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THE SYNTHESIS OF 2-*O*-α-D-GALACTOPYRANOSYL-D-GALACTOPYRANOSE AND 2-*O*-(2-*O*-α-D-GALACTOPYRANOSYL-α-D-GALACTOPYRANOSYL)-D-GLUCOPYRANOSE UNDECA-ACETATE

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ABSTRACT

The synthesis of 2-*O*-α-D-galactopyranosyl-D-galactopyranose was accomplished by condensation of 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride with 2,2,2-trichloroethyl 3,4,6-tri-*O*-benzyl-α-D-galactopyranoside in the presence of mercuric cyanide. The title trisaccharide undeca-acetate was prepared by condensing 1,3,4,6-tetra-*O*-acetyl-2-*O*-(3,4,6-tri-*O*-acetyl-α-D-galactopyranosyl)-α-D-glucopyranose with 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl chloride or bromide in the presence of various glycosidation catalysts, followed by debenzylation and acetylation.

INTRODUCTION

Gamian and Romanowska[1] have determined the structure **1** for the outer-core oligosaccharide which constitutes part of the *Shigella sonnei* lipopolysaccharide.

α-D-Gal*p*-(1→2)-α-D-Gal*p*
1
↓
2
β-D-Glc*p*-(1→3)-α-D-Glc*p*-(1→3)-α-D-Glc*p*

1

A pentasaccharide of this type has also been identified in the core oligosaccharides of *Shigella* flexneri 6[2] and *Escherichia coli* C[3], although some differences have been noted regarding the anomeric configuration in the (1→3)-glucan chain. A specific feature of **1** is the presence of four α linkages.

We now report the synthesis of two oligosaccharides derived from **1**, namely, α-D-Gal*p*-(1→2)-D-Gal*p* (**2**) and the undeca-acetate of α-D-Gal*p*-(1→2)-α-D-Gal*p*-(1→2)-D-Glc*p* (**3**); **2** is one of the galactobioses not synthesised hitherto; galactobioses involving (1→1)-α,α^4, -β,β^4, and -α,β^5, (1→3)-α^6 and -$\beta^{6,7}$, (1→4)-α^6

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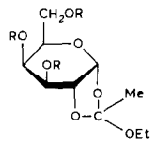
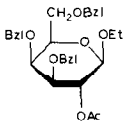
and -β^6, (1→5)-α^8, and (1→6)-α^9 and -β^{10} linkages have been obtained by synthesis [see below for comment on (1→2)-linked galactobioses].

RESULTS AND DISCUSSION

2,2,2-Trichloroethyl 3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (**10**), selected for the synthesis of **2**, was obtained as follows. 3,4,6-Tri-*O*-acetyl-1,2-*O*-ethoxyethylidene-α-D-galactopyranose (**4**) was obtained by a modification of the method of Lemieux and Morgan[11], which reduced the time of reaction from 12 h to 1 h with retention of the high yield. Treatment of **4** with benzyl chloride and sodium hydride in *N,N*-dimethylformamide gave **5** (41%). However, reaction of **5** with 2,2,2-trichloroethanol in the presence of mercuric bromide[12] did not give the expected 2,2,2-trichloroethyl glycoside but the ethyl β-glycoside **6** which was formed by an intramolecular rearrangement of **5** (*cf.* ref. 13).



4 R = Ac (*exo endo* 85 15)
5 R = Bzl (*exo endo* 88 12)



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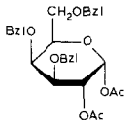

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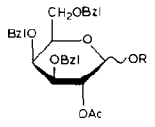
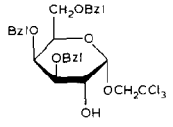


8 R = CH_2CCl_3
9 R = H



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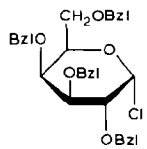
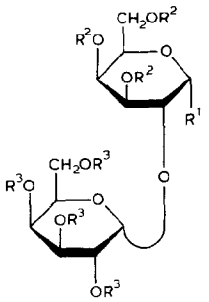
Conversion of **5** into the 1,2-diacetate **7** followed by treatment with 2,2,2-trichloroethanol in the presence of anhydrous zinc chloride[14] gave the expected glycoside **8** as a 3:1 α,β-mixture (69%). When stannic chloride was used as the catalyst[15], a complex mixture of products was formed. It is of interest that α-**8** was the main product, because β-glycosides are usually the main products of such glycosidation reactions[15]. Zemplén deacetylation of α-**8** afforded 2,2,2-trichloroethyl 3,4,6-tri-*O*-benzyl-α-D-galactopyranoside (**10**). 2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl chloride (**11**), which contains a non-participating group at C-2, and was chosen as the glycosylating agent, was obtained from 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose by reaction with methanesulfonyl chloride and 2,4,6-trimethylpyridine[16]. The glycosyl chloride **11** was unstable and had decomposed extensively after storage for 3 days at −30°. Therefore, it was prepared immediately before use.



