crystallized in 73% yield and of purity greater than 99% without further recrystallization. The soluble *N*-acetyl-D-tryptophan was racemized with acetic anhydride and again resolved. The acetyl derivative was hydrolyzed to L-tryptophan or reserved for resolution of α-phenylethylamine as needed. The diastereoisomeric (−)-amine salt crystallized from ethanol in 99% purity and 83% yield when the DL-form was mixed with 0.5 equivalent of *N*-acetyl-L-tryptophan and 0.5 equivalent of hydrochloric acid.

Our starting materials were 60.5 g. of (−)-α-phenylethylamine[7] and a plentiful supply of *N*-acetyl-DL-tryptophan and DL-α-phenylethylamine. By alternately resolving acid and base with the available quantities of each several times it was easily shown that 12.5 kg. of acetyl-L-tryptophan and 8.6 kg. of (−)-α-phenylethylamine could be realized after 17 reciprocal resolutions. Thus it is rather easy to work up to quite large scale resolutions with no initial large supply of resolving agent.[8]

These particular experiments were directed toward production of L-tryptophan. Through suitable modifications D-tryptophan and derivatives could be made equally readily, if desired.

EXPERIMENTAL

I. Resolution of acetyl-DL-tryptophan. A. Formation and separation of the diastereoisomers. Acetyl-DL-tryptophan[9] (246 g., 1.0 mole) was dissolved in 500 cc. of hot *N* KOH in 95% 3A ethanol. To the warm solution there was added 60.5 g. (0.5 mole) of (−)-alpha-phenylethylamine.[7] The solution was allowed to cool overnight at room temperature. The yield of crystalline salt [LA(−)B] was 134 g. (73%), $[\alpha]_D^{25}$ + 17.8° (C, 2 in water).[10]

B. Decomposition of the less soluble salt [LA(−)B]. The salt (134 g.) was suspended in about 250 cc. of water and about 50 cc. of benzene. The mixture was made alkaline to phenolphthalein with sodium hydroxide. The aqueous phase was separated and washed three times with 50-cc. portions of benzene. The combined benzene extracts were washed once with water which was combined with the aqueous phase.

C. Preparation of L-tryptophan. The aqueous solution of the sodium salt obtained as in Ib was adjusted with water and 3 equivalents of hydrochloric acid to be 2*N* with respect to acidity. After heating under reflux for 4 hr. the solution was decolorized with carbon and evaporated to dryness under reduced pressure. The residue was extracted with 95% 3A ethanol to separate the tryptophan hydrochloride from the sodium chloride. The alcoholic solution was neutralized with ammonium hydroxide to precipitate the L-tryptophan. This was removed by filtration, washed on the funnel with water followed by alcohol, and dried. The yield was 95%; $[\alpha]_D^{25}$ −31.2° (C, 1 in water).

D. Recovery of acetyl-L-tryptophan. The aqueous solution from Ib was decolorized with activated carbon as necessary and acidified to *p*H 3 with hydrochloric acid. About 96% of the acetyl-L-tryptophan precipitated. This was removed by filtration, washed with water and dried. $[\alpha]_D^{25}$ + 29.1° (C, 1 in H_2O + 1 equivalent NaOH).

E. Decomposition of the more soluble salt and racemization of acetyl-D-tryptophan. The alcoholic solution from Ia was evaporated to dryness and the residue dissolved in about 250 cc. of water and the salt decomposed with NaOH as in Ib. The aqueous solution was decolorized with activated carbon as necessary and 150 cc. of acetic anhydride added. The solution was seeded with *N*-aectyl-DL-tryptophan and kept at 40° overnight, whereupon acetyl-DL-tryptophan crystallized in about 92% yield. After chilling the mixture, the crystalline product was removed by filtration, washed with water, and dried. Specific rotation was zero, m.p. 205–206° (uncorr.). The yield of product was increased to 97% by combining similar filtrates and obtaining additional crops after evaporation of solvent.

II. Resolution of DL-α-phenylethylamine. *N*-Acetyl-L-tryptophan (123 g., 0.5 mole) was dissolved in 250 cc. of warm 95% 3A ethanol. To this solution there was added 0.5 mole of concentrated hydrochloric acid followed by 121 g. (1.0 mole) of DL-α-phenylethylamine (prepared from acetophenone using formamide and formic acid as described by Moore[11]). The solution was seeded and allowed to crystallize at room temperature overnight. The yield of LA(−)B salt was 151 g. (83%), $[\alpha]_D^{25}$ +17.7° (C, 2 in water).[7] The salt was decomposed as in Ia. The (−)-amine was recovered by drying the benzene extracts over sodium hydroxide pellets and distilling the benzene and amine through a short column; b.p. 185–187°, $[\alpha]_D^{25}$ −38.8° to −39.3° (without solvent) depending upon whether the salt was recrystallized before decomposition.

The more soluble material from the original alcohol filtrate was decomposed as in Ie to recover *N*-acetyl-L-tryptophan and the amine rich in the dextro-rotatory form.

