[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Ring-cleavage Reactions of 1,1,1-Trifluoro-2,3-epoxypropane

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The ring-cleavage reactions of 1,1,1-trifluoro-2,3-epoxypropane with ethanol under basic and acidic conditions, lithium aluminum hydride, ammonia, diethylamine, methylmagnesium bromide, anhydrous magnesium bromide and hydrogen bromide occur at the terminal carbon–oxygen bond.

Discussion

The literature relating to the direction of cleavage of the substituted epoxide ring is extensive and various hypotheses to explain the observed isomer distribution have been considered. Electronic factors such as relative electron densities at the two carbon atoms of the epoxide,[2] allylic[3] or hyperconjugative stabilization of a carbonium ion,[4] substituent inductive effects[2b,5] and complexing[3a] or solvent effects[3c,d,6] as well as steric factors such as degree of substitution of the epoxide,[7] size of the substituent on the ring[5a,8] and the size of the attacking group[2a,6b,8] have been used. Knowledge of the isomer distribution of the cleavage products for a base-stable, monosubstituted epoxide with steric requirements approximating those of propylene oxide (I), with a known $-I_s$ effect and in which the possibility of hyperconjugative stabilization of a carbonium ion is eliminated, was considered of importance in the development of an understanding of ring-cleavage reactions.

This paper reports the results of an investigation of the cleavage reactions of 1,1,1-trifluoro-2,3-epoxypropane (II) with a series of nucleophilic reagents.[9] Both I and II undergo strictly C_1 cleavage under basic conditions,[10] but in the presence of acid compound I gives a mixture of both types of cleavage in contrast to the sole C_1 cleavage shown by II. The ethanolysis of II in the presence of ethoxide ion and sulfuric acid has been reported previously by Burton, who concluded on the basis of boiling point and refractive index that both reactions gave the same products.[11] Independent synthesis of pure 3-ethoxy-1,1,1-trifluoro-2-propanol (III) and 2-ethoxy-3,3,3-trifluoro-1-propanol (IV) has now shown that the two isomers have almost identical physical properties but do differ markedly in their infrared spectra in the region of 10–14 μ (Fig. 1). Their respective acetates were found to differ sufficiently, however, to allow purification through rectification, followed by regeneration of the pure alcohol under basic hydrolysis. Crude III was obtained by the base-catalyzed ethanolysis of II. Crude IV was obtained by a sequence of reactions involving the addition of ethanol to 1-nitro-3,3,3-trifluoropropene, reduction to the amino ether and diazotization to IV. Infrared analysis indicated that less than 2% rearrangement of the primary carbonium ion had occurred.

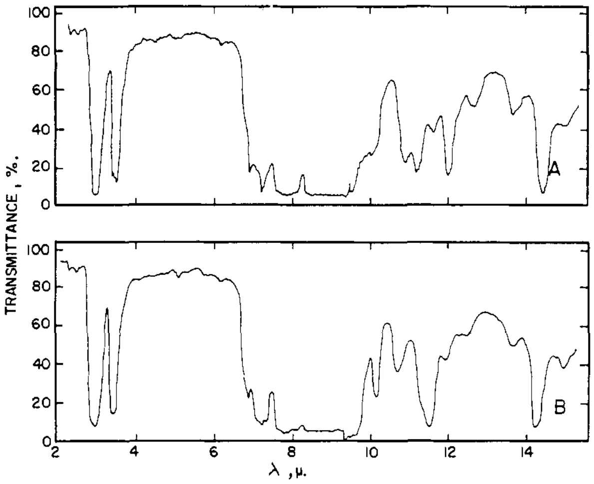

Fig. 1.—Infrared spectra: A, 3-ethoxy-1,1,1-trifluoro-2-propanol; B, 2-ethoxy-3,3,3-trifluoro-1-propanol.

