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Efficient C(sp^3_{alkyl})–SCF_3 bond formations *via* copper-mediated trifluoromethylthiolation of alkyl halides†

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A general and convenient copper-mediated trifluoromethylthiolation of primary and secondary alkyl halides was described. Variation of the solvent, additives and time allowed optimization of the reaction. A wide range of alkyl halides were explored to give a set of alkyl trifluoromethyl thioethers in moderate to excellent yields. A variety of functional groups, including ethers, thioether, esters, nitriles, amides, and ketal groups, were well tolerated in the electrophilic partner.

Introduction

Over the past several decades, organic molecules that contain a trifluoromethylthio group (–SCF_3) have been an important class of compounds, due to their remarkable stability, electronegativity, and lipophilicity properties.[1,2] These have found potential applications in a variety of areas, including pharmaceutical and agrochemical, as well as in advanced materials industries.[3–5] Consequently, there has been an immense effort to develop novel methods and reagents to access this class of compounds.[6,7]

Aryl trifluoromethyl thioethers ($ArSCF_3$) have typically been prepared by nucleophilic,[8–11] electrophilic,[12–14] or radical[15–20] trifluoromethylation of sulfur substrates with a trifluoromethylation reagent or nucleophilic reaction of trifluoromethylthiolate with aryl halides.[21–26] Metal-mediated trifluoromethylthiolation has been developed as an attractive route for the formation of C(sp^2_{aryl})–SCF_3 bonds under mild reaction conditions. The catalytic systems reported by the groups of Buchwald,[27] Qing,[28] Vicic,[29,30] Daugulis,[31] Shibata[32] and Rueping[33] illustrate the major importance of these transformations.

However, compared with these well-established procedures, relatively limited methods are currently available for the construction of C(sp^3_{alkyl})–SCF_3 bonds, which mainly rely on the strategy of employing electrophilic trifluoromethylthiolation reagents. For instance, Billard and co-workers have developed the electrophilic trifluoromethylthiolation of alkenes and organometallic nucleophiles with trifluoromethanesulfanylamides as reagents.[34–36] Lu, Shen and co-workers recently reported the electrophilic α-trifluoromethylthiolation of β-ketoesters using an electrophilic hypervalent iodine reagent.[37] More recently, Rueping and co-workers have demonstrated a highly enantioselective trifluoromethylthiolation of β-ketoesters with *N*-trifluoromethylthiophthalimide as the electrophilic SCF_3 source.[38] The successful implementation of these strategies has greatly expanded the utility of these transformations.

Alkyl trifluoromethyl sulfides have been involved in numerous synthetic applications, mainly devoted to the synthesis of bioactive molecules. Examples include trifluoromethylthioacetic acid and its derivatives, which serve as useful intermediates in the synthesis of the cephalosporin antibiotic cefazaflur.[39,40] From a preparative point of view, nucleophilic trifluoromethylthiolation with a large pool of readily available alkyl halides, particularly with secondary alkyl halides, would be an attractive alternative for the generation of C(sp^3_{alkyl})–SCF_3 bonds. One of the greatest challenges associated with using alkyl halides is to achieve high selectivity for trifluoromethylthiolation with suppressed β-hydride elimination.[41] Thus, efficient and selective methods to access this class of compounds are actively being sought.[9,11,16,18,19,42–44]

Recently, we invented a copper reagent (bpy)Cu(SCF_3) **1** for the nucleophilic trifluoromethylthiolation of aryl halides,[45] benzyl bromides[46] and allylic bromides.[47] These reactions provided a novel and convenient synthetic route for preparing new trifluoromethylthiolated derivatives. Herein, we report an efficient and general preparation of alkyl trifluoromethyl sulfides by means of copper-mediated trifluoromethylthiolation of alkyl halides.

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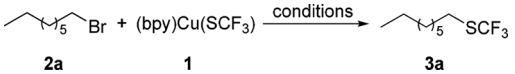
†Electronic supplementary information (ESI) available: Copies of ^1H, ^{13}C, ^{19}F NMR of synthesized products. See DOI: 10.1039/c4ob00403e

Results and discussion

Our initial experiment with 1-bromooctane (**2a**) and (bpy)Cu(SCF_3) (**1**),[45] by using CH_3CN as the solvent at 110 °C for 15 h provided 62% of trifluoromethylthiolated product **3a** (Table 1, entry 1). It is worthwhile to note that no β-hydride elimination by-products were observed in this reaction. Taking into account these preliminary results, we then examined the influence of the solvent, additive and reaction time on the efficiency of our model reaction. Studies on the effect of the solvent revealed that CH_3CN was the solvent of choice (Table 1, entry 1). This finding is consistent with our previous work on the trifluoromethylthiolation of aryl halides.[45] When dimethylformamide (DMF), dimethyl sulfoxide (DMSO), toluene, THF and CH_2Cl_2 were employed, the transformation was dramatically retarded (Table 1, entries 2–6).

We next examined the additive effect of this newly designed trifluoromethylthiolation. During the course of our work on the trifluoromethylthiolation/selenolation of α-halo-α,β-unsaturated carbonyl compounds, we found that the addition of CsF as a additive was beneficial in terms of yield of the desired products.[48] Therefore, we examined several fluorides to accelerate the subsequent reactions. Indeed, a significant increase in the yield of trifluoromethylthiolated product **3a** was observed when KF (1.0 equiv.) was employed as an additive (71%; Table 1, entry 7). Additionally, increasing the amount of KF to 2.0 equiv. accelerated the reaction to give **3a** in 91% yield (Table 1, entry 8). It was subsequently found that the reaction using CsF afforded the product in comparable yield (Table 1, entry 9). Although the reasons for the improved yield from the addition of an excess amount of alkaline fluoride salts are unclear, the presence of these fluorides accelerates the rate of reaction probably by facilitating the formation of active intermediate.[48] There are numerous cited examples of improving chemical processes by using CsF or KF as additive.[49–52]

Table 1 Optimization of the trifluoromethylthiolation of 1-bromooctane[a]



2a **1** **3a**

Entry	Additive (equiv.)	Solvent	T (°C)	Time (h)	Yield[b] (%)
1	—	CH_3CN	110	15	62
2	—	DMF	110	15	9
3	—	DMSO	110	15	12
4	—	Toluene	110	15	1
5	—	THF	90	15	3
6	—	CH_2Cl_2	40	15	1<
7	KF (1.0)	CH_3CN	110	15	71
8	KF (2.0)	CH_3CN	110	15	91
9	CsF (2.0)	CH_3CN	110	15	81
10	AgF (2.0)	CH_3CN	110	15	45
11	Bu_4NF (2.0)	CH_3CN	110	15	46
12	KF (2.0)	CH_3CN	110	8	48

[a] Reaction conditions: **1** (0.060 mmol), **2a** (0.050 mmol), solvent (1.0 mL), under N_2 atmosphere. [b] The yield was determined by ^{19}F NMR spectroscopy with $PhOCF_3$ as internal standard.

