tube which could be constricted by means of a pinch clamp. The apparatus was adjusted to deliver formalin solution at the prescribed rate and provided a very convenient method of accurately controlling the rate of addition.

The reaction mixture was stirred by means of the magnetic stirrer and held at the specified temperature for the required time. During the entire experiment the evolution of carbon dioxide was followed volumetrically using a "wet-test meter". The reaction mixture was then treated with 50 ml. of concentrated hydrochloric acid and 100 ml. of liquid was distilled from the mixture. The residue was made strongly basic with a 50% solution of sodium hydroxide and this mixture was fractionally distilled through a 3-ft. bubble-cap column which was equipped with a reflux head set at a reflux ratio of ten to one. The yield of secondary and tertiary amine and the amount of recovered primary amine was determined from a plot of the boiling point and refractive index of the distillate.

t-Butyldimethylamine is obtained as an azeotrope with water (86.3% amine, 13.7% water) under these conditions. The composition of the azeotrope (b.p. 76°, d_4^{25} 0.771) was determined by titration, vapor phase chromatography (Perkin-Elmer, Column Material "F"), and density. The pure *t*-butyldimethylamine could be obtained by distillation of the azeotrope from solid sodium hydroxide.

t-Butyldimethylamine. The described general procedure was used. Optimum conditions were: a 4:1 molar ratio of formic acid to amine, a 2.5:1 molar ratio of formaldehyde, a reaction temperature of 90–100°, and a reaction time of 2 hr. These conditions gave a 95% yield of product[6,10] b.p. 89°, n_D^{25} 1.4015, d_4^{25} 0.735, MR_D calcd.: 33.86. Found: 33.49. The melting point of the quaternary ammonium salt, *t*-butyltrimethylammonium iodide, m.p. 225–226° (with decomposition) agrees with the value previously reported.[10]

t-Butylmethylamine. The described general procedure was followed. Experimental conditions which gave the best yield were: A 3:1 molar ratio of formic acid to amine, a 1.25:1 molar ratio of formaldehyde, a reaction temperature of 50°, and a reaction time of 6 hr. The product[10] was obtained in 60% yield and 46% conversion; b.p. 69°, n_D^{25} 1.393, d_4^{25} 0.727, MR_D calcd.: 28.89%. Found: 28.61.

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[CONTRIBUTION FROM INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE]

Studies in Dieckmann Cyclization. I. Cyclization of Triethyl Pentane-1,2,5-tricarboxylate[1]

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Received January 10, 1958

Dieckmann cyclization of triethyl pentane-1,2,5-tricarboxylate has been shown to give diethyl cyclohexanone-2,3-dicarboxylate.

In connection with a research project on the synthesis of diterpenoid resin acids, in progress in this laboratory for some years, it became necessary to undertake the study of the Dieckmann cyclization of triethyl pentane-1,2,5-tricarboxylate (I).

Dieckmann cyclization of triethyl pentane-1,2,5-tricarboxylate was studied by Perkin and coworkers.[2] It was proved by them that a six-membered ring was formed in preference to a five-membered one, since the product of cyclization on hydrolysis furnished cyclohexanone-3-carboxylic acid. They did not, however, establish whether the intermediate β-keto ester had structure IIa or IIb representing the two possible modes of cyclization.

From a consideration of the inductive effect of substituents in the β-position on an α-methylene group Chakravarti[3] predicted that the cyclization of I should predominantly proceed *via* the route A rather than *via* B or C, resulting in the product IIa. Our results corroborate this view.

Triethyl pentane-1,2,5-tricarboxylate employed in these studies was prepared by two different methods. In the first method ethyl cyclopentanone-2-carboxylate was condensed with ethyl chloroacetate in benzene to produce diethyl cyclopentanone-2-acetate-2-carboxylate which, on being subjected to ring fission with catalytic amount of sodium ethoxide in ethanol, furnished the tri-ester (I). In the second method ethyl chloroacetate was condensed with diethyl sodiomalonate resulting in the formation of diethyl 1-carbethoxysuccinate. The succinic ester derivative was further condensed with ethyl γ-bromobutyrate to yield tetraethyl pentane-1,2,2,5-tetracarboxylate (IV). The tetra-

(1) Taken from the thesis submitted by Kalyanmay Sen for the degree of Doctor of Philosophy (Science) of the University of Calcutta, April 1957. A preliminary communication on this subject appeared in *Science and Culture*, **19**, 312 (1953).

