HYDROGENOLYSIS OF CARBOHYDRATES

VIII. COMPARATIVE STUDIES ON METHYL GLYCOPYRANOSIDES[1]

P. A. J. GORIN

ABSTRACT

Several methyl glycopyranosides have been hydrogenated under pressure at 180° C with copper chromite catalyst in dioxane. Many glycosides underwent hydroxyl group inversion and another reaction observed consisted of hydrogenolytic removal of the methoxyl group coupled with reduction of a hydroxyl group to a methylene group. Other glycosides were stable under these conditions, and these included methyl β- and methyl α-D-glucopyranosides and unexpectedly methyl β-D-mannopyranoside and methyl α-D-talopyranoside. The data indicated that generally β-glycosides are more stable than their α-anomers in the hexopyranoside series and that the methyl hexopyranosides are more stable than the methyl pentopyranosides. Explanations have been made in the theoretical section in order to cover these observations. At 240° C, however, methyl α-D-glucopyranoside is hydrogenolyzed giving 11% of 1,5-anhydro-4-deoxy-hexitols. These polyols have been fractionated and the mixture shown to contain lyxo- and arabo-1,5-anhydro-4-deoxy-D-hexitols.

The earlier findings of von Rudloff, Bauer, and Stuetz (1) showed that the hydrogenolysis of methyl α-D-glucopyranoside yields 1,5-anhydro-4-deoxy-hexitol (11% yield) along with many other products. The hydrogenolytic procedure was vigorous, the experiments being carried out with Adkins' copper chromite catalyst (2) at 240° C using dioxane as solvent under a hydrogen pressure of 170 atmospheres. More recent investigations (3, 4, 5, 6, 7) have indicated that at lower temperatures (180–220° C) some inversion of the asymmetric centers occurs as well as hydrogenolysis. However, methyl α- and methyl β-D-glucopyranosides were found to be virtually unaffected at 180° C. Since the hydroxyl groups on methyl β-L-arabopyranoside are readily inverted by catalytic hydrogenation (3) the behavior of the methyl glucosides seemed anomalous. Therefore, another hexopyranoside methyl α-D-mannopyranoside was hydrogenated at 180° C and was found to yield a mixture of isomeric glycosides.* By fractionation, on a cellulose column (8), methyl α-D-talopyranoside has been isolated from the mixture† together with unchanged methyl α-D-mannopyranoside and a small amount of methyl α-D-glucopyranoside. As the hydroxyl configurations in the substrate appeared to play a role in determining its susceptibility to hydrogenation other methyl α-D-hexopyranosides were examined. Methyl α-D-galacto- and -altro-pyranosides were transformed by hydrogenation to other isomers, mainly methyl α-D-talopyranoside, which is a stable methyl glycoside under the conditions used (Table I). This was confirmed by synthesizing methyl α-D-talopyranoside, hydrogenating it, and isolating the unchanged glycoside.

As well as the α-glycosides, several methyl β-D-hexopyranosides were tested. These included methyl β-D-allo-, -altro-, -galacto-, -gluco-, and -manno-pyranosides (Table I) and as a group these compounds were more stable to hydrogenation than the α-glycosides, a greater percentage of substrate being recovered unchanged. This stability was most pronounced in methyl β-D-gluco- and -manno-pyranosides which were virtually unaffected and were found to be the main end products of hydrogenation of the other β-glycosides.

In contrast to the hexopyranosides the methyl pentopyranosides, as represented by

[1]*Manuscript received January 4, 1960.*
Contribution from the National Research Council of Canada, Prairie Regional Laboratory, Saskatoon, Saskatchewan.
Issued as N.R.C. No. 5604.
The author wishes to thank Dr. A. S. Perlin for this unpublished information.
†*This would appear to be a simple route by which to prepare methyl α-D-talopyranoside.*

TABLE I

Products isolated from hydrogenation of methyl hexopyranosides at 180° C

Substrate	Product (% w/w)
Methyl α-D-glucopyranoside	98% Unchanged material
Methyl α-D-mannopyranoside	Methyl α-D-mannopyranoside (30%) Methyl α-D-talopyranoside (27%) Methyl α-D-glucopyranoside (3%)
Methyl α-D-galactopyranoside	Methyl α-D-glucopyranoside (33%) Methyl α-D-talopyranoside (9%) Polyols (7%) Methyl α-D-galactopyranoside (5%)
Methyl α-D-altropyranoside	Methyl α-D-talopyranoside (20%) Polyols (18%) Methyl α-D-mannopyranoside (11%)
Methyl α-D-talopyranoside	Mainly unchanged material
Methyl β-D-glucopyranoside	Unchanged material
Methyl β-D-mannopyranoside	87% Unchanged material
Methyl β-D-galactopyranoside	Methyl β-D-glucopyranoside (25%) Methyl β-D-galactopyranoside (17.5%) Polyols (16%) Methyl β-D-allopyranoside (3%)
Methyl β-D-altropyranoside	Methyl β-D-altropyranoside (24%) Polyols (16%) Methyl β-D-mannopyranoside (15%)
Methyl β-D-allopyranoside	Polyols (35%) Methyl β-D-allopyranoside } 25% Methyl β-D-glucopyranoside }

methyl α-L-arabo- and -D-lyxo-pyranosides and methyl β-L-arabo- (cf. ref. 3), -D-ribo-, and -D-xylo-pyranosides, were much more prone to hydroxyl group inversion at 180° C (Table II). Acid hydrolysis of the product and detection of the free sugars by paper

