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Ag-Mediated Trifluoromethylthiolation of Inert Csp^3−H Bond

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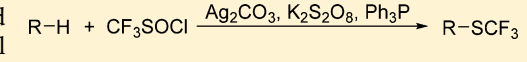
Supporting Information

ABSTRACT: Ag-mediated trifluoromethylthiolation of inert Csp^3−H bond with CF_3SOCl is described. Widely available reagents and operational simplicity make this protocol attractive.



Due to its strong electron-withdrawing nature (Hammett constants σ_p = 0.50, σ_m = 0.40) and high lipophilicity (Hansch parameter π = 1.44),[1] the trifluoromethylthio group (CF_3S) has received increasing attention in medicinal chemistry, agrochemistry, and material science.[2] Consequently, determined efforts have been devoted to the development of efficient methods for the installation of a CF_3S moiety to organic molecules.[2d,3] As C−H functionalization is an attractive concept because of its step economy, C−H trifluoromethylthiolation has become a straightforward strategy for CF_3S installation. Compared with trifluoromethylthiolation of the Csp^2−H bond[4] and Csp−H bond,[5] trifluoromethylthiolation of the inert Csp^3−H bond remains a challenging task.

In 2014, Qing reported a Cu-catalyzed Csp^3−H trifluoromethylthiolation, in which the Csp^3−H bond has to be an activated benzylic C−H bond (Scheme 1, eq 1).[6] Shortly afterward, Besset disclosed a Pd-catalyzed trifluoromethylthiolation of inert Csp^3−H bond. The desired products could be obtained in moderate yields, but a bulky directing group is required to be incorporated into the substrates (eq 2).[7] Almost at the same time, Chen[8] and Tang[9] independently described a radical trifluoromethylthiolation of alkanes with $AgSCF_3$ under oxidative conditions (eqs 3 and 4). A wide substrate scope and good functional group compatibility were observed in both approaches. Recently, photocatalytic radical trifluoromethylthiolation was achieved by the group of Glorius (eq 5).[10] Although good site selectivity and high yields were obtained, an expensive photocatalyst is needed. Apparently, the trifluoromethylthiolation reagents used in the above methods are expensive or have to be prepared via tedious synthetic procedures. We have been interested in the development of effective protocols for the incorporation of fluorine-containing functionalities into organic molecules.[11] We found that trifluoromethanesulfinic chloride (CF_3SOCl) could act as a trifluoromethylthio source to realize Ag-mediated radical trifluoromethylthiolation of inert Csp^3−H bond (eq 6). All reagents in this protocol are widely available and easy to handle.

As it has been previously reported that phosphorus species could reduce CF_3SO_2Cl to provide active trifluoromethylthiolation intermediates,[12] Ph_3P was used as a reducing agent in our initial attempts at the trifluoromethylthiolation of octane with CF_3SOCl (Table 1). A brief survey of the metal complex (entries 1−5) revealed that Ag_2CO_3 was quite effective (entry 2). Interestingly, no desired product was observed in other solvents (entries 6−8) except CH_3CN. An oxidant is necessary in the reaction, and replacing $K_2S_2O_8$ with other oxidants dramatically decreased the yield (entries 9 and 10). A reaction temperature of 60 °C proved superior to a lower or higher temperature (entry 2 vs entries 11 and 12). Increasing the loading of oxidant from 1.0 equiv to 1.5 equiv increased the yield to 77% (entry 13). However, the results were not reproducible (yields varied between 47% and 77%) if substrate **1a** was used in the same equivalent with reagent **2** (entry 13). To our delight, the reaction could be well reproduced by using slight excess of substrate **1a** (entry 14). A lower yield was obtained within a shorter reaction time (entry 15). One equivalent of Ag_2CO_3 was necessary, and decreasing the loading of Ag_2CO_3 led to the dramatic decrease in the yield (entries 16−19). No desired product was observed by replacing Ag_2CO_3 with K_2CO_3 (entry 20), suggesting that Ag_2CO_3 played a crucial role in the reaction.

