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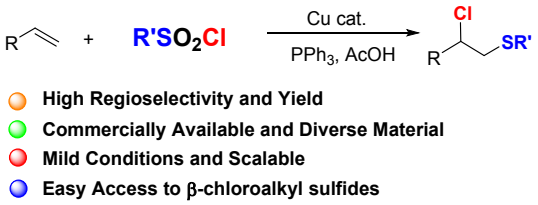
Regioselective Chloro-thiolation of Alkenes with Sulfonyl Chlorides

Jingjing Wei, §Shuaishuai Liang, § Lvqi Jiang,* Yasir Mumtaz, Wen-bin Yi*

School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing 210094, P. R. China



ABSTRACT: A newly developed sulfonyl chlorides-based regioselective chloro-thiolation of alkenes has been disclosed, the reaction is compatible with a variety of functional groups and can be scaled up to the gram-scale with no loss in yield. The employment of readily available reactants, mild reaction conditions, and high regioselectivity make this process very practical. Mechanistic studies revealed a possible free radical reaction pathway.

INTRODUCTION

Difunctionalization of alkenes is one of the most powerful synthetic methods to incorporate two functional groups to carbon−carbon double bond efficiently in one step,[1] providing tremendous step economy and convenience for the synthesis of complex multifunctional compounds. Among them, chloro-thiolation of alkenes is a topic of current interest because sulfur-containing compounds are valuable synthetic intermediates and important building blocks, and the chloro moieties can be converted into a wide variety of functional groups.[2] Moreover, the chloro-thiolation of alkenes have been shown to possess insecticidal, antibacterial and antifungal properties.[3]

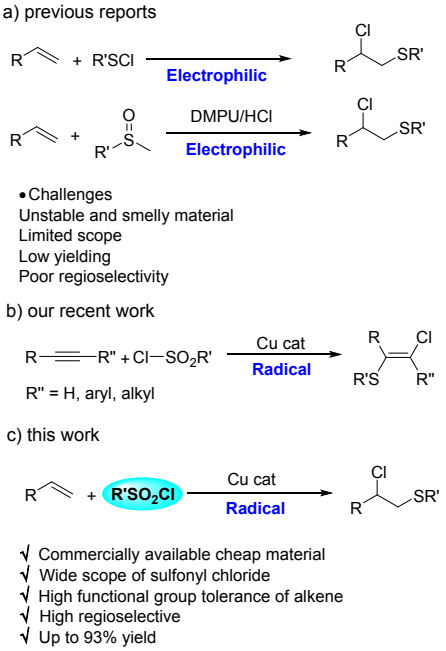
One general and routinely used approach for the preparation of *β*-chloroalkyl sulfides typically involves the electrophilic addition of sulfenyl chlorides to alkene (Scheme 1, a).[4] However, sulfenyl chlorides are really unstable compounds and the formation of sulfenyl chlorides suffer from toxic and foul-smelling reagents and poor functional group compatibility. Recently, Hammond's group has reported the chloro-thiolation of alkenes using DMPU-HCl and sulfoxides (Scheme 1, a).[5] This approach proves to be an efficient route to generate *β*-chloroalkyl sulfides with conventional materials, but it also encounters disadvantages: the reagents employed have to be prepared through cautious and inert conditions, and the limited variety of sulfoxides and low functional group tolerance also reduces the attractiveness of this reaction. In addition, compared with free radical addition, these electrophilic addition are often poorly regioselective, which further limit their usage. Thus, the use of convenient reagents for the high regioselective chloro-thiolation of alkenes with broad substrate scope and good functional tolerance continues to be an important goal.

Sulfonyl chlorides are inexpensive, easily available reagent and have been widely used in the field of

organic and medicinal chemistry as well as material science.[6] Our group recently reported its application in the chloro-thiolation of alkynes. Sulfur-centered radical was proved to be the key intermediate of the reaction (Scheme 1, b).[7] Encouraged by this result, we reasoned that under suitable conditions, high regioselective chloro-thiolation of alkenes could be achieved *via* free radical reaction pathway. In this paper, we report a practical protocol for the synthesis of various *β*-chloroalkyl sulfides by using readily available and diversified sulfonyl chlorides under mild reaction conditions (Scheme 1, c).

RESULTS AND DISCUSSION

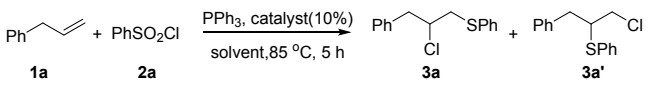
We embarked upon this investigation using allylbenzene **1a** as the benchmark substrate, $PhSO_2Cl$ **2a** as the chloro-thiolation reagent and CuCl as the catalyst, the results were summarized in Table 1. Initially, the



Scheme 1. Chloro-thiolation of alkenes

effect of solvent on the reaction was examined (entries 1−6). Among the various solvents examined, AcOH was the most suitable solvent for the reaction, affording the desired Markovnikov product **3a** in 83% with high regioselectivity (entry 6). Other solvents, such as DMF, DCE, or 1,4-dioxane were inferior. These results indicated that AcOH is crucial for both the high yield and regioselectivity of this transformation. Only 15% yield of the chloro-thiolated product was observed when no catalyst was employed (entry 7). Next, a series of copper catalysts were examined.. After screening copper catalysts of different valence states, CuBr proved to be the best option in the transformation, and the desired product **3a** was obtained in 94% yield in the presence of CuBr (10 mol%) (entry 8). Other copper catalysts, such as CuI, $CuCl_2$, and $Cu(OAc)_2$, were less effective, affording lower yields and regioselectivity of **3a**. Thus, 1:1.5:3:0.1 alkene/RSO_2Cl/PPh_3/CuBr in AcOH at 85°C for 5h was selected as the optimized reaction conditions. Notably, the present reaction is scalable, and 2.19 g (84%) of **3a** was isolated when the reaction was performed on a 10 mmol scale (Table 1, entry 14).

