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Iododifluoromethyl alkenes [$ICF_2CH{=}CHR$]: a labile system generated from 1,1-difluoro-1,3-diiodoalkanes and its trapping with nucleophiles

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Abstract

Treatment of 1,1-difluoro-1,3-diiodoalkanes ($ICF_2CH_2CHIR^1$, **1**) with NEt_3 in various solvents or with $KF/Al_2O_3/CH_3CN$ gave no alkenes ($ICF_2CH{=}CHR^1$, **2**), whereas with NaOH afforded α,β-unsaturated carboxylic acids, although a signal of **2** in ^{19}F NMR spectroscopy could be observed momentarily sometimes. However, the labile **2** can be trapped either with thiolate or phenoxide ions. The former reaction gives a mixture of $CF_2{=}CHCH(SR)R^1$ and $RSCF_2CH{=}CHR^1$, whereas the latter affords only $ArOCF_2CH{=}CHR^1$. The nucleophilic substitution of the bromoanalogues, $BrCF_2CH_2CHBrR^1$ and $BrCF_2CH{=}CHR^1$, has also been investigated. A mechanism involving S_N2' and an allene intermediate is proposed.

Keywords: 1,1-Difluoro-1,3-diiodoalkanes; Thiolate ions; Phenoxides; 1,1-Difluoroallene

1. Introduction

The iododifluoromethyl substituted alkenes, $ICF_2CH{=}CIR$, derived from the addition of difluorodiiodomethane to alkynes, could not be obtained through the initiation either by lead tetraacetate in alcohol [1] or aqueous hydrogen peroxide in acetone [2]. Instead, non-fluorinated compounds, i.e., β-iodo-α,β-unsaturated carboxylic esters and acids were formed. The alkene could not be isolated from the reaction of difluorodiiodomethane with phenylacetylene initiated by benzoyl peroxide (BPO) at 100°C for 20 min except that the desired compound could be detected by ^{19}F nuclear magnetic resonance (NMR) spectroscopy (in $CDCl_3$, −39.0 ppm, d, $J = 12.7$ Hz, *E*-form and −40.0 ppm, d, $J = 12.4$ Hz, *Z*-form, the ratio = 3:1) [3]. On the other hand, it is known that the bromoanalogues, i.e., bromodifluoromethylated alkenes, $BrCF_2CH{=}CHR$, are rather stable in most cases which are usually prepared from the addition of CF_2Br_2 to alkenes followed by the dehydrobromination with base [4,5]. However, the instability of some bromodifluoroalkenes is also well known. For example, 1-bromodifluoromethylcyclohexene or $PhCH{=}CHCF_2Br$ could not be obtained from the reaction of 1-difluorobromomethyl-2-bromocyclohexane or 1,1-difluoro-1,3-dibromo-3-phenylpropane with base due to the further hydrolysis of the bromodifluoromethyl group [5–7]. It is reasonable to assume that iododifluoromethyl alkenes will behave in a similar way. However, we are able to show that the thionate and phenoxide ions can trap the olefins. The results are presented herein.

2. Results and discussion

The starting materials, 1,1-difluoro-1,3-diiodoalkanes ($ICF_2CH_2CHIR^1$, **1**) are readily prepared from the reaction of difluorodiiodomethane and alkenes in the presence of BPO [8], Fe [9], Zn [9], $Na_2S_2O_4/NaHCO_3$ [10] or $Pb(OAc)_4$ [1]. In order to synthesize the corresponding iododifluoroalkenes, **2**, we tried to eliminate hydrogen iodide from **1** with base (Scheme 1). It was found that treatment of **1a** with sodium bicarbonate in acetonitrile, diethyl ether, tetrahydrofuran, 1,4-dioxane, diglyme, *N*,*N*-dimethylformamide (DMF), ethanol, methanol or benzene at room temperature did not give **2a**, **1a** being recovered. However, triethylamine in DMF overnight caused the complete consumption of **1a**, whereas the reaction was complete in diethyl ether or

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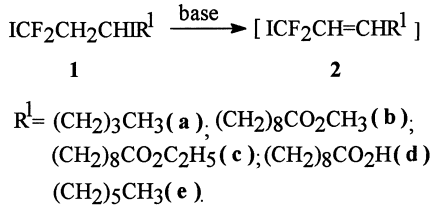
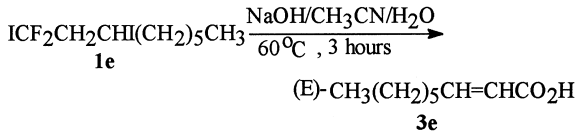


Scheme 1.



Scheme 2.

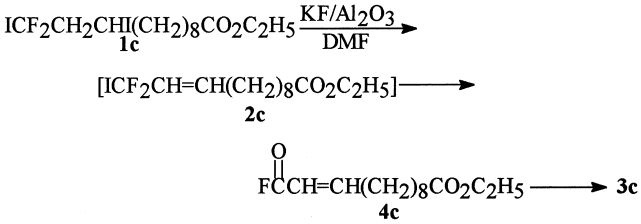
1,4-dioxane in 3 days as indicated by the disappearance of the $\delta_F = -39$ ppm peak during ^{19}F NMR monitoring, but no new signal was observed. When **1e** was reacted with aqueous sodium hydroxide in acetonitrile at 60°C for 3 h, a fluorine-free product, α,β-unsaturated carboxylic acid, **3e** was obtained (Scheme 2).

