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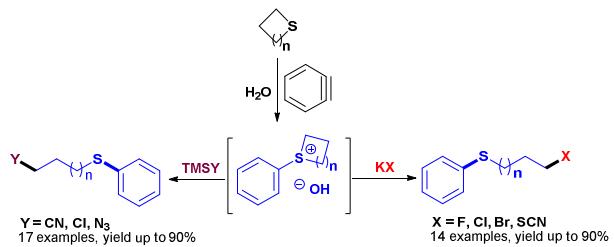
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Benzyne-induced synthesis of diverse functionalized thioethers



Divergent synthesis of functionalized thioethers via multicomponent reaction of benzenes

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Abstract: Diverse functionalized thioethers were efficiently synthesized through the multicomponent reaction of benzenes, cyclic thioethers and different nucleophiles. Both inorganic salts (KF, KCl, KBr, and KSCN) and silylated reagents (TMSCN, TMSN₃, TMSCl) can be utilized as efficient nucleophiles for the reaction.

Keywords: benzyne, thioether, multicomponent reaction

Introduction

Thioethers are privileged motifs found in many natural products, biologically active compounds and pharmaceuticals.¹ Over the past several decades, considerable efforts have been exerted to develop new methodologies for the synthesis of these significant frameworks. Several different strategies,² such as transition metal catalyzed cross-coupling reaction and hydrothiolation, organocatalytic sulfa-Michael reaction and sulfenylation reaction, have been well established for the construction of thioethers. Despite remarkable progress made in this research field, the development of efficient protocols for the synthesis of thioethers that bearing some specific functional groups, such as fluorine atom³ and cyano group,⁴ is still lacking.

Benzenes are highly reactive intermediates that are utilized widely in organic synthesis.⁵ The electrophilic benzyne can undergo N-, O-, C-insertion with different nucleophiles and trigger a broad variety of transformations.⁶ However, reactions initiated by S-insertion of benzyne are very limited. Recently, Studer⁷ and co-workers reported that the linear vinyl thioethers can react with benzyne

through [3+2] cycloaddition to form cyclic sulfonium ylide, and after proton transfer and β -elimination reaction, afford trisubstituted alkenes. Subsequently, through the S-insertion of linear thioethers and benzyne, Xu⁸ and co-workers developed a novel method to generate sulfonium ylide, which can be intercepted by isatin to form spiroepoxy oxindoles in high yield. Tan, Xu⁹ and co-workers further extended the study to allyl and propargyl thioethers, which can undergo [2,3] sigmatropic rearrangement with benzyne through sulfonium intermediate. Very recently, Tan, Xu^{10a}, Hoye^{10b} and their co-workers reported independently that benzynes can undergo multicomponent reaction with cyclic thioethers and different acidic proton-containing nucleophiles, such as acetic acid, phenol and amide, to give the ring-opening products. As part of our ongoing project,¹¹ we envisaged that the S-arylation of cyclic ethers can lead to the formation of sulfonium intermediate, which can undergo ring-opening reaction with different nucleophiles to produce various functionalized thioethers. And herein, we wish to report this result.

Results and discussion

We initiated our studies with the commercially available Kobayashi's reagent¹² **1a** and tetrahydrothiophene **2a**. To our delight, with 3.0 equiv KF/18-crown-6 and 2.0 equiv H₂O as additives, benzyne reacted with tetrahydrothiophene and fluoride anion smoothly at room temperature in THF to produce the fluorinated thioether **3a** in 59% yield (Table 1, entry 1). However, when H₂O was excluded from the same reaction conditions, only a small amount of product was formed (Table 1, entry 2). Used 2.0 equiv ethanol as the additive, the product can be obtained in 45% yield (Table 1, entry 3). A brief screening of the reaction media revealed that DCM was the best choice with respect to the reaction yield (Table 1, entries 4-7). Other fluoride sources, such as CsF/18-crown-6, TBAF and TBAT can also promote the reaction in good yield (Table 1, entries 8-10). In the absence of the crown ether, KF or CsF can only promote the reaction in very low efficiency (Table 1, entries 11 and 12). Increasing the amount of

tetrahydrothiophene to 5.0 equiv cannot improve the reaction yield (Table 1, entry 13). Neither reducing the amount of water to 1.0 equiv nor increasing to 3.0 equiv can improve the the yield (Table 1, entries 14 and 15).

Table 1 Optimization of reaction conditions ^a

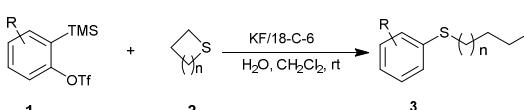
Entry	Additives	solvent	Time (h)	Yield (%) ^b
1	KF (3 equiv), 18-C-6 (3 equiv), H ₂ O (2 equiv)	THF	12	59
2	KF (3 equiv), 18-C-6 (3 equiv)	THF	12	<10
3	KF (3 equiv), 18-C-6 (3 equiv), EtOH (2 equiv)	THF	12	45
4	KF (3 equiv), 18-C-6 (3 equiv), H ₂ O (2 equiv)	CH ₃ CN	12	58
5	KF (3 equiv), 18-C-6 (3 equiv), H ₂ O (2 equiv)	DCM	12	76
6	KF (3 equiv), 18-C-6 (3 equiv), H ₂ O (2 equiv)	DCE	12	64
7	KF (3 equiv), 18-C-6 (3 equiv), H ₂ O (2 equiv)	toluene	12	<10
8	CsF (3 equiv), 18-C-6 (3 equiv), H ₂ O (2 equiv)	DCM	12	72
9	TBAF (3 equiv), H ₂ O (2 equiv)	DCM	12	60
10	TBAT (3 equiv), H ₂ O (2 equiv)	DCM	12	72
11	CsF (3 equiv), H ₂ O (2 equiy)	THF	24	<10
12 ^c	KF (3 equiv), H ₂ O (2 equiv)	THF	24	<10
13	KF (3 equiv), 18-C-6 (3 equiv), H ₂ O (2 equiv)	THF	12	70
14	KF (3 equiv), 18-C-6 (3 equiv) , H ₂ O (1 equiv)	DCM	12	51
15	KF (3 equiv), 18-C-6 (3 equiv) , H ₂ O (3 equiv)	DCM	12	70

^a Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), solvent 1 mL, room temperature ; ^b Isolated yield; ^c **2a** (0.5 mmol).

