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The perfluoroalkylthiolation/decarbonylation reaction of 1,3-diketones with perfluoroalkanesulfenic acids†

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The perfluoroalkylthiolation/decarbonylation reactions of 1,3-dicarbonyl compounds with *in situ* formed perfluoroalkanesulfenic acids were achieved. Using trifluoromethanesulfonic acid as an additive, a series of α -perfluoroalkylthiolated arylethanones were obtained in moderate to good yields. A possible mechanism was proposed based on the reaction results and control experiments.

Introduction

In recent decades, the introduction of fluorine-containing groups into organic compounds has received considerable attention and has become an important synthetic approach in labs and industries.¹ Among various fluorine-containing groups, trifluoromethylthio (CF₃S) plays an important role in organofluorine chemistry due to its high electronegativity, hydrophobicity, metabolic activity and bioavailability. Some compounds bearing fluoroalkylthio groups have been applied in the field of agrochemicals and pharmaceuticals.²

On the other hand, carbonyl compounds constitute a large family of interesting building blocks for organic synthesis, and a wide range of bioactive and natural compounds possess a carbonyl moiety.³ For example, the structure of β -keto thioether is found in many bioactive molecules and some β -keto thioethers have been used as useful intermediates in organic synthesis,⁴ and various synthetic methods for β -keto arylthioethers have been developed.⁵ Consequently, introducing the fluorine-containing group into carbonyl compounds could be of great value for further applications, and the α -functionalization of the carbonyl group appears to be a privileged strategy.⁶ Since the trifluoromethylthiolation of ethyl formylacetate has been achieved in 1973,⁷ a large number of electrophilic trifluoromethylthiolation reagents have been devel-

oped and great success has been achieved in the trifluoromethylthiolation reactions of keto-esters, ketones and aldehydes by different research groups.⁸ However, the perfluoroalkylthiolation of carbonyl compounds has been less studied. In 2016, Shibata *et al.*⁹ reported the perfluoroalkylthiolation of α -methylene- β -keto esters with perfluoroalkyl-DAST giving α -perfluoroalkylthio- β -keto esters, but an electron-withdrawing group at the β -position of the substrate was necessary. Therefore, the development of practical methods for the perfluoroalkylthiolation of carbonyl compounds is of great importance.

Results and discussion

Recently, our group has been working on the chemistry of perfluoroalkylsulfenic acids (R_fSOH). These solution-stable perfluoroalkanesulfenic acids are highly reactive and versatile fluorinated reagents due to the strong electron-withdrawing effect of the perfluoroalkyl group.¹⁰ Previous studies have shown that they could undergo addition reactions with some unsaturated compounds, such as alkenes, alkynes and allenes, to afford the corresponding perfluoroalkyl sulfoxides,¹¹ and electrophilic reactions with carbon nucleophiles, such as indoles, activated benzenes and pyrroles to give perfluoroalkylthiolated compounds.¹² To explore the reaction with more carbon nucleophiles and the synthetic applications of perfluoroalkanesulfenic acids, we further studied the reactions of perfluoroalkanesulfenic acids with carbonyl compounds. The results are reported in this paper.

Initially, phenyl acetone was chosen as the substrate. Based on our previous work,¹² a mixture of phenyl acetone, 4.0 equivalents of *i*-propyl perfluorobutyl sulfoxide (**1a**) and 2.0 equivalents of trifluoromethanesulfonic acid (TfOH) was directly stirred at 100 °C. However, ¹⁹F NMR monitoring

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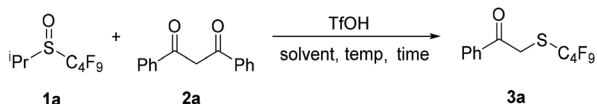


showed that the reaction was complicated and no perfluoroalkylthiolated product was isolated (Scheme 1, eqn (1)). Considering the higher nucleophilicity of 1,3-diketone, we prepared 1,3-diphenylpropane-1,3-dione (**2a**) and studied its reaction with perfluorobutanesulfenic acid generated *in situ* from *i*-propyl perfluorobutyl sulfoxide (**1a**). Interestingly, the reaction occurred readily and α -perfluorobutylthio acetophenone (**3a**) was formed as the major product, whereas the expected product, 2-perfluorobutylthio-1,3-diphenyl-1,3-propanedione was not obtained (Scheme 1, eqn (2)). Furthermore, benzoic acid was also isolated from the reaction system. It is obvious that a perfluorobutylthiolation/decarbonylation process was involved in this reaction.

