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OXIDATION OF SOME DERIVATIVES OF D-GALACTOSE WITH METHYL SULPHOXIDE–ACID ANHYDRIDE MIXTURES: A ROUTE TO DERIVATIVES OF D-GLUCOSE AND D-TALOSE*

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ABSTRACT

Methyl sulphoxide–acid anhydride oxidation of some suitably blocked derivatives of D-galactopyranose has led to the corresponding keto sugars in good yield. Metal hydride reduction of the ketones was shown to be stereospecific and gave some new derivatives of D-gulose and D-talose. An improved procedure for the preparation and isolation of 1,6-anhydro-β-D-gulopyranose is also described.

INTRODUCTION

A variety of reagents are now available for the oxidation of "isolated" secondary hydroxyl groups in carbohydrates to give keto sugars[1]. Methyl sulphoxide–acetic anhydride[2,3] and methyl sulphoxide–phosphorus pentaoxide[4,5] are particularly useful for this purpose. Their main advantage over the similar Pfitzner–Moffatt oxidant[6] is the ready isolation of the keto sugar. A wide variety of protecting groups have been found to be stable to both reagents[1,5]. Reduction of the keto sugars produced in the reaction has led to syntheses of a number of rare sugar derivatives[1].

The present report describes the use of these two reagents in converting some derivatives of D-galactopyranose, having "isolated" secondary hydroxyl groups at C-2 or C-3, into a number of new derivatives of the rare hexoses D-gulose and D-talose. Alternative routes[7,8] to derivatives of these two sugars, using the same reagents, are available. The reactions described compare favourably with these.

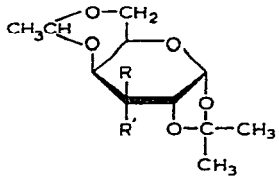
RESULTS AND DISCUSSION

Acetonation of 4,6-*O*-ethylidene-D-galactose[9], by a slight modification of the published method[10], gave the corresponding 1,2-*O*-isopropylidene derivative **1** in improved yield, and this was characterised as the benzoate and the known toluene-*p*-sulphonate. Oxidation of **1** with methyl sulphoxide–acetic anhydride afforded 44% of 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-α-D-*xylo*-3-hexulopyranose (**2**) which gave

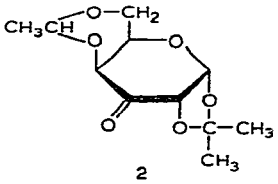
*For a preliminary report of part of this work, see G. J. F. CHITTENDEN, *Chem. Commun.*, (1968) 779.

a crystalline *p*-nitrophenylhydrazone. Treatment of the acetal **1** with methyl sulphoxide–phosphorus pentaoxide[5] gave the ketone **2** in improved yield (63%).

Reduction of the ketone **2** with sodium borohydride in aqueous ethanol gave 86% of 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-α-D-gulopyranose (**3**) which was characterised as the 3-toluene-*p*-sulphonate, 3-benzoate, and 3-methyl ether. The reduction appeared to be essentially stereospecific, since none of the acetal **1** was isolated when the crude reduction product was subjected to chromatography, although a faint trace was detected by t.l.c. Reduction of the crude oxidation product, without isolation of the intermediate ketone **2**, followed by chromatography on silica gel, gave the D-gulose compound **3** in 58–65% yield.



1 R = OH; R′ = H
3 R = H; R′ = OH
4 R = OCH_2SCH_3; R′ = H
5 R = OMe; R′ = H



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The main by-product of the oxidation with methyl sulphoxide–acetic anhydride was shown to be the 3-methylthiomethyl ether **4**, desulphurization of which with Raney nickel gave a syrupy product that was chromatographically indistinguishable (t.l.c.) from 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-galactopyranose (**5**). Similar thio-ether derivatives have been isolated as by-products in methyl sulphoxide–acetic anhydride oxidations of alkaloids[11], steroids[3], and other carbohydrates[11,12]. Their mode of formation has been discussed[3], and desulphurization with Raney nickel is known[12] to yield the corresponding methyl ether.

