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Note

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Copper-catalyzed TBHP-mediated radical cross-coupling reaction of sulfonylhydrazides with thiols leading to thiosulfonates

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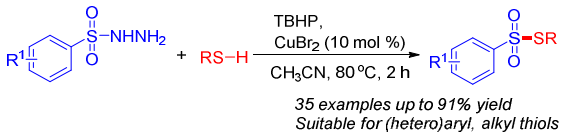


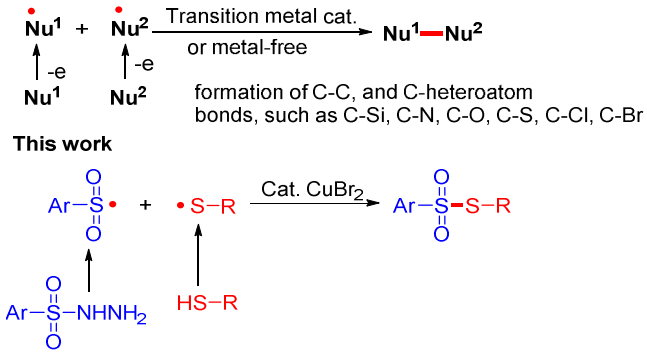
ABSTRACT: A *tert*-butyl hydroperoxide (TBHP)–mediated coupling of sulfonylhydrazides with thiols catalyzed by $CuBr_2$ to afford thiosulfonates *via* a radical process is described.

Oxidative radical cross-coupling reactions are becoming increasingly important for the construction of carbon-carbon and carbon-heteroatom bonds (Scheme 1).[1, 2] Most common types of organic reactions involving free radicals have so far been well studied and understood.[3] In contrast, the oxidative radical cross-coupling reaction still remains underdeveloped due to the issue of poor selectivity caused by the inherent activity of radicals. Therefore, the challenge is how to conduct these reactions in a highly efficient and selective manner.[1c, 1e] In general terms, only the radical coupling between a persistent radical (long-lived) and a transient radical would lead to a selective bond formation.[4]

Sulfonylhydrazides are important intermediates in organic synthesis. [5a] They are easily transformed into sulfonyl radicals that can further add to unsaturated carbon-carbon bonds.[5b-k] To the best of our knowledge however, the selective cross-coupling of sulfonylhydrazides with thiols has not been reported. According to the previous reports on thiyl radical reactions,[6] we hypothesized that a radical cross-coupling strategy for the construction of sulfur−sulfone bond could be developed. We

envisioned that a thiyl radical can be generated from thiol and then stabilized by a suitable transition metal catalyst (transient radical) which can subsequently couple with a persistent sulfonyl radical. Thiosulfonates have found widespread use as reagents or intermediates, so far several protocols for synthesis of thiosulfonates have been developed through the oxidation of thiols and disulfides, the cross-coupling reaction of sulfinic acid salts with disulfides or sulfonyl chlorides with thiols.[7] Herein, a new copper-catalyzed selective radical cross-coupling between sulfonylhydrazides and thiols for the formation of thiosulfonates is described.

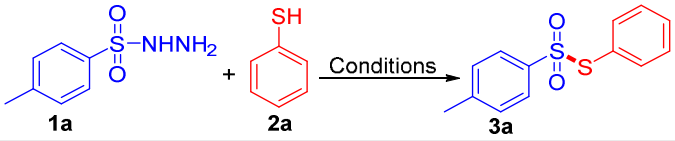
Scheme 1. **Oxidative radical cross-coupling reactions**



We began our investigation by focusing on the reaction between 4-methylbenzenesulfonyl hydrazide (**1a**) and benzenethiol (**2a,** 2 equiv.) in the presence of $CuBr_2$ (10 mol%) and *tert*-butyl hydroperoxide (TBHP, 7.5 equiv) in CH_3CN at room temperature (Table 1, entry 1). We were pleased to find that 72% yield of product **3a** could be obtained after 2 hours. In order to improve the yield of **3a**, other transition metal catalysts were screened. Whereas a similar result was obtained with CuCl (Table 1, entry 2), the use of other metal catalyst such as $FeCl_3$, $AgNO_3$ and $NiCl_2$ proved to be detrimental to the reaction. This indicates that only copper catalysts could significantly stabilize the thiyl radical. It is worthy to note that product **3a** was not detected in the absence of a metal catalyst (Table 1, entry 6). Next, we found that an increase in the temperature led to an increase in the yield of **3a**, with an optimal yield of 84% at 80 ^{o}C (Table 1, entries 7-10). Furthermore, a variation in the ratio of the amount of **1a** and **2a** impacted upon the yield negatively (Table 1, entries 11-13). Also, we discovered that 7.5 equiv. of TBHP was optimal for this reaction (Table 1, entries

14-19). Finally, CH_3CN remained the solvent of choice as the results obtained with other solvents were unsatisfactory (Table 1, entries 20-24).