(2) M. E. Dobson, J. Ferns, and W. H. Perkin, *J. Chem. Soc.*, **95**, 2010 (1909).

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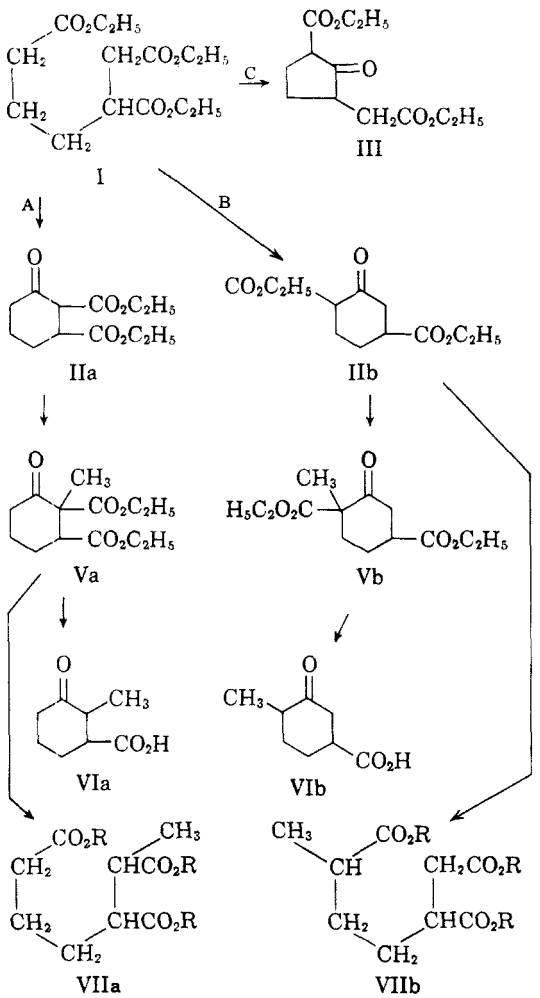
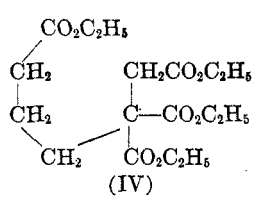


ester (IV) on hydrolysis with concentrated hydrochloric acid and subsequent esterification furnished I.



(IV)

Diekmann cyclization of I was conducted in benzene solution using 1.2 atoms of pulverized sodium. The course of cyclization was deduced from the following experiments.

The Dieckmann product was methylated *in situ* with methyl iodide. A portion of the methylated product was hydrolyzed directly with 25% hydrochloric acid whereupon an acid of m.p. 97° was formed[4] which was found to be identical with an authentic specimen of 2-methylcyclohexanone-3-carboxylic acid (VIa) through mixed m.p. determination and comparison of derivatives. Alternative method of cyclization of I would have led to the formation of 2-methylcyclohexanone-5-carboxylic acid (VIb).

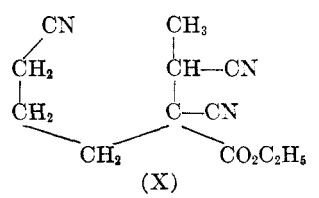
(4) O. Baudisch and W. H. Perkin, *J. Chem. Soc.*, **95**, 1886 (1909).