TABLE II

Products isolated from hydrogenation of methyl pentopyranosides at 180° C

Substrate	Product (% w/w)
Methyl α-L-arabopyranoside	Polyols (23%) Methyl β-D-ribopyranoside (12%) Methyl α-L-lyxopyranoside (6%) Methyl β-D-xylopyranoside (1%)
Methyl α-D-lyxopyranoside	Polyols (44%) Methyl ribopyranoside (?%) Methyl arabopyranoside Methyl xylopyranoside } 15% Methyl lyxopyranoside Methyl α-D-lyxopyranoside (13%)
Methyl β-L-arabopyranoside	Polyols (30%) Methyl β-L-arabopyranoside (10%) Methyl α-D-xylopyranoside (5%)
Methyl β-D-xylopyranoside	Polyols (29%) Methyl β-D-ribopyranoside (17%) Methyl xylopyranoside } 12% Methyl arabopyranoside }
Methyl β-D-ribopyranoside	Polyols (35%) Methyl ribopyranoside (16%) Methyl xylopyranoside Methyl lyxopyranoside } 7% Methyl arabopyranoside

chromatography indicated in each instance easy interconversion since two to four chemically different pentoses were present. Also, the pentopyranosides were hydrogenolyzed with greater ease to dihydroglycals (tetrahydropyrandiols) by reductive elimination of the methoxyl group coupled with reduction of a hydroxyl to a methylene group. The hydrogenation products of the methyl glycopyranosides are summarized in Tables I and II with the percentage of each compound contained in the reaction product as determined on column chromatographic separation.

It appears likely that resistance to catalytic hydroxyl inversion is affected by the shape of the substrate. For example, the 6-hydroxymethyl group seems to exert an influence in limiting hydroxyl group inversion and formation of compounds of the dihydroglycal type. The large substituent on C-5 would render the molecule more bulky and perhaps less flexible so that it could adopt fewer positions suited to reaction on the surface of the catalyst. Unfortunately too little is known about the surface properties of copper chromite to generalize on the probability of individual hydroxyls in the glycosides to invert. If, as has been assumed (7), inversion results from dehydrogenation followed by hydrogenation this ability would be concerned firstly, with the ease of dehydrogenation of the alcohol group to a ketone, and secondly with the specificity of reduction of the ketone to the two possible alcohols (Fig. 1). It has been shown that the rate of dehydrogenation

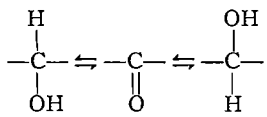

FIG. 1.

of a secondary alcohol with chromic acid in cyclohexane ring systems (9) to a ketone depends on the accessibility of the C-hydrogen atom (10) and not the rate of intermediate ester formation. The dehydrogenation rate was shown to be greater when the C-hydrogen atom was in the less sterically hindered equatorial position (9). However, this is in solution rather than on the surface of a catalyst. In order to explain the surprising observations that methyl β-D-mannopyranoside and methyl α-D-talopyranoside are virtually unaffected under hydrogenation conditions it must be assumed that the catalyst plays a role in limiting dehydrogenation. This may well be because the surface contours of the copper chromite prevent the C-hydrogen atoms, some of which are equatorial (11), from becoming available. On the other hand, methyl α- and β-D-glucopyranosides, which are also stable do not contain equatorial C-hydrogen atoms in their stable C-1 chair forms (11).

Since hydroxyl inversion readily occurs in polyhydroxyl compounds, even at temperatures as low as 180° C, it appeared likely that the syrupy 1,5-anhydro-4-deoxy-D-hexitol formed by hydrogenation of methyl α-D-glucopyranoside at 240° C (1) was a mixture of stereoisomers and accordingly, this product has been examined further. Cellulose column chromatography of the syrupy polyols derived by catalytic deacetylation of the fractionated acetate contained two main components which were distinguishable on paper chromatograms. The fraction which was slower on paper was syrupy but gave a crystalline tris-*p*-nitrobenzoate derivative from which a crystalline polyol (I) of R_{Rh} 1.1* was regenerated. The 1,5-anhydro-4-deoxy-hexitol structure for the substance was indicated by carbon and hydrogen composition and its consumption of 1.0 molar equivalent of sodium periodate. If it is assumed that no inversion at C-5 takes place and that the six-membered ring is not modified in the course of hydrogenolysis the only

**Throughout the text R_{Rh} denotes the distance moved by a spot on a paper chromatogram compared with rhamnose in the n-butanol – ethanol – water (40:11:19) v/v solvent.*

alternative structure fitting the data is that of a dihydroglycal (IV). However, since periodic acid oxidation of I followed by sodium borohydride reduction gave an optically active triol (III) the dihydroglycal formula is invalidated since it would have given a triol (V) with no asymmetric centers (Fig. 2).

