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Note

Synthesis of α- and β-cellotriose hendecaacetates and of several 6,6′,6″-trisubstituted derivatives of methyl β-cellotrioside

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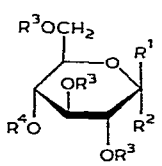
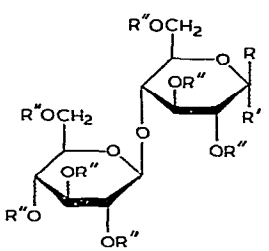
Hall and Lawler[1] reported that condensation of methyl 2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (**1**) with hepta-*O*-acetyl-α-cellobiosyl bromide (**6**) in the presence of silver oxide or silver carbonate gave methyl deca-*O*-acetyl-β-cellotrioside (**15**), which was then successively transformed into hendeca-*O*-acetyl-α- (**12**) and β-cellotriose (**13**) by a reaction sequence that involved acetolysis, saponification, and acetylation. The m.p. and optical rotation values given[1] for **15** differed significantly from those reported previously by Wolfrom and Haq[2], and the optical rotation values for **12** and **13**, obtained in the reaction described by Hall and Lawler[1] were not reported. In our hands, the reaction of **1** with **6** under the exact conditions described[1] gave no **15**, but led to extensive formation of crystalline 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-glucopyranose[3] (**7**), the physical constants of which were consistent with those of the compound that, Hall and Lawler[1] claimed, had structure **15**. Hall *et al.*[4] also reported that where 1,2,3,6-tetra-*O*-acetyl-α- (**2**) and -β-D-glucopyranose (**3**) were used, instead of **1**, as the aglycons in a similar condensation with **6**, *O*-β-D-glucopyranosyl-(1→4)-*O*-β-D-glucopyranosyl-(1→6)-α-



1 R^1 = OMe, R^2 = R^4 = H, R^3 = Ac
2 R^1 = R^4 = H, R^2 = OAc, R^3 = Ac
3 R^1 = OAc, R^2 = R^4 = H, R^3 = Ac
4 R^1 = H, R^2 = Br, R^3 = R^4 = Ac
5 R^1 = R^2 = H, OH, R^3 = R^4 = Ac



6 R = H, R′ = Br, R″ = Ac
7 R = H, R′ = OH, R″ = Ac

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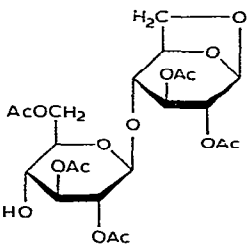
and -β-D-glucopyranose hendecaacetates, respectively, were formed, instead of the expected **12** and **13**, due to the migration of an acetyl group from O-6 to -4 in **2** and **3** during glycosidation; the physical constants given[4] for the latter trisaccharide derivative, however, differed from those of the compound prepared by other routes[5-7]. We were not able to repeat the condensation of **3** with **6** as described by Hall *et al.*[4]; under the conditions described, neither the (1→6)-linked trisaccharide derivative nor **13** could be obtained. We report here the synthesis of **12** and **13** by alternative routes, and the preparation of several 6,6′,6″-trisubstituted derivatives of methyl β-cellotrioside (**16**).

In the synthesis of **12**, treatment of 2,3,2′,3′,6′-penta-*O*-acetyl-1,6-anhydro-β-cellobiose[8] (**8**) with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**4**) in di-



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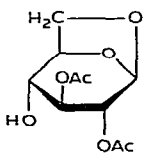

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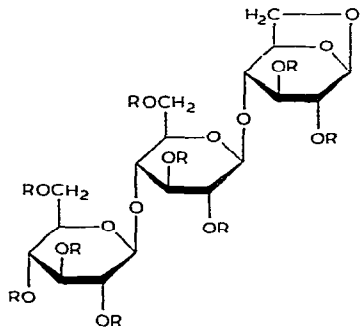
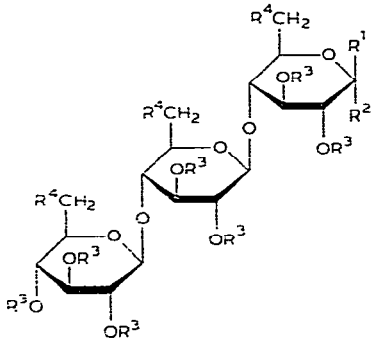


