

Preparations of carboxylic acid esters containing heptafluoroisopropyl groups

T. Suyama*, S. Kato[†] and Y. Mizutani

Corporate Planning Division, Tokuyama Soda Co. Ltd., 1-4-5 Nishi-shinbashi, Minato-ku, Tokyo 105 (Japan)

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Abstract

The reaction of fluoroglyoxylic acid esters and fluoroformic acid esters with perfluoropropene (PFP) yielded perfluoro(3-methyl-2-oxobutyric) acid esters and perfluoroisobutyric acid esters, respectively. Oxamide derivatives and 2,3-quinoxalinediol have been prepared by the reaction of perfluoro(3-methyl-2-oxobutyric) acid esters with amines and *o*-phenylenediamine, respectively. Perfluoro(3-methyl-2-oxobutyric) acid esters give perfluoroisobutyric acid esters on heating in the presence of fluoride ion in an aprotic solvent.

Introduction

There have been many reports on the reaction of perfluoropropene (PFP) with electrophilic reagents in the presence of the fluoride ion in an aprotic solvent. For example, Smith *et al.* [1] obtained perfluoro(alkyl isopropyl ketones) by the reaction between perfluoroacyl fluoride and PFP in the presence of fluoride ion. Aryl perfluoroisopropyl ketones have been prepared by the reaction between benzoyl chloride and PFP in the presence of potassium fluoride in *N,N*-dimethylformamide at 120–130 °C [2]. We found that perfluoro(3-methyl-2-oxobutyric) acid esters and perfluoroisobutyric acid esters could be obtained by the reaction of PFP with fluoroglyoxylic acid esters and fluoroformic acid esters as the electrophilic reagents, respectively. In comparison with much of the previous work on the preparation of perfluorocarboxylic acid derivatives, for example electrofluorination and reaction using perfluoro Grignard reagents, our method does not need the special apparatus of an electrofluorination system, harmful or special reagents such as hydrogen fluoride and perfluoro Grignard reagents [3–6]. Hence the reaction described here affords a valuable and convenient method for the preparation of perfluorocarboxylic acid derivatives. The perfluoro(3-methyl-2-oxobutyric) acid

*Author to whom correspondence should be addressed.

[†]Tsukuba Research Laboratory, Tokuyama Soda Co. Ltd., 40 Wadai, Tsukuba, Ibaraki 300-42 (Japan).

esters obtained here have not been reported previously except for perfluoropyruvic acid derivatives. In addition to the synthesis, we wish to report some reactivities of perfluoro(3-methyl-2-oxobutyric) acid esters.

Experimental

Boiling points are uncorrected. Infrared spectra were recorded on a Hitachi Grating Infrared Spectrometer model EPI-G3. The proton NMR spectra were recorded on a Japan Electron NMR Instrument model JNM-4H-100. The fluorine NMR spectra were recorded on a Japan Electron NMR Instrument model FTNMR-FX60. The mass spectra were recorded on a Hitachi Mass Spectrometer model RMU-6MG. The elementary analyses were carried out by the use of a Yanagimoto Yanaco CHN Corder model MT2. Most solvents used were purified by pre-drying over calcium hydride, followed by distillation from lithium aluminium hydride under a reduced pressure. All metal fluorides were completely oven dried before use.

Preparation of octyl fluoroglyoxylate

A mixture of octyl chloroglyoxylate (29.8 g, 0.14 mol) and well-dried potassium fluoride (4.7 g, 0.08 mol) in dry diglyme (32 ml) was refluxed at 130 °C for 3 h. The reaction mixture was then distilled under reduced pressure to give 20.2 g (74%) of octyl fluoroglyoxylate, b.p. 98–103 °C/12 mmHg. IR (neat): 1860 (CF); 1765 (C=O) cm^{-1} . Analysis: Found: C, 58.91; H, 8.34%. Calc. for $\text{C}_{10}\text{H}_{17}\text{O}_3\text{F}$: C, 58.80; H, 8.39%.