The *gulo* configuration of compound **3** was proved by hydrolysis with aqueous acetic acid, which gave D-gulose characterised as the known phenylhydrazone. Hydrolysis of compound **3** with aqueous mineral acid gave a mixture of D-gulose and its 1,6-anhydride. The latter compound (31%) was isolated after chromatography on Dowex-1 (HO^-) resin, and a new and useful route to this compound is thereby provided. Acetolysis of compound **3**, with acetic anhydride–sulphuric acid in the usual manner, gave the known α-D-gulopyranose pentaacetate.

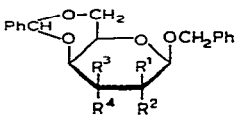
As expected, attempted nucleophilic displacement of the sulphonate groups in 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-3-*O*-toluene-*p*-sulphonyl-α-D-galactopyranose and the D-gulose analogue by using sodium benzoate or sodium azide in *N*,*N*-dimethylformamide at 140° (for 10 days) was unsuccessful. In each compound, there is an axial substituent at C-4 vicinal to the sulphonate group, an arrangement which is known to hinder S_N2 displacement[13].

Treatment of benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside 3-benzoate[14] (**6**) with methyl sulphoxide–acetic anhydride did not yield the expected ketone but gave 81% of the 2-methylthiomethyl ether **7**, a reaction observed hitherto mainly with primary hydroxyl groups[15]. Attempted desulphurization of **7** with Raney nickel was unsuccessful, and loss of the benzylidene group occurred (*cf.* ref. 16).

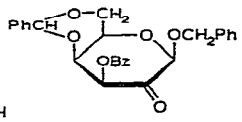
Treatment of the 3-benzoate **6** with 3–4 moles of methyl sulphoxide and 1 mole of phosphorus pentoxide per mole in *N,N*-dimethylformamide[5] for 15 h at 60° gave 73.5% of the D-*lyxo*-2-hexulopyranoside **8**, which had an i.r. band at 1760 cm^{-1} indicative of preponderent existence in the keto form and not as the *gem*-diol. It has been suggested that formation of *gem*-diols from pyran-2-osuloses is particularly favourable due to the electron-withdrawing effect at C-1. The ketone **8** was characterised as the *p*-nitrophenylhydrazone.

Reduction of compound **8** with lithium aluminium hydride in tetrahydrofuran gave 73% of benzyl 4,6-*O*-benzylidene-β-D-talopyranoside (**9**), which was characterised as the diacetate. Removal of the benzylidene group from **9** by treatment with 60% acetic acid gave syrupy benzyl β-D-talopyranoside which was characterised as the tetra(*p*-nitrobenzoate).

The *talo* configuration of **9** was shown by acid hydrolysis which gave D-talose and a trace of 1,6-anhydro-β-D-talopyranoside (identified chromatographically). Exhaustive hydrogenation of **9** over a palladium catalyst gave crystalline D-talose.



6 $R^1=R^4=H; R^2=OH; R^3=OBz$
7 $R^1=R^4=H; R^2=OCH_2SCH_3; R^3=OBz$
9 $R^1=R^3=OH; R^2=R^4=H$
10 $R^1=R^4=H; R^2=OBz; R^3=OH$



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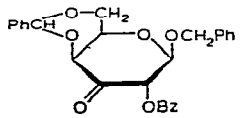

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Treatment of benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside 2-benzoate (**10**) with methyl sulphoxide–acetic anhydride gave a complex mixture of products (t.l.c.) but, with methyl sulphoxide–phosphorus pentaoxide, the D-*xylo*-3-hexulopyranoside **11** was obtained as a syrup and characterised as the *p*-nitrophenylhydrazone. Compound **11** showed a characteristic i.r. absorption for a ketone group (1755 cm^{-1}).

Reduction of compound **11** with sodium borohydride in methanol and lithium aluminium hydride in tetrahydrofuran gave high yields of benzyl 4,6-*O*-benzylidene-β-D-galactoside. Paper chromatography on the acid hydrolysate of the crude reduction product showed only a trace of gulose in addition to galactose.

The stereospecificity of the reduction of the foregoing keto sugars **2**, **8**, and **11** with metal hydrides may be explained on the basis of the reagent's approach from the less-hindered side of the carbonyl function[1,8,18–20].

It was interesting to note the extremely high specific rotations of the *p*-nitrophenylhydrazones derived from the ketones **2**, **8**, and **11**. High rotational values of other arylhydrazones derivatives of osuloses and osulosides have been previously observed[21–23].