The isomeric alcohols are easily differentiated by the failure of III to give a ceric nitrate test, whereas IV gives a weak but very definite coloration.[12] The reaction of ethoxide with I leads to 83.2% monomeric adduct, whereas reaction with II yields 90% polymeric but only 10% monomeric product under reflux conditions.[11] The formation of a preponderant amount of the polymeric product supports the concept of a bimolecular, nucleophilic displacement to form an intermediate anion (VII), which is capable of acting as a base by picking up a proton from the solvent or as a nucleophilic species in the cleavage of another molecule of epoxide.

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(1) A portion of a thesis submitted by C. E. Hathaway to Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, January, 1956.

(2) (a) R. R. Russell and C. A. VanderWerf, THIS JOURNAL, **69**, 11 (1947); (b) D. Swern, G. N. Billen and H. B. Knight, *ibid.*, **71**, 1152 (1949).

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(7) E. E. van Tamelen, G. Van Zyl and C. E. Zuidema, *ibid.*, **72**, 488 (1950).

(8) R. M. Adams and C. A. VanderWerf, *ibid.*, **72**, 4368 (1950).

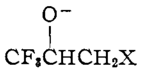
(9) For purposes of this discussion, the terms C_1 and C_2 cleavage refer, respectively, to nucleophilic displacement of the terminal carbon–oxygen bond and the secondary carbon–oxygen bond of the epoxide.

(10) Stewart and VanderWerf[6b] report up to 23% C_2 cleavage of I with ammonium bromide and a smaller percentage with both magnesium bromide and sodium bromide. A general acid catalysis is proposed to explain their results.

(11) T. M. Burton, Ph.D. Thesis, Purdue University, 1951.

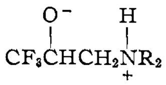
(12) Alcohols containing an α-trifluoromethyl group such as trifluoroethanol, 1,1,1-trifluoro-2-propanol, 3-bromo-1,1,1-trifluoro-2-propanol and 3-diethylamino-1,1,1-trifluoro-2-propanol in general fail to give a positive ceric nitrate test.

The three fluorine atoms on the α-methyl group exert sufficient inductive effect to decrease the basicity of VII toward a proton while labilizing the terminal carbon–oxygen bond with a resultant preferred polymerization. The contrasting formation of monomeric product upon reaction of II with diethylamine is evidence for the formation of VII as a reaction intermediate since an intermediate zwitterion (VIII) would be formed which would be expected to tautomerize more easily to the monomeric alcohol than polymerize.



$CF_3CH(O^-)CH_2X$

VII



$CF_3CH(O^-)CH_2\overset{+}{N}HR_2$

VIII

Since the inductive effect of a trifluoromethyl group increases the acidity of an adjacent carbinol group[13] and since the inductive effect diminishes rapidly with increasing chain length,[14] an attempt was made to distinguish between an alcohol with a carbinol grouping adjacent to a perfluoroalkyl group and one with a methylene group interposed by quantitative titration of the α-trifluoromethylcarbinol grouping in a strongly basic solvent.[15] Whereas phenol in butylamine gives a sharp equivalence point,[16] trifluoroethanol by a similar technique shows an inflection but no sharp break at the calculated equivalence point.

Reaction of compound II with lithium aluminum hydride gave only 1,1,1-trifluoro-2-propanol. Reaction of compound II with anhydrous ammonia gave 3-amino-1,1,1-trifluoro-2-propanol having identical properties, and a hydrochloride indistinguishable from the product resulting from the lithium aluminum hydride reduction of fluoral cyanohydrin. Reaction of compound II with diethylamine gave 3-diethylamino-1,1,1-trifluoro-2-propanol identical to the product isolated from the diethylation of 3-amino-1,1,1-trifluoro-2-propanol. Reaction of compound II with magnesium bromide, methylmagnesium bromide and hydrogen bromide gave 3-bromo-1,1,1-trifluoro-2-propanol, 1,1,1-trifluoro-2-butanol and 3-bromo-1,1,1-trifluoro-2-propanol, respectively. There were no data indicating rearrangement.

