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Difluorocarbene for Dehydroxytrifluoromethylthiolation of Alcohols

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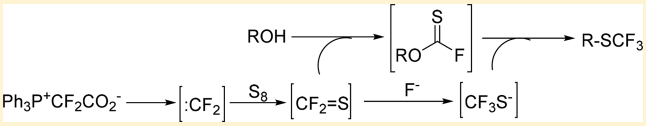
Supporting Information

ABSTRACT: Dehydroxytrifluoromethylthiolation of alcohols with a $Ph_3P^+CF_2CO_2^-/S_8/F^-$ system is described. Difluorocarbene generated from $Ph_3P^+CF_2CO_2^-$ would readily combine with elemental sulfur to furnish S=CF_2. S=CF_2 can be considered as a bifunctional intermediate, activating alcohol and providing scaffold for CF_3S^- formation, thus allowing for the convenient dehydroxytrifluoromethylthiolation of alcohols.



As fluorine-containing compounds have found widespread application in pharmaceuticals, agrochemicals, and functional materials,[1] determined efforts have been directed toward the development of efficient methods for the incorporation of fluorinated moieties into organic molecules.[2] The Trifluoromethylthio group (CF_3S) has received particular attention due to its strong electron-withdrawing effects (Hammett constants $\sigma_p = 0.50$, $\sigma_m = 0.40$) and high lipophilicity (Hansch parameter $\pi = 1.44$), effects which could be highly beneficial in modifying pharmacokinetic properties of target molecules.[3] The past years have witnessed significant advances in trifluoromethylthiolation.[4] A variety of trifluoromethylthiolation reagents and mild trifluoromethylthiolation approaches have continuously appeared.[5] Apparently, trifluoromethylthiolation of easily available starting materials would be one of the most attractive strategies. Despite the wide availability of alcohols, dehydroxytrifluoromethylthiolation of alcohols remains largely unexplored.

In 1994, Kolomeitsev reported a two-step method for dehydroxytrifluoromethylthiolation of alcohols, which suffers from a tedious procedure and the use of toxic CF_3SSCF_3.[6] In 2014, Rueping and co-workers described the Lewis acid-promoted dehydroxytrifluoromethylthiolation of alcohols with $CuSCF_3$. Although good yields were obtained, the reaction is limited to benzylic and allylic alcohols, and the alcoholic substrates have to be activated by a Lewis acid.[7] Qing disclosed a convenient method for the conversion of alcohols with $AgSCF_3$, which features high functional group compatibility and a wide substrate scope.[8] Recently, Billard reported an umpolung strategy for trifluoromethylthiolation of alcohols with electrophilic N-SCF_3 reagent.[9] The above dehydroxytrifluoromethylthiolation approaches require the use of excessive expensive transition metals or trifluoromethylthiolation reagents which are toxic, expensive, or prepared from hazardous agents, thus limiting their synthetic utility.

Difluorocarbene has found widespread application in organic synthesis.[10] We have previously found that it can be applied to the construction of trifluoromethylthio anion (CF_3S^-) in the presence of fluoride (F^-) and elemental sulfur (S_8), thus enabling the ^{18}F-trifluoromethylthiolation of alkyl electrophiles[11] and α-bromo carbonyl compounds.[12] We originally speculated that the trifluoromethylthio anion was formed via trifluoromethyl anion (CF_3^-).[11] Further mechanistic investigations revealed that the key process is the generation of thiocarbonyl fluoride (S=CF_2),[12] which is an important fluorinated material previously prepared by hazardous agents and/or under harsh conditions.[13] These unprecedented findings open up new opportunities for the chemistry of difluorocarbene and thiocarbonyl fluoride.

Herein, we report the application of difluorocarbene in dehydroxytrifluoromethylthiolation of alcohols. The easily accessible difluoromethylene phosphobetaine $Ph_3P^+CF_2CO_2^-$ (PDFA), which was developed by us[11,12,14] and also applied by other groups,[15] was found to be an efficient difluorocarbene precursor. In this strategy, thiocarbonyl fluoride can be considered as a bifunctional intermediate, activating alcohol and providing scaffold for CF_3S^- formation. In contrast to Qing's[8] and Billard's[9] process that S=CF_2 is derived from the decomposition of CF_3S^-, here it is formed in situ and further gives the CF_3S^- anion. This protocol allows for the convenient construction of Csp^3–SCF_3 bond under mild conditions.

