Following another 10 min of reaction the characteristic fluorescence of the immonium salt (9) had almost disappeared and the reaction mixture was cooled to room temperature. After filtration and basifying to a pH of 9 with concentrated ammonium hydroxide, 10 ml of chloroform was added. The layers were separated and the aqueous layer was extracted twice with 5-ml portions chloroform. The chloroform extracts were combined, dried with sodium sulfate, filtered, and evaporated under a reduced nitrogen atmosphere. The residue (71 mg) was triturated with 10 ml of boiling ethanol, filtered hot, and concentrated to 3 ml. With constant stirring, 15 ml of ether was added and the resulting precipitate (54 mg, 0.086 mmol, 56%) of (±)-1-deaza-1-thiareserpine was collected. A small quantity (~1 mg) was subjected to thin layer chromatography on Woelm activity II alumina elution with a mixture of chloroform–methanol–benzene (10:3:1)) and showed a single dark spot (R_f 0.65) under ultraviolet light. Recrystallization from ethanol–ether (9:1) gave an analytical sample (21 mg), mp 188–191° (sealed capillary), of fine, pure white crystals. The infrared spectrum of thiareserpine ($CHCl_3$) showed absorption at 3032, 2930, 2860, 1735, 1590, 1505, 1465, 1420, 1340, 935, 800, 720, 680 cm^{-1}. The ultraviolet spectrum had λ_{max} at 213 mμ (ε 58,700), 231 shoulder (27,100), 244 shoulder (20,200), 267 (22,200).

Anal. Calcd for $C_{33}H_{39}O_9NS$: C, 63.34; H, 6.28; N, 2.24. Found: C, 63.08; H, 6.75; N, 2.53.

Registry No.—4-Methoxythianaphthyl-3-acetamide, 14679-05-1; 6-methoxythianaphthyl-3-acetamide, 14679-06-2; **3**, 14679-07-3; picrate of **3**, 14679-49-3; 2,4-dinitrophenylhydrozone of **7** (R = H), 14679-08-4; **8**, 14745-99-4; **9**, 14679-09-5; **10**, 14679-10-8.

The Synthesis of Three Fully Acetylated Aldobiouronic Acid Methyl Esters, Including 6-*O*-(Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate)-tetra-*O*-acetyl-β-D-glucopyranose

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6-*O*-α-D-Glucopyranuronosyl-D-glucose (isomaltouronic acid) is a possible moiety in the capsular polysaccharide of *Diplococcus pneumoniae* Type II. The synthesis of its fully acetylated methyl ester starting from β-isomaltose octaacetate is described. Improvements in the syntheses of the fully acetylated methyl esters of 6-*O*-β-D-glucopyranuronosyl-D-glucose (gentiobiouronic acid) and 4-*O*-α-D-glucopyranuronosyl-D-glucose (maltouronic acid) are also reported.

The structure of the capsular polysaccharide of *Diplococcus pneumoniae* Type II has been under investigation for some time.[2-5] It is known that this antigenic capsular polysaccharide, S-II, contains terminal as well as intercatenary glucuronic acid residues. Recent additional findings[6] concerning the structure of S-II have clarified much about the type of linkages involved in this polysaccharide as well as some of the anomeric configurations. Still, the anomeric configuration of the intercatenary, presumably 1–6 linked, glucuronosylglucose is still open to question. Comparison of the inhibition of the antigen–antibody precipitation in the S-II–anti S-II system by isomaltouronic acid and gentiobiouronic acid could yield information about the anomeric configuration of this linkage. Similarly, the inhibition of the same system by maltouronic and cellobiouronic acids could shed light on the immunological importance of the anomeric configuration of the terminal glucuronosyl linkage.

The terminal uronic acid in S-II behaves unexpectedly, in that, although the molecule has terminal cellobiouronic acid units,[6] rabbit serum obtained against a synthetic antigen containing this acid as terminal side chains will not agglutinate cells of *D. pneumoniae* Type II, although this serum will agglutinate cells of *D. pneumoniae* Type III or VIII,[7] even though the latter two types only have *intercatenary* cellobiouronic acid.[8-10] It appears that the immunological specificity attributable to the terminal acid group in S-II does not seem to be very sensitive to the fact that the acid is glycosidically linked to glucose by a β linkage.

