# Convenient preparation of difluoromethylene-functionalized compounds from chlorodifluoroacetic acid

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(Received April 29, 1993; accepted September 27, 1993)

**Abstract**

A convenient route for the synthesis of difluoromethylene-functionalized compounds from chlorodifluoroacetic acid has been investigated. Bis(chlorodifluoroacetyl) peroxide, which was synthesized from chlorodifluoroacetic acid via its acid anhydride, was found to be a good reagent for the chlorodifluoromethylation of electron-rich aromatic compounds and olefins. The chlorine atom of the chlorodifluoromethylated compounds, thus prepared, exchanged hydrogen and allyl groups by reaction with tributyltin hydride and allyltributyltin, respectively, under radical conditions.

## Introduction

The introduction of one or two fluorines into a particular position in organic molecules leads to significant changes in chemical, physical and biological properties [1]. The direct introduction of fluorine into desired positions of organic compounds using fluorinating agents such as sulfur tetrafluoride [2] and diethylaminosulfur trifluoride [3] has provided a great challenge to fluorine chemists [4]. However, the construction of complex organofluorine compounds from easily available fluorinated molecules provides another approach and has been widely investigated by organic chemists [5]. Various types of fluorinated alkanoic acids are readily available and easy to handle; hence, the construction of fluorine compounds from fluoroalkanoic acids may be expected to provide useful and convenient routes.

We have been exploring the introduction of perfluoroalkyl groups into organic compounds using bis(perfluoroalkanoyl) peroxides [$(R_FCO_2)_2$] which are readily synthesized from fluoroalkanoic acids via acid chlorides and/or acid anhydrides [6]. In this paper, chlorodifluoromethylation with bis(chlorodifluoroacetyl) peroxide and successive conversions of the chlorine into other functional groups are reported in connection with interest in the development of convenient routes for the synthesis of difluoromethylene-functionalized compounds from chlorodifluoroacetic acid.

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## Experimental

$^1H$, $^{13}C$ and $^{19}F$ NMR spectra were taken with a JEOL JNM EX400 spectrometer. Fluorine chemical shifts are given in ppm from external $CF_3CO_2H$. IR spectra were recorded on a Hitachi 260-10 spectrometer. Gas chromatography was performed by means of a Hitachi G-3000 gas chromatograph using a 10% SE30 packed 1 m stainless-steel column. Gel-permeation chromatography (GPC) was performed by means of a JAI model LC-08 liquid chromatograph equipped with two JAIGEL-1H columns (20 mm×600 mm) with chloroform as eluent. Mass spectra were obtained with a JEOL JMS AX-505 spectrometer using an electron-impact (EI) ionization technique at 70 eV.

*Synthesis of bis(chlorodifluoroacetyl) peroxide (1)*

Hydrogen peroxide (30%, 2.5 ml) and then Freon 113 (15 ml) were added to a solution of sodium carbonate (4.4 g) and sodium chloride (4.8 g) in 80 ml water. The heterogeneous solution was cooled to −3 °C, stirred vigorously and chlorodifluoroacetic anhydride (4.5 g) in 5 ml of Freon 113 was added drop-by-drop for 5 min. After all of the chlorodifluoroacetic anhydride had been added, the reaction mixture was stirred for 2 min and the Freon layer separated. The peroxide was not isolated, being used as a solution in Freon 113. The concentration of the peroxide was determined by iodometry.

*Reaction of benzene with 1*

Benzene (10 mmol) was reacted with **1** (5 mmol) in 50 ml of Freon 113 at 40 ° C in a sealed tube for 18

0022-1139/94/$07.00 
*SSDI* 0022-1139(93)02985-N

h. The reaction mixture was washed with 5% aq. $NaHCO_3$ and then water. The organic layer was dried over anhydrous $MgSO_4$ and the solvent removed by evaporation. From the residue, $PhCF_2Cl$ [7] was obtained.

*Reduction of $PhCF_2Cl$ with tributyltin hydride*

$PhCF_2Cl$ (0.5 mmol) was reacted with tributyltin hydride (0.6 mmol) in the presence of AIBN (0.06 mmol) in benzene at 90 °C for 20 h in a sealed tube to give $PhCF_2H$ [8] in 82% yield; the formation of $PhCF_2H$ was confirmed by GC/MS (*m/z* 128 ($M^+$); 109; 78) and $^{19}F$ NMR spectroscopy ($\delta_F$ −35.19 (d, $J_{HF}$ = 57.4 Hz) ppm), and the yield also determined by $^{19}F$ NMR spectroscopy.