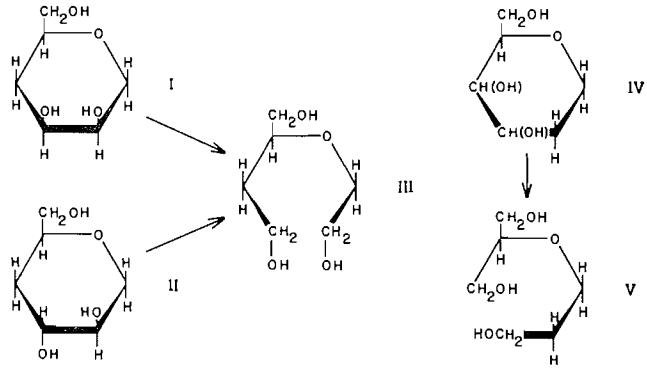

FIG. 2.

The other fraction having R_{Rh} 1.3, from the cellulose column, also gave a crystalline tris-*p*-nitrobenzoate, which on debenzoylation yielded a syrupy polyol (II) which consumed 1.0 molar equivalent of sodium periodate. Periodic acid oxidation and sodium borohydride reduction of the resulting dialdehyde formed the same compound as obtained from I. Their identity was confirmed by comparison of their crystalline tris-*p*-nitrobenzoates.

Comparison of the rates at which I and II consumed lead tetraacetate showed that the former was oxidized 4 times faster in the initial stages. This difference which is appreciable considering that the α-glycol groups are in a six-membered ring (4, 12, 13, 14) is interpreted as evidence that they are *cis* in I and *trans* in II. By consideration of the molecular rotations of various methyl hexopyranosides and 1,5-anhydro-hexitols theoretical values for the specific rotations of the four structural isomers of 1,5-anhydro-4-deoxy-D-hexitol can be calculated by use of Hudson's rules of optical superposition and isorotation (see Table III) (15). Since I has $[\alpha]_D$ $-50°$ it is probably lyxo-1,5-anhydro-4-deoxy-D-hexitol and II ($[\alpha]_D$ $+19°$) corresponds to arabo-1,5-anhydro-4-deoxy-D-hexitol. These compounds are different in hydroxyl configuration from methyl α-D-glucopyranoside and it is likely that the other two possible stereoisomers are present in the hydrogenolysis product, but were not isolated through the limitations of the fractionation procedures. Although the 1,5-anhydro-4-deoxy-hexitols are difficult to distinguish chromatographically from the dihydroglycals of the hexose series, shown to be formed by hydrogenolysis under milder conditions (4), it seems unlikely that they are present, because they are extensively degraded by hydrogenolysis at 220° C (26).

The readiness of methyl glycopyranosides to form polyols on hydrogenolysis parallels their tendency to undergo hydroxyl inversion in the hexose as well as pentose series (except that with the hexoses a higher temperature is generally needed to remove the methoxyl group). For instance, methyl β-D-galactopyranoside is much more reactive at 180° C than methyl α-D-glucopyranoside as far as hydroxyl group inversion is concerned. At 200° C the former is degraded to a mixture of dihydro-D-altral (12%), dihydro-D-glucal (31%), and dihydro-D-galactal (12%). But methyl α-D-glucopyranoside is relatively inert at this temperature and complete hydrogenolysis only takes place at 240° C,

TABLE III

Calculated specific rotations of 1,5-anhydro-4-deoxy-D-hexitols

Polyols and calculated specific rotations	Reference compounds
ribo-1,5-Anhydro-4-deoxy-D-hexitol +46°	Methyl β-D-allopyranoside ($[M]_D$ −9,510°) Methyl α-D-glucopyranoside (16) ($[M]_D$ +23,210°)
lyxo-1,5-Anhydro-4-deoxy-D-hexitol (I) −31°	Methyl α-D-talopyranoside ($[M]_D$ +4,070°) Methyl β-D-mannopyranoside (17) ($[M]_D$ −13,390°)
−34°	1,5-Anhydro-D-mannitol (18) ($[M]_D$ −8,360°) 1,5-Anhydro-D-talitol (19) ($[M]_D$ −1,800°)
xylo-1,5-Anhydro-4-deoxy-D-hexitol +106°	Methyl α-D-galactopyranoside (20) ($[M]_D$ +38,050°) Methyl β-D-glucopyranoside (21) ($[M]_D$ −6,640°)
+67°	1,5-Anhydro-D-glucitol (22) ($[M]_D$ +7,050° 1,5-Anhydro-D-galactitol (23) ($[M]_D$ +12,790°)
arabo-1,5-Anhydro-4-deoxy-D-hexitol (II) +20°	Methyl α-D-altropyranoside (24) ($[M]_D$ +24,420°) Methyl β-D-idopyranoside (25) ($[M]_D$ −18,430°)

to form the more stable 1,5-anhydro-4-deoxy-hexitols and degradation products such as ethylene and propylene glycols. Much of these lower molecular weight materials may therefore have been formed through an unstable 1,2-dihydroglycal intermediate rather than 1,5-anhydro-4-deoxy-D-hexitol which does not contain the 1,3-dihydroxy grouping which is susceptible to hydrogenolysis (27).

