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SYNTHESES OF 3-*O*-(2-ACETAMIDO-2-DEOXY-β-D-GLUCOPYRANOSYL)-α-D-GALACTOPYRANOSE ("LACTO-*N*-BIOSE II") AND 3,4-DI-*O*-(2-ACETAMIDO-2-DEOXY-β-D-GLUCOPYRANOSYL)-D-GALACTOPYRANOSE*

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ABSTRACT

3-*O*-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-α-D-galactopyranose (**10**, "Lacto-*N*-biose II") was synthesized by treatment of benzyl 6-*O*-allyl-2,4-di-*O*-benzyl-β-D-galactopyranoside with 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline (**5**), followed by selective *O*-deallylation, *O*-deacetylation, and catalytic hydrogenolysis. Condensation of **5** with benzyl 6-*O*-allyl-2-*O*-benzyl-α-D-galactopyranoside, followed by removal of the protecting groups, gave **10** and a new, branched trisaccharide, 3,4-di-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactopyranose (**27**).

INTRODUCTION

In 1956, Kuhn and Baer[2] isolated, by partial acid hydrolysis of the human-milk oligosaccharide "lacto-*N*-tetraose", a disaccharide (**10**, "lacto-*N*-biose II"). Later, this disaccharide was isolated, by Yosizawa[3], in crystalline form from a blood-group A glycoprotein prepared from hog gastric mucus. In 1963, Painter *et al.*[4] demonstrated that **10** is part of the structure of all four human blood-group A, B, H, and Le^a substances. This important disaccharide has never been synthesized until now, although Shapiro *et al.*[5] obtained the α-hepta-*O*-acetyl derivative by acetolysis of a 1,6-anhydro derivative; because of the well known lability to alkali of (1→3)-linked disaccharides, *O*-deacetylation of the acetyl derivative was accompanied by complete rupture of the glycosidic bond. As part of a program of synthesis of various oligosaccharides obtained as hydrolysis products of blood-group substances, we now describe a synthesis of **10** according to a scheme which allows further glycosylation at C-6 of the reducing D-galactose residue.

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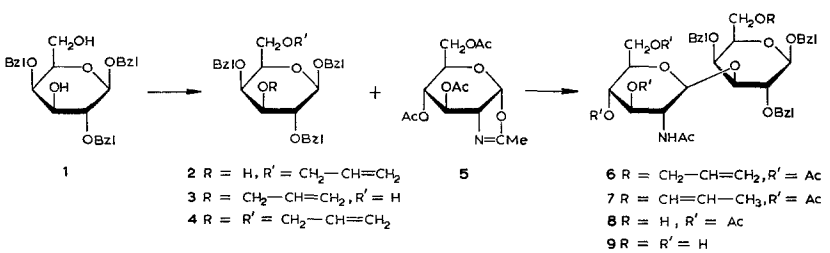
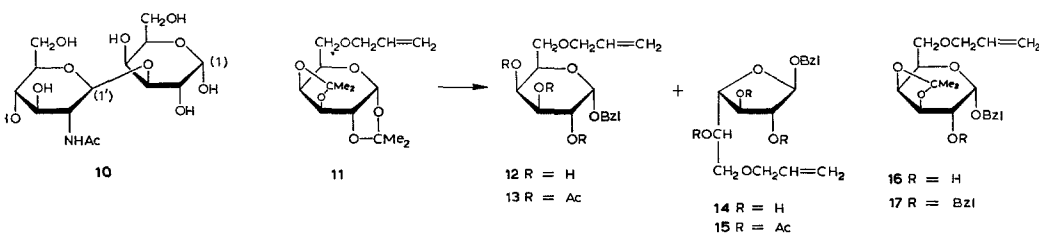
RESULTS AND DISCUSSION

Recently, we reported[6] the synthesis of benzyl 6-*O*-allyl-2,4-di-*O*-benzyl-β-D-galactopyranoside (**2**), a potentially useful derivative for the preparation of branched oligosaccharides where the reducing unit is a 3,6-disubstituted D-galactose residue. Treatment of the diol[6] **1** with allyl bromide in benzene at reflux, in the presence of 1.1 equiv. of sodium hydride gave more rapidly **2** in 21% yield, together with the 3-*O*-allyl (**3**, 46%), and the 3,6-di-*O*-allyl (**4**, 7.5%) derivatives. Reaction of 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline[7] (**5**) with **2** in 1:1 nitromethane–toluene in the presence of *p*-toluenesulfonic acid afforded the crystalline disaccharide **6** in 40% yield (based on **2**).

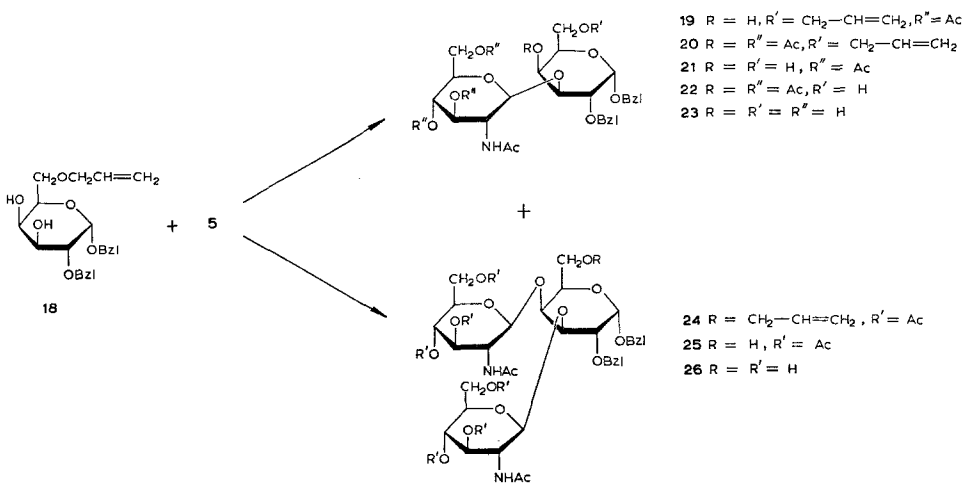
Tris(triphenyl)phosphinerhodium chloride, which catalyzes the isomerization of allyl ethers to give 1-propenyl ethers under neutral conditions[8], is useful in oligosaccharide syntheses where *O*-allyl groups are used for "temporary" blocking in the presence of *O*-acetyl groups. Treatment of **6** with the rhodium complex in the presence of 1,4-diazabicyclo[2.2.2]octane gave the crystalline *O*-(1-propenyl) disaccharide **7** in 80% yield, without detectable cleavage of the *O*-acetyl groups. Hydrolysis of **7** with mercuric chloride and mercuric oxide gave crystalline **8**, a disaccharide derivative suitably protected for subsequent condensation at C-6 of the D-galactose unit.