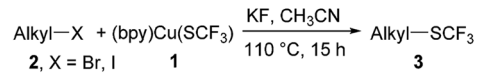
However, when AgF and Bu_4NF were used, product **3a** was formed with a lower yield (Table 1, entries 10 and 11). Further screening of the reaction conditions revealed that the reaction time has a profound impact on the reaction rate and efficiency. Shortening the time to 8 h led to a reduced yield (48%; Table 1, entry 12). Consequently, the optimized reaction conditions were determined as the combination of (bpy)Cu(SCF_3) **1** (1.2 equiv.), alkyl bromide (1.0 equiv.), KF (2.0 equiv.) in CH_3CN at 110 °C with a reaction time of 15 h.

The scope of this copper-mediated trifluoromethylthiolation was further examined by using various alkyl halides under the optimized conditions (Table 2). Importantly, a variety of functional groups such as ethers, thioether, esters, nitriles, amides, and ketal were well tolerated under the reaction conditions.

The unfunctionalized alkyl bromides **2a** and **2b** reacted with (bpy)Cu(SCF_3) (**1**) to give the trifluoromethylthiolated products **3a** and **3b** in excellent yields (90% and 96%, respectively; Table 2, entries 1 and 2). Alkyl bromides bearing an arene unit (**2c** and **2d**) smoothly afforded the corresponding products **3c** and **3d** in 90% and 95% yields, respectively (Table 2, entries 3 and 4). The alkyl bromides **2e** possessing a methoxy substituent at the *para* position of the aromatic ring reacted with **1** to give product **3e** in 98% yield (Table 2, entry 5). However, lower yields were observed for electrophiles containing electron-poor *para*-NO_2-substituted aromatic rings, as found in the reaction with **2f**, which led to **3f** in 34% isolated yield and 1-nitro-4-vinylbenzene as major side products (Table 2, entry 6). The alkyl bromides **2g–2i** carrying ether and thioether substituents furnished high yields of the corresponding products **3g–3i** (98, 96 and 89%, respectively; Table 2, entries 7–9). However, in the case of 2-(2-bromoethoxy)tetrahydro-2*H*-pyran **2j**, product **3j** was obtained in a moderate yield of 42% along with some unidentified by-products (Table 2, entry 10), which could be a result of the inherent instability of this compound. In addition, alkyl bromide **2k** having a nitrile substituent reacted with **1** to afford the corresponding product **3k** in 99% yield (Table 2, entry 11). Interestingly, the presence of sensitive ester groups in the alkyl moiety (**2l** and **2m**) did not affect the process, and the corresponding products **3l** and **3m** were isolated in excellent yields (98 and 99%, respectively; Table 2, entries 12 and 13). Likewise, an alkyl bromide **2n** bearing a ketal group also allowed the formation of the desired product **3n** in 70% yield (Table 2, entry 14). Furthermore, 2-(3-bromopropyl)isoindoline-1,3-dione **2o** also reacted to afford the product **3o** in 99% yield (Table 2, entry 15).

The substrate scope of the reaction was also extended to include unactivated alkyl electrophiles. The secondary alkyl iodides **2p** and **2q** proceeded smoothly to form the products **3p** and **3q** in 86 and 63% yield, respectively (Table 2, entries 16 and 17). Furthermore, heterocycle-containing secondary alkyl bromide **2r** could be converted to **3r**, albeit in modest yield after an extended reaction time (Table 2, entry 18). However, this method has its limitations. The reactions of cyclic secondary bromide **2s** and alkyl chloride **2c′** failed to produce the targeted compounds **3s** and **3c**, respectively (Table 2, entries 19

Table 2 Substrate scope of trifluoromethylthiolation of alkyl halides[a]



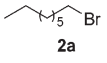
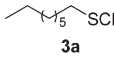
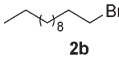
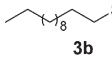
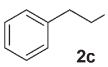
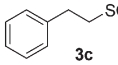
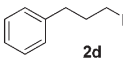
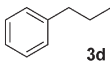
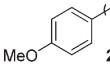
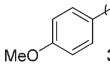
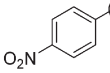
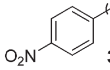
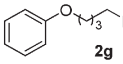
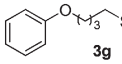
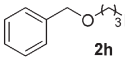
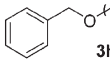
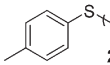
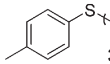
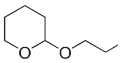
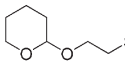
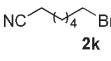
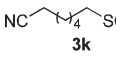
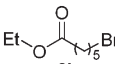
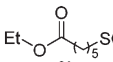
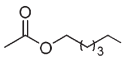
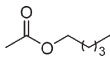
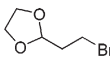
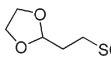
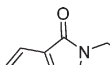
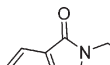
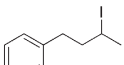
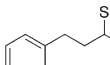
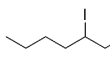
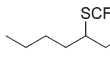
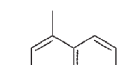
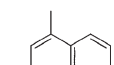
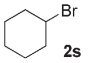
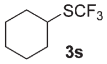
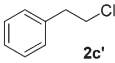
Entry	Alkyl halide	Product	Yield (%)
1	 2a	 3a	90
2	 2b	 3b	96
3	 2c	 3c	90
4	 2d	 3d	95
5	 2e	 3e	98
6	 2f	 3f	34
7	 2g	 3g	98
8	 2h	 3h	96
9	 2i	 3i	89
10	 2j	 3j	42
11	 2k	 3k	99
12	 2l	 3l	98
13	 2m	 3m	99
14	 2n	 3n	70
15	 2o	 3o	99
16	 2p	 3p	86
17	 2q	 3q	63
18	 2r	 3r	37
19	 2s	 3s	Trace
20	 2c'	3c	Trace

Table 2 *(Contd.)*

Entry	Alkyl halide	Product	Yield (%)
21	2t	3t	48
22	2s'	3s	12[b]
23	2u	3u	32
24	2v	3v	11[b]
25	2w	3w	13[b]

[a] Reaction conditions: **1** (0.30 mmol), alkyl halide **2** (0.25 mmol), KF (0.50 mmol, 2 equiv.), 15 h, N_2, 110 °C. Yields shown are of isolated products. [b] The yield was determined by ^{19}F NMR spectroscopy with $PhOCF_3$ as internal standard.

and 20) under the standard reaction conditions. Nevertheless, the cyclic secondary iodides **2t**, **2s′**, **2u** and **2v** could be transferred through this procedure although reduced yields of the corresponding products **3t**, **3s**, **3u** and **3v** were produced (48, 12, 32 and 11%, respectively; Table 2, entries 21–24). Similarly, the reaction has been extended to tertiary alkyl iodide **2w** which gave a relatively low yield of the desired product **3w** (13%; Table 2, entry 25).

