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# SYNTHESIS OF CELLOBIOSE, CELLOTRIOSE, CELLOTETRAOSE, AND LACTOSE

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ABSTRACT

Condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) with benzyl 2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**6**) in 1:1 benzene–nitromethane in the presence of mercuric cyanide gave, in 86% yield after *O*-deacetylation followed by column chromatography, benzyl 2,3,6-tri-*O*-benzyl-β-cellobioside, which was catalytically hydrogenolyzed to afford cellobiose. In a similar way, methyl α-cellobioside, cellotriose, methyl α- and β-cellotriosides, cellotetraose, lactose, and methyl α-lactoside were synthesized with high stereospecificity and in good yield by the coupling reaction, using methyl 2,3,6-tri-*O*-benzyl-α- and -β-D-glucopyranoside, **6**, and benzyl 2,3,6,2′,3′,6′-hexa-*O*-benzyl-β-cellobioside as the glycosyl acceptors, and **1**, 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide, and hepta-*O*-acetyl-α-cellobiosyl bromide as the glycosyl donors.

## INTRODUCTION

The practical, chemical synthesis of cellobiose (**13**) and lactose (**31**) has principally been hampered, by the low reactivity towards glycosylation of the equatorially disposed, HO-4 group in D-glucopyranose derivatives in the $^4C_1$ conformation, and partly by some difficulty in obtaining a suitably substituted D-glucopyranose derivative having only HO-4 unsubstituted. The disaccharide **13** has been synthesized in low yields (1.9–10%) by condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) with 1,6-anhydro-β-D-glucopyranose[1] or 1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranose[2], and in 35% yield[3] from epicellobiose octaacetate by a series of reactions involving inversion of the configuration at C-2.

The disaccharide **31** had been prepared[4] in 27% yield by rearrangement of epilactose octaacetate. Curtis and Jones[5] and Shapiro *et al.*[6] used 2,3:5,6-di-*O*-isopropylidene-D-glucose diethyl acetal and 2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose, respectively, to circumvent the low reactivity of HO-4 of D-glucopyranose derivatives in the $^4C_1$ conformation, and, by coupling with 2,3,4,6-tetra-

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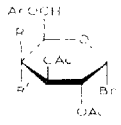
*O*-acetyl-α-D-galactopyranosyl bromide (**2**), obtained **31** and 1,6-anhydro-β-lactose hexaacetate in 39 and 41% yield, respectively. The disaccharide **31** has also been synthesized[7,8] in low yields by conversion of **13** *via* the 4',6'-di-*O*-(methylsulfonyl) derivatives.

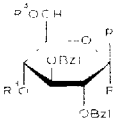
Takeo and co-workers[9] and Schmidt and Michel[10] have reported the synthesis of derivatives of cellotriose (**19**), and of derivatives of **13**, **19**, and cellotetraose (**29**), by methods respectively based on the Koenigs–Knorr type of condensation and the imidate procedure. However, neither method has proved satisfactory for the preparation of fairly large quantities of **13**, **19**, and **29**, and their derivatives, as the glycosyl acceptors used for the syntheses[9,10] are not readily prepared in the quantities needed. Sinaÿ[11] studied the influence of the nature of the substituents on the reactivity of HO-4 towards glycosylation for derivatives of methyl α-D-glucopyranoside and benzyl 2-acetamido-2-deoxy-α-D-glucopyranoside, and showed that substitution at O-3 by ether groups is essential for obtaining β-D-(1→4)-linked disaccharide derivatives in high yields. Recently, Garegg *et al.*[12,13] developed a highly regioselective, reductive opening of benzylidene acetals of hexopyranosides using cyanoborohydride–hydrochloric acid, giving high yields of the 2,3,6-tri-*O*-benzyl derivatives of D-glucopyranosides. These two results prompted us to re-investigate the synthesis of lower member of the series of cello-oligosaccharides, and of **31**. We report here a practical synthesis of **13**, **19**, **29**, and **31**, as well as of methyl α-cellobioside (**17**), methyl α- (**22**) and β-cellotrioside (**25**), and methyl α-lactoside (**33**) by the Koenigs–Knorr reaction of readily available glycosyl acceptors and donors.