With the optimal reaction conditions in hand (Table 1, entry 4), the generality of the reaction was subsequently studied and the results are summarized in Table 2. Symmetrical benzynes with electron-donating or withdrawing groups efficiently undergo the multicomponent reaction to produce the desired products in moderate to good yields (Table 2, entries 1-4). On the other hand, unsymmetrical benzynes can also react with **2a** and KF smoothly, affording the corresponding products as an

inseparable mixture of two regioisomers in good yield (Table 2, entries 5-8). Notably, when unsymmetrical 3-methoxy substituted benzene precursor **1i** was employed for the reaction, the fluorinated product **3i** was obtained in 78% yield with complete regioselectivity (Table 2, entry 9).¹³ Thietane **2b** was proved to be a good candidate for the reaction, providing **3j** in 74% yield (Table 2, entry 10). However, when thiane was used for the reaction, **3k** was only obtained in 28% yield (Table 2, entry 11). Different inorganic salts, such as KCl, KBr and KSCN were also proved to be competent nucleophiles for the reaction, giving chloro-, bromo- and thiocyanate-substituted thioethers in good to high yields (Table 2, entries 12-14).

Table 2 Evaluation of substrate scope ^a



Entry	1	2	Time (h)	Product	Yield (%) ^b
1	1a	2a	12	3a	76
2 ^c	1b	2a	24	3b	63
3	1c	2a	24	3c	56
4 ^d	1d	2a	24	3d	57
5	1e	2a	24	m-3e : o-3e' = 2:1 ^e	77
6	1f	2a	24	m-3f : p-3f' = 1.1:1 ^e	69
7					

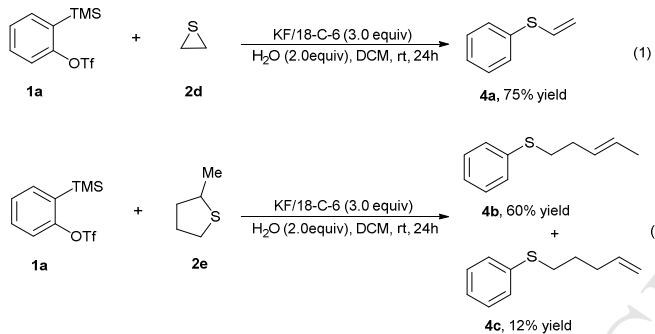
	1g		m-3g : p-3g' = 1:1.4^e
8		2a	24
	1h		
			alpha-3h : beta-3h' = 1:1.25^e
9		2a	24
	1i		
10			24
	1a	2b	
11 ^f			24
	1a	2c	
12 ^g		2a	24
	1a	2a	
13 ^h		2a	24
	1a	2a	
14 ⁱ		2a	24
	1a	2a	
			76
			78
			74
			28
			90
			58
			61
			3n

^a Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), solvent 2.0 mL, room temperature; ^b Isolated yield; ^c Using 3.0 equiv TBAF as fluoride source; ^d Using 3.0 equiv TBAT as fluoride source; ^e the regioselectivity was determined by ¹⁹F NMR analysis of the crude products; ^f Conducted the reaction at 40 °C; ^g Added 3.0 equiv KCl; ^h Added 3.0 equiv KBr; ⁱ Added 3.0 equiv KSCN.

Surprisingly, under the same reaction conditions, thiirane reacted with benzyne to provide vinyl thioether **4a** in 75% yield, and no fluorinated product was obtained (Scheme 1, eq 1). We postulated that the high ring strain of the three-membered cyclic sulfonium leads to very fast intramolecular β-elimination and resulted in the formation of the vinyl thioether products.¹⁴ More interestingly, when α-methyl substituted tetrahydrothiophene **2e** was used for the reaction, a similar β-elimination

reaction was observed and vinyl thioethers **4b** and **4c** were obtained as an inseparable mixture of 5:1 regioisomers in 72% total yield (Scheme 1, eq 2).

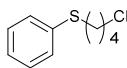
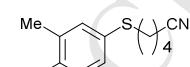
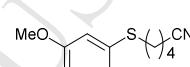
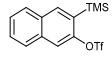
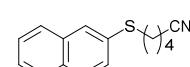
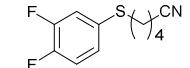
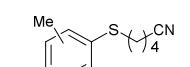
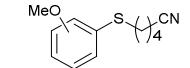
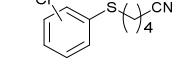
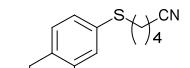
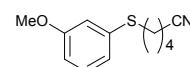
Scheme 1 Reaction of benzyne with thiirane and α -methyl tetrahydrothiophene

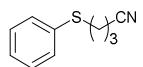
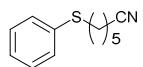
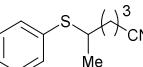
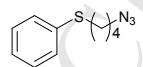
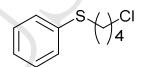
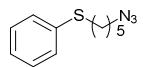
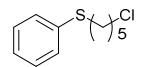
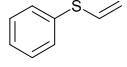


Silylated reagents such as trimethylsilyl cyanide, Ruppert–Prakash reagent and trimethylsilyl azide are important nucleophiles in organic synthesis. We subsequently explored the multicomponent reaction of benzenes, cyclic thioethers and different silylated nucleophiles. When trimethylsilyl cyanide (**5a**) was used as a nucleophile and the reaction was conducted in THF, the desired thioether **6a** was obtained in 89% yield (Table 3, entry 1). Electron-donating groups substituted benzenes gave higher yield than those bearing electron withdrawing substituents (Table 3, entries 2-5). Unsymmetrical benzenes underwent the reaction efficiently to deliver the corresponding cyanated products as an inseparable mixture of two regioisomers (Table 3, entries 6-9). Once again, **1i** provided the desired product with complete regioselectivity (Table 3, entry 10). Both thietane and thiane reacted very well, giving the corresponding products **6k** and **6l** in 90% and 88% yields, respectively (Table 3, entries 11 and 12). α -Methyl tetrahydrothiophene underwent the reaction smoothly to afford **6m** in 72% yield and no β -elimination product was formed (Table 3, entry 13). Trimethylsilyl azide and trimethylsilyl chloride were also proved to be suitable reactants for the reaction, producing the corresponding functionalized thioethers in high yields (Table 3, entries 14-17). However, other silylated reagents, such as the Ruppert–Prakash reagent and (difluoromethyl)trimethylsilane didn't afford the desired product under the same reaction conditions (Table 3, entries 18 and 19). Interestingly, thiirane underwent a β -elimination reaction to give vinyl thioether **4a** in good 66%

yield under the same reaction conditions (Table 3, entry 20).