Inspired by these results, we screened different conditions to find a suitable protocol for the selective formation of **3a**. It was found that decreasing the temperature led to a lower yield of **3a** and a longer reaction time (entries 2 and 3). Investigating the ratio of reactants indicated that increasing the amount of **1a** or additive was beneficial for the perfluoroalkylthiolation/decarbonylation reaction (entries 4–7). With a ratio of 1 : 4 : 6 (**2a**/**1a**/TfOH), the yield of **3a** could be improved to 85% (entry 7). Control experiments showed that TfOH was important for the reaction (entry 8). Other organic acids such as trifluoroacetic acid and acetic acid failed to promote this reaction with full recovery of **2a** (entries 9 and 10). We also studied the solvent effect. It was found that the reaction hardly occurred in *N,N*-dimethylformamide (DMF), acetonitrile or tetrahydrofuran (entries 11–13), and much lower yields were obtained in dichloromethane or *n*-hexane (entries 14 and 15). Thus, the optimal conditions were set to 4.0 equivalents of perfluoroalkyl sulfoxide and 6.0 equivalents of TfOH in toluene at 100 °C (Table 1).

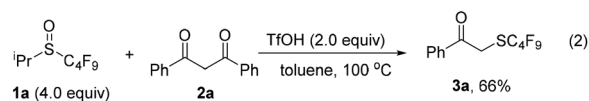
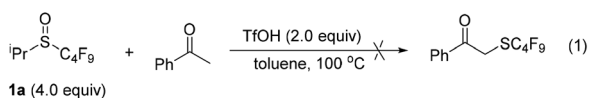
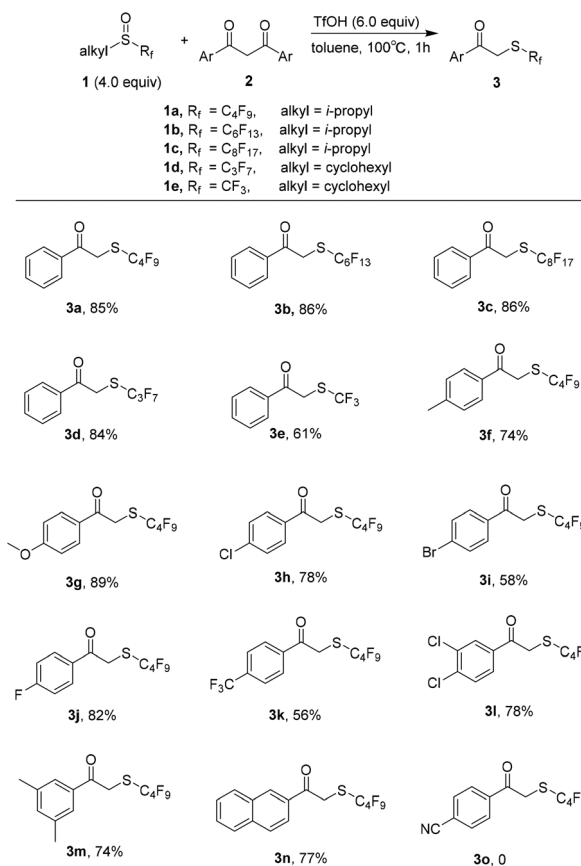
With the optimized reaction conditions in hand, we then examined the reactions of other perfluoroalkyl sulfoxides with **2a**. As shown in Scheme 2, the reactions of **2a** with *in situ* formed *n*-C₆F₁₃SOH, *n*-C₈F₁₇SOH, *n*-C₃F₇SOH or CF₃SOH also took place smoothly to give the corresponding products **3b–3e** in moderate to good yields. Furthermore, a range of 1,3-diarylpropane-1,3-diones **2** with different substituents in the phenyl group reacted readily with **1a**, giving the expected products in moderate to good yields. 1,3-Diketones containing both electron-rich and electron-deficient phenyl groups were compatible with the reaction conditions. For example, the reactions of diketones bearing methyl or methoxy groups gave the corres-

Table 1 Optimization of the reaction conditions

					
Entry ^a	2a / 1a /TfOH	Temp. (°C)	Time (h)	Solvent	3a ^b (%)
1	1 : 4 : 2	100	1	Toluene	66
2	1 : 4 : 2	80	4	Toluene	60
3	1 : 4 : 2	60	6	Toluene	56
4	1 : 1 : 2	100	1	Toluene	38
5	1 : 3 : 2	100	1	Toluene	53
6	1 : 4 : 4	100	1	Toluene	77
7	1 : 4 : 6	100	1	Toluene	85
8	1 : 4 : 0	100	1	Toluene	NR
9 ^c	1 : 4 : 6	100	4	Toluene	NR
10 ^d	1 : 4 : 6	100	4	Toluene	NR
11	1 : 4 : 6	100	1	DMF	Trace
12	1 : 4 : 6	100	1	CH ₃ CN	Trace
13	1 : 4 : 6	100	1	THF	Trace
14	1 : 4 : 6	100	1	DCM	28
15	1 : 4 : 6	100	1	<i>n</i> -Hexane	25

^a Reaction conditions: **2a** (0.2 mmol), *i*-propyl perfluorobutyl sulfoxide **1a** (1.0–4.0 equiv.), TfOH (0–6.0 equiv.), toluene. ^b Determined by ¹⁹F NMR spectroscopy using PhCF₃ as the internal standard.

