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A Selectfluor-promoted oxidative reaction of disulfides and amines: access to sulfinamides†

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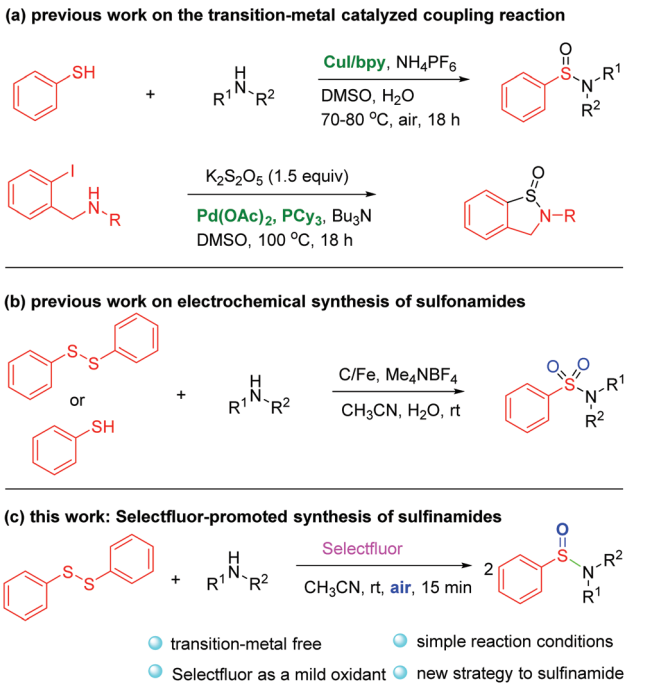
An unprecedented transition-metal-free oxidative reaction of disulfides and amines with Selectfluor as a mild oxidant under aerobic conditions was developed. This reaction was conducted under mild conditions and tolerated a wide range of coupling partners including disulfides and amines, affording the corresponding sulfinamide products in good chemical yields. Furthermore, this reaction could be used in gram-scale synthesis. This reaction enriches the research content of Selectfluor and provides a valuable vista for the convenient synthesis of sulfinamides.

Introduction

Sulfinamides belong to an important class of organosulfur compounds in drug research due to their fascinating role in the design of bioactive molecules and new pharmaceuticals.[1] Also, sulfinamides exist widely in N–S bond-containing natural products.[2] Furthermore, sulfinamides represent a valuable synthetic block in organic synthesis for the construction of drugs and natural products,[3] such as the anti-HIV drug maraviroc[4] and the natural product (−)-vindoline.[5] On the other hand, chiral sulfinamides play unique roles in asymmetric synthesis, and they can be used as chiral ligands or organocatalysts in asymmetric catalysis, and as chiral auxiliaries in the synthesis of chiral nitrogen-containing skeletons.[6–8] Therefore, the development of new methods for the preparation of sulfinamides is in great demand.

The traditional method for the synthesis of sulfonamides is well developed by the condensation reaction of sulfonyl chlorides and amines. In contrast, the N–S bond formation for the preparation of sulfinamides remains much less explored. The reaction between sulfonyl chlorides and amines has been reported for the synthesis of sulfinamides.[9] However, this reaction requires the use of triphenylphosphine as a reductant and has the disadvantage of the formation of sulfonamides as the by-product. In recent years, the Taniguchi group developed a transition-metal-catalyzed oxidative coupling reaction between thiols or disulfides with amines in the presence of NH_4PF_6 under air to afford sulfinamides as the product (Scheme 1a).[10] On the other hand, the Pd-catalyzed reactions of amino-substituted iodoarenes have also been developed for the synthesis of sulfinamides with $K_2S_2O_5$ as a sulfur dioxide surrogate (Scheme 1a).[11] Despite the fact that some progress has been



Scheme 1 Synthesis of sulfinamides and sulfonamides.

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made in the synthesis of sulfinamides, the development/design of highly efficient new synthetic procedures, especially from inexpensive and commercially available reagents, still remains a great challenge.[12]

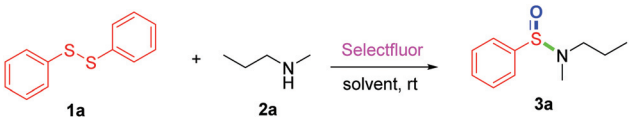
Selectfluor is a safe, commercially available, and highly reactive compound,[13] which has been widely used as an efficient electrophilic fluorinating reagent[14] and a mild chemical oxidant.[15] Notably, the synthesis of functionalized heterocyclic compounds has been achieved successfully using Selectfluor as a mild oxidant.[16] On the other hand, Selectfluor has been used in the synthesis of thiosulfonates *via* oxidation of disulfides.[17] Very recently, the Noël group reported an elegant work on the electrochemical reaction between thiols and amines, which afforded sulfonamides as the product (Scheme 1b).[18] However, to the best of our knowledge, oxidation of easily available thiols or disulfides using Selectfluor to obtain sulfinamides has never been explored to date. Herein, we report an unprecedented one-pot oxidative reaction of disulfides and amines promoted by Selectfluor under aerobic conditions (Scheme 1c). Furthermore, this process demonstrates a new oxidative transformation reaction of disulfides and also provides a new strategy for the synthesis of sulfinamides.