Our initial attempts at trifluoromethylthiolation of alcohol **1a** with PDFA/S_8/CsF revealed that solvent played an important role (Table 1, entries 1–4). The desired product could be formed in polar solvent (DMA) albeit in a low yield (entry 4). A brief survey of molar ratio of **1a**:PDFA:S:CsF (entries 5–10) indicated that excessive loading of PDFA, sulfur source, and CsF would lead to a significant rise in the yield (entry 10). Surprisingly, the absence of CsF could still affords **3a** in 50% yield (entry 11). This is because the activation of alcohol by thiocarbonyl fluoride would generate fluoride anion (F^-), a process which is shown in the proposed mechanism. Besides CsF, both KF and TBAT [*tetra-n*-butylammonium triphenyldifluorosilicate, ($^nBu_4N^+Ph_3SiF_2^-$)] were also effective to provide F^- (entries 12 and 13), but TBAT seemed more efficient. Commercial TBAF resulted in complete suppression of the

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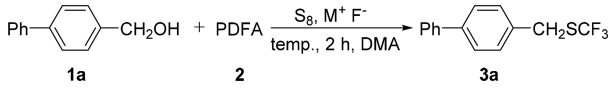
Table 1. Screening Reaction Conditions[a]



1a 2 3a

entry	M^+F^-	ratio	temp. (°C)	yield (%)
1	CsF	1:1:3:2	60	N.D
2	CsF	1:1:3:2	60	3
3[a]	CsF	1:1:3:2	60	6
4	CsF	1:1:3:2	60	21
5	CsF	1:2:3:2	60	29
6	CsF	1:2:5:2	60	42
7	CsF	1:2:10:2	60	51
8	CsF	1:2.5:10:2	60	64
9	CsF	1:4:10:2	60	72
10	CsF	1:4:10:4	60	82
11	–	1:4:10:0	60	50
12	KF	1:4:10:4	60	77
13	TBAT	1:4:10:4	60	88
14	TBAF	1:4:10:4	60	N.D
15	AgF	1:4:10:4	60	10
16	TBAT	1:4:10:4	50	80
17	TBAT	1:4:10:4	70	90
18	TBAT	1:4:10:4	100	68
19	TBAT	1:4:10:4	70	90
20	CsF	1:4:10:4	70	82

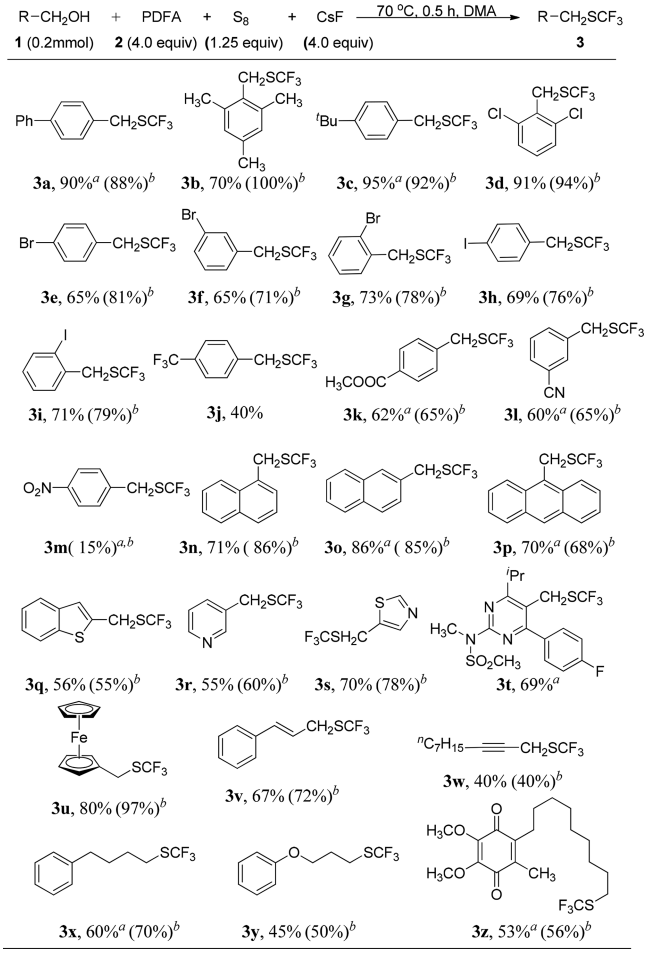
[a]CH_3CN was used as the solvent.

desired conversion, which should be due to the unavoidable presence of water in the commercial source (entry 14). The use of AgF produced $AgSCF_3$ and only gave product **3a** in 10% yield (entry 15). The reaction was slightly temperature-sensitive (entries 16–18 vs 13), and a high yield was obtained at 70 °C (entry 17). Full conversion was achieved within 0.5 h by using either TBAT (entry 19) or CsF (entry 20). Although TBAT was more favorable than CsF (entry 19 vs 20), CsF was still a preferred fluoride source because of its lower price and higher atom economy.