^c Trifluoroacetic acid was used instead of TfOH. ^d Acetic acid was used instead of TfOH.



Scheme 1 The reaction of carbonyl compounds with *in situ* generated perfluorobutanesulfenic acid.

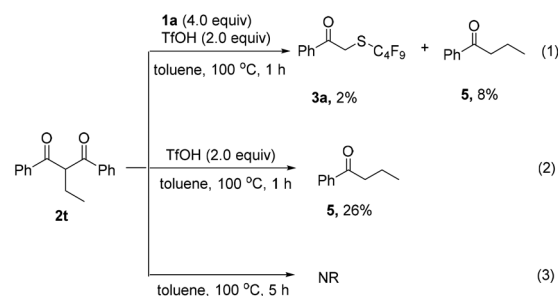
Scheme 2 Scope of the perfluoroalkylthiolation/decarbonylation reaction.



ponding products **3f** and **3g** in good yields. Diketones containing a halide or trifluoromethyl substituent also reacted well to give products **3h–k** in moderate yields. It was found that the yield of **3g** with a methoxy substituent was higher than those of α -perfluoroalkylthio- β -ketones bearing electron-withdrawing groups, indicating that the electronic effect of the substituent had some influence on the reaction. Diketones bearing dichloro or dimethyl substituents were also used and the corresponding products **3l** and **3m** were obtained in reasonable yields. A similar result was obtained with 1,3-bis(2-naphthyl)-1,3-propanedione (**2n**). However, 1,3-diketone **2o** containing a cyano substituent in both phenyl groups failed to give the desired product **3o** due to the weak nucleophilicity of 1,3-diketone **2o**. Furthermore, the perfluoroalkylthiolation/decarbonylation reaction didn't occur when ethyl benzoylacetate, pentane-2,4-dione or 1,3-cyclohexanedione was used as the substrate with full recovery of starting materials **2**.

We also studied the reaction of **1a** with 1,3-diketones **2p–s** containing different phenyls. As shown in Table 2, both products were obtained in the cases of 1,3-diketones containing methyl, methoxy or chlorine-substituted phenyls, but only product **3g** was obtained when compound **2s** bearing a methoxyl and a cyano substituent was used as the substrate.

In order to investigate the effect of substituents at the methylene position on the reaction, we synthesized 2-ethyl-1,3-diphenyl-1,3-propanedione (**2t**) and studied its reaction with **1a** under standard conditions. ^{19}F NMR monitoring showed that a small amount of perfluoroalkylthiolated product was formed. After separation by column chromatography, **3a** and **5** were isolated in 2% and 8% yield, respectively (Scheme 3). It is interesting to find that heating the solution of **2t** in the presence of trifluoromethanesulfonic acid at 100 °C for 1 hour gave the decarbonylation product **5** in 26% yield, while **2t**



Scheme 3 Reactions of **2t**.

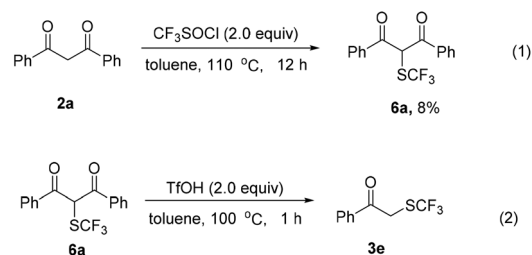
remained unchanged in the absence of TfOH under similar conditions. According to the literature, the decarbonylation of β -substituted diketones occurs under basic conditions.¹³ We hypothesized that 2-perfluoroalkylthiodiketone might be formed as an intermediate under the reaction conditions, which then underwent decarbonylation to give compound **3**. Therefore, we prepared 2-trifluoromethylthio-1,3-diphenylpropane-1,3-dione (**6a**) by the reaction of **2a** with CF_3SOCl and studied its reaction under standard conditions (Scheme 4). After being treated with TfOH in toluene at 100 °C, **6a** was fully converted to **3e**.

Based on the experimental results and the related literature, a plausible mechanism was proposed for the above reactions as shown in Scheme 5. In the presence of trifluoromethanesulfonic acid, the sulfur atom in perfluoroalkanesulfenic acid becomes more electrophilic and is easily attacked by nucleophilic 1,3-diketone **2** to give intermediate **6**. Subsequently, the decarbonylation of **6** takes place rapidly to give the final product **3** under the reaction conditions (Scheme 5).

