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Formation of 1,6- and 1,7-Anhydro-D-*glycero*-β-D-*gulo*-heptopyranoses from D-*glycero*-D-*gulo*-Heptose in Acid Solution[1,2]

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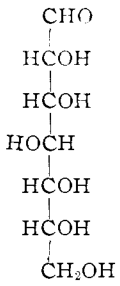
The sugar D-*glycero*-D-*gulo*-heptose is transformed by hot dilute acid to the extent of about 19% to a mixture of the previously known 1,6-anhydro-D-*glycero*-β-D-*gulo*-heptopyranose and a new crystalline monomeric anhydroheptose. The structure of the new anhydride was established conclusively through periodate oxidation methods as 1,7-anhydro-D-*glycero*-β-D-*gulo*-heptopyranose. The compound is thus the first example of an anhydroheptose with a 1,5:1,7 combination of rings and is the second example of anhydride formation by the action of acid on a sugar of the *gulo* configuration.

Earlier work has shown that the transformation of reducing sugars with the *altro* or *ido* configuration to non-reducing monomeric anhydrides under acidic conditions occurs to the following extents: D-altrose, 57%; D-*altro*-heptulose, 80%; D-idose, 75%; D-*ido*-heptulose, 85%; and D-*glycero*-D-*ido*-heptose, 43%. The crystalline anhydrides thus obtained from the aldoses are 1,6-anhydropyranoses and those from the heptuloses are the analogous 2,7-anhydropyranoses.[3]

Recently we discovered that L-*gulo*-heptulose also is sensitive to acids, and is converted, readily and in 80% yield, to a crystalline anhydride whose structure was proved to be 2,7-anhydro-β-L-*gulo*-heptulopyranose.[4] The behavior toward acid of a second sugar with a *gulo* configuration, namely, D-*glycero*-D-*gulo*-heptose (I) (formerly called D-α-glucoheptose and D-gluco-D-*gulo*-heptose) is the subject of the present communication. When a solution of that sugar in 0.5 *N* sulfuric acid was boiled gently for 24 hours it lost about 19% of its original reducing power. Removal of most of the unchanged heptose by crystallization, and the remainder by alkaline oxidation followed by deionization, left a non-reducing sirup. Benzoylation of the sirup yielded two products, one of which was identified as the tetrabenzoate of the known 1,6-anhydro-D-*glycero*-β-D-*gulo*-heptopyranose,[5] and the other, corresponding to about 12% of the original heptose, was the tetrabenzoate of a new monomeric anhydroheptose. Debenzoylation of the latter compound furnished the anhydride itself in crystalline form, with melting point originally 135–137°, later changing to 169–171°, and $[\alpha]^{20}\mathrm{D}$ +60.0° in water; the values 95° and +52.9°, respectively, had been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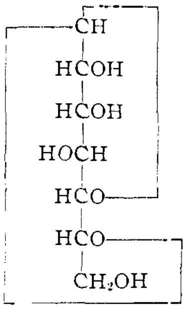
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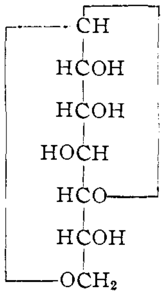
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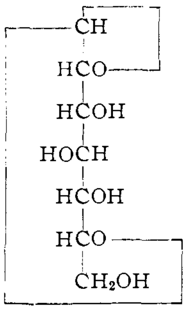
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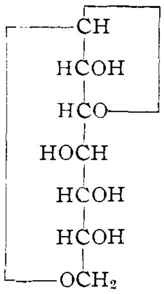
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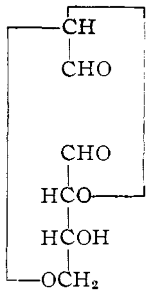
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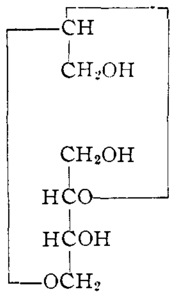
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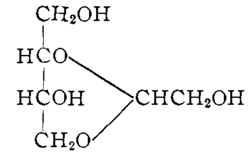
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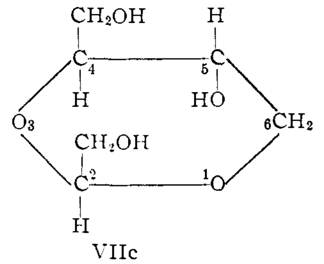
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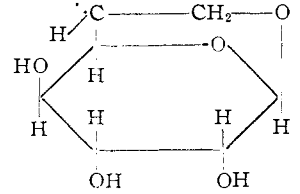
IIIa

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[1] Presented in part before the Division of Sugar Chemistry at the Atlantic City Meeting of the American Chemical Society, September 15, 1952.