Results and discussion

Initially, we started our investigation of the conditions for this envisioned oxidative reaction between 1,2-diphenyldisulfide (**1a**) and methylpropylamine (**2a**) (Table 1). It was pleasing to note that the reaction could proceed at room temperature and the desired sulfinamide product **3a** was obtained in 65% isolated yield with 4.0 equiv. of Selectfluor as an oxidant and acetonitrile as a solvent under air after 30 min (entry 1). Subsequently, the loading amount of Selectfluor was varied to improve the reaction yield. No improvement was observed upon switching the amount of Selectfluor from 4.0 equiv. to 3.0 or 5.0 equiv. (entries 2 and 3). When the reaction was stopped at 15 min, the yield increased to 75% (entry 4). However, the yield decreased markedly to 52% when the reaction was prolonged to 60 min (entry 5), which is mainly because of the over oxidation of product **3a** by Selectfluor. On the other hand, the loading amount of amine **2a** was found to be crucial for this reaction, and decreasing the amount of amine **2a** to 5 equiv. led to a poor yield of product **3a** (23%, entry 6). Solvents were found to be important for this transformation, as evidenced by almost no desired product obtained when using THF or CH_2Cl_2 as the reaction medium (0% yield, entries 7 and 8). It should be mentioned that almost all the starting disulfide **1a** remained in these two reactions. Further evaluation of the reaction conditions showed that the reaction could not proceed without the use of Selectfluor as an oxidant, and no desired product was observed when the reaction was conducted under a nitrogen atmosphere (entries 9 and 10).

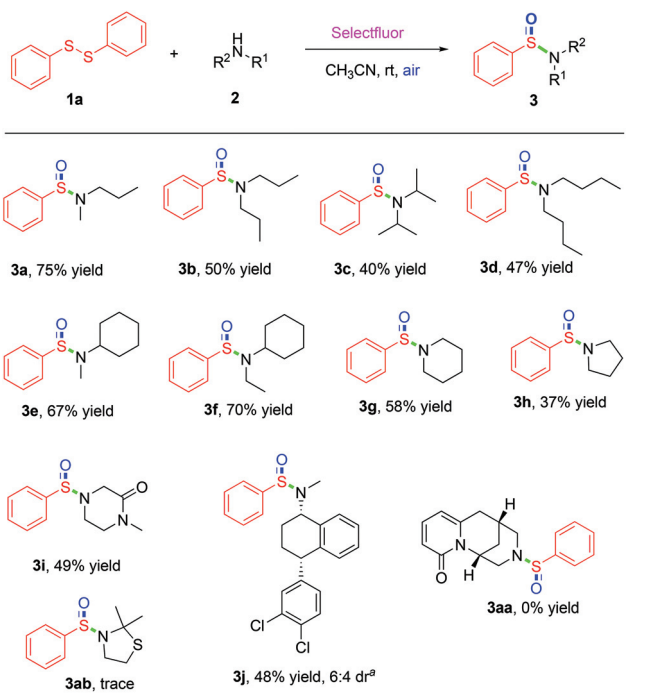
Then, the substrate generality of this Selectfluor-promoted oxidative reaction of diphenyl disulfide (**1a**) with various amines was explored under the optimized reaction conditions (Scheme 2).

Table 1 Optimization of reaction conditions[a]



Entry	2a (equiv.)	Solvent	Selectfluor (equiv.)	Time (min)	Yield[b] (%)
1	10	CH_3CN	4.0	30	65
2	10	CH_3CN	5.0	30	32
3	10	CH_3CN	3.0	30	53
4	10	CH_3CN	4.0	15	75
5	10	CH_3CN	4.0	60	52
6	5	CH_3CN	4.0	15	23
7	10	THF	4.0	15	0
8	10	CH_2Cl_2	4.0	15	0
9	10	CH_3CN	0	15	nr[c]
10[d]	10	CH_3CN	4.0	15	0

[a] Reaction conditions: Diphenyl disulfide (0.2 mmol), Selectfluor and solvent (3 mL) were stirred at room temperature for 5 minutes. Then, amine **2a** in CH_3CN (2 mL) was added to the mixture over 30 minutes and stirred at room temperature. [b] Isolated yield. [c] No reaction. [d] Under nitrogen.



