JOC The Journal of Organic Chemistry

Note

NH4I-Promoted and H2O-Controlled Intermolecular Bis-sulfenylation and Hydroxysulfenylation of Alkenes via a Radical Process

Runfa He, Xiuwen Chen, Yibiao Li, Qiang Liu, Chunshu Liao, Lu Chen, and Yubing Huang

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b01047 • Publication Date (Web): 11 Jun 2019

Just Accepted

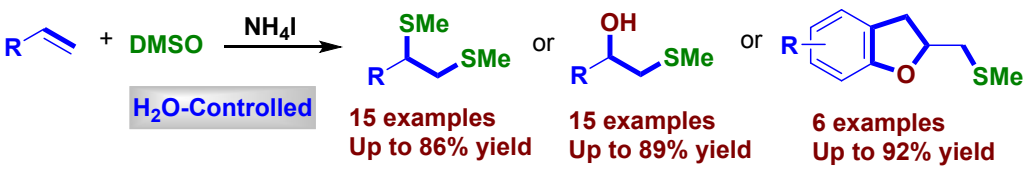
is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

NH_4I-Promoted and H_2O-Controlled Intermolecular Bis-sulfenylation and Hydroxysulfenylation of Alkenes *via* a Radical Process

Runfa He[a], Xiuwen Chen[a], Yibiao Li[a]*, Qiang Liu[a,b], Chunshu Liao[a], Lu Chen*, Yubing Huang

[a]School of Biotechnology and Health Sciences, Wuyi University, Jiangmen, Guangdong Province 529090, China; [b]Center of Basic Molecular Science, Department of Chemistry, Tsinghua University, Beijing 100084, China

E-mail: leeyib268@126.com; wyuchemcl@126.com

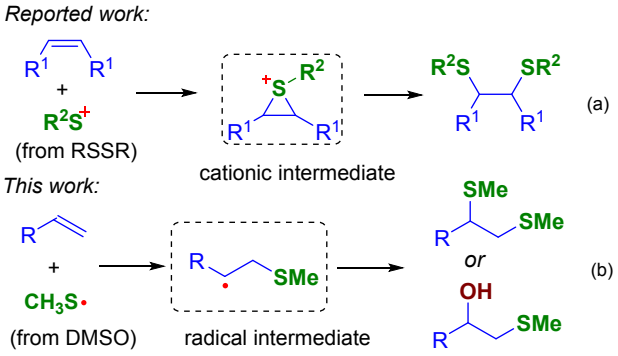


ABSTRACT: An NH_4I-promoted and H_2O-controlled intermolecular difunctionalization of alkenes for the synthesis of bis-methylsulfane and β-hydroxysulfides is presented. Mechanistic investigation revealed the reaction proceeds *via* methylthiyl radical addition to C=C double bond of alkenes to give a carbon-centered radical and immediately cyclize to a thiiranium ion, followed by combination with H_2O to afford *β*-hydroxysulfides in 52–89% yield with chemo- and regioselectivity. In the absence of the water, 1,2-disulfenylation takes place to give bis-methylsulfane in moderate to good yields.

In recent decades, the difunctionalization of olefins has become one of the most practical methods for synthesizing functional molecules or organic synthons bearing two vicinal carbon−carbon bonds or carbon−heteroatom bonds.[1] Among them, the bis-sulfenylation[2] and hydroxysulfenylation[3] of allylbenzene derivatives to prepare synthetically useful vicinal

dithioethers is attracting increasing attention due to their synthetic utility in drug development[4] and fine chemical synthesis[5]. Previously reported sulfur etherification reagents mainly focused on alkyl and aromatic sulphides, such as thiol,[6] sulfonyl hydrazides,[7] disulfides,[8] sulfonamides,[9] sulfenyl halides,[10] sulfenate esters,[11] (methylthio)-sulfonium salts[12] and sodium methanethiolate.[13] In particular, Lei and co-workers developed that the first efficiently electrocatalytic dehydrogenative C−H/S−H cross-coupling construct C-S bond, which was use the aryl/heteroaryl thiols and electron-rich arenes as reaction substrates.[14] Simultaneously, Jiang and co-workers use the organic thiosulfate salts to adjust the nature of free radicals by using the "masked strategy" and achieve selective sulphoxide and thioetherification.[15] However, these systems involve unpleasant odors, expensive catalysts and reagents, low chemo- and regio-selectivity and harsh conditions. There are hardly any reports of the use of dimethyl sulfoxide (DMSO) as a sulfur etherification reagent in bis-sulfenylation and hydroxysulfenylation reactions of alkenes. DMSO, however, has been used as source of groups such as $–C_1$, $–CH_2–$, =CH–, $–CH_3$, –CHO, –CN, –SMe, $–SO_2Me$ group and as an oxygen source[16] in various organic synthesis methodology over recent decades. In addition, most bis-sulfenylation reactions are generally initiated through an episulfonium ion intermediate, with nucleophilic attack ultimately leading to vicinal dithioethers (Scheme 1a)[2a-e ,17]. In contrast, the bis-sulfenylation of alkenes to give vicinal dithioethers *via* a radical approach has rarely been explored. When the bis-sulfenylation reaction was initiated through a $CH_3S•$ radical originating from DMSO, a subsequent carbon radical intermediate was formed. Herein, we report the realization of this

hypothesis via an NH_4I-promoted and H_2O-controlled intermolecular bis-sulfenylation and hydroxysulfenylation reaction of alkenes with DMSO as a MeS radical surrogate (Scheme 1b).

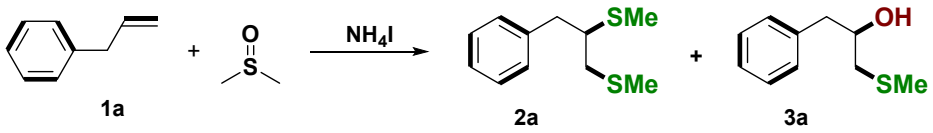


Scheme 1. Outline for the Bis-sulfenylation and Hydroxysulfenylation of Alkenes

In order to test the above bis-sulfenylation hypothesis, we screened reaction conditions using allylbenzene **1a**, NH_4I and anhydrous DMSO as a model reaction. The DMSO was used as both solvent and a MeS radical surrogate. To our delight, at a reaction temperature of 100 °C, the bis-sulfenylation reaction proceeded to afford the vicinal dithioether product **2a** in 19% yield, along with a small amount of the hydroxysulfenylation product **3a** in the presence of 2 equiv. NH_4I (Table 1, entry 1). Further studies demonstrated that the yield was significantly improved upon increasing the reaction temperature (Table 1, entries 2−4). When the reaction temperature was increased to 140 °C, the yield of the bis-sulfenylation product **2a** was slightly lower, and the yield of the hydroxysulfenylation product **3a** was slightly increased to 15% (Table 1, entry 5). Increasing or decreasing the amount of NH_4I did not improve the yield of the bis-sulfenylation reaction (Table 1, entries 6-7). It is noteworthy that H_2O concentration had a significant effect on the yield of **2a** and **3a** (Table 1, entries 8−12). The yield of the hydroxysulfenylation product **3a** was greatly improved if DMSO and H_2O

were used as the reaction solvent. We observed that when the ratio of DMSO: H_2O was 1:1, the hydroxysulfenylation product was afforded in 87% yield and the yield of the bis-sulfenylation reaction did not exceed 5% (Table 1, entries 8-12). Subsequently, we investigated various halide sources, such as Et_4NI, NH_4Br and HI (Table 1, entries 15-17). None of these promoted the reaction well, and only I_2 generated the 1-(methylthio)-3-phenylpropan-2-ol **3a** in 53% yield (Table 1, entry 18). When 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or butylated hydroxytoluene (BHT) were added as radical scavengers, the sulfenylation reaction was completely inhibited (Table 1, entries 19-20). This indicates that the current intermolecular difunctionalization reaction proceeds *via* a radical pathway.

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

Entry	Halide (equiv.)	Solvent(v/v)	Temp (°C)	Yield[b] (%)	
				2a	**3a**
1	NH_4I (2 eq)	DMSO	100	19	<5
2	NH_4I (2 eq)	DMSO	110	21	<5
3	NH_4I (2 eq)	DMSO	120	72	<5
4	**NH_4I (2 eq)**	**DMSO**	**130**	**84**	**<5**
5	NH_4I (2 eq)	DMSO	140	73	15
6	NH_4I (3 eq)	DMSO	130	82	<5
7	NH_4I (1 eq)	DMSO	130	67	13
8	NH_4I (2 eq)	DMSO/H_2O (20:1)	130	56	12
9	NH_4I (2 eq)	DMSO/H_2O (2:1)	130	<5	69

