EDGE ARTICLE

Check for updates

An efficient and mild oxidative approach from thiols to sulfonyl derivatives with DMSO/HBr†

Hongye Wang, Zhaoting Li, Rongheng Dai, Ning Jiao [ID] and Song Song [ID]*

A mild and practical method for synthesizing sulfonyl derivatives, which have a wide range of applications in pharmaceuticals, materials, and organic synthesis, was described through the oxidative functionalization of thiols with DMSO/HBr. The simple conditions, low cost and ready availability of DMSO/HBr, as well as the versatility of the transformations, make this strategy very powerful in synthesizing a variety of sulfonyl derivatives including sulfonamides, sulfonyl fluorides, sulfonyl azides, and sulfonates. Mechanistic studies revealed that DMSO served as the terminal oxidant, and HBr acted as both a nucleophile and a redox mediator to transfer the oxygen atom.

Introduction

Sulfonyl derivatives including sulfonyl halides, sulfonamides, sulfonyl azides *etc.* have a myriad of applications in pharmaceuticals, agrochemicals, and materials (Fig. 1).[1] For instance, sulfonyl halides are vital protecting reagents, versatile partners for cross-coupling reactions, and important synthetic intermediates.[2] Sulfonamides are some of the most important motifs in pharmaceuticals, and 25% of the FDA approved drugs from 2016 to 2018 contain the sulfonamide moiety.[3] Many strategies for the synthesis of sulfonyl derivatives have been developed, including transition-metal catalyzed coupling reactions,[4] electrochemical C–H activation,[5] nucleophilic reaction of sulfinate salts,[6] and the design of new sulfonylating reagents.[7] These elegant strategies provide new protocols to access sulfonyl derivatives and push this field forward.

Compared with the above strategies, the oxidative functionalization of commercially available thiols with nucleophiles represents one of the most convenient protocols to synthesize sulfonyl derivatives. In this transformation, the thiol motif couples with a nucleophile with two oxygen atoms introduced into the sulfur center simultaneously. Thus, the oxidant plays a dominant role in these reactions.[8] Many oxidative functionalization reactions of thiols employed stoichiometric oxidants, such as oxone,[8a] Cu(OAc)$_2$,[8b] PhI(OAc)$_2$,[8c] I$_2$O$_5$,[8d] TBHP,[8e] selectfluor[8f] *etc.*, which suffer from narrow substrate scope, low atom economy, and sometimes harsh reaction conditions[8a] (Scheme 1A). Recently, Noël[9] and coworkers developed an elegant electrochemical oxidative functionalization of thiols with KF or amines for the efficient synthesis of sulfonyl fluorides and

sulfonamides, which features broad substrate scope, high atom economy, and environmentally friendly reagents (Scheme 1B). Despite the significance of previous work, it is still highly desirable to develop a practical and efficient protocol to access sulfonyl derivatives with commercially available chemicals, mild reaction conditions, and broad substrate scope.

DMSO, as a common solvent, could serve as an oxidant, catalyst, or reagent in organic synthesis.[10] Compared with other solvents, DMSO could donate its O atom in many reactions to construct diverse C=O or C–OH bonds.[11] However, it is very
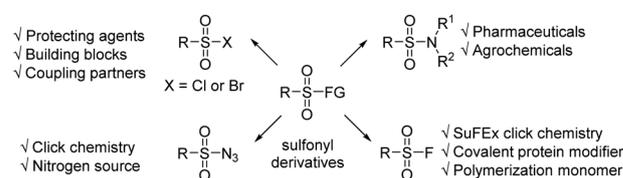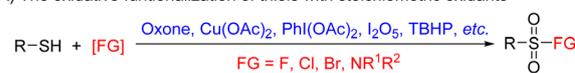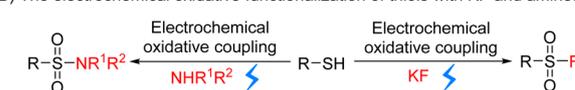

Fig. 1 The application of sulfonyl derivatives.

Scheme 1 Oxidative functionalization of thiols.

State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Xue Yuan Rd 38, Beijing 100191, China. E-mail: ssong@bjmu.edu.cn; Fax: +86-10-82805294

hard to donate the O atom of DMSO to heteroatoms. HBr, as the byproduct of the bromination industry, is inexpensive and readily available. The combination of DMSO and HBr could achieve many brominations[12] and has been widely applied in the synthesis of natural products, drugs, and materials.[13] Recently, Chen and coworkers reported a cyclization reaction enabling convenient construction of thiophene derivatives with DMSO/HBr.[14] Based on our previous research on halogenation,[15] herein, we disclose the Ni(OTf)$_2$ catalyzed oxidative bromination of thiols with DMSO and HBr to afford sulfonyl bromides (Scheme 1C). The synthesis of other sulfonyl derivatives is also achieved by a one-pot procedure. Mechanistic studies reveal that HBr acts as both a nucleophile and a redox mediator to transfer the O atom of DMSO, which serves as the terminal oxidant.

