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Note

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Air Oxidative Radical Hydroxysulfurization of Styrenes Leading to β-Hydroxysulfides

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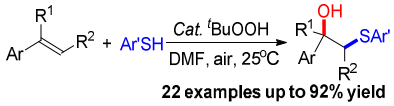


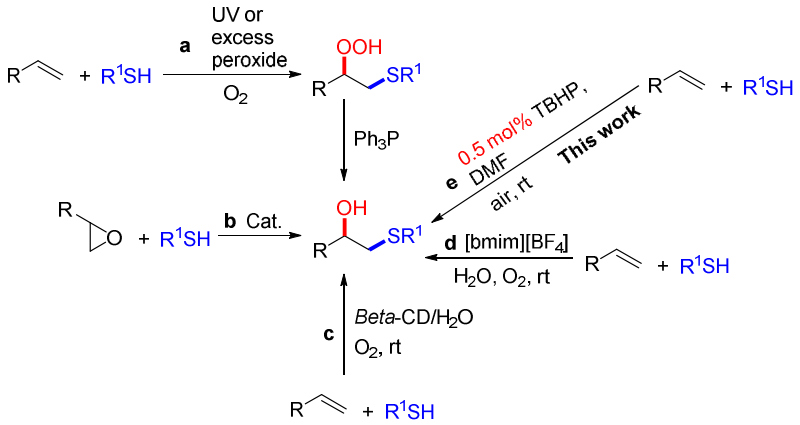
ABSTRACT: Air oxidative radical hydroxysulfurization of styrenes initiated by 0.5 mol % TBHP with arylthiols is described, a new type of difunctionalization of alkenes was achieved.

Difunctionalization has become a powerful tool in modern synthetic chemistry.[1] The radical difunctionalization reaction has attracted more attention in recent years because of its mild conditions, high selectivity and convenient work-up.[2] Thiol-oxygen cooxidation (TOCO) of olefins first reported by Kharasch in 1951,[3] is a well-known difunctionalization reaction, usually initiated by UV irradiation or excess of peroxides. It has been widely applied to the synthesis of TOCO products such as β-hydroperoxysulfides and β-hydroxysulfoxides, but not β-hydroxysulfides unless a reductant is added to the resultant compound *in situ* (Scheme 1, a). [4] Hence, it is still a challenge to prepare β-hydroxysulfides directly by TOCO reaction.

β-Hydroxysulfides are important starting materials for the synthesis of higher functionalized organic molecules, [5] pharmaceuticals, [6] and natural products.[7] One of the most straightforward synthetic route to β-hydroxysulfides is the reaction of epoxides, commonly derived from alkenes, with thiols in the presence of promoters and/or catalysts (Scheme 1, b).[5, 8] These methods are useful

but suffer from some drawbacks such as drastic reaction conditions, poor regioselectivity, lower yields and undesirable byproducts.[9] Recently, the methods of synthesizing β-hydroxysulfides *via* the reaction of alkenes with thiols were developed by Rao and Kamal groups, these reactions were conducted in β-cyclodextrin/H_2O[10] or ionic liquid [bmim][BF_4]/H_2O [11] medium through non-radical process (Scheme 1, c and d). Yadav group performed the same reaction utilizing eosin Y as an organophoto-redox catalyst in the visible light to afford the exclusive β-ketosulfoxides. The experiment confirmed that the reaction proceeds *via* a radical pathway. [12] To the best of our knowledge, no work on the direct one-pot synthesis of β-hydroxysulfides *via* TOCO reaction has been reported. In continuation of our effort on difunctionalization of alkenes, [13] herein, we report a new radical hydroxysulfurization of styrenes for the direct synthesis of β-hydroxysulfides based on the reaction of alkenes and arylthiols initiated by 0.5 mol % *tert*-butyl hydroperoxide (TBHP) (Scheme 1, e) .

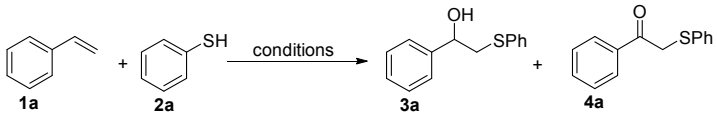
Scheme 1. Protocols for Synthesis of *β*-Hydroxysulfides



At the initial stage, the reaction of styrene (**1a**) with thiophenol (**2a**) in the presence of 0.5 mol % *tert*-butyl hydroperoxide (TBHP) was used as a model reaction. Solvents screening indicated that the reaction in DMF afforded β-hydroxysulfide (**3a**) as a major product in 70 % yield, accompanied by a byproducts β-oxosulfide (**4a**), benzaldehyde and diphenyldisulfide (Table 1, entry 5). Thus using DMF as solvent, the ratio of **1a**/**2a**, TBHP loading, temperature and time were screened (Table 1,

entries 10-21), optimum reaction conditions were determined to be: styrene (**1a**, 1.0 equiv), thiophenol (**2a**, 2 equiv) in DMF at 25°C for 48h (Table 1, entry 15) to afford the selective β-hydroxysulfide (**3a**) in 74% yield.

