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IODINOLYSIS OF C-2 MERCURATED HEXOSE DERIVATIVES

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ABSTRACT

Reaction of the C-2 mercurated methyl hexopyranoside acetates **1–3** with an excess of iodine resulted in nearly quantitative replacement of mercury by iodine with retention and inversion of configuration at C-2. Similar replacement was observed with 2-acetoxymercuri-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranose (**4**). In the iodinolysis of 2-acetoxymercuri-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose (**5**) in methanol, however, replacement at C-2 was accompanied to a considerable extent by solvolysis of the 1-acetoxyl group, and a mixture of 1,2-*trans* isomers of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-hexopyranosides having the D-*gluco* and D-*manno* configurations was obtained, together with 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranose.

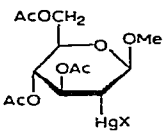
INTRODUCTION

Oxymercuration of glycals is an attractive reaction that proceeds readily at room temperature to give, in most cases quantitatively, easily crystallized C-2 mercurated carbohydrate derivatives. The carbon–mercury bond in these compounds is readily cleaved by a variety of reagents, some of which lead to carbohydrate derivatives of biochemical and synthetic interest. Demercuration reactions leading to 2-deoxy sugars[1–3] and 1,2- and/or 2,3-unsaturated sugars[2,4] have been already published. Brominolysis of typical mercurial adducts has been discussed earlier in relation to the configurational assignment of these adducts[5]. We describe herein chromatographic and p.m.r. studies on the reaction of some C-2 mercurated hexose derivatives with iodine. These iodinolysis reactions provide an alternative route to C-2 iodinated carbohydrate derivatives.

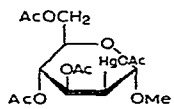
RESULTS AND DISCUSSION

When a methanolic solution of methyl 2-acetoxymercuri-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**1a**) and an excess of iodine was kept at room temperature, rapid uptake of iodine was observed, reaching a maximum of 1.5 moles per mole of the adduct within 1.5 h. Examination of the reaction mixture indicated

that it contained equivalent amounts of mercuric iodide, acetic acid, and iodinated sugars. Chromatographic fractionation of the sugar portion on a column of silica gel afforded the crystalline iodo compounds **8** (a known compound[6]) and **13**, in yields of 47% and 46%, respectively. The anomeric proton for **13** resonated as a doublet at τ 6.29, with a spacing of 1.4 Hz. Deacetylation of **8** and **13** gave the crystalline glycosides **9** and **14**. The melting point of **14** coincided with that of methyl 2-deoxy-2-iodo-α-D-mannopyranoside, but it was much more levorotatory than the recorded specific rotation for this compound (+48.8°) indicating apparent disagreement with the literature. Hydrolysis of **9** and **14** under mildly acidic conditions yielded 2-deoxy-2-iodo-D-glucose and 2-deoxy-2-iodo-D-mannose, respectively, as evidenced by t.l.c. G.l.c. examination of the sodium borohydride reduction-products obtained from their hydrolyzates was also indicative of these component sugars. The preceding observations establish that the iodinolysis of **1a** resulted in quantitative replacement of the mercury atom at C-2 by iodine, producing nearly equal amounts of the isomeric methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-hexopyranosides **8** and **13**.



1a X = OAc
1b X = I



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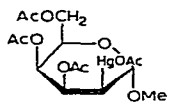

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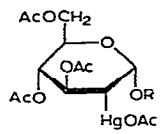
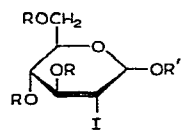
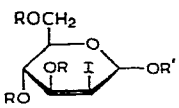


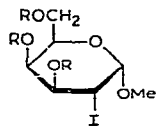
4 R = H
5 R = Ac



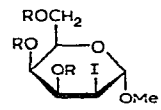
6 R = Ac R' = Me α-anomer
7 R = H R' = Me α-anomer
8 R = Ac R' = Me β-anomer
9 R = H R' = Me β-anomer
10 R = Ac R' = H α-anomer



11 R = Ac R' = Me α-anomer
12 R = H R' = Me α-anomer
13 R = Ac R' = Me β-anomer
14 R = H R' = Me β-anomer
15 R = Ac R' = H α-anomer
16 R = Ac R' = Ac α-anomer



17 R = Ac
18 R = H



19 R = Ac
20 R = H

1a, 1b ⟶ 8 + 13
2 ⟶ 6 + 11
3 ⟶ 17 + 19
4 ⟶ 10 + 15
5 ⟶ 8 + 11 + 16

Iodinolysis of **2**, the α-D-*manno* isomer of the mercurical glycoside **1a**, gave a syrupy mixture of chromatographically indistinguishable components **6** and **11** in a total yield of 90%. The p.m.r. spectrum of this mixture gave two sets of signals, one of which was identical with that from authentic methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranoside prepared by the Prévost reaction[6]. The other set of signals included one at τ 6.56 attributable to the methoxyl-proton signal of the *α-gluco* isomer. Deacetylation of the mixture of **6** and **11** yielded a syrupy mixture of the corresponding glycosides **7** and **12**. G.l.c. examination of the trimethylsilylated products obtained from this syrup demonstrated two well-resolved peaks having retention times (relative to methyl α-D-glucopyranoside) of 1.65 and 2.90. The former peak corresponded to that observed from authentic methyl 2-deoxy-2-iodo-α-D-

mannopyranoside[6], but the latter peak was not identical with peaks from any known methyl 2-deoxy-2-iodo-hexopyranosides.

