of 78% of pure crystalline levoglucosan was isolated from the aqueous filtrate by usual manipulations.

2,4,6-Tribromophenyl β-D-Xylopyranoside Triacetate.—It was prepared by the procedure used for its glucose analog and the yield was 75%. After recrystallization from three parts of ethanol, the substance melted at 129–131° and showed $[\alpha]^{20}\text{D}$ −66° (*c*, 0.8 in chloroform).

Anal. Calcd. for $C_{17}H_{17}O_8Br_3$: C, 34.66; H, 2.89. Found: C, 34.80; H, 2.93.

2,4,6-Tribromophenyl β-D-Xyloside (IV).—Deacetylation of the triacetate with ammoniacal methanol resulted in a nearly quantitative yield of the free xyloside. When recrystallized twice from forty parts of ethanol, the substance formed large prisms of m. p. 182–183° and showed $[\alpha]^{20}\text{D}$ −57° (*c*, 0.8 in pyridine).

Anal. Calcd. for $C_{11}H_{11}O_5Br_3$: C, 28.54; H, 2.40. Found: C, 28.68; H, 2.49.

Reaction of 2,4,6-Tribromophenyl β-D-Xylopyranoside with Sodium Methoxide.—Treated as has been described in the case of the glucose analog, 5 g. of this xyloside gave tribromophenol in 98% yield and methyl β-D-xylopyranoside in 96% yield, identified by its m. p., mixed m. p., crystalline habit (prisms) and specific rotation, ($[\alpha]^{20}\text{D}$ −63.3° in water).

Summary

Fischer and Strauss[1] found that tribromophenyl β-D-glucopyranoside is very labile in alkaline solution, splitting off tribromophenol and, in their opinion, generating D-glucose. Present study of the glucoside shows that levoglucosan rather than D-glucose is formed in high yield in aqueous barium hydroxide solution. The reaction of the glucoside in methanol solution with sodium methoxide produces tribromophenol (100%), methyl β-D-glucopyranoside (21%) and levoglucosan (75%), with retention of configuration for both carbohydrates. Tribromophenyl β-D-xyloside yields similarly methyl β-D-xylopyranoside (96%) and tribromophenol (98%); in aqueous barium hydroxide the aryl xyloside yields tribromophenol; apparently the xylose moiety suffers alkaline decomposition since the solution soon develops much color.

BETHESDA, MARYLAND RECEIVED SEPTEMBER 30, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Synthesis of Bicyclo[4.2.0]octane-7,8-diol, A Derivative of "Cycloöctatetraene Dichloride"[1]

BY ARTHUR C. COPE AND ELBERT C. HERRICK

One of the reactions of cycloöctatetraene which is reported to proceed with rearrangement and yield a derivative of bicyclo[4.2.0]octane is the addition of chlorine.[2] Part of the evidence supporting this conclusion consisted in conversion of the dichloride to a diacetate, which was converted to bicyclo[4.2.0]octane-7,8-diol (III, whether *cis* or *trans* was not determined) by hydrogenation followed by hydrolysis. The structure of III was established by oxidation to *cis*-hexahydrophthalic acid, and cleavage with lead tetraacetate to *cis*-hexahydrophthalaldehyde.

Relatively few syntheses of bicyclo[4.2.0]-octane derivatives have been reported, and none by routes which appeared to be useful for a synthesis of III which would confirm its structure and furnish direct evidence for the presence of a cyclobutane ring in the molecule. We have investigated a relatively direct synthesis, consisting of the acyloin condensation of *cis*-diethyl hexahydrophthalate (I) to bicyclo[4.2.0]octan-7-ol-8-one (II), followed by catalytic hydrogenation of II to III.

The application of the acyloin condensation to the synthesis of cyclic acyloins containing large rings has been investigated thoroughly. The reaction conditions used by Hansley[3] for the preparation of acyclic acyloins were later applied to the synthesis of cyclic acyloins with a ring size of seven or more carbon atoms.[4] Prelog, Frenkiel, Kobelt and Barman,[5] and Stoll, Hulstkamp and Rouvé[6] have used similar reaction conditions very successfully for the preparation of cyclic acyloins with rings containing nine to twenty carbon atoms. The acyloin condensation does not appear to have been used for the closure of four-membered rings.

cis-Diethyl hexahydrophthalate (I) was prepared conveniently by the addition of butadiene to maleic anhydride to give *cis*-Δ^4-tetrahydrophthalic anhydride, followed by esterification to *cis*-diethyl-Δ^4-tetrahydrophthalate and catalytic hydrogenation to (I). Under conditions previously used for the synthesis of cyclic acyloins,[4,5,6] by slow addition of the ester (I) to four equivalents of sodium in refluxing xylene with high-speed stirring, a product was obtained which consisted largely of a polymer and the recovered ester (I). The ester appeared to contain some of the acyloin, however, for it absorbed a small amount of hydrogen on catalytic reduction, and after saponification to remove the ester, small amounts of a liquid with the properties of a glycol were isolated. By modifying the conditions of

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(1) Supported in part by the Office of Naval Research under Contract N5ori-07822, Project Designation NR-055-96. Presented at the Atlantic City meeting of the American Chemical Society, Division of Organic Chemistry, September 20, 1949.

