[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF FLORIDA]

The Preparation of Some Derivatives of Chlorofluoroacetic Acid

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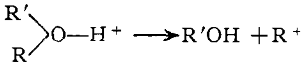
The preparation of di- and trifluoroacetic acids is easily accomplished by the oxidation of olefins containing the —CHF_2 and —CF_3 groups, respectively.[1] Monofluoroacetic acid derivatives are obtained by a reaction of the corresponding chloro- or bromo- compound with thallous fluoride or potassium fluoride.[2] The preparation of mixed fluorohaloacetic acids has received less attention although Swarts prepared some of the bromofluoroacetic acids[3] and chlorodifluoroacetic acid.[4] Recently, methyl chlorofluoroacetate[5] was prepared by the reaction of methanol on the product from the reaction of sulfuryl chloride and fluoroacetic acid. During the course of another investigation, we have found that esters of chlorofluoroacetic acid may be made in good yields by treatment of ethers of the type $CHClFCF_2OR$ with concentrated sulfuric acid. Inasmuch as these ethers may be synthesized by the reaction of the readily obtainable $CF_2{=}CFCl$ with alcohols,[6] this reaction offers a convenient method of preparation of esters of chlorofluoroacetic acid, from which other compounds containing the CHClFCO group may be made by conventional methods.

Discussion

The ease of hydrolysis of ethers such as $CHClFCF_2OC_2H_5$ is surprising in view of the supposed unreactivity of compounds containing the —CF_2— group. Experimentally, the hydrolysis of ethers of this type is best carried out in an ice–water-bath since a considerable amount of heat is evolved once the reaction begins. When the temperature is higher the yield is greatly reduced due no doubt to side reactions since no unreacted starting material was recovered in most of the experiments on the hydrolysis of $CHClFCF_2OC_2H_5$. The hydrolysis velocity decreases with dilution of the acid, possibly because of the lower solubility of the ether. The best yield of ethyl chlorofluoroacetate was obtained in glass apparatus at 10° using two moles of 96% sulfuric acid for each mole of ether. Etching of the glass apparatus was not serious when the experiments were carried out at 10°. Two hydrolyses were conducted in copper equipment but lower yields of chlorofluoro-ester were obtained. Lower yields of ester were also obtained when 85% phosphoric acid was substituted for sulfuric acid.

Hydrolysis of alkyl ethers may proceed, as suggested by Hammett,[7] by initial proton attack on the ether oxygen. The resulting ion then splits into one molecule of alcohol and a carbonium ion which in turn reacts to give another alcohol, according to the scheme

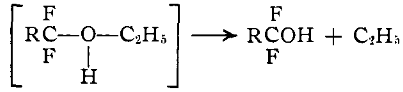


$$\begin{matrix}R' \\ R\end{matrix}\!\!>\!O{-}H^+ \longrightarrow R'OH + R^+$$

$$R^+ + H_2O \longrightarrow ROH + H^+$$

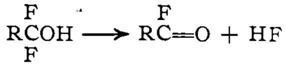
If the hydrolysis of α-difluoro ethers is to be explained in this way, a possible mechanism for the reaction is as follows

$$R = CHFCl{-}$$



$$\left[R\overset{F}{\underset{F}{C}}{-}\underset{\underset{H}{|}}{O}{-}C_2H_5\right] \longrightarrow R\overset{F}{\underset{F}{C}}OH + C_2H_5^+$$

$$C_2H_5^+ + H_2O \longrightarrow C_2H_5OH + H^+$$



$$R\overset{F}{\underset{F}{C}}OH \longrightarrow R\overset{F}{C}{=}O + HF$$

The acid fluoride so formed would react with the alcohol to give the ester.

If the reaction were carried out using a large amount of methanol as a solvent, it seems likely that some methyl chlorofluoroacetate would be produced. An attempt was made to carry out the hydrolysis of 2-chloro-1-ethoxy-1,1,2-trifluoroethane in the presence of 4 moles of methanol but no esters were obtained. However, when such a reaction was run using equimolar quantities of the ethoxy-compound and methanol, only ethyl chlorofluoroacetate was found, thus indicating that no chlorofluoroacetyl fluoride was formed. If such is the case, then the transformation of ether to ester probably takes place without the ethoxy group being released from the carbon to which it is attached.