Table 1. Optimization of the Reaction Conditions[a]



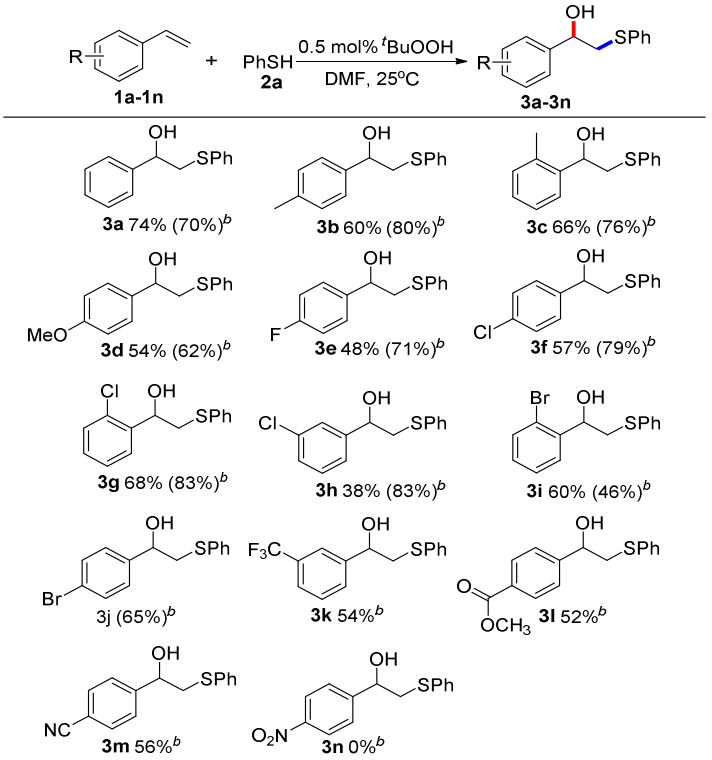
Entry	1a:2a	Solvent	Temp(°C)	Time(h)	Yield[b] 3a	4a
1	1:2	THF	13	48	33	13
2	1:2	CH_3CN	13	48	trace	trace
3	1:2	1,4-Dioxane	13	48	<5	trace
4	1:2	CH_3OH	13	48	<5	trace
5[c]	1:2	DMF	13	48	70	<5
6	1:2	CH_2Cl_2	13	48	trace	trace
7	1:2	Benzene	13	48	30	trace
8	1:2	Toluene	13	48	39	trace
9	1:2	*n*-hexane	13	48	17	6
10	1:1	DMF	13	48	28	<5
11	1:3	DMF	13	48	73	<5
12[d]	1:2	DMF	13	48	58	<5
13[e,f]	1:2	DMF	13	48	0	13
14	1:2	DMF	0	48	38	<5
15	1:2	DMF	25	48	74	<5
16	1:2	DMF	40	48	70	<5
17	1:2	DMF	80	48	44	<5
18	1:2	DMF	120	48	61	<5
19	1:2	DMF	25	24	52	9
20	1:2	DMF	25	72	71	17
21	1:2	DMF	25	96	70	<5

[a]Using 0.5 % mol TBHP as initiator in all the reactions except otherwise noticed; [b]Isolated yield; [c]Benzaldehyde (15% yield) and diphenyldisulfide (50% yield calculated based on the thiophenol (**2a**) were isolated; [d]5% mol TBHP; [e]No TBHP; [f]The effect of temperature on the reaction for 24 h and the effect of time on the reaction at 13 °C, please refer the supporting information.

Under the optimized reaction conditions, the reactions of a variety of substituted styrenes **1** with thiophenol (**2a**) were carried out. Styrenes bearing Me, F and Cl groups on the phenyl ring were tolerated to afford the selective β-hydroxysulfides in good yields although with prolonged reaction time (Table 2, **3b-c**, **3e-h**). It is noteworthy that the reaction of 4-methoxystyrene (**1d**) gave the desired product **3d** in slightly low yield, this may be attributed to some of **1d** being oxidized in the

reaction. The reactions of styrenes bearing strong electron-withdrawing groups such as CF_3, $COOCH_3$ and CN with **2a** gave low yield of β-hydroxysulfides (Table 2, **3k**, **3l** and **3m**), while no reaction was observed with the NO_2 derivative (Table 2, **3n**).