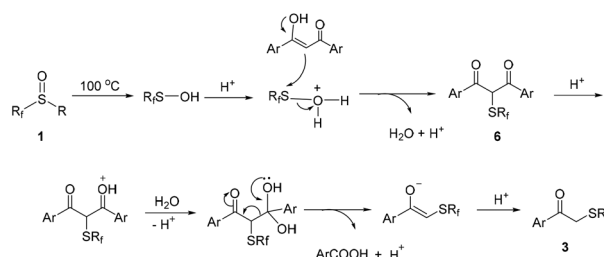
Table 2 The perfluoroalkylthiolation/decarbonylation reaction of 1,3-diketones containing different phenyls

$\text{I}^{\text{Pr}}\text{S}-\text{C}_6\text{F}_9 + \text{Ar}^1-\text{CH}_2-\text{C}(=\text{O})-\text{CH}_2-\text{C}(=\text{O})-\text{Ar}^2 \xrightarrow[\text{toluene, 100}^\circ\text{C, 1h}]{\text{TfOH (6.0 equiv)}} \text{Ar}^1-\text{CH}_2-\text{C}(=\text{O})-\text{CH}_2-\text{C}(=\text{O})-\text{S}-\text{C}_6\text{F}_9 + \text{Ar}^2-\text{CH}_2-\text{C}(=\text{O})-\text{CH}_2-\text{C}(=\text{O})-\text{S}-\text{C}_6\text{F}_9$		
Entry	Substrate	Products
1	4-MeOC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-C ₆ H ₄ -Me-4	4-MeOC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉ 4-MeOC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉
	2p	3g , 73% 3f , 26%
2	4-MeOC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-C ₆ H ₄ -Cl-4	4-MeOC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉ 4-ClC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉
	2q	3g , 26% 3h , 46%
3	4-MeC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-C ₆ H ₄ -Cl-4	4-MeC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉ 4-ClC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉
	2r	3f , 37% 3h , 45%
4	4-MeOC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-C ₆ H ₄ -CN-4	4-MeOC ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉ 4-CN-C ₆ H ₄ -C(=O)-CH ₂ -C(=O)-S-C ₆ F ₉
	2s	3g , 58% 3o , 0%

Reaction conditions: **2** (0.2 mmol), **1** (4.0 equiv.), TfOH (6.0 equiv.), toluene, 100 °C, isolated yield.



Scheme 4 Preparation and transformation of **6**.



Scheme 5 The proposed mechanism.



Conclusions

In conclusion, we have demonstrated the reaction of perfluoroalkanesulfenic acids with 1,3-diketones. In the presence of trifluoromethanesulfonic acid, various 1,3-diarylpropane-1,3-diones reacted readily with perfluoroalkanesulfenic acids formed *in situ* from perfluoroalkyl sulfoxides to give the corresponding α -perfluoroalkylthio- β -ketone products in moderate to good yields. Mechanism studies indicated that 2-perfluoroalkylthiodiketone might be formed as the intermediate in the reaction system. Having advantages including cheap reagents, easy-to-handle and transition metal-free conditions, this protocol is expected to find applications in organic synthesis.

Experimental

General information

Unless otherwise mentioned, solvents and reagents were purchased from commercial sources and used as received. Solvents were freshly distilled using a standard procedure prior to use. Melting points were measured on RY-I apparatus and uncorrected. ^1H NMR spectra were recorded in CDCl_3 on a Bruker AM 400 spectrometer (400 MHz) with TMS as the internal standard. ^{19}F NMR spectra were recorded on a Bruker AM 400 (376 MHz) spectrometer with CFCl_3 as the external standard. ^{13}C NMR spectra were recorded in CDCl_3 on a Varian AM-400 spectrometer (100 MHz) or an Agilent AM-400 (100 MHz) spectrometer with TMS as the internal standard. For compounds **3**, the peaks for fluorine-containing carbon atoms in perfluoroalkyl groups are difficult to find in ^{13}C NMR spectra because of their multiplicity. High Resolution Mass Spectra (HRMS) were obtained with a Waters Micromass GCT (EI) or an IonSpec FT-ICR mass spectrometer (FI).

General procedure for the perfluoroalkylthiolation/decarbonylation reaction

To a sealed tube containing a solution of 1,3-diketones **2** (0.2 mmol) and sulfoxide **1** (0.8 mmol) in dry toluene (2.0 mL) was added TfOH (1.2 mmol). The mixture was stirred at 100 °C for 1 hour. After the completion of the reaction, solvent was removed under reduced pressure and the resulting crude product was purified by column chromatography on silica gel to give the corresponding product **3** (PE : EA = 30/1, v/v).

Compound 3a: brown liquid, 85% yield, 63 mg. ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 4.55 (s, 2H) ppm; ^{19}F NMR (376 MHz, CDCl_3) δ -81.01 (t, J = 8.0 Hz, 3F), -87.41 to -81.49 (m, 2F), -121.54 to -120.63 (m, 2F), -125.54 to -125.62 (m, 2F) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 191.86, 134.74, 134.29, 128.99, 128.39, 37.11 ppm; MS (EI) m/z (%): 370 (1) $[\text{M}]^+$, 135 (3), 119 (3), 105 (100), 91 (6), 77 (60), 69 (5), 51 (8); HRMS (FI) calcd for $\text{C}_{12}\text{H}_7\text{F}_9\text{OS}$ $[\text{M}]^+$ requires 370.0068, found 370.0063.