Table 1. Optimization of the reaction conditions[a]



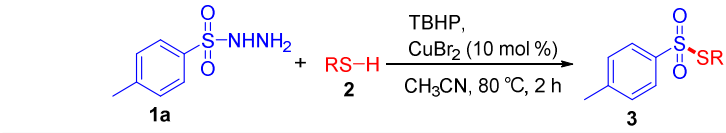
Entry	Catalyst (10 mo%)	Oxidant (equiv)	Solvent (5 mL)	Temp. (°C)	**1a** : **2a**	Yield (%)[b]
1	$CuBr_2$	TBHP (7.5)	CH_3CN	25	1 : 2	72
2	CuCl	TBHP (7.5)	CH_3CN	25	1 : 2	71
3	$FeCl_3$	TBHP (7.5)	CH_3CN	25	1 : 2	trace
4	$AgNO_3$	TBHP (7.5)	CH_3CN	25	1 : 2	30
5	$NiCl_2$	TBHP (7.5)	CH_3CN	25	1 : 2	25
6	--	TBHP (7.5)	CH_3CN	25	1 : 2	N.D.[c]
7	$CuBr_2$	TBHP (7.5)	CH_3CN	40	1 : 2	76
8	$CuBr_2$	TBHP (7.5)	CH_3CN	60	1 : 2	81
9	$CuBr_2$	TBHP (7.5)	CH_3CN	80	1 : 2	84
10	$CuBr_2$	TBHP (7.5)	CH_3CN	100	1 : 2	74
11	$CuBr_2$	TBHP (7.5)	CH_3CN	80	2 : 1	33
12	$CuBr_2$	TBHP (7.5)	CH_3CN	80	1 : 1	58
13	$CuBr_2$	TBHP (7.5)	CH_3CN	80	1 : 1.5	69
14	$CuBr_2$	TBHP (0)	CH_3CN	80	1 : 2	0
15	$CuBr_2$	TBHP (1.5)	CH_3CN	80	1 : 2	51
16	$CuBr_2$	TBHP (3.0)	CH_3CN	80	1 : 2	64
17	$CuBr_2$	TBHP (4.5)	CH_3CN	80	1 : 2	70
18	$CuBr_2$	TBHP (6.0)	CH_3CN	80	1 : 2	76
19	$CuBr_2$	TBHP (9.0)	CH_3CN	80	1 : 2	84
20	$CuBr_2$	TBHP (7.5)	$PhCH_3$	80	1 : 2	21
21	$CuBr_2$	TBHP (7.5)	DMSO	80	1 : 2	34
22	$CuBr_2$	TBHP (7.5)	1,4-Dioxane	80	1 : 2	50
23	$CuBr_2$	TBHP (7.5)	H_2O : CH_3CN (1 : 1)	80	1 : 2	61
24	$CuBr_2$	TBHP (7.5)	THF	80	1 : 2	77

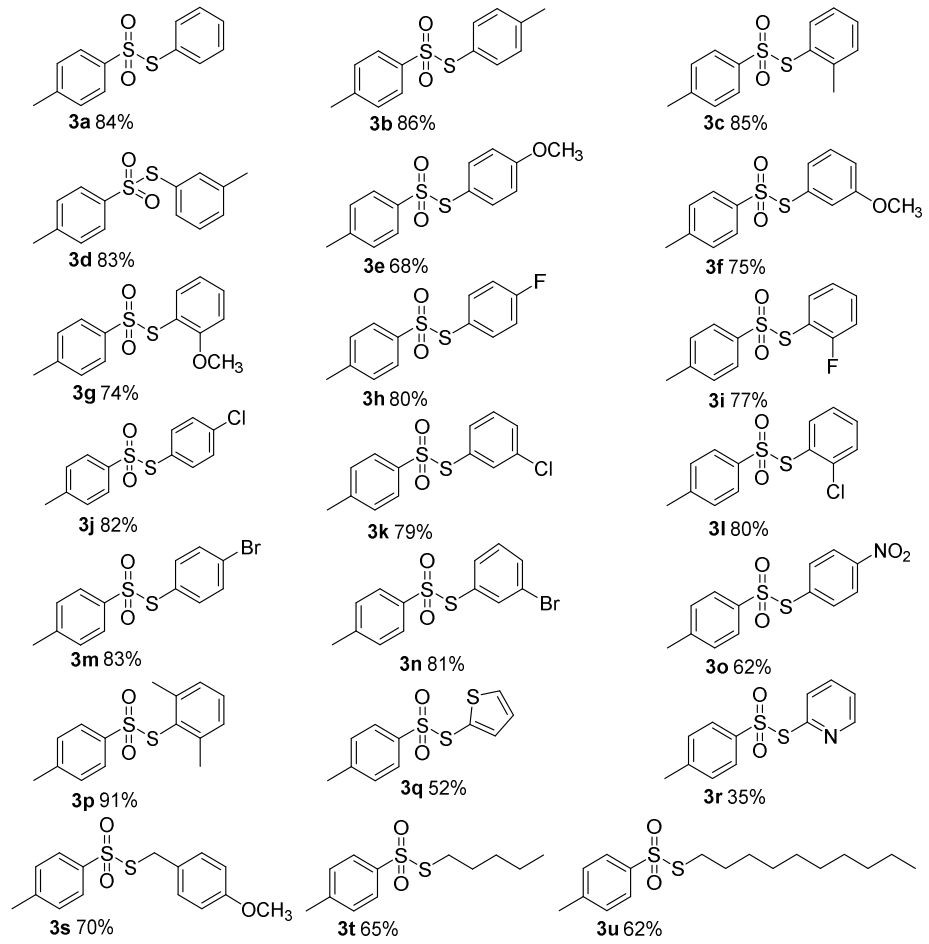
[a] Reaction conditions: **1a** (1 mmol), **2a** (2 mmol) and TBHP (7.5 mmol, 70 % in water) in CH_3CN (5.0 mL) in air at 80 °C for 2 h in the presence of $CuBr_2$ (10 mol %); [b] Isolated yield; [C] N.D. means none detected.