Recently, potassium fluoride supported on alumina was reported to be an efficient dehydrohalogenating agent [4,5,11]. However, when **1a** was treated with $KF/Al_2O_3/CH_3CN$, the formation of **2a** could be deduced spectroscopically only ($\delta_F = -37$ ppm, s). But on treatment of **1c** with KF/Al_2O_3/DMF, a small amount of α,β-unsaturated carboxylic acid fluoride, **4c** (10%), can be isolated, which is considered to be the precursor of the α,β-unsaturated carboxylic acid **3c** (Scheme 3).

Therefore, these results seem to show that iododifluoromethyl alkenes are indeed more labile than their bromo-analogues. Interestingly, when some nucleophiles were used both as dehydroiodination agent and trapper, derivatives of **2** might be formed. For example, the reaction of **1c** with sodium phenoxide in DMF at room temperature for 4 h gave *E*-difluoroallylphenyl ether **5ca** exclusively in high yield. (Table 1 and Scheme 4).

Sodium thionates **6** in DMF were found to react quickly with **1** at room temperature to give two products **7** and **8** (Table 2 and Scheme 5).

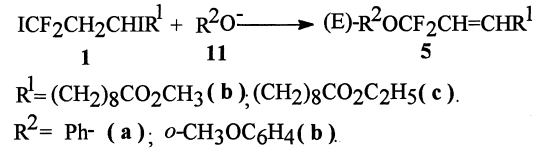
The yields and ratios of the products, **7**:**8**, were dependent on the ratios of the starting materials (**1** and **6**) used and the



Scheme 3.

Table 1
The reaction of **1** with **11** at room temperature in DMF for 4 h

Entry	Reactants	Isolated yield (%)
1	**1b** + **11a**	**5ba** (75)
2	**1b** + **11b**	**5bb** (70)
3	**1c** + **11a**	**5ca** (80)



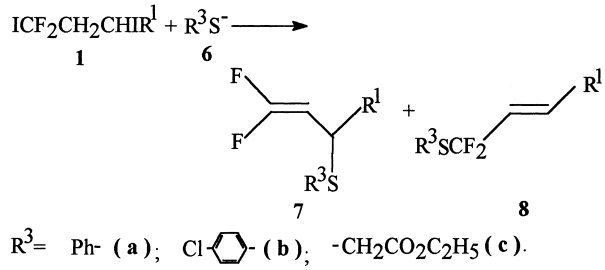
Scheme 4.

structure of **6**. For thiophenoxides **6a** and **6b**, when **6**:**1** ≥ 2:1, **7** was the major product, the ratio of **7**:**8** being 6:1 (determined by ^{19}F NMR). Higher ratio of **6**/**1** favored the formation of **7** (Entries 3, 4 and 5 in Table 2). On the contrary, when more nucleophilic alkylthionate **6c** was used, **8** became the main product (Entries 10 and 13 in Table 2). Under suitable conditions, either **7** or **8** may be formed exclusively (Entries 8 and 12 in Table 2). However, heating of either **7bb** or **7bc** at 150°C in DMF for 3 h did not result in the formation of **8bb** or **8bc**. The starting materials were recovered almost quantitatively. Similarly, **8bb** or **8bc** was not isomerized to **7bb** or **7bc** under similar conditions (Scheme 6).

In order to explain the formation of **5**, **7** and **8** from **1**, an S_N2' mechanism is proposed as shown in Scheme 7.

In a general case, **2** is first formed when treating **1** with a base or nucleophile. Addition of the nucleophile to **2** followed by elimination of iodide ion gives **7** as observed experimentally in the case in which nucleophile is **6a** or **6b**. Intramolecular S_N2' of **7** to **8** may be excluded by the above mentioned fact, i.e., even under severe conditions (in DMF at 150°C for 3 h), **7** was not changed to **8**. How about intermolecular S_N2' (see Table 3 and Scheme 8)?

It is indeed true that **8bc** was formed in high yield via S_N2' attack of the stronger nucleophile, **6c**, on **7bc** (Entry 6 in Table 3). However, for the weaker nucleophiles, **6a** and **6b**, a similar S_N2' did not occur (Entries 1 and 4 in Table 3) in spite of the fact that a more powerful sulfur nucleophile can

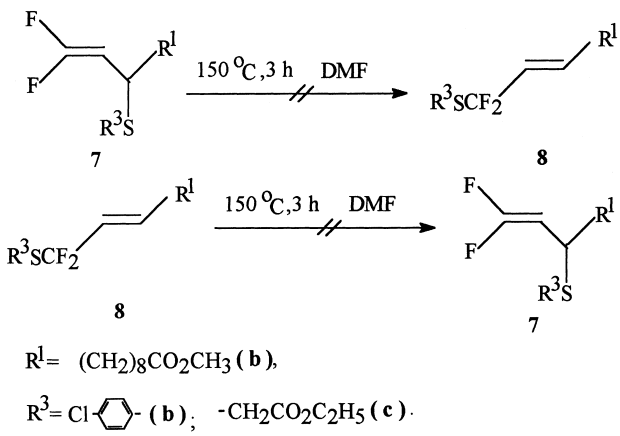


Scheme 5.

