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Journal of Fluorine Chemistry 123 (2003) 189–195
JOURNAL OF FLUORINE CHEMISTRY
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The chemistry of tetrafluoroallene: nucleophilic addition reactions with phenols and amines

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Received 28 February 2003; received in revised form 14 April 2003; accepted 19 April 2003

Abstract

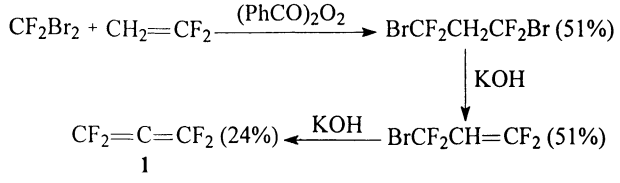
Treatment of tetrafluoroallene or its precursor, $ICF_2CH_2CF_2I$, with phenols in the presence of K_2CO_3 gave the corresponding unsaturated ethers. Tetrafluoroallene also reacted readily with amines in THF at room temperature to afford 3,3,3-trifluoropropionamides.

Keywords: Tetrafluoroallene; Nucleophilic addition reactions; Phenol; Amine

1. Introduction

It is known that fluoroallene and 1,1-difluoroallene, as allene derivatives, are prone to cycloaddition to alkenes [1], dienes [1a,2], nitrone [3] and diazo compounds [4] to give a quite variety of useful compounds. However, their analog, tetrafluoroallene (**1**), was less investigated. In 1959 Jacobs and Bauer first reported the synthesis of **1** by three-step procedure starting from dibromodifluoromethane [5] as shown follows (Scheme 1).

They also studied the chlorination [5] and dimerization [5] of **1**. After certain modification of the procedure, Banks et al. carried the ionic reaction of **1** with hydrogen halides, HX (X = Br, Cl, F) and fluoride ion to give $XCF_2CH{=}CF_2$ and $CF_3CH{=}CF_2$, respectively [6]. Fluoroallene **1** readily dimerizes to perfluoro-(1,2-dimethylenecyclobutane) and homopolymerized to $[-C(=CF_2)CF_2-]_n$ [5–7]. The cycloaddition of **1** to CF_3NO [8] or $CF_3C{\equiv}CCF_3$ [9] gives the corresponding [2 + 2]-adducts. Some interesting heterocyclic compounds were also obtained through 1,3-dipolar cycloaddition of **1** to *N*-phenylsydone [10], phenylazide [10], nitrone [11], diazophenylmethane [11] and diazodiphenylmethane [11]. Apparently, the chemistry of **1** has not been significantly developed because of its still difficult preparation. Recently, we reported that the yield of **1** was greatly improved by using 1,3-diiodo-1,1,3,3-tetrafluoropropane ($ICF_2CH_2CF_2I$, **2**) as its precursor which can be smoothly synthesized by the reaction of CF_2I_2 with $CF_2{=}CH_2$ in the presence of $Pb(OAc)_4$ [12]. Elimination of hydrogen iodide from **2** with K_2CO_3 in CH_3CN afforded **1** in good yield [12]. Thus, our new synthetic method for **1** makes the possibility for further expanding the chemistry of **1**. For example, very recently, we found that trifluoromethylindolizines could be obtained by 1,3-dipolar cycloaddition either from **1** to pyridinium bromide or from **2** in the presence of K_2CO_3 in CH_3CN at 65 °C [13] (Scheme 2).



Scheme 1.

Herein, we present the results of nucleophilic additions of phenols and amines to **1**.

2. Results and discussion

Although it was reported that **1** reacted with H_2O, MeOH and MeSH to give the corresponding $X{-}CF_2CH{=}CF_2$ (X = OH, OMe, SMe) [10], the experimental data of these compounds in detail were not available. We found that treatment of **2** with phenol (**3a**) in the presence of K_2CO_3 (10 mmol) in CH_3CN at 65 °C for 8 h gave the phenyl ether

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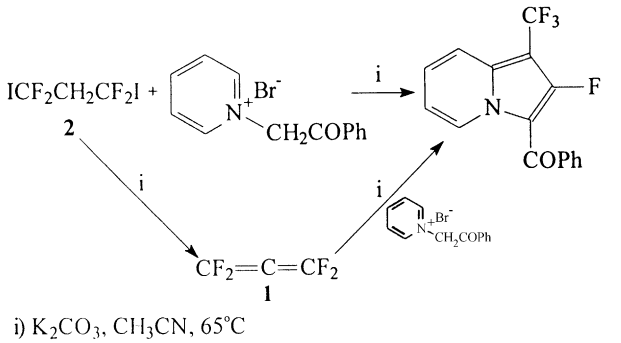
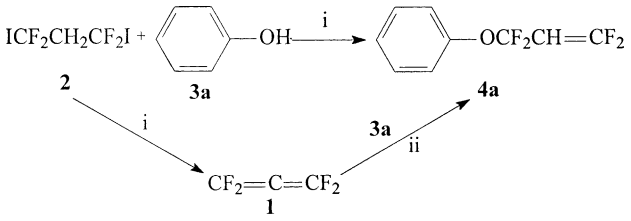
doi:10.1016/S0022-1139(03)00133-7



Scheme 2.



