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A New Approach for the Synthesis of Perfluoroalkanesulfenic Acids

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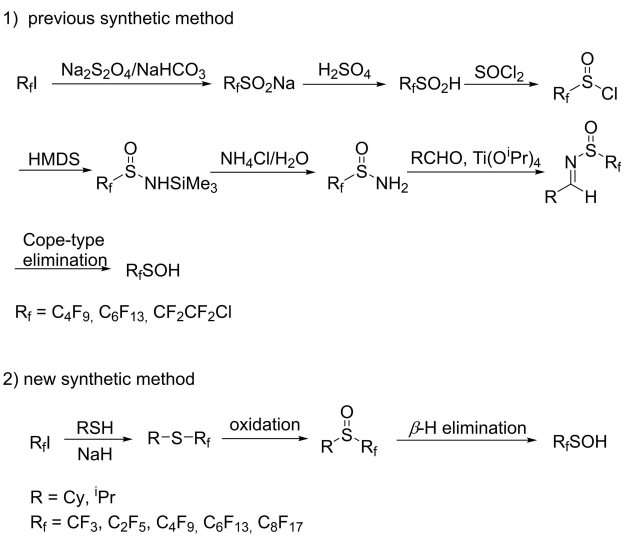
A new and more practical method for the preparation of solution-stable perfluoroalkanesulfenic acids was successfully developed. Starting from perfluoroalkyl iodides, perfluoroalkyl sulfoxides were synthesized by their substitution reaction with alkyl mercaptans and the following oxidation of resulting perfluoroalkyl sulfides with *m*-CPBA. Subsequent β-H elimination of perfluoroalkyl sulfoxides under heating conditions gave the corresponding perfluoroalkanesulfenic acids in good yields.

Introduction

Sulfenic acids (RSOH) have been recognized as active sulfur-containing intermediates which widely exist in organisms and play important roles in the life process.[1] They are key intermediates to regulate protein redox and have catalytic or regulatory functions in many redox-sensitive proteins, which are related to a variety of signal transduction pathways.[2] These signal transduction processes are closely related to the pathogenesis and drug design of many diseases. Sulfenic acids have both nucleophilic and electrophilic properties[3] and easily undergo self-condensation to give thiosulfinates in the absence of suitable trapping agents, which further transform into thiosulfonates and disulfides through redox conversion.[4] Therefore, most sulfenic acids are unstable and only exist as active intermediates in some reactions,[5] and many efforts have been made to synthesize and isolate stable sulfenic acids.[6] In general, either a huge steric hindrance[7] or intramolecular hydrogen bond,[8] or a combination of both,[9] is necessary for a sulfenic acid to be stable enough for isolation or characterization. Although some stable sulfenic acids have been synthesized so far, most of them are not suitable for directly studying the chemistry of the sulfenic group (–SOH) due to difficulties in their preparation, multireactive sites, or huge steric hindrance. As a result, research on the chemistry of sulfenic acids is still fragmentary.

In 2014, we reported a special type of solution-stable perfluoroalkanesulfenic acids, in which the strong electron-withdrawing perfluoroalkyl groups played an important role to stabilize the SOH group.[10] Further studies showed that these perfluorinated sulfenic acids have good reactivities and could undergo addition reactions with alkenes, alkynes, or allenes.[11] In many cases, similar reaction behaviors to those of normal non-fluorine sulfenic acids were observed with these perfluorinated sulfenic acids, indicating that perfluoroalkanesulfenic acids could provide a simple and stable model to study the chemistry of sulfenic acids and mimic some life processes involving sulfenic acids. Previously, perfluoroalkanesulfenic acids were obtained by Cope-type elimination reaction of the corresponding perfluoroalkanesulfinimines. As shown in Scheme 1, the synthesis of perfluoroalkanesulfinimine required multi-step reactions and made the preparation of perfluoroalkanesulfenic acids less efficient and uneconomic. Therefore, it is very desirable to develop a more convenient synthetic method for perfluoroalkanesulfenic acids.