Table 3 Reaction of benzynes, cyclic thioethers and silylated reagents ^a

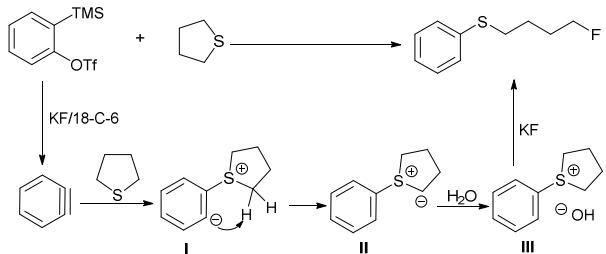
Entry	1	2	5	Time (h)	Product	Yield (%) ^b
					TMS-CN	
1	1a	2a	5a	6		89
2	1b	2a	5a	7		94
3	1c	2a	5a	8		86
4		2a	5a	7		64
5	1d	2a	5a	24		49
6	1e	2a	5a	8		82
					<i>m</i> - 6f : <i>o</i> - 6f' = 1.7:1 ^c	
7	1f	2a	5a	7		80
					<i>m</i> - 6g : <i>p</i> - 6g' = 1:1 ^c	
8	1g	2a	5a	6		70
					<i>p</i> - 6h : <i>m</i> - 6h' = 1.5:1 ^c	
9	1h	2a	5a	7		76
					<i>α</i> - 6i : <i>β</i> - 6i' = 1:1 ^c	
10	1i	2a	5a	7		84

					6j	
11	1a	2b	5a	7		90
					k	
12	1a	2c	5a	24		88
					6l	
13	1a	2e	5a	7		72
					6m	
14	1a	2a	5b	7		84
					6n	
15	1a	2a	5c	24		89
					6o	
16	1a	2c	5b	24		65
					6p	
17 ^d	1a	2c	5c	12		86
					6q	
18	1a	2a	5d	24	/	/
19	1a	2a	5e	24	/	/
20	1a	2d	5a	7		66
					4a	

^a Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **5a** (0.3 mmol), solvent 2 mL; ^b Isolated yield; ^c the regioselectivity was determined by ¹⁹F NMR analysis of the crude products; ^d The reaction was conducted in refluxing THF.

Based on the pioneering work of Tan, Xu^{10a} and Hoye,^{10b} a plausible mechanism was proposed and depicted in Scheme 1. Tetrahydrothiophene undergoes nucleophilic addition with benzyne to form zwitterion species **I**, and after 1,4-proton shift, to form

the unstable cyclic sulfonium ylide **II**. The intermediate **II** gets a proton from water to give species **III**, and after the following nucleophilic attack of the fluorine anion, to produce the final product.



Scheme 2 Proposed Mechanism

Conclusions

In summary, a multicomponent reaction of benzenes, cyclic thioethers and non-proton containing nucleophiles has been described. The transition-metal free conditions, simple procedure and divergent nucleophiles provide a new methodology for the synthesis of functionalized thioethers.

Experimental Section

General experimental Methods

Unless otherwise indicated, all reactions were conducted under nitrogen atmosphere in oven-dried glassware with magnetic stirring bar. ¹H NMR (400 MHz, CDCl₃), ¹³C NMR (100 MHz, CDCl₃) and ¹⁹F NMR (376 MHz, CDCl₃) spectra were recorded on a Bruker-DMX 400 spectrometer in CDCl₃, with tetramethylsilane as an internal standard and reported in ppm (δ). Benzyne precursors, cyclic thioethers and silylated reagents are obtained from commercial supplies and used without purification. Anhydrous THF, toluene, DCM, CH₃CN were distilled from sodium or calcium hydride. Petroleum ether (PE), where used, has a boiling point range of 60–90 °C.

General experimental Methods

General procedure for synthesis the functionalized thioethers (3a-3n)

To a suspension of KF (35 mg, 0.6 mmol), 18-crown-6 (158 mg, 0.6 mmol) in

anhydrous DCM (2.0 mL) was added H₂O (7.2 µL, 0.4 mmol), cyclic thioether **2** (0.3 mmol) and benzyne precursor **1** (0.2 mmol). The mixture was stirred at room temperature until full consumption of the aryne precursor as indicated by TLC. The solvent was then removed under reduced pressure and the crude material was purified by column chromatography (PE) to afford the desired product.

(4-fluorobutyl)(phenyl)sulfane(3a): Colorless oil; 28 mg, Yield: 76 %, ¹H NMR (400 MHz, CDCl₃) δ 7.30 – 7.24 (m, 2H), 7.24 – 7.17 (m, 2H), 7.14 – 7.05 (m, 1H), 4.44 (t, *J* = 5.8 Hz, 1H), 4.32 (t, *J* = 5.7 Hz, 1H), 2.89 (t, *J* = 7.1 Hz, 2H), 1.91 – 1.56 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 136.4, 129.4, 129.0, 126.1, 83.6 (d, *J* = 165.2 Hz), 33.4, 29.5 (d, *J* = 19.9 Hz), 25.1 (d, *J* = 4.8 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ -218.50; FTIR (film) 3431, 2971, 2925, 1633, 1480, 1438, 1384, 1088, 1047, 1025, 737 cm⁻¹; HRMS (ESI) m/z calcd for C₁₀H₁₄FS⁺ [M+H]⁺ 185.0795, found 185.0799.

(3,4-dimethylphenyl)(4-fluorobutyl)sulfane(3b): Colorless oil; 26.7 mg, Yield: 63 %, ¹H NMR (400 MHz, CDCl₃) δ 7.14 (s, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 4.50 (t, *J* = 5.9 Hz, 1H), 4.38 (t, *J* = 5.7 Hz, 1H), 2.91 (t, *J* = 7.0 Hz, 2H), 2.23 (s, 3H), 2.22 (s, 3H), 1.91 – 1.68 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 137.3, 135.0, 132.6, 131.4, 130.2, 127.6, 83.6 (d, *J* = 165.0 Hz), 34.1, 29.4 (d, *J* = 19.6 Hz), 25.1 (d, *J* = 4.8 Hz), 19.7, 19.3. ¹⁹F NMR (376 MHz, CDCl₃) δ -218.55; FTIR (film) 3441, 3012, 2961, 2857, 2360, 1597, 1457, 1384, 1187, 1040, 810 cm⁻¹; HRMS (ESI) m/z calcd for C₁₂H₁₈FS⁺ [M+H]⁺ 213.1108, found 213.1107.

