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Short Communication

Difluorocarbene-based trifluoromethylthiolation of terminal alkynes

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ABSTRACT

A large number of trifluoromethylthiolation methods have been developed, but a trifluoromethylthiolation reagent usually has to be used in these methods. Herein we describe a difluorocarbene-based trifluoromethylthiolation of terminal alkynes to construct a Csp—SCF_3 bond catalysed by a copper complex. $Ph_3P^+CF_2CO_2^-/S_8/F^-$ was used as a reagent system to form the CF_3S^- anion, and the sequential formation of CF_2═S, F—CF_2S and C—SCF_3 bonds was achieved in a one-step process.

1. Introduction

Due to its strong electron-withdrawing (Hammett constants $\sigma_p = 0.50$, $\sigma_m = 0.40$) and high lipophilicity (Hansch lipophilicity parameter $\pi = 1.44$) effects [1–3], the trifluoromethylthio group (CF_3S) has received particular attention in the design of pharmaceuticals and agrochemicals [4–6]. Many CF_3S-containing biologically active molecules have emerged recently, such as Toltrazuril, Tiflorex and Cefazaflur [6]. Therefore, significant efforts have been devoted to the development of efficient methods for the incorporation of a CF_3S group into organic molecules [6–16]. A large number of trifluoromethylthiolation reagents have been developed, including nucleophilic reagents, such as $AgSCF_3$ [17], $CuSCF_3$ [18–23] and $[R_4N]^+ {}^-SCF_3$ [24,25], and electrophilic reagents, such as N—SCF_3 type [26–32], O—SCF_3 type [33,34], and C—SO_2CF_3 type [35] reagents. The emergence of the general trifluoromethylthiolation reagents has allowed the development of a variety of trifluoromethylthiolation approaches, including nucleophilic [36–39], electrophilic [40–43] and radical [44–48] reactions, by which various C—SCF_3 bond could be effectively constructed.

The formation of a Csp—SCF_3 bond was usually achieved by trifluoromethylthiolation of terminal alkynes. Qing described an oxidative trifluoromethylthiolation with a nucleophilic reagent, $TMSCF_3/S_8$ system [49] or $AgSCF_3$ [50] in the presence of an oxidant, to afford CF_3S-alkynes in moderate to high yields (Scheme 1, eq 1). Billard [40,51,52], Rueping [29] and Shen [31,33,53] independently disclosed the trifluoromethylthiolation of terminal alkynes with electrophilic reagents (eq 1). The conversions were quite efficient, but suffered from strong basic reaction conditions or the need of tedious procedures to prepare the "CF_3S" reagents. Other alkynes, including alkynyl silanes [54], alkynyl acids [55], alkynyliodonium tosylates [56] and alkynyl bromides [57], could also be converted into CF_3S-alkynes by trifluoromethylthiolation transformation (eq 2). Obviously, the need for prefunctionalization of the substrates may limit their synthetic utility. Therefore, the development of convenient protocols for the formation of a Csp—SCF_3 bond is desirable.

Difluorocarbene has proved to be a versatile intermediate for the incorporation of CF_2 unit into molecules [58,59]. We recently developed a difluorocarbene reagent, $Ph_3P^+CF_2CO_2^-$ [60,61], and found that difluorocarbene could react with a suitable sulfur source to generate thiocarbonyl fluoride (CF_2═S) [62–64]. CF_2═S is an electrophilic species and could be readily trapped by F^- anion to provide CF_3S^- anion. This process was developed into a synthetic tool to enable ^{18}F-trifluoromethylthioaltion of alkyl electrophiles [62,63] and dehydroxytrifluoromethylthiolation of alcohols [65]. On the basis of these trifluoromethylthiolation conversions, we have now investigated the difluorocarbene-based trifluoromethylthiolation of terminal alkynes