The above results indicate that the cyclization of I proceeded through the route A. Further confirmation of this fact was obtained by subjecting the methylated product to ring fission with a catalytic amount of sodium ethoxide in ethanol. The triester so obtained on being hydrolyzed with concentrated hydrochloric acid furnished a gum which on trituration with dioxane gave crystals melting at 145° after two crystallizations from ethyl acetate. This acid was found to be identical with 1-methylpentane-1,2,5-tricarboxylic acid (VIIa, R = H), synthesized by an unambiguous method. 1-Methylpentane-1,4,5-tricarboxylic acid (VIIb, R = H) which should have resulted had the cyclization proceeded along route B was also synthesized for comparison and was found to possess quite different properties.

Our results clearly show that the cyclization of triethyl pentane-1,2,5-tricarboxylate in benzene proceeded predominantly *via* route A and that the by-product, if any, is formed only in minor amounts.

Certain compounds were synthesized and employed for comparison purposes. 2-Methylcyclohexanone-3-carboxylic acid (VIa) was prepared by converting 2-methylcyclohexanone to 2-methyl-2-cyclohexenone (VIII)[5] *via* pyridine-catalyzed dehydrochlorination of 2-methyl-2-chlorocyclohexanone, the addition of hydrogen cyanide to VIII, and hydrolysis of the keto nitrile.

1-Methylpentane-1,2,5-tricarboxylic acid (VIIa, R = H) was prepared in the following way. Ethyl α,β-dicyanobutyrate, synthesized by a convenient procedure developed in this laboratory,[6] was con-



(X)

densed with γ-bromobutyronitrile. The resulting ethyl 1-methyl-1,2,5-tricyanopentane-2-carboxylate (X) was hydrolyzed with concentrated hydrochloric acid. The triacid formed was purified through the triester (VIIa, R = C_2H_5).

1-Methylpentane-1,4,5-tricarboxylic acid (VIIb, R = H) was prepared as follows. Ethyl 2-methylcyclopentanone-2-carboxylate was subjected to ring fission by treatment with a catalytic amount of sodium ethoxide in ethanol to give diethyl 1-methylbutane-1,4-dicarboxylate. The latter was cyclized with sodium dust in benzene and the product was condensed *in situ* with ethyl bromoacetate giving diethyl 5-methylcyclopentanone-2-acetate-2-carboxylate.[7] This on being subjected to

(5) E. W. Warnhoff and W. S. Johnson, *J. Am. Chem. Soc.*, **75**, 494 (1953).

(6) K. Sen and P. Bagchi, *J. Org. Chem.*, **20**, 845 (1955).

(7) A. E. Bradfield, E. M. Frances, A. R. Penfold, and J. L. Simonsen, *J. Chem. Soc.*, 1619 (1936).

ring fission with catalytic amount of sodium ethoxide in ethanol furnished triethyl 1-methylpentane-1,4,5-tricarboxylate (VII,R = C_2H_5) which gave 1-methylpentane-1,4,5-tricarboxylic acid (VIIb,R = H) on hydrolysis with the concentrated hydrochloric acid.

EXPERIMENTAL

(All melting points and boiling points are uncorrected).

Triethyl pentane-1,2,5-tricarboxylate (I). *A. From diethyl cyclopentanone-2-carboxylate-2-acetate.* To a solution of sodium ethoxide (0.53 g. sodium and 15 ml. ethanol) was added the diester (55 g.). The mixture at once became deep wine red and heat was evolved. It was heated on a water bath for 2 hr. To the cooled solution was added glacial acetic acid (1 ml.) and water. A nearly colorless oil separated which gave a color reaction with ethanolic ferric chloride indicating the presence of a trace of β-ketoester. It was extracted with benzene and the benzene layer was washed thoroughly with 5% sodium hydroxide solution and then with water. After removing benzene an oil was obtained which distilled at 162–163°/5 mm. (54.2 g., 82.8%), n_D^{28} 1.4373. The product did not show a ferric chloride test.

Anal. Calcd. for $C_{14}H_{24}O_6$: C, 58.33; H, 8.33. Found: C, 58.56; H, 8.45.