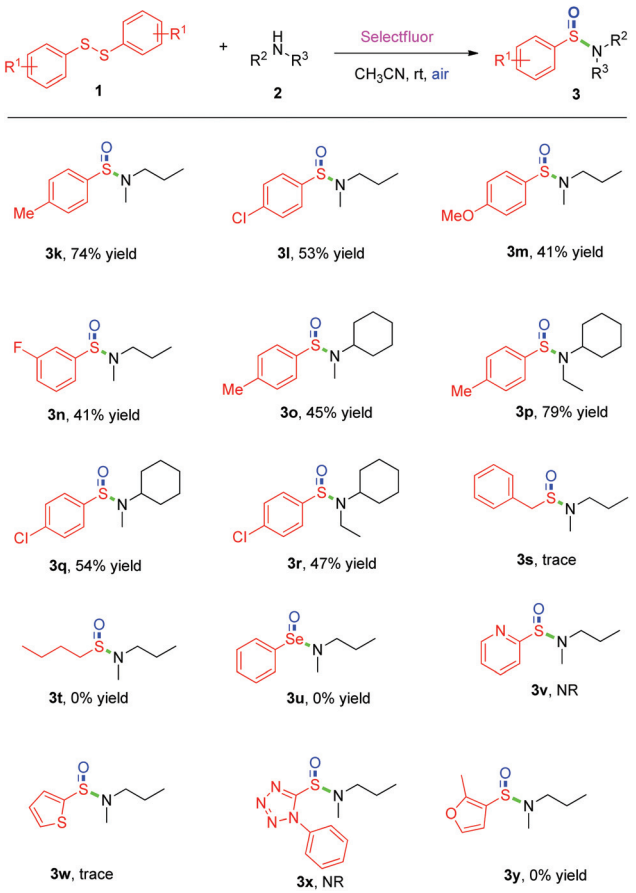
Scheme 2 Substrate study with variation of amine **2**. Reaction conditions: Diphenyl disulfide (**1a**) (0.2 mmol) and Selectfluor (4.0 equiv.) in acetonitrile (3 mL) were stirred at room temperature for 5 minutes. Then, amine **2** (10 equiv.) in CH_3CN (2 mL) was added to the mixture over 30 minutes and stirred for an additional 15 minutes. Isolated yields. [a] Determined by ^1H NMR.

Amines with different alkyl chains were well tolerated in this reaction, leading to the formation of the corresponding sulfinamides in moderate to good chemical yields (40–75%, **3a–d**). Extending the length of the alkyl chains on amines showed an obvious effect on the reaction performance. *N*-Methyl-substituted sulfinamide (**3a**) was obtained in the best yield (75%), while only 47% yield (**3d**) was obtained when dibutylamine was used as the substrate. Then, amines with cycloalkyl substituents on the nitrogen atom were used for this reaction. Fortunately, these amines performed equally well in this reaction, and the desired products **3e** and **3f** were obtained in good yields (67 and 71%, respectively). Besides linear amines, cyclic amines, including piperidines and pyrrolidines, were also suitable substrates, which reacted smoothly with disulfides to furnish the corresponding products **3g** and **3h** in 58 and 37% yields, respectively. To further demonstrate the utility of this Selectfluor-promoted oxidative coupling reaction, we used bioactive amines as substrates for this reaction. For example, 1-methyl-piperazin-2-one could react well with diphenyl disulfide (**1a**) under the standard conditions, giving the expected sulfonamide **3i** in 49% yield. Furthermore, an antidepressant drug, sertraline hydrochloride, was also employed in this reaction, which provided the desired product **3j** in 46% yield with 60 : 40 diastereoselectivity. Other amines, including 2,2-dimethylthiazolidine and cytisine, were examined in this system, which were demonstrated to be unsuitable substrates.

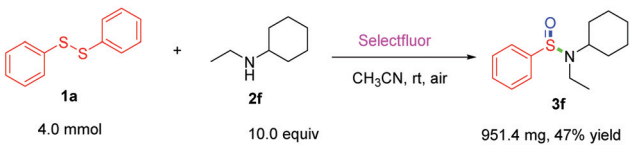
To further probe the applicability of this oxidative reaction, the coupling reaction of a series of substituted diaryl disulfides **1** with *N*-methylpropylamine (**2a**) was carried out under the standard reaction conditions (Scheme 3).

We found that the reactions of disulfide substrates bearing electron-donating groups (methyl and methoxyl) or electron-withdrawing groups (chloro and fluoro) could all proceed smoothly, resulting in the formation of the corresponding sulfinamides **3** in good yields (41–74%, **3k–3n**). Notably, methyl- and chloro-substituted diphenyl sulfides could also participate well in the reaction with *N*-cycloalkyl amines to form the desired products in 47–79% yields (**3o–3r**). In the cases of dibenzyl disulfide and dibutyl disulfide, the reaction did not occur and almost no desired products **3s** and **3t** were obtained, which is presumably due to the instability of the cation intermediate. We also used 1,2-diphenyldiselane as the substrate for this reaction. However, no desired product **3u** was obtained with the starting material used. Finally, several diheteroaryl disulfides were examined in this system. Unfortunately, almost no desired products (**3v–3y**) were detected. It should be mentioned that these pure sulfinamide products are not very stable when they are stored in a flask at room temperature.

In order to further demonstrate the scale applicability of this newly explored oxidative reaction, we conducted the reaction of disulfide **1a** and *N*-ethylcyclohexanamine (**2f**) on a gram scale under the optimized reaction conditions. The formation of sulfonamide **3f** in 47% yield (951.4 mg) from this large-scale synthesis was observed, which discloses the practical application of the current system (Scheme 4).