11

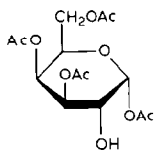


12 R^1 = OCH_2CCl_3, R^2 = R^3 = Bzl
13 R^1 = OH, R^2 = R^3 = Bzl
16 R^1 = Br, R^2 = R^3 = Bzl
19 R^1 = Br, R^2 = Ac, R^3 = Bzl

The condensation of **11** and **10** was performed under Helferich conditions in the presence of mercuric cyanide. After 5 days, 94% of the disaccharide derivative **12** could be isolated and appeared to be the sole product of the reaction. The chemical shift of the C-1′ signal was 96.7 p.p.m., a value which is characteristic[17] of α-D-galactopyranosides.

Removal of the 2,2,2-trichloroethyl group from **12** by zinc powder and pentane-2,4-dione[18] gave 21% of 3,4,6-tri-*O*-benzyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl)-D-galactopyranose (**13**). The formation of several degradation products was observed in contrast to **8** which, under similar conditions, afforded 87% of **9**.

The low yield of the foregoing deglycosidation reaction seriously hampered the planned synthesis of **2**. An alternative synthesis employing 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (**14**) as the alcohol component in the Helferich condensation was therefore investigated. Compound **14** was obtained by controlled acid hydrolysis of **4**[19]. Condensation of **11** and **14** under Helferich conditions afforded the disaccharide derivative **15** as a 4:1 α,β-mixture (95%). The anomers were isolated by flash chromatography, and catalytic hydrogenation followed by deacetylation gave pure **2** and the (1→2)-β-linked galactobiose. Gakhokidze[20] reported a synthesis of D-Gal-(1→2)-D-Gal; however, the paper appeared in an inaccessible journal which was not abstracted. During the synthesis of β-D-Gal*p*-(1→4)-D-Gal*p*, Curtis and Jones[21] obtained a substance which was presumably a (1→2)-β-linked galactobiose, but only periodate oxidation data were given. Toba and Adachi[22] re-



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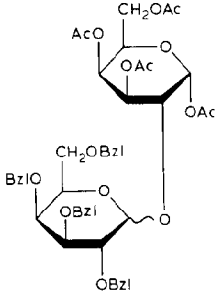

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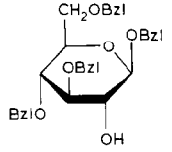

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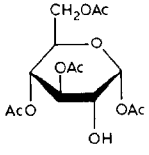

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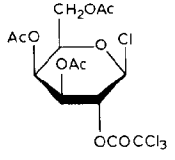

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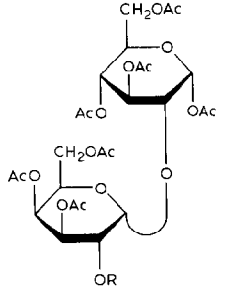


21 R = $COCCl_3$

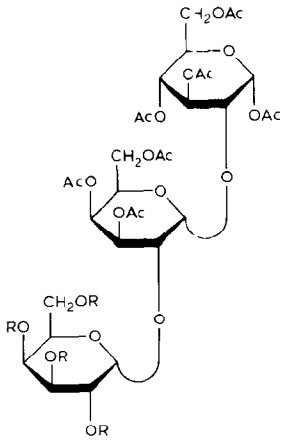
22 R = H

ported the synthesis of β-D-Gal*p*-(1→2)-D-Gal*p*, but their communication is not fully clear. The first unequivocal synthesis of this disaccharide was described recently by Fontana *et al.*[23]. Lipták and Nánási[24], Gorin[25], and Takeo *et al.*[26] described the syntheses of glycosides of (1→2)-linked galactobioses.

Attempts to synthesise derivatives of the trisaccharide α-D-Gal*p*-(1→2)-α-D-Gal*p*-(1→2)-D-Glc*p* by condensation of the glycosyl bromide **16** (obtained from **13**) with benzyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**17**) in the presence of tetraethylammonium bromide or mercuric cyanide led to decomposition of **16** into polar products (t.l.c.). Replacement of **17** by 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (**18**) in the condensation with **16** did not produce any isolable amounts of the trisaccharide. The bromide **19** was obtained from **15**, and condensed with **18** under Helferich conditions. Again, the trisaccharide was not obtained.