EXPERIMENTAL

Methyl sulphoxide and *N,N*-dimethylformamide were redistilled from calcium hydride. Descending paper chromatography was carried out on Whatman No. 1 paper with propyl alcohol–ethyl acetate–water[24] (7:1:2). Aniline hydrogen phthalate[25] and silver nitrate[26] were used as location reagents. T.l.c. was performed on Silica Gel G

(Merck) with detection by iodine vapour or by 3% ethanolic sulphuric acid at 140°. I.r. spectra were determined for KBr discs.

4,6-O-Ethylidene-1,2-O-isopropylidene-α-D-galactopyranose (**1**). — Anhydrous, finely ground 4,6-*O*-ethylidene-D-galactose[9] (20 g) suspended in "Analar" acetone (600 ml) was stirred vigorously with granular zinc chloride (70 g) and then processed[10] to yield, after chromatography[9] of the product on silica gel, 1,2:3,4 di-*O*-isopropylidene-α-D-galactopyranose (3.6 g) and **1** (8.2 g, 34.6%), m.p. 71–73°, $[\alpha]_D^{21}$ +57° (*c* 1.4, chloroform); lit.[10], m.p. 72–74°, $[\alpha]_D$ +58° (ethanol).

The following derivatives were prepared by conventional procedures: 3-toluene-*p*-sulphonate, m.p. 115–117°, $[\alpha]_D$ +117° (*c* 0.68, chloroform), lit.[9], m.p. 116–118°, $[\alpha]_D$ +119°; 3-benzoate, m.p. 175.5–176°, $[\alpha]_D^{21}$ +120° (*c* 1.0, chloroform) (Found: C, 62.01; H, 6.28. $C_{18}H_{22}O_7$ calc.: C, 61.72; H, 6.3%).

Oxidation of 4,6-O-ethylidene-1,2-O-isopropylidene-α-D-galactopyranose (**1**). — (*a*) *With methyl sulphoxide–acetic anhydride.* A solution of the acetal **1** (4 g) in methyl sulphoxide (45 ml) and acetic anhydride (30 ml) was stored for 36 h at 25°. Removal of excess reagents and by-products at 40–45°/0.1 mmHg and crystallization of the residue from carbon tetrachloride–cyclohexane (5:1, 35 ml) gave material (1.89 g) which was recrystallized from hexane to give 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-α-D-*xylo*-3-hexulopyranose (**2**) (1.74 g, 44%), m.p. 62–63°, $[\alpha]_D^{21}$ −47° (*c* 0.6, chloroform), ν_{max} 1740 cm^{-1} (C=O) (Found: C, 53.6; H, 6.7. $C_{11}H_{16}O_6$ calc.: C, 54.1; H, 6.6%).

(*b*) *With methyl sulphoxide–phosphorous pentoxide.* A solution of the acetal **1** (1.22 g) in methyl sulphoxide (1.6 g, 4 mol.) and *N,N*-dimethylformamide (5 ml) was stirred with phosphorous pentoxide (0.8 g, 1 mol.) for 2 h at 65°. The mixture was then diluted with dichloromethane (100 ml) and shaken with water (50 ml). The organic layer was washed with ice–water until neutral. Evaporation *in vacuo* of the dried (Na_2SO_4) extract gave a clear syrup, which was stored overnight at 37° over phosphorus pentoxide and then crystallized from hexane to give **2** (0.76 g, 63%), m.p. 60–62°, $[\alpha]_D^{20}$ − 45.4° (*c* 1.0, chloroform).

4,6-O-Ethylidene-1,2-O-isopropylidene-3-O-methylthiomethyl-α-D-galactopyranose (**4**). — The mother liquors from the reaction of the acetal **1** in (*a*) were concentrated *in vacuo*. Elution of the resulting oil from silica gel with benzene–ether (10:1) gave the 3-methylthiomethyl ether **4** (0.94 g, 19%), b.p. 148–152°/0.5 mmHg, $[\alpha]_D^{21}$ +15.5° (*c* 0.84, chloroform) (Found: C, 50.75; H, 6.8; S, 10.5 $C_{13}H_{22}O_6S$ calc.: 50.9; H, 7.2; S, 10.45%).