O-Deacetylation of **8** gave **9** as a crystalline monohydrate, in 70% yield. The hydrogenolysis of the benzyl groups of **9** in the presence of 10% palladium-on-charcoal at atmospheric pressure and ambient temperature in glacial acetic acid was nearly complete after 48 h, and the free disaccharide **10** was isolated in 57% yield by crystallisation of its dihydrate. Its physical properties were identical in all respects with those of the natural product isolated by Yosizawa[3].

In view of the rather tedious route required for the preparation[6] of **2**, a more accessible derivative of D-galactose was desirable. Gent and Gigg[9] recently reported the synthesis of benzyl 6-*O*-allyl-α-D-galactopyranoside (**12**), a compound readily obtained from 6-*O*-allyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**11**) by the action of benzyl alcohol under acid conditions. Repetition of this procedure gave **12** in similar yield (39%) together with benzyl 6-*O*-allyl-β-D-galactofuranoside (**14**, 25%), a syrupy compound that was isolated from the mother liquors of **12** by column chromatography. The structure of **14** was established as follows: no formic acid was released when **14** was oxidized by sodium periodate, whereas under the same conditions 1 mole of **12** liberated 0.9 mole of formic acid. Moreover, **14** could be partially converted into **12** by treatment with benzyl alcohol under acid conditions. The β-D configuration of **14** was tentatively assigned from the low value of the optical rotation, and also from the well-known[10] distribution of isomeric glycosides obtained from D-galactose by the Fischer procedure. Compound **12** was converted into the 3,4-*O*-isopropylidene derivative **16** as described by Gent and Gigg[9]. Benzylation of **16** gave, in quantitative yield, syrupy benzyl 6-*O*-allyl-2-*O*-benzyl-3,4-*O*-isopropylidene-α-D-galactopyranoside (**17**), which was hydrolyzed with acid in aqueous methanol to yield syrupy benzyl 6-*O*-allyl-2-*O*-benzyl-α-D-galactopyranoside (**18**) in 87% yield.



This compound, obtained in six steps from D-galactose with a reasonable yield, has free hydroxyl groups at C-3 and C-4. According to Flowers[11], it should be predominantly glycosylated at C-3. In our hands, however, treatment of **18** with an excess of **5** in the presence of *p*-toluenesulfonic acid gave a mixture of the β-D-(1→3)-linked disaccharide **19** and of the branched trisaccharide **24**; only traces of an unidentified condensation product, possibly a β-D-(1→4)-linked disaccharide were detectable. When only 1 equiv. of **5** was added, the disaccharide **19** could be isolated in 33% yield, large amounts of the starting material **18** being still present. This moderate yield was obviously due to the tendency of the oxazoline **5** to isomerize into 2-

acetamido-1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol and also to decompose. When further additions of **5** (up to 2.5 equiv.) were made, t.l.c. showed the increased formation of **19**, but also its transformation into a branched trisaccharide by subsequent glycosylation at C-4 of the D-galactose unit. Separation of condensation products was rather difficult: extraction of the crude reaction mixture with dry ether left an insoluble residue that contained mainly **19**, which was isolated in crystalline form by column chromatography in 25% yield (based on **18**). The ether extract contained the trisaccharide **24**, some **19**, and large amounts of isomerization or decomposition products derived from **5**; this extract was *O*-acetylated and submitted to column chromatography to give the crystalline 4-*O*-acetyl derivative of **19** (**20**, 5%), small quantities of an unidentified product [which may be the 3-*O*-acetyl derivative of a β-D-(1→4)-linked disaccharide (2%)], and the crystalline trisaccharide **24** (9%).

Selective removal of the *O*-allyl group of **19**, **20**, and **24** proceeded without difficulty by isomerization with the rhodium complex, followed by hydrolysis with mercuric chloride and mercuric oxide, to give crystalline **21** and **22**, and amorphous **25**, respectively. Compound **22**, which has only one free hydroxyl group at C-6 of the D-galactose unit, may prove of value for further condensations at that position.

Conventional *O*-deacetylation, followed by hydrogenolysis in glacial acetic acid converted **21** into the free disaccharide **10**, which was identical with the compound synthesized from **2**, except that the sample used for elemental analysis had lost one molecule of crystallization water by drying at 60°. Compound **25** was similary *O*-deacetylated and hydrogenolyzed to give the free, branched trisaccharide **27** which was obtained as a crystalline dihydrate after chromatography on silica gel.

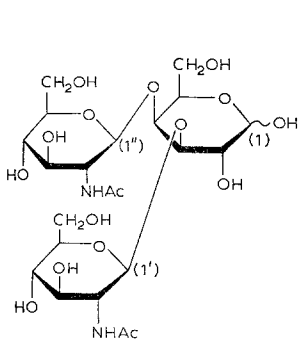
TABLE I

250-MHz N.M.R. SPECTRAL DATA[a] FOR COMPOUNDS **10**, **27**, AND **28** IN DEUTERIUM OXIDE AT 80°

Compounds[b]	*Chemical shifts* (δ) (*first-order couplings, Hz, in parentheses*)			
	H-1 ($J_{1,2}$)	*H-1′* ($J_{1',2'}$)	*H-1″* ($J_{1'',2''}$)	*Ac*
α-**10** (46)	5.28[c]	4.76 (8.4)		2.06
β-**10** (54)	4.58[d]	4.77 (8.4)		
α-**27** (39)	5.23 (3.9)	4.94 (8.3)	4.68 (8.3)	2.06[e]
β-**27** (61)	4.56 (8.0)	4.95 (8.3)	4.69 (8.3)	
α-**28** (49)	5.26[c]	4.77 (8.0)	4.62 (8.0)[g]	2.08[f]
β-**28** (51)	4.58 (7.8)	4.78 (8.0)		
α-D-Galactose[h] (ref. 18)	5.34 (2.8)			
β-D-Galactose[h]	4.68 (7.1)			
α-D-Galactose[i] (ref. 19)	5.29			
β-D-Galactose[i]	4.63			

[a]Spectra were recorded at 250 MHz with a Cameca Model TSN 250 spectrometer, with Fourier transformer. Tetramethylsilane was the external standard. [b]Percent of pyranose isomer in parentheses. [c]Broadened signal. [d]Second-order effects from virtual long-range coupling were observed[18]. [e]Minor peak at δ 2.04. [f]Minor peak at δ 1.94. [g]Same signal for α- and β-anomer. [h]At 35°. [i]At 80–100°.

