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Two Nitriles Derived from 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl Bromide. A 2-Cyano-2-methyl-1,3-dioxolane Derivative

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The supposed 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl cyanide, recorded in the literature as a product of the condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with silver cyanide in boiling xylene, is shown to be a 2-cyano-2-methyl-1,3-dioxolane derivative. The same substance may be prepared through the reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with mercuric cyanide in nitromethane solution, a reaction which gives a second, isomeric nitrile; this new substance is shown to be 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide. The formation from *cis*-α-acyloxy halides of products normally characteristic of those from *trans*-α-acyloxy halides is discussed.

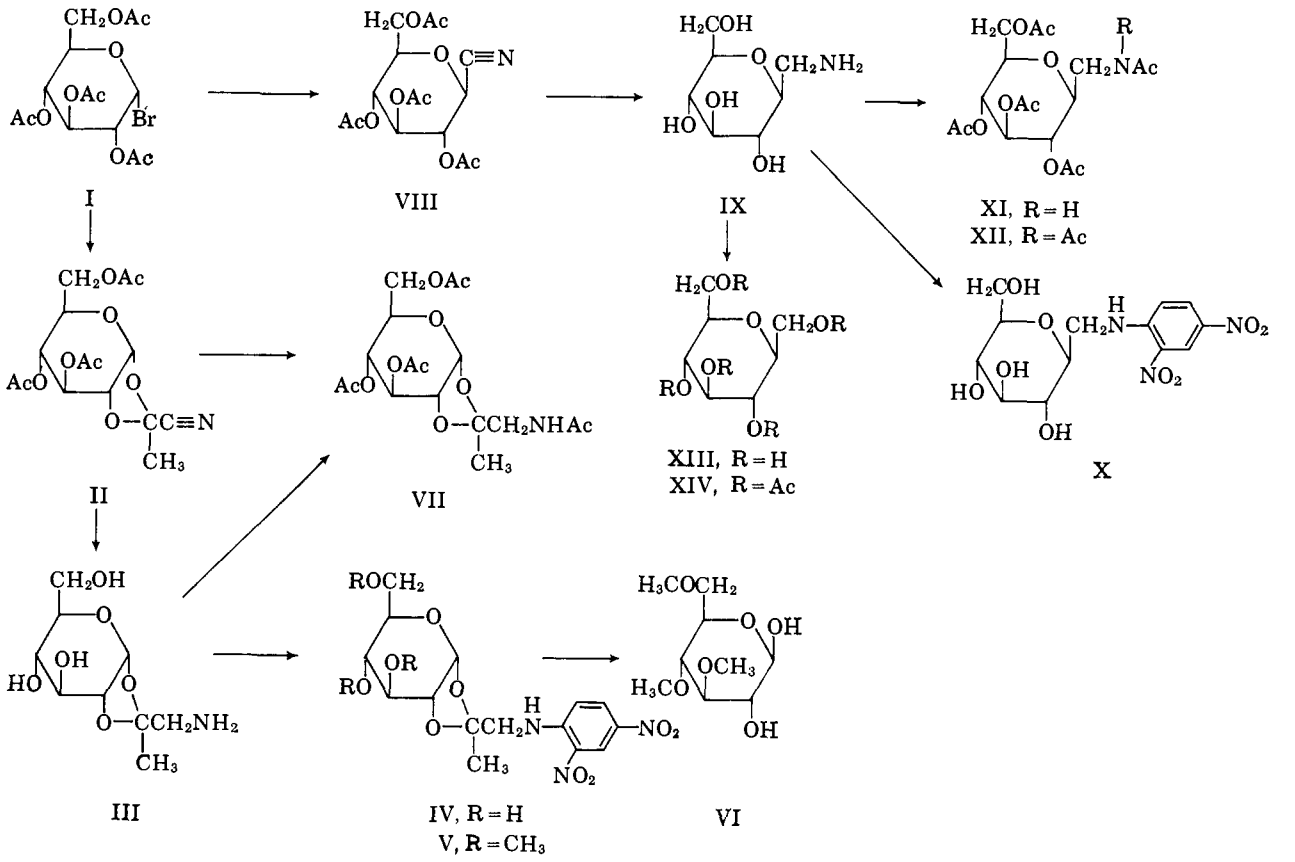
Sixty years ago Koenigs and Knorr[1] announced the discovery of what is now termed 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (I) and, more important, showed that the substance could be condensed with alcohols and phenols in the presence of silver carbonate to give acetylated β-D-glucopyranosides. Over the subsequent years this condensation has become the most important synthetic pathway to the glycosides and oligosaccharides. Efforts to improve the yields from the reaction have been numerous and, in particular, much attention has been directed to the role of those substances which appear to serve merely as acid acceptors but which often doubtless play a vital role in facilitating the displacement of the halide ion. Although still most commonly used, silver carbonate and silver oxide are less than ideal for this purpose since, obviously, in neutralizing hydrogen halides, they produce water which, in turn, may cause the hydrolysis of some of the remaining acylated glycosyl halide. While this difficulty may be minimized through the addition of a solid desiccant to the reaction mixture,[2,3] Goldschmid and Perlin[4] have shown that acylated glycosyl halides react with silver carbonate in the absence of a potential aglycon and that this reaction competes with the desired condensation leading to a glycoside.

In 1949, Helferich and Wedemeyer[5] found that mercuric cyanide could serve as a combined acid acceptor and catalyst in the Koenigs–Knorr reaction between 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide and excess methanol. Subsequently, Helferich and Weis[6] showed that the use of mercuric cyanide, with nitromethane as a solvent, produced an outstanding improvement in the Koenigs–Knorr reaction. Not only were good yields obtained, but these were not contingent upon the use of a large molar excess of the potential aglycon. This modification of the Koenigs–Knorr reaction has been widely adopted[7] but here another side reaction appears, for mercuric cyanide itself condenses with acylated glycosyl halides. Constantzas and Kocourek[8] found that 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide condenses with mercuric cyanide in boiling xylene to give what may be 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl cyanide, while Helferich and Bettin,[9] later and independently, noted the formation of the same compound when mercuric cyanide was used in nitromethane at room temperature. Subsequently Helferich and Ost[10] observed the formation of an analogous compound in the D-xylopyranose series.