(2) Reppe, Schlichting, Klager and Toepel, *Ann.*, **560**, 1 (1948).

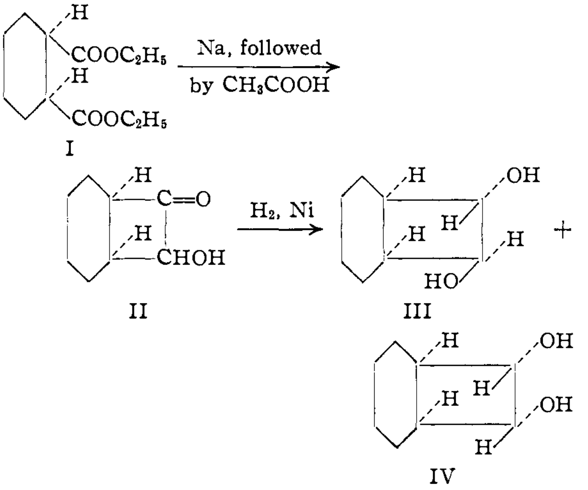
(3) Hansley, THIS JOURNAL, **57**, 2303 (1935).

(4) Hansley, U. S. Patent 2,228,268 (Jan. 14, 1941); *C. A.*, **35**, 2534 (1941).

(5) Prelog, Frenkiel, Kobelt and Barman, *Helv. Chim. Acta*, **30**, 1741 (1947).

(6) Stoll and Hulstkamp, *ibid.*, **30**, 1815 (1947); Stoll and Rouvé, *ibid.*, **30**, 1822 (1947).

the acyloin reaction and the method of isolating the product, a procedure described in the Experimental Part was developed, by which it was possible to isolate the pure acyloin (II) in 12% yield..



This yield was obtained by adding the ester very slowly under conditions of high dilution to slightly more than four equivalents of sodium in refluxing xylene. The acyloin condensation and subsequent neutralization of the sodium salts with acetic acid were conducted in an atmosphere of purified nitrogen.[6] After concentration and removal of acidic by-products by extraction with sodium carbonate, a small amount of a crystalline product separated which on the basis of its analysis and molecular weight is believed to be a mixture of isomeric forms of the eight-membered cyclic *dimeric* acyloin, $C_{16}H_{24}O_4$. After a preliminary short-path distillation of the remainder of the material at as low a temperature as possible to separate the product from polymers, II was isolated by distillation as a colorless liquid. Two stereoisomeric forms of II are possible, in which the hydroxyl group is either *cis* or *trans* to the hydrogens at the points of ring fusion (assuming that these hydrogens must have a *cis* relationship to each other because of the strain which would result in the four-membered ring if they were *trans*). Both a 3,5-dinitrobenzoate and a *p*-phenylazobenzoate of II were prepared and purified by chromatography, but no evidence for the existence of a second isomer of either derivative was obtained. Another derivative which was prepared from II was the 2,4-dinitrophenylosazone.

Catalytic hydrogenation of II gave a liquid mixture of stereoisomeric glycols, from which 17% of a crystalline isomer (III), m. p. 140.5–141.5°, was separated. This compound proved to be identical (m. p. and mixed m. p.) with a sample of III derived from cycloöctatetraene,[2] thus confirming the structure of the glycol from the latter source. Bis-*p*-phenylazobenzoates prepared from samples of III derived from these two sources also were identical. Samples of the isomer (III) with m. p. 140.5–141.5° from both sources produced no significant change in the acidity of boric acid,[7] and accordingly this isomer is believed to be the *trans* or DL-form.

After distillation of the glycol remaining in the mother liquor following separation of III another isomer crystallized; it melted at 71.5–73.5°, and gave a bis-*p*-phenylazobenzoate different from the corresponding derivative of III. This isomer (IV) did increase the acidity of boric acid, and consequently is believed to be one of the two possible *cis* or *meso* forms. The liquid glycol remaining after crystallization of IV was converted into the bis-*p*-phenylazobenzoate and chromatographed. A derivative was separated which melted lower than the derivatives of III or IV, but mixed melting points with both of them showed very little depression, and the infrared spectrum of the low melting derivative coincided closely with the spectra of the derivatives of III and IV. From this evidence it is considered more likely that the low melting derivative is a eutectic of the derivatives of III and IV, rather than a derivative of the second possible *cis* or *meso* isomer.