10 R = Ac
11 R = H

chloromethane, in the presence of silver trifluoromethanesulfonate (triflate) and 1,1,3,3-tetramethylurea[9], afforded a mixture that was shown by t.l.c. to contain 2,3,2′,3′,6′,2″,3″,4″,6″-nona-*O*-acetyl-1,6-anhydro-β-cellotriose (**10**) and unreacted **8**, in addition to 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (**5**), which arose from the hydrolysis of **4**. Compounds **8** and **10** have similar mobilities on t.l.c., so that acetylation was necessary to facilitate the isolation of **10**. The mixture was acetylated with acetic anhydride and sodium acetate, and the resulting mixture of products was fractionated by chromatography[10] on a dry-packed column of silica gel to give, in 53% yield, **10** as an amorphous powder. In the alternative synthesis of **10**, condensation of 2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose[11] (**9**) with **6** in 1,2-dichloroethane in the presence of mercuric cyanide[12] gave a mixture containing **10** and unreacted **9**, in addition of **7** derived from the hydrolysis of **6** (t.l.c.). Because of the similar rates of migration of **7**, **9**, and **10** in t.l.c., the mixture was acetylated, and the resulting acetylated mixture was fractionated by chromatography on a dry-packed column of silica gel to afford **10** in 40% yield. The samples of **10** obtained by both routes were identical in all respects. *O*-Deacetylation of **10** gave, in 95% yield, 1,6-anhydro-β-cellotriose (**11**) as an amorphous solid. The n.m.r. spectrum of **11** for a solution in deuterium oxide showed the H-1 resonance at the lowest field (δ 5.45)

as a broad singlet, in agreement with the previous observations obtained with 1,6-anhydro-β-maltotriose[13] and 1,6-anhydro-1(6)-thio-β-maltotriose[14], indicating the $^1C_4$(D) conformation of the 1,6-anhydro ring of **11** as the favored conformation. Acetolysis of **10** gave, in 82% yield, crystalline **12**, which was characterized by comparison with an authentic specimen obtained by the controlled acetolysis of cellulose[15].



12 R^1 = H, R^2 = R^4 = OAc, R^3 = Ac
13 R^1 = R^4 = OAc, R^2 = H, R^3 = Ac
14 R^1 = H, R^2 = Br, R^3 = Ac, R^4 = OAc
15 R^1 = OMe, R^2 = H, R^3 = Ac, R^4 = OAc
16 R^1 = OMe, R^2 = R^3 = H, R^4 = OH
17 R^1 = OMe, R^2 = H, R^3 = Ac, R^4 = OTs
18 R^1 = OMe, R^2 = H, R^3 = Ac, R^4 = I
19 R^1 = OMe, R^2 = R^4 = H, R^3 = Ac
20 R^1 = OMe, R^2 = R^3 = R^4 = H
21 R^1 = OMe, R^2 = H, R^3 = Ac, R^4 = Cl
22 R^1 = OMe, R^2 = R^3 = H, R^4 = Cl
23 R^1 = OMe, R^2 = H, R^3 = Ac, R^4 = N_3
24 R^1 = OMe, R^2 = H, R^3 = Ac, R^4 = NHAc
25 R^1 = OMe, R^2 = R^3 = H, R^4 = NHAc

In the synthesis of **13**, reaction[16,17] of **3** with **6** in the presence of silver triflate and 1,1,3,3-tetramethylurea in dichloromethane gave a mixture that contained **13**, unreacted **3**, and **7** (t.l.c.). As **3**, **7**, and **13** have similar t.l.c. mobilities, the mixture was acetylated to provide, in 39% yield after chromatographic fractionation, crystalline **13**, which was identified by comparison with an authentic specimen obtained from **12** by the procedure previously described[18].