The synthesis of the trisaccharide was therefore approached from the reducing unit. Thus, 3,4,6-tri-*O*-acetyl-2-*O*-trichloroacetyl-β-D-galactopyranosyl chloride (**20**) was condensed[27] with **18** in the presence of silver perchlorate–silver carbonate as catalyst. The trichloroacetyl group in the disaccharide derivative **21** was readily removed with pyridine in dichloromethane–methanol[28] to furnish the hepta-acetate **22** in high yield. Condensation of **22** with 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranosyl bromide in the presence of tetraethylammonium bromide as catalyst gave the desired trisaccharide derivative **23** (13% after 4 days). With mercuric bromide as the catalyst, 30% of **23** was obtained. Condensation of **22** with 2,3,4,6-tetra-*O*-benzyl-α,β-D-galactopyranosyl chloride in the presence of silver perchlorate and silver carbonate afforded the trisaccharide derivative **23** (58% after 24 h). These results essentially confirm the catalyst activity gradation proposed[29] by Paulsen and Kólař.

Catalytic hydrogenolysis of **23** followed by acetylation afforded the undeca-



23 R = Bzl
24 R = Ac

acetate **24**, the structure of which was confirmed by analytical data and by its ^{1}H- and ^{13}C-n.m.r. spectra.

Both syntheses present the first stages in the planned synthesis of the pentasaccharide **1**.

EXPERIMENTAL

^{1}H-N.m.r. spectra were recorded with a Jeol JNM-4H-100 (100 MHz) spectrometer. Fully decoupled ^{13}C-n.m.r. spectra were recorded with Jeol 90-Q and Varian CFT 20 spectrometers. All spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si). The resonances of aromatic protons and aromatic carbon atoms are not listed in the spectral data. Optical rotations were measured with a Perkin–Elmer 141 automatic polarimeter at 19 ±1°. Column chromatography was performed on silica gel 60 Merck (230–400 mesh), and t.l.c. on silica gel G (Merck).

All glycosidation reactions and syntheses of tetra-*O*-benzylglycopyranosyl halides were performed under argon, under rigorous anhydrous conditions. Solvents were distilled over calcium hydride before use.

*3,4,6-Tri-*O*-acetyl-1,2-*O*-ethoxyethylidene-α-*D*-galactopyranose* (**4**). — To a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide[30] (26 g) in chloroform (110 mL) were added dry ethanol (7 mL), 2,4,6-trimethylpyridine (14 mL), and tetrabutylammonium bromide (5.5 g), and the mixture was boiled under reflux. After 1 h, the substrate had disappeared (t.l.c.), and the mixture was washed with 0.5M hydrochloric acid and water, dried, and concentrated under reduced pressure. The resulting oil (~25 g), which was a mixture of *exo* and *endo* isomers, had $[\alpha]_D$ +70° (*c* 3.8, chloroform); lit.[12] $[\alpha]_D$ +78° (*c* 1, chloroform). N.m.r. data: ^{1}H, δ 5.80 (d, $J_{1,2}$ 4.8 Hz, H-1 of the *exo* isomer), 5.68 (d, $J_{1,2}$ 5.1 Hz, H-1 of the *endo* isomer), 5.44 (t, 1 H, $J_{3,4}$ 3.2, $J_{4,5}$ 2.5 Hz, H-4), 5.06 (dd, 1 H, $J_{2,3}$ 6.3 Hz, H-3), 4.07–4.42 (m, 4 H, H-2,5,6,6′), 3.57 and 1.20 (q and t, 5 H, OCH_2CH_3), 2.04, 2.08 (9 H, 3 OAc), 1.68 [s, >C(OEt)*Me exo*], 1.58 [s, >C(OEt)*Me endo*; *exo,endo* ratio 85:15]; ^{13}C, δ 97.53, 98.07 (C-1), 73.99, 73.35 (C-2), 71.41, 71.70 (C-3), 69.15 (C-4, for both isomers), 66.08, 66.33 (C-5), 61.43, 61.58 (C-6), 121.26, 121.56 [>*C*(OEt)Me], 58.41, 59.25 (OCH_2CH_3), 15.21 (OCH_2CH_3), 170.38, 169.75 ($OCOCH_3$), and 20.67, 20.54 ($OCOCH_3$).