With the optimized set of conditions in hand, the scope of this radical cross-coupling reaction was examined in detail. A variety of substituted benzenethiols were screened and results showed that both electron-withdrawing and electron-donating substituents on the benzene ring had no influence on product formation (Table 2). Also, this reaction was insensitive to steric effect as exemplified by substrates bearing *ortho*-substituents (Table 2, **3c**, **3g**, **3i**, **3l** and **3p**). Substrates containing methoxy substituent gave relatively lower yields probably due to the partial oxidation of substrates (Table 2,

3e-g). With heterocyclic thiols however, products such as **3q** and **3r** were formed in lower yields while alkylthiols gave the corresponding products in moderate yields (Table 2, **3s-u**).

Table 2. Scope of thiols[a,b]

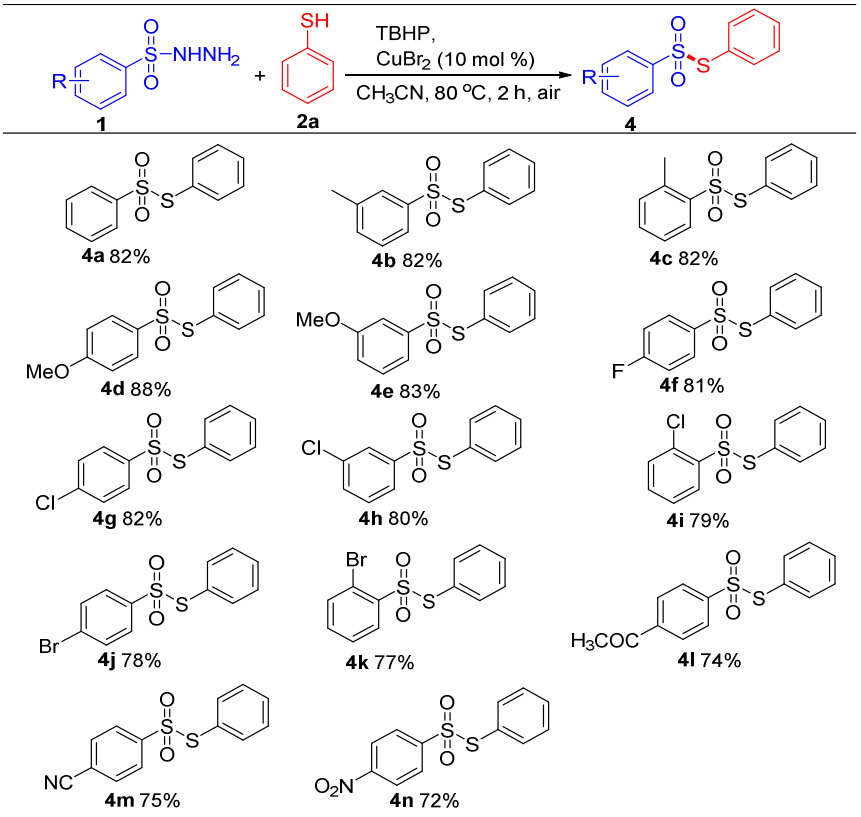




[a] Reaction conditions: **1a** (1 mmol), **2** (2 mmol) and TBHP (7.5 mmol, 70 % in water) in CH_3CN (5.0 mL) in air at 80 °C for 2 h in the presence of $CuBr_2$ (10 mol %); [b] Isolated yield.

Furthermore, the radical cross-coupling reaction was tested over a broad range of sulfonylhydrazides (Table 3). Again, we found that neither steric (Table 3, **4b**, **4i** and **4k**) nor electronic effect (Table 3, **4a-n**) had any significant influence on the yield of products, all of the sulfonylhydrazides gave the desired products in good yields, indicating that this reaction has good substituent group tolerance.