In view of the importance of the Koenigs–Knorr reaction we have turned our attention to the general problem of the structure of these interesting by-products. What is apparently the first representative of this class of substances was reported, in 1934, by Buerger,[11] who had condensed 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (I) with silver cyanide in dry, boiling xylene and obtained, in 45% yield, a crystalline substance which had the composition of a tetraacetylhexosyl cyanide. Buerger noted that the substance was not attacked by mercuric oxide at 75–80° and concluded that it was a nitrile rather than an isonitrile. The lability of the cyano group was particularly notable; even on warming with water the substance evolved hydrogen cyanide. With acetic anhydride at 200° or with glacial acetic acid at 150° the substance gave β-D-glucopyranose pentaacetate. On the basis of these pieces of evidence, Buerger termed the substance "1-cyano-2,3,4,6-tetra-*O*-acetyl-*d*-glucose." We have repeated Buerger's preparation and have obtained, in 53% yield, a substance with the melting point and composition which he reported (he gave no optical rotation). Reduction of the compound with lithium aluminum hydride afforded a primary amine, confirming the fact that the substance is a nitrile rather than an isonitrile. The primary amine did not, however, have the composition of the 1-amino-2,6-anhydro-1-deoxyheptitol which one might expect to obtain by the reduction of a 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl cyanide. Furthermore, acid hydrolysis of the amine led to the isolation of D-glucose and aminoacetone, the latter being identified as its crystalline salt with *p*-toluenesulfonic acid.[12] Methylation of the *N*-2,4-dinitrophenyl derivative of the amine afforded a tri-*O*-methyl derivative; hydrolysis of this latter gave the well known 3,4,6-tri-*O*-methyl-D-glucose (VI). The amine itself was further characterized through its *N*-acetyltri-*O*-acetyl derivative, a substance which could also be made through the catalytic reduction of the original nitrile in the presence of acetic anhydride.[13]

The above facts indicate that the primary amine has the structure represented by III, a cyclic acetal derived from D-glucopyranose and aminoacetone, while the nitrile first described by Buerger is not a 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl cyanide but II, which may be regarded as a cyclic acetal formally related to D-glucopyranose and pyruvic acid nitrile or, alternatively, as a cyanide of a cyclic orthoacetate. The nitrile II, which may be designated as 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose, is assumed to have

(1) W. Koenigs and E. Knorr, *Sitzber. Math. Naturw. Kl. Bayer. Akad. Wiss. München*, **30**, 108 (1900); *Ber.*, **34**, 957 (1901).
(2) B. Helferich, E. Bohm, and S. Winkler, *ibid.*, **63**, 990 (1930).
(3) D. D. Reynolds and W. L. Evans, *J. Am. Chem. Soc.*, **60**, 2559 (1938).
(4) H. R. Goldschmid and A. S. Perlin, *Can. J. Chem.*, **39**, 2025 (1961).
(5) B. Helferich and K. F. Wedemeyer, *Ann.*, **563**, 139 (1949).
(6) B. Helferich and K. Weis, *Chem. Ber.*, **89**, 314 (1956).
(7) *Cf.*, for instance, D. Shapiro and H. M. Flowers, *J. Am. Chem. Soc.*, **83**, 3327 (1961).
(8) N. Constantzas and J. Kocourek, *Collection Czech. Chem. Commun.*, **24**, 1099 (1959).
(9) B. Helferich and K. L. Bettin, *Chem. Ber.*, **94**, 1159 (1961).
(10) B. Helferich and W. Ost, *ibid.*, **95**, 2612 (1962).
(11) L. R. Buerger, *J. Am. Chem. Soc.*, **56**, 2494 (1934).
(12) W. H. Elliott, *Nature*, **183**, 1051 (1959).
(13) W. H. Carothers and G. A. Jones, *J. Am. Chem. Soc.*, **47**, 3051 (1925).



the α-D-configuration at C-1, a *trans* fusion of the two rings appearing somewhat unlikely; the configuration of the carbon atom bearing the cyano function remains unknown.

As far as the present authors are aware, structure II is unique in being the derivative of a 2-cyano-1,3-dioxolane. It is of interest to point out that the α,α-dialkoxynitriles have been reported[14] as being spontaneously hydrolyzed by atmospheric moisture. These substances may be construed as acyclic analogs of II; that II appears to be somewhat more stable may be attributed to its cyclic structure.

The conditions which Helferich and Bettin[9] used for the condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide with mercuric cyanide were now applied in the D-glucose series. Condensation of I with mercuric cyanide in nitromethane at room temperature afforded 11.5% of II, together with an equal quantity of a second, isomeric substance. One condensation, conducted in liquid hydrogen cyanide rather than nitromethane, gave II in 24% yield and the second substance in 3% yield. Reduction of the new isomer with lithium aluminum hydride led to the isolation of a crystalline primary amine; hence, the new isomer is a nitrile rather than an isonitrile. The primary amine did not prove to be an isomer of III but had the composition of an aminoanhydrodeoxyheptitol. The substance was characterized through conversion into a variety of derivatives: acetylation with acetic anhydride in pyridine gave an *N*-acetyltetra-*O*-acetyl derivative while boiling acetic anhydride in the presence of anhydrous sodium acetate converted the amine (as well as its pentaacetyl derivative) into a di-*N*-acetyltetra-*O*-acetyl derivative. The crystalline *N*-2,4-dinitrophenyl derivative of the amine reduced two molar equivalents of periodate, approximately one molar equivalent of formic acid being liberated, indicating the presence of three contiguous hydroxyl groups.

(14) J. G. Erickson, *J. Am. Chem. Soc.*, **73**, 1338 (1951).

On deamination with nitrous acid, the amine afforded an anhydroheptitol which consumed 2.01 molar equivalents of periodate and liberated 0.77 molar equivalent of formic acid, thus suggesting a 2,6-anhydro ring. Assuming that the D-*gluco* configuration has been preserved here, the only remaining problem is that of the configuration of the atom which had originally been the anomeric carbon; *i.e.*: is the substance 2,6-anhydro-D-*glycero*-D-*gulo*-heptitol (XIII) or 2,6-anhydro-D-*glycero*-D-*ido*-heptitol? Fortunately, the decision is simple since the former structure has a plane of symmetry while the latter has not. Actually, the anhydroheptitol obtained, as well as its pentaacetate, were devoid of optical activity[15] and so the substance is 2,6-anhydro-D-*glycero*-D-*gulo*-heptitol (= 2,6-anhydro-L-*glycero*-L-*gulo*-heptitol (XIII)), the amine is 1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (IX), and the parent nitrile has the structure shown by VIII. This nitrile is conveniently designated as 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide; alternatively it might be named 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptononitrile.