## RESULTS AND DISCUSSION

Methyl 2,3,6-tri-*O*-benzyl-α- (**3**) and -β-D-glucopyranoside (**4**) were prepared according to the procedure of Garegg *et al.*[12,13] using sodium cyanoborohydride–hydrochloric acid. Similarly, treatment of benzyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside[14,15] (**5**) with sodium cyanoborohydride–hydrochloric acid in oxolane (tetrahydrofuran) gave a mixture that was fractionated by chromatography on a column of silica gel, to afford benzyl 2,3,6-[15] (**6**) and 2,3,4-



1 R = H, R' = OAc
2 R = OAc, R' = H



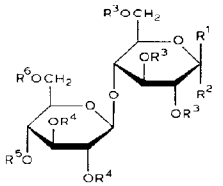
3 R = R' = H, R'' = OMe, R''' = Bzl
4 R = OMe, R' = R'' = H, R''' = Bzl
5 R = OBzl, R' = H, R'', R''' = PhCH
6 R = OBzl, R' = R'' = H, R''' = Bzl
7 R = OBzl, R' = R'' = H, R''' = Bzl

Bzl = PhCH

tri-*O*-benzyl-β-D-glucopyranoside[15] (**7**) in 85 and 6% yield, respectively. Reductive removal of the benzylidene group of benzyl 2,3,6,2′,3′-penta-*O*-benzyl-4′,6′-*O*-benzylidene-β-cellobioside[16] (**8**) with sodium cyanoborohydride–hydrochloric acid gave, after column chromatography, benzyl 2,3,6,2′,3′,6′- (**9**) and 2,3,6,2′,3′,4′-hexa-*O*-benzyl-β-cellobioside[16] (**10**) in 86 and 5% yield, respectively. Methylation[17] of **9**, followed by hydrogenolysis, hydrolysis, reduction with sodium borohydride, and acetylation, produced a 1:1 mixture of the peracetates of 4-*O*-methyl-D-glucitol and D-glucitol (g.l.c.), confirming the structure of **9**.

The condensation reactions were performed in 1:1 benzene–nitromethane in the presence of mercuric cyanide, the reaction temperature and time for each coupling reaction are specified in the Experimental section. When 2.5–3 molar proportions of the glycosyl donors, namely, **1**, **2**, and hepta-*O*-acetyl-α-cellobiosyl bromide (**11**), were used, the glycosyl acceptors **3**, **4**, **6**, and **9** reacted almost completely. Examination by t.l.c. of each reaction mixture showed the presence of a major product, invariably accompanied by traces of a marginally slower-migrating, unidentified product that could not be removed by column chromatography. Therefore, each reaction mixture was *O*-deacetylated to facilitate separation of the major product, and the resulting mixture of the products was chromatographed on a column of silica gel.

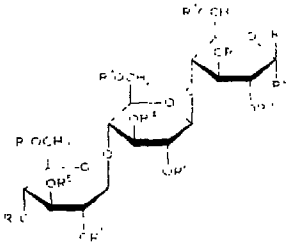
Condensation of **6** with **1**, followed by *O*-deacetylation, gave, after chromatographic fractionation, benzyl 2,3,6-tri-*O*-benzyl-β-cellobioside (**12**) in 86% yield. Catalytic hydrogenolysis of **12** in acetic acid in the presence of palladium-on-charcoal furnished, in 92% yield, compound **13**, which was identified by comparison with an authentic specimen[18], obtained by the acetolysis of cellulose.



**8** $R^1$ = OBzl, $R^2$ = H, $R^3$ = $R^4$ = Bzl, $R^5$, $R^6$ = PhCH
**9** $R^1$ = OBzl, $R^2$ = $R^5$ = H, $R^3$ = $R^4$ = $R^6$ = Bzl
**10** $R^1$ = OBzl, $R^2$ = $R^6$ = H, $R^3$ = $R^4$ = $R^5$ = Bzl
**11** $R^1$ = H, $R^2$ = Br, $R^3$ = $R^4$ = $R^5$ = $R^6$ = Ac
**12** $R^1$ = OBzl, $R^2$ = $R^4$ = $R^5$ = $R^6$ = H, $R^3$ = Bzl
**13** $R^1$ = OH, $R^2$ = $R^3$ = $R^4$ = $R^5$ = $R^6$ = H
**14** $R^1$ = OBzl, $R^2$ = H, $R^3$ = Bzl, $R^4$ = $R^5$ = $R^6$ = Ac
**15** $R^1$ = OBzl, $R^2$ = $R^6$ = H, $R^3$ = Bzl; $R^5$, $R^6$ = PhCH
**16** $R^1$ = $R^4$ = $R^5$ = $R^6$ = H, $R^2$ = OMe, $R^3$ = Bzl
**17** $R^1$ = $R^3$ = $R^4$ = $R^5$ = $R^6$ = H, $R^2$ = OMe

