

Received: December 4, 1981

NEW SYNTHESIS AND REACTIONS OF PERFLUORO-TERT-BUTYL CHLOROFORMATE

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SUMMARY

A new synthesis of perfluoro-tert-butyl chloroformate (perfluoro-tert-butoxycarbonyl chloride) is based on the reaction of potassium perfluoro-tert-butoxide with one equivalent of phosgene in xylene or mesitylene. Perfluoro-tert-butyl chloroformate reacts readily with hydroxy, sulfhydryl and amino compounds to give the corresponding perfluoro-tert-butyl alkyl carbonates, thiolcarbonates or carbamates, respectively. Dialkyl carbonates, diaryl carbonates, and symmetrically substituted ureas are formed as by-products and, with some compounds, as exclusive products. Primary amines form isocyanates.

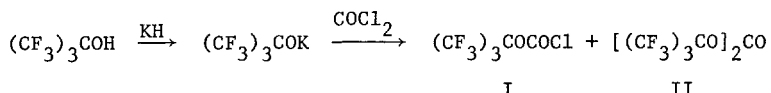
INTRODUCTION

Perfluoro-tert-butyl group has been known to be one of the most electronegative groups as evidenced by its effect on the acidity of 2-hydroperfluoroisobutane [1] and perfluoro-tert-butyl alcohol [2,3]. It was of interest to find out how this group would behave under conditions of nucleophilic displacement, whether it would be a suitable protecting group, and whether it could be utilized as a probe in ^{19}F NMR analysis. For this purpose, perfluoro-tert-butyl alcohol was converted to perfluoro-tert-butyl chloroformate (perfluoro-tert-butoxycarbonyl chloride) which was used for incorporating perfluoro-tert-butoxycarbonyl group into organic compounds.

RESULTS AND DISCUSSION

Perfluoro-tert-butyl chloroformate was first synthesized from carbon monoxide and perfluoro-tert-butyl hypochlorite which in turn was prepared from perfluoro-tert-butyl alcohol and chlorine monofluoride [4]. This synthesis requires autoclaves for the reaction of carbon monoxide, and involves work with extremely corrosive chlorine monofluoride.

Perfluoro-tert-butyl chloroformate can be obtained more conveniently in conventional glass equipment from phosgene and potassium perfluoro-tert-butoxide according to the equation:

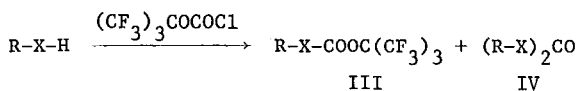


Perfluoro-tert-butyl alcohol is first converted to its potassium salt by potassium hydride according to the literature [5]. The salt is then treated with phosgene in toluene, xylene or mesitylene to give perfluoro-tert-butyl chloroformate (I) and bis(perfluoro-tert-butyl) carbonate (II). Since perfluoro-tert-butyl chloroformate is a very reactive acylating agent formation of bis(perfluoro-tert-butyl) carbonate can hardly be avoided even if a large excess of phosgene is used. (Bis(perfluoro-tert-butyl) carbonate was prepared earlier from potassium perfluoro-tert-butoxide and carbonyl fluoride [6] or from sodium perfluoro-tert-butoxide and phosgene [7]).

Perfluoro-tert-butyl chloroformate can be isolated by fractional distillation of the reaction mixture. It boils at 65-67° at atmospheric pressure. However, its separation from bis(perfluoro-tert-butyl) carbonate (b.p. 108-111°) is difficult because of a very high vapor pressure of the latter. (Crystals of bis(perfluoro-tert-butyl) carbonate vaporize at room temperature in a matter of hours).

Perfluoro-tert-butyl chloroformate was also prepared from perfluoro-tert-butyl alcohol and phosgene in the presence of triethylamine. However, the yield was very low (20%).