Preparation of octyl perfluoro(3-methyl-2-oxobutyrate)

A suspension of well-dried caesium fluoride (1.4 g, 9.2 mmol) in tetraglyme (25 ml) and octyl fluoroglyoxylate (7.8 g, 38 mmol) was put into a glass tube vessel equipped with a mechanical stirrer. Perfluoropropene (18 ml) was added to the vessel at -70 °C. After 12 h stirring under autogenous pressure at room temperature, the upper layer of the reaction mixture was separated and subjected to distillation to give 8.6 g (63%) of octyl perfluoro(3-methyl-2-butyrate), b.p. 67–69 °C/2 mmHg. MS(20 eV) m/z : 197 ($\text{C}_3\text{F}_7\text{CO}^+$, 6); 169 (C_3F_7 , 10); 111 (10); 83 (21); 71 (88); 57 (100); 43 (88); 29 (79). IR (neat): 2950; 2910; 2840; 1790 (C=O); 1770 (C=O); 1280; 1240 (CF) cm^{-1} . ^{19}F NMR (ext.ref. CFCl_3): δ -74.1 (d, $J=7.4$ Hz, 3F, CF_3); -186.0 (m, $J=7.4$ Hz, 1F, CF) ppm. ^{13}C NMR (60 MHz, CDCl_3 , ext.ref. TMS): δ 180.7 (d, $J=33.1$ Hz, C=O); 159.0 (C=OO) ppm. Analysis: Found: C, 43.95; H, 5.09; F, 37.63%. Calc. for $\text{C}_{13}\text{H}_{17}\text{F}_7\text{O}_3$: C, 44.07; H, 4.84; F, 37.57%.

Preparation of nonyl perfluoroisobutyrate

A suspension of well-dried caesium fluoride (2.2 g, 14 mmol) with 20 ml tetraglyme and nonyl fluoroformate (6.6 g, 35 mmol) was put into a glass tube vessel equipped with a mechanical stirrer. Perfluoropropene (20 ml) was added to the vessel at -70 °C. The whole was then warmed gradually

to room temperature, and stirred for 6 h under autogenous pressure. The upper layer of the reaction mixture was separated and subjected to distillation to give 6.2 g (53%) of nonyl perfluoroisobutyrate, b.p. 66–67 °C/1 mmHg. MS(20 eV)*m/z*: 197 (C₃F₇CO⁺, 6); 169 (C₃F₇⁺, 8); 126 (18); 97 (62); 83 (73); 69 (90); 55 (97); 43 (100); 29 (46). IR (neat): 2950; 2910; 2840; 1790; 1770 (C=O); 1280; 1240 (CF) cm⁻¹. ¹⁹F NMR (ext.ref CFCl₃): δ -75.1(d, *J*=7.4 Hz, 3F, CF₃); -181.0 (m, *J*=7.4 Hz, 1F, CF) ppm. ¹³C NMR (60 MHz, CDCl₃, ext.ref. TMS): δ 158.2 (d, *J*=33.1 Hz) ppm. Analysis: Found: C, 45.88, H, 5.63; F, 39.08%. Calc. for C₁₃H₁₉F₇O₂: C, 44.15; H, 5.15; F, 39.98%.

Decarbonylation reaction of 2-chloroethyl perfluoro(3-methyl-2-oxobutyrate)

After stirring well-dried caesium fluoride (1.0 g, 6.6 mmol) and tetraglyme (7 ml) at room temperature, 2-chloroethyl perfluoro(3-methyl-2-oxobutyrate) (4.8 g, 16 mmol) was added and the mixture was then heated for 3 h under stirring in an oil bath kept at 100–120 °C. After the disappearance of 2-chloroethyl perfluoro(3-methyl-2-oxobutyrate) confirmed by GC (silicon SE-30), 2.1 g (50%) of 2-chloroethyl perfluoro(3-methyl-2-oxobutyrate), b.p. 51–52 °C/20 mmHg was isolated by fractional distillation. MS(20 eV)*m/z*: 241 (M⁺-Cl, 0.1); 227 (M⁺-CH₂Cl, 15); 197 (C₃F₇CO⁺, 64); 167 (C₃F₇⁺, 32); 119 (C₂F₅⁺, 2); 65 (44); 63 (CH₂CH₂Cl⁺, 100). IR (neat): 2970; 1790 (C=O); 1770 (sh); 1280 (CF) cm⁻¹. ¹⁹F NMR (neat, ext. CFCl₃): δ -75.4(d, *J*=7.6 Hz, 3F, CF₃); -181.2 (m, *J*=7.6 Hz, 1F, CF) ppm. ¹³C NMR (60 MHz, CDCl₃, ext. TMS): δ 157.7 (d, *J*=33.1 Hz, C=O) ppm. Analysis: Found: C, 26.06; H, 1.46; Cl, 12.82; F, 48.09%. Calc. for C₆H₄O₂ClF₇: C, 25.96; H, 1.41; Cl, 12.85; F, 51.01%.

