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CHEMICAL MODIFICATION OF THE NONREDUCING, TERMINAL GROUP OF MALTOTRIOSE*

KEN'ICHI TAKEO†, TOSHINARI MATSUNAMI, AND TAKASHI KUGE

Department of Agricultural Chemistry, Kyoto Prefectural University, Shimogamo, Kyoto (Japan)

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ABSTRACT

O-α-D-Galactopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-glucopyranose (**12**) was prepared by inversion of configuration at C-4″ of 2,3,2′,3′,6′,2″,3″-hepta-*O*-acetyl-1,6-anhydro-4″,6″-di-*O*-methylsulfonyl-β-maltotriose (**7**), followed by *O*-deacylation, acetylation, acetolysis, and de-*O*-acetylation. The intermediate **7** was obtained by treatment of 1,6-anhydro-β-maltotriose (**2**) with benzal chloride in pyridine, followed by acetylation, removal of the benzylidene group, and methanesulfonylation. Selective tritylation of **2** and subsequent acetylation afforded 2,3,2′,3′,6′,2″,3″,4″-octa-*O*-acetyl-1,6-anhydro-6″-*O*-trityl-β-maltotriose (**6**), which was *O*-detritylated and *p*-toluenesulfonylated to give 2,3,2′,3′,6′,2″,3″,4″-octa-*O*-acetyl-1,6-anhydro-6″-*O*-*p*-tolylsulfonyl-β-maltotriose (**13**). Nucleophilic displacement of **13** with thioacetate, iodide, bromide, chloride, and azide ions gave 6″-*S*-acetyl- (**14**), 6″-iodo- (**15**), 6″-bromo- (**16**), 6″-chloro- (**19**), and 6″-azido- (**20**) 1,6-anhydro-β-maltotriose octaacetates, respectively. 6″-Deoxy- (**18**) and 6″-acetamido-6″-deoxy (**21**) derivatives of 1,6-anhydro-β-maltotriose decaacetates were also prepared from **15** and **16**, and **20**, respectively. Acetolysis of **14**, **15**, **16**, **18**, **19**, and **21** afforded 1,2,3,6,2′,3′,6′,2″,3″,4″-deca-*O*-acetyl-6″-*S*-acetyl (**22**), -6″-iodo (**23**), -6″-bromo (**24**), -6″-deoxy (**25**), -6″-chloro (**26**), and -6″-acetamido-6′-deoxy (**27**) derivatives of α-maltotriose, respectively. *O*-Deacetylation of **24**, **25**, and **26** furnished 6″-bromo- (**28**), 6″-deoxy- (**29**), and 6″-chloro- (**30**) maltotrioses, respectively, which on acetylation gave the corresponding β-decaacetates.

INTRODUCTION

We have previously reported the synthesis of 1,6-anhydro-β-maltotriose[2] (**2**) which is a useful starting material for the chemical transformation of the reducing[1] and nonreducing terminal residues of maltotriose (**1**). As a part of our studies on the chemistry of maltotriose[1–3], we have modified the nonreducing terminal residue,

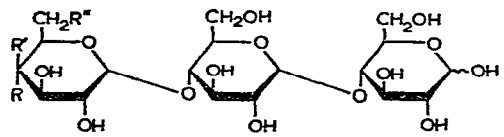
*Chemical modification of maltotriose. Part IV. For Part III, see Ref. 1.

†To whom inquiries should be addressed.

starting from **2**, and report here the conversion of **1** into *O*-α-D-galactopyranosyl-(1→4)-*O*-α-D-glucopyranosyl-(1→4)-D-glucopyranose (**12**) and the preparation of a homologous series of 6″-substituted maltotriose derivatives.

RESULTS AND DISCUSSION

Conversion of **1** into the *galacto* derivative **12** was accomplished by use of a reaction sequence similar to that described for the synthesis of *galacto* analogs of disaccharides[4–7], which involves sequential benzylidenation, acylation, removal of

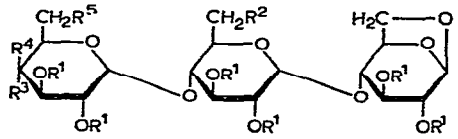


1 R = R″ = OH, R′ = H
12 R = H, R″ = R′ = OH
28 R = OH, R′ = H, R″ = Br
29 R = OH, R′ = R″ = H
30 R = OH, R′ = H, R″ = Cl

the benzylidene group, methanesulfonylation, and inversion of configuration by SN2 displacement of the 4-*O*-sulfonyloxy groups.

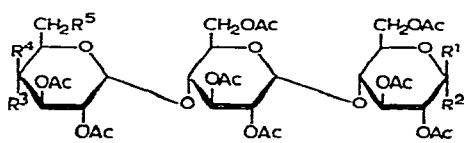
Initial attempts to synthesize 1,6-anhydro-4″,6″-*O*-benzylidene-β-maltotriose, the precursor of 2,3,2′,3′,6′,2″,3″-hepta-*O*-acetyl-1,6-anhydro-4″,6″-*O*-benzylidene-β-maltotriose (**3**), by the condensation of **2** with benzaldehyde in the presence of zinc chloride were not successful; under the conventional conditions, the reaction was sluggish and incomplete. Such modification of the reaction conditions as increasing the amount of benzaldehyde or zinc chloride did not improve the yield, and any increase in the reaction time caused extensive hydrolysis of both glycosidic linkages.