*Allylation of $PhCF_2Cl$ with allyltributyltin*

$PhCF_2Cl$ (0.5 mmol) was reacted with allyltributyltin (2.5 mmol) in the presence of AIBN in benzene (5 ml) at 90 °C for 20 h in a sealed tube; the allylation proceeded to give a yield of 99%. From the reaction mixture, 4,4-difluoro-4-phenyl-1-butene ($PhCF_2-CH_2-CH=CH_2$) was isolated by column chromatography (Wakogel C-200; eluent, hexane). 4,4-Difluoro-4-phenyl-1-butene: $^1H$ NMR ($CDCl_3$) $\delta$: 2.90 (td, $J_{HF}$ = 15.9, $J_{HH}$ = 6.8 Hz, 1H); 5.15 (d, $J$ = 17.1 Hz, 1H); 5.17 (d, $J$ = 10.3 Hz, 1H); 5.74 (ddt, $J$ = 17.1; 10.3, 6.8 Hz, 1H); 7.41–7.48 (m, 5H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$: 43.76 (t, $J_{CCF}$ = 28.5 Hz); 120.52, 121.76 (t, $J_{CF}$ = 242.7 Hz); 125.07 (t, $J_{CCCF}$ = 6.4 Hz); 128.35, 129.08 (t, $J_{CCCF}$ = 4.6 Hz); 129.72, 136.98 (t, $J_{CCF}$ = 25.8 Hz) ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: −19.75 (t, $J_{HF}$ = 15.9 Hz) ppm. MS *m/z*: 168 ($M^+$); 127; 77. Exact. MS: Calc. for $C_{10}H_{10}F_2$: 168.0751. Found: 168.0703.

*Reaction of naphthalene with 1*

Naphthalene (10 mmol) was reacted with **1** (5 mmol) in 50 ml of Freon 113 under reflux for 4 h. Chlorodifluoromethylation of naphthalene proceeded in 53% yield (the ratio of 1-chlorodifluoromethylnaphthalene/2-chlorodifluoromethylnaphthalene, 87: 13, determined by $^{19}F$ NMR spectroscopy). The reaction mixture was subjected to column chromatography on silica gel (Wakogel C-200; eluent, hexane) when a mixture of 1-chlorodifluoromethylnaphthalene and 2-chlorodifluoromethylnaphthalene was obtained. 1-Chlorodifluoromethyl and 2-chlorodifluoromethylnaphthalene were separated from each other by GPC. Each isomer was identified by $^{13}C$ NMR spectroscopy; one tertiary carbon split to a triplet by CCCF coupling was observed at $\delta$ 123.36 ppm in 1-chlorodifluoromethylnaphthalene and two tertiary carbons split to a triplet by CCCF coupling were observed at $\delta$ 121.46 and $\delta$ 124.49 ppm in 2-chlorodifluoromethylnaphthalene.

1-Chlorodifluoromethylnaphthalene: $^1H$ NMR ($CDCl_3$) $\delta$: 7.13–8.46 (m, 7H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$: 123.36 (t, $J_{CCCF}$ = 8.5 Hz); 124.11, 124.71, 126.50, 126.50 (t, $J_{CF}$ = 293.0 Hz); 127.42; 128.39, 128.88, 131.48 (t, $J_{CCF}$ = 23.1 Hz); 132.62, 134.24 ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: 28.54 ppm. MS *m/z*: 212 ($M^+$); 177; 127. Exact. MS: Calc. for $C_{11}H_7ClF_2$: 212.2051. Found: 212.0187.

2-Chlorodifluoromethylnaphthalene: m.p. 56.0–57.5 °C (from EtOH): $^1H$ NMR ($CDCl_3$) $\delta$: 7.20–8.18 (m, 7H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$: 121.46 (t, $J_{CCCF}$ = 4.9 Hz); 124.49 (t, $J_{CCCF}$ = 6.1 Hz); 125.79, 126.77 (t, $J_{CF}$ = 293.2 Hz); 127.20, 127.85, 128.01, 128.94; 132.19; 133.34; 134.35 (t, $J_{CCF}$ = 19.3 Hz) ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: 26.88 ppm. MS *m/z*: 212 ($M^+$); 177; 127.