(3,4-dimethoxyphenyl)(4-fluorobutyl)sulfane(3c): Colorless oil; 27.3mg, Yield: 56 %, ¹H NMR (400 MHz, CDCl₃) δ 6.98 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.94 (d, *J* = 2.1 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 4.51 (t, *J* = 5.9 Hz, 1H), 4.39 (t, *J* = 5.7 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 2.88 (t, *J* = 7.0 Hz, 2H), 1.93 – 1.64 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 149.1, 148.5, 126.7, 124.2, 115.0, 111.6, 83.6 (d, *J* = 165.1 Hz), 55.9, 35.4, 29.3 (d, *J* = 19.8 Hz), 25.2 (d, *J* = 4.7

Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.57; FTIR (film) 3442, 2959, 2838, 2360, 1639, 1584, 1505, 1252, 1137, 1026, 804 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{18}\text{FO}_2\text{S}^+ [\text{M}+\text{H}]^+$ 245.1006, found 245.1005.

(3,4-difluorophenyl)(4-fluorobutyl)sulfane(3d): Colorless oil; 25 mg, Yield: 57 %, ^1H NMR (400 MHz, CDCl_3) δ 7.21 – 7.11 (m, 1H), 7.12 – 7.02 (m, 2H), 4.52 (t, $J = 5.7$ Hz, 1H), 4.40 (t, $J = 5.5$ Hz, 1H), 2.93 (t, $J = 7.0$ Hz, 2H), 1.94 – 1.66 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 150.9 (dd, $J = 118.7, 12.9$ Hz), 148.5 (dd, $J = 116.0, 12.9$ Hz), 132.7 (dd, $J = 5.9, 4.0$ Hz), 125.9 (dd, $J = 6.1, 3.6$ Hz), 118.7 (d, $J = 18.3$ Hz), 117.7 (d, $J = 17.6$ Hz), 83.5 (d, $J = 165.2$ Hz), 34.2, 29.3 (d, $J = 19.8$ Hz), 24.9 (d, $J = 4.5$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -136.59, -140.52, -218.80; FTIR (film) 3450, 2964, 2871, 1598, 1504, 1406, 1273, 1200, 905, 811 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{10}\text{H}_{12}\text{F}_3\text{S}^+ [\text{M}+\text{H}]^+$ 221.0606, found 221.0612.

(4-fluorobutyl)(m-tolyl)sulfane(3e) and (4-fluorobutyl)(o-tolyl)sulfane(3e') A mixture of inseparable regioisomers in 2:1 ratio; Colorless oil; 30.5 mg, Yield: 77 %, ^1H NMR (400 MHz, CDCl_3) of 3e: δ 7.25 (d, $J = 8.0$ Hz, 1H), 7.19 – 7.13 (m, 3H), 4.52 (t, $J = 6.0$ Hz, 1H), 4.40 (t, $J = 5.8$ Hz, 1H), 2.94 (t, $J = 5.6$ Hz, 2H), 2.37 (s, 3H), 1.82 – 1.71 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 137.6, 135.7, 130.1, 127.9, 126.4, 125.6, 83.6 (d, $J = 165.1$ Hz), 32.5, 29.6 (d, $J = 19.8$ Hz), 24.9 (d, $J = 4.8$ Hz), 20.4. ^{19}F NMR (376 MHz, CDCl_3) δ -218.61. ^1H NMR (400 MHz, CDCl_3) of 3e': δ 7.13 – 7.11 (m, 1H), 7.10 – 7.06 (m, 2H), 6.99 (d, $J = 4.0$ Hz, 1H), 4.51 (t, $J = 6.0$ Hz, 1H), 4.39 (t, $J = 7.0$ Hz, 1H), 2.95 (t, $J = 8.0$ Hz, 2H), 2.32 (s, 3H), 1.92 – 1.82 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 138.7, 136.1, 129.9, 128.8, 126.9, 126.2, 83.6 (d, $J = 165.3$ Hz), 33.3, 29.4 (d, $J = 13.8$ Hz), 25.1 (d, $J = 4.8$ Hz), 21.4. ^{19}F NMR (376 MHz, CDCl_3) δ -218.60; FTIR (film) 3439, 2965, 2923, 2358, 1635, 1471, 1384, 1066, 1047, 881, 744 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{11}\text{H}_{16}\text{FS}^+ [\text{M}+\text{H}]^+$ 199.0951, found 199.0959.

(4-fluorobutyl)(3-methoxyphenyl)sulfane(3f) and (4-fluorobutyl)(4-methoxyphenyl)sulfane(3f') A mixture of inseparable

regioisomers in 1.1:1 ratio: Colorless oil; 29 mg, Yield: 69 %. ^1H NMR (400 MHz, CDCl_3) of 3f: δ 7.19 (t, $J = 8.0$ Hz, 1H), 6.92 – 6.89 (m, 1H), 6.88 – 6.87 (m, 1H), 6.73 – 6.70 (m, 1H), 4.49 (t, $J = 6.0$ Hz, 1H), 4.37 (t, $J = 5.8$ Hz, 1H), 3.79 (s, 3H), 2.85 (t, $J = 8.0$ Hz, 2H), 1.79 – 1.66 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.9, 137.8, 129.7, 126.3, 121.2, 114.5, 83.6 (d, $J = 165.0$ Hz), 55.3, 35.5, 29.3 (d, $J = 19.8$ Hz), 25.2 (d, $J = 4.8$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.52. ^1H NMR (400 MHz, CDCl_3) of 3f': δ 7.36 – 7.32 (m, 2H), 6.86 – 6.82 (m, 2H), 4.51 (t, $J = 6.0$ Hz, 1H), 4.40 (t, $J = 5.8$ Hz, 1H), 3.79 (s, 3H), 2.96 (t, $J = 6.0$ Hz, 2H), 1.91 – 1.79 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 159.9, 133.3, 114.6, 111.6, 83.6 (d, $J = 165.1$ Hz), 55.3, 33.1, 29.5 (d, $J = 19.8$ Hz), 25.0 (d, $J = 4.7$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.63; FTIR (film) 3442, 2960, 2360, 1636, 1493, 1384, 1244, 1171, 913, 743 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{11}\text{H}_{16}\text{FOS}^+ [\text{M}+\text{H}]^+$ 215.0900, found 215.0900.