A small amount of **4** was desulphurized by refluxing a solution in ethanol (20 ml) containing Raney nickel (1 g) for 2 h. T.l.c. (benzene) indicated a single product having the same mobility as the known[27] 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-galactopyranose (**5**).

4,6-O-Ethylidene-1,2-O-isopropylidene-α-D-xylo-3-hexulopyranose p-nitrophenylhydrazone. — A solution of the ketone **2** (0.61 g) and *p*-nitrophenylhydrazine (0.36 g) in propan-2-ol (15 ml) was refluxed for 1 h. Cooling gave a yellow, crystalline product which was recrystallized from propan-2-ol to give the *p*-nitrophenylhydrazone (0.58 g,

61%), m.p. 118–189°, $[\alpha]_D^{21}$ +466° (*c* 0.44, chloroform) (Found: C, 54.3; H, 5.9; N, 11.2. $C_{17}H_{21}N_3O_7$ calc.: C, 53.8; H, 5.7; N, 11.1%).

4,6-O-Ethylidene-1,2-O-isopropylidene-α-D-gulopyranose (**3**). — A solution of the ketone **2** (3 g) in 70% aqueous ethanol (120 ml) was cooled to 0° and treated with sodium borohydride (4 g) for 1 h. The mixture was concentrated *in vacuo* to approximately half volume, diluted with water (40 ml), and extracted with ethyl acetate (7 × 100 ml). The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give a syrup which contained only a trace of **1** (t.l.c., ether) and which crystallized on treatment with warm hexane. Recrystallization of the product (2.8 g) from hexane gave **3** (2.62 g, 86%), m.p. 133–134°, $[\alpha]_D^{21}$ −19° (*c* 0.64, chloroform) (Found: C, 53.8; H, 7.4. $C_{11}H_{18}O_6$ calc.: C, 53.65; H, 7.4%).

Reduction of the crude product (1 g) from treatment of the acetal **1** with methyl sulphoxide–acetic anhydride as described above, followed by elution of the product from silica gel with benzene–ether (10:1), gave the methylthiomethyl compound **4** (0.23 g, 18%), $[\alpha]_D^{21}$ +16° (*c* 0.9, chloroform). Subsequent elution with ether gave **3** (0.58 g, 58%), m.p. 130–133° (from hexane), $[\alpha]_D^{20}$ −18.4° (*c* 0.95, chloroform).

Similar fractionation of the product from the reaction of **1** with methyl sulphoxide–phosphorus pentaoxide gave **3** (0.85 g, 65%), m.p. 131–133°, $[\alpha]_D^{21}$ −18° (*c* 1.4, chloroform).

By conventional procedures, **3** was converted into the 3-toluene-*p*-sulphonate (78%), m.p. 138–139° (decomp.) (from propan-2-ol or isopropyl ether), $[\alpha]_D^{21}$ +34.6° (*c* 0.75, *N,N*-dimethylformamide) (Found: C, 54.6; H, 6.2; S, 7.9. $C_{18}H_{24}O_8S$ calc.: C, 54.0; H, 6.2; S, 8.1%); and the 3-benzoate (60%), m.p. 117–118° (from isopropyl ether), $[\alpha]_D^{22}$ +61° (*c* 0.65, dichloromethane) (Found: C, 55.1; H, 7.7. $C_{12}H_{20}O_6$ calc.: C, 55.4; H, 7.7%).

Hydrolysis of compound **3**. — (*a*) *With 0.5M sulphuric acid.* Compound **3** (20 mg) was heated with 0.5M sulphuric acid (2.5 ml) for 1 h at 100°. The hydrolysate was diluted with water (2.5 ml), neutralized with barium carbonate, and centrifuged, and the clear supernatant was evaporated to dryness *in vacuo*. Paper chromatography of the residue revealed D-gulose (R_{Gal} 1.36) and 1,6-anhydro-β-D-gulopyranose (R_{Gal} 2.2) as shown by comparison with the products from the hydrolysis of methyl α-D-gulopyranoside.