Work on the serological inhibition reaction now in progress in collaboration with Dr. M. Heidelberger, might be expected to shed light on this point and will be reported elsewhere.

The synthesis of 6-*O*-α-D-glucopyranuronosyl-D-glucose (isomaltouronic acid), was initiated starting from 6-*O*-[α-D-glucopyranosyl]-β-D-glucopyranose octaacetate (β-isomaltose octaacetate) (**1**) which was obtained from the acid reversion of glucose following the method of Wolfrom and Thompson.[11] It was deacetylated and tritylated at the 6′ position in pyridine solution. Without further isolation, it was then acetylated and the resulting hepta-*O*-acetyl-6′-*O*-tritylisomaltose (**2**) was isolated by chromatography on silica gel in 61.5% yield. The nmr spectrum indicated that **2** was a mixture of α and β anomers, a finding that was expected, as tritylation in pyridine prior to acetylation would cause anomerization. Detritylation of **2** by brief treatment in acetic acid with 1 mol equiv of hydrogen bromide[12] gave 1,2,3,4,2′,3′,4′-hepta-*O*-acetylisomaltose (**3**) in 83% yield. The heptaacetate **3** was then oxidized with potassium permanganate in acetic acid, and the car-

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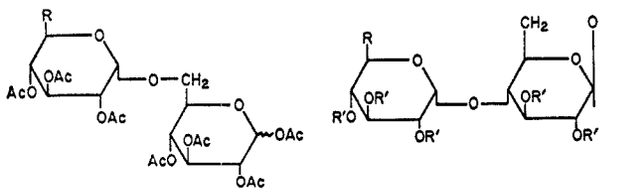
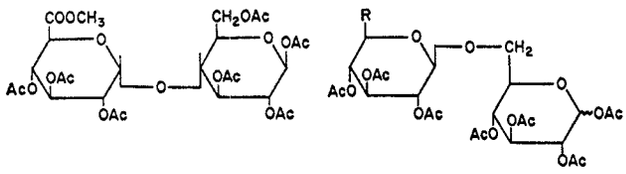


1, R = CH_2OAc (β 1-O-acetyl)
2, R = CH_2O trityl
3, R = CH_2OH
4, R = $COOCH_3$
5, R = $COOCH_3$ (β 1-O-acetyl)
6, R = CH_2OAc; R′ = Ac
7, R = CH_2O trityl; R′ = COC_6H_5
8, R = CH_2OH; R′ = COC_6H_5
9, R = COOH; R′ = COC_6H_5
10, R = $COOCH_3$; R′ = COC_6H_5



11

12, R = CH_2O trityl
13, R = CH_2OH
14, R = $COOCH_3$ (β 1-O-acetyl)

boxylic acid produced was directly esterified with diazomethane to give methyl hepta-*O*-acetylisomaltouronate (**4**) in 58% yield, showing that acetyl migration[13] in 1,2,3,4,2′,3′,4′-hepta-*O*-acetylisomaltose is insignificant under these conditions. This compound, a mixture of the α and β anomers, could not be induced to crystallize. Consequently, **4** was converted into the 1-bromo derivative, hepta-*O*-acetylisomaltouronosyl bromide methyl ester, which was treated with silver acetate in benzene according to Wolfrom and Fields[14] to give crystalline methyl hepta-*O*-acetyl-β-D-isomaltouronate (**5**) in 66% yield.