(3-chlorophenyl)(4-fluorobutyl)sulfane(3g) and
(4-chlorophenyl)(4-fluorobutyl)sulfane(3g') A mixture of inseparable regioisomers in 1:1.4 ratio: Colorless oil; 26 mg, Yield: 60 %. ^1H NMR (400 MHz, CDCl_3) of 3g: δ 7.30 – 7.27 (m, 1H), 7.22 – 7.16 (m, 2H), 7.15 – 7.11 (m, 1H), 4.52 (t, $J = 6.0$ Hz, 1H), 4.41 (t, $J = 5.8$ Hz, 1H), 2.97 (t, $J = 7.0$ Hz, 2H), 1.91 – 1.80 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 134.7, 132.0, 129.9, 128.3, 126.8, 125.9, 83.5 (d, $J = 165.3$ Hz), 32.9, 29.4 (d, $J = 19.9$ Hz), 24.9 (d, $J = 4.6$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.76. ^1H NMR (400 MHz, CDCl_3) of 3g': δ 7.27 – 7.22 (m, 4H), 4.51 (t, $J = 4.0$ Hz, 1H), 4.39 (t, $J = 5.8$ Hz, 1H), 2.94 (t, $J = 8.0$ Hz, 2H), 1.80 – 1.72 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 138.7, 134.9, 130.6, 129.0, 83.5 (d, $J = 165.3$ Hz), 33.6, 29.4 (d, $J = 19.9$ Hz), 24.9 (d, $J = 4.7$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.73; FTIR (film) 3441, 2961, 2853, 2359, 2341, 1636, 1476, 1384, 1095, 1010, 811 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{10}\text{H}_{13}\text{ClFS}^+ [\text{M}+\text{H}]^+$ 219.0405, found 219.0407.

(4-fluorobutyl)(naphthalen-1-yl)sulfane(3h) and
(4-fluorobutyl)(naphthalen-2-yl)sulfane(3h') A mixture of inseparable

regioisomers in 1:1.25 ratio: Colorless oil; 35.5 mg, Yield: 76 %. ^1H NMR (400 MHz, CDCl_3) of 3h: δ 7.57 – 7.54 (m, 2H), 7.53 – 7.51 (m, 1H), 7.44 – 7.37 (m, 4H), 4.50 (t, J = 6.0 Hz, 1H), 4.38 (t, J = 5.8 Hz, 1H), 3.05 (t, J = 8.0 Hz, 2H), 1.92 – 1.82 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 133.9, 133.8, 133.5, 133.1, 128.4, 127.4, 126.9, 126.6, 126.3, 125.7, 83.6 (d, J = 165.1 Hz), 33.2, 29.5 (d, J = 19.8 Hz), 25.1 (d, J = 5.0 Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.54. ^1H NMR (400 MHz, CDCl_3) of 3h': δ 8.40 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.78 – 7.76 (m, 1H), 7.73 – 7.71 (m, 3H), 7.50 – 7.45 (m, 1H), 4.48 (t, J = 6.0 Hz, 1H), 4.36 (t, J = 5.8 Hz, 1H), 3.00 (t, J = 8.0 Hz, 2H), 1.82 – 1.72 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 134.0, 131.8, 128.6, 128.2, 127.7, 127.3, 127.1, 126.4, 125.6, 125.1, 83.6 (d, J = 165.1 Hz), 33.9, 29.5 (d, J = 19.8 Hz), 25.1 (d, J = 5.0 Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.50; FTIR (film) 3441, 3054, 2961, 2867, 1926, 1589, 1501, 1384, 1268, 1038, 813, 790 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{16}\text{FS}^+ [\text{M}+\text{H}]^+$ 235.0951, found 235.0953.

(4-fluorobutyl)(3-methoxyphenyl)sulfane(3i): Colorless oil; 33.4 mg, Yield: 78 %, ^1H NMR (400 MHz, CDCl_3) δ 7.20 (t, J = 8.0 Hz, 1H), 6.95 – 6.89 (m, 1H), 6.87 (t, J = 2.1 Hz, 1H), 6.76 – 6.69 (m, 1H), 4.52 (t, J = 5.8 Hz, 1H), 4.40 (t, J = 5.6 Hz, 1H), 3.80 (s, 3H), 2.97 (t, J = 7.0 Hz, 2H), 1.98 – 1.69 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 159.9, 137.7, 129.7, 121.2, 114.5, 111.6, 83.6 (d, J = 165.1 Hz), 55.3, 33.1, 29.4 (d, J = 19.8 Hz), 25.0 (d, J = 4.8 Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -218.66; FTIR (film) 3452, 2960, 1590, 1575, 1479, 1283, 1248, 1041, 862, 771 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{11}\text{H}_{16}\text{FOS}^+ [\text{M}+\text{H}]^+$ 215.0900, found 215.0904.

(3-fluoropropyl)(phenyl)sulfane(3j): Colorless oil; 25 mg, Yield: 74 %, ^1H NMR (400 MHz, CDCl_3) δ 7.37 – 7.32 (m, 2H), 7.32 – 7.24 (m, 2H), 7.22 – 7.14 (m, 1H), 4.61 (t, J = 5.7 Hz, 1H), 4.49 (t, J = 5.7 Hz, 1H), 3.04 (t, J = 7.2 Hz, 2H), 2.09 – 1.91 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 135.9, 129.4, 129.0, 126.2, 82.2 (d, J = 165.6 Hz), 30.1 (d, J = 20.2 Hz), 29.4 (d, J = 4.7 Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -221.05; FTIR (film) 3432, 2969, 2923, 1630,

1584, 1480, 1438, 1384, 1050, 1021, 738 cm⁻¹; HRMS (ESI) m/z calcd for C₉H₁₂FS⁺ [M+H]⁺ 171.0638, found 171.0630.

(5-fluoropentyl)(phenyl)sulfane (3k): Colorless oil; 11 mg, Yield: 28 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.30 (m, 2H), 7.31 – 7.25 (m, 2H), 7.21 – 7.13 (m, 1H), 4.49 (t, J = 6.0 Hz, 1H), 4.37 (t, J = 6.0 Hz, 1H), 2.93(t, J = 8.0 Hz, 2H), 1.79 – 1.63 (m, 4H), 1.60 – 1.50 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 136.7, 129.1, 128.9, 125.8, 83.9 (d, J = 164.7 Hz), 33.5, 29.9 (d, J = 19.7 Hz), 28.8, 24.5 (d, J = 5.3 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ -218.41; FTIR (film) 3431, 2969, 2926, 2359, 2342, 1633, 1480, 1384, 1045, 879, 740 cm⁻¹; HRMS (ESI) m/z calcd for C₁₁H₁₆FS⁺ [M+H]⁺ 199.0951, found 199.0950.

