457. *Organic Fluorine Compounds. Part IX.* The Preparation of Fluoroacetone and* 1 : 3-*Difluoroacetone.*

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Satisfactory procedures for these preparations are described.

NONE of the methods of preparing fluoroacetone [1] lends itself to large-scale preparations, so other methods have been studied. Attempts to fluorinate the ethylene ketals of chloro- or bromo-acetone with potassium fluoride in glycols, acetamide, or nitrobenzene failed, as did reaction of dimethylcadmium with fluoroacetyl chloride (cf. the unreactivity of fluoroacetyl chloride towards Grignard reagents [2]). Oxidation of 1-fluoro-2-methylpropan-2-ol by means of hydrogen peroxide in the presence of ferrous ion [3] gave promising results, but its usefulness was limited by the fact that the preparation of this alcohol by the action of hydrogen fluoride on *iso*butene oxide [4] or by reaction between ethyl fluoroacetate and methylmagnesium bromide gave unsatisfactory yields.

Fluoroacetone is best prepared by chromic acid oxidation of 1-fluoropropan-2-ol, which is obtained more conveniently by fluorination of commercial 1-chloropropan-2-ol with potassium fluoride by Hoffmann's method [5] than from propene oxide and hydrogen fluoride.[4] The overall yield of fluoroacetone is only 16—20%, but as much as 1 mole can be prepared at a time. α-Fluoropropionic acid was isolated as a by-product; this was attributed at first to the presence of as much as 25% of the isomeric 2-chloropropan-1-ol in the chloropropanol, but pure material gave exactly the same result. One must assume that 1-chloropropan-2-ol is converted by potassium fluoride into propene oxide which then adds hydrogen fluoride in the two possible directions. Indeed, the product always contains a certain amount of propene oxide, and Smith [6] has found that this compound also surprisingly adds hydrogen chloride in both directions.

Both 1-fluoropropan-2-ol and fluoroacetone give constant-boiling mixtures with water.

For the preparation of 1 : 3-difluoroacetone [7] 1 : 3-difluoropropan-2-ol [5] appeared to be the starting material of choice. The reaction of 1 : 3-dichloropropan-2-ol with potassium fluoride gave low yields. However, refluxing epichlorohydrin with potassium hydrogen fluoride in diethylene glycol gave 39% of 1 : 3-difluoropropan-2-ol and 17·5% of 1-chloro-3-fluoropropan-2-ol. In our experience, epichlorohydrin is unaffected by

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* Part VIII, *Chem. and Ind.*, 1957, 394.

[1] Ray, Goswami, and Ray, *J. Indian Chem. Soc.*, 1935, **12**, 93; Fukuhara and Bigelow, *J. Amer. Chem. Soc.*, 1941, **63**, 788; E. D. Bergmann and Ikan, *Chem. and Ind.*, 1957, 394; Knuyants, Kisel, and Bykhovskaya, *Isvest. Akad. Nauk. S.S.S.R., Otdel. Khim. Nauk*, 1956, 377; Fraser, Millington, and Pattison, *J. Amer. Chem. Soc.*, 1957, **79**, 1959; Olah and Kuhn, *Chem. Ber.*, 1956, **89**, 864.

[2] Howell, Scott, and Pattison, *J. Org. Chem.*, 1957, **22**, 255.

[3] Merz and Waters, *J.*, 1949, 15.

[4] Knuyants, Kil'disheva, and Petrov, *Zhur. obshchei Khim.*, 1949, **19**, 95, 101.

[5] Hoffmann, *J. Amer. Chem. Soc.*, 1948, **70**, 2596.

[6] Smith, *Z. physik. Chem.*, 1918, **93**, 59.

[7] McBee, Pierce, Kilbourne, and Wilson, *J. Amer. Chem. Soc.*, 1953, **75**, 3152.

potassium fluoride in diethylene glycol; Olah and Pavlath[8] claim the formation of epifluorohydrin by this method, but Pattison and Norman[9] had to use prolonged heating of epichlorohydrin with potassium fluoride in an autoclave in order to bring about the halogen exchange. We assume, therefore, that the first step in the reaction between epichlorohydrin and potassium hydrogen fluoride is the opening of the epoxide ring by hydrogen fluoride to yield the chlorofluoropropanol which in turn, gives rise to 1 : 3-difluoropropan-2-ol. Dehydrohalogenation of 1-chloro-3-fluoropropan-2-ol yields only epifluorohydrin.