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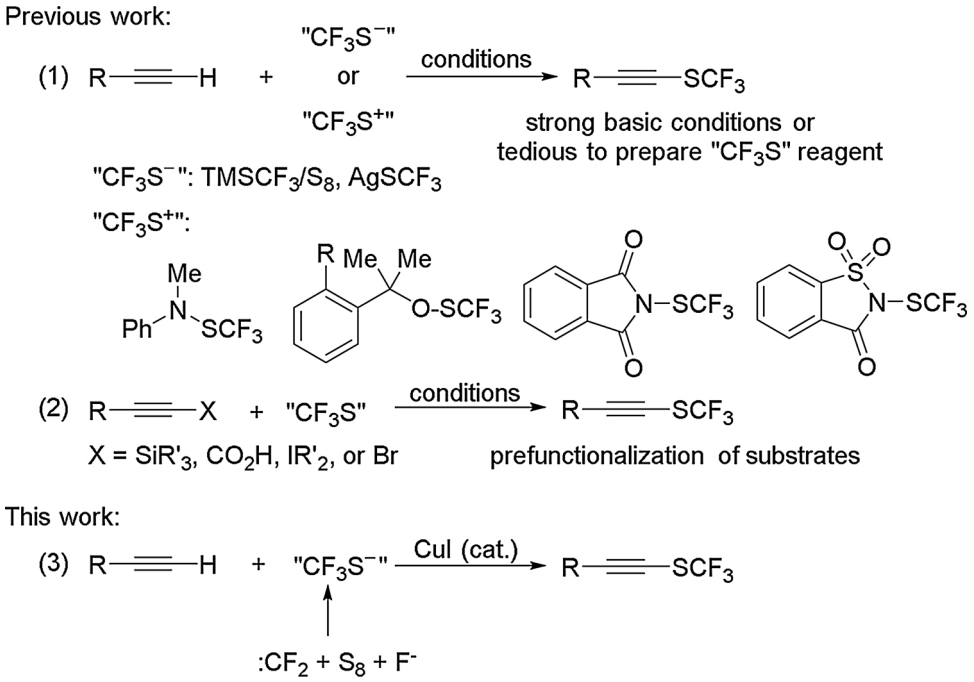


Scheme 1. The formation of Csp—SCF_3 bond by trifluoromethylthiolation.

catalyzed by a copper complex (Scheme 1, eq 3). A sequential formation of CF_2═S, F—CF_2S and C—SCF_3 bonds was achieved in a one-step process. $Ph_3P^+CF_2CO_2^-$, which was used as the difluorocarbene source in the transformations, could be easily prepared by a one-step reaction and purified by a simple washing procedure, and therefore the operationally convenient trifluoromethylthiolation protocol would be quite attractive.

2. Results and discussion

Although DMF was found to be a suitable solvent in the oxidative trifluoromethylthiolation [49], no desired product was observed in our initial attempts at the trifluoromethylthiolation of alkyne **1a** with the $Ph_3P^+CF_2CO_2^-/S_8/F^-$ system (Table 1, entry 1). To our delight, a 3 % yield was obtained by using ethyl acetate as the solvent (entry 2), which encouraged us to further screen other solvents. After the identification of the suitable solvent, THF (entry 4), we then examined various fluoride sources (entries 4–7). The lower solubility of KF did not lead to the decrease in the yield. Instead, the yield was increased to 26 % (entry 5 vs entry 4). Interestingly, decreasing the loadings of the copper complex gave higher yields (entries 8–9 vs entry 5), but no expected product was generated without using the copper complex (entry 11), indicating that the copper complex is essential for this conversion. A brief survey of the copper sources revealed that CuI was a superior choice (entry 9 vs entries 12–14). The use of a tertiary amine as the base afforded moderate yields (entries 9 and 15), but the desired transformation was completely suppressed when using a secondary amine (entry 16). The yield was increased by increasing the loadings of $Ph_3P^+CF_2CO_2^-$ and S_8 (entries 17–18). A high yield was obtained by replacing the ligand **L1** with **L4** (entry 21).

With the optimal reaction conditions in hand (Table 1, entry 21), we then investigated the substrate scope of the difluorocarbene-based trifluoromethylthiolation of terminal alkynes. As shown in Scheme 2, a wide range of terminal alkynes could be converted smoothly into the desired products in moderate to good yields. The examination of electronic effects showed that neither electron-donating nor -withdrawing groups had obvious side effects on the conversion of phenyl alkynes (**3a-3 l**). Pyridine heterocylces could be tolerated under these conditions (**3 m**). Besides phenyl alkynes, alkyl alkynes were also found to be reactive towards this conversion, but lower yields were obtained (**3n-3o**).