The 250-MHz n.m.r. data for solutions of **10**, **27**, and 3,6-di-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-D-galactopyranose[12] (**28**) at equilibrium in deuterium oxide at 80° are summarized in Table I. The values for the anomeric-proton resonances for the inter-sugar β-D linkage (d, $J_{1',2'}$ or $J_{1'',2''}$ 8.0–8.4 Hz) are concentrated in the region δ 4.60–4.95 and are in good agreement with the values reported for various D-glucooligosaccharides[13]. The anomeric equilibria were determined from the intensities of the H-1α and H-1β signals of the reducing D-galactose unit.



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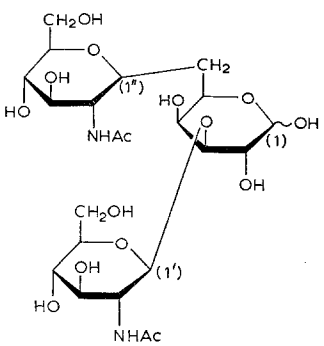

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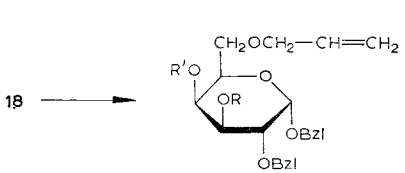

29 R = R' = Bzl
30 R = Bzl, R' = Ac
31 R = Ac, R' = Bzl
32 R = Bzl, R' = H
33 R = H, R' = Bzl

The diol **18** was less convenient than **2** as a starting compound for the synthesis of β-D-(1→3)-linked disaccharides because of the appreciable reactivity of the hydroxyl group at C-4. From our results, this reactivity seemed to be enhanced by previous glycosylation at C-3, whereas others using similar derivatives of D-galactose with an ester substituent at C-6 found either an almost exclusive glycosylation[11,14] at O-3 or comparable glycosylations[15,16] at both O-3 and O-4.

Therefore, monobenzylation of **18** was attempted by treatment with benzyl bromide in *N*,*N*-dimethylformamide at room temperature in the presence of 1.1 equiv. of sodium hydride. Separation of the isomeric 3- and 4-*O*-benzyl derivatives was only possible after acetylation of the reaction mixture. Column chromatography afforded 9% of benzyl 6-*O*-allyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranoside (**29**), identical with the product described by Gent and Gigg[9], 16% of benzyl 4-*O*-acetyl-6-*O*-allyl-2,3-di-*O*-benzyl-α-D-galactopyranoside (**30**), 44% of benzyl 3-*O*-acetyl-6-*O*-allyl-2,4-di-*O*-benzyl-α-D-galactopyranoside (**31**), and 19% of starting material **18**. This distribution was in good agreement with the higher reactivity of the hydroxyl group at

C-4 observed by Flowers[17] in similar alkylations. *O*-Deacetylation of **30** and **31** afforded syrupy **32** and **33**, respectively.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with a Roussel–Jouan electronic, digital micropolarimeter. I.r. spectra were recorded with a Unicam model SP 1100 spectrometer, n.m.r. spectra with a Jeol C-60-H n.m.r. spectrometer at 60 MHz, with chloroform-*d* as solvent and Me_4Si as internal standard. T.l.c. was performed on plates of silica gel (with fluorescence indicator; layer thickness 0.25 mm; E. Merck, Darmstadt, Germany). The compounds were detected by spraying the plates with 1:19 (v/v) conc. H_2SO_4–ethanol. Silica gel Merck (70–325 mesh; E. Merck) was used for column chromatography. Paper chromatography was performed on Whatman No. 1 paper. Free sugars were detected with the aniline hydrogenphthalate reagent. G.l.c. was conducted with a Girdel model 3000 instrument fitted with a flame-ionization detector and a stainless-steel column (250 × 0.3 cm) packed with 3% of SE-30 on Gas-Chrom Q (80–100 mesh), and with N_2 as the carrier gas. Per(trimethylsilyl)ation was performed with hexamethyldisilazane–chlorotrimethylsilane–pyridine (1:1:5) for 3 h at room temperature. Microanalyses were performed by the Laboratoire Central de Micro-Analyse du C.N.R.S.

*Allylation of benzyl 2,4-di-*O*-benzyl-β-*D*-galactopyranoside* (**1**). — A solution of benzyl 2,4-di-*O*-benzyl-β-D-galactopyranoside[6] (**1**, 4.50 g, 10 mmol) in dry benzene (100 ml) was boiled until 50 ml of the solvent had distilled, then cooled to room temperature. Sodium hydride (0.33 g, 11 mmol, 80% dispersion in oil, Merck-Schuchardt, Munich, Germany) and allyl bromide (2.0 ml, 22 mmol) were added, and the mixture was boiled under reflux for 2 h. Methanol was added cautiously to the cooled mixture. The solvents were evaporated and the residue was extracted with chloroform; the extract was washed with water, dried ($MgSO_4$), and evaporated. The residue was chromatographed on silica gel (500 g) with 4:1 (v/v) toluene–ether. A number of components were separated from the mixture as homogeneous fractions and are reported in the order of their emergence from the column [R_1 is the R_F relative to that of **1** in t.l.c. with 4:1 (v/v) benzene–ether]:

(*a*). *Benzyl 3,6-di-*O*-allyl-2,4-di-*O*-benzyl-β-*D*-galactopyranoside* (**4**, 0.40 g, 7.5%), R_1 14.6, b.p.$_{0.01\,mm}$ 200°, $[\alpha]_D^{20}$ −35° (*c* 1.51, chloroform).

Anal. Calc. for $C_{33}H_{38}O_6$: C, 74.69; H, 7.22; O, 18.09. Found: C, 74.50; H, 7.07; O, 17.99.

(*b*). *Benzyl 6-*O*-allyl-2,4-di-*O*-benzyl-β-*D*-galactopyranoside* (**2**, 1.03 g, 21%), R_1 7.3, $[\alpha]_D^{20}$ −20° (*c* 1.02, chloroform); lit.[6]: $[\alpha]_D^{20}$ −19° (*c* 0.905, chloroform).

(*c*). *Benzyl* 3-O-*allyl*-2,4-di-O-*benzyl-β-*D*-galactopyranoside* (**3**, 2.25 g, 46%), R_1 4.5, m.p. 101°, $[\alpha]_D^{20}$ −57° (*c* 1.30, chloroform); lit.[6]: m.p. 101°, $[\alpha]_D^{20}$ −58° (*c* 1.15, chloroform).

(*d*). *Benzyl 2,4-di-*O*-benzyl-β-*D*-galactopyranoside* (**1**, 0.90 g, 20%), R_1 1.0.

