# THE REACTION OF UNSATURATED CARBOHYDRATES WITH CARBON MONOXIDE AND HYDROGEN

## V. ABSOLUTE STEREOCHEMISTRY OF ANHYDRODEOXYHEPTITOLS FROM 3,4,6-TRI-*O*-ACETYL-D-GLUCAL. STEREOCHEMISTRY OF HYDROFORMYLATION. CONFORMATIONAL ANALYSIS

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Received November 13, 1964

*Dedicated to Professor R. B. Sandin on the Occasion of his Sixty-Eighth Birthday*

ABSTRACT

3,4,6-Tri-*O*-acetyl-D-glucal reacted with carbon monoxide and hydrogen in the presence of dicobalt octacarbonyl to yield a mixture of two epimeric anhydrodeoxyheptitols, namely, 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*manno*-heptitol (I) and 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*gluco*-heptitol (II). De-*O*-acetylation of the mixture, followed by chromatographic separation, yielded crystalline 2,6-anhydro-3-deoxy-D-*manno*-heptitol (III) and 2,6-anhydro-3-deoxy-D-*gluco*-heptitol (IV). Reaction of the mixture of heptitols (I) and (II) with *p*-bromobenzenesulfonyl chloride, followed by fractional crystallization of the brosylates, gave pure 4,5,7-tri-*O*-acetyl-2,6-anhydro-1-*O*-(*p*-bromophenylsulfonyl)-3-deoxy-D-*gluco*-heptitol (VII). The absolute configuration of (VII) has been previously established by X-ray crystallographic analysis. The absolute configuration of (III) was established by correlation with that of (VII). The conversion of compound (II) into various derivatives is described.

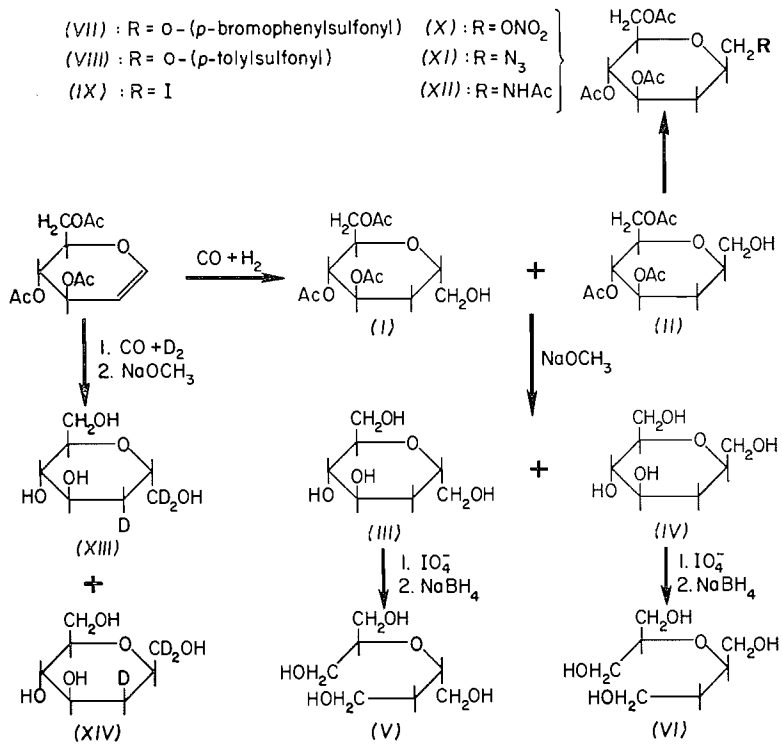
Reaction of 3,4,6-tri-*O*-acetyl-D-glucal with carbon monoxide and deuterium afforded 2,6-anhydro-3-deoxy-D-*manno*-heptitol-1,1,3-$^2H_3$ (XIII) and 2,6-anhydro-3-deoxy-D-*gluco*-heptitol-1,1,3-$^2H_3$ (XIV). Examination of the nuclear magnetic resonance (n.m.r.) spectra of the normal and deuterated anhydrodeoxyheptitols confirmed the structural assignments and showed that *cis* addition to the double bond took place to give (XIV).