Therefore, **2** was treated with benzal chloride[8] in boiling pyridine, followed by acetylation with acetic anhydride, to give a mixture from which **3** was directly isolated in crystalline form in 45% yield. The structure of **3** was demonstrated by conversion into 2,3,2′,3′,6′,2″,3″,4″-octa-*O*-acetyl-1,6-anhydro-6″-*O*-trityl-β-maltotriose (**6**) in the following sequence of reactions: Treatment with aqueous acetic acid removed the benzylidene group to afford crystalline 2,3,2′,3′,6′,2″,3″-hepta-*O*-acetyl-1,6-anhydro-β-maltotriose (**4**). Tritylation of **4** with 1.3 molar equivalents of reagent in pyridine, followed by acetylation gave crystalline **6** in high yield. Alternatively, treatment of **2** with 1.5 molar equivalents of chlorotriphenylmethane in pyridine and subsequent acetylation afforded, after column-chromatography fractionation, 2,3,2′,3′,2″,3″,4″-hepta-*O*-acetyl-1,6-anhydro-6′,6″-di-*O*-trityl-β-maltotriose (**5**) and the 6″-trityl ether **6** in 21% and 41% yield, respectively. The monotrityl ethers obtained by both routes were shown to be identical by comparison of their m.p., optical rotation, u.v. and n.m.r. spectra, and behavior in t.l.c. This not only supports the structure assigned to **3**, but also indicates the trityl group of **6** to be located at O-6″.



2 $R^1 = R^4 = H$, $R^2 = R^3 = R^5 = OH$
3 $R^1 = Ac$, $R^2 = OAc$, R^3, $R^5 = PhCHO_2$, $R^4 = H$
4 $R^1 = Ac$, $R^2 = OAc$, $R^3 = R^5 = OH$, $R^4 = H$
5 $R^1 = Ac$, $R^2 = R^5 = OTr$, $R^3 = OAc$, $R^4 = H$
6 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = OTr$
7 $R^1 = Ac$, $R^2 = OAc$, $R^3 = R^5 = OMs$, $R^4 = H$
8 $R^1 = Ac$, $R^2 = R^4 = R^5 = OAc$, $R^3 = H$
9 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = OH$
13 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = OTs$
14 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = SAc$
15 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = I$
16 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = Br$
17 $R^1 = Ac$, $R^2 = H$, $R^3 = OBz$, $R^4 = H$, $R^5 = Br$
18 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = R^5 = H$
19 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = Cl$
20 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = N_3$
21 $R^1 = Ac$, $R^2 = R^3 = OAc$, $R^4 = H$, $R^5 = NHAc$

Methanesulfonylation of **4** gave crystalline 2,3,2′,3′,6′,2″,3″-hepta-*O*-acetyl-1,6-anhydro-4″,6″-di-*O*-methylsulfonyl-β-maltotriose (**7**). Replacement of the sulfonyloxy groups of **7** with sodium benzoate in *N*,*N*′,*N*″-hexamethylphosphoric triamide gave a product which on *O*-deacylation and reacetylation afforded, in 76% yield, the crystalline *galacto* nonaacetate **8** with inversion of configuration at C-4″. Acetolysis[2,3,9] of **8** opened the 1,6-anhydro ring without cleavage of the glycosidic linkages to give an amorphous solid that was homogeneous on t.l.c. with various solvent systems, but n.m.r. spectroscopy showed it to be a 3:2 mixture of the α- and β-hendecaacetates **10** and **11** and attempts to separate the mixture failed. The mixture was *O*-deacetylated with sodium methoxide in methanol to give **12** as an amorphous solid, the structure of which was confirmed by methanolysis and g.l.c. examination of the trimethylsilyl derivatives of the methanolizate. Acetylation of free **12** gave the crystalline β-hendecaacetate **11**.



10 $R^1 = R^3 = H$, $R^2 = R^4 = R^5 = OAc$
11 $R^1 = R^4 = R^5 = OAc$, $R^2 = R^3 = H$
22 $R^1 = R^4 = H$, $R^2 = R^3 = OAc$, $R^5 = SAc$
23 $R^1 = R^4 = H$, $R^2 = R^3 = OAc$, $R^5 = I$
24 $R^1 = R^4 = H$, $R^2 = R^3 = OAc$, $R^5 = Br$
25 $R^1 = R^4 = R^5 = H$, $R^2 = R^3 = OAc$
26 $R^1 = R^4 = H$, $R^2 = R^3 = OAc$, $R^5 = Cl$
27 $R^1 = R^4 = H$, $R^2 = R^3 = OAc$, $R^5 = NHAc$
31 $R^1 = R^3 = OAc$, $R^2 = R^4 = H$, $R^5 = Br$
32 $R^1 = R^3 = OAc$, $R^2 = R^4 = R^5 = H$
33 $R^1 = R^3 = OAc$, $R^2 = R^4 = H$, $R^5 = Cl$

The direct synthesis of 2,3,2′,3′,6′,2″,3″,4″-octa-*O*-acetyl-1,6-anhydro-6″-*O*-*p*-tolylsulfonyl-β-maltotriose (**13**), the key intermediate in the synthesis of a homologous series of 6″-substituted maltotriose derivatives, was attempted by selective *p*-toluenesulfonylation of **2**, followed by acetylation. *p*-Toluenesulfonylation of **2** with 1.1 molar equivalents of reagent in pyridine gave, however, a complex mixture comprising at least six products (t.l.c.). Accordingly, **13** was prepared from the 6″-trityl ether **6** by *O*-detritylation with aqueous acetic acid to give 2,3,2′,3′,4′,2″,3″,4″-octa-*O*-acetyl-1,6-anhydro-β-maltotriose (**9**). Formation of **6** by retritylation of **9** eliminated the possibility of a (4″ → 6″) acetyl migration during the *O*-detritylation of **6**. Subsequent *p*-toluenesulfonylation of **9** gave crystalline **13** in a high yield.