With the optimized reaction conditions in hand (Table 1, entry 14), we then investigated the substrate scope of the Ag-mediated trifluoromethylthiolation of inert Csp^3−H bond. As shown in Scheme 2, a variety of alkanes could be converted smoothly into the desired products in moderate to high yields. A large-scale reaction (10 mmol CF_3SOCl) could also give the desired product in a good yield (**3a**, 75% ^{19}F NMR yield), demonstrating the potential application of this reaction. Some trifluoromethylthiolation products are volatile, and therefore, lower isolated yields compared to ^{19}F NMR yields were obtained. Although C−H bond dissociation energies decrease in the order of secondary > tertiary, both secondary and tertiary carbons were found to be quite reactive, and tertiary carbon showed a higher reactivity. If two tertiary carbons were present in the substrates, trifluoromethylthiolation would prefer to take place at the position which is remote from electron-withdrawing groups (**3q**−**3t**). A wide range of

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Scheme 1. Csp^3−H Trifluoromethylthiolation

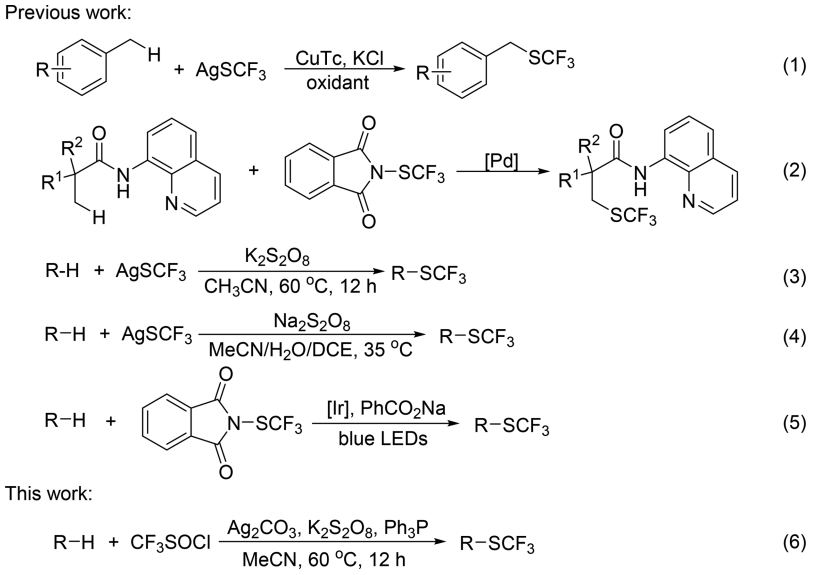
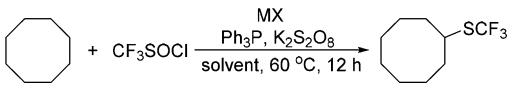


Table 1. Optimization of the Reaction Conditions



entry	MX	solvent	ratio[b]	yield (%)[c]
1	$AgNO_3$	CH_3CN	1:1:1:1.5:1	0
2	Ag_2CO_3	CH_3CN	1:1:1:1.5:1	55
3	AgF	CH_3CN	1:1:1:1.5:1	21
4	CuSCN	CH_3CN	1:1:1:1.5:1	0
5	CuCl	CH_3CN	1:1:1:1.5:1	0
6	Ag_2CO_3	DMF	1:1:1:1.5:1	0
7	Ag_2CO_3	DCM	1:1:1:1.5:1	0
8	Ag_2CO_3	$PhCH_3$	1:1:1:1.5:1	0
9[d]	Ag_2CO_3	CH_3CN	1:1:1:1.5:1	trace
10[e]	Ag_2CO_3	CH_3CN	1:1:1:1.5:1	trace
11[f]	Ag_2CO_3	CH_3CN	1:1:1:1.5:1	46
12[g]	Ag_2CO_3	CH_3CN	1:1:1:1.5:1	57
13	Ag_2CO_3	CH_3CN	1:1:1:1.5:1.5	77
14	Ag_2CO_3	CH_3CN	1.5:1:1:1.5:1.5	80
15[h]	Ag_2CO_3	CH_3CN	1.5:1:1:1.5:1.5	65
16	Ag_2CO_3	CH_3CN	1.5:1:0.8:1.5:1.5	57
17	Ag_2CO_3	CH_3CN	1.5:1:0.6:1.5:1.5	35
18	Ag_2CO_3	CH_3CN	1.5:1:0.5:1.5:1.5	0
19	–	CH_3CN	1.5:1:0:1.5:1.5	0
20	K_2CO_3	CH_3CN	1.5:1:1:1.5:1.5	0