With the optimized reaction conditions in hand (Table 1, entry 20), we then investigate the substrate scope for dehydroxytrifluoromethylthiolation of primary alcohols with PDFA/S_8/F^- system (Scheme 1). A series of electron-rich, -neutral, and -deficient benzyl alcohols were converted smoothly into the desired products in good to excellent yields (**3a**–**3p**), but the presence of strong electron-withdrawing group on the benzyl ring would lead to an obvious decrease in the yield (**3m**). The conversion is not particularly sensitive to steric effects, as evidenced by the good yields of **3b**, **3n**, and **3p**. Moderate yields were obtained for the transformation of heteroaryl substrates (**3q**–**3t**). The incorporation of the CF_3S motif into ferrocene scaffold (**3u**) may improve catalytic activity of ferrocene, which has found widespread application in catalysis. The reaction is applicable not only to benzyl alcohols but also to allyl alcohol (**3v**), propargyl alcohol (**3w**), and alkyl alcohols (**3x**–**3z**). But lower yields were obtained in the case of propargyl- and alkyl-alcohols.

Under the same optimal conditions for trifluoromethylthiolation of primary alcohols (Table 1, entry 19 or 20), low yields were obtained (<16%) for secondary alcohols. After screening various reaction conditions [see Supporting Information (SI)], we were delighted to find that a high concentration, the use of KF/18-crown-6 instead of CsF, and the addition of activator (CuI or $^nBu_4NI$) would increase the

Scheme 1. Dehydroxytrifluoromethylthiolation of Primary Alcohols



[a]TBAT was used instead of CsF. [b]The yields in parentheses were determined by ^{19}F NMR.

yield (see SI). We then investigated the substrate scope for the conversion of secondary alcohols. As shown in Scheme 2, moderate yields were obtained. The low reactivity of secondary alcohols should be because of its severe steric effects and strong possibility for dehydration to produce olefins.

We have previously shown that difluorocarbene would readily combine with elemental sulfur to give thiocarbonyl fluoride ($S{=}CF_2$).[12] In this dehydroxytrifluoromethylthiolation, $S{=}CF_2$ generated in situ would be readily trapped by F^- to produce CF_3S^- or react with alcohol to form thiolate **A** (Scheme 3). F^- might be generated from the formation of thiolate **A**. This is why trifluoromethylthiolation could still happen even without any external fluoride (Table 1, entry 11). The $-OC(=S)F$ group in thiolate **A** is a good leaving group, meaning that the nucleophilic attack of CF_3S^- at thiolate **A** would readily occur to give the final product.

In order to get more information on the proposed mechanism, efforts were made to isolate thiolate **A**. Since thiolate **A** would be easily converted by CF_3S^-, suppressing the formation of CF_3S^- anion may lead to accumulation of thiolate **A**. Obviously, the absence of external fluoride would suppress the formation of CF_3S^- anion, and thus thiolate **A** may persist to be isolated. For benzyl alcohols, the reaction cannot stop at thiolate **A** even without the addition of external fluoride, which

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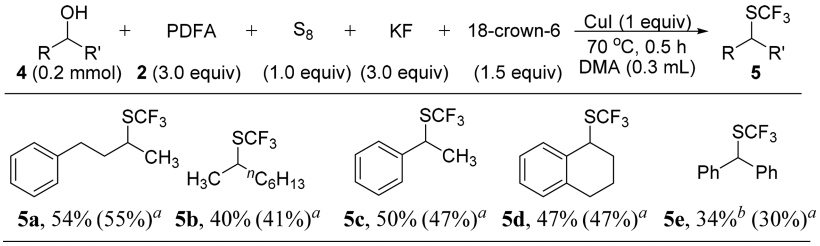
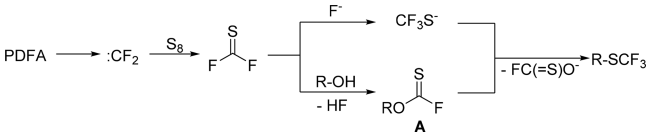
Scheme 2. Dehydroxytrifluoromethylthiolation of Secondary Alcohols



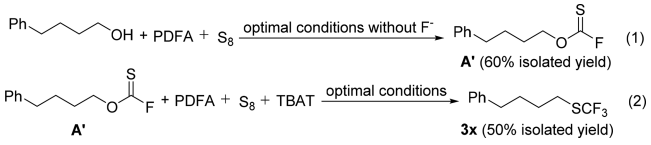
[a]The yields in parentheses were determined by ^{19}F NMR. [b]Two mL of DMA was used.