*Reduction of 1-chlorodifluoromethyl and 2-chlorodifluoromethylnaphthalene with tributyltin hydride*

1-Chlorodifluoromethylnaphthalene (0.5 mmol) was reacted with tributyltin hydride (0.6 mmol) in the presence of AIBN (0.06 mmol) in 5 ml of benzene under reflux for 20 h. 1-Difluoromethylnaphthalene was isolated by column chromatography in a yield of 87% (Wakogel C-200; eluent, hexane). 1-Difluoromethylnaphthalene: oil (78–79 °C/0.4 mmHg) [9]: $^1H$ NMR ($CDCl_3$) $\delta$: 7.08 (t, $J_{HF}$ = 54.0 Hz, 1H); 7.38–8.34 (m, 7H) ppm. $^{13}C$ NMR ($CDCl_3$): 115.45 (t, $J_{CF}$ = 238.0 Hz); 123.57, 124.71, 124.82 (t, $J_{CCCF}$ = 8.6 Hz); 126.39; 127.20, 128.83, 129.52 (t, $J_{CCF}$ = 19.3 Hz); 129.75, 131.48, 133.92 ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: −35.59 (d, $J_{HF}$ = 54.0 Hz) ppm.

Similarly, 2-difluoromethylnaphthalene was obtained in a yield of 88%. 2-Difluoromethylnaphthalene: m.p. 70.0–71.0 °C (from hexane): $^1H$ NMR ($CDCl_3$) $\delta$: 6.67 (t, $J_{HF}$ = 56.1 Hz, 1H); 7.17–8.00 (m, 7H) ppm. $^{13}C$ NMR ($CDCl_3$) $\delta$: 115.12 (t, $J_{CF}$ = 238.7 Hz); 122.06 (t, $J_{CCCF}$ = 4.9 Hz); 125.90 (t, $J_{CCCF}$ = 7.3 Hz); 126.82, 127.42; 127.91, 128.56, 128.94, 131.81 (t, $J_{CCF}$ = 21.4 Hz); 132.7, 134.46 ppm. $^{19}F$ NMR ($CDCl_3$) $\delta$: −34.56 (d, $J_{HF}$ = 56.1 Hz) ppm. MS *m/z*: 178 ($M^+$); 157; 128. Exact. MS: Calc. for $C_{11}H_8F_2$: 178.0594. Found: 178.0583.

*Allylation of 1-chlorodifluoromethylnaphthalene and 2-chlorodifluoromethylnaphthalene with allyltributyltin*

1-Chlorodifluoromethylnaphthalene (0.5 mmol) was reacted with allyltributyltin (2.5 mmol) in the presence of AIBN (0.06 mmol) in 5 ml of benzene under reflux. The reaction was monitored by GC methods; allylation proceeded in 94% yield in 20 h. 4,4-Difluoro-4-(1-naphthyl)-1-butene ($ArCF_2-CH_2-CH=CH_2$) was isolated from the reaction mixture by column chromatography (Wakogel C-200; eluent, hexane). 4,4-Difluoro-4-(1-naphthyl)-1-butene: $^1H$ NMR ($CDCl_3$) $\delta$: 3.13 (td, $J_{HF}$ = 15.9, $J_{HH}$ = 6.8 Hz, 2H); 5.10 (d, $J$ = 17.1 Hz, 1H); 5.12 (d, $J$ = 10.1 Hz, 1H); 5.17 (ddt, $J$ = 17.1, 10.3, 6.8

Hz, 1H); 7.37–8.24 (m, 7H). $^{13}$C NMR ($CDCl_3$) $\delta$: 43.50 (t, $J_{CCF}$ = 26.7 Hz); 120.22, 122.74 (t, $J_{CF}$ = 244.5 Hz); 124.34 (t, $J_{CCCF}$ = 9.3 Hz); 124.40, 124.70, 125.85, 126.78, 128.96, 129.19 (t, $J_{CCCF}$ = 5.1 Hz); 129.30, 130.88, 132.27 (t, $J_{CCF}$ = 23.9 Hz); 134.13 ppm. $^{19}$F NMR ($CDCl_3$) $\delta$: −15.66 (t, $J_{HF}$ = 15.9 Hz) ppm. MS *m/z*: 218 ($M^+$); 177; 127. Exact. MS: Calc. for $C_{14}H_{12}F_2$ 218.0908. Found: 218.0879.