Perfluoro-tert-butyl chloroformate reacts readily with hydroxy, sulfhydryl and amino compounds to form the corresponding perfluoro-tert-butyl alkyl or aryl carbonates, S-thiolcarbonates, or carbamates (III). In addition, dialkyl or diaryl carbonates and symmetrical ureas are formed (IV):



R=alkyl or aryl, X=O, S, NH or NR

The symmetrical dialkyl or diaryl carbonates or ureas result evidently from the reaction of the primarily formed perfluoro-*tert*-butyl derivatives with the yet unreacted alcohols, phenols, thiols or amines. In some cases the symmetrical compounds are the main and even exclusive products. This means that in the reactions of perfluoro-*tert*-butyl chloroformate with nucleophiles not only chlorine but perfluoro-*tert*-butoxy group as well is being displaced, the latter one more sluggishly. This assumption was confirmed when bis(perfluoro-*tert*-butyl) carbonate reacted with hydroxy or amino compounds to give the same sym. carbonates or ureas (IV) as perfluoro-*tert*-butyl chloroformate.

From nine compounds reacting with perfluoro-*tert*-butyl chloroformate 1-octanol, cyclohexanol, benzyl alcohol, *p*-thiocresol, diethylamine, and dibenzylamine gave, respectively, perfluoro-*tert*-butyl octyl carbonate (IIIa), perfluoro-*tert*-butyl cyclohexyl carbonate (IIIb), perfluoro-*tert*-butyl benzyl carbonate (IIIc), perfluoro-*tert*-butyl *S-p*-cresyl thiol-carbonate (IIId), perfluoro-*tert*-butyl *N,N*-diethyl carbamate (IIIe), and perfluoro-*tert*-butyl *N,N*-dibenzyl carbamate (IIIf). Phenol, aniline and benzylamine gave little, if any, perfluoro-*tert*-butoxycarbonyl derivatives but instead diphenyl carbonate (IVa), *N,N'*-diphenylurea (IVb) and *N,N'*-dibenzylurea (IVc), respectively. Phenyl isocyanate (Va) and benzyl isocyanate (Vb) were isolated as intermediates.

The reaction of perfluoro-*tert*-butyl chloroformate with hydroxy, sulfhydryl and amino compounds was carried out in ether-carbon tetrachloride solutions in the presence of a tertiary amine such as pyridine, or better still, triethylamine. The reaction was instantaneous even at a temperature below 10° as evidenced by immediate formation of a precipitate of amine hydrochlorides. The products were isolated by suction filtration and evaporation of the filtrate in vacuo.

Since perfluoro-*tert*-butoxy residue is a very good leaving group (comparable to chlorine) it was expected that it will be possible to remove it from the perfluoro-*tert*-butyloxycarbonyl derivatives. However, heating of *N,N*-dibenzyl perfluoro-*tert*-butyl carbamate with trifluoroacetic acid, with trifluoroethanol or with aqueous ethanol was ineffective. Dilute hydrochloric and acetic acid were necessary for the hydrolysis.

Perfluoro-tert-butyl group containing nine equivalent fluorine atoms gives a very strong singlet in ^{19}F NMR. Perfluoro-tert-butyl alcohol has the chemical shift of +75 ppm, perfluoro-tert-butyloxycarbonyl derivatives at +70 ppm (upfield from fluorotrichloromethane F11). Signals of perfluoro-tert-butyl chloroformate I and bis(perfluoro-tert-butyl) carbonate differ only by 0.2 ppm. Perfluoro-tert-butoxycarbonyl derivatives of hydroxy, sulfhydryl and amino compounds give all signals in the vicinity of +70 ppm with a very little spread, if any, of the chemical shift. It is, therefore, not possible to use perfluoro-tert-butoxycarbonylation as a means of identifying hydroxy, sulfhydryl and amino compounds in their mixtures by ^{19}F NMR.

On the other hand, it might be possible to use the ^{19}F NMR for quantitative determination of primary amines in the presence of secondary amines. Perfluoro-tert-butyl chloroformate converts secondary amines to perfluoro-tert-butyl N,N-disubstituted carbamates having chemical shift +70 ppm. Primary amines form isocyanates and release one equivalent of perfluoro-tert-butyl alcohol whose signal (+75) differs both from that of the products of secondary amines and from that of unreacted perfluoro-tert-butyl chloroformate (+70 ppm).