[a]Reaction conditions: **1a**, **2** (0.4 mmol), MX (1 equiv), Ph_3P (1.5 equiv), and $K_2S_2O_8$ in CH_3CN (3 mL) at 60 °C for 12 h. [b]Molar ratio of **1a**/**2**/MX/Ph_3P/$K_2S_2O_8$. [c]The yields were determined by ^{19}F NMR spectroscopy. [d]$NaIO_4$ was used instead of $K_2S_2O_8$. [e]$PhI(OAc)_2$ was used instead of $K_2S_2O_8$. [f]The reaction temperature was 50 °C. [g]The reaction temperature was 70 °C. [h]The reaction time was 6 h.

functional groups could be tolerated, such as ketones, esters, amides, ethers, halides, and nitriles, demonstrating the synthetic utility of this protocol. To our surprise, the benzylic C−H bond is inert under these conditions. For instance, no desired product was observed for the conversion of toluene or 1-ethylnaphthalene.

Some preliminary experimental results were collected to gain more mechanistic insights into the C−H trifluoromethylthiolation process. The reaction gave the desired product in low yields in the presence of a radical scavenger, such as TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl), hydroquinone, or 1,4-dinitrobenzene, suggesting that a radical pathway may be involved (Scheme 3, eq 1). For the conversion of substrate **1o**, a cyclization product (**3o′**) was produced in 45% yield (eq 2), further supporting the radical mechanism. Without the presence of the CF_3SOCl/Ph_3P system, substrate **1o** could also be converted into cyclization product **3o′**, indicating that the $Ag_2CO_3/K_2S_2O_8$ system would lead to the generation of a radical intermediate from the substrate (eq 3).

Although Ph_3P is a reducing agent and $K_2S_2O_8$ is an oxidizing agent, the reaction between them is quite slow, whereas the reaction of Ph_3P with CF_3SOCl occurred rapidly. Almost no Ph_3P was converted by heating the mixture of Ph_3P and $K_2S_2O_8$ at 60 °C for 10 min. But, after the mixture of Ph_3P and CF_3SOCl was stirred for 10 min, CF_3SOCl was completely consumed to produce a major product, CF_3SSCF_3, which was confirmed by ^{19}F NMR spectroscopy (δ: −46.2 ppm)[13] and GC-MS (M^+: 201.9) (Scheme 4, eq 1). ^{31}P NMR analysis of the reaction mixture revealed that Ph_3P was completely converted into two species, $Ph_3P{=}O$ and ($Ph_3P^+Cl\ Cl^-$) (δ: +65 ppm)[14] (eq 1). The molar ratio of these two species determined by ^{31}P NMR spectroscopy was 3.4:1 [$Ph_3P{=}O$/($Ph_3P^+Cl\ Cl^-$)]. After the complete conversion of CF_3SOCl into CF_3SSCF_3, substrate **1a** and the $Ag_2CO_3/K_2S_2O_8$ reagent system were added, and the resultant mixture was stirred at 60 °C for 12 h (eq 2). A 60% ^{19}F NMR yield of the desired product was obtained, suggesting that CF_3SSCF_3 is a key intermediate for this trifluoromethylthiolation process.

On the basis of the above results, the plausible mechanism is proposed as shown in Scheme 5. CF_3SOCl could be reduced by Ph_3P to form CF_3SCl (trifluoromethanesulfenyl chloride) via a halogen bonding process to form chlorophosphonium salt (ClP^+Ph_3) and an Arbuzov conversion to release $Ph_3P{=}O$.[12] A further halogen bonding process between Ph_3P and CF_3SCl generates chlorophosphonium salt (ClP^+Ph_3) and trifluoromethylthio anion (CF_3S^-), which attacks CF_3SCl to produce CF_3SSCF_3 and a chloride anion. The disproportionation of peroxydisulfate anion in the presence of a Ag^+ salt gives a sulfate radical anion.[15] The abstraction of a hydrogen atom