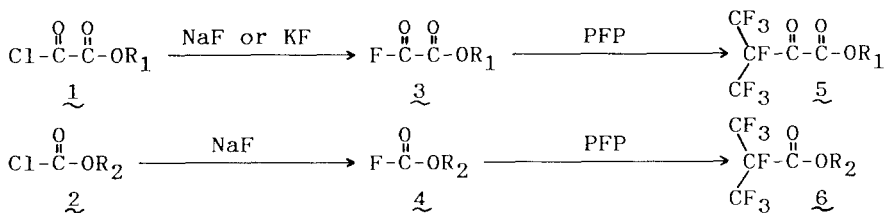
Reaction of ethyl perfluoro(3-methyl-2-oxobutyrate) with o-phenylenediamine

Ethyl perfluoro(3-methyl-2-oxobutyrate) (1.4 g, 5.2 mmol) was added to a solution of *o*-phenylenediamine (0.6 g, 5.5 mmol) in acetonitrile (10 ml) at 0 °C. After 30 min stirring at room temperature, the separated crystals were collected by filtration to give 0.65 g (80%) of 2,3-quinoxalinediol, which was identified by means of its spectroscopic data in comparison with those of an authentic sample.

Results and discussion

The synthetic pathways is shown in Scheme 1.

Chloroglyoxylic acid esters (**1**) were prepared according to the method of Rhoads and Michel [7]. The fluoroglyoxylic acid esters (**3**) and the fluoroformic acid esters (**4**) obtained are listed in Table 1. The reaction was mainly carried out by the method of Tullock and Coffman (method A) [8]. When the reaction did not proceed or resulted in low yields using method



Scheme 1.

TABLE 1

Preparation of FCO-COOR₁ (3) and FCOOR₂ (4)

Substituent	Method ^a	B.p. (°C)	Yield (%)
R ₁ = C ₂ H ₅	A	107-109	81
n-C ₈ H ₁₇	B	98-100/12 mmHg	73
c-C ₆ H ₁₁	B	61-62/5 mmHg	84
CH ₂ CH=CH ₂	A	120-123	63
C ₂ H ₄ OC ₂ H ₅	A	54-56/6 mmHg	57
CH ₂ CH ₂ Cl	A	58-62/5 mmHg	62
CH ₂ CH ₂ Ph	B	88/1 mmHg	61
Ph	C	58/1 mmHg	82
R ₂ = CH ₃	A	35-37	12
C ₂ H ₅	A	53-58	59
CH ₂ CH=CH ₂	A	75-76	48
n-C ₉ H ₁₉	A	66-67/1 mmHg	56
Ph	A	38-40/9 mmHg	27

^aA: NaF⁻-sulfolane; B: KF-diglyme; C: KF in a glass tube.

A, these compounds were obtained by heating with potassium fluoride in diglyme (method B). In the case of phenyl fluoroglyoxylate, the starting material was recovered almost quantitatively using both methods. The target fluoride was obtained in high yield by heating the neat chloride with potassium fluoride in a glass tube (method C). The fluoroglyoxylic acid esters (3) and fluoroformic acid esters (4) obtained were purified by distillation. The perfluoro(3-methyl-2-oxobutyric) acid esters thus prepared are listed in Table 2. They were identified by IR, MS, ¹⁹F NMR and ¹³C NMR spectroscopies. ¹³C NMR spectroscopy was an especially effective method for confirming the α-keto structure of these compounds. Ethyl perfluoro(3-methyl-2-oxobutyrate) showed two types of carbonyl signals at 158.5 ppm and 180.3 ppm, respectively. The latter signal appeared as a doublet, caused by the adjacent single fluorine atom and indicating the existence of a carbonyl carbon at the α position. The preparation of perfluoroisobutyric acid esters using the fluoroformic acid esters (4) and PFP is summarized in Table 3. Fluoroformic acid esters were allowed to react with PFP in the presence of caesium fluoride in a similar manner as with the fluoroglyoxylic acid esters. In this case there was a tendency towards a low reaction rate, so that the formation of PFP

