Lithium Aluminum Hydride Reduction of Difluoroacetic Acid[1]

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In earlier publications (2,8), alcohols are reported as the only products from the reaction between lithium aluminum hydride and carboxylic acids. However it was shown recently (5) that perfluoro acids can be reduced to perfluoro aldehydes by lithium aluminum hydride. The esters of perfluoro acids can be converted to the aldehydes by reduction with lithium aluminum hydride at Dry Ice temperature (10) and carbon dioxide has been reduced to methanol (3) or formaldehyde (9), depending on the amount of the hydride. It was of interest to study the reduction of difluoroacetic acid and to study the properties of difluoroacetaldehyde if formed, since this aldehyde can perhaps be used for the introduction of the CHF_2-group into various molecules.

Reduction of difluoroacetic acid with lithium aluminum hydride gave an 18% yield of difluoroacetaldehyde (27% when based on isolated 2,4-dinitrophenylhydrazone) and 12% of 2,2-difluoroethanol. Yields of isolated aldehyde are lower than derivatives because treatment with phosphorus pentoxide or sulfuric acid appears to result in polymerization and decomposition of the aldehyde. The mixture of aldehydrol and sulfuric acid decomposes when heated (above 118°), giving hydrogen fluoride and a black tar.

The yield of aldehyde in the reduction is increased by decreasing the quantity of lithium aluminum hydride. When a ratio of one-fourth of a mole of hydride per mole of acid is used, 20% of the unreacted acid is recovered. The yield of the aldehyde is increased to 34% (isolated as the 2,4-dinitrophenylhydrazone) but that of the alcohol is decreased to 2%.

A mechanism for reductions by lithium aluminum hydride has been postulated by Trevoy and Brown (12). They proposed that a hydride ion functions as a nucleophilic reagent in a bimolecular nucleophilic displacement reaction. This postulated mechanism may be used to explain the results obtained with difluoroacetic acid. The CHF_2- group causes the carbonyl carbon atom to be electron deficient; this not only permits an easier hydride attack but also makes it more difficult for an aluminate ion to leave. If the R group in the acid, RCOOH is changed to CF_3- or C_2F_5-, its electron withdrawing power is enhanced which results in a more stable ion and a greater formation of aldehydrol. This prediction agrees with the experimental results. The yield of perfluoroacetaldehyde and perfluoropropionaldehyde from acids is 46% (1) and 40-49% (7) respectively and substantially greater than that of difluoroacetaldehyde.

The structure of difluoroacetaldehyde was established by physical and chemical methods. Its infrared absorption spectrum shows the presence of bands characteristic of C-F (9.90-7.41 μ), C=O 5.65 μ) and C-H (3.5μ), but there are no bands for the OH group (3.22-2.68 μ) (4). In

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contrast to the aldehyde, the infrared absorption spectrum of aldehydrol exhibits the bands characteristic of C-F, C-H and OH groups but no bands for the C=O group. The aldehyde grouping is indicated by a positive Schiff's test and the formation of derivatives with semicarbazide hydrochloride and 2,4-dinitrophenylhydrazine. It reacts rapidly with water and acetic anhydride, yielding respectively difluoroacetaldehydrol and the diacetate of difluoroacetaldehydrol. This aldehydrol, unlike the solid perfluoro aldehydrols, is a liquid having a boiling point of 105.5-106°.

Further evidence for the typical carbonyl reactivity is obtained by the reaction of difluoroacetaldehyde with methylmagnesium iodide to give 1,1-difluoro-2-propanol in 53% yield.

Experimental[1]

Difluoroacetaldehyde.—Two pounds of anhydrous ether and 30 g. (0.8 mole) of lithium aluminum hydride were placed in a 2-l., 3-necked flask, fitted with a Hershberg stirrer, a 125 ml. dropping funnel and a reflux condenser protected by a calcium chloride tube. One mole (96 g.) of difluoroacetic acid was added dropwise from the dropping funnel to the stirred reaction mixture, which was cooled in an ice bath. The addition of the acid was kept at such a rate that the ether did not reflux. Upon completion of the addition of the acid, the mixture was stirred for two hours. The excess lithium aluminum hydride was destroyed by the cautious addition of 20 ml. of 95% ethanol and 20 ml. of water. The mixture was poured into a beaker containing 1 kg. of cracked ice and 200 ml. of concentrated sulfuric acid. The mixture was agitated well and the ether layer was separated. The aqueous layer was extracted three times with 200 ml. portions of ether. The ether layer and the ether extracts were distilled to remove the ether. An oily residue was obtained composed mainly of difluoroacetaldehydrol and 10 g. (12%) of 2,2-difluoroethanol. The oily residue was dried over Drierite and treated with phosphorus pentoxide. The aldehyde was distilled from the acid mixture directly into a cooled receiver (b.p. 31-43°). Redistillation through an eight-inch helix packed column yielded 14 g. (18%) of difluoroacetaldehyde, b.p. 27-28°. This aldehyde gave a positive Schiff's test.