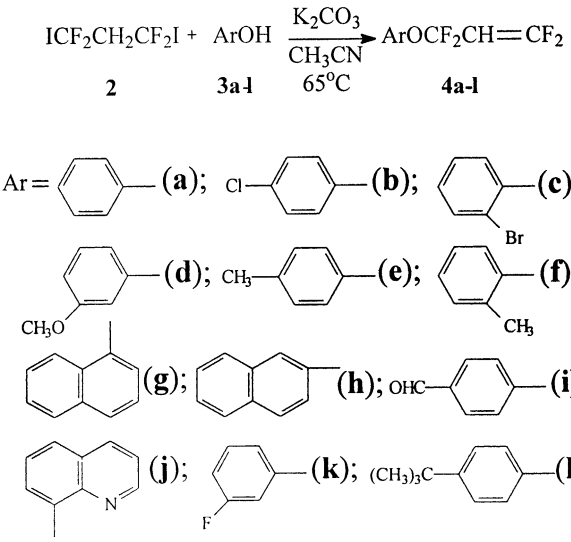
Scheme 3.

4a in high yield. The control experiment, i.e. using **1** as a reactant instead of **2** in the presence of catalytic amount of K_2CO_3 at room temperature for 6 h afforded the same product with a comparable yield. The absence of K_2CO_3 did not initiate the reaction showing that phenol is not a good nucleophile towards **1** (Scheme 3).

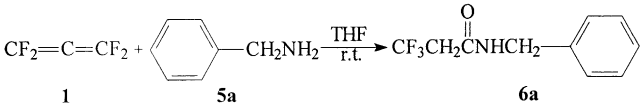
Similarly, several aromatic ethers were obtained either by the reactions of **2** with substituted phenols (one-pot procedure) or by that of **1** (two-step procedure) in comparable high yields (Scheme 4).

The results are listed in Table 1.

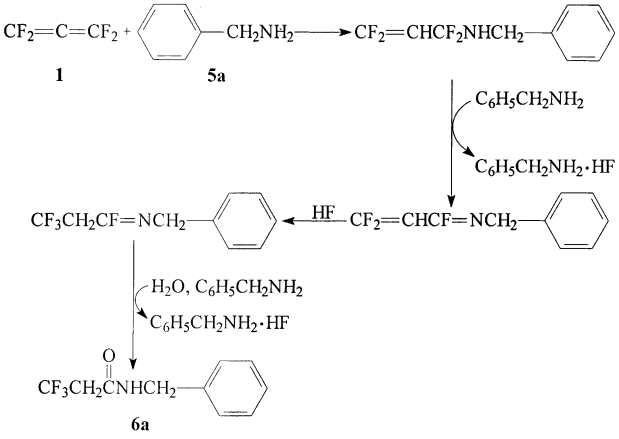
Amines, different from phenols, reacted with **2** sluggishly in one pot, the products being very complicated. However, mixing **1** and benzyamine (**5a**) in THF at room temperature quickly gave the unexpected β,β,β-trifluoropropionamide (**6a**) (Scheme 5). The structure for **6a** was established by its spectral data (IR, MS, NMR) and elemental analysis as well as X-ray diffraction. (Fig. 1).



Scheme 4.



Scheme 5.



Scheme 6.

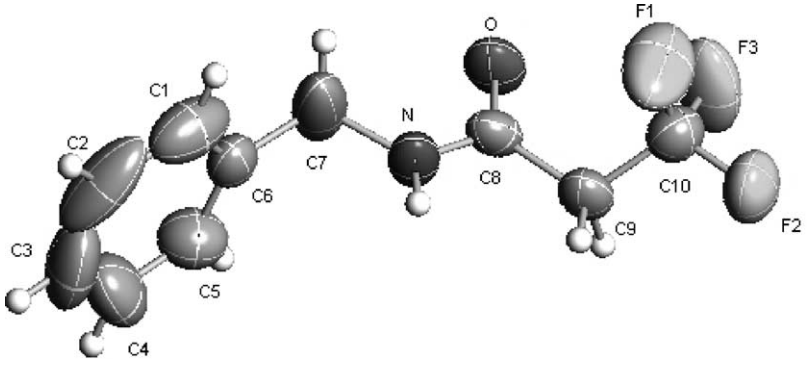
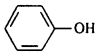
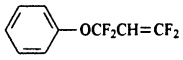
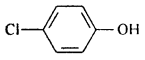
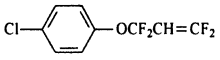
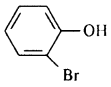
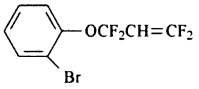
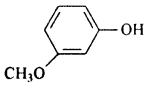
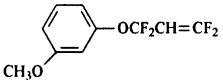
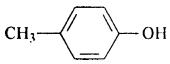
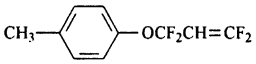
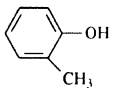
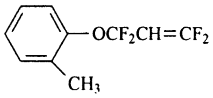
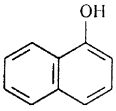
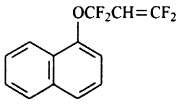
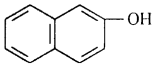
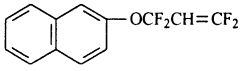
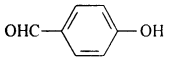
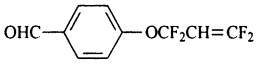
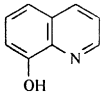
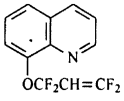
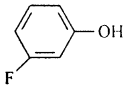
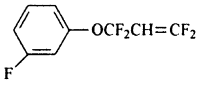
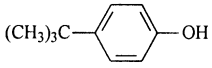
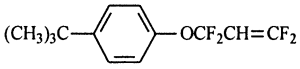