TABLE 2

Preparation of $(CF_3)_2CFCOOR_1$ (5)

R_1	Yield (%)	B.p. (°C)	^{19}F NMR (δ ppm) ^a		
			IR (cm^{-1}) C=O	CF_3	CF
C_2H_5	63	116–117	1770(sh), 1760	–74.8(d)	–186.6(m)
n- C_8H_{17}	63	67–69/2 mmHg	1765(sh), 1775	–74.1(d)	–186.0(m)
c- C_6H_{11}	79	47–49/2 mmHg	1770(sh), 1755	–73.8(d)	–185.9(m)
$CH_2CH=CH_2$	52	131–132	1775(sh), 1760	–75.5(d)	–188.5(m)
$C_2H_4OC_2H_5$	75	42–43/3 mmHg	1770(sh), 1755	–74.5(d)	–186.3(m)
CH_2CH_2Cl	55	35–37/4 mmHg	1775(sh), 1755	–74.2(d)	–186.0(m)
CH_2CH_2Ph	54	87–89/5 mmHg	1775(sh), 1760	–72.8(d)	–185.3(m)

d: doublet; m: multiplet.

^aChemical shifts are given in δ ppm upfield from $CFCl_3$ as an external reference.

TABLE 3

Preparation of $(CF_3)_2CFCOOR_2$ (6)

R_2	Yield (%) ^a	B.p. (°C)	^{19}F NMR (δ ppm) ^b		
			IR (cm^{-1}) C=O	CF_3	CF
CH_3	51	35–37	1795, 1780	–76.4(d)	–182.0(m)
C_2H_5	63	53–58	1790, 1780	–76.2(d)	–181.9(m)
$CH_2CH=CH_2$	73	75–76	1790, 1780	–75.9(d)	–181.5(m)
n- C_9H_{19}	53	66–67/1 mmHg	1790, 1770	–75.1(d)	–181.0(m)
Ph	43	38–40/9 mmHg	1805, 1790	–75.3(d)	–180.1(m)

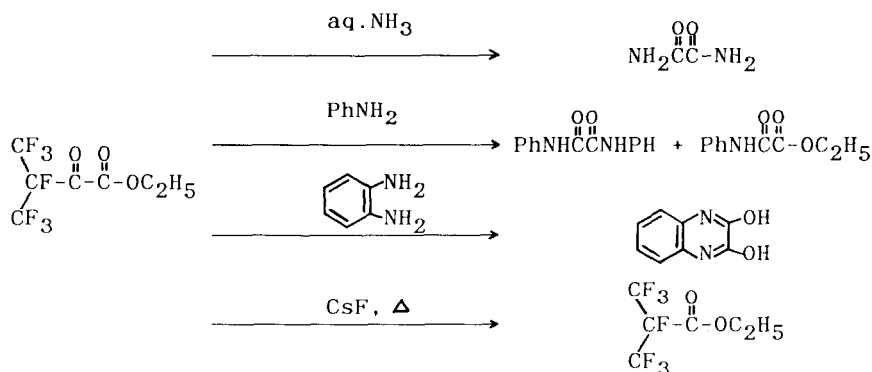
d: doublet; m: multiplet.

^aCalculated by gas chromatography.^bChemical shifts are given in δ ppm upfield from $CFCl_3$ as an external reference.

oligomers was also observed. The perfluoroisobutyric acid esters obtained here were purified by distillation. In both the preparation of the perfluoro(3-methyl-2-oxobutyric) acid esters (5) and the perfluoroisobutyric acid esters (6), the reaction also proceeded when potassium fluoride was used in place of caesium fluoride. However there was a marked tendency towards decreasing reaction rates and/or the necessity for heating in some cases when potassium fluoride was used.

