[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AT THE OHIO STATE UNIVERSITY]

The Preparation of Trifluorinated Aldehydes

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Syntheses for aldehydes bearing a CF_3 group have been examined, and recommended procedures devised. When the CF_3 group is not adjacent to the carbonyl group, conventional methods can be used; specifically, we have prepared CF_3CH_2CHO by dichromate oxidation of $CF_3CH_2CH_2OH$ and McBee[1] has just reported that he has obtained $CF_3CH_2CH_2CHO$ by treating $CF_3CH_2CH_2MgX$ with ethyl orthoformate. In contrast, attempts to prepare the first member of the series, CF_3CHO, by most of the conventional procedures were failures, and only one good method was found, the reduction of CF_3CN with lithium aluminum hydride at low temperature. We have noted that this reduction of nitriles is now generally recommended,[2] and that some perfluorobutyraldehyde was obtained as a by-product in the reduction of the acid to the alcohol.[3]

The boiling point of trifluorinated aldehydes is substantially the same as that of unfluorinated aldehydes, except for trifluoroacetaldehyde which boils about 40° below acetaldehyde.

Experimental

CF_3CH_2CHO.—$CF_3CH_2CH_2OH$ was prepared by oxidation of $CF_3CH_2CH_2MgCl$.[4] For convenience the needed $CF_3CH_2CH_2Cl$ was made by a conventional fluorination of commercial[4,5] $CCl_3CH_2CH_2Cl$ with antimony fluoride, rather than from $CCl_2{=}CHCH_3$.[6] We also found that in the presence of an excess of magnesium, and in dilute solution,[7] the Grignard derivative could be made practically quantitatively; its oxidation by a stream of oxygen was found to be particularly efficient at $-78°$ because the formation of $CF_3CH{=}CH_2$ was avoided. With these improvements, the yield of $CF_3CH_2CH_2OH$ from the chloride reached 80–85%.

Trifluoropropanol was oxidized to the aldehyde with acidified sodium dichromate. Concentrated sulfuric acid (38 g. or 0.36 mole), trifluoropropanol (29.8 g. or 0.26 mole) and water (150 ml.) were heated in a round-bottom flask fitted with a Claisen distilling head. When the temperature of the reaction mixture reached 70°, sodium dichromate (30 g. or 0.1 mole in 100 ml. of water) was added slowly from a dropping funnel. The temperature of the reaction mixture rose to 85°, and 16.5 g. (0.15 mole, 57% yield) of material distilled over into the receiver. This material gave a positive Fehling test, and a 2,4-dinitrophenylhydrazone m. p. 150.2–150.8° after recrystallization from 95% alcohol, with a nitrogen content of 19.0% found, 19.1% calculated. Its physical properties were: b. p. 56.0–56.5° at 745 mm.; $n^{22}{}_D$ 1.3168; $d^{20}{}_4$ 1.365. The atomic refraction for fluorine was computed as $AR_F = 1.1$.

This oxidation procedure was then modified to yield the acid rather than the aldehyde. When the dichromate was added at 70° but under reflux, it was observed that the oxidation proceeded vigorously during the addition of about one-half of the dichromate, after which it subsided markedly. The mixture was therefore refluxed overnight. After cooling, it was extracted with ether, and the extract was dried. At 14–15 mm., trifluoropropionic acid distilled at 27–30°, without visible decomposition; it became pink on standing at room temperature, but remained undecomposed in a refrigerator; it solidified close to 0°, and had a neutral equivalent of 126, compared to a calculated value of 128; its anilide had a m. p. of 117.5 to 118°, and a nitrogen content of 7.0%; the calculated value is 6.9%. Values of 12° for m. p. and 146° for b. p. are reputed to have been observed in the laboratories of I. G. Farbenindustrie.

CF_3CHO.—Trifluoroacetic acid was converted into its amide in 90% yield.[8] The amide (34 g. or 0.3 mole) was mixed with an equal weight of phosphorus pentoxide and dry-distilled to yield CF_3CN (26 g. or 85% yield). Redistilled nitrile (22 g. or 0.23 mole) was placed in a 250-ml. three-necked flask cooled with Dry Ice, and fitted with a stirrer, a Dry Ice reflux condenser and a dropping funnel. At this low temperature, an ether solution of lithium aluminum hydroxide (0.06 mole in 70 ml.) was added dropwise with stirring. A bright yellow color appeared. While the mixture was warming to room temperature, its color changed to brown. Concentrated hydrochloric acid was then cautiously fed, until the mixture became clear. The solution was extracted continuously with ether for forty-eight hours. The ether extract containing the aldehyde hydrate was fractionally distilled until reduced to 10% of its volume. This concentrate was then dropped on 15 g. of phosphorus pentoxide, and the mixture heated; the distillate obtained therefrom was refractionated through a column cooled to 0°, to give the desired aldehyde (10.5 g.) in 46% yield.