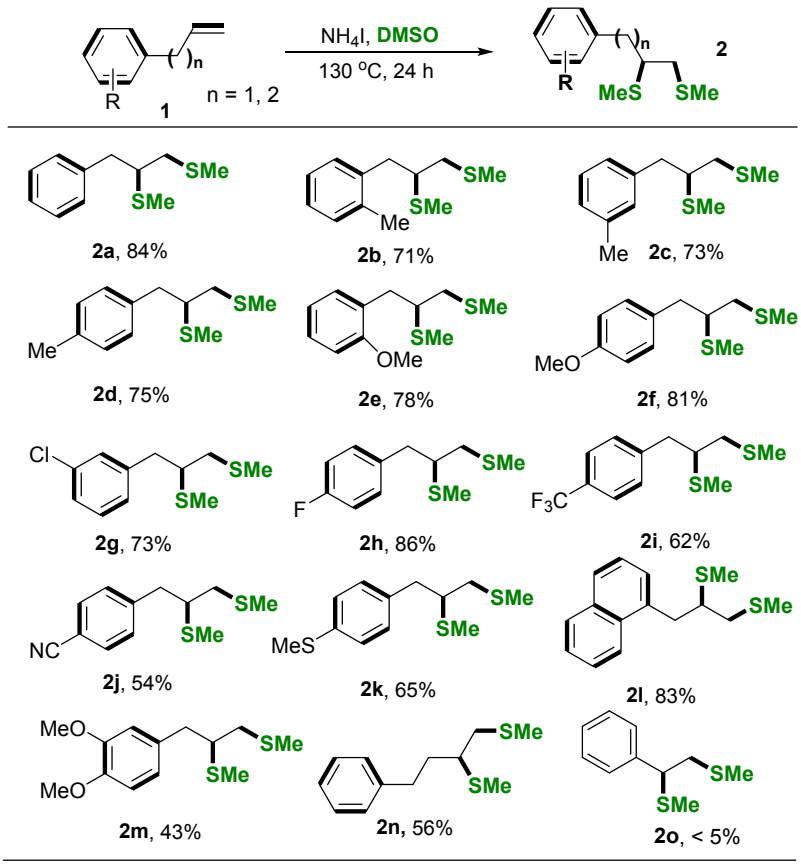
10	NH_4I (1 eq)	DMSO/H_2O (2:1)	130	<5	65
11	NH_4I (3 eq)	DMSO/H_2O (2:1)	130	<5	72
12	**NH_4I (2 eq)**	**DMSO/H_2O (1:1)**	**130**	**<5**	**87**
13	NH_4I (2 eq)	DMSO/H_2O (1:1)	120	<5	48
14	NH_4I (2 eq)	DMSO/H_2O (1:2)	130	<5	35
15	Et_4NI (2 eq)	DMSO/H_2O (1:1)	130	0	<5
16	NH_4Br (2 eq)	DMSO/H_2O (1:1)	130	0	<5
17	HI (2 eq)	DMSO/H_2O (1:1)	130	<5	32
18	I_2 (1 eq)	DMSO/H_2O (1:1)	130	<5	53
19[c]	NH_4I (2 eq)	DMSO/H_2O (1:1)	130	trace	trace
20[d]	NH_4I (2 eq)	DMSO/H_2O (1:1)	130	trace	trace

[a] Reaction conditions: alkene **1a** (1.0 mmol), halide, solvent(v/v) (3.0 mL), 24h; [b] Isolated yield. [c]BHT (1.5 mmol); [d]TEMPO (1.5 mmol).

With the optimized conditions in hand, the generality of this bis-sulfenylation reaction was investigated. As shown in Scheme 2, allylbenzene derivatives with different substituents on the phenyl ring, including electron-withdrawing and electron-donating groups, were successfully converted to the corresponding bis-sulfenylation products **2a**−**m** in moderate to good yields. The addition of substituents at different positions on the aromatic ring of the allylbenzenes had no significant effect on the yield. The reaction tolerated a range of substituents including: -Me, -OMe, -F, -Cl, -CF_3, -CN and -SMe. It is noteworthy that 2-allylnaphthalene gave product **2l** in 83% yield under the standard reaction condition. It is important to note that substrates bearing two electron-donating groups such as a 3,4-dimethoxy group also proceeded smoothly to afford the target product **2m** in 43% yield.

Furthermore, the optimized conditions are equally effective for other unactivated alkenes (such as but-3-en-1-ylbenzene), to afford the bis-sulfenylation product **2n** in good yields. Unfortunately, the reaction with styrene, failed under the current reaction conditions (Scheme 2, **2o**). The yield of the bis-sulfenylation products was slightly lower because there is always accompanied by the hydroxysulfenylation product **3** (Scheme 3).

Scheme 2. Substrate scope for bis-sulfenylation reaction of alkenes [a, b]

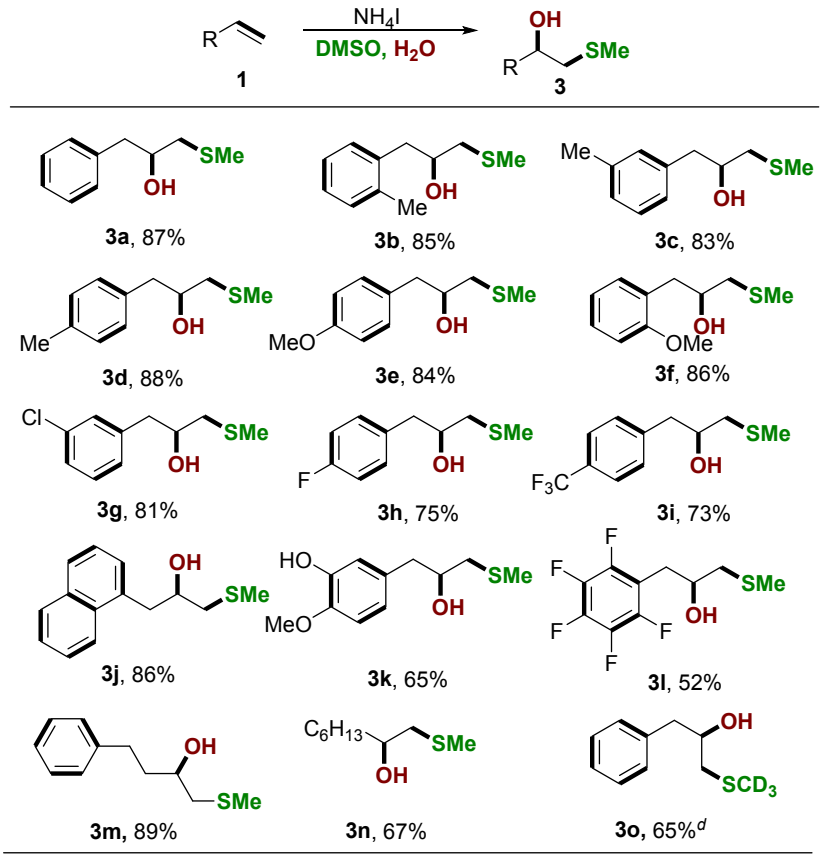


[a] Reaction conditions: alkene 1 (1.0 mmol), NH_4I (2.0 mmol) in DMSO (3.0 mL) at 130 °C for 24 h; [b] Isolated yield.

To further explore the application of our approach, we turned our attention to the NH_4I-promoted and H_2O-controlled hydroxysulfenylation of inactivated alkenes (Scheme 3). First, the various allylbenzene derivatives underwent hydroxysulfenylation under the standard conditions: NH_4I (2.0

equiv), DMSO (1.5 mL), H_2O (1.5 mL) and allylbenzene (1.0 mmol) at 130 °C for 24 h, which provided products **3a** in 87% yield (Table 1, entry 12). Similar to the bis-sulfenylation reaction, by varying the R substituents of allylbenzene derivatives **1**, it was observed that both electron-withdrawing and electron-donating substituents could be introduced to afford the hydroxysulfenylation products in moderate to good yields. The results indicated that the steric hindrance of allylbenzenes had no obvious influence on the efficiency of the desired transformation (Scheme 2, **3b** and **3f**), while electronic effects reduced the yields of **3** slightly (Scheme 2, **3h** and **3i**). It is noteworthy that 5-allyl-2-methoxyphenol also reacted smoothly with DMSO and H_2O to afford **3k** in 65% yield. As the phenolic hydroxyl group can quench the radical, the yield could be improved by prolonging the reaction time. Interestingly, the use of 1-allyl-2,3,4,5,6-pentafluorobenzene resulted in the formation of the corresponding β-hydroxysulfide product **3l** in moderate yield. Furthermore, the hydroxysulfenylation of but-3-en-1-ylbenzene with DMSO under the optimized conditions gave **3m** in 89% yield. Various substituted alkyl alkenes were found to be compatible under the optimized condition. The terminal alkenes 1-octenes successfully completed the hydroxysulfenylation reaction and gave the design product **3n** in 67% yields. When deuterated-DMSO was used as the reaction solvent and reagent, deuterium-labeled hydroxysulfenylation product **3o** were isolated in 65% yield, respectively.

Scheme 3. Substrate scope for the hydroxysulfenylation reaction[a,b]

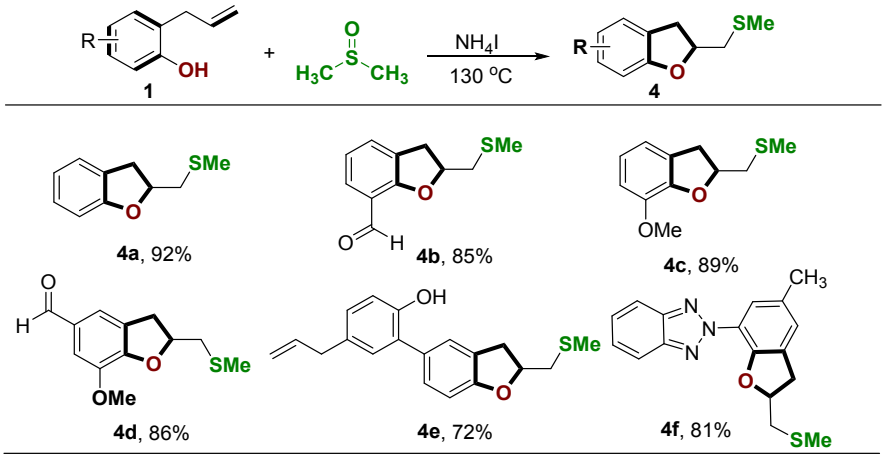


[a] Reaction conditions: alkene **1** (1.0 mmol), NH_4I (2.0 mmol) and H_2O (1.5 mL) in DMSO (1.5 mL) at 130 °C for 24 h; [b] Isolated yield; [c] Detected by ^{1}H-NMR; [d] DMSO-d^6 was used instead of DMSO.

To continue our investigation of the reaction scope, we explored various 2-allylphenol substrates for this process under the optimized reaction conditions (Scheme 4). Compared with hydroxysulfenylation of inactivated alkenes , Synthesis of 2-((methylthio)methyl)-2,3-dihydrobenzofuran by 2-hydroxylylylation of 2-allylphenol was achieved.[18] In this oxidizing system, both the methoxy group and the aldehyde group are not affected. The aldehyde group substituted 2-hydroxyallylbenzene can smoothly gave the target product 2-((methylthio)methyl)-2,3-dihydrobenzofuran-7-carbaldehyde **4b** and **4d** in good yields. It is important to note that substrates bearing electron-donating group such as phenolic hydroxy group

and allyl group also proceeded smoothly to afford the target product **4e** in 72% yield. It is interesting to note that 2-allyl-6-(2*H*-benzo[*d*][1,2,3]triazol-2-yl)-4-methylphenol gave product **4f** in 81% yield under the standard reaction condition.