[2] For the preceding paper on anhydro sugars see J. W. Pratt, N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **75**, 4503 (1953).

[3] See ref. 2 for further details and pertinent references. In addition, 1,6-anhydro-β-D-glucopyranose (= levoglucosan) has been obtained from D-glucose in about 0.2% yield [A. Thompson, K. Anno, M. L. Wolfrom and M. Inatome, THIS JOURNAL, **76**, 1309 (1954)] and still more recently has been reported to exist in the equilibrium mixture to the extent of 2% [L. D. Ough and R. G. Rohwer, Abstracts of Papers, New York Meeting of the American Chemical Society, Sept. 12–17, 1954, page 16D, and personal communication from the authors]. A new anhydride, tentatively identified as 2,7-anhydro-β-D-*altro*-heptulofuranose, has been reported in 2% yield from the action of acid on the well-known 2,7-anhydro-β-D-*altro*-heptulopyranose (= sedoheptulosan) [L. P. Zill and N. E. Tolbert, *Federation Proc.*, **13**, 327 (1954); THIS JOURNAL, **76**, 2929 (1954)].

[4] L. C. Stewart, N. K. Richtmyer and C. S. Hudson, *ibid.*, **74**, 2206 (1952).

[5] E. M. Montgomery, N. K. Richtmyer and C. S. Hudson, *ibid.*, **65**, 1848 (1943); see also ref. 2 for a definitive proof of structure.

reported previously for the melting point and rotation of the 1,6-anhydride.[5] Both new and old anhydrides are converted by acetolysis to mixtures of the known hexaacetates of D-*glycero*-D-*gulo*-heptose.

The structure of the new anhydride was established through application of periodate oxidation methods. The consumption of two molar equivalents of oxidant and the liberation of one molar equivalent of formic acid indicated the presence of three contiguous secondary hydroxyl groups in the anhydride molecule. The possible structures are thus limited to four, as shown in formulas II-V, and of these, II had been proved already to apply to the first anhydride.[5] To decide among the other three choices, we submitted the periodate oxidation product to hydrogenation and obtained a six-carbon-atom trihydric alcohol that on subsequent hydrolysis yielded erythritol. Such treatment of IV and V would have produced glycerol and ethylene glycol, respectively. The remaining structure III must therefore apply to our new anhydride; its Haworth-type projection formula is shown in IIIa. Direct confirmation of that structure was secured readily through characterization of the trihydric alcohol as a crystalline tri-*p*-nitrobenzoate. In contrast to the optically inactive derivative obtained similarly from II,[2] our tri-*p*-nitrobenzoate showed $[\alpha]^{20}\text{D}$ $-55.8°$ in chloroform; the compound from II was a symmetrically substituted 2,3-acetal of erythritol and was thus a *meso* form, whereas the compound VIIa, from III *via* the optically active dialdehyde VI, should be optically active. It may be written also as VIIb and named as an erythritol derivative (as we have done in the Experimental part) or as VIIc and named 5-D-*glycero*-2,4-*cis*-di-(hydroxymethyl)-5-*trans*-hydroxy-1,3-dioxane, in which manner we have attempted to show its complete configuration and to indicate that the arrangement at C_5 is the same as that at C_6 in the original D-*glycero*-D-*gulo*-heptose.

In summary, the action of acid had been found previously to convert L-*gulo*-heptulose in 80% yield to what we may designate the "normal" anhydride, which is the 2,7-anhydroheptulopyranose form. D-*glycero*-D-*gulo*-Heptose, however, has now been found to produce about 7% of the analogous "normal" 1,6-anhydroheptopyranose form, together with about 12% of a new type of anhydride whose structure has been proved to be a 1,7-anhydroheptopyranose. The acid transformation of D-gulose to 1,6-anhydro-β-D-guloheptopyranose in about 43% yield has recently been announced,[6] and will be described in a subsequent publication.