Discussion

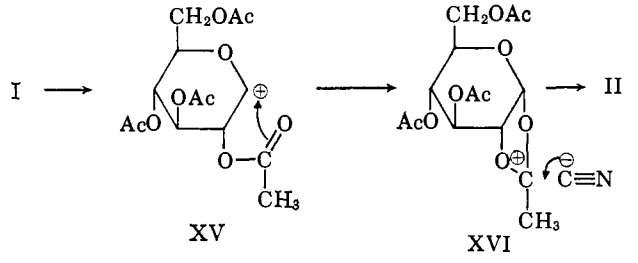
The formation of two isomeric nitriles (II and VIII) from 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (I) deserves special comment. Under normal conditions, acylated glycosyl halides, bearing a halogen atom *cis* to the acyloxy group at C-2, undergo simple inversion at C-1 as occurs in the formation of VIII. On the other hand, cyclic orthoester derivatives are generally regarded as characteristic products of the acylated *trans*-glycosyl halides,[16] and the formation of a structure such as II from the *cis*-glycosyl halide I must be regarded as unusual. Such a reaction is not, however,

(15) It may be noted that deamination of the parent amine did not result in total loss of optical activity and that the anhydroheptitol was obtained in inactive form only after rigorous purification. It is apparent, therefore, that the deamination leads to at least two products here.

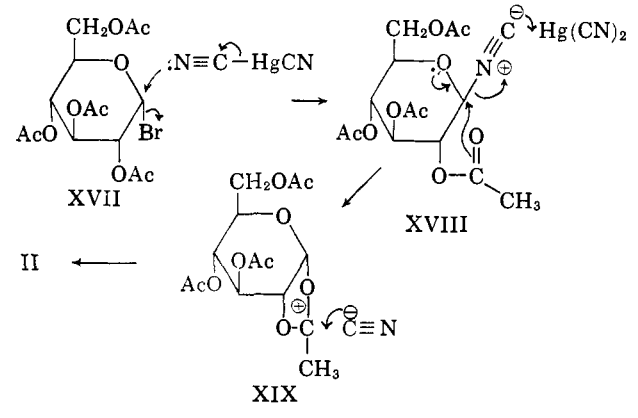
(16) E. Pacsu, *Advan. Carbohydrate Chem.*, **1**, 77 (1945).

completely without precedent. Helferich, Doppstadt, and Gottschlich[17] noted that heating I with isopropyl alcohol in the presence of a sterically hindered tertiary amine (2,6-dimethylpyridine or 2,4,6-trimethylpyridine) gave an isopropyl orthoacetate and none of the normal glucoside. Later, Helferich and Weis[6] reported that both methyl and benzyl alcohols react with 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide in nitromethane in the presence of 2,4,6-trimethylpyridine to give orthoester derivatives. Hurd and Holysz[18] found that I reacts with di-*n*-butyl- and dibenzylcadmium in boiling toluene to give compounds analogous to II, there being an *n*-butyl or benzyl group in place of the cyano group.

All of the cases cited above appear to have one factor in common with the formation of II from I: the displacement of the halogen of a *cis*-halide under conditions (high temperature, solvent of high dielectric constant, or presence of a hindered amine) which, by one means or other, tend to prolong the life of the carbonium ion initially formed so that the "shielding effect"[19] of the departing halide ion is no longer operative, thus allowing the sequence



No evidence of isonitrile formation was found in the condensation of I with silver and mercuric cyanides, although a significant proportion of the condensation product remained unidentified as uncrystallizable sirup. The possibility cannot be excluded, however, that the *ortho* structure II arises by rearrangement of a β-isonitrile (XVIII), a process (XVII → XVIII → XIX → II) which would be assisted by the electromeric effect of the ring oxygen and by the presence of a Lewis acid catalyst such as silver or mercuric cyanide.



It should be mentioned that both II and VIII appear completely stable when dissolved in nitromethane containing mercuric cyanide.

Studies of the structure of a nitrile from the condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide with mercuric cyanide are under way and will form the topic of a forthcoming communication.

(17) B. Helferich, A. Doppstadt, and G. A. Gottschlich, *Naturwissenschaften*, **40**, 441 (1953).

(18) C. D. Hurd and R. P. Holysz, *J. Am. Chem. Soc.*, **72**, 2005 (1950).

(19) E. D. Hughes, *Quart. Rev.* (London), **5**, 245 (1951).

Experimental[20]

3,4,6-Tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose (II) was readily prepared through the condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with silver cyanide in boiling xylene as described by Buerger.[11] However, the following procedure afforded the desired product in somewhat higher yield.

A mixture of 2.07 g. of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide, 3 g. of dry silver cyanide, and 20 ml. of dry xylene was boiled under reflux with stirring for 1 hr. After cooling, the insoluble material was filtered off and washed with 100 ml. of xylene; concentration of the combined filtrate and washings gave a pale yellow sirup which was dried *in vacuo* at 60°. The crude product (1.82 g.) was dissolved in a mixture of 10 ml. of warm benzene, the solution diluted with 50 ml. of ether, and then adsorbed on a column of 70 g. of neutralized Alcoa alumina (grade F-20). Elution with 60 ml. of 1:5 benzene–ether, followed by 200 ml. of ether, gave 1.22 g. of sirup which, from ethanol at −5°, yielded 0.958 g. (53%) of 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose as thick needles, m.p. 77–78°. Further recrystallization failed to change this value; Buerger[11] reported m.p. 76°. A second crop of less pure material (m.p. 66–72°) was obtained from the ethanolic mother liquor. The pure product showed $[\alpha]^{20}D$ +13.8° in chloroform (*c* 1.02).

Anal. Calcd. for $C_{15}H_{19}NO_9$ (357.31): C, 50.42; H, 5.36; N, 3.92; Ac, 36.14. Found: C, 50.22; H, 5.58; N, 3.94; Ac, 36.02.

In dichloromethane solution or potassium bromide plate the substance shows ν_{max} (cm.$^{-1}$) 1755s (OAc) but no absorption in the 2000 to 2300 cm.$^{-1}$ region, the C≡N absorption being quenched[21]; n.m.r. data: τ 8.11 ($H_3CC(=O)-$), 7.94 (×2), 7.90 (OAc).

1,2-*O*-Aminoisopropylidene-α-D-glucopyranose (III).—A solution of 9 g. of 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose in 180 ml. of ether was added to a stirred suspension of 6 g. of lithium aluminum hydride in 80 ml. of ether at such a rate as to maintain a gentle refluxing. The reaction mixture was boiled under reflux with stirring for 0.5 hr. and the excess lithium aluminum hydride then destroyed through the cautious addition of ethanol. Water was added until the gray suspension became white, followed by 60 ml. of concentrated ammonium hydroxide (*d* 0.9) and a quantity of Filter-Cel which had previously been washed with water and 5 *N* ammonium hydroxide. The mixture was stirred and then filtered through a thin layer of Filter-Cel (washed as above), the solid being washed with 500 ml. of 5 *N* ammonium hydroxide. The combined filtrate and washings were concentrated to a volume of 60 ml. and then passed through a column (2.5 × 35 cm.) of Amberlite IR-120(H) which was thereafter washed with 3 l. of water. Elution of the resin with 2 l. of 0.5 *N* ammonium hydroxide, followed by concentration of the ninhydrin-positive eluate, yielded a nearly colorless solid which was extracted six times with *ca.* 50-ml. portions of boiling ethanol. The combined extracts were filtered through Filter-Cel and concentrated to *ca.* 200 ml.; on standing at −5° overnight the solution deposited 5.08 g. (86%) of product as colorless rhombohedral plates, m.p. 182–184° (preliminary sintering) and $[\alpha]^{20}D$ +37.5° in water (*c* 2.36). A second crop (0.251 g., 4%) of slightly less pure material (m.p. 180–182°) was obtained. Recrystallization of the first crop gave the pure amino alcohol: 4.49 g., m.p. 182–184°, $[\alpha]^{20}D$ +37.7° (*c* 1.75, H_2O).