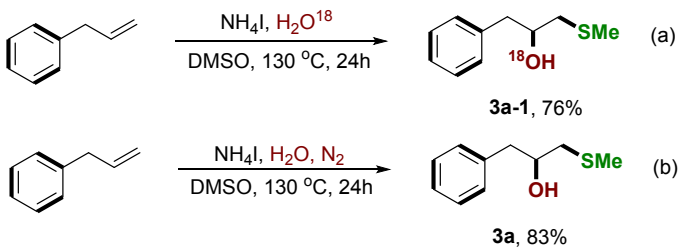
Scheme 4 Synthesis of dihydrobenzofurans from alkenes [a, b]



[a] Reaction conditions: alkene **1** (1.0 mmol), NH_4I (2.0 mmol) in DMSO (1.5 mL) at 130 °C for 18 h; [b] Isolated yield.

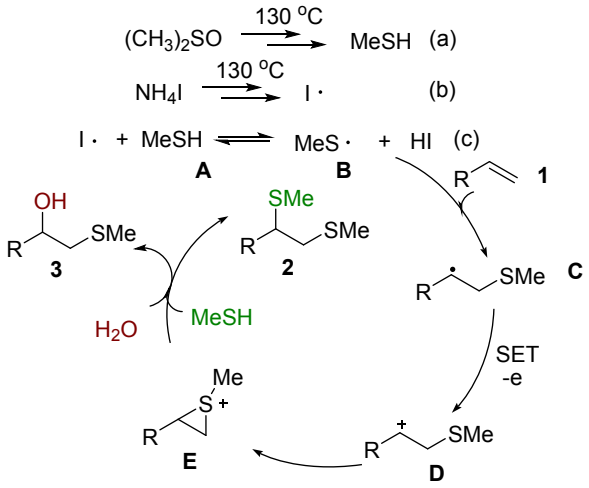
To gain mechanistic insights, isotopic labelling experiment using H_2O^{18} were conducted to verify the oxygen atom of the hydroxysulfenylation products. These results indicate that water acts as a hydroxy donor in this transformation (Scheme 5a). Under N_2 condition, the hydroxysulfenylation product **3a** was obtained in 83% yield (Scheme 5b). The result indicated that the formation of a thiiranium ion intermediate could be the dominant pathway.

Scheme 5. Control experiments.



On the basis of our findings and previous literature, a possible mechanism is illustrated in Scheme 6.[19] Initially, the iodine radical (I•)[20] and methanthiol (CH_3SH)[21] are produced through a series of transformations with NH_4I and DMSO at high temperature. Iodine radicals can form through a thermal decomposition process originating from NH_4I, which can react with methanthiol to liberate CH_3S• radicals. The methylthiyl radical (CH_3S•) **B** initiated by iodine radical selectively adds to the terminal C=C double bond of **1** to form intermediate carbon radical **C** [22], which undergoes further single-electron oxidation to afford a β-MeS-substituted carbocation **D** [23]. Then the β-MeS-substituted carbocation **D** should immediately cyclize to a gives thiiranium ion **E.** Subsequently, the nucleophilic attack of MeSH or H_2O on the thiiranium ion **E** produces bis-sulfenylation products **2** or hydroxysulfenylation products **3** [2a-e, 3c].

Scheme 6. Proposed reaction mechanism.



In conclusion, we have demonstrated an efficient and attractive strategy for synthesis of valuable bis-methylsulfane and β-hydroxysulfides through an NH_4I-promoted and H_2O-controlled intermolecular bis-sulfenylation and hydroxysulfenylation of terminal alkenes. The method complements existing approaches involving methylthiyl radical allylic C−H activation. The water

played a critical role in this reaction. This reaction chemo- and regioselectively afforded the bis-sulfenylation and hydroxysulfenylation products by varying the proportion of water. This unique bis-sulfenylation and hydroxysulfenylation procedure used readily available, stable and odorless DMSO as a thioetherification reagent, and has potential applications in modern organic synthesis chemistry and pharmaceutical chemistry.

EXPERIMENTAL SECTION

General Information: Unless otherwise noted, all commercial materials and solvents were used without further purification and all the reactions were carried out in a Schlenk tube equipped with magnetic stir bar. ^{1}H NMR spectra were recorded in $CDCl_3$ at 400 MHz (or 600 MHz) and ^{13}C $\{^{1}H\}$ NMR NMR spectra were recorded in $CDCl_3$ at 100 MHz (or 150 MHz) respectively, ^{1}H and ^{13}C $\{^{1}H\}$ NMR NMR were referenced to $CDCl_3$ at δ 7.26 and 77.0 respectively. GC–MS was obtained using electron ionization (Agilent Technologies 7890A/5975C). HRMS spectra were acquired using an Agilent 6210 ESI/TOF mass spectrometer and MAT 95XP (Double-focusing Magnetic Sector Analyzer), Thermo (EI, 70eV). TLC was performed using commercially prepared 100-400 mesh silica gel plates (GF_{254}), and visualization was effected at 254 nm. All the other chemicals were purchased from Aldrich Chemicals. Commercial reagents were used without further purification.

Typical procedure for synthesis of 1-(2,3-bis(methylthio)propyl)benzene derivatives: A mixture of allylbenzene (1 mmol), NH_4I (2 mmol), DMSO (2 mL) was added successively in a 20 mL Schlenk tube. The Schlenk tube was then immersed in an oil bath at 130 ^{o}C stirring for 24 h. After cooling down to room temperature, the solution was filtered through a small amount of silica gel. Then the residue was concentrated in vacuo and the crude was purified by flash chromatography

with n-hexane/ethyl acetate (10/1, v/v) to afford the (3-phenylpropane-1,2-diyl)bis(methylsulfane) as a pale-yellow oil in 84% yield.

Typical procedure for synthesis of 1-(methylthio)-3-phenylpropan-2-ol derivatives: A mixture of allylbenzene (1 mmol), NH_4I (2 mmol), DMSO (1.5 mL) and H_2O (1.5 mL) was added successively in a 20 mL Schlenk tube. The Schlenk tube was then immersed in an oil bath at 130 °C stirring for 24 h. After cooling down to room temperature, the solution was filtered through a small amount of silica gel. Then the residue was concentrated in vacuo and the crude was purified by flash chromatography with n-hexane/ethyl acetate (8/1, v/v) to afford the 1-(methylthio)-3-phenylpropan-2-ol as a pale-yellow oil in 87% yield.

1-(2,3-bis(methylthio)propyl)benzene (2a): Pale-yellow liquid (178 mg, 84% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.17 (m, 2H), 7.13 (dd, J = 7.5, 3.8 Hz, 3H), 3.03 (dd, J = 13.6, 5.8 Hz, 1H), 2.88 – 2.80 (m, 1H), 2.71 (ddd, J = 18.6, 13.5, 6.4 Hz, 2H), 2.57 (dd, J = 13.3, 7.6 Hz, 1H), 2.02 (s, 3H), 1.95 (s, 3H); ^{13}C {^{1}H} NMR NMR (100 MHz, $CDCl_3$) δ 138.7, 129.1 (2C), 128.1 (2C), 126.2, 48.0, 39.4, 38.8, 16.2, 13.7. GC-MS (EI, 70 eV) m/z: 212, 164, 151, 121; HRMS (EI) m/z: $[M]^+$ Calcd for $C_{11}H_{16}S_2$ 212.0688; Found, 212.0687.

1-(2,3-bis(methylthio)propyl)-2-methylbenzene (2b): Pale-yellow liquid (160 mg, 71% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20-7.18 (m, 1H), 7.16-7.14 (m, 3H), 3.17 (dd, J = 14.1, 6.3 Hz, 1H), 2.98 – 2.90 (m, 1H), 2.86 – 2.76 (m, 2H), 2.72 (dd, J = 13.3, 7.4 Hz, 1H), 2.36 (s, 3H), 2.14 (s, 3H), 2.05 (s, 3H); ^{13}C {^{1}H} NMR NMR (150 MHz, $CDCl_3$) δ 137.4, 136.2, 130.4, 130.2, 126.6, 125.8, 47.4, 39.6, 37.4, 19.6, 16.6, 14.0. GC-MS (EI, 70 eV) m/z: 226, 178, 165, 121; HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}S_2$ 226.0844; Found, 226.0843.

1-(2,3-bis(methylthio)propyl)-3-methylbenzene (2c): Pale-yellow liquid(165 mg, 73% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 1H), 7.08 – 6.96 (m, 3H), 3.08 (dd, J = 13.8, 6.2 Hz, 1H), 2.97 – 2.90 (m, 1H), 2.84 – 2.74 (m, 2H), 2.68 (dd, J = 13.3, 7.5 Hz, 1H), 2.34 (s, 3H), 2.14 (s, 3H), 2.07 (s, 3H); ^{13}C {^{1}H} NMR NMR (150 MHz, $CDCl_3$) δ 138.9, 137.9, 130.0, 128.2, 127.2, 126.3, 48.2, 39.6, 39.0, 21.4, 16.4, 13.9. GC-MS (EI, 70 eV) m/z: 226, 178, 165, 131, 121; HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}S_2$ 226.0844; Found, 226.0846.

1-(2,3-bis(methylthio)propyl)-4-methylbenzene (2d): Pale-yellow liquid (170 mg, 75% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.13-7.10 (m, 4H), 3.08 (dd, J = 13.9, 6.1 Hz, 1H), 2.95 – 2.89 (m, 1H), 2.84 – 2.77 (m, 2H), 2.67 (dd, J = 13.3, 7.7 Hz, 1H), 2.32 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H); ^{13}C {^{1}H} NMR NMR (150 MHz, $CDCl_3$) δ 136.0, 135.8 (2C), 129.2 (2C), 129.0, 48.3, 39.1, 39.0, 21.1, 16.4, 13.9. GC-MS (EI, 70 eV) m/z: 226, 178, 165, 121; HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}S_2$ 226.0844; Found, 226.0843.