Experimental

Conversion of D-*glycero*-D-*gulo*-Heptose (I) with Acid to a Non-reducing Sirup.—In a typical preparation, 100 g. of D-*glycero*-D-*gulo*-heptose in 1 liter of 0.5 *N* sulfuric acid was boiled gently under a reflux condenser for 24 hours; longer heating caused further destruction of the unchanged sugar without increasing the amount of non-reducing anhydrides. A portion of the brown solution and accompanying small amount of carbon-like material was clarified with activated carbon and the rotation found to have changed from $[\alpha]^{20}\text{D}$ $-20°$ to $-5°$ (calcd. as heptose). The sulfuric acid was neutralized by adding 100 g. of barium carbonate in small amounts and stirring until the solution was no longer acid to litmus. Twenty-five grams of activated carbon was added, the mixture filtered, and the solution concentrated *in vacuo*. When crystals of the sugar began to separate, the solution was heated and transferred to a beaker where it could be stirred occasionally as it crystallized at room temperature and then at $-5°$ for 2 days. The product was filtered and washed with 80% ethanol. An additional amount could be obtained by diluting the filtrate with 25 ml. of 95% ethanol. The average recovery of D-*glycero*-D-*gulo*-heptose by this procedure was 53 g. The mother liquor was diluted with water and concentrated *in vacuo* to remove the ethanol; the aqueous solution was then heated with excess barium hydroxide in an open beaker on the steam-bath for about 1 day to destroy the remaining heptose. Carbon dioxide was bubbled into the solution until it was no longer alkaline to phenolphthalein. Decolorizing carbon was added and the mixture heated on the steam-bath for 1 hour, filtered and finally deionized completely by passage through Amberlite IR-120 and Duolite A-4 ion-exchange resins. The resulting solution, upon concentration to a small volume, showed $[\alpha]^{20}\text{D}$ $+6°$, calcd. on the basis of the original 100 g. of heptose; further concentration left 14 g. of a sirup, whose rotation accordingly would be about $[\alpha]^{20}\text{D}$ $+ 43°$. This non-reducing sirup showed no tendency to crystallize until seed crystals of the 1,7-anhydride became available later. Acetylation failed to yield any crystalline derivative.

Benzoylation of the Non-reducing Sirup and Isolation of 1,7-Anhydro-2,3,4,6-tetra-*O*-benzoyl-D-*glycero*-β-D-*gulo*-heptopyranose.—The reaction of 12 g. of sirup with benzoyl chloride and pyridine overnight at room temperature, with subsequent isolation of the product in the usual manner, gave two crystalline benzoates. The less-soluble component, after four recrystallizations from a mixture of acetone and *n*-pentane, weighed 6 g. and the clusters of fine needles melted at 175–178°; by several additional recrystallizations the m.p. could be raised to a constant value of 182–183°. The rotation was $[\alpha]^{20}\text{D}$ $+99.0°$ in chloroform (*c* 2).

Anal. Calcd. for $C_{35}H_{28}O_{10}$: C, 69.07; H, 4.64. Found: C, 68.92; H, 4.78.

Isolation of 1,6-Anhydro-2,3,4,7-tetra-*O*-benzoyl-D-*glycero*-β-D-*gulo*-heptopyranose.—After tosylation of the non-reducing sirup, as described in a later paragraph, had indicated the presence of the known 1,6-anhydro-D-*glycero*-β-D-*gulo*-heptose,[5] confirmatory evidence was sought in the lower-melting fractions of the benzoylation product. Chromatography of a portion of that material by adsorption on a column of activated alumina and fractional elution with benzene yielded first the new 1,7-anhydride tetrabenzoate, and later the slower-moving 1,6-anhydride derivative. Subsequently, the laborious fractional crystallization of a large amount of the mixed benzoates from benzene–pentane afforded a total of 16 g. of the 1,6-anhydro-2,3,4,7-tetra-*O*-benzoyl-D-*glycero*-β-D-*gulo*-heptopyranose with m.p. 149–150° and $[\alpha]^{20}\text{D}$ $+146°$ in chloroform (*c* 2) as compared with the recorded values of m.p. 154–155° and $[\alpha]^{20}\text{D}$ $+144.4°$ in chloroform (*c* 2).[5]

Debenzoylation of 15.5 g. of the tetrabenzoate thus obtained produced 4.2 g. of 1,6-anhydro-D-*glycero*-β-D-*gulo*-heptopyranose; recrystallized from methanol–ethyl acetate, it showed m.p. 95–97° and $[\alpha]^{20}\text{D}$ $+51.1°$ in water (*c* 1.3) as compared with the recorded values of m.p. 95° and $[\alpha]^{20}\text{D}$ $+52.9°$ in water (*c* 2).[5] The molecular weight, not previously determined, was found to be 193 (calcd. 192) by the lowering of the freezing point of water.