Preliminary kinetic data (Fig. 2) for the acid-catalyzed ethanolysis of II shows a marked increase in the rate of C_1 cleavage for the protonated species. The over-all effect of the trifluoromethyl group on epoxide ring cleavage reactions appears to be a labilization of the terminal carbon–oxygen bond through an inductive effect operating on the polarizable epoxide function.

Acknowledgment.—The authors wish to express their appreciation to the Carbide and Carbon Chemicals Co. for financial assistance during this investigation.

Experimental[17]

Starting Materials.—3-Bromo-1,1,1-trifluoro-2-propanol and 1,1,1-trifluoro-2,3-epoxypropane were prepared by the method previously described,[18] except the epoxide was distilled with calcium hydride. 1,1,1-Trifluoro-2-butanol was prepared by the reaction of ethylmagnesium bromide with fluoral.[19] Raney nickel was prepared by the method of Mozingo.[20]

Infrared Analysis of Mixtures of 3-Ethoxy-1,1,1-trifluoro-2-propanol (III) and 2-Ethoxy-3,3,3-trifluoro-1-propanol (IV).—All infrared spectra were made on a Perkin–Elmer double-beam recording infrared spectrograph, model 21, using a standard 0.025-mm. sodium chloride cell. An analytical calibration curve was established on the basis of relative absorption maxima characteristic of 2-ethoxy-3,3,3-trifluoro-1-propanol at 11.6 μ and 3-ethoxy-1,1,1-trifluoro-2-propanol at 12.0 μ (Fig. 1). The relative values for absorption maxima were measured from a base line connecting absorption minima at 10.5 and 13.9 μ, which were common to both spectra.[21] In Table I are summarized absorption data for a series of possible mixtures of the isomeric ether alcohols obtained from the base and acid-catalyzed reaction and from the diazotization of 2-ethoxy-3,3,3-trifluoro-1-propanamine. The method is accurate to ±0.5% (see duplicate runs a and b, Table I).

Table I

Infrared Analysis of Mixtures of 3-Ethoxy-1,1,1-trifluoro-2-propanol (III) and 2-Ethoxy-3,3,3-trifluoro-1-propanol (IV)

Unknown[a]	Absorption A (11.6 μ)	Absorption B (12.0 μ)	Ratios A/B	Ratios B/A	Composition, % III	Composition, % V
a	24.7	45.9	0.539		99.4	
b	24.5	46.0	.533		99.2	
c	23.6	43.4	.541		99.1	
d	52.5	17.8		0.339		98.0

[a] (a,b) products from duplicate runs for the acid-catalyzed ethanolysis of 1,1,1-trifluoro-2,3-epoxypropane (II), (c) product from the ethoxide ion-catalyzed ethanolysis of II and (d) product from the diazotization of 2-ethoxy-3,3,3-trifluoro-1-propanamine.

Ethanolysis of 1,1,1-Trifluoro-2,3-epoxypropane (II). (a) Sulfuric Acid Catalysis.—1,1,1-Trifluoro-2,3-epoxypropane (50 g., 0.45 mole) was slowly added to a refluxing solution of 205 g. of ethanol containing 1.5 g. of concentrated sulfuric acid. The reflux temperature gradually fell to about 46° but rose again to the boiling point of ethanol in 48 hr. Excess ethanol and epoxide were then distilled off, the residue was crudely distilled under reduced pressure and rectified to give 54.0 g. (77%) of liquid, b.p. 135°, $n^{20}D$ 1.3568 to 1.3561. Infrared analysis of this liquid (Table I) indicated a composition of over 99.4% 3-ethoxy-1,1,1-trifluoro-2-propanol.

(b) Ethoxide Ion Catalysis.—A solution of 54 g. (0.48 mole) of 1,1,1-trifluoro-2,3-epoxypropane in 20 ml. of absolute ethanol was added during 2 hr. to a stirred solution of 0.1 g. of sodium in 350 g. of ethanol at 25°. After 40 hr. the mixture was acidified with sulfuric acid and filtered. The ethanol and unreacted epoxide were distilled and the residue rectified to obtain 2.4 g. of product, b.p. 57.1° (29 mm.), $n^{20.5}D$ 1.3572, which gave a negative ceric nitrate test. Infrared analysis of this liquid (Table I) indicated a com-

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(13) (a) E. T. McBee, W. F. Marzluff and O. R. Pierce, This Journal, **74**, 444 (1952); (b) A. L. Henne and R. L. Pelley, *ibid.*, **75**, 1426 (1953); (c) A. L. Henne and W. C. Francis, *ibid.*, **75**, 991 (1953).

