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EQUIMOLAR OXYMERCURATION OF D-GLUCAL TRIACETATE WITH MERCURIC PERCHLORATE AND ITS APPLICATION TO THE SYNTHESIS OF 2′-DEOXY DISACCHARIDES

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ABSTRACT

A search for appropriate reaction conditions for the equimolar methoxymercuration of D-glucal triacetate was made by using various mercuric salts, bases, and reaction solvents. Under optimum conditions with mercuric perchlorate, *sym*-collidine, and acetonitrile, D-glucal triacetate underwent methoxymercuration with an equimolar amount of methanol to afford methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-perchloratomercuri-β-D-glucopyranoside (**1**, 26%) and its α-D-*manno* isomer (**2**, 49%). Equimolar oxymercuration of D-glucal triacetate with partially protected sugars, followed by subsequent demercuration of the products with sodium borohydride, afforded α- and β-linked 2′-deoxy disaccharide derivatives in moderate yields. The partially protected sugars used were 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose, and the corresponding products were *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-(1→6)-1,2,3,4-tetra-*O*-acetyl-D-glucopyranose (**4**, 23%) and its β-linked isomer (**5**, 11%) from the former, and *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexapyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**9**, 29%) and its β-linked isomer (**10**, 10%) from the latter. Deacetylation of these 2′-deoxy disaccharides was effected with methanolic sodium methoxide, but deacetonation was unsuccessful owing to simultaneous cleavage of the glycosidic linkage.

INTRODUCTION

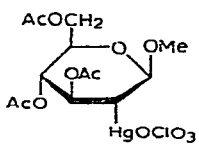
It is well established[1–4] that methoxymercuration of glycal acetates produces high yields of methyl glycosides bearing a mercury atom at C-2. These mercurial methyl glycosides can be conveniently converted into methyl 2-deoxyglycoside acetates by reductive demercuration with sodium borohydride. Similarly, the solvo-oxymercuration of D-glucal triacetate in such volatile alcohols as ethanol[2], propyl alcohol[5] and isopropyl alcohol[2,5] gives crystalline mercurial products that are readily transformed into the corresponding alkyl 2-deoxyglycoside acetates[6]. Thus, the oxymercuration–borohydride demercuration method may provide an excellent synthetic route to glycosides of 2-deoxy sugars. However all of these oxymercuration reactions were effected with large excesses of the alcohols, which were readily removable after reaction by simple evaporation. For reactions with alcohols that are difficulty remova-

ble from reaction mixtures, the amount of alcohol should be decreased to facilitate purification of the products. The present paper describes a search for appropriate reaction conditions to effect equimolar methoxymercuration of D-glucal triacetate, together with an application of the oxymercuration–borohydride demercuration method to the synthesis of disaccharides having a 2-deoxy sugar at the non-reducing part, as an approach to the synthesis of oligosaccharide moieties of cardiac glycosides.

RESULTS AND DISCUSSION

The methoxymercuration of D-glucal triacetate with an equimolar amount of methanol was examined by use of various mercuric salts. Rapid methoxymercuration occurred with mercuric perchlorate, as evidenced by p.m.r. spectroscopy and by t.l.c. examination of reaction mixtures, whereas mercuric salts such as the bromide, chloride, cyanide, nitrate, and sulfate were unreactive. Although a mercurial product slow-moving on t.l.c. was observed with mercuric acetate, this product was the acetoxymercurial compound reported previously[7]; acetoxymercuration took precedence over methoxymercuration in this instance.

Reaction solvents suitable for equimolar methoxymercuration of D-glucal triacetate with mercuric perchlorate are limited. Benzene, toluene, ether, and chloroform were unsuitable because of the low solubility of the mercuric salt. *N*,*N*-Dimethylformamide and dimethyl sulfoxide were undesirable because of their low volatility. Acetone, nitromethane, and tetrahydrofuran were to be avoided, as they are darkened by interaction with the mercuric salt. Pyridine retarded the reaction, presumably by increasing the electron density of the mercury atom through formation of a complex. Of the various solvents examined, acetonitrile was selected as the reaction solvent most appropriate.