Table 2. Reactions of Styrenes 1 and Thiophenol 2a[a]

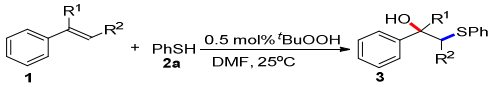


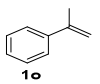
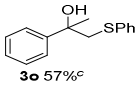
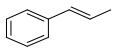
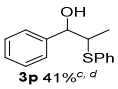
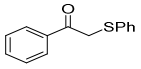
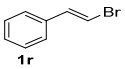
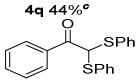
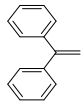
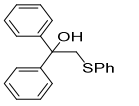
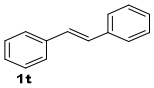
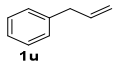
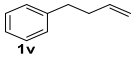
[a]Reaction conditions: styrenes (1 mmol), PhSH (2 mmol) in DMF at 25°C for 48h; [b]25 °C, 96h; Yield means isolated yield.

To evaluate the effect of *α*- or *β*-substituents of styrene on the reaction, CH_3, Br and Ph substituted styrenes were utilized for this purpose. The reactions of α-methylstyrene (**1o**) and β-methylstyrene (**1p**) with **2a** both afforded the expected β-hydroxysulfides **3o** and **3p** in 57% and 41% yield, respectively (Table 3, entries 1-2). It was noted that the methyl substituent located at α or β-position of styrene has steric effect on the reaction leading to the decreased yield of products. Then the reaction of α-bromostyrene (**1q**) with **2a** was carried out, and β-oxosulfide **4q** was isolated in 44% yield (Table 3, entry 3), while the reaction of β-bromostyrene (**1r**) with **2a** gave the β-oxythioacetal **4r** in 15% yield (Table 3, entry 4). Also, the reaction of α-phenylstyrene (**1s**) with **2a** was performed, and the corresponding β-hydroxysulfide **3s** was isolated in 71% yield (Table 3, entry

5). On the contrary, no reaction was observed for β-phenylstyrene (**1t**) (Table 3, entry 6). Based on the results aforementioned, using α- or β-substituted (CH_3, Br and Ph) styrenes as substrates, different products or yields were obtained, which depended on both the kind of substituents and their location. Finally, non-conjugated terminal alkenes (**1u-v**) were used in place of styrene but no reactions were observed (Table 3, entries 7-8).

Table 3. Reactions of α- and β-Substituted Styrenes 1 with Thiophenol 2a[a]



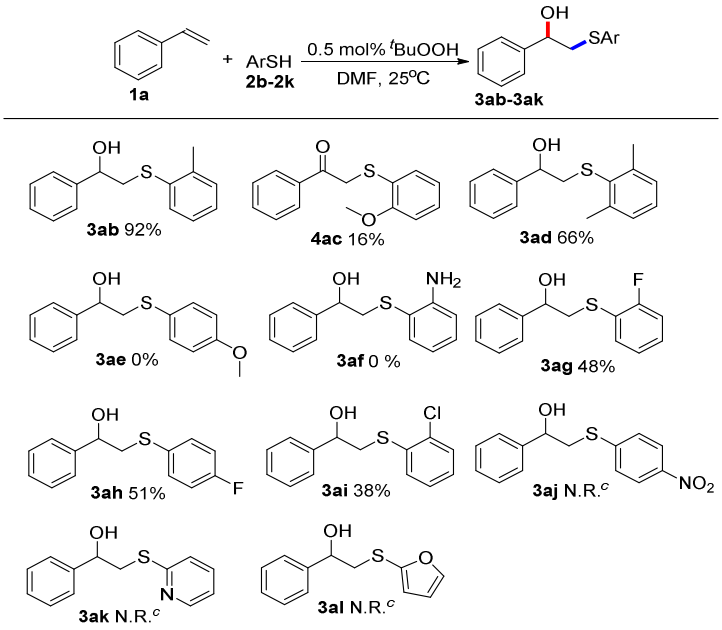
Entry	Olefin	Product and yield[b]
1	 1o	 3o 57%[c]
2	 1p	 3p 41%[c, d] (*dr* = 86/14)[e]
3	 1q	 4q 44%[e]
4	 1r	 4r 15%[e]
5	 1s	 3s 71% (78%)[c]
6	 1t	N.R[f]
7	 1u	N.R[f]
8	 1v	N.R[f]

[a]Reaction conditions: Olefin (1 mmol), PhSH (2 mmol) in DMF at 25°C for 48h; [b]Isolated yield; [c]96h; [d]Combined yield of two diastereomers; [e]Determined by ^{1}H NMR. [f]N.R. means the alkene is not consumed and the desired β -hydroxysulfide was not isolated (0% yield).

With the promising results at hand, the reaction was extended to other arylthiols. The results indicated that the kind of substituents and their location had an effect on the outcome of the reaction. The reaction of *o*-tolylthiol (**2b**) with styrene (**1a**) gave the desired β-hydroxysulfide **3ab** in 92% yield, while the *o*-methoxybenzenethiol (**2c**) afforded the β-oxosulfide **4ac** in 16% yield, the *p*-methoxybenzenethiol (**2e**) and *o*-aminobenzenethiol (**2f**) gave no desired β-hydroxysulfides **3ae** and **3af** (Table 4). The arylthiols bearing F and Cl groups reacted with **1a** to afford the expected β-

hydroxysulfides **3ag**, **3ah** and **3ai** in moderate yields (Table 4), while the NO_2 derivative did not react (Table 4, **3aj**). Also, no reactions were observed with pyridylthiol and furylthiol (Table 4, **3ak** and **3al**).