Scheme 3. Proposed Reaction Mechanism



should be because the benzyl position is highly reactive toward nucelophilic substitution. Fortunately, the absence of external fluoride could furnish thiolate **A′** in a good isolated yield for the conversion of 4-phenylbutanol (Scheme 4, eq 1). Thiolate **A′** could be further transformed into the desired trifluoromethylthiolation product in 50% yield (eq 2), suggesting that the proposed mechanism is plausible.

Scheme 4. Evidence for the Proposed Mechanism



In conclusion, the combination of difluorocarbene with sulfur and fluoride anion was developed into an efficient synthetic tool for dehydroxytrifluoromethylthiolation of alcohols. Thiocarbonyl fluoride generated in situ can not only activate alcohols but also provide the scaffold for the formation of trifluoromethylthio anion. This protocol is attractive since the Csp^3–SCF_3 bond is formed by trifluoromethylthiolation of easily available substrates under mild conditions. This process may also find application in other research areas.

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 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 or LC-MS (ESI). High-resolution mass data were recorded on a high-resolution mass spectrometer in the EI, ESI, or MALDI mode. The mass analyzer types for HRMS-EI, HRMS-ESI, and HRMS-MALDI are time-of-flight, Fourier transform mass spectrometer, and Fourier transform mass spectrometer, respectively. Unless otherwise noted, all reagents were obtained commercially and used without further purification.

General Procedure for Dehydroxytrifluoromethylthiolation of Primary Alcohols. Into a mixture of substrate (0.2 mmol, 1.0 equiv), PDFA (0.8 mmol, 285.0 mg, 4.0 equiv), S_8 (0.25 mmol, 64.1 mg, 1.25 equiv), cesium fluoride (0.8 mmol, 121.5 mg, 4.0 equiv), or TBAT(0.8 mmol, 431.8 mg, 4.0 equiv) and DMA (2 mL) were added sequentially into a flame-dried sealed tube under N_2 atmosphere. After the tube was sealed, the resulting mixture was stirred at 70 °C for 30 min. When the reaction was completed, as monitored by ^{19}F NMR, the crude reaction mixture was diluted with CH_2Cl_2 (20 mL). The solution was washed with water (3 × 20 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was subjected to flash column chromatography (eluent: hexane or dichloromethane) to give the final product **3**.

*([1,1′-Biphenyl]-4-ylmethyl)(trifluoromethyl)sulfane (**3a**).*[8] Fluoride source was TBAT. White solid, 48.3 mg, 90%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.61–7.54 (m, 4H), 7.49–7.31 (m, 5H), 4.16 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.6 (s, 3F).

*(Trifluoromethyl)(2,4,6-trimethylbenzyl)sulfane (**3b**).* Fluoride source was CsF. Colorless oil, 32.8 mg, 70%.. ^1H NMR (500 MHz, $CDCl_3$) δ 6.89 (s, 2H), 4.22 (s, 2H), 2.41 (s, 6H), 2.28 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −42.4 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.9 (s), 137.5 (s), 130.8 (q, J = 307.0 Hz), 129.3 (s), 126.8 (s), 28.8 (q, J = 2.4 Hz), 20.9 (s), 19.3 (s). IR (neat) ν = 2923, 2861, 1614, 1458, 1379, 1249, 1112, 853, 752, 690, 457 cm^{-1}. HRMS (EI): calcd for $C_{11}H_{13}F_3S$ $[M]^+$: 234.0690, Found: 234.0697.

*(4-(tert-Butyl)benzyl)(trifluoromethyl)sulfane (**3c**).*[8] Fluoride source was TBAT. Colorless oil, 42.9 mg, 92%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 4.11 (s, 2H), 1.32 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.8 (s, 3F).

