

azo compounds have likewise been characterized (R = cyclopropyl, isobutyl and the hydrazine from cyclohexanone). Hydrochlorides of two new 1,2-disubstituted hydrazines (R = isopropyl, R = cyclopropyl) have likewise been characterized.

2. Three new succinonitriles, decomposition products from three of the azo nitriles (R = iso-butyl, *n*-propyl and the azo compound from cyclohexanone) have been prepared and characterized.

3. Rates of decomposition of seven aliphatic azo compounds at 80.2° have been determined in toluene and the reaction shown to be first order.

4. Activation energies have been determined for five of the azo compounds by additional rate measurements at 69.8°.

5. The rate of decomposition of 2,2'-azo-bis-isobutyronitrile has been studied in toluene, isobutyl alcohol, *t*-amyl alcohol and aniline and has been shown to be essentially independent of solvent type.

6. It has been demonstrated that free radicals are produced in the decomposition of the azo compounds. A mechanism for the decomposition reaction is proposed. Major differences in rate constants are ascribed largely to steric factors.

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Polyglycerols. II. Syntheses of Diglycerol¹

BY HAROLD WITTCOFF, J. ROBERT ROACH AND SIDNEY E. MILLER

Diglycerol has long been known to be a constituent of the mixture resulting from the base-catalyzed, thermal condensation of glycerol. The recovery of diglycerol as the tetraallyl ether or as the diisopropylidene derivative from such mixtures has been described by Wittcoff, Roach and Miller.^{1a} The isolation of diglycerol as well as higher polyglycerols as the acetates has been reported by Rangier² and by Wright and DuPuis,³ whereas conditions for the direct distillation of polyglycerol mixtures have been published by Istin.⁴

A very interesting reaction which yielded a mixture of glycerol and diglycerol has been carried out by Wright and DuPuis³ who pyrolyzed the substance resulting from the action of carbon dioxide on calcium glyceroxide. A direct synthesis of diglycerol was accomplished many years ago by Nef⁵ who hydrolyzed 2-epoxypropyl ether which he obtained by the interaction of silver oxide and epichlorohydrin.

This paper describes three direct syntheses of diglycerol: (a) by the hydroxylation of allyl ether; (b) by the hydrolysis of the dichlorohydrin resulting from the addition of hypochlorous acid to allyl ether; and (c) by the hydrolysis of 2-epoxypropyl ether prepared from this dichlorohydrin.

Although hydroxylation of allyl ether by action of permanganate proved feasible, considerably

better yields of diglycerol were obtained in this work by the use of performic acid⁶ as the hydroxylating agent. In both cases, however, it was observed that the product could be distilled from the reaction mixture only with difficulty. Accordingly, the crude reaction mixture was subjected to the action of acidic acetone in order to obtain diisopropylidenediglycerol which could be distilled readily. In addition, some isopropylidenediglycerol was also formed and both of these derivatives were easily hydrolyzed to diglycerol.

The addition of hypochlorous acid to allyl ether occurred readily when the reagent was prepared as described by Kadesch,⁷ a procedure which was found superior in this work to the one described in "Organic Syntheses."⁸ The dichlorohydrin was hydrolyzed directly to diglycerol by the action of a weak base such as sodium bicarbonate. Sodium hydroxide, on the other hand, converted the dichlorohydrin to 2-epoxypropyl ether, first described by Nef,⁵ which likewise was hydrolyzed to diglycerol by the action of dilute aqueous sulfuric acid.

Experimental

Isopropylidene- and Diisopropylidenediglycerol from the Oxidation of Allyl Ether with Performic Acid.—A mixture of allyl ether (57.8 g., 0.59 mole), formic acid (87%, 325 cc.) and hydrogen peroxide (29%, 146.0 g., 1.2 moles) was stirred mechanically, the reaction vessel having been placed behind a safety glass shield. The temperature rose to 40° in fifteen minutes and was maintained there first by external cooling and then by heating for four and one-half hours. When titration of a test sample indicated that practically no peroxide remained, the reaction mixture, having been stirred with sodium bisulfite (7.0 g.) to ensure the absence of peroxides, was concentrated under

(6) D. Swern, G. N. Billen, T. W. Findley and J. T. Scanlan, *THIS JOURNAL*, **67**, 1786 (1945).