T.l.c. examination of the hydrolyzate of the mixture gave somewhat tailing spots indistinguishable from those given by a mixture of 2-deoxy-2-iodo-D-glucose and 2-deoxy-2-iodo-D-mannose. G.l.c. of the sodium borohydride reduction-product obtained from this hydrolyzate demonstrated also that the product was composed of these two iodinated hexoses. The proportions of **6** and **11** were estimated from peak areas to be 58 and 42% of the syrup, respectively. From these data, the yields of **6** and **11** were calculated to be 52 and 38%, respectively.

Thus, iodinolysis of the mercurial glycoside **2** at room temperature resulted again in replacement of mercury by iodine without any change elsewhere in the molecule.

These results indicate that all four possible stereoisomers of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-hexopyranosides having the D-*gluco* and D-*manno* configurations can be derived quantitatively from D-glucal triacetate by successsive application of methoxymercuration, followed by iodinolysis, These reactions contrast with the results of Prévost methoxyiodination[6], whereby only *trans*-disposed isomers are obtained.

Iodinolysis of methyl 2-acetoxymercuri-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-talopyranoside (**3**) gave a syrupy mixture of the iodo compounds **17** and **19**, which could not be separated chromatographically. However, after deacetylation, a part of the product crystallized spontaneously, and the crystalline product **18** was reconverted by acetylation into one of the original acetates (**17**). On the basis of p.m.r. data for pure **17** and the syrupy mixture, the structures methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-galactopyranoside and its α-D-*talo* isomer were proposed for **17** and **19**, respectively. The mixture of trimethylsilyl derivatives obtained from the deacetylation product was well resolved by g.l.c., and the proportions of **17** and **19** were estimated to be 63 and 37%, respectively. These values correspond to yields of 57 and 33%, respectively.

Mercury–iodine replacement was also observed with 2-acetoxymercuri-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranose (**4**). From this mercurial adduct a syrupy mixture of 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-glucopyranose (**10**) and its α-D-*manno* isomer (**15**) was obtained. After chromatographic resolution on a column of silica gel, the α-D-*gluco* isomer (**10**) crystallized. The other isomer (**15**) was not obtained crystalline. The configurations of these products at C-2 were confirmed by g.l.c. comparison of their methylation products. Anomeric methyl glycosides of 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-D-glucopyranose and its D-*manno* isomer were detected for compounds **10** and **15**, respectively.

The first stage of these iodinolysis reactions is considered to be the replacement of the mercury-bound acetate by iodide to form iodomercurial compounds, since when a small amount of iodine was used in the iodinolysis of **1a** and the reaction mixture was processed immediately after dissolution of iodine, there was isolated a considerable amount of the iodomercury compound **1b**. In addition, t.l.c. and p.m.r.

spectroscopy revealed that the reaction of **1b** with an excess of iodine yielded the same products as did its precursor **1a**. It has been shown from a kinetic study that the reaction of 4-camphylmercuric iodide with iodine in 1,4-dioxane is a free-radical process[8]. However, in a polar solvent, such as aqueous 1,4-dioxane, electrophilic substitution has been observed. Similarly, the brominolysis of *cis*- and *trans*-4-methylcyclohexylmercuric bromides[9] and also *sec*-butylmercuric bromide[10] has been reported to occur by both polar and free-radical mechanisms. Brominolysis of **1a** in carbon disulfide has been reported[5] to yield a mixture of isomeric 2-bromo sugars with retention and inversion of configuration at C-2. It is noteworthy, however, that configurational retention only was observed for brominolysis in such polar solvents, as methanol, ethanol, and pyridine. These solvent effects are consistent with those already cited[9,10]. In the iodinolysis of the mercurial glycosides **1a** and **2**, the percentage of configurational retention (as determined by g.l.c.) increased with increasing polarity of the solvent. Interconversion of the iodo sugars can be ruled out, because the products **8** and **13** were not epimerized when subjected independently to the iodinolysis medium. Although the configurational retention varied within a narrower range (~40–60%), the dependency of configurational retention of the polarity of solvents that was observed in these iodinolysis reactions also paralleled the solvent effect on the brominolysis of organomercuric bromides[4,9,10] already mentioned. Accordingly, it is probable that in these reactions also, electrophilic and free-radical mechanisms (which proceed with retention and inversion of configuration at C-2, respectively) operate competitively both in polar and non-polar solvents.

The product from iodinolysis in methanol of 2-acetoxymercuri-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose (**5**) was fractionated on a column of silica gel. Two chromatographically homogeneous fractions, A and B, were obtained in yields of 61 and 27%, respectively. The p.m.r. spectrum of the faster-moving, syrupy fraction A exhibited two methoxyl proton signals at τ 6.43 and 6.59, identical with those for compounds **8** and **11**, respectively, and other signals were also identical with those from a mixture of authentic **8** and **11**. Fraction A was deacetylated to give a syrupy mixture of glycosides. G.l.c. examination of the *O*-trimethylsilyl derivatives obtained from this mixture indicated again that fraction A was a mixture of **8** and **11**, as there was observed good separation of peaks corresponding to those from authentic glycosides **9** and **12**. The proportions of **8** and **11**, as estimated from specific rotations as well as from peak areas of their methoxyl-proton signals and g.l.c. peaks, amounted to 36 and 64% of fraction A, respectively. From these data, the yields of **8** and **11** were calculated to be 22 and 39%, respectively. The slower-moving fraction B was also a syrup, but its p.m.r. spectrum suggested that it was homogeneous. The spectrum was essentially same as that of **11** except for an upfield shift of the H-1 doublet, and the structure of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranose (**16**) is proposed for this compound.