EXPERIMENTAL

Optical rotations were measured at 25° C. Evaporations were carried out under reduced pressure. The solvent used for paper chromatographic separations was *n*-butanol – ethanol – water (40:11:19 v/v). Reducing sugars were detected with the *p*-anisidine hydrochloride spray (28) and non-reducing sugars with ammoniacal silver nitrate (29). Acid hydrolysis of glycosides was carried out with *N* H_2SO_4 at 100° C for 3 hours, the solutions neutralized with $BaCO_3$, filtered, and evaporated.

A. Preparation of Reference Compounds

Methyl β-D-Allopyranoside

D-Allose (500 mg), kindly supplied by Dr. A. C. Neish, was refluxed in 3% methanolic hydrogen chloride (20 ml) for 5 hours, and the solution neutralized, after it was cooled, with silver oxide which was then filtered off. The filtrate was evaporated to a syrup which crystallized and three recrystallizations from ethanol – ethyl acetate afforded material with m.p. 155–157° C and $[\alpha]_D$ −49° (*c*, 1.0, H_2O), yield 95 mg. Calculated for $C_7H_{14}O_6$: C, 43.3%; H, 7.3%. Found: C, 43.2%; H, 7.3%. The constants of the product agree with those given by Lindberg and Theander (30).

Methyl α-D-Talopyranoside and Derivative

Syrupy D-talose (1.26 g) was heated for 4 hours in refluxing 3% methanolic hydrogen chloride (40 ml), the acid was neutralized (Ag_2O), the solution filtered and evaporated to a syrup (1.17 g). Examination on a paper chromatogram indicated a main spot having R_{Rh} 1.4 with a minor component of R_{Rh} 1.1. The faster material was isolated by cellulose chromatography using benzene–ethanol–water (500:50:1 v/v) as the mobile phase. The product was a syrup (0.56 g) with $[\alpha]_D$ +105° (*c*, 1.0, H_2O). Calculated for $C_6H_{11}O_5 \cdot OCH_3$: OCH_3, 16.0%. Found: OCH_3, 16.0%. The glycoside was designated the α-configuration because of its strong dextrorotation.

The syrupy product (30 mg) was heated at 100° C for 2 hours in pyridine (0.5 ml) containing triphenylchloromethane (61 mg). After it was cooled, acetic anhydride (0.5 ml) was added and the solution left overnight. Then it was added to aqueous sodium bicarbonate and the insoluble material which formed was isolated and recrystallized twice from aqueous ethanol, then ethanol. The crystals (25 mg) had m.p. 177–178° C and $[\alpha]_D$ +21° (*c*, 1.3, pyridine) and analyzed for 2,3,4-tri-*O*-acetyl-6-*O*-triphenylmethyl methyl α-D-talopyranoside. Calculated for $C_{32}H_{34}O_9$: C, 68.3%; H, 6.1%. Found: C, 68.2%; H, 6.2%.

B. Hydrogenation of Methyl Glycopyranosides at 180° C

In hydrogenation of the following methyl hexopyranosides identical procedures were used. The glycoside was added to one-third its weight of copper chromite in 50 parts of dioxane (v/w). The mixture was shaken at 180° C for 6 hours at a hydrogen pressure of 600 p.s.i. and after it was cooled the solution was filtered and evaporated. An attempt was then made to crystallize any sugars from solution and the resulting syrup was chromatographed on a cellulose column. The solvents for cellulose chromatography were benzene–ethanol–water (500:50:1 v/v) to isolate materials moving faster than rhamnose on a paper chromatogram. For compounds moving slower than rhamnose *n*-butanol one-quarter saturated with water was used.

When methyl pentopyranosides were hydrogenated the procedure was the same as above except for the relative proportion of components in the reaction mixture. In this case the weight of catalyst was 30% that of the methyl pentoside and the solvent used was 45 times that of the pentoside on a volume per unit weight basis.

(*i*) *Methyl α-D-glucopyranoside.*—From the hydrogenation product of the glucoside (2.00 g) mainly unchanged material was recovered by crystallization from ethanol, m.p. and mixed m.p. 165–166° C. Column chromatography yielded only 42 mg of substance that ran at a different rate than methyl glucoside on a paper chromatogram.

(*ii*) *Methyl β-D-glucopyranoside.*—Using the same procedure as with the above α-anomer only 9 mg of material was obtained not corresponding to methyl β-D-glucopyranoside. From ethyl acetate – ethanol the crystals had m.p. and mixed m.p. 115–116° C.

(*iii*) *Methyl α-D-mannopyranoside.*—The mannoside (1.75 g) was hydrogenated and some unchanged glycoside (0.47 g) was recovered from the reaction mixture having m.p. and mixed m.p. 192–195° C. The remainder was fractionated on a cellulose column to give material containing methyl α-D-talopyranoside (0.47 g) with $[\alpha]_D$ +83° (*c*, 3.3, H_2O). Calculated for $C_6H_{11}O_5 \cdot OCH_3$: OCH_3, 16.0%. Found: OCH_3, 16.7%. Acid hydrolysis yielded a sugar which corresponded to talose and ran faster than galactose on a paper chromatogram, and which gave D-lyxohexose phenylosazone on treatment with aqueous phenylhydrazine acetate at 80° for 6 hours. The phenylosazone gave an X-ray diffraction pattern identical with authentic D-lyxohexose phenylosazone and different

from D-arabohexose, D-ribohexose, and L-xylohexose phenylosazones. The next fraction contained unchanged methyl α-D-mannopyranoside (63 mg), m.p. and mixed m.p. 192–194° C. A later fraction (46 mg) from the column crystallized and two recrystallizations from ethanol – ethyl acetate yielded methyl α-D-glucopyranoside, m.p. and mixed m.p. 167–168° C. Calculated for $C_7H_{14}O_6$: C, 43.3%; H, 7.3%. Found: C, 43.4%; H, 7.35%.