EXPERIMENTAL

Commercial chemicals were used throughout the work. Perfluoro-tert-butyl alcohol was the product of PCR and was chromatographically pure. Boiling points and melting points (determined on Thomas Hoover Unimelt apparatus) are uncorrected. Gas-liquid chromatography was carried out on Varian Aerograph 920 using silicone elastomer SE 30, thermal conductivity detector, and flow rates of helium 60 ml/min. IR spectra were measured on Unicam SP 1025 Infrared Spectrophotometer, ^1H and ^{19}F NMR on Varian EM 390 spectrophotometer at 90 and 84.6 MHz, respectively, using carbon tetrachloride as a solvent and TMS, F11 and F112 as internal standards. Fluorine chemical shifts upfield from fluorotrichloromethane are positive.

Perfluoro-tert-butyl Chloroformate I

(a) From Perfluoro-tert-butyl Alcohol

Triethylamine (1.01 g, 0.01 mol) was added to a solution of 2.36 g (0.01 mol) of perfluoro-tert-butyl alcohol in 5 ml of mesitylene. The mixture warmed up to 40°. After cooling it was added dropwise over a period of 25 minutes to 11.5 g of a 13% solution of phosgene in mesitylene (0.015

mol) placed in a flask immersed in an ice bath and kept under argon. After 6 hours at room temperature the white precipitate of triethylamine hydrochloride was removed by suction filtration, and the filtrate was distilled to give 0.82 g of a fraction boiling at 66-70° and containing 76% of I and 24% of unreacted perfluoro-tert-butyl alcohol as determined by ^{19}F NMR. The yield of I was 20%.

(b) From Potassium Perfluoro-tert-butoxide

Potassium perfluoro-tert-butoxide was prepared according to the literature [5] by adding, under argon, 4.31 g (0.011 mol) of potassium hydride to a stirred solution of 9.45 g (0.04 mol) of perfluoro-tert-butyl alcohol in 83 ml of dry ethyl ether, by filtering off the unreacted potassium hydride, and by evaporating the filtrate to dryness at 45° at 25 mm and finally at 0.2 mm. Yield of the dry salt was 9.99 g (90.5%).

The powdered potassium perfluoro-tert-butoxide (9.99 g, 0.036 mol) was added under argon portionwise over a period of 75 minutes to 42 g of a stirred and ice-cooled solution containing 5.45 g (0.055 mol, 52% molar excess) of phosgene in mesitylene. The mixture was stirred overnight at room temperature and then distilled at 16 mm up to a temperature of 60° into a dry-ice cooled receiver connected to a dry ice trap.

Redistillation of the contents of the dry ice trap (1.59 g) gave 0.89 g of perfluoro-tert-butyl chloroformate (I), redistillation of the contents of the receiver (9.23 g) yielded 4.75 g of I (89% pure based on NMR) boiling at 60-70° (mainly 65-67°), and 1.55 g of a less pure product (50%) distilling at 70-100°. The total yield of pure I was 5.88 g (54.5% based on potassium perfluoro-tert-butoxide).

When p-xylene was used as the solvent instead of mesitylene separation of pure perfluoro-tert-butyl chloroformate was incomplete. In addition to an almost pure product distilling at 54-70°, a higher boiling fraction (70-83°) was collected which contained 30% of xylene as found by gas liquid chromatography. However, it could be used for the preparation of perfluoro-tert-butoxycarbonyl derivatives.

Bis(perfluoro-tert-butyl) Carbonate II

When only a 30% molar excess of phosgene in mesitylene over potassium perfluoro-tert-butoxide was used in the above-mentioned procedure, the reaction gave 39% yield of perfluoro-tert-butyl chloroformate and 38% yield

of crude (22.4% yield of pure) bis(perfluoro-tert-butyl) carbonate, distilling at 108-110° (710 mm), m.p. 42-43.5°.

Lit. [6] m.p. 43.0°, b.p. 119.7°; [7] m.p. 40-42°, b.p. 84-87°.

Preparation of Perfluoro-tert-butoxycarbonyl Derivatives (General Procedure)

A hydroxy, sulfhydryl or amino compound (0.001 mol) was placed in a 25 ml Erlenmeyer flask, was diluted with 3 ml of dry ethyl ether, 1 ml of 1 M solution of triethylamine in carbon tetrachloride was pipetted in, and the flask was immersed in an ice bath.

While the contents of the flask were stirred 1 ml of 1 M solution of I in carbon tetrachloride was added dropwise over a period of 3-4 minutes. After the first drops had been added a white precipitate was formed. It was filtered with suction, usually after allowing the mixture to stand at room temperature for 15 minutes. The filtrate was evaporated at 30-40° at 10-25 mm, and the residue was recrystallized or distilled under reduced pressure.