The formation of methyl glycosides might intuitively be ascribed to solvolysis of preformed acetates of iodinated hexose(s). However, this is not the case, as a methanolic solution of fraction B containing the same amounts of iodine, acetic acid,

and mercuric iodide as liberated from the iodinolysis mixture underwent no change within the reaction time used for the iodinolysis of the mercurial adduct **5**. That the 1-acetoxyl group in **5** is extremely labile was demonstrated by its demercuration by thiourea[4]. The intermediate formation of 1,2-cyclic iodonium ions, as proposed for the mechanism of the Prévost reaction[6], can be postulated also in this instance. Attack of the methoxyl ion on these iodonium ions would afford the *trans*-disposed methyl glycosides **8** and **11**.

EXPERIMENTAL

General. — Melting points were determined on a hot stage with a Yanagimoto micro melting-point apparatus and are uncorrected. Specific rotations were determined in a 1-dm tube. P.m.r. spectra were measured at 90 MHz on a Hitachi R-22 spectrometer. Chemical shifts are expressed on the τ scale for $\sim$10% solutions in chloroform-*d* at 35°, with tetramethylsilane as the internal standard. Descending paper chromatography (p.c.) was carried out on Whatman No. 1 filter paper with 4:1:5 butanol–acetic acid–water (upper phase, solvent *A*) and 6:4:3 butanol–pyridine–water (solvent *B*). The spots were detected with alkaline silver nitate[11]. R_{Glc} denotes the mobility relative to D-glucose. T.l.c. was performed on glass plates (20 × 20 cm) coated with Wakogel B-5 by using 7:2 benzene–ethyl acetate (solvent *C*), 7:3 ether–hexane (solvent *D*), and 30:9:1 chloroform–methanol–water (solvent *E*) as eluants. Spots were visualized by spraying with concentrated sulfuric acid, followed by heating the plates in an oven. Mercuric compounds were also detected with diphenylcarbazide as violet spots. $R_{Me\,\alpha\text{-}G}$ and $R_{Me\,\alpha\text{-}GAc}$ denote the mobilities relative to methyl α-D-glucopyranoside and methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside, respectively. G.l.c. was performed with a Hitachi K-23 instrument equipped with a flame-ionization detector. Samples were trimethylsilylated according to the procedure of Sweeley *et al.*[12] before being applied to a column (2 m) at 180° containing 15% butanediol succinate polyester absorbed on Celite 545. The carrier gas (nitrogen) was regulated at a flow-rate of 30 ml/min. $RRT_{Me\,\alpha\text{-}G}$ denotes the retention time relative to methyl tetra-*O*-trimethylsilyl-α-D-glucopyranoside. Evaporations were effected below 40° under diminished pressure.

Iodinolysis of methyl 2-acetoxymercuri-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranoside (**1a**). — *A. Uptake of iodine and liberation of acetic acid.* The mercurial glycoside **1a** (0.56 g, 1.00 mmole) was dissolved in methanol (20.0 ml) and to this solution was added iodine (0.51 g, 2.00 mmoles). Aliquots (1.00 ml) were titrated at intervals with 10mM sodium thiosulfate and a starch solution as the indicator. The consumption of titrant became constant after 1.5 h, indicating an uptake of 1.5 moles of iodine per mole of **1a**. After 1.5 h, a part of the reaction solution (10.0 ml) was decolorized with sodium thiosulfate and titrated potentiometrically with 0.1M sodium hydroxide. The total acid liberated was estimated to be 1.0 mole per mole of **1a**. The neutralized solution was evaporated to dryness, and the residue was extracted with D_2O. P.m.r. examination of the D_2O solution indicated the presence of a signal at τ 8.10 for the acetic acid liberated. The amount of acetic acid was estimated to be

1.0 mole per mole of **1a** by using sodium 4,4-dimethyl-4-silapentanesulfonate as an internal standard.

B. Isolation of the iodomercurial derivative **1b**. The mercurial glycoside **1a** (1.13 g, 2.00 mmoles) was dissolved in methanol (10 ml), and to this solution was added iodine (0.51 g, 2.00 mmoles). A considerable amount of crystalline **1b** precipitated immediately after dissolution of iodine. The reaction mixture was immediately evaporated to dryness and the residue was extracted into chloroform (25 ml). The chloroform solution was washed with 5% sodium thiosulfate, followed by saturated sodium hydrogen carbonate, and finally with water. Evaporation of solvent afforded a syrup (1.10 g), which crystallized from methanol to give plates of **1b** (0.48 g, 38%), m.p. and mixed m.p.[3] 172–173°. The p.m.r. spectrum was identical with that of authentic methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodomercuri-β-D-glucopyranoside[3].