Anal. Calcd. for $C_2H_2F_2O$: C, 30.00; H, 2.50. Found: C, 30.35; H, 2.85.

Difluoroacetaldehyde polymerized slowly either at room temperature or ice temperature to a white rubbery material. This polymerization was catalyzed by one drop of concentrated sulfuric acid, but was inhibited by very low temperatures. The aldehyde could be kept in the liquid state at Dry Ice temperature. The difluoroacetaldehyde polymer softens at 130° and starts to depolymerize at 165°. Solubility tests for this polymer indicate that it is soluble in acetone and insoluble in water, ethanol, butanol, chloroform, carbon tetrachloride, benzene and n-heptane. It swells in glacial acetic acid, ethyl acetate, methyl ethyl ketone, cyclohexanone and

1. All temperatures are uncorrected; the melting points were determined with a Fischer-Johns melting point apparatus. Carbon, hydrogen and nitrogen analysis by H. Galbraith, Knoxville, Tennessee, and Mrs. C. S. T. Yeh of this department.

ether. It is also insoluble in cold dilute acid (10% hydrochloric acid) and cold dilute base (10% sodium hydroxide).

The **semicarbazone** of difluoroacetaldehyde was prepared following the method of Kling (6) with aqueous ethanol as solvent. The product was purified by two crystallizations from aqueous ethanol, m.p. 156-157°.

Anal. Calcd. for $C_3H_5F_2N_3O$: N, 30.65. Found: N, 30.86.

The **2,4-dinitrophenylhydrazone** was prepared according to the procedure of Shriner and Fuson (11). The orange-yellow needles were recrystallized from an ethanol-water mixture, m.p. 156-157°.

Anal. Calcd. for $C_8H_6F_2N_4O_4$: N, 21.54. Found: N, 21.69.

Difluoroacetaldehydrol.—Difluoroacetaldehyde (6.5 g., 0.081 mole) was placed in a 100 ml. flask equipped with a dropping funnel and a Dry Ice condenser. While shaking the flask, 1.4 g. (0.078 mole) of water was added dropwise. A reaction took place immediately with evolution of heat. After all the water was added, the flask was allowed to cool to room temperature. The resulting solution was distilled giving 4.6 g. (60%) of difluoroacetaldehydrol, b.p. 105.5-106°, n_D^{20} 1.3743.

Anal. Calcd. for $C_2H_4F_2O_2$: C, 24.49; H, 4.08. Found: C, 24.53; H, 4.22.

Diacetate of Difluoroacetaldehydrol.—In a 100 ml flask, fitted with a Dry Ice condenser, were placed 5 g. (0.063 mole) of difluoroacetaldehyde and 14 g. (0.137 mole) of acetic anhydride. One drop of concentrated sulfuric acid was added as a catalyst. The solution was refluxed for 15 min. and the product was recovered by washing with water, drying with anhydrous magnesium sulfate and rectifying. The yield of diacetate was 4.7 g. (41%), b.p. 176-178° (or 75°/13 mm.), n_D^{20} 1.3821.

Anal. Calcd. for $C_6H_8F_2O_4$: C, 39.56; H, 4.39. Found: C, 39.52; H, 4.52.

1,1-Difluoro-2-propanol.—Two-tenths of a mole (16 g.) of difluoroacetaldehyde in 100 ml. of anhydrous ether was added to an ether solution of a Grignard reagent, prepared from 6 g. (0.25 g. atom) of magnesium and 35.5 g. (0.25 mole) of methyl iodide, contained in a 3-necked, 300 ml. flask equipped with a stirrer, a dropping funnel and a reflux condenser. After the aldehyde solution was added, the mixture was allowed to stir for one hour and then poured onto cracked ice. The precipitate was dissolved in dilute (20%) sulfuric acid, the ether layer was separated and the aqueous layer was extracted three times with ether. The combined ether solutions were washed with a saturated sodium sulfite solution and dried over Drierite. Rectification yielded 10.1 g. (53%) of 1,1-difluoro-2-propanol, b.p. 93-93.5°, n_D^{20} 1.3494.

Anal. Calcd. for $C_3H_6F_2O$: C, 37.50; H, 6.24. Found: C, 37.39; H, 6.42.

Summary

Difluoroacetaldehyde has been prepared by the reduction of difluoroacetic acid with lithium aluminum hydride. Several reactions of this aldehyde were investigated and its infrared absorption spectrum has been determined.

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