*3,4,6-Tri-*O*-benzyl-1,2-*O*-ethoxyethylidene-α-*D*-galactopyranose* (**5**). — To a cooled (0°) solution of **4** (18 g) in *N,N*-dimethylformamide (230 mL) was gradually added sodium hydride (20 g, 50% dispersion in oil) followed by benzyl chloride (30 mL). The mixture was stirred for 18 h, the excess of sodium hydride was then decomposed with methanol, the mixture was poured into water and extracted with chloroform, and the extract was dried and concentrated. Column chromatography of the oily residue with light petroleum–ether (5:1) gave **5** (10.2 g, 41%), $[\alpha]_D$ +34° (*c* 2, toluene); lit.[31] $[\alpha]_D$ +31° (*c* 1, toluene). ^{1}H-n.m.r. data: δ 5.70 (d, $J_{1,2}$ 4.5 Hz, H-1 of the *exo* isomer), 5.54 (d, $J_{1,2}$ 5.0 Hz, H-1 of the *endo* isomer), 4.24–5.01 (m, 7 H, 3 CH_2Ph, H-2), 3.90–4.09 (m, 2 H, H-3,4), 3.47–3.63 (m, 5 H, H-5,6,6′ and

OCH_2CH_3), 1.57 [s, >C(OEt)*Me exo*], 1.54 [s, >C(OEt)*Me endo*], and 1.18 (t, 3 H, OCH_2CH_3).

Ethyl 2-O-acetyl-3,4,6-tri-O-benzyl-β-D-galactopyranoside (**6**). — To a solution of **5** (0.56 g) in nitromethane (7 mL) were added 2,2,2-trichloroethanol (0.14 mL) and mercuric bromide (0.1 g). The substrate had disappeared after 15 h (t.l.c.). The solution was then concentrated to dryness and the residue was purified by column chromatography (light petroleum–ethyl acetate, 85:15) to give **6** (0.32 g, 57%), m.p. 62–63.5° (from hexane–ether), $[\alpha]_D$ −2° (*c* 20, chloroform). ^{1}H-N.m.r. data: δ 5.35 (dd, 1 H, $J_{1,2}$ 7.7, $J_{2,3}$ 10 Hz, H-2), 4.34 (d, 1 H, H-1), 4.40–5.02 (s and 2 ABq, 6 H, 3 CH_2Ph), 3.33–4.03 (m, 7 H, H-3,4,5,6,6′ and OCH_2CH_3), 1.99 (s, 3 H, OAc), and 1.14 (t, 3 H, OCH_2CH_3).

Anal. Calc for $C_{31}H_{36}O_7$: C, 71.52; H, 6.97. Found: C, 71.51; H, 7.03.

1,2-Di-O-acetyl-3,4,6-tri-O-benzyl-α-D-galactopyranose (**7**). — A solution of **5** (10.2 g) in acetone (100 mL) was treated with M hydrochloric acid (2.5 mL). After 5 min, the solution was neutralised with triethylamine and concentrated to dryness. A solution of the residue in dichloromethane (30 mL) was treated with acetic anhydride (10 mL), pyridine (30 mL), and a few crystals of 4-dimethylaminopyridine. After 1 h, the mixture was concentrated and a solution of the residue in dichloromethane was washed with water, dried, and concentrated to give **6** (10.3 g, 98%) as a colorless oil, $[\alpha]_D$ +56.5° (*c* 2, chloroform). ^{1}H-N.m.r. data: δ 6.32 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.50 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 4.38–5.01 (2 s and ABq, 6 H, 3 CH_2Ph), 3.46–4.12 (m, 5 H, H-3,4,5,6,6′), and 2.03, 2.11 (2 s, 6 H, 2 OAc).

Anal. Calc. for $C_{31}H_{34}O_8$: C, 69.65; H, 6.41. Found: C, 69.20; H, 6.37.