1-(2,3-bis(methylthio)propyl)-2-methoxybenzene (2e): Pale-yellow liquid (189 mg, 78% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (td, J = 8.0, 1.7 Hz, 2H), 6.85 (d, J = 8.1 Hz, 2H), 3.82 (s, 3H), 3.11 (dt, J = 9.4, 6.8 Hz, 2H), 2.87 (td, J = 9.7, 5.0 Hz, 1H), 2.80 – 2.74 (m, 1H), 2.74 – 2.66 (m, 1H), 2.12 (s, 3H), 2.07 (s, 3H); ^{13}C {^{1}H} NMR NMR (150 MHz, $CDCl_3$) δ 157.5, 131.2, 127.8, 127.4, 120.3, 110.2, 55.2, 46.3, 39.3, 35.1, 16.3, 13.6. GC-MS (EI, 70 eV) m/z: 242, 194, 181, 147. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}OS_2$ 242.0794; Found, 242.0792.

1-(2,3-bis(methylthio)propyl)-4-methoxybenzene (2f): Pale-yellow liquid (196 mg, 81% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 – 7.10 (m, 2H), 6.87 – 6.80 (m, 2H), 3.79 (s, 3H), 3.06 (dd, J = 13.9, 6.0 Hz, 1H), 2.95 – 2.85 (m, 1H), 2.80 – 2.75 (m, 2H), 2.66 (dd, J = 13.2, 7.7 Hz, 1H), 2.13 (s, 3H),

2.06 (s, 3H); ^{13}C {^{1}H} NMR NMR (150 MHz, $CDCl_3$) δ 158.2, 130.9, 130.6 (2C), 113.7 (2C), 55.2, 48.4, 38.9, 38.6, 16.4, 14.0. GC-MS (EI, 70 eV) m/z: 242, 194, 181, 147. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}OS_2$ 242.0794; Found, 242.0792.

(3-(3-chlorophenyl)propane-1,2-diyl)bis(methylsulfane) (2g): Pale-yellow liquid (180 mg, 73% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.20 (m, 3H), 7.13 (d, J = 6.6 Hz, 1H), 3.13 (dd, J = 13.8, 5.5 Hz, 1H), 2.90 (ddd, J = 10.6, 7.9, 5.3 Hz, 1H), 2.79 (dt, J = 11.5, 5.0 Hz, 2H), 2.65 (dd, J = 13.3, 8.0 Hz, 1H), 2.14 (s, 3H), 2.06 (s, 3H); ^{13}C {^{1}H} NMR NMR (100 MHz, $CDCl_3$) δ 141.0, 134.1, 129.5, 129.4, 127.6, 126.7, 48.0, 39.1 (2C), 16.4, 14.0. GC-MS (EI, 70 eV) m/z: 246, 210, 163, 150, 137, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{11}H_{15}ClS_2$ 246.0298; Found, 246.0297.

1-(2,3-bis(methylthio)propyl)-4-fluorobenzene (2h): Pale-yellow liquid (198 mg, 86% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 2H), 7.04 – 6.95 (m, 2H), 3.11 (dd, J = 14.0, 5.6 Hz, 1H), 2.89 (tt, J = 7.9, 5.4 Hz, 1H), 2.78 (dd, J = 13.3, 5.2 Hz, 2H), 2.66 – 2.58 (m, 1H), 2.14 (s, 3H), 2.06 (s, 3H); ^{13}C {^{1}H} NMR NMR (150 MHz, $CDCl_3$) δ 161.6 (d, $J_{C\text{-}F}$ = 243.0 Hz, 1C), 134.6 (d, $J_{C\text{-}F}$ = 3.15 Hz, 1C), 130.7 (d, $J_{C\text{-}F}$ = 7.8 Hz, 2C), 115.1 (d, $J_{C\text{-}F}$ = 21.0 Hz, 2C), 48.3, 39.0, 38.6, 16.4, 14.0. GC-MS (EI, 70 eV) m/z: 230, 182, 169, 135, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{11}H_{15}FS_2$ 230.0594; Found, 230.0592.

1-(2,3-bis(methylthio)propyl)-4-(trifluoromethyl)benzene (2i): Pale-yellow liquid (174 mg, 62% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.7 Hz, 2H), 7.36 (d, J = 7.8 Hz, 2H), 3.23 (dd, J = 13.5, 4.5 Hz, 1H), 2.95 – 2.77 (m, 3H), 2.65 (dd, J = 12.6, 8.3 Hz, 1H), 2.15(d, J = 1.2 Hz, 3H), 2.06 (d, J = 1.2 Hz, 3H); ^{13}C {^{1}H} NMR NMR (100 MHz, $CDCl_3$) δ 143.1, 129.7 (4C), 128.8 (d, $J_{C\text{-}F}$ =

32.1 Hz, 1C), 125.2 (q, J_{C-F} = 3.8 Hz, 1C), 47.9, 39.2, 39.1, 16.4, 14.0. GC-MS (EI, 70 eV) m/z: 280, 232, 219, 185, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{15}F3S_2$ 280.0562; Found, 280.0564.

4-(2,3-bis(methylthio)propyl)benzonitrile (2j): Pale-yellow liquid (128 mg,54% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 3.25 (dd, *J* = 13.8, 4.9 Hz, 1H), 2.89 (dt, *J* = 13.3, 4.3 Hz, 1H), 2.87 – 2.78 (m, 2H), 2.62 (dd, *J* = 13.3, 8.6 Hz, 1H), 2.15 (s, 3H), 2.05 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 144.7, 132.1 (2C), 130.2 (2C), 118.9, 110.4, 47.7, 39.3, 39.2, 16.4, 14.0. GC-MS (EI, 70 eV) m/z: 237, 189, 176, 142, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{15}NS_2$ 237.0640; Found, 237.0642.

(3-(4-(methylthio)phenyl)propane-1,2-diyl)bis(methylsulfane) (2k): Pale-yellow liquid (168 mg, 65% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.2 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 3.09 (dd, *J* = 13.9, 5.9 Hz, 1H), 2.90 (ddd, *J* = 13.3, 7.6, 5.8 Hz, 1H), 2.83 – 2.74 (m, 2H), 2.66 (dd, *J* = 13.3, 7.8 Hz, 1H), 2.47 (s, 3H), 2.14 (s, 3H), 2.06 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 136.2, 135.9, 129.8 (2C), 126.8 (2C), 48.2, 38.99, 38.95, 16.4, 16.0, 14.0. GC-MS (EI, 70 eV) m/z: 258, 210, 163, 150, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}S_3$, 258.0565; Found, 258.0564.

1-(2,3-bis(methylthio)propyl)naphthalene (2l): Pale-yellow liquid (217 mg, 83% yield), ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.16 (d, *J* = 8.3 Hz, 1H), 7.87 (s, 1H), 7.76 (dt, *J* = 6.3, 3.3 Hz, 1H), 7.57 – 7.46 (m, 2H), 7.44 – 7.36 (m, 2H), 3.71 (q, *J* = 9.4 Hz, 1H), 3.19 – 3.07 (m, 2H), 2.88 (dd, *J* = 13.3, 4.5 Hz, 1H), 2.81 – 2.68 (m, 1H), 2.15 (s, 3H), 2.02 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, CDCl3) *δ* 135.1, 133.9, 131.9, 128.9, 127.9, 127.4, 126.0, 125.5, 125.3, 123.6, 47.4, 39.9, 37.4, 16.6, 13.9. GC-MS (EI, 70 eV) m/z: 262, 214, 167, 153, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{15}H_{18}S_2$, 262.0844; Found, 262.0845.

4-(2,3-bis(methylthio)propyl)-1,2-dimethoxybenzene (2m): Pale-yellow liquid (117 mg, 43% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.84 – 6.73 (m, 3H), 3.87 (d, J = 10.0 Hz, 6H), 3.06 – 3.02 (m, 1H), 2.94 – 2.89 (m, 1H), 2.86 – 2.74 (m, 2H), 2.68 – 2.64 (m, 1H), 2.14 (s, 3H), 2.08 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 148.7, 147.7, 131.4, 121.4, 112.6, 111.1, 55.9, 55.9, 48.4, 39.2, 39.0, 16.5, 14.1. GC-MS (EI, 70 eV) m/z: 272, 224, 177, 151; GC-MS (EI, 70 eV) m/z: 226, 165, 117. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{13}H_{20}O_2S_2$, 272.0899; Found, 272.0897.

1-(3,4-bis(methylthio)butyl)benzene (2n): Pale-yellow liquid (127 mg, 56% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (s, 2H), 7.21 (dd, J = 17.1, 5.0 Hz, 3H), 2.89-2.83 (m, 2H), 2.81 – 2.73 (m, 2H), 2.66 (d, J = 6.6 Hz, 2H), 2.22 – 2.12 (m, 1H), 2.09 (s, 3H), 2.07 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 141.6, 128.5 (2C), 128.4 (2C), 125.9, 45.4, 39.8, 34.1, 32.8, 16.1, 13.0. GC-MS (EI, 70 eV) m/z: 226, 165, 117. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{12}H_{18}S_2$, 226.0844; Found, 226.0848.

1-(methylthio)-3-phenylpropan-2-ol (3a): Pale-yellow liquid(158 mg, 87% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.24 – 7.21 (m, 3H), 3.93 – 3.92 (m, 1H), 2.84 (d, J = 6.3 Hz, 2H), 2.66 (dd, J = 13.6, 3.8 Hz, 1H), 2.59 (s, 1H), 2.50 (dd, J = 13.6, 8.5 Hz, 1H), 2.09 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.9, 129.3 (2C), 128.4 (2C), 126.5, 69.9, 42.4, 41.2, 15.6. GC-MS (EI, 70 eV) m/z: 182, 164, 117, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{14}OSNa$ 205. 0658; Found 205.0658.

1-(methylthio)-3-o-tolylpropan-2-ol (3b): Pale-yellow liquid(167 mg, 85% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dp, J = 9.2, 5.2, 4.4 Hz, 4H), 3.96 – 3.92 (m, 1H), 2.86 (d, J = 6.5 Hz, 2H), 2.69 (dd, J = 13.6, 3.9 Hz, 1H), 2.59 – 2.49 (m, 2H), 2.34 (s, 3H), 2.10 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.5, 136.2, 130.4, 130.0, 126.6, 125.9, 69.3, 41.5, 39.7, 19.6, 15.7. GC-MS (EI, 70

eV) m/z: 196, 178, 131, 106, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{16}OSNa$ 219.0814; Found 219.0802.

