POLYFLUOROALKYLATION OF CARBONYL COMPOUNDS BY POLYFLUOROALKYL ANIONS GENERATED FROM POLYFLUOROCARBOXAMIDES

Natshumi Wakita and Shoji Hara*

Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan
E-mail: shara@eng.hokudai.ac.jp

Abstract – Polyfluoroalkyl anions, generated by reduction of (polyfluoroalkanoyl)piperidines with Et$_3$BHK, were used for the polyfluoroalkylation of carbonyl compounds. Trifluoromethylation of aromatic aldehydes proceeded in good yields, and that of aliphatic aldehydes afforded a moderate yield. In contrast, the yield was low when the reaction involved benzophenone. Pentafluoroethylation and octafluorobutylation of aldehydes were also carried out by using the corresponding (polyfluoroalkanoyl)piperidines, which were prepared from commercially available polyfluorocompounds. The (polyfluoroalkanoyl)piperidines were also prepared through polyfluorination, and were used in the polyfluoroalkylation of aldehydes.

INTRODUCTION

Nucleophilic trifluoromethylation of carbonyl compounds has been widely performed to introduce a trifluoromethyl group into the substrate.\textsuperscript{1} The trifluoromethyl anion is unstable. Therefore, it is generated from the precursor in the presence of an electrophile such as a carbonyl compound. Although a number of various trifluoromethyl compounds have been used as precursors, trifluoromethyltrimethylsilane has been most frequently used and is well-studied.\textsuperscript{1c,1d,2}

Dedicated to Professor Victor Snieckus on the occasion of his 77th birthday.
Recently, trifluoroacetaldehyde hemiaminals (1) have attracted much attention as an accessible trifluoromethyl source, because they can be prepared from economical materials such as fluoroform\textsuperscript{1j,3} and trifluoroacetaldehyde hemiacetal.\textsuperscript{1j,4} They are converted to their metal salts (2) to generate the trifluoromethyl anion.\textsuperscript{5} We can obtain 2 by the reduction of trifluoroacetamide (3).\textsuperscript{6} Moreover, various (polyfluoroalkanoyl)amides are obtainable from either commercially available polyfluorocompounds or through polyfluorination reactions, and they can be used as a source for polyfluoroalkyl anions (Scheme 1).

\begin{center}
\begin{tikzpicture}
  \node (N1) at (0,0) {OH};
  \node (N2) at (1,0) {\text{CF}_3\text{H}N\text{R}^{12}};
  \node (N3) at (0,-1) {\text{CF}_3\text{CONR}^{12}};

  \node (O1) at (2,0) {OH};
  \node (O2) at (3,0) {\text{CF}_3\text{R}^2};
  \node (O3) at (2,-1) {\text{CF}_3\text{R}^3};

  \node (BuOM) at (1.5,-0.5) {tBuOM};
  \node (OM) at (2.5,-0.5) {OM};
  \node (MH) at (1,-1) {MH};

  \draw[->] (N1) -- (N2) node[pos=0.5,above] {\text{CF}_3\text{H}N\text{R}^{12}};
  \draw[->] (N2) -- (N3) node[pos=0.5,above] {\text{CF}_3\text{CONR}^{12}};
  \draw[->] (N1) -- (O1) node[pos=0.5,above] {OH};
  \draw[->] (N2) -- (O2) node[pos=0.5,above] {\text{CF}_3\text{R}^2};
  \draw[->] (N3) -- (O3) node[pos=0.5,above] {\text{CF}_3\text{R}^3};

  \draw[->] (BuOM) -- (OM) node[pos=0.5,above] {BuOM};
  \draw[->] (OM) -- (MH) node[pos=0.5,above] {OM};
  \draw[->] (MH) -- (MH) node[pos=0.5,above] {OM};