(*b*) *With 0.25M sulphuric acid.* Compound **3** (1 g) was suspended in 0.25M sulphuric acid (11 ml) and heated for 11-12 h at 100° (constant rotation). The solution was neutralized with barium carbonate and concentrated *in vacuo* to *ca.* 10 ml. The solution was then allowed to percolate through a column (15 × 1.5 cm.) of Dowex-1 (HO^-) resin. The resin was then washed with 5–6 bed volumes of CO_2-free water, and the combined eluate and washings were evaporated. One recrystallization of the residue from ethanol gave 1,6-anhydro-β-D-gulopyranose (0.21 g, 31%), m.p. 153–156°, $[\alpha]_D^{20}$ +51° (*c* 0.77, water); lit.[28] m.p. 154–155°, $[\alpha]_D^{20}$ +50.4°.

(*c*) *With aqueous acetic acid.* Compound **3** was heated for 3 h at 100° with 80% aqueous acetic acid (15 ml). Evaporation of the hydrolysate gave a syrup which was re-evaporated several times with portions of benzene (25 ml) to give a pale-yellow

syrup (0.31 g). The product was shown by paper chromatography to be essentially homogeneous D-gulose (R_{Gal} 1.37).

A portion of the product (100 mg) in 25% aqueous acetic acid (0.4 ml) was treated with redistilled phenylhydrazine (0.1 ml). After 1 h at room temperature, the crystalline product was collected and washed, first with water and then ether. Recrystallization from hot ethanol gave D-gulose phenylhydrazone, m.p. 141–143°, lit.[29], m.p. 143°.

Acetolysis of **3**. — A solution of **3** (0.5 g) in acetic anhydride (13 ml) was cooled to −5°, treated with conc. sulphuric acid (0.12 ml), and then kept for 5 days at 0° (constant rotation). The mixture was poured into ice–water (100 ml) and extracted with chloroform (3 × 50 ml), and the combined extracts were shaken successively with water, saturated, aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated. A solution of the resulting yellow syrup (0.72 g) was eluted from silica gel (100 g) with benzene to give an unidentified yellow syrup (0.17 g) having a peppermint odour. Elution with benzene–ether (5:3) and recrystallization of the product from ether–pentane gave α-D-gulopyranose pentaacetate (0.39 g, 49.5%), m.p. 104–106°, $[\alpha]_D^{21}$ +85.8° (*c* 0.7, chloroform); lit. [30], m.p. 106°, $[\alpha]_D$ +86.2°.

Benzyl 4,6-O-benzylidene-2-O-methylthiomethyl-β-D-galactopyranoside 3-benzoate (**7**). — Compound[14] **6** (4.62 g) dissolved in methyl sulphoxide (30 ml) and acetic anhydride (20 ml) was allowed to stand for 4 days (constant rotation) at 25°. Removal of excess reagents and by-products at 40–45°/1 mmHg and recrystallization of the residue from propan-2-ol–acetone gave **7** (4.23 g, 81%), m.p. 169.5–170°, $[\alpha]_D^{23}$ +83° (*c* 1.45, dichloromethane) (Found: C, 66.7; H, 5.7; S, 5.9. $C_{29}H_{30}O_7S$ calc.: C, 66.7; H, 5.8; S, 6.1%).

T.l.c. (benzene–ether, 4:1) on the concentrated mother liquor revealed some unchanged starting compound **6** and a trace of the ketone **8**.

Treatment of **6** *with methyl sulphoxide–phosphorus pentaoxide*[5]. — The benzoate **6** (1.16 g) dissolved in *N,N*-dimethylformamide (5 ml) and methyl sulphoxide (0.8 ml) was stirred with phosphorus pentoxide (0.4 g) for 15 h at 60°. The mixture was then poured into ice–water (100 ml) containing sodium hydrogen carbonate (1 g), and the solid product was collected, washed thoroughly with water, and dried *in vacuo*. The crude product, which contained no starting compound **6** (t.l.c.), was recrystallized from propan-2-ol–dichloromethane or propan-2-ol–acetone to give benzyl 4,6-*O*-benzylidene-α-D-*lyxo*-2-hexulopyranoside 3-benzoate (**8**) (0.85 g, 73.5%), m.p. 160–162° (decomp.), $[\alpha]_D^{21}$ +67° (*c* 0.9, dichloromethane), ν_{max} 1765 (C=O) and 1725 cm^{-1} (COPh) (Found: C, 70.8; H, 4.8. $C_{27}H_{24}O_7$ calc.: C, 70.4; H, 5.2%).

Treatment of **6** as above, but with heating for only 2 h at 65–70°, gave the ketone **8** (61.5%).