Anal. Calc. for $C_{13}H_{19}HgIO_8$: C, 24.75; H, 3.04; Hg, 31.80. Found: C, 24.45; H, 2.98; Hg, 31.91.

C. Isolation of methyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-β-D-glucopyranoside (**8**) *and its β-D-manno isomer* (**13**). The mercurial glycoside **1a** (1.13 g, 2.00 mmoles) was dissolved in methanol (25 ml) and to this solution was added iodine (1.02 g, 4.00 mmoles). Immediately after dissolution of iodine there was observed the separation of crystalline **1b**, which then redissolved gradually. After 2 h, the reaction mixture was evaporated to dryness and the residue was extracted with chloroform (25 ml). Crystalline mercuric iodide (0.87 g, 96%) remained unextracted.

Anal. Calc. for HgI_2: Hg, 44.14. Found: Hg, 44.10.

The chloroform extract was washed with 5% sodium thiosulfate, followed by saturated sodium hydrogen carbonate, and finally with water. Evaporation of the solvent gave a syrupy mixture (0.85 g, 95%) of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-β-D-glucopyranoside (**8**) and its β-D-*manno* isomer (**13**). The syrup was applied to a column of silica gel (Wakogel C-200, 50 g, 2.0 × 45 cm) and fractionated with 7:3 ether–hexane. From the 110–150-ml fraction the crystalline glycoside **8** (0.42 g, 47%) was obtained after evaporation of solvent. Recrystallization from ether–hexane afforded needles, m.p. 97–97.5° (lit.[6] 94–95°); $[\alpha]_D^{27}$ +68.9° (*c* 2.3, chloroform; lit.[6] +61.1°; *c*, 2 chloroform); $R_{Me\,\alpha\text{-}GAc}$ (t.l.c.) 1.47 (solvent *C*), 1.25 (solvent *D*); p.m.r. data: τ 4.71 (1-proton quartet, H-3, $J_{3,4}$ 10.7 Hz), 5.05 (1-proton triplet, H-4, $J_{4,5}$ 9.2 Hz), 5.46 (1-proton doublet, H-1, $J_{1,2}$ 9.0 Hz), 5.66 (1-proton quartet, H-6), 5.88 (1-proton quartet, H-6'), 6.12 (1-proton quartet, H-2, $J_{2,3}$ 9.0 Hz), 6.24 (1-proton octet, H-5), 6.43 (3-proton singlet, OMe), 7.90 (6-proton singlet, OAc), and 7.96 (3-proton singlet, OAc).

Anal. Calc. for $C_{13}H_{19}IO_8$: C, 36.30; H, 4.45; I, 29.50. Found: C, 36.36; H, 4.58; I, 29.40.

From the 190–250-ml fraction the other glycoside **13** (0.41 g, 46%) was obtained crystalline. Recrystallization from ether–hexane afforded needles, m.p. 118–118.5°, $[\alpha]_D^{27}$ −97.8° (*c* 1.9, chloroform); $R_{Me\,\alpha\text{-}GAc}$ 1.28 (solvent *C*), 0.67 (solvent *D*); p.m.r.

data: τ 4.60 (1-proton triplet, H-4, $J_{4,5}$ 9.2 Hz), 5.34 (1-proton quartet, H-2, $J_{2,3}$ 4.1 Hz), 5.56 (1-proton quartet, H-3, $J_{3,4}$ 9.0 Hz), 6.29 (1-proton doublet, H-1, $J_{1,2}$ 1.4 Hz), 5.4–6.5 (3-proton multiplet, H-5, H-6, H-6'), 6.43 (3-proton singlet, OMe), 7.90 (6-proton singlet, OAc), and 7.96 (3-proton singlet, OAc).

Anal. Calc. for $C_{13}H_{19}IO_8$: C, 36.30; H, 4.45; I, 29.50. Found: C, 36.29; H, 4.53; I, 29.20.

When the iodinolysis of **1a** was conducted under reflux for 2 h, the chloroform extract obtained by similar processing of this reaction mixture gave a faint spot on t.l.c., together with two major spots of the foregoing products; $R_{Me\,\alpha\text{-}GAc}$ 0.96 (solvent *C*), 0.49 (solvent *D*). Acetylation with a 2:1 mixture of pyridine and acetic anhydride however, eliminated this faint spot and the chromatogram was identical with that exhibited by the chloroform extract obtained from the iodinolysis for 2 h at room temperature.

*Iodinolysis of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodomercuri-β-*D*-glucopyranoside* (**1b**). — The mercurial glycoside **1b** (0.3 mmole) was dissolved in methanol (10 ml), and to this solution was added iodine (0.6 mmole). After 2 h the reaction mixture was processed as described for the iodinolysis of **1a**. T.l.c. examination of the chloroform extract revealed two spots, $R_{Me\,\alpha\text{-}GAc}$ 1.47 and 1.28 (solvent *C*). The p.m.r. spectrum of the syrup obtained after evaporation of solvent was identical with the spectrum of a mixture of **8** and **13**.