Fig. 1. The X-ray structure of compound **6a**.

Table 1
Reaction of **2** or **1** with ArOH (**3**)

Entry	Substrate		Product		Yield[a] (%)	
					One-pot[b]	Two-step[c]
1		**3a**		**4a**	90	93
2		**3b**		**4b**	92	91
3		**3c**		**4c**	85	88
4		**3d**		**4d**	88	90
5		**3e**		**4e**	83	85
6		**3f**		**4f**	80	87
7		**3g**		**4g**	91	95
8		**3h**		**4h**	90	95
9		**3i**		**4i**	93	92
10		**3j**		**4j**	87	9
11		**3k**		**4k**	84	93
12		**3l**		**4l**	93	95

[a] Isolated yields based on phenols used.
[b] **2**:ArOH:K_2CO_3 = 5:3:10 in CH_3CN at 65 °C for 10 h.
[c] **1**:ArOH:K_2CO_3 = 4:3:0.3 in CH_3CN at room temperature for 8 h.

Based on the presence of fluoride ion in aqueous layer after workup of the reaction mixture, we proposed that amine was not only used as a reactant but also as a dehydrofluorination reagent, thus the base was unnecessary for the reaction (Scheme 6).

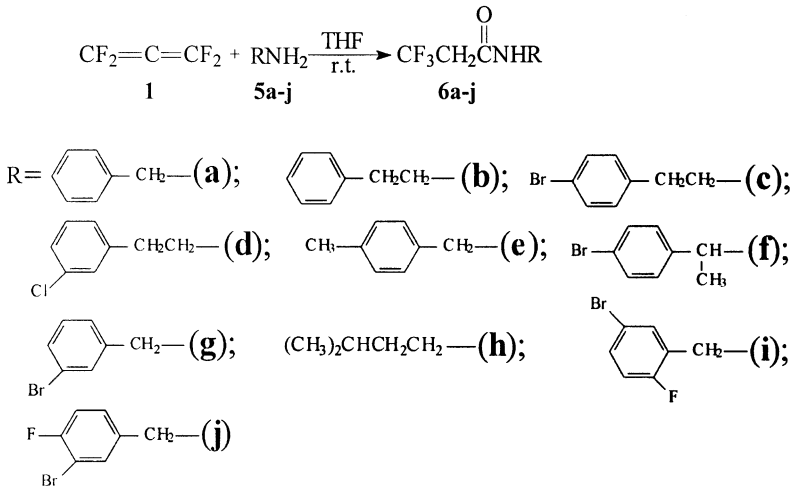
Substituted benzylamines (**5a–g**, **5i** and **5j**) and simple aliphatic amine (**5h**) underwent a similar reaction with **1** (Scheme 7).

The results are listed in Table 2.

In conclusion, we provided several examples of the nucleophilic addition reactions of phenols and amines to tetrafluoroallene. The studies on the electrophilic and free radical reactions of **1** are in progress.