Similarly, allylation of 2-chlorodifluoromethylnaphthalene proceeded in 96% yield. 4,4-Difluoro-4-(2-naphthyl)-1-butene; m.p. 34.0–35.0 °C (from hexane): $^1$H NMR ($CDCl_3$) $\delta$: 2.97 (td, $J_{HF}$ = 15.9, $J_{HH}$ = 6.8 Hz, 2H); 5.14 (d, $J$ = 17.6 Hz, 1H); 5.15 (d, $J$ = 9.8 Hz, 1H); 5.76 (ddt, $J$ = 17.6, 9.8, 6.8 Hz, 1H); 7.49–7.95 (m, 7H) ppm. ($CDCl_3$) $\delta$: 43.72 (t, $J_{CCF}$ = 28.1 Hz); 120.54, 121.95 (t, $J_{CF}$ = 242.9 Hz); 122.33 (t, $J_{CCCF}$ = 5.5 Hz); 124.82 (t, $J_{CCCF}$ = 7.3 Hz); 126.61, 127.04, 127.69, 128.34, 128.56, 129.04 (t, $J_{CCCF}$ = 5.5 Hz); 132.56; 133.70, 134.24 (t, $J_{CCF}$ = 28.2 Hz) ppm. ($CDCl_3$) $\delta$: −19.34 (t, $J_{HF}$ = 15.9 Hz) ppm. MS *m/z*: 218 ($M^+$); 177; 127. Exact. MS: Calc. for $C_{14}H_{12}F_2$: 218.0908. Found: 218.0982. Analysis: Calc. for $C_{14}H_{12}F_2$: C, 77.05; H, 5.54%. Found: C, 76.59; H, 5.35%.

*Reaction of styrene with 1*

Styrene (3.0 mmol) was reacted with **1** (1.5 mmol) in Freon 113 (15 ml) at 40 °C for 6 h in a sealed tube. From the reaction mixture, 1-chloro-3-chlorodifluoroacetoxy-1,1-difluoro-3-phenylpropane (**2**) was isolated by column chromatography (Wakogel C-200; eluent, 20:1 hexane/ethyl acetate). Compound **2**: $^1$H NMR ($CDCl_3$) $\delta$: 2.80 (m, 1H); 3.17 (m, 1H); 6.26 (dd, $J$ = 9.3, 2.4 Hz, 1H); 7.39 (s, 5H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 47.60 (t, $J_{CCF}$ = 23.9 Hz); 74.71, 116.71 (t, $J_{CF}$ = 300.6 Hz); 126.33; 127.07 (t, $J_{CF}$ = 292.3 Hz); 129.28, 129.72, 136.34, 157.84 (t, $J_{CCF}$ = 34.9 Hz) ppm. MS *m/z*: 318 ($M^+$); 189; 153.

Compound **2**, thus obtained, was stirred in 10% aq NaOH for 3 h at room temperature. The aqueous solution was washed with ether (2×10 ml) and the combined ether extracts dried over anhydrous $MgSO_4$. Evaporation of the ether gave almost pure 1-chloro-1,1-difluoro-3-phenylpropan-3-ol (**3**). Compound **3**: $^1$H NMR ($CDCl_3$) $\delta$: 2.39 (s, 1H); 2.63 (m, 1H); 2.81 (m, 1H); 5.10 (d, $J$ = 9.1 Hz, 1H); 7.35 (s, 5H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 50.42 (t, $J_{CCF}$ = 22.1 Hz); 69.70, 125.68, 128.31, 128.37 (t, $J_{CF}$ = 293.2 Hz); 128.78, 142.28 ppm. MS *m/z*: 206 ($M^+$); 107; 79.

Compound **3** was refluxed in benzene (10 ml) in the presence of *p*-toluenesulfonic acid (0.15 mmol) for 24 h. From the reaction mixture, 2-(chlorodifluoromethyl)styrene (**4**) was obtained by column chromatography (Wakogel C-200; eluent, hexane). 2-(Chlorodifluoromethyl)styrene (**4**): $^1$H NMR ($CDCl_3$) $\delta$: 6.39 (dt, $J_{HH}$ = 16.1, $J_{HF}$ = 9.0 Hz, 1H); 7.07 (d, $J$ = 16.1 Hz, 1H); 7.37–7.46 (m, 5H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 122.13 (t, $J_{CCF}$ = 26.7 Hz); 125.44 (t, $J_{CF}$ = 284.9 Hz); 127.61; 128.93; 129.94; 133.37, 134.93 (t, $J_{CCCF}$ = 7.4 Hz) ppm. MS *m/z*: 188 ($M^+$); 153; 133. Exact. MS: Calc. for $C_9H_7F_2Cl$: 188.0205. Found: 188.0332.