(14) A. L. Henne and C. J. Fox, *ibid.*, **73**, 2323 (1951).

(15) J. S. Fritz, "Acid and Base Titrations in Nonaqueous Solvents," G. Frederick Smith Chemical Co., Columbus, Ohio, 1952.

(16) J. S. Fritz and N. M. Lisicke, *Anal. Chem.*, **23**, 589 (1951).

(17) All temperatures are uncorrected. Melting points were taken in capillaries. Microanalyses were performed by Mrs. P. T. Yeh, Chemistry Department, Purdue University.

(18) E. T. McBee and T. M. Burton, This Journal, **74**, 3022 (1952).

(19) E. T. McBee, O. R. Pierce and J. F. Higgins, *ibid.*, **74**, 1636 (1952).

(20) R. Mozingo, *Org. Syntheses*, **21**, 15 (1941).

(21) The reproducibility of spectra and sensitivity of the instrument were established by comparing two spectra of 3-ethoxy-1,1,1-trifluoro-2-propanol obtained at a 3-day interval; the ratio of absorption maxima checked to the third decimal place. All analytical spectra were obtained in one day at a speed of 2 min./μ. The instrument resolution was checked at 3 min./μ and gave identical peak values with those obtained at the faster rate. No spurious peaks were noted in any spectra.

position of over 99.1% 3-ethoxy-1,1,1-trifluoro-2-propanol. There was also isolated 6.7 g. of higher boiling liquid which has been shown by Burton[11] to consist of dimeric and polymeric product arising through the reaction of the product alcohol with more epoxide.

2-Ethoxy-3-nitro-1,1,1-trifluoropropane.—A mixture of 100 ml. of ethanol and 65 g. (0.46 mole) of 1-nitro-3,3,3-trifluoropropene[22] was heated under reflux for 72 hr. during which time the characteristic pale green color of the nitroolefin disappeared. Rectification of the mixture gave 60 g. (69%) of colorless product, b.p. 147–149° (52.5° (19 mm.)), $n^{25.5}\mathrm{D}$ 1.3630, d^{25}_4 1.266.

Anal. Calcd. for $C_5H_8F_3NO_3$: C, 32.12; H, 4.28; *MR*, 32.97. Found: C, 32.06; H, 4.31; *MR*, 32.84.

2-Ethoxy-3,3,3-trifluoro-1-propanamine.—2-Ethoxy-3-nitro-1,1,1-trifluoropropane (20 g., 0.11 mole) was dissolved in 75 ml. of absolute ethanol and reduced under a pressure of 27–50 lb. of hydrogen in the presence of 3 g. of Raney nickel. After the calculated pressure drop corresponding to a 1:3 mole ratio was obtained, the catalyst was removed by filtration and the alcohol was removed by distillation. The residue was rectified under reduced pressure to give 5.03 g. (30%) of crude product. Considerable decomposition was noted but essentially quantitative conversion was obtained by isolating the amine directly as the hydrochloride. The crude product was rerectified to give a liquid, b.p. 63.7° (101 mm.), $n^{20}\mathrm{D}$ 1.3606, d^{25}_4 1.135.

Anal. Calcd. for $C_5H_{10}F_3NO$: C, 38.12; H, 6.42; *MR*, 30.90. Found: C, 37.89; H, 6.43; *MR*, 30.99.

The hydrochloride of this compound was formed quantitatively and when recrystallized from ethyl acetate had a m.p. 188–190°.

Anal. Calcd. for $C_5H_{11}ClF_3NO$: C, 31.02; H, 5.73. Found: C, 31.31; H, 5.43.