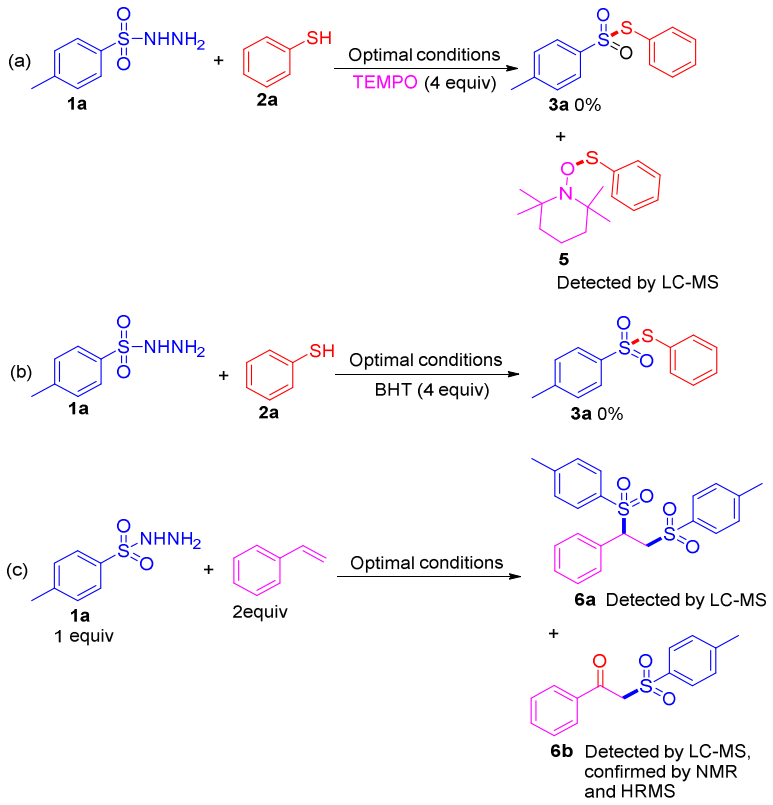
Table 3. Scope of sulfonylhydrazides[a, b]



[a] Reaction conditions: **1a** (1 mmol), **2** (2 mmol), $CuBr_2$ (10 mol %), TBHP (7.5 mmol, 70 % in water), CH_3CN (5.0 mL), 80 °C in air for 2 h; [b] Isolated yield.

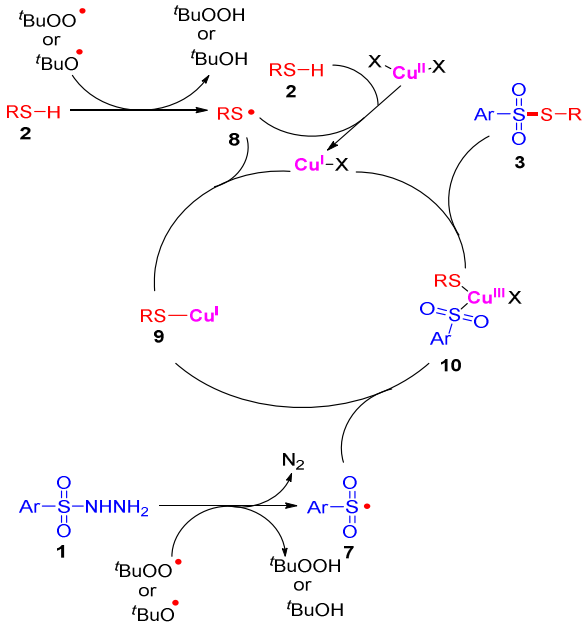
In order to understand the mechanism of the reaction, a series of control experiments were carried out (Scheme 2). Initially, a well-known radical trapping agent, 2,2,6,6-tetramethylpiperidine oxide (TEMPO), was added to the reaction mixture containing 4-methylbenzenesulfonylhydrazide (**1a**) and benzenethiol (**2a**) under the optimal conditions. As expected, the reaction was inhibited while the capture of a thiyl radical by TEMPO was detected by LC-MS (Scheme 2(a)). Also, the product formation was completely suppressed upon the addition of the radical inhibitor BHT to the reaction (Scheme 2(b)). Furthermore, when **1a** was reacted with styrene under the optimal conditions, the styrene adducts **6a** and **6b** were detected by LC-MS, in which **6b** was isolated and confirmed by NMR and HRMS further (Scheme 2(c)). These results therefore confirmed the involvement of thiyl and sulfonyl radical intermediates.

Scheme 2. The control experiments



On the basis of the results above and literature[1e, 2f], a plausible mechanism was proposed as shown in Scheme 3. Initially, sulfonyl radical **7** could be formed from sulfonylhydrazide **1** *via* a multi-step reaction with *tert*-butoxy radical (*t*-BuO•) or *tert*-butylperoxy radical (*t*-BuOO•) alongside the release of a nitrogen molecule. On the other hand, thiyl radical **8** could be generated from the oxidation of thiol **2** by the *t*-BuO• or *t*-BuOO• radicals, which can further coordinate with the copper species to form the complex **9**. Finally, the sulphur-sulfone bond can be formed *via* the coupling of sulfonyl radical **7** with complex **9** through intermediate **10** to give thiosulfonate **3.** Meanwhile, the copper species is released for the next cycle.

Scheme 3. Plausible mechanism



In conclusion, we have developed a convenient copper-catalyzed TBHP-mediated radical cross-coupling of sulfonylhydrazides with thiols. The procedure is simple, mild, and tolerant to different functional groups and affords a variety of thiosulfonates in good yields. The reaction proceeded through the cross-coupling of sulfonyl radicals with thiyl radical copper complex process to form new sulfur-sulfone bonds in a highly selective manner. This method represents a useful contribution to the area of radical cross-coupling reaction.