  \node at (1.5,-1) {Scheme 1};
\end{tikzpicture}
\end{center}

**RESULTS AND DISCUSSION**

Trifluoromethylation of benzaldehyde was carried out using \textit{N}-(trifluoroacetyl)piperidine, \textit{N}-(trifluoroacetyl)pyrrolidine, and \textit{N,N}-diethyltrifluoroacetamide as trifluoromethyl anion sources, and potassium triethylborohydride, DIBAH and potassium triisopropoxyborohydride as reducing reagents under various conditions (Table 1). A reducing reagent and benzaldehyde were successively added to the amide in THF at -78 °C (Entries 1–5) or at room temperature (Entry 6), and the resulting mixture was stirred for 24 h at 50 °C. Maintaining an interval between each addition of the reagents did not improve the results. The expected trifluoromethylated product (2a) was formed, only when \textit{N}-(trifluoroacetyl)piperidine or \textit{N}-(trifluoroacetyl)pyrrolidine was treated with potassium triethylborohydride (Entries 1, 4, and 6). The best yield was obtained by adding potassium triethylborohydride and benzaldehyde to \textit{N}-(trifluoroacetyl)piperidine at room temperature (Entry 6).
Table 1. Trifluoromethylation of benzaldehyde under various conditions$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>NR$_2$</th>
<th>MH</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>N</td>
<td>KB$_2$Et$_3$H</td>
<td>57</td>
</tr>
<tr>
<td>2</td>
<td>N</td>
<td>DIBAH</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>N</td>
<td>KB(OPr-i)$_3$</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>NEt$_2$</td>
<td>KB$_2$Et$_3$H</td>
<td>47</td>
</tr>
<tr>
<td>5</td>
<td>N</td>
<td>KB$_2$Et$_3$H</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>N</td>
<td>KB$_2$Et$_3$H</td>
<td>99$^c$</td>
</tr>
</tbody>
</table>

$^a$ If otherwise not mentioned, 2 eq of the amide and MH to benzaldehyde were used. The reagents were added at -78 °C, and the mixture was stirred at 50 °C for 24 h. $^b$ $^{19}$F NMR yield based on benzaldehyde. $^c$ The reagents were added at room temperature.

The present trifluoromethylation reaction was applied to various carbonyl compounds. In the reaction with aromatic aldehydes and cinnamaldehyde, the corresponding trifluoromethylated products were obtained in good yield (Entries 1-5 in Table 2). From adamantane-1-carbaldehyde that has no $\alpha$-proton, the trifluoromethylated product was obtained in 60% yield (Entry 6). In contrast, the reaction with cyclohexanecarbaldehyde that has $\alpha$-proton, afforded an aldol reaction product as the main product. However, when the reaction was carried out in CH$_2$Cl$_2$ instead of THF, the trifluoromethylated product was obtained in 45% yield (Entry 7). In the reaction with benzophenone, most of the starting material remained unchanged (Entry 8).
Table 2. Trifluoromethylation of carbonyl compounds\(^{a}\)

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Carbonyl compound</th>
<th>Product</th>
<th>Yield (%)(^{b})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCHO</td>
<td><img src="image" alt="2a" /></td>
<td>(99)</td>
</tr>
<tr>
<td>2</td>
<td>Br-Ph-CHO</td>
<td><img src="image" alt="2b" /></td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>Ph-CH=CHO</td>
<td><img src="image" alt="2c" /></td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>CHO</td>
<td><img src="image" alt="2d" /></td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>Furan-CHO</td>
<td><img src="image" alt="2e" /></td>
<td>(81)</td>
</tr>
<tr>
<td>6</td>
<td>Bicyclo[2.2.1]hept-2-en-5-CHO</td>
<td><img src="image" alt="2f" /></td>
<td>60</td>
</tr>
<tr>
<td>7</td>
<td>Cyclohexan CHO</td>
<td><img src="image" alt="2g" /></td>
<td>45(^{c})</td>
</tr>
<tr>
<td>8</td>
<td>Ph-CHO</td>
<td><img src="image" alt="2h" /></td>
<td>14</td>
</tr>
</tbody>
</table>