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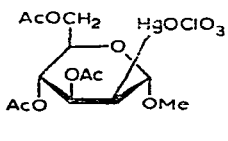

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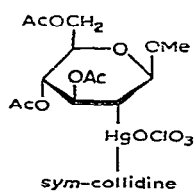

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The p.m.r. spectra of the reaction products obtained by equimolar methoxymercuration with mercuric perchlorate showed two methoxyl-proton signals for the isomeric methyl glycosides (**1** and **2**) at τ 6.49 and 6.64, respectively. These chemical shifts accord with those of the methyl glycosides of β-D-glucose and α-D-mannose derivatives respectively, bearing a mercury atom at C-2, that were obtained by the solvomethoxymercuration of D-glucal triacetate[1]. The percentages of these isomeric products formed were determined by using *p*-(*tert*-butyl)benzoic acid (which gave a singlet for methyl protons at τ 8.68) as an internal standard.

TABLE I

EFFECT OF BASES ON THE EQUIMOLAR METHOXYMERCURATION OF D-GLUCAL TRIACETATE WITH MERCURIC PERCHLORATE (2 h, 25°)

Base	*Yield (%) of methyl 3,4,6-tri-O-acetyl-2-deoxy-2-perchloratomercuri-hexopyranoside*[a]		
	β-D-gluco	*α*-D-manno	*Total*
sym-Collidine	26	49	75
Pyridine	13	32	45
$NaHCO_3$[b]	19	48	67

[a]The molar ratios of bases: methanol were 1:1 in all cases. [b]Finely pulverized Drierite (molar ratio to methanol, 1:1) was added and the reaction was conducted with continuous stirring.

The perchloric acid liberated as the methoxymercuration of D-glucal triacetate proceeded catalyzed the degradation of reaction products. Various bases, as in table I, were evaluated for neutralizing this acid. Pyridine, and especially *sym*-collidine, were effective. Sodium hydrogen carbonate was also useful, but had to be used together with a desiccant to eliminate the water formed simultaneously, otherwise the yields of mercurial products dropped markedly. Stronger bases were unsuitable as they caused the concurrent deacetylation and demercuration of products.

TABLE II

COMPARISON OF THE YIELDS OF MERCURIAL METHYL GLYCOSIDES FORMED IN VARIOUS TYPES OF EQUIMOLAR METHOXYMERCURATION OF D-GLUCAL TRIACETATE (2 h, 25°)

Reaction type	*Yield (%) of methyl 3,4,6-tri-O-acetyl-2-deoxy-2-perchloratomercuri-hexopyranoside*[a]		
	β-D-gluco	*α*-D-manno	*Total*
i D-Glucal triacetate + $Hg(ClO_4)_2$ + MeOH (simultaneously)	7	22	29
ii[b] D-Glucal triacetate + $Hg(ClO_4)_2$, followed by addition of MeOH	0	0	0
iii D-Glucal triacetate + $Hg(ClO_4)_2$ + MeOH + *sym*-collidine (simultaneously)	26	49	75
iv[c] D-Glucal triacetate + $Hg(ClO_4)_2$, followed by addition of MeOH + *sym*-collidine	0	0	0

[a]Both of the molar ratios, $Hg(ClO_4)_2$: methanol and *sym*-collidine: methanol, were 1:1. [b]Methanol was added after the reaction of D-glucal triacetate with mercuric perchlorate for 1 h. [c]Methanol and *sym*-collidine were added after treating D-glucal triacetate with mercuric perchlorate for 1 h.

The combination mercuric perchlorate–*sym*-collidine–acetonitrile proved to be the most effective for the equimolar methoxymercuration of D-glucal triacetate. This combination exhibited an interesting phenomenon (Table II): methoxymercuration

occurred only when D-glucal triacetate, mercuric perchlorate, and methanol were dissolved simultaneously (reaction type *i* and *iii*); no mercurial methyl glycosides were produced when D-glucal triacetate and mercuric perchlorate were first dissolved, and methanol was then added (*ii* and *iv*). T.l.c. monitoring indicated that the mobile spot of D-glucal triacetate disappeared rapidly after mercuric perchlorate was added, and intense "tailing" spots positive to diphenylcarbazide spray appeared near the origin. These spots were ascribed to rather stable mercurial derivatives that did not react with methanol during 2 h, and thus were not considered to be reactive intermediates in the manner of the mercurinium complexes described previously[3]. As methoxymercuration occurred only when methanol was present at the stage of mixing other reactants, the velocity of the methoxymercuration reaction with mercuric perchlorate seemed to be faster than that of the reaction between D-glucal triacetate and mercuric perchlorate without methanol.