Table 4. Reactions of Styrene 1a with Arylthiols 2[a,b]



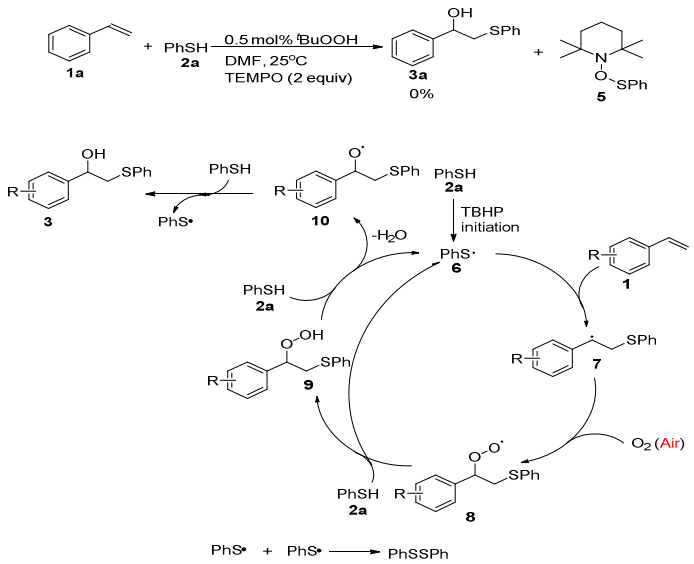
[a]Reaction conditions: Styrene (1 mmol), ArSH (2 mmol) in DMF at 25°C for 96h; [b]Isolated yield; [c]N.R. means the styrene is not consumed and the desired β -hydroxysulfide was not isolated (0% yield).

Finally, the scale-up reaction of **1a** (10.4 g, 0.1 mol) with **2a** (22.0 g, 0.2 mol) in DMF at room temperature for 48 h in the presence of 0.5 mol % TBHP was performed, the expected product **3a** was obtained in 64% yield (14.7 g).

To confirm that the reaction proceeded *via* a radical pathway, TEMPO was added to the reaction mixture of styrene (**1a**) with thiophenol (**2a**), only the product **5** was isolated, which was confirmed to be 2,2,6,6-tetramethyl-1-((phenylthio)oxy)piperidine formed from the reaction of TEMPO and thiophenyl radical, but no β-hydroxysulfide (**3a**) was formed (Scheme 2). This result strongly supported the free radical mechanism. On the basis of results obtained, a mechanism for the reaction of styrenes **1** with thiophenol (**2a**) was proposed in Scheme 2. Thiyl radical **6** initiated by TBHP selectively adds to the terminal C=C double bond of **1** to form intermediate radical **7**. It reacts with O_2 to form peroxy radical **8**, followed by reacting with **2a** to form hydroperoxide **9** and thiyl radical **6**

is regenerated. **9** reacts with thiophenol (**2a**) to give radical **10**, which then get hydrogen atom from **2a** to afford product **3** and regenerate thiyl radical **6**, which continues to drive the reaction further.

Scheme 2. Proposed Mechanism for the Reaction of Styrenes with Thiophenol



In conclusion, a new type of difunctionalization of alkenes *via* the reaction of arylthiols with styrenes has been developed. The reaction was initiated by 0.5 mol % TBHP at room temperature, with air (O_2) as sole oxidant to afford the hydroxysulfurization products in moderate to good yields. The reaction can be effectively scaled up and product conveniently obtained in a one-pot process. This method is straightforward, requires no additives or other oxidant, and involves simple manipulations. The β-hydroxysulfides obtained can be directly applied in syntheses of organic and medicinal compounds, and can also be transformed into a variety of other useful functionalized compounds.

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. All alkenes were purified by flash column chromatography (Al_2O_3) before use.

Preparation of 1-Aryl-2-(arylthio)ethan-1-ol 3. *Typical Procedure for the Preparation of 1-Phenyl-2-(phenylthio)ethan-1-ol (**3a**).* To a solution of dimethylformamide (DMF, 10 mL), styrene (0.104 g, 1 mmol) and benzenethiol (0.22 g, 2 mmol) was added *t*-butyl hydroperoxide (70% aqueous solution, 0.7 μL, 0.005 mmol), the mixture was stirred at room temperature in air for 48 h. After the completion of the reaction, water (10 mL) was added to the reaction mixture, extracted with ethyl acetate (10 mL × 3). The combined organic fractions were dried over anhydrous Na_2SO_4, and concentrated under vacuum to yield the crude product, which was purified by column chromatography (silica gel, petroleum ether/EtOAc = 40:1) to give 1-phenyl-2-(phenylthio) ethan-1-ol (**3a**) .