On the basis of the above results and our previous observations on difluorocarbene-based trifluoromethylthiolation [62,63,65], we propose that the mechanism shown in Scheme 3 is plausible. The CF_3S^- anion generated from $Ph_3P^+CF_2CO_2^-$ via :CF_2 followed by CF_2═S coordinates to the copper center to give Cu^ISCF_3 complex. The coordination of the terminal alkynes to Cu^ISCF_3 (intermediate **A**) increases the acidity of the terminal proton and thus a deprotonation would readily occur to provide copper acetylide (intermediate **B**). Elemental sulfur (S_8) may oxidize Cu^I to Cu^{III} (intermediate **C**), and the subsequent reductive elimination delivers the final products and releases the catalyst.

3. Conclusions

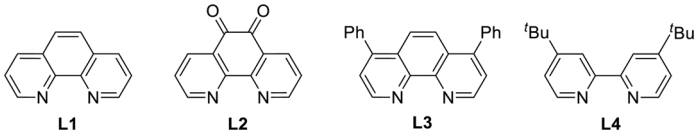
In summary, we have described the difluorocarbene-based trifluoromethylthiolation of terminal alkynes with the $Ph_3P^+CF_2CO_2^-/S_8/F^-$ system. A sequential formation of CF_2═S, F—CF_2S and C—SCF_3 bonds was achieved in a one-step transformation. The trifluoromethylthiolation protocol is attractive as $Ph_3P^+CF_2CO_2^-$ is easily available and shelf-stable. This process may find application in ^{18}F-trifluoromethylthiolation since an external fluoride anion is involved for the construction of the CF_3S moiety.

4. Experimental section

4.1. General remark

^1H, ^{13}C and ^{19}F NMR spectra were detected on a 400 MHz or 300 MHz NMR spectrometer. Data for ^1H NMR, ^{13}C NMR 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 GC–MS (EI). High resolution mass data were recorded on a high resolution mass spectrometer in the EI mode.

Table 1
The optimization of the reaction contidions.[a]



Entry	F^-	[Cu] (mol %)	Ligand (mol %)	Base	Molar ratio[b]	Yield (%)[c]
1[d]	CsF	CuI (100)	**L1** (100)	Et_3N	1 : 2.5 : 0.9	0
2[e]	CsF	CuI (100)	**L1** (100)	Et_3N	1 : 2.5 : 0.9	3
3[f]	CsF	CuI (100)	**L1** (100)	Et_3N	1 : 2.5 : 0.9	8
4[g]	CsF	CuI (100)	**L1** (100)	Et_3N	1 : 2.5 : 0.9	14
5	KF	CuI (100)	**L1** (100)	Et_3N	1 : 2.5 : 0.9	26
6	NaF	CuI (100)	**L1** (100)	Et_3N	1 : 2.5 : 0.9	13
7	TBAT	CuI (100)	**L1** (100)	Et_3N	1 : 2.5 : 0.9	10
8	KF	CuI (50)	**L1** (50)	Et_3N	1 : 2.5 : 0.9	31
9	KF	CuI (20)	**L1** (20)	Et_3N	1 : 2.5 : 0.9	44
10	KF	CuI (10)	**L1** (10)	Et_3N	1 : 2.5 : 0.9	30
11	KF	–	–	Et_3N	1 : 2.5 : 0.9	0
12	KF	CuBr (20)	**L1** (20)	Et_3N	1 : 2.5 : 0.9	trace
13	KF	CuCl (20)	**L1** (20)	Et_3N	1 : 2.5 : 0.9	trace
14	KF	CuOTf (20)	**L1** (20)	Et_3N	1 : 2.5 : 0.9	trace
15	KF	CuI (20)	**L1** (20)	TMEDA	1 : 2.5 : 0.9	46
16	KF	CuI (20)	**L1** (20)	Et_2NH	1 : 2.5 : 0.9	0
17	KF	CuI (20)	**L1** (20)	TMEDA	1 : 3 : 1.1	57
18	KF	CuI (20)	**L1** (20)	TMEDA	1 : 4 : 1.5	73
19[h]	KF	CuI (20)	**L2** (20)	TMEDA	1 : 4 : 1.5	82
20[h]	KF	CuI (20)	**L3** (20)	TMEDA	1 : 4 : 1.5	77
21[h]	KF	CuI (20)	**L4** (20)	TMEDA	1 : 4 : 1.5	84