Comparison of the exchange reaction of sodium iodide with 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*gluco*-heptitol (VIII) and with 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*manno*-heptitol (XV) revealed that the equatorial primary tosyloxy group of (VIII) was exchanged by iodine twice as readily as the axial primary tosyloxy group of (XV).

Preceding papers in this series (1, 2) have reported that pentals react preferentially at C-1 with carbon monoxide and hydrogen to yield epimeric anhydrodeoxyhexitols. This paper deals with the extension of the oxo reaction to 3,4,6-tri-*O*-acetyl-D-glucal. A preliminary report of part of this work has already appeared (3).

When 3,4,6-tri-*O*-acetyl-D-glucal was subjected to the oxo reaction at a temperature of about 130°, an almost quantitative yield of a mixture of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*manno*-heptitol (I) and 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*gluco*-heptitol (II) was obtained. De-*O*-acetylation of this mixture with methanolic sodium methoxide afforded the crystalline parent anhydrodeoxyheptitols (III) and (IV) which were readily separated by paper chromatography or cellulose column chromatography. Both heptitols were also converted into crystalline acetates.

Alternatively, the oxo product mixture was separated in the following ways. Tosylation of the mixture of (I) and (II) yielded the monotosylate esters (VIII) and (XV), which, on fractional crystallization, afforded pure crystalline 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*gluco*-heptitol (VIII). Chromatographic separation of the monotosylates by thin-layer chromatography (t.l.c.) gave both epimers. Similarly, treatment of (I) and (II) with *p*-bromobenzenesulfonyl bromide, followed by fractional crystallization of the




brosylates, produced pure 4,5,7-tri-*O*-acetyl-2,6-anhydro-1-*O*-(*p*-bromobenzenesulfonyl)-3-deoxy-D-*gluco*-heptitol (VII). The purity of the tosylate and brosylate esters was established by their conversion into 4,5,7-tri-*O*-acetyl-2,6-anhydro-1,3-dideoxy-1-iodo-D-*gluco*-heptitol (IX), which, on treatment with silver nitrate, yielded the 1-*O*-nitro derivative (X). Reduction of the latter substance with hydrogen over palladium, followed by de-*O*-acetylation, gave the crystalline anhydrodeoxyheptitol (IV).

In order that the point of attachment of the hydroxymethyl group to the glycal might be ascertained, the heptitols (III) and (IV) were first oxidized with periodate (1 mole consumed by each) and the resulting dialdehydes were then reduced with sodium borohydride. The fact that enantiomeric tetrol ethers (V) and (VI) were produced established that the heptitols (III) and (IV) are epimers which differ in the configuration of C-2. This assignment of structure was confirmed by analysis of the n.m.r. spectra of the heptitols. The spectra of both heptitols (see Fig. 1, *a* and *c*) exhibit a multiplet of peaks at $\delta = 1.5$ to 2 having an area which corresponds to the two methylenic hydrogens on C-3.

The configuration of C-2 of both epimeric 2,6-anhydro-3-deoxyheptitols was then readily established by application of n.m.r. spectroscopy, as previously described (1), to the 3-deoxy-3-deuterioanhydroheptitols (XIII) and (XIV) which were produced when 3,4,6-tri-*O*-acetyl-D-glucal was caused to react with carbon monoxide and deuterium. Thus, as shown in Fig. 1, *b*, the chemical shift and quartet structure (width of 17.7 c.p.s.) of the signal of intensity one at around $\delta = 1.7$ require the C-3 proton to be in an axial orientation and coupled with the C-4 axial and C-2 equatorial hydrogens. On the other hand, as depicted in Fig. 1, *d*, the corresponding narrower quartet of signals (width 7.3 c.p.s.) of intensity one at the lower field ($\delta = 1.94$) necessitates that the C-3 proton of compound (XIV) is in an equatorial orientation and coupled with the C-4 and C-2 axial hydrogens.