*Scale-up procedure for the Preparation of 1-Phenyl-2-(phenylthio)ethan-1-ol (**3a**).* To a solution of DMF (200 mL), styrene (10.4 g, 0.1 mol) and benzenethiol (22.0 g, 0.2 mol) was added *t*-butyl hydroperoxide (70% aqueous solution, 0.05 g, 0.5 mmol), the mixture was stirred at room temperature for 48 h. Then, water (100 mL) was added into the reaction mixture, and extracted with ethyl acetate (100 mL × 3). The combined organic fractions were dried over anhydrous Na_2SO_4, and vaporized under vacuum to give concentrated solution, which was cooled to 0 ^oC, diphenyldisulfide (PhSSPh) precipitated. The solid was filtered, the filtrate was concentrated and purified with chromatography (silica gel, petroleum ether/EtOAc = 40:1) to afford **3a** (yellow oil, 14.7 g, 64% yield).

*1-Phenyl-2-(phenylthio)ethan-1-ol (**3a**)*[10]. Yellow oil, 70% yield (161 mg). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33−7.10 (m, 10H), 4.62 (dd, J = 9.4, 3.5 Hz, 1H), 3.22 (dd, J = 13.8, 3.5 Hz, 1H), 3.00 (dd, J = 13.8, 9.4 Hz, 1H), 2.73 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.2, 135.0, 130.2, 129.2,

128.6, 128.0, 126.8, 125.9, 71.7, 44.0. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{14}H_{13}S$ 213.1, found 213.1.

*2-(Phenylthio)-1-(p-tolyl)ethan-1-ol (**3b**)*[10]. Yellow oil, 80% yield (195 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.46 (m, 2H), 7.40−7.36 (m, 2H), 7.34−7.27 (m, 3H), 7.22 (d, J = 8.0 Hz, 2H), 4.76 (dd, J = 9.1, 3.9 Hz, 1H), 3.35 (dd, J = 13.7, 3.9 Hz, 1H), 3.18 (dd, J = 13.7, 9.1 Hz, 1H), 3.09 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.4, 137.7, 135.4, 130.1, 129.3, 129.2, 126.7, 126.0, 71.7, 43.8, 21.3. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{15}H_{16}OS$ 244.0922, found 244.0933.

*2-(Phenylthio)-1-(o-tolyl)ethan-1-ol (**3c**)*. Yellow oil, 76% yield (185 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 7.4 Hz, 1H), 7.52−7.48 (m, 2H), 7.41−7.20 (m, 5H), 7.16 (d, J = 7.5 Hz, 1H), 4.97 (dd, J = 9.6, 3.1 Hz, 1H), 3.32 (dd, J = 13.9, 3.1 Hz, 1H), 3.07 (dd, J = 13.9, 9.6 Hz, 1H), 2.97 (s, 1H), 2.22 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.2, 135.0, 134.5, 130.7, 130.5, 129.16, 127.7, 127.0, 126.5, 125.4, 68.3, 43.1, 18.9. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{15}H_{16}OS$ 244.0922, found 244.0925.

*1-(4-Methoxyphenyl)-2-(phenylthio)ethan-1-ol (**3d**)*[10]. Yellow oil, 62% yield (161 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.42 (m, 2H), 7.38−7.22 (m, 5H), 6.91 (d, J = 8.7 Hz, 2H), 4.72 (dd, J = 9.2, 3.8 Hz, 1H), 3.82 (s, 3H), 3.31 (dd, J = 13.7, 3.9 Hz, 1H), 3.14 (dd, J = 13.7, 9.2 Hz, 1H), 2.94 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.4, 135.1, 134.4, 130.1, 129.1, 127.2, 126.7, 114.0, 71.4, 55.3, 43.8. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{15}H_{15}OS$ 243.1, found 243.1.

*1-(4-Fluorophenyl)-2-(phenylthio)ethan-1-ol (**3e**).* Yellow oil, 71% yield (176 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.42 (m, 2H), 7.39−7.23 (m, 5H), 7.15−6.99 (m, 2H), 4.72 (dd, J = 9.1, 3.8 Hz, 1H), 3.30 (dd, J = 13.8, 3.9 Hz, 1H), 3.20−2.95 (m, 2H, -O<u>H</u>, -C<u>H</u>-). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.4 (d, J = 264.0 Hz), 138.0 (d, J = 3.1 Hz), 134.8, 130.3, 129.2, 127.7 (d, J = 8.1 Hz), 126.9, 115.4 (d, J = 21.5 Hz), 71.2, 44.0. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{14}H_{13}FOS$ 248.0671, found 248.0679.

*1-(4-Chlorophenyl)-2-(phenylthio)ethan-1-ol (**3f**)*[10]. Yellow oil, 79% yield (208 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.40 (m, 2H), 7.39−7.15 (m, 7H), 4.71 (dd, J = 9.3, 3.6 Hz, 1H), 3.30 (dd, J = 13.8, 3.7 Hz, 1H), 3.07 (dd, J = 13.8, 9.3 Hz, 1H), 2.94 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.6, 134.6, 133.6, 130.4, 129.2, 128.7, 127.2, 127.0, 71.0, 44.0. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{14}H_{12}ClS$ 247.0, found 247.0.