Table 1. Optimization of reaction conditions[a, b]



1a 2a 3a 3a'

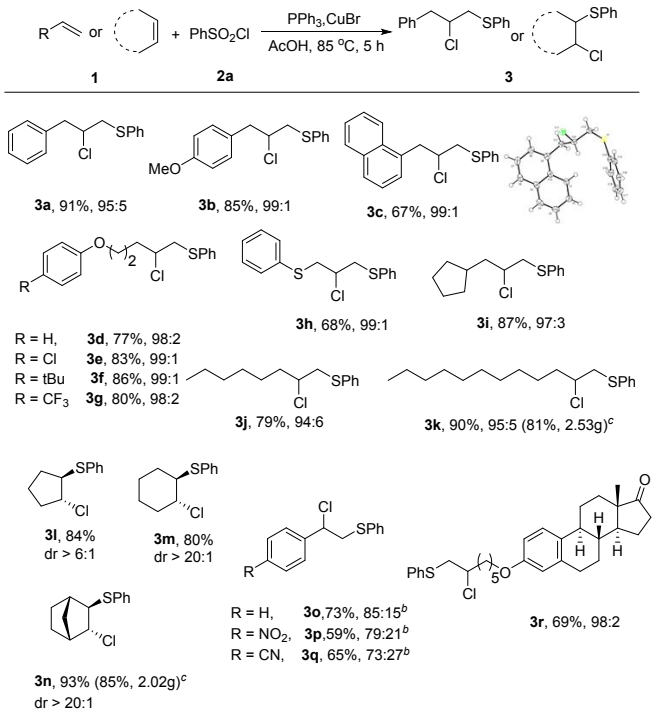
entry	cat.(10%)	solvent	yield(%)[b][c]	**3a**/**3a'**
1	CuCl	DMF	21	76/24
2	CuCl	DCE	22	72/28
3	CuCl	1,4-dioxane	16	60/40

4	CuCl	chlorobenzene	27	65/35
5	CuCl	THF	20	57/43
6	CuCl	AcOH	81	92/8
7		AcOH	15	74/26
8	CuBr	AcOH	93	95/5
9	CuI	AcOH	34	90/10
10	Cu	AcOH	60	88/12
11	$CuBr_2$	AcOH	83	94/6
12	$CuCl_2$	AcOH	67	91/9
13	$Cu(OAc)_2$	AcOH	70	90/10
14	CuBr	AcOH	84[c](2.19g)	92/8

[a]Reaction conditions: allylbenzene (0.5 mmol), benzenesulfonyl chloride (0.75 mmol), PPh_3 (1.5 mmol), AcOH (2.5 mL), 85 °C for 5 h. [b]Yield and ratio determined by ^1H NMR using desyl chloride as an internal standard on crude products, the regioisomers were assigned according to the value of chemical shift of the proton attached to the secondary carbon center (downfield for the chloro-substituted **3a** and up field for the sulfur- substituted **3a'**). [c]Yield was obtained at 10 mmol scale.

With the optimized reaction conditions in hand, we then explored the scope of the reaction with a structurally diverse alkene. As displayed in Scheme 2. Aromatic terminal alkenes reacted smoothly to yield the corresponding chloro-thiolated products **3a**–**3h** in good to excellent yields. Substrates bearing electron-donating (tert-butyl and methoxy) and electron-withdrawing groups (chlorine and trifluoromethyl) proceeded well under the mild reaction conditions and gave the desired product in 67%–91% yields. The precise configuration was unambiguously confirmed by single-crystal X-ray analysis of **3c**. Aliphatic alkenes, such as oct-1-ene and cyclic alkenes, resulted in corresponding products **3i**-**3n** in 79-93% yields. Additionally, the reaction was also practicable in styrene (**3o**-**3q**), but the products hydrolyze easily and, therefore, cannot be isolated by using flash columnchromatography.[5] To demonstrate the applicability of this methodology further on, the chloro-thiolation of drug-like molecule was investigated, reaction of the substrate bearing estrone gave the corresponding product **3r** in 69% yield.

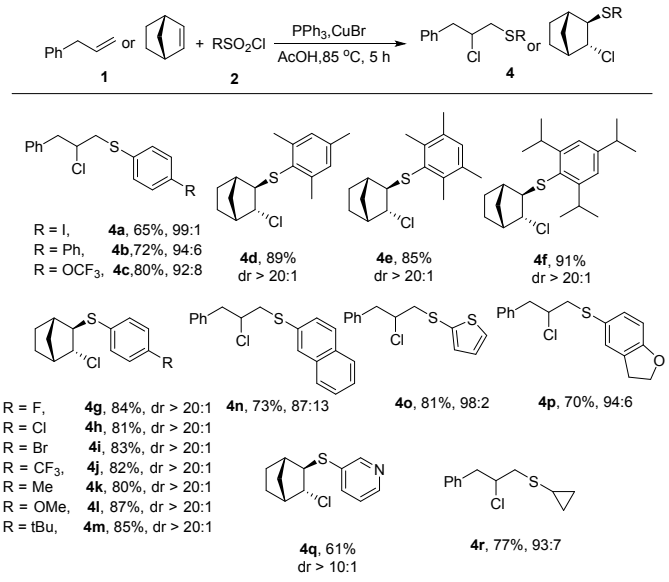
Scheme 2. Scope of alkenes[a]



[a]Reaction conditions: alkene (0.5 mmol), $PhSO_2Cl$ (0.75 mmol), PPh_3 (1.5 mmol) in AcOH (2.5 mL) at 85 °C for 5 h; ratio determined by GC or ^1H NMR on crude products. . [b]Yield determined by GC using *p*-tolyl disulfide as an internal standard on crude products. [c]Yield was obtained at 10 mmol scale.

Next, we selected allylbenzene and norbornene to test the scope of sulfonyl chloride and the results are presented in Scheme 3. To our delight, In all the cases, good regioselectivity was observed. As for benzenesulfonyl chlorides, a wide range of relevant functional groups are well tolerated, including halogen (**4a**, **4g**, **4h** and **4i**), phenyl (**4b**), trifluoromethoxy (**4c**), methoxy (**4l**) and trifluoromethyl (**4j**) groups. Sterically hindered benzenesulfonyl chlorides survived the optimal conditions to generate the desired products in good yields (**4d**–**4f**). Pleasingly, naphthalene-2-sulfonyl chloride and heterocyclic sulfonyl chlorides (thiophene-2-sulfonyl chloride, 2,3-dihydrobenzofuran-5-sulfonyl chloride and pyridine-3-sulfonyl chloride) could work well under the standard conditions to afford the corresponding *β*-chloroalkyl sulfides of good yields (**4n**–**4q**). A limitation of this method is that most alkylsulfonyl chloride is not suitable for this reaction except cyclopropanesulfonyl chloride (**4r**), only large amount of Ph_3PS was detected as the byproduct.[8]

Scheme 3. Scope of sulfonyl chlorides[a]