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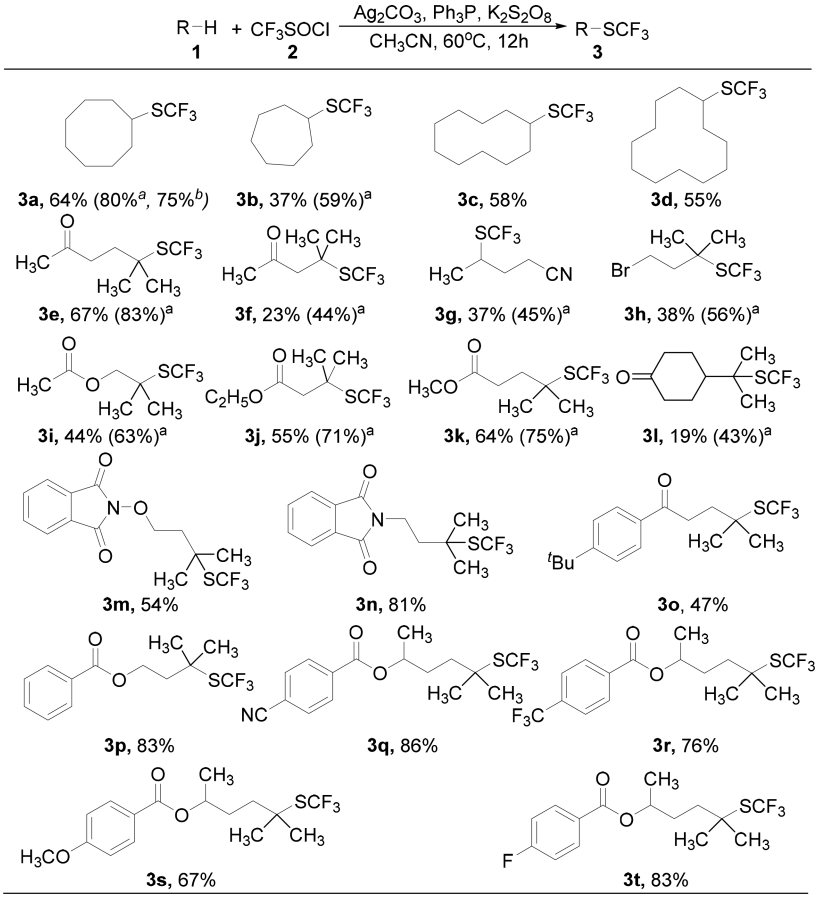
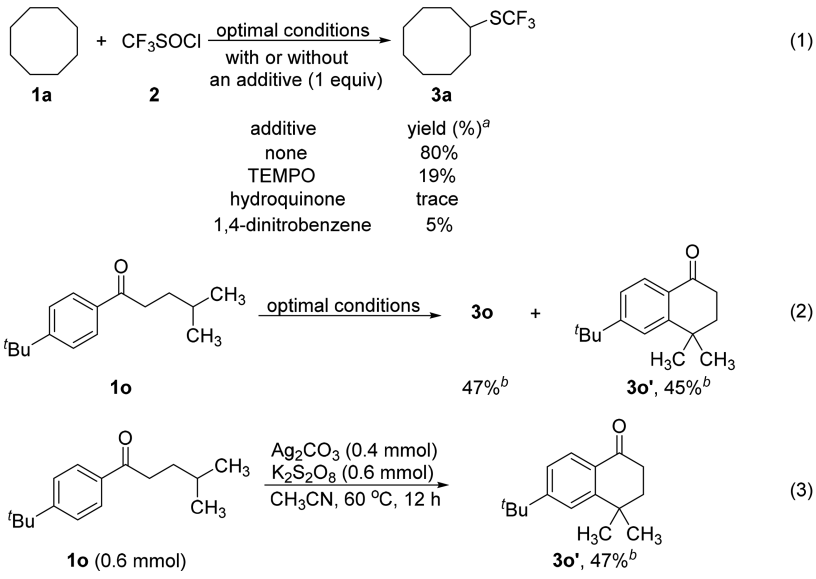
Scheme 2. Ag-Mediated Trifluoromethylthiolation of Inert Csp^3–H Bond[c]



[c]Isolated yields. Reaction conditions: substrate **1** (1.5 equiv), CF_3SOCl (0.4 mmol, 1 equiv), Ag_2CO_3 (1 equiv), Ph_3P (1.5 equiv), and $K_2S_2O_8$ (1.5 equiv) in CH_3CN (3 mL) at 60 °C for 12 h. Within the schematic: [a]the yields were determined by ^{19}F NMR spectroscopy; [b]a 75% ^{19}F NMR yield was obtained by increasing the reaction scale to 10 mmol (CF_3SOCl).