Experimental[8]

***cis*-Δ^4-Tetrahydrophthalic Anhydride.**—An assembly of apparatus consisting of a 2-l. three-necked flask fitted with a gas-dispersing stirrer,[9] gas inlet tube, thermometer and reflux condenser was placed in a hood. Bubbler tubes containing benzene were attached to the gas inlet tube and the top of the reflux condenser, and 500 ml. of dry benzene and 196 g. (2 moles) of maleic anhydride was added to the flask. Stirring was begun, the flask was heated with a pan of hot water, and butadiene was introduced rapidly (0.6–0.8 l. per minute) from a commercial cylinder. Heating was discontinued after three to five minutes, when the temperature of the solution reached 50°. The heat of reaction caused the temperature to reach 70–75° in fifteen to twenty-five minutes. Absorption of the rapid stream of butadiene was nearly complete for thirty to forty minutes, after which it was introduced at progressively slower rates (without further heating) for a total reaction time of two to two and one-half hours, at which time reaction was complete, as evidenced by equal rates of bubbling in the two bubbler tubes. The solution was poured into a 1-l. beaker, which was covered and kept at 0–5° overnight. The product was collected on a large Büchner funnel and washed with 250 ml. of 35–60° petroleum ether. A second crop (5–15 g.) obtained by diluting the filtrate with an additional 250 ml. of petroleum ether was combined with the first crop of crystals. After drying to constant weight in an oven at 70–80° the yield of *cis*-Δ^4-tetrahydrophthalic anhydride was 281.5–294.5 g. (93–97%), m. p. 99–102°. This product was analytically pure and suitable for use in preparing esters. Recrystallization from ligroin or ether raised its m. p. to 103–104°.

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[7] Böeseken, *Rec. trav. chim.*, **40**, 553 (1921).

[8] Melting points are corrected and boiling points are uncorrected. We are indebted to Mr. S. M. Nagy and Mrs. Louise W. Spencer for analyses.

[9] Designed by Frank S. Crossley of Sharp and Dohme, Inc., Glenolden, Pa., for use in catalytic hydrogenations. The stirrer is made from a length of glass tubing which is sealed at the upper end and contains a hole below the glass sleeve bearing and above the surface of the liquid. Rotation of the stirrer pumps the gas through the liquid.

Most of the previous preparations of the compound have used closed reaction vessels under positive pressure.[10]

***cis*-Diethyl and Dimethyl Δ^4-Tetrahydrophthalates and Hexahydrophthalates.**—*cis*-Δ^4-Tetrahydrophthalic anhydride, m. p. 99-102° (228 g., 1.5 moles), 525 ml. (9 moles) of commercial absolute ethanol and 2.5 g. of *p*-toluenesulfonic acid monohydrate were heated under reflux for twelve to sixteen hours. Toluene (270 ml.) then was added and an azeotropic mixture of ethanol, water and toluene was distilled at 75-78°, with a heating bath temperature of 105-110°, until the distillation temperature began to drop, after five to eight hours. An additional 525 ml. of absolute ethanol was added and the procedure of refluxing followed by azeotropic distillation with toluene was repeated, after which the remaining toluene and ethanol were distilled under reduced pressure. The residue was cooled, diluted with 200 ml. of ether, and washed with 3% aqueous sodium carbonate solution until the aqueous layer remained alkaline. The ether solution was combined with ether extracts of the sodium carbonate solution, washed with water, dried over magnesium sulfate and distilled. The yield of *cis*-diethyl Δ^4-tetrahydrophthalate was 280-292 g. (83-87%); b. p. 129-131° (5 mm.); $n^{25}\mathrm{D}$ 1.4610.[11] *cis*-Dimethyl Δ^4-tetrahydrophthalate was prepared by substituting an equimolar amount of dry methanol for ethanol in the above procedure; yield 239 g. (80%); b. p. 120-122° (5 mm.); $n^{25}\mathrm{D}$ 1.4700.

Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.38; H, 7.12.

cis-Diethyl hexahydrophthalate was prepared by hydrogenating 226 g. of *cis*-diethyl Δ^4-tetrahydrophthalate at room temperature in the presence of 0.5 g. of Adams platinum oxide catalyst, prereduced in 20 ml. of absolute ethanol, or in the presence of 1 g. of 10% palladium-on-carbon[12] without a solvent, at a pressure of 30-15 p. s. i. during three to five hours. The yield was 215-219 g. (94-96%), b. p. 130-132° (9 mm.); $n^{25}\mathrm{D}$ 1.4510.[13] *cis*-Dimethyl hexahydrophthalate was prepared in a similar manner by hydrogenation of 198 g. of *cis*-dimethyl Δ^4-tetrahydrophthalate in the presence of 0.5 g. of prereduced Adams platinum oxide catalyst; yield 196 g. (98%); b. p. 110-112° (5 mm.); $n^{25}\mathrm{D}$ 1.4570.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06. Found: C, 59.86; H, 8.05.