Anal. Calcd. for $C_9H_{17}NO_6$ (235.24): C, 45.95; H, 7.29; N, 5.96; C–CH_3, 11.5. Found: C, 46.12; H, 7.38; N, 5.85; C–CH_3 (Kuhn–Roth), 8.04.

The substance showed ν_{max}^{Nujol} (cm.$^{-1}$) 3320s, 3300s, 3200s (OH and NH), 1628m (NH_2). The amine gave a positive ninhydrin test but did not reduce hot Fehling solution; its nuclear magnetic resonance was measured in D_2O using tetramethylsilane as an external reference: τ 8.37 ($CH_3C(=O)-$), 7.22 (CH_2N). The be-

(20) Melting points are corrected. Selected maxima, together with probable assignments, are given for infrared spectra, intensities being indicated as s (strong), m (medium), and w (weak). Paper chromatography was conducted in the descending manner using ethyl acetate–acetic acid–water, 9:2:2 (v./v.). N.m.r. spectra were measured on either a Varian A-60 or an HR-60 spectrometer and, unless otherwise specified, were measured in $CDCl_3$ solution using tetramethylsilane as an internal reference at 10.0. Selected proton resonances are given in p.p.m. with probable assignments.

(21) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen & Co., Ltd., London, 1956, p. 225.

havior of the substance with sodium metaperiodate is described later in this paper.

Acetonylammonium *p*-Toluenesulfonate. (a) **From *N*-Acetonylphthalimide.**—A mixture of 5 g. of *N*-acetonylphthalimide,[22] 15 ml. of concentrated hydrochloric acid, and 7.5 ml. of water was boiled under reflux for 4 hr., diluted with 60 ml. of water, and cooled. A small quantity of pink, crystalline material was removed, washed with 50 ml. of 2 *N* hydrochloric acid, and discarded. The combined filtrate and washings were concentrated to give a pink-brown crystalline mass which was dried over sodium hydroxide pellets at 50° and then extracted with 50 ml. of water, the insoluble material being washed with a further 60 ml. of water. The aqueous extract was then passed through a column (2 × 15 cm.) of Amberlite IR-120(H), the resin washed with 570 ml. of water and the amine eluted with 450 ml. of 2 *N* hydrochloric acid; concentration gave a semicrystalline mass of crude aminoacetone hydrochloride (2.4 g.) which was dissolved in 50 ml. of water and mixed with a solution of 6.11 g. of silver *p*-toluenesulfonate in 100 ml. of water. The silver chloride was filtered off on a bed of charcoal and Filter-Cel; concentration of the pale yellow filtrate gave a semicrystalline mass from which absolute ethanol was twice distilled. Extraction with boiling ethanol, filtration of the extract through decolorizing carbon, and cooling the filtrate at 0° for 5 hr. gave 2.53 g. (42%) of aminoacetone *p*-toluenesulfonate as fine, colorless needles, m.p. 133–134°. Recrystallized successively from aqueous acetone–ether, dioxane, and methanol–ether, the product was obtained as irridescent plates, m.p. 139°, R_f 0.74 (ninhydrin spray: orange-brown spot becoming purple on standing). Elliott[12] reported m.p. 130.5° for acetonylammonium *p*-toluenesulfonate.

Anal. Calcd. for $C_{10}H_{15}NO_4S$ (245.29): C, 48.96; H, 6.16; N, 5.71; S, 13.07. Found: C, 48.80; H, 6.39; N, 5.48; S, 12.80. ν_{max}^{Nujol} (cm.$^{-1}$) 3160s (NH_3^+), 2715m, 2600m; 1735s (C=O), 1608m, 1482s.

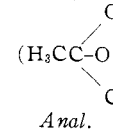
(b) **From 1,2-*O*-Aminoisopropylidene-α-D-glucopyranose (III).**—A solution of 0.704 g. of 1,2-*O*-aminoisopropylidene-α-D-glucopyranose in 5 ml. of concentrated hydrochloric acid was heated at 100° for 2 min., cooled rapidly, diluted with 50 ml. of water, and treated, portionwise, with 48 g. of damp Amberlite IR-45(OH) until the pH had risen to 4.0–4.5. The resin was filtered off and the solution passed through a column (2 × 22 cm.) of Amberlite IR-120(H). The reducing, highly acidic effluent was neutralized as it flowed from the column by stirring with Amberlite IR-45(OH). The resin and solvent were removed to give a colorless sirup (0.408 g., 76%) which was shown by paper chromatography to consist largely of **D-glucose** (R_f 0.41) with a trace of a slower moving impurity R_f 0.24 (periodate–silver nitrate spray). From methanol–ethanol, containing a drop of glacial acetic acid, crystalline D-glucose was isolated. Its rotation, $[\alpha]^{20}D$ +53.8° (equil., H_2O), and infrared spectrum served to identify it.[23]

Elution of the thoroughly washed IR-120 resin with 500 ml. of 2 *N* hydrochloric acid, followed by concentration of the eluate and drying of the resulting light brown sirup by two distillations with benzene and, finally, over sodium hydroxide at 60° for 18 hr., afforded crude aminoacetone hydrochloride as a dark brown sirup, 0.338 g. The hydrochloride was converted to the *p*-toluenesulfonate using 0.861 g. of silver *p*-toluenesulfonate in a manner similar to that described earlier for the authentic specimen. Crystallization from ethanol–ether yielded the salt as hard clusters of needles in three crops: (1) 0.14 g. (19%), m.p. 132–135° (incomplete); (2) 0.114 g. (15.5%), m.p. 131–133° (with preliminary sintering); (3) 0.137 g. (19%), m.p. 127–132° (with preliminary sintering and decomposition). The first and second crops were combined and dissolved in hot ethanol and the solution was filtered through a pad of Darco X on Filter-Cel; addition of ether to the filtrate gave long, colorless needles, m.p. 134–136°. Recrystallization from methanol–ether and then from isopropyl alcohol raised the m.p. to 135–137°; on admixture with an authentic sample of acetonylammonium *p*-toluenesulfonate, the product melted at 137–138°. Paper chromatography and infrared spectra confirmed the identity of the two specimens.