The synthesis of maltouronic acid, 4-*O*-α-D-glucopyranuronosyl-D-glucose, was first reported by Hirasaka,[15] who subjected benzyl β-maltoside to catalytic oxidation. That the C-6′, rather than the C-6, position was attacked, may probably be attributed to steric hindrance of C-6 by the phenyl group at C-1. Since the removal of small amounts of the C-6 oxidized material may prove cumbersome, and since the presence of such an impurity might cloud results of immunochemical tests, we used an alternative route for the preparation of **11** analogous to that used by Lindberg and Selleby[16] for the preparation of cellobiouronic acid. 1,6-Anhydro-4-*O*-α-D-glucopyranosyl-β-D-glucopyranose hexaacetate was prepared *via* phenyl β-maltoside by the procedure of Lindberg.[17] The hexaccetate (**6**) was deacetylated, monotritylated, and then benzoylated to yield crystalline 1,6-anhydro-4-*O*-(6′-*O*-trityl-α-D-glucopyranosyl)-β-D-glucopyranose pentabenzoate (**7**) in 54% yield. Next, **7** was reductively detritylated with hydrogen over palladium black to give, after purification by chromatography over silica gel, 1,6-anhydro-2,3,2′,3′,4′-penta-*O*-benzoylmaltose (**8**) as colorless needles in 92% yield. When **8** was oxidized with potassium permanganate in glacial acetic acid, the product, 1,6-anhydropenta-*O*-benzoylmaltouronic acid (**9**), was obtained in crystalline form, also in 92% yield. Reaction of **9** with diazomethane yielded crystalline methyl 1,6-anhydropenta-*O*-benzoylmaltouronate (**10**). Treatment of **9** with sodium methoxide and subsequent acid-catalyzed hydrolysis of the deacetylated **9** with aqueous 0.5 *N* sulfuric acid gave a product from which amorphous maltouronic acid was isolated in 48% yield by cellulose chromatography. Its rotation is in excellent agreement with the one reported previously, while the derived methyl hepta-*O*-acetyl-β-D-maltouronate (**11**) also has constants in close agreement with the ones reported.[18] Of course it has previously been established that, especially in hexuronosyl hexoses, the 1,6-anhydro bridge may be opened without hydrolysis of the intersaccharidic linkage.[16,19,20]

Gentiobiouronic acid was first synthesized by Hotchkiss and Goebel.[21] These workers obtained the aldobiouronic acid by Koenigs–Knorr condensation of methyl acetobromoglucuronate with 1,2,3,4-tetra-*O*-acetyl-β-D-glucose. The synthesis reported here starts from 6-*O*-[β-D-glucopyranosyl]-D-glucose (gentiobiose) and takes a course analogous to that of our synthesis of isomaltouronic acid. Gentiobiose was monotritylated in pyridine solution. The reaction could be conveniently followed by thin layer chromatography on Avicel microcrystalline cellulose.[22] After the completion of the reaction, the compound was acetylated *in situ* and purified by chromatography on silica gel to give 1,2,3,4,2′,3′,4′-hepta-*O*-acetyl-6′-*O*-tritylgentiobiose (**12**) in 55% yield as a mixture of the anomeric acetates, as shown by its nmr spectrum. Detritylation of **12** was achieved by brief treatment with 1 mol equiv of hydrogen bromide[12] to give crystalline 1,2,3,4,2′,3′,4′-hepta-*O*-acetylgentiobiose (**13**), a mixture of anomers as shown by its nmr. Potassium permanganate oxidation of **13** in acetic acid solution gave hepta-*O*-acetylgentiobiouronic acid which was esterified directly with diazomethane to yield crystalline methyl hepta-*O*-acetylgentiobiouronate in 50% yield. The material, although crystalline, was shown by nmr spectroscopy to be a mixture of anomeric acetates. Treatment of this ester with hydrogen bromide in acetic acid, followed by reaction of the 1-bromo derivative with silver acetate in benzene,[14] gave, in 50% yield, crystalline methyl hepta-*O*-acetyl-β-D-gentiobiouronate (**14**) identical in melting point and optical rotation with that obtained by Hotchkiss and Goebel.[21]

A few comments concerning the nmr spectra of some of the intermediates are in order. The spectrum of β-isomaltose octaacetate (**1**) with its H-1 showing as a doublet at τ 4.2 ($J_{1,2}$ = 8 Hz) had signals for six protons in the region τ 5.7–6.4. Obviously they were two H-6′, two H-6, H-5′, and H-5 protons. On the basis of higher deshielding effect of an –OAc compared to an –*O*–glycosyl group, the broad signal at τ 5.8 was assigned to two H-6′ protons and that at 6.23 was assigned to two H-6 protons. When the 6′-*O*-acetyl group was removed, as in the hepta-*O*-acetate **3**, the signal at τ 5.8 of compound **1** shifted to 6.38, undoubtedly owing to the removal of this more de-