*(2,6-Dichlorobenzyl)(trifluoromethyl)sulfane (**3d**).* Fluoride source was CsF. Colorless oil, 47.5 mg, 91%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.18 (m, 3H), 4.46 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.6(s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.9 (s), 131.8(s), 130.7 (q, J = 307.1 Hz), 129.9 (s), 128.6 (s), 29.7 (q, J = 2.6 Hz). IR (neat) ν = 2925, 1582, 1559, 1438, 1112, 897, 875, 780, 764, 689, 417 cm^{-1}. HRMS (EI): calcd. for $C_8H_5Cl_2F_3S$ $[M]^+$: 259.9441, Found: 259.9446.

*(4-Bromobenzyl)(trifluoromethyl)sulfane (**3e**).*[8] Fluoride source was CsF. Colorless oil, 35.2 mg, 65%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.3 Hz, 2H), 7.20 (d, J = 8.2 Hz, 2H), 4.04 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.6(s, 3F).

*(3-Bromobenzyl)(trifluoromethyl)sulfane (**3f**).* Fluoride source was CsF. Colorless oil, 35.2 mg, 65%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.43 (d, J = 7.5 Hz, 1H), 7.30–7.16 (m, 2H), 4.05 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.6 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5(s), 131.9 (s), 131.2 (s), 130.4(q, J = 307.1 Hz), 130.4(s), 127.5 (s), 122.8 (s), 33.6 (q, J = 2.4 Hz). IR (neat) ν = 2958, 2922, 1260, 1054, 800, 752, 665, 534, 521 cm^{-1}. HRMS (EI): calcd for $C_8H_6BrF_3S$ $[M]^+$: 269.9326, Found: 269.9322.

*(2-Bromobenzyl)(trifluoromethyl)sulfane (**3g**).* Fluoride source was CsF. Colorless oil, 39.6 mg, 73%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.17 (t, J = 7.7 Hz, 1H), 4.21 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.4 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.1(s), 133.2 (s), 131.0 (s), 130.6(q, J = 308.0 Hz), 129.7 (s), 127.8 (s), 124.5 (s), 34.8 (q, J = 2.4 Hz). IR (neat) ν = 2925, 1593, 1570, 1471, 1441, 1384, 1258, 1206, 1150, 1113, 1045, 1027, 870, 805, 755, 730, 676, 658, 439 cm^{-1}. HRMS (EI): calcd for $C_8H_6F_3BrS$ $[M]^+$: 269.9326, Found: 269.9322.

*(4-Iodobenzyl)(trifluoromethyl)sulfane (**3h**).*[8] Fluoride source was CsF. Pale yellow oil, 43.9 mg, 69%. ^1H NMR (400 MHz, $CDCl_3$) δ

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7.68 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 4.05 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.5 (s, 3F).

*(2-Iodobenzyl)(trifluoromethyl)sulfane (**3i**).* Fluoride source was CsF. Colorless oil, 45.2 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.9 Hz, 1H), 7.39 (d, J = 7.6 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 6.98 (t, J = 7.6 Hz, 1H), 4.20 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0 (s), 138.2 (s), 130.6 (q, J = 307.3 Hz), 130.3 (s), 129.7 (s), 128.7 (s), 100.2 (s), 39.6 (q, J = 2.4 Hz). IR (neat) ν = 1566, 1465, 1437, 1251, 1204, 1150, 1114, 1014, 756, 647, 435 cm^{-1}. HRMS (EI): calcd for $C_8H_6F_3IS$ $[M]^+$: 317.9187, Found: 317.9184.

*(Trifluoromethyl)(4-(trifluoromethyl)benzyl)sulfane (**3j**).*[8] Fluoride source was CsF. Colorless oil, 20.8 mg, 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 8.1 Hz, 2H), 4.13 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.5 (s, 3F), −62.72 (s, 3F).

*Methyl 4-(((trifluoromethyl)thio)methyl)benzoate (**3k**).*[8] Fluoride source was TABT. Yellow oil, 30.6 mg, 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 4.14 (s, 2H), 3.91 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.5 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7 (s), 140.5 (s), 130.6 (q, J = 306.5 Hz), 130.2 (s), 130.0 (s), 129.0 (s), 52.3 (s), 34.0 (q, J = 2.4 Hz),

*3-(((Trifluoromethyl)thio)methyl)benzonitrile (**3l**)*[8]. Fluoride source was TABT. Yellow oil, 26.0 mg, 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.60 (d, J = 8.3 Hz, 2H), 7.47 (t, J = 7.7 Hz, 1H), 4.12 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.4 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.3 (s), 133.3 (s), 132.4 (s), 131.7 (s), 130.4 (q, J = 308.2 Hz) 129.8 (s), 118.3 (s), 113.2 (s), 33.5 (q, J = 2.5 Hz).