Tosylation of the Non-reducing Sirup and Isolation of 1,6-Anhydro-D-*glycero*-β-D-*gulo*-heptopyranose Derivatives.—A mixture of 7 g. of sirup, 35 g. of *p*-toluenesulfonyl chloride and 150 ml. of dry pyridine was allowed to stand at room temperature for 2 days and at $+5°$ for an additional 3 days. The product, isolated in the usual manner, was a sirup that was dissolved in hot methanol and seeded with crystals of the known tritosyl derivative of the 1,6-anhydride. Overnight two types of crystals deposited; these were filtered, separated by hand and each type recrystallized several times from methanol. The one—acicular prisms—melted at 151–152° and showed $[\alpha]^{20}\text{D}$ $+33.3°$ in chloroform (*c* 2); these values, together with an analysis (Calcd. for $C_{28}H_{30}O_{12}S_3$: C, 51.36; H, 4.62. Found: C, 51.49; H, 4.63), identified the substance as 1,6-anhydro-2,3,7-tri-*O*-*p*-tolylsulfonyl-D-*glycero*-β-D-*gulo*-heptopyranose whose m.p.

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[6] L. C. Stewart and N. K. Richtmyer, Abstracts of Papers, Chicago Meeting of the American Chemical Society, Sept. 6-11, 1953, page 18D.

and rotation had been reported previously[5] as 157° and $[\alpha]^{20}\mathrm{D}$ +34.6° in chloroform (*c* 2), respectively. A small sample remaining from the earlier work now melted at 148–150° and apparently was not pure, but a mixture of the two substances showed no depression in melting point. The second compound—clusters of fine needles—melted at 178–179° and showed $[\alpha]^{20}\mathrm{D}$ −37.0° in chloroform (*c* 1); these data, plus the analysis (Calcd. for $C_{21}H_{22}O_9S_2$: C, 52.27; H, 4.60; S, 13.29. Found: C, 52.19; H, 4.57; S, 13.46), identified the substance as the 1,6:4,7-dianhydro-2,3-di-*O*-*p*-tolylsulfonyl-D-*glycero*-*β*-D-*gulo*-heptopyranose, with m.p. 180–182° and $[\alpha]^{20}\mathrm{D}$ −37.0°, that had been described earlier. The formation of a 4,7-anhydride in this instance, presumably through the 2,3,7-tritosyl derivative as an intermediate, recalls the conversion of 1,2-*O*-isopropylidene-D-glucofuranose to 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-D-glucose by tosylation in boiling pyridine–chloroform.[7]

1,7-Anhydro-D-*glycero*-*β*-D-*gulo*-heptopyranose (III).—Six grams of the new, higher-melting tetrabenzoate described above was debenzoylated by refluxing it in 100 ml. of methanol containing 1 ml. of 3% sodium methoxide for 1 hour. The solution was concentrated *in vacuo* to a thick sirup that crystallized when rubbed with ethanol. Several recrystallizations from ethanol gave prisms with m.p. 135–137° and $[\alpha]^{20}\mathrm{D}$ +60.0° in water (*c* 1.6). With seed crystals available it was possible to inoculate the original nonreducing sirups in ethanol and obtain the 1,7-anhydride by direct crystallization, although the process was very slow. The first crystals obtained in this manner, however, melted at 169–171°, and it was discovered that the original preparation, after standing for a month, meanwhile had acquired the higher melting point; the lower-melting modification was never observed again. Acetylation of the 1,7-anhydride did not produce a crystalline acetate.

Anal. Calcd. for $C_7H_{12}O_6$: C, 43.75; H, 6.30; mol. wt., 192. Found: C, 44.01; H, 6.40; mol. wt. (by lowering of the freezing point of water), 193.