Bicyclo[4.2.0]octan-7-ol-8-one (II). Acyloin Condensation of I.—A 5-l. three-necked creased flask was fitted with a stainless steel stirrer[14] attached to a 10,000 r. p. m. motor controlled by a variable transformer, a thermometer well and a high dilution apparatus[15] consisting of a still-head for distillation of xylene and a reflux condenser for its condensation, which returned the xylene to the flask through a U-tube. A side arm of the U-tube was attached to a 1-l. Hershberg dropping funnel, through which a xylene solution of *cis*-diethyl hexahydrophthalate was added slowly, so that it was diluted with the xylene returned by the reflux condenser before entering the reaction flask. All of the apparatus was dried in an oven before assembling and was protected with drying tubes, and by maintenance of an atmosphere of prepurified nitrogen containing less than 0.001% oxygen through connections at the top of the reflux condenser and the dropping funnel and the lower end of the stirrer shaft. The nitrogen in the system was kept under a positive pressure of 1 cm. of mercury by a pop-valve. One liter of xylene (dried over sodium and redistilled, b. p. 137-140°) and 31.3 g. (1.36 g. atoms) of clean sodium were placed in the flask. The xylene was heated to the boiling point with an electric heating mantle and stirred at 2600 r. p. m. After fifteen minutes, addition of a solution of 76 g. (0.33 mole) of *cis*-diethyl hexahydrophthalate (I) in 2130 ml. of dry xylene was begun at a rate of one drop in two seconds, with a ratio of xylene reflux to addition of the xylene solution of the ester of about 25 to 1. Addition of the solution of the ester was completed in forty-five and one-half hours, and heating and stirring were continued for one-half hour longer. The mixture was cooled with an air blast and then with an ice-salt-bath. After three-quarters of an hour the sodium salts had settled to the bottom of the flask and 1.5 l. of xylene was separated with a siphon and discarded. Dry ether (500 ml.) was added to the flask and when the mixture had cooled to 6° (still protected with nitrogen), dropwise addition with stirring of a solution of 78.5 ml. of glacial acetic acid in 500 ml. of dry ether was begun. The addition was completed in one-half hour, and the maximum temperature reached was 12°. The sodium acetate was separated by filtering the mixture through three 20-cm. Büchner funnels. The filter cakes were covered with rubber dams. When no more filtrate could be separated the cakes of sodium acetate were combined and extracted twice with 750-ml. portions of ether by stirring vigorously for thirty minutes and refiltering. Distillation of the extracts left 140 ml. of a xylene solution of the product, which was combined with the xylene filtrate and concentrated to a residue of 48.5 g. by distillation at 1-2 mm. The residue was dissolved in 275 ml. of ether and extracted with four 50-ml. portions of 3% sodium carbonate solution. The sodium carbonate extracts were washed with 50 ml. of ether, and the combined ether solutions were washed with 50 ml. of 1 *N* hydrochloric acid, twice with 50 ml. of water, dried over magnesium sulfate, filtered and placed in a refrigerator to allow separation of the dimeric acyloin described below. Acidification of the sodium carbonate extracts followed by extraction with ether separated 3.35 g. of acidic material formed in the acyloin reaction, which appeared to be largely polymeric.

Crystalline material amounting to 1.1 g., m. p. 181-191°, separated from the cold ether solution of the product during twelve hours. An analytical sample recrystallized twice from 95% ethanol melted at 178-184.5°. The following analytical data and molecular weight indicate that this product is the eight-membered cyclic dimeric acyloin formed by condensation of two moles of I. Two structural isomers and several stereoisomeric forms of the dimer are possible, and the melting point range indicates that the solid isolated is a mixture of isomers.

Anal. Calcd. for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63; mol. wt., 280. Found: C, 68.77; H, 8.49; mol. wt., 283 (Rast method in borneol).