Benzyl 3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-6-O-allyl-2,4-di-O-benzyl-β-D-galactopyranoside (**6**). — To a solution of benzyl 6-*O*-allyl-2,4-di-*O*-benzyl-β-D-galactopyranoside (**2**, 0.810 g, 1.65 mmol) in dry nitromethane (5 ml) were added *p*-toluenesulfonic acid (20 mg) and a solution of 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)[2,1-*d*]-2-oxazoline (**5**, 0.550 g, 1.68 mmol) in dry toluene (6 ml). The mixture was stirred at 60° under N_2 for 72 h, further additions of **5** being made after 24 and 48 h (1.68 mmol each time). T.l.c. (7:7:1, v/v, benzene–ether–methanol) showed the presence of a main component (R_F 0.47) and only traces of **2** (R_F 0.69). The solution was cooled, neutralized with a few drops of pyridine, and evaporated. The residue was chromatographed on silica gel (200 g) with 49:1 (v/v) chloroform–ethanol; the main fraction was crystallized twice from ethanol–ether (**6**, 0.544 g, 40% from **2**), m.p. 146–147°, $[\alpha]_D^{20}$ −41° (*c* 1.03, chloroform); i.r. data: ν_{max}^{KBr} 3300 (NH), 3100 and 3020 (Ph), 1752 (OAc), 1660 (Amide I), 1565 (Amide II), 1500 (Ph), 1240 (OAc), 732 and 698 cm^{-1} (Ph); n.m.r. data: δ 7.30–7.25 (m, 15 H, 3 Ph), 5.74 (m, 1 H, OCH_2–C*H*=CH_2), 2.04–1.96 (9 H, NAc and 2 OAc), and 1.54 (s, 3 H, OAc).

Anal. Calc. for $C_{44}H_{53}NO_{14}$: C, 64.45; H, 6.52; N, 1.71; O, 27.32. Found: C, 64.25; H, 6.54; N, 1.98; O, 27.26.

Benzyl 3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2,4-di-O-benzyl-6-O-(1-propenyl)-β-D-galactopyranoside (**7**). — To a solution of **6** (0.410 g, 0.50 mmol) in 7:3:1 (v/v) ethanol–benzene–water (13 ml) were added tris(triphenyl)phosphinerhodium chloride (7 mg, 8 μmol) and 1,4-diazabicyclo[2.2.2]-octane (48 mg, 0.4 mmol). The mixture was boiled under reflux for 4 h. T.l.c. in 7:7:1 (v/v) benzene–ether–methanol showed nearly complete conversion of the starting material (R_F 0.47) into one product having R_F 0.51. The solution was cooled and evaporated, the residue dissolved in chloroform, and the extract washed with water until neutral, dried ($MgSO_4$), and then evaporated. The residue was crystallized from ethanol–ether (**7**, 0.328 g, 80%), m.p. 150°, $[\alpha]_D^{20}$ −43° (*c* 1.05, chloroform); i.r. data: ν_{max}^{KBr} 3290 (NH), 3100, 3070 and 3040 (Ph), 1755 (OAc), 1665 (Amide I and –OCH=C*H*CH_3), 1565 (Amide II), 1500 (Ph), 1240 (OAc), 735 and 695 cm^{-1} (Ph).

Anal. Calc. for $C_{44}H_{53}NO_{14}$: C, 64.45; H, 6.52; N, 1.71; O, 27.32. Found: C, 64.32; H, 6.52; N, 1.97; O, 27.18.

Benzyl 3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2,4-di-O-benzyl-β-D-galactopyranoside (**8**). — To a solution of **7** (0.410 g, 0.50 mmol) in 10:1 (v/v) acetone–water (4.5 ml) were added yellow HgO (0.136 g, 0.63 mmol), and then dropwise under stirring a solution of $HgCl_2$ (0.136 g, 0.50 mmol) in 10:1 (v/v) acetone–water (1.5 ml). After 10 min at room temperature, t.l.c. in 7:7:1 (v/v) benzene–ether–methanol showed one spot (R_F 0.31). The solid was removed by centrifugation, the supernatant evaporated, and chloroform was added. The chloroform extract was washed with 4.2M KI, and then with water, dried ($MgSO_4$), and evaporated. The residue crystallized from ethanol–ether–light petroleum (**8**, 0.332 g, 85%), m.p. 197°, $[\alpha]_D^{20}$ −47° (*c* 1.03, chloroform); i.r. data: ν_{max}^{KBr} 3525 (OH), 3350

(NH), 3080, 3060 and 3020 (Ph), 1740 (OAc), 1662 (Amide I), 1515 (Amide II), 1260 (OAc), 730 and 692 cm^{-1} (Ph).

Anal. Calc. for $C_{41}H_{49}NO_{14}$: C, 63.14; H, 6.33; N, 1.80; O, 28.73. Found: C, 62.85; H, 6.45; N, 1.98; O, 28.49.

*Benzyl 3-*O*-(2-acetamido-2-deoxy-β-*D*-glucopyranosyl)-2,4-di-*O*-benzyl-β-*D*-galactopyranoside* (**9**). — A solution of **8** (0.300 g, 0.38 mmol) in methanol (10 ml) and water (2.5 ml) was treated with triethylamine (1 ml, 7 mmol) overnight at room temperature. The solvents were evaporated, and the residue, after being dried by repeated additions and evaporations of ethanol, crystallized from ethanol–ether (**9**, 0.175 g, 70%), m.p. 142–145°, $[\alpha]_D^{20}$ −25° (*c* 1.035, methanol).

Anal. Calc. for $C_{35}H_{43}NO_{11}\cdot H_2O$: C, 62.58; H, 6.75; N, 2.09; O, 28.58. Found: C, 62.82; H, 7.36; N, 1.99; O, 28.19.

*Benzyl 6-*O*-allyl-α-*D*-galactopyranoside* (**12**). — A solution of 6-*O*-allyl-1,2:3,4-di-*O*-isopropylidene-α-*D*-galactopyranose (**11**, 27 g, 90 mmol) in benzyl alcohol (250 ml) containing HCl (7.5 g) was boiled under reflux for 2 h according to the procedure of Gent and Gigg[9]. Crystallization from ether, and then from water afforded benzyl 6-*O*-allyl-α-*D*-galactopyranoside (**12**, 5.1 g, 18%), m.p. 129–130°, $[\alpha]_D^{20}$ +134° (*c* 1.065, methanol); n.m.r. data: δ 7.53–7.28 (m, 5 H, Ph), 6.02 (m, 1 H, $-OCH_2CH{=}CH_2$), 5.50–5.02 (m, 3 H, $-OCH_2CH{=}CH_2$ and H-1), 4.85 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$), and 4.55 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$); lit.[9]: m.p. 130–131.5°, $[\alpha]_D$ +132.3° (*c* 0.8, methanol).