Perfluoro(3-methyl-2-oxobutyric) acid esters (5) are new compounds and have some interesting reactivities. They are relatively stable in acids; for example, they are stable on heating in sulfuric acid. However they are prone to react with nucleophiles such as amines giving oxamide derivatives. The reactions of ethyl perfluoro(3-methyl-2-oxobutyrate) with some amines are summarized in Scheme 2.

When ethyl perfluoro(3-methyl-2-oxobutyrate) was reacted with aniline in diethyl ether at room temperature, the oxanilide and ethyl oxanilate were



Scheme 2.

TABLE 4

Preparation of $(\text{CF}_3)_2\text{CFCOOR}_1$ by decarbonylation of 5

R_1	Yield (%)	B.p. ($^{\circ}\text{C}$)	^{19}F NMR (δ ppm) ^a	
			IR (cm^{-1}) C=O	CF ₃ CF
n-C ₆ H ₁₇	53	60/11 mmHg	1790, 1775	-75.2(d) -180.8(m)
n-C ₆ H ₁₁	33	43-44/5 mmHg	1785, 1770	-75.5(d) -181.0(m)
C ₂ H ₄ OC ₂ H ₅	72	37/65 mmHg	1785, 1770sh	-75.4(d) -181.2(m)
CH ₂ CH ₂ Cl	50	51-52/20 mmHg	1790, 1770sh	-75.4(d) -181.2(m)

d: doublet; m: multiplet.

^aChemical shifts are given in δ ppm upfield from CFCl_3 as an external reference.

obtained in 25% and 45% yield, respectively. It should be noted that the perfluoroisopropyl moiety appears to be released more readily than the ethoxy group to form 1,1,1,2,3,3,3-heptafluoropropane. The formation of the latter was confirmed by trapping the effluent gas during the reaction and its subsequent identification by mass spectroscopy. Similarly, on reacting ethyl perfluoro(3-methyl-2-oxobutanoate) with *o*-phenylenediamine in acetonitrile at 0 $^{\circ}\text{C}$, 2,3-quinoxalinediol was obtained in 80% yield. Although Knunyants *et al.* [9] have reported the preparation of perfluoro-2-oxoalkanamide by the reaction of perfluoroacyl chloride with *N,N*-dimethylformamide, we failed to obtain perfluoro(3-methyl-2-oxobutan)amide derivatives. The reactivity of ethyl perfluoro(3-methyl-2-oxobutanoate) with various amines seems to be quite different from that of the perfluoroacyl chloride.

Perfluoro(3-methyl-2-oxobutanoic) acid esters are particularly interesting, for they undergo a decarbonylation reaction upon heating with caesium fluoride in tetraglyme to yield the perfluoroisobutyric acid esters. The corresponding data are listed in Table 4.

There have been some reports that α -keto esters cause decarbonylation upon heating or in the presence of glass powder as a catalyst [10, 11]. The reaction described here is a unique example of decarbonylation using caesium

fluoride as a catalyst, and has already been reported briefly [12, 13]. The decarbonylation reaction proceeded readily in high yield over the temperature range 100–180 °C. Above the latter temperature the esters tended to decompose and the yield of decarbonylated product decreased. The effect of the catalyst and the solvent has been investigated. Of the various possibilities, caesium fluoride in tetraglyme appears the most appropriate for the decarbonylation reaction. Recently, Kurykin and German [14] have reported that a similar reaction also occurs with certain perfluorinated α -diketones.

This report highlights the novel synthesis of perfluoroisobutyric acid esters. These are new compounds with many interesting reactivities. For example, the perfluoro(3-methyl-2-oxobutyric) acid esters are stable in the presence of moisture and can be used as easy-to-handle substitutes for oxalyl dihalides. Similar reactions also proceed by the use of perfluoro olefins other than PFP [15]. We intend to develop the method further for the preparation of perfluorocarboxylic acid derivatives.

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