3. Experimental

Melting points were recorded at atmospheric pressure and were uncorrected. ^1H NMR and ^{19}F NMR spectra were recorded on a Varian-360L instrument or Bruker AM-300 spectrometer for solution in $CDCl_3$ with TMS and $CFCl_3$ as the internal and external standards respectively, and the upfields are negative. Coupling constants are given in Hz. IR spectra were obtained with a Perkin-Elmer 983G spectrophotometer. Lower resolution mass spectra (LRMS) and higher resolution mass spectra (HRMS) were obtained on a HP-5989a and Finnigan MAT-8430 instruments, respectively. Organic solvents were dried by standard methods



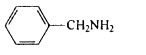
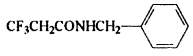
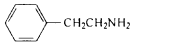
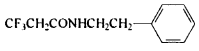
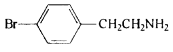
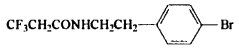
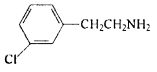
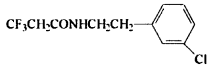
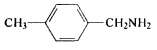
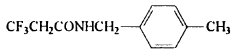
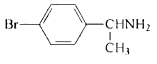
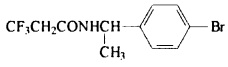
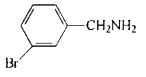
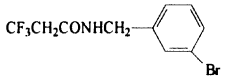
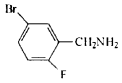
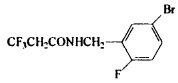
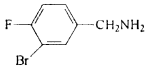
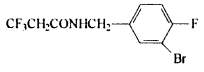
Scheme 7.

when necessary. All the commercially available reagents were of analytical grade and were used without further purification. Flash column chromatography was carried out using 300–400 mesh silica gel.

3.1. General procedure for the preparation of unsaturated polyfluoroaryl ethers

Procedure A. One-pot method: A 6 ml Pyrex tube was placed $ICF_2CH_2CF_2I$ (**2**) (5 mmol, 1.84 g), phenol (3 mmol) and anhydrous acetonitrile (3 ml). After addition of K_2CO_3 (10 mmol, 1.38 g), the tube was immediately sealed and then heated in an oil bath at 65 °C for 8 h. Cooled the tube to −50 °C for 5 min, opened it and then warmed again to room temperature. The mixture was poured into H_2O (40 ml) and extracted with Et_2O 3 ml × 15 ml). Then the combined organic layer was washed with brine (3 ml × 20 ml). The organic layer was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography to give the product.

Table 2
The results of **1** with amines[a]

Entry	Substrate		Product		Yield[b] (%)
1		**5a**		**6a**	62
2		**5b**		**6b**	57
3		**5c**		**6c**	59
4		**5d**		**6d**	52
5		**5e**		**6e**	58
6		**5f**		**6f**	55
7		**5g**		**6g**	53
8	$(CH_3)_2CHCH_2CH_2NH_2$	**5h**	$CF_3CH_2CONHCH_2CH_2CH(CH_3)_2$	**6h**	46
9		**5i**		**6i**	60
10		**5j**		**6j**	51

[a] **1**:RNH_2 = 4:3 at room temperature for 4 h.
[b] Based on amine.

Procedure B. Two-step method: Tetrafluoroallene (**1**) was prepared according to [12]. Into a 6 ml Pyrex tube containing phenol (3 mmol), K_2CO_3 (4 mmol, 0.553 g), anhydrous CH_3CN (3 ml) was condensed $CF_2{=}C{=}CF_2$ (**1**) (0.448 g, 4 mmol). The tube was sealed and allowed to warm to room temperature and then stirred for 6 h. The subsequent operation was the same as procedure A.

*3.1.1. 3-Phenoxy-1,1,3,3-tetrafluoro-1-propene (**4a**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.18–7.39 (m, 5H, ArH), 4.88 (dtd, $J = 22.3$, 7.2, 1.9 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.5 (m, 2F), −73.2 (m, 1F), −78.7 (m, 1F). IR (ν_{max} (cm^{-1})): 1660(w), 1633(m), 1468(m), 1260(m), 1093(m), 1016(s), 798(m). MS (EI) *m/z* (relative intensity): 206 (M^+, 23), 187 (1), 113 (100), 94 (17), 77 (12), 69 (6). HRMS (EI) Calcd. for $C_9H_6F_4O$ 206.0353; Found: 206.0365.

*3.1.2. 3-(4-Chlorophenoxy)-1,1,3,3-tetrafluoro-1-propene (**4b**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.11–7.35 (m, 4H, ArH), 4.87 (dtd, $J = 22.4$, 7.0, 1.6 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −61.5 (m, 2F), −72.8 (m, 1F), −78.3 (m, 1F). IR (ν_{max} (cm^{-1})): 1726(vs), 1489(vs), 1375(s), 1235(s), 1165(m), 1105(vs), 976(m). MS (EI) *m/z* (relative intensity): 240 (M^+, 37), 221 (2), 193 (2), 149 (3), 128 (11), 113 (100), 75 (6). Anal. Calcd. for $C_9H_5ClF_4O$: C 44.93, H 2.09, F 31.59; Found: C 44.92, H 2.11, F 31.58.

*3.1.3. 3-(2-Bromophenoxy)-1,1,3,3-tetrafluoro-1-propene (**4c**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.10–7.64 (m, 4H, ArH), 4.95 (dtd, $J = 22.5$, 7.6, 2.2 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.6 (m, 2F), −72.2 (m, 1F), −77.9 (m, 1F). IR (ν_{max} (cm^{-1})): 1724(vs), 1475(s), 1376(vs), 1234(s), 1213(s), 1106(s), 1050(m), 978(m). MS (EI) *m/z* (relative intensity): 284 (M^+, 5), 220 (10), 194 (8), 113 (100), 108 (17). Anal. Calcd. for $C_9H_5BrF_4O$: C 37.92, H 1.77, F 26.66; Found: C 37.62, H 1.75, F 26.52.