*1-(2-Chlorophenyl)-2-(phenylthio)ethan-1-ol (**3g**)*. Yellow oil, 83% yield (219 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70−7.66 (m, 1H), 7.48−7.52 (m, 2H), 7.38−7.28 (m, 4H), 7.29−7.21 (m, 2H), 5.13 (dd, J = 9.7, 2.7 Hz, 1H), 3.55 (dd, J = 14.0, 2.7 Hz, 1H), 3.03 (s, 1H), 2.92 (dd, J = 14.0, 9.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.5, 134.3, 131.6, 130.4, 129.4, 129.1, 128.9, 127.2, 127.1, 126.9, 68.1, 42.2. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{14}H_{13}ClOS$ 264.0376, found 264.0379.

*1-(3-Chlorophenyl)-2-(phenylthio)ethan-1-ol (**3h**)* . Yellow oil, 83% yield (219 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.27 (m, 2H), 7.24−7.18 (m, 3H), 7.17−7.03 (m, 4H), 4.55 (dd, J = 9.3, 3.6 Hz, 1H), 3.17 (dd, J = 13.8, 3.6 Hz, 1H), 3.01 (s, 1H), 2.93 (dd, J = 13.8, 9.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 144.3, 134.6, 134.5, 130.4, 129.8, 129.2, 128.1, 127.0, 126.1, 124.1, 71.1, 44.0. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{14}H_{13}ClOS$ 264.0376, found 264.0384.

*1-(2-Bromophenyl)-2-(phenylthio)ethan-1-ol (**3i**)*. Yellow oil, 60% yield (185 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, J = 7.8, 1.6 Hz, 1H), 7.56−7.48 (m, 3H), 7.42−7.31 (m, 3H), 7.31−7.24 (m, 1H), 7.16 (td, J = 7.7, 1.7 Hz, 1H), 5.08 (dd, J = 9.7, 2.6 Hz, 1H), 3.53 (dd, J = 14.0, 2.8 Hz, 1H), 3.15 (s, 1H), 2.90 (dd, J = 14.0, 9.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.1, 134.3, 132.8, 130.7, 129.3, 129.1, 127.9, 127.5, 127.0, 121.8, 70.4, 42.4. HRMS (CI-TOF) *m/z*: $(M+H)^+$ Calcd for $C_{14}H_{14}BrOS$ 308.9949, found 308.9936.

*1-(4-Bromophenyl)-2-(phenylthio)ethan-1-ol (**3j**)*[10]. Yellow oil, 65% yield (201 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.45 (m, 2H), 7.44−7.40 (m, 2H), 7.39−7.30 (m, 2H), 7.24−7.30 (m, 1H), 7.24−7.17 (m, 2H), 4.68 (dd, J = 9.0, 3.8 Hz, 1H), 3.30 (s, 1H), 3.27 (dd, J = 13.8, 3.9 Hz, 1H), 3.08

(dd, J = 13.8, 9.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.3, 134.8, 131.7, 130.3, 129.3, 127.7, 127.0, 121.8, 71.2, 43.8. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{14}H_{12}BrS$ 291.0, found 291.0.

*2-(Phenylthio)-1-(3-(trifluoromethyl)phenyl)ethan-1-ol (**3k**)*. Yellow oil, 54% yield (161 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (s, 1H), 7.58−7.52 (m, 2H), 7.50−7.41 (m, 3H), 7.39−7.32 (m, 2H), 7.31−7.26 (m, 1H), 4.79 (dd, J = 9.2, 3.7 Hz, 1H), 3.34 (dd, J = 13.9, 3.8 Hz, 1H), 3.30 (s, 1H), 3.11 (dd, J = 13.9, 9.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.2, 134.4, 130.8 (q, J = 32.3 Hz), 130.5, 129.3, 129.3, 129.3, 129.0, 127.1, 124.8 (q, J = 3.8 Hz), 122.8 (q, J = 3.8 Hz), 71.2, 44.0. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{15}H_{13}F_3OS$ 298.0639, found 298.0652.

*Methyl 4-(1-hydroxy-2-(phenylthio)ethyl)benzoate (**3l**)*. Yellow oil, 52% yield (150 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46−7.42 (m, 2H), 7.41−7.32 (m, 4H), 7.30−7.30 (m, 1H), 7.08−7.10 (m, 2H), 4.74 (dd, J = 9.5, 3.3 Hz, 1H), 3.33 (dd, J = 13.9, 3.5 Hz, 1H), 3.09 (dd, J = 13.9, 9.5 Hz, 1H), 2.93 (s, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.6, 150.2, 140.0, 135.1, 130.1, 129.2, 127.1, 126.8, 121.7, 71.3, 43.7, 21.2. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{16}H_{16}O_3S$ 288.0820, found 288.0826.