The ether filtrate containing the product was concentrated to 60 ml. and washed into a 100-ml. short-path still[16] with 25 ml. of ether. Glass wool (0.2 g.) was added to minimize bumping, the ether was distilled under reduced pressure, and a low-boiling forerun (1.7 g.) was distilled at a bath temperature of 85° and 0.4 mm. pressure. A crude acyloin fraction of 8.6 g. was separated from the polymeric residue (28 g.) by slow distillation at a bath temperature of 115-125° and 0.05-0.1 mm. pressure during eighteen hours. The acyloin was fractionated through a 30 × 0.7 cm. semi-micro column containing a wire spiral.[17] Seven fractions were separated. The first two were yellow, indicating the probable presence of the diketone derived from the acyloin by oxidation; (1) 0.11 g., b. p. 46-55.5° (0.1 mm.), $n^{25}\mathrm{D}$ 1.4801; (2) 0.5 g., b. p. 59.5-67° (0.06 mm.), $n^{25}\mathrm{D}$ 1.4850. The remaining five fractions had b. p. 66.5-67.5° (0.04 mm.), and $n^{25}\mathrm{D}$ from

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[10] Diels and Alder, *Ann.*, **460**, 113 (1928); Farmer and Warren, *J. Chem. Soc.*, 903 (1929); Kohler and Jansen, This Journal, **60**, 2144 (1938); Fieser and Novello, *ibid.*, **64**, 806 (1942); Jenkins and Costello, *ibid.*, **68**, 2733 (1946).

[11] Brooks and Cardarelli, U. S. Patent 1,824,069 (Sept. 22, 1931); *C. A.*, **26**, 152 (1932), describe the preparation of this ester from the anhydride or acid, ethanol and sulfuric acid.

[12] "Organic Syntheses," Vol. 26, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 32.

[13] This ester has been prepared by reaction of the acid or its anhydride with absolute ethanol and sulfuric acid; von Auwers and Ottens, *Ber.*, **57**, 437 (1924); Hückel and Goth, *ibid.*, **58**, 447 (1925); Price and Schwarcz, This Journal, **62**, 2891 (1940).

[14] Morton and Redman, *Ind. Eng. Chem.*, **40**, 1190 (1948).

[15] See Ziegler, Eberle and Ohlinger, *Ann.*, **504**, 123 (1933).

[16] Similar to the boiling point still described by Hickman and Weyerts, This Journal, **52**, 4714 (1930).

[17] Gould, Holzman and Niemann, *Anal. Chem.*, **20**, 361 (1948).

1.4950 to 1.4993. Fractions 4-7 differed only slightly in refractive index ($n^{25}\text{D}$ 1.4980-1.4993), and carbon-hydrogen analyses of the third, fifth and seventh fractions gave results which were in agreement with the values calculated for the acyloin. The yield based on fractions three to seven was 5.7 g. (12%); the following physical properties of II were determined, using fraction five: $n^{25}\text{D}$ 1.4992; d^{25}_4 1.1218; $M\text{D}$ calcd. 36.66 (including the value 0.5 for the cyclobutane ring[18]); $M\text{D}$ found 36.71.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.84; H, 8.78.

The procedure described for preparation of II was developed in a series of thirty-five acyloin condensations of dialkyl hexahydrophthalates, from which the following information was obtained. Reaction conditions analogous to those used for the preparations of other cyclic acyloins,[4,5,6] in which the ester was added to the sodium during one and one-half to seventeen hours without the use of a high-dilution apparatus gave much smaller yields of the monomeric acyloin and a high proportion of polymer. Use of toluene as a solvent gave somewhat lower yields, as did prolongation of the period of heating after addition of the ester to two to sixteen hours. Use of a mixture of *cis*- and *trans*-diethyl and dibutyl hexahydrophthalates obtained by hydrogenation of the dialkyl phthalates in the presence of Raney nickel gave lower yields of II, as would be expected, and *cis*-dimethyl hexahydrophthalate appeared to offer no advantage over I. It was necessary to employ an amount of sodium in excess of four molar equivalents in order to remove *cis*-diethyl hexahydrophthalate completely in the reaction, for the ester differed little from the acyloin in boiling point, and mixtures of the two could not be separated by fractionation. Use of prepurified nitrogen instead of ordinary commercial nitrogen improved the yield.[6] Attempts to remove the ester by saponification with 10% alcoholic potassium hydroxide appeared to destroy the acyloin. Acidification of the sodium salts with 50% sulfuric acid, which is a common practice in the preparation of acyclic acyloins,[19] gave poorer results, and the optimum temperature for acidification with acetic acid in ether was 5 ± 5° rather than −30 to −15° because of the slowness with which the viscous slurry of sodium salts was neutralized at the lower temperature. The acyloin proved to be sufficiently stable to bases to permit separation of acidic by-products by extraction with sodium carbonate solution, with obvious advantage in purification of the product. The acyloin was not obtained free from impurities until the purification procedure was modified to include a preliminary short-path distillation at as low a temperature as possible to separate the product from polymers. Presumably simple distillation at low pressures, which was employed in early preparations, led to contamination of the product with material formed by decomposition of the polymer which could not be separated completely in the subsequent fractionation.