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were determined with $CDCl_3$ or DMSO-d_6 as solvent and tetramethylsilane (TMS) as internal standard. Chemical shifts were reported in ppm from internal TMS (δ), all coupling constants (J values) were reported in Hertz (Hz). High resolution mass spectra were recorded on a TOF machine (ESI). Column chromatography was performed with 300-400 mesh silica gel using flash column techniques. All of the reagents were used directly as obtained commercially unless otherwise noted.

General procedure for the preparation of thiosulfonates 3 and 4. To a acetonitrile (5 mL) solution of sulfonylhydrazide **1** (1 mmol), thiol **2** (2 mmol) and $CuBr_2$ (0.1 mmol) in Schlenk tube equipped a magnetic bar was added *tert*-butyl hydroperoxide (TBHP, 7.5 mmol) dropwise over a minute. The reaction mixture was stirred at 80 ^oC for 2 hours in air. After the substrates were completely consumed, the solvent was evaporated off and the residue was purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 40:1) to afford the thiosulfonates **3** and **4**.

*S-phenyl-4-methylbenzenesulfonothioate (**3a**).*[7d] Yellow solid, mp 73.5−74.8 ^oC, 84% yield (216 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.44 (m, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.37 – 7.30 (m, 4H), 7.19 (d, J = 10 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.3, 139.7, 136.1, 130.9, 129.0, 128.9, 127.5, 127.1, 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{13}O_2S_2$ 265.0357, found 265.0353.

*S-p-tolyl-4-methylbenzenesulfonothioate (**3b**).* [7d] Yellow solid, mp 76.7−77.5 ^oC, 86% yield (240 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 2.42 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 142.0, 140.5, 136.5, 130.2, 129.4, 127.6, 124.6, 21.7, 21.5. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{14}H_{15}O_2S_2$ 279.0513, found 279.0504.

*S-o-tolyl-4-methylbenzenesulfonothioate (**3c**).* [7d] Yellow solid, mp 104.1−104.6 ^oC, 85% yield (236 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J = 8.3 Hz, 2H), 7.35 (dd, J = 13.1, 7.1 Hz, 2H), 7.22 (t, J = 8.1 Hz, 3H), 7.16 (t, J = 7.6 Hz, 1H), 2.43 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.7, 144.2, 140.8, 138.3, 131.8, 131.0, 129.4, 127.5, 127.3, 126.9, 21.7, 20.7. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{14}H_{15}O_2S_2$ 279.0513, found 279.0499.

*S-m-tolyl-4-methylbenzenesulfonothioate (**3d**).* [7d] Yellow solid, mp 76.5−77.0 ^oC, 83% yield (230 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 6.8 Hz, 1H), 7.23 – 7.19 (m, 3H), 7.17 (s, 1H), 7.13 (d, J = 7.5 Hz, 1H), 2.42 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 144.1, 139.8, 138.9, 136.7, 133.0, 131.6, 128.8, 128.7, 127.2, 127.2, 21.2, 20.6. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{14}H_{15}O_2S_2$ 279.0513, found 279.0525.

*S-(4-methoxyphenyl)-4-methylbenzenesulfonothioate (**3e**).* [7d] White solid, mp 127.2−128.0 °C, 68% yield (199 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.2 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 3.83 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 144.1, 139.9, 137.9, 128.9, 127.1, 118.3, 114.5, 55.0, 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{14}H_{15}O_3S_2$ 295.0463, found 295.0477.

*S-(3-methoxyphenyl)-4-methylbenzenesulfonothioate (**3f**).* [7d] White solid, mp 97.8−98.6 °C, 75% yield (220 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.3 Hz, 2H), 7.23 (t, J = 8.1 Hz, 3H), 7.00 (ddd, J = 8.4, 2.6, 0.9 Hz, 1H), 6.93 (ddd, J = 7.6, 1.5, 1.0 Hz, 1H), 6.88 (dd, J = 2.4, 1.7 Hz, 1H), 3.72 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 144.2, 139.8, 129.6, 128.9, 128.3, 128.3, 127.2, 120.3, 117.6, 54.9, 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{14}H_{15}O_3S_2$ 295.0463, found 295.0470.

*S-(2-methoxyphenyl)-4-methylbenzenesulfonothioate (**3g**).* [7d] White solid, mp 103.5−104.0 °C, 74% yield (217 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 – 7.47 (m, 3H), 7.47 – 7.42 (m, 1H), 7.21 (d, J = 8.1 Hz, 2H), 6.97 (td, J = 7.6, 1.1 Hz, 1H), 6.79 (d, J = 8.3 Hz, 1H), 3.48 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2, 144.2, 141.6, 139.5, 133.8, 129.1, 127.7, 121.3, 115.6, 113.1, 55.4, 21.6. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{14}H_{15}O_3S_2$ 295.0463, found 295.0475.