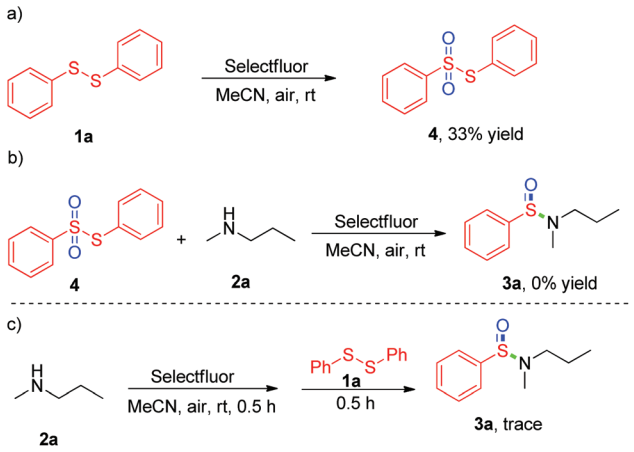


Scheme 3 Substrate study with variation of disulfide **1**. Reaction conditions: Disulfide **1** (0.2 mmol) and Selectfluor (4.0 equiv.) in acetonitrile (3 mL) were stirred at room temperature for 5 minutes. Then, amine **2** (10 equiv.) in CH_3CN (2 mL) was added to the mixture over 30 minutes and stirred at room temperature for an additional 15 minutes. Isolated yield.



Scheme 4 Large-scale synthesis.

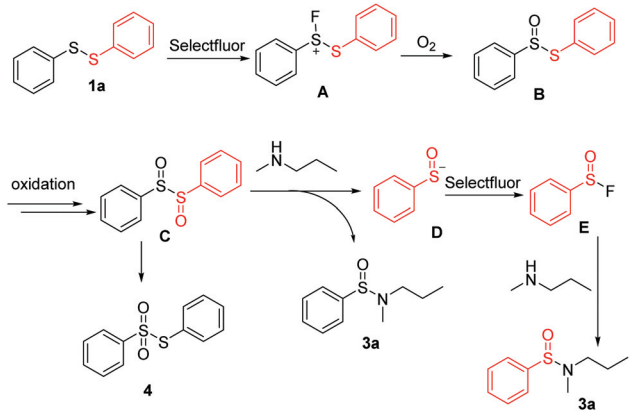
To gain insight into this oxidative reaction, a mixture of diphenyl disulfide (**1a**) and Selectfluor in acetonitrile was stirred at room temperature for 30 minutes under air. After careful isolation of the reaction mixture, *S*-phenyl benzenesulfonothioate (**4**) was obtained in 33% yield (Scheme 5a). Then, we used it as the starting material to perform the reaction under the standard reaction conditions. However, no reaction occurred and no desired product **3a** was obtained (Scheme 5b). Thus, compound **4** may not be the intermediate or the captured intermediate of this oxidative coupling procedure. On the other hand, Selectfluor and amine **2a** were stirred in acetonitrile for 30 min, followed by the addition of disulfide **1a**.



Scheme 5 Control experiments.

Almost no desired sulfinamide **3a** was obtained (Scheme 5c). In addition, the oxidative reaction process was detected by ^{19}F NMR, which indicated that a fluorine-containing intermediate[17] was formed in the initial step and disappeared along with the formation of product **3a** (see the ESI†).

On the basis of the above experimental results and previous reports,[17–19] an oxidative cross-coupling pathway *via* a disulfoxide intermediate was proposed for this reaction (Scheme 6). Initially, the reaction between Selectfluor and diphenyl disulfide (**1a**) affords the active sulfonium intermediate **A**,[17] which undergoes the oxidation reaction with oxygen to give thiosulfinate (**B**).[18,19] Thiosulfinate (**B**) is subsequently oxidized into an unstable disulfoxide (**C**) *via* a similar two-step process. The formation of the by-product thiosulfonate **4** is probably due to the rearrangement of the unstable disulfoxide (**C**).[17] Then, the substitution reaction of disulfoxide (**C**) with amine occurs to form the final product **3a** and intermediate **D**. Intermediate **D** reacts with Selectfluor to give benzenesulfinic fluoride (**E**), which finally reacts with amine to afford product **3a** again. It should be mentioned that the pathway including the initial generation of *N*-fluoro amine, reaction with disulfide to generate phenyl sulfamate (PhSNHR) and subsequent oxidation to give the corresponding sulfinamide may not be possible for the current reaction.[20]



Scheme 6 Possible mechanism.

Experimental section

General information

All the commercial reagents including solvents were used directly without further purification. All the experiments were monitored by thin layer chromatography (TLC) with UV light using 0.25 mm silica gel coated on glass plates. Column chromatography was performed with silica gel 60 (300–400 mesh). NMR spectra were recorded using Bruker 600 MHz and 400 MHz spectrometers. High-resolution mass spectra (HRMS) were recorded using an Agilent 6210 ESI/TOF MS instrument.

Typical procedure of the reaction of disulfides and amines

Into a 10 mL vial were taken disulfide **1** (0.2 mmol), Selectfluor (4 equiv.) and acetonitrile (3 mL). The mixture was stirred at room temperature for 5 minutes. Then, amine **2** (10 equiv.) dissolved in acetonitrile (2 mL) was added dropwise within 30 minutes. After stirring for another 15 minutes, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography using hexane/EtOAc (4 : 1, v/v) as an eluent to afford the desired product **3**.