Compounds **12** and **13** were converted into deca-*O*-acetyl-α-cellotriosyl bromide[19] (**14**) in crystalline form with hydrogen bromide in acetic acid. Methanolysis of **14** in the presence of mercuric cyanide in benzene gave, in 84% yield, crystalline **15** having physical constants in good agreement with those reported by Wolfrom and Haq[2]. *O*-Deacetylation of **15** furnished crystalline **16**; the optical rotation value agreed well with that described[2], but the m.p. was higher than that reported[2], suggesting that **16** crystallizes in two isomorphic forms.

Selective *p*-toluenesulfonylation of **16** with 3.6 mol. equiv. of reagent in pyridine, followed by acetylation, gave a mixture from which methyl 2,3,2′,3′,2″,3″,4″-hepta-*O*-acetyl-6,6′,6″-tri-*O*-*p*-tolylsulfonyl-β-cellotrioside (**17**) was obtained, in 66% yield after column chromatography, as an amorphous powder. Treatment of **17** with sodium iodide in *N*,*N*-dimethylformamide displaced the tosyloxy by iodo groups to

give the crystalline 6,6′,6″-trideoxy-6,6′,6″-triiodo derivative **18**, proving that the three sulfonyloxy groups of **17** were located at C-6, -6′, and -6″. Reductive dehalogenation of **18** with Raney nickel in the presence of hydrazine[20] afforded the crystalline 6,6′,6″-trideoxy derivative **19** which was *O*-deacetylated to give crystalline methyl 6,6′,6″-trideoxy-β-cellotrioside (**20**), the structure of which was confirmed by methanolysis and g.l.c. examination of the trimethylsilyl derivatives of the methanolyzates. The n.m.r. spectrum of **20** for a solution in dimethyl sulfoxide-d_6 showed three doublets (J 6.0 Hz) at high field (δ 1.05, 1.18, and 1.28), which were together integrated for nine protons, but could not be differentiated. Displacement of the tosyloxy groups in **17** with the chloride ion in *N*,*N*-dimethylformamide gave the crystalline 6,6′,6″-trichloro-6,6′,6″-trideoxy derivative **21**, which on *O*-deacetylation furnished methyl 6,6′,6″-trichloro-6,6′,6″-trideoxy-β-cellotrioside (**22**) as an amorphous solid. Hydrolysis of **22** in aqueous sulfuric acid followed by zinc chloride-catalyzed acetylation[21] gave 1,2,3,4-tetra-*O*-acetyl-6-chloro-6-deoxy-α-D-glucopyranose[22], thus establishing the structure of **22**. Treatment of **17** with sodium azide in *N*,*N*-dimethylformamide afforded the 6,6′,6″-triazido-6,6′,6″-trideoxy derivative **23**, which was successively hydrogenated and acetylated to give the crystalline 6,6′,6″-triacetamido-6,6′,6″-trideoxy derivative **24**, further *O*-deacetylated into methyl 6,6′,6″-triacetamido-6,6′,6″-trideoxy-β-cellotrioside (**25**) obtained in crystalline form.

EXPERIMENTAL

General methods. — Unless otherwise stated, the general experimental conditions were the same as those described previously[23]. Dry-column chromatography was performed on Silica gel No 7734 (Merck) according to the procedure described earlier[10]. Gas-liquid chromatography was performed on a Hitachi gas chromatograph 063 using a column (200 × 0.25 mm) of 5% Silicone SE-30 on 80–100 mesh Chromosorb W (operating temperature 190°), and a flame-ionization detector. The following solvent systems (v/v) were used: (*A*) 2:1, (*B*) 1:1, and (*C*) 3:2 ethyl acetate–benzene, (*D*) 3:2 benzene–methanol, and (*E*) 3:2 benzene–ethanol.