2,2,2-Trichloroethyl 2-O-acetyl-3,4,6-tri-O-benzyl-α,β-D-galactopyranoside (**8**). — To a solution of **7** (10.3 g) in dichloromethane (15 mL) were added 2,2,2-trichloroethanol (20 mL) and freshly melted zinc chloride (8 g), and the mixture was stirred. After 48 h, water was added, the product was extracted with chloroform, and the extract was dried and concentrated to dryness. The residue was subjected to column chromatography (light petroleum–ether, 9:1). Elute first was the α anomer (6.2 g), m.p. 70.5–71.5°, $[\alpha]_D$ +97° (*c* 1.5, chloroform). N.m.r. data: ^{1}H (CCl_4), δ 5.31 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.15 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 4.07 (ABq, 2 H, OCH_2CCl_3), 3.85–4.08 (m, 3 H, H-3,4,5), 4.34–4.97 (2 s and ABq, 6 H, 3 (CH_2Ph), 3.39–3.65 (m, 2 H, H-6,6′), and 1.99 (s, 3 H, OAc); ^{13}C ($CDCl_3$), δ 97.20 (C-1), 76.50, 73.47, 70.98, 70.38 (C-2,3,4,5), 68.59 (C-6), 96.44 (OCH_2CCl_3), 79.32 (OCH_2CCl_3), 74.77, 74.44, 72.93 (3 CH_2Ph), 170.40 ($OCOCH_3$), and 20.81 ($OCOCH_3$).

Anal. Calc. for $C_{31}H_{33}Cl_3O_7$: C, 59.67; H, 5.33; Cl, 17.05. Found: C, 59.72; H, 5.30; Cl, 16.88.

Eluted next was the β anomer (2.1 g), m.p. 83.5–85°, $[\alpha]_D$ −12° (*c* 2, chloroform). ^{1}H-N.m.r. data (CCl_4): δ 4.48 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 5.33 (dd, 1 H, $J_{2,3}$ 9.8 Hz, H-2), 3.87 (d, 1 H, $J_{3,4}$ 2.5 Hz, H-4), 4.14 (ABq, 2 H, OCH_2CCl_3), 3.41–3.64 (m, 4 H, H-3,5,6,6′), 4.37–4.96 (2 s and ABq, 6 H, 3 CH_2Ph), and 1.95 (s, 3 H, OAc).

Anal. Found: C, 59.69; H, 5.50; Cl, 17.00.

2-O-Acetyl-3,4,6-tri-O-benzyl-α-D-galactopyranose (**9**). — A solution of **α-8** (1 g) in benzene (1 mL) was treated with pentane-2,4-dione (0.3 mL) at 60°. To this solution was added a suspension of zinc powder (0.5 g) in cyclohexane (1 mL). After ~10 s, vigorous evolution of 1,1-dichloroethylene started, and the reaction was finished after ~30 s. The solution was filtered and concentrated, and the residue was purified by column chromatography (light petroleum–ether, 7:3) to give **9** as a thick syrup (0.69 g, 87%), $[\alpha]_D$ +45° (*c* 3, chloroform). ^{1}H-N.m.r. data: δ 5.39 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 5.32 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 4.36–5.0 (2 s and ABq, 6 H, 3 CH_2Ph), 3.30–4.21 (m, 6 H, H-3,4,5,6,6′ and OH), and 2.09 (s, 3 H, OAc).

Anal. Calc. for $C_{29}H_{32}O_7$: C, 70.71; H, 6.55. Found: C, 70.72; H, 6.60.

2,2,2-Trichloroethyl 3,4,6-tri-O-benzyl-α-D-galactopyranoside (**10**). — Zemplén deacetylation of **α-8** (2 g) furnished **10** (1.7 g, 91%) as a viscous oil, $[\alpha]_D$ +79° (*c* 1, chloroform). ^{1}H-N.m.r. data (CCl_4): δ 4.96 (d, 1 H, $J_{1,2}$ 3.9 Hz, H-1), 3.64 (dd, 1 H, $J_{2,3}$ 9.2, $J_{3,4}$ 2.3 Hz, H-3), 4.07 (ABq, 2 H, OCH_2CCl_3), 4.32–4.87 (s and 2 ABq, 6 H, 3 CH_2Ph), 3.82–4.19 (m, 3 H, H-2,4,5), and 3.31–3.56 (m, 2 H, H-6,6′).

Anal. Calc. for $C_{29}H_{31}Cl_3O_6$: C, 59.86; H, 5.37; Cl, 18.28. Found: C, 59.65; H, 5.33; Cl, 18.00.

2,3,4,6-Tetra-O-benzyl-α-D-galactopyranosyl chloride (**11**). — To a solution of 2,3,4,6-tetra-*O*-benzyl-D-galactopyranose[32] (5.55 g) in dichloromethane (50 mL) and 2,4,6-trimethylpyridine (10.4 mL) at −10° was added methanesulfonyl chloride (3.4 mL), and the mixture was stored at room temperature. After 1 h, the solution was washed with M hydrochloric acid and twice with water, dried, and concentrated under reduced pressure. Toluene was twice evaporated from the residue to leave **11** as an oil (5.4 g), $[\alpha]_D$ +128° (*c* 1, benzene); lit.[33] $[\alpha]_D$ +147° (*c* 2, benzene). ^{1}H-N.m.r. data: δ 6.11 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1).