*Benzyl 2,3,4-tri-*O*-acetyl-6-O-allyl-α-*D*-galactopyranoside* (**13**). — Acetylation of **12** with acetic anhydride and pyridine overnight at room temperature gave crystalline **13**, m.p. 51.5–53° (from ether–light petroleum), $[\alpha]_D^{20}$ +144° (*c* 0.915, chloroform); n.m.r. data: δ 7.45–7.32 (m, 5 H, Ph), 6.02 (m, 1 H, $-OCH_2CH{=}CH_2$), 4.82 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$), 4.52 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$), 4.26 (t, 1 H, $J_{5,6}$ 6 Hz, H-5), 3.97 (d, 2 H, $-OCH_2CH{=}CH_2$), 3.47 (d, 2 H, $J_{5,6}$ 6 Hz, H-6), 2.13 (3 H, OAc_{ax}), and 2.03–1.97 (6 H, 2 OAc_{eq}).

Anal. Calc. for $C_{22}H_{28}O_9$: C, 60.54; H, 6.47; O, 32.99. Found: C, 60.82; H, 6.55; O, 32.69.

*Benzyl 6-*O*-allyl-β-*D*-galactofuranoside* (**14**). — The mother liquor of **12** was fractionated by column chromatography on silica gel (100 × 5 cm) with 9:1 (v/v) chloroform–ethanol, 20-ml fractions being collected. Fractions 85–119 contained pure benzyl 6-*O*-allyl-β-*D*-galactofuranoside (**14**, 7.0 g, 25%), which could not be crystallized, $[\alpha]_D^{20}$ −45.5° (*c* 1.12, chloroform); n.m.r. data: δ 7.29 (m, 5 H, Ph), 5.96 (m, 1 H, $-OCH_2CH{=}CH_2$), 5.42–4.95 (m, 3 H, $-OCH_2CH{=}CH_2$ and H-1), 4.75 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$), and 4.47 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$).

Anal. Calc. for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15; O, 30.93. Found: C, 61.57; H, 7.15; O, 31.53.

*Benzyl 2,3,5-tri-*O*-acetyl-6-O-allyl-β-*D*-galactofuranoside* (**15**). — Acetylation of **14** with acetic anhydride and pyridine overnight at room temperature gave syrupy **15** which was distilled, $b.p._{0.01\,mm}$ 180°, $[\alpha]_D^{20}$ −28° (*c* 5.00, chloroform); n.m.r. data: δ 7.32 (m, 5 H, Ph), 5.92 (m, 1 H, $-OCH_2CH{=}CH_2$), 4.80 (d, 1 H, $J_{a,b}$ 12 Hz,

$PhCH_aH_bO$), 4.50 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$), 4.00 (d, 2 H, $-OCH_2CH{=}CH_2$), 3.62 (d, 2 H, $J_{5,6}$ 6 Hz, H-6), and 2.13–2.05 (9 H, 3 OAc).

Anal. Calc. for $C_{22}H_{28}O_9$: C, 60.54; H, 6.47; O, 32.99. Found: C, 60.39; H, 6.40; O, 32.95.

Fractions 125–160 gave more crystalline **12** (5.8 g, 21%). When **14** was treated with benzyl alcohol and HCl under reflux, t.l.c. in 9:1 (v/v) chloroform–ethanol showed the reaction mixture to contain, after 2 h, **12** (R_F 0.16) and **14** (R_F 0.27) in the ratio 2:1.

A solution of **12** or **14** (62 mg, 0.2 mmol) in 0.16M $NaIO_4$ (10 ml, 1.6 mmol) was diluted with water to 40 ml and kept in the dark at 5°. Release of formic acid was followed by adding 1,2-ethanediol (1 ml) to 10-ml aliquots of the solution and titrating after 15 min with 0.01M NaOH: **12** released 0.9 mmol of formic acid per mmol after 48 h, whereas **14** released no formic acid.

*Benzyl 6-*O*-allyl-2-*O*-benzyl-3,4-*O*-isopropylidene-α-*D*-galactopyranoside* (**17**). — A solution of benzyl 6-*O*-allyl-3,4-*O*-isopropylidene-α-D-galactopyranoside[9] (**16**, 14.62 g, 42 mmol) in dry benzene (300 ml) was treated with NaH (2.00 g, 84 mmol) and benzyl bromide (10 ml, 84 mmol) for 1 h at room temperature, and then under reflux for 4 h. T.l.c. in 5:1 (v/v) toluene–acetone showed complete conversion of **16** (R_F 0.49) into **17** (R_F 0.70). The excess of hydride was decomposed by the addition of methanol to the cooled mixture; the solution was washed with water, dried ($MgSO_4$), and evaporated to a syrup (18.50 g, 100%). An analytical sample of **17** was obtained by distillation, b.p.$_{0.01\,mm}$ 195°, $[\alpha]_D^{20}$ +124° (*c* 2.59, chloroform); i.r. data: ν_{max}^{film} 3080, 3040, 2990, 1500, 740, and 700 cm^{-1} (Ph); n.m.r. data: δ 7.35–7.27 (m, 10 H, 2 Ph), 5.97 (m, 1 H, $-OCH_2CH{=}CH_2$), 5.40–5.08 (m, 2 H, $-OCH_2CH{=}CH_2$), 4.88 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.77 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$), 4.48 (d, 1 H, $J_{a,b}$ 12 Hz, $PhCH_aH_bO$), 1.37 and 1.31 (2 s, 6 H, CMe_2).

Anal. Calc. for $C_{26}H_{32}O_6$: C, 70.89; H, 7.32; O, 21.79. Found: C, 71.31; H, 7.51; O, 21.01.

*Benzyl 6-*O*-allyl-2-*O*-benzyl-α-*D*-galactopyranoside* (**18**). — A solution of crude **17** (19 g, 43 mmol) in methanol (54 ml) and 0.5M HCl (18 ml) was heated under reflux. T.l.c. in 5:1 (v/v) toluene–acetone after 30 min showed complete conversion of **17** (R_F 0.70) into **18** (R_F 0.18). An excess of $NaHCO_3$ was added and the solvents were evaporated. The residue was extracted with chloroform; the extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel with 19:1 (v/v) chloroform–ethanol to give a syrup (15.1 g, 87% from **16**). An analytical sample of **18** was obtained by distillation, b.p.$_{0.01\,mm}$ 220–230°, $[\alpha]_D^{20}$ +125° (*c* 1.475, chloroform); i.r. data: ν_{max}^{film} 3450 (OH), 3070, 3040, 1500, 740, and 700 cm^{-1} (Ph); n.m.r. data: δ 7.33–7.25 (m, 10 H, 2 Ph), 5.96 (m, 1 H, $-OCH_2CH{=}CH_2$), 5.45–5.08 (m, 2 H, $-OCH_2CH{=}CH_2$), 4.92 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 4.68 (d, 1 H, $J_{a,b}$ 11 Hz, $PhCH_aH_bO$), and 4.42 (d, 1 H, $J_{a,b}$ 11 Hz, $PhCH_aH_bO$).