1,7-Anhydro-2,3,6(?)-tri-*O*-*p*-tolylsulfonyl-D-*glycero*-*β*-D-*gulo*-heptopyranose.—The reaction of 4.2 g. of the 1,7-anhydride (III) with 25 g. of *p*-toluenesulfonyl chloride (6 molar equivalents) in 50 ml. of pyridine for 42 hours at room temperature yielded a sirupy tosylation product. A portion of the sirup in benzene was adsorbed on a column of activated alumina and eluted with successive portions of benzene and of benzene–ether mixtures The larger part of the eluate, composed of the less-polar fractions and hence presumed to contain the tetratosyl derivative, could not be crystallized. The later fractions, however, gave crystals that were used to inoculate the remainder of the sirupy tosylation product. In this way, 6 g. of the tritosyl derivative was isolated. It separated from benzene–pentane as needles that melted at 75–85°, resolidified at about 120°, and melted again at 148–149°; analyses indicated that the original needles represented a partially solvated form. Recrystallization from methanol or ether–pentane furnished short chunky prisms of solvent-free tritosyl compound, with m.p. 149–150° and $[\alpha]^{20}\mathrm{D}$ +37.7° in chloroform (*c* 2). While the m.p. and rotation are close to the values reported for the tritosyl-1,6-anhydride (151–152°; +33.3°),[5] mixed melting points and infrared absorption spectra clearly established the non-identity of the two substances. It should be noted that there is no experimental evidence to substantiate the allocation of the tosyl groups to the positions indicated in the paragraph heading; however, models indicate that the hydroxyl at carbon 4 is the most hindered and hence probably the least readily substituted.

Anal. Calcd. for $C_{28}H_{30}O_{12}S_3$: C, 51.36; H, 4.62; S, 14.69. Found: C, 51.43; H, 4.94; S, 14.48.

Acetylation of this tritosyl derivative, unlike that of the isomeric tritosyl-1,6-anhydride, failed to give a crystalline acetate.

Estimation of the Amounts of the 1,6- and 1,7-Anhydrides in the Equilibrium Mixture with D-*glycero*-D-*gulo*-Heptose.—Although some carbonization of material occurs when D-*glycero*-D-*gulo*-heptose is heated with acid, it was of interest to determine the position of equilibrium between sugar and anhydrides at the point chosen for stopping the reaction. Accordingly, in one preparation, 218 g. of heptose was refluxed gently for 24 hours in 0.5 *N* sulfuric acid; the acid was removed by cautious neutralization with barium hydroxide; and the solution was clarified by subsequent filtration through activated carbon. An aliquot of this solution was dried to constant weight and the total amount of heptose and anhydrides found to be 175 g. The rotation, $[\alpha]^{20}\mathrm{D}$ −6.85°, was then determined for the mixture. From the $[\alpha]^{20}\mathrm{D}$ values of −20° for the unchanged heptose and +58° for the mixed anhydrides (a weighted average derived from the data recorded in the following paragraph), the total amount of the two anhydrides was calculated as 17% by weight, or 19% on a molar basis. These figures were confirmed by determining the amount of heptose in the same solution by a standard ferricyanide titration method. Thus we could estimate that about 19% of the D-*glycero*-D-*gulo*-heptose is transformed by acids to a mixture of the two anhydrides.

The relative amounts of the anhydrides were determined in a portion of the solution by destroying the unchanged heptose with barium hydroxide, deionizing, and concentrating the mixed anhydrides to dryness. The residue was benzoylated with benzoyl chloride and pyridine in the usual manner and the rotation $[\alpha]^{20}\mathrm{D}$ +115° determined for a known weight of the mixed benzoates in chloroform solution. Knowing the specific rotations of the two tetrabenzoates, we could then estimate the ratio of 1,7- to 1,6-anhydride as nearly 2:1 and that the original equilibrium mixture contained, on a molar basis, about 81% of the heptose, 12% of the 1,7-anhydride and 7% of the 1,6-anhydride.