Condensation of methyl 2,3,6-tri-O-acetyl-β-D-glucopyranoside (**1**) *with 2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-glucopyranosyl bromide* (**6**) *in the presence of silver oxide.* — A solution of **1** (1.20 g) in anhydrous chloroform (4 mL) was mixed with silver oxide (2 g) and Drierite (12 g), and the suspension was shaken for a few minutes. A solution of **6** (4.80 g) in absolute chloroform (16 mL) was added, and the mixture was shaken for 1 h, and then boiled under reflux for 3 h. The suspension was processed as described[1], and the resulting syrup was crystallized from ethanol and recrystallized from the same solvent to give 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-α-D-glucopyranose (**7**) (2.35 g; 54% calculated on the basis of **6**), m.p. 209–210°, $[\alpha]_D^{20}$ +34.0° (*c* 3.1, chloroform), $[\alpha]_D^{20}$ +32.8 (5 min)→+23.6° (24 h, *c* 2.0, pyridine); lit.[3] m.p. 209°, $[\alpha]_D^{22}$ +33.4→+23.0° (24 h; *c* 2.22, pyridine).

T.l.c. examination (solvent *A*) of the mother liquors from **7** showed the presence

of unreacted **1** (R_F 0.54) besides **7** (R_F 0.46), in addition to three unknown components (R_F 0.64, 0.59, and 0.36). On the same t.l.c. plate, authentic **15**, prepared by the procedure described earlier[2], showed a mobility similar to that of **1**. The mother liquors from **7** were evaporated, and the residue was dissolved in pyridine (30 mL). The solution was cooled to 0°, acetic anhydride (20 mL) was added, and the mixture was kept overnight at room temperature. Isolation in the usual way by pouring into ice–water gave a syrup that was crystallized from ethanol to give α-cellobiose octaacetate (0.78 g; 18%, calculated on the basis of **6**), m.p. 228–229°, $[\alpha]_D^{20}$ +40.2° (*c* 2.5, chloroform); lit.[24] m.p. 229.5°, $[\alpha]_D$ +41.5° (chloroform). T.l.c. examination (solvent *B*) of the mother liquor showed the presence of methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (R_F 0.50) and additional α-cellobiose octaacetate (R_F 0.41), together with some minor products, but did not show the presence of **15**. On the same t.l.c. plate, authentic **15** had an R_F value of 0.27.

O-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-β-D-glucopyranosyl)-(1→4)-2,3-di-O-acetyl-1,6-anhydro-β-D-glucopyranose (**10**). — (*a*) A solution of **8** (5 g, 9.4 mmol) in anhydrous dichloromethane (50 mL) containing silver triflate (5.29 g, 20.6 mmol) and 1,1,3,3-tetramethylurea (7.39 mL, 61.8 mmol) was cooled to −30° under a dry nitrogen atmosphere. A solution of **4** (7.69 g, 18.7 mmol) in dry dichloromethane (30 mL) was added dropwise over a period of 20 min with stirring. After 1 h at −20°, the mixture was allowed to reach room temperature, and then stirred overnight. The suspension was filtered through a Celite pad, and the residue was washed with dichloromethane. The combined filtrate and washings were washed successively with aqueous sodium hydrogencarbonate, water, dried (sodium sulfate), and evaporated. The residue was acetylated with acetic anhydride (55 mL) and sodium acetate (7 g) under reflux for 20 min. Isolation in the usual way gave a syrup which was eluted from a dry-packed column of silica gel (600 g) with solvent *A* to afford **10** as an amorphous powder (4.29 g, 53%), $[\alpha]_D^{21}$ −29.4° (*c* 1.7, chloroform); t.l.c. (solvent *A*): R_F 0.35.

Anal. Calc. for $C_{36}H_{48}O_{24}$: C, 50.00; H, 5.59. Found: C, 50.13; H, 5.52.