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shielding moiety. The anomeric acetates of methyl isomaltouronate (**4**) showed doublets centered at τ 3.76 and 4.33 for α and β diastereoisomers, respectively, in close resemblance to the heptaacetate **3** which is also a mixture of two anomers. In addition, the H-5′ of **4** was shifted downfield to τ 5.7 ($J_{4,5}$ = 10.5 Hz) owing to the deshielding effect of the –COOMe group. The CH_3 of the methyl ester, appearing as a sharp singlet at τ 6.28, was overlapped with the two H-6 protons and the H-5 proton in about the same region. The spectrum of methyl hepta-*O*-acetyl-β-D-isomaltouronate showed only one anomeric hydrogen as a doublet at τ 4.35 ($J_{1,2}$ = 8.5 Hz).

The spectra of the gentiobiose series could be explained on a similar type of reasoning. The spectrum of 1,6-anhydro-6′-*O*-tritylpenta-*O*-benzoylmaltose (**7**) showed five benzoyl groups, one trityl group, and a two-proton signal at τ 6.60 along with other peaks. The signal at τ 6.60, which was assigned to two H-6′ hydrogens (shielded by the trityl group), was shifted to 6.16 when the trityl group was replaced by hydrogen as in compound **8**. The hydroxy compound **8** and the acid **9** which were crystallized from ether, showed exactly 1 mol of ether of crystallization in their nmr spectra. The acid **9** gave an ester with diazomethane which also gave a characteristic signal for the methyl ester in the nmr spectrum. Pure methyl hepta-*O*-acetylmaltouronate had a signal for H-1 at τ 4.20 as a doublet ($J_{1,2}$ = 8 Hz) and a singlet for the methyl ester at 6.23.

Experimental Section[23]

1,2,3,4,2′,3′,4′-Hepta-*O*-acetyl-6′-*O*-tritylisomaltose (2).—Crystalline β-isomaltose octaacetate (**1**, 10 g) was deacetylated with 0.03 *N* sodium methoxide in methanol for 2 hr. The reaction mixture was concentrated to dryness and pyridine was distilled off twice under vacuum. The residue was taken up in dry pyridine (200 ml) and tritylated with 15 g of tritylchloride with stirring for 3 days. Acetic anhydride (40 ml) was added and after 3 days the mixture was poured into ice water (1.5 l.) with stirring. The solid material was collected by filtration, dried under vacuum, dissolved in a small volume of benzene, and added to the top of a column of silica gel (400 g, Merck Darmstad 0.05–0.2 mm) which was eluted with benzene–ether (2:1). After removal of some triphenylcarbinol and higher tritylated derivatives there was obtained amorphous 8 g (61.5% yield) of 1,2,3,4,2′,3′,4′-hepta-*O*-acetyl-6′-*O*-tritylisomaltose (**2**), $[\alpha]^{20}D$ +100.2° (*c* 1, chloroform).

The nmr spectrum showed two doublets for H-1, centered around τ 3.68 and 4.26, indicating the presence of both α- and β-acetates. The spectrum had a general resemblance to **1** and also confirmed the presence of one trityl group in the molecule.

Anal. Calcd for $C_{45}H_{50}O_{18}$: C, 61.50; H, 5.73. Found: C, 61.72; H, 5.68.

1,2,3,4,2′,3′,4′-Hepta-*O*-acetylisomaltose (3).—A solution of **2** (4.5 g) in acetic acid (30 ml) was treated for 2 min with a solution of hydrogen bromide (0.4 g) dissolved in acetic acid (10 ml), while shaking vigorously. The mixture was immediately filtered through a sintered glass funnel into ice water (300 ml), and the heptaacetate was extracted with four 100-ml portions of chloroform. The extract was washed with water, saturated sodium bicarbonate, and, again, water. The solution was dried over magnesium sulfate and concentrated to dryness; the product was purified by chromatography on silica gel using benzene–ether (20:60). The pure 1,2,3,4,2′,3′,4′-hepta-*O*-acetylisomaltose (**3**) was obtained in a yield of 2.7 g, $[\alpha]^{20}D$ +117.8° (*c* 0.7, chloroform).