Compound **8** (0.5 g) dissolved in propan-2-ol (15 ml) and dichloromethane (5 ml) was treated with *p*-nitrophenylhydrazine (0.165 g) for 1 h under reflux. Dichloromethane was then distilled off, and the product which separated from the residual, cooled solution was recrystallized from propan-2-ol–dichloromethane to give benzyl 4,6-*O*-benzylidene-β-D-*lyxo*-2-hexulopyranoside 3-benzoate *p*-nitrophenylhydrazone

(0.56 g, 67%), m.p. 174–175°, $[\alpha]_D^{20}$ +273° (*c* 0.6, dichloromethane) (Found: C, 66.0; H, 5.0; N, 6.75. $C_{33}H_{29}N_3O_8$ calc: C, 66.5; H, 4.9; N, 7.1%).

Benzyl 4,6-O-benzylidene-β-D-talopyranoside (**9**). – A solution of **8** (2.2 g) in dry tetrahydrofuran (50 ml) was added dropwise, with stirring, to a mixture of lithium aluminium hydride (2.5 g) and tetrahydrofuran (50 ml). On completion of the addition the mixture was heated for 4 h under reflux. Cautious addition of water (10 ml) gave a gelatinous precipitate which was separated by filtration and washed well with hot dichloromethane (200 ml). The combined filtrate and washing were concentrated *in vacuo*, and the residue was recrystallized from propan-2-ol–methanol to give **9** (1.26 g, 73%), m.p. 171°, $[\alpha]_D^{20}$ −70° (*c* 1.1, dichloromethane) (Found: C, 66.6; H, 6.3. $C_{20}H_{22}O_6$ calc: C, 67.0; H, 6.2%).

With acetic anhydride–pyridine in the usual manner, **9** gave the diacetate, m.p. 137° (from propan-2-ol), $[\alpha]_D^{23}$ +19° (*c* 0.84, dichloromethane) (Found: C, 64.7; H, 5.9, $C_{24}H_{26}O_8$ calc.: C, 65.1; H, 5.9%).

Hydrolysis of **9**. — (*a*) *With 60% acetic acid.* Compound **9** (0.5 g) suspended in 60% aqueous acetic acid (50 ml) was heated for 3 h at 100°. Concentration *in vacuo* of the clear solution, followed by re-evaporation with several portions of benzene (50 ml), gave syrupy benzyl β-D-talopyranoside (0.37 g), $[\alpha]_D^{22}$ −61° (*c* 1.4, ethanol).

The product was dissolved in pyridine (10 ml), treated with *p*-nitrobenzoyl chloride (2 g), and kept for 4 days at room temperature. Work up in the usual way gave the tetra(*p*-nitrobenzoate), m.p. 206–207° (from propan-2-ol–acetone), $[\alpha]_D^{20}$ −68° (*c* 1.48, dichloromethane) (Found: C, 58.4; H, 3.5; N, 6.7. $C_{41}H_{30}N_4O_{18}$ calc.: C, 57.9; H, 3.4; N, 6.6%).

(*b*) *With* 0.5M *sulphuric acid.* Compound **9** (50 mg) was heated for 1 h at 100° with 0.5M sulphuric acid (5 ml). The solution was neutralized with barium carbonate and centrifuged, and the clear supernatant was concentrated *in vacuo*. Paper chromatography of the residue revealed D-talose (R_{Gal} 1.7) and 1,6-anhydro-β-D-talopyranose (R_{Gal} 2.47). Hydrolysis of the crude reduction product from compound **8**, in the same manner, showed the same components and, in addition, a trace of galactose.

Hydrogenolysis of **9**. — Compound **9** (1 g) dissolved in 70% aqueous ethanol (150 ml) was hydrogenated exhaustively (41 h) in the presence of palladium (from 1 g of the oxide). Filtration and concentration *in vacuo* of the mixture gave a syrupy residue (0.49 g) which crystallized on nucleation with D-talose. Recrystallation was achieved by dissolution in water (2 ml), followed by evaporation to a syrup and adding an equal volume of methanol, to yield α-D-talose (0.29 g, 58%), m.p. 130–133°, $[\alpha]_D^{21}$ +64→+23° (*c* 1, water); lit.[31] m.p. 133–134°, $[\alpha]_D^{20}$ +68→ +21°.