During our study on the reaction of polyfluoroalkanesulfenic acids with alkenes, it was found that the addition of sulfenic acids to alkenes and the reverse *syn*-β-H elimination of resulted sulfoxides could take place at the same time.[11] Inspired by this, we tried a new synthetic method and found that using β-H elimination of perfluoroalkyl sulfoxides as a key step, perfluor-



Scheme 1. Synthetic methods for perfluoroalkanesulfenic acids.

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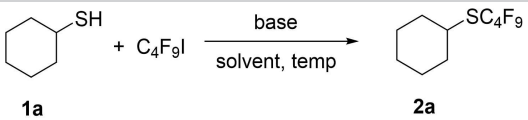
oalkanesulfenic acids could be easily obtained from perfluoroalkyl iodides with high efficiency and good yields (Scheme 1, eq 2). The results are reported in this paper.

Results and Discussion

Initially, we tried to synthesize alkyl perfluoroalkyl sulfides and embarked on our investigation with the reaction of perfluorobutyl iodide with cyclohexanethiol (**1a**) in the presence of sodium bisulfite and sodium formate in a mixed solvent of dimethyl formamide (DMF) and water referring to the literature.[12] Unfortunately, cyclohexyl perfluorobutyl sulfide (**2a**) was only obtained in 10% yield (Table 1, entry 1).

Other bases, such as KH_2PO_4, $NaHCO_3$, *t*-BuOK, Na_2HPO_4, NaOH, K_2CO_3, Cs_2CO_3, K_3PO_4, and NaH, were also tested (entries 2–10). It was found that KH_2PO_4, $NaHCO_3$, *t*-BuOK, Na_2HPO_4, and NaOH could not promote the reaction (entries 2–6). Gratefully, NaH afforded **2a** in 41% yield (entry 10). Solvents were also screened, and lower yields were obtained in tetrahydrofuran (THF), dimethyl sulfoxide (DMSO), and dichloromethane (DCM) (entries 11–13). Changing the addition sequence of reactants showed that the yield of **2a** could be improved to 58% when perfluorobutyl iodide was added to the pre-stirred mixture of cyclohexanethiol and NaH (entry 14). Further investigation indicated that a slightly higher yield of **2a** could be achieved with a ratio of **1a**/C_4F_9I/NaH = 1:1.2:1.1 (entries 15–16), and a better result was obtained at −20 °C (entries 17–19). As a comparison, the reaction at −20 °C in the presence of K_3PO_4 was also tried and a lower yield was obtained (44%, entry 20). Therefore, the optimal conditions for the formation of **2a** were set as follows: 1.0 equiv. of alkyl mercaptan, 1.2 equiv. of perfluoroalkyl iodide, and 1.1 equiv. of NaH in DMF at −20 °C.

Table 1. Optimization of reaction conditions for the formation of sulfide **2a**.



1a **2a**

Entry[a]	Base	C_4F_9I (equiv.)	Solvent	Temp [°C]	Yield [%][b]
1	Na_2SO_3/HCOONa	1.0	DMF/H_2O	RT	10
2	KH_2PO_4	1.0	DMF	RT	trace
3	$NaHCO_3$	1.0	DMF	RT	trace
4	^{t}BuOK	1.0	DMF	RT	trace
5	Na_2HPO_4	1.0	DMF	RT	trace
6	NaOH	1.0	DMF	RT	trace
7	K_2CO_3	1.0	DMF	RT	20
8	Cs_2CO_3	1.0	DMF	RT	13
9	K_3PO_4	1.0	DMF	RT	30
10	NaH	1.0	DMF	RT	41
11	NaH	1.0	THF	RT	10
12	NaH	1.0	DMSO	RT	34
13	NaH	1.0	DCM	RT	trace
14[c]	NaH	1.0	DMF	RT	58
15[c]	NaH	1.2	DMF	RT	63
16[c]	NaH	1.5	DMF	RT	54
17[c]	NaH	1.2	DMF	0	55
18[c]	NaH	1.2	DMF	−20	85
19[c]	NaH	1.2	DMF	−40	80
20	K_3PO_4	1.2	DMF	−20	44

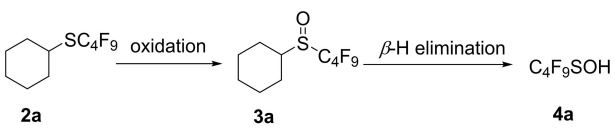
[a] Reaction conditions: **1a** (1.0 mmol), C_4F_9I (1.0–1.5 mmol), base (1.1 mmol) for 1 h. [b] Determined by ^{19}F NMR spectroscopy using $PhCF_3$ as internal standard. [c] After stirring the mixture of **1a** and NaH for 1 h at room temperature, perfluorobutyl iodide was added at the specified temperature.