(4-chlorobutyl)(phenyl)sulfane(3l)¹⁵: Colorless oil; 36 mg, Yield: 90 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.29 (m, 2H), 7.33 – 7.22 (m, 2H), 7.22 – 7.11 (m, 1H), 3.53 (t, J = 6.5 Hz, 2H), 2.94 (t, J = 7.1 Hz, 2H), 1.98 – 1.85 (m, 2H), 1.86 – 1.71 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 136.3, 129.3, 128.9, 126.1, 44.5, 33.0, 31.4, 26.4.

(4-bromobutyl)(phenyl)sulfane(3m)¹⁶: Colorless oil; 28 mg, Yield: 58 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.31 (m, 2H), 7.31 – 7.24 (m, 2H), 7.22 – 7.13 (m, 1H), 3.40 (t, J = 6.6 Hz, 2H), 2.94 (t, J = 7.1 Hz, 2H), 2.07 – 1.94 (m, 2H), 1.89 – 1.73 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 136.3, 129.3, 128.9, 126.1, 33.1, 32.9, 31.6, 27.6.

phenyl(4-thiocyanatobutyl)sulfane(3n): Colorless oil; 20.4 mg, Yield: 61 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.32 (m, 2H), 7.32 – 7.25 (m, 2H), 7.23 – 7.15 (m, 1H), 2.99 – 2.90 (m, 4H), 2.05 – 1.90 (m, 2H), 1.85 – 1.73 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 135.8, 129.6, 129.0, 126.3, 112.1, 33.6, 33.1, 28.8, 27.3; FTIR (film) 3436, 2930, 2858, 2359, 2341, 2151, 1630, 1437, 1280, 1024, 907 cm⁻¹; HRMS (ESI) m/z calcd for C₁₁H₁₄NS₂⁺ [M+H]⁺ 224.0562, found 224.0564.

phenyl(vinyl)sulfane(4a)¹⁷: Colorless oil; 20.4 mg, Yield: 75 %, ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.34 (m, 2H), 7.37 – 7.27 (m, 2H), 7.30 – 7.20 (m, 1H),

6.54 (dd, $J = 16.6, 9.6$ Hz, 1H), 5.36 (d, $J = 1.7$ Hz, 1H), 5.33 (d, $J = 8.7$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 134.3, 131.9, 130.5, 129.1, 127.1, 115.5.

(E)-pent-3-en-1-yl(phenyl)sulfane(4b**)** **and**

pent-4-en-1-yl(phenyl)sulfane(4c**)¹⁸** A mixture of inseparable regioisomers in 5:1 ratio: Colorless oil; 25.6 mg, Yield: 72 %. ^1H NMR (400 MHz, CDCl_3) of 4b: δ 7.35 – 7.23 (m, 5H), 5.55 – 5.42 (m, 2H), 2.93 (t, $J = 5.8$ Hz, 2H), 2.34 – 2.29 (m, 2H), 1.65 (d, $J = 4.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 136.7, 129.1, 128.9, 128.8, 126.9, 125.8, 33.6, 32.3, 17.9. ^1H NMR (400 MHz, CDCl_3) of 4c: δ 7.18 – 7.14 (m, 5H), 5.83 – 5.73 (m, 1H), 5.06 – 4.97 (m, 2H), 2.92 – 2.90 (m, 2H), 2.22 – 2.16 (m, 2H), 1.78 – 1.70 (m, 2H), ^{13}C NMR (100 MHz, CDCl_3) δ 137.6, 131.1, 129.2, 129.1, 127.0, 115.4, 32.9, 32.7, 28.3.

General procedure for synthesis the functionalized thioethers (6a-6q**)**

To a solution of KF (35 mg, 0.6 mmol), 18-crown-6 (158 mg, 0.6 mmol) in anhydrous THF (2.0 mL) was added H_2O (7.2 μL , 0.4 mmol), benzyne precursor **1** (0.2 mmol), cyclic thioether **2** (4 mmol) and silylated reagent **5** (0.3 mmol). The mixture was stirred at room temperature until full consumption of the benzyne precursor as indicated by TLC. The solvent was then removed under reduced pressure and the crude material was purified by column chromatography (Al_2O_3) to afford the desired product.

5-(phenylthio)pentanenitrile(6a**)¹⁹:** Colorless oil; 33.9 mg, Yield: 89 %, ^1H NMR (400 MHz, CDCl_3) δ 7.38 – 7.31 (m, 2H), 7.31 – 7.24 (m, 2H), 7.23 – 7.16 (m, 1H), 2.94 (t, $J = 6.7$ Hz, 2H), 2.34 (t, $J = 6.9$ Hz, 2H), 1.91 – 1.70 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 135.9, 129.6, 129.0, 126.3, 119.4, 32.9, 27.9, 24.3, 16.8.

5-((3,4-dimethylphenyl)thio)pentanenitrile(6b**):** Colorless oil; 41.6 mg, Yield: 94 %, ^1H NMR (400 MHz, CDCl_3) δ 7.14 (s, 1H), 7.09 (dd, $J = 7.8, 2.0$ Hz, 1H), 7.05 (d, $J = 7.8$ Hz, 1H), 2.89 (t, $J = 6.7$ Hz, 2H), 2.33 (t, $J = 6.8$ Hz, 2H), 2.23 (s, 3H), 2.22 (s, 3H), 1.88 – 1.65 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 137.5, 135.3, 132.1, 131.7, 130.3, 127.9, 119.4, 33.6, 28.1, 24.3, 19.8, 19.4,

16.8; FTIR (film) 3425, 2972, 2925, 2359, 2246, 1635, 1456, 1384, 1264, 1049, 882 cm⁻¹; HRMS (ESI) m/z calcd for C₁₃H₁₈NS⁺ [M+H]⁺ 220.1155, found 220.1154.

5-((3,4-dimethoxyphenyl)thio)pentanenitrile(6c): Colorless oil; 43 mg, Yield: 86 %, ¹H NMR (400 MHz, CDCl₃) δ 6.98 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.94 (d, *J* = 2.1 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 2.86 (t, *J* = 6.6 Hz, 2H), 2.35 (t, *J* = 6.7 Hz, 2H), 1.88 – 1.64 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 149.1, 148.7, 126.2, 124.5, 119.4, 115.2, 111.7, 56.0, 55.9, 34.9, 28.1, 24.2, 16.8; FTIR (film) 3440, 2936, 2837, 2245, 1583, 1504, 1463, 1395, 1252, 1178, 853 cm⁻¹; HRMS (ESI) m/z calcd for C₁₃H₁₇NO₂S⁺ [M+H]⁺ 251.0975, found 251.0975.