TABLE III

EFFECT OF *sym*-COLLIDINE ON THE EQUIMOLAR METHOXYMERCURATION OF D-GLUCAL TRIACETATE WITH MERCURIC PERCHLORATE (2 h, 25°)

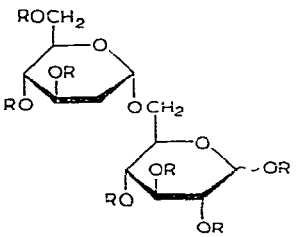
Molar ratio of sym-*collidine: methanol*	*Yield (%) of methyl 3,4,6-tri-O-acetyl-2-deoxy-2-perchloratomercuri-hexopyranoside*		
	β-D-gluco	α-D-manno	*Total*
1.0	26	49	75
1.5	20	27	47
2.0	14	25	39
3.0	6	23	29

On the basis of these observations, the following investigation of reaction conditions was made by mixing all of the reactants at one time. Table III illustrates the dependency of the yields of isomeric mercurial products on the ratios of *sym*-collidine: methanol. P.m.r. determination indicated that the yields of both isomeric products were maximal at a ratio of 1.0, giving a total yield of 75% after reaction for 2 h, whereas they decreased with increasing proportions of *sym*-collidine until no production of mercurials was observed when *sym*-collidine was used alone as the reaction solvent. This tendency may be rationalized by postulating a complex between the mercuric salt and *sym*-collidine that greatly retards the addition reaction of the complexed mercuric salt to the double bond. This hypothesis is further supported by the isolation of a considerable amount of a 1:1 *sym*-collidine–mercurial glycoside complex (3, m.p. 168–169°), which underwent dissociation into its components upon acidification.

As expected from the discussion on Table II, the reaction is very rapid, and the yields of both isomers reach maximal after reaction for only 1 h, giving a total yield of 75% (β-D-*gluco* isomer, 26%; α-D-*manno* isomer, 49%). It is noteworthy that the β-D-*gluco*:α-D-*manno* ratio (0.53) in the products varied greatly from that[3] in the

solvomethoxymercuration of D-glucal triacetate with mercuric acetate (0.82). The products were stable for at least several h; owing to slight acidity, gradual degradation of the β-D-*gluco* isomer ensured, as indicated by darkening of the reaction solution. The total yield after 24 h was 62% (β-D-*gluco* isomer, 14%; α-D-*manno* isomer, 48%).

In consequence, methoxymercuration of D-glucal triacetate was conducted with equimolar amounts of methanol, mercuric perchlorate, and *sym*-collidine in acetonitrile for 2 h at 25°. Although the perchloratomercuri derivatives (**1** and **2**) were not obtained crystalline, their treatment with sodium chloride afforded 25% of a crystalline product identified as methyl 3,4,6-tri-*O*-acetyl-2-chloromercuri-2-deoxy-β-D-glucopyranoside from its physical data. The specific rotation and p.m.r. spectrum of the syrupy isomer (the chloromercuri derivative of **2**, 48%) obtained from the mother liquor were identical with those of methyl 3,4,6-tri-*O*-acetyl-2-chloromercuri-2-deoxy-α-D-mannopyranoside.



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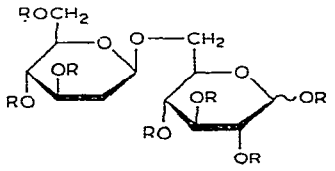
7 R = H



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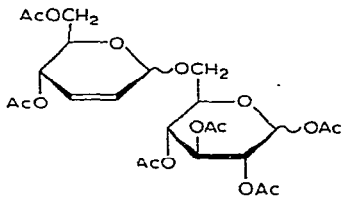

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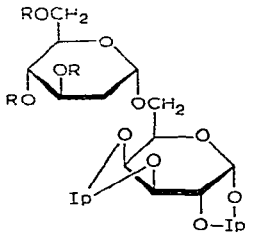
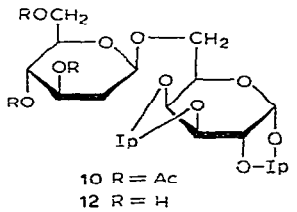