Anal. Calc. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05; O, 23.97. Found: C, 68.85; H, 7.14; O, 23.98.

Benzyl 3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-6-O-allyl-2-O-benzyl-α-D-galactopyranoside (**19**), *benzyl 3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-4-O-acetyl-6-O-allyl-2-O-benzyl-α-D-galactopyranoside* (**20**), *and benzyl 3,4-di-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-6-O-allyl-2-O-benzyl-α-D-galactopyranoside* (**24**). — To a solution of **18** (2.00 g, 5 mmol) in dry nitromethane (17 ml) were added *p*-toluenesulfonic acid (60 mg) and a solution of 2-methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (**5**, 1.65 g, 5 mmol) in dry toluene (18 ml). The mixture was stirred at 60° under N_2 for 24 h. T.l.c. in 7:7:1 (v/v) benzene–ether–methanol showed the presence of unchanged **18** (R_F 0.47), traces of **5** (R_F 0.37), and a major condensation product (R_F 0.35). A further amount of **5** (1.65 g, 5 mmol) in dry toluene (18 ml) was added, and the solution was stirred at 60° for a further 24 h. T.l.c. indicated traces of **18**, an increase of condensation product of R_F 0.35, and a new condensation product (R_F 0.32). After a further addition of **5** (0.82 g, 2.5 mmol) in dry toluene (9 ml), heating and stirring were continued for a further 24 h, after which time t.l.c. showed the complete disappearance of **18**. The resulting brown solution was cooled to room temperature, brought to pH 7 with a few drops of pyridine, and evaporated. The residue was triturated with dry ether to give a solid material (**A**) which was thoroughly washed with ether and dried (2.8 g). The filtrate and washings were combined, washed with water, dried (Na_2SO_4), and evaporated to a syrup (**B**, 6.0 g).

Material **A** was chromatographed on silica gel (200 g) with 7:7:1 (v/v) toluene–ether–methanol, 12-ml fractions being collected. Fractions 26–45 gave **19**, which was crystallized from ethanol (0.93 g, 25% from **18**), m.p. 226–228°, $[\alpha]_D^{20}$ +46° (*c* 0.91, chloroform); i.r. data: ν_{max}^{KBr} 3600 (OH), 3300 (NH), 1755 (OAc), 1670 (Amide I), 1555 (Amide II), 1250 (OAc), 735, and 695 cm^{-1} (Ph); n.m.r. data: δ 7.34–7.26 (m, 10 H, 2 Ph), 2.88 (1 H, OH), 2.06–2.01 (9 H, NAc and 2 OAc), and 1.71 (3 H, OAc).

Anal. Calc. for $C_{37}H_{47}NO_{14}$: C, 60.89; H, 6.49; N, 1.92; O, 30.70. Found: C, 61.11; H, 6.47; N, 2.17; O, 30.21.

Fractions 46–69 contained the slower-moving condensation product (fraction **C**, R_F 0.32, 0.28 g) slightly contaminated with **19**. The ether-soluble material **B** was chromatographed on silica gel (200 g) with 19:1 (v/v) chloroform–ethanol, 12-ml fractions being collected. Fractions 48–52 gave a mixture (**D**, 1.10 g) of condensation products that were combined with fraction **C**. The last fractions contained 2-acetamido 1,5-anhydro-2-deoxy-D-*arabino*-hex-1-enitol (R_F 0.27) and other degradation products from **5**.

The mixture of condensation products (**D** and **C**) was acetylated in pyridine and acetic anhydride to facilitate the isolation of the compound having R_F 0.32. After the usual processing, the mixture was fractionated by column chromatography on silica gel (150 g) with 7:7:1 (v/v) toluene–ether–methanol as eluant 9-ml fractions being collected. Fractions 62–68 gave **20**, which was crystallized from ethanol–ether–light petroleum (0.20 g, 5% from **18**), m.p. 148.5–150°, $[\alpha]_D^{20}$ +43° (*c* 0.675, chloroform); i.r. data: ν_{max}^{KBr} 3290 (NH), 3100 and 3040 (Ph), 1750 (OAc), 1655 (Amide I), 1565 (Amide II), 1250 (OAc), 735, and 700 cm^{-1} (Ph); n.m.r. data: δ 7.35–7.28

(m, 10 H, 2 Ph), 5.90 (m, 1 H, $-OCH_2CH{=}CH_2$), 2.08–1.98 (12 H, NAc and 3 OAc), and 1.70 (3 H, OAc).

Anal. Calc. for $C_{39}H_{49}NO_{15}$: C, 60.69; H, 6.40; N, 1.81; O, 31.10. Found: C, 60.30; H, 6.42; N, 1.81; O, 30.90.

Fractions 73–80 gave a product that was not investigated; it may be a (1→4)-linked disaccharide (80 mg, 2% from **18**). Fractions 85–100 gave pure **24**, which was crystallized from ethanol–ether (0.475 g, 9% from **18**), m.p. 182–183°, $[\alpha]_D^{20}$ +10° (*c* 0.825, chloroform); i.r. data: ν_{max}^{KBr} 3300 (NH), 3100, 3080 and 3040 (Ph), 1760 (OAc), 1670 (Amide I), 1565 (Amide II), 1250 (OAc), 740 and 700 cm^{-1} (Ph); n.m.r. data: δ 7.35–7.31 (m, 10 H, 2 Ph), 5.86 (m, 1 H, $-OCH_2CH{=}CH_2$), 2.02–1.98 (21 H, NAc and 6 OAc), and 1.76 (3 H, OAc).

Anal. Calc. for $C_{51}H_{66}N_2O_{22}$: C, 57.83; H, 6.28; N, 2.65; O, 33.24. Found: C, 57.89; H, 6.18; N, 2.72; O, 33.40.

Condensation of **18** (2.00 g, 5 mmol) with **5** (1.98 g, 6 mmol) in 1:1 (v/v) toluene–nitromethane (35 ml) at 60° for 24 h gave pure **19** (0.93 g, 25%) by precipitation with ether of the crude condensation mixture and crystallization from ethanol. Chromatography on silica gel with 7:7:1 (v/v) toluene–ether–methanol of the mother-liquor gave additional **19** (0.28 g, 8%).