Results and discussion

Compared with aromatic thiols, the oxidative bromination of aliphatic thiols is less documented. Thus, we chose octane-1-thiol **1** as the model substrate (Table 1). The oxidative bromination of **1** was performed with 48% aqueous HBr (1.5 equiv.) in DMSO at 40 °C for 12 hours under air, and no sulfonyl bromide **2** was obtained (entry 1). We then investigated the influence of solvent with 5 equiv. of DMSO as the oxidant (entries 2–4) and found that DCM was the best solvent to deliver **2** in 32% yield (entry 4). The study on the equivalent of DMSO revealed that 3.5 equiv. of DMSO as the oxidant afforded **2** in 57% yield (entries 4–6). The yield increased to 74% when acetic acid solution of HBr was employed instead of aqueous solution (entry 7). The

Lewis acid catalyst was beneficial for present oxidative bromination (entries 8–10). With 10 mol% Ni(OTf)$_2$ as the catalyst, this reaction delivered **2** in 91% yield (entry 8), and other Lewis acid catalysts such as AgOTf and Sc(OTf)$_3$ were also suitable (entries 9 and 10). The oxidative bromination of **1** underwent smoothly under an argon atmosphere, which indicated that the molecular oxygen was not the oxidant (entry 11). Without DMSO, the sulfonyl bromide **2** was not detected, revealing the dominant role of DMSO in the present reaction (entry 12). This reaction could not proceed when HBr was replaced by NaBr, revealing that the acidic conditions were crucial for the transformation (entry 13). 40 °C is the optimal temperature for this reaction. The yield of **2** decreased to 74% at room temperature (entry 14).

With the optimum conditions in hand, we explored the substrate scope of this oxidative bromination (Table 2). A broad range of aliphatic and (hetero)aromatic thiols were all converted to sulfonyl bromides smoothly with good to high yields. Several linear, branched and cyclic aliphatic thiols were valid substrates to deliver sulfonyl bromides **2–17** in satisfactory yields, regardless of the steric hindrance or chain length. The reactivity of secondary thiols (**14–16**) was lower than that of primary thiols, so the equivalent of DMSO and HBr should be enlarged to ensure the full conversion of substrates. Functional groups such as ether (**8**), ester (**7, 9**), arene (**5**), amide (**13, 37**) and sulfonamide (**17**) were tolerated in the reaction. Besides aliphatic thiols, aromatic thiols were also compatible with the current conditions (**18–40**). *Para*-substituted thiophenols bearing electron-donating groups (**18–21**) or weak electron-withdrawing groups (**22–24**) furnished the products in moderate to good yields. However, thiophenols bearing strong electron-withdrawing groups such as CN (**26**) or NO$_2$ (**27**) suffered from a reduced reactivity, affording the corresponding disulfides as the byproduct. *Meta*- (**28–30**), *ortho*- (**31–32**), and di-substituted (**34–35**) thiophenols were also successfully converted to sulfonyl bromides in good yields. To our pleasure, the thioether group was unaffected under the standard conditions (**33**), although it's considered as a reductant motif. This result proves the good selectivity of the reaction. Besides thiophenols, 2-naphthalenethiol (**36**) and heteroaromatic thiols including *N*-oxide pyridine (**38**), thiophene (**39**), and furan (**40**) also worked well under the standard conditions, although the isolated yields were lower. This was probably because the products **38–40** were unstable and easily hydrolyzed to the corresponding sulfonic acids during the isolating process. Tertiary thiol failed to deliver the corresponding sulfonyl bromide under the standard conditions. Although the DMSO/HBr system showed high reactivity in bromination of electron-rich arenes,[12a,c] no aromatic bromination was detected in our present reaction. It is worth mentioning that without the Ni(OTf)$_2$ catalyst, the oxidative bromination could also work smoothly to afford products with good yields in some cases.

As sulfonyl bromides are important intermediates to access sulfonamides. We speculated that the sulfonyl bromide generated could be converted to sulfonamide *via* a one-pot procedure. By adding the reaction mixture to the DCM solution of amines, the sulfonamides were prepared conveniently with good to high

Table 1 Optimization of the reaction conditions[a]

Entry	Catalyst	HBr	DMSO	Solvent	Yield of **2**[b]
1	—	48% HBr in H$_2$O	—	DMSO	0%
2	—	48% HBr in H$_2$O	5 equiv.	MeCN	0%
3	—	48% HBr in H$_2$O	5 equiv.	EtOAc	11%
4	—	48% HBr in H$_2$O	5 equiv.	DCM	32%
5	—	48% HBr in H$_2$O	3.5 equiv.	DCM	57%
6	—	48% HBr in H$_2$O	2 equiv.	DCM	27%
7	—	33% HBr in AcOH	3.5 equiv.	DCM	74%
8	**Ni(OTf)$_2$**	**33% HBr in AcOH**	**3.5 equiv.**	**DCM**	**91% (86%)[c]**
9	AgOTf	33% HBr in AcOH	3.5 equiv.	DCM	84%
10	Sc(OTf)$_3$	33% HBr in AcOH	3.5 equiv.	DCM	87%
11[d]	Ni(OTf)$_2$	33% HBr in AcOH	3.5 equiv.	DCM	87%
12	Ni(OTf)$_2$	33% HBr in AcOH	—	DCM	0%
13	Ni(OTf)$_2$	NaBr in AcOH	3.5 equiv.	DCM	0%
14[e]	Ni(OTf)$_2$	33% HBr in AcOH	3.5 equiv.	DCM	74%