Compound 3a. Colorless oil, 75% yield. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.67–7.65 (m, 2H), 7.52–7.48 (m, 3H), 3.19–3.14 (m, 1H), 3.07–3.02 (m, 1H), 3.27 (s, 3H), 1.67–1.59 (m, 2H), 0.94 (t, J = 7.35 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 144.0, 130.7, 128.8, 126.2, 54.3, 32.3, 21.4, 11.3. HRMS (ESI): calculated for $C_{10}H_{15}NNaOS^+$ $[M + Na]^+$ 220.0767, found 220.0769.

Compound 3b. Colorless oil, 50% yield. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.67–7.65 (m, 2H), 7.50–7.44 (m, 3H), 3.03–2.95 (m, 4H), 1.61–1.55 (m, 2H), 1.50–1.44 (m, 2H), 0.82 (t, J = 7.38 Hz, 6H). HRMS (ESI): calculated for $C_{12}H_{19}NNaOS^+$ $[M + Na]^+$ 248.1080, found 248.1083.

Compound 3c. Colorless oil, 40% yield. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.67–7.65 (m, 2H), 7.50–7.47 (m, 2H), 7.45–7.43 (m, 1H), 3.60–3.53 (m, 2H), 1.42 (d, J = 6.72 Hz, 6H), 1.13 (d, J = 6.84 Hz, 6H). HRMS (ESI): calculated for $C_{12}H_{19}NNaOS^+$ $[M + Na]^+$ 248.1080, found 248.1084.

Compound 3d. Colorless oil, 47% yield. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.67–7.66 (m, 2H), 7.51–7.45 (m, 3H), 3.05 (t, J = 7.59 Hz, 4H), 1.58–1.51 (m, 2H), 1.47–1.39 (m, 2H), 1.29–1.19 (m, 4H), 0.85 (t, J = 7.41 Hz, 6H). HRMS (ESI): calculated for $C_{14}H_{23}NNaOS^+$ $[M + Na]^+$ 276.1393, found 276.1397.

Compound 3e. Colorless oil, 67% yield. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.63–7.62 (m, 2H), 7.49–7.43 (m, 3H), 3.29–3.23 (m, 1H), 2.40 (s, 3H), 2.04–2.00 (m, 1H), 1.97–1.94 (m, 1H), 1.87–1.80 (m, 2H), 1.66–1.63 (m, 1H), 1.62–1.50 (m, 2H), 1.37–1.27 (m, 2H), 1.16–1.08 (m, 1H). HRMS (ESI): calculated for $C_{13}H_{19}NNaOS^+$ $[M + Na]^+$ 260.1080, found 260.1082.

Compound 3f. Colorless oil, 70% yield. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.65–7.64 (m, 2H), 7.47–7.42 (m, 3H), 3.12–3.07 (m, 2H), 2.92–2.86 (m, 1H), 2.15–2.11 (m, 1H), 1.84–1.78 (m, 3H),

1.66–1.57 (m, 3H), 1.29–1.22 (m, 2H), 1.16–1.09 (m, 1H), 0.89 (t, J = 7.14 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 144.7, 130.3, 128.5, 126.4, 59.8, 37.9, 33.7, 33.2, 26.3, 26.2, 25.6, 15.8. HRMS (ESI): calculated for $C_{14}H_{21}NNaOS^+$ $[M + Na]^+$ 274.1236, found 274.1239.

Compound 3g. White solid, 58% yield, mp 78–79 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.67–7.66 (m, 2H), 7.51–7.47 (m, 3H), 3.14–3.10 (m, 2H), 2.98–2.94 (m, 2H), 1.66–1.57 (m, 4H), 1.55–1.51 (m, 2H). HRMS (ESI): calculated for $C_{11}H_{15}NNaOS^+$ $[M + Na]^+$ 232.0767, found 232.0770.

Compound 3h. Colorless oil, 37% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.69–7.67 (m, 2H), 7.50–7.45 (m, 3H), 3.37–3.33 (m, 2H), 3.03–2.99 (m, 2H), 1.87–1.84 (m, 4H). HRMS (ESI): calculated for $C_{10}H_{13}NNaOS^+$ $[M + Na]^+$ 218.0610, found 218.0614.

Compound 3i. Colorless oil, 49% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.65–7.63 (m, 2H), 7.52–7.50 (m, 3H), 3.76 (d, J = 16.8 Hz, 1H), 3.52–3.45 (m, 2H), 3.38–3.32 (m, 3H), 2.95 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.3, 141.7, 131.5, 129.1, 125.9, 48.9, 46.6, 44.7, 34.2. HRMS (ESI): calculated for $C_{11}H_{14}N_2NaO_2S^+$ $[M + Na]^+$ 261.0668, found 261.0670.