1-(methylthio)-3-m-tolylpropan-2-ol (3c): Pale-yellow liquid(163 mg, 83% yield), ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, J = 7.7 Hz, 1H), 7.04 (t, J = 7.6 Hz, 3H), 3.96 – 3.89 (m, 1H), 2.81 (d, J = 6.4 Hz, 2H), 2.68 (dd, J = 13.6, 3.8 Hz, 1H), 2.58 – 2.46 (m, 2H), 2.34 (s, 3H), 2.11 (s, 3H); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.1, 137.8, 130.1, 128.4, 127.3, 126.3, 67.0, 42.5, 41.3, 21.4, 15.6. GC-MS (EI, 70 eV) m/z: 196, 178, 131, 106, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{16}OSNa$ 219.0814; Found 219.0812.

1-(methylthio)-3-p-tolylpropan-2-ol (3d): Pale-yellow liquid(172 mg, 88% yield), ^1H NMR (400 MHz, $CDCl_3$) δ 7.11 (s, 4H), 3.94 – 3.88 (m, 1H), 2.80 (d, J = 6.4 Hz, 2H), 2.67 (dd, J = 13.6, 3.8 Hz, 1H), 2.58 – 2.44 (m, 2H), 2.32 (s, 3H), 2.09 (s, 3H); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 136.1, 134.8, 129.3 (2C), 129.3 (2C), 70.1, 42.1, 41.3, 21.1, 15.7. GC-MS (EI, 70 eV) m/z: 196, 178, 131, 106, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{16}OSNa$ 219.0814; Found 219.0815.

1-(4-methoxyphenyl)-3-(methylthio)propan-2-ol (3e): Pale-yellow liquid(178 mg, 84% yield), ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 3.88 (dq, J = 8.2, 4.7, 4.1 Hz, 1H), 3.79 (s, 3H), 2.79 (d, J = 6.3 Hz, 2H), 2.71 – 2.62 (m, 1H), 2.50 (dd, J = 13.7, 8.6 Hz, 2H), 2.10 (s, 3H); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.3, 130.3 (2C), 129.8, 113.9 (2C), 70.0, 55.2, 41.6, 41.2, 15.6. GC-MS (EI, 70 eV) m/z: 212, 194, 147, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{11}H_{16}O_2S$, 212.0866; Found, 212.0864.

1-(2-methoxyphenyl)-3-(methylthio)propan-2-ol (3f): Pale-yellow liquid(182 mg, 86% yield), ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.10 (m, 2H), 6.98 – 6.78 (m, 2H), 4.01 (d, J = 11.1 Hz, 1H), 3.82

(s, 3H), 2.99 – 2.82 (m, 2H), 2.79 (s, 1H), 2.65 (dd, J = 13.6, 4.3 Hz, 1H), 2.54 (dd, J = 13.6, 8.0 Hz, 1H), 2.11 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.5, 131.4, 128.0, 126.4, 120.7, 110.5, 69.5, 55.3, 41.4, 37.2, 15.8. GC-MS (EI, 70 eV) m/z: 212, 194, 147, 121. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{11}H_{16}O_2S$, 212.0866; Found, 212.0867.

1-(3-chlorophenyl)-3-(methylthio)propan-2-ol (3g): Pale-yellow liquid(175 mg, 81% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 7.5 Hz, 3H), 7.16 – 7.09 (m, 1H), 3.92 (ddt, J = 12.4, 6.2, 3.9 Hz, 1H), 2.82 (d, J = 6.3 Hz, 2H), 2.73 – 2.58 (m, 2H), 2.50 (dd, J = 13.7, 8.7 Hz, 1H), 2.11 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 140.1, 134.2, 129.7, 129.4, 127.6, 126.7, 69.5, 42.0, 41.4, 15.6. GC-MS (EI, 70 eV) m/z: 216, 198, 151, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{13}ClOSNa$ 239.0268; Found 239.0268.

1-(4-fluorophenyl)-3-(methylthio)propan-2-ol (3h): Pale-yellow liquid(170 mg, 85% yield), 1H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 2H), 7.04 – 6.95 (m, 2H), 3.93 – 3.85 (m, 1H), 2.81 (d, J = 6.3 Hz, 2H), 2.67 (dd, J = 13.7, 3.7 Hz, 1H), 2.56 (s, 1H), 2.49 (dd, J = 13.7, 8.7 Hz, 1H), 2.10 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 161.7 (d, $J_{C\text{-}F}$ = 93 Hz, 1C), 133.6 (d, $J_{C\text{-}F}$ = 3.15 Hz, 1C), 130.8 (d, $J_{C\text{-}F}$ = 7.8 Hz, 2C), 115.3 (d, $J_{C\text{-}F}$ = 21 Hz, 2C), 69.7, 41.6, 41.3, 15.6. GC-MS (EI, 70 eV) m/z: 200, 169, 109, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{13}FOSNa$ 223.0563; Found 223.0563.

1-(4-(trifluoromethyl)phenyl)-3-(methylthio)propan-2-ol (3i): Pale-yellow liquid(183 mg, 73% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 3.95 (ddq, J = 8.7, 5.8, 3.2 Hz, 1H), 2.90 (d, J = 6.6 Hz, 2H), 2.69 (dd, J = 13.7, 3.7 Hz, 1H), 2.65 – 2.56 (m, 1H), 2.51 (dd, J = 13.7, 8.8 Hz, 1H), 2.11 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.2, 129.7 (4C),

128.9 (d, $J_{C\text{-}F}$ = 32.2 Hz, 1C), 125.3 (q, $J_{C\text{-}F}$ = 3.7 Hz, 1C), 69.3, 42.2, 41.5, 15.5. GC-MS (EI, 70 eV) m/z: 250, 232, 185, 159, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{13}F_3OSNa$ 273.0531; Found 273.0533.

1-(methylthio)-3-(naphthalen-4-yl)propan-2-ol (3j): Pale-yellow liquid (200 mg, 86% yield), ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.3 Hz, 1H), 7.92 – 7.85 (m, 1H), 7.77 (d, J = 7.7 Hz, 1H), 7.62 – 7.48 (m, 2H), 7.47 – 7.37 (m, 2H), 4.21 – 4.02 (m, 1H), 3.38 (dd, J = 13.9, 5.5 Hz, 1H), 3.29 (dd, J = 14.0, 7.4 Hz, 1H), 2.73 (dd, J = 13.6, 4.3 Hz, 1H), 2.68 – 2.49 (m, 2H), 2.10 (s, 3H); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 134.1, 133.9, 132.1, 128.8, 127.6, 127.4, 126.0, 125.6, 125.4, 123.7, 69.5, 41.6, 39.6, 15.8. GC-MS (EI, 70 eV) m/z: 232, 214, 167, 142. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{14}H_{16}OS$, 232.0916; Found, 232.0915.

5-(2-hydroxy-3-(methylthio)propyl)-2-methoxyphenol (3k): Pale-yellow liquid (148 mg, 65% yield), ^1H NMR (600 MHz, $CDCl_3$) δ 6.88 – 6.81 (m, 1H), 6.74 (d, J = 1.8 Hz, 1H), 6.70 (dd, J = 8.0, 1.8 Hz, 1H), 5.71 (s, 1H), 3.92 – 3.87 (m, 1H), 3.86 (s, 3H), 2.77 (d, J = 6.0 Hz, 2H), 2.67 (dd, J = 13.6, 3.9 Hz, 1H), 2.62 (s, 1H), 2.50 (dd, J = 13.6, 8.5 Hz, 1H), 2.10 (s, 3H); ^{13}C $\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 146.4, 144.2, 129.6, 121.9, 114.4, 111.9, 70.1, 55.8, 42.0, 41.1, 15.6. GC-MS (EI, 70 eV) m/z: 228, 210, 163, 137. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{11}H_{16}O_3S$, 228.0815; found, 228.0813.

1-(methylthio)-3-(perfluorophenyl)propan-2-ol (3l): Pale-yellow liquid (141 mg, 52% yield), ^1H NMR (600 MHz, $CDCl_3$) δ 3.99 – 3.86 (m, 1H), 2.92 (d, J = 6.5 Hz, 2H), 2.78 – 2.68 (m, 2H), 2.55 (dd, J = 13.8, 8.8 Hz, 1H), 2.13 (s, 3H); ^{13}C $\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 146.3-144.5 (m, 2C), 140.9-139.0 (m, 1C), 138.4-138.1 (m, 2C), 111.5 (dd, J = 20.6, 16.7 Hz, 1C), 67.7, 41.6, 29.1, 15.5.

GC-MS (EI, 70 eV) m/z: 272, 207, 154. HRMS (APCI-TOF) m/z: $[M-H_2O+H]^+$ Calcd for $C_{10}H_8F_5S$ 255.0261; Found 255.0261.

1-(methylthio)-4-phenylbutan-2-ol (3m) :Pale-yellow liquid (174 mg, 89% yield), ^1H NMR (600 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.6 Hz, 2H), 7.20 (dd, *J* = 16.6, 7.6 Hz, 3H), 3.75 – 3.64 (m, 1H), 2.90 – 2.81 (m, 1H), 2.76 – 2.67 (m, 2H), 2.60 (s, 1H), 2.48 (dd, *J* = 13.7, 9.2 Hz, 1H), 2.10 (s, 3H), 1.87 – 1.75 (m, 2H); ^{13}C $\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 141.8, 128.43 (2C), 128.42 (2C), 125.9, 67.7, 42.3, 37.8, 32.1, 15.5. GC-MS (EI, 70 eV) m/z: 196, 148, 137, 117. HRMS (EI) m/z: $[M]^+$ Calcd for $C_{11}H_{16}OS$, 196.0916; Found 196.0915.