*S-(4-fluorophenyl)-4-methylbenzenesulfonothioate (**3h**).*[8] Yellow solid, mp 92.8−93.5 °C, 80% yield (226 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 8.2 Hz, 2H), 7.35 (dd, J = 8.6, 5.3 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.03 (t, J = 8.5 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3 (d, J = 253.7 Hz), 144.5, 139.6, 138.4 (d, J = 9.1 Hz), 129.0, 127.1, 123.1 (d, J = 3.3 Hz), 116.3 (d, J = 22.3 Hz), 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}FO_2S_2$ 283.0263, found 283.0257.

*S-(2-fluorophenyl)-4-methylbenzenesulfonothioate (**3i**).*[8] Yellow solid, mp 65.8−66.2 °C, 77% yield (221 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.41 (m, 4H), 7.23 (d, J = 8.1 Hz, 2H), 7.18 (t, J = 7.1 Hz, 1H), 7.06 (td, J = 8.7, 1.1 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.4 (d, J = 253.7 Hz), 144.5, 140.2, 138.6, 133.7 (d, J = 8.3 Hz), 129.0, 127.0, 124.5, 115.9 (d, J = 22.7 Hz), 114.9 (d, J = 17.8 Hz), 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}FO_2S_2$ 283.0263, found 283.0250.

*S-(4-chlorophenyl)-4-methylbenzenesulfonothioate (**3j**).*[7d] Yellow solid, mp 86.1−87.2 °C, 83% yield (247 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J = 8.3 Hz, 2H), 7.35 – 7.28 (m, 4H), 7.24 (d, J = 8.2 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.5, 139.7, 137.7, 137.2, 129.2, 129.1, 127.1, 126.1, 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}ClO_2S_2$ 298.9967, found 298.9961.

*S-(3-chlorophenyl)-4-methylbenzenesulfonothioate (**3k**).* Yellow solid, mp 77.6−78.5 °C, 79% yield (235 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J = 8.4 Hz, 2H), 7.46 – 7.41 (m, 1H), 7.32 – 7.27 (m, 3H), 7.25 (d, J = 8.1 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 140.0, 136.1, 134.8, 134.6, 131.4, 130.4, 129.7, 129.5, 127.7, 21.7. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}ClO_2S_2$ 298.9967, found 298.9962.

*S-(2-chlorophenyl)-4-methylbenzenesulfonothioate (**3l**).* White solid, mp 117.6−118.2 °C, 80% yield (238 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8.2 Hz, 1H), 7.47 (d, J = 8.3 Hz, 2H), 7.43 – 7.37 (m, 2H), 7.34 – 7.29 (m, 1H), 7.22 (d, J = 8.1 Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 140.3, 139.8, 139.1, 132.4, 129.8, 129.1, 127.2, 127.1, 126.7, 21.2.HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}ClO_2S_2$ 298.9967, found 298.9962.

*S-(4-bromophenyl)-4-methylbenzenesulfonothioate (**3m**).*[7d] Yellow solid, mp 102.5−103.4 °C, 83% yield (283 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 2.7 Hz, 2H), 7.47 (d, J = 2.6 Hz, 2H), 7.26 – 7.21 (m, 4H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 140.0, 136.1, 134.6,

131.4, 130.4, 129.5, 127.7, 21.7. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}BrO_2S_2$ 342.9462, found 342.9453.

*S-(3-bromophenyl)-4-methylbenzenesulfonothioate (**3n**).* Yellow solid, mp 73.9−74.8 °C, 81% yield (277 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (ddd, J = 8.0, 1.9, 1.1 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.26 – 7.18 (m, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 139.9, 138.9, 135.1, 134.3, 130.7, 130.0, 129.5, 127.7, 122.6, 21.7. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}BrO_2S_2$ 342.9462, found 342.9464.

*S-(4-nitrophenyl)-4-methylbenzenesulfonothioate (**3o**).*[7d] Yellow solid, mp 129.9−130.2 °C, 62% yield (192 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J = 8.9 Hz, 2H), 7.59 (d, J = 8.9 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 6.6 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.6, 140.2, 137.1, 135.8, 129.8, 127.6, 126.4, 124.1, 21.7. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{12}NO_4S_2$ 310.0208, found 310.0200.

*S-(2,6-dimethylphenyl)-4-methylbenzenesulfonothioate (**3p**).* White solid; mp 95.3−95.7 °C, 91% yield (266 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.3 Hz, 2H), 7.26 – 7.21 (m, 3H), 7.10 (d, J = 7.5 Hz, 2H), 2.44 (s, 3H), 2.20 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1, 144.3, 141.1, 131.0, 129.2, 128.3, 126.9, 126.40, 21.2, 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{15}H_{17}O_2S_2$ 293.0670, found 293.0656.

*S-thiophen-2-yl-4-methylbenzenesulfonothioate (**3q**).* Purple solid, mp 51.8−52.0 °C, 52% yield (140 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, J = 5.3, 1.3 Hz, 1H), 7.54 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 7.16 (dd, J = 3.7, 1.3 Hz, 1H), 7.07 (dd, J = 5.3, 3.7 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 139.0, 138.9, 134.6, 129.0, 127.9, 127.4, 124.9, 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{11}H_{11}O_2S_3$ 270.9921, found 270.9927.