Next, the oxidation of cyclohexyl perfluorobutyl sulfide was studied. It was found that **2a** could be easily oxidized by 3-chloroperbenzoic acid (*m*-CPBA), giving the corresponding sulfoxide **3a** in good yield along with a small amount of sulfone as a byproduct. Screening the ratio of reactants, reaction temperature and time showed that the best result was obtained when 1.0 equivalent of *m*-CPBA was used and the reaction was carried out at room temperature (Scheme 2). Other oxidants such as hydrogen peroxide, oxone, and $NaIO_4$ were also tried but did not give a better result.

On the basis of our previous reaction conditions for the synthesis of perfluoroalkanesulfenic acids via Cope-type elimination of perfluoroalkanesulfinimines,[10] β-H elimination of **3a** was firstly carried out in toluene at 80 °C for 10 h. However, ^{19}F NMR monitoring showed that perfluoro-*n*-butanesulfenic acid (**4a**) was formed in only 14% yield. When the reaction temperature was increased to 110 °C, 100% conversion of **3a** and 88% yield of **4a** were obtained after 8 hours (Scheme 2).

Considering an alkene was also produced in the β-H elimination reaction of alkyl perfluoroalkyl sulfoxide, and the alkene with a shorter carbon chain and a lower boiling point would be easier to remove from the reaction mixture, several perfluorobutyl sulfoxides (**3b**–**3f**) were prepared from different alkyl mercaptans and their β-H elimination reactions were studied to find a more practical method for perfluoroalkanesulfenic acids. As shown in Scheme 3, perfluoroalkyl sulfoxides **3b**–**3e** with 2-butyl, *n*-propyl, 2-methyl-1-propyl, or *n*-butyl group could not completely convert into sulfenic acid, whether increasing temperature or prolonging reaction time. Fortunately, 100% conversion was obtained with sulfoxide **3f** containing a shorter *iso*-propyl group under similar conditions.

Using cyclohexyl or *iso*-propyl as the counterpart alkyl group, a series of alkyl perfluoroalkyl sulfoxides were synthesized from different perfluoroalkyl iodides and their β-H elimination reactions were studied to prepare the correspond-

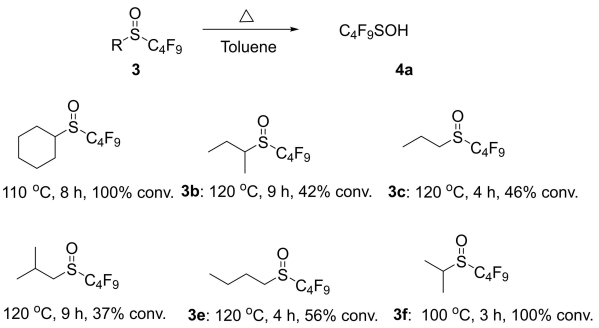


2a **3a** **4a**

oxidation:
m-CPBA (1.0 equiv), CH_2Cl_2, 0 °C, 3 h, 77%
m-CPBA (1.0 equiv), CH_2Cl_2, rt, 3 h, 80%
m-CPBA (1.0 equiv), CH_2Cl_2, rt, 12 h, 88%
m-CPBA (1.2 equiv), CH_2Cl_2, rt, 3 h, 87%
H_2O_2 (4.0 equiv), AcOH, 50 °C, 12 h, 70%
oxone (1.0 equiv), CH_2Cl_2+H_2O, rt, 12 h, NR
$NaIO_4$ (1.0 equiv), MeOH, rt, 12 h, NR

elimination:
toluene, 80 °C, 10 h, 14%
toluene, 110 °C, 8 h, 88%

Scheme 2. Synthesis of perfluoro-*n*-butanesulfenic acid.



