

PREPARATION OF DIFLUOROACETIC ACID AND ITS DERIVATIVES FROM CHLOROTRIFLUOROETHYLENE*

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Received January 28th, 1977

Chlorofluoroacet-diethylamide (*I*) has been converted into difluoroacet-diethylamide (*II*) by the action of potassium fluoride in diethylene glycol. Alkaline hydrolysis of amide *II* furnished difluoroacetic acid (*IIIa*). By acidolysis of esters of aromatic carboxylic acids with acid *IIIa* its methyl ester *IIIb* and ethyl ester *IIIc* were prepared.

Of the fluorinated derivatives of acetic acid, difluoroacetic acid (*IIIa*) is still accessible only with difficulty, as no technologically simple procedure for its preparation has been found so far. On this ground also the use of difluoroacetic acid and its derivatives in the synthesis of fluorinated organic compounds is substantially limited. The up to now known procedures for preparing acid *IIIa* may be divided essentially into two groups. One part is based on the oxidation of 1,1-difluoro-2,3-unsaturated hydrocarbons which themselves are, however, products of multi-stage syntheses¹⁻³. The second group of syntheses starts from tetrafluoroethylene⁴⁻⁹. These syntheses are comparatively simple, but the starting olefin is not always commonly accessible. Other reactions by which acid *IIIa* or its derivatives are formed are rather of theoretical interest¹⁰⁻¹⁴.

Recently, a three-stage synthesis of the methyl ester *IIIb* has been described¹⁵ starting from chlorotrifluoroethylene (*IV*). This procedure is of advantage on account of the easy accessibility of the starting material, but is less suitable for the preparation on a larger scale. The present paper describes the use of olefin *IV* for the synthesis of acid *IIIa* and its derivatives by a different procedure. The simple realization of this synthesis together with its high yields facilitate the preparation of these compounds even in larger quantities.

N,N-diethyl-2-chloro-2-fluoroacetamide (*I*) was prepared according to cit.¹⁶, in a yield of about 80%, by addition of diethylamine to olefin *IV* and hydrolysis of the N-(2-chloro-1,1,2-trifluoroethyl)-N,N-diethylamine (*V*) formed. This substance is also formed as a by-product in all reactions where the amine *V* is used

* Patent protection has been applied for at the Czechoslovak Patent Office under number PV 7603-72 (November 9th, 1972).

as a fluorinating agent (Yarovenko reagent^{17,18}). Treatment of amide *I* with potassium fluoride in diethylene glycol gave a 75% yield of N,N-diethyl-2,2-difluoroacetamide (*II*). This is the first example of a direct conversion of a chlorofluoroacetic acid derivative to the corresponding difluoro derivative. Alkaline hydrolysis of amide *II* leads to the free acid *IIIa*, as has been described earlier⁷.

The direct esterification of acid *IIIa* with alcohols is complicated by formation of an azeotropic mixture of the alcohol and the formed ester¹⁹. The removal of alcohol from these mixtures is cumbersome and may unfavourably affect the yield owing to the lability of esters of acid *IIIa* in presence of water¹⁵. Another procedure was therefore worked out, which was based on the acidolysis of high boiling esters with acid *IIIa*, where the formed esters *IIIb* and *IIIc*, resp. distilled from the reaction mixture in yields of about 75%. For this purpose aromatic carboxylic acid esters, e.g. benzoic and phthalic acid esters have been found to be most suitable. When using diethyl oxalate, the resulting ester *IIIc* was contaminated with ethyl formate (arising under the reaction conditions from the intermediately formed ethyl hydrogen oxalate and identified by gas chromatography) and the final yield dropped to 45%.

EXPERIMENTAL

Temperature data are uncorrected. Gas chromatography was carried out on Packard 7731 apparatus (stationary phase 15% SE-30 on Gas-Chrom P, flow rate 50 ml/min, carrier gas nitrogen).

N,N-Diethyl-2,2-difluoroacetamide (*II*)

A mixture of amide *I* (250 g), anhydrous potassium fluoride (110 g), and anhydrous diethylene glycol (640 g) was stirred at 140°C and 100 Torr, whereby the crude product distilled over. In the course of the reaction the temperature was gradually raised to 180°C. Redistillation provided 171 g (75%) of the difluoro derivative *II* of at least 99% purity (GLPC at 110°C), b.p. 70–74°C/22 Torr, n_D^{22} 1.4150. The sample for analysis had b.p. 68°C/19 Torr and n_D^{20} 1.4150 (lit.¹⁹ gives b.p. 75–75.5°C/22 Torr and n_D^{20} 1.4140).

Ethyl Difluoroacetate

To acid *IIIa* (37.9 g) and ethyl benzoate (119 g) concentrated sulphuric acid (2.2 ml) was added and the mixture heated to 150°C under stirring. The formed ester was removed by distillation through a column. In the course of 5 h the bath temperature was raised to 220°C, the distillate (b.p. 95–102°C; 40.8 g) dried overnight over a small quantity of phosphorus pentoxide and redistilled. Yield of ester *IIIc* was 35.5 g (73%) of at least 99% purity (GLPC at 45°C), b.p. 98–100°C, n_D^{20} 1.3466 (lit.²⁰ gives b.p. 99°C, n_D^{20} 1.3463).

Methyl Difluoroacetate (*IIIb*)

From acid *IIIa* (32.0 g), dimethyl phthalate (90 g), and concentrated sulphuric acid (2 ml) there was obtained, by the same procedure as in the foregoing section, 28.9 g (78%) of ester *IIIb* of 98 to 99% purity (GLPC at 37°C). B.p. 84–85°C, n_D^{20} 1.3371 (lit.¹² gives b.p. 85–86°C).

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Translated by V. Čermáková.