*Deacetylation of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-β-*D*-glucopyranoside* (**8**). — Compound **8** (0.15 g) was dissolved in 0.1M methanolic sodium methoxide and the solution was kept for 1 h. Decationization with Amberlite IR-120 (H^+) resin, followed by evaporation of solvent yielded crystalline methyl 2-deoxy-2-iodo-β-D-glucopyranoside (**9**, 0.10 g, 98%). Recrystallization from methanol–ether afforded needles, m.p. 190–190.5° (lit.[7] 189–189.5°), $[\alpha]_D^{28}$ +29.0° (*c* 1.5, methanol; lit.[7] +6.9°, *c* 2.1, methanol); R_{Glc} (p.c.) 3.77 (solvent *A*), 2.83 (solvent *B*) [the R_{Glc} value of authentic methyl 2-deoxy-2-iodo-β-D-glucopyranoside[7] was 3.77 (solvent *A*) and 2.83 (solvent *B*)]; $RRT_{Me\,\alpha\text{-}G}$ (g.l.c.) 3.22 (the $RRT_{Me\,\alpha\text{-}G}$ value of authentic methyl 2-deoxy-2-iodo-β-D-glucopyranoside was 3.22).

Anal. Calc. for $C_7H_{13}IO_5$: C, 27.65; H, 4.31; I, 41.74. Found: C, 27.61; H, 4.33; I, 41.65.

Hydrolysis of a portion of **9** in 0.05M sulfuric acid for 2 h at 100°, followed by neutralization with barium hydroxide, yielded a syrup that on t.l.c. gave a spot having $R_{Me\,\alpha\text{-}G}$ 1.36 (solvent *E*). The $R_{Me\,\alpha\text{-}G}$ value of authentic 2-deoxy-2-iodo-D-glucose, prepared by hydrolysis of its methyl β-D-glycoside[7] was 1.36 (solvent *E*). To the hydrolyzate was added an excess of sodium borohydride. After 1 h the solution was decationized and evaporated to dryness. The residue was dissolved in methanol and evaporated. After repeating this procedure three times, the residual syrup was subjected to trimethylsilylation, and the product was examined by g.l.c. One main peak was detected, $RRT_{Me\,\alpha\text{-}G}$ 1.49. Authentic 2-deoxy-2-iodo-D-glucose was reduced with sodium borohydride and trimethylsilylated similarly to give a peak having $RRT_{Me\,\alpha\text{-}G}$ 1.49.

Deacetylation of methyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-β-D-mannopyranoside (**13**). — By the procedure described for **8** deacetylation of **13** yielded quantitatively the crystalline methyl 2-deoxy-2-iodo-β-D-mannopyranoside (**14**). Recrystallization from methanol–ether afforded needles, m.p. 147–148°, $[\alpha]_D^{28}$ −6.3° (*c* 0.7, methanol); R_{Glc} (p.c.) 3.14 (solvent *A*), 2.64 (solvent *B*); $RRT_{Me\,\alpha-G}$ (g.l.c.) 3.84.

Anal. Calc. for $C_7H_{13}IO_5$: C, 27.65; H, 4.31; I, 41.74. Found: C, 27.54; H, 4.31; I, 41.60.

Hydrolysis of a portion of **14** as for **9** gave a spot on t.l.c. having $R_{Me\,\alpha-G}$ 1.43 (solvent *E*). The $R_{Me\,\alpha-G}$ value of authentic 2-deoxy-2-iodo-D-mannose, prepared by hydrolysis of its methyl α-D-glycoside[7] was 1.43 (solvent *E*). G.l.c. examination of the sodium borohydride reduction-product obtained from the hydrolyzate gave a main peak having $RRT_{Me\,\alpha-G}$ 1.10. Authentic 2-deoxy-2-iodo-D-mannose was reduced with sodium borohydride and trimethylsilylated similarly to give a peak having $RRT_{Me\,\alpha-G}$ 1.10.

Iodinolysis of methyl 2-acetoxymercuri-3,4,6-tri-O-acetyl-2-deoxy-α-D-mannopyranoside (**2**). — The mixture obtained by reaction of the mercurial glycoside **2** (2.00 mmoles) and iodine (4.00 mmoles) in methanol (25 ml) for 2 h was processed as described for the iodinolysis of **1a**. The yield of mercuric iodide was 0.84 g (92%). From the chloroform extract there was obtained a syrup (0.83 g), which gave a single spot on t.l.c. This product was purified on a column of silica gel (Wakogel C-200, 50 g, 2.0 × 45 cm) with 7:3 ether–hexane to give a syrupy mixture (0.80 g, 90%) of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-glucopyranoside (**6**) and its α-D-*manno* isomer (**11**), $[\alpha]_D^{35}$ +70.5° (*c* 3.6, chloroform); $R_{Me\,\alpha-GAc}$ (t.l.c.) 1.52 (solvent *C*), 1.29 (solvent *D*); p.m.r. data: τ 4.54 (1-proton quartet, H-3 of **6**, $J_{3,4}$ 9.1 Hz), 4.67 (1-proton triplet, H-4 of **11**, $J_{4,5}$ 9.1 Hz), 4.95 (1-proton singlet, H-1 of **11**, $J_{1,2}$ 0.2 Hz), 5.03 (1-proton triplet, H-4 of **6**, $J_{4,5}$ 8.6 Hz), 5.15 (1-proton doublet, H-1 of **6**, $J_{1,2}$ 2.5 Hz), 5.40 (1-proton quartet, H-3 of **11**, $J_{3,4}$ 9.5 Hz), 5.80 (1-proton doublet, H-2 of **11**, $J_{2,3}$ 4.1 Hz), 5.93 (1-proton quartet, H-2 of **6**, $J_{2,3}$ 11.2 Hz), 5.4–6.2 (6-proton multiplet, H-5, H-6, H-6′ of **6** and **11**), 6.56 (3-proton singlet, OMe of **6**), 6.59 (3-proton singlet, OMe of **11**), 7.90 (3-proton singlet, OAc of **11**), 7.93 (6-proton singlet, OAc of **6** plus 3-proton singlet, OAc of **11**), 7.96 (3-proton singlet, OAc of **11**), and 8.00 (3-proton singlet, OAc of **6**). The relative peak-areas of two methoxyl proton signals resonating at τ 6.56 (**6**) and 6.59 (**11**) were 42:58, respectively. Attempted crystallization of this syrup from various solvents was unsuccessful.