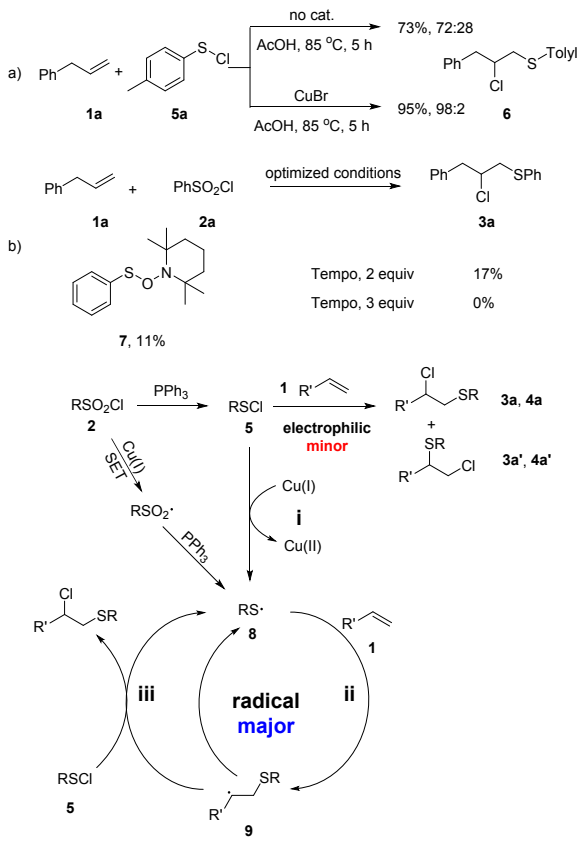


[a] Reaction conditions: alkene (0.5 mmol), RSO_2Cl (0.75 mmol), PPh_3 (1.5 mmol) in AcOH (2.5 mL) at 85 °C for 5 h; ratio determined by GC or ^1H NMR on crude products.

To gain some insight into the reaction mechanism, control experiments with possible intermediates were designed and investigated (Scheme 4). Addition of sulfenyl chloride **5a** to allylbenzene gave 73% yield of **6** with a regioselectivity of 72:28. Better yields (95%) and regioselectivity (98:2) were observed when the reaction was performed under the catalysis of CuBr, which proved that sulfenyl chloride was a possible intermediate and CuBr indeed played as a catalyst. (Scheme 4, a). The reaction was inhibited in the presence of TEMPO (3 equiv), and a 11% yield of radical scavengers **7** was generated, this result provides substantial evidence that sulfenyl radical was generated in the reactions (Scheme 4, b). Based on the present results and previous reports,[9] a proposed mechanism for the synthesis of *β*-chloroalkyl sulfides was illustrated (Scheme 4). At first, sulfenyl chloride is generated from sulfuryl chloride by the reduction of PPh_3.[9a, 9b] Hence, there are two plausible paths during the reaction. ***Major Path***: the in situ generated sulfenyl chloride then underwent a single electron transfer from the copper catalyst to yield the corresponding sulfenyl radical **8** (Scheme 4, step i). then, sulfur-centered radical **8** adds to the terminal carbon of **1** to form the alkenyl radical **9.** This step (Scheme 4, step ii) is reversible[10] and has excellent regioselectivity due to the radical stability and steric hindrance. Finally, the radical S_H2 substitution of **9** with **5** affords the product and regenerates the sulfenyl radical **8** to complete the radical chain (Scheme 4, step iii). ***Minor Path***: sulfenyl chloride then underwent a direct electrophilic addition to alkene, and due to the poor regioselectivity of this process, small

amount of the anti-Markovnikov product was generated. Alternated, path way in which sulfenyl radical **8** generated from sulfonyl radical cannot be rule out.

Scheme 4. Control Experiment and Proposed Reaction Mechanism



CONCLUSIONS

In summary, we have developed a new and efficient method for the regioselective chloro-thiolation of alkenes using sulfonyl chlorides by employing copper catalyst. The reaction itself features high functional group tolerance, broad substrate scope, good selectivity and mild reaction conditions. Mechanistic investigations revealed a plausible radical process involving a sulfur-centered radical intermediate via copper-mediated homolysis of the Cl-S bond. The current method is complementary to the established synthesis of *β*-chlorothiolated compounds and represents a valuable addition to the synthetic toolbox.

EXPERIMENTAL SECTION

General information

All chemical reagents are obtained from commercial suppliers and used without further purification. All known compounds are identified by appropriate technique such as ^{1}H NMR, ^{13}C{^{1}H} NMR, ^{19}F NMR and compared with previously reported data. All unknown compounds are characterized by ^{1}H NMR, ^{13}C{^{1}H} NMR, ^{19}F NMR and HRMS. Analytical thin-layer chromatography is performed on glass plates precoated with silica gel impregnated with a fluorescent indicator (254 nm), and the plates are visualized by exposure to ultraviolet light. ^{1}H, ^{13}C{^{1}H} and ^{19}F NMR spectra were recorded on a 500 MHz Bruker DRX 500 and tetramethylsilane (TMS) was used as a reference. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.0). and chemical shifts are reported in ppm. GC-MS data was recorded on a ISQ LT Single Quadrupole Mass Spectrometer, coupled with a Trace 1300 Gas Chromatograph (Thermo Fisher Scientific). Melting points were measured on a melting point apparatus and were uncorrected. High resolution mass spectral data were acquired on Waters Micromass GCT Premier spectrometer (electro ionization: EI) and

Waters Q-Tof micro™ (electrospray ionization: ESI).

A typical procedure for preparation of *β*-chloroalkyl sulfides

A 15 mL oven-dried reaction vessel was charged with CuBr (7.2 mg, 0.05 mmol, 0.1 equiv), PPh_3 (393 mg, 1.5 mmol, 3 equiv), allylbenzene **1a** (59 mg, 0.5 mmol, 1 equiv) and $PhSO_2Cl$ **2a** (132 mg, 0.75 mmol, 1.5 equiv) dissolved in AcOH (2.5 mL) was added to the sealed reaction vessel by syringe. The resulting solution was stirred at 85 ºC for 5 h (oil bath). After cooling to room temperature the volatiles were removed under vacuum and the residue was purified by column chromatography to give the corresponding chloro-thiolated products.

A typical procedure of gram-scale synthesis

In a round-bottomed flask (150mL) was consecutively placed CuBr (143 mg, 1 mmol, 0.1 equiv), PPh_3 (7.86 g, 30 mmol, 3 equiv), allylbenzene **1a** (1.18 g, 10 mmol, 1 equiv) and $PhSO_2Cl$ **2a** (2.63 g, 15 mmol, 1.5 equiv) dissolved in AcOH (50 mL) was added to the sealed reaction vessel by syringe, then the mixture was heated at 85 ℃ by oil bath for 5 h. Upon completion, the reaction was cooled to room temperature, the reaction mixture was extracted with CH_2Cl_2 and the organic extracts were concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel to obtain **3a** in 84% yield (2.19 g).

(1-chloro-3-phenylpropan-2-yl)(phenyl)sulfane 3a.[5] Colorless oil, yield 91% (119.2 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.34 (dd, *J* = 7.8, 2.1 Hz, 2H), 7.32 – 7.23 (m, 5H), 7.23 – 7.17 (m, 3H), 4.14 (ddd, *J* = 7.9, 5.3, 2.5 Hz, 1H), 3.33 (tdd, *J* = 14.1, 5.4, 2.2 Hz, 2H), 3.18 (ddd, *J* = 14.0, 7.9, 2.3 Hz, 1H), 3.00 (ddd, *J* = 14.3, 8.0, 2.2 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 136.1 , 134.0 , 129.1 , 128.6 , 128.2 , 127.4 , 126.0 , 125.8 , 60.2 , 41.6 , 40.3.