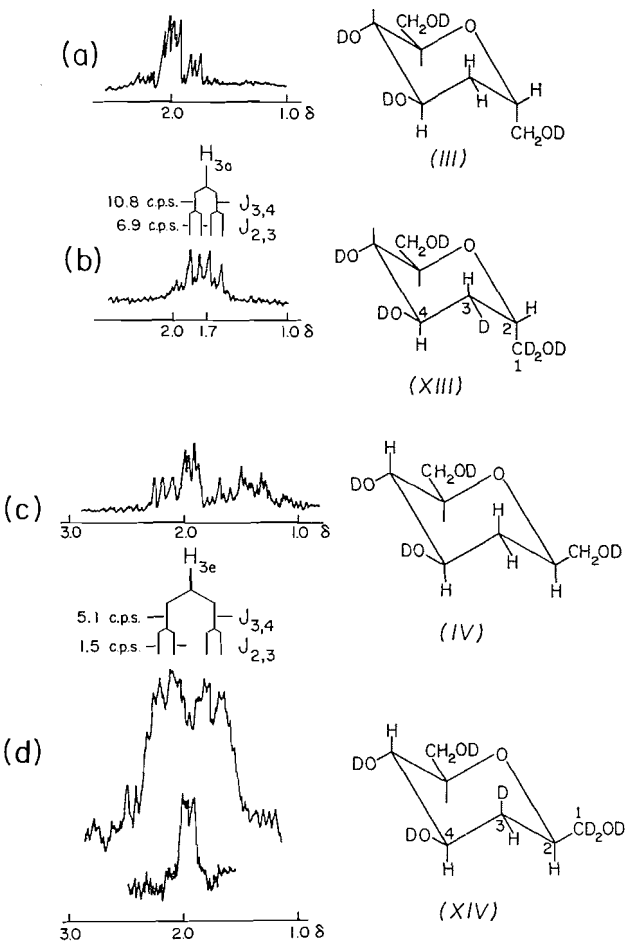



FIG. 1. Proton n.m.r. spectra in $D_2O$ solution at 60 Mc/s with chemical shifts given in p.p.m. from tetramethylsilane as zero: (*a*) 2,6-anhydro-3-deoxy-D-*manno*-heptitol; (*b*) 2,6-anhydro-3-deoxy-D-*manno*-heptitol-1,1,3-$^2H_3$; (*c*) 2,6-anhydro-3-deoxy-D-*gluco*-heptitol; (*d*) 2,6-anhydro-3-deoxy-D-*gluco*-heptitol-1,1,3-$^2H_3$. (Only signals of protons attached to C-4 are shown.)

Therefore, compounds (XIII) and (XIV) are 2,6-anhydro-3-deoxy-D-*manno*-heptitol-1,1,3-$^2H_3$ (*cis*) and 2,6-anhydro-3-deoxy-D-*gluco*-heptitol-1,1,3-$^2H_3$ (*cis*), respectively. Evidently, the deuterated heptitols (XIII) and (XIV) must have been formed by a *cis* addition of the hydroxymethyl group and of the deuterium to the 1,2-unsaturated bond of 3,4,6-tri-*O*-acetyl-D-glucal. Unequivocal confirmation of the structures of the heptitols was provided by carrying out an independent X-ray crystallographic analysis (4) of a derivative of compound (II), namely, 4,5,7-tri-*O*-acetyl-2,6-anhydro-1-*O*-(*p*-bromobenzenesulfonyl)-3-deoxy-D-*gluco*-heptitol (VII).