1-(methylthio)octan-2-ol (3n), Pale-yellow liquid (118 mg, 67% yield), H NMR (500 MHz, $CDCl_3$) δ 3.64 (dd, *J* = 11.3, 4.5 Hz, 1H), 3.47 (dd, *J* = 11.3, 7.3 Hz, 1H), 2.72 – 2.58 (m, 1H), 2.21 (s, 1H), 2.01 (s, 3H), 1.55 – 1.37 (m, 4H), 1.27 (t, *J* = 14.4 Hz, 6H), 0.87 (t, *J* = 6.7 Hz, 3H); ^{13}C $\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 62.6, 50.0, 31.7, 30.7, 29.1, 27.0, 22.6, 14.1, 11.7. HRMS (EI) m/z: $[M]^+$ Calcd for $C_9H_{20}OS$, 176.1229; found 176.1226,

1-((methyl-d_3)thio)-3-phenylpropan-2-ol (3o): Pale-yellow liquid (120 mg, 65% yield), ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.34 – 7.27 (m, 2H), 7.23 (d, *J* = 7.2 Hz, 3H), 3.93 (s, 1H), 2.84 (d, *J* = 6.3 Hz, 2H), 2.67 (d, *J* = 13.1 Hz, 1H), 2.51 (dd, *J* = 13.7, 8.9 Hz, 2H); ^{13}C $\{^1H\}$ NMR (100 MHz, $CDCl_3$) *δ* 137.9, 129.4, 128.5, 126.5, 70.01, 42.5 (2C), 41.1. GC-MS (EI, 70 eV) m/z: 185, 167, 117. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{11}D_3NaOS$ 208.0846; Found 208.0843.

1-(methylthio)-3-phenylpropan-2-ol-^{18}O (3a-1): Pale-yellow liquid (140 mg, 76% yield), ^1H NMR (400 MHz, $CDCl_3$) ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.29 – 7.24 (m, 3H), 4.03 – 3.89 (m, 1H), 2.88 (dd, *J* = 6.4, 2.9 Hz, 2H), 2.71 (d, *J* = 12.4 Hz, 1H), 2.59 (s, 1H), 2.54 (dd, *J* =

13.5, 8.8 Hz, 1H), 2.13 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 207.1, 137.9, 129.4 (2C), 128.5(2C), 126.5, 69.8, 42.45, 41.3, 15.6. GC-MS (EI, 70 eV) m/z: 184, 164, 117, 91. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{10}H_{14}{}^{18}OSNa$ 207.0700; Found 207.0700.

2,3-dihydro-2-((methylthio)methyl)benzofuran (4a): Pale-yellow liquid (166 mg, 92% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (d, *J* = 7.3 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.97 (dq, *J* = 9.0, 6.6 Hz, 1H), 3.38 (dd, *J* = 15.6, 9.1 Hz, 1H), 3.08 (dd, *J* = 15.6, 6.9 Hz, 1H), 2.91 (dd, *J* = 13.7, 6.0 Hz, 1H), 2.79 (dd, *J* = 13.7, 6.6 Hz, 1H), 2.23 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 159.1, 128.0, 126.2, 125.0, 120.5, 109.4, 82.0, 39.2, 34.9, 16.4. HRMS (APCI-TOF) m/z: $[M+H]^+$ calcd for $C_{10}H_{13}OS$, 181.0687; Found, 181.0681.

2-((methylthio)methyl)-2,3-dihydrobenzofuran-7-carbaldehyde (4b): Pale-yellow liquid(177 mg, 85% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.18 (s, 1H), 7.56 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.42 – 7.30 (m, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 5.14 (dtd, *J* = 9.2, 6.8, 5.3 Hz, 1H), 3.36 (dd, *J* = 15.9, 9.2 Hz, 1H), 3.09 (dd, *J* = 15.9, 6.8 Hz, 1H), 2.94 (dd, *J* = 13.9, 5.3 Hz, 1H), 2.81 (dd, *J* = 13.9, 6.9 Hz, 1H), 2.20 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 188.6, 161.4, 130.9, 128.8, 127.0, 120.7, 119.4, 84.2, 38.9, 33.6, 16.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$: Calcd for $C_{11}H_{12}O_2SNa$ 231.0450; Found, 231.0450.

7-methoxy-2-((methylthio)methyl)-2,3-dihydrobenzofuran (4c), Pale-yellow liquid: 187 mg, 89% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 – 6.78 (m, 2H), 6.74 (dd, *J* = 6.8, 3.8 Hz, 1H), 5.08 – 4.92 (m, 1H), 3.86 (s, 3H), 3.37 (dd, *J* = 15.6, 9.0 Hz, 1H), 3.12 (dd, *J* = 15.6, 7.2 Hz, 1H), 2.97 (dd, *J* = 13.6, 4.8 Hz, 1H), 2.79 (dd, *J* = 13.6, 7.8 Hz, 1H), 2.19 (s, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ

147.5, 144.5, 127.4, 121.1, 117.2, 111.2, 82.5, 55.9, 38.9, 35.3, 16.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{11}H_{15}O_2S$ 211.0787; Found, 211.0789.

7-methoxy-2-((methylthio)methyl)-2,3-dihydrobenzofuran-5-carbaldehyde (4d), Pale-yellow liquid: (195 mg, 82% yield), ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.30 (d, *J* = 13.6 Hz, 2H), 5.20 – 5.00 (m, 1H), 3.89 (d, *J* = 2.6 Hz, 3H), 3.41 (dd, *J* = 14.9, 10.0 Hz, 1H), 3.25 – 3.08 (m, 1H), 3.01 – 2.88 (m, 1H), 2.81 (ddd, *J* = 13.7, 7.4, 2.3 Hz, 1H), 2.17 (d, *J* = 2.5 Hz, 3H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 190.3, 153.3, 144.8, 131.1, 127.84, 121.4, 111.2, 84.1, 55.9, 38.7, 34.2, 16.2. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{15}O_3S$ 239.0736; Found, 239.0735.

4-allyl-2-(2-((methylthio)methyl)-2,3-dihydrobenzofuran-5-yl)phenol (4e), Pale-yellow liquid: (237 mg, 76% yield), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (s, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.15 – 7.00 (m, 2H), 6.91 (dd, *J* = 13.1, 8.2 Hz, 2H), 5.99 (ddt, *J* = 16.8, 10.0, 6.7 Hz, 1H), 5.14 – 5.07 (m, 2H), 5.07 – 5.02 (m, 1H), 3.44 (dd, *J* = 15.9, 9.1 Hz, 1H), 3.37 (d, *J* = 6.7 Hz, 2H), 3.15 (dd, *J* = 15.9, 7.0 Hz, 1H), 3.00 – 2.91 (m, 1H), 2.84 (dd, *J* = 13.7, 6.5 Hz, 1H), 2.26 (s, 3H); ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$) δ 159.1, 150.8, 137.7, 132.2, 130.3, 129.3, 129.0, 128.7, 128.0, 127.6, 125.9, 115.6, 115.5, 110.0, 82.5, 39.4, 39.2, 34.8, 16.4. HRMS (APCI-TOF) m/z: $[M+H]^+$ calcd for: $C_{19}H_{21}O_2S$ 313.1262; Found, 313.1252.

2-(5-methyl-2-((methylthio)methyl)-2,3-dihydrobenzofuran-7-yl)-2H-benzo[d][1,2,3]triazole (4f),: Pale-yellow liquid (252 mg, 81% yield), ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.71 (s, 1H), 7.46 – 7.35 (m, 2H), 7.09 (s, 1H), 5.30 – 5.16 (m, 1H), 3.47 (dd, *J* = 15.8, 9.1 Hz, 1H), 3.18 (dd, *J* = 15.8, 6.3 Hz, 1H), 2.96 (dd, *J* = 13.8, 4.8 Hz, 1H), 2.79 (dd, *J* = 13.8, 7.9 Hz, 1H), 2.37 (s, 3H), 2.17 (s, 3H); ^{13}C {^{1}H} NMR (150 MHz, $CDCl_3$) δ 149.1, 144.7, 131.0, 129.8, 126.8 (2C)

, 126.5, 123.8, 123.0, 118.3 (2C), 83.8, 38.6, 34.7, 20.6, 16.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{17}H_{18}N_3OS$ 312.1165, found 312.1159.

ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Authors

Leeyib268@126.com; wyuchemcl@126.com

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We thank the Foundation of the Department of Education of Guangdong Province (2017KZDXM085, 2018KZDXM070 and 2017KSYS010), Science and Technology Foundation of Jiangmen City (2017012) and Science Foundation for Young Teachers of Wuyi University (2016zk03) and Chemical Industry Collaborative Innovation Center of Yueshan Town 2017(368) for financial support.

REFERENCES

1 (a) Jensen, K. H., Sigman, M. S. Mechanistic approaches to palladium-catalyzed alkene difunctionalization reactions, *Org. Biomol. Chem*., **2008**, *6*, 4083-4088; (b) Lu, Q., Zhang, J., Zhao, G., Qi, Y., Wang, H., Lei, A. Dioxygen-triggered oxidative radical reaction: direct

aerobic difunctionalization of terminal alkynes toward *β*-keto sulfones, *J. Am. Chem. Soc*. **2013**, *135*, 11481-11484; (c) Yin, G., Mu, X., Liu, G. Palladium(II)-catalyzed oxidative difunctionalization of alkenes: bond forming at a high-valent palladium center, *Acc. Chem. Res*. **2016**, *49*, 2413−2423; (d) Wang, F., Wang, D., Wan, X., Wu, L., Chen, P., Liu, G. Enantioselective copper-catalyzed intermolecular cyanotrifluoromethylation of alkenes via radical process, *J. Am. Chem. Soc*. **2016**, *138*, 15547−15550; (e) Wu, L., Wang, F., Wan, X., Wang, D., Chen, P., Liu, G. Asymmetric Cu-catalyzed intermolecular trifluoromethylarylation of styrenes: enantioselective arylation of benzylic radicals, *J. Am. Chem. Soc*. **2017**, *139*, 2904−2907; (f) Chen, C., Luo, Y., Fu, L., Chen, P., Lan, Y., Liu, G. Palladium-Catalyzed intermolecular ditrifluoromethoxylation of unactivated alkenes: CF_3O-palladation initiated by Pd(IV), *J. Am. Chem. Soc*. **2018**, *140*, 1207−1210; (g) Yasu, Y., Koike, T., Akita, M. Three-component oxytrifluoromethylation of alkenes: highly Efficient and regioselective difunctionalization of C=C bonds mediated by photoredox catalysts, *Angew. Chem. Int. Ed*. **2012**, *51*, 9567-9571; (h) Pathak, T. P. Gligorich, K. M., Welm, B. E., Sigman, M. S. Synthesis and preliminary biological Studies of 3-substituted indoles accessed by a palladium-catalyzed enantioselective alkene difunctionalization reaction, *J. Am. Chem. Soc*. **2010**, *132*, 7870-7871.