(*iv*) *Methyl β-D-mannopyranoside.*—Methyl β-D-mannopyranoside (1.16 g) on hydrogenation followed by acid hydrolysis yielded 137 mg of material from a cellulose column that did not correspond to mannose. In another experiment the unchanged glycoside was characterized as its tetraacetate, m.p. and mixed m.p. 161–163° C.

(*v*) *Methyl α-D-galactopyranoside.*—Methyl α-D-galactopyranoside (1.60 g) was hydrogenated and crystals were obtained from an ethanolic ethyl acetate solution of the product. The material (0.36 g) corresponded to methyl α-D-glucopyranoside since it had m.p. and mixed m.p. 163–165° C and $[\alpha]_D$ +161° (*c*, 3.5, H_2O). The mother liquor on cellulose chromatography gave three main fractions. These were a mixture (0.26 g) of polyols and methyl α-D-talopyranoside having OCH_3, 9.3%, and $[\alpha]_D$ +27° (*c*, 1.2, H_2O). The methoxyl content of the mixture corresponded to 58% of glycoside and it was acid hydrolyzed to give free aldose (R_F = talose) which was converted to D-lyxohexose phenylosazone by heating at 80° C for 6 hours with 4 moles of aqueous phenylhydrazine acetate. The identity of the phenylosazone was proved by its X-ray diffraction pattern, which was identical to that of an authentic specimen. The other two fractions which both crystallized from ethyl acetate – ethanol consisted of methyl α-D-glucopyranoside (0.16 g), m.p. and mixed m.p. 165–166° C, and methyl α-D-galactopyranoside (80 mg), m.p. and mixed m.p. 117–118° C.

(*vi*) *Methyl β-D-galactopyranoside.*—Hydrogenation of methyl β-D-galactopyranoside (2.0 g) gave a syrup from which methyl β-D-glucopyranoside (0.34 g), m.p. and mixed m.p. 116–117° C, was isolated. Cellulose chromatography gave as one of the main products a polyol fraction (0.32 g) and another contained glycosides (0.77 g) having R_{Rh} 0.7. The latter was fractionated by crystallization from ethyl acetate – ethanol to give methyl β-D-glucopyranoside (163 mg) as thick prisms with m.p. and mixed m.p. 116–117° C and $[\alpha]_D$ −37° (*c*, 1.0, H_2O) after two further recrystallizations. Calculated for $C_7H_{14}O_6$: C, 43.3%; H, 7.3%. Found: C, 43.2%; H, 7.5%. After the bulky prisms were removed a fluffy solid (62 mg) remained which on two recrystallizations from the same solvent yielded methyl β-D-allopyranoside with m.p. and mixed m.p. 157–158° C and $[\alpha]_D$ −52° (*c*, 1.6, H_2O). Calculated for $C_7H_{14}O_6$: C, 43.3%; H, 7.3%. Found: C, 43.25%; H, 7.4%. The last fraction from the column consisted of unchanged methyl β-D-galactopyranoside (0.35 g) with m.p. and mixed m.p. 179–180° C.

(*vii*) *Methyl α-D-altropyranoside.*—Methyl α-D-altropyranoside (1.80 g) on hydrogenation gave a syrup which yielded crystals (0.19 g) from ethyl acetate – ethanol that corresponded to methyl α-D-mannopyranoside with m.p. and mixed m.p. 191–193° C. Cellulose chromatography afforded three main fractions, the first of which (66 mg) appeared to be a polyol. The next fraction (0.13 g) afforded a sugar with R_{Rh} 1.0 on hydrolysis which was not identified. The last portion of the column eluate gave a mixture (0.61 g) of polyol and methyl α-D-talopyranoside which had OCH_3 9.4% which indicated a glycoside content of 59%. Acid hydrolysis of the mixture afforded an aldose of R_F = talose which, on treatment with 4 moles of aqueous phenylhydrazine acetate at 80° C for 6 hours, gave D-lyxohexose phenylosazone identified by its X-ray diffraction pattern.

(*viii*) *Methyl β-D-altropyranoside.*—Cellulose chromatography of the hydrogenation product of methyl β-D-altropyranoside (1.04 g) afforded three fractions. The first was a

mixture of materials (164 mg) with mobility on a paper chromatogram greater than methyl β-altroside. The following fraction (253 mg) consisted of unchanged glycoside characterized as its tetraacetate, m.p. and mixed m.p. 98–99° C. Calculated for $C_{14}H_{19}O_9 \cdot OCH_3$: OCH_3, 8.35%. Found: OCH_3, 8.6%. The last material from the column was methyl β-D-mannopyranoside (155 mg), characterized as its tetraacetate, m.p. and mixed m.p. 161–163° C. Calculated for $C_{15}H_{22}O_{10}$: C, 49.7%; H, 6.1%. Found: C, 49.8%; H, 6.2%.