An attempt was made to determine the b. p. by Engler distillation, but part-polymerization was seen to occur and no better than an estimation of $-20 \pm 1°$ can be offered. A hydrate is formed with great ease, which sublimes markedly at about 50°. Both the aldehyde and the hydrate give a 2,4-dinitrophenylhydrazone melting at 150–151° after recrystallization from 50% alcohol, identical with the analyzed product of Shechter and Conrad.[9]

The aldehyde reacted with an ether solution of phenylmagnesium bromide. The reaction mixture was extracted with ether, and the ether was evaporated; the residue was oxidized with cold acid permanganate until a pink color persisted. After bleaching the solution with a little bisulfite, a 2,4-dinitrophenylhydrazone was made, which after recrystallization from 50% alcohol, melted at 95°; this agrees with the known value for trifluoroacetophenone.[10]

Attempted Preparations of CF_3CHO.—(1) CF_3CO_2H and formic acid did not react on manganous oxide at high temperature until carbonization set in. (2) CF_3CONH_2 was reduced to the alcohol with hydrogen on platinum and to the amine on copper chromite, broke down completely with sodium in liquid ammonia, condensed with a Grignard reagent without reduction to a tertiary carbinol. (3) CF_3CN failed to give an imine in the Stephens reduction with stannous chloride and hydrochloric acid. (4) CF_3COCl was reduced to the alcohol by lithium aluminum hydride, condensed with two moles of Grignard reagent but was not reduced to a ketone, was not reduced by sodium hydride or borohydride, did not react in the Rosenmund reduction or was reduced directly to the alcohol.

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(1) McBee, Kelley and Rapkin, Abstracts of 116th meeting, p. 10K, Atlantic City, 1949.

(2) Friedman, *ibid.*, p. 5M.

(3) Husted, *ibid.*, p. 10K.

(4) McBee and Truchan, THIS JOURNAL, **70**, 2910 (1948).

(5) Gift of Dr. E. C. Ladd, United States Rubber Corp., Passaic, N. J.

(6) Henne and Whaley, THIS JOURNAL, **64**, 1157 (1942).

(7) Adams, M.S. Thesis, The Ohio State University, 1949.

(8) Zimmer, M.S. Thesis, The Ohio State University, 1949.

(9) Shechter and Conrad, THIS JOURNAL, **72**, 3371 (1950).

(10) Simons, *ibid.*, **65**, 389 (1943).

(5) CF_3COSR and Raney nickel led to the alcohol. (6) Hydrolysis of CF_3CHCl_2 by a variety of procedures led nowhere. (7) CF_3CH_2OH was oxidized directly to the acid by sodium dichromate, and was recovered intact after treatment with acetone and aluminum isopropoxide.

Summary

To synthesize an aldehyde bearing a CF_3 group, conventional oxidation of the corresponding alcohol is adequate if the CF_3 is not adjacent to the carbonyl group. For the synthesis of fluoral, CF_3CHO, only the low temperature reduction of CF_3CN with lithium aluminum hydride was found effective. The preparation of CF_3CHO, CF_3CH_2CHO and $CF_3CH_2CO_2H$ are described,

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Oxidative Nitration of 1,1,1-Trifluoropropane. Trifluoroacetaldehyde

BY HAROLD SHECHTER AND FRANKLIN CONRAD[1]

Nitration of alkanes in the vapor-phase at temperatures above 350° yields each nitroalkane derived from the replacement of any hydrogen atom or alkyl group in the hydrocarbon.[2]

In reactions of the "atom-radical" type it has been shown that the trifluoromethyl group has a marked deactivating effect on replacement of hydrogen atoms in alpha positions; however, the effect of the trifluoromethyl group is greatly diminished in beta positions.[3] Since nitration reactions in the vapor-phase usually involve the substitution of nitro groups for hydrogen atoms and alkyl radicals, it is of interest to determine the influence of the trifluoromethyl group on the specificity of nitration of 1,1,1-trifluoropropane.