[a] The solution of **1** (0.50 mmol), catalyst, DMSO, and HBr (0.75 mmol) in anhydrous DCM (2.0 mL) was heated at 40 °C for 12 h. [b] Yields were determined by ^{1}H-NMR using 1,1,2,2-tetrachloroethane as the internal standard. [c] Isolated yield. [d] Under an argon atmosphere. [e] At room temperature.
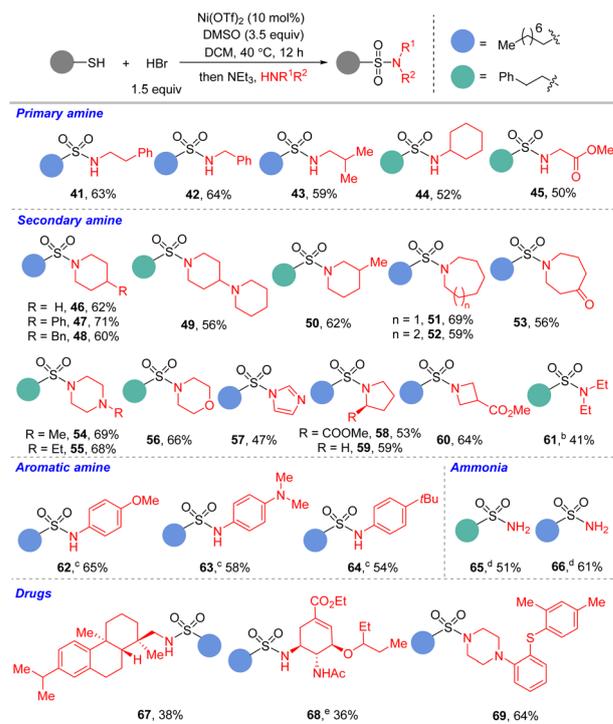
Table 2 The oxidative bromination of thiols[a]
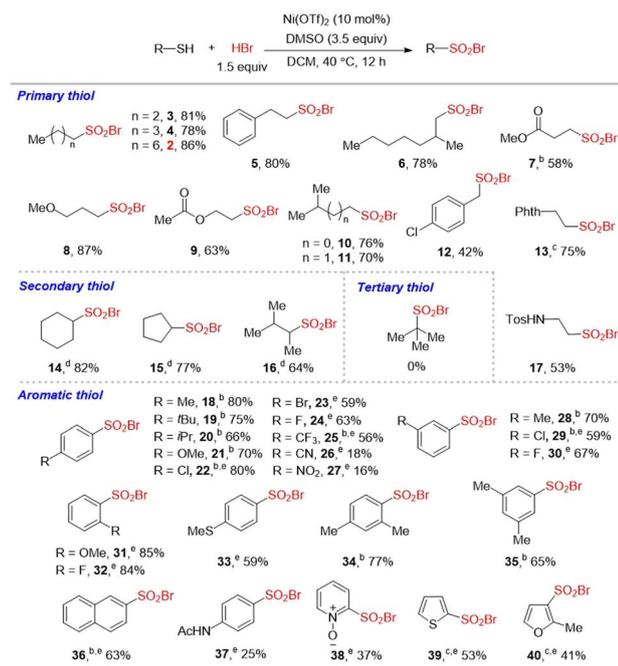
Table 3 One-pot synthesis of sulfonamides[a]

[a] The solution of thiol (0.50 mmol), Ni(OTf)$_2$ (0.05 mmol), DMSO (1.75 mmol) and HBr (33% in AcOH, 0.75 mmol) in anhydrous DCM (2.0 mL) was heated at 40 °C for 12 h. Isolated yield. [b] DMSO (2.3 mmol) and HBr (33% in AcOH, 1 mmol) was added. [c] HBr (48% aqueous solution) in EtOAc (2.0 mL) was used. [d] DMSO (3.2 mmol) and HBr (33% in AcOH, 1.2 mmol) were used. [e] Without Ni(OTf)$_2$.
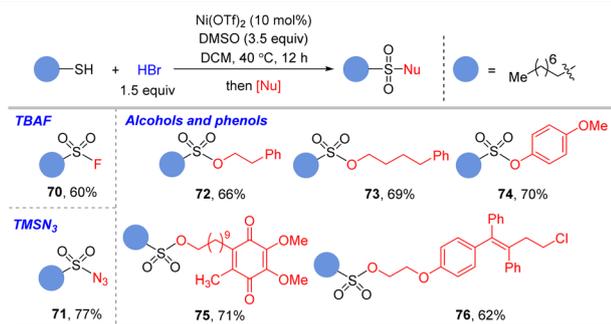
[a] The solution of thiol (0.50 mmol), Ni(OTf)$_2$ (0.05 mmol), DMSO (1.75 mmol) and HBr (33% in AcOH, 0.75 mmol) in anhydrous DCM (2.0 mL) was heated at 40 °C for 12 h. The reaction mixture was added dropwise into the solution of amine (1.5 mmol) and NEt$_3$ (4 mmol) in DCM (1 mL) in an ice-salt bath, and then reacted for 8 h. Isolated yield. [b] The reaction mixture was added into the DCM (1 mL) solution of amines (5 mmol) and NEt$_3$ (4 mmol). [c] The reaction mixture was added into the DCM (1 mL) solution of amine (1.5 mmol) and NEt$_3$ (4 mmol) under a N$_2$ atmosphere. [d] The reaction mixture was added into the DCM (1 mL) solution of NEt$_3$ (4 mmol) under an NH$_3$ atmosphere. [e] The reaction mixture was added into the THF (2 mL) solution of amine (5 mmol) and NEt$_3$ (4 mmol).