Compound 3b: yellow solid, m.p. 32–34 °C, 86% yield, 80 mg; ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 4.55 (s, 2H)

ppm; ^{19}F NMR (376 MHz, CDCl_3) δ -80.90 (t, J = 10.2 Hz, 3F), -86.95 to -87.67 (m, 2F), -119.76 (s, 2F), -121.51 (s, 2F), -122.89 (s, 2F), -126.22 to -126.34 (m, 2F) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 191.87, 134.74, 134.30, 129.00, 128.40, 37.17 ppm; MS (EI) m/z (%): 470 (3) $[\text{M}]^+$, 365 (40), 135 (20), 105 (100), 91 (86), 77 (98), 65 (30), 51 (90); HRMS (EI) calcd for $\text{C}_{14}\text{H}_7\text{F}_{13}\text{OS}$ $[\text{M}]^+$ requires 470.0005, found 470.0011.

Compound 3c: yellow solid, m.p. 63–65 °C, 86% yield, 98 mg; ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 4.55 (s, 2H) ppm; ^{19}F NMR (376 MHz, CDCl_3) δ -80.90 (t, J = 11.2 Hz, 3F), -87.21 to -87.29 (m, 2F), -119.67 (s, 2F), -121.26 (s, 2F), -121.82 to -122.34 (m, 4F), -122.87 (s, 2F), -126.19 to -126.28 (m, 2F) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 191.87, 134.74, 134.28, 128.98, 128.39, 37.13 ppm; MS (EI) m/z (%): 570 (2) $[\text{M}]^+$, 551 (8), 465 (10), 179 (15), 105 (100), 91 (56), 77 (85), 51 (50); HRMS (FI) calcd for $\text{C}_{16}\text{H}_7\text{F}_{17}\text{OS}$ $[\text{M}]^+$ requires 569.9941, found 569.9947.

Compound 3d: yellow liquid, 84% yield, 54 mg; ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 4.55 (s, 2H) ppm; ^{19}F NMR (376 MHz, CDCl_3) δ -80.08 (t, J = 11.2 Hz, 3F), -88.08 to -88.13 (m, 2F), -124.02 (t, J = 3.7 Hz, 2F) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 191.86, 134.73, 134.32, 129.01, 128.41, 37.04 ppm; MS (EI) m/z (%): 320 (2) $[\text{M}]^+$, 215 (3), 169 (5), 105 (100), 91 (10), 77 (58), 69 (8), 51 (18); HRMS (FI) calcd for $\text{C}_{11}\text{H}_7\text{F}_7\text{OS}$ $[\text{M}]^+$ requires 320.0100, found 320.0104.

Compound 3e: brown liquid, 61% yield, 27 mg; ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 8.0 Hz, 2H), 7.63 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 2H), 4.51 (s, 2H) ppm; ^{19}F NMR (376 MHz, CDCl_3) δ -41.46 (s, 3F) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 192.00, 134.73, 134.26, 131.14 (q, J = 197 Hz), 128.99, 128.42, 38.39 (d, J = 2.0 Hz) ppm; MS (EI) m/z (%): 220 (2) $[\text{M}]^+$, 182 (5), 105 (100), 83 (3), 77 (45), 69 (3), 65 (2), 51 (5); HRMS (FI) calcd for $\text{C}_9\text{H}_7\text{F}_3\text{OS}$ $[\text{M}]^+$ requires 220.0164, found 220.0159. Some unidentified impurities were hard to separate from the reaction mixture. So, the clean ^1H NMR spectrum was not obtained.

Compound 3f: white solid, m.p. 89–91 °C, 74% yield, 56 mg; ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 4.52 (s, 2H), 2.42 (s, 3H) ppm; ^{19}F NMR (376 MHz, CDCl_3) δ -80.98 (t, J = 11.2 Hz, 3F), -87.39 to -81.46 (m, 2F), -121.53 to -120.61 (m, 2F), -125.50 to -125.61 (m, 2F) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 191.45, 145.45, 132.27, 129.67, 128.52, 37.07, 21.76 ppm; MS (EI) m/z (%): 384 (1) $[\text{M}]^+$, 292 (22), 265 (5), 149 (3), 119 (100), 105 (7), 91 (60), 65 (20); HRMS (FI) calcd for $\text{C}_{13}\text{H}_9\text{F}_9\text{OS}$ $[\text{M}]^+$ requires 384.0225, found 384.0226.

