The Synthesis of 1,2,3-Cyclopropanetriamine[1]

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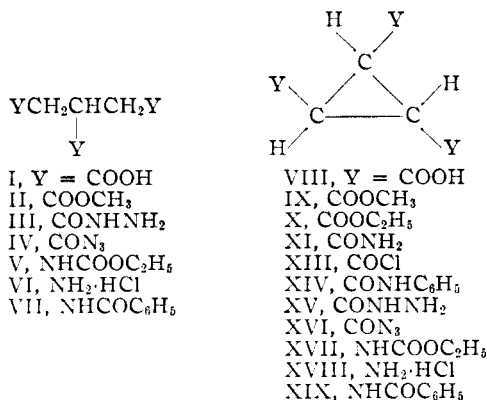
1,2,3-Cyclopropanetriamine was prepared by the degradation of ethyl trans-1,2,3-cyclopropanetricarboxylate by the Curtius reaction. It was identified through its benzoate and carbamate derivatives. Infrared spectra of the tricarbamate show that the cyclopropane ring remained intact during the degradation. Linear 1,2,3-propanetriamine was used as a model compound and ethyl 1,2,3-propanetricarbamate was prepared in analytically pure form.

Although several examples of the simultaneous degradation of more than one carboxyl or carboxylate group on the same molecule to a polyamine or amine derivative are described in the literature,[3] only one example could be found in which three carbethoxyl groups on contiguous carbon atoms had been so degraded. In 1900, Curtius and Hesse[4] described the preparation of 1,2,3-propanetriamine by the well known Curtius reaction sequence starting from esters of tricarballylic acid.

It seemed probable, in view of the latter account, that a similar reaction sequence applied to esters of trans-1,2,3-cyclopropanetricarboxylic acid would give trans-1,2,3-cyclopropanetriamine, provided the conditions of the reaction did not cause ring fission, and also provided no inversion occurred.

The work of Curtius and Hesse was repeated in order to obtain a sample of ethyl 1,2,3-propanetricarbamate which, in the earlier work, had not been prepared in pure form. At the same time, the known reaction sequence was studied to obtain optimum reaction conditions.

YCH₂CHCH₂Y
|
Y

I, Y = COOH
II, COOCH₃
III, CONHNH₂
IV, CON₃
V, NHCOOC₂H₅
VI, NH₂·HCl
VII, NHCOC₆H₅

VIII, Y = COOH
IX, COOCH₃
X, COOC₂H₅
XI, CONH₂
XIII, COCl
XIV, CONHC₆H₅
XV, CONHNH₂
XVI, CON₃
XVII, NHCOOC₂H₅
XVIII, NH₂·HCl
XIX, NHCOC₆H₅

trans-1,2,3-Cyclopropanetricarboxylic acid (VIII) was prepared initially according to the method of Ing and Perkin,[5] but it was found more convenient to prepare the ethyl ester (X) either by an adaptation of the method of Büchner,[6] or in better yields, by means of the isolable pyrazoline of Darapsky.[7]

(1) This article is taken from work done under Contract W-19-020-ORD-6436 with the Office of the Chief of Ordnance and has been approved for publication by the Public Information Division, National Military Establishment. Presented before the Division of Organic Chemistry, 121st Meeting of the American Chemical Society, Buffalo, N. Y., March 23-27, 1952.

(2) (a) Arthur D. Little, Inc., Postdoctorate Fellow, University of Virginia, 1951; (b) Arthur D. Little, Inc., Cambridge, Mass.

(3) See P. A. S. Smith, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, pp. 390-449.

(4) T. Curtius and A. Hesse, J. prakt. Chem., 62, 232 (1900).

(5) H. R. Ing and W. H. Perkin, J. Chem. Soc., 125, 1814 (1924).

(6) E. Büchner, Ber., 21, 2637 (1888).

(7) A. Darapsky, ibid., 43, 1112 (1910).