(*b*) To a solution of **9** (1.2 g, 4.9 mmol) in anhydrous 1,2-dichloroethane (50 mL) were added mercuric cyanide (1.40 g, 5.5 mmol) and **6** (3.86 g, 5.5 mmol), and the mixture was stirred for 4 days at 40° with rigorous protection from moisture and light. The cooled solution was diluted with dichloromethane, washed successively with aqueous potassium bromide and water, dried (sodium sulfate), and evaporated. The residue was acetylated with acetic anhydride (25 mL) and sodium acetate (3 g), as just described. After the usual processing, the resulting syrup was eluted from a dry-packed column of silica gel (300 g) with solvent *A* to give **10** (1.69 g, 40%), $[\alpha]_D^{23}$ −29.3° (*c* 1.5, chloroform); the n.m.r. spectrum and behavior in t.l.c. were identical with those of the compound prepared by method *a*.

O-β-D-Glucopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose (**11**). — A solution of **10** (337 mg) in dry methanol (5 mL) was treated with methanolic 0.1M sodium methoxide (0.1 mL). The solution was kept for 2 h at room temperature, neutralized with Amberlite IR-120 (H^+) ion-exchange resin,

filtered, and evaporated to give **11** as an amorphous solid (181 mg, 95%), $[\alpha]_D^{21}$ −36.3° (*c* 1.4, water); t.l.c. (solvent *D*): R_F 0.24; the compound did not reduce boiling Fehling's solution.

Anal. Calc. for $C_{18}H_{30}O_{15}$: C, 44.45; H, 6.22. Found: C, 44.56; H, 6.13.

O-(*2,3,4,6-Tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-*1,2,3,6-tetra*-O-*acetyl*-α-D-*glucopyranose* (**12**). — Compound **10** (5.2 g) was dissolved in an acetolysis mixture (80 mL) of 70:30:1 (v/v) acetic anhydride–acetic acid–sulfuric acid. After being stirred for 3 h at room temperature, the solution was poured into ice–water containing sodium carbonate, and then extracted with chloroform. The extract was washed successively with aqueous sodium hydrogencarbonate and water, dried (sodium sulfate), and evaporated to give a crystalline mass which on recrystallization from ethanol afforded **12** (4.76 g, 82%), m.p. 221–222°, $[\alpha]_D^{18}$ +23.0° (*c* 4.4, chloroform); n.m.r. (chloroform-*d*): δ 6.26 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1); lit.[15] m.p. 221.7–222.7°, $[\alpha]_D$ +22.6° (*c* 5.10, chloroform).

O-(*2,3,4,6-Tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-*1,2,3,6-tetra*-O-*acetyl*-β-D-*glucopyranose* (**13**). — A solution of **6** (3.95 g, 5.6 mmol) in dichloromethane (20 mL) was added dropwise under a flow of dry nitrogen to a solution (cooled to −30°) of **3** (1.31 g, 3.8 mmol) in dichloromethane (30 mL) containing silver triflate (1.74 g, 6.8 mmol) and 1,1,3,3-tetramethylurea (2.43 mL, 20.3 mmol). After being stirred at −30° for 1 h, the reaction mixture was allowed to warm to room temperature, and then stirred overnight. The solid was removed by filtration and washed with dichloromethane. The combined filtrates were washed successively with aqueous sodium hydrogencarbonate and water, dried (sodium sulfate), and evaporated. The residue was acetylated with acetic anhydride (30 mL) and sodium acetate (4 g), as described previously, and the resulting syrup was fractionated on a dry-packed column of silica gel (500 g) with solvent *B* to give **13** (1.42 g, 39%), m.p. 209–210° (aqueous ethanol), $[\alpha]_D^{20}$ −18.0° (*c* 4.1, chloroform); n.m.r. (chloroform-*d*): δ 5.68 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1); lit.[18] m.p. 209.5–210.5° (95% ethanol), $[\alpha]_D$ −17.9° (chloroform).

O-(*2,3,4,6-Tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl bromide* (**14**). — To a chilled solution of **12** (4.96 g) in anhydrous dichloromethane (15 mL) was added a saturated (at 0°) solution of hydrogen bromide in acetic acid (15 mL). The mixture was kept for 1 h at room temperature, and then diluted with dichloromethane. The solution was washed successively with iced water, aqueous sodium hydrogencarbonate, and water, dried (magnesium sulfate), and evaporated to a syrup which crystallized from ethyl acetate–ether to give **14** (4.26 g, 84%), m.p. 184–185° (dec.), $[\alpha]_D^{18}$ +58.9° (*c* 5.2, chloroform); lit.[19] m.p. 183° (dec.), $[\alpha]_D^{18}$ +58.0° (*c* 11.4, chloroform).