Oxidation of the halogeno-alcohols with chromic acid yields 1 : 3-difluoroacetone and 1-chloro-3-fluoroacetone. Both ketones failed to give dinitrophenylhydrazones and their semicarbazones proved unstable. Analogous observations have been made for 1 : 3-dichloroacetone.[10] Difluoroacetone, like the monofluoro-compound, gives with water a constant-boiling mixture.

After this study had been completed, Kitano and Fukui[11] claimed that fluoroacetone is formed in 66% yield from chloroacetone and potassium fluoride in ethylene glycol and that 1 : 3-difluoropropan-2-ol is obtained from 1 : 3-dichloropropan-2-ol and potassium fluoride. As the original Japanese paper was not available and, therefore, the exact operating conditions are not known to us, we cannot account for the fact that we were unable to carry out these reactions.

EXPERIMENTAL

1-*Fluoro*-2-*methylpropan*-2-*ol*.—To a solution of methylmagnesium bromide [from magnesium (24 g.), methyl bromide (110 g.), and ether (500 c.c.)], ethyl fluoroacetate (53 g.) in ether (100 c.c.) was added with stirring during 90 min. at 0—5°. The mixture was decomposed with ice and hydrochloric acid, and the ethereal solution separated, washed with dilute sodium hydrogen carbonate solution, dried (Na_2SO_4), and fractionated. The fraction (19 g.) boiling from 85° to 105° was redistilled; it had b. p. 96—98°, n_D^{28} 1·3895 (15 g., 32%) (lit.,[4] b. p. 58°/82 mm., n_D^{20} 1·3913) (Found: C, 52·3; H, 9·9. Calc. for C_4H_9OF: C, 52·2; H, 9·8%).

Fluorination of 1-*Chloropropan*-2-*ol*.—The technical chlorohydrin (336 g.) (Eastman), containing 25% of 2-chloropropan-1-ol, was added dropwise to a stirred mixture of potassium fluoride (310 g.), ethylene glycol (280 g.), and diethylene glycol (80 g.), at 170—180°. The fluorinated material was allowed to distil through a downward condenser, the temperature at the still head being maintained at 100—110° by controlling the rate of addition of the chlorohydrin. The crude distillate (165 g.), on redistillation in an efficient column, gave the following fractions: (*a*) Propylene oxide (23 g.), b. p. 34—40°; (*b*) 1-fluoropropan-2-ol (128 g., 46%), b. p. 95—110°. Fraction (*b*) was redistilled, to give the fluorohydrin (103 g., 37%), b. p. 103—105°, n_D^{28} 1·3718 (lit.,[4] b. p. 107—108°, n_D^{20} 1·3822) (Found: C, 44·7; H, 9·2. Calc. for C_3H_7OF: C, 44·9; H, 9·1%).

When the chlorohydrin, b. p. 124—128°, prepared from propylene oxide and hydrochloric acid, or pure 1-chloropropan-2-ol, prepared from allyl chloride and sulphuric acid,[6] was used in this preparation, very similar results were obtained.

Fluoroacetone.—To a stirred mixture of crude fluorohydrin, b. p. 95—110° (144 g.), sodium dichromate dihydrate (340 g.), and water (180 c.c.), a mixture of sulphuric acid (260 c.c.) and water (144 c.c.) was added during 3—4 hr., the temperature being kept at 20—25°. The mixture was diluted with water (100 c.c.) and distilled, finally for a few minutes after the temperature at the still head had reached 100°. The fluoroacetone in the distillate was salted out with sodium chloride, separated, dried ($CaCl_2$), and redistilled. It (60 g., 43%) had b. p 78—79°, n_D^{28} 1·3627 (lit.,[1] b. p. 72·5°, 78°, 77—79°, n_D^{20} 1·3693), $\nu_{max.}$ (liquid) 1721 cm. (C=O). The dinitrophenylhydrazone had m. p. 134—135° (from ethanol) (lit., 118—119°,[1] 132°[11]) (Found: C, 41·9; H, 3·7. Calc. for $C_9H_9O_4N_4F$: C, 42·2; H, 3·5%).