(2-chloro-3-(4-methoxyphenyl)propyl)(phenyl)sulfane 3b. Colorless oil, yield 85% (124.1 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.36 (m, 2H), 7.35 – 7.29 (m, 2H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.21 – 7.10 (m, 2H), 6.95 – 6.81 (m, 2H), 4.16 (tt, *J* = 7.7, 5.4 Hz, 1H), 3.82 (d, *J* = 1.4 Hz, 3H), 3.38 – 3.28 (m, 2H), 3.22 (ddd, *J* = 13.9, 7.8, 1.7 Hz, 1H), 3.02 (ddd, *J* = 14.4, 7.7, 1.7 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 159.6 , 136.0 , 131.6 , 131.0 , 130.2 , 130.0 , 127.8 , 114.8 , 62.5 , 56.2 , 42.7 , 42.1 . HR-MS (EI) m/z: M^+ Calcd. For $C_{16}H_{17}ClOS$ 292.0689; Found 292.0697.

(2-chloro-3-(naphthalen-1-yl)propyl)(phenyl)sulfane 3c. White solid, M.p. 60.8-62.2 ºC, yield 67% (104.5 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 8.2 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.79 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.51 – 7.39 (m, 4H), 7.38 – 7.33 (m, 2H), 7.28 (d, *J* = 7.5 Hz, 2H), 7.24 – 7.19 (m, 1H), 4.41 – 4.32 (m, 1H), 4.02 (dd, *J* = 14.5, 4.8 Hz, 1H), 3.51 (dd, *J* = 14.1, 5.3 Hz, 1H), 3.36 – 3.28 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 136.0 , 134.9 , 134.3 , 132.7 , 130.6 , 130.2 , 129.9 , 129.2 , 128.8 , 127.7 , 127.1 , 126.6 , 126.3 , 124.3 , 61.5 , 42.9 , 41.4 . HR-MS (EI) m/z: M^+ Calcd. For $C_{19}H_{17}ClS$ 312.0740; Found 312.0732.

(2-chloro-5-phenoxypentyl)(phenyl)sulfane 3d. Colorless oil, yield 77% (117.8 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.43 – 7.33 (m, 2H), 7.30 – 7.23 (m, 4H), 7.22 – 7.17 (m, 1H), 6.96 – 6.90 (m, 1H), 6.89 – 6.81 (m, 2H), 4.01 (tdd, *J* = 8.6, 5.5, 3.2 Hz, 1H), 3.93 (tt, *J* = 4.8, 2.6 Hz, 2H), 3.38 (dd, *J* = 13.8, 5.5 Hz, 1H), 3.15 (dd, *J* = 13.9, 8.2 Hz, 1H), 2.35 – 2.25 (m, 1H), 2.09 – 1.98 (m, 1H), 1.85 (dddd, *J* = 23.3, 18.9, 9.7, 5.1 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 157.8 , 133.9 , 129.4 , 128.4 , 128.2 , 125.9 , 119.7 , 113.5 , 65.8 , 59.8 , 41.2 , 32.2 , 25.0 . HR-MS (EI) m/z: M^+ Calcd. For $C_{17}H_{19}ClOS$ 306.0845; Found 306.0838.

(2-chloro-5-(4-chlorophenoxy)pentyl)(phenyl)sulfane 3e. Colorless oil, yield 83% (141.1 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 – 7.33 (m, 2H), 7.30 – 7.25 (m, 2H), 7.24 – 7.17 (m, 3H), 6.81 – 6.74 (m, 2H), 4.00 (tdd, *J* = 8.4, 5.3, 3.1 Hz, 1H), 3.95 – 3.88 (m, 2H),

3.42 – 3.36 (m, 1H), 3.15 (dd, *J* = 13.9, 8.5 Hz, 1H), 2.34 – 2.21 (m, 1H), 2.03 (dqd, *J* = 11.9, 6.0, 3.7 Hz, 1H), 1.85 (dddt, *J* = 21.2, 14.4, 9.5, 4.5 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 156.4 , 133.9 , 129.3 , 128.3 , 128.2 , 125.9 , 124.5 , 114.7 , 66.3 , 59.6 , 41.1 , 32.0 , 24.9 .HR-MS (EI) m/z: M^+ Calcd. For $C_{17}H_{18}Cl_2OS$ 340.0455; Found 340.0445.

(5-(4-(tert-butyl)phenoxy)-2-chloropentyl)(phenyl)sulfane 3f. Colorless oil, yield 86% (155.7 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.33 (m, 2H), 7.30 – 7.22 (m, 4H), 7.21 – 7.17 (m, 1H), 6.84 – 6.77 (m, 2H), 4.01 (dtd, *J* = 11.7, 5.5, 3.2 Hz, 1H), 3.92 (td, *J* = 6.0, 1.9 Hz, 2H), 3.41 – 3.35 (m, 1H), 3.16 (dd, *J* = 13.8, 8.2 Hz, 1H), 2.35 – 2.22 (m, 1H), 2.02 (ddt, *J* = 12.0, 9.5, 5.9 Hz, 1H), 1.92 – 1.76 (m, 2H), 1.29 (d, *J* = 1.7 Hz, 9H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 155.6 , 142.4 , 134.0 , 129.4 , 128.2 , 125.9 , 125.2 , 113.0 , 65.9 , 59.9 , 41.3 , 33.1 , 32.2 , 30.6 , 25.1 . HR-MS (EI) m/z: M^+ Calcd. For $C_{21}H_{27}ClOS$ 362.1471; Found 362.1472.

(2-chloro-5-(4-(trifluoromethyl)phenoxy)pentyl)(phenyl)sulfane 3g. Colorless oil, yield 80% (149.6 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.52 (d, *J* = 8.6 Hz, 2H), 7.37 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.29 – 7.18 (m, 3H), 6.91 (d, *J* = 8.5 Hz, 2H), 4.08 – 3.92 (m, 3H), 3.45 – 3.37 (m, 1H), 3.16 (dd, *J* = 13.9, 8.6 Hz, 1H), 2.31 (dddd, *J* = 14.0, 10.3, 5.2, 2.8 Hz, 1H), 2.11 – 2.02 (m, 1H), 1.95 – 1.80 (m, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 162.3 , 135.8 , 131.3 , 130.2 , 127.9 , 127.8 (q, *J* = 3.8 Hz), 125.4 (q, *J* = 270.9 Hz), 115.4 , 68.2 , 61.6 , 43.1 , 34.0 , 26.8 ; ^{19}F NMR (470 MHz, Chloroform-*d*) δ -58.92. HR-MS (EI) m/z: M^+ Calcd. For $C_{18}H_{18}ClF_3OS$ 374.0719; Found 374.0712.