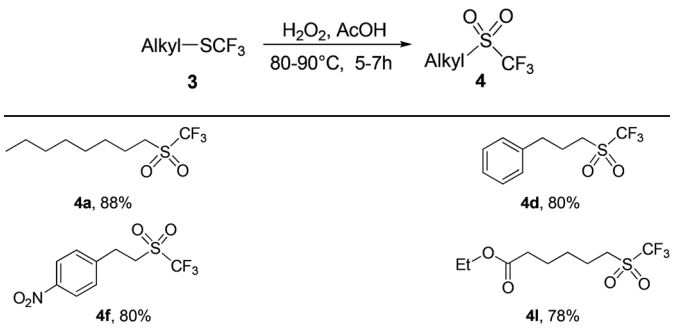
To demonstrate the practical utility, the trifluoromethylthiolation of **2o** was carried out on a 0.5-g scale (Scheme 1). As a result, the product **3o** was isolated in 99% yield (0.538 g).

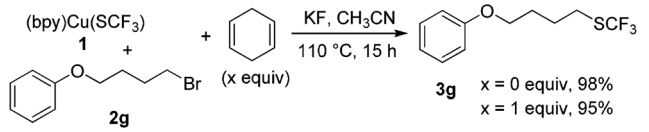
To further illustrate the synthetic potential of these alkyl trifluoromethyl thioethers, the subsequent oxidation was performed. As shown in Table 3, the trifluoromethylthiolated compound **3** underwent smooth oxidation with H_2O_2 in acetic acid to give the corresponding alkyl trifluoromethanesulfones **4** in good yields.

In an attempt to examine whether any radical intermediates are generated during trifluoromethylthiolation, a series of experiments were carried out under the optimized conditions. The addition of a radical scavenger, cyclohexa-1,4-diene (CHD), to the reaction of **1** with **2g** did not suppress this transformation (Scheme 2). The trifluoromethylthiolated product **3g** was formed in similar yield both in the absence (98%; Table 2,

Scheme 1 Scalability of the trifluoromethylthiolation of **2o**.

Table 3 Synthesis of alkyl trifluoromethyl sulfones



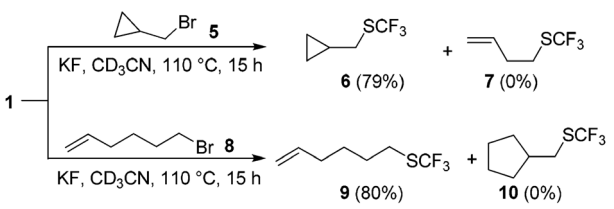


Scheme 2 Radical scavenger experiments.

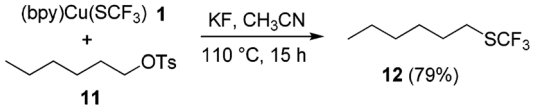
entry 7) and presence of 1.0 equiv. of the radical scavenger (95%; ^{19}F NMR yield).

Subsequently, the intermediacy of alkyl radical was probed by reactions with a radical clock, such as (bromomethyl)cyclopropane **5** and 6-bromo-1-hexene **8**. The rates of radical ring-opening of **5** and the cyclization of **8** are known to be 1.3×10^8 and 1.0×10^5 s^{-1}, respectively.[53] The reaction of **1** with **5** or **8** was conducted in CD_3CN solvent at 110 °C for 15 h (Scheme 3). These reactions formed the products **6** and **9** from $C(sp^3{}_{alkyl})$–SCF_3 coupling in 79 and 80% yields (^{19}F NMR), respectively. No ring-opened product **7** or cyclized product **10** were detected. These results indicate that radicals are not produced in this trifluoromethylthiolation.

Additionally, trifluoromethylthiolation with alkyl tosylates was also examined (Scheme 4). Reaction of **1** with 1 equiv. of hexyl *p*-toluenesulfonate **11** for 15 h at 110 °C in CH_3CN formed the desired product **12** in 79% yield (^{19}F NMR). Given the good reactivity of alkyl tosylates, the mechanism of the present trifluoromethylthiolation might involve an S_N2-type substitution with **1**.



Scheme 3 Radical clock experiments.



Scheme 4 Reaction of **1** with alkyl tosylates.

Conclusions

In conclusion, an efficient method for the preparation of alkyl trifluoromethyl thioethers *via* the copper-mediated trifluoromethylthiolation of primary and secondary alkyl halides has been developed. The reactions proceeded smoothly with yields up to 99% and demonstrated good compatibility with a wide range of functional groups, *e.g.*, ethers, thioether, esters, nitriles, amides, and ketal, *etc*.

Experimental

General remarks

^{1}H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded using a 400 Hz spectrometer. ^{1}H NMR and ^{13}C NMR chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane and ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard and low field is positive. Coupling constants (*J*) are reported in hertz (Hz). The residual solvent peak was used as an internal reference: ^{1}H NMR (chloroform δ 7.26) and ^{13}C NMR (chloroform δ 77.0). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. HRMS data were obtained at the Shanghai Institute of Organic Chemistry. Alkyl bromides **2i** and **2r**, alkyl iodide **2p** and **2r**,[54] **2t**,[55] **2q**,[56] **2u–v**,[56] and (bpy)Cu(SCF_3) (**1**),[45] were prepared according to the published procedures. Other reagents were received from commercial sources. Solvents were freshly dried and degassed according to published procedures[57] prior to use. Column chromatography purifications were performed by flash chromatography using silica gel 60.

General procedure for trifluoromethylthiolation of alkyl bromide with [(bpy)Cu(SCF_3)] (1)

[(bpy)Cu(SCF_3)] (**1**) (96 mg, 0.30 mmol, 1.2 equiv.), alkyl bromide **2** (0.25 mmol), KF (29 mg, 0.50 mmol, 2 equiv.), and CH_3CN (1.0 mL) were added to a reaction tube equipped with a magnetic stirrer bar. The tube was sealed and the solution was placed into a preheated 110 °C oil bath for 15 h. The tube was removed from the oil bath and allowed to cool. The reaction mixture was then filtered through Celite to remove metal salts. Water (10.0 mL) was added to the mixture at 0 °C. The resulting mixture was extracted with diethyl ether (3 × 6.0 mL), and the combined organic layers were dried over magnesium sulfate. The solvent was removed by rotary evaporation in an ice bath and the resulting product was purified by column chromatography on silica gel with *n*-pentane.

General procedure for synthesis of alkyl trifluoromethyl sulfones

A 30% (w/w) aqueous solution of H_2O_2 (0.21 mL, 2 mmol) was added dropwise to a solution of **3** (0.50 mmol) in acetic acid (5 mL) at room temperature. The mixture was stirred at 80–90 °C for 5–7 h. The resulting solution was cooled to room temperature, and poured into water (5 mL) and then extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with water (3 × 10 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL) and water again (2 × 10 mL), then dried over $MgSO_4$ and concentrated under vacuum at room temperature. The crude product was purified by column chromatography on silica gel, eluting with (*n*-pentane–diethyl ether).

Octyl(trifluoromethyl)sulfane.[20] (3a). Obtained as a pale yellow oil in 90% yield (68 mg). R_f (*n*-pentane): 0.91. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (t, J = 7.4 Hz, 2H), 1.83–1.63 (m, 2H), 1.49–1.22 (m, 10H), 0.91 (t, J = 6.6 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.3 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.2 (q, J = 305.1 Hz), 31.7 (s), 29.9 (s), 29.4 (s), 29.0 (s), 28.9 (s), 28.5 (s), 22.6 (s), 14.0 (s). IR (KBr): ν 2929, 2858, 1458, 1152, 1118, 756 cm^{-1}. GC-MS m/z 214 (M^+), 145 ($M^+ - CF_3$ 100%).