Anal. Calc. for $C_{13}H_{19}IO_8$: C, 36.30; H, 4.45; I, 29.50. Found: C, 36.52; H, 4.53; I, 29.71.

Deacetylation of the iodinated glycoside mixture of **6** *and* **11**. — The mixture of **6** and **11** was deacetylated as described for the deacetylation of **8**, to give quantitatively a syrupy mixture of methyl 2-deoxy-2-iodo-α-D-glucopyranoside (**7**) and its α-D-*manno* isomer (**12**), $[\alpha]_D^{36}$ +88.0° (*c* 2.2, methanol); R_{Glc} (p.c.) 3.78 (solvent *A*), 2.84 (solvent *B*); R_{Glc} of authentic methyl 2-deoxy-2-iodo-α-D-mannopyranoside[7] 3.80 (solvent *A*), 2.84 (solvent *B*). G.l.c. of the trimethylsilyl derivatives obtained from this syrup gave peaks, $RRT_{Me\,\alpha-G}$ 1.65 and 2.90, having relative peak-areas of 58.3:41.7. The

$RRT_{Me\,\alpha\text{-}G}$ value of authentic methyl 2-deoxy-2-iodo-α-D-mannopyranoside was 1.65.

Hydrolysis of this syrup in 0.05M sulfuric acid for 2 h at 100° yielded a syrup that by t.l.c. showed two closely adjacent spots, $R_{Me\,\alpha\text{-}G}$ 1.36 and 1.43 (solvent *E*). The $R_{Me\,\alpha\text{-}G}$ values for authentic 2-deoxy-2-iodo-D-glucose and 2-deoxy-2-iodo-D-mannose were 1.36 and 1.43, respectively.

Solvent effect on the iodinolysis of mercurial glycosides **1a** *and* **2**. — In each experiment the mercurial glycoside (0.10 mmole) was dissolved (or suspended in the case of carbon disulfide and carbon tetrachloride) in a solvent (2.00 ml) and to this solution (or suspension) was added iodine (0.20 mmole) and methyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside (0.050 mmole, internal standard), and the mixture was kept for 2 h at 25°. The reaction mixture was evaporated to dryness and the residue was extracted with chloroform (2.00 ml). The unextracted solid mass was washed with chloroform (1.00 ml). The combined extract and washings were shaken with 2% sodium thiosulfate (3.00 ml), followed by water (3.00 ml) twice. The chloroform layer was evaporated to dryness to give a syrup. The yields of iodinated derivatives were almost quantitative in all instances. Subsequently, the syrup was dissolved in 0.05M methanolic sodium methoxide (1.00 ml). After 1 h the solution was decationized with Amberlite IR-120 (H^+) resin (0.1 g) and evaporated to dryness. G.l.c. examination of the trimethylsilyl derivatives indicated that all reaction mixtures obtained from the mercurial glycoside **1a** gave peaks having $RRT_{Me\,\alpha\text{-}G}$ 3.22 and 3.84, which correspond to methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-β-D-glucopyranoside (**8**) and its β-D-*manno* isomer (**13**), respectively. All reaction mixtures obtained from the mercurial glycoside **2** gave peaks having $RRT_{Me\,\alpha\text{-}G}$ 1.65 and 2.90, which correspond to methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranoside (**11**) and its α-D-*gluco* isomer (**6**). The yields (%) of **8** and **13** from **1a** for the solvents indicated were: carbon disulfide 45.5, 54.5; carbon tetrachloride 45.8, 54.2; chloroform 45.6, 54.4; dichloromethane 45.8, 54.2; acetone 49.6, 50.4; ethanol 50.2, 49.8; methanol 50.5, 49.5; and acetonitrile 50.7, 49.3, respectively. The yields (%) of **6** and **11** from **2** for the solvents indicated were: carbon disulfide 61.6, 38.4; carbon tetrachloride 53.2, 46.8; chloroform 51.7, 48.3; dichloromethane 49.8, 50.2; acetone 43.5, 56.5; ethanol 43.3, 56.7; methanol 41.7, 58.3; and acetonitrile 38.1, 61.9, respectively.