*(Naphthalen-1-ylmethyl)(trifluoromethyl)sulfane (**3n**).* Fluoride source was CsF. Colorless oil, 34.4 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.1 Hz, 1H), 7.84 (d, J = 8.2 Hz, 1H), 7.64−7.57 (m, 1H), 7.57−7.47 (m, 2H), 7.47−7.39 (m, 1H), 4.60 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.8 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.0 (s), 131.2 (s), 130.8 (q, J = 307.0 Hz), 130.1 (s), 129.3 (s), 129.1 (s), 128.1 (s), 126.8 (s), 126.2(s), 125.4 (s), 123.2 (s), 32.1 (q, J = 2.4 Hz). IR (neat) ν = 3065, 1597, 1512, 1398, 1352, 1250, 1111, 1017, 791, 586, 465 cm^{-1}. HRMS (EI): calcd for $C_{12}H_9F_3S$ $[M]^+$: 242.0377, Found: 242.0377.

*(Naphthalen-2-ylmethyl)(trifluoromethyl)sulfane (**3o**).*[8,16] Fluoride source was TABT. White solid, 41.7 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89−7.72 (m, 4H), 7.57−7.40 (m, 3H), 4.28 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.5 (s, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.4 (s), 133.0 (s), 132.5 (s), 130.8 (q, J = 307.9 Hz) 128.9 (s), 128.0 (s), 127.90 (s), 127.87(s), 126.64(s), 126.62(s), 126.5(s), 34.7 (q, J = 2.3 Hz).

*(Anthracen-9-ylmethyl)(trifluoromethyl)sulfane (**3p**).* Fluoride source was TABT. White solid, 40.9 mg, 70%. M.P.: 99 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.26 (d, J = 8.9 Hz, 2H), 8.02 (d, J = 8.4 Hz, 2H), 7.67−7.56 (m, 2H), 7.54−7.45 (m, 2H), 5.16 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −42.1 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.5 (s), 130.9 (q, J = 307.4 Hz), 130.2 (s), 129.4 (s), 128.9 (s), 127.0 (s), 125.3 (s), 123.9(s), 123.3 (s), 27.1 (q, J = 2.4 Hz). IR (neat) ν = 3439, 3052, 1623, 1445, 1345, 1116, 886, 737, 722, 605, 519 cm^{-1}. HRMS (EI): calcd for $C_{16}H_{11}F_3S$ $[M]^+$: 292.0534, Found: 292.0539.

*2-(((Trifluoromethyl)thio)methyl)benzo[b]thiophene (**3q**).*[8] Fluoride source was CsF. White solid, 27.1 mg, 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.2 Hz, 1H), 7.72 (d, J = 7.2 Hz, 1H), 7.39−7.29 (m, 3H), 4.41 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.6 (s, 3F).

*3-(((Trifluoromethyl)thio)methyl)pyridine (**3r**)*[8]. Fluoride source was CsF. Brown oil, 21.2 mg, 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.56(d, J = 4.1 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.41−7.01 (m, 1H), 4.09 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.5 (s, 3F).

*5-(((Trifluoromethyl)thio)methyl)thiazole (**3s**)*[8]. Fluoride source was CsF. Brown oil, 27.9 mg, 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.79 (s, 1H), 4.34 (s, 2H).^{19}F NMR (376 MHz, $CDCl_3$) δ −41.6 (s, 3F).

*N-(4-(4-Fluorophenyl)-6-isopropyl-5-(((trifluoromethyl)thio)-methyl)pyrimidin-2-yl)-N-methylmethanesulfonamide (**3t**).*[8] Fluoride source was TABT. Pale yellow solid, 56.7 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, J = 8.4, 5.4 Hz, 2H), 7.20 (t, J = 8.5 Hz, 2H), 4.16 (s, 2H), 3.55 (s, 3H), 3.50 (s, 3H), 3.43 (hep, J = 6.5 Hz, 1H), 1.35 (d, J = 6.6 Hz, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −42.3 (s, 3F), −110.6 (s, 1F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.4 (s), 166.9 (s), 163.8 (d, J = 250.6 Hz), 158.3 (s) 133.6 (d, J = 3.4 Hz), 130.9 (d, J = 8.5 Hz), 130.0 (q, J = 307.7 Hz) 115.8 (d, J = 21.8 Hz), 115.0 (s), 42.6 (s), 33.2 (s), 31.8 (s), 28.0 (q, J = 2.4 Hz), 22.3 (s).