2 (a) Yamagiwa, N., Suto, Y., Torisawa, Y. Convenient method for the addition of disulfides to alkenes, *Bioorg. Med. Chem. Lett*., **2017**, *17*, 6197–6201; (b) Shukla, G., Srivastava, A., Nagaraju, A., Raghvanshi, K., Singh, M. S. Iodine-mediated copper-catalyzed efficient α-C(sp^2)-thiomethylation of α-oxoketene dithioacetals with dimethyl sulfoxide in one pot, *Adv. Synth. Catal.* **2015**, *357*, 3969 –3976; (c) Jin, Z., Xu, B., Hammond, G. B. Green synthesis of vicinal dithioethers and alkenyl thioethers from the reaction of alkynes and thiols in water, *Eur. J. Org. Chem.* **2010**, 168–173; (d) Wang, X. R., Chen, F. *Tetrahedron*, Iodine-catalyzed disulfidation of alkenes, **2011**, *67*, 4547–4551; (e) Yadav, L. D. S., Awasthi, C. The first one-pot oxidative 1, 2-acetoxysulfenylation and 1, 2-disulfenylation of Baylis–Hillman alcohols in an ionic liquid, *Tetrahedron Lett*., **2009**, *50*, 3801–3804; (f) Li, J., Li, C., Ouyang, L., Li, C., Yang, S., Wu, W., Jiang, H. Palladium-catalyzed regioselective

three-component cascade bisthiolation of terminal alkynes, *Adv. Synth. Catal.* **2018**, *360*, 1138–1150.

3 (a) Wang, H., Lu, Q., Qian, C., Liu, C., Liu, W., Chen, K., Lei, A. Solvent-enabled radical selectivities: controlled syntheses of sulfoxides and sulfides, *Angew. Chem. Int. Ed.* **2016**, *55*, 1094–1097; (b) Gao, X., Pan, X., Gao, J., Jiang, H., Yuan, G., Li, Y. *Org. Lett.*, NH_4I-Mediated three-component coupling reaction: metal-free synthesis of *β*-alkoxy methyl sulfides from DMSO, alcohols, and styrenes, **2015**, *17*, 1038–1041; (c) Taniguchi, N., Copper-catalyzed 1, 2-hydroxysulfenylation of alkene using disulfide via cleavage of the S−S bond, *J. Org. Chem.*, **2006**, *71*, 7874–7876; (d) Ueda, M., Miyabe, H., Shimizu,H., Suino, H.,. Miyata, O. Regioselective hydroxysulfenylation of *α, β*-unsaturated imines: enhanced stability of an intermediate radical, *Angew. Chem. Int. Ed.*, **2008**, *47*, 5600–5604; (e) Xi, H., Deng, B., Zong, Z., Lu,S., Li, Z. Hydroxysulfenylation of electron-deficient alkenes through an aerobic copper catalysis, *Org. Lett.*, **2015**, *17*,1180–1183; (f) Huo, C., Wang, Y., Yuan, Y., Chen, F., Tang, J. Auto-oxidative hydroxysulfenylation of alkenes, *Chem. Commun.*, **2016**, *52*, 7233-7236; (g)Yu, J., Gao, C., Song, Z., Yang, H., Fu, H. Metal-free oxysulfenylation of alkenes with 1-(arylthio) pyrrolidine-2, 5-diones and alcohols, *Org. Biomol. Chem.*, **2015**, *13*, 4846–4850; (h) Sun, Li.; Yuan, Y.; Yao, M.; Wang, H.; Wang, D.; Gao, M.; Chen, Y.; Lei, A, Electrochemical aminoselenation and oxyselenation of styrenes with hydrogen evolution, *Org. Lett.*, **2019**, DOI: 10.1021/acs.orglett.8b03274.

4 (a) Mosberg, M. I.; Yeomans, L.; Anand, J. P.; Porter, V.; Sobczyl-Kojiro, K.; Traynor, J. R.; Jutkiewicz, E. M. Development of a bioavailable μ opioid Receptor (MOPr) agonist, δ opioid receptor (DOPr) antagonist peptide that evokes antinociception without development of qcute tolerance, *J. Med. Chem.*, **2014**, *57*, 3148–3153; (b) Li, P.; Jiang, S.; Lee, S.; Lin, C. Y.; Johnson, M. D.; Dickson, R. B.; Michejda, C. J.; Roller, P. P, Design and synthesis of novel and potent inhibitors of the type II transmembrane serine protease, matriptase, based upon the sunflower trypsin inhibitor-1, *J. Med. Chem.*, **2007**, *50*, 5976–5983; (c) Viola, F.; Balliano, G.; Milla, P.; Cattel, L.; Rocco, F.; Ceruti, M. Stereospecific syntheses of *trans*-vinyldioxidosqualene and *β*-hydroxysulfide derivatives, as potent and time-dependent 2,

3-oxidosqualene cyclase inhibitors, *Bioorg. Med. Chem*. **2000**, *8*, 223-232; (d) Luly, J. R.; Yi, N.; Soderquist, J.; Stein, H.; Cohen, J.; Perun, T. J.; Plattner, J. J. New inhibitors of human renin that contain novel Leu-Val replacements, *J. Med. Chem*. **1987**, *30*, 1609-1616.

5 (a) Beckerle, K.; Manivannan, R.; Lian, B.; Meppelder, G. M.; Raabe, G.; Spaniol, T. P.; Ebeling, H.; Pelascini, F.; Mülhaupt, R.; Okuda, J. Stereospecific styrene enchainment at a titanium site within a helical ligand framework: evidence for the formation of homochiral polystyrene, *Angew. Chem. Int. Ed.* **2007**, *46*, 4790–4793; (b) Meppelder, G. M.; Beckerle, K.; Manivannan, R.; Lian, B.; Raabe, G.; T. Spaniol, P.; Okuda, J. Enantiomerically pure titanium complexes containing an [OSSO]-type bis(phenolate) ligand: synthesis, structure, and formation of optically active oligostyrenes, *Chem. Asian J.* **2008**, *3*, 1312–1323; (c) Gall, B. T.; Pelascini, F.; Ebeling, H.; Beckerle, K.; Okuda, J.; Mülhaupt, R. Molecular weight and end group control of isotactic polystyrene using olefins and nonconjugated diolefins as chain transfer agents, *Macromolecules* **2008**, *41*, 1627–1633; (d) Lian, B.; Beckerle, K.; Spaniol, T. P.; Okuda, J, Regioselective 1-hexene oligomerization using cationic bis(phenolato) group 4 metal catalysts: switch from 1,2-to 2,1-insertion, *Angew. Chem. Int. Ed.* **2007**, *46*, 8507–8510.

6 (a) Johnson, M. W., Hannoun, K. I., Tan, Y., Fu, G. C., Peters, J. C. A mechanistic investigation of the photoinduced, copper-mediated cross-coupling of an aryl thiol with an aryl halide, *Chem*. *Sci*., **2016**, *7*, 4091-4100; (b) Chen, Q.; Yu, G.; Wang, X.; Ou, Y.; Huo, Y. Catalyst-free direct C(sp^3)–H sulfenylation of xanthene derivatives using air as the oxidant, *Green Chem*., **2019**, DOI:10.1039/C8GC03898H; (c) Rajeshkumar, V., Neelamegama, C., Anandana, S. A one-pot metal-free protocol for the synthesis of chalcogenated furans from 1,4-enediones and thiols, *Org. Biomol. Chem*., **2019**, *17*, 982-991; (d) Chen, M., Luo, Y., Zhang, C., Guo, L., Wang, Q., Wu, Y. Graphene oxide mediated thiolation of indoles in water: a green and sustainable approach to synthesize 3-sulfenylindoles, *Org. Chem. Front*., **2019**, *6*, 116-120; (e) Lida, H., Demizu, R., Ohkado, R. Tandem flavin-iodine-catalyzed aerobic oxidative sulfenylation of imidazo[1,2-*a*]pyridines with thiols, *J. Org. Chem*., **2018**, *83* 12291–12296; (g) Siddaraju, Y., Ramaiah, K., Prabhu, R. Regioselective sulfenylation of

α′-CH_3 or α′-CH2 Groups of α, β-unsaturated ketones with heterocyclic thiols, *J. Org. Chem*., **2018**, *83*, 2986–2992.

7 (a) Yang, F. L., Wang, F. X., Wang, T. T., Wang, Y. J., Tian, S. K. Iodine-catalyzed three-component oxysulfenylation of alkenes with sulfonyl hydrazides and alcohols, *Chem. Commun*., **2014**, *50*, 2111-2113; (b) Yang, F. L., Tian, S. K. Iodine-catalyzed regioselective sulfenylation of indoles with sulfonyl hydrazides, *Angew. Chem. Int. Ed*., **2013**, *52*, 4929–4932; (c) Yang, F. L., Cui, Y., Yu, B. K., Jin, Y. X., Yian, S. K. By-product-catalyzed redox-neutral sulfenylation/deiodination/aromatization of cyclic alkenyl iodides with sulfonyl hydrazides, *Adv. Syn. Catal*., **2016**, *358*, 3368-3372; (d) Yu, Q., Yang, Y., Wan, J., Liu, Y. Copper-catalyzed C_5–H sulfenylation of unprotected 8-aminoquinolines using sulfonyl hydrazides, *J. Org. Chem.*, **2018**, *83*, 11385-11391; (e) Mo, Z. Y., Swaroop, T. R., Tong, W., Zhang, Y. Z., Yang, H. T., Pan, Y. M., Sun, H. B., Chen, Z. F. Electrochemical sulfonylation of thiols with sulfonyl hydrazides: a metal- and oxidant-free protocol for the synthesis of thiosulfonates, *Green Chem*., **2018**, *20*, 4428-4432; (f) Bao, Y., Yang, X., Zhou, Q., Yang, F. Iodine-promoted deoxygenative iodization/olefination/sulfenylation of ketones with sulfonyl hydrazides: access to *β*-iodoalkenyl sulfides, *Org. Lett*., **2018**, *20*, 1966–1969.