*3.1.4. 3-(3-Methoxyphenoxy)-1,1,3,3-tetrafluoro-1-propene (**4d**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 6.79–7.33 (m, 4H, ArH), 4.92 (dtd, $J = 22.2$, 7.0, 1.6 Hz, 1H, CH), 3.85 (s, 3H, CH_3). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.6 (m, 2F), −73.3 (m, 1F), −78.8 (m, 1F). IR (ν_{max} (cm^{-1})): 1722(vs), 1614(s), 1493(vs), 1382(s), 1267(s), 1228(vs), 1140(vs), 1101(vs), 991(m). MS (EI) *m/z* (relative intensity): 236 (M^+, 30), 217 (1), 124 (44), 113 (100), 107 (6), 95 (9). Anal. Calcd. for $C_{10}H_8F_4O_2$: C 50.86, H 3.41, F 32.18; Found: C 50.73, H 3.39, F 31.90.

*3.1.5. 3-(4-Methylphenoxy)-1,1,3,3-tetrafluoro-1-propene (**4e**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.05–7.24 (m, 4H, ArH), 4.85 (dtd, $J = 22.2$, 7.0, 1.9 Hz, 1H, CH), 2.33 (s, 3H, CH3). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.6 (m, 2F), −73.4 (m, 1F), −78.9 (m, 1F). IR (ν_{max} (cm^{-1})): 1724(vs), 1508(vs), 1382(vs), 1272(m), 1228(vs), 1194(vs), 1123(vs), 1102(vs), 978(s). MS (EI) *m/z* (relative intensity): 220 (M^+, 25), 201 (2), 113 (89), 108 (45), 91 (100), 77 (26). HRMS (EI) Calcd. for $C_{10}H_8F_4O$ 220.0510; Found: 220.0482.

*3.1.6. 3-(2-Methylphenoxy)-1,1,3,3-tetrafluoro-1-propene (**4f**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.12–7.25 (m, 4H, ArH), 4.90 (dtd, $J = 22.4$, 6.7, 1.8 Hz, 1H, CH), 2.27 (s, 3H, CH3). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.0 (m, 2F), −73.2 (m, 1F), −78.9 (m, 1F). IR (ν_{max} (cm^{-1})): 1764(m), 1722(vs), 1588(m), 1493(s), 1385(vs), 1274(s), 1222(vs), 1174(vs), 1116(vs), 1098(vs), 979(s). MS (EI) *m/z* (relative intensity): 220 (M^+, 1), 201 (44), 181 (5), 108 (10), 91 (100), 77 (18). HRMS (EI) Calcd. for $C_{10}H_8F_4O$ 220.0510; Found: 220.0462.

*3.1.7. 3-(1-Naphthoxy)-1,1,3,3-tetrafluoro-1-propene (**4g**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.38–8.12 (m, 7H, ArH), 4.99 (dtd, $J = 22.3$, 7.1, 2.0 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.1 (m, 2F), −72.8 (m, 1F), −78.3 (m, 1F). IR (ν_{max} (cm^{-1})): 3064(w), 1720(vs), 1601(m), 1510(m), 1390(s), 1234(vs), 1222(vs), 1111(vs), 1078(s), 961(m), 773(s). MS (EI) *m/z* (relative intensity): 256 (M^+, 58), 237 (1), 144 (71), 115 (100), 113 (83), 89 (12). Anal. Calcd. for $C_{13}H_8F_4O$: C 60.95, H 3.15, F 29.66; Found: C 60.84, H 3.28, F 29.38.

*3.1.8. 3-(2-Naphthoxy)-1,1,3,3-tetrafluoro-1-propene (**4h**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.31–7.85 (m, 7H, ArH), 4.93 (dtd, $J = 22.3$, 7.0, 1.8 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.4 (m, 2F), −73.0 (m, 1F), −78.5 (m, 1F). IR (ν_{max} (cm^{-1})): 3066(w), 1724(vs), 1600(m), 1391(s), 1240(vs), 1209(s), 1158(s), 1119(vs), 1104(vs), 990(vs). MS (EI) *m/z* (relative intensity): 256 (M^+, 100), 144 (74), 113 (46). Anal. Calcd. for $C_{13}H_8F_4O$: C 60.95, H 3.15, F 29.66; Found: C 60.92, H 3.12, F 29.37.