(7) R. C. Kadesch, *ibid.*, **68**, 41 (1946).

(8) H. Gilman and A. H. Blatt, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 158.

(1) Paper No. 86, Journal Series, Research Laboratories, General Mills, Inc.

(1a) H. Wittcoff, J. R. Roach and S. E. Miller, *THIS JOURNAL*, **69**, 2655 (1947). See footnote 2 for a discussion of nomenclature.

(2) M. Rangier, *Compt. rend.*, **187**, 345 (1928); *C. A.*, **22**, 4468 (1928).

(3) H. J. Wright and R. N. DuPuis, *THIS JOURNAL*, **68**, 446 (1946).

(4) M. Istin, *Ann. faculte sci. Marseille*, **13**, 5 (1946); *C. A.*, **41**, 2392 (1947).

(5) J. Nef, *Ann.*, **335**, 238 (1904).

reduced pressure to a sirupy residue. This was dissolved in absolute ethyl alcohol; the solution was filtered and the filtrate concentrated once more to a sirupy residue. The residue was made slightly alkaline with dilute methanolic sodium hydroxide and then methyl alcohol and methyl formate were removed by slow distillation. The residue was allowed to stand overnight with a solution of sodium hydroxide (7.0 g.) in 90% aqueous methanol (200 cc.). After neutralization with concentrated hydrochloric acid, the reaction mixture was filtered and concentrated under reduced pressure. The residue was extracted with absolute methanol, and from the extract the solvent was removed under reduced pressure. The sequence of operations was repeated twice to eliminate inorganic material. Finally, the residue was dissolved in absolute ethanol; the solution was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The product (95 g., theoretical is 98.0 g.) could not be distilled directly since it foamed excessively.

The hydroxylation product (90.0 g.) was stirred with a solution of hydrogen chloride (9.0 g.) in acetone (600 cc.) in the presence of anhydrous sodium sulfate (90 g.), the mixture having been cooled initially because of the exothermic nature of the reaction. The reaction mixture, having been stirred overnight at room temperature, was made slightly basic with alcoholic sodium hydroxide; it was filtered and concentrated to yield the acetonated product (100 g., 74.8% yield, assuming complete acetonation) which was fractionated under reduced pressure, twelve cuts having been taken. The first six cuts (58.5 g., distillation range 85–108° (0.4 mm.)) were diisopropylidenediglycerol. The next cut (6.0 g.) was an intermediate fraction, whereas the next three cuts (19.0 g., distillation range 137–150° (0.8 mm.)) comprised incompletely acetonated diglycerol from which pure diglycerol was obtained by hydrolysis. Repeated fractional distillation of this higher boiling material yielded pure isopropylidenediglycerol. The yield of diglycerol calculated on the basis of the isopropylidene derivatives was about 71%.

Diisopropylidenediglycerol¹⁸ prepared by this procedure distilled at 97° (1 mm.) and had a constant n_D^{25} of 1.4375. Isopropylidenediglycerol distilled at 114–117° (3 mm.) and had an n_D^{25} of 1.4607.

*Anal.*⁹ Calcd. for $C_9H_{18}O_5$: C, 52.42; H, 8.73. Found: C, 52.16, 52.17; H, 8.85, 8.90.