Compound 3g: white solid, m.p. 69–71 °C, 89% yield, 71 mg; ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.0 Hz, 2H), 4.50 (s, 2H), 3.88 (s, 3H) ppm; ^{19}F NMR (376 MHz, CDCl_3) δ -80.99 (t, J = 11.2 Hz, 3F), -87.41 to -81.48 (m, 2F), -121.54 to -120.61 (m, 2F), -125.54 to -125.61 (m, 2F) ppm; ^{13}C NMR (101 MHz, CDCl_3) δ 190.27, 164.44, 130.81, 127.73, 114.17, 55.59, 36.88 ppm; MS (EI) m/z (%): 400 (2) $[\text{M}]^+$, 265 (3), 135 (100), 121 (5), 107 (7), 92 (9), 77



(12), 69 (3); HRMS (FI) calcd for $C_{13}H_9F_9O_2S$ $[M]^+$ requires 400.0174, found 400.0168.

Compound **3h**: brown liquid, 78% yield, 63 mg; 1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 4.50 (s, 2H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.03 (t, J = 11.2 Hz, 3F), -87.39 to -87.46 (m, 2F), -120.56 to -120.63 (m, 2F), -125.56 to -125.64 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.76, 140.97, 133.01, 129.78, 129.37, 36.89 ppm; MS (EI) m/z (%): 404 (2) $[M]^+$, 265 (6), 139 (100), 125 (8), 111 (47), 89 (3), 75 (36), 50 (5); HRMS (FI) calcd for $C_{12}H_6ClF_9OS$ $[M]^+$ requires 403.9676, found 403.9682.

Compound **3i**: white solid, m.p. 52–54 °C, 58% yield, 51 mg; 1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 4.49 (s, 2H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.94 (t, J = 11.2 Hz, 3F), -87.33 to -87.41 (m, 2F), -121.50 to -120.58 (m, 2F), -125.49 to -125.57 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.95, 133.43, 132.40, 129.84, 129.75, 36.83 ppm; MS (EI) m/z (%): 448 (2) $[M]^+$, 350 (6), 265 (10), 185 (98), 183 (100), 157 (79), 155 (80), 76 (50); HRMS (FI) calcd for $C_{12}H_6BrF_9OS$ $[M]^+$ requires 447.9174, found 447.9172.

Compound **3j**: yellow solid, m.p. 26–28 °C, 82% yield, 64 mg; 1H NMR (400 MHz, $CDCl_3$) δ 8.19–7.79 (m, 2H), 7.19–7.14 (m, 2H), 4.51 (s, 2H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.00 to -81.14 (m, 3F), -87.44 to -87.52 (m, 2F), -100.04 to -107.02 (m, 1F), -120.58 to -120.66 (m, 2F), -125.59 to -125.67 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.34, 166.40 (d, J = 257.1 Hz), 131.12, 131.22, 116.24 (d, J = 22.2 Hz), 36.90 ppm; MS (EI) m/z (%): 388 (2) $[M]^+$, 123 (100), 109 (10), 95 (41), 83 (3), 75 (15), 69 (12), 50 (2); HRMS (FI) calcd for $C_{12}H_6F_{10}OS$ $[M]^+$ requires 387.9974, found 387.9969.

Compound **3k**: yellow solid, m.p. 40–41 °C, 56% yield, 49 mg; 1H NMR (400 MHz, $CDCl_3$) 8.06 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.0 Hz, 2H), 4.53 (s, 2H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.39 (s, 3F), -80.98 (td, J = 9.8, 2.7 Hz, 3F), -87.33 to -87.40 (m, 2F), -121.53 to -120.60 (m, 2F), -125.54 to -125.59 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.08, 137.32, 135.55 (q, J = 33.3 Hz), 128.79, 126.11 (q, J = 3.1 Hz), 123.31 (d, J = 273.7 Hz), 36.92 ppm; MS (EI) m/z (%): 438 (2) $[M]^+$, 419 (20), 265 (10), 173 (100), 159 (20), 145 (85), 125 (9), 95 (10); HRMS (FI) calcd for $C_{13}H_6F_{12}OS$ $[M]^+$ requires 437.9942, found 437.9940.

Compound **3l**: brown liquid, 78% yield, 68 mg; 1H NMR (400 MHz, $CDCl_3$) 8.02 (d, J = 4.0 Hz, 1H), 7.77 (dd, J = 8.3, 2.1 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 4.47 (s, 2H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.93 (t, J = 7.5 Hz, 3F), -87.30 to -87.38 (m, 2F), -121.52 to -120.60 (m, 2F), -125.53 to -125.61 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.86, 139.17, 134.15, 133.94, 131.17, 130.35, 127.33, 36.73 ppm; MS (EI) m/z (%): 438 (3) $[M]^+$, 175 (98), 173 (100), 159 (59), 145 (95), 138 (20), 109 (85), 75 (70); HRMS (FI) calcd for $C_{12}H_5Cl_2F_9OS$ $[M]^+$ requires 437.9298, found 437.9286.