5-(naphthalen-2-ylthio)pentanenitrile(6d)²⁰: Colorless oil; 31 mg, Yield: 64 %, ¹H NMR (400 MHz, CDCl₃) δ 7.82 – 7.70 (m, 4H), 7.54 – 7.34 (m, 3H), 3.03 (t, *J* = 6.7 Hz, 2H), 2.33 (t, *J* = 6.8 Hz, 2H), 1.89 – 1.74 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 133.8, 133.3, 131.9, 128.6, 127.8, 127.5, 127.4, 127.1, 126.7, 125.8, 119.4, 32.8, 27.9, 24.3, 16.8.

5-((3,4-difluorophenyl)thio)pentanenitrile(6e): Colorless oil; 22 mg, Yield: 49 %, ¹H NMR (400 MHz, CDCl₃) δ 7.21 – 7.13 (m, 1H), 7.13 – 7.04 (m, 2H), 2.92 (t, *J* = 6.6 Hz, 2H), 2.37 (t, *J* = 6.7 Hz, 2H), 1.87 – 1.73 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 151.1 (dd, *J* = 100.6, 12.9 Hz), 148.6 (dd, *J* = 98.2, 13.0 Hz), 132.3 – 131.9 (m), 126.3 (dd, *J* = 6.1, 3.7 Hz), 119.2 (d, *J* = 6.3 Hz), 118.9, 117.8 (d, *J* = 17.6 Hz), 33.8, 27.9, 24.2, 16.8; FTIR (film) 3431, 2974, 2927, 2359, 2245, 1635, 1500, 1384, 1269, 1049, 771 cm⁻¹; HRMS (ESI) m/z calcd for C₁₁H₁₂F₂NS⁺ [M+H]⁺ 228.0653, found 228.0657.

5-(m-tolylthio)pentanenitrile(6f) and 5-(o-tolylthio)pentanenitrile(6f') A mixture of inseparable regioisomers in 1.7:1 ratio: Colorless oil; 33.6 mg, Yield: 82 %. ¹H NMR (400 MHz, CDCl₃) of 6f: δ 7.20 – 7.13 (m, 4H), 2.91 (t, *J* = 5.8 Hz, 2H), 2.37 (s, 3H), 2.36 – 2.33 (m, 2H), 1.85 – 1.80 (m, 4H), ¹³C NMR (100 MHz, CDCl₃) δ 137.8, 135.2, 130.3, 128.2, 126.5, 125.9, 119.4, 32.1, 28.0, 24.5,

20.4, 16.9. ^1H NMR (400 MHz, CDCl_3) of 6f': δ 7.28 – 7.25 (m, 1H), 7.12 – 6.97 (m, 3H), 2.93 (t, $J = 5.8$ Hz, 2H), 2.36 – 2.33 (m, 2H), 2.32 (s, 3H), 1.80 – 1.74 (m, 4H), ^{13}C NMR (100 MHz, CDCl_3) δ 138.8, 135.6, 130.2, 128.9, 127.2, 126.5, 119.4, 32.9, 28.0, 24.3, 21.4, 16.8; FTIR (film) 3431, 2973, 2926, 2359, 2341, 1634, 1456, 1384, 1049, 880, 742 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{16}\text{NS}^+ [\text{M}+\text{H}]^+$ 206.0998, found 206.0996.

5-((3-methoxyphenyl)thio)pentanenitrile(6g) and

5-((4-methoxyphenyl)thio)pentanenitrile (6g') A mixture of inseparable regioisomers in 1:1 ratio: Colorless oil; 35 mg, Yield: 80 %. ^1H NMR (400 MHz, CDCl_3) of 6g: δ 7.20 (t, $J = 8.0$ Hz, 1H), 6.91 – 6.89 (m, 1H), 6.87 – 6.86 (m, 1H), 6.75 – 6.72 (m, 1H), 3.79 (s, 3H), 2.95 (t, $J = 6.0$ Hz, 2H), 2.35 (t, $J = 8.0$ Hz, 2H), 1.84 – 1.78 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 159.9, 137.2, 129.8, 125.8, 121.4, 119.3, 114.8, 55.3, 35.1, 27.9, 24.3, 16.8. ^1H NMR (400 MHz, CDCl_3) of 6g': δ 7.36 – 7.32 (m, 2H), 6.86 – 6.83 (m, 2H), 3.79 (s, 3H), 2.83 (t, $J = 8.0$ Hz, 2H), 2.33 (t, $J = 8.0$ Hz, 2H), 1.78 – 1.67 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 159.1, 133.6, 119.4, 114.7, 111.8, 55.4, 32.7, 28.1, 24.1, 16.8; FTIR (film) 3431, 2973, 2925, 2359, 2341, 1635, 1456, 1384, 1239, 1049, 880 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{16}\text{NOS}^+ [\text{M}+\text{H}]^+$ 222.0947, found 222.0944.

5-((4-chlorophenyl)thio)pentanenitrile(6h) and

5-((3-chlorophenyl)thio)pentanenitrile (6h') A mixture of inseparable regioisomers in 1.5:1 ratio: Colorless oil; 31.6 mg, Yield: 70 %. ^1H NMR (400 MHz, CDCl_3) of 6h: δ 7.26 – 7.23 (m, 4H), 2.92 (t, $J = 6.0$ Hz, 2H), 2.36 (t, $J = 6.0$ Hz, 2H), 1.81 – 1.79 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 134.4, 130.9, 130.0, 129.2, 126.3, 33.2, 27.9, 24.2, 16.8. ^1H NMR (400 MHz, CDCl_3) of 6h': δ 7.29 (s, 1H), 7.22 – 7.14 (m, 3H), 2.96 (t, $J = 6.0$ Hz, 2H), 2.37 (t, $J = 6.0$ Hz, 2H), 1.79 – 1.73 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 138.2, 134.8, 132.3, 129.2, 128.6, 127.1, 119.3, 32.6, 27.8, 24.3, 16.8; FTIR (film) 3432, 2973,

2926, 2360, 2342, 1635, 1384, 1071, 1051, 903, 720 cm⁻¹; HRMS (ESI) m/z calcd for C₁₁H₁₃ClNS⁺ [M+H]⁺ 226.0452, found 226.0450.