Compound 3j. Colorless oil, 48% yield (dr = 3 : 2). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.80–7.78 (m, 0.8H), 7.73–7.72 (m, 1.8H), 7.69–7.67 (m, 0.4H), 7.58–7.47 (m, 3H), 7.36–7.32 (m, 2H), 7.24–7.20 (m, 1H), 7.14–7.13 (m, 0.6H), 7.09–7.08 (m, 0.4H), 6.97–6.94 (m, 1H), 6.87–6.85 (m, 0.6H), 6.84–6.82 (m, 0.4H), 4.91–4.88 (m, 0.4H), 4.85–4.83 (m, 0.6H), 4.18–4.12 (m, 1H), 2.42 (s, 1.8H), 2.39 (m, 1.2H), 2.31–2.21 (m, 1H), 2.16–2.07 (m, 1H), 2.04–1.89 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 146.9, 146.8, 144.2, 144.1, 138.6, 138.5, 136.1, 135.8, 132.3, 132.2, 130.9, 130.8, 130.73, 130.70, 130.6, 130.5, 130.2, 130.1, 129.1, 129.0, 128.9, 128.4, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4, 126.2, 126.1, 61.9, 61.7, 60.4, 43.4, 43.2, 29.9, 29.8, 28.0, 27.1, 24.3, 23.4, 14.2. HRMS (ESI): calculated for $C_{23}H_{21}Cl_2NNaOS^+$ $[M + Na]^+$ 452.0613, found 452.0615.

Compound 3k. Colorless oil, 74% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.53–7.51 (m, 2H), 7.30–7.28 (m, 2H), 3.15–3.11 (m, 1H), 3.04–2.99 (m, 1H), 2.50 (s, 3H), 2.40 (s, 3H), 1.66–1.56 (m, 2H), 0.92 (t, J = 7.38 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 141.0, 140.9, 129.4, 126.1, 54.1, 32.2, 21.4, 21.3, 11.3. HRMS (ESI): calculated for $C_{11}H_{17}NNaOS^+$ $[M + Na]^+$ 234.0923, found 234.0925.

Compound 3l. Colorless oil, 53% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.60–7.57 (m, 2H), 7.48–7.46 (m, 2H), 3.16–3.12 (m, 1H), 3.05–3.00 (m, 1H), 2.52 (s, 3H), 1.67–1.57 (m, 2H), 0.93 (t, J = 7.38 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 142.6, 137.0, 129.0, 127.6, 54.3, 32.3, 21.4, 11.3. HRMS (ESI): calculated for $C_{10}H_{14}ClNNaOS^+$ $[M + Na]^+$ 254.0377, found 254.0381.

Compound 3m. Colorless oil, 41% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57–7.54 (m, 2H), 7.01–6.98 (m, 2H), 3.85 (s, 3H), 3.14–3.09 (m, 1H), 3.03–2.98 (m, 1H), 2.50 (s, 3H), 1.65–1.56 (m, 2H), 0.92 (t, J = 7.38 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.6, 135.3, 127.7, 114.2, 55.5, 53.9, 32.1, 21.4, 11.3. HRMS (ESI): calculated for $C_{11}H_{18}NO_2S^+$ $[M + H]^+$ 228.1053, found 228.1056.

Compound 3n. Colorless oil, 41% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.49–7.46 (m, 1H), 7.44–7.42 (m, 1H), 7.39–7.37 (m, 1H), 7.18–7.14 (m, 1H), 3.18–3.13 (m, 1H), 3.06–3.01 (m, 1H), 2.53 (s, 3H), 1.67–1.60 (m, 2H), 0.93 (t, J = 7.38 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 163.7 (d, J = 249.3 Hz), 146.8 (d, J = 5.8 Hz), 130.4 (d, J = 7.7 Hz), 121.9 (d, J = 3.4 Hz), 117.9 (d, J = 21.4 Hz), 113.5 (d, J = 23.6 Hz), 54.4, 32.4, 21.4, 11.3. ^{19}F NMR (565 MHz, $CDCl_3$): δ = −110.9. HRMS (ESI): calculated for $C_{10}H_{14}FNNaOS^+$ $[M + Na]^+$ 238.0672, found 238.0675.

Compound 3o. Colorless oil, 45% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.51 (d, J = 8.28 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 3.28–3.23 (m, 1H), 2.40 (s, 6H), 2.03–2.00 (m, 1H), 1.97–1.94 (m, 1H), 1.87–1.80 (m, 2H), 1.67–1.63 (m, 1H), 1.62–1.50 (m, 2H), 1.37–1.28 (m, 2H), 1.16–1.09 (m, 1H). HRMS (ESI): calculated for $C_{14}H_{21}NNaOS^+$ $[M + Na]^+$ 274.1236, found 274.1239.

Compound 3p. Colorless oil, 79% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.53 (d, J = 8.16 Hz, 2H), 7.26 (d, J = 7.92 Hz, 2H), 3.12–3.05 (m, 2H), 2.92–2.86 (m, 1H), 2.39 (s, 3H), 2.14–2.11 (m, 1H), 1.84–1.78 (m, 3H), 1.66–1.55 (m, 3H), 1.29–1.22 (m, 2H), 1.17–1.09 (m, 1H), 0.91 (t, J = 7.17 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 141.5, 140.5, 129.3, 126.4, 59.7, 37.8, 33.7, 33.3, 26.3, 26.2, 25.6, 21.3, 15.8. HRMS (ESI): calculated for $C_{15}H_{23}NNaOS^+$ $[M + Na]^+$ 288.1393, found 288.1395.