8 (a) Trost, B. M., Ochiai, M., Mcdougal, P. G. Hydroxysulfenylation of olefins. An olefin cleavage with functional group differentiation, *J. Am. Chem. Soc*., **1978**, *100*, 7103–7106; (b) Xin, Y. X., Pan, S., Huang, Y., Xu, X. H., Qing, F. L. Copper-catalyzed sulfenylation, sulfonylation, and selenylation of 2,3-allenoic acids with disulfides or diselenides, *J. Org. Chem*., **2018**, *83*, 6101-6109; (c) Movassagh, B., Navidi, M. One-pot synthesis of *β*-hydroxysulfides from styrenes and disulfides using the Zn/$AlCl_3$ system, *Tetrahedron Letters*, **2008**, *49*, 6712–6714.

9 (a) Wang, H., Huang, D., Cheng, D., Li, L., Shi, Y. Acid-Catalyzed regioselective sulfetherification of alkenols and stereoselective rearrangement of tetrahydrofuran to tetrahydropyran, *Org. Lett*., **2011**, *13*, 1650–1653; (b) Ye, S., Li, Y.,Wu, J., Li, Z. Thiourea dioxide as a source of sulfonyl groups: photoredox generation of sulfones and sulfonamides from heteroaryl/aryl halides, *Chem. Commun*., **2019**, DOI:10.1039/C9CC00008A.

10 (a) Scoffone, E., Fontana, A. R. Sulfenyl halides as modifying reagents for polypeptides and proteins. I. Modification of tryptophan residues, *Rocchi Biochem*, **1968**, *7*, 971–979; (b) Nicolaou, K. C., Seitz, S. P., Sipio, W. J., Blount, J. F. Phenylseleno-and phenylsulfenolactonizations. Two highly efficient and synthetically useful cyclization procedures, *J. Am. Chem. Soc.* **1979**, *101*, 3884-3893. (c) Young, R. N., Coombs, W., Guindon, Y., Rokach, J. The preparation of octahydro leukotrienes C, D, and E via a stereoselective sulfenyllactonization reaction, *Tetrahedron Let*t. **1981**, *22*, 4933-4936.

11 (a) Ito, Y., Ogawa, T. Sulfenate esters as glycosyl acceptors: a novel approach to the synthesis of 2-deoxyglycosides, *Tetrahedron Lett*. **1987**, *28*, 2723-2726; (b) Kharasch, N., McQuarrie, D. P., Buess, C. M. Derivatives of Sulfenic Acids. X. The reaction of 2, 4-dinitrobenzenesulfenyl chloride with alcohols, *J. Am. Chem. Soc.* **1953**, *75*, 2658-2660.

12 (a) Saeva, F. D., Morgan, B. P., Luss, H. R. Photochemical conversion of sulfonium salts to sulfides via a 1,3-sigmatropic rearrangement. Photogeneration of broensted acids, *J. Org. Chem.*, **1985**, *50*, 4360–4362; (b) Minkwitz, R., kornath, A., Sawodny, W., Typke, V., Boatz, J. A. Synthesis and characterization of the tris(methylthio)sulfonium salt $[(CH_3S)_3S]^+SbF_6^{-1}$, *J. Am. Chem. Soc*., **2000**, *122*, 1073–1078.

13 (a) Kohn, H., Abuzar, S., Reinterpretation of the bicyclomycin-sodium methanethiolate reaction, *J. Am. Chem. Soc.*, **1988**, *110*, 3661-3663.

14 (a) Wang, P., Tang, S., Huang, P., Lei, A., Electrocatalytic oxidant-free dehydrogenative C-H/S-H cross-coupling, *Angew*. *Chem*. *Int*. *Ed*., **2017**, *56*, 3009 –3013; (b) Wang, H., Wang, G., Lu, Q., Chiang, C., Peng, P., Zhou, J., Lei, A. Catalyst-free difunctionalization of activated alkenes in water: efficient synthesis of *β*-keto sulfides and sulfones, *Chem*. *Eur*. *J*., **2016**, *22*, 14489–14493.

15 (a) Qiao, Z., Ge, N., Jiang, X. CO_2-promoted oxidative cross-coupling reaction for C–S bond formation via masked strategy in an odourless way, *Chem. Commun*., **2015**, *51*, 10295-10298; (b) Xiao, X., Feng, M., Jiang, X. New Design of a disulfurating reagent: facile and straightforward pathway to unsymmetrical disulfanes by copper-catalyzed oxidative cross-coupling, *Angew*. *Chem*. *Int*. *Ed*., **2016**, *55*, 14121-14125; (c) Wei, J., Li, Y., jiang, X.

Aqueous compatible protocol to both alkyl and aryl thioamide synthesis, *Org. Lett*., **2016**, *18*, 340-343; (d) Li, Y., Wang, M., Jiang, X. Controllable sulfoxidation and sulfenylation with organic thiosulfate salts *via* dual electron- and energy-transfer photocatalysis, *ACS Catal*., **2017**, *11*, 7587–7592.

16 (a) Epstein, W. W., Sweat, F. W. Dimethyl sulfoxide oxidations, *Chem Rev*., **1967**, *67*, 247-260; (*b*) Wu, X. F., Natte, K. The applications of dimethyl sulfoxide as reagent in organic synthesis, *Adv*. *Synth*. *Catal*., **2016**, *358*, 336 – 352; (c) Jones-Mensad, E., Karki, M., Magolan, J. Dimethyl sulfoxide as a synthon in organic chemistry, *Synthesis*, **2016**, *48*, 1421-1436; (d) Russell, G. A., S. A. Weiner, Methylation of aromatic hydrocarbons by dimethyl sulfoxide in the presence of base, *J. Org. Chem*., **1966**, *31*, 248–251; (d) Omura, K., Sharma, A. K., Swern, D. Dimethyl sulfoxide-trifluoroacetic anhydride. New reagent for oxidation of alcohols to carbonyls, *J. Org. Chem*., **1976**, *41*, 957–962; (e) Pfitzner, K. E., Moffatt, J. G. A new and selective oxidation of alcohols, *J. Am. Chem*. *Soc*. **1963**, *85*, 3027–3028; (f) Brennfürer, A., Neumann, H., Beller, M. Palladium-catalyzed carbonylation reactions of aryl halides and related compounds, *Angew. Chem. Int. Ed*., **2009**, *48*, 4114–4133; (g) Ren, X., Chen, J., Chen, F., Cheng, J. The palladium-catalyzed cyanation of indole C-H bonds with the combination of NH_4HCO_3 and DMSO as a safe cyanide source, *Chem. Commun*., **2011**, *47*, 6725–6727; (h) Zhao, W., Xie, P., Bian, Z., Zhou, A., Ge, H., Zhang, M., Ding, Y., Zheng, L. Ammonium iodide induced nonradical regioselective sulfenylation of flavones *via* a C-H functionalization process, *J. Org. Chem*., **2015**, *80*, 9167−9175.

17 (a) Cui, H., Liu, X., Wei, W., Yang, D., He, C., Zhang, T., Wang, H. Molecular iodine-mediated difunctionalization of alkenes with nitriles and thiols leading to *β*-acetamido sulfides, *J. Org. Chem*., **2016**, *81*, 2252−2260; (b) Zhu, Z., Luo, J., Zhao, X. Combination of Lewis Basic selenium catalysis and redox selenium chemistry: synthesis of trifluoromethylthiolated tertiary alcohols with alkenes, *Org*. *Lett*., **2017**, *19*, 4940−4943; (c) Wang, D., Zhang, R., Lin, S., Yan, Z., Cuo, S. Tetrabutylammonium iodide mediated synthesis of *β*-alkoxy sulfides and vinyl sulfones by using benzenesulfonyl chlorides as the sulfur sources under acidic or alkaline conditions, *Synlett,* **2016**, *27*, 2003–2008.

18 (a) Gao, Y., Gao, Y., Tang, X., Peng, J., Hu, M., Wu, W., Jiang, H. Copper-catalyzed oxysulfenylation of enolates with sodium sulfinates: A strategy To construct sulfenylated cyclic ethers, *Org. Lett*., **2016**, *18*, 1158-1161; (b) Wang, D., Zhang, R., Ning, W., Yan, Z., Lin, S. Three-component oxysulfenylation reaction: two simple and convenient approaches to *β*-alkoxy sulfides, *Org. Biomol. Chem*., **2016**, *14*, 5136-5140.

19 (a) Dénès, F., Pichowicz, M., Povie, G., Renaud, P. Thiyl radicals in organic synthesis, *Chem. Rev.*, **2014**, *114*, 2587–2693; (b) Zhou, S. F., Pan, X., Zhou, Z. H., Shoberu, A., Zou, J. P. Air Oxidative Radical Hydroxysulfurization of Styrenes Leading to β-Hydroxysulfides, *J. Org. Chem*., **2015**, *80*, 3682–3687.

20 (a) Gao, X., Pan, X., Gao, J., Huang, H., Yuan, G., Li, Y. Ammonium iodide-induced sulfonylation of alkenes with DMSO and water toward the synthesis of vinyl methyl sulfones, *Chem*. *Commun*., **2015**, *51*, 210-212; (b) Gromada, J., Matyjaszewski, K. Simultaneous reverse and normal initiation in atom transfer radical polymerization, *Macromolecules*, **2001**, *34*, 7664–7671.

21 (a) Sharma, P., Pohilla, S., Jain, N. Copper acetate–DMSO promoted methylthiolation of arenes and heteroarenes, *J. Org. Chem*., **2015**, *80*, 4116–4122; (b) Chu, L., Yue, X., Qing, F. F. Cu(II)-mediated methylthiolation of aryl C-H bonds with DMSO, *Org*. *Lett*., **2010**, *12*, 1644–1647; (c) Dai, C., Xu, Z., Huang, F., Yu, Z., Gao, Y. F. Lewis acid-catalyzed, copper(II)-mediated synthesis of heteroaryl thioethers under base-free conditions, *J. Org. Chem*., **2012**, *77*, 4414–4419.

22 Ruan, H., Meng, L., Zhu, L., Wang, L. Visible-Light-Induced hydroxysulfurization and alkoxysulfurization of styrenes in the absence of photocatalyst: synthesis of β-hydroxysulfides and β-alkoxysulfides, *Adv. Synth. Catal*., **2019**, DOI: 10.1002/adsc.201900140.

23 Shen, W., Wu, Q., Gong, X., Ao, G., Liu, F. A facile method for hydroxytrifluoromethylation of alkenes with Langlois reagent and DMSO, *Green Chem*., **2019**, DOI: 10.1039/c9gc00886a.