Oxidation of 1,7-Anhydro-D-*glycero*-*β*-D-*gulo*-heptopyranose (III) with Sodium Metaperiodate and Subsequent Hydrogenation to 1,3-*O*-(2-Hydroxyethylidene)-L-erythritol (VIIa, b, c).—A preliminary oxidation of 0.5 g. of the 1,7-anhydride showed a final constant rotation of $[\alpha]^{20}\mathrm{D}$ −35.8° (calcd. as the expected dialdehyde VI) as contrasted with the value of −58.7° obtained from the 1,6-anhydride.[5] Titrations after 12 and 36 hours corresponded to the liberation of 0.99 and 1.02 molar equivalents of formic acid and the consumption of 2.01 and 2.10 molar equivalents of oxidant, respectively. No formaldehyde was detected in the solution. In a larger run, the oxidation of 15.00 g. of 1,7-anhydride by 400 ml. of 0.43 *M* aqueous sodium metaperiodate in a total volume of 1 liter produced considerable heat and was complete within 1 hour; the rotation $[\alpha]^{20}\mathrm{D}$ −36.4° and the values 0.95 and 2.01 for formic acid liberated and periodate consumed, respectively, are in good agreement with the corresponding data of the preliminary experiment. The solution was neutralized cautiously with aqueous barium hydroxide, and 25 g. of barium chloride dihydrate in water was added to precipitate most of the iodate and periodate ions. After filtration, the solution was concentrated *in vacuo* and the dialdehyde extracted with ethanol from the remaining salts. An aqueous solution of the dialdehyde was hydrogenated, with Raney nickel as catalyst, for 16 hours at 100° and 2800 p.s.i. The solution was filtered, deionized, and concentrated *in vacuo;* it showed $[\alpha]^{20}\mathrm{D}$ −41°, calculated as the expected trihydric alcohol VII. Neither the trihydric alcohol nor the benzoate prepared from it could be crystallized. However, when 3 g. of the sirupy alcohol with an excess of *p*-nitrobenzoyl chloride in 50 ml. of pyridine was allowed to stand overnight at room temperature and the reaction mixture poured into water, 10 g. of dark-colored crystalline material was obtained. After several decolorizations with activated carbon in various solvents and several recrystallizations from aqueous acetone, the product consisted of very pale yellow, flattened prismatic needles with m.p. 163–164° and $[\alpha]^{20}\mathrm{D}$ −55.8° in chloroform (*c* 1.3); its composition agreed with that of the expected 1,3-*O*-(2-hydroxyethylidene)-L-erythritol tri-*p*-nitrobenzoate.

Anal. Calcd. for $C_{27}H_{21}O_{14}N_3$: C, 53.03; H, 3.46; N, 6.87. Found: C, 53.09; H, 3.50; N, 7.10.

Hydrolysis of 1,3-*O*-(2-Hydroxyethylidene)-L-erythritol (VII) to Glycolaldehyde and Erythritol.—A solution containing about 2.8 g. of the erythritol derivative VII in 100 ml. of 0.5 *N* sulfuric acid was heated in a boiling waterbath for 2 hours; its rotation had become practically negligible. The presence of glycolaldehyde in the solution was inferred from its restoration of color instantly to Schiff reagent and from its reduction of cold Fehling solution, and confirmed by the characteristic green that it developed in the

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[7] H. Ohle and E. Dickhäuser, *Ber.*, **58**, 2593 (1925); for some other examples, see R. S. Tipson, in *Advances in Carbohydrate Chem.*, **8**, 117 (1953).

specific color reaction described by Dische and Borenfreund.[8] The major portion of the hydrolysis mixture was neutralized with aqueous barium hydroxide, filtered and concentrated to a sirup that was benzoylated with benzoyl chloride and pyridine in the usual manner. The four grams of product thus obtained was identified as erythritol tetrabenzoate, melting at 190–191° and showing no depression of m.p. when mixed with an authentic specimen.

Acetolysis of 1,7-Anhydro-D-*glycero*-β-D-*gulo*-heptopyranose (III).—In the same way as had been done previously with the 1,6-anhydride,[6] a 0.5-g. sample of the new 1,7-anhydride was dissolved in a 2:1 mixture of acetic anhydride and glacial acid containing 2.5% (v./v.) of concentrated sulfuric acid. After the rotation had become constant at $[\alpha]^{20}_D$ +20.2° (calcd. as heptose hexaacetate) in the course of 5 days at 20°, the reaction mixture was decomposed in the usual manner. The product was fractionally crystallized from chloroform–pentane to yield the known α- and β-anomers of D-*glycero*-D-*gulo*-heptose hexaacetate, which were identified by m.p. and mixed m.p. with authentic materials prepared especially for that purpose.