Anal. Calcd for $C_{26}H_{36}O_{18}$: C, 49.06; H, 5.70. Found: C, 49.10; H, 5.66.

6-*O*-(Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate)-tetra-*O*-acetyl-β-D-glucopyranose (5).—To a solution of **3** (1.9 g) in acetic acid (20 ml), finely powdered potassium permanganate (1.3 g) was added slowly with stirring at room temperature for 5 days, at which time thin layer chromatography on silica gel G (benzene–ether–acetic acid, 33:66:2.5) showed the reaction to be nearly complete. Excess permanganate was destroyed with sodium oxalate, and the mixture was poured into water (250 ml). The acid was extracted with five 80-ml portions of chloroform, and the extract was washed with water, dried over magnesium sulfate, and concentrated to a white amorphous foam. This product was esterified in methanol solution with diazomethane in ether and purified by chromatography over silica gel, using benzene–ether (1:2), to yield methyl hepta-*O*-acetylisomaltouronate (**4**, 1.15 g) as an anomeric mixture of the acetates as revealed by the nmr spectrum. The material could not be induced to crystallize. Consequently, **4** (0.6 g) was dissolved in 32% hydrogen bromide in glacial acetic acid (10 ml) and the mixture shaken at room temperature for 7 min. Chloroform was added and the solution was washed thrice with water, dried over sodium sulfate, and concentrated to dryness. It was taken up in dry benzene (50 ml), and silver acetate (6 g) was added. Stirring was continued for 16 hr after which solids were removed by filtration through Celite, and the filtrate was concentrated to dryness. The product was then purified by chromatography over silica gel, using benzene–ether (1:1) as the eluent. From ethanol, pure 6-*O*-(methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate)tetra-*O*-acetyl-β-D-glucopyranose (**5**) was obtained as fine needle-shaped crystals: mp 169–170°; $[\alpha]^{20}D$ +96.1° (*c* 0.5, chloroform).

The nmr spectrum showed a signal for H-1 at τ 4.35 and the signal at 6.28 for the methyl ester.

Anal. Calcd for $C_{27}H_{36}O_{19}$: C, 48.80; H, 5.46. Found: C, 48.66; H, 5.41.

1,6-Anhydropenta-*O*-benzoyl-6′-*O*-tritylmaltose (7).—A 6.7-g sample of 1,6-anhydromaltose hexaacetate[17] (**6**) was deacetylated in 0.03 *N* barium methoxide. The product was dissolved in pyridine (140 ml) and trityl chloride (5.7 g) was added. After 3 days benzoyl chloride (16 g) was added while cooling, and the reaction mixture was left at room temperature overnight. Methanol (10 ml) was added, and after 0.5 hr the solution was concentrated at 40° under vacuum to about 30 ml. Chloroform (200 ml) was added, and the solution was washed thrice with water and dried over magnesium sulfate. Concentration, followed by dissolution of the residue in ethyl acetate (30 ml) and ethanol (100 ml), gave crystalline 1,6-anhydropenta-*O*-benzoyl-6′-*O*-tritylmaltose (**7**), mp 230–231°. From the mother liquor, an additional 2 g was recovered after chromatography over silica gel (benzene–ether, 7:3) for a total yield of 6.8 g (54%) of **7**, $[\alpha]^{20}D$ +49° (*c* 1.0, chloroform).

Anal. Calcd for $C_{66}H_{56}O_{15}$: C, 72.78; H, 5.18. Found: C, 72.67; H, 5.22.