Diisopropylidenediglycerol from the Oxidation of Allyl Ether with Permanganate.—To a mixture of allyl ether (49.0 g., 0.5 mole) and water (600 cc.) cooled to 2° was added, with stirring, a solution of potassium permanganate (160.0 g., 1.01 moles) in water (3200 cc.) over a period of four hours. The mixture at first was a fairly thick gel which became more fluid in the last hour when the temperature rose to 5°. After three hours at room temperature the mixture was filtered. The filtrate was neutralized with concentrated hydrochloric acid and the solution was concentrated under reduced pressure to a viscous, light-colored residue. When most of the water had been removed, ethyl alcohol (50 cc.) and benzene (50 cc.) were added in order to dry the product by azeotropic distillation. After the residual sirup was dissolved in methyl alcohol, the mixture was filtered and the alcohol was removed under reduced pressure. There was obtained 91.8 g. of product (theoretical yield, 83.0 g.) which possessed an hydroxyl content of 21.7%⁹ (theoretical for diglycerol, 40.8%). These data indicate that the product was very impure, possibly as a result of the presence of inorganic salts and oxidation products of diglycerol.

This product (80.0 g.) together with a solution of hydrogen chloride (6.0 g.) in acetone (350 cc.) and anhydrous sodium sulfate (100.0 g.) were stirred overnight at room temperature. The acetonation products were isolated as indicated in the preceding preparation. The sodium sulfate in this case became gummy and the adhering unre-

acted polyhydric alcohol was removed by extraction with absolute methyl alcohol. Evaporation of the solvent yielded 23.8 g. of sirup which was again subjected to acetonation (250 cc. acetone, 1.8 g. hydrogen chloride, 30.0 g. sodium sulfate). From these two acetonations there resulted 34.0 g. (31.8%) of diisopropylidenediglycerol whose physical constants checked those of the preceding preparation. No isopropylidenediglycerol was obtained in this case.

Addition of Hypochlorous Acid to Allyl Ether.—Carbon dioxide was bubbled into a stirred, cooled (3°) mixture of allyl ether (24.5 g., 0.25 mole), water (2500 cc.) and calcium hypochlorite (35%, 102 g., 0.25 mole) in a flask equipped with a Dry Ice-condenser to prevent loss of allyl ether. After two hours, titration of a test sample indicated that all of the calcium hypochlorite had reacted. To ensure completion of the reaction, 51 g. more of calcium hypochlorite was added, and stirring and carbon dioxide addition were continued for two hours longer. Titration for calcium hypochlorite at hourly intervals indicated that the reaction was complete. The filtered reaction mixture was saturated with sodium chloride and extracted with ether, and the ether extract was dried and concentrated. The residue (50.0 g.) on distillation under reduced pressure yielded 47.9 g. (94.4%) of material (distillation range 150–165° (3 mm.)). A sample was redistilled for analysis at 138–139° (1 mm.). It possessed the constants n_D^{25} 1.4913, d_4^{25} 1.3450.

*Anal.*⁹ Calcd. for $C_9H_{18}O_5Cl_2$: Cl, 34.91. Found: Cl, 34.82, 34.75.

Isopropylidene- and Diisopropylidenediglycerol from the Hydrolysis Product of the Hypochlorous Acid Addition Product of Allyl Ether.—A mixture containing the above-described hypochlorous acid addition product (40.6 g., 0.2 mole) and sodium bicarbonate solution (10%, 672 cc., 0.8 mole) was heated at 140–160° in an autoclave for two hours. The cooled solution was neutralized with concentrated hydrochloric acid after which it was concentrated under reduced pressure. The resulting sirup was dissolved in absolute ethanol, the solution filtered and the solvent removed under reduced pressure. The residue weighed 32.0 g. (theoretical, 33.6 g.).

This sirup (20.0 g.) was acetonated (150 cc. acetone, 5.0 g. hydrogen chloride, 25.0 g. anhydrous sodium sulfate) as indicated previously to obtain 13.5 g. of diisopropylidenediglycerol and 7.0 g. of isopropylidenediglycerol. On the basis of the weights of isopropylidene derivatives, the yield of diglycerol was 71%.