Derivatives Prepared from Bicyclo[4.2.0]octan-7-ol-8-one. (a) **3,5-Dinitrobenzoate** of II.—A solution of 0.14 g. of II and 0.25 g. of 3,5-dinitrobenzoyl chloride in 6 ml. of dry benzene and 2.5 ml. of dry pyridine was heated under reflux for one hour.[20] The solution was diluted with 80 ml. of ether and washed successively with two 25-ml. portions of 3 *N* hydrochloric acid, two 25-ml. portions of 3% sodium carbonate solution, and twice with water. The ether solution was dried over magnesium sulfate and concentrated under reduced pressure. The oily residue crystallized on trituration with hexane, and the crystalline product was separated by filtration; yield 0.121 g. (36%), m. p. 127.5-130°. A sample from a similar preparation was recrystallized from methylcyclohexane to a constant m. p. of 131-132° for analysis.

Anal. Calcd. for $C_{15}H_{14}N_2O_7$: C, 53.89; H, 4.22; N, 8.38; mol. wt., 334. Found: C, 54.12; H, 4.40; N, 8.42; mol. wt., 361 (Rast method in borneol).

The 3,5-dinitrobenzoate (121 mg.) in 10 ml. of benzene and 20 ml. of hexane was adsorbed on a 32 × 1.8 cm. column of 2:1 silicic acid-Hyflo Super Cel (containing 27 mg. of Rhodamine 6G, Color Index No. 752, in 610 g. of adsorbent[21]). The band of the derivative (dark against a fluorescent background when illuminated with ultraviolet light) was developed to a length of 13 cm. with 2:1 hexane-benzene followed by hexane containing 5% of ether, and cut in half. The derivative recovered from each half by elution with benzene containing a little ethanol and recrystallized from methylcyclohexane melted at 130.5-131.5°, indicating no separation into isomers by chromatography under these conditions.

(b) *p*-**Phenylazobenzoate** of II.—A solution of 0.28 g. of II and 0.735 g. of *p*-phenylazobenzoyl chloride in 15 ml. of pyridine (refluxed over barium oxide and distilled) was heated under reflux on a steam-bath for three hours and cooled.[22] Water (0.5 ml.) was added and the solution was allowed to stand for fifteen minutes. The solvent was removed under reduced pressure, and the residue was washed twice with water and air-dried. Chloroform (30 ml.) was added, the mixture was heated, and most of the undissolved *p*-phenylazobenzoic acid was separated by filtration. The remainder was removed by filtering the solution through 8 g. of 5:1 activated alumina (Alcoa 325 mesh)-Hyflo Super Cel. The crude product obtained on removal of the solvent amounted to 0.537 g., m. p. 110-131°. It was dissolved in a mixture of 10 ml. of chloroform and 20 ml. of hexane and placed on a 38 × 2.5 cm. column packed dry with suction with 2:1 silicic acid-Hyflo Super-Cel and prewashed with 100 ml. of 1:1 hexane-benzene. The column was developed with 600 ml. of benzene containing 0.1% of absolute ethanol under air pressure of 30 cm. of mercury. Eleven successive fractions of the eluate, approximately equal in volume, were separated and evaporated to dryness by warming on a steam-bath in an air stream. The residues from fractions 1 and 2 (67 mg., m. p. 120.5-151°) were combined and rechromatographed twice, but no pure product was obtained. The residues from fractions 3 to 6 (200 mg., m. p. 124-138.5°) were combined, rechromatographed and again eluted; fractions 3 to 8 from this chromatogram (0.071 g., m. p. 138-139°) were combined. The residues from fractions 7 to 11 of the original chromatogram (162 mg., m. p. 137.5-139°) were combined with this material; total yield 0.233 g. (34%). An analytical sample was rechromatographed and crystallized from hexane; m. p. 138-139°.

Anal. Calcd. for $C_{21}H_{18}N_2O_3$: C, 72.39; H, 5.79; N, 8.04; mol. wt., 348. Found: C, 72.57; H, 5.97; N, 8.23; mol. wt., 357 (Rast method in borneol).

(c) **2,4-Dinitrophenylosazone Prepared from II.**—2,4-Dinitrophenylhydrazine (1.2 g.) was dissolved in 6 ml. of concentrated sulfuric acid and 4 ml. of water was added, followed by 30 ml. of 95% ethanol. The solution was added to a solution of 0.28 g. of II in 20 ml. of 95% ethanol, and the mixture was heated under reflux in an atmosphere of nitrogen. After thirty minutes the brownish-orange precipitate (0.343 g.) was separated, and combined with the additional material (6 mg.) which separated when the filtrate was heated under reflux for another hour. A solution of the solid in 60 ml. of chloroform and 20 ml. of hexane was placed on a 26 × 2.5 cm. column of 2:1 silicic acid-Hyflo Super-Cel, packed dry with suction and prewashed with 100 ml. of benzene. The chromatogram was developed with 3:1 chloroform-hexane, which separated an upper dark orange band and a lower light orange band. The column was extruded and sectioned into these bands, which were eluted with chloroform containing 10% of ethanol. The residue from the dark orange band proved to be the 2,4-dinitrophenylosazone derived from II; yield

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[18] Eisenlohr and Wohlisch, *Ber.*, **53**, 1746 (1920).