(*ix*) *Methyl α-D-talopyranoside.*—Paper chromatography of the product (0.31 g) from hydrogenated methyl talopyranoside (0.34 g) indicated that the material was mainly unchanged taloside with R_{Rh} 1.4. Only a trace of slower-moving material was detected. The product had OCH_3 16.2% indicating that removal of the methoxyl group had not occurred. Acid hydrolysis of the product furnished an aldose, which on treatment with 1 mole of 1-methylphenylhydrazine (31) in refluxing ethanol gave crystals characterized as D-talose 1-methylphenylhydrazone, m.p. and mixed m.p. 150–152° C.

(*x*) *Methyl β-D-allopyranoside.*—Hydrogenation of the glycoside (0.48 g) yielded a syrup (0.36 g) which on cellulose chromatography was found to consist of 0.17 g of materials with $R_{Rh} > 1.0$ on a paper chromatogram and 122 mg of a mixture of methyl β-D-allo- and -gluco-pyranosides. Fractional crystallization from ethyl acetate – ethanol gave 19 mg of the former with m.p. and mixed m.p. 154–156° C and 29 mg of the latter which had m.p. and mixed m.p. 115–116° C.

(*xi*) *Methyl α-L-arabopyranoside.*—The glycoside (2.22 g) was hydrogenated and the resulting mixture chromatographed on cellulose. The first fraction consisted of polyols (0.50 g) and tosylation of the mixture (14) gave a product which was fractionally crystallized to yield ditosyl-*trans*-tetrahydropyrandiol, m.p. and mixed m.p. 157–161° C, and ditosyl-*cis*-tetrahydropyrandiol, m.p. 125–129° C. A second fraction (0.26 g), $[\alpha]_D$ −98° (*c*, 1.0, H_2O), from the column crystallized to give methyl β-D-ribopyranoside from Skelly "F"–ethyl acetate, m.p. and mixed m.p. 83–84° C. The next material eluted (0.13 g) was shown to be methyl α-L-lyxopyranoside, m.p. 109–110° C and $[\alpha]_D$ −57° (*c*, 1.0, H_2O), after two recrystallizations from ethyl acetate – ethanol, which gave an X-ray diffraction pattern identical with that of the D-isomer. Calculated for $C_6H_{12}O_5$: C, 43.9%; H, 7.4%. Found: C, 44.1%; H, 7.4%. The last fraction from the column weighed 0.16 g and from this 16 mg of methyl β-D-xylopyranoside, m.p. and mixed m.p. 159–161° C, was obtained after two recrystallizations from ethanol – ethyl acetate.

(*xii*) *Methyl β-L-arabopyranoside.*—The hydrogenolysis product from methyl β-L-arabopyranoside (2.22 g) was very complex and acid hydrolysis showed that it contained all four chemically different pentosides. On cellulose chromatography a polyol fraction (0.66 g) was obtained corresponding to the two possible tetrahydropyrandiols. Very little further fractionation was obtained although methyl β-L-arabopyranoside (0.22 g), m.p. and mixed m.p. 167–168° C, was crystallized from ethanol and later 109 mg of a syrupy glycoside, with $[\alpha]_D$ +128° (*c*, 2.2, H_2O) which gave xylose on acid hydrolysis, was obtained. Although the latter product did not crystallize it appears that it was methyl α-D-xylopyranoside.

(*xiii*) *Methyl α-D-lyxopyranoside.*—The glycoside (2.22 g) was hydrogenated and on cellulose chromatography three fractions were obtained. A considerable proportion of tetrahydropyrandiols (0.97 g) was shown to be present. In this fraction it appeared that some methyl riboside was present since ribose was obtained on a paper chromatogram by hydrolyzing the syrup with acid. The next fraction (0.29 g) contained methyl α-D-lyxopyranoside, m.p. and mixed m.p. 107–109° C and the last portion (0.33 g) from

the column was shown to contain xyloside, arabinoside, and lyxoside by acid hydrolysis followed by paper chromatography.

(*xiv*) *Methyl β-D-ribopyranoside.*—When methyl β-D-ribopyranoside (2.20 g) was hydrogenolyzed and the product chromatographed on cellulose a considerable proportion of polyol (1.11 g) was found. The polyol had OCH_3 6.3% and on acid hydrolysis some ribose was formed, which indicates that 31% of the mixture consisted of methyl riboside. The remainder of the column eluate (0.16 g) consisted of a mixture of xyloside, riboside, and arabinoside as shown by paper chromatography of the acid hydrolyzate.

(*xv*) *Methyl β-D-xylopyranoside.*—The xyloside (1.11 g) was hydrogenolyzed and chromatographed on cellulose in the usual way. The initial fraction appeared to be tetrahydropyrandiols (0.32 g) and later portions were obtained which consisted of methyl-β-D-ribopyranoside (m.p. and mixed m.p. 80–81° C; 0.19 g) from ethyl acetate – Skelly F, and a xyloside (0.13 g) which could not be crystallized but which gave xylose on acid hydrolysis.