Treatment of **13** with potassium thioacetate in *N*,*N*-dimethylformamide gave crystalline 6″-*S*-acetyl-1,6-anhydro-6″-thio-β-maltotriose octaacetate (**14**), with sodium iodide in *N*,*N*-dimethylformamide crystalline 1,6-anhydro-6″-deoxy-6″-iodo-β-maltotriose octaacetate (**15**), and with sodium bromide in *N*,*N*′, *N*″-hexamethylphosphoric triamide, crystalline 1,6-anhydro-6″-bromo-6″-deoxy-β-maltotriose octaacetate (**16**). This last-named compound was also prepared by an alternative route: oxidative removal of the benzylidene group of **3** with *N*-bromosuccimide[10] yielded crystalline 2,3,2′,3′,6′,2″,3″-hepta-*O*-acetyl-1,6-anhydro-4″-*O*-benzoyl-6″-bromo-6″-deoxy-β-maltotriose (**17**) which was sequentially de-*O*-acylated and reacetylated to give **16**. Reductive dehalogenation of **15** and **16** with Raney nickel in the presence of hydrazine[11] gave crystalline 1,6-anhydro-6″-deoxy-β-maltotriose octaacetate (**18**). Substitution reaction of **13** with lithium chloride in *N*,*N*′,*N*″-hexamethylphosphoric triamide afforded crystalline 1,6-anhydro-6″-chloro-6″-deoxy-β-maltotriose octaacetate (**19**), which was identical with that prepared directly from **9** by reaction with sulfuryl chloride and pyridine in chloroform. Treatment of **13** with sodium azide in *N*,*N*-dimethylformamide gave crystalline 1,6-anhydro-6″-azido-6″-deoxy-β-maltotriose octaacetate (**20**), which was successively hydrogenated and acetylated to yield crystalline 6″-acetamido-1,6-anhydro-6″-deoxy-β-maltotriose octaacetate (**21**).

Acetolysis of **14**, **15**, **16**, **18**, **19**, and **21** gave the 6″-*S*-acetyl-6″-thio- (**22**), 6″-deoxy-6″-iodo- (**23**), 6″-bromo-6″-deoxy- (**24**), 6″-deoxy- (**25**), 6″-chloro-6″-deoxy- (**26**), and 6″-acetamido-6″-deoxy- (**27**) derivatives of α-maltotriose decaacetate, respectively, all the compounds being obtained in crystalline form. Each of the n.m.r. spectra of **22**–**27** in chloroform-*d* showed the anomeric proton signal at τ 3.75 as a doublet with $J_{1,2}$ 3.3–3.7 Hz, which is consistent with an α anomeric configuration.

O-De-acetylation of **24**, **25**, and **26** with methanolic sodium methoxide, gave 6″-bromo-6″-deoxy- (**28**), 6″-deoxy- (**29**), and 6″-chloro-6″-deoxy-maltotriose (**30**) as hygroscopic powders, respectively, which on acetylation were transformed into 6″-bromo-6″-deoxy- (**31**), 6″-deoxy- (**32**), and 6″-chloro-6″-deoxy-β-maltotriose (**33**) decaacetate, respectively. The n.m.r. spectra (chloroform-*d*) of **31**, **32**, and **33** showed the H-1 resonances at τ 4.27 as a doublet with $J_{1,2}$ 7.5 Hz, which is consistent with the β-anomeric configuration.

Each of the n.m.r. spectra of the 6″-deoxy derivatives **18**, **25**, and **32** exhibited a three-proton doublet (*J* 6.0–6.5 Hz) at τ 8.84 for the methyl group at C-5″, the

chemical shift being in good agreement with that of the methyl group at C-5′ in methyl 2,3,6,2′,3′,4′-hexa-*O*-acetyl-6′-deoxy-β-maltoside[12].

EXPERIMENTAL

General methods. — Unless otherwise stated, experimental conditions were as described[2] in Part I. Gas-liquid chromatography was performed on a Hitachi gas chromatograph 063, equipped with a column (200 × 0.25 cm) of 5% Silicone SE-30 on 80–100 mesh Chromosorb W and a flame-ionization detector; operation was isothermal, at 185°, with nitrogen as carrier gas at a flow rate of 80 ml/min. The following solvent-systems were used; (*A*) 3:2 (v/v) ethyl acetate–benzene, (*B*) 1:1 (v/v) ethyl acetate–benzene, and (*C*) 9:1 (v/v) benzene–ethanol.

O-(*2,3-Di*-O-*acetyl-4,6*-O-*benzylidene*-α-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro*-β-D-*glucopyranose* (**3**). — To a solution of **2** (10 g) in pyridine (200 ml) was added benzal chloride (4 ml), and the mixture was gently heated with for 4 h under reflux with exclusion of moisture. After a further addition of benzal chloride (4 ml), the mixture was again heated for 4 h under reflux. The mixture was cooled to 0° and treated with acetic anhydride (80 ml) and pyridine (40 ml), and then kept overnight at room temperature. The solution was poured into ice–water and extracted with chloroform. The organic layer was successively washed with cold 5% HCl, aqueous $NaHCO_3$, and water, and dried (Na_2SO_4). The solution was treated with charcoal and evaporated to a syrup, which crystallized from methanol–chloroform to give **3** (8 g, 45%), m.p. 221–222°, $[\alpha]_D^{15}$ +64.6° (*c* 1.5, chloroform); n.m.r. (chloroform-*d*): τ 4.51 (s, 1 H, benzylic H).