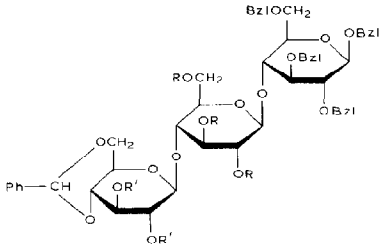
Acetylation of **12** afforded crystalline benzyl 2',3',4',6'-tetra-*O*-acetyl-2,3,6-tri-*O*-benzyl-β-cellobioside (**14**). Conventional treatment of **12** with benzaldehyde in the presence of zinc chloride gave crystalline benzyl 2,3,6-tri-*O*-benzyl-4',6'-*O*-benzylidene-β-cellobioside (**15**), a useful starting-material for chemical modification of HO-2' and -3' in **13**. Reaction of **3** with **1**, and subsequent *O*-deacetylation, gave, in 84% yield after column chromatography, methyl 2,3,6-tri-*O*-benzyl-α-cellobioside (**16**), which was submitted to hydrogenolysis, furnishing **17** in 90% yield. Compound **17** had previously been prepared by the anomerization of methyl β-cellobioside with titanium tetrachloride[19], and by methanolysis of β-cellobiosyl *N*,*N*-dimethyldithiocarbamate[11] and of 3,6,2',3',4',6'-hexa-*O*-acetyl-β-cellobiosyl chloride[21].

Reaction of **6** with **11**, followed by *O*-deacetylation, gave a mixture from which benzyl 2,3,6-tri-*O*-benzyl-β-cellotrioside (**18**) crystallized in 39% yield. Fractionation of the mother liquor from **18** on a column of silica gel afforded a further



**18** R = OBzl, R' = R'' = R''' = H, R'''' = Bzl
**19** R = R' = R'' = R''' = H, R'''' = OH
**20** R = OBzl, R' = R''' = H, R'' = R'''' = Bzl
**21** R = R'' = R''' = H, R' = OMe, R'''' = Bzl
**22** R = R' = R'' = R''' = H, R'''' = OMe
**23** R = R' = OMe, R'' = R''' = R'''' = Ac
**24** R = OMe, R' = R'' = R''' = H, R'''' = Bzl
**25** R = OMe, R' = R'' = R''' = R'''' = H

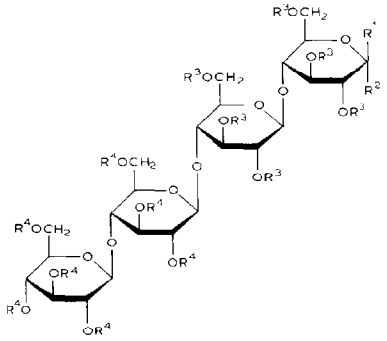
38% yield of **18**. Hydrogenolysis of **18** furnished, in 90% yield, compound **19**, which was characterized by comparison with an authentic sample[18]. In the alternative synthesis of **19**, compound **9** was allowed to react with **1**, to give, in 80% yield after *O*-deacetylation followed by column chromatography, benzyl 2,3,6,2',3',6'-hexa-*O*-benzyl-β-cellotrioside (**20**), which, on hydrogenolysis, afforded **19**. Benzylidenation of **18** gave crystalline benzyl 2,3,6-tri-*O*-benzyl-4'',6''-*O*-benzylidene-β-cellotrioside (**26**), whereas that of **20** produced crystalline benzyl 2,3,6,2',3',6'-hexa-*O*-benzyl-4'',6''-*O*-benzylidene-β-cellotrioside (**27**), which is a useful intermediate for the chemical modification of HO-2'' and -3'' in **19**.



**26** R = R′ = H
**27** R = Bzl, R′ = H

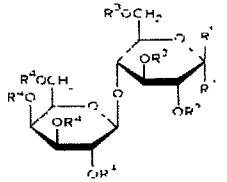
Condensation of **3** with **11**, followed by *O*-deacetylation and column chromatography, gave, in 77% yield, methyl 2,3,6-tri-*O*-benzyl-α-cellotrioside (**21**), which was hydrogenolyzed to furnish **22** in crystalline form in 92% yield. Acetylation of **22** afforded methyl α-cellotrioside decaacetate (**23**) in crystalline form. Compound **23** had previously been obtained[22] as an amorphous solid by the anomerization of methyl β-cellotrioside decaacetate with titanium tetrachloride. Reaction of **4** with **11**, followed by *O*-deacetylation and column chromatography, afforded, in 80% yield, methyl 2,3,6-tri-*O*-benzyl-β-cellotrioside (**24**), which was hydrogenolyzed to furnish the known[9] **25** in 93% yield.