1,2-*O*-(2,4-Dinitrophenylaminoisopropylidene)-α-D-glucopyranose (IV).—A mixture of 0.660 g. of 1,2-*O*-aminoisopropylidene-α-D-glucopyranose and 5 g. of powdered calcium carbonate in 25 ml. of water was stirred at room temperature and 0.524 g. (1.0 mole with respect to the amine) of 2,4-dinitrofluorobenzene washed into the mixture with 25 ml. of ethanol. The suspension, which rapidly became bright yellow, was stirred at room temperature for 12 hr. when a further 1 g. of calcium carbonate was added and the solution stirred 15 min. The solid was filtered off and washed with ethanol until free of color; concentration of the combined filtrate and washings gave a sirup (1.15 g.) which was crystallized from aqueous ethanol at +5°. The fine, bright yellow needles (1.079 g., 96%) melted at 103–105°; after two recrystallizations from water containing a little ethanol the 2,4-dinitrophenyl derivative melted at 105–107°, showed $[\alpha]^{20}D$ +37.7° in acetone (*c* 1.51), and had R_f 0.85 (no spray); spectral data: ν_{max}^{Nujol} (cm.$^{-1}$) 3550m, 3350s, and 3200m (shoulder) (OH and NH), 1625s, 1588s, and 1500s (Ar), 1547w (NH), 1525s (NO_2). The behavior of the substance with sodium metaperiodate is described later in this paper.

Anal. Calcd. for $C_{15}H_{19}N_3O_{10}$ (401.32): C, 44.89; H, 4.77; N, 10.47. Found: C, 45.20; H, 5.01; N, 10.40; mol. wt. (Signer), 420.

1,2-*O*-(2,4-Dinitrophenylaminoisopropylidene)-3,4,6-tri-*O*-methyl-α-D-glucopyranose (V).—A mixture of 0.843 g. of 1,2-*O*-(2,4-dinitrophenylaminoisopropylidene)-α-D-glucopyranose, 5 g. of silver oxide, 10 g. of Drierite, 20 ml. of methyl iodide, and 20 ml. of dry acetone was boiled under reflux with stirring for 15 hr. After removal of the solid, the solution was concentrated to a sirup which was dissolved in 50 ml. of benzene and poured onto a column (2 × 22 cm.) of 64 g. of Woelm alumina (acidic, grade II) in cyclohexane. Elution with 450 ml. of benzene and then with 500 ml. of 4:1 benzene–ether removed the bright yellow major component from the column while bright red and pink by-products remained on the alumina; these were not further investigated. Concentration of the yellow eluate afforded a sirup which crystallized from methanol as bright yellow clusters of needles. Recrystallization from isopropyl alcohol gave 0.636 g. (68%) of product melting at 84°; two further recrystallizations from ethanol raised the m.p. to 86°. The trimethyl ether showed $[\alpha]^{20}D$ +25.6° in chloroform (*c* 1.08); ν_{max}^{Nujol} (cm.$^{-1}$) 3330m (NH), 1625s, 1588s, and 1498m (Ar), 1528s (NO_2); n.m.r., τ 8.30



Anal. Calcd. for $C_{18}H_{25}N_3O_{10}$ (443.40): C, 48.75; H, 5.68; N, 9.48; CH_3–C, 6.10; CH_3O, 21.00. Found: C, 49.02; H, 5.74; N, 9.56; CH_3–C, 6.28; CH_3O, 20.83; mol. wt. (Signer), 440.

3,4,6-Tri-*O*-methyl-β-D-glucopyranose (VI) from 1,2-*O*-(2,4-Dinitrophenylaminoisopropylidene)-3,4,6-tri-*O*-methyl-α-D-glucopyranose (V).—To a solution of 1.28 g. of V in 15 ml. of dioxane was added 15 ml. of concentrated hydrochloric acid and the mixture heated on the steam bath for 8 min. The dark brown solution was cooled, diluted with 30 ml. of ice-water, and passed successively through columns of Amberlite IR-45(OH) (2.5 × 36 cm.) and Amberlite IR-120(H) (2.5 × 10 cm.). The neutral, colorless solution was concentrated to a small volume, treated with a little Amberlite IR-45(OH), and filtered through Darco X on Filter-Cel to remove a slight opalescence. Washing of the charcoal with ethanol, followed by concentration of the resulting extract, afforded a clear sirup from which absolute ethanol was twice distilled and which was finally held at 60° over phosphorus pentoxide: 0.42 g. (65%). The sirup was extracted with boiling ether, 4 mg. of insoluble material being filtered off; at −5° the ethereal extract crystallized as clusters of fine colorless needles when seeded with authentic 3,4,6-tri-*O*-methyl-β-D-glucopyranose. A total of 0.1634 g. (25%) of crystalline product was obtained in two crops; two recrystallizations from ether at −5° afforded pure 3,4,6-tri-*O*-methyl-β-D-glucopyranose as clusters of thick needles, m.p. 99–102°, $[\alpha]^{20}D$ +41.3° (4 min.) → +78.2° (24 hr., constant) in water (*c* 1.23), and R_f 0.84 (periodate–silver nitrate spray). The material cochromatographed with an authentic sample; its infrared spectrum (in Nujol mull) was identical with that of an authentic sample. Sundberg, *et al.*,[24] reported 3,4,6-tri-*O*-methyl-β-D-glucopyranose to show $[\alpha]^{25}D$ +41.1° (2.5 min.) → +78.0° in water.

1,2-*O*-Acetamidoisopropylidene-3,4,6-tri-*O*-acetyl-α-D-glucopyranose (VII). (a) **From 1,2-*O*-Aminoisopropylidene-α-D-glucopyranose (III).**—A mixture of 0.478 g. of 1,2-*O*-aminoisopropylidene-α-D-glucopyranose, 15 ml. of acetic anhydride, and 1.5 g. of powdered anhydrous sodium acetate was heated at 100° for 5 hr., cooled, and poured onto a mixture of crushed ice and sodium bicarbonate, and left overnight. Extraction of the solution with chloroform (4 × 50 ml.), followed by washing the combined extracts twice with water and then concentration, yielded a pale yellow sirup which was dissolved in warm ethanol and filtered through Darco X; concentration then gave 0.813 g. of colorless sirup which crystallized as fine needles on the addition of ether. Crystallization from chloroform–ether yielded the tetraacetyl derivative as fine needles which changed to irregular plates on exposure to the atmosphere following filtration. Washing with pentane and drying over phosphorus pentoxide gave 0.572 g. (70%) of product, m.p. 110–112° (with preliminary sintering). Two further recrystallizations from chloroform–ether at −5°

(22) R. E. Lancaster, Jr., and C. A. VanderWerf, *J. Org. Chem.*, **23**, 1208 (1958).