In preliminary investigations with trans-1,2,3-cyclopropanetricarboxylic acid, the trimethyl ester (IX) was prepared. When treated with ammonia, (IX) gave the triamide (XI). trans-1,2,3-Cyclopropanetricarboxylic acid did not give a triacid chloride with thionyl chloride, but rather a monoacid chloride anhydride, as proved by the formation of the dianilide (XII). With phosphorus pentachloride (VIII) yielded trans-1,2,3-cyclopropanetricarbonyl chloride (XIII) as proved by its conversion to the trianilide (XIV), the triamide (XI) and the trimethyl ester (IX).
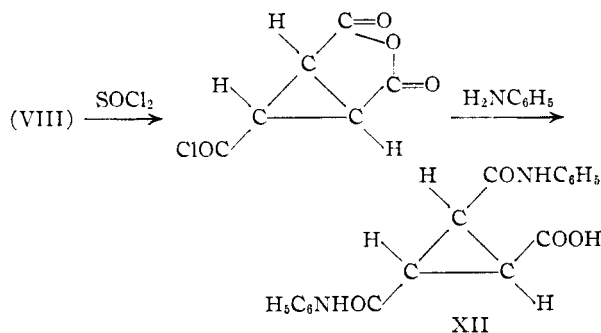
Ethyl trans-1,2,3-cyclopropanetricarboxylate (X) was treated with hydrazine hydrate (100%) in methanol solution to give trans-1,2,3-cyclopropanetricarboxylic acid trihydrazide (XV) which was then diazotized in aqueous solution containing an excess of hydrochloric acid. The triazide (XVI) was taken up in ether but not isolated. The ether was exchanged for absolute ethanol and the solution refluxed to give ethyl trans-1,2,3-cyclopropanetricarbamate (XVII). The trans configuration was assigned to the latter compound on the assumption that inversion during the rearrangement seemed unlikely, although absolute proof of configuration was not obtained. (XVII) was converted to the triamine trihydrochloride (XVIII) which proved too unstable to obtain in analytically pure condition. However, the latter compound was converted to the tribenzamide (XIX).

trans-1,2,3-Cyclopropanetricarboxamide did not undergo the Hofmann reaction, and the Schmidt reaction on trans-1,2,3-cyclopropanetricarboxylic acid gave no isolable product. It was not found feasible to apply the Curtius reaction by way of the acid chloride, acid azide, carbamate sequence owing to the difficulties of isolation in pure form of the unstable triazide.

Figure 1 shows the infrared spectra for both the linear and cyclic tricarbamate derivatives. The maxima occurring at 810, 958 and 1185 cm.⁻¹ (in 1-B) are probably perturbations of bands at
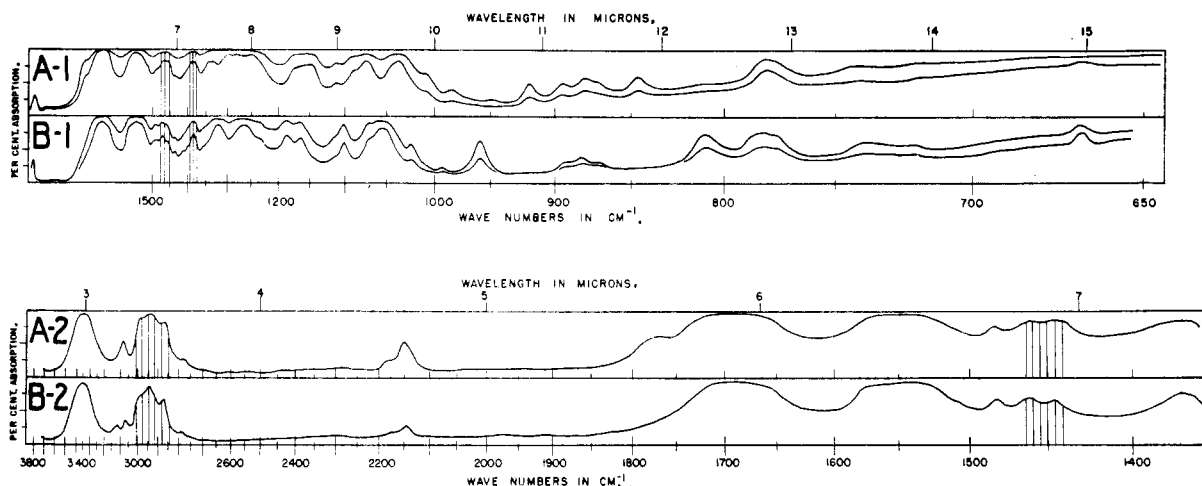
Fig. 1.—A, Ethyl 1,2,3-propanetricarbamate in mineral oil; B, ethyl *trans*-1,2,3-cyclopropanetricarbamate in mineral oil.