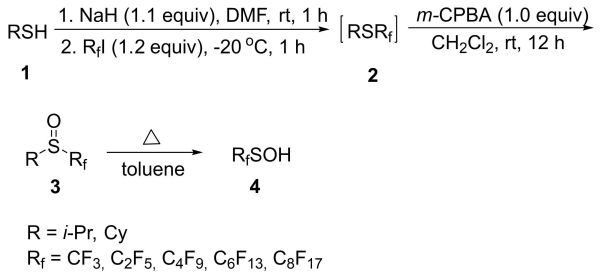
Scheme 3. β-H elimination of various perfluorobutyl sulfoxides.

ing perfluoroalkanesulfenic acids. As shown in Table 2, trifluoromethanesulfenic acid (**4b**), perfluoroethanesulfenic acid (**4c**), perfluoro-*n*-hexanesulfenic acid (**4d**), and perfluoro-*n*-octanesulfenic acid (**4e**) were successfully prepared in good yields under the optimized conditions, and similar results were obtained with isopropyl and cyclohexyl. It is worth mentioning that crude products **2** could be used directly in this process without purification.

Conclusions

In summary, we have developed a convenient and more practical method for the synthesis of perfluoroalkanesulfenic acids. Using perfluoroalkyl iodides as starting materials, the corresponding perfluoroalkyl sulfides could be easily prepared by the substitution reaction with alkyl mercaptans. Subsequent oxidation with *m*-CPBA and β-H elimination reaction of resulted perfluoroalkyl sulfoxides gave desired perfluoroalkanesulfonic acids. With advantages such as high efficiency, easy-to-handle, and mild conditions, this new method would find applications in organic syntheses and researches on the chemistry of sulfonic acids.

Table 2. Synthesis of perfluoroalkanesulfenic acids.



Entry	R/R_f	3 Yield [%][a]	Elimination	4 Yield [%][b]
1	Cy/C_4F_9	**3a**, 60	110 °C, 8 h	**4a**, 86
2	*i*-Pr/C_4F_9	**3f**, 61	100 °C, 3 h	**4a**, 88
3	Cy/CF_3	**3g**, 23	160 °C, 10 min	**4b**, 70
4	Cy/C_2F_5	**3h**, 48	110 °C, 8 h	**4c**, 86
5	Cy/C_6F_{13}	**3i**, 51	110 °C, 8 h	**4d**, 84
6	*i*-Pr/C_6F_{13}	**3j**, 55	100 °C, 3 h	**4d**, 86
7	Cy/C_8F_{17}	**3k**, 55	110 °C, 8 h	**4e**, 87
8	*i*-Pr/C_8F_{17}	**3l**, 56	100 °C, 3 h	**4e**, 85

[a] Overall isolated yields for two steps. [b] Determined by ^{19}F NMR spectroscopy using $PhCF_3$ as internal standard.

Experimental Section

General information

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

Typical procedure for the prepartion of compound 2: In a 50 mL three-necked flask, the solution of sodium hydride (11 mmol) and alkyl mercaptan (10 mmol) in DMF (15 mL) was stirred at room temperature for 1 hour. Then the mixture was cooled to −20 °C and perfluoroalkyl iodide (12 mmol) was quickly added. After 1 hour, the reaction mixture was warmed to room temperature and quenched with water. The resulting solution was extracted with DCM for three times (3×10 mL). The organic layers were combined, dried over $MgSO_4$, and concentrated to give crude product **2**.

Typical procedure for the prepartion of compound 3: To a solution of *m*-CPBA (1.0 equiv) in DCM (20 mL) was added dropwise the solution of above crude product **2** in DCM (10 mL) in 5 minutes. The mixture was stirred overnight at room temperature. The resulting mixture was quenched with aqueous $NaHCO_3$ solution. The resulting solution was extracted with DCM for three times (3× 20 mL). The combined organic solution was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (PE: DCM = 5:1) to give product **3**.

Typical procedure for the preparation of compound 4: A solution of sulfoxide **3** in dry toluene (0.2 M) was stirred at 100–160 °C in a sealed tube. After the completion of the reaction, the mixture was cooled to room temperature and the yield of **4** was determined by ^{19}F NMR spectroscopy.