Anal. Calc. for $C_{39}H_{48}O_{22}$: C, 53.92; H, 5.57. Found: C, 54.08; H, 5.54.

O-(*2,3-Di*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro*-β-D-*glucopyranose* (**4**). — A solution of **3** (5 g) in acetic acid (50 ml) was heated at 80°, water (30 ml) was added in small portions within a few min, and the mixture was kept for 10 min at 80°. The solvents were evaporated and the last traces of volatile compounds were removed by repeated codistillation with toluene to give a syrup which was purified on a column of silica gel (100 g) with solvent *A* to afford **4** (3.75 g, 84%), m.p. 114–115.5° (from methanol), $[\alpha]_D^{15}$ +82.4° (*c* 1.5, chloroform).

Anal. Calc. for $C_{32}H_{44}O_{22}$: C, 49.23; H, 5.68. Found: C, 49.18; H, 5.75.

O-(*2,3,4-Tri*-O-*acetyl-6*-O-*trityl*-α-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro*-β-D-*glucopyranose* (**6**). — (*a*). A solution of **2** (12 g) and chlorotriphenylmethane (10.32 g, 1.5 molar equiv.) in pyridine (120 ml) was stirred for 48 h at room temperature. It was cooled to 0° and treated with acetic anhydride (70 ml) and pyridine (30 ml); the mixture was kept for 24 h at room temperature and then poured into ice–water. The resulting precipitate was filtered off, washed well with water, and dried. This was shown by t.l.c. (solvent *A*) to be composed of two major components having R_F 0.64 (**5**) and R_F 0.43 (**6**), and some minor components. The two major components were isolated by column

chromatography on silica gel (500 g) with solvent *A*. The initial fractions gave *O*-(2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranosyl)-(1→4)-*O*-(2,3-di-*O*-acetyl-6-*O*-trityl-α-D-glucopyranosyl)-(1→4)-2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (**5**) (6.6 g, 21%), m.p. 137–137.5° (from methanol–chloroform), $[\alpha]_D^{15}$ +79.8° (*c* 1.5, chloroform); u.v.: λ_{max}^{MeOH} 259 nm (ε 1340).

Anal. Calc. for $C_{70}H_{72}O_{22}$: C, 66.45; H, 5.74. Found: C, 66.28; H, 5.90.

Compound **6** (11.6 g, 44%) was next eluted and crystallized from methanol–chloroform, m.p. 233–234°, $[\alpha]_D^{15}$ +97.5° (*c* 1.5, chloroform); u.v.: λ_{max}^{MeOH} 259 nm (ε 675).

Anal. Calc. for $C_{53}H_{60}O_{23}$: C, 59.77; H, 5.68. Found: C, 59.62; H, 5.75.

(*b*). A solution of **4** (293 mg) and chlorotriphenylmethane (136 mg, 1.3 molar equiv.) in pyridine (1.5 ml) was stirred for 20 h at room temperature, and then for 4 h at 70°. The cooled solution was treated with acetic anhydride (0.6 ml) and pyridine (0.7 ml), and kept overnight at room temperature. The precipitate, which separated on addition of ice–water, was purified by elution from a short column of silica gel with solvent *A* to give **6** (360 mg, 90%), m.p. and mixed m.p. 233–234° (from methanol–chloroform), $[\alpha]_D^{20}$ +98.0° (*c* 1.9, chloroform); the u.v. and n.m.r. spectra were identical with those of the compound prepared by method *a*.

O-(*2,3-Di*-O-*acetyl-4,6-di*-O-*methylsulfonyl*-α-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro*-β-D-*glucopyranose* (**7**). — A solution of **4** (2.5 g) in pyridine (12 ml) was treated with methanesulfonyl chloride (2.5 ml) at −10° and stored overnight at 5°. The solution was poured into ice–water and the precipitate formed was collected by filtration, washed with water, and dried. Crystalllization from ethanol–ethyl acetate gave **7** (2.6 g, 87%), m.p. 179–180°, $[\alpha]_D^{15}$ +75.8° (*c* 1.5, chloroform); n.m.r. (chloroform-*d*): τ 6.90, 6.92 (s, 6 H, 2 $MeSO_2$).

Anal. Calc. for $C_{34}H_{48}O_{26}S_2$: C, 43.59; H, 5.18; S, 6.85. Found: C, 43.70; H, 5.12; S, 6.71.

O-(*2,3,4,6-Tetra*-O-*acetyl*-α-D-*galactopyranosyl*)-(*1→4*)-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro*-β-D-*glucopyranose* (**8**). — Compound **7** (2.0 g) was heated in *N,N',N''*-hexamethylphosphoric triamide (30 ml) with sodium benzoate (2.3 g) for 26 h at 100°. The mixture was poured into ice–water, and the precipitate formed was filtered off and dissolved in chloroform. The solution was washed well with water, dried ($MgSO_4$), and evaporated. A solution of the residue in anhydrous methanol (20 ml) was treated with methanolic M sodium methoxide (2 ml), and the solution was stirred for 5 h at room temperature. After neutralization with Amberlite IR-120 (H^+) ion-exchange resin, the solution was evaporated to a syrup which was dissolved in 1:1 acetic anhydride–pyridine (20 ml). The mixture was kept overnight at room temperature, poured into ice–water, and the resulting precipitate was filtered off, washed with water, and dried. Crystallization from methanol afforded **8** (1.4 g, 76%), m.p. 198–199°, $[\alpha]_D^{20}$ +85.0° (*c* 1.4, chloroform).