*3.1.9. 4-(1,1,3,3-Tetrafluoroallyloxy)benzaldehyde (**4i**)*

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 9.99 (s, 1H, CHO), 7.30–8.14 (m, 4H, ArH), 4.93 (dtd, $J = 22.2$, 7.3, 2.0 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −61.5 (m, 2F), −72.3 (m, 1F), −77.7 (m, 1F). IR (ν_{max} (cm^{-1})): 3087(m), 1757(vs), 1705(s), 1604(s), 1373(s), 1289(m), 1211(s), 1113(vs), 1052(vs), 960(vs). MS (EI) *m/z* (relative intensity): 234 (M^+, 10), 121 (6), 113 (100), 105 (1). Anal. Calcd. for $C_{10}H_6F_4O_2$: C 51.30, H 2.58, F 32.46; Found: C 51.13, H 2.69, F 32.12.

*3.1.10. 3-(8-Quinolyloxy)-1,1,3,3-tetrafluoro-1-propene (**4j**)*

Yellow liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 9.01 (m, 1H, ArH), 7.44–8.20 (m, 5H, ArH), 5.13 (dtd, $J = 22.3$,

8.3, 1.9 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.9 (m, 2F), −73.0 (m, 1F), −78.2 (m, 1F). IR (ν_{max} (cm^{-1})): 3071(w), 1758(vs), 1502(s), 1371(vs), 1221(s), 1126(vs), 1048(s), 958(s), 796(m). MS (EI) *m/z* (relative intensity): 257 (M^+, 3), 238 (8), 191 (96), 159 (53), 145 (100), 113 (59), 89 (43). Anal. Calcd. for $C_{12}H_7F_4NO$: C 56.04, H 2.74, N 5.45, F 29.55; Found: C 56.08, H 2.79, N 5.61, F 29.44.

3.1.11. 3-(3-Fluorophenoxy)-1,1,3,3-tetrafluoro-1-propene (**4k**)

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 6.93–7.33 (m, 4H, ArH), 4.88 (dtd, J = 22.4, 7.1, 1.7 Hz, 1H, CH). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −61.1 (m, 2F), −72.3 (m, 1F), −78.1 (m, 1F), −111.2 (m, 1F, ArF). IR (ν_{max} (cm^{-1})): 1759(vs), 1607(s), 1490(s), 1376(s), 1294(m), 1228(s), 1130(vs), 1056(m), 972(m). MS (EI) *m/z* (relative intensity): 224 (M^+, 13), 205 (1), 113 (100), 95 (9), 69 (11). HRMS (EI) Calcd. for $C_9H_5F_5O$ 224.0259; Found 224.0239.

3.1.12. 3-[4-(tert-Butyl)phenoxy]-1,1,3,3-tetrafluoro-1-propene (**4l**)

Colorless liquid: ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.11–7.39 (m, 4H, ArH), 4.89 (dtd, J = 22.4, 7.2, 1.9 Hz, 1H, CH), 1.33 (s, 9H, $C(CH_3)_3$). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −60.5 (m, 2F), −73.3 (m, 1F), −78.9 (m, 1F). IR (ν_{max} (cm^{-1})): 2968(s), 1759(vs), 1512(vs), 1373(vs), 1291(m), 1230(s), 1208(s), 1174(m), 1130(s), 1051(s), 961(vs). MS (EI) *m/z* (relative intensity): 263 ($M^+ + 1$, 14), 247 (93), 135 (74), 113 (34), 105 (100), 77 (38), 57 (27). Anal. Calcd. for $C_{13}H_{14}F_4O$: C 59.54, H 5.38, F 28.98; Found: C 59.50, H 5.21, F 29.06.

3.2. General procedure for the reaction of CF_2=C=CF_2 (**1**) with amine

Tetrafluoroallene (**1**) was prepared according to [12]. Into a 6 ml Pyrex tube containing amine (3 mmol), anhydrous THF (3 ml) was condensed CF_2=C=CF_2 (**1**) (0.448 g, 4 mmol). The tube was immediately sealed and allowed to warm to room temperature and then stirred for 4 h. Cooled the tube to −50 °C for 5 min, opened it and then warmed again to room temperature. The mixture was poured into H_2O (30 ml) and extracted with Et_2O (3 ml × 15 ml). Then the combined organic layer was washed with brine (3 ml × 20 ml). The organic layer was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography to give the product.

3.2.1. N-Benzyl-3,3,3-trifluoropropionamide (**6a**)

White solid: mp 125–127 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.28–7.36 (m, 5H, ArH), 6.07 (br., 1H, NH), 4.49 (d, J = 5.4 Hz, 2H, CH_2), 3.10 (q, J = 10.6 Hz, 2H, CF_3CH_2). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.3 (t, J = 11.5 Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3314(s), 1645(vs), 1553(s), 1234(s), 1139(s), 1106(s), 698(m). MS (EI) *m/z* (relative intensity): 217 (M^+, 100), 148 (8), 106 (57), 91 (68). Anal. Calcd. for $C_{10}H_{10}F_3NO$: C 55.30, H 4.64, N 6.45, F 26.24; Found: C 55.38, H 4.62, N 6.34, F 26.36.