\(^{a}\) If otherwise not mentioned, the reaction was carried out in THF using 2 eq of KBE\(\text{t}_{3}\)H and amide to carbonyl compound. The reagents were mixed at room temperature and stirred at 50 °C for 24 h. Isolated yield base on carbonyl compound used. In parentheses, \(^{19}\)F NMR yield. c. CH\(_2\)Cl\(_2\) was used as solvent.
As various (polyfluoroalkanoyl)piperidines are obtainable from commercially available polyfluoro-compounds, the present method is applicable to the various polyfluoroalkylation of carbonyl compounds. For example, \(N\)-(pentafluoropropanoyl)piperidine (1b) was prepared from methyl pentafluoropropionate\(^7\) and was used for the pentafluoroethylation of 1-naphthaldehyde. The reaction proceeded similar to trifluoromethylation, and the pentafluoroethylated product (2i) was obtained in high yield. \(N\)-(2,2,3,3,4,4,5,5-Octafluoropetanoyl)piperidine (1c) was prepared from commercially available 2,2,3,3,4,4,5,5-octafluoropentanol in three steps\(^7\)\(^-\)\(^9\) and was used in the reaction with 1-naphthaldehyde. The reaction of 1c with aldehyde was sluggish and the octafluorobutylated product 2j was formed in poor yield under the trifluoromethylation conditions. However, 2j was obtained in 61% yield by carrying the reaction at 40 °C for 24 h using 4 equivalents of 1c and KBEt\(_3\)H to 1-naphthaldehyde without solvent (Scheme 2).

\[
\begin{align*}
\text{1b} & \quad \text{KBEt}_3\text{H} / \text{THF} \quad \text{CHO} \quad \text{11b} \\
\text{1c} & \quad \text{KBEt}_3\text{H} \quad \text{CHO} \quad \text{11c}
\end{align*}
\]

\(89\%\)

\(61\%\)

\text{Scheme 2}

(Polyfluoroalkanoyl)piperidines can be also prepared through polyfluorination reactions. For example, methyl 2-(arylsulfanyl)-2,2-difluoroacetate (3) was prepared by difluorination of methyl 2-(arylsulfanyl)acetate using IF\(_5\)-Et\(_3\)N-3HF\(^{10}\) and then converted to \(N\)-(arylsulfanyl)-2,2-difluoroacetyl}piperidine (4).\(^7\) The reaction of 4 with an aldehyde was performed as in the case of 2a, and the (arylsulfanyl)difluoromethylated product (5) was obtained in high yield (Scheme 3).
Methyl 2,2,3,3-tetrafluoro-3-phenylpropionate (7) was prepared from methyl 2-(arylsulfanyl)propionate in 74% yield by using our recently developed method, and the resulting 7 was converted to the amide (8). Although the reaction of 8 with aldehyde was sluggish, the expected polyfluoroalkylated product (9) was obtained in 60% yield by performing the reaction at 40 °C for 24 h using 4 equivalents of 8 and KEt₃BH to the aldehyde (Scheme 4).

**EXPERIMENTAL**

**4.1. General**

The melting points were measured with a Yanagimoto micro melting-point apparatus. The IR spectra were recorded using a JASCO FT/IR-410. The ¹H NMR (400 MHz) spectra, ¹⁹F NMR (376 MHz) spectra, and ¹³C NMR (100 MHz) were recorded in CDCl₃ on a JEOL JNM-A400II FT NMR and the chemical shift, δ, is referred to TMS (¹H, ¹³C) and CFCl₃ (¹⁹F), respectively. The EI-high-resolution mass spectra were measured on a JEOL JMS-700TZ. KBEt₃H (1.0 M in THF) was purchased from Aldrich Chemica and
KB(OPr)₃H was prepared from B(OPr)₃ and KH according to the literature.¹² IF₅ in a stainless-steel cylinder was supplied by Asahi Glass Co., Ltd. IF₅ was transferred through a Teflon™ tube from the cylinder under an N₂ atmosphere. IF₅ was transferred quickly from the bottle to the reaction vessel made of Teflon™ in open air. IF₅ decomposes in air emitting HF fume, and, therefore, it should be carefully handled in a bench hood with rubber-gloved hands.¹¹

2,2,3,3,4,4,5,5-Octafluoropentanol was donated from Daikin Industries, Ltd.