When compound **9** reacted with **11**, benzyl 2,3,6,2′,3′,6′-hexa-*O*-benzyl-β-cellotetraoside (**28**) was obtained in 69% yield, after *O*-deacetylation followed by column chromatography. Hydrogenolysis of **28** furnished, in 84% yield, compound **29**, which was identified by comparison with an authentic specimen[18].



**28** $R^1$ = OBzl, $R^2$ = $R^4$ = H, $R^3$ = Bzl
**29** $R^1$ = OH, $R^2$ = $R^3$ = $R^4$ = H

Reaction of **6** with **2**, followed by *O*-deacetylation and column chromatography, gave, in 84% yield, benzyl 2,3,6-tri-*O*-benzyl-β-lactoside (**30**), which, on hydrogenolysis, provided **31** in 92% yield. Coupling of **3** with **2**, followed by *O*-deacetylation and column chromatography, gave, in 86% yield, methyl 2,3,6-tri-*O*-benzyl-α-lactoside (**32**), which was debenzylated to afford **33** in 92% yield. Compound **33** had previously been prepared[20] by methanolysis of β-lactosyl *N,N*-dimethyldithiocarbamate.



**30** R¹ = OBzl, R² = R⁴ = H, R³ = Bzl
**31** R = R¹ = R⁴ = H, R² = OH
**32** R = R⁴ = H, R² = OMe, R³ = Bzl
**33** R = R¹ = R⁴ = H, R² = OMe

## EXPERIMENTAL

*General methods.* — Unless stated otherwise, the general experimental conditions were the same as those described previously[23]. Retention times are given relative to that of 1,2,3,4,5,6-hexa-*O*-acetyl-D-glucitol as unity. The following solvent systems (v/v) were used: (*1*) 2:1 hexane–ethyl acetate, (*2*) 9:1 benzene–ethyl acetate, (*3*) 9:1 benzene–ethanol, and (*4*) 9:1 chloroform–methanol.

*Benzyl 2,3,6-tri-O-benzyl-β-D-glucopyranoside* (**6**) *and benzyl 2,3,4-tri-O-benzyl-β-D-glucopyranoside* (**7**). — To a stirred mixture of **5** (22.0 g), sodium cyanoborohydride (25 g), and molecular sieves 3A (20 g) in anhydrous oxolane (330 mL), cooled to 0°, was added dropwise diethyl ether saturated with hydrogen chloride until the evolution of gas ceased. After 1 h, t.l.c. (solvent *1*) showed that the reaction was complete. The mixture was processed as described earlier[12,13], and the resulting mixture was fractionated on a column of silica gel with solvent *1*. The first fraction gave **6** (18.8 g, 85%); m.p. 64–65° (hexane–ether), $[\alpha]_D^{20}$ −44.2° (*c* 1.8, chloroform); lit.[15] m.p. 66–67° (ethanol–water), $[\alpha]_D^{20}$ −42° (*c* 1.07, chloroform).

The second fraction afforded **7** (1.35 g, 6%); m.p. 105–106° (hexane–ether), $[\alpha]_D^{20}$ −9.1° (*c* 1.5, chloroform); lit.[15] m.p. 104–105° (ethanol–water), $[\alpha]_D^{20}$ −9° (*c* 0.9, chloroform).

*Benzyl 2,3,6-tri-O-benzyl-4-O-(2,3,6-tri-O-benzyl-β-D-glucopyranosyl)-β-D-glucopyranoside* (**9**) *and benzyl 2,3,6-tri-O-benzyl-4-O-(2,3,4-tri-O-benzyl-β-D-*

*glucopyranosyl)-β-*D*-glucopyranoside* (**10**). — Compound **8** (11.0 g) was treated, in oxolane (180 mL) containing sodium cyanoborohydride (15 g) and molecular sieves 3A (10 g), with diethyl ether saturated with hydrogen chloride, as just described, to give a mixture which was chromatographed on a column of silica gel with solvent *2*. The initial fraction gave **9** (9.5 g, 86%); m.p. 82–83° (hexane); $[\alpha]_D^{20}$ −7.5° (*c* 1.3, chloroform).

*Anal.* Calc. for $C_{61}H_{64}O_{11}$: C, 75.29; H, 6.63. Found: C, 75.57; H, 6.49.

Successive methylation[17] of a portion of **9**, hydrogenolysis in acetic acid in the presence of 10% palladium-on-charcoal, hydrolysis with 0.5M sulfuric acid for 6 h at 100°, neutralization with barium carbonate, reduction with sodium borohydride, and acetylation, gave compounds that had the retention times of the peracetates of 4-*O*-methyl-D-glucitol (*T* 0.85, 50%) and D-glucitol (*T* 1.00, 50%).