*Reaction of butyl vinyl ether with 1*

Butyl vinyl ether (3.0 mmol) was reacted with **1** (1.5 mmol) in Freon 113 (15 ml) at 40 °C for 6 h in a sealed tube. Although the formation of the adduct (**5**) arising from the introduction of $CF_2Cl$ and $CF_2ClCO_2$ groups into butyl vinyl ether was estimated by GC/MS measurement of the reaction mixture, **5** was too unstable to be isolated. After removal of Freon 113, methanol was added to the residue and the resulting solution allowed to stir for 3 h. This led to the conversion of compound **5** into 3-butoxy-1-chloro-1,1-difluoro-3-methoxypropane (**6**), which was isolated by column chromatography. Compound **6**: $^1$H NMR ($CDCl_3$) $\delta$: 0.93 (t, $J$ = 7.3 Hz, 3H); 1.40 (sext., $J$ = 7.3 Hz, 2H); 1.58 (quint., $J$ = 7.3 Hz, 2H); 2.66 (td, $J_{HF}$ = 13.2, $J_{HH}$ = 5.4 Hz, 2H); 3.36 (s, 3H); 3.48, 3.62 (ABqt, $J$ = 9.3, 7.3 Hz, 2H); 4.80 (t, $J$ = 5.4 Hz, 1H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 13.84, 19.33, 31.75, 45.50 (t, $J_{CCF}$ = 23.0 Hz); 53.00, 66.51, 99.03, 127.50 (t, $J_{CF}$ = 292.3 Hz) ppm. $^{19}$F NMR ($CDCl_3$) $\delta$: 26.62 (t, $J_{HF}$ = 13.2 Hz) ppm. MS *m/z*: 185 ($M^+$ −31); 143; 117. Exact. MS: Calc. for $C_7H_{12}OClF_2$ ($M^+$ −OMe): 185.0545. Found: 185.0582.

*Reduction of 6 with tributyltin hydride*

Reduction of **6** was carried out by a method similar to that described for the reduction of $ArCF_2Cl$. 3-Butoxy-1,1-difluoro-3-methoxypropane (**7**) was isolated by GPC. Compound **7**: $^1$H NMR ($CDCl_3$) $\delta$: 0.93 (t, $J$ = 7.3 Hz, 3H); 1.39 (sext., $J$ = 7.3 Hz, 2H); 1.57 (quint., $J$ = 7.3 Hz, 2H); 2.17 (tt, $J_{HF}$ = 15.9, $J_{HH}$ = 5.4 Hz, 2H); 3.35 (s, 3H); 3.45, 3.62 (ABqt, $J$ = 9.3, 7.3 Hz, 2H); 4.61 (t, $J$ = 5.4 Hz, 1H); 5.88 (tt, $J_{HF}$ = 56.2, $J_{HH}$ = 5.4 Hz, 1H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 13.84, 19.37, 31.84, 38.48 (t, $J_{CCF}$ = 21.1 Hz); 53.20, 66.61, 99.34, 115.68 (t, $J_{CF}$ = 232.2 Hz) ppm. $^{19}$F NMR ($CDCl_3$) $\delta$: −41.02 (dt, $J_{HFgem}$ = 56.2, $J_{HFvic}$ = 15.9 Hz) ppm. Exact. MS: Calc. for $C_{10}F_{17}OF_2$ ($M^+$ −OMe): 151.0935. Found: 151.0883.

*Allylation of 6 with allyltributyltin*

Allylation of **6** (0.5 mmol) was carried out with allyltributyltin (2.5 mmol) in the presence of AIBN (0.06 mmol) in 5 ml of benzene under reflux for 72 h. After removal of the solvent, the residual oil was subjected to column chromatography on silica gel (Wakogel C-200) and eluted with hexane to give excess allyltributyltin and then with ethyl acetate to give crude allylated product (**8**), which was further purified by GPC. 6-Butoxy-4,4-difluoro-6-methoxy-1-hexene (**8**): $^1$H NMR ($CDCl_3$) $\delta$: 0.93 (t, $J$ = 7.3 Hz, 3H); 1.39 (sext.,

$J$=7.3 Hz, 2H); 1.57 (quint., $J$=7.3 Hz, 2H); 2.20 (td, $J_{HF}$=16.4, $J_{HH}$=5.4 Hz, 2H); 2.66 (td, $J_{HF}$=16.4, $J_{HH}$=7.3 Hz, 2H); 3.34 (s, 3H); 3.45, 3.60 (ABqt, $J$=9.3, 7.3 Hz, 2H); 4.70 (t, $J$=5.4 Hz, 1H); 5.21 (d, $J$=16.1 Hz, 1H); 5.22 (d, $J$=11.2 Hz, 1H); 5.81 (ddt, $J$=16.1, 11.2, 7.3 Hz, 1H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 13.86, 19.39, 31.80, 39.85 (t, $J_{CCF}$=23.9 Hz); 41.42 (t, $J_{CCF}$=25.7 Hz); 52.80, 66.20, 99.34, 120.46, 122.79 (t, $J_{CF}$=241.8 Hz); 129.55 ppm. ($CDCl_3$) $\delta$: −18.82 (quint., $J_{HF}$=16.4 Hz) ppm. Exact. MS: Calc. for $C_7H_{13}OF_2$ ($M^+$ −OMe): 191.1248. Found: 191.1186.