*4-(1-Hydroxy-2-(phenylthio)ethyl)benzonitrile (**3m**)*[14]. Yellow oil, 56% yield (143 mg). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.79 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.43−7.23 (m, 4H), 7.21− 7.11 (m, 1H), 5.93 (d, J = 4.7 Hz, 1H), 4.82 (dd, J = 11.1, 6.0 Hz, 1H), 3.25 (d, J = 6.2 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 154.7, 141.5, 137.2, 134.2, 133.3, 132.5, 130.9, 124.2, 115.1, 75.9, 46.2. MS (ESI-TOF) *m/z*: $(M+H)^+$ Calcd for $C_{15}H_{14}NOS$ 256.1, found 256.1.

*2-Phenyl-1-(phenylthio)propan-2-ol (**3o**)*[15]. Yellow oil, 57% yield (139 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 7.4 Hz, 2H), 7.42−7.28 (m, 4H), 7.35−7.26 (m, 3H), 7.26−7.20 (m, 1H), 3.60 (d, J = 13.3 Hz, 1H), 3.42 (d, J = 13.3 Hz, 1H), 3.06 (s, 1H), 1.69 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 146.3, 136.6, 130.0, 129.0, 128.3, 127.2, 126.5, 124.9, 74.1, 49.6, 29.4. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{15}H_{15}S$ 227.1, found 227.1.

*1-Phenyl-2-(phenylthio)propan-1-ol (**3p**)*[16]. Yellow oil, 41% yield (combined yield of two diastereomers) (*dr* = 86/14, determined by ^{1}H NMR) (100 mg).

Major diastereomer of **3p**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.24 (m, 10H), 4.81 (s, 1H), 3.60 (qd, J = 7.0, 3.0 Hz, 1H), 2.88 (s, 1H), 1.21−1.18 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.0, 133.8, 132.4, 129.2, 128.2, 127.6, 127.4, 126.0, 73.3, 51.4, 13.2.

Minor diastereomer of **3p**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56−7.52 (m, 10H), 4.44 (d, J = 8.6 Hz, 1H), 3.49 (s, 1H), 3.41−3.29 (m, 1H), 1.13 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.9, 134.2, 133.7, 129.1 128.4, 128.1, 127.9, 127.1, 73.3, 52.7, 18.3.

MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{15}H_{15}S$ 227.1, found 227.1.

*1-Phenyl-2-(phenylthio)ethan-1-ol (**4q**)*. White solid, mp 58−60 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02−7.92 (m, 2H), 7.69−7.59 (m, 1H), 7.53−7.46 (m, 2H), 7.44−7.38 (m, 2H), 7.40−7.21 (m, 3H), 4.31 (s, 2H). MS (ESI-TOF) *m/z*: $(M+H)^+$ Calcd for $C_{14}H_{13}$ OS 229.1, found 229.1.

*1-Phenyl-2,2-bis(phenylthio)ethan-1-ol (**4r**)*. Yellow oil, 15% yield (50 mg). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.07 (d, J = 7.2 Hz, 2H), 7.79−7.63 (m, 1H), 7.54 (t, J = 7.7 Hz, 2H), 7.48−7.40 (m, 4H), 7.38−7.34 (m, 6H), 6.68 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 191.8, 134.8, 134.2, 133.6, 132.0, 129.5, 129.2, 128.9, 60.3. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{20}H_{16}OS_2$ 336.0643, found 336.0660.

*1,1-Diphenyl-2-(phenylthio)ethan-1-ol (**3s**)*[15]. Yellow oil, 78% yield (240 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.41 (m, 4H), 7.40−7.36 (m, 2H), 7.34−7.30 (m, 4H), 7.28−7.11 (m, 5H), 3.87 (s, 2H), 3.55 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.2, 136.5, 130.3, 129.1, 128.3, 127.4, 126.7, 126.2, 77.7, 49.1. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{20}H_{17}S$ 289.1, found 289.1.

*1-Phenyl-2-(o-tolylthio)ethan-1-ol(**3ab**)*. Yellow oil, 92% yield (230 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47−7.33 (m, 6H), 7.27−7.18 (m, 3H), 4.79 (dd, J = 9.3, 3.6 Hz, 1H), 3.33 (dd, J = 13.6, 3.6 Hz, 1H), 3.16 (dd, J = 13.6, 9.3 Hz, 1H), 3.05 (s, 1H), 2.49 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$):

δ 142.4, 138.5, 134.4, 130.5, 129.3, 128.7, 128.6, 128.1, 126.7, 126.6, 126.0, 71.9, 43.1, 20.7. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{15}H_{15}S$ 227.1, found 227.1.