Benzyl 3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2-O-benzyl-α-D-galactopyranoside (**21**). — To a solution of **19** (0.660 g, 0.9 mmol) in 7:3:1 (v/v) ethanol–benzene–water (23 ml) were added tris(triphenyl)phosphinerhodium chloride (12 mg, 13 μmol) and 1,4-diazabicyclo[2.2.2]octane (88 mg, 0.8 mmol). The mixture was boiled under reflux for 4 h. T.l.c. in 7:7:1 (v/v) benzene–ether–methanol showed the nearly complete conversion of **19** (R_F 0.35) into the 6-*O*-(1-propenyl) disaccharide (R_F 0.37). The solution was cooled and evaporated, the residue dissolved in chloroform, and the extract washed with water until neutral, dried ($MgSO_4$), and evaporated. The residue (0.564 g) was dissolved in 10:1 (v/v) acetone–water (7 ml). To the solution were added yellow HgO (0.220 g, 1 mmol), and then dropwise under stirring during 5 min a solution of $HgCl_2$ (0.220 g, 0.8 mmol) in 10:1 (v/v) acetone–water (3 ml). After 10 min, t.l.c. in 19:1 (v/v) chloroform–ethanol indicated complete conversion of the starting material into **21** (R_F 0.16). The solid was removed by centrifugation, the supernatant evaporated, and chloroform was added. The chloroform extract was washed with 4.2M KI, and then with water, dried ($MgSO_4$), and evaporated. The residue (0.552 g) was crystallized from ethanol to give **21** (0.300 g, 48%), m.p. 237–242°, $[\alpha]_D^{20}$ +45° (*c* 0.51, chloroform).

Anal. Calc. for $C_{34}H_{43}NO_{14}$: C, 59.20; H, 6.28; N, 2.03; O, 32.48. Found: C, 59.07; H, 6.08; N, 2.11; O, 32.27.

Benzyl 3-O-(2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-4-O-acetyl-2-O-benzyl-α-D-galactopyranoside (**22**). — Tris(triphenyl)phosphinerhodium chloride (7 mg, 8 μmol) and 1,4-diazabicyclo[2.2.2]octane (50 mg, 0.4 mmol) were added to a solution of **20** (0.386 g, 0.5 mmol) in 7:3:1 (v/v) ethanol–benzene–water. The mixture was heated under reflux for 4 h, and then processed as described for **21**. The dry residue (0.380 g) was dissolved in 10:1 (v/v) acetone–water (4 ml). To

the solution were added yellow HgO (0.141 g, 0.65 mmol), and then dropwise under stirring a solution of $HgCl_2$ (0.141 g, 0.5 mmol) in 10:1 (v/v) acetone–water (2 ml). After 10 min, t.l.c. in 19:1 (v/v) chloroform–ethanol showed one major product (R_F 0.39) and traces of **20** (R_F 0.53). After being processed as described for **21**, the crude product (0.276 g) was purified by column chromatography on silica gel (20 g) with 19:1 (v/v) chloroform–ethanol to give **22** (0.182 g, 50%) which crystallized by addition of ether, m.p. 163–165° and 233°, $[\alpha]_D^{20}$ +57° (*c* 1.40, chloroform); n.m.r. data: δ 7.38–7.32 (m, 10 H, 2 Ph), 2.17 (s, 3 H, OAc_{ax}), 2.08 and 2.00 (2 s, 9 H, OAc and NAc), and 1.71 (s, 3 H, OAc).

Anal. Calc. for $C_{36}H_{45}NO_{15}$: C, 59.09; H, 6.20; N, 1.91; O, 32.80. Found: C, 58.81; H, 6.32; N, 1.68; O, 32.52.

*Benzyl 3-*O*-(2-acetamido-2-deoxy-β-*D*-glucopyranosyl)-2-*O*-benzyl-α-*D*-galacto-pyranoside* (**23**). — A solution of **21** (0.240 g, 0.35 mmol) in methanol (10 ml) and water (2.5 ml) was treated with triethylamine (1 ml, 7 mmol) overnight at room temperature. T.l.c. in 3:1 (v/v) chloroform–ethanol indicated the formation of only one product (R_F 0.12). The solution was evaporated and the residue, after being dried by repeated additions and evaporations of ethanol, was crystallized from ethanol–water (**23**, 0.168 g, 86%), m.p. 274–277°, $[\alpha]_D^{20}$ +61.5° (*c* 0.765, methanol); i.r. data: ν_{KBr}^{max} 3500–3300 (OH and NH), 1655 (Amide I), 1560 (Amide II), 735 and 695 cm^{-1} (Ph).

Anal. Calc. for $C_{28}H_{37}NO_{11}$: C, 59.66; H, 6.61; N, 2.49; O, 31.23. Found: C, 59.82; H, 6.69; N, 2.61; O, 31.21.

*3-*O*-(2-Acetamido-2-deoxy-β-*D*-glucopyranosyl)-α-*D*-galactopyranose* (**10**). — *A. From* **9**. A solution of **9** (0.150 g, 0.23 mmol) in glacial acetic acid (10 ml) was hydrogenated in the presence of 10% palladium-on-charcoal (0.150 g) for 48 h at room temperature and atmospheric pressure. The catalyst was removed and the filtrate evaporated; the residue was dried by repeated additions and evaporations of toluene, and then crystallized from methanol–ether (**10**, 50 mg, 57%), m.p. 132–134° (shrinking at 125°), $[\alpha]_D^{20}$ +44 → +35° (*c* 0.92, water); paper chromatography: R_{Glc} 0.61 and $R_{Lactose}$ 1.27 (5:3:2, v/v, butanol–pyridine–water), R_{Glc} 0.69 and $R_{Lactose}$ 1.14 (2:1:2, v/v, ethyl acetate–pyridine–water); i.r. data: ν_{max}^{KBr} 3500–3300 (OH and NH), 1650 (Amide I), 1575 (Amide II), 995, and 900 cm^{-1}. The analytical sample was dried for 18 h at room temperature (0.01 mm Hg) in the presence of P_2O_5.

Anal. Calc. for $C_{14}H_{25}NO_{11}\cdot 2H_2O$: C, 40.09; H, 6.97; N, 3.34; O, 49.60. Found: C, 40.33; H, 6.59; N, 3.29; O, 48.97.

G.l.c. at 240° of the per-*O*-(trimethylsilyl)ated derivative gave one peak (56%) at 18.2 min and a second peak (44%) at 22.5 min [per-*O*-(trimethylsilyl)sucrose: 11.0 min].

For the natural disaccharide, Yosizawa[3] reported m.p. 131–133° (with preliminary softening), $[\alpha]_D^{23}$ +45.5 (5 min) → +35.7° (constant, *c* 0.9, water); paper chromatography: R_{Glc} 0.62 and $R_{Lactose}$ 1.34 (5:3:2, v/v, butanol–pyridine–water), R_{Glc} 0.70 and $R_{Lactose}$ 1.11 (2:1:2, v/v, ethyl acetate–pyridine–water); i.r. data: ν_{max}^{KBr} 950 and 895 cm^{-1}.