[19] Snell and McElvain, THIS JOURNAL, **53**, 750 (1931).

[20] Based on an esterification procedure described by Reichstein, *Helv. Chim. Acta*, **9**, 799 (1926).

[21] White and Dryden, *Anal. Chem.*, **20**, 853 (1948).

[22] Based on an esterification procedure described by Coleman, Rees, Sundberg and McCloskey, THIS JOURNAL, **67**, 381 (1945).

0.075 g. (8%), m. p. 248.5–252° (dec.). An analytical sample was purified by rechromatographing and crystallizing from ethyl acetate; m. p. 256–257.5° (dec.).

Anal. Calcd. for $C_{20}H_{18}N_8O_8$: C, 48.20; H, 3.65; N, 22.49. Found: C, 48.60; H, 3.94; N, 22.41.

The residue from the eluate of the light orange band was yellow in color; yield 0.156 g., m. p. 150–153°. An analytical sample was rechromatographed and crystallized twice from methylcyclohexane; m. p. 152.5–153.5°. The structure of this compound was not determined.

Anal. Found: C, 55.63; H, 6.06; N, 16.45.

Reduction of II, *trans*-Bicyclo[4.2.0]octane-7,8-diol (III).—A solution of 1.89 g. of II in 40 ml. of absolute ethanol was hydrogenated at atmospheric pressure in the presence of 2 g. of W-7 Raney nickel.[23] Absorption of hydrogen stopped after forty minutes at 109% of one molar equivalent. The catalyst was separated, heated with 30 ml. of benzene, and the combined alcohol and benzene solutions were concentrated under reduced pressure. Part of the residue crystallized on trituration with 30 ml. of hexane. The crystalline *trans*-glycol (III) was separated by filtration; yield 0.315 g. (17%), m. p. 136.5–140.5°. Two recrystallizations from benzene gave III with a constant m. p. of 140.5–141.5°; mixed m. p. with a sample of III derived from cycloöctatetraene,[2] 140.5–141.5°. A sample of III with the same m. p. from another preparation was analyzed.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.37; H, 9.97.

Hydrogenation of II in the presence of Adams platinum catalyst in absolute ethanol also gave a mixture of glycols, from which less of the crystalline *trans* glycol III was isolated than from the Raney nickel reduction.

A solution of III (0.043 g.) derived from cycloöctatetraene and 0.326 g. of *p*-phenylazobenzoyl chloride in 10 ml. of dry pyridine was heated under reflux for eleven hours. The solution was cooled to room temperature, 0.5 ml. of water was added, and after fifteen minutes the solvent was removed under reduced pressure. The residue was washed with two 15-ml. portions of water, air-dried, and heated with 15 ml. of chloroform. The undissolved *p*-phenylazobenzoic acid was removed by filtration, and the solution was filtered through 6 g. of 5:1 activated alumina–Hyflo Super Cel to remove the small amount of the acid which had dissolved. Evaporation of the solvent gave 170 mg. of the bis-*p*-phenylazobenzoate of III, m. p. 172–173.5°. A solution of the derivative in 5 ml. of chloroform and 15 ml. of *n*-hexane was placed on a 29 × 1.8 cm. column packed dry (with suction) with 2:1 silicic acid–Celite No. 503 filter aid. The chromatogram was developed under air pressure of 30 cm. of mercury with 20 ml. of 3:1 *n*-hexane–chloroform, followed by 75 ml. of benzene containing 0.1% of absolute ethanol. The dark orange band was sectioned, eluted with chloroform containing 10% of ethanol, and the bis-*p*-phenylazobenzoate of III was crystallized from methylcyclohexane; yield 0.132 g., m. p. 174.8–175.8°.

Anal. Calcd. for $C_{34}H_{30}N_4O_4$: C, 73.10; H, 5.41; N, 10.03. Found: C, 73.20; H, 5.63; N, 10.04.

A sample of III prepared by hydrogenation of II was converted to the bis-*p*-phenylazobenzoate in the same manner and purified by chromatography followed by crystallization from methylcyclohexane; m. p. and mixed m. p. with the derivative prepared from III derived from cyclooctatetraene, 174.8–175.8°. A mixed m. p. of this derivative with the bis-*p*-phenylazobenzoate of the *cis*-glycol (described below, m. p. 165–166°) was depressed to 146–169.5°.