The utility of the monotosylate ester (VIII) in synthesis was demonstrated by its conversion into the 1-amino derivative. Treatment of compound (VIII) with ammonia in methanol afforded the 1-amino derivative, which was isolated in the fully acetylated form (XII). Attempts to convert the tosylate ester (VIII) into the amino derivative via the monoiodo derivative (IX), thence into the azido derivative, followed by catalytic reduction of the azido compound to (XII), were not successful and were abandoned.

Very little work has been reported (5) on correlating the reactivity of primary hydroxyl groups of carbohydrates with their orientation. From this work, which has dealt mainly with the polyol bicyclic acetal derivatives, it has been adduced that the axially oriented tosyloxy group reacts with sodium iodide with greater ease than the equatorial group when both groups are in similar environments (5). Preferential reaction at the axial tosyloxy group would not be expected in a reaction that seems to be (6) rather strongly retarded by an increase in the size of substituents in the vicinity of tosyloxy groups.

Since an acetal ring is known to greatly reduce the chemical reactivity of adjacent tosyloxy groups (7–9), we believed that carbohydrates possessing the pyran ring and only one tosyloxy group would be suitable model substances for correlating chemical reactivity of the tosyloxy group and its orientation. The mono-1-*O*-tosylate derivative of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*gluco*-heptitol and of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*manno*-heptitol appeared to be ideal model compounds because these epimers differ in one aspect only, namely, one possesses an equatorial tosyloxy group whereas the other has an axial tosyloxy group. X-ray crystallographic studies have definitely established that 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*gluco*-heptitol (VIII) exists in the chair conformation with all groups in equatorial positions (4). On the bases of the facts that 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*manno*-heptitol (XV) was prepared by tosylation of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*manno*-heptitol following the same procedure as utilized in the preparation of its epimer, and the n.m.r. spectra of the two tosylates were similar, the tosyl group was assumed to be on C-1. If there had been acetyl migration before the tosylation, then the tosyl group would have been on a secondary hydroxyl group. Because replacements by iodide of a tosyloxy group on a secondary hydroxy under the conditions used in our work are not known to occur (10), the assumption that compound (XV) had its tosylate group on C-1 appears to be valid.

Samples of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*gluco*-heptitol (VIII) and of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*manno*-heptitol (XV) were allowed to react with sodium iodide in acetone at 100° in closed tubes for varying periods of time as shown in the Experimental section. The solutions were equimolecular with respect to each other. The extent of the exchange reaction was determined by weighing the sodium *p*-toluenesulfonate precipitated. In the figures quoted in the Experimental section, the solubility of sodium *p*-toluenesulfonate in a solution of acetone and sodium iodide was taken into account. The results clearly show that the equatorial tosyloxy group at C-1 of (VIII) was replaced at about double the rate by iodine than was the axial tosyloxy group at C-1 of (XV).

When a 0.01-mole mixture of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*manno*-heptitol (I) and 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*gluco*-heptitol (II) was allowed to react with 0.011 mole of *p*-toluenesulfonyl chloride at room temperature for 22 h, all of compound (II) was tosylated, whereas only a trace of compound (I) was converted into the tosylate (XV).

## EXPERIMENTAL

### *General Considerations*

General conditions for chromatographic separations have been described previously (1). Preparation of *p*-nitrobenzoyl derivatives was carried out by a procedure similar to that described by Gorin (11).

### *Reaction of 3,4,6-Tri-O-acetyl-D-glucal with Carbon Monoxide and Hydrogen to Yield 2,6-Anhydro-3-deoxy-D-manno-heptitol (III) and 2,6-Anhydro-3-deoxy-D-gluco-heptitol (IV)*

3,4,6-Tri-*O*-acetyl-D-glucal (12) was caused to react with carbon monoxide and hydrogen in the presence of preformed dicobalt octacarbonyl according to a procedure previously described (1). The product was de-*O*-acetylated with sodium methoxide to yield a mixture of compounds (III) and (IV). Fractionation of

the mixture of anhydrodeoxyheptitols was carried out by preparative paper chromatography or by cellulose column chromatography at 37°.