*Iodinolysis of methyl 2-acetoxymercuri-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-talopyranoside* (**3**). — The mixture obtained from the reaction of the mercurial glycoside **3** (2.00 mmoles) and iodine (4.00 mmoles) in methanol (25 ml) for 2 h was processed as described for the iodinolysis of **1a**. The yield of mercuric iodide was 0.84 g (92%). From the chloroform extract there was obtained a syrup (0.82 g), which gave a single spot on t.l.c. The crude product was purified on a column of silica gel to give a syrupy mixture (0.80 g, 90%) of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-galactopyranoside (**17**) and its α-D-*talo* isomer (**19**), $[\alpha]_D^{35}$ −15.3° (*c* 5.7, chloroform); $R_{Me\,\alpha\text{-}GAc}$ (t.l.c.) 1.56 (solvent *C*), 1.26 (solvent *D*). The p.m.r. spectrum indicated the presence of methoxyl protons resonating at τ 6.56 (**19**) and 6.59 (**17**) and having relative peak-areas of 37:63, respectively. Anomeric-proton signals were observed at τ 5.12 (**17**) and 5.14 (**19**), having spacings of 3.0 and 3.2 Hz, respectively.

Anal. Calc. for $C_{13}H_{19}IO_8$: C, 36.30; H, 4.45; I, 29.50. Found: C, 36.42; H 4,.44; I, 29.47.

Deacetylation of the iodinated glycoside mixture **17** *and* **19**. — The mixture of **17** and **19** was deacetylated as described for the deacetylation of **8** to give quantitatively a syrupy mixture of methyl 2-deoxy-2-iodo-α-D-galactopyranoside (**18**) and its α-D-*talo* isomer (**20**). The trimethylsilyl derivatives obtained from this syrup gave two peaks on g.l.c. having $RRT_{Me\,\alpha-G}$ 2.08 (**18**) and 2.85 (**20**) and relative peak-areas of 63.1:36.9, respectively. A portion (57%) of this syrup crystallized from methanol–ether, and recrystallization from methanol afforded prisms of **18**, m.p. 140–142° (decomp), $[\alpha]_D^{35}$ +172° (*c* 0.9, methanol); R_{Glc} (p.c.) 3.69 (solvent *A*), 2.72 (solvent *B*).

Anal. Calc. for $C_7H_{13}IO_5$: C, 27.65; H, 4.31; I, 41.74. Found: C, 27.45; H, 4.40; I, 41.34.

Acetylation of the crystalline glycoside **18** with 2:1 pyridine–acetic anhydride yielded syrupy **17**, $[\alpha]_D^{35}$ +133° (*c* 1.3, chloroform); p.m.r. data: τ 4.72 (1-proton quartet, H-3, $J_{3,4}$ 3.2 Hz), 4.74 (1-proton quartet, H-4, $J_{4,5}$ 1.6 Hz), 5.12 (1-proton doublet, H-1, $J_{1,2}$ 3.0 Hz), 5.75 (1-proton octet, H-2, $J_{2,3}$ 12.6 Hz, $J_{2,5}$ 1.1 Hz), 5.7–6.0 (3-proton multiplet, H-5, H-6, H-6'), 6.59 (3-proton singlet, OMe), 7.78 (3-proton singlet, OAc), and 7.96 (6-proton singlet, OAc).

Anal. Calc. for $C_{13}H_{19}IO_8$: C, 36.30; H, 4.45; I, 29.50. Found: C, 36.24; H, 4.51; I, 29.72.

From the mother liquor of **18**, syrupy **20** (42%) (contaminated with a small amount of **18**) was obtained; R_{Glc} (p.c.) 3.67 (solvent *A*), 2.74 (solvent *B*).

Anal. Calc. for $C_7H_{13}IO_5$: C, 27.65; H, 4.31; I, 41.74. Found: C, 27.38; H, 4.42; I, 41.57.

*Iodinolysis of 2-acetoxymercuri-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-glucopyranose* (**4**). — The mixture obtained from the reaction of the mercurial adduct **4** (2.00 mmoles) and iodine (4.00 mmoles) in methanol (25 ml) for 2 h was processed as in the iodinolysis of **1a**. The yield of mercuric iodide was 0.91 g (100%). From the chloroform extract there was obtained a syrup (0.83 g), which was fractionated on a column of silica gel (Wakogel C-200, 50 g, 2.0×45 cm) with 7:3 ether–hexane. From the 130–160-ml fraction syrupy 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-glucopyranose (**10**, 0.42 g, 50%) was obtained. This syrup crystallized during one week from ether–hexane as prisms, m.p. 122–123°, $[\alpha]_D^{35}$ +166° (*c* 1.1, chloroform); $R_{Me\,\alpha-GAc}$ (t.l.c.) 1.09 (solvent *C*), 1.08 (solvent *D*); p.m.r. data: τ 4.45 (1-proton quartet, H-4, $J_{4,5}$ 11.2 Hz), 4.57 (1-proton doublet, H-1, $J_{1,2}$ 3.0 Hz), 5.01 (1-proton quartet, H-3, $J_{3,4}$ 9.1 Hz), 5.85 (1-proton quartet, H-2, $J_{2,3}$ 9.3 Hz), 5.5–6.2 (3-proton multiplet, H-5, H-6, H-6'), 6.7 (1-proton broadened singlet, OH), 7.93 (6-proton singlet, OAc), and 7.98 (3-proton singlet, OAc).