*((Trifluoromethylthio)methyl)ferrocene (**3u**).*[8] Fluoride source was CsF. Brown oil, 48.0 mg, 80%.. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.22−4.17(m, 9H), 3.93 (s, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.7 (s, 3F).

*Cinnamyl(trifluoromethyl)sulfane (**3v**).*[8,17] Fluoride source was CsF. Yellow oil, 29.2 mg, 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.20 (m, 5H), 6.60 (d, J = 15.7 Hz, 1H), 6.30−6.15 (m, 1H), 3.71 (d, J = 7.3 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −40.9 (s, 3F).

*Dec-2-yn-1-yl(trifluoromethyl)sulfane (**3w**).*[8] Fluoride source was CsF. Colorless oil, 19.1 mg, 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 2H), 2.19 (t, J = 6.4 Hz, 2H), 1.61−1.42 (m, 2H), 1.43−1.21 (m, 8H), 0.89 (t, J = 5.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −42.0 (s, 3F).

*(4-Phenylbutyl)(trifluoromethyl)sulfane (**3x**).*[18] Fluoride source was TBAT. Colorless oil, 28.1 mg, 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.14 (m, 5H), 2.89 (t, J = 6.7 Hz, 2H), 2.64 (t, J = 6.9 Hz, 2H), 1.76−1.70 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.2 (s, 3F).

*(3-Phenoxypropyl)(trifluoromethyl)sulfane (**3y**).*[19] Fluoride source was CsF. Colorless oil, 21.3 mg, 45%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (t, J = 7.8 Hz, 2H), 6.96 (t, J = 7.4 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 4.06 (t, J = 5.7 Hz, 2H), 3.10 (t, J = 7.2 Hz, 2H), 2.23−2.11 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.1 (s, 3F).

*2,3-Dimethoxy-5-methyl-6-(10-((trifluoromethyl)thio)decyl)-cyclohexa-2,5-diene-1,4-dione (**3z**).*[8] Fluoride source was TABT. Orange oil, 35.7 mg, 53%.^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (s, 6H), 2.84 (t, J = 7.4 Hz, 2H), 2.41 (t, J = 7.8 Hz, 2H), 1.98 (s, 3H), 1.70−1.60 (m, 2H), 1.40−1.22 (m, 14H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −41.3 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.8 (s), 184.2 (s), 144.37 (s), 144.35 (s), 143.1 (s), 138.7 (s), 131.3 (q, J = 305.6 Hz), 61.2 (s), 30.0 (q, J = 1.8 Hz), 29.9 (s), 29.5 (s), 29.43 (s), 29.41 (s), 29.37 (s), 29.0 (s), 28.8 (s), 28.5 (s), 26.5 (s), 12.0 (s).

Dehydroxytrifluoromethylthiolation of Secondary Alcohols. Into a mixture of substrate (0.2 mmol, 1.0 equiv), PDFA (0.6 mmol, 285.0 mg, 3.0 equiv), S_8 (0.2 mmol, 64.1 mg, 1.0 equiv), potassium fluoride (0.6 mmol, 34 mg, 3.0 equiv), 18-crown-6 (0.3 mmol, 79.4 mg, 1.5 equiv), CuI (0.2 mmol, 38 mg, 1.0 equiv) or Bu_4NI (0.2 mmol, 74 mg, 1.0 equiv), and DMA (0.3 or 2 mL) were added sequentially into a flame-dried sealed tube under N_2 atmosphere. After the tube was sealed, the resulting mixture was stirred at 70 °C for 30 min. When the reaction was completed, as monitored by ^{19}F NMR, the crude reaction mixture was diluted with CH_2Cl_2 (20 mL). The solution was washed with water (3 × 20 mL), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was subjected to flash column chromatography (eluent: hexane) to give the final product **5**.

*(4-Phenylbutan-2-yl)(trifluoromethyl)sulfane (**5a**).*[8] 0.3 mL DMA was used. Yellow oil, 25.3 mg, 54%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.15 (m, 5H), 3.37−3.23 (m, 1H), 2.83−2.70 (m, 2H), 2.02−1.84 (m, 2H), 1.46 (d, J = 6.9 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −38.9 (s, 3F).