yields. We then evaluated different amine fragments under these conditions with octane-1-thiol or 2-phenylethane-1-thiol as model substrates. Aliphatic and aromatic amines, NH$_3$, and bioactive molecules bearing amino group performed well in the reaction (Table 3). The chained amines including phenylethylamine (**41**), benzylamine (**42**), and cyclohexylamine (**44**), or cyclic amines including piperidine (**46–50**), azepane (**51**), azocane (**52–53**), piperazine (**54–55**), morpholine (**56**), and imidazole (**57**) were compatible with the standard conditions, delivering sulfonamides in moderate to good yields. α- or β-Amino acid derivatives which are common motifs in drug design were also suitable substrates (**45**, **58**, and **60**). The chained secondary amine was converted into the corresponding sulfonamide (**61**) with moderate yield. With the modification of reaction conditions, electron-rich anilines furnished the conversion (**62–64**) successfully with satisfactory yields. When NH$_3$ was used as the nucleophile, primary sulfonamides (**65–66**) were obtained in moderate yields. Pleasingly, the present method was successfully applied in the late-stage sulfonylation of drugs bearing amino groups. Olefin, amide, or thioether groups (**67–69**) were all well tolerated. As a result, this approach provides a novel way to prepare a set of sulfonamide analogues, which are very important for drug discovery.[16]

Besides sulfonamides, the present oxidative bromination method was also successfully applied in the synthesis of other

valuable sulfonyl derivatives (Table 4). With inorganic Bu$_4$NF as the nucleophile, sulfonyl fluoride **70** was conveniently obtained in 60% yield. The sulfonyl azide **71** was prepared by the one-pot procedure in 77% yield with TMSN$_3$ as the nucleophile. Several alcohols or phenols were successfully coupled with thiol to deliver sulfonates (**72–76**) in good yields. Olefin, ether, halogen, and ketone groups were tolerated under the reaction conditions.

To test the scalability of this method, the synthesis of **18** was scaled up to 10 mmol with 72% yield (Scheme 2A). To further demonstrate the importance of our method, it was applied in the synthesis of tolbutamide, which is used in the management of type II diabetes mellitus.[17] Oxidative functionalization of *p*-toluenethiol produced sulfonamide **77** in 71% yield, which underwent further acylation to deliver tolbutamide (Scheme 2B).[18]

To further understand the mechanism of the reaction, some control experiments were conducted. In order to detect the possible intermediates, we monitored the reaction at different times under standard conditions. The reaction afforded product **2** in 40% yield along with disulfide **78** in 55% yield at

Table 4 One-pot synthesis of sulfonyl derivatives[a]

[a] The solution of thiol (0.50 mmol), Ni(OTf)$_2$(0.05 mmol), DMSO (1.75 mmol) and HBr (33% in AcOH, 0.75 mmol) in anhydrous DCM (2.0 mL) was heated at 40 °C for 12 h. Then, for oxidative fluorination: the reaction mixture was added dropwise into the solution of TBAF (2.5 mmol) and NEt$_3$ (3.5 mmol) in DCM (1 mL) in an ice-salt bath. The mixture was stirred at r.t. for 8 h. For oxidative azidation: the reaction mixture was added dropwise into the solution of TMSN$_3$ (1.5 mmol) and NEt$_3$ (4 mmol) in DCM (1 mL) in an ice-salt bath. The mixture was stirred at r.t. for 8 h. For oxidative esterification: the reaction mixture was added dropwise into the solution of alcohol (1.5 mmol) and NEt$_3$ (4 mmol) in DCM (1 mL) in an ice-salt bath. The mixture was stirred at r.t. for 8 h. Isolated yield.

1 h (Scheme 3A). As the reaction proceeded, the yield of **2** increased while disulfide **78** was consumed continuously, revealing that **78** was the intermediate of this reaction (Scheme 3A). When the reaction was performed with 0.2 equiv. of HBr, only 12% yield of **2** was obtained along with disulfide **78** (33%) and *S*-octyl octane-1-sulfonothioate **79** (54%) (Scheme 3B, eqn (a)). 75% yield of **78** and 23% yield of **2** were detected with 1.5 equiv. of DMSO as the oxidant (Scheme 3B, eqn (b)). These results indicate that DMSO and HBr both play important roles in this oxidative bromination reaction. Then we isolated the plausible intermediates disulfide **78** and *S*-octyl octane-1-sulfonothioate **79**, which were subjected to the reaction system with different amounts of DMSO (Scheme 3C, eqn (c) and (d)). Disulfide **78** could not be converted to **2** without DMSO, and the yield of **2** increased with the addition of DMSO (eqn (c)). **79** could be converted to **2** (31%) and **78** (46%) by simply stirring with HBr without DMSO. An enhanced amount of **2** was produced with the addition of DMSO (eqn (d)). It should be noted that using 2 equiv. of DMSO gave the highest yield of **2**. This result suggests that **78** and **79** are intermediates for the formation of **2**. When DMSO[18] was used in the standard reaction, the ^{18}O-labeled product **46** was detected although the
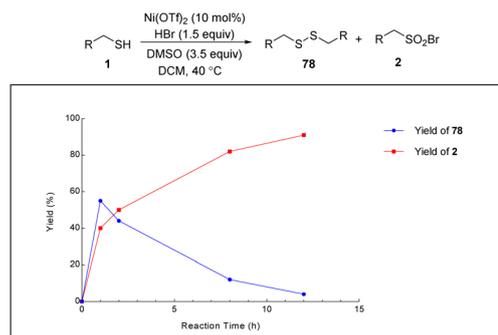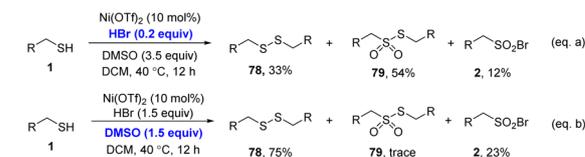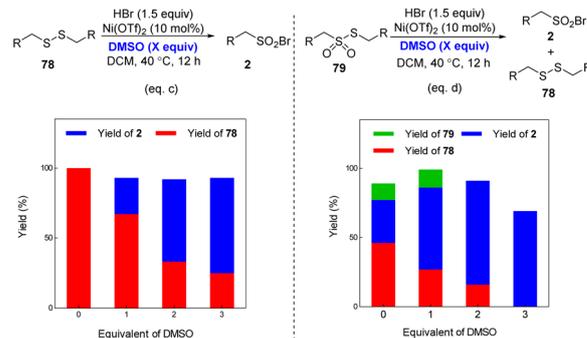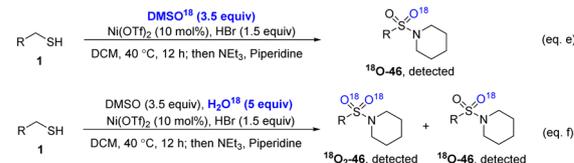

Scheme 3 Mechanistic studies.