2,2,2-Trichloroethyl 3,4,6-tri-O-benzyl-2-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-α-D-galactopyranoside (**12**). — To a solution of **10** (1.41 g, 2.4 mmol) in benzene (30 mL) were added mercuric cyanide (1.37 g, 5.54 mmol) and a solution of **11** (3.1 g, 5.5 mmol) in nitromethane (30 mL). The mixture was stirred at 45°. After 5 days, **10** had disappeared (t.l.c.). The mixture was then concentrated to dryness and the residue was purified by column chromatography (light petroleum–ether, 9:1) to give **12** (2.52 g, 94%), $[\alpha]_D$ +73° (*c* 4, chloroform). ^{13}C-N.m.r. data: δ 97.27 (C-1), 96.70 (C-1′), 96.44 and 79.23 (OCH_2CCl_3), 68.35 and 68.66 (C-6,6′), 78.89, 78.41, 77.41, 77.02, 76.16, 75.59, 74.68, 74.55, 73.34, 73.21, 72.77, 72.43, 70.43, and 69.53 (remaining carbon atoms and CH_2Ph).

Anal. Calc. for $C_{63}H_{65}Cl_3O_{11}$: C, 68.51; H, 5.93. Found: C, 68.46; H, 5.79.

3,4,6-Tri-O-benzyl-2-O-(2,3,4,6-tetra-O-benzyl-α-D-galactopyranosyl)-D-galactopyranose (**13**). — A solution of **12** (0.488 g) in benzene (1 mL) and pentane-2,4-dione was boiled under reflux and a suspension of activated zinc powder (0.5 g) in cyclohexane (2 mL) was added. The mixture was stirred for 30 min and then con-

centrated, and the residue was purified by column chromatography (light petroleum–ether, 7:3) to give **13** (0.09 g, 21%), m.p. 125.5–126.5° (from hexane–ether), $[\alpha]_D$ +50° (*c* 1, chloroform).

Anal. Calc. for $C_{61}H_{64}O_{11}$: C, 75.29; H, 6.63. Found: C, 75.28; H, 6.71.

*1,3,4,6-Tetra-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-benzyl-α- and -β-*D*-galactopyranosyl)-α-*D*-galactopyranose* (**α-15** *and* **β-15**). — To a solution of 1,3,4,6-tetra-*O*-acetyl-α-D-galactopyranose (**14**; 1.3 g, 3.7 mmol) in nitromethane (28 mL) were added mercuric cyanide (2.52 g) and a solution of **11** (5.8 g, 10 mmol) in benzene (28 mL). The mixture was kept at 45° for 7 days and then concentrated, and the residue was subjected to flash chromatography (light petroleum–ethyl acetate, 2:1). Eluted first was **α-15** (2.504 g, 77%), m.p. 109.5–110° (from ethanol–water), $[\alpha]_D$ +69° (*c* 1, chloroform). N.m.r. data ^{1}H, δ 6.40 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.43 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4), 5.25 (dd, 1 H, $J_{2,3}$ 10.3 Hz, H-3), 4.90 (d, 1 H, $J_{1',2'}$ 3.0 Hz, H-1'), 3.37–4.98 (m, 18 H), and 1.89 (12 H, 4 OAc); ^{13}C, δ 89.07 (C-1), 96.59 (C-1'), 74.95, 74.76, 73.50 (C-2 and 2 CH_2Ph), 61.72 (C-6), 72.91, 70.01, 69.18, 68.80, 68.34, and 67.63 (remaining carbon atoms).

Anal. Calc. for $C_{48}H_{54}O_{15}$: C, 66.20; H, 6.25. Found: C, 65.92; H, 6.13.

Eluted second was amorphous **β-15** (0.584 g, 18%), $[\alpha]_D$ +61° (*c* 1, chloroform). N.m.r. data: ^{1}H, δ 6.39 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.40 (m, 1 H, H-4), 5.30 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 3.36–4.97 (m, 19 H), 1.70, 1.98, and 2.08 (3 s, 12 H, 4 OAc); ^{13}C, δ 104.96 (C-1'), 91.63 (C-1), 61.24 (C-6), 74.75, 74.58, 74.47, 73.66, 73.58, 73.20, 72.93, 69.13, 68.63, 67.90, and 67.80 (remaining carbon atoms).