*Reaction of cyclopentadiene and cycloheptatriene with 1*

Typically, olefin (3.0 mmol) was reacted with **1** (1.5 mmol) in 15 ml of Freon 113 at 40 °C in a sealed tube for 6 h. The products were isolated by column chromatography (Wakogel C-200; eluent, 20:1 hexane/ethyl acetate) and GPC. In the reaction with cyclopentadiene, 3-chlorodifluoroacetoxy-5-chlorodifluoromethyl-1-cyclopentene (**9**) and 3,5-bis(chlorodifluoroacetoxy)-1-cyclopentene (**10**) were obtained.

3-Chlorodifluoroacetoxy-5-chlorodifluoromethyl-1-cyclopentene (**9**): $^1$H NMR ($CDCl_3$) $\delta$: 2.25 (ddd, $J$=15.1, 7.8, 2.9 Hz, 1H); 2.53 (ddd, $J$=15.1, 7.3, 5.4 Hz, 1H); 3.82–3.88 (m, 1H); 5.96 (d, $J$=5.4 Hz, 1H); 6.17–6.21 (m, 2H) ppm. MS *m/z*: 280 ($M^+$); 151; 116. Exact. MS: Calc. for $C_8H_6O_2F_4Cl_2$: 279.9680. Found: 279.9697.

3,5-Bis(chlorodifluoroacetoxy)-1-cyclopentene (**10**): $^1$H NMR ($CDCl_3$) $\delta$: 2.51 (t, $J$=4.9 Hz, 2H); 6.05 (t, $J$=4.9 Hz, 2H); 6.32 (s, 2H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 36.50, 82.17, 116.70 (t, $J_{CF}$=295.3 Hz); 135.57, 159.01 (t, $J_{CCF}$=35.2 Hz) ppm.

In the reaction with cycloheptatriene, 5-chlorodifluoroacetoxy-7-chlorodifluoromethyl-1,3-cycloheptadiene (**11**) and 5,7-bis(chlorodifluoroacetoxy)-1,3-cycloheptadiene (**12**) were obtained.

5-Chlorodifluoroacetoxy-7-chlorodifluoromethyl-1,3-cycloheptadiene (**11**): $^1$H NMR ($CDCl_3$) $\delta$: 1.98 (ddd, $J$=15.0, 10.7, 2.9 Hz, 1H); 2.55 (dd, $J$=15.0, 2.9 Hz, 1H); 3.19 (td, $J$=10.7, 10.7 Hz, 1H); 5.71 (d, $J$=3.9 Hz, 1H); 5.97 (dd, $J$=11.5, 4.9 Hz, 1H); 6.07–6.12 (m, 1H); 6.18–6.23 (m, 2H) ppm. MS *m/z*: 306 ($M^+$); 141, 91. Exact. MS: Calc. for $C_{10}H_8O_2F_4Cl_2$: 305.9836. Found: 305.9811.

5,7-Bis(chlorodifluoroacetoxy)-1,3-cycloheptadiene (**12**): $^1$H NMR ($CDCl_3$) $\delta$: 2.44 (d, $J$=13.2 Hz; 1H); 2.80 (dt, $J$=13.2, 9.5 Hz, 1H); 5.82–5.88 (m, 4H); 5.96–5.98 (m, 2H) ppm. $^{13}$C NMR ($CDCl_3$) $\delta$: 35.19, 73.12, 116.70 (t, $J_{CF}$=301.5 Hz); 125.90, 130.94, 158.94 (t, $J_{CCF}$=35.0 Hz) ppm.