Scheme 3. Mechanistic Evidence[c]



[c]Within the schematic: [a]the yield was determined by ^{19}F NMR spectroscopy; [b]isolated yield.

from the substrates by the sulfate radical anion would readily occur to generate an alkyl radical. The reaction of the alkyl radical with CF_3SSCF_3 provides the final trifluoromethylthiolation product and a trifluoromethylthio radical ($CF_3S^{\bullet}$), the combination of which with the alkyl radical also furnishes the trifluoromethylthiolation product.

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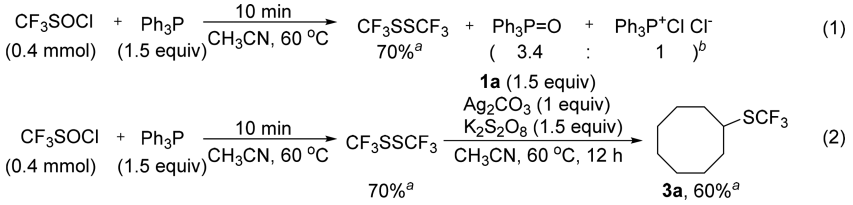
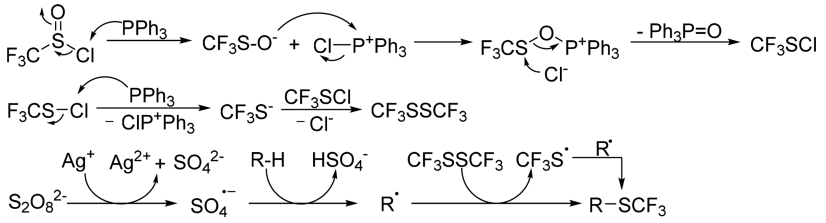
Scheme 4. Mechanistic Investigations[c]



[c]Within the schematic: [a]the yield was determined by ^{19}F NMR spectroscopy; [b]the molar ratio was determined by ^{31}P NMR spectroscopy.

Scheme 5. Proposed Reaction Mechanism



In summary, we have described the Ag-mediate trifluoromethylthiolation of inert Csp^3–H bond with CF_3SOCl. All reagents used in this process were widely available, and the reactions occurred smoothly under mild conditions. A broad substrate scope and good functional group compatibility were observed, demonstrating the synthetic utility of this trifluoromethylthiolation protocol. Due to its operational convenience and step economy, the protocol may find application in the synthesis of CF_3S-containing pharmaceuticals and agrochemicals.

EXPERIMENTAL SECTION

General Information. ^1H, ^{13}C, and ^{19}F NMR spectra were detected on a 500, 400, or 300 MHz NMR spectrometer. Data for ^1H, ^{13}C, and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, coupling constant (s) in Hz). Mass spectra were obtained on a GC-MS or LC-MS (ESI) instrument. High-resolution mass data were recorded on a high-resolution mass spectrometer in the ESI mode. The mass analyzer type for HRMS-ESI is a Fourier transform mass spectrometer. Unless otherwise noted, all reagents, including CF_3SOCl (95% purity), were obtained commercially and used without further purification.

General Procedure for Trifluoromethylthiolation. Under an N_2 atmosphere, into a 15 mL sealed tube was added triphenylphosphine (0.6 mmol, 1.5 equiv), $K_2S_2O_8$ (0.6 mmol, 1.5 equiv), Ag_2CO_3 (0.4 mmol, 1.0 equiv), CH_3CN (3 mL), alkane substrate (0.6 mmol, 1.5 equiv), and trifluoromethanesulfinic chloride (0.4 mmol, 1.0 equiv). The tube was sealed, and the mixture was stirred at 60 °C for 12 h. After being cooled to room temperature, the mixture was filtered to remove the solid. The solid was washed with dichloromethane, and the combined organic phase was concentrated to remove the solvent. The residue was subjected to flash column chromatography to give the pure product.