Diazotization of 2-Ethoxy-3,3,3-trifluoro-1-propanamine.—2-Ethoxy-3,3,3-trifluoro-1-propanamine hydrochloride (85 g., 0.44 mole) was dissolved in 300 ml. of cold water and placed in a 3-necked flask fitted with an addition funnel, Tru-bore stirrer and a 20-cm. glass-helices-packed column with a reflux head. A precooled solution of 87 g. (1.26 moles) of sodium nitrite in 150 ml. of water was added slowly. After standing for 0.5 hr., the mixture was heated to reflux on a steam-bath. During 2.5 hr. there was slowly added 150 ml. of 1 *N* hydrochloric acid at a rate to maintain the solution slightly acidic. There was obtained a 2-phase distillate, b.p. to 75°, the lower layer of which weighed 20 g., decolorized permanganate and was assumed to be 2-ethoxy-3,3,3-trifluoropropene. The product was taken up in ether from the distillate and reaction flask, dried and the ether removed by distillation. Rectification of the residue gave 23.7 g. (34%) of product, b.p. 56.6–56.8° (31.5 mm.), $n^{20}\mathrm{D}$ 1.3580, d^{25}_4 1.213, which gave a positive ceric nitrate test and was shown by infrared analysis (Table I) to be 98% 2-ethoxy-3,3,3-trifluoro-1-propanol.

Anal. Calcd. for $C_5H_9F_3O_2$: C, 37.98; H, 5.73. Found: C, 37.90; H, 5.45.

2-Ethoxy-3,3,3-trifluoro-1-propanol.—Acetyl chloride (14 g., 0.18 mole) was added slowly to a cooled, stirred solution of 25 g. (0.16 mole) of the product from the diazotization of 2-ethoxy-3,3,3-trifluoro-1-propanamine dissolved in 5 times its volume of anhydrous pyridine. After 1 hr. the mixture was allowed to warm to 25° and poured into a slurry of 200 ml. of concentrated hydrochloric acid and ice. The product was taken up in ether, washed with sodium carbonate solution, dried and the ether removed by distillation. Rectification of the residue gave 12.2 g. (38%) of isomerically pure 2-ethoxy-3,3,3-trifluoro-1-propyl acetate, b.p. 73.0 to 73.1° (37 mm.), $n^{20}\mathrm{D}$ 1.3632, d^{25}_4 1.1578.

Anal. Calcd. for $C_7H_{11}F_3O_3$: C, 41.99; H, 5.54; *MR*, 38.24. Found: C, 42.28; H, 5.80; *MR*, 38.42.

A mixture of 10.7 g. (0.06 mole) of the isomerically pure acetate, 18 g. of 20% sodium hydroxide solution and 10 ml. of water was heated under reflux for 4 hr. and allowed to stand for 48 hr. The product was taken up in ether, washed with 5 ml. of 5% hydrochloric acid and then dilute sodium carbonate until neutral. The solution was dried, the ether was distilled off and the residue was rectified to give 5.6 g. (61%) of 2-ethoxy-3,3,3-trifluoro-1-propanol, b.p. 57.0° (29 mm.), $n^{20}\mathrm{D}$ 1.3575 to 1.3576, d^{25}_4 1.2076; *MR* calcd. 28.88, *MR* found 28.56; positive ceric nitrate test, which was used to establish the infrared calibration curve.