Compound 3q. White solid, 54% yield, mp 59–60 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57–7.55 (m, 2H), 7.46–7.44 (m, 2H), 3.27–3.22 (m, 1H), 2.40 (s, 3H), 2.02–1.99 (m, 1H), 1.95–1.92 (m, 1H), 1.87–1.80 (m, 2H), 1.67–1.63 (m, 1H), 1.61–1.49 (m, 2H), 1.36–1.27 (m, 2H), 1.16–1.08 (m, 1H). HRMS (ESI): calculated for $C_{13}H_{18}ClNNaOS^+$ $[M + Na]^+$ 294.0690, found 294.0693.

Compound 3r. Colorless oil, 47% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.60–7.58 (m, 2H), 7.46–7.43 (m, 2H), 3.12–3.05 (m, 2H), 2.94–2.88 (m, 1H), 2.15–2.11 (m, 1H), 1.86–1.80 (m, 3H), 1.66–1.55 (m, 3H), 1.31–1.23 (m, 2H), 1.18–1.12 (m, 1H), 0.93 (t, J = 7.17 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 143.3, 136.6, 128.8, 127.9, 59.8, 38.0, 33.7, 33.2, 26.2, 26.1, 25.5, 15.8. HRMS (ESI): calculated for $C_{18}H_{20}ClNNaOS^+$ $[M + Na]^+$ 308.0846, found 308.0847.

Compound 4. Yellow oil, 33% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.56 (m, 3H), 7.50–7.46 (m, 1H), 7.45–7.41 (m, 2H), 7.37–7.32 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.9, 136.6, 133.8, 131.5, 129.5, 128.9, 127.8, 127.6. HRMS (ESI): calculated for $C_{12}H_{11}O_2S_2^+$ $[M + H]^+$ 251.0195, found 251.0196.

Conclusions

In summary, we have developed a new two-fold coupling reaction of disulfides and amines with Selectfluor as a mild oxidant. The reaction was carried out under mild conditions and tolerated a wide range of amine substrates, resulting in the formation of sulfinamides in good yields. This reaction does not require any metal catalyst and uses easily available reagents as starting materials, and provides a new and efficient strategy for the preparation of sulfinamides.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (*a*) M. Frings, C. Bolm, A. Blum and C. Gnamm, *Eur. J. Med. Chem.*, 2017, **126**, 225–245; (*b*) J. Uetrecht, *Drug Metab. Rev.*, 2002, **34**, 651–665; (*c*) G. R. Revankar, N. B. Hanna, N. Imamura, A. F. Lewis, S. B. Larson, R. A. Finch, T. L. Avery and R. K. Robins, *J. Med. Chem.*, 1990, **33**, 121–128; (*d*) H. Mei, J. Han, S. Fustero, M. Medio-Simon, D. M. Sedgwick, C. Santi, R. Ruzziconi and V. A. Soloshonok, *Chem. – Eur. J.*, 2018, **25**, 11797–11819; (*e*) T. L. Avery, R. A. Finch, K. M. Vasquez, S. Radparvar, N. B. Hanna, G. R. Revankar and R. K. Robins, *Cancer Res.*, 1990, **50**, 2625–2630.

2 J. J. Petkowski, W. Bains and S. Seager, *J. Nat. Prod.*, 2018, **81**, 423–446.

3 U. Lücking, *Org. Chem. Front.*, 2019, **6**, 1319–1324.

4 Y. Zhu, H. Li, K. Lin, B. Wang and W. Zhou, *Synth. Commun.*, 2019, **49**, 1721–1728.

5 W. Chen, H. Tian, W. Tan, X. Liu, X. Yang and H. Zhang, *Tetrahedron*, 2019, **75**, 1751–1759.

6 (*a*) X. Su, W. Zhou, Y. Li and J. Zhang, *Angew. Chem., Int. Ed.*, 2015, **54**, 6874–6877; (*b*) H. Mei, J. L. Han, S. Fustero, R. Román, R. Ruzziconi and V. A. Soloshonok, *J. Fluorine Chem.*, 2018, **216**, 57–70; (*c*) F. A. Davis, *J. Org. Chem.*, 2006, **71**, 8993–9003.

7 M. T. Robak, M. A. Herbag and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 3600–3740.

8 (*a*) F. A. Davis, R. E. Reddy, J. M. Szewczyk, G. V. Reddy, P. S. Portonovo, H. Zhang, D. Fanelli, P. Zhou and P. J. Carroll, *J. Org. Chem.*, 1997, **62**, 2555–2563; (*b*) F. A. Davis, Y. Zhang, Y. Andemichael, T. Fang, D. L. Fanelli and H. Zhang, *J. Org. Chem.*, 1999, **64**, 1403–1406.

9 M. Harmata, P. Zheng, C. Huang, M. G. Gomes, W. Ying, K. O. Ranyanil, G. Balan and N. L. Calkins, *J. Org. Chem.*, 2007, **72**, 683–685.

10 (*a*) N. Taniguchi, *Eur. J. Org. Chem.*, 2016, 2157–2162; (*b*) N. Taniguchi, *Eur. J. Org. Chem.*, 2010, 2670–2673.