*Cyclooctyl(trifluoromethyl)sulfane (**3a**).*[8] 64% yield; 54 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.53–3.46 (m, 1H), 2.11–2.04 (m, 2H), 1.83–1.69 (m, 4H), 1.63–1.49 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 131.7 (q, J = 306.1 Hz), 45.9, 32.9, 27.5, 25.9, 25.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −39.70 (s, 3F). GC-MS (EI) m/z: 212.2 (M^+).

*Cycloheptyl(trifluoromethyl)sulfane (**3b**).*[8] 37% yield; 29 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.49–3.42 (m, 1H), 2.13–2.06 (m, 2H), 1.78–1.66 (m, 4H), 1.63–1.49 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 131.6 (q, J = 306.2 Hz), 46.3, 35.8, 28.4, 25.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −39.68 (s, 3F). GC-MS (EI) m/z: 198.1 (M^+).

*Cyclodecyl(trifluoromethyl)sulfane (**3c**).*[8] 58% yield; 56 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.59–3.53 (m, 1H), 1.97–1.79 (m, 4H), 1.71–1.61 (m, 4H), 1.57–1.52 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 131.7 (q, J = 306.1 Hz), 44.0, 32.2, 25.6, 25.1, 24.9, 23.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −39.61 (s, 3F). GC-MS (EI) m/z: 240.2 (M^+).

*Cyclododecyl(trifluoromethyl)sulfane (**3d**).*[8] 55% yield; 59 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.35–3.29 (m, 1H), 1.86–1.77 (m, 2H), 1.69–1.61 (m, 2H), 1.57–1.50 (m, 2H), 1.42–1.31 (m, 16H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 131.8 (q, J = 306.1 Hz), 42.9, 31.3, 24.2, 24.0, 23.8, 23.7, 22.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −39.59 (s, 3F). GC-MS (EI) m/z: 268.1 (M^+).

*5-Methyl-5-((trifluoromethyl)thio)hexan-2-one (**3e**).*[8] 67% yield; 57 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.60 (t, J = 8.1 Hz, 2H), 2.15 (s, 3H), 1.92 (t, J = 7.6 Hz, 2H), 1.41 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 207.6, 131.1 (q, J = 308.1 Hz), 51.7, 39.4, 36.4, 30.2, 29.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.97 (s, 3F). GC-MS (EI) m/z: 214.0 (M^+).

*4-Methyl-4-((trifluoromethyl)thio)pentan-2-one (**3f**).*[8] 23% yield; 18 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.90 (s, 2H), 2.16 (s, 3H),1.58 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 205.5, 131.2 (q, J = 307.7 Hz), 54.8, 49.4, 32.1, 29.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.68 (s, 3F). GC-MS (EI) m/z: 200.0 (M^+).

*4-((Trifluoromethyl)thio)pentanenitrile (**3g**).*[8] 37% yield; 27 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.42–3.34 (m, 1H), 2.54 (t, J = 7.3 Hz, 2H), 2.07–1.91 (m, 2H), 1.49 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 130.9 (q, J = 308.1 Hz), 118.8, 40.2, 32.7, 22.4, 15.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −38.94 (s, 3F). GC-MS (EI) m/z: 183.0 (M^+).

*(4-Bromo-2-methylbutan-2-yl)(trifluoromethyl)sulfane (**3h**).*[8] 38% yield; 38 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.48 (t, J = 8.3 Hz, 2H), 2.28 (t, J = 8.0 Hz, 2H), 1.48 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 130.9 (q, J = 307.9 Hz), 52.0, 46.4, 29.7, 27.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.95 (s, 3F). GC-MS (EI) m/z: 251.9 (M^+).

*2-Methyl-2-((trifluoromethyl)thio)propyl Acetate (**3i**).* 44% yield; 38 mg; colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ: 4.14 (s, 2H), 2.10 (s, 3H), 1.46 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.8, 130.9 (q, J = 309.1 Hz), 71.1, 50.1, 26.5, 21.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.45 (s, 3F). HRMS-ESI (m/z): calcd for $C_7H_{15}F_3O_2SN$ $[M + NH_4]^+$, 234.0770; found, 234.0770. IR(KBr): 2962, 1261, 1096, 1027, 799, 704 cm^{-1}.