(23) In a separate experiment the D-glucose was further identified through conversion to β-D-glucopyranose pentaacetate which had m.p. 130–131°, undepressed by authentic material.

(24) R. L. Sundberg, C. M. McCloskey, D. E. Rees, and G. H. Coleman, *J. Am. Chem. Soc.*, **67**, 1080 (1945).

afforded pure 1,2-*O*-acetamidoisopropylidene-3,4,6-tri-*O*-acetyl-α-D-glucopyranose as hygroscopic, irregular plates (0.408 g.), m.p. 114°, $[\alpha]^{20}D$ +40° in chloroform (*c* 1.35); infrared absorption: ν_{max}^{Nujol} (cm.$^{-1}$) 3740w (H_2O), 3320m (NH), 1747s (OAc), 1662m and 1630m (NAc), 1548m (NH). N.m.r. data: τ 8.44 ($CH_3C(=O)-$), 7.99, 7.90, and 7.89 (NAc and OAc) doublet at 6.65 ($-C(=O)CH_2N$) (J = 6.5 c.p.s.) (CH_2N). The substance is soluble in water.

Anal. Calcd. for $C_{17}H_{25}NO_{10}$ (403.38): C, 50.61; H, 6.25; N, 3.47; (O)Ac, 32.07; total Ac, 42.69. Found: C, 50.66; H, 6.34; N, 3.60; (O)Ac, 31.91; total Ac (hot acid hydrolysis), 43.73.

(b) **From 3,4,6-Tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose (II).**—Platinum oxide catalyst (0.5 g.), suspended in 5 ml. of acetic anhydride, was saturated with hydrogen and then a solution of 2.01 g. of 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose in 25 ml. of acetic anhydride was added. The mixture was shaken with hydrogen at 23° and atmospheric pressure until absorption of gas had virtually ceased (19.5 hr.). Catalyst and solvent were removed to yield a mobile sirup which was freed of residual acetic anhydride by repeated distillations with ethanol. From chloroform–ether, on seeding, the product crystallized as clusters of needles which, after filtration, became irregular plates; 0.91 g. (40%), m.p. 111–112°. Two further recrystallizations from chloroform–ether gave pure material as irregular, hygroscopic plates, m.p. 113–114°, undepressed on admixture with the product made as described in (a) above. It showed $[\alpha]^{20}D$ +41° in chloroform (*c* 1.33). The infrared spectra of the products made in (a) and (b) above were identical.

Condensation of 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl Bromide (I) with Mercuric Cyanide in Nitromethane. 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl Cyanide (VIII).—A mixture of 20.5 g. of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide, 12.6 g. of dry mercuric cyanide (1 mole equivalent), and 100 ml. of pure nitromethane (dried over Drierite) was stirred at room temperature for 24 hr.[25] and then concentrated *in vacuo* (bath temperature 30°) to give a thick paste; this was dissolved in 200 ml. of methanol and the solution diluted with a mixture of 400 ml. of *N* potassium bromide and 250 g. of ice. The sirup which precipitated was extracted with chloroform (4 × 200 ml.) and the combined extracts were washed twice with water and concentrated to yield a stiff, pale yellow sirup; 18.69 g., $[\alpha]^{20}D$ +40° (*c* 8.9 in chloroform); ν_{max}^{film} (cm.$^{-1}$) 3600w (OH), 1755s (OAc), 1480m. A portion (16.82 g.) of the crude sirup was dissolved in 300 ml. of warm benzene, the solution cooled to room temperature and chromatographed on 665 g. of neutralized Alcoa alumina. Elution with 3 l. of ether yielded 2.33 g. of a pale yellow sirup which crystallized from ethanol; 1.84 g. (11.5%), m.p. 78–79° alone or in admixture with 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-D-glucopyranose, $[\alpha]^{20}D$ +12.9° in chloroform (*c* 4.57). A second crop (92 mg., 0.6%, m.p. 77.5–79°) was obtained from the mother liquor.

Elution of the adsorbent with a further 500 ml. of ether gave only 0.23 g. of sirupy material which was discarded. Elution with 2 l. of 4:1 (v./v.) ether–ethyl acetate gave 2.88 g. of pale yellow sirup which crystallized from ethanol as fine needles; 1.97 g. (12%), m.p. 114–115°. Recrystallization from ethanol gave pure **2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide (VIII)**, m.p. 116°, $[\alpha]^{20}D$ +10.1° (*c* 2.64 in $CHCl_3$); infrared absorption: ν_{max}^{Nujol} (cm.$^{-1}$) 1750s (OAc); no absorption in 2000–2300 cm.$^{-1}$ region; n.m.r. data: τ 7.96 and 7.88 (OAc).

Anal. Calcd. for $C_{15}H_{19}NO_9$ (357.31): C, 50.42; H, 5.36; N, 3.92; Ac, 48.19. Found: C, 50.57; H, 5.14; N, 4.05; Ac, 48.77.

1-Amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (IX).—A solution of 4.47 g. of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl cyanide in 300 ml. of warm ether was added to a stirred suspension of 2.85 g. of lithium aluminum hydride in 25 ml. of ether at such a rate as to maintain the reaction mixture under gentle reflux (*ca.* 0.25 hr.). The residual cyano derivative was washed in with a further 250 ml. of ether and the mixture boiled under reflux for 0.5 hr., excess hydride then being destroyed through the cautious addition of ethanol. Water was added until the reaction mixture turned white and then were added 80 ml. of concentrated ammonium hydroxide and Filter-Cel (which had previously been washed with water, 5 *N* ammonium hydroxide, and ethanol). The mixture was then filtered on a thin bed of Filter-Cel (previously washed as described above) and the residue washed with 500 ml. of 5 *N* ammonium hydroxide. The combined filtrate and washings were concentrated to a volume of *ca.* 80 ml. and passed through a column (2.5 × 21 cm.) of Amberlite IR-120(H). The resin was washed with water and the amine then eluted at a rapid rate with 2 l. of 0.5 *N* ammonium hydroxide. Concentration of the alkaline eluate afforded a solid, lithium-free residue which was dried by distilling absolute ethanol therefrom two times and then extracted with boiling ethanol (4 × 75 ml.). The combined extracts were filtered through a thin layer of Filter-Cel, concentrated somewhat, and left at −5° overnight to give 1.85 g. (77%) of 1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol, m.p. 164–165°. A second crop (89 mg., 4%) of less pure material was obtained; m.p. 156–159°. Recrystallization of the first crop from methanol and then from aqueous ethanol failed to change its m.p.; material thus purified showed $[\alpha]^{20}D$ −6.7° in water (*c* 3.15) and $R_{glucose}$ 1.3 (ninhydrin and periodate–silver nitrate sprays); infrared spectrum: ν_{max}^{Nujol} (cm.$^{-1}$) 3380s and 3175s (OH and NH), 1620m (NH_2). The behavior of the substance with sodium metaperiodate is described later in this paper.