C. Hydrogenation of Glycosides at Temperatures > 180° C

1,5-Anhydro-4-deoxy-D-hexitols from Hydrogenolysis of Methyl α-D-glucopyranoside at 240° C

The hydrogenolysis of methyl α-D-glucopyranoside at 240° C was described by von Rudloff, Bauer, and Stuetz, who acetylated the product and fractionally distilled the acetates (1). Their still residue contained acetates of the 1,5-anhydro-4-deoxy-D-hexitols and this (7.32 g) was deacetylated with 0.1 mole of sodium methoxide in methanol (150 ml) for 3 hours. The polyols (4.92 g) obtained on evaporation consisted of two main fractions of R_{Rh} 1.1 and 1.3. Cellulose chromatography gave a syrup (1.81 g) consisting of mainly the former and this was heated at 80° C for 1 hour with *p*-nitrobenzoyl chloride (13 g) in pyridine (30 cc). The solution was poured into excess aqueous sodium bicarbonate and after 30 minutes stirring the precipitate was collected, washed with water, and dried. Three recrystallizations from ethyl acetate – Skelly F brought the tris-*p*-nitrobenzoate (4.84 g) to a constant m.p. of 113–115° C; it had $[\alpha]_D$ −83° (*c*, 1.1, $CHCl_3$). Calculated for $C_{27}H_{21}O_{13}N_3$: C, 54.6%; H, 3.6%. Found: C, 54.7%; H, 3.3%. Debenzoylation of the product (4.8 g) with 0.1 mole of sodium for 1 hour in boiling methanol (200 cc), followed by evaporation and deionization yielded crystals which were recrystallized twice from ethyl acetate – methanol. Yield, 0.37 g. The 1,5-anhydro-4-deoxy-D-hexitol corresponded to the fraction having R_{Rh} 1.1 and had m.p. 80–81° C, $[\alpha]_D$ −50° (*c*, 0.8, H_2O) and consumed 1.0 mole of aqueous sodium periodate overnight. Calculated for $C_6H_{12}O_4$: C, 48.6%; H, 8.2%. Found: C, 48.7%; H, 8.2%.

The polyol having R_{Rh} 1.3 was eluted later from the cellulose column and it (1.08 g) gave a tris-*p*-nitrobenzoate having m.p. 115–119° C and $[\alpha]_D$ +59° (*c*, 1.1, $CHCl_3$). Calculated for $C_{27}H_{21}O_{13}N_3$: C, 54.6%; H, 3.6%. Found: C, 54.5%; H, 3.9%. Catalytic debenzoylation furnished a syrupy 1,5-anhydro-4-deoxy-D-hexitol with R_{Rh} 1.3 and $[\alpha]_D$ +19° (*c*, 1.1, H_2O), which consumed 1.0 mole of aqueous sodium periodate in 18 hours.

Structure of the 1,5-Anhydro-4-deoxy-D-hexitols

The anhydro deoxyhexitol of R_{Rh} 1.1 (150 mg) was oxidized with 0.1 *M* periodic acid (1.5 moles) for 18 hours, the solution neutralized ($BaCO_3$) and filtered into an aqueous solution (10 ml) of sodium borohydride (100 mg). After 30 minutes the solution was acidified with acetic acid, treated with Amberlite IR-120, filtered, and evaporated to a

crust which was repeatedly dissolved in methanol which was then evaporated. The syrupy polyol (132 mg) had $[\alpha]_D$ −20° (*c*, 2.0, H_2O) and 75 mg of it was *p*-nitrobenzoylated in a manner similar to that described above to yield after three recrystallizations from ethyl acetate – pentane a tris-*p*-nitrobenzoate with m.p. 103–104° C and $[\alpha]_D$ −26° (*c*, 2.3, $CHCl_3$). Calculated for $C_{27}H_{23}O_{13}N_3$: C, 54.3%; H, 3.9%. Found: C, 54.3%; H, 3.9%.

Similar treatment of the anhydro deoxyhexitol of R_{Rh} 1.3 (60 mg) with periodic acid and sodium borohydride gave the open chain polyol with $[\alpha]_D$ −16° (*c*, 1.0, H_2O) from which gave an identical tris-*p*-nitrobenzoate, m.p. 98–102° and $[\alpha]_D$ −22° (*c*, 1.4, $CHCl_3$) was prepared. It had an X-ray crystal diagram similar to that of the *p*-nitrobenzoate obtained from the triol of R_{Rh} 1.1. Calculated for $C_{27}H_{23}O_{13}N_3$: C, 54.3%; H, 3.9%. Found: C, 54.5%; H, 3.9%.