Compound **14** (0.29 g, 81%) was also obtained from **13** (0.35 g) by an analogous procedure.

Methyl O-(*2,3,4,6-tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-β-D-*glucopyranosyl*)-(*1*→*4*)-*2,3,6-tri*-O-*acetyl*-β-D-*glucopyranoside* (**15**). —

Compound **14** (4.19 g) was dissolved in a mixture of anhydrous methanol (3 mL) and dry benzene (30 mL) containing mercuric cyanide (1.07 g). The mixture was stirred for 4 h at room temperature, and concentrated to a syrup, which was dissolved in chloroform. The solution was washed successively with water, aqueous potassium bromide, and water, dried (sodium sulfate), and evaporated. Crystallization of the residue from methanol gave **15** (3.34 g, 84%), m.p. 197–198°, $[\alpha]_D^{18}$ −25.3° (*c* 3.7, chloroform): lit.[2] m.p. 198–199° (methanol), $[\alpha]_D^{20}$ −25.9° (*c* 4.7, chloroform).

Methyl O-*β*-D-*glucopyranosyl*-(*1*→*4*)-O-*β*-D-*glucopyranosyl*-(*1*→*4*)-*β*-D-*glucopyranoside* (**16**). — *O*-Deacetylation of **15** (3 g), as described for the preparation of **11**, and crystallization of the residue from aqueous ethanol gave **16** (1.53 g, 92%), m.p. 265–267° (dec.), $[\alpha]_D^{17}$ −13.9° (*c* 3.2, water); lit.[2] m.p. 240–242° (aqueous ethanol), $[\alpha]_D^{20}$ −13.7° (*c* 3.1, water).

Methyl O-(*2,3,4-tri*-O-*acetyl*-*6*-O-p-*tolylsulfonyl*-*β*-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3-di*-O-*acetyl*-*6*-O-p-*tolylsulfonyl*-*β*-D-*glucopyranosyl*)-(*1*→*4*)-*2,3-di*-O-*acetyl*-*6*-O-p-*tolylsulfonyl*-*β*-D-*glucopyranoside* (**17**). — To a solution of **16** (1.42 g) in anhydrous pyridine (35 mL), cooled to −20°, was added portionwise *p*-toluenesulfonyl chloride (1.88 g, 3.6 mol. equiv.). The reaction mixture was further stirred for 1 h at −20°, kept overnight at 0°, treated with acetic anhydride (20 mL), kept overnight at room temperature, and then diluted with chloroform. The solution was washed successively with dilute sulfuric acid, aqueous sodium hydrogencarbonate, and water, and dried (sodium sulfate). The residual syrup, obtained after evaporation of the solvent, was applied to a silica gel column (250 g). Elution with solvent *B* gave **17** as an amorphous powder (2.30 g, 66%), $[\alpha]_D^{14}$ −9.0° (*c* 1.6, chloroform); t.l.c. (solvent *C*): R_F 0.52; n.m.r. (chloroform-*d*): δ 3.39 (s, 3 H, OMe), 2.46 (s, 9 H, 3 aryl-CH_3), and 2.13–2.03 (overlapping singlets, 21 H, 7 OAc).

Anal. Calc. for $C_{54}H_{66}O_{29}S_3$: C, 50.86; H, 5.22; S, 7.54. Found: C, 50.94, H, 5.28; S, 7.40.