Extraction of the oxidation mixture with ether, drying of the ethereal solution (Na_2SO_4),

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[8] Olah and Pavlath, *Acta Chim. Hung.*, 1953, **3**, 431.

[9] Pattison and Norman, *J. Amer. Chem. Soc.*, 1957, **79**, 2311.

[10] von Romburgh, *Verslag Akad. Wetenschapp. Amsterdam*, 1922, **31**, 655.

[11] Kitano and Fukui, *Kogyo Kagashu Zasshi*, 1956, **59**, 395; *Chem. Abs.*, 1957, **51**, 11,282.

removal of the solvent, and distillation of the residue under reduced pressure, gave α-fluoropropionic acid (9 g.), b. p. 82—83°/30 mm., n_D^{28} 1·3810 (lit.,[12] b. p. 60°/5—8 mm.) (Found: C, 38·5; H, 5·2. Calc. for $C_3H_5O_2F$: C, 38·2; H, 5·4%).

1 : 3-*Difluoropropan-2-ol.*—1 : 3-Dichloropropan-2-ol (203 g.) was added dropwise to a stirred mixture of potassium fluoride (270 g.), ethylene glycol (250 g.), and diethylene glycol (80 g.) at 190—200°, as described for the chlorohydrin. The product was distilled at 130—140°. Redistillation gave the following fractions after a small fore-run: (*a*) 1 : 3-difluoropropan-2-ol (10 g.), b. p. 50—60°/34 mm., and, upon redistillation, 54—55°/34 mm. (6·5 g., 4·3%), n_D^{28} 1·3745 (lit.,[4] b. p. 59°/40 mm., n_D^{20} 1·380) (Found: C, 37·3; H, 6·2. Calc. for $C_3H_6OF_2$: C, 37·2; H, 6·2%); (*b*) 1-chloro-3-fluoropropan-2-ol, b. p. 64—65°/34 mm. (6 g., 4%), n_D^{28} 1·4141 (lit.,[4] b. p. 153—156°, n_D^{20} 1·4360) (Found: C, 32·1; H, 5·5. Calc. for C_3H_6OClF: C, 32·0; H, 5·3%).

Reaction between Epichlorohydrin and Potassium Hydrogen Fluoride.—A stirred mixture of epichlorohydrin (500 g.), potassium hydrogen fluoride (Baker and Adamson) (470 g.), and diethylene glycol (500 g.) was heated under reflux for 2·5 hr. (oil-bath, 160—170°). The mixture was allowed to cool, and the material distilled under reduced pressure, both condenser and receiver being cooled with ice-water. The distillate (325 g.), b. p. 40—90°/30 mm., upon redistillation through an efficient column, gave a fore-run (7 g.), b. p. 90—124°, 1 : 3-difluoropropan-2-ol (182° g., 36%), b. p. 124—134°, and upon redistillation (154 g., 30%), b. p. 127—128°, n_D^{28} 1·3737 (Found: C, 37·0; H, 6·2. Calc. for $C_3H_6OF_2$: C, 37·2; H, 6·2%), and 1-chloro-3-fluoropropan-2-ol (100 g., 17·5%), b. p. 135—155°, and upon redistillation, 146—148°, n_D^{28} 1·4269.

When epichlorohydrin was added dropwise to a stirred mixture of potassium fluoride and diethylene glycol or potassium fluoride and glycerol, as described above, and at a temperature as high as 220° (oil-bath), it was recovered in 50—60% yield.

Dehydrochlorination of 1-*Chloro*-3-*fluoropropan*-2-*ol to Epifluorohydrin.*—1-Chloro-3-fluoropropan-2-ol (112·5 g.) was treated with powdered sodium hydroxide (44 g.) and ether (300 ml.) according to the method used for epichlorohydrin.[13] Epifluorohydrin distilled at 85—86°, (50 g., 66%), n_D^{28} 1·3680 (lit., b. p. 85—86°,[4] 83—84°,[9] n_D^{20} 1·373,[4] n_D^{25} 1·3679 [9]) (Found: C, 47·3; H, 6·7. Calc. for C_3H_5OF: C, 47·3; H, 6·6%).