(2-chloropropane-1,3-diyl)bis(phenylsulfane) 3h.[11] Colorless oil, yield 68% (99.4 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 – 7.29 (m, 4H), 7.25 (d, *J* = 1.7 Hz, 4H), 7.23 – 7.18 (m, 2H), 4.05 (p, *J* = 6.4 Hz, 1H), 3.47 (dd, *J* = 14.1, 6.6 Hz, 2H), 3.32 (dd, *J* = 14.2, 6.2 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 133.6 , 129.4 , 128.1 , 125.9 , 57.8 , 39.9 , 28.7 .

(2-chloro-3-cyclopentylpropyl)(phenyl)sulfane 3i. Colorless oil, yield 87% (110.5 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.23 (q, *J* = 6.9 Hz, 1H), 3.95 (tdd, *J* = 8.8, 5.5, 3.4 Hz, 1H), 3.37 (dd, *J* = 13.7, 5.5 Hz, 1H), 3.15 (dd, *J* = 13.7, 8.0 Hz, 1H), 2.12 – 2.01 (m, 1H), 1.95 (ddd, *J* = 13.2, 9.4, 3.4 Hz, 1H), 1.82 – 1.72 (m, 3H), 1.61 (td, *J* = 6.8, 3.0 Hz, 2H), 1.53 (dtd, *J* = 15.8, 7.8, 3.3 Hz, 2H), 1.12 (dq, *J* = 12.0, 8.0 Hz, 1H), 0.99 (dq, *J* = 11.8, 8.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 137.5, 135.9, 132.6, 131.1, 129.6, 128.4, 128.0, 127.8, 126.2, 116.6, 20.3. HR-MS (EI) m/z: M^+ Calcd. For $C_{14}H_{19}ClS$ 254.0896; Found 254.0900.

(2-chlorooctyl)(phenyl)sulfane 3j. Colorless oil, yield 79% (101.2 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 3.96 (tdd, *J* = 8.8, 5.5, 3.5 Hz, 1H), 3.36 (dd, *J* = 8.7, 5.0 Hz, 1H), 3.15 (dd, *J* = 13.8, 8.2 Hz, 1H), 2.04 – 1.96 (m, 1H), 1.69 (dtd, *J* = 14.2, 9.5, 4.6 Hz, 1H), 1.55 – 1.48 (m, 1H), 1.38 (td, *J* = 9.0, 7.9, 5.0 Hz, 1H), 1.29 – 1.24 (m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 136.3 , 131.2 , 130.2 , 127.8 , 62.3 , 43.2 , 37.5 , 32.7 , 29.7 , 27.1 , 23.6 , 15.1 .HR-MS (EI) m/z: M^+ Calcd. For $C_{14}H_{21}ClS$ 256.1053; Found 256.1047.

(2-chlorododecyl)(phenyl)sulfane 3k.[12] Colorless oil, yield 90% (140.5 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 3.96 (tdd, *J* = 8.8, 5.5, 3.4 Hz, 1H), 3.36 (dd, *J* = 13.8, 5.6 Hz, 1H), 3.16 (dd, *J* = 13.8, 8.2 Hz, 1H), 2.00 (tdd, *J* = 9.7, 6.1, 2.9 Hz, 1H), 1.69 (dtd, *J* = 14.2, 9.5, 4.6 Hz, 1H), 1.54 – 1.48 (m, 1H), 1.42 – 1.37 (m, 1H), 1.25 (s, 14H), 0.88 (t, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 136.3 , 131.2 , 130.2 , 127.8 , 62.3 , 43.2 , 37.5 , 33.0 , 30.6 , 30.6 , 30.5 , 30.4 , 30.1 , 27.1 , 23.8 , 15.2 .

((1R,2R)-2-chlorocyclopentyl)(phenyl)sulfane 3l.[13] Colorless oil, yield 84% (89.1 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 4.25 (d, *J* = 5.4 Hz, 1H), 3.86 – 3.79 (m, 1H), 2.49 – 2.35 (m, 2H), 2.03 – 1.95 (m, 2H), 1.91 – 1.84 (m, 1H), 1.68 (q, *J* = 4.8 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 131.2 , 130.2 , 127.7 , 66.8 , 55.7 , 35.5 , 30.9 , 23.3 .

((1R,2R)-2-chlorocyclohexyl)(phenyl)sulfane 3m.[14] Colorless oil, yield 80% (90.4 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.46 (dd, *J* = 7.3, 1.7 Hz, 2H), 7.33 – 7.30 (m, 2H), 7.29 – 7.26 (m, 1H), 4.02 (dt, *J* = 10.0, 4.8 Hz, 1H), 3.32 (q, *J* = 6.2 Hz, 1H), 2.35 (ddd, *J* = 14.0, 7.9, 3.5 Hz, 1H), 2.23 (ddt, *J* = 13.1, 8.4, 3.8 Hz, 1H), 1.76 (dtd, *J* = 14.2, 8.1, 7.6, 3.0 Hz, 2H), 1.71 – 1.58 (m, 2H), 1.41 (dtd, *J* = 12.4, 9.2, 8.6, 4.1 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 134.9 , 133.8 , 130.1 , 128.5 , 63.1 , 53.9 , 34.3 , 31.2 , 24.5 , 23.9 .

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(phenyl)sulfane 3n.[15] Colorless oil, yield 93% (110.7 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 – 7.33 (m, 2H), 7.29 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.24 – 7.18 (m, 1H), 4.04 (td, *J* = 4.1, 1.8 Hz, 1H), 3.08 (dd, *J* = 4.0, 2.8 Hz, 1H), 2.48 (q, *J* = 3.7 Hz, 1H), 2.29 (d, *J* = 4.6 Hz, 1H), 2.00 (q, *J* = 1.7 Hz, 1H), 1.82 (dt, *J* = 10.6, 2.0 Hz, 1H), 1.75 – 1.65 (m, 1H), 1.52 – 1.42 (m, 2H), 1.39 (q, *J* = 2.6 Hz, 1H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 134.3 , 129.6 , 127.9 , 125.6 , 66.2 , 58.1 , 43.2 , 42.7 , 34.8 , 27.8 , 20.7 .