Benzyl 4,6-O-benzylidene-β-D-xylo-3-hexulopyranoside 2-benzoate (**11**). — The benzoate[14] **10** (1.2 g) dissolved in *N,N*-dimethylformamide (5 ml) and methyl sulphoxide (0.9 ml) was stirred with phosphorus pentoxide (0.45 g) for 14 h at 60–65°. The mixture was poured into ice–water (150 ml) containing sodium hydrogen carbonate (1.3 g) and shaken with dichloromethane (150 ml). The organic layer was washed several times with water, dried (Na_2SO_4), and evaporated to give a gum which was dissolved in benzene (200 ml) and stirred with charcoal for 24 h at 25°. The

filtered mixture was evaporated to give a syrup which contained (t.l.c.; benzene–ether, 4:1) two compounds, one of which corresponded to the 2-benzoate **10**. Elution of the mixture from silica with benzene and benzene–ether (4:1) gave the D-*xylo*-3-hexulopyranoside **11** (0.75 g, 62.5%) as a colourless gum, $[\alpha]_D^{22}$ −30° (*c* 0.58, tetrahydrofuran), ν_{max} 1755 cm^{-1} (C=O).

Further elution with benzene–ether (4:1) gave, on vaporation, unreacted **10** (0.22 g, 18%), m.p. 187–188°, $[\alpha]_D^{22}$ +22.5° (*c* 2, chloroform); lit.[14] m.p. 188–189° $[\alpha]_D$ +24°.

Compound **11** (0.4 g) dissolved in propan-2-ol (15 ml) and dichloromethane (5 ml) was treated with *p*-nitrophenylhydrazine (0.13 g) for 1 h under reflux. The dichloromethane was then distilled off. The product which separated from the residual, cooled solution was recrystallized from propan-2-ol–dichloromethane to give the *p*-nitrophenylhydrazone (0.38 g, 58%), m.p. 145–146° (decomp.), $[\alpha]_D^{21}$ +520° (*c* 0.3, dichloromethane) (Found: C, 66.9; H, 4.6; N, 6.75. $C_{33}H_{29}N_3O_8$ calc.: C, 66.5; H, 4.9; N, 7.1%).

*Reduction of benzyl 4,6-O-benzylidene-β-*D-xylo-*3-hexulopyranoside 2-benzoate.* — (*a*) *With lithium aluminium hydride.* Compound **11** (1.2 g) dissolved in dry tetrahydrofuran (50 ml) was added dropwise, with stirring, to a mixture of lithium aluminium hydride (2 g) in tetrahydrofuran (30 ml), and the mixture was then heated under reflux for 4 h. The reaction was terminated and processed as described earlier for compound **8** to give, after recrystallization from methanol, benzyl 4,6-*O*-benzylidene-β-D-galactopyranoside (0.93 g, 89%), m.p. 207–209°, $[\alpha]_D^{21}$ −61.5° (*c* 0.9, dichloromethane); lit.[32], m.p. 209–210°, $[\alpha]_D^{20}$ −62.4°. The dibenzoate had m.p. 175–177°, lit.[14] m.p. 177–178°.

(*b*) *With sodium borohydride.* — A solution of compound **11** (1 g) in methanol (35 ml) was cooled to 5° and stirred with sodium borhydride (1.5 g) over 1 h. At the end of this time, 2.7M methanolic sodium methoxide (3 ml) was added, and the solution was stored overnight at 5°. The mixture was neutralized with M sulphuric acid, concentrated *in vacuo* to small volume (*ca.* 10 ml), diluted with water (10 ml), and extracted with dichloromethane (3 × 50 ml). The combined extracts were washed with water, dried (Na_2SO_4), and concentrated *in vacuo* to give a white residue which, on recrystallization from methanol, gave the benzyl 4,6-*O*-benzylidene-β-D-galactoside (0.67 g, 87%), m.p. 206–208°, $[\alpha]_D^{21}$ −61° (*c* 0.67, dichloromethane).

Hydrolysis of samples of both crude reduction products with 0.5M sulphuric acid, as described earlier for compound **9**, followed by chromatography on paper, showed galactose to be the main product, with a faint trace of gulose (R_{Gal} 1.36). No 1,6-anhydro-β-D-gulopyranose (R_{Gal} 2.2) was detectable.

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