Dodecyl(trifluoromethyl)sulfane.[12] (3b). Obtained as a pale yellow oil in 96% yield (65 mg). R_f (*n*-pentane): 0.89. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (t, J = 7.4 Hz, 2H), 1.82–1.64 (m, 2H), 1.52–1.14 (m, 18H), 0.91 (t, J = 6.6 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.3 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.2 (q, J = 305.7 Hz), 31.9 (s), 29.9 (q, J = 2.0 Hz), 29.6 (s), 29.5 (s), 29.4 (s), 29.3 (s), 28.9 (s), 28.5 (s), 22.7 (s), 14.1 (s). IR (KBr) ν 2926, 2855, 1466, 1159, 1118, 756 cm^{-1}. GC-MS m/z 270 (M^+), 269 ($M^+ - SCF_3$ 100%).

Phenethyl(trifluoromethyl)sulfane.[58] (3c). Obtained as a pale yellow oil in 90% yield (50 mg). R_f (*n*-pentane): 0.92. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 7.4 Hz, 2H), 7.34–7.27 (m, 1H), 7.25 (d, J = 7.4 Hz, 2H), 3.18 (t, J = 7.7 Hz, 2H), 3.04 (t, J = 7.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.0 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0 (s), 131.2 (q, J = 306.0 Hz), 128.7 (s), 128.5 (s), 126.9 (s), 36.0 (s), 31.2 (q, J = 1.9 Hz). IR (KBr) ν 3031, 2929, 1497, 1455, 1112, 757, 712, 697 cm^{-1}. GC-MS m/z 205 (M^+), 104 ($M^+ - SCF_3$ 100%).

(3-Phenylpropyl)(trifluoromethyl)sulfane.[59] (3d). Obtained as a pale yellow oil in 95% yield (52 mg). R_f (*n*-pentane): 0.86. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (t, J = 7.3 Hz, 2H), 7.29–7.23 (m, 3H), 2.93 (t, J = 7.3 Hz, 2H), 2.80 (t, J = 7.5 Hz, 2H), 2.19–1.95 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.0 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.5 (s), 131.2 (q, J = 305.8 Hz), 128.6 (s), 128.5 (s), 126.3 (s), 34.4 (s), 31.0 (s), 29.2 (q, J = 2.0 Hz). IR (KBr) ν 3029, 2931, 1497, 1455, 1114, 744, 699 cm^{-1}. GC-MS m/z 220 (M^+), 119 ($M^+ - SCF_3$ 100%).

(4-Methoxyphenethyl)(trifluoromethyl)sulfane (3e). Obtained as a pale yellow oil in 98% yield (65 mg). R_f (*n*-pentane): 0.78. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 3.82 (s, 3H), 3.12 (t, J = 7.7 Hz, 2H), 2.96 (t, J = 7.7 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.0 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5 (s), 131.2 (q, J = 305.8 Hz), 131.0 (s), 129.6 (s), 114.1 (s), 55.3 (s), 35.1 (s), 31.6 (q, J = 1.8 Hz). IR (KBr) ν 3005, 2956, 2936, 2837, 1612, 1585, 1514, 1466, 1320, 1250, 1112, 1037, 822, 756, 699 cm^{-1}. GC-MS m/z 236 (M^+), 135 ($M^+ - SCF_3$ 100%). HRMS (EI) calcd for $C_{10}H_{11}F_3OS$: 236.0483; Found: 236.0487.

(4-Nitrophenethyl)(trifluoromethyl)sulfane (3f). Obtained as a pale yellow oil in 34% yield (22 mg). R_f (*n*-pentane): 0.25. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 3.24–3.11 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −40.9 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.1 (s), 146.2 (s), 130.9 (q, J = 308.1 Hz), 129.5 (s), 124.0 (s), 35.72 (s), 30.5 (q, J = 2.2 Hz). IR (KBr) ν 3081, 2946, 2855, 1606, 1520, 1348, 1111, 855, 746, 695 cm^{-1}. GC-MS m/z 251 (M^+), 150 ($M^+ - SCF_3$ 100%). HRMS (EI) calcd for $C_9H_8F_3NO_2S$: 251.0228; Found: 251.0230.

(4-Phenoxybutyl)(trifluoromethyl)sulfane (3g). Obtained as a pale yellow oil in 98% yield (61 mg). R_f (*n*-pentane): 0.67. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 7.7 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 6.94 (d, J = 7.4 Hz, 2H), 4.03 (t, J = 4.4 Hz, 2H), 3.00 (t, J = 7.7 Hz, 2H), 2.01–1.91 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.1 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9 (s), 131.2 (q, J = 305.8 Hz), 129.5 (s), 120.8 (s), 114.5 (s), 66.9 (s), 29.7 (q, J = 2.1 Hz), 28.1 (s), 26.4 (s). IR (KBr) ν 3041, 2948, 2873, 1600, 1587, 1497, 1245, 1117, 754, 691 cm^{-1}. GC-MS m/z 249 (M^+), 148 ($M^+ - SCF_3$ 100%). HRMS (EI) calcd for $C_{11}H_{13}F_3OS$: 250.0639; Found: 250.0641.

(3-(Benzyloxy)propyl)(trifluoromethyl)sulfane (3h). Obtained as a pale yellow oil in 96% yield (60 mg). R_f (*n*-pentane): 0.62. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.31 (m, 5H), 4.54 (s, 2H), 3.61 (t, J = 5.8 Hz, 2H), 3.05 (t, J = 7.2 Hz, 2H), 2.06–1.99 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.2 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2 (s), 131.2 (q, J = 305.9 Hz), 128.4 (s), 127.7 (s), 127.6 (s), 73.1 (s), 67.8 (s), 29. 8 (s), 26.9 (q, J = 2.2 Hz). IR (KBr) ν 3032, 2861, 1455, 1114, 912, 741, 697 cm^{-1}. GC-MS m/z 249 (M^+), 148 ($M^+ - SCF_3$ 100%). HRMS (EI) calcd for $C_{11}H_{13}F_3OS$: 250.0639; Found: 250.0638.

***p*-Tolyl(3-((trifluoromethyl)thio)propyl)sulfane (3i).** Obtained as a pale yellow oil in 89% yield (39 mg). R_f (*n*-pentane): 0.56. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 7.2 Hz, 2H), 7.15 (d, J = 7.2 Hz, 2H), 3.06–2.99 (m, 4H), 2.36 (s, 3H), 2.13–1.81 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.0 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8 (s), 131.6 (s), 131.0 (q, J = 306.6 Hz), 130.8 (s), 129.8 (s), 33.1 (s), 28.8 (s), 28.5 (q, J = 2.0 Hz), 21.0 (s). IR (KBr) ν 3021, 2924, 2860, 1493, 1456, 1419, 1115, 805, 756 cm^{-1}. GC-MS m/z 265 (M^+), 164 ($M^+ - SCF_3$ 100%). HRMS (EI) calcd for $C_{11}H_{13}F_3S_2$: 266.0411; Found: 266.0410.