2-Epoxypropyl Ether.—An apparatus and procedure similar to that described in "Organic Syntheses"¹⁰ was used. The above-described hypochlorous acid addition product (152.3 g., 0.75 mole) in anhydrous ether (300 cc.) was converted to 2-epoxypropyl ether by the action of powdered and sieved sodium hydroxide (66.0 g., 1.65 moles) which had been mixed with an equal amount of sand. Approximately twenty minutes was required for the addition of alkali, during which time the mixture was agitated vigorously and the temperature was maintained at 25–30°. The reaction was continued under reflux for four hours and the caustic was scraped from the sides of the vessel at intervals. The reaction mixture was filtered and the solid material was washed well with ether. Evaporation of the filtrate and washings yielded the product which was distilled under reduced pressure and collected in five fractions which weighed 74.3 g. (distilling range, 70–91° (2 mm.)). The residue (8.0 g.) was probably chiefly unreacted chlorohydrin. By more careful fractional distillation of the above distillate there was obtained 62.8 g. (64.4%) of 2-epoxypropyl ether, as indicated by a plot of refractive index *versus* sample weights. The product, previously reported by Nef,⁵ distilled at 98–99° (11 mm.) and had an n_D^{25} of 1.4455 and d_4^{25} of 1.1262. The product was readily hydrolyzed to diglycerol as indicated in the next experiment.

Diglycerol by the Hydrolysis of 2-Epoxypropyl Ether.—A mixture of 2-epoxypropyl ether (25.0 g., 0.192 mole)

(9) The authors are indebted to Mr. Harold Boyd and to Miss Katherine Teller for the micro carbon and hydrogen analyses, to Mrs. Eileen Smith for the hydroxyl analysis and to Mrs. Janice Floyd for the chlorine analysis.

(10) H. Gilman and A. H. Blatt, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 233.

and dilute sulfuric acid (5%, 400 cc.) was refluxed for four and one-half hours. The cooled solution was neutralized with saturated barium hydroxide solution, centrifuged to remove barium sulfate, and concentrated under reduced pressure. The residue was dissolved in absolute ethanol, filtered and again concentrated. The product (28.0 g.) was fractionally distilled under reduced pressure and yielded 21.5 g. (67.4%) of product distilling at 207° (1.2 mm.) and possessing a n_D^{20} of 1.4885.^{1a}

Diglycerol from Isopropylidene- and Diisopropylidene-diglycerols.—Diisopropylidenediglycerol was hydrolyzed to diglycerol as previously described.^{1a} The monoisopropylidene derivative was hydrolyzed similarly to yield a theoretical quantity of the parent compound.

Summary

1. Diglycerol has been synthesized directly by the hydroxylation of allyl ether by the action

of permanganate and by the action of performic acid.

2. Diglycerol has also been synthesized by hydrolysis of the dichlorohydrin resulting from the addition of hypochlorous acid to allyl ether. The dichlorohydrin has likewise been converted to 2-epoxypropyl ether which has also been hydrolyzed to diglycerol.

3. Fractional distillation of diglycerol as diisopropylidenediglycerol has provided a simple means for isolating diglycerol from the reaction mixtures. Isopropylidenediglycerol forms as a by-product.

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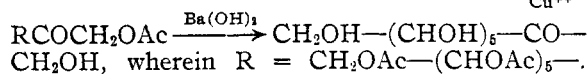
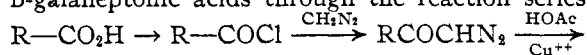
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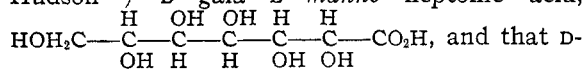
Two Ketoöctoses from the D-Galaheptonic Acids¹

BY M. L. WOLFROM AND PASCAL W. COOPER,

In continuation of our studies on the synthesis of higher ketoses, we report herein two new ketoöctoses prepared from the two isomeric D-galaheptonic acids through the reaction series



The more readily isolable form of D-galaheptonic acid, obtained through the cyanohydrin reaction on D-galactose, was described by Maquenne,² Kiliani³ and Fischer⁴ and was designated D- α -galaheptonic acid by the latter. The epimeric D- β -galaheptonic acid was first obtained by Fischer.⁴ Peirce⁵ proved that D- α -galaheptonic acid was configurationally (nomenclature of Hudson^{6,7}) D-gala-L-manno-heptonic acid,