Anal. Calc. for $C_{12}H_{17}IO_8$: C, 34.63; H, 4.12; I, 30.50. Found: C, 34.68; H, 4.12; I, 30.19.

A portion of **10** was methylated with a large excess of methyl iodide and silver carbonate in acetone overnight. The reaction mixture was filtered and the filtrate was evaporated to dryness. The residual syrup was deacetylated with methanolic sodium

methoxide as described for the deacetylation of **8**, and the product was subjected to trimethylsilylation. G.l.c. indicated the presence of intense peaks having $RRT_{Me\,\alpha\text{-}G}$ 2.90 and 3.22. These retention values were identical with those for the corresponding derivatives of **7** and **9**, respectively.

From the 210–280-ml fraction syrupy 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranose (**15**, 0.24 g, 29%) was obtained, $[\alpha]_D^{35}$ −18.8° (*c* 1.4, chloroform); $R_{Me\,\alpha\ GAc}$ (t.l.c.) 1.00 (solvent *C*), 0.86 (solvent *D*); p.m.r. data: τ 4.43 (1-proton doublet, H-1, $J_{1,2}$ 1.0 Hz), 4.65 (1-proton sextet, H-4, $J_{4,5}$ 9.3 Hz), 5.24 (1-proton quartet, H-2, $J_{2,3}$ 4.7 Hz), 5.39 (1-proton quartet, H-3, $J_{3,4}$ 9.3 Hz), 5.4–5.9 (3-proton multiplet, H-5, H-6, H-6'), 4.5 (1-proton broadened signal, OH), 7.90 (3-proton singlet, OAc), 7.93 (3-proton singlet, OAc), and 7.96 (3-proton singlet, OAc).

Anal. Calc. for $C_{12}H_{17}IO_8$: C, 43.63; H, 4.12; I, 30.50. Found: C, 34.69; H, 4.59; I, 30.41.

Methylation, followed by deacetylation yielded a syrup, which, after trimethylsilylation, gave intense peaks having $RRT_{Me\,\alpha\text{-}G}$ 1.65 and 3.84. These retention values were identical with those of the corresponding derivatives of **12** and **14**, respectively.

From the 160–210-ml fraction a syrupy mixture of **10** and **15** (0.16 g, 19%) was obtained, which was not further fractionated.

*Iodinolysis of 2-acetoxymercuri-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose* (**5**). — The mixture obtained from the reaction of the mercurial adduct **5** (2.00 mmoles) and iodine (4.00 mmoles) in methanol (25 ml) for 4 h was processed as described for the iodinolysis of **1a**. The yield of mercuric iodide was 0.86 g (96%). From the chloroform extract there was obtained a syrupy mixture (0.89 g) of iodo compounds, which was fractionated on a column of silica gel (Wakogel C-200, 50 g, 2.0 × 45 cm) with 7:3 benzene–ethyl acetate. From the 80–110-ml and 150–180-ml fractions were obtained syrupy products, A (0.28 g) and B (0.08 g), respectively, after evaporation of solvent. From the 110–150-ml fraction a mixture of A and B (0.51 g) was obtained, which was further fractionated on a similar silica gel column with 4:1 ether–hexane. From the 100–130-ml and 140–190-ml fractions additional crops of A (0.27 g) and B (0.17 g) were obtained.

The combined crops of A (total yield, 61%) had $[\alpha]_D^{21}$ +53.5° (*c* 2.2, chloroform); $R_{Me\,\alpha\text{-}GAc}$ (t.l.c.) 1.50 (solvent *C*), 1.27 (solvent *D*). The p.m.r. spectrum was identical with that of a mixture of methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-β-D-glucopyranoside (**8**) and its α-D-*manno* isomer (**11**). The relative areas of methoxyl-proton signals appearing at τ 6.43 (**8**) and 6.59 (**11**) were 36:64. The syrupy mixture A was deacetylated and trimethylsilylated. G.l.c. examination showed two peaks, $RRT_{Me\,\alpha\text{-}G}$ 3.22 and 3.84, with relative peak-areas of 36:64.

Anal. Calc. for $C_{13}H_{19}IO_8$: C, 36.30; H, 4.45; I, 29.50. Found: C, 36.17; H, 4.51; I, 28.82.

The syrup B (total yield, 27%) had $[\alpha]_D^{21}$ +21.2° (*c* 3.2, chloroform); $R_{Me\,\alpha\text{-}GAc}$ (t.l.c.) 1.31 (solvent *C*), 0.75 (solvent *D*); p.m.r. data: τ 3.65 (1-proton singlet, H-1, $J_{1,2}$ 0.3 Hz), 4.57 (1-proton triplet, H-4, $J_{4,5}$ 9.1 Hz), 5.43 (1-proton quartet, H-3, $J_{3,4}$ 9.3 Hz), 5.79 (1-proton doublet, H-2, $J_{2,3}$ 4.1 Hz), 5.4–6.0 (3-proton multiplet,

H-5, H-6, H-6'), 7.85 (3-proton singlet, OAc) 7.90 (6-proton singlet, OAc), and 7.93 (3-proton singlet, OAc).

Anal. Calc. for $C_{14}H_{19}IO_9$: C, 36.81; H, 4.31; I, 27.29. Found: C, 36.78; H, 4.34; I, 27.69.

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