Anal. Found: C, 65.87; H, 6.27.

*2-*O*-α-*D*-Galactopyranosyl-*D*-galactopyranose* (**2**) *and its β isomer.* — A solution of **α-15** (200 mg) in ethanol (25 mL) was hydrogenolysed at atmospheric pressure in the presence of 10% Pd/C (200 mg) for 8 h, filtered, and concentrated to dryness. The residue was deacetylated (Zemplén), and the methanolic solution was treated with Amberlite IR-120 (H^+) resin and concentrated to dryness to give **2** (58 mg, 74%), m.p. 173–175° (from water), $[\alpha]_D$ +105° (*c* 2, water). ^{13}C-N.m.r. data (D_2O): 99.07 and 98.83 (C-1'α and β), 97.31 and 90.46 (C-1α and β), 77.80 (C-2β), 75.81 (C-2α and C-5β), 74.07 (C-3β), 72.34, 72.13 (C-5'α and β), 61.72 (C-6,6'), 71.78, 71.47, 71.21, 70.00, 69.74, 69.09, 68.87, and 68.53 (remaining carbon atoms).

Anal. Calc. for $C_{12}H_{22}O_{11}$: C, 42.11; H, 6.48. Found: C, 41.97; H, 6.67.

Deprotection of **β-15** (214 mg) gave β-D-Gal*p*-(1→2)-D-Gal*p* (64 mg, 76%) as an amorphous powder, $[\alpha]_D$ +46° (*c* 1, water); lit.[21] $[\alpha]_D$ +35°; lit.[23] m.p. 164–167°, $[\alpha]_D$ +66→ +50°.

*1,3,4,6-Tetra-*O*-acetyl-2-*O*-(3,4,6-tri-*O*-acetyl-α-*D*-galactopyranosyl)-α-*D*-glucopyranose* (**22**). — A solution of 1,3,4,6-tetra-*O*-acetyl-2-*O*-(3,4,6-tri-*O*-acetyl-2-*O*-trichloroacetyl-α-D-galactopyranosyl)-α-D-glucopyranose[27] (**21**, 0.36 g) in dichloromethane–methanol–pyridine (5 mL, 10:1:1) was stored for 1.5 h at room temperature. Toluene (10 mL) was then added and the solvents were evaporated under reduced pressure. The residue was eluted from a short column of silica

gel with benzene–ethyl acetate (1:1.3), to give **22** (0.24 g, 81%), $[\alpha]_D$ +134° (*c* 1, chloroform). N m.r. data: ^{1}H, δ 6.42 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.41 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.3 Hz, H-3), 5.37 (d, 1 H, $J_{3',4'}$ 2.8 Hz, H-4'), 5.08 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.3 Hz, H-4), 5.04 (d, 1 H, $J_{1',2'}$ 3.8 Hz, H-1'), 4.92 (dd, 1 H, $J_{2',3'}$ 10.5 Hz, H-3'), 3.80–4.41 (m, 9 H, H-2,5,6,6,2',5',6',6' and OH), 2.02, 2.04, 2.06, 2.09, and 2.19 (21 H, 7 OAc); ^{13}C, δ 99.96 (C-1'), 89.45 (C-1), 75.91 (C-2), 71.25 (C-3), 69.95 (C-5,3'), 67.78 (C-4,4',5'), 66.70 (C-2'), 61.49 and 61.12 (C-6,6'), 169.49–170.56 ($OCOCH_3$), and 20.59–21.46 ($OCOCH_3$).

Anal. Calc. for $C_{26}H_{36}O_{18}$: C, 49.06; H, 5.70. Found: C, 48.94; H, 5.81.

1,3,4,6-Tetra-O-*acetyl-2*-O-[*3,4,6-tri*-O-*acetyl-2*-O-*(2,3,4,6-tetra*-O-*benzyl-α*-D-*galactopyranosyl)-α*-D-*galactopyranosyl*]-*α*-D-*glucopyranose* (**23**). — (*a*) A solution of 2,3,4,6-tetra-*O*-benzyl-*α*-D-galactopyranosyl bromide[34] (0.25 g, 0.4 mmol) and **22** (0.06 g, 0.09 mmol) in dichloromethane (5 mL) was stirred with tetraethylammonium bromide (0.1 g) and molecular sieves (4 Å, 0.15 g) for 4 days at room temperature, to give **23** (0.014 g, 13%), isolated by chromatography [see (*c*)].