9 R = Ac
11 R = H



10 R = Ac
12 R = H

Application of this method for oxymercuration with non-volatile alcohols is demonstrated by the synthesis of 2′-deoxy disaccharides. The reaction of D-glucal triacetate with equimolar amounts of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose, mercuric perchlorate, and *sym*-collidine gave a syrupy mixture of mercurial products, which, on subsequent demercuration with sodium borohydride, followed by fractionation on a column of silica gel, afforded a chromatographically homogeneous mixture of the acetates of α- and β-linked *O*-(2-deoxy-D-*arabino*-hexopyranosyl)-(1→6)-D-glucopyranoses (**4** and **5**, respectively) in a total yield of 34%, together with a small amount (2%) of a disaccharide, possibly the acetate of *O*-(2,3-dideoxy-D-*erythro*-hex-2-enopyranosyl)-(1→6)-D-glucopyranose (**6**). From the 2′-deoxy disaccharide fraction were obtained, two crystalline products, having m.p. 126–128°,

$[\alpha]_D$+54.2°, and m.p. 196–198°, $[\alpha]_D$+51.2°. These were determined to be the β-anomer of **4** (**4β**) and the α-anomer of **5** (**5α**), respectively, on the basis of their specific rotations (the value calculated from methyl 3,4,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranosides and 1,2,3,4-tetra-*O*-acetyl-D-glucopyranoses based on the isorotation rule: **4α**, +103°; **4β**, +54°; **5α**, +56°; **5β**, −7°) and $J_{1,2}$ coupling constants (**4β**, 8.2 Hz; **5α**, 3.3 Hz) obtained from their p.m.r. spectra. The inversion of the anomeric acetoxyl group during the reaction appears analogous to behavior in the Königs–Knorr condensation when silver perchlorate is used as a catalyst[8]. The crystalline products **4** and **5** were deacetylated with methanolic sodium methoxide to give the corresponding 2′-deoxy disaccharides **7** and **8**, respectively. The paper-chromatographic behavior of these isomeric disaccharides was identical, but they differend considerably in their retention volumes on liquid chromatography. The retention volume of **7**, as well as its specific rotation and p.m.r. data, were identical with those of authentic *O*-(2-deoxy-α-D-*arabino*-hexopyranosyl)-(1→6)-D-glucose prepared by the oxyiodination–hydrogenation method[9], whereas the low $[\alpha]_D$ value (+11.3°) of **8** and large couplings exhibited by the H-2′*a* proton ($J_{1',2'a}$ 10.0 Hz, $J_{2'a,2'e}$ 12.3 Hz, $J_{2'a,3'}$ 10.0 Hz) were apparently indicative of a β-D-linkage. As the syrup obtained from the mother liquor of **4β** was highly dextrorotatory (+76.0°), and as the l.c. determination of the proportion of α- and β-linkages in this syrup (57:30) indicated preponderance of the α-linkage, the greater proportion of this syrup is considered to be the α-anomer of **4**. In total, the yields of α-D-and β-D-linked disaccharides amounted to 23% and 11%, respectively. It should be pointed out that a considerable proportion of the β-D-linked isomer is formed in this series of reactions, in contrast to the oxyiodination–hydrogenation method[9], in which only the α-linked isomer was obtained.

Similarly, the oxymercuration of D-glucal triacetate with equimolar amounts of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose and mercuric perchlorate in the presence of *sym*-collidine, followed by demercuration of product with sodium borohydride, afforded 10% of crystalline *O*-(3,4,6-tri-*O*-acetyl-2-deoxy-β-D-*arabino*-hexopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose **10** and 29% of its syrupy isomer **9**. Although the H-2′*a* couplings of these compounds were not available because of overlap of signals, the specific rotations (−46° and +21°) were in good agreement with the expected values for β- and α-linked isomers (−42° and +29°), respectively. Deacetylation of **9** and **10** yielded the corresponding di-*O*-isopropylidene derivatives of α-D- and β-D-linked *O*-(2-deoxy-D-*arabino*-hexopyranosyl)-(1→6)-α-D-galactopyranose, **11** and **12**, respectively. Deacetonaton of **11** and **12** under mild conditions [either by heating at 90° in 60% acetic acid or by stirring with Amberlite IR-120 (H^+) resin] was, however, unsuccessful because of the simultaneous cleavage of glycosidic linkages.