Anal. Calc. for $C_{36}H_{48}O_{24}$: C, 50.00; H, 5.60. Found: C, 50.11; H, 5.55.

O-α-D-*Galactopyranosyl*-(*1→4*)-O-α-D-*glucopyranosyl*-(*1→4*)-D-*glucopyranose*

(**12**) *and* O-(*2,3,4,6-tetra*-O-*acetyl*-α-D-*galactopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*1,2,3,6-tetra*-O-*acetyl*-β-D-*glucopyranose* (**11**). — Compound **8** (800 mg) was dissolved in the acetolysis mixture[9] (16 ml; 70:30:1, v/v, acetic anhydride–acetic acid–sulfuric acid). After being stirred for 2 h at room temperature, the mixture was poured into ice–water and extracted with chloroform. The extract was successively washed with aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated to give an amorphous solid (700 mg, 78%) which was a 3:2 mixture of **10** and **11** (deduced from the relative proton intensities of the H-1 resonances), $[\alpha]_D^{20}$ +116.3° (*c* 1.1, chloroform); t.l.c.: R_F 0.58 (solvent *B*); n.m.r. (chloroform-*d*): τ 3.75 (d, $J_{1,2}$ 3.8 Hz, H-1 of **10**) and 4.25 (d, $J_{1,2}$ 7.5 Hz, H-1 of **11**).

Anal. Calc. for $C_{40}H_{54}O_{27}$: C, 49.69; H, 5.63. Found: C, 49.57; H, 5.81.

A solution of the mixture of **10** and **11** (600 mg) in dry methanol (8 ml) was treated with methanolic 0.5M sodium methoxide (0.5 ml), and the solution was kept for 3 h at room temperature. After neutralization with Amberlite IR-120 (H^+) ion-exchange resin, the solution was evaporated to give **12** (297 mg, 95%) as an amorphous powder, $[\alpha]_D^{20}$ +155.0° (equil., *c* 1.1, water); n.m.r. (deuterium oxide): τ 4.63 (d, 2 H, $J_{1',2'}$ and $J_{1'',2''}$ 3.5 Hz, H-1′ and H-1″), 4.80 (d, $J_{1,2}$ 3.5 Hz, H-1 of the α-anomer), and 5.38 (d, $J_{1,2}$ 7.7 Hz, H-1 of the β-anomer); ratio of α to β: ~2:1.

Anal. Calc. for $C_{18}H_{32}O_{16}$: C, 42.86; H, 6.40. Found: C, 42.65; H, 6.65.

Methanolysis of **12** (40 mg; 1% methanolic HCl, 5 ml; reflux, 16 h) and g.l.c. of the resulting methyl glycosides as the trimethylsilyl derivatives gave peaks corresponding to methyl D-galactopyranosides (10.9 and 12.5 min, 33%) and methyl D-glucopyranosides (13.8 and 15.2 min, 67%). No other peaks were detected.

Conventional acetylation of **12** (150 mg) with acetic anhydride (1 ml) and pyridine (2 ml) gave **11** (193 mg, 76%), m.p. 181–182° (from methanol), $[\alpha]_D^{20}$ +86.3° (*c* 1.5, chloroform); n.m.r. (chloroform-*d*): τ 4.25 (d, 1 H, 7.5 Hz, H-1).

Anal. Calc. for $C_{40}H_{54}O_{27}$: C, 49.69; H, 5.63. Found: C, 49.51; H, 5.70.

O-(*2,3,4-Tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro*-β-D-*glucopyranose* (**9**). — A solution of **6** (7.4 g) in 80% aqueous acetic acid (180 ml) was stirred for 1.5 h at 70°. Removal of the solvents by codistillation with toluene gave a solid. Purification by elution from the column of silica gel (100 g) with solvent *C* afforded **9** (4.8 g, 84%), m.p. 196–196.5° (from methanol), $[\alpha]_D^{15}$ +82.7° (*c* 1.0, chloroform).

Anal. Calc. for $C_{34}H_{46}O_{23}$: C, 49.64; H, 5.64. Found: C, 49.55: H, 5.66.

Compound **9** (100 mg) was treated with chlorotriphenylmethane (50 mg) in pyridine (1 ml) for 3 h at 100°. Isolation, in the usual way, gave **6** (110 mg, 85%).

O-(*2,3,4-Tri*-O-*acetyl-6*-O-p-*tolylsulfonyl*-α-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro*-β-D-*glucopyranose* (**13**). — A solution of **9** (4.02 g) in dry pyridine (20 ml) was treated with *p*-toluenesulfonyl chloride (4.66 g) at 0°. The reaction mixture was allowed to reach room temperature, stored overnight, and poured into ice–water. The resulting precipitate was filtered off, washed with water, and dried. Crystallization from ethanol

gave **13** (4.0 g, 84%), m.p. 118–118.5°, $[\alpha]_D^{15}$ +85.6° (*c* 1.5, chloroform); n.m.r. (chloroform-*d*): τ 2.08–2.74 (m, 4 H, aryl-H) and 7.55 (s, 3 H, aryl-CH_3).