1,6-Anhydro-2,3,2′,3′,4′-penta-*O*-benzoylmaltose (8).—Palladium chloride (1.2 g) was added to a solution of the trityl compound **7** (6.2 g) dissolved in dioxane (150 ml, purified by passage through a column of aluminum oxide, Brockman Grade I) and the suspension was stirred under hydrogen at atmospheric pressure for 18 hr. Silver carbonate (4 g) was added and the solids were removed by filtration. The filtrate was concentrated and chromatographed over silica gel using chloroform–ether (9:1) as the eluent. After pooling of the correct fractions, they were concentrated and dissolved in ether. Crystallization was almost immediate. A yield of 4.8 g (92%) of 1,6-anhydro-2,3,2′,3′,4′-penta-*O*-benzoylmaltose was obtained: mp 136–138°; $[\alpha]^{20}D$ +53.6° (*c* 0.85, chloroform). The nmr spectrum showed the presence of exactly 1 mol of ether of crystallization. Tritylation of **8** yielded the original 6′-*O*-trityl derivative **7**.

Anal. Calcd for $C_{47}H_{40}O_{15}O \cdot (C_2H_5)_2$: C, 66.66; H, 5.48. Found: C, 66.53; H, 5.66.

1,6-Anhydropenta-*O*-benzoylmaltouronic Acid (9).—The detritylated compound **8** (4.6 g) dissolved in glacial acetic acid (45 ml) was oxidized with potassium permanganate (3 g) for 3 days as described for **4**. The product, which was obtained as a colored syrup (4.3 g, 92%), was purified by chromatography over silica gel, using chloroform–ether–acetic acid (3:3:0.2) as the eluent. From ether, crystals were obtained which contained

(23) All melting points are corrected. Nmr spectra were taken in $CdCl_3$ on a 60-Mc Varian Instrument using tetramethylsilane as an internal reference. Elemental analyses were performed by the Section on Analytical Services and Instrumentation of this laboratory, for which we wish to express our graditude.

1 mol of ether of crystallization, as shown by its nmr spectrum. The 1,6-anhydropenta-*O*-benzoylmaltouronic acid (**9**) has mp 152–153°, $[\alpha]^{20}D$ +46° (*c* 0.4 chloroform).

Anal. Calcd for $C_{47}H_{36}O_{16}\cdot O(C_2H_5)_2$: C, 65.66; H, 5.19. Found: C, 65.98; H, 4.90.

Treatment of **9** with diazomethane in the usual fashion gave the methyl ester (**10**), mp 169–171°.

4-*O*-(Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate)-tetra-*O*-acetyl-β-D-glucose (11).—The crystalline acid **9** (3.5 g) was debenzoylated in 0.05 *N* sodium methoxide solution (60 ml) for 2 hr. The solution, after neutralization with Amberlite IR-120 exchange resin, was freed from methyl benzoate. The deacetylated product was heated at 95–100° in 0.5 *N* aqueous sulfuric acid for 12 hr. After neutralization with barum carbonate, and removal of cations by ion exchange, the product was isolated by chromatography over cellulose, using ethyl acetate–acetic acid–water (18:7:8) as the eluent to yield 650 mg (48%) of 4-*O*-α-D-glucopyranuronosyl-D-glucose (maltouronic acid), $[\alpha]^{20}D$ +115° (*c* 0.17, water). Dutton and Slessor[18] have reported $[\alpha]^{20}D$ +116° for this acid. The derived 4-*O*-(methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranosyluronate)tetra-*O*-acetyl-β-D-glucose (**11**), prepared by esterification of maltouronic acid with diazomethane followed by acetylation with sodium acetate and acetic anhydride and crystallization from ethanol, had mp 199–200°, $[\alpha]^{20}D$ +71° (*c* 0.72 chloroform).

Anal. Calcd for $C_{27}H_{36}O_{19}$: C, 48.80; H, 5.46. Found: C, 48.95; H, 5.58.

1,2,3,4,2′,3′,4′-Hepta-*O*-acetyl-6′-*O*-tritylgentiobiose (12).—Gentiobiose (8 g) was tritylated in pyridine solution and then acetylated *in situ* as described in the preparation of **2**. The hepta-*O*-acetyl-6′-*O*-tritylgentiobiose (**12**) (12.5 g) obtained had $[\alpha]^{20}D$ +38° (*c* 1.5, chloroform). The nmr spectrum showed the presence of both anomeric acetates.