Compound **3a**: light yellow liquid; 2.10 g, 60% yield; IR (neat, cm^{-1}): ν 2939, 2862, 1454, 1235, 1138, 1047, 862, 746; ^1H NMR (400 MHz, $CDCl_3$) δ 3.09–3.19 (m, 1H), 1.97–2.01 (m, 1H), 1.82–1.92 (m, 3H), 1.51–1.69 (m, 3H), 1.30–1.43 (m, 2H), 1.17–1.27 (m, 1H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.31 ~ −81.41 (m, 3F), −116.82 (AB, J = 248.1 Hz, 2F), −122.27 (AB, J = 300.8 Hz, 2F), −126.45 (AB, J = 293.3 Hz, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.95, 27.08, 25.26, 24.94, 24.80, 23.90 ppm; MS (FI) (m/z, %): 351 (3) $[M+H]^+$; HRMS (FI) calcd for $C_{10}H_{12}F_9OS$ $[M+H]^+$ requires 351.0456, found 351.0460.

Compound **3b**: light yellow liquid; 1.40 g, 43% yield; IR (neat, cm^{-1}): ν 2968, 2937, 1468, 1351, 1237, 1139, 866, 725; ^1H NMR (400 MHz, $CDCl_3$) δ 3.02–3.08 (m, 1H), 2.51–2.58 (m, 1H), 2.24–2.31

(m, 1H), 1.08–1.12 (m, 6H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.20 ~ −81.35 (m, 3F), −119.26 (AB, J = 248.2 Hz, 2F), −121.83 (AB, J = 308.3 Hz, 2F), −126.48 (AB, J = 304.6 Hz, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.12 (t, J = 17.0 Hz), 23.23, 22.60, 20.98 ppm; MS (FI) (m/z, %): 324 (34) $[M]^+$; HRMS (FI) calcd for $C_8H_9F_9OS$ $[M]^+$ requires 324.0218, found 324.0225.

Compound **3c**: light yellow liquid; 0.91 g, 29% yield; IR (neat, cm^{-1}): v 2975, 2942, 1465, 1351, 1236, 1013, 865, 725; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.04–3.11 (m, 1H), 2.72–2.80 (m, 1H), 1.79–1.98 (m, 2H), 1.09 (t, J = 7.4 Hz, 3H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.30 ~ −81.35 (m, 3F), −119.25 (AB, J = 248.2 Hz, 2F), −122.03 (AB, J = 304.6 Hz, 2F), −126.57 (AB, J = 293.3 Hz, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 49.50, 15.61, 12.87 ppm; MS (EI) (m/z, %): 311 (3) $[M+H]^+$, 219 (19), 131 (50), 119 (28), 100 (38), 91 (54), 69 (100), 63 (18); HRMS (ESI) calcd for $C_7H_7F_9OS$ $[M+H]^+$ requires 311.0145, found 311.0147.

Compound **3d**: light yellow liquid; 0.94 g, 29% yield; IR (neat, cm^{-1}): v 2968, 2937, 1468, 1350, 1237, 1099, 866, 725; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.04–3.09 (m, 1H), 2.52–2.59 (m, 1H), 2.26–2.33 (m, 1H), 1.11–1.14 (m, 6H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.10 ~ −81.18 (m, 3F), −118.65 (AB, J = 251.9 Hz, 2F), −121.73 (AB, J = 293.3 Hz, 2F), −126.39 (AB, J = 293.3 Hz, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.19 (t, J = 4.1 Hz), 23.25, 22.70, 21.07 ppm; MS (FI) (m/z, %): 324 (30) $[M]^+$; HRMS (FI) calcd for $C_8H_9F_9OS$ $[M]^+$ requires 324.0222, found 324.0225.

Compound **3e**: light yellow liquid; 1.33 g, 41% yield; IR (neat, cm^{-1}): v 2967, 2939, 1468, 1350, 1236, 1139, 864, 724; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00–3.07 (m, 1H), 2.73–2.82 (m, 1H), 1.74–1.85 (m, 2H), 1.40–1.53 (m, 2H), 0.86–0.94 (m, 3H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.43 ~ −81.67 (m, 3F), −119.93 (AB, J = 248.2 Hz, 2F), −122.11 (AB, J = 312.1 Hz, 2F), −126.70 (AB, J = 293.3 Hz, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 47.42 (t, J = 4.4 Hz), 23.74, 21.69, 13.11 ppm; HRMS (ESI) calcd for $C_8H_9F_9OS$ $[M+H]^+$ requires 325.0301, found 325.0303.