Methyl O-(*2,3,4-tri*-O-*acetyl*-*6*-*deoxy*-*6*-*iodo*-*β*-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3-di*-O-*acetyl*-*6*-*deoxy*-*6*-*iodo*-*β*-D-*glucopyranosyl*)-(*1*→*4*)-*2,3-di*-O-*acetyl*-*6*-*deoxy*-*6*-*iodo*-*β*-D-*glucopyranoside* (**18**). — Sodium iodide (0.9 g) was added to a solution of **17** (450 mg) in *N,N*-dimethylformamide (10 mL), and the mixture was heated for 2 h at 100°. The mixture was evaporated and the residue was extracted with chloroform. The extract was washed with water, dried (sodium sulfate), and evaporated. Crystallization from ethanol gave **18** (334 mg, 83%), m.p. 199–200°, $[\alpha]_D^{14}$ −21.8° (*c* 1.34, chloroform).

Anal. Calc. for $C_{33}H_{45}I_3O_{20}$: C, 34.69; H, 3.97; I, 33.33. Found: C, 34.57; H, 3.86; I. 33.19.

Methyl O-(*2,3,4-tri*-O-*acetyl*-*6*-*deoxy*-*β*-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3-di*-O-*acetyl*-*6*-*deoxy*-*β*-D-*glucopyranosyl*)-(*1*→*4*)-*2,3-di*-O-*acetyl*-*6*-*deoxy*-*β*-D-*glucopyranoside* (**19**). — A solution of **18** (380 mg) in ethanol (20 mL) was mixed with barium carbonate (2 g) and heated to boiling with stirring. A small amount of Raney nickel was then added to the mixture and, after 5 min, hydrazine hydrate (1 mL) was added portionwise during 5 min. The mixture was boiled for 20 min under reflux,

and then filtered through a Celite pad, and the filtrate was evaporated to dryness. The residue was dissolved in chloroform, and the solution was washed successively with water, 5% sodium thiosulfate, and water, dried (sodium sulfate), and evaporated to a solid which was recrystallized from ethanol–2-propanol to give **19** (215 mg, 86%), m.p. 231–232° (dec.), $[\alpha]_D^{14}$ −36.6° (*c* 1.3, chloroform).

Anal. Calc. for $C_{33}H_{48}O_{20}$: C, 51.83; H, 6.33. Found: C, 51.91; H, 6.26.

Methyl O-(*6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-O-(*6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-*6-deoxy-β-*D-*glucopyranoside* (**20**). — *O*-Deacetylation of **19** (211 mg), as described for the preparation of **11**, afforded **20** (116 mg, 89%), m.p. 152–153° (ethanol), $[\alpha]_D^{15}$ −23.1° (*c* 1.1, water).

Anal. Calc. for $C_{19}H_{34}O_{13}$: C, 48.51; H, 7.28. Found: C, 48.61; H, 7.22.

Methanolysis of **20** [20 mg; 1% methanolic hydrogen chloride (3 mL) at reflux for 8 h] and g.l.c. of the resulting methyl glycosides as the per(trimethylsilyl) ethers gave peaks corresponding to methyl 6-deoxy-α,β-D-glucopyranoside. No other peaks were detected.

Methyl O-(*2,3,4-tri-*O-*acetyl-6-chloro-6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-O-(*2,3-di-*O-*acetyl-6-chloro-6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-*2,3-di-*O-*acetyl-6-chloro-6-deoxy-β-*D-*glucopyranoside* (**21**). — A solution of **17** (989 mg) in *N,N*-dimethylformamide (9 mL) containing lithium chloride (1.8 g) was stirred for 3 h at 100°. The reaction mixture was processed as described for the preparation of **18** to give **21** (565 mg, 84%), m.p. 207–208° (ethanol), $[\alpha]_D^{14}$ −40.4° (*c* 1.7, chloroform).

Anal. Calc. for $C_{33}H_{45}Cl_3O_{20}$: C, 45.66; H, 5.23; Cl, 12.25. Found: C, 45.54; H, 5.28; Cl, 12.16.

Methyl O-(*6-chloro-6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-O-(*6-chloro-6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-*6-chloro-6-deoxy-α-*D-*glucopyranoside* (**22**). — *O*-Deacetylation of **21** (450 mg), as described previously, gave **22** as an amorphous solid (279 mg, 94%), $[\alpha]_D^{15}$ −23.8° (*c* 1.1, water).