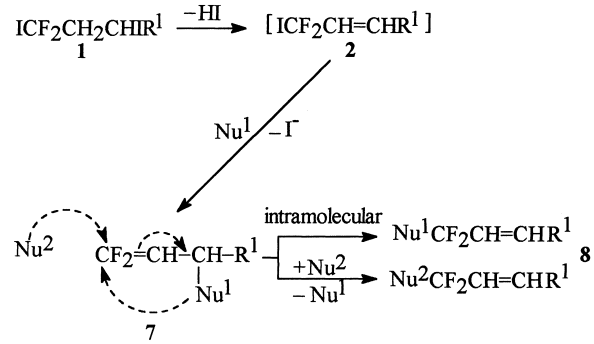
Table 2
The reaction of **1** or **12b** with **6** at room temperature in DMF for 4 h

Entry	Reactants	**1**:**6**	Conversion[a] (%)	Crude products[a], **7**:**8**	Isolated products[a], **7**:**8**	Isolated yield **7** or **8** (%)
1	**1a** + **6a**	1:2.2	100	61	121	71 (**7** + **8**)
2	**1b** + **6a**	1:2.4	100	–	–	99 (**7** + **8**)
3	**1b** + **6b**	1:2.4	100	71	–	81 (**7** + **8**)
4		1:4	100	>201	–	–
5		1:1	50	61	–	–
6	**1c** + **6a**	1:2.4	100	–	–	90 (**7** + **8**)
7	**1c** + **6b**	1:2.4	100	71	–	100 (**7** + **8**)
8	**1d** + **6a**	1:2.4	100	–	–	65 (**7**)
9	**1d** + **6b**	1:2.4	100	71	–	88 (**7** + **8**)
10	**1b** + **6c**	1:2.4	100	116	–	59 (**8**)
11		1:2	100	11	0.7:1	71 (**7** + **8**)
12		1:4	100	01	–	62 (**8**)
13	**1c** + **6c**	1:2.4	100	15	–	60 (**7** + **8**)
14		1:2	100	21	–	55 (**7** + **8**)
15		1:1	64	21	–	–
16	**12b** + **6a**	1:1	50	101	–	–
17		1:2.4	100	61	71	76 (**7** + **8**)
18	**12b** + **6b**	1:2.4	80	71	71	74 (**7** + **8**)
19	**12b** + **6c**	1:2	100	31	31	82 (**7** + **8**)
20		1:2.4	100	16	01	49 (**8**)
21		1:4	100	01	01	91 (**8**)

[a] Determined by ^{19}F NMR.



Scheme 6

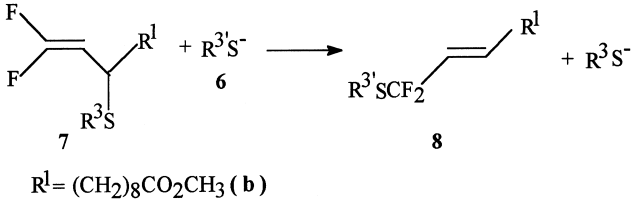


Scheme 7

Table 3
The reaction of **7** with **6** at room temperature in DMF for 4 h

Entry	Reactants	R^3	$R^{3'}$	**7**:**6**	Products (isolated yield %)
1	**7ba** + **6a**	C_6H_5 (**a**)	C_6H_5 (**a**)	1:2	No reaction
2	**7ba** + **6c**	C_6H_5 (**a**)	$CH_2CO_2C_2H_5$ (**c**)	1:1.3	**8bc** (69), **6a** (73)
3	**7bb** + **6a**	*p*-ClC_6H_4 (**b**)	C_6H_5 (**a**)	1:6.3	**8ba** (39), 7**bb** (22)[a]
4	**7bb** + **6b**	*p*-ClC_6H_4 (**b**)	*p*-ClC_6H_4 (**b**)	1:4.8 or 1:2	No reaction
5	**7bb** + **6c**	*p*-ClC_6H_4 (**b**)	$CH_2CO_2C_2H_5$ (**c**)	1:1.3	**8bc** (70), **6b** (69)
6	**7bc** + **6c**	$CH_2CO_2C_2H_5$ (**c**)	$CH_2CO_2C_2H_5$ (**c**)	1:4.8	**8bc** (95)

[a] Compound **6b** was not determined through the formation of *p*-ClC_6H_4SH because there was difficulty in separating latter from C_6H_5SH by chromatography (SiO_2).



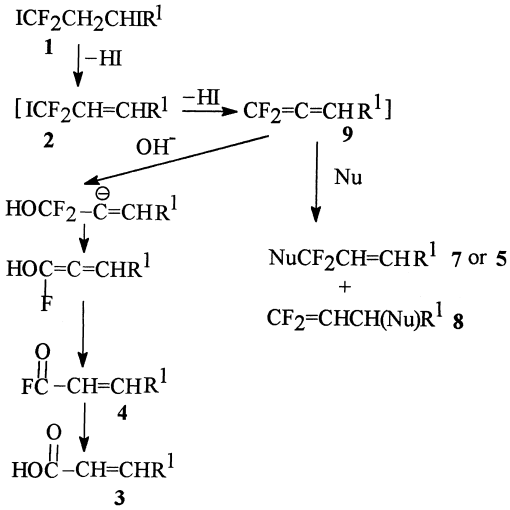
Scheme 8.

displace the less powerful one from **7** through the same mechanism (Entries 2, 3 and 5 in Table 3). Therefore, a simple S_N2' mechanism cannot give a satisfactory explanation of the formation of **8** and **5**.

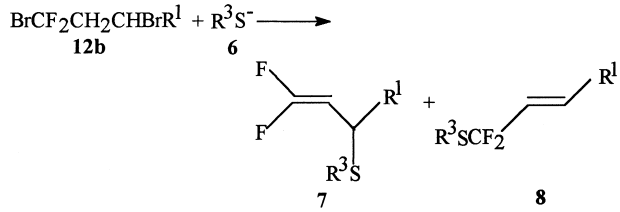
Furthermore, one can hardly illustrate the hydrolysis of the iododifluoromethyl group of **1** by means of base either. An alternative explanation is through a difluoroallene intermediate, CF_2=C=CHR[1], **9**, resulting from the double eliminations of hydrogen iodide from **1** as proposed previously for the reaction of $PhCHBrCH_2CF_2Br$ with $KF/Al_2O_3/CH_3CN$ [5]. In **9**, there are two electrophilically attacked sites, i.e., methinic carbon and CF_2 terminal. A weaker nucleophile, such as **6a** or **6b** mainly adds to methinic group to give **7** as well as to difluoromethyl group to afford **8** (Scheme 9). The opposite results are obtained for the stronger nucleophile such as **6c** and phenoxide ion. When a simple base was used as mentioned above, the products, α,β-unsaturated carbonyl fluoride and carboxylic acid, can be also rationalized in terms of attacking of hydroxyl ion on the terminal CF_2 of allene (Scheme 9).