2-(2-((Trifluoromethyl)thio)ethoxy)tetrahydro-2*H*-pyran (3j). Obtained as a pale yellow oil in 42% yield (28 mg). R_f (*n*-pentane): 0.65. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 (t, J = 3.2 Hz, 1H), 4.04–3.82 (m, 2H), 3.75–3.50 (m, 2H), 3.13 (t, J = 6.4 Hz, 2H), 1.90–1.68 (m, 2H), 1.64–1.52 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.3 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.1 (q, J = 305.9 Hz), 98.9 (s), 65.9 (s), 62.2 (s), 30.4 (s), 29.8 (q, J = 2.1 Hz), 25.3 (s), 19.2 (s). IR (KBr) ν 2946, 2874, 1201, 1116, 1081, 1032 cm^{-1}. GC-MS m/z 230 (M^+), 129 ($M^+ - SCF_3$ 100%). HRMS (EI) [$M^+ - H$] calcd for $C_8H_{12}F_3O_2S$: 229.0510; Found: 229.0512.

7-((Trifluoromethyl)thio)heptanenitrile (3k). Obtained as a pale yellow oil in 99% yield (68 mg). R_f (*n*-pentane): 0.71. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91 (t, J = 7.2 Hz, 2H), 2.37 (t, J = 7.2 Hz, 2H), 1.78–1.66 (m, 4H), 1.58–1.41 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.2 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.1 (q, J = 305.7 Hz), 119.5 (s), 29.7 (q, J = 2.1 Hz), 29.1 (s), 28.0 (s), 27.6 (s), 25.2 (s), 17.1(s). IR (KBr) ν 2941, 2863, 2246, 1464, 1427, 1116, 755 cm^{-1}. GC-MS m/z 211 (M^+), 110 (M^+ − SCF_3 100%). HRMS (EI) calcd for $C_8H_{12}F_3NS$: 211.0643; Found: 211.0638.

Ethyl 6-((trifluoromethyl)thio)hexanoate (3l). Obtained as a pale yellow oil in 98% yield (28 mg). R_f (*n*-pentane): 0.74. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (q, J = 7.2 Hz, 2H), 2.90 (t, J = 7.2 Hz, 2H), 2.33 (t, J = 7.4 Hz, 2H), 1.77–1.64 (m, 4H), 1.53–1.40 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.2 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.4 (s), 131.1 (q, J = 305.7 Hz), 60.3 (s), 34.0 (s), 29.6 (q, J = 2.2 Hz), 29.1 (s), 27.9 (s), 24.3 (s), 14.2 (s). IR (KBr) ν 2939, 2863, 1734, 1301, 1115, 1032 cm^{-1}. GC-MS m/z 244 (M^+), 143 (M^+ − SCF_3 100%). HRMS (EI) calcd for $C_9H_{15}F_3O_2S$: 244.0745; Found: 244.0747.

5-((Trifluoromethyl)thio)pentyl acetate (3m). Obtained as a pale yellow oil in 99% yield (68 mg). R_f (*n*-pentane): 0.74. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (t, J = 6.5 Hz, 2H), 2.90 (t, J = 7.4 Hz, 2H), 2.06 (s, 3H), 1.82–1.59 (m, 4H), 1.57–1.38 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.3 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0 (s), 131.1 (q, J = 305.7 Hz), 64.0 (s), 29.6 (q, J = 1.9 Hz), 29.1 (s), 28.0 (s), 24.9 (s), 20.8 (d, J = 1.2 Hz). IR (KBr) ν 2943, 2866, 1741, 1367, 1238, 1117, 1044 cm^{-1}. GC-MS m/z 230 (M^+), 129 (M^+ − SCF_3 100%). HRMS (EI) [M^+ + H] calcd for $C_8H_{14}F_3O_2S$: 231.0667; Found: 231.0663.

2-(2-((Trifluoromethyl)thio)ethyl)-1,3-dioxolane (3n). Obtained as a colorless oil in 70% yield (39 mg). R_f (*n*-pentane): 0.62. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.00 (t, J = 4.1 Hz, 1H), 4.04–3.96 (m, 2H), 3.94–3.87 (m, 2H), 3.02 (t, J = 4.1 Hz, 2H), 2.16–2.06 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.7 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.1 (q, J = 305.9 Hz), 102.4 (s), 65.1 (s), 33.7 (s), 23.9 (q, J = 2.3 Hz). IR (KBr) ν 2889, 2359, 1115, 913, 742 cm^{-1}. GC-MS m/z 200 (M^+), 99 (M^+ − SCF_3 100%). HRMS (EI) [M^+ − H] calcd for $C_6H_8F_3O_2S$: 201.0197; Found: 201.0202.

2-(3-((Trifluoromethyl)thio)propyl)isoindoline-1,3-dione (3o). Obtained as a white solid in 99% yield (72 mg). Mp: 48–50 °C. R_f (*n*-pentane): 0.35. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88–7.81 (m, 2 H), 7.76–7.69 (m, 2H), 3.82 (t, J = 7.0 Hz, 2H), 2.92 (t, J = 7.0 Hz, 2H), 2.10 (p, J = 7.0 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.2 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2 (d, J = 0.8 Hz), 134.1 (s), 132.0 (s), 131.0 (q, J = 306.1 Hz), 123.3 (d, J = 1.1 Hz), 36.5 (s), 28.9 (s), 27.3 (q, J = 2.2 Hz). IR (KBr) ν 3469, 3063, 2943, 1772, 1716, 1615, 1583, 1395, 1117, 1016, 756, 719 cm^{-1}. GC-MS m/z 289 (M^+), 188 (M^+ − SCF_3 100%). HRMS (EI) calcd for $C_{12}H_{10}F_3NO_2S$: 289.0384; Found: 289.0382.

(4-Phenylbutan-2-yl)(trifluoromethyl)sulfane (3p). Obtained as a pale yellow oil in 86% yield (50 mg). R_f (*n*-pentane): 0.65. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 7.3 Hz, 2H), 7.26–7.19 (m, 3H), 3.39–3.25 (m, 1H), 2.86–2.71 (m, 2H), 2.07–1.85 (m, 2H), 1.49 (d, J = 6.9 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −38.9 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9 (s), 131.2 (q, J = 306.3 Hz), 128.6 (s), 128.4 (s), 126.2 (s), 40.6 (q, J = 1.4 Hz), 38.5 (s), 32.8 (s), 22.5 (s). IR (KBr) ν 3029, 2929, 2861, 1496, 1455, 1382, 1116, 747, 699 cm^{-1}. GC-MS m/z 234 (M^+), 133 (M^+ − SCF_3 100%). HRMS (EI) calcd for $C_{11}H_{13}F_3S$: 234.0690; Found: 234.0693.