5-(naphthalen-1-ylthio)pentanenitrile(6i)²⁰ and

5-(naphthalen-2-ylthio)pentanenitrile(6i') A mixture of inseparable regioisomers in 1:1 ratio: Colorless oil; 36.2 mg, Yield: 76 %. ¹H NMR (400 MHz, CDCl₃) of 6i: δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.75 – 7.73 (m, 4H), 7.58 – 7.56 (m, 2H), 3.02 (t, *J* = 6.0 Hz, 2H), 2.32 (t, *J* = 5.8 Hz, 2H), 1.85 – 1.80 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 134.0, 133.4, 132.9, 128.6, 127.7, 127.4, 126.7, 126.3, 125.6, 125.0, 119.4, 33.5, 28.1, 24.4, 16.8. ¹H NMR (400 MHz, CDCl₃) of 6i': δ 8.39 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.54 – 7.38 (m, 5H), 2.97 (t, *J* = 6.0 Hz, 2H), 2.30 (t, *J* = 5.8 Hz, 2H), 1.80 – 1.71 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 133.8, 133.1, 131.9, 128.8, 128.7, 127.8, 127.5, 127.1, 126.6, 125.8, 119.4, 32.8, 27.9, 24.3, 16.8.

5-((3-methoxyphenyl)thio)pentanenitrile(6j): Colorless oil; 37 mg, Yield: 84 %, ¹H NMR (400 MHz, CDCl₃) δ 7.20 (t, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 7.7 Hz, 1H), 6.87 (t, *J* = 2.1 Hz, 1H), 6.73 (dd, *J* = 8.6, 2.7 Hz, 1H), 3.79 (s, 3H), 2.95 (t, *J* = 6.0 Hz, 2H), 2.35 (t, *J* = 8.0 Hz, 2H), 1.87 – 1.73 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 159.9, 137.2, 129.8, 121.4, 119.4, 114.8, 111.8, 55.3, 32.7, 27.9, 24.3, 16.8; FTIR (film) 3425, 2972, 2926, 2359, 2339, 1657, 1630, 1384, 1245, 1047, 880; HRMS (ESI) m/z calcd for C₁₂H₁₆NOS⁺ [M+H]⁺ 222.0947, found 222.0948.

4-(phenylthio)butanenitrile(6k)²⁰: Colorless oil; 32.1 mg, Yield: 90 %, ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.33 (m, 2H), 7.33 – 7.27 (m, 2H), 7.25 – 7.18 (m, 1H), 3.02 (t, *J* = 6.9 Hz, 2H), 2.50 (t, *J* = 7.1 Hz, 2H), 1.98 – 1.91 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 134.8, 130.1, 129.2, 126.8, 119.1, 32.6, 24.9, 15.9.

6-(phenylthio)hexanenitrile(6l):²¹ Colorless oil; 36.3 mg, Yield: 88 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.24 (m, 4H), 7.22 – 7.14 (m, 1H), 2.92 (t, *J* = 7.0 Hz, 2H), 2.32 (t, *J* = 6.9 Hz, 2H), 1.75 – 1.52 (m, 6H). ¹³C NMR (100

MHz, CDCl₃) δ 136.3, 129.2, 128.9, 126.0, 119.6, 33.3, 28.3, 27.7, 25.0, 17.1.

5-(phenylthio)hexanenitrile(6m): Colorless oil; 29.6 mg, Yield: 72 %, ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.36 (m, 2H), 7.36 – 7.25 (m, 2H), 7.30 – 7.20 (m, 1H), 3.20 (m, 1H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.93 – 1.79 (m, 2H), 1.75 – 1.64 (m, 2H), 1.30 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 134.4, 132.5, 128.9, 127.2, 119.4, 42.8, 35.5, 22.9, 21.3, 17.1; FTIR (film) 3441, 2960, 2924, 2359, 2244, 1635, 1437, 1383, 1246, 1052, 743 cm⁻¹; HRMS (ESI) m/z calcd for C₁₂H₁₆NS⁺ [M+H]⁺ 206.0998, found 206.0996.

(4-azidobutyl)(phenyl)sulfane(6n)²²: Colorless oil; 34.8 mg, Yield: 84 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.31 (m, 2H), 7.31 – 7.23 (m, 2H), 7.22 – 7.12 (m, 1H), 3.27 (t, *J* = 6.3 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H), 1.82 – 1.64 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 136.3, 129.3, 128.9, 126.1, 50.9, 33.3, 27.9, 26.3.

(4-chlorobutyl)(phenyl)sulfane(6o)¹⁵: Colorless oil; 36 mg, Yield: 89 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.31 (m, 2H), 7.31 – 7.23 (m, 2H), 7.22 – 7.13 (m, 1H), 3.54 (t, *J* = 6.4 Hz, 2H), 2.94 (t, *J* = 7.1 Hz, 2H), 2.01 – 1.87 (m, 2H), 1.86 – 1.74 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 136.3, 129.3, 128.9, 126.1, 44.4, 33.0, 31.4, 26.4.

(5-azidopentyl)(phenyl)sulfane(6p): Colorless oil; 28.2 mg, Yield: 65 %, ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.22 (m, 4H), 7.22 – 7.11 (m, 1H), 3.25 (t, *J* = 6.7 Hz, 2H), 2.92 (t, *J* = 7.2 Hz, 2H), 1.73 – 1.56 (m, 4H), 1.56 – 1.46 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 136.6, 129.1, 128.9, 125.9, 51.3, 33.5, 28.7, 28.5, 25.9; FTIR (film) 3430, 2972, 2931, 2095, 1630, 1480, 1438, 1384, 1288, 1050, 913 cm⁻¹; GC-MS (EI) m/z calcd for C₁₁H₁₅N₃S⁺ [M]⁺ 221.09, found 221.1

(5-chloropentyl)(phenyl)sulfane(6q)¹⁵: Colorless oil; 37.4 mg, Yield: 86 %, ¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.28 (m, 2H), 7.32 – 7.22 (m, 2H), 7.22 – 7.10 (m, 1H), 3.51 (t, *J* = 6.6 Hz, 2H), 2.92 (t, *J* = 7.1 Hz, 2H), 1.81 – 1.74 (m, 2H), 1.75 – 1.60 (m, 2H), 1.64 – 1.51 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ

136.6, 129.1, 128.9, 125.9, 44.8, 33.5, 32.1, 28.5, 26.1.

Conflicts of interest

There are no conflicts to declare.

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