[18]O-labeled ratio was low. The result reveals that DMSO participates in the oxygenation process (Scheme 3D, eqn (e)). Performing the reaction in the presence of H$_2$O[18] (5 equiv.) afforded **46** in a higher ^{18}O-labeled ratio (eqn (f)). These results indicate that DMSO performs the oxygenation process *via* H$_2$O as the intermediary, and HBr is the key mediator to transfer the oxygen atom of DMSO to the product.

On the basis of the above results, a plausible mechanism was proposed (Scheme 4). Initially, HBr is oxidized by DMSO to afford H$_2$O and DMS·Br$_2$,[12a,19] which disproportionates to produce HBrO, HBr and DMS. The Br$^+$ species can oxidize thiol to afford disulfide and regenerate HBr simultaneously, which would be oxidized by DMSO again to deliver DMS·Br$_2$ or HBrO. The disulfide is further oxidized to deliver R–S(O)–S(O)–R *via* R–S(O)–S–R by HBrO.[20] As a result, HBrO serves as a direct oxidant while DMSO serves as a terminal oxidant. Next, the rearrangement of R–S(O)–S(O)–R produces R–SO$_2$–SR through a free radical process.[21] In the subsequent step, R–SO$_2$–SR undergoes
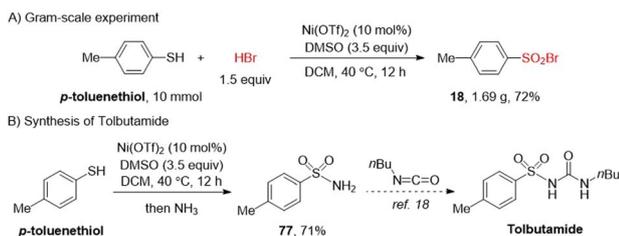
Scheme 2 Gram-scale experiment and application.
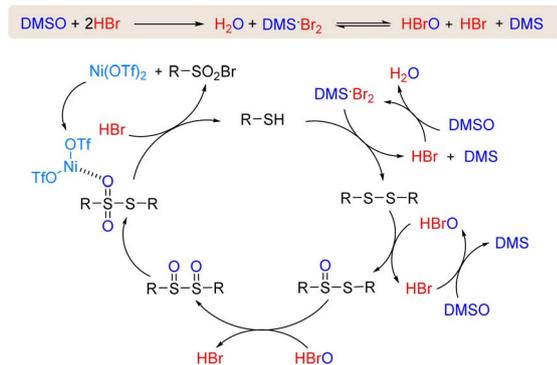
Scheme 4 Proposed mechanism.

nucleophilic attack by HBr to afford the target product sulfonyl bromide and thiol with the assistance of Ni(OTf)$_2$. The produced thiol enters a new reaction cycle to be converted to sulfonyl bromides by DMSO/HBr.

Conclusions

In summary, we describe a novel and general approach to access various sulfonyl derivatives through oxidative functionalization of thiol with DMSO and HBr. This method features mild reaction conditions, available reagents, and broad substrate scope, and thus proved useful in the synthesis of various sulfonyl derivatives. Mechanistic studies reveal that DMSO served as the terminal oxidant, and HBr acts as a nucleophile and a redox mediator to transfer the oxygen atom of DMSO.

Data availability

All of the necessary data had been included in the ESI.†

Author contributions

S. S. and H. W. conceived and designed the experiments; H. W. carried out most of experiments; S. S., H. W., Z. L., R. D. and N. J. analysed data; S. S. and H. W. wrote the paper; S. S. directed the project.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

1 (a) A. S. Barrow, C. J. Smedley, Q. Zheng, S. Li, J. Dong and J. E. Moses, *Chem. Soc. Rev.*, 2019, **48**, 4731–4758; (b) B. R. Beno, K.-S. Yeung, M. D. Bartberger, L. D. Pennington and N. A. Meanwell, *J. Med. Chem.*, 2015, **58**, 4383–4438; (c) T. S.-B. Lou and M. C. Willis, *Nat. Rev. Chem.*, 2022, **6**, 146–162; (d) A. Narayanan and L. H. Jones, *Chem. Sci.*, 2015, **6**, 2650–2659.

2 (a) X.-Q. Chu, D.-H. Ge, Y.-Y. Cui, Z.-L. Shen and C.-J. Li, *Chem. Rev.*, 2021, **121**, 12548–12680; (b) L. Kvaerno, M. Werder, H. Hauser and E. M. Carreira, *Org. Lett.*, 2005, **7**, 1145–1148; (c) S. R. Dubbaka and P. Vogel, *Angew. Chem., Int. Ed.*, 2005, **44**, 7674–7684; (d) S. R. Dubbaka and P. Vogel, *J. Am. Chem. Soc.*, 2003, **125**, 15292–15293; (e) X. Zhao, E. Dimitrijevic and V. M. Dong, *J. Am. Chem. Soc.*, 2009, **131**, 3466–3467; (f) O. Saidi, J. Marafie, A. E. W. Ledger, P. M. Liu, M. F. Mahon, G. Kociok-Koehn, M. K. Whittlesey and C. G. Frost, *J. Am. Chem. Soc.*, 2011, **133**, 19298–19301.