EXPERIMENTAL

General. — Melting points were determined on a hot stage with a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were measured

in a 1-dm tube. The p.m.r. determination of mercurial methyl glycosides were performed at 60 MHz on a Hitachi R-20A spectrometer, and the p.m.r. spectra of compound **3** and disaccharides were obtained at 100 MHz with a JEOL JNM 4H-100 spectrometer. Chemical shifts are expressed on the τ scale in p.p.m. for the chloroform-*d* (compound **3** and disaccharide derivatives) and D_2O (free disaccharides) solutions at room temperature, with tetramethylsilane as the standard. T.l.c. was performed on glass plates (20 × 20 cm) coated with Wakogel B-5, by using 7:3 benzene–ethyl acetate, and detection with sulfuric acid. Descending p.c. was performed on Whatman No. 1 filter paper with 4:1:5 butyl alcohol–acetic acid–water (upper phase, solvent *A*) and 6:4:3 butyl alcohol–pyridine–water (solvent *B*). Detection of spots was effected with alkaline silver nitrate[10]. Liquid chromatography (l.c.) of disaccharides was performed with a JEOL JLC-3BC apparatus. A glass column (0.8 × 15 cm) packed with LC-R-3 resin was used at 55°, and the column was eluted with pH 9.0 (88 ml), followed by pH 9.6 borate buffer, at a flow rate of 0.49 ml/min. Samples were applied in pH 9.0 buffer solutions, and the effluent, colored with the orcinol–sulfuric acid reagent, was submitted automatically to spectrophotometric analysis at 440 nm. All evaporations were effected below 40° under diminished pressure.

P.m.r. determination of mercurial methyl glycosides. — D-Glucal triacetate (68.0 mg, 0.25 mmoles) was dissolved in acetonitrile (1.00 ml) containing methanol (8.01 mg, 0.25 mmoles). In the examples where bases were used, one of the bases was added to this solution. The solution was cooled in an ice–salt mixture and mixed with a cold 0.5M solution (0.50 ml) of mercuric perchlorate in acetonitrile that had been prepared by dissolving a slight excess of commercial mercuric perchlorate dihydrate (Shimakyu Pure Chemicals Co., Ltd.) in acetonitrile, with subsequent dehydration of the resulting solution with a large excess of pulverized Drierite. The concentration was adjusted to 0.5M after titrating against ammonium thiocyanate with ferric ammonium sulfate as the indicator. The reaction solution was kept for 2 h at 25° and then the solvent was evaporated. The residual syrup was dissolved in a chloroform-*d* containing *p*-(*tert*-butyl)benzoic acid (τ CH_3 8.68, 1.00 mg) as the internal standard. After washing the chloroform-*d* solution three times with equal volumes of water, the signals of methyl protons resonating at τ 6.49 (*β*-D-*gluco*) and 6.64 (*α*-D-*manno*) were determined.

Methoxymercuration of D-*glucal triacetate with equimolar amounts of methanol and mercuric perchlorate.* — D-Glucal triacetate (1.36 g, 5.00 mmoles), methanol (160 mg, 5.00 mmoles), and *sym*-collidine (606 mg, 5.00 mmoles) were dissolved in dehydrated acetonitrile (10.0 ml), and the solution was cooled in an ice–salt mixture. To this solution was added an 0.5M solution (10.0 ml) of mercuric perchlorate in acetonitrile. The solution was kept for 2 h at 25° and then the solvent was evaporated off. The residual syrup was taken up in chloroform (30 ml) and the solution was washed three times with cold water (50 ml). The chloroform solution was then shaken with M aqueous sodium chloride (50 ml) for 30 min, and then water (50 ml). After evaporation of solvent, the residual syrup (1.97 g, 73%) was crystallized from acetone–isopropyl ether to give minute crystals of the chloromercuri derivative of **1** (670 mg,

25%), m.p. 176–177°. Recrystallization from methanol afforded needles, m.p. and mixed m.p. 178–179°, $[\alpha]_D^{22}+11.4°$ (*c* 1.0, chloroform). The p.m.r. spectrum was identical with that of authentic methyl 3,4,6-tri-*O*-acetyl-2-chloromercuri-2-deoxy-β-D-glucopyranoside prepared by the solvomethoxymercuration of D-glucal triacetate with mercuric acetate[3]. The mother liquor was evaporated to dryness to give a syrup of the chloromercuri derivative of **2**, $[\alpha]_D^{22}-14.6°$ (*c* 1.0, chloroform), whose p.m.r. spectrum was identical with that of methyl 3,4,6-tri-*O*-acetyl-2-chloromercuri-2-deoxy-α-D-mannopyranoside.