β -galaheptonic acid was D-gala-L-gluco-heptonic acid, $HOH_2C \begin{array}{cccc} H & OH & OH & H & OH \\ | & | & | & | & | \\ -C & -C & -C & -C & -CO_2H. \text{ In} \\ | & | & | & | & | \\ OH & H & H & OH & H \end{array}$

our work we followed the preparative directions of Hudson and co-workers^{8,9} for obtaining these two acids. Incidental to the isolation of D- α -galaheptonic acid as the amide, we describe the dihydrate of D-gala-L-manno-heptonamide.

(1) Paper No. 11 in the series entitled "The Action of Diazomethane upon Acyclic Sugar Derivatives"; previous communication, M. L. Wolfrom, J. M. Berkebile and A. Thompson, THIS JOURNAL, **71**, 2360 (1949).

(2) L. Maquenne, *Compt. rend.*, **106**, 286 (1888).

(3) H. Kiliani, *Ber.*, **21**, 915 (1888).

(4) E. Fischer, *Ann.*, **388**, 139 (1895).

(5) G. Peirce, *J. Biol. Chem.*, **22**, 327 (1915).

(6) C. S. Hudson, THIS JOURNAL, **60**, 1537 (1938).

(7) C. S. Hudson, *Advances in Carbohydrate Chem.*, **1**, 28 (1945).

(8) R. M. Hann, Alice T. Merrill and C. S. Hudson, THIS JOURNAL, **67**, 2100 (1935).

(9) R. M. Hann and C. S. Hudson, *ibid.*, **59**, 548 (1937).

D-Gala-L-manno-heptonic acid crystallizes in the unlactonized form and Robbins and Upson¹⁰ found it to be directly acetylatable to its crystalline hexaacetate. Treatment of the acetylated acid with phosphorus pentachloride yielded the crystalline hexaacetyl-D-gala-L-manno-heptonyl chloride which gave the crystalline acetylated diazomethyl ketone with diazomethane. The keto acetate resisted crystallization but was obtained in an analytically pure condition by chromatographic purification. Low temperature deacetylation with barium hydroxide yielded D-gala-L-tagato-octose, $HOH_2C \begin{array}{cccc} H & OH & OH & H & H \\ | & | & | & | & | \\ -C & -C & -C & -C & -CO-CH_2OH. \\ | & | & | & | & | \\ OH & H & H & OH & OH \end{array}$

This substance was unfortunately amorphous but was characterized further by a crystalline phenylosotriazole.

The crystalline epimeric hexaacetyl-D-gala-L-gluco-heptonic acid was obtained by the acetylation of the amorphous cadmium salt with acetic anhydride and hydrogen chloride according to the general procedure of Ladenburg, Tishler, Wellman and Babson.¹¹ It was further characterized as its methyl ester. The corresponding acetylated acid chloride failed to crystallize but the acetylated diazomethyl ketone and the keto acetate were obtained crystalline. Deacetylation of the latter yielded D-gala-L-sorbo-

octose, $HOH_2C \begin{array}{cccc} H & OH & OH & H & OH \\ | & | & | & | & | \\ -C & -C & -C & -C & -CO-CH_2OH, \\ | & | & | & | & | \\ OH & H & H & OH & H \end{array}$

again unfortunately not crystallized. It was characterized further by its known phenylosazone.

D-Gluco-L-tagato-octose has been described.¹² Its properties and those of two derivatives are

(10) G. B. Robbins and F. W. Upson, *ibid.*, **62**, 1074 (1940).

(11) K. Ladenburg, M. Tishler, J. W. Wellman and R. D. Babson, *ibid.*, **66**, 1217 (1944).

(12) M. L. Wolfrom and A. Thompson, *ibid.*, **63**, 1453 (1946).