Anal. Calcd. for $C_7H_{15}NO_5$ (193.20): C, 43.51; H, 7.83; N, 7.25. Found: C, 43.54; H, 7.69; N, 7.25.

2,6-Anhydro-1-deoxy-1-(2,4-dinitrophenylamino)-D-*glycero*-D-*gulo*-heptitol (X).—To a stirred solution of 0.401 g. of 1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol in 25 ml. of water was added 5 g. of powdered calcium carbonate and 0.39 g. of 2,4-dinitrofluorobenzene (1 mole equivalent) was then washed into the mixture with 25 ml. of ethanol. The suspension was stirred at room temperature for 23 hr., filtered through a thin layer of Filter-Cel, and the residue washed with ethanol until colorless. The combined filtrate and washings were concentrated to a bright yellow sirup which crystallized from aqueous ethanol on standing overnight at +5°. Recrystallization from isopropyl alcohol at −5°, followed by drying *in vacuo* at 50° over phosphorus pentoxide for 2.5 days, gave bright yellow needles of 2,6-anhydro-1-deoxy-1-(2,4-dinitrophenylamino)-D-*glycero*-D-*gulo*-heptitol monoisopropyl alcoholate: 0.757 g. (87%), m.p. 88–90° (with foaming). Two further recrystallizations from isopropyl alcohol at −5° gave the pure solvate, m.p. 89–91° (foaming), $[\alpha]^{20}D$ −14.5° (*c* 1.41 in acetone).

Anal. Calcd. for $C_{13}H_{17}N_3O_9 \cdot C_3H_7OH$ (419.38): C, 45.82; H, 6.01; N, 10.02. Found: C, 45.50; H, 5.93; N, 10.06.

A small sample of the crystalline solvate, when heated in a microdistillation apparatus, afforded a colorless condensate indistinguishable from authentic isopropyl alcohol by gas–liquid partition chromatography on a 1.83-m. column of 15% w./w. Dow–Corning silicone fluid Q.F.1 on Chromosorb A at 27°.

Drying of a melted sample of the solvate *in vacuo* at 100° removed the isopropyl alcohol, the residue being amorphous.

Anal. Calcd. for $C_{13}H_{17}N_3O_9$ (359.29): C, 43.45; H, 4.77. Found: C, 43.62; H, 4.84.

The behavior of the substance with sodium metaperiodate is described later in this paper.

1-Acetamido-3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (XI).—A suspension of 0.302 g. of 1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol in a mixture of 5 ml. of dry pyridine and 5 ml. of redistilled acetic anhydride was stirred at room temperature for 0.25 hr. and, solution being complete, the reaction mixture left at room temperature for 24 hr. It was then poured into ice-water and the product extracted with dichloromethane; the combined extracts were washed successively with 2 *N* hydrochloric acid, aqueous sodium bicarbonate, and water. The solution was concentrated to a sirup from which absolute ethanol was evaporated. From ether containing a little ethanol the product crystallized as elongated hexagonal prisms; 0.502 g. (80%), m.p. 119–121°. After successive recrystallization from ether containing a little ethanol and then from ether containing a little dichloromethane, the pure product melted at 120° and showed $[\alpha]^{20}D$ −0.5° in chloroform (*c* 2.1); infrared absorption: ν_{max}^{Nujol} (cm.$^{-1}$) 3350m (NH), 1745s (OAc), 1670s (NAc), 1540m (NH); n.m.r. data: τ 8.02, 7.98, 7.95, 7.92 (NAc, OAc). The compound is soluble in water.

Anal. Calcd. for $C_{17}H_{25}NO_{10}$ (403.38): C, 50.61; H, 6.25; N, 3.47; (O)Ac, 42.69; total Ac, 53.36. Found: C, 50.81; H, 6.10; N, 3.43; (O)Ac, 43.14; total Ac, 53.24.

Di-*N*-acetyl-3,4,5,7-tetra-*O*-acetyl-1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (XII).—A mixture of 0.257 g. of 1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol, 0.5 g. of powdered anhydrous sodium acetate, and 10 ml. of acetic anhydride was boiled under reflux for 2 hr., cooled, and poured into a mixture of ice and sodium bicarbonate. On stirring, crystallization was spontaneous; the product was extracted with chloroform (3 × 50 ml.). The combined extracts were washed thrice with water and concentrated to a pale yellow sirup which was dissolved in ethanol and decolorized with Darco X. The ethanol was removed and the product crystallized from isopropyl alcohol; 0.391 g. (66%), m.p. 101–102°. Recrystallized from isopropyl alcohol, twice from aqueous ethanol, and finally from ethanol alone, the product had m.p. 104–106° (preliminary sintering,

(25) After 0.5 hr. a test with cupric acetate–benzidine paper showed that hydrogen cyanide was being evolved. A similar observation was made when carbon tetrachloride was substituted for nitromethane. However, mercuric cyanide in nitromethane, without the 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl bromide, did not evolve detectable traces of hydrogen cyanide.

TABLE I

PERIODATE OXIDATIONS IN UNBUFFERED SOLUTION[a]

Compound	Time, hr.	0.25	0.75	1.5	3	7	24	48
1,2-*O*-Aminoisopropylidene-α-D-glucopyranose (III)	Uptake	1.18	1.19	1.30	1.42	1.62	1.95	2.07
	Acid	0	0	0	0	0	0	0
1,2-*O*-(2,4-Dinitrophenylaminoisopropylidene)-α-D-glucopyranose (IV)[b]	Uptake	0.90	0.94	0.94	0.91	0.88	0.81	0.71
	Acid	0	0	0	0	0	0	0
1-Amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (IX)	Uptake	1.84	2.96	3.57	3.96	4.27	4.52	4.90[c]
	Acid	0.06	0.53	0.83	1.17	1.45	1.72	2.26[c]
2,6-Anhydro-1-deoxy-1-(2,4-dinitrophenylamino)-D-*glycero*-D-*gulo*-heptitol (X)	Uptake	1.32	1.79	1.91	1.91	2.02	2.02	2.03
	Acid	0.58	0.71	0.74	0.74	0.87	0.93	0.93
2,6-Anhydro-D-*glycero*-D-*gulo*-heptitol (XIII)	Uptake	1.17	1.56	1.66	1.82	1.95	2.01	2.01[d]
	Acid	0.39	0.46	0.54	0.61	0.68	0.76	0.77

[a] The results are expressed in moles of sodium metaperiodate consumed (and/or moles of formic acid liberated) per mole of substrate. [b] In 20% methanol. The blank decreased in titer with time. The decrease in consumption of periodate in the oxidation is apparently due to inhibition of the oxidation of the methanol by the product of the oxidation of IV. [c] At 102 hr. [d] Solution optically inactive throughout oxidation.