4.2. Preparation of N-(polyfluoroalkanoyl)piperidine

N-(Polyfluoroalkanoyl)piperidines were prepared from the corresponding ethyl or methyl polyfluoroalkanoate with piperidine according to the literature.⁷

4.2.1. N-(Trifluoroacetyl)piperidine (1a)

IR (neat) 2945, 1691, 1193, 1128 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 1.65-1.71 (6H, m), 3.54-3.63 (4H, m). ¹³C NMR (100MHz, CDCl₃) δ 23.8, 25.1, 26.0, 44.2, 46.5 (t, J_C-F = 3.5 Hz), 116.4 (t, J_C-F = 287.8 Hz), 154.9 (t, J_C-F = 35.3 Hz). ¹⁹F NMR (373MHz, CDCl₃) δ -69.49 (3F, s) (lit. -68.02).

4.2.2. N-(2,2,3,3,3-Pentafluoropropanoyl)piperidine (1b)

IR (neat) 2947, 1684, 1175 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 1.64-1.71 (6H, m), 3.61 (4H, brs). ¹³C NMR (100MHz, CDCl₃) δ 23.7, 25.0, 26.0, 44.0, 46.2 (tq, J_C-F = 270.6 Hz, J_C-F = 36.0 Hz), 117.9 (tq, J_C-F = 34.4 Hz, J_C-F = 285.6 Hz), 155.6 (t, J_C-F = 24.8 Hz). ¹⁹F NMR (373MHz, CDCl₃) δ -82.77 (3F, s), -115.44 (2F, s). HRMS (EI) calcd for C₈H₁₀F₅NO (M⁺) 231.06825, found 231.06888.

4.2.3. N-(2,2,3,3,4,4,5,5-Octafluoropentanoyl)piperidine (1c)

Ethyl 2,2,3,3,4,4,5,5-octafluoropentanoate was prepared from 2,2,3,3,4,4,5,5-octafluoropentanol according to the literature,⁸ and then converted to 1c according to the literature.⁷

IR (neat) 2950, 1682, 1175 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 1.65-1.71 (6H, m), 3.61 (4H, brs), 6.33 (1H, tt, J = 52.3, 5.7 Hz). ¹³C NMR (100MHz, CDCl₃) δ 23.7, 25.1, 26.0, 44.5, 46.5 (t, J_C-F = 6.3 Hz), 105.0-114.1 (4C, m), 156.3 (t, J_C-F = 24.6 Hz). ¹⁹F NMR (373MHz, CDCl₃) δ -112.13 (2F, t, J = 9.0 Hz), -124.50 to -124.56 (2F, m), -129.02 to -129.12 (2F, m), -138.17 (2F, dm, J = 52.0 Hz). HRMS (EI) calcd for C₁₀H₁₁F₈NO (M⁺) 313.07129, found 313.07058.

4.2.4. N-2-{(4-Chlorophenyl)sulfanyl}-2,2-difluoroacetylpiperidine (4)

Methyl 2-{(4-chlorophenyl)sulfanyl}-2,2-difluoroacetate (3) was prepared from methyl 2-{(4-chlorophenyl)sulfanyl}acetate according to the literature,¹⁰ and converted to 4 according to the literature.⁷ White solid. Mp 77-79 °C. IR (KBr) 2935, 1671, 1038 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 1.62-1.69 (6H, m), 3.60-3.64 (4H, m), 7.37 (2H, d, J = 8.3 Hz), 7.56 (2H, d, J = 8.3 Hz). ¹³C NMR (100MHz, CDCl₃) δ 24.2, 25.5, 26.3, 44.8, 47.0 (t, J_C-F = 5.0 Hz), 124.2, 124.6 (t, J_C-F = 291.4 Hz), 129.2 (2C), 136.8, 137.9 (2C), 159.2 (t, J_C-F = 26.2 Hz). ¹⁹F NMR (373MHz, CDCl₃) δ -73.52 (2F, s). HRMS (EI)
cald for C_{13}H_{14}Cl F_{2}NOS (M^+) 305.04494, found 305.04527.