[a] Reaction conditions: substrate **1a** (0.2 mmol), **2**, S_8, F^- (1.2 mmol), copper source [Cu], ligand, base (0.4 mmol) in THF (2 mL) at 60 °C for 2 h under a N_2 atmosphere; TBAT = *n*-tetrabutylammonium triphenyldifluorosilicate; TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.
[b] Molar ratio of **1a**:**2**:S_8.
[c] Determined by ^{19}F NMR spectroscopy.
[d] DMF was used as the solvent.
[e] EtOAc was used as the solvent.
[f] 1,4-dioxane was used as the solvent.
[g] THF was used as the solvent.
[h] The reaction time was 3 h.

4.2. General procedure for trifluoromethylthiolation

In to a 10 ml sealed tube were added alkynes **1** (0.4 mmol), $Ph_3P^+CF_2CO_2^-$ (570.1 mg, 1.6 mmol), S_8 (153.9 mg, 0.6 mmol), CuI (15.2 mg, 0.08 mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (21.5 mg, 0.08 mmol), KF (139.4 mg, 2.4 mmol), TMEDA (92.9 mg, 0.8 mmol) and anhydrous THF (4 mL) under a N_2 atmosphere. The tube was sealed and the resulting mixture was stirred at 60 °C for 3 h. After being cooled to room temperature, the mixture was filtered through a plug of Celite, and the solid was washed with DCM. The combined organic phase was washed with brine (10 mL × 3) and water (10 mL × 3) and dried with Na_2SO_4. The solvent was removed by concentration under vacuum, and the residue was subjected to flash column chromatography to give the final products.

4.3. Characterization of the products

(**3a**) [49]: White solid, 85 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.57 (m, 6 H), 7.47 (t, *J* = 7.4 Hz, 2 H), 7.43 – 7.37 (m, 1 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.6 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6 (s), 140.0 (s), 132.7 (s), 129.0 (s), 128.2 (q, *J* = 312.5 Hz), 128.0 (s), 127.2 (s), 127.1 (s), 120.4 (s), 101.3 (s), 67.3 (q, *J* = 4.1 Hz). GC–MS (EI): Calculated for $C_{15}H_9F_3S$ $[M]^+$: 278.0; Found: 278.1.

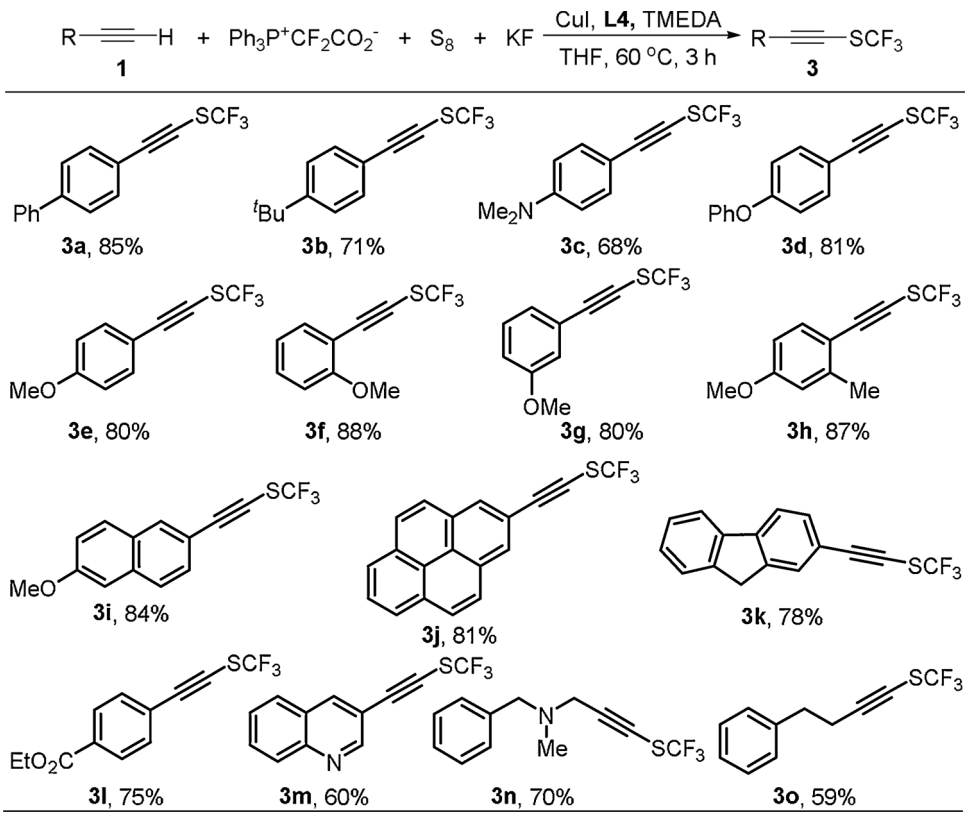
(**3b**) [49]: Colorless oil, 71 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.6 Hz, 2 H), 7.37 (d, *J* = 8.6 Hz, 2 H), 1.32 (s, 9 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.9 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3 (s), 131.1 (s), 127.1 (q, *J* = 312.5 Hz), 124.5 (s), 117.5 (s), 100.5 (s), 64.8 (q, *J* = 4.1 Hz), 33.9 (s), 30.0 (s). GC–MS (EI): Calculated for $C_{13}H_{13}F_3S$ $[M]^+$: 258.1; Found: 258.1.