*Ethyl 3-Methyl-3-((trifluoromethyl)thio)butanoate (**3j**).* 55% yield; 51 mg; colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ: 4.15 (q, J = 7.1 Hz, 2H), 2.75 (s, 2H), 1.59 (s, 6H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 169.9, 131.1 (q, J = 307.9 Hz), 61.0, 49.2, 47.8, 29.4, 14.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.91

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(s, 3F). HRMS-ESI (m/z): calcd for $C_8H_{17}F_3O_2SN$ $[M + NH_4]^+$, 248.0927; found, 248.0926. IR(KBr): 2962, 2929, 1734, 1466, 1371, 1119, 1035, 869, 805, 756, 721 cm^{-1}.

*Methyl 4-Methyl-4-((trifluoromethyl)thio)pentanoate (**3k**).*[9] 64% yield; 59 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.66 (s, 3H), 2.47 (t, J = 8.3 Hz, 2H), 2.01 (t, J = 8.1 Hz, 2H), 1.43 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.7, 131.1 (q, J = 307.6 Hz), 52.1, 51.5, 37.9, 30.1, 29.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.97 (s, 3F). GC-MS (EI) m/z: 129.1 ($[M - SCF_3]^+$).

*4-(2-((Trifluoromethyl)thio)propan-2-yl)cyclohexan-1-one (**3l**).*[10] 19% yield; 18 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.45−2.21 (m, 6H), 2.05−1.99 (m, 1H), 1.62−1.51 (m, 2H), 1.46 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 210.9, 131.3 (q, J = 309.1 Hz), 55.5, 46.4, 40.9, 27.7, 27.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.01 (s, 3F). GC-MS (EI) m/z: 240.1 (M^+).

*2-(3-Methyl-3-((trifluoromethyl)thio)butoxy)isoindoline-1,3-dione (**3m**).*[8] 54% yield; 72 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.83−7.79 (m, 2H), 7.76−7.73 (m, 2H), 4.38 (t, J = 6.4 Hz, 2H), 2.22 (t, J = 6.4 Hz, 2H), 1.56 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.7, 134.9, 131.0 (q, J = 307.6 Hz), 129.2, 123.9, 75.5, 50.8, 40.9, 30.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.89 (s, 3F). MS (EI) m/z: 232.1 ($[M - SCF_3]^+$).

*2-(3-Methyl-3-((trifluoromethyl)thio)butyl)isoindoline-1,3-dione (**3n**).*[8] 81% yield; 103 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.82−7.80 (m, 2H), 7.70−7.68 (m, 2H), 3.82 (t, J = 7.9 Hz, 2H), 2.04 (t, J = 7.9 Hz, 2H), 1.52 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 168.3, 134.3, 132.4, 131.0 (q, J = 307.9 Hz), 123.5, 50.4, 41.1, 34.5, 29.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.76 (s, 3F). GC-MS (EI) m/z: 317.1 (M^+).

*1-(4-(tert-Butyl)phenyl)-4-methyl-4-((trifluoromethyl)thio)-pentan-1-one (**3o**).* 47% yield; 62 mg; colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, J = 8.5 Hz, 2H), 7.49 (d, J = 8.5 Hz, 2H), 3.14 (t, J = 7.8 Hz, 2H), 2.14 (t, J = 7.7 Hz, 2H), 1.51 (s, 6H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 199.1, 157.3, 134.5, 131.3 (q, J = 309.1 Hz), 128.4, 125.9, 52.1, 37.1, 35.5, 34.4, 31.4, 30.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.77 (s, 3F). HRMS-ESI (m/z): calcd for $C_{17}H_{24}F_3OS$ $[M + H]^+$, 333.1494; found, 333.1494. IR(KBr): 2967, 2907, 2870, 1683, 1606, 1568, 1470, 1392, 1318, 1225, 1098, 999, 842, 755, 583 cm^{-1}.

*3-Methyl-3-((trifluoromethyl)thio)butyl benzoate (**3p**).*[9] 83% yield; 97 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.03 (d, J = 8.0 Hz, 1H), 7.56 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 4.52 (t, J = 6.7 Hz, 2H), 2.21 (t, J = 6.7 Hz, 2H), 1.56 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.7, 133.4, 131.1 (q, J = 307.6 Hz), 130.4, 129.9, 128.7, 61.9, 50.6, 41.6, 30.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.76 (s, 3F). GC-MS (EI) m/z: 292.1 (M^+).