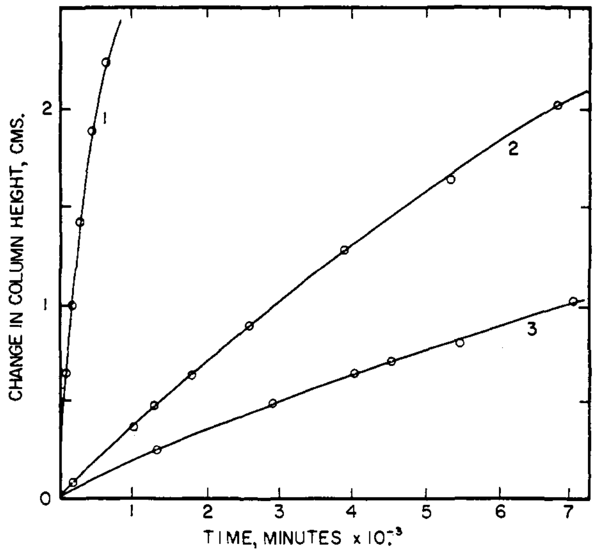

Fig. 2.—Change in height of liquid column in dilatometer during reaction of 1,1,1-trifluoro-2,3-epoxypropane with ethanol: 1, 0.26% sodium ethoxide; 2, 0.76% sulfuric acid; 3, no catalyst.

3-Ethoxy-1,1,1-trifluoro-2-propanol.—The reaction product from the acid-catalyzed ethanolysis of 1,1,1-trifluoro-2,3-epoxypropane was assumed to be largely 3-ethoxy-1,1,1-trifluoro-2-propanol and was purified isomerically by isolation as the acetate, b.p. 66.0° (38 mm.), $n^{20}\mathrm{D}$ 1.3596, d^{25}_4 1.1685.

Anal. Calcd. for $C_7H_{11}F_3O_3$: C, 41.99; H, 5.54; *MR*, 38.24. Found: C, 41.75; H, 5.80; *MR*, 37.56.

The acetate was heated to 70° with a slight excess of 20% sodium hydroxide solution for 1 hr. The product was taken up in ether, washed with 2% hydrochloric acid until acidic, washed with dilute sodium carbonate solution, dried and the ether distilled. Rectification of the residue gave 4 fractions of a liquid, b.p. 57.3° (26.5 mm.), $n^{20}\mathrm{D}$ 1.3572, d^{25}_4 1.2078, negative ceric nitrate test, which was assumed to be isomerically pure 3-ethoxy-1,1,1-trifluoro-2-propanol and was used to establish the infrared calibration curve.

Anal. Calcd. for $C_5H_9F_3O_2$: C, 37.98; H, 5.73; *MR*, 28.88. Found: C, 38.20; H, 5.68; *MR*, 28.56.

Rate of Ethanolysis of 1,1,1-Trifluoro-2,3-epoxypropane: Dilatometric Technique.—The rate of ethanolysis of 1,1,1-trifluoro-2,3-epoxypropane was studied in a dilatometer constructed by sealing an inverted 0.2-ml. pipet to the cap of a 2-ml. specific gravity bottle. Ethanol (2.00 ml.) and 1,1,1-trifluoro-2,3-epoxypropane (0.40 ml.) were brought to the bath temperature and then mixed in a test-tube with no observed temperature rise. The pycnometer bulb was filled with this reaction mixture, keeping a small column of liquid in the capillary. The tip of the pipet was covered with a rubber policeman to minimize evaporation. The reaction vessel was maintained at 25 ± 0.2° and the difference in height of the liquid column was observed with a cathetometer accurate to ±0.01 cm.

Similar experiments were run using (a) a 0.26% solution of sodium ethoxide in ethanol and (b) a 0.76% solution of sulfuric acid in ethanol. Since the reaction products from all three situations were subsequently shown to be identical, the relative rates for the three reactions are ethoxide ion catalyzed >> acid catalyzed > uncatalyzed. The rate data are summarized in Fig. 2. All runs were duplicated.

Reaction of 1,1,1-Trifluoro-2,3-epoxypropane with Lithium Aluminum Hydride.—1,1,1-Trifluoro-2,3-epoxypropane (30 g., 0.27 mole) was dissolved in 200 ml. of anhydrous ethyl ether and added dropwise to a stirred solution of 7.0 g. (0.18 mole) of lithium aluminum hydride in 400 ml. of ether under a nitrogen atmosphere at a rate sufficient to maintain constant reflux. After 1.5 hr. 50 ml. of wet ether, 20 ml. of water, 62 ml. of 50% sulfuric acid and 100 ml. of water were

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[22] D. J. Cook, O. R. Pierce and E. T. McBee, THIS JOURNAL, 76, 83 (1954).

added in sequence. The ether layer was separated and the water layer was washed with three 50-ml. portions of ether and then continuously extracted for 2 days. The ether layer and extracts were combined, dried and rectified to give 24.5 g. (80%) of 1,1,1-trifluoro-2-propanol, b.p. 76°, $n^{20}\text{D}$ 1.3160 (lit.[23] b.p. 76–77°). The product was shown by infrared analysis to be at least 99.4% pure.