The mixture obtained by similar reaction of 3.0 mmoles of D-glucal triacetate, methanol, mercuric perchlorate, and 4.5 mmoles of *sym*-collidine, was evaporated to dryness and the residual syrup taken up in chloroform. The chloroform solution was washed with water until the aqueous layer became neutral. After evaporation of the solvent, the residual syrup was crystallized from methanol–isopropyl ether to give a 1:1 *sym*-collidine–methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-perchloratomercuri-β-D-glucopyranose complex (**3**, 350 mg). Recrystallization from the same solvent system afforded prisms, m.p. 168–169°, $[\alpha]_D^{30}+34.7°$ (*c* 0.97, chloroform); p.m.r. data: τ 2.80 (2-proton singlet, ring protons of *sym*-collidine), 4.76 (1-proton quartet, H-3, $J_{3,4}$ 8.5 Hz), 5.08 (1-proton triplet, H-4, $J_{4,5}$ 8.5 Hz), 5.10 (1-proton doublet, H-1, $J_{1,2}$ 9.7 Hz), 5.82 (1-proton quartet, H-6, $J_{5,6}$ 4.5 Hz, $J_{6,6'}$ 12.1 Hz), 5.86 (1-proton quartet, H-6′, $J_{5,6}$, 3.2 Hz), 6.2–6.5 (1-proton multiplet, H-5), 6.48 (3-proton singlet, OMe), 7.23 (6-proton singlet, α-Me of *sym*-collidine), 7.37 (1-proton quartet, H-2, $J_{2,3}$ 11.4 Hz), 7.59 (3-proton singlet, β-Me of *sym*-collidine), 7.93 (3-proton singlet, OAc), 7.98 (6-proton singlet, OAc). When a chloroform-*d* solution of **3** was washed with cold M perchloric acid, followed by water, the signals due to *sym*-collidine disappeared, indicating rapid dissociation of the complex.

Anal. Calc. for $C_{21}H_{30}ClHgNO_{12}$: Hg, 27.69. Found: Hg, 27.35.

O-(*3,4,6-Tri*-O-*acetyl-2-deoxy*-α-D-arabino-*hexopyranosyl*)-(*1→6*)-*1,3,2,4-tetra*-O-*acetyl*-D-*glucopyranose* (**4**) *and its isomer* (**5**). — D-Glucal triacetate (2.72 g, 10.0 mmoles), 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose [prepared by detritylation of pure 1,2,3,4-tetra-*O*-acetyl-6-*O*-trityl-β-D-glucopyranose according to the literature[11] and purified carefully by repeated recrystallization of product, m.p. 126–128°, $[\alpha]_D^{19}+9.6°$ (*c* 1.6, chloroform)] (3.48 g, 10.0 mmoles) and *sym*-collidine (1.21 g, 10.0 mmoles) were dissolved in dehydrated acetonitrile (10 ml). To this solution was added, under cooling, a solution (14.5 ml, 0.689 mmoles/ml) of mercuric perchlorate in acetonitrile. After 2 h at 25°, the solution was evaporated and the residual syrup taken up in chloroform (100 ml). The solution was washed three times with ice–water (100 ml) and the chloroform layer was evaporated to dryness. The residual syrup was dissolved in methanol (40 ml), and sodium borohydride (170 mg) was added in small portions, keeping the reaction temperature below 0°. The reaction mixture was deionized with a mixture of Amberlite IR-120 (H^+, 3 g) and Amberlite IRA-400 (OH^-, 3 g), evaporated, and the residue dried over phosphorus pentaoxide overnight *in vacuo*. The demercuration product was then acetylated conventionally with pyridine (20 ml) and acetic anhydride (10 ml) to convert unreacted D-glucose tetraacetate into

the pentaacetate for better resolution, and the resulting syrup was fractionated on a column of silica gel (Wakogel C-200, 150 g, 3.5 × 60 cm) with 4:1 benzene–ethyl acetate. A small proportion of unreacted D-glucal triacetate and D-glucose pentaacetate present were eluted at early stage.