3.2.2. N-(2-Phenylethyl)-3,3,3-trifluoropropionamide (**6b**)

White solid: mp 76–78 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.18–7.36 (m, 5H, ArH), 5.72 (br., 1H, NH), 3.58 (q, J = 6.6 Hz, 2H, NCH_2), 3.02 (q, J = 10.8 Hz, 2H, CF_3CH_2), 2.85 (t, J = 6.7 Hz, 2H, $ArCH_2$). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.0 (t, J = 10.5 Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3308(s), 1658(vs), 1562(s), 1393(m), 1364(m), 1261(s), 1240(s), 1157(s), 1109(s), 699(s). MS (EI) *m/z* (relative intensity): 231 (M^+, 6), 111 (11), 104 (100), 91 (31), 69 (2). Anal. Calcd. for $C_{11}H_{12}F_3NO$: C 57.14, H 5.23, N 6.05, F 24.65; Found: C 56.82, H 4.85, N 5.92, F 24.86.

3.2.3. N-[2-(4-Bromophenyl)ethyl]-3,3,3-trifluoropropionamide (**6c**)

White solid: mp 118–120 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.04–7.45 (m, 4H, ArH), 5.81 (br., 1H, NH), 3.53 (q, J = 6.5 Hz, 2H, NCH_2), 3.02 (q, J = 10.6 Hz, 2H, CF_3CH_2), 2.80 (t, J = 6.9 Hz, 2H, $ArCH_2$). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.4 (t, J = 11.6 Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3305(s), 1654(vs), 1568(s), 1489(m), 1403(m), 1276(m), 1240(s), 1141(s), 1109(m). MS (EI) *m/z* (relative intensity): 312 ($M^+ + 2$, 5), 310 (M^+, 5), 182 (100), 169 (16), 111 (19), 90 (20), 69 (3). Anal. Calcd. for $C_{11}H_{11}BrF_3NO$: C 42.60, H 3.58, N 4.52, F 18.38; Found: C 42.59, H3.31, N 4.34, F 18.35.

3.2.4. N-[2-(3-Chlorophenyl)ethyl]-3,3,3-trifluoropropionamide (**6d**)

White solid: mp 64–66 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.06–7.28 (m, 4H, ArH), 5.74 (br., 1H, NH), 3.56 (q, J = 6.6 Hz, 2H, NCH_2), 3.03 (q, J = 10.6 Hz, 2H, CF_3CH_2), 2.83 (t, J = 7.0 Hz, 2H, $ArCH_2$). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.0 (t, J = 10.6 Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3319(s), 1654(vs), 1558(s), 1394(m), 1365(s), 1266(s), 1235(s), 1141(vs), 1108(s), 797(m). MS (EI) *m/z* (relative intensity): 265 (M^+, 8), 138 (100), 125 (22), 111 (34), 89 (23), 69 (7). Anal. Calcd. for $C_{11}H_{11}ClF_3NO$: C 49.73, H 4.17, N 5.27, F 21.45; Found: C 50.01, H 4.06, N 5.25, F 21.45.

3.2.5. N-[(4-Methylphenyl)methyl]-3,3,3-trifluoropropionamide (**6e**)

White solid: mp 130–132 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.15 (m, 4H, ArH), 5.94 (br., 1H, NH), 4.44 (d, J = 5.4Hz, 2H, NCH_2), 3.09 (q, J = 10.6 Hz, 2H, CF_3CH_2), 2.34 (s, 3H, CH_3). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −62.9 (t, J = 11.0 Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3302(s), 1651(vs), 1560(s), 1421(w), 1273(m), 1237(m), 1134(s), 1106(m), 807(m). MS (EI) *m/z* (relative intensity): 231 (M^+, 62), 216 (33), 120 (39), 111 (30), 106 (100), 91 (52), 77 (37). Anal. Calcd. for $C_{11}H_{12}F_3NO$: C 57.14, H

5.23, N 6.05, F 24.65; Found: C 57.14, H 5.30, N 6.00, F 24.26.

*3.2.6. N-[1-(4-Bromophenyl)ethyl]-3,3,3-trifluoropropionamide (**6f**)*

White solid: mp 151–153 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.17–7.51 (m, 4H, ArH), 5.94 (br., 1H, NH), 5.11 (m, 1H, CH), 3.08 (q, $J = 10.6$ Hz, 2H, CF_3CH_2), 1.51 (d, $J = 7.1$ Hz, 3H, CH_3). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −62.9 (t, $J = 10.9$ Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3310(s), 1660(vs), 1558(s), 1420(m), 1394(m), 1238(s), 1140(s), 1109(s), 1009(m), 824(m). MS (EI) *m/z* (relative intensity): 311 ($M^+ + 1$, 36), 309 ($M^+ - 1$, 37), 294 (57), 184 (100), 120 (23), 111 (40), 104 (39), 91 (16), 77 (43). Anal. Calcd. for $C_{11}H_{11}BrF_3NO$: C 42.60, H 3.58, N 4.52, F 18.38; Found: C 42.96, H 3.64, N 4.36, F 18.29.