(8R,9S,13S,14S)-3-((6-chloro-7-(phenylthio)heptyl)oxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro -17H-cyclopenta[a]phenanthren-17-one 3r. Colorless oil, yield 69% (176.0 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.39 – 7.34 (m, 2H), 7.29 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.24 – 7.17 (m, 2H), 6.69 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.63 (d, *J* = 2.7 Hz, 1H), 3.99 – 3.89 (m, 3H), 3.36 (dd, *J* = 13.8, 5.5 Hz, 1H), 3.15 (dd, *J* = 13.8, 8.3 Hz, 1H), 2.92 – 2.84 (m, 2H), 2.52 – 2.45 (m, 1H), 2.38 (dt, *J* = 14.2, 3.6 Hz, 1H), 2.23 (td, *J* = 10.7, 4.4 Hz, 1H), 2.16 – 2.08 (m, 1H), 2.06 – 1.97 (m, 3H), 1.96 – 1.91 (m, 1H), 1.75 (tdd, *J* = 14.5, 13.6, 6.6, 2.4 Hz, 3H), 1.64 – 1.58 (m, 2H), 1.53 – 1.36 (m, 8H), 0.89 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 158.1 , 138.8 , 136.3 , 133.0 , 131.2 , 130.2 , 127.9 , 127.4 , 115.6 , 113.2 , 68.7 , 62.2 , 51.5 , 49.1 , 45.0 , 43.2 , 39.4 , 37.4 , 37.0 , 32.7 , 30.7 , 30.2 , 27.6 , 27.0 , 26.9 , 26.6 , 22.7 , 14.9 . HR-MS (ESI) m/z: $[M+H]^+$ Calcd. For $C_{31}H_{40}ClSO_2$ 511.2432; Found 511.2431.

(2-chloro-3-phenylpropyl)(4-iodophenyl)sulfane 4a. Colorless oil, yield 65% (126.1 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.67 – 7.53 (m, 2H), 7.37 – 7.16 (m, 5H), 7.10 – 7.00 (m, 2H), 4.15 (tt, *J* = 7.5, 5.6 Hz, 1H), 3.30 (td, *J* = 14.2, 5.6 Hz, 2H), 3.20 (dd, *J* = 14.0, 7.3 Hz, 1H), 3.05 (dd, *J* = 14.2, 7.6 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 137.9 , 136.7 , 135.0 , 131.2 , 129.3 , 128.3 , 126.9 , 91.5 , 60.7 , 42.6 , 40.8 . HR-MS (EI) m/z: M^+ Calcd. For $C_{15}H_{14}ClIS$ 387.9550; Found 387.9548.

[1,1'-biphenyl]-4-yl(2-chloro-3-phenylpropyl)sulfane 4b. Colorless oil, yield 72% (121.7 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.63 – 7.59 (m, 2H), 7.57 – 7.54 (m, 2H), 7.49 – 7.43 (m, 4H), 7.41 – 7.33 (m, 3H), 7.31 – 7.25 (m, 3H), 4.23 (ddd, *J* = 7.8, 5.3, 2.5 Hz, 1H), 3.41 (ddd, *J* = 13.8, 8.4, 5.3 Hz, 2H), 3.26 (dd, *J* = 14.0, 7.8 Hz, 1H), 3.08 (dd, *J* = 14.3, 7.9 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 141.3 , 140.9 , 138.2 , 135.0 , 131.5 , 130.7 , 130.0 , 129.5 , 128.9 , 128.6 , 128.1 , 128.0 , 62.2 , 43.7 , 42.4 . HR-MS (EI) m/z: M^+ Calcd. For $C_{21}H_{19}ClS$ 338.0896; Found 338.0902.

(2-chloro-3-phenylpropyl)(4-(trifluoromethoxy)phenyl)sulfane 4c. Colorless oil, yield 80% (138.4 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.38 – 7.25 (m, 5H), 7.19 (d, *J* = 7.4 Hz, 2H), 7.13 (d, *J* = 8.3 Hz, 2H), 4.22 – 4.09 (m, 1H), 3.29 (td, *J* = 13.8, 5.7 Hz, 2H), 3.20 (dd, *J* = 14.0, 7.1 Hz, 1H), 3.05 (dd, *J* = 14.3, 7.6 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 149.1 ,

137.8 , 134.8 , 132.4 , 130.5 , 129.5 , 128.0 , 122.7 , 121.4 (q, *J* = 257.5 Hz), 61.8 , 43.8 , 42.5; ^{19}F NMR (470 MHz, Chloroform-*d*) δ -55.43. HR-MS (EI) m/z: M^+ Calcd. For $C_{16}H_{14}ClF_3OS$ 346.0406; Found 346.0403.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(mesityl)sulfane 4d.[14] Colorless oil, yield 89% (124.6 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.93 (s, 2H), 3.94 (td, *J* = 4.1, 1.8 Hz, 1H), 2.78 (dd, *J* = 3.9, 2.8 Hz, 1H), 2.52 (s, 6H), 2.47 – 2.42 (m, 1H), 2.26 (s, 3H), 2.10 (d, *J* = 4.6 Hz, 1H), 1.93 (ttd, *J* = 12.8, 4.1, 2.2 Hz, 2H), 1.61 (dd, *J* = 12.5, 4.5 Hz, 1H), 1.42 (tddd, *J* = 10.6, 8.5, 4.4, 2.1 Hz, 2H), 1.20 (ddt, *J* = 11.5, 4.5, 2.6 Hz, 1H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 137.5, 135.9, 132.6, 131.1, 129.6, 128.4, 128.0, 127.8, 126.2, 116.6, 20.3.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(2,3,5,6-tetramethylphenyl)sulfane 4e. White solid, M.p. 55.4-57.6 ºC, yield 85% (125.0 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 6.95 (s, 1H), 3.93 (d, *J* = 1.9 Hz, 1H), 2.72 (dd, *J* = 4.0, 2.8 Hz, 1H), 2.52 (s, 6H), 2.46 – 2.42 (m, 1H), 2.24 (s, 6H), 2.07 (d, *J* = 4.6 Hz, 1H), 1.92 (ttd, *J* = 11.7, 4.2, 2.2 Hz, 2H), 1.56 (dt, *J* = 12.4, 4.5 Hz, 1H), 1.46 – 1.38 (m, 2H), 1.18 (dddd, *J* = 11.6, 8.6, 4.5, 2.3 Hz, 1H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 137.8 , 133.2 , 131.8 , 131.1 , 65.9 , 59.4 , 43.3 , 42.3 , 34.8 , 27.8 , 20.8 , 19.9 , 17.6 . HR-MS (EI) m/z: M^+ Calcd. For $C_{17}H_{23}ClS$ 294.1209; Found 294.1207.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(2,4,6-triisopropylphenyl)sulfane 4f. White solid, M.p. 72.2-73.9 ºC, yield 91% (165.7 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.00 (s, 2H), 4.09 – 3.90 (m, 3H), 2.88 (p, *J* = 6.9 Hz, 1H), 2.67 (t, *J* = 3.3 Hz, 1H), 2.45 (d, *J* = 4.4 Hz, 1H), 2.12 (d, *J* = 4.6 Hz, 1H), 1.99 – 1.83 (m, 2H), 1.60 (ddt, *J* = 12.3, 8.9, 4.4 Hz, 1H), 1.42 (tddd, *J* = 11.2, 9.4, 4.5, 1.9 Hz, 2H), 1.28 – 1.18 (m, 19H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 152.0 , 148.6 , 126.2 , 120.8 , 66.0 , 60.9 , 43.2 , 42.1 , 34.7 , 33.1 , 30.4 , 27.9 , 23.7 , 23.2 , 22.8 , 20.8 . HR-MS (EI) m/z: M^+ Calcd. For $C_{22}H_{33}ClS$ 364.1992; Found 364.2001.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(4-fluorophenyl)sulfane 4g. Colorless oil, yield 84% (107.5 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.45 – 7.39 (m, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 4.01 (td, *J* = 4.1, 1.8 Hz, 1H), 2.98 (dd, *J* = 3.9, 2.8 Hz, 1H), 2.51 – 2.45 (m, 1H), 2.25 (d, *J* = 4.6 Hz, 1H), 1.98 (dddd, *J* = 13.3, 9.2, 4.5, 2.4 Hz, 1H), 1.81 (dp, *J* = 10.7, 1.9 Hz, 1H), 1.68 (tt, *J* = 12.5, 4.6 Hz, 1H), 1.50 – 1.40 (m, 2H), 1.34 (dddd, *J* = 11.9, 9.2, 4.6, 2.3 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 161.2 (d, *J* = 247.4 Hz), 132.8 (d, *J* = 8.1 Hz), 128.9 , 115.0 (d, *J* = 21.8 Hz), 66.2 , 59.2 , 43.3 , 42.5 , 34.7 , 27.8 , 20.7; ^{19}F NMR (470 MHz, Chloroform-*d*) δ -113.56. HR-MS (EI) m/z: M^+ Calcd. For $C_{13}H_{14}ClFS$ 256.0489; Found 256.0493.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(4-chlorophenyl)sulfane 4h.[16] Colorless oil, yield 81% (110.2 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H), 4.01 (td, *J* = 4.1, 1.8 Hz, 1H), 3.04 (dd, *J* = 3.9, 2.7 Hz, 1H), 2.49 (q, *J* = 3.7 Hz, 1H), 2.26 (d, *J* = 4.6 Hz, 1H), 1.99 (dddd, *J* = 13.2, 9.1, 4.5, 2.4 Hz, 1H), 1.80 (dp, *J* = 10.5, 1.9 Hz, 1H), 1.70 (tt, *J* = 12.5, 4.6 Hz, 1H), 1.51 – 1.41 (m, 2H), 1.37 (dddd, *J* = 11.8, 9.1, 4.6, 2.3 Hz, 1H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 132.7 , 131.7 , 131.0 , 128.0 , 66.1 , 58.3 , 43.2 , 42.6 , 34.8 , 27.8 , 20.7.