The second fraction eluted from the column afforded **10** (0.6 g, 5%); m.p. 94–95° (hexane–ether), $[\alpha]_D^{20}$ +6.6° (*c* 1.0, chloroform); lit.[16] m.p. 96–98°, $[\alpha]_D$ +7.5° (*c* 1.06, chloroform).

*Benzyl 2,3,6-tri-O-benzyl-4-O-β-*D*-glucopyranosyl-β-*D*-glucopyranoside* (**12**). — A solution of **6** (5.51 g, 10.2 mmol) in 1:1 (v/v) benzene–nitromethane (280 mL) was concentrated until 110 mL of the solvent mixture had distilled, and the concentrate was then cooled to 50°. Compound **1** (4.19 g, 10.2 mmol) and mercuric cyanide (2.51 g, 10.2 mmol) were added, and the mixture was stirred for 8 h at 50°. Further additions of **1** (6.29 g, 15.3 mmol) and mercuric cyanide (3.86 g, 15.3 mmol) were made, and stirring was continued for another 16 h. The mixture was evaporated to dryness, and the residue was dissolved in chloroform. The solution was washed successively with water, aqueous potassium iodide, aqueous sodium hydrogencarbonate, and water, dried (sodium sulfate), and evaporated. A solution of the residual syrup in anhydrous methanol (100 mL) was treated with M sodium methoxide (5 mL). The solution was kept for 2 h at room temperature, made neutral with aqueous acetic acid, and evaporated to a syrupy product, which was applied to a column of silica gel that had been packed by using benzene. Elution of the column with solvent *3* gave **12** as an amorphous powder (6.16 g, 86%); $[\alpha]_D^{20}$ +10.4°(*c* 0.8, chloroform).

*Anal.* Calc. for $C_{40}H_{46}O_{11}$: C, 68.36; H, 6.60. Found: C, 68.64; H, 6.43.

*4-O-β-*D*-Glucopyranosyl-β-*D*-glucopyranose* (**13**). — A solution of **12** (2.15 g) in acetic acid (40 mL) was hydrogenolyzed in the presence of 10% palladium-on-charcoal (1.5 g) at atmospheric pressure for 1 day at room temperature. The catalyst was filtered off through a Celite pad, and washed with boiling water (50 mL). The filtrate and washings were combined, and evaporated to a syrup, which crystallized from aqueous ethanol, to give **13** (0.97 g, 92%); m.p. and mixed m.p. 224–225°, $[\alpha]_D^{20}$ +13.0 (3 min)→ +34.0° (*c* 5.0, water); lit.[18] m.p. 225°, $[\alpha]_D^{20}$ +14→ +34.6° (*c* 8, water).

*Benzyl 2,3,6-tri-O-benzyl-4-O-(2,3,4,6-tetra-O-acetyl-β-*D*-glucopyranosyl)-β-*D*-glucopyranoside* (**14**). — A solution of **12** (0.49 g) in 1:1 (v/v) acetic anhydride–pyridine (5 mL) was kept overnight at room temperature. The solvents were

removed by codistillation with toluene, to give a solid which was recrystallized from ether–hexane, to afford **14** (0.57 g, 93%): m.p. 100–101°, $[\alpha]_D^{20}$ −13.2° (*c* 1.4, chloroform); n.m.r. data (chloroform-*d*): δ 7.37–7.21 (m, 20 H, aromatic), 1.98 (s, 6 H, 2 OAc), 1.95 (s, 3 H, OAc), and 1.93 (s, 3 H, OAc).

*Anal.* Calc. for $C_{48}H_{54}O_{15}$: C, 66.20; H, 6.25. Found: C, 66.39; H, 6.34.

*Benzyl 2,3,6-tri-O-benzyl-4-O-(4,6-O-benzylidene-β-D-glucopyranosyl)-β-D-glucopyranoside* (**15**). — A suspension of **12** (2.50 g) and powdered, anhydrous zinc chloride (2.5 g) in freshly distilled benzaldehyde (12 mL) was stirred for 5 h at room temperature. The solution was poured into a mixture of petroleum ether and ice-water, and the precipitate formed was filtered off, successively washed with cold water and petroleum ether, and dried. Crystallization from ethanol gave **15** (2.45 g, 87%): m.p. 151–152°, $[\alpha]_D^{20}$ 0° (*c* 1.4, chloroform); n.m.r. data (chloroform-*d*): δ 5.40 (s, 1 H, benzylic H).

*Anal.* Calc. for $C_{47}H_{50}O_{11}$: C, 71.38; H, 6.37. Found: C, 71.51; H, 6.46.