868, 1028 and 1189 cm.$^{-1}$, respectively, the latter having been assigned in the literature[8] as being characteristic of the cyclopropyl ring structure.

Acknowledgment.—The authors wish to thank Dr. Gilbert W. King of Arthur D. Little, Inc., for his aid in interpretation of the infrared data.

Experimental[9]

Ethyl 1,2,3-Propanetricarbamate (V).—This compound was obtained by following the general procedure of Curtius and Hesse.[4] Several recrystallizations from ethanol–water gave material melting at 109.0–109.5° (Curtius and Hesse give 91–92°).

Anal. Calcd. for $C_{12}H_{23}N_3O_6$: C, 47.20; H, 7.59; N, 13.76. Found: C, 47.76; H, 7.51; N, 13.80.

***trans*-1,2,3-Cyclopropanetricarboxylic Acid (VIII).**—The suggested procedure of Ing and Perkin[5] was followed for this material but proved quite laborious. It was found more convenient to prepare **ethyl *trans*-1,2,3-cyclopropanetricarboxylate** according to the method of Büchner[6] or, in higher yield, by the method of Darapsky.[7]

***trans*-1,2,3-Cyclopropanetricarboxamide (XI).**—Methyl *trans*-1,2,3-cyclopropanetricarboxylate (0.5 g., 0.0023 mole) was treated with 2.0 ml. of concentrated aqueous ammonia. Vigorous shaking produced a clear solution followed by almost immediate precipitation of fine, white needles. The mixture was allowed to stand for 15 minutes; the triamide was filtered and washed with two 5-ml. portions of methanol. After recrystallization from boiling water, 0.30 g. (77%) was obtained, m.p. 258–260°.

Anal. Calcd. for $C_6H_9N_3O_3$: N, 24.55. Found: N, 24.22.

Action of Thionyl Chloride on *trans*-1,2,3-Cyclopropanetricarboxylic Acid.—*trans*-1,2,3-Cyclopropanetricarboxylic acid (2.0 g., 0.012 mole) was refluxed with 100 ml. of redistilled thionyl chloride for 36 hours. After removal of excess reagent, the brown solid remaining was dissolved in boiling benzene–petroleum ether and treated with decolorizing charcoal. After filtration, the orange filtrate soon deposited yellow-white crystals melting at 87–89°. A Mohr titration for chlorine on a hydrolyzed sample (0.1049 g.) of this rather unstable material gave a value for chlorine of 18.6% (theoretical value 20.6 for the acid chloride anhydride). To 0.2 g. of the crude acid chloride anhydride was added an excess (1.0 ml.) of freshly distilled aniline in 10 ml. of benzene. A yellow solid separated immediately. The semi-crystalline material was washed with dilute hydro-

chloric acid and recrystallized three times from ethanol–water. The pure white crystals melted at 236–239°.

Anal. Calcd. for $C_{18}H_{16}N_2O_4$ (dianilide, XIII): N, 8.64. Found: N, 8.84.

***trans*-1,2,3-Cyclopropanetricarbonyl Chloride (XIV).**—Using the method of Emery,[10] *trans*-1,2,3-cyclopropanetricarboxylic acid (10.0 g., 0.0574 mole) and phosphorus pentachloride (37.0 g., 0.178 mole) were mixed in a small flask fitted with a reflux condenser. A spontaneous reaction took place, the flask warmed, hydrogen chloride fumes were evolved and a yellow solution formed. The mixture was warmed on the steam-bath for three hours, and then distilled. The distilland, *trans*-1,2,3-cyclopropanetricarbonyl chloride (8.6 g., 65%) boiled at 90–93° at 0.9 mm. When several drops of the acid chloride were added to an excess of ammonium hydroxide, a precipitate formed immediately. Recrystallized from hot water, the product melted at 262°. A mixture melting point with the triamide obtained from methyl *trans*-1,2,3-cyclopropanetricarboxylate was 262–264°. With methanol, a sample of the acid chloride gave methyl *trans*-1,2,3-cyclopropanetricarboxylate, as proved by an undepressed mixture melting point with the authentic ester.

***trans*-1,2,3-Cyclopropanetricarboxanilide (XV).**—*trans*-1,2,3-Cyclopropanetricarbonyl chloride (0.5 g.) was dropped into a solution of 1.5 g. of redistilled aniline in ether. A white precipitate formed with considerable evolution of heat. After the reaction subsided, the product was filtered and washed with ethanol. Recrystallization from a large amount of ethanol gave a product melting at 313–315°.