Twenty-five milligrams of each 1,5-anhydro-4-deoxy-hexitol was dissolved in water (0.3 ml) and acetic acid (10 ml). A 1% solution of lead tetraacetate in acetic acid (10 ml) was added, the consumption of oxidant followed and the following values obtained:

Time (minutes)	10	35	70	135	205
Material of R_{Rh} 1.1, uptake in moles/mole	0.26	0.62	0.79	0.89	0.88
Material of R_{Rh} 1.3, uptake in moles/mole	0.07	0.16	0.25	0.30	0.34

Hydrogenolysis of Methyl β-D-galactopyranoside at 200° C

Methyl β-D-galactopyranoside (2.00 g) was hydrogenolyzed at 200° C using the proportions described previously. Paper chromatographic examination of the product indicated that all the starting material had been destroyed. In order to decompose any deoxy glycosides that may have been formed in the reaction, the product was heated for 18 hours at 100° C in *N* H_2SO_4. The solution was then neutralized ($BaCO_3$), filtered, and evaporated to a syrup (1.56 g), 0.69 g of which was fractionated on a cellulose column using benzene–ethanol–water (500:50:1 v/v) as solvent. From the column, dihydro-D-altral (80 mg), m.p. 105–106° C, dihydro-D-glucal (213 mg), m.p. 75–76° C, and dihydro-D-galactal (82 mg), m.p. 130–132° C, were obtained. All the above melting points were undepressed on admixture of the crystals with authentic specimens.

ACKNOWLEDGMENTS

The author wishes to thank Dr. A. S. Perlin for helpful discussions during the course of this work, and to Drs. E. von Rudloff, H. F. Bauer, and D. E. Stuetz for the gift of 1,5-anhydro-4-deoxy-hexitol acetates. Thanks are also due to Mr. J. A. Baignée and Mr. M. Mazurek for microanalytical determinations and Miss S. Lubin for technical assistance.

REFERENCES

1. E. von Rudloff, H. F. Bauer, and D. E. Stuetz. Can. J. Chem. **35**, 315 (1957).
2. W. H. Zartman and H. Adkins. J. Am. Chem. Soc. **55**, 4559 (1933).
3. A. S. Perlin, E. von Rudloff, and A. P. Tulloch. Can. J. Chem. **36**, 921 (1958).
4. E. von Rudloff and A. P. Tulloch. Can. J. Chem. **35**, 1504 (1957).
5. P. A. J. Gorin and A. S. Perlin. Can. J. Chem. **36**, 661 (1958).
6. T. Francis and A. S. Perlin. Can. J. Chem. **37**, 1229 (1959).
7. P. A. J. Gorin. J. Org. Chem. **24**, 49 (1959).
8. L. Hough, J. K. N. Jones, and W. H. Wadman. J. Chem. Soc. 2511 (1949).
9. S. Winstein and N. J. Holness. J. Am. Chem. Soc. **77**, 5562 (1955).
10. F. H. Westheimer and N. Nicolaides. J. Am. Chem. Soc. **71**, 25 (1949).
11. R. E. Reeves. *In* Advances in carbohydrate chemistry. Vol. 6. *Edited by* W. W. Pigman and M. L. Wolfrom. Academic Press Inc., New York. 1951. p. 130.
12. R. Criegee, L. Kraft, and B. Rank. Ann. **507**, 159 (1933).
13. A. S. Perlin. J. Am. Chem. Soc. **76**, 5505 (1954).

14. H. F. BAUER and D. E. STUETZ. J. Am. Chem. Soc. **78**, 4097 (1956).
15. C. S. HUDSON. Rapports sur les hydrates de carbone (glucides). Union Internationale de Chimie, Paris. 1931. pp. 59–78.
16. H. S. ISBELL. J. Research Natl. Bur. Standards, **8**, 1 (1932).
17. E. L. JACKSON and C. S. HUDSON. J. Am. Chem. Soc. **61**, 959 (1939).
18. R. C. HOCKETT and M. CONLEY. J. Am. Chem. Soc. **66**, 464 (1944).
19. D. A. ROSENFELD, N. K. RICHTMYER, and C. S. HUDSON. J. Am. Chem. Soc. **70**, 2201 (1948).
20. C. N. RIIBER, J. MINSAAS, and R. T. LYDE. J. Chem. Soc. 2173 (1929).
21. W. KOENIGS and E. KNORR. Chem. Ber. **34**, 961 (1901).
22. R. K. NESS, H. G. FLETCHER, and C. S. HUDSON. J. Am. Chem. Soc. **72**, 4547 (1950).
23. H. G. FLETCHER and C. S. HUDSON. J. Am. Chem. Soc. **70**, 310 (1948).
24. N. K. RICHTMYER and C. S. HUDSON. J. Am. Chem. Soc. **63**, 1727 (1941).
25. E. SORKIN and R. REICHSTEIN. Helv. Chim. Acta, **28**, 1 (1945).
26. P. A. J. GORIN. Unpublished results.
27. H. ADKINS. Reactions of hydrogen. 4th ed. The University of Wisconsin Press, Madison, Wisconsin. 1946. p. 71.
28. L. HOUGH, J. K. N. JONES, and W. H. WADMAN. J. Chem. Soc. 1702 (1950).
29. S. M. PARTRIDGE. Nature, **158**, 270 (1946).
30. B. LINDBERG and O. THEANDER. Acta Chem. Scand. **8**, 1870 (1954).
31. P. A. LEVENE and R. S. TIPSON. J. Biol. Chem. **93**, 631 (1931).