*Methyl 2,3,6-tri-O-benzyl-4-O-β-D-glucopyranosyl-α-D-glucopyranoside* (**16**). — Treatment of **3** (3.05 g, 6.6 mmol) in 1:1 benzene–nitromethane (90 mL) with **1** (6.75 g, 16.4 mmol) and mercuric cyanide (4.15 g, 16.4 mmol) for 28 h at 50°, followed by *O*-deacetylation, as described for the preparation of **12**, gave a mixture which was chromatographed on a column of silica gel that had been packed by using benzene. Elution with solvent *3* afforded **16** as an amorphous powder (3.45 g, 84%); $[\alpha]_D^{20}$ +34.5° (*c* 3.6, chloroform).

*Anal.* Calc. for $C_{34}H_{42}O_{11}$: C, 65.16; H, 6.76. Found: C, 65.33; H, 6.69.

*Methyl 4-O-β-D-glucopyranosyl-α-D-glucopyranoside* (**17**). — Hydrogenolysis of **16** (1.87 g), as described for **12**, gave **17** (0.95 g, 90%), m.p. 143–144° (ethanol), $[\alpha]_D^{20}$ +97.6° (*c* 2.0, water); lit.[21] m.p. 144–145° (ethanol), $[\alpha]_D^{25}$ +97.4° (*c* 1.4, water).

*Benzyl O-β-D-glucopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→4)-2,3,6-tri-O-benzyl-β-D-glucopyranoside* (**18**). — Treatment of **6** (7.0 g, 12.9 mmol) in 1:1 benzene–nitromethane (220 mL) with **1** (27.2 g, 38.9 mmol) and mercuric cyanide (9.82 g, 38.9 mmol) for 60 h at 60°, followed by *O*-deacetylation, as described for the preparation of **12**, gave a syrup which was extracted with water to remove **13**. The resulting residue crystallized from ethanol–ether and was recrystallized from ethanol, to give **18** (4.37 g, 39%): m.p. 193–194°, $[\alpha]_D^{20}$ +4.9° (*c* 2.0, chloroform).

*Anal.* Calc. for $C_{40}H_{56}O_{11}$: C, 63.88; H, 6.53. Found: C, 64.15; H, 6.69.

The mother liquors were evaporated to a syrup that was eluted from a column of silica gel (that had been packed by using chloroform) with solvent *4*, to afford an additional amount of **18** (4.25 g, 38%).

*O-β-D-Glucopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→4)-α-D-glucopyranose* (**19**). — Hydrogenolysis of **18** (3.43 g), as described for **12**, gave **19** (1.79 g, 90%); m.p. and mixed m.p. 206–208.5° (dec.) (aqueous ethanol), $[\alpha]_D^{21}$ +32.8° (3 min)→ +21.0° (*c* 4.2, water); lit.[18] m.p. 206–209° (dec.), $[\alpha]_D^{20}$ +35° → +22° (*c* 4, water).

Benzyl O-β-D-*glucopyranosyl-(1→4)-O-(2,3,6-tri-O-benzyl-β-D-glucopyra-*

*nosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**20**). — Treatment of **9** (3.98 g, 4.1 mmol) in 1:1 benzene–nitromethane (120 mL) with **1** (5.05 g, 12.3 mmol) and mercuric cyanide (3.10 g, 12.3 mmol) for 57 h at 60°, followed by *O*-deacetylation, as described for the preparation of **12**, gave a syrup which was chromatographed on a column of silica gel (that had been packed by using benzene) with solvent *3*, to afford **20** as an amorphous powder (3.71 g, 80%); $[\alpha]_D^{20}$ +9.3° (*c* 3.2, chloroform).

*Anal.* Calc. for $C_{67}H_{74}O_{16}$: C, 70.88; H, 6.57. Found: C, 71.04; H, 6.40.

Hydrogenolysis of **20** (1.23 g), as described for **12**, gave **19** (0.48 g, 87%); m.p. 206–209° (dec.) (aqueous ethanol), $[\alpha]_D^{20}$ +32.5 (3 min)→ +21.3° (*c* 3.5, water).

*Benzyl* O-*(4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1→4)-*O*-β-*D*-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**26**). — Treatment of **18** (1.33 g) with benzaldehyde (7 mL) in the presence of zinc chloride (1.3 g) for 7 h at room temperature, as described for **12**, gave **26** (1.26 g, 86%); m.p. 190–191° (ethanol–ether), $[\alpha]_D^{20}$ −4.3° (*c* 1.8, chloroform); n.m.r. data (chloroform-*d*): δ 5.42 (s, 1 H, benzylic H).