Nonan-5-yl(trifluoromethyl)sulfane (3q). Obtained as a pale yellow oil in 63% yield (36 mg). R_f (*n*-pentane): 0.84. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31–2.83 (m, 1H), 1.78–1.59 (m, 4H), 1.50–1.29 (m, 8H), 0.94 (t, J = 7.1 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −39.1 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.4 (q, J = 305.8 Hz), 46.7 (q, J = 1.2 Hz), 34.8 (s), 28.5 (s), 22.4 (s), 13.9 (s). IR (KBr) ν 2960, 2932, 1466, 1112 cm^{-1}. GC-MS m/z 228 (M^+), 159 (M^+ − CF_3 100%). HRMS (EI) calcd for $C_{10}H_{19}F_3S$: 228.1160; Found: 228.1164.

4-Methyl-7-(3-(trifluoromethylthio)butoxy)-2*H*-chromen-2-one (3r). Obtained as a colourless oil in 37% yield (35 mg). R_f (*n*-pentane): 0.72. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.8 Hz, 1H), 6.89 (dd, J = 8.8, 2.5 Hz, 1H), 6.84 (d, J = 2.4 Hz, 1H), 6.17 (s, 1H), 4.25–4.13 (m, 2H), 3.62 (dq, J = 13.6, 6.7 Hz, 1H), 2.43 (s, 3H), 2.25–2.01 (m, 2H), 1.56 (d, J = 6.9 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −39.0 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6 (s), 161.3 (s), 155.2 (s), 152.6 (s), 131.0 (q, J = 306.4 Hz), 125.6 (s), 113.8 (s), 112.5 (s), 112.2 (s), 101.5 (s), 65.2 (s), 37.9 (q, J = 1.6 Hz), 36.0 (s), 22.7 (s), 18.7 (s). IR (KBr) ν 3029, 2929, 2861, 1496, 1455, 1382, 1116, 747, 699 cm^{-1}. GC-MS m/z 332 (M^+), 233 (M^+ − SCF_3 100%). HRMS (EI) calcd for $C_{15}H_{15}F_3O_3S$: 332.0694; Found: 332.0691.

Cyclohexyl(trifluoromethyl)sulfane.[36] (3s). 12% yield (^{19}F NMR). This volatile compound was identified by ^{19}F NMR spectra and GC-MS of reaction mixtures. ^{19}F NMR (376 MHz, CH_3CN) δ −38.9 (s). GC-MS m/z 184 (M^+), 83 (M^+ − SCF_3 100%).

(2,3-Dihydro-1*H*-inden-2-yl)(trifluoromethyl)sulfane (3t). Obtained as a pale yellow oil in 48% yield (26 mg). R_f (*n*-pentane): 0.91. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.19 (m, 4H), 4.10 (p, J = 7.6 Hz, 1H), 3.46 (dd, J = 16.1, 7.7 Hz, 2H), 3.09 (dd, J = 16.0, 7.5 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −40.4 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.6 (s), 131.0 (q, J = 306.3 Hz), 127.1 (s), 124.3 (s), 42.3 (q, J = 1.7 Hz), 40.6 (d, J = 0.8 Hz). IR (KBr) ν 3212, 2926, 2853, 1715, 1683, 1539, 1116, 743 cm^{-1}. GC-MS m/z 217 (M^+ − H), 116 (M^+ − SCF_3 100%). HRMS (EI) calcd for $C_{10}H_9F_3S$: 218.0377; Found: 218.0375.

Cycloheptyl(trifluoromethyl)sulfane (3u). Obtained as a pale yellow oil in 32% yield (16 mg). R_f (*n*-pentane): 0.91. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45–3.51 (m, 1H), 2.19–2.03 (m, 2H), 1.83–1.65 (m, 4H), 1.65–1.48 (m, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −39.6 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.2 (q, J = 306.1 Hz), 45.9 (q, J = 1.2 Hz), 35.5 (s), 28.0 (s), 25.4 (s). IR (KBr) ν 2930, 2857, 1460, 1125 cm^{-1}. GC-MS m/z 198 (M^+), 129 (M^+ − CF_3 100%). HRMS (EI) calcd for $C_8H_{13}F_3S$: 198.0690; Found: 198.0691.

Cyclooctyl(trifluoromethyl)sulfane (3v). 11% yield (^{19}F NMR). This compound was identified by ^{19}F NMR spectra and GC-MS of reaction mixtures. ^{19}F NMR (376 MHz, CH_3CN) δ −39.1 (s). GC-MS m/z 212 (M^+), 143 (M^+ − SCF_3 100%).

***tert*-Butyl(trifluoromethyl)sulfane.[36] (3w).** 13% yield (^{19}F NMR). This volatile compound was identified by ^{19}F NMR

spectra of reaction mixtures. ^{19}F NMR (376 MHz, CH_3CN) δ −36.2 (s).

1-((Trifluoromethyl)sulfonyl)octane.[60] (4a). Obtained as a colorless oil in 88% yield (54 mg). R_f (*n*-pentane–diethyl ether = 3 : 1): 0.87. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28–3.18 (m, 2H), 1.96 (dt, J = 15.7, 7.9 Hz, 2H), 1.56–1.45 (m, 2H), 1.42–1.22 (m, 8H), 0.91 (t, J = 6.8 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −78.2 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 119.5 (q, J = 327.2 Hz), 49.6 (q, J = 1.0 Hz), 31.6 (s), 28.8 (s), 28.4 (s), 22.6 (s), 20.6 (s), 14.1 (s). IR (KBr) ν 3086, 3032, 2931, 1647, 1112, 963, 749, 693 cm^{-1}. GC-MS *m*/*z* 246 (M^+), 113 ($M^+ - SO_2CF_3$ 100%).

(3-((Trifluoromethyl)sulfonyl)propyl)benzene.[61] (4d). Obtained as a pale yellow oil in 80% yield (50 mg). R_f (*n*-pentane–diethyl ether = 3 : 1): 0.77. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.15 (m, 5H), 3.28–3.13 (m, 2H), 2.86 (t, J = 7.3 Hz, 2H), 2.37–2.24 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −78.1 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8 (s), 128.9 (s), 128.4 (s), 126.9 (s), 119. 5 (q, J = 327.1 Hz), 48.8 (s), 34.0 (s), 22.3 (s). IR (KBr) ν 2962, 2917, 2849, 2360, 1456, 1367, 1260, 1198, 1120, 1112, 912, 799, 699 cm^{-1}. GC-MS *m*/*z* 251 (M^+), 118 ($M^+ - SO_2CF_3$ 100%).

1-Nitro-4-(2-((trifluoromethyl)sulfonyl)ethyl)benzene (4f). Obtained as a white solid in 80% yield (18 mg). Mp: 134–136 °C. R_f (*n*-pentane–diethyl ether = 3 : 1): 0.27. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 8.6 Hz, 2H), 3.55 (dd, J = 10.1, 6.1 Hz, 2H), 3.38 (dd, J = 9.9, 6.3 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −77.8 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4 (s), 129.5 (s), 124.4 (s), 119.4 (q, J = 323.2 Hz), 50.2 (q, J = 1.0 Hz), 26.7 (s). IR (KBr) ν 3083, 2993, 2933, 1521, 1353, 1211, 1108, 855, 737 cm^{-1}. GC-MS *m*/*z* 283 (M^+), 150 ($M^+ - SO_2CF_3$ 100%). HRMS (EI) calcd for $C_9H_8F_3NO_4S$: 283.0126; Found: 283.0130.