Anal. Calc. for $C_{41}H_{52}O_{25}S$: C, 50.41; H, 5.37; S, 3.28. Found: C, 50.29; H, 5.49; S, 3.49.

O-(*2,3,4-Tri*-O-*acetyl*-6-S-*acetyl*-6-*thio*-α-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1*→*4*)-*2,3-di*-O-*acetyl*-*1,6-anhydro*-β-D-*glucopyranose* (**14**). — A solution of **13** in *N,N*-dimethylformamide (8 ml) containing potassium thioacetate (155 mg) was heated for 30 min at 100°. The solution was cooled and poured into ice–water. The precipitate was filtered off, washed with water, and dried. Crystallization from ethanol gave **14** (360 mg, 80%), m.p. 145–146°, $[\alpha]_D^{15}$ +76.8° (*c* 1.5, chloroform); n.m.r. (chloroform-*d*): τ 7.66 (s, 3 H, SAc).

Anal. Calc. for $C_{36}H_{48}O_{23}S$: C, 49.09; H, 5.49; S, 3.64. Found: C, 49.22; H, 5.41; S, 3.75.

O-(*2,3,4-Tri*-O-*acetyl*-6-*deoxy*-6-*iodo*-α-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1*→*4*)-*2,3-di*-O-*acetyl*-*1,6-anhydro*-β-D-*glucopyranose* (**15**). — A solution of **13** (2.7 g) in *N,N*-dimethylformamide (110 ml) containing NaI (9 g) was heated for 3 h at 90° with stirring. The reaction mixture was processed as just described to give **15** (1.26 g, 83%), m.p. 177–178° (from 2-propanol), $[\alpha]_D^{15}$ +83.5° (*c* 1.2, chloroform).

Anal. Calc. for $C_{34}H_{45}IO_{22}$: C, 43.79; H, 4.86; I, 13.61. Found: C, 43.90; H, 4.77; I, 13.51.

O-(*2,3-Di*-O-*acetyl*-*4*-O-*benzoyl*-*6*-*bromo*-*6*-*deoxy*-α-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1*→*4*)-*2,3-di*-O-*acetyl*-*1,6-anhydro*-β-D-*glucopyranose* (**17**). — A mixture of **3** (3.25 g), $BaCO_3$ (7.5 g), and *N*-bromosuccimide (863 mg) in anhydrous carbon tetrachloride (130 ml) and 1,1,2,2-tetrachloroethane (110 ml) was heated for 3 h under reflux, while being stirred. The mixture was filtered, and the inorganic precipitate was washed extensively with chloroform. The combined filtrate and washings were evaporated to a syrup which was dissolved in chloroform. The solution was washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue was crystallized from 2-propanol to give **17** (2.56 g, 72%), m.p. 185–185.5°, $[\alpha]_D^{15}$ +59.0° (*c* 1.0, chloroform); n.m.r. (chloroform-*d*): τ 1.85–2.60 (m, 5 H, aryl-H).

Anal. Calc. for $C_{39}H_{47}BrO_{22}$: C, 49.43; H, 5.00; Br, 8.43. Found: C, 49.32; H, 4.92; Br, 8.55.

O-(*2,3,4-Tri*-O-*acetyl*-*6*-*bromo*-*6*-*deoxy*-α-D-*glucopyranosyl*)-(*1*→*4*)-O-(*2,3,6-tri*-O-*acetyl*-α-D-*glucopyranosyl*)-(*1*→*4*)-*2,3-di*-O-*acetyl*-*1,6-anhydro*-β-D-*glucopyranose* (**16**). — (*a*). Compound **13** (340 mg) was added to a suspension of NaBr (350 mg) in *N,N',N''*-hexamethylphosphoric triamide (2 ml), and the mixture was heated for 3 h at 100° while being stirred. The reaction mixture was processed as just described, and the resulting material was crystallized from ethanol–chloroform to give **16** (300 mg, 86%), m.p. 199–199.5°, $[\alpha]_D^{25}$ +87.4° (*c* 1.0, chloroform).

Anal. Calc. for $C_{34}H_{36}BrO_{22}$: C, 46.06; H, 5.23; Br, 9.01. Found: C, 45.89; H, 5.35; Br, 9.14.

(*i*). A solution of **17** (1 g) in anhydrous methanol (10 ml) was treated with methanolic 0.5M sodium methoxide (1 ml). The solution was stirred for 6 h at room temperature, neutralized with Amberlite IR-120 (H^+) ion-exchange resin, filtered, and concentrated to dryness. The residue was acetylated with acetic anhydride (6 ml) and pyridine (8 ml) overnight at room temperature. Isolation in the usual way gave a white material that crystallized from ethanol–chloroform to give **16** (776 mg, 83%), m.p. and mixed m.p. 199–199.5°, $[\alpha]_D^{23}$ +88.7° (*c* 1.5, chloroform). The n.m.r. spectrum was identical with that of the compound obtained by method *a*.