11 H. Konishi, H. Tanaka and K. Manabe, *Org. Lett.*, 2017, **19**, 1578–1581.

12 (*a*) Q. Dai and J. Zhang, *Adv. Synth. Catal.*, 2018, **360**, 1123–1127; (*b*) L. J. Ma, S. S. Chen, G. X. Li, J. Zhu, Q. W. Wang and Z. Tang, *ACS Catal.*, 2019, **9**, 1525–1530; (*c*) G. J. Li, Y. L. Pan, Y. L. Liu, H. F. Xu and J. Z. Chen, *Tetrahedron Lett.*, 2019, **60**, 151260; (*d*) E. Wenschuh, W. Günther and K. Plewinski, *Adv. Synth. Catal.*, 1977, **319**, 297–304.

13 P. T. Nyffeler, S. G. Durón, M. D. Burkart, S. P. Vincent and C. H. Wong, *Angew. Chem., Int. Ed.*, 2005, **44**, 192–212.

14 (*a*) H. G. Cheng and G. Yin, *Chem*, 2019, **5**, 1022–1024; (*b*) R. Szpera, D. F. J. Moseley, L. B. Smith, A. J. Sterling and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2019, **58**, 14824–14848; (*c*) S. H. Wood, S. Etridge, A. R. Kennedy, J. M. Percy and D. J. Nelson, *Chem. – Eur. J.*, 2019, **25**, 5574–5585; (*d*) K. K. Laali and G. I. Borodkin, *J. Chem. Soc., Perkin Trans. 2*, 2002, 953–957; (*e*) N. Shibata, E. Suzuki and Y. Takeuchi, *J. Am. Chem. Soc.*, 2000, **122**, 10728–10729; (*f*) N. Shibata, E. Suzuki, T. Asahi and M. Shiro, *J. Am. Chem. Soc.*, 2001, **123**, 7001–7009.

15 For selected examples, see: (*a*) L. Y. Xie, S. Peng, F. Liu, J. Y. Yi, M. Wang, Z. Tang, X. Xu and W. M. He, *Adv. Synth. Catal.*, 2018, **360**, 4259–4264; (*b*) J. Zhou, Y. Zou, P. Zhou, Z. Chen and J. Li, *Org. Chem. Front.*, 2019, **6**, 1594–1598; (*c*) J. D. Galloway, D. N. Mai and R. D. Baxter, *Org. Lett.*, 2017, **19**, 5772–5775; (*d*) C. X. Wang, J. W. Cai, M. Zhang and X. M. Zhao, *J. Org. Chem.*, 2017, **82**, 1260–1265; (*e*) G. Zhou, Y. W. Tian, X. M. Zhao and W. Y. Dan, *Org. Lett.*, 2018, **20**, 4858–4861; (*f*) J. Hu, G. Zhou, Y. Tian and X. Zhao, *Org. Biomol. Chem.*, 2019, **17**, 6342–6345.

16 (*a*) L. Niu, J. Liu, X. A. Liang, S. Wang and A. Lei, *Nat. Commun.*, 2019, **10**, 467; (*b*) X. A. Liang, L. Niu, S. Wang, J. Liu and A. Lei, *Org. Lett.*, 2019, **21**, 2441; (*c*) J. W. Yuan, J. L. Zhu, B. Li, L. Y. Yang, P. Mao, S. R. Zhang, Y. C. Li and L. B. Qu, *Org. Biomol. Chem.*, 2019, **17**, 10178–10187; (*d*) J. S. Yadav, B. V. S. Reddy and Y. J. Reddy, *Tetrahedron Lett.*, 2007, **48**, 7034–7037; (*e*) J. Yuan, F. Zeng, W. Mai, L. Yang, Y. Xiao, P. Mao and D. Wei, *Org. Biomol. Chem.*, 2019, **17**, 5038–5046; (*f*) W. P. Mai, J. W. Yuan, J. L. Zhu, Q. Q. Li, L. R. Yang, Y. M. Xiao, P. Mao and L. B. Qu, *ChemistrySelect*, 2019, **4**, 11066–11070.

17 M. Kirihara, S. Naito, Y. Ishizuka, H. Hanai and T. Noguchi, *Tetrahedron Lett.*, 2011, **52**, 3086–3089.

18 G. Laudadio, E. Barmpoutsis, C. Schotten, L. Struik, S. Govaerts, D. L. Browne and T. Noël, *J. Am. Chem. Soc.*, 2019, **141**, 5664–5668.

19 C. Ai, H. Shen, D. Song, Y. Li, X. Yi, Z. Wang, F. Ling and W. Zhong, *Green Chem.*, 2019, **21**, 5528–5531.

20 (*a*) R. P. Singh and J. M. Shreeve, *Chem. Commun.*, 2001, 1196–1197; (*b*) M. S. Chauhan, G. D. Yadav, F. Hussain and S. Singh, *Catal. Sci. Technol.*, 2014, **4**, 3945–3952; (*c*) O. Carmona, R. Greenhouse, R. Landeros and J. M. Muchowski, *J. Org. Chem.*, 1980, **45**, 5336–5339.