## Results and discussion

In our previous paper, we showed that bis(chlorodifluoroacetyl) peroxide (**1**) acts as a good reagent for the chlorodifluoromethylation of aromatic rings [10]. The chlorodifluoromethylarenes, thus prepared, were readily converted into $ArCF_2H$ and $ArCF_2CH_2CH{=}CH_2$ via $ArCF_2$ radicals with tributyltin hydride and allyltributyltin, respectively. As peroxide **1** is synthesized from chlorodifluoroacetic acid via its acid anhydride formally, the COOH group in chlorodifluoroacetic acid is replaced by aromatic rings and the chlorine then exchanged for hydrogen or allyl groups, respectively (Scheme 1).

Fluorine-substituted carbocation intermediates are usually difficult to prepare due to the strong electronegativity of fluorine [11]. Furthermore, $\alpha$-fluorocarbanions are also unstable and tend to undergo defluorination due to the electrostatic repulsions between the unshared electron pair of the carbanion and lone pairs of fluorine [12]. Hence, radical species are likely to play important roles in the synthesis of organofluorine compounds [13]. Although C–F bonds are too strong for the abstraction of fluorine, chlorine is relatively easy to abstract under radical conditions. Thus, $CF_2Cl$ is expected to be a useful functional group for the synthesis under radical conditions of compounds containing $CF_2$ units*. In order to extend the method to the synthesis of various chlorodifluoromethylated compounds, we further investigated the reactions of olefins with **1**, with the results shown in Table 1.

In the reaction of styrene with **1**, the adduct (**2**) arising from the introduction of $CF_2Cl$ and $CF_2ClCO_2$ groups into styrene was obtained in 51% yield (Table 1, run 1). Plausible mechanisms are shown in Scheme 2; the reaction is initiated by electron transfer from styrene to **1** to give the radical cation of styrene, the fluoromethyl radical and the fluoroacetate within a solvent cage. Since the reaction proceeds in a solvent cage, $CF_2Cl$ and $CF_2CO_2$ groups are introduced selectively into styrene without the formation of polymeric products.

$$ClCF_2{-}CO_2H \longrightarrow (CF_2ClCO)_2O \longrightarrow (CF_2ClCO_2)_2$$

$$(CF_2ClCO_2)_2 + ArH \longrightarrow ArCF_2Cl + CF_2ClCO_2H + CO_2$$

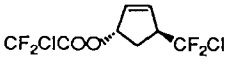
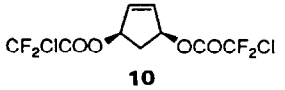
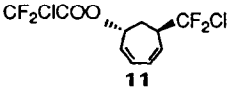
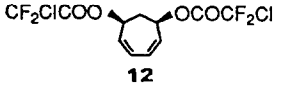
$$ArCF_2Cl \xrightarrow{Bu_3Sn^\bullet} ArCF_2^\bullet \xrightarrow{Bu_3SnH} ArCF_2H$$

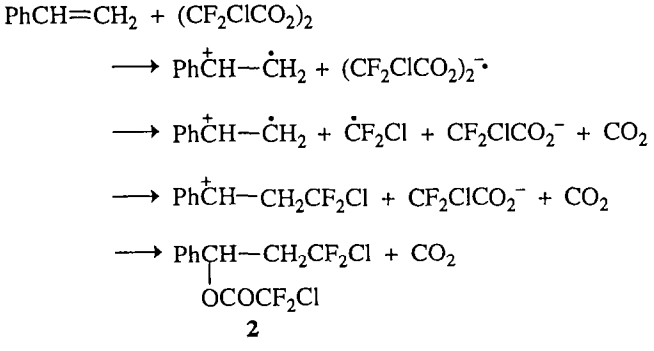
$$ArCF_2^\bullet \xrightarrow{Bu_3SnCH_2CH{=}CH_2} ArCF_2CH_2CH{=}CH_2$$

Scheme 1.

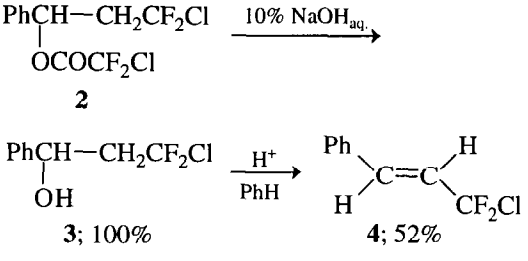
*Radical cyclizations of $CF_2Cl$ derivatives have recently been reported [14].

TABLE 1. Reactions of olefins with compound **1**

| Run No. | Substrate | Product (yield, %) |
|---|---|---|
| 1 | $PhCH{=}CH_2$ | $PhCH(OCOCF_2Cl)-CH_2CF_2Cl$ **2** (51) |
| 2 | $BuOCH{=}CH_2$ | $BuOCH(OCOCF_2Cl)-CH_2CF_2Cl$ **5** (61) |
| 3 |  | Unidentified polymeric products |
| 4 |  |  (17) **9**;  (8) **10** |
| 5 |  |  (34) **11**;  (21) **12** |



Scheme 2.