Ethyl 6-((trifluoromethyl)sulfonyl)hexanoate (4l). Obtained as a colorless oil in 78% yield (54 mg). R_f (*n*-pentane–diethyl ether = 3 : 1): 0.60. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (q, J = 7.1 Hz, 2H), 3.28–3.17 (m, 2H), 2.35 (t, J = 7.2 Hz, 2H), 1.97 (dt, J = 15.7, 7.8 Hz, 2H), 1.71 (dt, J = 14.7, 7.2 Hz, 2H), 1.61–1.51 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −78.2 (s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1 (s), 119.5 (q, J = 327.1 Hz), 60.5 (s), 49.4 (s), 33.6 (s), 27.8 (s), 24.1 (s), 20.5 (s), 14.2 (s). IR (KBr) ν 2939, 2873, 1731, 1464, 1366, 1199, 1122, 913, 735, 614 cm^{-1}. GC-MS *m*/*z* 276 (M^+), 143 ($M^+ - SO_2CF_3$ 100%). HRMS (EI) calcd for $C_9H_{15}F_3O_4S$: 276.0643; Found: 276.0647.

Procedure for the reaction of 1 with 4-phenoxybutyl bromide 2g in the presence of 1.0 equiv. CHD

1 (19.2 mg, 0.060 mmol), **2g** (11.4 mg, 0.050 mmol), KF (5.8 mg, 0.10 mmol), and 0.6 mL CH_3CN were added to a oven-dried 5 mL test tube with Teflon screw cap. CHD (2.0 mg, 0.025 mmol) was added into the mixture by syringe. The tube was sealed and the reaction solution was placed into a pre-heated 110 °C oil bath for 15 h. The tube was removed from the oil bath and cooled to room temperature, and then 10 μL (trifluoromethoxy)benzene was added as an internal standard. The resulting mixture was filtered through a layer of Celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of the (4-phenoxybutyl)(trifluoromethyl)sulfane **3g** was calculated to be 95%.

Procedure for the reaction of 1 with (bromomethyl) cyclopropane 5

1 (19.2 mg, 0.060 mmol), **5** (6.8 mg, 0.050 mmol), KF (5.8 mg, 0.10 mmol), and 0.6 mL CD_3CN were added to an NMR tube containing a septum-lined screw cap. The tube was sealed and an initial ^{1}H NMR spectrum was acquired. The reaction solution was then placed into a pre-heated 110 °C oil bath for 15 h. The tube was removed from the oil bath and cooled to rt, and a final ^{1}H NMR spectrum was also acquired. 10 μL (trifluoromethoxy)benzene was then added as an internal standard. The reaction mixture was analyzed by ^{19}F NMR and GC-MS. The yield of (cyclopropylmethyl)(trifluoromethyl)sulfane **6** was calculated to be 79%. Formation of but-3-enyl(trifluoromethyl)-sulfane **7** was not detected from ^{1}H NMR.

Procedure for the reaction of 1 with 6-bromohex-1-ene 8

1 (19.2 mg, 0.060 mmol), **8** (8.2 mg, 0.050 mmol), KF (5.8 mg, 0.10 mmol), and 0.6 mL CD_3CN were added to an NMR tube containing a septum-lined screw cap. The tube was sealed and an initial ^{1}H NMR spectrum was acquired. The reaction solution was then placed into a pre-heated 110 °C oil bath for 15 h. The tube was removed from the oil bath and cooled to room temperature, and a final ^{1}H NMR spectrum was also acquired. 10 μL (trifluoromethoxy)benzene was then added as an internal standard. The reaction mixture was analyzed by ^{19}F NMR and GC-MS. The yield of the hex-5-enyl(trifluoromethyl)-sulfane **9** was calculated to be 80%. Formation of (cyclopentylmethyl)(trifluoromethyl)sulfane **10** was not detected from ^{1}H NMR.

Procedure for the reaction of 1 with hexyl *p*-toluenesulfonate 11

1 (19.2 mg, 0.060 mmol), **11** (12.8 mg, 0.050 mmol), KF (5.8 mg, 0.10 mmol), and 0.6 mL CH_3CN were added to a oven-dried 5 mL test tube with Teflon screw cap. The tube was sealed and the reaction solution was placed into a pre-heated 110 °C oil bath for 15 h. The tube was removed from the oil bath and cooled to room temperature, and then 10 μL (trifluoromethoxy)benzene was added as an internal standard. The resulting mixture was filtered through a layer of Celite. The filtrate was analyzed by ^{19}F NMR and GC-MS. The yield of the hexyl(trifluoromethyl)sulfane **12** was calculated to be 79%.