Experimental

The physical properties of the derivatives of chlorofluoroacetic acid are given in Table I. Properties were measured on fractions of the various compounds corresponding to the boiling points listed in the table.

Esters of Chlorofluoroacetic Acid.—The methyl, ethyl and propyl esters were obtained by the reaction of the corresponding alkoxytrifluorochloroethane with sulfuric acid as illustrated below; yields of 55, 83 and 66%, respectively, were obtained.

One mole (163 g.) of $CHClFCF_2OC_2H_5$ was placed in a one-liter flask equipped with a stirrer, thermometer and dropping funnel and cooled to 0°. Approximately two moles (200 g.) of sulfuric acid (96%) was added over a period of one-half hour with vigorous stirring. When

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(1) McBee, *Ind. Eng. Chem.*, **40**, 1611 (1948).

(2) Bacon, Bradley, Hoegberg, Tarrant and Cassaday, THIS JOURNAL, **70**, 2653 (1948).

(3) Swarts, *Bull. Acad. Roy. Belg.*, 319 (1898); *Chem. Zentr.*, **74**, II, 710 (1903).

(4) Swarts, *Chem. Zentr.*, **77**, I, 1237 (1906); **78**, II, 581 (1907).

(5) Gryszkiewics-Trochimowski, A. Sporzynski and J. Wnuk, *Rec. trav. chim.*, **66**, 424 (1947).

(6) (a) Hanford and Rigby, U. S. Patent 2,409,274; (b) Park, Vail, Lea and Lacher, THIS JOURNAL, **70**, **1553** (1948); (c) Miller, Fager and Griswold, *ibid.*, **70**, 431 (1948).

(7) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1949, p. 300.

TABLE I

PHYSICAL CONSTANTS OF CHLOROFLUOROACETIC ACID AND DERIVATIVES

Compound	B. p., °C.	n^{25}_D	d^{25}_4	Chlorine, % Calcd.	Chlorine, % Found	MR_D[a]	AR_F[b]
$CHClFCOOH$	162	1.4085	1.532	31.52	31.35	18.14	1.40
$CHClFCOCl$	69.5	1.3992	1.468	54.15	54.17[c]	21.57	1.49
$CHClFCONH_2$	72/1 mm.	1.4535	1.510	31.79	31.52	19.97	1.01
$CHClFCN$	66	1.3627	1.267	37.92	37.98	16.40	1.45
$CHClFCOOCH_3$	116	1.3903	1.323	28.02	27.93	22.69	1.22
$CHClFCOOC_2H_5$	128	1.3927	1.225	25.22	24.91	27.38	1.29
$CHClFCOOC_3H_7(n)$	147	1.3994	1.170	22.94	22.85	31.98	1.27
$CHClFCOOC_4H_9(n)$[d]	165-166	1.4067	1.124	21.03	20.82	36.90	1.58

[a] Molecular refraction as calculated from Lorentz-Lorenz equation. [b] Atomic refractivity of fluorine was obtained by subtracting the sum of the values for the individual atoms other than *F* from *MR*. [c] Ionic chlorine: Found 26.85; Calcd. 27.08. [d] Molecular weight: Found 161; Calcd. 168.6.

the addition was complete, the reaction was continued for one and one-half hours at 10°. The contents were then poured onto crushed ice, washed with water and dried with calcium chloride. Ethyl chlorofluoroacetate, (116 g.), boiling at 128-130°, was obtained by distilling the product through a 24" column packed with helices; there was no indication of unreacted ether, which boils at 88°. Butyl chlorofluoroacetate was obtained by transesterification of the methyl ester. About 0.5 mole (62 g.) of $CHClFCOOCH_3$ was refluxed for two hours with one mole (74.8 g.) of *n*-butanol and 3 ml. of 85% phosphoric acid. After removal of methanol and unreacted butanol, 59 g. of butyl chlorofluoroacetate boiling at 165-166° was obtained. This corresponds to a yield of 70%.