The formation of the allene **9** apparently depends on the strength of nucleophile or base used as well as the presence of iodine in allylic position which possesses a good leaving ability.

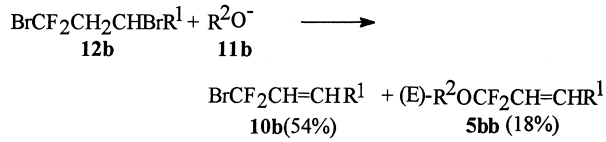
In order to verify the latter point, the synthesis of bromoanalogues **12b**, **10b** and their reactions with **6b**, **6c** and **11b** have been carried out.



Scheme 9.



Scheme 10.



Scheme 11.

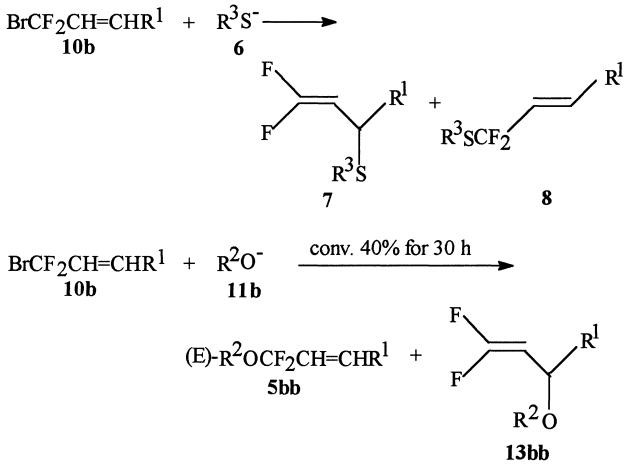
Treatment of **12b** with **6b** in the ratio of 1:2.4 gave a mixture of **7** and **8** with the ratio of 7:1, whereas with **6c** afforded only **8** even in the presence of excess of **6c** (Entries 18 and 21 in Table 2 and Scheme 10). The results are consistent with those from the alkene, **10b** (Entries 5 and 6 in Table 4 and Scheme 12) with the initial nucleophilic substitution of sulfur nucleophile, **6**, on **12b** to give the intermediate, alkene, **10b**. Because comparing the results of the reactions with sulfur nucleophile, **6**, between **12b** and **1**, we are unable to differentiate their reactivities. However, it became quite clear when they reacted with phenoxides, respectively. Treatment of **12b** with **11b** at room temperature for 4 h afforded not only **5bb** (18%) but also **10b** (54%) (Scheme 11).

These data are quite different from that of the reaction of **1** under the same conditions, in which **5bb** was the only product with a 70% yield (see Table 1). The formation of

Table 4
The reaction of **10b** and **6** or **11b** at room temperature in DMF for 2 h

Entry	Reactants	Ratio	Conversion (%)	Products (isolated yield %)
1	**10b** + **6a**	1:1.2	100	**7ba** (73), **8ba** (0)
2	**10b** + **6a**	1:2.4	100	**7bb** (79), **8bb** (5)
3	**10b** + **6b**	1:1.2	100	**7bb** (74), **8bb** (0)
4		1:2.4	100	**7bb** (60), **8bb** (<3)
5	**10b** + **6c**	1:1.2	100	**7bc** (52), **8bc** (0)
6		1:2.4	100	**7bc** (8), **8bc** (47)
7[a]	**10b** + **11b**	1:1.2	40	**5bb** (87), **13bb** (17)

[a] For 30 h.



Scheme 12.

10b as the major product from **12b** as compared with its absence from the reaction of **1** seems to show that the alkene, **2**, is more labile than **10**. Further reaction of the intermediate **10b** with **11b** occurred only sluggishly giving both CF_2-terminal and allylic substituted products at room temperature for 30 h with 40% conversion (Entry 7 in Table 4; Scheme 12). This may imply that the allene formed from **10b** is indeed much more difficult than that from **1** due to the difference in the reactivities of an allylic bromine and iodine.

In conclusion, we present evidence to show that iododifluromethylalkenes formed through eliminating HI from 1,1-difluoro-1,3-diiodoalkanes are very labile compounds. However, the alkenes can be trapped with thionate and phenoxide ions.

3. Experimental

IR spectra were recorded on a Shimadzu IR-440 or Perkin-Elmer Jeol 983 spectrometer. ^{19}F NMR spectra were obtained on a Varian EM-360L (56.4 MHz) spectrometer using trifluoroacetic acid as external standard and Bruker AM-300 (282 MHz) spectrometer, downfield shift being designated as negative. ^1H NMR spectra were carried out on a Varian EM-390 (90 MHz) spectrometer with Me_4Si as an external standard or Bruker AM-300 (300 MHz) spectrometer with Me_4Si as an internal standard. Mass spectra were taken on a Hewlett-Packard HP-5989A spectrometer and HRMS data were obtained on a Finnigan MAT-8430 spectrometer. All reactions were routinely monitored by using thin layer chromatography (TLC) or ^{19}F NMR spectroscopy.