Hexa-*O*-acetyl-D-*glycero*-α-D-*gulo*-heptopyranose has been reported by Fischer[9] to melt at 156°. Hudson and Yanovsky[10] later prepared the substance by the zinc chloride–acetic anhydride rearrangement of the β-anomer and reported m.p. 164° (uncor.) and $[\alpha]^{20}_D$ +87.0° for the pure substance. One of us has now repeated the zinc chloride procedure[10] and, after five recrystallizations from a mixture of chloroform, ether, and pentane, obtained a product with m.p. 171–172° (cor.) and $[\alpha]^{20}_D$ +94.7° in chloroform (*c* 1.6, *l* 4); these values were unchanged by five additional recrystallizations. Independently, the second author then acetylated 10 g. of D-*glycero*-D-*gulo*-heptose with 150 ml. of acetic anhydride containing 1% sulfuric acid. The rotation, after 3 days, was $[\alpha]^{20}_D$ +22° and corresponded roughly to the presence of 20% of the α-form. The crude product, from chloroform–pentane, weighed 15.6 g. and melted at 116–136°. One recrystallization from a large volume of ether yielded 6.2 g. with m.p. 140–155°. A second recrystallization, from chloroform–ether, produced cauliflower-like aggregates of small needles weighing 2.7 g. and melting at 166–168°. Five additional recrystallizations from chloroform–ether finally yielded 0.5 g. of flattened, shiny, prismatic needles, with m.p. 171–172° (cor.) and $[\alpha]^{20}_D$ +94.8° in chloroform (*c* 2.5; *l* 2) in excellent agreement with the values obtained for the product isolated in the first preparation.

Anal. Calcd. for $C_{19}H_{26}O_{13}$: C, 49.35; H, 5.67; CH_3CO, 55.9. Found: C, 49.41; H, 5.83; CH_3CO, 55.7.

Acknowledgment.—The authors wish to thank Mr. John T. Sipes for preparing the D-*glycero*-D-*gulo*-heptose and Mr. Edward W. Tracy for his aid in the preparation of the anhydrides; Dr. James W. Pratt for his determination of the molecular weights; and Dr. William C. Alford and his associates of the Institutes' microanalytical laboratory for carrying out the microanalyses.

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[8] Z. Dische and E. Borenfreund, *J. Biol. Chem.*, **180**, 1297 (1949).

[9] E. Fischer, *Ann.*, **270**, 64 (1892).

[10] C. S. Hudson and E. Yanovsky, THIS JOURNAL, **38**, 1575 (1916).

[CONTRIBUTION FROM THE STARCH AND DEXTROSE SECTION, NORTHERN UTILIZATION RESEARCH BRANCH[1]]

The Polyesterification of 2,4;3,5-Di-*O*-methylene-D-gluconic Acid[2]

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The polyesterification of the difunctional substituted sugar acid 2,4;3,5-di-*O*-methylene-D-gluconic acid is reported. Rapid condensation of this substance occurs in dry pyridine solution on addition of an equivalent amount of benzoyl chloride or benzoic anhydride. Other aromatic acid chlorides also were effective for this purpose The molecular size of polymer fractions isolated, established by elementary analysis and end-carboxyl-group determination, was in the range of 3 to 45 basic monomer units. The behavior of the products in various solvents also was indicative of polymer formation.

Intermolecular condensation of ω-hydroxyaliphatic acids to form polymers has been demonstrated adequately.[3,4] Examples of condensation polymerization of structurally related acids derived from natural sugars, however, is limited to that of 2,3,4-tri-*O*-methyl-L-arabonic acid.[5] It was of interest, therefore, to study the polyesterification of the difunctional substituted sugar acid 2,4;3,5-di-*O*-methylene-D-gluconic acid.[6,7] Efforts to achieve such condensation by heating *in vacuo* by the method of Lycan and Adams[3] gave only decomposition products, while attempts to transesterify the methyl ester caused methylene cyclic acetal rearrangement and produced methyl 2,4;5,6-di-*O*-methylene-D-gluconate.[8] However, in an attempt to benzoylate 2,4;3,5-di-*O*-methylene-D-gluconic acid, it was found that this substance was rapidly polymerized in dry pyridine solution on addition of an equivalent amount of benzoyl chloride or benzoic anhydride.[9] An extension of the study showed that such highly electronegative acid chlorides as *m*- and *p*-nitro-, 3,5-dinitro- and *p*-chlorobenzoyl chloride and *p*-toluenesulfonyl chloride also favored polyesterification. On the other hand, thionyl chloride, acetyl chloride and acetic anhydride were ineffective for this purpose.

Polyesterification of dimethylenegluconic acid presumably involves intermediate formation of a mixed anhydride from dimethylenegluconic acid and acid chloride or anhydride used.[10–12] Both functional groups of dimethylenegluconic acid must be present to effect polymerization. Neither the methyl ester nor the 6-acetyl derivative of dimethylenegluconic acid in pyridine solution gave a precipitate on addition of benzoyl chloride. As

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