The ratio of (I) and (II) depended on the temperature of the reaction. At 130° it was almost equimolar.

*Characterization of Fractions (III) and (IV)*

*Fraction (III) (2,6-anhydro-3-deoxy-*D*-manno-heptitol).*—This fraction was crystallized from methanol – isopropyl ether; m.p. 152–153°, $[\alpha]_D^{20}$ +60° (*c*, 1.4, water), $R_F$ = 0.21.

Anal. Calcd. for $C_7H_{14}O_5$: C, 47.18; H, 7.92. Found: C, 47.30; H, 7.82.

*1,4,5,7-Tetra-O-acetyl-2,6-anhydro-3-deoxy-*D*-manno-heptitol.*—Fraction (III) was acetylated with acetic anhydride in the presence of sodium acetate to yield a tetra-*O*-acetyl derivative which was first purified by chromatography on silica gel using 2.5% methanol in benzene as developer and then crystallized from ether – light petroleum ether; m.p. 123–124°, $[\alpha]_D^{20}$ +28° (*c*, 0.5, acetone).

Anal. Calcd. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.40. Found: C, 52.53; H, 6.55.

*Fraction (IV) (2,6-anhydro-3-deoxy-*D*-gluco-heptitol).*—This fraction was crystallized from methanol – isopropyl ether; m.p. 137–138°, $[\alpha]_D^{20}$ −1° (*c*, 3.5, water), $R_F$ = 0.30.

Anal. Calcd. for $C_7H_{14}O_5$: C, 47.18; H, 7.92. Found: C, 47.19; H, 7.63.

*1,4,5,7-Tetra-O-acetyl-2,6-anhydro-3-deoxy-*D*-gluco-heptitol.*—Fraction (IV) was acetylated and purified in the same way as described above to yield a tetra-*O*-acetyl derivative; m.p. 79–80°, $[\alpha]_D^{21}$ +2° (*c*, 0.5, acetone).

Anal. Calcd. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.40. Found: C, 52.48; H, 6.50.

*Structure and Stereochemistry of Compounds (III) and (IV)*

*2-Deoxy-3-O-(1,3-dihydroxy-2-propyl)-*D*-glycero-tetritol (V) from 2,6-Anhydro-3-deoxy-*D*-manno-heptitol (III)*

Oxidation of 2,6-anhydro-3-deoxy-D-*manno*-heptitol with 0.1 *M* periodic acid (1 mole consumed), followed by reduction of the resulting dialdehyde with sodium borohydride in water according to the procedure described by Gorin (11), gave the tetrol ether (V) as a sirup; $[\alpha]_D^{19}$ −25° (*c*, 0.7, methanol). This sirup was converted into a tetra-*O*-(*p*-nitrobenzoyl) derivative; m.p. 149–150.5°, $[\alpha]_D^{22}$ −22° (*c*, 1.5, chloroform).

Anal. Calcd. for $C_{35}H_{28}O_{17}N_4$: C, 54.13; H, 3.63; N, 7.21. Found: C, 54.55; H, 3.71; N, 7.30.

*2-Deoxy-3-O-(1,3-dihydroxy-2-propyl)-*L*-glycero-tetritol (VI) from 2,6-Anhydro-3-deoxy-*D*-gluco-heptitol (IV)*

Periodate oxidation and sodium borohydride reduction of the dialdehyde from (IV) under similar conditions to those described above gave the tetrol ether (VI); $[\alpha]_D^{22}$ +26° (*c*, 2.9, water). This formed a tetra-*O*-(*p*-nitrobenzoyl) derivative which was recrystallized from ethyl acetate – petroleum ether; m.p. 151–152°; $[\alpha]_D^{21}$ +22° (*c*, 1.2, chloroform).

Anal. Calcd. for $C_{35}H_{28}O_{17}N_4$: C, 54.13; H, 3.63; N, 7.21. Found: C, 54.50; H, 3.94; N, 7.50.