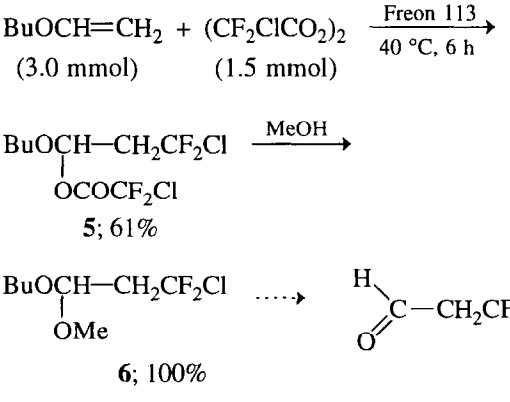


Scheme 3.

Hydrolysis of adduct **2** gave an alcohol **3** under basic conditions and the alcohol was then converted into the fluoroalkylated olefin **4** by refluxing in benzene in the presence of *p*-toluenesulfonic acid (Scheme 3).

The electron-rich olefin (butyl vinyl ether) also reacted with **1** to give adduct **5** in 61% yield (Table 1, run 2). Adduct **5** was too unstable to be isolated. However, when methanol was added to the mixture of butyl vinyl ether with **1**, the $CF_2ClCO_2$ group in **5** was converted into a methoxy group to give **6**, which corresponds to the protected aldehyde (Scheme 4). Product **6** was isolated by column chromatography.

The reactions of cyclohexene with **1** gave only unidentified polymeric products (Table 1, run 3). Electron transfer from cyclohexene to **1** did not take place due to the high ionization potential, but unimolecular homolytic decomposition of **1** occurred. Reactions of conjugated olefins (which have lower ionization potentials relative to cyclohexene) with **1** were also investigated (Table 1, runs 4 and 5). In these reactions two types of products were obtained; one was the adduct arising from the introduction of a $CF_2Cl$ and $CF_2ClCO_2$ group (type A, compounds **9** and **11**), and the other was the adduct arising from the introduction of two $CF_2ClCO_2$ groups (type B, compounds **10** and **12**). Interestingly, type A adducts have a *trans* configuration between the $CF_2Cl$ and $CF_2ClCO_2$ groups, whereas in contrast type

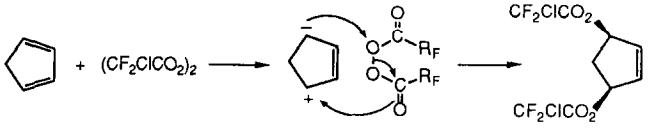


Scheme 4.

B adducts have a *cis* configuration between the two $CF_2ClCO_2$ groups. Type A adducts were formed via an electron-transfer process as shown by the reaction of styrene with **1**. Type B compounds are probably produced via a concerted reaction of the $\pi$-electrons of the olefin with the O--O bond of **1** as shown in Scheme 5.

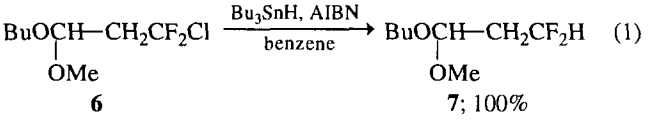
The substitution of the chlorine atom of **6** by hydrogen and allyl was also investigated. Reduction of **6** with 1.2 equiv. of tributyltin hydride proceeded almost quantitatively [Scheme 6, eqn. (1)]. Allylation of **6** also proceeded in 69% yield with 5.0 equiv. of allyltributyltin [Scheme 6, eqn. (2)].

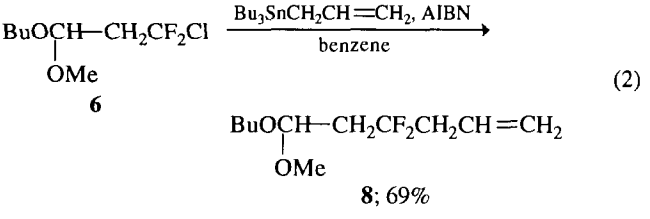
Since the allyl group can be converted further into useful functional groups, the method described in this paper is expected to provide useful and convenient routes for the synthesis of difluoromethylene-functionalized compounds.




**10**

Scheme 5.




Scheme 6.

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