(4-bromophenyl)((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)sulfane 4i. Colorless oil, yield 83% (131.1 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.44 – 7.39 (m, 2H), 7.28 – 7.23 (m, 2H), 4.01 (td, *J* = 4.1, 1.8 Hz, 1H), 3.08 – 3.02 (m, 1H), 2.50 (d, *J* = 4.4 Hz, 1H), 2.27 (d, *J* = 4.7 Hz, 1H), 2.00 (dddd, *J* = 13.2, 9.1, 4.6, 2.4 Hz, 1H), 1.81 (dp, *J* = 10.7, 2.0 Hz, 1H), 1.70 (tt, *J* = 12.4, 4.6 Hz, 1H), 1.53 – 1.44 (m, 2H), 1.38 (dddd, *J* = 11.7, 9.0, 4.5, 2.2 Hz, 1H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 137.5, 135.9, 132.6, 131.1, 129.6, 128.4, 128.0, 127.8, 126.2, 116.6, 20.3. HR-MS

(EI) m/z: M^+ Calcd. For $C_{13}H_{14}ClBrS$ 315.9688; Found 315.9691.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(4-(trifluoromethyl)phenyl)sulfane 4j. White solid, M.p. 50.8-52.6 ºC, yield 82% (125.5 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.1 Hz, 2H), 7.42 (d, *J* = 8.1 Hz, 2H), 4.12 – 3.94 (m, 1H), 3.17 (t, *J* = 3.3 Hz, 1H), 2.53 (d, *J* = 4.4 Hz, 1H), 2.31 (d, *J* = 4.6 Hz, 1H), 2.04 (ddt, *J* = 12.7, 8.7, 2.9 Hz, 1H), 1.87 – 1.71 (m, 2H), 1.56 – 1.44 (m, 3H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 140.1 , 127.6 , 126.9 (q, *J* = 32.5 Hz), 124.6 , 123.0 (q, *J* = 271.7 Hz), 65.9 , 57.0 , 43.2 , 42.7 , 35.0 , 27.8 , 20.7; ^{19}F NMR (470 MHz, Chloroform-*d*) δ -61.61. HR-MS (EI) m/z: M^+ Calcd. For $C_{14}H_{14}ClF_3S$ 306.0457; Found 306.0458.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(p-tolyl)sulfane 4k.[17] Colorless oil, yield 80% (100.8 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H), 4.02 (d, *J* = 1.9 Hz, 1H), 3.01 (d, *J* = 1.2 Hz, 1H), 2.54 – 2.41 (m, 1H), 2.32 (s, 3H), 2.27 (d, *J* = 4.6 Hz, 1H), 1.98 (dddd, *J* = 13.3, 9.2, 4.5, 2.4 Hz, 1H), 1.81 (dt, *J* = 10.6, 2.0 Hz, 1H), 1.67 (tt, *J* = 12.4, 4.6 Hz, 1H), 1.52 – 1.39 (m, 2H), 1.35 (ddq, *J* = 11.8, 6.8, 2.3 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 135.9 , 130.6 , 130.3 , 128.7 , 66.2 , 58.7 , 43.2 , 42.6 , 34.7 , 27.8 , 20.8 , 20.0.

((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)(4-methoxyphenyl)sulfane 4l. Colorless oil, yield 87% (116.6 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 8.7 Hz, 2H), 6.88 – 6.82 (m, 2H), 4.01 (td, *J* = 4.1, 1.8 Hz, 1H), 3.79 (s, 3H), 2.92 (dd, *J* = 4.0, 2.7 Hz, 1H), 2.50 – 2.40 (m, 1H), 2.24 (d, *J* = 4.7 Hz, 1H), 1.95 (dddd, *J* = 13.2, 9.1, 4.5, 2.3 Hz, 1H), 1.79 (dp, *J* = 10.5, 1.9 Hz, 1H), 1.65 (tt, *J* = 10.1, 3.5 Hz, 1H), 1.46 – 1.36 (m, 2H), 1.31 (ddd, *J* = 9.8, 4.6, 2.3 Hz, 1H).; ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 158.4 , 133.6 , 124.0 , 113.5 , 66.2 , 59.7 , 54.3 , 43.3 , 42.5 , 34.7 , 27.9 , 20.8 . HR-MS (EI) m/z: M^+ Calcd. For $C_{14}H_{17}ClOS$ 268.0689; Found 268.0692.