B. Unambiguous synthesis. To a solution of sodium ethoxide (2.3 g. sodium and 40 ml. ethanol) was added diethyl α-carbethoxysuccinate (24.6 g., b.p. 140°/7 mm., prepared in 65% yield from diethyl sodiomalonate and ethyl chloroacetate) followed immediately by ethyl γ-bromobutyrate (23 g., prepared in almost quantitative yield from γ-butyrolactone by the action of hydrogen bromide in ethanol solution). After refluxing until neutral (18 hr.) water was added and the precipitated oil was taken up in ether. The ether extract was washed and dried. After removal of ether and distillation of the residual oil, tetraethyl pentane-1,2,2,5-tetracarboxylate (IV) (19 g., 50.4%) b.p. 155°/0.4 mm. was obtained.

Anal. Calcd. for $C_{17}H_{28}O_8$: C, 56.66; H, 7.77. Found: C, 56.29; H, 7.62.

The above ester (16.4 g.) and concentrated hydrochloric acid (60 ml.) were refluxed over an oil bath for 18 hr. The resulting clear solution was evaporated, dried, and subjected to esterification with 5% ethanolic sulfuric acid (75 ml.). After addition of water the oil was extracted with ether, washed successively with water, saturated sodium bicarbonate solution, and finally with water. After drying and removal of solvent the product triethyl pentane-1,2,5-tricarboxylate distilled at 162–163°/5 mm. (9.4 g., 72%).

Anal. Calcd. for $C_{14}H_{24}O_6$: C, 58.33; H, 8.33. Found: C, 58.42; H, 8.32.

Cyclization of triethyl pentane-1,2,5-tricarboxylate (I). The triester (52 g.) was heated with sodium dust (5 g.) in benzene (170 ml.) in a nitrogen atmosphere for 3 hr. The contents became wine red colored, sodium being completely dissolved. The product was decomposed with ice cold hydrochloric acid (1:1, 60 ml.). The water layer was extracted once with benzene and the total benzene solution was washed thrice with water. The solvent was removed and the product (IIa) distilled at 130–135°/3 mm. (31.7 g., 72.5%), n_D^{29} 1.4637.

Anal. Calcd. for $C_{12}H_{18}O_5$: C, 59.5; H, 7.4. Found: C, 59.8; H, 7.2.

Methylation of the ester (IIa). To a well cooled suspension of sodium dust (3 g.) in benzene (175 ml.) was added the above cyclized ester (28.7 g.) dropwise in 10 min. and the mixture was refluxed. A deep red solution of the sodiosalt was formed. Methyl iodide (12 ml.) was added to the solution and slow heating was continued. Sodium iodide appeared within 5 min. Refluxing was continued until the solution became neutral. Water was added and the benzene layer was separated and washed thoroughly with water and the solvent was removed. The product (Va) distilled at 142–144°/3.5 mm. (24.6 g., 81%), n_D^{31} 1.4567.

Anal. Calcd. for $C_{13}H_{20}O_5$: C, 60.94; H, 7.81. Found: C, 61.28; H, 7.84.

Hydrolysis of the ester (Va). The above ester (3 g.) was boiled with 25% hydrochloric acid (75 ml.) for 21 hr. over an oil bath. The contents were filtered and the filtrate evaporated. The residue was subjected to evaporative distillation at 165–170°/1.5 mm. An oil was deposited which solidified to a hygroscopic solid m.p. 97°. Mixed melting point with an authentic sample of 2-methylcyclohexanone-3-carboxylic acid gave no depression. Semicarbazone m.p. 204° (lit.[4] 204°). The 2,4-dinitrophenylhydrazone, m.p. 209°, was crystallized twice from alcohol.

Anal. Calcd. for $C_{14}H_{16}O_6N_4$: N, 16.66. Found: N, 16.48.

Ring fission of the ester (Va). The ester (24.1 g.) was treated with an ice cold solution of sodium ethoxide (0.216 g. sodium and 7 ml. ethanol). The product was isolated in the usual way and distilled at 146°/0.6 mm. (27.7 g., 97.5%), n_D^{31} 1.4358.

Anal. Calcd. for $C_{15}H_{26}O_6$: C, 59.60; H, 8.61. Found: C, 59.60; H, 8.24.