3.1. The experiment of dehydroiodination from **1** by bases

3.1.1. With sodium bicarbonate

A mixture of $NaHCO_3$ (0.17 g, 2 mmol) and **1a** (0.39 g, 1 mmol) in CH_3CN (5 ml) were stirred for 3 days at room temperature. The signal at −39 ppm [1] assigned to **1a** did not change and **1a** was recovered. In other solvents such as diethyl ether, tetrahydrofuran, 1,4-dioxane, diglyme, *N*,*N*-dimethylformamide (DMF), ethanol, methanol or benzene, the similar phenomenon was observed.

3.1.2. With triethylamine

A mixture of triethylamine (0.20 g, 2 mmol) and **1a** (0.39 g, 1 mmol) in DMF (5 ml) were stirred overnight. The signal at −39 ppm assigned to **1a** disappeared and none of new signals was detected by ^{19}F NMR, indicative of the hydrolysis of the difluoromethylene group. An attempt to isolate the non-fluorine products from the reaction mixture only met failure. So did in diethyl ether or in 1,4-dioxane for 3 days.

3.1.3. With sodium hydroxide

A mixture of NaOH (1.15 g, 28.8 mmol) and **1e** (3.00 g, 7.2 mmol) in acetonitrile (20 ml) was stirred overnight, a new signal (−37 ppm, s) appeared. A 3 ml of the solution of acetonitrile was poured into water and acidified by HCl (5 ml, 1N). The aqueous layer was extracted three times with ether (3 × 5 ml). The combined extracts were washed with water (3 × 3 ml) and dried over Na_2SO_4. After evaporation of the ether, the residue was turned black and detected by ^{19}F NMR, a very small peak at −100 ppm being observed and the peak at about −40 ppm not being found. To other acetonitrile solution was added water (5 ml), the mixture was heated to 60°C for 3 h, poured into water and acidified by 1N HCl. The aqueous layer was extracted three times with ether (3 × 40 ml). The combined extracts were washed with water (3 × 10 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **3e** (0.95 g, 84%).

3e: Colorless oil. IR (film) (cm^{-1}): 2955, 2927, 2857, 1694, 1647, 1460, 1420, 1311, 1289, 1231, 1182, 1149, 1083, 980, 942, 690. ^1H NMR (CD_3COCD_3, 300 MHz) δ (ppm): 0.83 (3H), 1.29 (m, 6H), 1.43 (2H), 2.20 (2H), 5.80 (dt, J = 15.4, 1.5 Hz, 1H), 6.92 (dtt, J = 15.4, 7.0, 1.5 Hz, 1H). ^1H NMR (CCl_4, 90 MHz) δ (ppm): 12.4 (s, 1H). MS *m*/*z* (relative intensity): 157 (100), 139 (66.78), 96 (16.33), 73 (20.59), 69 (16.52), 55 (24.40), 43 (26.92), 41 (29.09). Analysis: calc. for $C_9H_{16}O_2$: C, 69.19%; H, 10.32%. Found: C, 69.23%; H, 10.66%.

3.1.4. With KF/Al_2O_3

A suspension consisting of DMF (2 ml), KF/Al_2O_3 power (3 g, 20 mmol) [5] and **1c** (1.00 g, 2 mmol) was stirred at 60°C for 1 h, while **1c** was completely consumed, detected by ^{19}F NMR. A small peak (−102 ppm) appeared. After acidified by 1N HCl, the mixture was filtered off. The filtrate

was poured into water and extracted three times with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **4c** (0.05 g, 10%).

4c: Colorless oil. IR (film) (cm^{-1}): 2900, 1800, 1740, 1640, 1200, 1100. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.20–1.73 (m, 15H), 2.28 (t, $J = 7.5$ Hz, 2H), 2.31 (d, $J = 6.4$ Hz, 2H), 4.12 (q, $J = 7.1$ Hz, 2H), 5.80 (dtt, $J = 15.6$, 8.2, 1.4 Hz, 1H), 7.18 (dt, $J = 14.6$, 7 Hz, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): −102.2 (d, $J = 7.7$ Hz). MS *m/z* (relative intensity): 239 (1.33), 213 (32.19), 164 (21.86), 55 (100.00).

3.2. General procedure for the reactions of **1** with **11**

Compound **1c** (1.02 g, 2 mmol) was added to **11a** (0.42 g phenol reacted with equimolar amount of NaH) in DMF (10 ml) at room temperature. After 4 h, the mixture was poured into water, to which HCl (10 ml, 1N) was added. The aqueous layer was extracted three times with ether (3 × 20 ml). The combined extracts were washed with water (3 × 10 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **5ca** (0.57 g, yield 80%).

5ca: Colorless oil. IR (film) (cm^{-1}): 2930, 1730, 1590, 1490, 1120. ^1H NMR (CD_3COCD_3, 300 MHz) δ (ppm): 1.18–1.59 (m, 15H), 2.14 (d, $J = 2.4$ Hz, 2H), 2.19 (t, $J = 7.4$ Hz, 2H), 4.08 (q, $J = 7.1$ Hz, 2H), 5.81 (dtt, $J = 15.5$, 6.9, 1.5 Hz, 1H), 6.42 (dtt, $J = 15.6$, 6.9, 2.2 Hz, 1H), 7.20–7.44 (m, 5H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): −16.1 (s). MS *m/z* (relative intensity): 335 (8.56), 309 (25.83), 261 (44.39), 175 (32.03), 133 (52.37), 94 (100.00). Analysis: calc. for $C_{20}H_{28}F_2O_3$: C, 67.77%; H, 7.96%; F, 10.72%. Found: C, 67.13%; H, 8.13%; F, 10.76%.