1 : 3-*Difluoroacetone.*—To a stirred mixture of 1 : 3-difluoropropan-2-ol (b. p. 124—130°) (60 g.), sodium dichromate dihydrate (84 g.), and water (50 c.c.), a mixture of concentrated sulphuric acid (120 g.) and water (30 c.c.) was added during 3—4 hr. at 15—20°. The mixture was stirred for 2 hr., diluted with water (200 c.c.), and distilled until about 170—200 c.c. of distillate had collected, the portion of the distillate at 97—98° containing most of the ketone. Excess of calcium chloride was added to the distillate until the ketone was salted out. This was separated, the calcium chloride solution extracted once with ether, and the ethereal solution added to the ketone, dried ($CaCl_2$), and fractionated, giving 1 : 3-difluoroacetone (24·5 g., 42%), b. p. 124—126°/760 mm., 52—53°/30 mm., n_D^{28} 1·3719, $\nu_{max.}$ (liquid) 1750 cm.$^{-1}$ (C=O) (Found: C, 38·3; H, 4·3. Calc. for $C_3H_4OF_2$: C, 38·2; H, 4·3%). Difluoroacetone is extremely soluble in water, probably through hydrate formation, as shown by evolution of heat when it is added to water; it forms an azeotrope, b. p. 97—98°, with water. It cannot be salted out with sodium chloride or sodium sulphate, nor is it possible to extract it efficiently from water by means of ether. This makes its recovery from oxidation mixtures by means of extraction a very tedious and inefficient procedure. The *semicarbazone*, obtained from an aqueous solution, is very unstable; it cannot be purified by recrystallization; it had m. p. 143—146° (Found: C, 31·8; H, 4·9. $C_4H_7ON_3F_2$ requires C, 31·8; H, 4·6%).

2 : 2-*Di*(*fluoromethyl*)-1 : 3-*dioxolan.*—Since difluoroacetone could not be characterised by a stable solid derivative, and in order to differentiate it from the 1 : 3-difluoropropan-2-ol, which has a very similar b. p., a ketal was prepared: difluoroacetone (10 g.), ethylene glycol (7·0 g.), and toluene-*p*-sulphonic acid (0·25 g.) in benzene were refluxed azeotropically for 5—6 hr., about 2 c.c. of water being collected; The acid was neutralized, the solvent was removed by distillation, and the *ketal* distilled under reduced pressure (yield, 8 g., 54%; b. p. 64—65°/30 mm., n_D^{27} 1·3989) (Found: C, 44·3; H, 6·2. $C_5H_8O_2F_2$ requires C, 43·5; H, 5·8%).

Oxidation of 1-*Chloro*-3-*fluoropropan*-2-*ol to* 1-*Chloro*-3-*fluoroacetone.*—To a stirred mixture of the propanol, b. p. 140—150° (64 g.), sodium dichromate dihydrate (96 g.), and water (54 c.c.), a mixture of sulphuric acid (114 g.) and water (50 c.c.) was added at 20—25° during 4—5 hr. Stirring was continued for 2 hr. more, and the mixture diluted with water (250 c.c.) and distilled

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[12] Gryszkiewicz-Trochimowski and Gryszkiewicz-Trochimowski, *Bull. Soc. chim. France*, 1949, 928.

[13] Clarke and Hartman, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 233.

at 70—80 mm. until about 200 c.c. of distillate had been collected. To this was added calcium chloride in excess until the ketone separated as the bottom layer. This was separated, dried ($CaCl_2$), and fractionated, to yield 1-chloro-3-fluoroacetone (29 g., 46%), b. p. 142—144°, n_D^{28} 1·4195 (lit., b. p. 141·5—143·5°,[4] 55°/20 mm.,[1] n_D^{20} 1·4277 [1]) $\nu_{max.}$ (liquid) 1754 cm.$^{-1}$ (C=O) (Found: C, 32·6; H, 3·7. Calc. for C_3H_4OClF: C, 32·2; H, 3·6%). A very unstable semicarbazone, m. p. 116—118°, was obtained from an aqueous solution of the compound.

2-*Chloromethyl*-2-*fluoromethyl*-1 : 3-*dioxolan*.—This *compound*, obtained (78%) from fluorochloracetone (5·5 g.), ethylene glycol (3·1 g.), and toluene-*p*-sulphonic acid (0·25 g.) as described above, had b. p. 82—84°/30 mm., n_D^{27} 1·4320 (Found: C, 38·6; H, 5·3. $C_5H_8O_2ClF$ requires C, 38·8; H, 5·2%).

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