***cis*-Bicyclo[4.2.0]octane-7,8-diol (IV).**—The hexane solution remaining after separation of the crystalline *trans*-glycol (III) was concentrated and the residue was distilled through a 30 × 0.7 cm. semi-micro column.[17] The distillate partially crystallized on standing overnight at 0–5°. The crystals (0.060 g., m. p. 71.5–73.5°) were separated and combined with an additional quantity which separated from a cooled solution of the remainder in pentane (0.049 g., m. p. 71.5–73.5°; total yield 5%). An analytical sample from another preparation was recrystallized three times from hexane, and also melted at 71.5–73.5° after softening at 64°.

Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.24; H, 9.91.

A solution of IV (0.035 g.) and 0.366 g. of *p*-phenylazobenzoyl chloride in 10 ml. of dry pyridine was heated under reflux for eleven hours. The product was isolated and purified by chromatographic adsorption in the same manner as the corresponding derivative of III; yield 0.086 g., m. p. 164.5–166°, which on recrystallization from methylcyclohexane gave 0.071 g., m. p. 165–166°.

Anal. Calcd. for $C_{34}H_{30}N_4O_4$: C, 73.10; H, 5.41; N, 10.03. Found: C, 72.97; H, 5.57; N, 10.03.

The liquid glycol (0.78 g.) remaining after separation of the crystalline *trans* and *cis* isomers was treated with *p*-phenylazobenzoyl chloride in the manner previously described. The crude product (2.11 g.) was placed on a 35 × 3.5 cm. column of 2:1 silicic acid–Hyflo Super-Cel and eluted with benzene containing 0.1% of absolute ethanol. Combination of fractions of the eluate with similar m. p. and repetition of the process gave 0.43 g., m. p. 143–146°, which was crystallized twice from hexane; m. p. 144–146°.

Anal. Calcd. for $C_{34}H_{30}N_4O_4$: C, 73.10; H, 5.41; N, 10.03. Found: C, 73.13; H, 5.79; N, 10.28.

This derivative gave a mixed m. p. with the corresponding derivative of the *trans* glycol (m. p. 174.8–175.8°) of 140–170°, and a mixed m. p. with the derivative of the *cis* glycol (m. p. 165–166°) of 142–156°. The infrared absorption spectrum of the derivative with m. p. 144–146° appeared to contain no bands which were not present in the spectra of the corresponding *cis* and *trans* glycol derivatives. From these data it is probable that the derivative with m. p. 144–146° is a eutectic of the *cis* and *trans* glycol derivatives rather than a derivative of the second isomeric *cis* glycol which theoretically is capable of existence.

Evidence for the Configuration of III and IV.—Successive increments of III were added to 25 ml. of 0.1 *M* boric acid solution and the effect produced on the *p*H was determined with a Beckman model G *p*H meter using a glass electrode. The effect of IV and *trans*-cyclohexan-1,2-diol (a known *trans* glycol examined as a control) on the *p*H of 0.1 *M* boric acid was determined in the same way. After addition of 0, 10, 20, 30 and 50 mg. increments of III the *p*H was 5.21, 5.21, 5.23, 5.25 and 5.27. These values were obtained using III prepared from cycloöctatetraene; with III prepared from II the *p*H values were 5.18, 5.24, 5.26, 5.29 and (after addition of a 40 mg. increment) 5.31. After addition of 0, 10, 20, 30 and 50 mg. increments of *trans*-cyclohexane-1,2-diol the *p*H was 5.21, 5.23, 5.25, 5.27 and 5.31. After addition of 0, 10, 20, 30 and 40 mg. increments of IV the *p*H was 5.18, 5.05, 4.90, 4.70 and 4.45.

These data indicate that III has a *trans* and IV a *cis* relationship of the hydroxyl groups.

Summary

The acyloin condensation has been utilized for closure of the four-membered ring of bicyclo-[4.2.0]octan-7-ol-8-one (II), by the reaction of *cis*-diethyl hexahydrophthalate with sodium under conditions of high dilution. Hydrogenation of the cyclic acyloin (II) yielded a mixture of stereoisomeric bicyclo[4.2.0]octan-7,8-diols (III and IV). The high melting isomer, which apparently has the *trans* or DL configuration (III), proved to be identical with a sample of the glycol derived from cycloöctatetraene by a sequence of reactions involving molecular rearrangement.

CAMBRIDGE, MASSACHUSETTS

RECEIVED SEPTEMBER 3, 1949

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[23] Adkins and Billica, THIS JOURNAL, **70**, 695 (1948).