5ba: Colorless oil. IR (film) (cm^{-1}): 2926, 1736, 1676, 1626, 1590, 1491, 1437, 1320, 1200, 1182, 1123, 1035, 975, 756, 694. ^1H NMR (CD_3COCD_3, 300 MHz) δ (ppm): 1.43–1.61 (m, 12H), 2.17 (m, 2H), 2.27 (m, 2H), 3.61 (s, 3H), 5.81 (dtt, $J = 15.5$, 7.0, 1.5 Hz, 1H), 6.41 (dtt, $J = 15.7$, 7.0, 2.0 Hz, 1H), 7.21–7.44 (m, 5H). ^{19}F NMR (CD_3COCD_3, 282 MHz) δ (ppm): −16.1 (d, $J = 5.4$ Hz). MS *m/z* (relative intensity): 321 (100.00), 309 (7.75), 247 (13.05), 207 (6.10), 175 (9.10), 133 (10.51), 94 (9.60). Analysis: calc. for $C_{19}H_{26}F_2O_3$: C, 67.04%; H, 7.70%; F, 11.16%. Found: C, 66.81%; H, 7.51%; F, 11.04%.

5bb: Colorless oil. IR (film) (cm^{-1}): 2923, 1735, 1676, 1600, 1499, 1458, 1438, 1265, 1202, 1173, 1117, 1032, 975, 882, 783, 754. ^1H NMR (CD_3COCD_3, 300 MHz) δ (ppm): 1.24–1.59 (m, 12H), 2.13 (m, 2H), 2.25 (m, 2H), 3.60 (s, 3H), 3.82 (s, 3H), 5.75 (dtt, $J = 15.6$, 7.2, 1.4 Hz, 1H), 6.35 (dtt, $J = 15.5$, 7.0, 2.1 Hz, 1H), 6.89–7.34 (m, 4H). ^{19}F NMR (CD_3COCD_3, 282 MHz) δ (ppm): −16.2 (d, $J = 5.1$ Hz). MS *m/z* (relative intensity): 370 (M^+, 6.84%), 351 (40.40), 339 (6.64), 124 (100.00), 109 (11.65), 77 (14.24). Analysis: calc. for $C_{20}H_{28}F_2O_4$: C, 64.84%; H, 7.61%; F, 10.26%. Found: C, 64.68%; H, 7.57%; F, 10.30%.

3.3. General procedure for the reactions of **1** or **12b** with **6**

Compound **1b** (1.00 g, 2 mmol) was added to **6b** (0.69 g *p*-chlorothiophenol reacted with equimolar amount of NaH in DMF (10 ml). After the reaction was complete, the mixture was poured into water, to which HCl (10 ml, 1N) was added. The aqueous layer was extracted three times with ether (3 × 20 ml). The combined extracts were washed with water (3 × 10 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **7bb** and **8bb** (0.63 g, yield 81%).

A pure sample of **8aa**, **8ba**, **8ca**, **8da** or **8db** was not isolated from **7**, but identified by ^{19}F NMR.

7aa: Isolated from PhSSPh by distillation. Colorless oil, b.p. 73°C/mmHg. IR (film) (cm^{-1}): 2900, 1740, 1580, 1440, 1280, 1170. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.91 (t, $J = 7.2$ Hz, 3H), 1.30–1.78 (m, 6H), 3.84 (m, 1H), 4.18 (ddd, $J = 24.0$, 10.8, 2.0 Hz), 7.26–7.45 (m, 5H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 10.8 (d, $J = 41.8$), 12.2 (dd, $J = 41.7$, 24.0 Hz). MS *m/z* (relative intensity): 242 (M^+, 12.64%), 133 (16.41), 110 (75.16), 109 (33.68), 77 (100.00). HRMS: calc. for $C_{13}H_{16}F_2S$: 242.0941. Found: 242.0968.

7ba: Colorless oil. IR (film) (cm^{-1}): 2900, 1740, 1580, 1440, 1170. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.36–1.77 (m, 14H), 2.30 (t, $J = 7.5$ Hz, 2H), 3.65 (s, 3H), 3.80 (m, 1H), 4.16 (ddd, $J = 24.1$, 10.6, 2.0 Hz, 1H), 7.23–7.43 (m, 5H), ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 10.2 (d, $J = 41.7$ Hz), 11.4 (dd, $J = 41.6$, 24.0 Hz). MS *m/z* (relative intensity): 356 (M^+, 2.50%), 247 (100.00), 175 (58.25), 110 (71.79). Analysis: calc. for $C_{19}H_{26}F_2O_2S$: C, 64.01%; H, 7.35%; F, 10.66%. Found: C, 64.25%; H, 7.34%; F, 10.54%. HRMS: calc. for $C_{19}H_{26}F_2O_2S$: 356.1622. Found: 356.1641.

7bb: Colorless oil. IR (film) (cm^{-1}): 2931, 2857, 1738, 1574, 1477, 1178, 1096, 1014, 823. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 0.96–1.23 (m, 14H), 2.31 (t, $J = 7.5$ Hz, 2H), 3.67 (s, 3H), 3.78 (m, 1H), 4.15 (ddd, $J = 24.0$, 10.8, 1.9 Hz, 1H), 7.29 (m, 4H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 10.3 (d, $J = 40.9$ Hz), 11.8 (dd, $J = 41.2$, 24.0 Hz). MS *m/z* (relative intensity): 390 (M^+, 0.51%), 389 (1.79), 247 (79.81), 175 (54.29), 133 (74.74), 55 (100.00). Analysis: calc. for $C_{19}H_{25}ClF_2O_2S$: C, 58.37%; H, 6.45%; F, 9.72%. Found: C, 58.31%; H, 6.44%; F, 9.74%.