4.2.5. **N-(2,2,3,3-Tetrafluoro-3-phenylpapranoyl)piperidine (8)**

Methyl 3-phenyl-2,2,3,3-tetrafluoropropionate (7) was prepared from methyl 2-(4-chlorophenyl)sulfonyl)propionate in three steps according to the literature, and converted to 8 by the reaction with piperidine. IR (neat) 2941, 1675, 1452, 1294, 1120 cm^{-1}. \( ^1H \text{NMR (400MHz, CDCl}_3 \right) \delta 1.63-1.68 (6H, m), 3.59-3.64 (4H, m), 7.45-7.52 (3H, m), 7.62 (2H, d, J = 7.5 Hz). \( ^{13}C \text{NMR (100MHz, CDCl}_3 \right) \delta 24.2, 25.5, 26.4, 44.8, 46.9-47.1 (m), 111.6 (tt, J_{CF} = 264.6 Hz, J_{CF} = 37.4 Hz), 116.1 (tt, J_{CF} = 253.5 Hz, J_{CF} = 31.5 Hz), 126.8 (tt, J_{CF} = 6.5 Hz, J_{CF} = 1.5 Hz), 128.1 (2C), 130.3 (t, J_{CF} = 24.3 Hz), 131.1 (2C, t, J_{CF} = 1.7 Hz), 157.7 (t, J_{CF} = 26.0 Hz). \( ^{19}F \text{NMR (373MHz, CDCl}_3 \right) \delta -110.91 (2F, s), -111.62 (2F, s). \( \text{HRMS (EI) calcd for C}_{14}H_{15}F_{4}NO (M^+) 289.10898, found 289.10820.

4.3. **Perfluoroalkylation of carbonyl compounds**

4.3.1. **2,2,2-Trifluoro-1-phenylethanol (2a)**

To a THF solution (3 mL) of 1a (181 mg, 1 mmol) were added a 1.0 M THF solution of Et_{3}BH (1 mL, 1 mmol) and benzaldehyde (53 mg, 0.5 mmol) successively at room temperature under N\(_2\) atmosphere. The mixture was stirred at 50 °C for 24 h and then 30% aqueous H\(_2\)O\(_2\) (2 mL) was added at 0 °C. After stirring for 1 h, the mixture was extracted with Et\(_2\)O (30 mL X 3). The combined organic phase was dried over MgSO\(_4\) and the yield of 2a was determined by \(^{19}F\) NMR using fluorobenzene as internal standard (99%).

Pure 2a was obtained by column chromatography (silica gel/CH\(_2\)Cl\(_2\):hexane = 4:1). IR (neat) 3397, 1267, 1127 cm\(^{-1}\). \( ^{1}H \text{NMR (400MHz, CDCl}_3 \right) \delta 5.01-5.06 (1H, m), 7.41-7.49 (5H, m). \( ^{13}C \text{NMR (100MHz, CDCl}_3 \right) \delta 72.2 (q, J_{CF} = 32.2 Hz), 123.4 (q, J_{CF} = 282.3 Hz), 127.4, 128.6 (2C), 129.6 (2C), 133.9 (q, J_{CF} = 0.9 Hz). \( ^{19}F \text{NMR (373MHz, CDCl}_3 \right) \delta -78.99 (3F, d, J = 7.1 Hz) \{lit.14 \ -78.77 (d, J = 7.6 Hz)\}.

4.2.2. **1-(4-Bromophenyl)-2,2,2-trifluoroethanol (2b)**

IR (neat) 3397, 1492, 1268, 1173, 1130 cm\(^{-1}\). \( ^{1}H \text{NMR (400MHz, CDCl}_3 \right) \delta 4.98-5.03 (1H, m), 7.35-7.44 (2H, m), 7.54-7.56 (2H, m). \( ^{13}C \text{NMR (100MHz, CDCl}_3 \right) \delta 72.2 (q, J_{CF} = 32.2 Hz), 123.8, 123.9 (q, J_{CF} = 282.1 Hz), 129.0 (2C), 131.8 (2C), 132.7. \( ^{19}F \text{NMR (373MHz, CDCl}_3 \right) \delta -79.15 (3F, d, J = 7.1 Hz) \{lit.14 \ -78.94 (d, J = 6.8 Hz)\}.