The infrared spectra of the tetra-*O*-(*p*-nitrobenzoyl) derivatives of the tetrol ethers (V) and (VI) were identical.

*Alternative Methods of Separation of the Heptitols (I) and (II) by Conversion to 1-O-Sulfonate Esters (VII) and (VIII)*

*A. 4,5,7-Tri-O-acetyl-2,6-anhydro-1-O-(p-bromophenylsulfonyl)-3-deoxy-*D*-gluco-heptitol (VII)*

*p*-Bromobenzenesulfonyl bromide (2.6 g) was added to 2 g of an ice-cold anhydrous mixture of oxo product (I) and (II) dissolved in anhydrous pyridine (15 ml). After the mixture was left at room temperature for 30 h, 20 ml of water was added and the mixture left to stand for 24 h. The solution was then extracted with three portions of chloroform. The combined chloroform extracts were washed with water and then dried over anhydrous sodium sulfate. Evaporation of the chloroform left a residue which was twice recrystallized from methanol, and then from methanol–water; yield 1.01 g; m.p. 104°; $[\alpha]_D^{22}$ −10° (*c*, 3, chloroform).

Anal. Calcd. for $C_{19}H_{23}O_{10}SBr$: C, 43.58; H, 4.43; S, 6.13; Br, 15.27. Found: C, 43.57; H, 4.47; S, 6.32; Br, 15.26.

The proof of structure of compound (VII) by X-ray crystallographic studies has been described previously (4).

*B. 4,5,7-Tri-O-acetyl-2,6-anhydro-3-deoxy-1-O-tosyl-*D*-gluco-heptitol (VIII)*

The tosylate ester (VIII) was prepared by tosylation of the mixture of compounds (I) and (II) following the same procedure as used in the preparation of the brosylate ester (VII). Fractional crystallization of the tosylates gave compound (VIII) in pure form; m.p. 117–118°, $[\alpha]_D^{20}$ −5° (*c*, 0.5, chloroform); n.m.r. (given in $\delta$ units; spectra obtained in deuterated chloroform): 2.0 (acetyl and $CH_2$, area = 11H), 2.37 ($CH_3$, area = 3H), 3.55 (area = 2H), 3.95 (multiplet, area = 4H), 4.85 (area = 2H), 7.17 (doublet, area = 2H), 7.61 (doublet, area = 2H).

Anal. Calcd. for $C_{20}H_{26}O_{10}S$: C, 52.50; H, 5.52. Found: C, 52.20; H, 5.51.

*4,5,7-Tri-O-acetyl-2,6-anhydro-3-deoxy-1-O-tosyl-*D*-manno-heptitol (XV)*

An amount of 4.8 g of the oxo products (I) and (II) was allowed to react with 6.0 g of *p*-toluenesulfonyl chloride in 125 ml of anhydrous pyridine at room temperature for 12 h and then heated at 100° for 1 h. Work-up of the product in the usual way gave 5.06 g of a mixture of compounds (VIII) and (XV). Thin-layer chromatographic separation of this mixture (0.45 g) on silica gel using toluene–ether (2:1, v:v), or isopropyl

ether, as developer afforded 0.30 g of (VIII) and 0.08 g of (XV). The tosylates were detected by spraying the samples with diphenylamine in methanol (1% solution) and viewing them under ultraviolet light.

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*manno*-heptitol (XV) was obtained as an oil; $[\alpha]_D^{23}$ +30° (*c*, 1.7, chloroform); n.m.r.: 2.0 (11H), 2.40 (3H), 3.55 (2H), 4.00 (multiplet, 4H), 4.90 (multiplet, 2H), 7.17 (2H), 7.65 (2H).

Anal. Calcd. for $C_{20}H_{26}O_{10}S$: C, 52.50; H, 5.52. Found: C, 52.36; H, 6.18.