O-(*2,3,4-Tri*-O-*acetyl-6-deoxy-α*-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl-α*-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro-β*-D-*glucopyranose* (**18**). — (*a*). A mixture of **15** (1 g), $BaCO_3$ (3 g), and Raney Ni (one spatulaful) in ethanol (50 ml) was heated under reflux and stirred vigorously while hydrazine hydrate (3 ml) was added dropwise during 10 min. The mixture was further heated for 1 h under reflux, filtered through a Celite pad, and evaporated to give a crystalline solid which on recrystallization from methanol–chloroform afforded **18** (640 mg, 74%), m.p. 211–212°, $[\alpha]_D^{15}$ +89.3° (*c* 1.5, chloroform); n.m.r. (chloroform-*d*): τ 8.84 (d, 3 H, *J* 6.5 Hz, CH_3-5″).

Anal. Calc. for $C_{34}H_{46}O_{22}$: C, 50.62; H, 5.75. Found: C, 50.76; H, 5.63.

(*b*). A mixture of **16** (780 mg), $BaCO_3$ (2.5 g), and a small amount of Raney Ni in ethanol (40 ml) was treated with hydrazine hydrate (2 ml), as described in *a*, to give **18** (500 mg, 70%), m.p. and mixed m.p. 211–212° (from methanol–chloroform), $[\alpha]_D^{20}$ +88.0° (*c* 1.3, chloroform). The n.m.r. spectrum was identical with that of the compound prepared by method *a*.

O-(*2,3,4-Tri*-O-*acetyl-6-chloro-6-deoxy-α*-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl-α*-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro-β*-D-*glucopyranose* (**19**). — (*a*). LiCl (230 mg) was added to a solution of **13** (450 mg) in *N,N′,N″*-hexamethylphosphoric triamide (3 ml). The mixture was heated for 3.5 h at 100°, and then processed in the usual way to give **19** (298 mg, 77%), m.p. and mixed m.p. 201–202° (from ethanol–chloroform), $[\alpha]_D^{15}$ +90.5° (*c* 1.5, chloroform).

Anal. Calc. for $C_{34}H_{45}ClO_{22}$: C, 48.55; H, 5.39; Cl, 4.22. Found: C, 48.69; H, 5.24; Cl, 4.31.

(*b*). A solution of **9** (1 g) in pyridine (2 ml) and chloroform (15 ml) was treated with $SOCl_2$ (1 ml) for 1 h at −20°. The mixture was gradually allowed to reach room temperature (within 1 h), and then was kept for 2 h. It was diluted with chloroform, and the solution washed successively with M HCl, aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated to give a crystalline mass which, on recrystallization from ethanol–chloroform, afforded **19** (850 mg, 79%), m.p. 201–202°, $[\alpha]_D^{22}$ +89.0° (*c* 1.1, chloroform); the n.m.r. spectrum was identical with that of the compound obtained with method *a*.

O-(*2,3,4-Tri*-O-*acetyl-6-azido-6-deoxy-α*-D-*glucopyranosyl*)-(*1→4*)-O-(*2,3,6-tri*-O-*acetyl-α*-D-*glucopyranosyl*)-(*1→4*)-*2,3-di*-O-*acetyl-1,6-anhydro-β*-D-*glucopyranose* (**20**). — A solution of **13** (1.47 g) in *N,N*-dimethylformamide (70 ml) containing NaN_3 (1.4 g) was heated for 2.5 h at 100°. The reaction mixture was processed in the

usual way, and the resulting solid was crystallized from ethanol to afford **20** (1.16 g, 91%), m.p. 185–186°, $[\alpha]_D^{15}$ +94.6° (*c* 1.5, chloroform); i.r.: ν_{max}^{KBr} 2100 cm^{-1} (N_3).

Anal. Calc. for $C_{34}H_{45}N_3O_{22}$: C, 48.17; H, 5.35; N, 4.96. Found: C, 48.08; H, 5.42; N, 5.07.

O-(6-Acetamido-2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-D-glucopyranosyl)-(1→4)-2,3-di-O-acetyl-1,6-anhydro-β-D-glucopyranose (**21**). — Compound **20** was dissolved in dry methanol (20 ml), and $BaCO_3$ (1.6 g) and Raney Ni (one spatulaful) were added. The mixture was heated to boiling while hydrazine hydrate (1 ml) was added dropwise during 10 min. 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 (5 ml) overnight at room temperature. The mixture was concentrated to a syrup which was chromatographed on silica gel (20 g) with 17:3 (v/v) benzene–ethanol as eluent. The fractions containing the major product were evaporated to dryness, and the residue was crystallized from ether–petroleum ether to give **21** (260 mg, 64%), m.p. 128–130°, $[\alpha]_D^{15}$ +87.1° (*c* 1.3, chloroform).

Anal. Calc. for $C_{36}H_{49}NO_{23}$: C, 50.06; H, 5.72; N, 1.62. Found: C, 49.92; H, 5.95; N, 1.81.

O-(2,3,4-Tri-O-acetyl-6-S-acetyl-6-thio-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-α-D-glucopyranose (**22**), *O-(2,3,4-tri-O-acetyl-6-deoxy-6-iodo-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-α-D-glucopyranose* (**23**), *O-(2,3,6-tri-O-acetyl-6-bromo-6-deoxy-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-α-D-glucopyranose* (**24**), *O-(2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-α-D-glucopyranose* (**25**), *O-(2,3,4-tri-O-acetyl-6-chloro-6-deoxy-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-α-D-glucopyranose* (**26**), *and O-(6-acetamido-2,3,4-tri-O-acetyl-6-deoxy-α-D-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-α-D-glucopyranose* (**27**). — Compounds **14**, **15**, **16**, **18**, **19**, and **21** (200 mg) were treated with the acetolysis mixture, as described for the acetolysis of **8**, to give the corresponding 6″-substituted α-decaacetates **22**–**27**, respectively:

Compound **22** (129 mg, 58%), m.p. 129–130° (from ethanol), $[\alpha]_D^{20}$ +123.5° (*c* 1.5, chloroform).