Compound **3m**: brown liquid, 74% yield, 59 mg; 1H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 2H), 7.26 (s, 1H), 4.53 (s, 2H), 2.38 (s, 6H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.93 (t, J = 7.5 Hz, 3F), -87.30 to -87.38 (m, 2F), -121.53 to -120.60 (m, 2F), -125.50 to -125.62 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$)

δ 192.16, 138.77, 136.00, 134.82, 126.15, 37.36, 21.22 ppm; MS (EI) m/z (%): 398 (2) $[M]^+$, 265 (15), 133 (100), 119 (46), 105 (85), 91 (30), 77 (75), 69 (38); HRMS (FI) calcd for $C_{14}H_{11}F_9OS$ $[M]^+$ requires 398.0381, found 398.0378.

Compound **3n**: light yellow solid, m.p. 69–71 °C, 77% yield, 65 mg; 1H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.03–7.96 (m, 2H), 7.9–7.82 (m, 2H), 7.66–7.57 (m, 2H), 4.69 (s, 2H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.88 to -80.95 (m, 3F), -87.26 to -87.35 (m, 2F), -120.47 to -120.54 (m, 2F), -125.45 to -125.56 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.78, 136.04, 132.37, 132.07, 130.48, 129.70, 129.25, 129.03, 127.93, 127.28, 123.56, 37.23 ppm; MS (EI) m/z (%): 420 (8) $[M]^+$, 265 (3), 155 (100), 141 (10), 127 (50), 105 (5), 77 (8), 69 (7); HRMS (FI) calcd for $C_{16}H_9F_9OS$ $[M]^+$ requires 420.0225, found 420.0223.

Compound **6a**: yellow liquid, 8% yield, 5.2 mg; 1H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 4H), 7.59 (t, J = 8.0 Hz, 2H), 7.46 (t, J = 8.0 Hz, 4H), 6.40 (s, 1H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ -40.09 (s, 1.5F), -46.53 (s, 1.5F) ppm. MS (EI) m/z (%): 324 (28) $[M]^+$, 303 (5), 255 (8), 237 (9), 221 (5), 105 (100), 82 (8), 77 (36); HRMS (EI) calcd for $C_{16}H_{11}F_3O_2S$ $[M]^+$ requires 324.0426, found 324.0425.

Conflicts of interest

There are no conflicts to declare.

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References

- (a) T. Umemoto, *Chem. Rev.*, 1996, **96**, 1757–1778; (b) G. K. S. Prakash and A. K. Yudin, *Chem. Rev.*, 1997, **97**, 757–786; (c) O. A. Tomashenko and V. V. Grushin, *Chem. Rev.*, 2011, **111**, 4475–4521; (d) T. Furuya, A. S. Kamlet and T. Ritter, *Nature*, 2011, **473**, 470–477; (e) F. A. Carey and R. J. Sundberg, *Nucleophilic Substitution*, in *Advanced Organic Chemistry: Part A: Structure and Mechanisms*, ed. F. A. Carey and R. J. Sundberg, Springer US, Boston, MA, 2007; (f) T. Besset, C. Schneider and D. Cahard, *Angew. Chem., Int. Ed.*, 2012, **51**, 5048–5050, (*Angew. Chem.*, 2012, **124**, 5134–5136); (g) A. Studer, *Angew. Chem., Int. Ed.*, 2012, **51**, 8950–8958, (*Angew. Chem.*, 2012, **124**, 9082–9090); (h) X. Wang, Y. Zhang and J. Wang, *Sci. Sin.: Chim.*, 2012, **42**, 1417–1427; (i) B. E. Smart, *Chem. Rev.*, 1996, **96**, 1555–1556; (j) M. Hird, *Chem. Soc. Rev.*, 2007, **36**, 2070–2095; (k) Y. Li, *Acc. Chem. Res.*, 2012, **45**, 723–733; (l) M. Cametti, B. Crousse, P. Metrangolo, R. Milani and G. Resnati, *Chem. Soc. Rev.*, 2012, **41**, 31–42; (m) R. Berger, G. Resnati,