The solution of triethylamine in carbon tetrachloride must be kept in a freezer since at room temperature a reaction with the solvent produces a crystalline precipitate after a few days. Instead of triethylamine, a solution of pyridine in carbon tetrachloride could be used. However, triethylamine is preferable since its hydrochloride is not hygroscopic and is more convenient to handle.

Perfluoro-tert-butoxycarbonyl derivatives were also prepared by treating hydroxy or amino compounds with bis(perfluoro-tert-butyl) carbonate II. This procedure is slower than that using perfluoro-tert-butyl chloroformate and less advantageous since the by-product - perfluoro-tert-butyl alcohol - is difficult to recover.

Analyses, IR and NMR spectra of the compounds prepared are listed in Table I.

Octyl Perfluoro-tert-butyl Carbonate (IIIa) (nc)

1-Octanol and I gave 58.7% yield of IIIa, b.p. 95-97° (10 mm).

Cyclohexyl Perfluoro-tert-butyl Carbonate (IIIb) (nc)

Cyclohexanol and I yielded 40% of IIIb, b.p. 70-78° (12 mm) contaminated with cyclohexanol from which it could be hardly separated.

Benzyl Perfluoro-tert-butyl Carbonate (IIIc) (nc)

Benzyl alcohol and I afforded 70.3% yield of IIIc, b.p. 86-93.5° (13 mm).

When benzyl alcohol and I reacted in ether solution for 24 hours the main product was dibenzyl carbonate, distilling at 94-109° (0.005 mm), m.p. 32-33°.

Lit. [8] b.p. 180-190° (2 mm), m.p. 27-28°.

S-p-Cresyl Perfluoro-tert-butyl Thiocarbonate (IIIId) (nc)

p-Thiocresol and I yielded 90.6% of IIIId, m.p. 43.5-44.5° (hexane). Mixed m.p. with p-thiocresol (m.p. 42-44°) was 36°.

N,N-Diethylamino Perfluoro-tert-butyl Carbamate (IIIe) (nc)

Diethylamine and I gave 53.8% of IIIe, b.p. 54-57° (11 mm); 60-62° (13 mm).

N,N-Dibenzylamino Perfluoro-tert-butyl Carbamate (IIIIf) (nc)

Dibenzylamine and I afforded 69.7% yield of IIIIf, b.p. 85-90° (0.02 mm), 82-89° (0.005 mm).

Reaction of Perfluoro-tert-butyl Chloroformate with Phenol

Phenol and I reacted according to the general procedure to give 64.5% yield of impure perfluoro-tert-butyl phenyl carbonate IIIIf, (nc), b.p. 71-77.5° (13 mm).

When the two compounds reacted in ether solution for 24 hours diphenyl carbonate was obtained in 70% yield. M.p. 79.5-80.5° (ethanol). Lit. [9] m.p. 79°; [10] m.p. 83°.

Reaction of Perfluoro-tert-butyl Chloroformate with Aniline

Aniline and I reacted according to the general procedure to give 88% yield of phenyl isocyanate (Va), and 12% yield of N,N'-diphenylurea (ν NCO 2265 cm^{-1}), m.p. 241-242° (acetone). Lit [11] m.p. 239.5°.