*Anal.* Calc. for $C_{53}H_{60}O_{16}$: C, 66.79; H, 6.35. Found: C, 66.84; H, 6.37.

*Benzyl* O-*(4,6-*O*-benzylidene-β-*D*-glucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-benzyl-β-*D*-glucopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucopyranoside* (**27**). — Compound **20** (0.84 g) was treated with benzaldehyde (4 mL) in the presence of zinc chloride (0.8 g) for 7 h at room temperature, as described for **12**, to give **27** (0.77 g, 85%); m.p. 138.5–139.5° (ether–petroleum ether), $[\alpha]_D^{20}$ −1.4° (*c* 1.4, chloroform); n.m.r. data (chloroform-*d*): δ 5.40 (s, 1 H, benzylic H).

*Anal.* Calc. for $C_{74}H_{78}O_{16}$: C, 72.65; H, 6.43. Found: C, 72.81; H, 6.35.

*Methyl* O-β-*D*-glucopyranosyl-(1→4)-*O*-β-*D*-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-*D*-glucopyranoside* (**21**). — Treatment of **3** (2.35 g, 5.1 mmol) in 1:1 benzene-nitromethane (70 mL) with **11** (10.61 g, 15.2 mmol) and mercuric cyanide (3.83 g, 15.2 mmol) for 60 h at 60°, followed by *O*-deacetylation, as described for the preparation of **12**, gave a syrup which was fractionated on a column of silica gel (that had been packed by using chloroform) with solvent *4*, to afford **21** as an amorphous powder (3.07 g, 77%); $[\alpha]_D^{20}$ +24.7° (*c* 2.4, chloroform).

*Anal.* Calc. for $C_{40}H_{52}O_{16}$: C, 60.90; H, 6.64. Found: C, 61.10; H, 6.79.

*Methyl* O-β-*D*-glucopyranosyl-(1→4)-*O*-β-*D*-glucopyranosyl-(1→4)-α-*D*-glucopyranoside* (**22**). — Hydrogenolysis of **21** (2.75 g), as described for **12**, gave **22** (1.66 g, 92%); m.p. 253–255° (methanol–ethanol), $[\alpha]_D^{20}$ +68.8° (*c* 1.9, water); n.m.r. data (deuterium oxide): δ 4.79 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1) and 3.40 (s, 3 H, OMe).

*Anal.* Calc. for $C_{19}H_{34}O_{16}$: C, 44.02; H, 6.61. Found: C, 43.91; H, 6.75.

*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-α-*D*-glucopyranoside* (**23**). — Acetylation of **22** (0.52 g) with 1:1 acetic anhydride–pyridine (6 mL), as described for **12**, gave **23** (0.88 g, 94%); m.p. 177.5–179° (ether–petroleum ether–ethanol),

$[\alpha]_D^{20}$ +31.7° (*c* 1.9, chloroform); lit.[22] m.p. 110–115° (ether–petroleum ether). $[\alpha]_D^{20}$ +32 ±1° (*c* 1.3, chloroform).

*Anal.* Calc. for $C_{39}H_{54}O_{26}$: C, 49.89; H, 5.80. Found: C, 50.05; H, 5.69.

*Methyl* O-*β*-D-*glucopyranosyl-(1→4)*-O-*β*-D-*glucopyranosyl-(1→4)-2,3,6-tri*-O-*benzyl*-*β*-D-glucopyranoside (**24**). — The product obtained by treatment of **4** (4.0 g, 8.6 mmol) in 1:1 benzene–nitromethane (120 mL) with **11** (18.07 g, 25.8 mmol) and mercuric cyanide (6.53 g, 25.8 mmol) for 60 h at 60°, followed by *O*-deacetylation as described previously, was fractionated on a column of silica gel (that had been packed by using chloroform) with solvent *4*, to give **24** as an amorphous powder (5.43 g, 80%); $[\alpha]_D^{20}$ +15.7° (*c* 4.2, chloroform).

*Anal.* Calc. for $C_{40}H_{52}O_{16}$: C, 60.90; H, 6.64. Found: C, 61.11; H, 6.50.

Methyl O-*β*-D-*glucopyranosyl-(1→4)*-O-*β*-D-*glucopyranosyl-(1→4)*-*β*-D-*glucopyranoside* (**25**). — Hydrogenolysis of **24** (2.29 g), as described previously, gave **25** (1.40 g, 93%); m.p. 265–267° (dec.) (aqueous ethanol), $[\alpha]_D^{20}$ −13.7° (*c* 3.4, water); lit.[9] m.p. 265–267° (dec.) (aqueous ethanol), $[\alpha]_D^{17}$ −13.9° (*c* 3.2, water).