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(7) We are indebted to Professor A. W. Ingersoll of Vanderbilt University for this initial supply of active amine.

(8) Although it was not investigated in this study it is also possible to obtain an initial large supply of (−)-α-phenylethylamine through the method of DeWitt and Ingersoll using easily available *N*-acetyldibromo-L-tyrosine, *J. Am. Chem. Soc.*, **73**, 5782 (1951).

(9) Purchased from the Winthrop Chemical Co.

(10) Recrystallization from water increased the specific rotation of the salt to +18.8°, which was unchanged by further crystallization. The over-all yield of salt was reduced to 64%. Unless a product of exceptional antipodal purity was desired recrystallization was normally omitted.

(11) M. L. Moore, *Org. Reactions*, **5**, 321 (1949).

Preparation of 3-(1,1,2-Trifluoro-2-chloroethoxy)propanol and Some of Its Derivatives

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Received February 28, 1958

The preparation of ethers of the general formula RO—CF_2—CX_2H where R is an alkyl radical and X is halogen or hydrogen has received a good deal of attention in recent years.[2–4] However, very little has been done in the preparation of ethers of the type, $OH(CH_2)_n$-O-CF_2CX_2H. Coffman *et al.*[5]

(1) Abstracted from a thesis submitted by J. G. Abramo in partial fulfillment of the requirements for the Ph.D. degree, University of Colorado, June 1956.

(2) J. D. Park, D. K. Vail, and J. R. Lacher, *J. Am. Chem. Soc.*, **70**, 1550 (1948).

(3) J. D. Park, C. M. Snow, and J. R. Lacher, *J. Am. Chem. Soc.*, **73**, 861 (1951).

(4) Hanford and Rigby, U. S. Patent 2,409,274 [*Chem. Abstr.*, **41**, 982 (1942)].

(5) D. D. Coffman, M. S. Rausch, G. W. Rigby, P. L. Barrick, and W. E. Hanford, *J. Org. Chem.*, **14**, 747 (1949).

have prepared $HOCH_2CH_2$-O-CF_2CF_2H by the base-catalyzed addition of ethylene glycol to tetrafluoroethylene. The diether, CF_2H-CF_2-O-CH_2CH_2-O-CF_2CF_2H was also isolated. Lawson[6] reported the preparation of $HOCH_2CH_2$-O-CF_2CFClH and Chaney[7] prepared a series of derivatives of 1,1,1,-4,4,4-hexafluorobut-2-yne with ethylene glycol and trimethylene glycol through a base-catalyzed reaction. This paper presents our findings concerning the addition of trimethylene glycol to trifl ıoro-chloroethylene and the preparation of some of its derivatives obtained thereform.

The nucleophilic addition of trimethylene glycol to chlorotrifluoroethylene has been found to proceed in the presence of potassium hydroxide under autogenous pressure. The dispersion of the olefin through the solution of potassium hydroxide and trimethylene glycol under atmospheric conditions was unsuccessful.

Two products were obtained from the pressure reaction in the form of an azeotrope—a mixture of $CFClHCF_2$-$O(CH_2)_3OH$ (I) and $CFClHCF_2$-O-$(CH_2)_3$-OCF_2CFClH (II) which was not separable by ordinary fractional distillation.

Refractive index data later indicated that the mixture had the following composition: 59 mole per cent of I and 41 mole per cent of II.

Separation was achieved by conversion of I to the benzoate followed by purification of the benzoate and subsequent saponification of the benzoate (C_6H_5-$CO_2(CH_2)_3$-O-CF_2CFClH) to the ether-alcohol. The diether II was isolated by oxidation of the azeotrope (in which the ether-alcohol is converted to the ether-acid) and distillation of the solution remaining after extraction of the acid. Another product was obtained from the oxidation mixture, namely $CFClH$-$CF_2OCH_2CH_2$-$COO(CH_2)_3OCF_2C$-$FClH$, which would be expected from the oxidation of an ether-alcohol in an acid medium.

EXPERIMENTAL

The base catalyzed addition of trimethylene glycol to trifluorochloroethylene. A gas-tight 500-ml. Parr hydrogenation bomb was charged with 153 g. (2.0 moles) of trimethylene glycol in which 56 g. (1 mole) of potassium hydroxide had been dissolved. The bomb was then cooled to −78° and charged with 230 g. (2 moles) of trifluorochloroethylene, after which it was rocked for 36 hr. at room temperature. After removal of the unreacted olefin, the bomb was opened and the contents washed with water until neutral to litmus paper, and dried over anhydrous sodium sulfate. Fractionation on a "Helipak"-packed column yielded 175 g. of product distilling at 76–77° at 7-mm. Hg pressure. This product was found to be a mixture of the monoadduct, $CFClH$-CF_2-$O(CH_2)_3$-OH (I) and the di-adduct, $CFClH$-CF_2-$O(CH_2)_3O$-CF_2CFClH (II), which was not separable by simple distillation. The refractive index of this mixture at 20° was found to be 1.3852.