Anal. Calc. for $C_{19}H_{31}Cl_3O_{13}$: C, 39.77; H, 5.45; Cl, 18.54. Found: C, 39.59; H, 5.61; Cl, 18.38.

Hydrolysis of **22** (220 mg) in aqueous sulfuric acid, followed by acetylation[21] with acetic anhydride and zinc chloride, gave 1,2,3,4-tetra-*O*-acetyl-6-chloro-6-deoxy-α-D-glucopyranose (290 mg, 72%), m.p. 162–163° (ether), $[\alpha]_D^{15}$ +118.5° (*c* 0.5, chloroform); lit.[22] m.p. 164°, $[\alpha]_D$ +120° (*c* 1.0, chloroform).

Methyl O-(*2,3,4-tri-*O-*acetyl-6-azido-6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-O-(*2,3-di-*O-*acetyl-6-azido-6-deoxy-β-*D-*glucopyranosyl*)-(*1→4*)-*2,3-di-*O-*acetyl-6-azido-6-deoxy-β-*D-*glucopyranoside* (**23**). — A solution of **17** (612 mg) in *N,N*-dimethylformamide (12 mL) containing sodium azide (1.1 g) was heated for 3 h at 100°. The reaction mixture was processed as described for the preparation of **18**, and the resulting product was purified by elution from a column of silica gel (30 g) with solvent *B* to give **23** (345 mg, 81%) as an amorphous solid, $[\alpha]_D^{14}$ −7.4° (*c* 1.5, chloroform); ν_{max}^{KBr} 2100 cm^{-1} (N_3).

Anal. Calc. for $C_{33}H_{45}N_9O_{20}$: C, 44.65; H, 5.11; N, 14.20. Found: C, 44.46; H, 5.23; N, 14.34.

Methyl O-(*6-acetamido-2,3,4-tri*-O-*acetyl-6-deoxy-β*-D-*glucopyranosyl*)-(*1→4*)-O-(*6-acetamido-2,3-di*-O-*acetyl-6-deoxy-β*-D-*glucopyranosyl*)-(*1→4*)-*6-acetamido-2,3-di*-O-*acetyl-6-deoxy-β*-D-*glucopyranoside* (**24**). — Compound **23** (280 mg) was dissolved in methanol (20 mL), and a small amount of Raney nickel was added. The mixture was boiled to boiling while hydrazine hydrate (1 mL) was added dropwise. It was then heated for a further 40 min under reflux, filtered through a Celite pad, and evaporated to dryness. The residue was acetylated with acetic anhydride (3 mL) and pyridine (4 mL) overnight at room temperature. The mixture was concentrated to a syrup which was chromatographed on silica gel (20 g) with solvent *E* to give **24** (244 mg, 83%), m.p. 142–146° (ether-petroleum ether), $[\alpha]_D^{15}$ −55.2° (*c* 1.1, chloroform).

Anal. Calc. for $C_{39}H_{57}N_3O_{23}$: C, 50.05; H, 6.14; N, 4.49. Found: C, 50.20; H, 6.03; N, 4.35.

Methyl O-(*6-acetamido-6-deoxy-β*-D-*glucopyranosyl*)-(*1→4*)-O-(*6-acetamido-6-deoxy-β*-D-*glucopyranosyl*)-(*1→4*)-*6-acetamido-6-deoxy-β*-D-*glucopyranoside* (**25**). — *O*-Deacetylation of **24** (210 mg), as described previously, afforded **25** (132 mg, 92%), m.p. 165–170° (ethanol), $[\alpha]_D^{15}$ −13.9° (*c* 1.3, water); n.m.r. (dimethyl sulfoxide-d_6): δ 7.77 (broad s, 3 H, exchangeable with D_2O, 3 NH) and 1.85 (s, 9 H, 3 NAc).

Anal. Calc. for $C_{25}H_{43}N_3O_{16}$: C, 46.80; H, 6.76; N, 6.55. Found: C, 46.96; H, 6.90; N, 6.44.

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