From the 700–800 ml fraction there was obtained a chromatographically homogeneous, unstable, minor product **6** (120 mg, 2%), whose p.m.r. spectrum indicated the presence of alkenic signals at $\tau \sim 4$; a chloroform solution of this product absorbed bromine rapidly. Deacetylation of **6** gave a disaccharide, R_G 1.31 (solvent *A*), contaminated with a considerable proportion of D-glucose. The disaccharide was purified by preparative p.c., and heated in 0.1M hydrochloric acid for 2 h at 50°. Examination of the hydrolyzate (p.c.) showed a dense spot for D-glucose together with a faint mobile spot of an unidentified compound.

The 800–1650 ml fraction gave a chromatographically homogeneous mixture of 2′-deoxy disaccharides (2.13 g, 34%) as a syrup that was crystallized from methanol to give needles of the α-anomer of **5** (**5α**, 100 mg), m.p. 196–198°, $[\alpha]_D^{29} + 51.2°$ (*c* 1.2, chloroform), p.m.r. data: τ 3.20 (1-proton doublet, H-1, $J_{1,2}$ 3.3 Hz).

Anal. Calc. for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.85. Found: C, 50.44; H, 6.05.

The mother liquors were concentrated and refrigerated for a week to afford another crystalline product (**4β**, 295 mg), obtained from isopropyl ether as fibrous crystals, m.p. 126–128°, $[\alpha]_D^{28} + 54.2°$ (*c* 1.2, chloroform); p.m.r. data: τ 4.32 (1-proton doublet, H-1, $J_{1,2}$ 8.2 Hz).

Anal. Calc. for $C_{26}H_{36}O_{17}$: C, 50.32; H, 5.85. Found: C, 50.48; H, 5.74.

From the mother liquor of **4β**, a syrup of **4** contaminated with a considerable amount of **5** was obtained; $[\alpha]_D^{32} + 76.0°$ (*c* 1.9, chloroform). Attempted crystallization from various solvents was unsuccessful.

Deacetylation of **4** *and* **5**. — A 0.05M methanolic solution of sodium methoxide containing **4β** was kept for 1 h. The reaction solution was decationized with Amberlite IR-120 (H^+) to give quantitatively *O*-(2-deoxy-α-D-*arabino*-hexopyranosyl)-(1→6)-D-glucose (**7**), $[\alpha]_D^{29} + 89.2°$ (*c* 0.6, water, 24 h); R_G 0.60 (solvent *A*), 0.69 (solvent *B*); l.c. retention volume 162 ml, p.m.r. data: τ 7.50 (1-proton octet, H-2′*e*, $J_{1',2'e}$ 1.5 Hz, $J_{2'a,2'e}$ 13.3 Hz, $J_{2'e,3'}$ 5.0 Hz), 7.99 (1-proton octet, H-2′*a*, $J_{1',2'a}$ 3.3 Hz, $J_{2'a,3'}$ 11.3 Hz). All of these data for **7** accord with those of an authentic sample prepared from D-glucal triacetate and 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose by the oxyiodination–hydrogenation method[9]. Hydrolysis of **7** in 0.1M hydrochloric acid for 2 h at 60°, followed by neutralization with barium hydroxide, yielded a syrup that gave two spots on p.c., R_G 1.00 and 1.70 (solvent *A*, authentic 2-deoxy-D-*arabino*-hexose 1.70); 1.00 and 1.38 (solvent *B*, authentic 2-deoxy-D-*arabino*-hexose 1.38).

On the other hand, similar deacetylation of **5α** gave *O*-(2-deoxy-β-D-*arabino*-hexopyranosyl)-(1→6)-D-glucose (**8**) quantitatively, $[\alpha]_D^{20} + 11.3°$ (*c* 1.5, water, 24 h); R_G 0.60 (solvent *A*), 0.69 (solvent *B*); l.c. retention volume 184 ml, p.m.r. data: τ 6.82 (1-proton octet, H-2′*e*, $J_{1',2'e}$ 2.0 Hz, $J_{2'a,2'e}$ 12.3 Hz, $J_{2'e,3'}$ 5.0 Hz), 7.55 (1-proton sextet, H-2′*a*, $J_{1',2'a}$ 10.0 Hz, $J_{2'a,3'}$ 10.0 Hz). Hydrolysis of **8** in 0.1M hydrochloric acid for 2 h at 60° gave the same result as for **7**. Deacetylation of the

syrup obtained from the mother liquor of **4β** gave a mixture of **7** and **8**, l.c. retention volume 162 ml (intensity 0.57) and 184 ml (intensity 0.30).