(**3c**) [49]: Yellow solid, 68 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.7 Hz, 2 H), 6.60 (d, *J* = 8.9 Hz, 2 H), 2.99 (s, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −44.7 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.1 (s), 134.3 (s), 128.2 (q, *J* = 312.6 Hz), 111.5 (s), 107.8 (s), 103.2 (s), 63.9 (q, *J* = 4.4 Hz), 40.0 (s). GC–MS (EI): Calculated for $C_{11}H_{10}F_3NS$ $[M]^+$: 245.0; Found: 245.0.

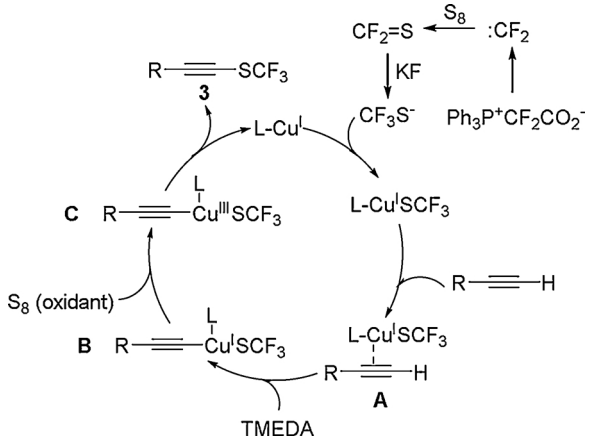
(**3d**): Pale yellow oil, 81 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.8 Hz, 2 H), 7.36 (t, *J* = 7.9 Hz, 2 H), 7.17 (t, *J* = 7.5 Hz, 1 H), 7.03 (d, *J* = 8.4 Hz, 2 H), 6.93 (d, *J* = 8.7 Hz, 2 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.9 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2 (s), 155.9 (s), 134.4 (s), 130.0 (s), 128.2 (q, *J* = 312.5 Hz), 124.3 (s), 119.9 (s), 118.1 (s), 115.7 (s), 101.0 (s), 66.0 (q, *J* = 4.2 Hz). HRMS (EI): Calculated for $C_{15}H_9OF_3S$ $[M]^+$: 294.0326; Found 294.0330. IR (neat) *ν*: 2962, 2176, 1588, 1504, 1489, 1281, 1246, 1165, 1104, 908, 880, 862, 837, 750, 735, 692 cm^{-1}.

(**3e**) [49]: Pale yellow oil, 80 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.7 Hz, 2 H), 6.85 (d, *J* = 8.8 Hz, 2 H), 3.81 (s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −44.1 (s, 3 F) ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9 (s), 134.4 (s), 128.2 (q, *J* = 312.4 Hz), 114.1 (s), 113.5 (s), 101.5 (s), 65.2 (q, *J* = 4.4 Hz)., 55.3 (s). GC–MS (EI): Calculated for $C_{10}H_7F_3OS$ $[M]^+$: 232.0; Found: 232.0.