7bc: Colorless oil. IR (film) (cm^{-1}): 2900, 1740, 1280, 1170. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.28–1.72 (m, 17H), 2.32 (t, $J = 7.6$ Hz, 2H), 3.23 (dd, $J = 20.7$, 15.2 Hz, 2H), 3.70 (m, 4H),4.20 (m, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 9.73 (d, $J = 41.5$ Hz), 12.0 (dd, $J = 41.6$, 24.1 Hz). MS *m/z* (relative intensity): 366 (M^+, 1.16%), 346 (1.53), 279 (49.15), 247 (100.00), 175 (38.03). Analysis: calc. for $C_{17}H_{28}F_2O_4S$: C, 55.71%; H, 7.70%; F, 10.37%. Found: C, 55.92%; H, 7.81%; F, 10.31%.

7ca: Colorless oil. IR (film) (cm^{-1}): 2900, 1740, 1580, 1440, 1170. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.18–1.79 (m, 17H), 2.28 (t, $J = 7.5$ Hz, 2H), 3.80 (m, 1H), 4.09–4.22 (m, 3H), 7.23–7.43 (m, 5H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 10.8 (d, $J = 41.7$ Hz), 12.1 (dd, $J = 41.8$, 24.1 Hz). MS *m/z* (relative intensity): 370 (M^+, 0.83%), 331 (15.30), 261 (100.00), 175 (42.76), 137 (43.22), 109 (46.63). Analysis: calc. for $C_{20}H_{28}F_2O_2S$: C, 64.83%; H, 7.62%; F, 10.25%. Found: C, 64.73%; H, 7.59%; F, 10.28%.

7cb: Colorless oil. IR (film) (cm^{-1}): 2900, 1740, 1570, 1480, 1180, 1090, 820. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.23–1.75 (m, 17H), 2.29 (t, $J = 7.6$ Hz, 2H), 3.78 (m, 1H), 4.08–4.21 (m, 3H), 7.24–7.41 (m, 4H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 10.3 (d, $J = 41.9$ Hz), 11.8 (dd, $J = 41.2$, 24.0 Hz). MS *m/z* (relative intensity): 403 (1.85), 358 (18.89), 261 (100.00), 175 (59.02), 147 (59.06), 133 (87.98). Analysis: calc. for $C_{20}H_{27}ClF_2O_2S$: C, 59.32%; H, 6.72%; F, 9.38%. Found: C, 59.06%; H, 6.59%; F, 9.79%.

7cc: Colorless oil. IR (film) (cm^{-1}): 2900, 1740, 1270, 1180. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.20–1.67 (m, 20H), 2.25 (t, $J = 7.5$ Hz, 2H), 3.19 (q, $J = 14.4$ Hz, 2H), 3.62 (m, 1H), 4.06–4.19 (m, 5H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 9.69 (d, $J = 41.4$ Hz), 12.0 (dd, $J = 41.4$, 24.0 Hz). MS *m/z* (relative intensity): 380 (M^+, 0.64%), 293 (19.68), 261 (34.26), 247 (40.93), 175 (31.45), 55 (100.00). Analysis: calc. for $C_{18}H_{30}F_2O_4S$: C, 56.82%; H, 7.95%. Found: C, 56.56%; H, 8.13%.

7da: ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.31–1.80 (m, 14H), 2.35 (t, $J = 7.4$ Hz, 2H), 3.80 (m, 1H), 4.16 (ddd, $J = 24.0$, 10.7, 1.7 Hz, 1H), 7.25–7.43 (m, 5H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 10.7 (d, $J = 41.6$ Hz), 12.1 (dd, $J = 41.7$, 24.1 Hz). MS *m/z* (relative intensity): 242 (M^+, 10.22%), 233 (4.26), 193 (13.65), 110 (100.00). Analysis: calc. for $C_{18}H_{24}F_2O_2S$: C, 63.13%; H, 7.06%; F, 11.10%. Found: C, 63.08%; H, 7.16%; F, 11.05%.

7db: IR (film) (cm^{-1}): 2900, 1740, 1480, 1090, 820. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.29–1.75 (m, 14H), 2.35 (t, $J = 7.5$ Hz, 2H), 3.77 (m, 1H), 4.12 (ddd, $J = 24.0$, 10.7, 2.0 Hz, 1H), 7.24–7.35 (m, 4H), 11.2 (0.4H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): 10.3 (d, $J = 41.0$ Hz), 11.7 (dd, $J = 40.4$, 24.0 Hz). MS *m/z* (relative intensity): 376 (M^+, 10.22%), 359 (17.80), 193 (100.00), 175 (65.58). Analysis: calc. for $C_{18}H_{23}ClF_2O_2S$: C, 57.36%; H, 6.15%; F, 10.08%. Found: C, 57.36%; H, 6.27%; F, 10.05%.

8bb: Colorless oil. IR (film) (cm^{-1}): 2928, 1736, 1666, 1476, 1262, 1199, 1098, 1018. ^1H NMR (CD_3COCD_3, 300 MHz) δ (ppm): 1.30–1.58 (m, 12H), 2.07 (m, 2H), 2.30 (t, $J = 7.4$ Hz, 2H), 3.61 (s, 3H), 5.82 (dtt, $J = 15.6$, 9.9, 1.5 Hz, 1H), 6.12 (dtt, $J = 15.6$, 7.0, 2.4 Hz, 1H), 7.36–7.64 (m, 4H). ^{19}F NMR (CD_3COCD_3, 282 MHz) δ (ppm): −11.1 (d, $J = 9.3$ Hz). MS *m/z* (relative intensity): 390 (M^+, 2.64%), 371 (8.33), 351 (33.48), 247 (57.92), 207 (52.31), 175 (92.58), 147 (64.52), 133 (100.00). Analysis: calc. for $C_{19}H_{25}ClF_2O_2S$: C, 58.37%; H, 6.45%. Found: C, 58.16%; H, 6.41%.