O-(3,4,6-Tri-O-acetyl-2-deoxy-α-D-arabino-hexopyranosyl)-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (**9**) *and its isomers* (**10**). — D-Glucal triacetate (2.72 g, 10.0 mmoles), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (2.60 g, 10.0 mmoles), and *sym*-collidine (1.21 g, 10.0 mmoles) were dissolved in dehydrated acetonitrile (20 ml). To this solution was added, under cooling, a solution (21 ml) of 0.48 mmoles/ml mercuric perchlorate in acetonitrile. The reaction solution was kept for 2 h at 25° and evaporated to dryness. The residual syrup was demercurated in a similar manner as for **4** and **5**, with subsequent fractionation on a column of silica gel (Wakogel C-200, 140 g, 3 × 70 cm) with 9:1 (400 ml), 6:1 (350 ml) and 4:1 (200 ml) benzene–ethyl acetate, in this order. From the 400–750 ml fraction a chromatographically homogeneous syrup (2.10 g, 39%) was obtained, which was crystallized from ether–hexane to give needles of **10** (530 mg, 10%), m.p. 119–120°, $[\alpha]_D^{28} -46.1°$ (*c* 1.3, chloroform), p.m.r. data: τ 4.4–6.5 (13-proton signals of sugar-ring protons), 7.5–8.5 (2-proton signals of H-2′*a* and H-2′*e*), 7.93 (3-proton singlet, OAc), 7.99 (6-proton singlet, OAc), 8.48 (3-proton singlet, C–Me), 8.57 (3-proton singlet, C–Me), 8.68 (6-proton singlet, C–Me).

Anal. Calc. for $C_{24}H_{36}O_{13}$: C, 54.13; H, 6.81. Found: C, 54.16; H, 6.81.

From the mother liquor syrupy **9** (1.56 g, 29%) was obtained after evaporation of the solvent; $[\alpha]_D^{35} +21.0°$ (*c* 1.9, chloroform), p.m.r. data: τ 4.4–6.5 (13-proton signals of sugar ring protons), 7.5–8.5 (2-proton signals of H-2′a and H-2′e), 7.94 (3-proton singlet, OAc), 7.98 (3-proton singlet, OAc), 8.02 (3-proton singlet, OAc), 8.46 (3-proton singlet, C–Me), 8.58 (3-proton singlet, C–Me), 8.67 (6-proton singlet, C–Me).

Deacetylation of **9** *and* **10**. — Deacetylation of crystalline **10** as described for **4β** gave (quantitatively) syrupy *O*-(2-deoxy-β-D-*arabino*-hexopyranosyl)-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**12**), which crystallized from isopropyl ether as needles, m.p. 112–113°; $[\alpha]_D^{32} -77.3°$ (*c* 4.0, chloroform).

Anal. Calc. for $C_{18}H_{30}O_{10}$: C, 53.19; H, 7.44. Found: C, 52.64; H, 7.44.

On the other hand, similar deacetylation of **9** gave a chromatographically homogeneous syrup of the α-linked isomer **11**, $[\alpha]_D^{32} +2.0°$ (*c* 2.5, chloroform). Attempted crystallization from various solvents was unsuccessful.

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REFERENCES

1 G. R. Inglis, J. C. P. Schwarz, and L. McLaren, *J. Chem. Soc.*, (1962) 1014.
2 P. T. Manolopoulos, M. Mednick, and N. N. Lichtin, *J. Amer. Chem. Soc.*, 84 (1962) 2203.
3 K. Takiura and S. Honda, *Carbohyd. Res.*, 21 (1972) 379.
4 S. Honda, K. Izumi, and K. Takiura, *Carbohyd. Res.*, 23 (1972) 427.

5 J. H. LEFTIN AND N. N. LICHTIN, *Israel J. Chem.*, 3 (1965) 107.
6 Our unpublished results.
7 K. TAKIURA AND S. HONDA, *Carbohyd. Res.*, 23 (1972) 369.
8 H. BREDERECK, A. WAGNER, G. FASER, H. OTT, AND J. RAUTER, *Chem. Ber.*, 92 (1959) 1135.
9 S. HONDA, K. KAKEHI, AND K. TAKIURA, *Carbohyd. Res.*, 29 (1973) 488.
10 N. E. TREVELYAN, D. P. PROCTER, AND J. S. HARRISON, *Nature*, 166 (1950) 444.
11 E. A. TALLEY, *Methods Carbohyd. Chem.*, 2 (1963) 339.