(**3f**): Pale yellow oil, 88 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.6, 1.7 Hz, 1 H), 7.34 (ddd, *J* = 8.4, 7.6, 1.7 Hz, 1 H), 6.91 (td, *J* = 7.5, 0.9 Hz, 1 H), 6.87 (d, *J* = 8.4 Hz, 1 H), 3.87 (s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.9 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8 (s), 134.2 (s), 131.4 (s), 128.2 (q, *J* = 312.5 Hz), 120.5 (s), 110.9 (s), 97.9 (s), 70.2 (q, *J* = 4.2 Hz), 55.8 (s). HRMS (EI): Calculated for $C_{10}H_7OF_3S$ $[M]^+$: 232.0170; Found: 232.0172. IR (neat) V: 2938, 2178, 1596, 1576, 1491, 1465, 1435, 1282, 1262, 1161, 1104, 1047, 1025,



Scheme 2. Difluorocarbene-based trifluoromethylthiolation of terminal alkynes. Isolated yields. Reaction conditions: substrate **1** (0.4 mmol), **2** (4 equiv), S_8 (1.5 equiv), KF (6 equiv), CuI (0.2 equiv), **L4** (0.2 equiv), TMEDA (2 equiv) in THF (4 mL) at 60 °C for 3 h under a N_2 atmosphere.



Scheme 3. The plausible reaction mechanism.

782, 752 cm^{-1}.

(**3 g**) [54]: Pale yellow oil, 80 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.9 Hz, 1 H), 7.08 (dt, *J* = 7.6, 1.1 Hz, 1 H), 7.00 (dd, *J* = 2.3, 1.5 Hz, 1 H), 6.94 (ddd, *J* = 8.4, 2.6, 0.9 Hz, 1 H), 3.79 (s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.6 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (s), 129.5 (s), 128.1 (q, *J* = 312.5 Hz), 124.7 (s), 122.4 (s), 116.8 (s), 116.4 (s), 101.3 (s), 66.5 (q, *J* = 4.4 Hz), 55.3 (s). GC–MS (EI): Calculated for $C_{10}H_7F_3OS$ $[M]^+$: 232.0; Found: 232.0.

(**3 h**): Pale yellow oil, 87 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 1 H), 6.74 (d, *J* = 2.5 Hz, 1 H), 6.69 (dd, *J* = 8.5, 2.6 Hz, 1 H), 3.80 (s, 3 H), 2.41(s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −44.4 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8 (s), 143.8 (s), 134.4 (s), 128.3 (q, *J* = 312.3 Hz), 115.2 (s), 113.6 (s), 111.4 (s), 100.6 (s), 68.4 (q, *J* = 4.2 Hz), 55.2 (s), 20.7 (s). HRMS (EI): Calculated for $C_{11}H_9OF_3S$ $[M]^+$: 246.0326; Found: 246.0330. IR (neat) *ν*: 2961, 2840, 2166, 1605, 1564, 1497, 1466, 1315, 1299, 1283, 1260, 1232, 1157, 1103, 1042, 869, 849, 808, 756 cm^{-1}.

(**3i**) [49]: White solid, 84 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1 H), 7.69 (d, *J* = 8.9 Hz, 1 H), 7.67 (d, *J* = 8.4 Hz, 1 H), 7.46 (dd, *J* = 8.5, 1.6 Hz, 1 H), 7.16 (dd, *J* = 8.9, 2.5 Hz, 1 H), 7.09 (d, *J* = 2.5 Hz, 1 H), 3.91 (s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.8 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9 (s), 134.9 (s), 132.8 (s), 129.6 (s), 128.9 (s), 128.18 (s), 128.15 (q, *J* = 312.7 Hz), 127.0 (s), 119.7 (s), 116.3 (s), 105.8 (s), 102.0 (s), 66.0 (s), 55.3 (s). GC–MS (EI): Calculated for $C_{14}H_9F_3OS$ $[M]^+$: 282.0; Found: 282.0.