Anal. Calc. for $C_{40}H_{54}O_{26}S$: C, 44.88; H, 5.54; S, 3.26. Found: C, 44.71; H, 5.65; S, 3.33.

Compound **23** (157 mg, 69%), m.p. 179–180° (from ethanol), $[\alpha]_D^{20}$ +126.0° (*c* 1.3, chloroform).

Anal. Calc. for $C_{38}H_{51}IO_{25}$: C, 44.11; H, 4.97; I, 12.27. Found: C, 44.20; H, 4.90; I, 12.12.

Compound **24** (161 mg, 72%), m.p. 139–141° (from methanol), $[\alpha]_D^{25}$ +122.1° (*c* 1.3, chloroform).

Anal. Calc. for $C_{38}H_{51}BrO_{25}$: C, 46.21; H, 5.20; Br, 8.09. Found: C, 45.99; H, 5.31; Br, 8.18.

Compound **25** (158 mg, 70%), m.p. 150–151° (from methanol), $[\alpha]_D^{20}$ +123.1° (*c* 1.3, chloroform).

Anal. Calc. for $C_{38}H_{53}O_{25}$: C, 50.17; H, 5.77. Found: C, 50.22; H, 5.88.

Compound **26** (169 mg, 75%), m.p. 170–171° (from methanol), $[\alpha]_D^{20}$ +125.2° (*c* 1.0, chloroform).

Anal. Calc. for $C_{38}H_{51}ClO_{25}$: C, 48.39; H, 5.45; Cl, 3.76. Found: C, 48.50; H, 5.29; Cl, 3.81.

Compound **27** (121 mg, 54%), m.p. 112–114° (from ether), $[\alpha]_D^{25}$ +124.2° (*c* 1.1, chloroform).

Anal. Calc. for $C_{40}H_{55}NO_{26}$: C, 49.74; H, 5.74; N, 1.45. Found: C, 49.68; H, 5.89; N, 1.51.

*O-6-Bromo-6-deoxy-α-*D*-glucopyranosyl-(1→4)-O-α-*D*-glucopyranosyl-(1→4)-*D*-glucopyranose* (**28**), *O-6-deoxy-α-*D*-glucopyranosyl-(1→4)-O-α-*D*-glucopyranosyl-(1→4)-*D*-glucopyranose* (**29**), *and O-6-chloro-6-deoxy-α-*D*-glucopyranosyl-(1→4)-O-α-*D*-glucopyranosyl-(1→4)-*D*-glucopyranose* (**30**). — Compounds **24**, **25**, and **26** (130 mg) were treated with 0.5M sodium methoxide (0.1 ml) in methanol (3 ml), as described for the preparation of **12**, to give the corresponding 6″-substituted maltotrioses **27**, **28**, and **29**, respectively, as hygroscopic powders, but these could not be crystallized:

Compound **28** (71 mg, 95%), $[\alpha]_D^{20}$ + 146.5° (equil., *c* 1.4, water). Compound **29** (66 mg, 94%), $[\alpha]_D^{25}$ +143.0° (equil., *c* 0.9, water); n.m.r. (D_2O): τ 8.75 (d, 3 H, *J* 6.0 Hz, CH_3-5″). Compound **30** (70 mg, 92%), $[\alpha]_D^{18}$ + 140.2° (equil., *c* 0.8, water).

*O-(2,3,4-Tri-O-acetyl-6-bromo-6-deoxy-α-*D*-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-*D*-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-β-*D*-glucopyranose* (**31**), *O-(2,3,4-tri-O-acetyl-6-deoxy-α-*D*-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-*D*-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-β-*D*-glucopyranose* (**32**), *and O-(2,3,4-tri-O-acetyl-6-chloro-6-deoxy-α-*D*-glucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-α-*D*-glucopyranosyl)-(1→4)-1,2,3,6-tetra-O-acetyl-β-*D*-glucopyranose* (**33**). — Each of the free sugars **28**, **29**, and **30** (50 mg) was acetylated with acetic anhydride (1 ml) and pyridine (2 ml) overnight at room temperature. Isolation in the usual way gave the corresponding 6″-substituted β-decaacetates **31**, **32**, and **33**, respectively.

Compound **31** (71 mg, 82%), m.p. 197–198° (from ethanol), $[\alpha]_D^{20}$ +92.3° (*c* 1.2, chloroform).

Anal. Calc. for $C_{38}H_{51}BrO_{25}$: C, 46.21; H, 5.20; Br, 8.09. Found: C, 46.33; H, 5.24; Br, 7.90.

Compound **32** (80 mg, 86%), m.p. 174–175° (from ethanol), $[\alpha]_D^{23}$ +88.0° (*c* 0.7, chloroform).

Anal. Calc. for $C_{38}H_{53}O_{25}$: C, 50.17; H, 5.77. Found: C, 50.00; H, 5.91.

Compound **33** (73 mg, 86%), m.p. 188–189° (from methanol), $[\alpha]_D^{20}$ +84.5° (*c* 0.8, chloroform).

Anal. Calc. for $C_{38}H_{51}ClO_{25}$: C, 48.39; H, 5.45; Cl, 3.76. Found: C, 48.31; H, 5.58; Cl, 3.90.

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