The above ester (5 g.) was hydrolyzed with concentrated hydrochloric acid (30 ml.) for 40 hr. The oily acid initially obtained on trituration with dioxane gave a solid which crystallized from ethyl acetate, m.p. 145°. Mixed m.p. with authentic 1-methylpentane-1,2,5-tricarboxylic acid (VIIa, R = H) showed no depression.

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.54; H, 6.42. Found: C, 49.61; H, 6.91.

Triethyl 1-methylpentane-1,4,5-tricarboxylate (VIIb, R = C_2H_5). Diethyl 5-methylcyclopentanone-2-acetate-2-carboxylate (23 g.) was treated with ice cold sodium ethoxide (0.21 g. sodium and 8.2 ml. ethanol) and the product was isolated in the usual manner. It distilled at 166–168°/2 mm. (21.2 g., 78.1%), n_D^{31} 1.4348.

Anal. Calcd. for $C_{15}H_{26}O_6$: C, 59.60; H, 8.61. Found: C, 59.94; H, 8.20.

The above ester (5 g.) was hydrolyzed with concentrated hydrochloric acid (50 ml.) for 25 hr. 1-Methylpentane-1,4,5-tricarboxylic acid (VIIb, R = H) was crystallized from glacial acetic acid m.p. 97°.

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.54; H, 6.42. Found: C, 49.64; H, 6.65.

Ethyl 1-methyl-1,2,5-tricyanopentane-2-carboxylate (X). To an ice cold solution of sodium ethoxide prepared from sodium (2.73 g.) and ethanol (42 ml.) was added ethyl α,β-dicyanobutyrate (18.6 g.). Instantaneously a thick reddish solution was formed and the mixture was kept in ice cold water for 10 min. γ-Bromobutyronitrile (18.3 g.) was added and the mixture was refluxed for 22 hr. until it became neutral to litmus. Water was then added and the separated oil was taken up in benzene. After washing the benzene solution with water the solvent was removed and the residual oil was distilled at 224–228°/4 mm. (17.9 g., 68.9%), n_D^{31} 1.4593.

Anal. Calcd. for $C_{12}H_{15}N_3O_2$: C, 61.80; H, 6.43. Found: C, 61.48; H, 6.50.

Triethyl 1-methylpentane-1,2,5-tricarboxylate (VIIa, R = C_2H_5). The trinitrile (X, 20 g.) was refluxed with concentrated hydrochloric acid (150 ml.) for 24 hr. The solution was evaporated over a water bath and extracted with ether. The ether solution was dried and the solvent was removed. The crude residual oil was dried carefully under vacuum and was refluxed with a mixture of ethanol (60 ml.) and concentrated sulfuric acid (8 ml.) for 34 hr. Water was added and the precipitated oil was extracted with ether. The ethereal solution was washed with sodium bicarbonate solution, dried, and evaporated. The residual oil distilled at 162–164°/3.5 mm. (15.1 g., 58.2%), n_D^{31} 1.4358.

Anal. Calcd. for $C_{15}H_{26}O_6$: C, 59.60; H, 8.61. Found: C, 59.59; H, 8.34.

The above ester (5 g.) was hydrolyzed to 1-methylpentane-1,2,5-tricarboxylic acid (VIIa, R = H) by boiling with 60 ml. concentrated hydrochloric acid for 30 hr. The solution on evaporation produced an oil which solidified on keeping for some days and was finally crystallized twice from ethyl acetate, m.p. 145°.

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.54; H, 6.42. Found: C, 49.61; H, 6.91.

2-Methyl-3-cyanocyclohexanone (IX). To an ethanolic solution of 2-methyl-2-cyclohexenone (16.7 g.) in a three necked flask fitted with a stirrer, a solution of sodium cyanide (6.4 g.) in water (20 ml.) was added with stirring. A reddish color developed which gradually intensified to wine red coloration. A slight rise in temperature was observed. After about 0.5 hr. a mixture of concentrated hydrochloric acid (6.9 ml.) and water (15 ml.) was added to this solution during 40 min., whereupon a light yellow oil separated. It was poured into a mixture of concd. hydrochloric acid (15 ml.) and water (200 ml.) and the oil was extracted with ether. The ether solution was dried and evaporated and the residual oil was distilled at 120°/3.5 mm. (5.2 g., 25%), n_D^{32} 1.4669.