8bc: Colorless oil. IR (film) (cm^{-1}): 2929, 1736, 1181, 1029. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm): 1.25–1.59 (m, 15H), 2.09 (m, 2H), 2.31 (t, $J = 7.5$ Hz, 2H), 3.58 (s, 2H), 3.67 (s, 3H), 4.20 (m, 2H), 5.69 (dt, $J = 15.7$, 9.4 Hz, 1H), 6.23 (dtt, $J = 15.6$, 6.8, 2.2 Hz, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz) δ (ppm): −5.55 (d, $J = 9.0$ Hz). MS *m/z* (relative intensity): 347 (31.91), 327 (59.26), 295 (72.14), 247 (62.68), 207 (49.89), 195 (100.00), 175 (85.17), 133 (87.05). Analysis: calc. for $C_{17}H_{28}F_2O_4S$: C, 55.71%; H, 7.70%; F, 10.37%. Found: C, 55.69%; H, 7.87%; F, 10.14%.

8cc: Colorless oil. IR (film) (cm^{-1}): 2900, 1740, 1290, 1170, 1120. ^1H NMR ($CDCl_3$, 282 MHz) δ (ppm): 1.23–1.63 (m, 18H), 2.12 (m, 2H), 2.27 (t, $J = 7.5$ Hz, 2H), 3.56 (s, 2H), 4.09 (q, $J = 7.1$ Hz, 2H), 4.20 (m, 2H), 5.67 (dtt, $J = 15.8$, 9.3, 1.5 Hz, 1H), 6.22 (dtt, $J = 15.6$, 6.7, 2.3 Hz, 1H). ^{19}F NMR (CD_3COCD_3, 300 MHz) δ (ppm): −5.45 (d, $J = 8.6$ Hz). MS *m/z* (relative intensity): 361 (63.02), 341 (100.00), 295 (21.95), 261 (33.85), 221 (24.27), 195 (28.83), 175 (28.96). Analysis: calc. for $C_{18}H_{30}F_2O_4S$: C, 56.82%; H, 7.95%. Found: C, 56.53%; H, 8.10%.

3.4. Test of the thermal stability of **7bb**, **8bb**, **7bc** *or* **8bc**

Compound **7bb** (0.39 g, 1 mmol) was in DMF (5 ml) heated at 150°C for 3 h. Then the mixture was poured into water. The aqueous layer was extracted three times with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was detected by ^{19}F NMR. Only **7bb** was left. No **8bb** was found.

The same results were obtained for **8bb**, **7bc** and **8bc**.

3.5. The reaction of **7bb** *with* **6b**

Compound **7bb** (0.39 g, 1 mmol) was added to **6b** (4.8 mmol) in DMF (5 ml) at room temperature. After 2 h, the mixture was poured into water, to which then HCl (5 ml, 1N) was added. The aqueous layer was extracted three times with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was detected by ^{19}F NMR. Only **7bb** was left. No **8bb** was found.

3.6. The general procedure of the reaction of **7ba**, **7bb** *or* **7bc** *with* **6c**

Compound **7bb** (0.70 g, 1.8 mmol) was added to **6c** (2.4 mmol) in DMF (5 ml) at room temperature. After 2 h, the mixture was poured into water, to which then HCl (5 ml, 1N) was added. The aqueous layer was extracted three times with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **8bc** (0.46 g, yield 70%).

3.7. The reaction of **12b** with **11b**

Compound **12b** (0.41 g, 1 mmol) was added to **11b** (2.4 mmol) in DMF (6 ml) at room temperature. After 4 h, the mixture was poured into water, to which then HCl (5 ml, 1N) was added. The aqueous layer was extracted three times with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **10b** (0.18 g, 54%) and **5bb** (0.07 g, yield 18%).

3.8. The general procedure of the reaction of **10b** with **6b** or **6c**

Compound **10b** (0.33 g, 1 mmol) was added to **6b** (1.2 mmol) in DMF (5 ml) at room temperature. After 2 h, the mixture was poured into water, to which then HCl (5 ml, 1N) was added. The aqueous layer was extracted three times with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **7bb** (0.30 g, yield 74%). No **8bb** was detected.

The similar reaction of **10b** (1 mmol) with **6c** (1.2 mmol) gave **7bc** (0.19 g, 52%).

3.9. The reaction of **10b** with **11b**

Compound **10b** (0.47 g, 1.4 mmol) was added to **11b** (1.7 mmol) in DMF (6 ml) at room temperature. After 30 h, the mixture was poured into water, to which then HCl (5 ml, 1N) was added. The aqueous layer was extracted three times with ether (3 × 10 ml). The combined extracts were washed with water (3 × 5 ml) and dried over Na_2SO_4. After the ether had been evaporated, the residue was subjected to chromatography on silica gel to give **10b** (0.28 g, 60%) and product 0.20 g (conversion 40%; yield: **5bb**, 87%; **13bb**, 13%). Compound **13bb** could not be isolated from **5bb**, but identified by ^{19}F NMR (CD_3COCD_3, 282 MHz) δ (ppm): 5.91 (d, $J = 40.7$ Hz), 6.24 (dd, $J =$ 43.2, 24.2 Hz).

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