*3.2.7. N-[(3-Bromophenyl)methyl]-3,3,3-trifluoropropionamide (**6g**)*

White solid: mp 114–116 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.20–7.44 (m, 4H, ArH), 6.08 (br., 1H, NH), 4.46 (d, $J = 5.9$ Hz, 2H, NCH_2), 3.13 (q, $J = 10.6$ Hz, 2H, CF_3CH_2). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.3 (t, $J = 10.2$ Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3313(s), 1647(vs), 1552(s), 1463(m), 1352(m), 1271(s), 1234(s), 1136(vs), 1110(s), 788(s), 694(m). MS (EI) *m/z* (relative intensity): 297 ($M^+ + 1$, 53), 295 ($M^+ - 1$, 51), 216 (25), 184 (23), 169 (24), 111 (23), 106 (100), 89 (20), 77 (23), 69 (3). Anal. Calcd. for $C_{10}H_9BrF_3NO$: C 40.57, H 3.06, N 4.73, F 19.25; Found: C 40.70, H 3.02, N 4.66, F 19.10.

*3.2.8. N-(3-Methylbutyl)-3,3,3-trifluoropropionamide (**6h**)*

White solid: mp 39–41 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 5.74 (br., 1H, NH), 3.32 (m, 2H, NCH_2), 3.06 (q, $J = 10.6$ Hz, 2H, CF_3CH_2), 1.25–1.66 (m, 3H, CH_2CH), 0.92 (d, $J = 6.8$ Hz, 6H, $C(CH_3)_2$). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.5 (t, $J = 11.1$ Hz, CF_3). IR (KBr) (ν_{max} (cm^{-1})): 3301(s), 2962(s), 1649(vs), 1569(s), 1371(m), 1312(m), 1267(s), 1245(s), 1146(s), 1105(s), 930(m). MS (EI) *m/z* (relative intensity): 197 (M^+, 1), 182 (4), 154 (34), 141 (100), 128 (21), 111 (32), 91 (9), 70 (35), 55 (43), 44 (50). HRMS (EI) Calcd. for $C_8H_{14}F_3NO$ 197.1024; Found: 197.1039.

*3.2.9. N-[(5-Bromo-2-fluorophenyl)methyl]-3,3,3-trifluoropropionamide (**6i**)*

White solid: mp 105–107 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 6.93–7.47 (m, 3H, ArH), 6.17 (br., 1H, NH), 4.50 (d, $J = 5.7$ Hz, 2H, NCH_2), 3.12 (q, $J = 10.6$ Hz, 2H, CF_3CH_2). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.3 (t, $J = 10.1$ Hz, CF_3), −121.4 (m, 1F, ArF). IR (KBr) (ν_{max} (cm^{-1})): 3302(s), 3095(w), 1657(vs), 1562(m), 1485(s), 1439(w), 1361(m), 1258(m), 1236(s), 1148(m), 814(m). MS (EI) *m/z* (relative intensity): 315 ($M^+ + 1$, 60), 313 ($M^+ - 1$, 62), 202 (23), 187 (39), 124 (100), 111 (48), 107 (34), 94 (15), 83 (20). HRMS (EI) Calcd. for $C_{10}H_8BrF_4NO$ 312.9724; Found: 312.9737.

*3.2.10. N-[(3-Bromo-4-fluorophenyl)methyl]-3,3,3-trifluoropropionamide (**6j**)*

White solid: mp 116–118 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ (ppm): 7.06–7.48 (m, 3H, ArH), 6.12 (br., 1H, NH), 4.44 (d, $J = 5.7$ Hz, 2H, NCH_2), 3.12 (q, $J = 10.6$ Hz, 2H, CF_3CH_2). ^{19}F NMR ($CDCl_3$, $CFCl_3$) δ (ppm): −63.3 (t, $J = 10.4$ Hz, CF_3), −109.0 (m, 1F, ArF). IR (KBr) (ν_{max} (cm^{-1})): 3308(s), 3095(w), 1654(vs), 1563(m) 1498(s), 1392(m), 1266(s), 1243(s), 1150(s), 1112(s), 828(m). MS (EI) *m/z* (relative intensity): 315 ($M^+ + 1$, 85), 313 ($M^+ - 1$, 90), 202 (39), 187 (54), 124 (100), 111 (51), 107 (46), 96 (21), 83 (23). HRMS (EI) Calcd. for $C_{10}H_8BrF_4NO$ 312.9724; Found: 312.9740.

Acknowledgements

We thank the Chinese National Natural Science Foundation (D20032010, 20272076) for the financial support.

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