Anal. Calcd for $C_{45}H_{50}O_{18}$: C, 61.50; H, 5.73. Found: C, 61.66; H, 6.03.

1,2,3,4,2′,3′,4′-Hepta-*O*-acetylgentiobiose (13).—In order to remove the trityl group from **12** (9 g) it was dissolved in acetic acid (60 ml) and treated with 1 equiv of hydrogen bromide exactly as described in the preparation of **3**. After purification by silica gel chromatography as described for **3**, the pure 1,2,3,4,2′,3′,4′-hepta-*O*-acetylgentiobioise (**13**), was crystallized from ethanol yielding 5.4 g (83%): mp 162–167°; $[\alpha]^{20}D$ +24.7° (*c* 1.0 chloroform).

Anal. Calcd for $C_{26}H_{36}O_{18}$: C, 49.06; H, 5.70. Found: C, 49.01; H, 5.81.

6-*O*-(Methyl-2,3,4-tri-*O*-acetyl-β-D-glucopyranosyluronate)-tetra-*O*-acetyl-β-D-glucopyranose (14).—Gentiobiose heptaacetate **13** (4 g), was dissolved in acetic acid (40 ml) and oxidized with potassium permanganate (2.7 g) exactly as described in the preparation of **4**. Direct esterification of the acid with diazomethane in ether gave 1.91 g (50%) of the desired 6-*O*-(methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosyluronate)tetra-*O*-acetyl-D-glucopyranose after purification by silica gel chromatography (benzene–ether, 1:2): mp 200–201° (after crystallization from methanol); $[\alpha]^{20}D$ −1.5° (*c* 1, chloroform).

Anal. Calcd for $C_{27}H_{36}O_{19}$: C, 48.80; H, 5.46. Found: C, 48.52; H, 5.36.

The above methyl ester, albeit crystalline, was still a mixture of anomeric acetates. It was therefore treated with hydrogen bromide, followed by silver acetate in benzene, as described for **5** to give 6-*O*-(methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranosyluronate)tetra-*O*-acetyl-β-D-glucose (**14**), in 50% yield: mp 200–202°, $[\alpha]^{20}D$ −11° (*c* 0.1, chloroform).

Registry No.—**2**, 15811-22-0; **3**, 15811-23-1; **5**, 15811-24-2; **7**, 15811-25-3; **8**, 15811-26-4; **9**, 15811-27-5; **10**, 15856-56-1; **11**, 4079-39-4; **12**, 15811-29-7; **13**, 15811-30-0; **14**, 15811-31-1.

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The Synthesis of 18,19-Dioxygenated Steroids by Intramolecular Radical Processes[1]

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By the application of known methods, especially intramolecular substitution reactions, pregnenolone has been converted into 18,19,20α- and 18,19,20β-trihydroxypregn-4-en-3-one. These compounds are possible metabolites from the perfusion of adrenal glands with progesterone.

The ability of adrenal tissue to oxygenate steroids at the angular methyl groups (C-18 and C-19) is well known.[2] Steroids functionalized at either of these positions have been isolated from adrenal tissue[2a–d] or formed by the action of adrenal preparations on exogenous steroidal substrates.[2e–g] These substances have been of considerable interest as a result of their intrinsic biological activity (aldosterone, for instance), their role in hormone biosynthesis (19-hydroxy steroids), and the chemical challenge inherent in their preparation. This challenge has been met by the development of several methods[3] for the selective functionalization of "unactivated" carbon atoms.

Although steroids substituted at either C-18 or C-19 are well known and now, for the most part, easily available, the occurrence of steroids functionalized at *both* angular methyls has not yet been reported. (Allusion has been made to functionalization at C-18 of a 19-substituted steroid. The nature of the products was not disclosed.[3g]) We now report the synthesis of the isomeric 18,19-disubstituted pregnanetriols **1a** and **1b**. This synthesis was undertaken as a portion of our continuing program of synthesis of 18- and 19-substituted steroids[4] and to provide standard materials for a program of adrenal perfusion. Compound

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