Compound **3f**: light yellow liquid; 1.89 g, 61% yield; IR (neat, cm^{-1}): v 2925, 1353, 1275, 1248, 1137, 1079, 749, 724; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.30–3.41 (m, 1H), 1.38–1.41 (m, 6H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.42 ~ −81.62 (m, 3F), −117.39 (AB, J = 247.9 Hz, 2F), −122.43 (AB, J = 304.6 Hz, 2F), −126.60 (AB, J = 293.3 Hz, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 49.36, 17.31, 13.99 ppm; MS (FI) (m/z, %): 311 (9) $[M+H]^+$; HRMS (FI) calcd for $C_7H_8F_9OS$ $[M+H]^+$ requires 311.0145, found 311.0147.

Compound **3g**: light yellow liquid; 0.46 g, 23%; IR (neat, cm^{-1}): v 2937, 2860, 1453, 1169, 1139, 1076, 1046, 745; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.04–3.11 (m, 1H), 2.04–2.11 (m, 1H), 1.82–1.96 (m, 3H), 1.51–1.71 (m, 3H), 1.21–1.49 (m, 3H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −70.09 (s, 3F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 123.93 (q, J = 336.3 Hz), 57.46, 26.17, 25.08, 25.04, 24.77, 24.40 ppm; MS (FI) (m/z, %): 201 (1) $[M+H]^+$; HRMS (FI) calcd for $C_7H_{12}F_3OS$ $[M+H]^+$ requires 201.0551, found 201.0555.

Compound **3h**: light yellow liquid; 1.21 g, 48% yield; IR (neat, cm^{-1}): v 2938, 2861,1454, 1331,1216, 1122, 949, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17–3.24 (m, 1H), 2.03–2.10 (m, 1H), 1.84–1.98 (m, 3H), 1.67–1.74 (m, 2H), 1.56–1.67 (m, 1H), 1.35–1.48 (m, 2H), 1.21–1.33 (m, 1H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.42 (s, 3F), −120.03 (AB, J = 244.4 Hz, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 118.01 (qt, J = 288.3, 32.1 Hz), 117.03 (ddq, J = 314.5, 304.2, 39.1 Hz), 56.75 (t, J = 3.0 Hz), 26.88 (d, J = 2.9 Hz), 25.15, 24.98, 24.79, 24.10 ppm; HRMS (ESI) calcd for $C_8H_{12}F_5OS$ $[M+H]^+$ requires 251.0522, found 251.0524.

Compound **3i**: white solid; m.p. 44–46°C; 2.31 g, 51% yield; IR (neat, cm^{-1}): v 2934, 2859, 1453, 1241, 1203, 1145, 1076, 666; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13–3.21 (m, 1H), 2.00–2.04 (m, 1H), 1.84–1.96 (m, 3H), 1.22–1.76 (m, 3H), 1.34–1.46 (m, 2H), 1.21–1.31 (m, 1H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.14 (t, J = 10.0 Hz, 3F), −116.44 (AB, J = 244.4 Hz, 2F), −121.17 (AB, J = 304.6 Hz, 2F), −122.02 ~ −122.17 (m, 2F), −122.93 ~ −123.08 (m, 2F), −126.34 ~ −126.47 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 57.01 (t, J = 3.6 Hz), 27.11, 25.31, 24.98, 24.84, 23.93 ppm; MS (EI) (m/z, %): 368 (1) $[M-C_6H_{11}]^+$, 169 (6), 131 (13), 119 (12), 100 (9), 83 (100), 69 (21), 55 (80); HRMS (ESI) calcd for $C_{12}H_{11}F_{13}OS$ $[M+Na]^+$ requires 473.0214, found 473.0215.