3-(1,1,2-Trifluoro-2-chloroethoxy)-1-propyl benzoate. About 170 g. of the mixture of the mono- and di-ether, I and II, was treated with 120 g. of benzoyl chloride and 100 ml. of pyridine under reflux conditions for about 1 hr. The reaction mixture was washed three times with water and then three times with a 10% solution of sodium hydroxide. Distillation at 3-mm. pressure yielded two fractions with the desired benzoate distilling over at 128–129°; n_D^{20} 1.4710; d_4^{20} 1.313. Molecular refraction: Calcd. for $C_{12}H_{12}O_3F_3Cl$ 62.6. Found, 63.16.

Anal. calcd. for $C_{12}H_{12}O_3F_3Cl$: C, 48.6; H, 4.27, Cl, 12.01. Found: C, 48.79; H, 4.18; Cl, 11.96.

Saponification of $C_6H_5CO_2(CH_2)_3O$-CF_2CFClH. About 53 g. (0.2 mole) of $C_6H_5CO_2(CH_2)_3O$-CF_2CFClH and 22 g. (0.4 mole) of potassium hydroxide pellets were dissolved in 200 milliliters of 75% aqueous ethanol and refluxed for about 0.5 hr. The reaction mixture was then poured into 200 ml. of water and extracted with three 100-ml. portions of ether. The ether fractions were combined and dried over anhydrous sodium sulfate. Distillation in a helix-packed column yielded 15 g. (39%) of $CFClH$-CF_2-$O(CH_2)_3OH$ boiling at 57–58° at 3 mm. of Hg pressure. n_D^{20} 1.3916; d_4^{20} 1.379. Molecular refraction: Calcd. for $C_5H_8O_2F_3Cl$, 33.11. Found, 33.11.

Anal. Calcd. for $C_5H_8O_2F_3Cl$: C, 31.01; H, 4.15; Cl, 18.50. Found: C, 30.8; H, 4.00; Cl, 18.80.

3-(1,1,2-Trifluoro-2-chloroethoxy)propionic acid. About 39 g. of the mixture of the mono- and diether, I and II, was charged to a three-neck flask with 70 g. of magnesium sulfate and 240 ml. of water. To this mixture was added 30 g. of potassium permanganate in 300 ml. of water over a 6-hr. period with constant stirring. The stirring was continued an additional 8 hr. to ensure completeness of reaction after which time, the reaction mixture was then treated with sodium bisulfite until the color of the permanganate was discharged and the manganese dioxide allowed to settle. After filtering and washing the manganese dioxide precipitate, the aqueous solution was treated with 50% sulfuric acid until acid to litmus paper. The aqueous solution was then extracted with 4-250-ml. portions of ether and the ether extracts combined and dried over anhydrous sodium sulfate. Distillation yielded 15 g. of $CHClFCF_2$-$O(CH_2)_2COOH$ boiling at 114–115° at 7 mm. of Hg pressure. n_D^{20} 1.3953; d_4^{20} 1.477. Molecular refraction: Calcd. for $C_5H_6ClF_3O_3$, 33.33. Found, 33.55. Neutralization equivalent: Calcd., 206.6; Found, 208.

The acid-catalyzed oxidation of the mixture of I and II was carried out through the courtesy of Mr. Wayne Severson, Minnesota Mining & Manufacturing Co., St. Paul, Minn.

Isolation of $CFClHCF_2$-$O(CH_2)_2COO(CH_2)_3O$-CF_2CFClH and $CFClH$-CF_2—$O(CH_2)_3OCF_2CFClH$. After the acid had been extracted from the oxidation mixture, distillation of the organic residue gave two main fractions, the first boiling at 73–73.5° (3 mm.) and the second boiling at 136–137° (3 mm.) The physical properties and analyses of the two fractions are given.

(1) $CFClH$-CF_2-$O(CH_2)_3OCF_2CFClH$. B.p. 73–73.5°/3 mm.; n_D^{20} 1.3758; d_4^{20} 1.476. MR_D: Calcd. 47.55; Found, 48.01.

Anal. Calcd. for $C_7H_8F_6Cl_2O_2$: Cl, 23. Found: Cl, 23.1.

(2) $CFClH$-CF_2-$O(CH_2)_2COO(CH_2)_3O$—CF_2CFClH. B.p. 136–137°/3 mm.; n_D^{20} 1.400; d_4^{20} 1.460. MR_D: Calcd. 63.1; Found, 63.1.

Anal. Calcd. for $C_{10}H_{12}F_7Cl_2O_4$: C, 31.42; F, 29.85. Found: C, 31.70; F, 29.90.

Acknowledgment. We wish to express our appreciation to the Minnesota Mining & Manufacturing Co., St. Paul, Minn., and to the Monsanto Chemical Co., St. Louis, Mo., for support of this work in the form of grants-in-aid.

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