(**3 j**) [49]: Pale yellow solid, 81 %. ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 9.1 Hz, 1 H), 8.25 – 8.01 (m, 8 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.6 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.7 (s), 132.1 (s), 130.9 (s), 130.7 (s), 123.0 (s), 128.8 (s), 128.8 (s), 128.3 (q, *J* = 312.7 Hz), 126.9 (s), 126.3 (s), 126.0 (s), 125.9 (s), 124.7 (s), 124.2 (s), 124.0 (s), 123.8 (s), 115.4 (s), 100.7 (s), 71.5 (q, *J* = 4.1 Hz). GC–MS (EI): Calculated for $C_{19}H_9F_3S$ $[M]^+$: 326.0; Found: 326.1.

(**3k**): Pale yellow solid (m.p. 100–101 °C), 78 %. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.3 Hz, 1 H), 7.73 (d, *J* = 7.9 Hz, 1 H), 7.66 (s, 1 H), 7.55 (d, *J* = 7.7 Hz, 1 H), 7.52 (d, *J* = 7.9 Hz, 1 H), 7.39 (t, *J* = 7.2 Hz, 1 H), 7.36 – 7.31 (m, 1 H), 3.87 (s, 2 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.8 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8 (s), 143.4 (s), 143.2 (s), 140.7 (s), 131.4 (s), 128.9 (s), 128.1 (q, J = 312.5 Hz), 127.6 (s), 127.0 (s), 125.2 (s), 120.5 (s), 119.9 (s), 119.4 (s), 102.1 (s), 66.4 (q, *J* = 4.3 Hz), 36.71 (s). HRMS (EI): Calculated for $C_{16}H_9F_3S$ $[M]^+$: 290.0377; Found: 290.0369. IR (neat) *ν* : 3070, 2173, 1607, 1464, 1454, 1418, 1399, 1176, 1162, 1150, 1131, 1101, 952, 875, 839, 770, 755, 737, 593 cm^{-1}.

(**3 l**) [49]: Yellow oil, 75 %. ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.6 Hz, 2 H), 7.52 (d, *J* = 8.6 Hz, 2 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.3 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7 (s), 131.6 (s), 131.1 (s), 129.5 (s), 127.9 (q, *J* = 312.6 Hz), 125.8 (s), 100.5 (s), 69.9 (q, *J* = 4.4 Hz), 61.3

(s), 14.2 (s). GC–MS (EI): Calculated for $C_{12}H_9F_3O_2S$ $[M]^+$: 274.0; Found: 274.1.

(**3 m**) [29]: Pale yellow solid, 60 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (d, J = 1.9 Hz, 1 H), 8.30 (s, 1 H), 8.09 (d, J = 8.5 Hz, 1 H), 7.81 – 7.72 (m, 2 H), 7.61 – 7.55 (m, 1 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −43.2 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6 (s), 147.3 (s), 139.8 (s), 131.0 (s), 129.5 (s), 128.0 (q, J = 312.6 Hz), 127.8 (s), 127.7 (s), 126.9 (s), 115.7 (s), 98.7 (s), 70.5 (q, J = 4.2 Hz). GC–MS (EI): Calculated for $C_{12}H_6F_3NS$ $[M]^+$: 253.0; Found: 253.0.

(**3n**) [52]: Orange yellow oil, 70 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 5 H), 3.55 (s, 2 H), 3.45 (s, 2 H), 2.35 (s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −44.0 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.0 (s), 129.1 (s), 128.4 (s), 128.3 (q, J = 311.8 Hz), 127.4(s), 99.0 (s), 63.1 (q, J = 4.1 Hz), 60.0 (s), 45.9 (s), 41.9 (s). GC–MS (EI): Calculated for $C_{12}H_{12}F_3NS$ $[M]^+$: 259.1; Found: 259.1.

(**3o**) [49]: Yellow oil, 59 %. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2 H), 7.26 – 7.20 (m, 3 H), 2.88 (t, J = 7.4 Hz, 2 H), 2.68 (t, J = 7.4 Hz, 2 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −44.1 (s, 3 F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.9 (s), 128.52 (s), 128.48 (q, J = 311.5 Hz), 128.45 (s), 126.6 (s), 103.0 (s), 58.0 (q, J = 4.3 Hz), 34.4 (s), 22.4 (s). GC–MS (EI): Calculated for $C_{11}H_9F_3S$ $[M]^+$: 230.0; $[M\text{-}CF_3]^+$: 161.0; Found $[M\text{-}CF_3]^+$: 161.1.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jfluchem.2019.109437.

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