*S-pyridin-2-yl-4-methylbenzenesulfonothioate (**3r**).*[9] Yellow solid, mp 51.1−52.0 °C, 35% yield (93 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (d, J = 4.5 Hz, 1H), 7.80 – 7.70 (m, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.38 – 7.32 (m, 1H), 7.24 (d, J = 8.1 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 150.7, 150.2, 144.5, 140.9, 137.3, 131.4, 129.1, 127.0, 124.4, 21.2. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{12}NO_2S_2$ 266.0309, found 266.0315.

S-p-methoxybenzyl-4-methylbenzenesulfonothioate ***(3s)***.[10] White solid, mp 61.8−62.7 °C, 70% yield (216 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 6.75 (d, J = 8.7 Hz, 2H), 4.21 (s, 2H), 3.76 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 144.1, 141.6, 129.9, 129.2, 128.5, 124.9, 113.7, 54.8, 39.4, 20.9. HRMS (ESI-TOF) *m/z*: $(M + Na)^+$ Calcd for $C_{15}H_{16}O_3S_2Na$ 331.0439, found 331.0440.

S-pentyl-4-methylbenzenesulfonothioate ***(3t)***.[11] Yellow liquid, 65% yield (168 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 3.04 – 2.92 (m, 2H), 2.45 (s, 3H), 1.58 – 1.56 (m, 2H), 1.29 – 1.24 (m, 4H), 0.84 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 142.1, 129.8, 127.0, 36.0, 30.7, 28.3, 22.0, 21.6, 13.8. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{19}O_2S_2$ 259.0826, found 259.0835.

S-decyl-4-methylbenzenesulfonothioate ***(3u)***. Yellow liquid, 62% yield (204 mg). ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.81 (d, J = 5.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 2.98 (t, J = 8.0 Hz, 2H), 2.45 (s, 3H), 1.58 (t, J = 7.4 Hz, 2H), 1.26 – 1.17 (m, 12H), 0.88 (t, J = 6.9 Hz, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 142.2, 129.8, 127.0, 36.0, 31.9, 29.5, 29.34, 29.26, 28.9, 28.6, 28.5, 22.7, 21.6, 14.1. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{17}H_{29}O_2S_2$ 329.1609, found 329.1619.

S-phenyl benzenesulfonothioate ***(4a)***.[7d] Yellow liquid, 82% yield (206 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 – 7.54 (m, 3H), 7.49 – 7.45 (m, 1H), 7.45 – 7.39 (m, 2H), 7.38 – 7.31 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 136.1, 133.1, 130.9, 129.0, 128.3, 127.4, 127.1. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{11}O_2S_2$ 251.0200, found 251.0209.

S-phenyl-3-methylbenzenesulfonothioate ***(4b)***. Yellow liquid, 82% yield (217 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 – 7.50 (m, 1H), 7.45 – 7.37 (m, 7H), 7.36 – 7.32 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3, 138.6, 136.2, 133.9, 130.9, 128.9, 128.1, 127.5, 127.4, 124.2, 20.7. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{13}O_2S_2$ 265.0357, found 265.0354.

*S-phenyl-2-methylbenzenesulfonothioate (**4c**).*[8] Yellow liquid, 82% yield (217 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.43 (m, 2H), 7.40 (dd, J = 8.0, 1.0 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.33 – 7.26 (m, 4H), 7.11 (t, J = 7.7 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 137.4, 136.1, 133.4, 132.4, 130.8, 129.7, 128.8, 127.3, 125.2, 20.0. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{13}O_2S_2$ 265.0357, found 265.0363.

*S-phenyl-4-methoxybenzenesulfonothioate (**4d**).*[8] Yellow liquid, 88% yield (246 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 – 7.41 (m, 3H), 7.40 – 7.27 (m, 4H), 6.85 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.1, 136.1, 134.4, 130.8, 129.4, 128.9, 127.7, 113.4, 55.3. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{13}H_{13}O_3S_2$ 281.0306, found 281.0317.

*S-phenyl-3-methoxybenzenesulfonothioate (**4e**).* Yellow liquid, 83% yield (232 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.42 (m, 1H), 7.37 – 7.27 (m, 5H), 7.12 (d, J = 7.7 Hz, 1H), 7.06 (d, J = 8.2 Hz, 1H), 6.95 (s, 1H), 3.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 143.4, 136.2, 131.0, 129.3, 129.0, 127.5, 120.2, 119.2, 111.1, 55.1. HRMS (ESI-TOF) *m/z*: $(M + Na)^+$ Calcd for $C_{13}H_{12}O_3S_2Na$ 303.0126, found 303.0106.