*Comparative Rate of Tosylation of Oxo Products (I) and (II)*

An amount of 0.010 mole of oxo product mixture (70% of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*manno*-heptitol (I) and 30% of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-D-*gluco*-heptitol (II)) was allowed to react with 0.011 mole of *p*-toluenesulfonyl chloride (0.011 mole) at room temperature for varying periods of time and the product analyzed by t.l.c. on silica gel using isopropyl ether as developer. Compound (II) was completely tosylated after 22 h whereas only a trace of compound (I) was converted into the tosylate (XV) during the same time.

*4,5,7-Tri-O-acetyl-2,6-anhydro-1,3-dideoxy-1-iodo-D-gluco-heptitol (IX)*

4,5,7-Tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*gluco*-heptitol was allowed to react with sodium iodide in acetone in a closed tube at 100° for 6 h to afford 4,5,7-tri-*O*-acetyl-2,6-anhydro-1,3-dideoxy-1-iodo-D-*gluco*-heptitol; m.p. 100°, $[\alpha]_D^{22}$ −13° (*c*, 0.1, chloroform).

Anal. Calcd. for $C_{13}H_{19}O_7I$: C, 37.69; H, 4.62; I, 30.64. Found: C, 37.58; H, 4.35; I, 30.58.

Treatment of the brosylate (VII) with sodium iodide in acetone also yielded compound (IX).

*4,5,7-Tri-O-acetyl-2,6-anhydro-3-deoxy-1-O-nitro-D-gluco-heptitol (X)*

4,5,7-Tri-*O*-acetyl-2,6-anhydro-1,3-dideoxy-1-iodo-D-*gluco*-heptitol dissolved in acetonitrile was caused to react with silver nitrate according to a procedure previously described (10). The product (X) was recrystallized from ether – light petroleum ether; m.p. 79°, $[\alpha]_D^{22}$ −8° (*c*, 0.7, acetone).

Anal. Calcd. for $C_{13}H_{19}O_{10}N$: C, 44.71; H, 5.48; N, 4.08. Found: C, 44.58; H, 5.12; N, 4.06.

*Conversion of 4,5,7-Tri-O-acetyl-2,6-anhydro-3-deoxy-1-O-nitro-D-gluco-heptitol (X) into 2,6-Anhydro-3-deoxy-D-gluco-heptitol (IV)*

An amount of 30 mg of compound (X) dissolved in anhydrous methanol (10 ml) was hydrogenated over palladium black (3 mg) at atmospheric pressure and room temperature for 75 min. After removal of the catalyst, the solvent was evaporated under vacuum and the product then dried. De-*O*-acetylation of the residual sirup with methanolic sodium methoxide gave a compound having a melting point, $R_F$ value, and infrared spectrum identical with those of authentic 2,6-anhydro-3-deoxy-D-*gluco*-heptitol (IV).

*1-Acetamido-4,5,7-tri-O-acetyl-2,6-anhydro-1,3-dideoxy-D-gluco-heptitol (XII)*

An amount of 0.148 g of 4,5,7-tri-*O*-acetyl-2,6-anhydro-3-deoxy-1-*O*-tosyl-D-*gluco*-heptitol was added to an ammonia-saturated solution of methanol (12 ml). The reactants were heated in a sealed tube at 100° for 65 h. After the ammonia evaporated, the methanol was removed under reduced pressure and the product then dried. Acetylation of the product with 4 ml of acetic anhydride and 4 ml of pyridine in the usual way gave the fully acetylated amino compound (XII). Purification of (XII) was achieved by column chromatography on silica gel using benzene–methanol (96:4, v:v) as developer. Recrystallization of the product (0.065 g) from acetone – isopropyl ether – heptane gave pure (XII); m.p. 136–137°, $[\alpha]_D^{22}$ −3° (*c*, 1.8, chloroform); n.m.r.: 2.05 (multiplet, area = 14H), 3.5 (multiplet, area = 4H), 4.1 (multiplet, area = 2H), 4.82 (multiplet, 2H), 5.75 (broad, area = 1H).