*2-((2-Methoxyphenyl)thio)-1-phenylethan-1-ol (**4ac**).* Yellow oil, 16% yield (40 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98−7.94 (m, 2H), 7.62−7.56 (m, 1H), 7.50−7.44 (m, 2H), 7.37 (dd, J = 7.6, 1.6 Hz, 1H), 7.30−7.24 (m, 1H), 6.90−6.86 (m, 2H), 4.25 (s, 2H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.5, 158.4, 135.7, 133.3, 132.7, 129.1, 128.7, 128.6, 122.1, 121.1, 110.8, 55.7, 39.6. HRMS (CI-TOF) *m/z*: $(M+H)^+$ Calcd for $C_{15}H_{15}O_2S$ 259.0793, found 259.0786.

*2-((2,6-Dimethylphenyl)thio)-1-phenylethan-1-ol (**3ad**).* Yellow oil, 66% yield (160 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.30 (m, 5H), 7.23−7.16 (m, 3H), 4.66 (dd, J = 9.4, 3.6 Hz, 1H), 3.10−3.04 (m, 2H, -C<u>H</u>$_2$-, O<u>H</u>), 2.97 (dd, J = 13.3, 9.4 Hz, 1H), 2.63 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 142.4, 142.0, 132.4, 128.1, 127.9, 127.4, 125.5, 72.2, 44.7, 21.7. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{16}H_{17}S$ 241.1, found 241.1.

*2-((2-Fluorophenyl)thio)-1-phenylethan-1-ol (**3ag**).* Yellow oil, 48% yield (120 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (td, J = 7.8, 1.8 Hz, 1H), 7.39−7.25 (m, 6H), 7.16−7.05 (m, 2H), 4.72 (dd, J = 9.3, 3.4 Hz, 1H), 3.33 (dd, J = 13.7, 3.6 Hz, 1H), 3.10 (dd, J = 13.7, 9.3 Hz, 1H), 3.06 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 161.5 (d, J = 245.6 Hz), 141.6, 132.9 (d, J = 1.4 Hz), 128.9 (d, J = 8.0 Hz), 128.1, 127.5, 125.4, 124.2 (d, J = 3.7 Hz), 121.2 (d, J = 17.7 Hz), 115.5 (d, J = 22.7 Hz), 71.5, 43.1 (d, J = 2.3 Hz). HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{14}H_{13}FOS$ 248.0671, found 248.0670.

*2-((4-Fluorophenyl)thio)-1-phenylethan-1-ol (**3ah**).* Yellow oil, 51% yield (130 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49−7.44 (m, 2H), 7.41−7.31 (m, 5H), 7.11−7.04 (m, 2H), 4.74 (dd, J = 9.2, 3.7 Hz, 1H), 3.36−3.25 (m, 1H), 3.13 (dd, J = 13.7, 9.2 Hz, 1H), 3.06 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.1 (d, J = 247.3 Hz), 142.1, 133.2 (d, J = 8.1 Hz), 130.0 (d, J = 3.4 Hz), 128.6, 128.1, 125.9, 116.3 (d, J = 21.9 Hz), 71.8, 45.1. MS (ESI-TOF) *m/z*: $(M\text{-}OH)^+$ Calcd for $C_{14}H_{12}FS$ 231.1, found 231.0.

*2-((2-Chlorophenyl)thio)-1-phenylethan-1-ol(**3ai**)*. Yellow oil, 38% yield (100 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48−7.32 (m, 7H), 7.29−7.22 (m, 1H), 7.20−7.14 (m, 1H), 4.79 (dd, J = 9.1, 3.7 Hz, 1H), 3.36 (dd, J = 13.5, 3.7 Hz, 1H), 3.18 (dd, J = 13.5, 9.2 Hz, 1H), 3.09 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.7, 134.3, 134.0, 129.8, 129.5, 128.2, 127.6, 127.0, 126.8, 125.4, 71.4, 42.3. HRMS (CI-TOF) *m/z*: M^+ Calcd for $C_{14}H_{13}ClOS$ 264.0376, found 264.0377.

*2,2,6,6-Tetramethyl-1-((phenylthio)oxy)piperidine (**5**)*. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 6.4 Hz, 2H), 7.44−7.42 (m, 2H), 7.40−7.36 (m, 1H), 1.95−1.75 (m, 1H), 1.74−1.30 (m, 15H), 1.00−0.80 (m, 2H). MS (ESI-TOF) *m/z*: $(M+H)^+$ Calcd for $C_{15}H_{24}NOS$ 266.2, found 266.2.

ASSOCIATED CONTENT

Supporting Information

The discussion and mechanism for the reactions of α−bromostyrene (**1q**), β−bromostyrene (**1r**) and alkenes (**1t-v**) with thiophenol, as well as the reactions of *o*-methoxythiophenol (**2c**), 4-methoxyphenylthiol (**2e**), 2-aminophenylthiol (**2f**), 4-nitrophenylthiol (**2j**), 2-pyridylthiol (**2k**) and 2-furylthiol (**2l**) with styrene; ^{1}H, ^{13}C NMR spectra for compounds **3**, **4** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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