*S-phenyl-4-fluorobenzenesulfonothioate (**4f**).*[8] Yellow liquid, 81% yield (217 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (dd, J = 8.9, 5.0 Hz, 2H), 7.52 – 7.45 (m, 1H), 7.40 – 7.31 (m, 4H), 7.08 (t, J = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0 (d, J = 256.9 Hz), 138.5 (d, J = 3.1 Hz), 136.1, 131.1, 130.0 (d, J = 9.7 Hz), 129.1, 127.2, 115.6 (d, J = 22.8 Hz). HRMS (ESI-TOF) *m/z*: $(M+H)^+$ Calcd for $C_{12}H_{10}FO_2S_2$ 269.0106, found 269.0116.

*S-phenyl-4-chlorobenzenesulfonothioate (**4g**).*[8] Yellow solid, mp 80.7−81.3 ^{o}C, 82% yield (233 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 – 7.47 (m, 3H), 7.43 – 7.35 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 139.8, 136.1, 131.2, 129.1, 128.6, 128.5, 127.1. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{10}ClO_2S_2$ 284.9811, found 284.9803.

*S-phenyl-3-chlorobenzenesulfonothioate (**4h**).* Yellow solid, mp 65.2−62.8 ^{o}C, 80% yield (227 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 – 7.49 (m, 3H), 7.46 (d, J = 8.0 Hz, 1H), 7.42 – 7.36 (m,

5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.7, 136.1, 134.6, 133.2, 131.3, 129.6, 129.1, 127.2, 126.9, 125.1. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{10}ClO_2S_2$ 284.9811, found 284.9801.

*S-phenyl-2-chlorobenzenesulfonothioate (**4i**).* Yellow solid, mp 84.0−84.6 °C, 79% yield (224 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 7.9 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.37 – 7.32 (m, 2H), 7.32 – 7.27 (m, 2H), 7.20 (td, J = 7.8, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 136.1, 134.1, 132.2, 131.9, 131.12, 131.07, 128.9, 127.0, 126.0. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{10}ClO_2S_2$ 284.9811, found 284.9801.

*S-phenyl-4-bromobenzenesulfonothioate (**4j**).*[8] Yellow solid, mp 76.2−76.8 °C, 78% yield (256 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.7 Hz, 2H), 7.57 – 7.52 (m, 1H), 7.45 (d, J = 8.7 Hz, 2H), 7.43 – 7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.4, 136.1, 131.6, 131.2, 129.1, 128.5, 128.4, 127.0. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{10}BrO_2S_2$ 328.9306, found 328.9298.

*S-phenyl-2-bromobenzenesulfonothioate (**4k**).* Yellow solid, mp 57.3−58.0 °C, 77% yield (254 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (dd, J = 7.9, 1.0 Hz, 1H), 7.54 (dd, J = 8.0, 1.6 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.36 – 7.21 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 136.2, 135.4, 133.9, 131.4, 131.0, 128.9, 127.1, 126.6, 120.3. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{12}H_{10}BrO_2S_2$ 328.9306, found 328.9302.

*S-phenyl-4-acetylbenzenesulfonothioate (**4l**).* Yellow liquid, 74% yield (216 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 8.6 Hz, 2H), 7.69 (d, J = 8.6 Hz, 2H), 7.57 – 7.53 (m, 1H), 7.43 – 7.39 (m, 4H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2, 145.9, 140.0, 136.1, 131.2, 129.2, 128.2, 127.3, 126.9, 26.4. HRMS (ESI-TOF) *m/z*: $(M + H)^+$ Calcd for $C_{14}H_{13}O_3S_2$ 293.0306, found 293.0316.

*S-phenyl-4-cyanobenzenesulfonothioate (**4m**).* White solid, mp 141.2−142.4 °C, 75% yield (207 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.1 Hz, 2H), 7.55 – 7.49

(m, 1H), 7.45 – 7.30 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.0, 136.0, 132.2, 131.5, 129.3, 127.6, 126.5, 116.8, 116.6. HRMS (ESI-TOF) *m/z*: $(M + Na)^+$ Calcd for $C_{13}H_9NO_2S_2Na$ 297.9972, found 297.9956.

*S-phenyl-2-nitrobenzenesulfonothioate (**4n**).*[12] Yellow liquid, 62% yield (183 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, J = 8.9 Hz, 2H), 7.73 (d, J = 11.2 Hz, 2H), 7.55 – 7.51 (m, 1H), 7.43 – 7.36 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.9, 147.4, 136.0, 131.6, 129.4, 128.3, 126.4, 123.6. HRMS (ESI-TOF) *m/z*: $(M + Na)^+$ Calcd for $C_{12}H_9NO_4S_2Na$ 317.9871, found 317.9892.

1-Phenyl-2-tosylethanone (***6b***). White solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 7.6 Hz, 2H), 7.70 (d, J = 8.1 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.7 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 4.65 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 187.09, 144.32, 134.66, 133.26, 128.77, 128.74, 128.26, 128.24, 127.77, 127.74, 127.54, 127.51, 62.5, 20.6. HRMS (ESI-TOF) *m/z*: $(M + Na)^+$ Calcd for $C_{15}H_{14}O_3SNa$ 297.0561, found 297.0558.

ASSOCIATED CONTENT

Supporting Information

^{1}H, and ^{13}C NMR spectra for compounds **3**, **4** and **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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