Anal. Calcd. for $C_{24}H_{21}N_3O_3$: N, 10.52. Found: N, 10.58.

***trans*-1,2,3-Cyclopropanetricarboxylic Trihydrazide (XVI).**—Ethyl *trans*-1,2,3-cyclopropanetricarboxylate (40.0 g., 0.156 mole) was diluted with 40 ml. of methanol. Hydrazine hydrate (100%, Fairmont Chemical Co.) (24.0 ml., excess of 0.458 mole) was added, the flask was stoppered with a foil-covered cork and allowed to stand at room temperature. After one-half hour, the mixture warmed and crystallization of the product began. The reaction was complete at the end of an hour. Filtration and drying gave 32.5 g. (96%) of white crystalline product. An analytical sample, m.p. 203–205°, was prepared by four recrystallizations from an ethanol–water mixture.

Anal. Calcd. for $C_6H_{12}N_6O_3$: N, 38.86. Found (after drying to constant weight at 100° in vacuum): N, 39.13.

Ethyl *trans*-1,2,3-Cyclopropanetricarbamate (XVIII).—A solution of *trans*-1,2,3-cyclopropanetricarboxylic trihydrazide (25.0 g., 0.116 mole) in 150 ml. of water was stirred rapidly in a flask surrounded by an ice–salt-bath. Concentrated hydrochloric acid (30 ml., slight excess of 0.348 mole) was added through a dropping funnel during one-half hour. Ether (200 ml.) was added, then a solution of 25.0 g. (slight excess of 0.348 mole) of sodium nitrite in 100 ml. of water

(8) G. Herzberg, "Infra Red & Raman Spectra of Polyatomic Molecules," D. Van Nostrand Co., Inc., New York, N. Y., 1945, p. 352; G. W. King, R. T. Armstrong and L. Harris, THIS JOURNAL, **58**, 1580 (1936).

(9) All boiling points and melting points are corrected. Microanalyses by Clark Microanalytical Laboratory, Urbana, Illinois.

(10) W. D. Emery, *Ber.*, **22**, 2929 (1889).

was added dropwise over one-half hour at a temperature under 5°. The yellow ether layer was carefully separated and washed with dilute sodium carbonate solution and finally with water. The aqueous solution was extracted with two 100-ml. ether portions which were washed with sodium carbonate solution and water. The combined ether extracts were allowed to stand at 7° over anhydrous sodium sulfate for one hour with occasional shaking, then over fresh sodium sulfate for three hours at 0–5°. A second drying with Drierite did not appreciably increase the final yield while lengthening of the drying time decreased the yield. A small amount of the ether solution was evaporated on a watch glass leaving the triazide (XVII) as a clear oil which could not be crystallized. This oil exploded violently when touched to a hot-plate (300°) and decomposed rapidly without explosion at 90–100°. The dried ether solution of XVII was added to 200 ml. of freshly prepared absolute ethanol and the ether was removed on the steam-bath. The ethanol solution was refluxed until all nitrogen evolution ceased (6 hours). After decolorizing with Norit, and reducing the volume of the ethanol solution to 100 ml., an equal amount of water was added and the solution was allowed to stand overnight at 0–5°. Lower temperatures caused oiling of the product. The yield was 4.1 g., m.p. 150–153°. Further evaporation and cooling of the mother liquor gave an additional 2.0 g. Approximately 6.0 g. of a thick, clear sirup was recovered from the mother liquor

from which additional small amounts of carbamate crystallized over a long period. The yield of crude, sirupy material was 34% (17.5% of carbamate melting at 150–153°). Recrystallization of the latter from ethanol–water gave white needles melting at 160–162°. This material did not decolorize bromine in carbon tetrachloride or potassium permanganate solution.

Anal. Calcd. for $C_{12}H_{21}N_3O_6$: C, 47.52; H, 6.98; N, 13.98. Found: C, 47.45; H, 6.98; N, 13.86.

trans-1,2,3-Tribenzamidocyclopropane (XX).—Ethyl *trans*-1,2,3-cyclopropanetricarbamate (1.0 g., 0.0033 mole) was hydrolyzed with concentrated hydrochloric acid for 8 hours. After decolorizing, the aqueous solution was extracted with ether, then evaporated to dryness. Approximately 0.3 g. (40–50%) of the crude triamine hydrochloride (XIX) melting at 185–195° with considerable decomposition, was obtained. This material could be recrystallized from ethyl acetate and ethereal hydrogen chloride (m.p. 190–195° (dec.)) but analyses were unsatisfactory. To a sample of the material (0.2 g.) in 2.0 ml. of 20% sodium hydroxide solution was added excess benzoyl chloride. The white flocculent solid (0.3 g., 75%) was recrystallized five times from 95% ethanol. The melting point was 288–290°.