Anal. Calcd. for $C_{15}H_{23}O_8N$: C, 52.17; H, 6.71; N, 4.06. Found: C, 51.94; H, 7.01; N, 3.94.

*Attempt to Prepare 1-Acetamido-2,6-anhydro-1,3-dideoxy-D-gluco-heptitol from Compound (IX)*

An amount of 0.24 g of 4,5,7-tri-*O*-acetyl-2,6-anhydro-1,3-dideoxy-1-iodo-D-*gluco*-heptitol (IX) was caused to react with sodium azide (0.5 g) in acetone (3 ml) and water (2 ml) for 10 h at a temperature of 110–120 °C in a sealed tube. After the tube was opened, 5 ml of ether was added. The ether layer was washed with water, dried over an anhydrous sodium sulfate, and then evaporated. The resulting azido compound (XI), dissolved in acetone, was decolorized by passage through a short column of charcoal; yield 0.083 g. Compound (XI) showed an azide peak at 2 120 $cm^{-1}$ in the infrared spectrum. After it was dissolved in ethanol (20 ml), it was hydrogenated at atmospheric pressure for 6 h over platinum oxide (0.022 g) according to a procedure previously described (13). After removal of the catalyst, the solvent was evaporated under reduced pressure. The product was then acetylated in the usual way using acetic anhydride and pyridine. Addition of water to the reaction product gave a trace of crystalline product which was removed by filtration. After removal of the volatile components, the product was analyzed by thin-layer chromatography and shown to contain a trace of compound (XII).

*Reaction of 3,4,6-Tri-O-acetyl-D-glucal with Carbon Monoxide and Deuterium to Yield 2,6-Anhydro-3-deoxy-D-manno-heptitol-1,1,3-$^2H_3$ (cis) (XIII) and 2,6-Anhydro-3-deoxy-D-gluco-heptitol-1,1,3-$^2H_3$ (cis) (XIV)*

3,4,6-Tri-*O*-acetyl-D-glucal was caused to react with carbon monoxide and deuterium at 130°, under

conditions similar to those used in the preparation of the normal anhydrodeoxyheptitols, to yield the above-mentioned deuterated heptitols (XIII) and (XIV). The stereochemisty of the deuterium atom on C-3 of both heptitols was determined by proton n.m.r. analysis (see Discussion).

*Comparative Iodine Exchange Experiments of Tosylates (VIII) and (XV)*

In each experiment each Carius tube contained 9.1 mg of the tosylate, 9.1 mg of sodium iodide, and 1.4 ml of acetone. After the tubes were cooled in solid carbon dioxide, they were sealed and then heated at 100° (±0.1) for varying periods of time. The amount of sodium *p*-toluenesulfonate was collected in a sintered-glass crucible, washed with 2 ml dry acetone, and dried under reduced pressure before they were weighed. A correction of 0.20 mg of sodium *p*-toluenesulfonate was added to each weight as this amount dissolved in the acetone at room temperature. The results are as follows: % exchange of tosylate by iodine of compound (VIII) 14 (5 min), 18 (10 min), 41 (23 min), 46 (41 min), 51 (60 min), 59 (90 min), 93 (162 min); % exchange of tosylate by iodine of compound (XV) 20 (30 min), 32 (60 min), 41 (120 min), 47 (300 min), 56 (420 min), 73 (630 min).

## ACKNOWLEDGMENTS

The authors gratefully acknowledge the financial assistance of the National Cancer Institute of Canada, the National Research Council of Canada, the University of British Columbia Research Grant, and the Petroleum Research Fund administered by the American Chemical Society for support of this work.

Part of the preliminary experimental work was done by Mr. T. Field and Mr. R. Bolster.

The senior author (A. R.) expresses his gratitude to University Chemical Laboratory, University of Cambridge, for use of its facilities during the writing of this manuscript.

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