3 (a) K. A. Scott and J. T. Njardarson, *Top. Curr. Chem.*, 2018, **376**, 1; (b) P. Bhutani, G. Joshi, N. Raja, N. Bachhav, P. K. Rajanna, H. Bhutani, A. T. Paul and R. Kumar, *J. Med. Chem.*, 2021, **64**, 2339–2381.

4 (a) G. Qiu, K. Zhou and J. Wu, *Chem. Commun.*, 2018, **54**, 12561–12569; (b) J. A. Andrews and M. C. Willis, *Synthesis*, 2022, **54**, 1695–1707; (c) Y. Chen, P. R. D. Murray, A. T. Davies and M. C. Willis, *J. Am. Chem. Soc.*, 2018, **140**, 8781–8787; (d) V. T. Nguyen, G. C. Haug, V. D. Nguyen, N. T. H. Vuong, H. D. Arman and O. V. Larionov, *Chem. Sci.*, 2021, **12**, 6429–6436; (e) Y. Chen and M. C. Willis, *Chem. Sci.*, 2017, **8**, 3249–3253; (f) Y. Meng, M. Wang and X. Jiang, *Angew. Chem., Int. Ed.*, 2020, **59**, 1346–1353.

5 (a) S. P. Blum, K. Hofman, G. Manolikakes and S. R. Waldvogel, *Chem. Commun.*, 2021, **57**, 8236–8249; (b) S. P. Blum, T. Karakaya, D. Schollmeyer, A. Klapars and S. R. Waldvogel, *Angew. Chem., Int. Ed.*, 2021, **60**, 5056–5062; (c) S. P. Blum, D. Schollmeyer, M. Turks and S. R. Waldvogel, *Chem.–Eur. J.*, 2020, **26**, 8358–8362; (d) S. P. Blum, L. Schaffer, D. Schollmeyer and S. R. Waldvogel, *Chem. Commun.*, 2021, **57**, 4775–4778; (e) Z. Li, L. Jiao, Y. Sun, Z. He, Z. Wei and W.-W. Liao, *Angew. Chem., Int. Ed.*, 2020, **59**, 7266–7270; (f) C. Zhang, M. Yang, Y. Qiu, M. Song, H. Wang, M. Yang, W. Xie, J. Wu and S. Ye, *Chem. Sci.*, 2022, **13**, 11785–11791.

6 (a) D. Kaiser, I. Klose, R. Oost, J. Neuhaus and N. Maulide, *Chem. Rev.*, 2019, **119**, 8701–8780; (b) D.-K. Kim, H.-S. Um, H. Park, S. Kim, J. Choi and C. Lee, *Chem. Sci.*, 2020, **11**, 13071–13078; (c) Q. Zhou, A. Ruffoni, R. Gianatassio, Y. Fujiwara, E. Sella, D. Shabat and P. S. Baran, *Angew. Chem., Int. Ed.*, 2013, **52**, 3949–3952; (d) C. S. Richards-Taylor, D. C. Blackmore and M. C. Willis, *Chem. Sci.*, 2014, **5**, 222–228; (e) P. S. Fier and K. M. Maloney, *J. Am. Chem. Soc.*, 2019, **141**, 1441–1445; (f) P. S. Fier, S. Kim and K. M. Maloney, *J. Am. Chem. Soc.*, 2019, **141**, 18416–18420; (g) G. K. S. Prakash, C. Ni, F. Wang, J. Hu and G. A. Olah, *Angew. Chem., Int. Ed.*, 2011, **50**, 2559–2563; for approachs generating sulfinate salts or sulfinate radicals *in situ*, see: ; (h) M. Wang and X. Jiang, *Chem. Rec.*, 2021, **21**, 3338–3355; (i) S. Ye, M. Yang and J. Wu, *Chem. Commun.*, 2020, **56**, 4145–4155; (j) T. Liu, D. Zheng, Z. Li and J. Wu, *Adv. Synth.*

Catal., 2017, **359**, 2653–2659; (*k*) X. Marset, J. Torregrosa-Crespo, R. M. Martinez-Espinosa, G. Guillena and D. J. Ramon, *Green Chem.*, 2019, **21**, 4127–4132; (*l*) M. Magre and J. Cornella, *J. Am. Chem. Soc.*, 2021, **143**, 21497–21502; (*m*) E. J. Emmett, B. R. Hayter and M. C. Willis, *Angew. Chem., Int. Ed.*, 2014, **53**, 10204–10208; (*n*) M. W. Johnson, S. W. Bagley, N. P. Mankad, R. G. Bergman, V. Mascitti and F. D. Toste, *Angew. Chem., Int. Ed.*, 2014, **53**, 4404–4407; (*o*) A. Shavnya, K. D. Hesp, V. Mascitti and A. C. Smith, *Angew. Chem., Int. Ed.*, 2015, **54**, 13571–13575; (*p*) A. S. Deeming, C. J. Russell and M. C. Willis, *Angew. Chem., Int. Ed.*, 2016, **55**, 747–750; (*q*) T. S.-B. Lou, S. W. Bagley and M. C. Willis, *Angew. Chem., Int. Ed.*, 2019, **58**, 18859–18863; (*r*) P. K. T. Lo, Y. Chen and M. C. Willis, *ACS Catal.*, 2019, **9**, 10668–10673; (*s*) Y. Meng, M. Wang and X. Jiang, *Angew. Chem., Int. Ed.*, 2020, **59**, 1346–1353; (*t*) D. Zheng, Y. An, Z. Li and J. Wu, *Angew. Chem., Int. Ed.*, 2014, **53**, 2451–2454; (*u*) Y. Meng, M. Wang and X. Jiang, *CCS Chem.*, 2021, **3**, 17–24; (*v*) Y. Li, S. Chen, M. Wang and X. Jiang, *Angew. Chem., Int. Ed.*, 2020, **59**, 8907–8911.

