.-Y. Chen and X.-Q. Yu, *J. Org. Chem.*, 2013, **78**, 11874.
- 19 For examples of coupling between sulfinates and aryl halides under photoredox catalysis, see: (a) H. Yue, C. Zhu and M. Rueping, *Angew. Chem., Int. Ed.*, 2018, **57**, 1371; (b) N.-W. Liu, K. Hofman, A. Herbert and G. Manolikakes, *Org. Lett.*, 2018, **20**, 760; (c) M. J. Cabrera-Afonso, Z.-P. Lu, C. B. Kelly, S. M. Lang, R. Dykstra, O. Gutierrez and G. A. Molander, *Chem. Sci.*, 2018, **9**, 3186.
- 20 For examples of coupling between sulfinates and aryl halides under irradiation, see: L. Chen, J. Liang, Z.-Y. Chen, J. Chen, M. Yan and X.-J. Zhang, *Adv. Synth. Catal.*, 2019, **361**, 956.
- 21 (a) J. J. Byerley and W. K. Teo, *Can. J. Chem.*, 1969, **47**, 3355; (b) Z. Jusys and A. Vaškelis, *Langmuir*, 1992, **8**, 1230; (c) D. Preti, S. Squarzialupi and G. Fachinetti, *Angew. Chem., Int. Ed.*, 2009, **48**, 4763; (d) O. A. Demchenko and D. I. Belkin, *Kinet. Catal.*, 2011, **52**, 26.
- 22 (a) S. G. Modha and M. F. Greaney, *J. Am. Chem. Soc.*, 2015, **137**, 1416; (b) N. Miralles, R. M. Romero, E. Fernández and K. Muñoz, *Chem. Commun.*, 2015, **51**, 14068; (c) M. Wang, J. Wei, Q. Fan and X. Jiang, *Chem. Commun.*, 2017, **53**, 2918; (d) C. J. Teskey, S. M. A. Sohel, D. L. Bunting, S. G. Modha and M. F. Greaney, *Angew. Chem., Int. Ed.*, 2017, **56**, 5263; (e) S. G. Modha, M. V. Popescu and M. F. Greaney, *J. Org. Chem.*, 2017, **82**, 11933.
- 23 Y. M. Markitanov, V. M. Timoshenko and Y. G. Shermolovich, *J. Sulfur Chem.*, 2014, **35**, 188.
- 24 The reaction of **2k**, **10s** and Na₂S₂O₅ under palladium catalysis (ref. 5c) did not produce the unsymmetrical sulfone **25**, but led mainly to the formation of 2-iodophenol *via* deallylation of **10s**. See the ESI† for details.
- 25 (a) B. J. A. Furr, B. Valcaccia, B. Curry, J. R. Woodburn, G. Chesterson and H. Tucker, *J. Endocrinol.*, 1987, **113**, R7; (b) H. Tucker, J. W. Crook and G. J. Chesterson, *J. Med. Chem.*, 1988, **31**, 954; (c) L. Thijs, R. Keltjens and G. J. B. Ettema, *US pat.*, 0,068,135, 2004.