*5-Methyl-5-((trifluoromethyl)thio)hexan-2-yl 4-Cyanobenzoate (**3q**).*[9] 86% yield; 119 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.11 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H), 5.18−5.13 (m, 1H), 1.95−1.68 (m, 4H), 1.44 (s, 6H), 1.37 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.7, 134.7, 132.5, 131.2 (q, J = 307.6 Hz), 130.3, 118.3, 116.6, 72.8, 51.8, 38.9, 31.4, 29.7, 20.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.80 (s, 3F). GC-MS (EI) m/z: 244.1 ($[M - SCF_3]^+$).

*5-Methyl-5-((trifluoromethyl)thio)hexan-2-yl 4-(Trifluoromethyl)benzoate (**3r**).*[9] 76% yield; 118 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.14 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.1 Hz, 2H), 5.30−4.93 (m, 1H), 1.98−1.66 (m, 4H), 1.46 (s, 6H), 1.39 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.3, 134.7 (q, J = 32.7 Hz), 134.2, 131.3 (q, J = 309.1), 130.3, 125.7 (q, J = 3.7 Hz), 124.0 (q, J = 272.6 Hz), 72.5, 51.9, 39.0, 31.5, 29.8, 20.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.83 (s, 3F), −63.18 (s, 3F). ESI (m/z): $C_{16}H_{18}F_6O_2SNa$ $[M + Na]^+$, 411.1.

*5-Methyl-5-((trifluoromethyl)thio)hexan-2-yl 4-Methoxybenzoate (**3s**):*[9] 67% yield; 93 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 5.13−5.09 (m, 1H), 3.85 (s, 3H), 1.93−1.67 (m, 4H), 1.45 (s, 6H), 1.35 (d, J = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.2, 163.6, 131.8, 131.3 (q, J = 307.6 Hz), 123.3, 113.9, 71.2, 55.7, 52.0, 39.1, 31.6, 29.8, 20.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.76 (s, 3F). GC-MS (EI) m/z: 350.2 (M^+).

*5-Methyl-5-((trifluoromethyl)thio)hexan-2-yl 4-Fluorobenzoate (**3t**).*[9] 83% yield; 112 mg. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.06−8.02 (m, 2H), 7.10 (t, J = 8.5 Hz, 2H), 5.15−5.11 (m, 1H), 1.92−1.68 (m, 4H), 1.45 (s, 6H), 1.36 (d, J = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.1 (d, J = 253.5 Hz), 165.5, 132.4 (d, J = 9.8 Hz), 131.3 (q, J = 307.6 Hz), 127.2 (d, J = 3.4 Hz), 115.8 (d, J = 21.9 Hz), 71.9, 51.9, 39.0, 31.6, 29.8, 20.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −35.80 (s, 3F), −105.96 ∼ −106.05 (m, 1F). GC-MS (EI) m/z: 237.1 ($[M - SCF_3]^+$).

*6-(tert-Butyl)-4,4-dimethyl-3,4-dihydronaphthalen-1(2H)-one (**3o′**).* 45% yield; 41 mg; colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, J = 8.3 Hz, 1H), 7.42 (d, J = 1.9 Hz, 1H), 7.33 (dd, J = 8.3, 19 Hz, 1H), 2.70 (t, J = 6.8 Hz, 2H), 2.01 (t, J = 6.8 Hz, 2H), 1.39 (s, 6H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 198.5, 157.7, 152.3, 129.1, 127.5, 123.9, 122.6, 37.6, 35.6, 35.4, 34.4, 31.4, 30.1. HRMS-ESI (m/z): calcd for $C_{16}H_{23}O$ $[M + H]^+$, 231.1743; found, 231.1743. IR(KBr): 3351, 2961, 2868, 1685, 1604, 1465, 1387, 1285, 1198, 1092, 1021, 880, 837, 810, 696, 655, 569, 485 cm^{-1}.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b02207.

Copies of ^1H, ^{19}F, and ^{13}C NMR spectra of compounds (PDF)

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The authors declare no competing financial interest.

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