Benzyl O-*β*-D-*glucopyranosyl-(1→4)*-O-*β*-D-*glucopyranosyl-(1→4)*-O-*(2,3,6-tri*-O-*benzyl*-*β*-D-*glucopyranosyl)-(1→4)-2,3,6-tri*-O-*benzyl*-*β*-D-*glucopyranoside* (**28**). — The product obtained by treatment of **9** (2.0 g, 2.1 mmol) in 1:1 benzene–nitromethane (60 mL) with **11** (4.31 g, 6.2 mmol) and mercuric cyanide (1.56 g, 6.2 mmol) for 66 h at 65°, followed by *O*-deacetylation, as described previously, was chromatographed on a column of silica gel (that had been packed by using chloroform) with solvent *4*, to afford **28** as an amorphous powder (1.84 g, 69%); $[\alpha]_D^{20}$ +5.2° (*c* 1.9, chloroform).

*Anal.* Calc. for $C_{73}H_{84}O_{21}$: C, 67.58; H, 6.53. Found: C, 67.75; H, 6.40.

O-*β*-D-*Glucopyranosyl-(1→4)*-O-*β*-D-*glucopyranosyl-(1→4)*-O-*β*-D-*glucopyranosyl-(1→4)*-*β*-D-*glucopyranose* (**29**). — Hydrogenolysis of **28** (1.45 g), as described previously, gave **29** (0.62 g, 84%); m.p. and mixed m.p. 251–253° (dec.) (aqueous ethanol), $[\alpha]_D^{20}$ +7.1 (3 min)→ +17.1° (*c* 2.5, water); lit.[18] m.p. 252–253° (dec.), $[\alpha]_D^{23}$ +8→ +16.5° (*c* 3.4, water).

*Benzyl 2,3,6-tri*-O-*benzyl*-4-O-*β*-D-*galactopyranosyl*-*β*-D-*glucopyranoside* (**30**). — The product obtained by treatment of **6** (3.0 g, 5.5 mmol) in 1:1 benzene–nitromethane (90 mL) with **2** (5.70 g, 13.9 mmol) and mercuric cyanide (3.50 g, 13.9 mmol) for 25 h at 40°, followed by *O*-deacetylation, as described previously, was chromatographed on a column of silica gel (that had been packed by using benzene) with solvent *3*, to give **30** as an amorphous powder (3.28 g, 84%); $[\alpha]_D^{20}$ +17.4° (*c* 3.4, chloroform).

*Anal.* Calc. for $C_{40}H_{46}O_{11}$: C, 68.36; H, 6.60. Found: C, 68.55; H, 6.70.

*4*-O-*β*-D-*Galactopyranosyl*-*α*-D-glucopyranose (**31**). — Hydrogenolysis of **30** (1.0 g), as described previously, afforded **31** as a monohydrate (0.47 g, 92%); m.p. 201–202° (dec.) (aqueous methanol), $[\alpha]_D^{20}$ +82 (2 min)→ +52.9° (*c* 1.9, water); lit.[4] m.p. 201 (dec.), $[\alpha]_D$ +81→ +52.7° (*c* 2.0, water).

*Methyl 2,3,6-tri*-O-*benzyl*-4-O-*β*-D-*galactopyranosyl*-*α*-D-*glucopyranoside* (**32**). — The product obtained by treatment of **3** (2.50 g, 5.4 mmol) in 1:1 benzene–

nitromethane (75 mL) with **2** (5.53 g, 13.4 mmol) and mercuric cyanide (3.39 g, 13.4 mmol) for 24 h at 40°, followed by *O*-deacetylation, as described previously, was fractionated on a column of silica gel (that had been packed by using benzene) with solvent *3*, to give **32** as an amorphous powder (2.90 g, 86%); $[\alpha]_D^{20}$ +38.5° (*c* 4.6, chloroform).

*Anal.* Calc. for $C_{34}H_{42}O_{11}$: C, 65.16; H, 6.76. Found: C, 65.29; H, 6.84.

*Methyl 4-O-β-D-galactopyranosyl-α-D-glucopyranoside* (**33**). — Hydrogenolysis of **32** (2.0 g), as described previously, gave **33** (1.14 g, 92%); m.p. 188–189° (ethanol), $[\alpha]_D^{20}$ +121.2° (*c* 1.6, water); lit.[20] m.p. 189–190° (ethanol), $[\alpha]_D^{25}$ +115.1° (*c* 1.03, water).

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