The reaction of 1,1,1-trifluoropropane, nitric acid, and oxygen at 437–462° yields 1,1,1-trifluoro-3-nitropropane as the only nitrated product; the principal product of reaction is trifluoroacetaldehyde (fluoral).[4]

The yield of 1,1,1-trifluoro-3-nitropropane, based on nitric acid consumed, is 16%; the yield of trifluoroacetaldehyde, as the monohydrate, is 20–24%. No direct evidence was obtained for the formation of nitromethane, nitroethane, trifluoronitromethane, 1,1,1-trifluoro-2-nitroethane, and 1,1,1-trifluoro-2-nitropropane, the products expected from a non-specific nitration reaction. 1,1,1-Trifluoro-3-nitropropane was identified by reaction of its sodium salt with sulfuric acid and 2,4-dinitrophenylhydrazine to yield 3,3,3-trifluoropropionaldehyde 2,4-dinitrophenylhydrazone.[5] The infrared spectrogram of the trifluoronitroalkane is given in Fig. 1.

Trifluoroacetaldehyde, the first completely fluorinated aldehyde to be reported,[6] was isolated from its hydrate by reaction with phosphoric anhydride. The aldehyde was identified by preparing the *p*-nitrophenylhydrazone and the 2,4-dinitrophenylhydrazone. Swarts[7] has reported that oxidation of trifluoroethanol with chromic acid yields trifluoroacetic acid; no trifluoroacetaldehyde was obtained. Whether trifluoroacetaldehyde is produced by oxidation of 1,1,1-trifluoropropane or by decomposition of 1,1,1-trifluoro-2-nitroethane has not been established. Since thermal decomposition of primary nitroalkanes yields the corresponding aldehyde, nitric oxide, and water,[8] it is probable that decomposition of 1,1,1-trifluoro-2-nitroethane yields much of the trifluoroacetaldehyde produced.

Fluoral gives typical reactions of the carbonyl group; however, its properties are greatly influenced by the strong inductive effect of the trifluoromethyl group. The aldehyde, b. p. −18.8 to −17.5°, (infrared spectrum, Fig. 2), dissolves very slowly in water; in dilute acids it forms the expected hydrate. During storage, trifluoroacetaldehyde polymerizes into a clear waxy resin[9] which is slightly soluble in diethyl ether and in acetone. The polymer, insoluble in water, carbon disulfide, chloroform, and carbon tetrachloride, serves as a convenient source of trifluoroacetaldehyde since, upon heating, it decomposes readily into the aldehyde. The polymer is hydrolyzed slowly by concentrated acids, but dissolves rapidly in dilute carbonate solutions to yield fluoral hydrate.

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[1] Abstracted from the thesis of Franklin Conrad, submitted in partial fulfillment of the requirements for the M.S. degree at The Ohio State University, Columbus, Ohio.

[2] Hass, Hodge and Vanderbilt, *Ind. Eng. Chem.*, **28**, 339 (1936); Hass and Shechter, *ibid.*, **39**, 817 (1947).

[3] Henne and Whaley, THIS JOURNAL, **64**, 1157 (1942); Henne and Hinkamp, *ibid.*, **67**, 1197 (1945); McBee, Hass, Elmore, Thomas, Toland and Truchan, *ibid.*, **69**, 944 (1947); Ash and Brown, *Rec. Chem. Prog.*, **9**, 81 (1948).

[4] After submission of this manuscript, McBee and Robinson, 116th Meeting of the American Chemical Society, Atlantic City, N. J., reported that nitration of 1,1,1-trifluoropropane at 390° in the absence of oxygen yields 1,1,1-trifluoro-3-nitropropane and 1,1,1-trifloro-2-nitroethane; no trifluoroacetaldehyde was obtained. It is likely that, at higher temperatures and in the presence of oxygen, trifluoroacetaldehyde is formed at the expense of 1,1,1-trifluoro-2-nitroethane. The conclusions from both studies concerning the effect of the trifluoromethyl group are essentially the same.

[5] Henne, Pelley and Alm, THIS JOURNAL, **72**, 3370 (1950).

[6] Since submission of this manuscript, Husted and Ahlbrecht, 116th Meeting of the American Chemical Society, Atlantic City, N. J., have reported the preparation of perfluorobutyraldehyde.

[7] Swarts, *Bull. soc. chim. Belg.*, **43**, 471 (1934).

[8] Gabriel, *Ber.*, **18**, 1254 (1885); Kon, *ibid.*, **28**, 1861 (1895) Holleman, *Rec. trav. chim.*, **14**, 121 (1895).

[9] Slow distillation of fluoral also yields a crystalline solid, m. p. 47–49°, which has not been identified. The structures of the various polymers of fluoral, perhaps linear and cyclic, are now being studied.