7 (*a*) T. Q. Davies and M. C. Willis, *Org. Lett.*, 2020, **22**, 9495–9499; (*b*) S. M. Hell and T. Noël, *J. Am. Chem. Soc.*, 2020, **142**, 720–725; (*c*) X. Nie, T. Xu, J. Song, A. Devaraj, B. Zhang, Y. Chen and S. Liao, *Angew. Chem., Int. Ed.*, 2021, **60**, 3956–3960; (*d*) P. Wang, H. Zhang, X. Nie, T. Xu and S. Liao, *Nat. Commun.*, 2022, **13**, 3370; (*e*) P. K. T. Lo and M. C. Willis, *J. Am. Chem. Soc.*, 2021, **143**, 15576–15581; (*f*) S. M. Hell, C. F. Meyer, A. Misale, J. B. I. Sap, K. E. Christensen, M. C. Willis, A. A. Trabanco and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2020, **59**, 11620–11626; (*g*) T. Guo, G. Meng, X. Zhan, Q. Yang, T. Ma, L. Xu, K. B. Sharpless and J. Dong, *Angew. Chem., Int. Ed.*, 2018, **57**, 2605–2610; (*h*) H.-L. Qin, Q. Zheng, G. A. L. Bare, P. Wu and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2016, **55**, 14155–14158; (*i*) G. Meng, T. Guo, T. Ma, J. Zhang, Y. Shen, K. B. Sharpless and J. Dong, *Nature*, 2019, **574**, 86–89; (*j*) J. E. Erchinger, R. Hoogesteger, R. Laskar, S. Dutta, C. Hümpel, D. Rana, C. G. Daniliuc and F. Glorius, *J. Am. Chem. Soc.*, 2023, **145**, 2364–2374.

8 (*a*) S. Madabhushi, R. Jillella, V. Sriramoju and R. Singh, *Green Chem.*, 2014, **16**, 3125–3131; (*b*) X. Huang, J. Wang, Z. Ni, S. Wang and Y. Pan, *Chem. Commun.*, 2014, **50**, 4582–4584; (*c*) A. Tota, S. St John-Campbell, E. L. Briggs, G. O. Estevez, M. Afonso, L. Degennaro, R. Luisi and J. A. Bull, *Org. Lett.*, 2018, **20**, 2599–2602; (*d*) M. Zhu, W. Wei, D. Yang, H. Cui, L. Wang, G. Meng and H. Wang, *Org. Biomol. Chem.*, 2017, **15**, 4789–4793; (*e*) J.-B. Feng and X.-F. Wu, *Org. Biomol. Chem.*, 2016, **14**, 6951–6954; (*f*) M. Kirihara, S. Naito, Y. Ishizuka, H. Hanai and T. Noguchi, *Tetrahedron Lett.*, 2011, **52**, 3086–3089; (*g*) H. Veisi, R. Ghorbani-Vaghei, S. Hemmati and J. Mahmoodi, *Synlett*, 2011, **16**, 2315–2320; (*h*) C. Silva-Cuevas, C. Perez-Arrieta, L. A. Polindara-Garcia and J. Armando Lujan-Montelongo, *Tetrahedron Lett.*, 2017, **58**, 2244–2247; (*i*) K. Bahrami, M. M. Khodaei and M. Soheilizadt, *J. Org. Chem.*, 2009, **74**, 9287–9291; (*j*)

P. Vedso, P. H. Olesen and T. Hoeg-Jensen, *Synlett*, 2004, **5**, 892–894; (*k*) K. Bahrami, M. M. Khodaei and M. Soheilizad, *Synlett*, 2009, **17**, 2773–2776; (*l*) T. Okada, H. Matsumuro, T. Iwai, S. Kitagawa, K. Yamazaki, T. Akiyama, T. Asawa, Y. Sugiyama, Y. Kimura and M. Kirihara, *Chem. Lett.*, 2015, **44**, 185–187; (*m*) M. Jereb and L. Hribernik, *Green Chem.*, 2017, **19**, 2286–2295; (*n*) M. Kirihara, S. Yamahara, T. Okada, H. Matsumuro, Y. Kinoshita, A. Kitajima, Y. Takamura, T. Odagiri, T. Asawa, Y. Sugiyama and Y. Kimura, *Synthesis*, 2022, **54**, 4120–4128; (*o*) E. Hayashi, Y. Yamaguchi, Y. Kita, K. Kamata and M. Hara, *Chem. Commun.*, 2020, **56**, 2095–2098; (*p*) A. K. Singh, H. Yi, G. Zhang, C. Bian, P. Pei and A. Lei, *Synlett*, 2017, **28**, 1558–1563.