- P. Metrangolo, E. Weber and J. Hulliger, *Chem. Soc. Rev.*, 2011, **40**, 3496–3508.
- 2 (a) F. Toulgoat, S. Alazet and T. Billard, *Eur. J. Org. Chem.*, 2014, 2415–2428; (b) C. Hansch, A. Leo and R. W. Taft, *Chem. Rev.*, 1991, **91**, 165–195; (c) T. Hiyama, *Organofluorine Compounds: Chemistry and Applications*, Springer, Berlin, 2000; (d) J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok and H. Liu, *Chem. Rev.*, 2014, **114**, 2432–2506; (e) M. Li, J. Guo, X. S. Xue and J. P. Cheng, *Org. Lett.*, 2016, **18**, 264–267; (f) X. H. Xu, K. Matsuzaki and N. Shibata, *Chem. Rev.*, 2015, **115**, 731–764.
 - 3 (a) T. Silverstone, J. Fincham and J. Plumley, *Br. J. Clin. Pharmacol.*, 1979, **7**, 353–356; (b) R. B. Strelkov and L. F. Semenov, *Radiobiologiya*, 1964, **4**, 756–759; (c) L. M. Yagupolskii, I. I. Maletina, K. I. Petko, D. V. Fedyuk, R. Handrock, S. S. Shavaran, B. M. Klebanov and S. Herzig, *J. Fluorine Chem.*, 2001, **109**, 87–94.
 - 4 (a) R. J. Cremllyn, *An Introduction to Organo-Sulfur Chemistry*, Wiley & Sons, New York, 1996; (b) H. Q. Zhang, J. M. Xi and W. W. Liao, *J. Org. Chem.*, 2020, **85**, 1168–1180; (c) H. Y. Chen, S. Kim, J. Y. Wu, E. T. Birzin, W. Chan, Y. T. Yang, J. Dahllund, F. DiNinno, S. P. Rohrer, J. M. Schaeffer and M. L. Hammond, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 2551–2554.
 - 5 (a) M. Liao and B. Wang, *Green Chem.*, 2007, **9**, 184–188; (b) J. Li, K. Ji, R. Zheng, J. Nelson and L. Zhang, *Chem. Commun.*, 2014, **50**, 4130–4133; (c) R. M. P. Dias and A. C. B. Burtoloso, *Org. Lett.*, 2016, **18**, 3034–3037; (d) Y. Xu, X. Huang, G. Lv, R. Lai, S. Lv, J. Li, L. Hai and Y. Wu, *Eur. J. Org. Chem.*, 2020, 4635–4638; (e) X. B. Xu, Z. H. Lin, Y. Liu, J. Guo and Y. He, *Org. Biomol. Chem.*, 2017, **15**, 2716–2720; (f) A. Jana, P. Bhaumick and L. H. Choudhury, *New J. Chem.*, 2020, **44**, 8442–8453; (g) A. Cadu, R. A. Watile, S. Biswas, A. Orthaber, P. J. R. Sjöberg and J. S. M. Samec, *Org. Lett.*, 2014, **16**, 5556–5559.
 - 6 (a) S. G. Li and S. Z. Zard, *Org. Lett.*, 2013, **15**, 5898–5902; (b) Z. Zhang, Z. Sheng, W. Yu, G. Wu, R. Zhang, W. D. Chu, Y. Zhang and J. Wang, *Nat. Chem.*, 2017, **9**, 970–976; (c) L. Xu, H. Wang, C. Zheng and G. Zhao, *Adv. Synth. Catal.*, 2017, **359**, 2942–2948; (d) H. B. Yang, X. Fan, Y. Wei and M. Shi, *Org. Chem. Front.*, 2015, **2**, 1088–1093.
 - 7 H. Bayreuther and A. Haas, *Chem. Ber.*, 1973, **106**, 1418–1422.
 - 8 (a) L. Hu, M. Wu, H. Wan, J. Wang, G. Wang, H. Guo and S. Sun, *New J. Chem.*, 2016, **40**, 6550–6553; (b) X. Shao, X. Wang, T. Yang, L. Lu and Q. Shen, *Angew. Chem., Int. Ed.*, 2013, **52**, 3457–3460, (*Angew. Chem.*, 2013, **125**, 3541–3544); (c) C. Xu, B. Ma and Q. Shen, *Angew. Chem., Int. Ed.*, 2014, **53**, 9316–9320, (*Angew. Chem.*, 2014, **126**, 9470–9474).
 - 9 I. Saidalimu, S. Suzuki, T. Yoshioka, E. Tokunaga and N. Shibata, *Org. Lett.*, 2016, **18**, 6404–6407.
 - 10 (a) X. B. Li, Z. F. Xu, L. J. Liu and J. T. Liu, *Eur. J. Org. Chem.*, 2014, 1182–1188; (b) J. H. Xu, M. Jiang, L. P. Song and J. T. Liu, *Eur. J. Org. Chem.*, 2021, 1919–1923.
 - 11 (a) X. B. Li, J. Zhao, J. Jiang and J. T. Liu, *J. Fluorine Chem.*, 2016, **185**, 24–30; (b) X. B. Li, J. Zhao, Q. Liu, M. Jiang and J. T. Liu, *Chin. J. Org. Chem.*, 2019, **39**, 183–191.
 - 12 J. H. Li, J. H. Xu, M. Jiang, L. P. Song and J. T. Liu, *Eur. J. Org. Chem.*, 2022, e202200885.
 - 13 T. Hirashita, S. Kuwahara, S. Okochi, M. Tsuji and S. Araki, *Tetrahedron Lett.*, 2010, **51**, 1847–1851.