4.2.3. **(E)-1,1,1-Trifluoro-4-phenylbut-3-en-2-ol (2c)**

White solid. Mp 42-43 °C (lit.15 42-43 °C). IR (KBr) 3315, 2924, 1453, 1371 cm\(^{-1}\). \( ^{1}H \text{NMR (400MHz, CDCl}_3 \right) \delta 4.61-4.68 (1H, m), 6.21 (1H, dd, J = 15.9, 6.5 Hz), 6.86 (1H, d, J = 15.9 Hz), 7.29-7.44 (5H, m). \( ^{13}C \text{NMR (100MHz, CDCl}_3 \right) \delta 72.2 (q, J_{CF} = 32.4 Hz), 120.5 (q, J = 1.9 Hz), 124.2 (q, J = 281.8 Hz), 126.9 (2C), 128.7 (2C), 128.8, 135.3, 136.4. \( ^{19}F \text{NMR (373MHz, CDCl}_3 \right) \delta -79.70 (3F, d, J = 6.8 Hz) \{lit.14 \ -79.7 (d, J = 6.4 Hz)\}.

4.2.4. **2,2,2-Trifluoro-1-(naphthalen-1-yl)ethanol (2d)**
IR (neat) 3399, 2941, 1265, 1168, 1126 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 2.69 (1H, d, J = 4.5 Hz), 5.85-5.94 (1H, m), 7.51-7.60 (3H, m), 7.84 (1H, d, J = 7.3 Hz), 7.90-7.93 (2H, m), 8.08 (1H, d, J = 8.4 Hz).
¹³C NMR (100MHz, CDCl₃) δ 68.8 (q, ²JC-F = 32.2 Hz), 122.7 (q, ⁴JC-F = 0.9 Hz), 124.6 (q, ¹JC-F = 282.5 Hz), 125.1, 125.7 (q, ³JC-F = 1.2 Hz), 125.9, 126.8, 129.0, 129.8 130.1, 131.0, 133.6. ¹⁹F NMR (373MHz, CDCl₃) δ -77.48 (3F, d, J = 7.2 Hz) {lit.14 -77.25 (d, J = 6.5 Hz)}.

4,2,5. 2,2,2-Trifluoro-1-(furan-2-yl)ethanol (2e)
IR (neat) 3399, 1669, 1504, 1152 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 2.59 (1H, d, J = 7.2 Hz), 5.03-5.10 (1H, m), 6.53-6.44 (1H, m), 6.54 (1H, d, J = 3.2 Hz), 7.47-7.48 (1H, m). ¹³C NMR (100MHz, CDCl₃) δ 67.1 (q, ²JC-F = 34.3 Hz), 110.1 (q, ⁴JC-F = 0.9 Hz), 110.7, 123.4 (q, ¹JC-F = 282.1 Hz), 143.6, 147.1 (q, ³JC-F = 1.6 Hz). ¹⁹F NMR (373MHz, CDCl₃) δ -78.59 (3F, d, J = 7.2 Hz) {lit.3c -78.42 (d, J = 6.4 Hz)}.

4,2,6. 1-(1-Adamantan-1-yl)-2,2,2-trifluoroethanol (2f)
Yellow solid. Mp 47-49 °C. IR (KBr) 3422, 2907, 2851, 1263, 1167, 1120 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 1.68-1.79 (11H, m), 2.02 (3H, brs), 3.44 (1H, q, J = 8.3 Hz). ¹³C NMR (100MHz, CDCl₃) δ 28.0 (3C), 35.7 (3C), 36.7 (3C), 37.6 (q, ⁴JC-F = 1.8 Hz), 77.5 (q, ²JC-F = 27.9 Hz), 125.6 (q, ¹JC-F = 285.1 Hz). ¹⁹F NMR (373MHz, CDCl₃) δ -71.55 (3F, d, J = 8.8 Hz). HRMS (EI) calcd for C₁₂H₁₆F₃O (M⁺) 233.11587, found 233.11668.