9 (*a*) G. Laudadio, E. Barmpoutsis, C. Schotten, L. Struik, S. Govaerts, D. L. Browne and T. Noël, *J. Am. Chem. Soc.*, 2019, **141**, 5664–5668; (*b*) G. Laudadio, A. d. A. Bartolomeu, L. M. H. M. Verwijlen, Y. Cao, K. T. de Oliveira and T. Noël, *J. Am. Chem. Soc.*, 2019, **141**, 11832–11836.

10 (*a*) X.-F. Wu and K. Natte, *Adv. Synth. Catal.*, 2016, **358**, 336–352; (*b*) Z. Tashrifi, M. M. Khanaposhtani, B. Larijani and M. Mahdavi, *Adv. Synth. Catal.*, 2020, **362**, 65–86.

11 (*a*) N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand and W. M. Weaver, *J. Am. Chem. Soc.*, 1957, **79**, 6562; (*b*) R. Xu, J. P. Wan, H. Mao and Y. Pan, *J. Am. Chem. Soc.*, 2010, **132**, 15531–15533; (*c*) Y. Ashikari, A. Shimizu, T. Nokami and J. Yoshida, *J. Am. Chem. Soc.*, 2013, **135**, 16070–16073; (*d*) Y. Ashikari, T. Nokami and J. Yoshida, *J. Am. Chem. Soc.*, 2011, **133**, 11840–11843; (*e*) R. N. Reddi, P. K. Prasad and A. Sudalai, *Angew. Chem., Int. Ed.*, 2015, **54**, 14150–14153; (*f*) Y.-F. Liang, X. Li, X. Wang, M. Zou, C. Tang, Y. Liang, S. Song and N. Jiao, *J. Am. Chem. Soc.*, 2016, **138**, 12271–12277; (*g*) S. Song, X. Huang, Y.-F. Liang, C. Tang, X. Li and N. Jiao, *Green Chem.*, 2015, **17**, 2727–2731; (*h*) X. Wu, Q. Gao, S. Liu and A. Wu, *Org. Lett.*, 2014, **16**, 2888–2891; (*i*) Q. Gao, X. Wu, S. Liu and A. Wu, *Org. Lett.*, 2014, **16**, 1732–1735; (*j*) N. Mupparapu, S. Khan, S. Battula, M. Kushwaha, A. P. Gupta, Q. N. Ahmed and R. A. Vishwakarma, *Org. Lett.*, 2014, **16**, 1152–1155.

12 (*a*) G. Majetich, R. Hicks and S. Reister, *J. Org. Chem.*, 1997, **62**, 4321–4326; (*b*) S. Song, X. Li, X. Sun, Y. Yuan and N. Jiao, *Green Chem.*, 2015, **17**, 3285–3289; (*c*) S. Song, X. Sun, X. Li, Y. Yuan and N. Jiao, *Org. Lett.*, 2015, **17**, 2886–2889; (*d*) M. Karki and J. Magolan, *J. Org. Chem.*, 2015, **80**, 3701–3707.

13 (*a*) S.-L. Fang, M.-X. Jiang, S. Zhang, Y.-J. Wu and B.-F. Shi, *Org. Lett.*, 2019, **21**, 4609–4613; (*b*) J.-Y. Kim, D.-H. Kim, T.-H. Jeon, W.-H. Kim and C.-G. Cho, *Org. Lett.*, 2017, **19**, 4688–4691; (*c*) D. Kamakura, H. Todoroki, D. Urabe, K. Hagiwara and M. Inoue, *Angew. Chem., Int. Ed.*, 2020, **59**, 479–486.

14 H. Liu, G.-C. He, C.-Y. Zhao, X.-X. Zhang, D.-W. Ji, Y.-C. Hu and Q.-A. Chen, *Angew. Chem., Int. Ed.*, 2021, **60**, 24284–24291.

15 (*a*) S. Song, X. Li, J. Wei, W. Wang, Y. Zhang, L. Ai, Y. Zhu, X. Shi, X. Zhang and N. Jiao, *Nat. Catal.*, 2020, **3**, 107–115; (*b*) W. Wang, X. Li, X. Yang, L. Ai, Z. Gong, N. Jiao and

S. Song, *Nat. Commun.*, 2021, **12**, 3873; (*c*) W. Wang, X. Yang, R. Dai, Z. Yan, J. Wei, X. Dou, X. Qiu, H. Zhang, C. Wang, Y. Liu, S. Song and N. Jiao, *J. Am. Chem. Soc.*, 2022, **144**, 13415–13425.

16 D. C. Blakemore, L. Castro, I. Churcher, D. C. Rees, A. W. Thomas, D. M. Wilson and A. Wood, *Nat. Chem.*, 2018, **10**, 383–394.

17 (*a*) M. N. Feinglos and H. E. Lebovitz, *Nature*, 1978, **276**, 184–185; (*b*) H. E. Lebovitz and M. N. Feinglos, *Diabetes Care*, 1978, **1**, 189–198.

18 J. Cervelló and T. Sastre, *Synthesis*, 1990, **3**, 221–222.

19 (*a*) K. Mislow, J. T. Melillo, T. Simmons and A. L. Ternay, *J. Am. Chem. Soc.*, 1964, **86**, 1452–1453; (*b*) M. B. Floyd, M. T. Du, P. F. Fabio, L. A. Jacob and B. D. Johnson, *J. Org. Chem.*, 1985, **50**, 5022–5027.

20 (*a*) M. M. Chau and J. L. Kice, *J. Am. Chem. Soc.*, 1976, **98**, 7711–7716; (*b*) S. Oae, Y. H. Kim, T. Takata and D. Fukushima, *Tetrahedron Lett.*, 1977, **13**, 1995–1998.

21 F. Freeman, *Chem. Rev.*, 1984, **84**, 117–135.