(*b*) Condensation of 2,3,4,6-tetra-*O*-benzyl-*α*-D-galactopyranosyl bromide (0.23 g, 0.38 mmol) with **22** (0.05 g, 0.08 mmol) in the presence of mercuric bromide (0.046 g) and molecular sieves (4 Å, 0.3 g) in dichloromethane (6 mL) for 3 days gave **23** (30%), isolated by chromatography [see (*c*)].

(*c*) A mixture of 2,3,4,6-tetra-*O*-benzyl-*α*,*β*-D-galactopyranosyl chloride (0.5 g, 0.89 mmol; obtained from 2,3,4,6-tetra-*O*-benzyl-*α*-D-galactopyranosyl bromide and tetraethylammonium chloride in acetonitrile), **22** (0.086 g, 0.14 mmol), dichloromethane (3 mL), silver carbonate (0.1 g), silver perchlorate (0.025 g), calcium sulphate (0.12 g), and molecular sieves (4 Å, 0.12 g) was stirred in the dark for 2 days. Column chromatography (light petroleum–ethyl acetate, 2:1) gave **23** (0.09 g, 58%) as a colorless syrup, $[\alpha]_D$ +91° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 6.58 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 3.51–5.25 (m, 28 H, remaining pyranose ring and methylene group protons), 1.81, 1.93, 1.96, and 1.99 (21 H, 7 OAc).

Anal. Calc. for $C_{60}H_{70}O_{23}$: C, 62.17; H, 6.09. Found: C, 62.23; H, 6.12.

1,3,4,6-Tetra-O-*acetyl-2*-O-[*3,4,6-tri*-O-*acetyl-2*-O-*(2,3,4,6-tetra*-O-*acetyl-α*-D-*galactopyranosyl)-α*-D-*galactopyranosyl*]-*α*-D-*glucopyranose* (**24**). — A solution of **23** (0.066 g) in ethanol (10 mL) was hydrogenolysed in the presence of 10% Pd/C (70 mg). The reaction was complete after 8 h (t.l.c.). The solution was then filtered and concentrated, and the product was acetylated conventionally. Elution of the product from a small column of silica gel (light petroleum–ethyl acetate, 3:1) gave **24** (0.04 g, 73%) as a thick syrup, $[\alpha]_D$ +149° (*c* 1, chloroform). N.m.r. data: ^{1}H (400 MHz), δ 6.49 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.40, 5.47 (2 dd, 2 H, $J_{4',5'}$ 1.0 Hz, H-4',4''), 5.43 (t, 1 H, $J_{2,3}$ 12.0, $J_{3,4}$ 10.0 Hz, H-3), 5.31 (dd, 1 H, $J_{2'',3''}$ 10.7, $J_{3'',4''}$ 3.1 Hz, H-3''), 5.16 (dd, 1 H, $J_{1'',2''}$ 3.5 Hz, H-2''), 5.13 (d, 1 H, H-1''), 5.09 (dd, 1 H, $J_{2',3'}$ 10.4, $J_{3',4'}$ 3.2 Hz, H-3'), 5.04 (t, 1 H, $J_{4,5}$ 10.4 Hz, H-4), 5.03 (d, 1 H, $J_{1',2'}$ 3.1 Hz, H-1'), 4.20, 4.32 (dt, 2 H, $J_{5',6'}$ 7.0 Hz, H-5',5''), 4.26 (dd, 1 H, H-2), 3.84–4.17 (m, 8 H, H-5,6,6,2',6',6',6'',6''), 1.97, 1.98, 2.03 (6 H), 2.0, 2.06, 2.07, 2.11, 2.13, 2.15, and 2.21 (10 s, 33 H, 11 OAc); ^{13}C, 98.34 (C-1'), 96.77 (C-1''), 89.07 (C-

1), 76.40 (C-2), 73.58 (C-2'), 71.84 (C-3), 69.62 (C-5), 68.59, 68.48, 68.00 (intensity of four C-atoms), 67.35 (intensity of two C-atoms) (C-4,3',4',5',2'',3'',4'',5''), 61.71, 61.06 (intensity of two C-atoms) (C-6,6',6''), 168.77–170.40 ($COCH_3$), and 20.59–20.75 ($COCH_3$).

Anal. Calc. for $C_{40}H_{54}O_{27}$: C, 49.69; H, 5.63. Found: C, 49.40; H, 5.90.

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