(4-(tert-butyl)phenyl)((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)sulfane 4m. Colorless oil, yield 85% (125.0 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 1.5 Hz, 4H), 4.03 (td, *J* = 4.1, 1.8 Hz, 1H), 3.04 (dd, *J* = 4.0, 2.8 Hz, 1H), 2.47 (td, *J* = 4.2, 1.6 Hz, 1H), 2.33 – 2.23 (m, 1H), 1.99 (ddq, *J* = 11.5, 6.8, 2.4 Hz, 1H), 1.81 (dt, *J* = 10.7, 2.1 Hz, 1H), 1.74 – 1.63 (m, 1H), 1.52 – 1.40 (m, 2H), 1.36 (tdd, *J* = 9.0, 4.5, 2.3 Hz, 1H), 1.30 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 148.9 , 130.7 , 129.6 , 124.9 , 66.2 , 58.3 , 43.2 , 42.8 , 34.7 , 33.4 , 30.2 , 27.8 , 20.7. HR-MS (EI) m/z: M^+ Calcd. For $C_{17}H_{23}ClS$ 294.1209; Found 294.1205.

(2-chloro-3-phenylpropyl)(naphthalen-2-yl)sulfane 4n. Colorless oil, yield 73% (113.9 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.81 – 7.69 (m, 4H), 7.50 – 7.40 (m, 3H), 7.33 – 7.18 (m, 5H), 4.20 (tt, *J* = 7.6, 5.4 Hz, 1H), 3.44 – 3.26 (m, 3H), 3.06 (dd, *J* = 14.2, 7.7 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 136.0 , 132.7 , 131.3 , 131.0 , 128.5 , 127.8 , 127.4 , 127.0 , 126.7 , 126.6 , 126.2 , 126.0 , 125.7 , 125.0 , 60.1 , 41.7 , 40.0 . HR-MS (EI) m/z: M^+ Calcd. For $C_{19}H_{17}ClS$ 312.0740; Found 312.0745.

2-((2-chloro-3-phenylpropyl)thio)thiophene 4o. Colorless oil, yield 81% (108.5 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.36 (dd, *J* = 5.4, 1.4 Hz, 1H), 7.30 (t, *J* = 7.3 Hz, 2H), 7.27 – 7.15 (m, 4H), 6.98 (dd, *J* = 5.4, 3.6 Hz, 1H), 4.16 (tt, *J* = 7.8, 5.0 Hz, 1H), 3.39 (dd, *J* = 14.3, 4.5 Hz, 1H), 3.18 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.02 (ddd, *J* = 31.4, 14.0, 8.0 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 138.0 , 135.5 , 133.8 , 131.1 , 130.5 , 129.4 , 128.8 , 127.9 , 61.9 , 46.7 , 43.3 . HR-MS (EI) m/z: M^+ Calcd. For $C_{13}H_{13}ClS_2$ 268.0147; Found 268.0151.

6-((2-chloro-3-phenylpropyl)thio)-2,3-dihydrobenzofuran 4p. Colorless oil, yield 70% (106.4 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.27 (m, 3H), 7.24 – 7.22 (m, 1H), 7.19 (dt, *J* = 7.8, 1.8 Hz, 3H), 6.71 (d, *J* = 8.3 Hz, 1H), 4.56 (t, *J* = 8.8 Hz, 2H), 4.08 (tdd, *J* = 8.1, 5.5, 4.6 Hz, 1H), 3.38 (dd, *J* = 14.3, 4.6 Hz, 1H), 3.21 – 3.14 (m, 3H), 3.05 (dd, *J* = 13.8, 8.0 Hz, 1H),

2.97 (dd, *J* = 14.2, 8.1 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 137.5, 135.9, 132.6, 131.1, 129.6, 128.4, 128.0, 127.8, 126.2, 116.6, 20.3. HR-MS (EI) m/z: M^+ Calcd. For $C_{17}H_{17}ClOS$ 304.0689; Found 304.0695.

3-(((1S,2R,3R,4R)-3-chlorobicyclo[2.2.1]heptan-2-yl)thio)pyridine 4q. Colorless oil, yield 61% (72.9 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 2.3 Hz, 1H), 8.24 (d, *J* = 4.7 Hz, 1H), 7.51 (dd, *J* = 7.8, 2.2 Hz, 1H), 7.01 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.81 (q, *J* = 3.0, 2.1 Hz, 1H), 2.85 (t, *J* = 3.3 Hz, 1H), 2.28 (d, *J* = 4.3 Hz, 1H), 2.06 (d, *J* = 4.6 Hz, 1H), 1.77 (tdt, *J* = 8.9, 4.5, 2.3 Hz, 1H), 1.60 (dd, *J* = 11.0, 2.5 Hz, 1H), 1.48 (dq, *J* = 12.2, 6.4, 4.7 Hz, 1H), 1.31 – 1.21 (m, 2H), 1.20 – 1.10 (m, 1H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 150.2 , 146.7 , 146.7 , 137.3 , 137.2 , 131.4 , 122.7 , 66.1 , 58.1 , 43.3 , 43.3 , 42.6 , 34.8 , 34.8 , 27.8 , 27.8 , 20.7 , 20.6. HR-MS (EI) m/z: M^+ Calcd. For $C_{12}H_{14}ClNS$ 239.0535; Found 239.0536.

(2-chloro-3-phenylpropyl)(cyclopropyl)sulfane 4r. Colorless oil, yield 77% (87.0 mg). Eluent: ethyl acetate/petroleum ether (1:99). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.33 (dd, *J* = 8.5, 6.5 Hz, 2H), 7.26 (d, *J* = 13.9 Hz, 3H), 4.30 (tt, *J* = 7.8, 5.2 Hz, 1H), 3.38 – 3.33 (m, 1H), 3.01 (dt, *J* = 14.1, 6.8 Hz, 2H), 2.91 (dd, *J* = 13.7, 7.6 Hz, 1H), 1.98 (tt, *J* = 7.6, 4.3 Hz, 1H), 0.88 (dd, *J* = 8.2, 4.4 Hz, 2H), 0.59 (q, *J* = 4.9, 4.5 Hz, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 138.5 , 130.6 , 129.5 , 127.9 , 63.2 , 43.9 , 42.2 , 14.3 , 9.9 , 9.4 .HR-MS (EI) m/z: M^+ Calcd. For $C_{12}H_{15}ClS$ 226.0583; Found 226.0584.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publication website at DOI:

X-ray crystallography data, CIF file, ^{1}H NMR, $^{13}C\{^{1}H\}$ NMR, and ^{19}F NMR for products (PDF).

AUTHOR INFORMATION

Corresponding Authors

* E-mail: yiwb@njust.edu.cn

Author Contributions

§ These authors contributed equally to this paper.

ORCID

Lvqi Jiang: 0000-0002-1921-985X

Wen-bin Yi: 0000-0003-4606-7668

Notes

The authors declare no competing financial interest.

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