Compound **3j**: white solid; m.p. 36–38°C; 2.26 g, 55% yield; IR (neat, cm^{-1}): v 2934, 2859, 1453, 1241, 1203, 1145, 1076, 666; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.32–3.39 (m, 1H), 1.38–1.41 (m, 6H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.95 ~ −81.01 (m, 3F), −116.73 (AB, J = 244.4 Hz, 2F), −120.99 ~ −121.08 (m, 1F), −121.16 ~ −121.27 (m, 1F), −121.90 ~ −122.07 (m, 2F), −122.82 ~ −123.01 (m, 2F), −126.21 ~ −126.35 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 49.39 (t, J = 3.5 Hz), 17.34, 13.9 ppm; MS (FI) (m/z, %): 411 (1) $[M+H]^+$; HRMS (FI) calcd for $C_9H_8F_{13}OS$ $[M+H]^+$ requires 411.0086, found 411.0081.

Compound **3k**: white solid; m.p. 72–74°C; 3.03 g, 55% yield; IR (neat, cm^{-1}): v 2931, 2859, 1371, 1204, 1148, 1120, 1076, 652; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.15–3.22 (m, 1H), 2.02–2.06 (m, 1H), 1.85–1.98 (m, 3H), 1.56–1.74 (m, 3H), 1.35–1.48 (m, 2H), 1.22–1.33 (m, 1H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.98 ~ −81.04 (m, 3F), −116.3 (AB, J = 248.2, 2F), −121.01 (AB, J = 300.8 Hz, 2F), −121.64 ~ −122.15 (m, 6H), −122.80 ~ −122.96 (m, 2F), −126.23 ~ −126.37 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 57.04 (t, J = 3.1 Hz), 27.16 (d, J = 2.8 Hz), 25.36, 25.01, 24.89, 23.96 ppm; HRMS (ESI) calcd for $C_{14}H_{11}F_{17}OS$ $[M+Na]^+$ requires 573.0149, found 573.0151.

Compound **3l**: white solid; m.p. 70–72°C; 2.86 g, 56% yield; IR (neat, cm^{-1}): v 2929, 1371, 1331, 1203, 1150, 1121, 928, 654; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31–3.42 (m, 1H), 1.39–1.42 (m, 6H) ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.93 ~ −80.99 (m, 3F), −116.68 (AB, J = 244.4, 2F), −120.92 ~ −121.01 (m, 1F), −121.08 ~ −121.18 (m, 1F), −121.71 ~ −122.07 (m, 6F), −122.77 ~ −122.93 (m, 2F), −126.23 ~ −126.32 (m, 2F) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 49.42 (t, J = 10.2 Hz), 17.36, 14.01 ppm; MS (FI) (m/z, %): 511 (17) $[M+H]^+$; HRMS (FI) calcd for $C_{11}H_8F_{17}OS$ $[M+H]^+$ requires 511.0013, found 511.0019.

Compound **4a**: ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.18 (t, J = 10.0 Hz, 3F), −102.72 (t, J = 12.7 Hz, 2F), −122.28 ~ −122.37 (m, 2F), −126.13 ~ −126.20 (m, 2F) ppm.

Compound **4b**: ^{19}F NMR (376 MHz, $CDCl_3$) δ −56.03 (s, 3F) ppm.

Compound **4c**: ^{19}F NMR (376 MHz, $CDCl_3$) δ −82.64 ~ −82.62 (m, 3F), −107.61 ~ −107.73 (m, 2F) ppm.

Compound **4d**: ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.13 (t, J = 10.3 Hz, 3F), −102.51 (t, J = 13.7 Hz, 2F), −121.40 ~ −121.48 (m, 2F), −121.92 ~ −121.99 (m, 2F), −122.81 ~ −122.90 (m, 2F), −126.21 ~ −126.31 (m, 2F) ppm.

Compound **4e**: ^{19}F NMR (376 MHz, $CDCl_3$) δ −81.11 ~ −81.22 (m, 3F), −102.41 ~ −102.50 (m, 2F), −121.36 ~ −121.41 (m, 2F), −121.74 ~ −121.95 (m, 6F), −122.78 (s, 2F), −126.21 ~ −126.32 (m, 2F) ppm.

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Conflict of Interest

The authors declare no conflict of interest.

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