Chlorofluoroacetamide.—The amide was obtained in 88% yield by the ammonolysis of ethyl chlorofluoroacetate. One mole (141 g.) of ester was cooled to 0° in a flask equipped with an efficient stirrer, dropping funnel and thermometer. About 200 ml. of concentrated ammonia solution was added over a period of one-half hour. After a short time a vigorous reaction resulted and external cooling was applied to keep the temperature below 10°. When the addition was complete, the water and alcohol were removed under reduced pressure so that the temperature of the mixture did not exceed 60°. Vacuum distillation of the residue gave 98 g. of amide boiling at 72-77° at 1 mm. pressure.

Chlorofluoroacetonitrile.—Chlorofluoroacetamide (0.5 mole) was slowly added to a 200-ml., 3-neck flask containing phosphorus pentoxide (0.25 mole). Distillation of the product gave 35 g. of material boiling at 50-70°. Redistillation gave 30 g. of chlorofluoroacetonitrile boiling at 66°. The crude product was not washed as it reacts rapidly with sodium hydroxide and to some extent with water.

Chlorofluoroacetic Acid.—One mole (140.5 g.) of ethyl chlorofluoroacetate was added to a 10% solution of sodium hydroxide while the temperature was maintained below 15°. The reaction mixture was allowed to warm to room temperature and was stirred thereafter for three hours. The mixture was concentrated to a pasty mass under reduced pressure; toluene was then added and the mixture distilled to remove additional water. About 100 ml. of 85% phosphoric acid was added and the mixture heated gently and stirred. Phosphorus pentoxide (50 g.) was then added and distillation of the chlorofluoroacetic acid begun at atmospheric pressure with a free flame. Frothing becomes troublesome if vigorous stirring is not applied during the distillation. The product was redistilled through a 24" column packed with glass helices. A 50% yield of chlorofluoroacetic acid boiling at 162-164° was obtained.

Sulfuric acid was used in one experiment but the yield of organic acid was low since considerable charring took place during its distillation.

Chlorofluoroacetyl Chloride.—Chlorofluoroacetic acid (0.47 mole, 53 g.) was added over a period of one-half hour to phosphorus pentachloride (0.51 mole, 105 g.) in a flask maintained at 25-30° and containing a reflux condenser cooled by ice water and a stirrer. The reaction was continued at room temperature for an additional half hour after the addition of the acid. The product was distilled twice through a short column packed with glass helices and 50 g. of chlorofluoroacetyl chloride boiling at 69-70° was obtained; this corresponds to an 81% yield.

Hydrolysis of 2-Chloro-1-ethoxy-1,1,2-trifluoroethane in the Presence of Methanol.—One mole (161 g.) of 2-chloro-1-ethoxy-1,1,2-trifluoroethane and one mole (32 g.) of methanol were cooled to 10° in a three-necked flask equipped with a stirrer, thermometer and dropping funnel and 200 g. (2 moles) of sulfuric acid (96%) was added over a period of one-half hour while the temperature was maintained at 5-10°. After the addition, the mixture was stirred an additional two hours. The products were poured onto ice and the organic layer separated, washed and dried. Distillation through a 30 inch column packed with glass helices gave 64 g. of recovered ether (b. p. 88-90°), 5 g. of material boiling between 89 and 127° and 50 g. of the ethyl ester boiling at 127-130°. There was no flat observed at 116-117° where the methyl ester boils. The yield of ethyl ester was 35%.

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Summary

1. A new method of synthesis of esters of chlorofluoroacetic acid is described. It consists of the reaction of 1-alkoxy-2-chloro-1,1,2-trifluoroethane with sulfuric acid to give the corresponding alkyl chlorofluoroacetate.

2. The following new compounds were prepared and characterized: chlorofluoroacetic acid and its amide, nitrile, acid chloride and its ethyl, *n*-propyl and *n*-butyl esters.

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