TABLE I

Analyses and Spectral Data of Perfluoro-tert-butoxycarbonyl Derivatives

Compound	CHN Analyses % (Calcd. %)	IR (cm ⁻¹)	¹ H NMR δ, ppm	¹⁹ F NMR φ, ppm ^a
(CF ₃) ₃ COCOCl I		732, 830, 990, 1011, b) 1062, 1120, 1268, 1288, 1834		+70.0 (s) c)
[(CF ₃) ₃ CO] ₂ CO II		724, 732, 990, 1028, d) 1096, 1120, 1180, 1270, 1289, 1860 (in CCl ₄)		+70.2 (s) e)
C ₈ H ₁₇ OCOOOC(CF ₃) ₃ IIIa	C, 39.92 ; H, 4.31 (39.80) (4.37)	732, 749, 775, 982, 1015, 1060, 1155, 1181, 1260-1280, 1398, 1472, 1810, 2870, 2940	4.21 (t, J=7Hz) 1.73 (t, J=7Hz) 1.30 (m) 0.88 (t, J=6Hz)	+70.2 (s)
c-C ₆ H ₁₁ OCOOOC(CF ₃) ₃ IIIb	C, 37.11 ; H, 2.91 (36.47) (3.06)	733, 756, 776, 895, 910, 921, 982, 1010, 1040, 1120, 1150, 1180, 1270-1290 1459, 1805, 2870, 2955	4.69 (broad m) 1.25-2.02 (m)	+70.2 (s)
C ₆ H ₅ CH ₂ OCOOOC(CF ₃) ₃ IIIc	C, 38.78 ; H, 2.17 (38.93) (1.91)	700, 732, 747, 760, 774, 839, 892, 911, 987, 1000, 1026, 1089, 1157, 1187, 1222, 1280, 1385, 1460, 1502, 1810, 3040, 3070	7.25 (s) 5.15 (s)	+70.2 (s)
p-CH ₃ C ₆ H ₄ SCOOOC(CF ₃) ₃ IIId	C, 37.07 ; H, 1.63 (37.32) (1.83)	730, 820, 985, 1006, 1014, 1035, 1112, 1194, 1260, 1285, 1308, 1499, 1600, 1785 (in CCl ₄)	7.26 (d, J=8Hz) 6.97 (d, J=8Hz) 2.92 (s)	+70.0 (s)

$(C_2H_5)_2NCOOC(CF_3)_3$ IIIe	C, 32.37 ; H, 2.95 ; N, 4.33 (32.25) (3.01) (4.18)	690, 730, 748, 781, 810, 930, 950, 981, 1001, 1032, 1087, 1102, 1140, 1175, 1228, 1250-1290, 1355, 1370, 1390, 1425, 1465, 1480, 1775, 2890, 2950, 2995	2.87 (q, J=7.5Hz) 1.28 (t, J=7.5Hz)	+70.0 (s)
$(C_6H_5CH_2)_2NCOOC(CF_3)_3$ III f	C, 49.74 ; H, 3.00 ; N, 3.09 (49.68) (3.07) (3.05)	704, 730, 755, 778, 825, 835, 961, 980, 1001, 1033, 1087, 1135, 1179, 1255-1290, 1360, 1370, 1425, 1459, 1500, 1590, 1610, 1770, 2900, 3040, 3070	7.25 (s) 4.39 (s)	+69.8 (s)
$C_6H_5OCOOOC(CF_3)_3$	f)	732, 747, 975, 985, 1020, 1130, 1210, 1234, 1275, 1492, 1500, 1822	7.10-7.45 (m)	+70.0 (s)

- a) ^{19}F chemical shifts were measured from F112 (CCl_2FCCl_2F) whose ϕ was found to be +67.7 ppm.
 b) The data match well those in the literature [4].
 c) Lit. [4] +70.0 ppm.
 d) IR spectra differ somewhat from the literature but the strong peaks match [6].
 e) Lit. [6] +70.2 ppm.
 f) This compound was not pure enough for elemental analysis.

Reaction of Perfluoro-tert-butyl Chloroformate with Benzylamine

Benzylamine and I reacted according to the general procedure to yield 91.5% of N,N'-dibenzylurea, m.p. 169-170° (acetone). Lit. [12] m.p. 171° (CHCl₃). When the reaction mixture was worked up immediately after the addition of I had been completed, dibenzyl isocyanate (Vb) (ν NCO 2275 cm⁻¹) was isolated in addition to the dibenzylurea.

Reaction of Bis(perfluoro-tert-butyl) Carbonate with Diethylamine

To 0.08 g (0.0011 mol) of diethylamine was added, at room temperature, 5 ml of a 0.2 M solution of bis(perfluoro-tert-butyl) carbonate II in carbon tetrachloride. The solution was allowed to stand at room temperature for 12 hours. A small amount of an amine hydrochloride (resulting from the reaction of diethylamine with perfluoro-tert-butyl chloroformate present as an impurity) was removed by suction filtration, the filtrate was evaporated at 40° at 10 mm, and the residue was distilled in vacuo to give 0.33 g (89%) of IIIe, identical with the compound prepared from diethylamine and I.

ACKNOWLEDGEMENT

The author would like to thank G. A. Iannaccone for elemental analyses.

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