Anal. Calcd. for $C_3H_5F_3O$: C, 31.58; H, 4.38. Found: C, 31.32; H, 4.48.

Reaction of 1,1,1-Trifluoro-2,3-epoxypropane with Anhydrous Ammonia.—A 100-ml., 3-necked flask was fitted with a Tru-Bore stirrer, Dry-Ice cooled condenser and addition funnel. Liquid ammonia (50 ml.) was transferred to the flask and 20 g. (0.18 mole) of 1,1,1-trifluoro-2,3-epoxypropane was added dropwise with stirring. After 0.5 hr., the excess ammonia was allowed to vaporize into a Dry-Ice cooled trap and a crystalline residue was obtained which was assumed to be a mixture of secondary and tertiary amino alcohols. After the vapor trap was allowed to warm to room temperature, there was obtained 6.22 g. (27%) of a white solid, m.p. 99°, which upon recrystallization from ether had a m.p. 98.9–99.0° and was identified as 3-amino-1,1,1-trifluoro-2-propanol.

Anal. Calcd. for $C_3H_6F_3NO$: C, 27.91; H, 4.65. Found: C, 27.92; H, 4.81.

The amine hydrochloride, m.p. 158.8–160°, was confirmed with an authentic sample prepared by Cook[22] by mixed melting point (lit. m.p. 154–155°,[22] 147–148°[24]).

Anal. Calcd. for $C_3H_7ClF_3NO$: C, 22.15; H, 3.63. Found: C, 22.20; H, 3.71.

Further confirmation of the structure of the above amino alcohol hydrochloride was obtained by mixed melting point with the hydrochloride of the product obtained from the lithium aluminum hydride[25] reduction of fluoral cyanohydrin.

Reaction of 1,1,1-Trifluoro-2,3-epoxypropane with Diethylamine.—1,1,1-Trifluoro-2,3-epoxypropane (18 g., 0.16 mole) was added dropwise to 35.3 g. (0.48 mole) of diethylamine at a rate such that gentle reflux was maintained. The mixture was held at reflux temperature for an additional 0.5 hr. and then allowed to stand at 25° for 10 hr. The mixture was rectified to give 22.9 g. (89%) of 3-diethylamino-1,1,1-trifluoro-2-propanol, b.p. 103.2° (104 mm.), $n^{20}\text{D}$ 1.3917, d^{25}_4 1.1096.

Anal. Calcd. for $C_7H_{14}F_3NO$: C, 45.41; H, 7.57. Found: C, 45.63; H, 7.74.

The hydrochloride was prepared, m.p. 126.0–126.5°, from ethyl acetate.

Anal. Calcd. for $C_7H_{15}ClF_3NO$: C, 38.00; H, 6.35. Found: C, 37.93; H, 6.70.

The N,N-diethylated product of 3-amino-1,1,1-trifluoro-2-propanol was prepared by refluxing 1.0 g. (0.008 mole) of the amino alcohol with 2.2 g. (0.02 mole) of ethyl bromide and a solution of 1.6 g. (0.04 mole) of sodium hydroxide in 10 ml. of water for 2 days. The product was extracted from the upper layer with ether, dried, the ether distilled and the residue distilled into a Dry-Ice cooled trap under reduced pressure. The crude distillate was converted into the hydrochloride by passing dry hydrogen chloride through an ether solution of the amine. After removal of solvent under reduced pressure, the product was recrystallized from ethyl acetate, m.p. 126.0–126.5°. This hydrochloride was shown by mixed melting point to be identical with the hydrochloride from the reaction of the epoxide with diethylamine. Both dialkylated products are identified as the hydrochloride of 3-diethylamino-1,1,1-trifluoro-2-propanol.