TABLE II

PERIODATE OXIDATIONS AT pH 5.1[a]

Compound	Time, hr.	0.08	0.25	0.75	1.5	3	25	93	Formaldehyde test[b]
1,2-*O*-Aminoisopropylidene-α-D-glucopyranose (III)		1.1	1.1	1.1	1.1	1.1	1.1	1.36	Negative
1,2-*O*-Benzylidene-α-D-glucopyranose[c]		0.73	0.95	0.97	0.97	0.98	...	..	Negative
1,2-*O*-Benzylidene-α-D-glucofuranose[d]		0.96	0.96	..	..	..	...	..	Positive

[a] The results are expressed in moles of sodium metaperiodate consumed per mole of substrate. The buffer was 0.02 *M* sodium acetate–acetic acid. [b] The method of J. F. O'Dea and R. A. Gibbons [*Biochem. J.*, **55**, 580 (1953)] was used. [c] H. B. Wood, Jr., H. W. Diehl, and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **79**, 1986 (1957). [d] J. C. Sowden and D. J. Kuenne, *ibid.*, **74**, 686 (1952).

variable) and showed $[\alpha]^{20}D$ −48.7° in chloroform (*c* 2.04); infrared absorption: ν_{max}^{Nujol} (cm.$^{-1}$) 3430w (H_2O or ethanol), 1750s (OAc), 1715s, and 1683s [$N(Ac)_2$]; no absorption in the regions of the spectrum associated with NH.

Anal. Calcd. for $C_{19}H_{27}NO_{11}$ (445.42): C, 51.23; H, 6.11; N, 3.15; Ac, 57.99. Found: C, 50.97; H, 6.25; N, 3.39; Ac, 57.87 (hot acid hydrolysis).

Acetylation of 1-acetamido-3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (XI) with sodium acetate and boiling acetic anhydride in a similar fashion gave the same di-*N*-acetyl-3,4,5,7-tetra-*O*-acetyl-1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol (XII) in 71% yield, m.p. 105–107°, $[\alpha]^{20}D$ −49.0° (*c* 1.24, $CHCl_3$). The product thus prepared showed infrared absorption indistinguishable from that made directly from the amino alcohol IX; a mixture melting point was undepressed; n.m.r. data: τ 8.01, 7.98, 7.95, and 7.905 (OAc), 7.61 [$N(Ac)_2$].

2,6-Anhydro-D-*glycero*-D-*gulo*-heptitol (XIII).—A mixture of 0.7011 g. of 1-amino-2,6-anhydro-1-deoxy-D-*glycero*-D-*gulo*-heptitol and 0.752 g. of sodium nitrite was dissolved in 20.0 ml. of 10% (v./v.) acetic acid and the solution left at room temperature. After 7 hr., evolution of gas had virtually ceased and the solution showed $\alpha^{20}D$ +1.59° in a 2-dm. tube, a value unchanged after a further 3 hr. at room temperature. The solution was passed successively through columns of Amberlite IR-120(H) (2 × 15 cm.) and Amberlite IR-45(OH) (2 × 12 cm.) and the effluent concentrated to give a slightly turbid pale yellow sirup containing rectangular, plate-like crystals. The crude product was dissolved in aqueous ethanol, the solution decolorized with Darco X, and the anhydroheptitol crystallized at −5°; 0.296 g. (42%), m.p. 199–201°, $[\alpha]^{20}D$ +3.1° (*c* 5.87 in water), $R_{glucose}$ 1.27 (periodate–silver nitrate spray). A second crop of less pure material was obtained from ethanol; 87 mg. (12%), m.p. 194–199° (preliminary browning), $[\alpha]^{20}D$ +7° (*c* 1.65 in water).

Three recrystallizations of the first crop from aqueous ethanol raised the m.p. of the anhydroheptitol to 204–205°; two additional recrystallizations from this solvent effected no further change.

Anal. Calcd. for $C_7H_{14}O_6$ (194.18): C, 43.29; H, 7.27. Found: C, 43.27; H, 7.41.

After each of five successive recrystallizations from aqueous ethanol, the anhydroheptitol gave the following corresponding rotations in water: $[\alpha]^{20}D$ +1.5° (*c* 4.02), +0.4° (*c* 2.2), +0.1° (*c* 1.94), 0.0 ± 0.3° (*c* 3.2) and 0.0 ± 1° (*c* 1.68).[26] Optical rotatory dispersion measurements then showed the substance to be inactive from 240–700 mμ (*c* 1.68, H_2O). The behavior of the substance with sodium metaperiodate is described later in this paper.

1,3,4,5,7-Penta-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptitol (XIV).—A mixture of 0.254 g. of 2,6-anhydro-D-*glycero*-D-*gulo*-heptitol, 0.5 g. of powdered anhydrous sodium acetate, and 10 ml. of acetic anhydride was heated under reflux for 2.5 hr., then cooled and poured into a mixture of ice and sodium bicarbonate. The mixture was stirred until the odor of acetic anhydride was no longer detectable and the product was then extracted with 3 × 50 ml. of chloroform. The combined brown extracts were washed thrice with water and concentrated to a sirup which was dried by distillation with absolute ethanol; crystallization was spontaneous. Recrystallized from isopropyl alcohol at −5°, the product (0.378 g., 71%) melted at 88–90°; a second crop (88 mg., 17%) melted at 91–98°. Successive recrystallization of the first crop from isopropyl alcohol, aqueous ethanol, and from aqueous acetone afforded the pure pentaacetate as fine needles, m.p. 89°, $[\alpha]^{20}D$ 0 ± 0.2° (*c* 1.57, $CHCl_3$); infrared absorption: ν_{max}^{Nujol}(cm.$^{-1}$) 1760s (OAc).

Anal. Calcd. for $C_{17}H_{24}O_{11}$ (404.36): C, 50.49; H, 5.98; Ac, 53.23. Found: C, 50.74; H, 6.10; Ac, 53.0.

The compound gave only a single peak when subjected to gas–liquid partition chromatography on a 60-cm. column of 1% S.E. 30 silicone gum on Chromosorb W at 215°.

Oxidations with Periodate.—Oxidations with sodium metaperiodate were carried out in unbuffered solution using conventional techniques. The results obtained are shown in Table I. It will be noted that the compounds III and IX consumed more oxidant than one might expect of structures of this type. However, in buffer (pH 5.1), III consumed the expected proportion of oxidant; two closely related compounds of known structure behave normally under these conditions. Table II summarizes the data obtained in buffer solution.

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(26) Subsequent work showed that the anhydroheptitol was most easily purified through its pentaacetate.