4,2,7. 1-Cyclohexyl-2,2,2-trifluoroethanol (2g)
IR (neat) 3399, 3055, 1476, 1162, 1060 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 1.10-1.34 (5H, m), 1.67-2.02 (6H, m), 3.68-3.77 (1H, m). ¹³C NMR (100MHz, CDCl₃) δ 25.7, 25.9, 26.0, 26.7 (q, ²JC-F = 1.0 Hz), 28.0 (3C), 35.7 (3C), 36.7 (3C), 37.6 (q, ⁴JC-F = 1.0 Hz), 74.3 (q, ²JC-F = 29.1 Hz), 125.3 (q, ¹JC-F = 283.3 Hz). ¹⁹F NMR (373MHz, CDCl₃) δ -76.2 (3F, d, J = 7.1 Hz) {lit.3c -75.98 (d, J = 7.5 Hz)}.

4,2,8. 2,2,2-Trifluoro-1,1-diphenylethanol (2h)
IR (neat) 3456, 3063, 1714, 1155 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 7.34-7.38 (6H, m), 7.48-7.50 (4H, m). ¹³C NMR (100MHz, CDCl₃) δ 79.36 (q, ²JC-F = 28.4 Hz), 125.3 (q, ¹JC-F = 286.1 Hz), 127.4 (2C, q, ³JC-F = 1.4 Hz), 128.2 (4C), 128.6 (4C), 139.4 (2C). ¹⁹F NMR (373MHz, CDCl₃) δ -74.91 (3F, s) (lit.16 -74.21).

4,2,9. 2,2,3,3,3-Pentafluoro-1-(naphthalen-1-yl)propan-1-ol (2i)
The reaction was carried out as in the case of 2a using 1b and 1-naphthaldehyde instead of 1a and benzaldehyde, and 2i was isolated by column chromatography (silica gel, hexane:CH₂Cl₂=4:1) in 89% yield. White solid. Mp 44-46 °C. IR (KBr) 3465, 3060, 1185, 1135, 1028 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 2.49 (1H, d, J = 4.1 Hz), 6.06 (1H, dt, J = 18.3, 4.5 Hz), 7.52-7.61 (3H, m), 7.84 (1H, d, J = 7.2 Hz), 7.90-7.95 (2H, m), 8.03 (1H, d, J = 8.3 Hz). ¹³C NMR (100MHz, CDCl₃) δ 79.36 (q, ²JC-F = 28.4 Hz), 125.3 (q, ¹JC-F = 286.1 Hz), 127.4 (2C, q, ³JC-F = 1.4 Hz), 128.2 (4C), 128.6 (4C), 139.4 (2C). ¹⁹F NMR (373MHz, CDCl₃) δ -74.91 (3F, s) (lit.16 -74.21).
To 1c (626 mg, 2 mmol) were added a 1.0 M THF solution of Et₃BHK (2 mL, 2 mmol) and 1-naphthaldehyde (78 mg, 0.5 mmol) successively at room temperature under N₂ atmosphere. Then a volatile part was removed under reduced pressure, and the resulting viscous mixture was stirred at 40 °C for 24 h. Then, 30% aqueous H₂O₂ (2 mL) was added at 0 °C, and after stirring for 1 h, the mixture was extracted with Et₂O (30 mL X 3). The combined organic phase was dried over MgSO₄ and 2j was isolated by column chromatography (silica gel/CH₂Cl₂:hexane = 1:4) in 61% yield. White solid. Mp 75-77 °C. IR (KBr) 3398, 1175, 1124, 1041 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 2.57 (1H, s), 6.11 (1H, tt, J = 52.1, 5.5 Hz), 7.51-7.60 (3H, m), 7.84 (1H, d, J = 7.3 Hz), 7.90-7.94 (2H, m), 8.00 (1H, d, J = 8.4 Hz). ¹³C NMR (100MHz, CDCl₃) δ 67.3 (dd, Jₑ₋ᵢ₈ = 21.8 Hz, Jₑ₋ᵢ₉ = 30.5 Hz), 104.8-118.3 (4C, m), 122.6, 125.1, 125.9, 126.5, 126.9, 129.0, 130.1, 130.2, 131.3, 133.5. ¹⁹F NMR (373MHz, CDCl₃) δ -116.37 (1F, d, J = 286.6 Hz), -123.50 to -125.38 (2F, m), -127.40 (1F, d, J = 284.8 Hz), -129.7 to -131.90 (2F, m), -136.94 to -138.82 (2F, m). HRMS (ESI) calcd for C₁₅H₉C₈F₈O (M⁺) 357.05311, found 357.05331.