Reaction of 1,1,1-Trifluoro-2,3-epoxypropane with Magnesium Bromide.—Anhydrous magnesium bromide (0.1 mole) was prepared in ether suspension by the direct reaction of magnesium and bromine under a nitrogen atmosphere. 1,1,1-Trifluoro-2,3-epoxypropane (11.2 g., 0.1 mole) was added to the mixture and an exothermic reaction occurred which caused the ether to reflux. The mixture was maintained at reflux temperature for 1 hr., poured into ice-water and acidified with dilute sulfuric acid. The ether layer was separated, the aqueous layer was extracted with three 20-ml. portions of ether which were combined with the original ether layer and dried. The ether was removed by distillation and the residue was rectified to yield 8.9 g. of liquid, b.p. 124°, which was shown to be 3-bromo-1,1,1-trifluoro-2-propanol by comparison of the infrared spectrum with that of an authentic sample.[18]

Reaction of 1,1,1-Trifluoro-2,3-epoxypropane with Methylmagnesium Bromide.—A solution of 0.42 equivalent of methylmagnesium bromide in 190 ml. of ether was added slowly to a solution of 47 g. (0.43 mole) of 1,1,1-trifluoro-2,3-epoxypropane in 150 ml. of anhydrous ethyl ether at the temperature of refluxing ether. The reaction mixture was stirred an additional 0.5 hr. at this temperature, hydrolyzed and the product was taken up in ether and dried. The ether was distilled and the residue rectified to yield 10.2 g. (19%) of 1,1,1-trifluoro-2-butanol as indicated by comparison of boiling point and infrared spectrum with an authentic sample.[19] There was also obtained 20.6 g. (25.6%) of 3-bromo-1,1,1-trifluoro-2-propanol. There was no evidence of the presence of the other possible cleavage product, 2-methyl-3,3,3-trifluoro-1-propanol,[26] b.p. 100°. The epoxide did not rearrange to a carbonyl function prior to or in the presence of the Grignard reagent[27] as evidenced by the absence of 2-methyl-1,1,1-trifluoro-2-propanol and 4,4,4-trifluoro-2-butanol.

Reaction of 1,1,1-Trifluoro-2,3-epoxypropane with Anhydrous Hydrogen Bromide.—1,1,1-Trifluoro-2,3-epoxypropane (15 g., 0.13 mole) was added to a solution of 16 g. (0.20 mole) of anhydrous hydrogen bromide dissolved in 100 ml. of ether at a rate to maintain gentle reflux. The mixture was allowed to stand overnight and rectified to give 20.9 g. (82%) of liquid, b.p. 118–126°, $n^{19.5}\text{D}$ 1.3880 to 1.3992, which was identified by infrared spectra as 3-bromo-1,1,1-trifluoro-2-propanol.

Fluoral Cyanohydrin.—Fluoral hydrate (58 g., 0.5 mole) was added slowly to a cooled solution of 27 g. (0.55 mole) of sodium cyanide in 118 g. of water at 5° in a good fume hood followed by 200 ml. of 6 *N* sulfuric acid. The reaction mixture was allowed to warm to 25° over a 10-hr. period, and excess hydrogen cyanide was removed by bubbling a slow stream of air through the solution for 4 hr. The reddish-colored aqueous solution was extracted with three 75-ml. portions of ether which were combined and dried. The ether was removed by distillation and the residue was crudely distilled at reduced pressure. Upon redistillation there was obtained 22.8 g. (36.5%) of a liquid, b.p. 59–60° (17 mm.), $n^{20}\text{D}$ 1.3330. Upon standing in a stoppered bottle for 30 days, polymerization to a brown solid occurred

Anal. Calcd. for $C_3H_2F_3NO$: C, 28.80; H, 1.60. Found: C, 29.45; H, 1.99.

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