*Octan-2-yl(trifluoromethyl)sulfane (**5b**).* 0.3 mL DMA was used. Yellow oil, 17.1 mg, 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.33−3.24 (m, 1H), 1.61−1.54 (m, 2H), 1.39 (d, J = 6.8 Hz, 3H), 1.35−1.16 (m, 8H), 0.87 (t, J = 5.4 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −39.2 (s, 3F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.3 (q, J = 306.0 Hz), 41.2 (q, J = 1.2 Hz), 36.9 (s), 31.63 (s), 28.9 (s), 26.6(s), 22.6 (s), 22.3 (s), 14.1 (s). IR (neat) ν = 3445, 2912, 1636, 1437, 1231, 1107, 1014, 961, 717, 639, 518 cm^{-1}. HRMS (EI): calcd for $C_9H_{17}F_3S$ $[M]^+$: 214.1003, Found: 214.1011.

*(1-Phenylethyl)(trifluoromethyl)sulfane (**5c**).*[8] 0.3 mL DMA was used. Yellow oil, 20.6 mg, 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−

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J. Org. Chem. 2017, 82, 11206−11211

7.21 (m, 5H), 4.52 (q, J = 7.1 Hz, 1H), 1.72 (d, J = 7.0 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −40.2 (s, 3F).

*(1,2,3,4-Tetrahydronaphthalen-1-yl)(trifluoromethyl)sulfane (**5d**).*[8] 0.3 mL DMA was used. Yellow oil, 21.8 mg, 47%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (m, 1H), 7.18 (m, 2H), 7.09 (m, 1H), 4.73 (s, 1H), 2.89−2.76 (m, 2H), 2.34−2.05 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −40.4 (s, 3F).

*Benzhydryl(trifluoromethyl)sulfane (**5e**).*[17] 2.0 mL DMA was used. Colorless oil, 18.2 mg, 34%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.37 (m, 4H), 7.34 (ddd, J = 7.7, 4.9, 2.1 Hz, 4H), 7.30−7.23 (m, 2H), 5.68 (s, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ −40.8 (s, 3F).

Preparation of Intermediate A′. Into a mixture of substrate (0.2 mmol, 1.0 equiv), PDFA (0.8 mmol, 285.0 mg, 4.0 equiv), sulfur powder (2.0 mmol, 64.1 mg, 10.0 equiv), and DMA (2 mL) were added sequentially into a flame-dried sealed tube under N_2 atmosphere. After the tube was sealed, the resulting mixture was stirred at 70 °C for 30 min. When the reaction was completed, as monitored by ^{19}F NMR, the crude reaction mixture was purified by flash column chromatography (eluent: hexane) to give the final product **A′** as a colorless oil.

*O-(4-phenylbutyl) carbonofluoridothioate (**A′**).* Colorless oil, 25.5 mg, 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−6.80 (m, 5H), 4.50 (t, J = 6.3 Hz, 2H), 2.68 (t, J = 7.4 Hz, 2H), 2.20−1.68 (m, 4H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 43.6 (s, 1F). ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.9 (d, J = 329.9 Hz), 141.4 (s), 128.4 (s), 128.4 (s), 126.0 (s), 76.7 (d, J = 5.6 Hz), 35.2 (s), 27.29 (s), 27.26 (s). IR (neat) ν = 3062, 2941, 2860, 1603, 1496, 1465, 1407, 1311, 1188, 1031, 748, 699, 638, 533, 521 cm^{-1}.

HRMS (EI): calcd for $C_{11}H_{13}FOS$ $[M]^+$: 212.0671, Found: 212.0676.

Transformation of Intermediate A′. Into a mixture of intermediate **A′** (0.2 mmol, 1.0 equiv), PDFA (0.8 mmol, 285.0 mg, 4.0 equiv), sulfur powder (2.0 mmol, 64.1 mg, 10.0 equiv), TBAT (0.8 mmol, 431.8 mg, 4.0 equiv), and DMA (2 mL) were added sequentially into a flame-dried sealed tube under N_2 atmosphere. After the tube was sealed, the resulting mixture was stirred at 70 °C for 30 min. When the reaction was completed, as monitored by ^{19}F NMR, the crude reaction mixture was diluted with CH_2Cl_2 (20 mL). The solution was washed with water (3 × 20 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The residue was subjected to flash column chromatography (eluent: hexane) to give the final product **3x**.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01701.

Copies of ^{1}H/^{19}F/^{13}C NMR. (PDF)

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Notes

The authors declare no competing financial interest.

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