Anal. Calcd. for $C_{24}H_{21}N_3O_3$: C, 72.13; H, 5.30; N, 10.52. Found: C, 71.85; H, 5.25; N, 10.59, 10.51.

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Physical Constants and Infrared Spectra of a Homologous Series of Dialkyl Sebacates

BY WILLIAM H. STAHL AND HELMUT PESSEN

The 18 diesters of sebacic acid with normal alcohols from methyl to octadecyl were prepared. Melting points, densities and refractive indices are given and the characteristics of the infrared absorption spectra are briefly discussed.

The compounds representing the homologous series of di-*n*-alkyl sebacates (dialkyl decanedioates) were synthesized primarily for use as substrates for the growth of certain bacteria and fungi as part of a study of the microbiological degradation of plasticizers.[1] Available data on these esters are scant; with the exception of di-*n*-octyl sebacate,[2] no physical constants for the esters above di-*n*-propyl sebacate appear in the literature. Although the first three members of the series have been described before, they are included here for the sake of completeness.

Experimental

Tridecyl, pentadecyl, hexadecyl, heptadecyl and octadecyl alcohols[3] were generously donated by Dr. E. Emmett Reid of Johns Hopkins University; nonyl alcohol was furnished by Dodge and Olcott, New York, with a specification of 98% purity, $n^{20}D$ 1.4340; tetradecanol was donated by Armour and Co., with a specification of 99% purity, m.p. 37.7°; hexyl alcohol was redistilled Eastman Kodak Co. technical grade, using the fraction boiling between 155–156°; all other alcohols were Eastman "white label" grade; methyl, ethyl and propyl were redistilled and all others used without further purification.

The sebacates were prepared by esterification of sebacic acid (Eastman "white label," recrystallized three times, m.p. 133.5°), with the appropriate alcohol in the presence of *p*-toluenesulfonic acid as catalyst. The crude product was dissolved in ether and thoroughly washed with 10% sodium bicarbonate. Those esters up to di-*n*-nonyl inclusive were distilled *in vacuo*, while the higher ones were further purified by repeated crystallization from acetone until

successive crops showed constant melting point. A further purification of all products was achieved by chromatographing them as ether solutions through a column packed with freshly activated adsorbents. For adsorption of acidic impurities, anhydrous alumina was used; for alcohols, silica gel; and for color and odor, fuller's earth. The liquid esters were finally subjected to a high vacuum for several hours to remove any remaining traces of solvent. All resulting products showed an acid number < 0.05.

Melting points of the esters up to di-*n*-nonyl inclusive were taken by freezing in a test-tube containing a narrow range thermometer, stirring constantly upon partial melting, and noting the melting point at the disappearance of the last crystal. Melting points of the esters above di-*n*-nonyl were taken by means of a calibrated Kofler micro hot-stage melting-point apparatus.

Results and Discussion

The esters up to and including di-*n*-nonyl sebacate at room temperature were colorless liquids of relatively low viscosity and with boiling points above 290°. The higher esters were white waxy crystalline solids.

Melting points and carbon–hydrogen analyses for the eighteen sebacates are listed in Table I. It is pertinent to point out that if these melting points are plotted as a function of carbon atoms in the alkyl radical, the curve is comparable to one obtained for the corresponding adipates (hexanedioates) by Feagan and Copenhaver,[4] which exhibited a definite alternation in melting point values between odd and even alkyls. In the present case the same general phenomenon is noticeable, particularly above C_{11}. A curve of the values for odd-

(1) W. H. Stahl and H. Pessen, *Applied Microbiology*, in press.

(2) J. T. Davies, *Trans. Faraday Soc.*, **44**, 909 (1948).

(3) J. D. Meyer and E. E. Reid, THIS JOURNAL, **55**, 1574 (1933).

(4) R. A. Feagan and J. E. Copenhaver, *ibid.*, **62**, 869 (1940).