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Notes and references

1 C. Hansch, A. Leo, S. H. Unger, K. H. Kim, D. Nikaitani and E. J. Lien, *J. Med. Chem.*, 1973, **16**, 1207–1216.
2 F. Leroux, P. Jeschke and M. Schlosser, *Chem. Rev.*, 2005, **105**, 827–856.
3 A. Becker, *Inventory of Industrial Fluoro-Biochemicals*, Eyrolles, Paris, 1996.
4 B. R. Langlois, T. Billard, S. Large and N. Roques, *Fluorinated Bio-active Compounds*, Fluorine Technology, Cheshire, 1999, Paper 24.
5 V. N. Boiko, *Beilstein J. Org. Chem.*, 2010, **6**, 880–921.
6 A. Tlili and T. Billard, *Angew. Chem., Int. Ed.*, 2013, **52**, 6818–6819.
7 G. Landelle, A. Panossian, S. Pazenok, J.-P. Vors and F. R. Leroux, *Beilstein J. Org. Chem.*, 2013, **9**, 2476–2536.
8 C. Pooput, W. R. Dolbier and M. Médebielle, *J. Org. Chem.*, 2006, **71**, 3564–3568.
9 G. Blond, T. Billard and B. R. Langlois, *Tetrahedron Lett.*, 2001, **42**, 2473–2475.
10 N. Roques, *J. Fluorine Chem.*, 2001, **107**, 311–314.
11 T. Billard and B. R. Langlois, *Tetrahedron Lett.*, 1996, **37**, 6865–6868.
12 U. Teruo and I. Sumi, *Tetrahedron Lett.*, 1990, **31**, 3579–3582.
13 T. Umemoto and S. Ishihara, *J. Am. Chem. Soc.*, 1993, **115**, 2156–2164.
14 I. Kieltsch, P. Eisenberger and A. Togni, *Angew. Chem., Int. Ed.*, 2007, **46**, 754–757.
15 C. Wakselman and M. Tordeux, *J. Org. Chem.*, 1985, **50**, 4047–4051.
16 C. Wakselman, M. Tordeux, J.-L. Clavel and B. Langlois, *J. Chem. Soc., Chem. Commun.*, 1991, 993–994.
17 B. Quiclet-Sire, R. N. Saicic and S. Z. Zard, *Tetrahedron Lett.*, 1996, **37**, 9057–9058.
18 T. Billard, N. Roques and B. R. Langlois, *J. Org. Chem.*, 1999, **64**, 3813–3820.
19 C. Pooput, M. Medebielle and W. R. Dolbier, *Org. Lett.*, 2004, **6**, 301–303.
20 A. Harsányi, É. Dorkó, Á. Csapó, T. Bakó, C. Peltz and J. Rábai, *J. Fluorine Chem.*, 2011, **132**, 1241–1246.
21 L. M. Yagupolskii, N. V. Kondratenko and V. P. Sambur, *Synthesis*, 1975, 721–723.
22 D. C. Remy, K. E. Rittle, C. A. Hunt and M. B. Freedman, *J. Org. Chem.*, 1976, **41**, 1644–1646.
23 Q.-Y. Chen and J.-X. Duan, *J. Chem. Soc., Chem. Commun.*, 1993, 918–919.
24 D. J. Adams, A. Goddard, J. H. Clark and D. J. Macquarrie, *Chem. Commun.*, 2000, 987–988.
25 D. J. Adams and J. H. Clark, *J. Org. Chem.*, 2000, **65**, 1456–1460.
26 W. Tyrra, D. Naumann, B. Hoge and Y. L. Yagupolskii, *J. Fluorine Chem.*, 2003, **119**, 101–107.
27 G. Teverovskiy, D. S. Surry and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2011, **50**, 7312–7314.
28 C. Chen, Y. Xie, L. Chu, R.-W. Wang, X. Zhang and F.-L. Qing, *Angew. Chem., Int. Ed.*, 2012, **51**, 2492–2495.
29 C.-P. Zhang and D. A. Vicic, *J. Am. Chem. Soc.*, 2012, **134**, 183–185.
30 C.-P. Zhang and D. A. Vicic, *Chem. – Asian J.*, 2012, **7**, 1756–1758.
31 L. D. Tran, I. Popov and O. Daugulis, *J. Am. Chem. Soc.*, 2012, **134**, 18237–18240.
32 Y.-D. Yang, A. Azuma, E. Tokunaga, M. Yamasaki, M. Shiro and N. Shibata, *J. Am. Chem. Soc.*, 2013, **135**, 8782–8785.
33 M. Rueping, N. Tolstoluzhsky and P. Nikolaienko, *Chem. – Eur. J.*, 2013, **19**, 14043–14046.
34 A. Ferry, T. Billard, B. R. Langlois and E. Bacqué, *Angew. Chem., Int. Ed.*, 2009, **48**, 8551–8555.
35 A. Ferry, T. Billard, E. Bacqué and B. R. Langlois, *J. Fluorine Chem.*, 2012, **134**, 160–163.
36 F. Baert, J. Colomb and T. Billard, *Angew. Chem., Int. Ed.*, 2012, **51**, 10382–10385.
37 X. Shao, X. Wang, T. Yang, L. Lu and Q. Shen, *Angew. Chem., Int. Ed.*, 2013, **52**, 3457–3460.
38 T. Bootwicha, X. Liu, R. Pluta, I. Atodiresei and M. Rueping, *Angew. Chem., Int. Ed.*, 2013, **52**, 12856–12859.
39 A. A. Kolomeitsev, K. Y. Chabanenko, G. V. Röschenthaler and Y. L. Yagupolskii, *Synthesis*, 1994, 145–146.
40 R. M. DeMarinis, J. R. E. Hoover, G. L. Dunn, P. Actor, J. V. Uri and J. A. Weisbach, *J. Antibiot.*, 1975, **28**, 463–470.
41 A. Rudolph and M. Lautens, *Angew. Chem., Int. Ed.*, 2009, **48**, 2656–2670.
42 E. Anselmi, J.-C. Blazejewski, M. Tordeux and C. Wakselman, *J. Fluorine Chem.*, 2000, **105**, 41–44.
43 T. Billard, S. Large and B. R. Langlois, *Tetrahedron Lett.*, 1997, **38**, 65–68.
44 N. V. Ignat'ev, V. N. Boiko and L. M. Yagupolskii, *Zh. Org. Khim.*, 1985, **21**, 653.
45 Z. Weng, W. He, C. Chen, R. Lee, D. Tan, Z. Lai, D. Kong, Y. Yuan and K.-W. Huang, *Angew. Chem., Int. Ed.*, 2013, **52**, 1548–1552.
46 D. Kong, Z. Jiang, S. Xin, Z. Bai, Y. Yuan and Z. Weng, *Tetrahedron*, 2013, **69**, 6046–6050.
47 J. Tan, G. Zhang, Y. Ou, Y. Yuan and Z. Weng, *Chin. J. Chem.*, 2013, **31**, 921–926.
48 P. Zhu, X. He, X. Chen, Y. You, Y. Yuan and Z. Weng, *Tetrahedron*, 2014, **70**, 672–677.
49 T. M. Figg, M. Wasa, J.-Q. Yu and D. G. Musaev, *J. Am. Chem. Soc.*, 2013, **135**, 14206–14214.
50 K. Urgin, C. Aubé, M. Pipelier, V. Blot, C. Thobie-Gautier, S. Sengmany, J. Lebreton, E. Léonel, D. Dubreuil and S. Condon, *Eur. J. Org. Chem.*, 2013, 117–124.
51 S. K. Gurung, S. Thapa, A. S. Vangala and R. Giri, *Org. Lett.*, 2013, **15**, 5378–5381.
52 H.-F. Duan, J.-H. Xie, W.-J. Shi, Q. Zhang and Q.-L. Zhou, *Org. Lett.*, 2006, **8**, 1479–1481.
53 B. Maillard, D. Forrest and K. U. Ingold, *J. Am. Chem. Soc.*, 1976, **98**, 7024–7026.
54 Y. Liu, C. Chen, H. Li, K.-W. Huang, J. Tan and Z. Weng, *Organometallics*, 2013, **32**, 6587–6592.
55 Y. Dai, F. Wu, Z. Zang, H. You and H. Gong, *Chem. – Eur. J.*, 2012, **18**, 808–812.

56 P. Ren, O. Vechorkin, K. v. Allmen, R. Scopelliti and X. Hu, *J. Am. Chem. Soc.*, 2011, **133**, 7084–7095.
57 W. L. F. Armerego and C. L. L. Chai, *Purification of Laboratory Chemicals*, Elsevier, Amsterdam, 6th edn, 2009.
58 V. M. Timoshenko and C. Portella, *J. Fluorine Chem.*, 2009, **130**, 586–590.
59 J. W. Cubbage, Y. Guo, R. D. McCulla and W. S. Jenks, *J. Org. Chem.*, 2001, **66**, 8722–8736.
60 A. Hasegawa, T. Ishikawa, K. Ishihara and H. Yamamoto, *Bull. Chem. Soc. Jpn.*, 2005, **78**, 1401–1410.
61 J. B. Hendrickson and P. L. Skipper, *Tetrahedron*, 1976, **32**, 1627–1635.