To a CH₂Cl₂ solution (1 mL) of 8 (578 mg, 2 mmol) were added a 1.0 M THF solution of Et₃BHK (2 mL, 2 mmol) and 4-isobutylbenzaldehyde (81 mg, 0.5 mmol) successively at room temperature under N₂ atmosphere. The mixture was stirred at 40 °C for 24 h and then 30% aqueous H₂O₂ (2 mL) was added at 0 °C. After stirring for 1 h, the mixture was extracted with Et₂O (30 mL X 3). The combined organic phase was dried over MgSO₄ and 9 was isolated by column chromatography (silica gel/AcOEt:hexane = 1:10) in 60% yield. White solid. Mp 54-55 °C. IR (KBr) 3466, 2960, 1069 cm⁻¹. ¹H NMR (400MHz, CDCl₃) δ 0.89 (6H, d, J = 6.7 Hz), 1.80-1.91 (1H, m), 2.39 (1H, d, J = 4.7 Hz), 2.47 (1H, d, J = 7.2 Hz), 5.14 (1H, dt, J = 17.3, 5.1 Hz), 7.15 (2H, d, J = 8.1 Hz), 7.34 (2H, d, J = 8.0 Hz), 7.43-7.52 (3H, m), 7.58 (2H, d, J = 7.4 Hz).
\(^{13}\text{C}\) NMR (100MHz, CDCl\(_3\)) \(\delta\) 22.3 (2C), 30.1, 45.1, 72.0 (dd, \(^{2}J_{C,F} = 28.8\) Hz, \(^{2}J_{C,F} = 22.4\) Hz), 115.4 (tt, \(^{1}J_{C,F} = 260.8\) Hz, \(^{2}J_{C,F} = 35.3\) Hz), 117.2 (tt, \(^{1}J_{C,F} = 253.0\) Hz, \(^{2}J_{C,F} = 34.1\) Hz), 126.7 (t, \(^{3}J_{C,F} = 6.7\) Hz), 127.8 (2C), 128.2 (2C), 129.1 (2C), 130.9 (2C, t, \(^{2}J_{C,F} = 24.3\) Hz), 131.0 (t, \(^{4}J_{C,F} = 1.4\) Hz), 132.5, 142.8. \(^{19}\text{F}\) NMR (373MHz, CDCl\(_3\)) \(\delta\) -109.50 to -110.99 (2F, m), -108.29 (1F, dd, \(J = 275.5, 6.2\) Hz), -108.29 (1F, dd, \(J = 275.5, 17.6\) Hz). HRMS (EI) calcd for C\(_{19}\)H\(_{19}\)F\(_{4}\)O (M\(^{+}\)) 339.13775, found 339.13808.

ACKNOWLEDGEMENTS

We are grateful to Asahi Glass Co., Ltd., and Daikin Industries, Ltd., for their donation of IF\(_{5}\) and 2,2,3,3,4,4,5,5-octafluoropentanol, respectively.

REFERENCES


6. Trifluoroacetamides were previously used to generate the trifluoromethyl anion by the reaction with base, but the trifluoromethylation successfully proceeded only in the reaction with aromatic ketones, see: L. Jablonski, J. Joubert, T. Billard, and B. R. Langlois, *Synlett*, 2003, 230.