Anal. Calcd. for $C_8H_{11}NO$: C, 70.07; H, 8.03. Found: C, 69.55; H, 8.36.

2-Methylcyclohexanone-3-carboxylic acid (VIa). The above nitrile (IX, 2.5 g.) was boiled first with concd. hydrochloric acid and then with a 20% solution of potassium hydroxide at 150–160° for 20 hr. The resultant solution was acidified and then extracted with ether. The ethereal solution after drying and evaporation gave an oil which on sublimation at 167°/0.2 mm. produced a solid acid, m.p. 97° (lit.[4] m.p. 97°).

The dinitrophenylhydrazone, crystallized from ethanol, m.p. 210°.

Anal. Calcd. for $C_{14}H_{16}N_4O_6$: N, 16.66. Found: N, 16.48.

Acknowledgment. We are grateful to Dr. P. C. Dutta, head of the Department of Organic Chemistry, Indian Association for the Cultivation of Science, for his active interest during the course of this investigation.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, CASE INSTITUTE OF TECHNOLOGY]

Reaction of *N*-Bromosuccinimide with Dihydropyran

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Received January 14, 1958

Products identified from the reaction of *N*-bromosuccinimide with dihydropyran were 3-bromo-5,6-dihydro-4*H*-pyran, 2,3-dibromotetrahydropyran, and both geometrical isomers of 2-succinimidyl-3-bromotetrahydropyran. A polar mechanism is indicated in which a positive bromine from *N*-bromosuccinimide first adds at the 3-position of dihydropyran to form a reactive intermediate which can either lose a proton or add a negative group to give the observed products. A small acceleration of rate in the presence of oxygen or peroxide suggests that a free-radical reaction is also involved to some extent. No product of direct alpha methylenic substitution on dihydropyran was obtained. The polarizing effect of the oxygen alpha to the double bond is considered to increase the nucleophilic character and thus favor a polar mechanism.

N-Bromosuccinimide can undergo either a homolytic dissociation to free radicals or a heterolytic dissociation to give a positive halogen. The reaction most often observed with this reagent and simple olefins[1] is an alpha substitution of bromine by a free-radical mechanism. In addition to these allylic brominations, there have been a number of examples of addition to the double bond. In some cases[2] where reactions were accelerated by peroxides, the addition would appear to proceed by a free-radical mechanism. Other examples are reported where addition leading to the corresponding dibromide is promoted by the presence of inorganic salts[3,4] and alkyl ammonium salts.[4] Bailey and Bello[3] report that whereas *N*-bromosuccinimide brominates crotonitrile in the allylic position, allylic bromination is inhibited by an electron-withdrawing group attached directly to the alpha carbon.

The presence of an electron-releasing group adjacent to a double bond should increase the tendency toward reaction by a polar mechanism with an electrophyllic reagent such as a positive halogen. Dihydropyran was selected for study as an example of such a compound which also contains an alpha methylene group. The object of the investigation was thus to see whether *N*-bromosuccinimide would react with this compound to give allylic bromination by a free-radical mechanism or attack on the double bond by a polar mechanism.

Previous studies of the reaction of *N*-bromosuccinimide with dihydropyran (I) have been reported to yield tars[5] and an addition product, 2-succinimidyl-3-bromotetrahydropyran VI.[6]

Discussion. *N*-Bromosuccinimide reacted with I to give a mixture of products which appeared as a very viscous, clear residue when solvent was removed. Attempts to distil the products gave only small amounts of I and a mixture of 3-bromo-5,6-dihydro-4*H*-pyran (II) and 2,3-dibromotetrahy-

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(2) P. L. Southwick, L. A. Pursglove, and P. Numerof, *J. Am. Chem. Soc.*, **72**, 1600, 1604 (1950).

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