B. From **23**. A solution of **23** (0.152 g, 0.27 mmol) in glacial acetic acid (10 ml) was hydrogenated in the presence of 10% palladium-on-charcoal (0.150 g) for 48 h at room temperature and atmospheric pressure. The catalyst was removed and the filtrate evaporated. The residue, after being dried by repeated additions and evaporations of toluene, was crystallized from methanol (**10**, 40 mg, 40%), m.p. 129–134°, $[\alpha]_D^{20}$ +41° → +34° (*c* 0.950, water). This compound was identical in all respects [i.r. spectrum, paper chromatography mobility, and g.l.c. pattern of the per-*O*-(trimethylsilyl)ated derivative] with the compound described under *A*. The analytical sample was dried for 18 h at 60° under a pressure of 0.01 mmHg in the presence of P_2O_5.

Anal. Calc. for $C_{14}H_{25}NO_{11}\cdot H_2O$: C, 41.90; H, 6.78; N, 3.49; O, 47.84. Found: C, 41.20; H, 6.78; N, 3.30; O, 47.45.

Benzyl 3,4-di-O-(*2-acetamido-3,4,6-tri*-O-*acetyl-2-deoxy-β*-D-*glucopyranosyl*)-*2*-O-*benzyl-α*-D-*galactopyranoside* (**25**). — Compound **24** (0.455 g, 0.43 mmol) was isomerized by treatment with tris(triphenyl)phosphinerhodium chloride (6 mg, 6 μmol) and 1,4-diazabicyclo[2.2.2]octane (42 mg, 0.3 mmol) in 7:3:1 (v/v) ethanol–benzene–water (11 ml) for 4 h under reflux. The mixture was processed in the usual way to give a syrup (0.450 g) that was hydrolyzed by treatment with $HgCl_2$ (0.109 g, 0.4 mmol) and yellow HgO (0.109 g, 0.5 mmol) in 10:1 (v/v) acetone–water (5 ml) for 10 min at room temperature. After the usual processing, the mixture was chromatographed on silica gel with 19:1 (v/v) chloroform–ethanol to give **25** (0.310 g, 71%) as a foam, $[\alpha]_D^{20}$ +17° (*c* 0.835, chloroform).

Anal. Calc. for $C_{48}H_{62}N_2O_{22}$: C, 56.57; H, 6.13; H, 2.75. O, 34.54. Found: C, 56.32; H, 6.10; N, 2.84; O, 34.67.

Benzyl 3,4-di-O-(*2-acetamido-2-deoxy-β*-D-*glucopyranosyl*)-*2*-O-*benzyl-α*-D-*galactopyranoside* (**26**). — Compound **25** (0.300 g, 0.3 mmol) was *O*-deacetylated overnight at room temperature in 20:5:2 (v/v) methanol–water–triethylamine (14 ml). The solution was evaporated and the residue chromatographed on silica gel with 3:3:2 (v/v) 2-propanol–ethyl acetate–water to give **26** (0.170 g, 75%) as a foam, which gave a solid by trituration with ether, m.p. 149–153°, $[\alpha]_D^{20}$ +60° (*c* 0.733, methanol).

Anal. Calc. for $C_{36}H_{50}N_2O_{16}\cdot H_2O$: C, 55.09; H, 6.68; N, 3.57; O, 34.66. Found: C, 54.53; H, 6.77; N, 3.30; O, 33.90.

3,4-Di-O-(*2-acetamido-2-deoxy-β*-D-*glucopyranosyl*)-D-*galactopyranose* (**27**). — Compound **26** (0.140 g, 0.18 mmol) was hydrogenated in the presence of 10% palladium-on-charcoal (0.140 g) in glacial acetic acid (10 ml) for 48 h at room temperature and atmospheric pressure. After removal of the catalyst and evaporation of the filtrate, the residue (0.117 g) was chromatographed on silica gel with 3:3:4 (v/v) 2-propanol–ethyl acetate–water to give **27** (0.075 g, 64%), which could be precipitated from a methanolic solution by addition of ether, m.p. 170–174°, $[\alpha]_D^{20}$ +24° (*c* 0.875, water, no mutarotation); paper chromatography: R_{Glc} 0.40 and $R_{Lactose}$ 0.90 (5:3:2, v/v, butanol–pyridine–water); g.l.c. at 280° of the per-*O*-(trimethylsilyl)ated derivative gave one peak (95%) at 9.3 min and a second peak (5%) at 4.6 min [per-*O*-(trimethyl-

silyl)raffinose: 4.6 min]; i.r. data: ν_{max}^{KBr} 3500–3300 (OH and NH), 1650 (Amide I), 1575 (Amide II), 955, and 900 cm^{-1}.

Anal. Calc. for $C_{22}H_{38}N_2O_{16}\cdot 2H_2O$: C, 42.44; H, 6.80; N, 4.50; O, 46.26. Found: C, 42.18; H, 6.78; N, 4.29; O, 46.98.

*Benzylation of benzyl 6-*O*-allyl-2-*O*-benzyl-α-*D*-halactopyranoside* (**18**). — To a solution of **18** (2.82 g, 7.05 mmol) in dry *N*,*N*-dimethylformamide (30 ml), NaH (0.23 g, 7.7 mmol) was added. The mixture was stirred for 90 min at room temperature. Benzyl bromide (0.96 ml, 8.1 mmol) was added dropwise and the mixture was stirred for a further 3 h at room temperature. The excess of hydride was decomposed by the addition of a few ml of methanol. The resulting solution was diluted with benzene (150 ml), washed with water, and evaporated. The residue (3.50 g) was chromatographed on silica gel with 1:1 (v/v) ether–light petroleum. The first fractions contained benzyl 6-*O*-allyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranoside (**29**, 0.38 g, 9%), which crystallized from methanol, m.p. 77.5–79°, $[\alpha]_D^{20}$ +61° (*c* 0.91, chloroform); lit.[9]: m.p. 78.5–80°, $[\alpha]_D^{20}$ +63.4° (*c* 0.8, chloroform). The following fractions contained a mixture of **32** and **33** (2.12 g, 60%), and pure ether eluted unreacted **18** (2.20 g, 19.5%).

*Benzyl 4-*O*-acetyl-6-*O*-allyl-2,3-di-*O*-benzyl-α-*D*-galactopyranoside* (**30**) *and benzyl 3-*O*-acetyl-6-*O*-allyl-2,4-di-*O*-benzyl-α-*D*-galactopyranoside* (**31**). — The mixture of **32** and **33** (2.12 g) was treated with acetic anhydride (8 ml) and pyridine (8 ml) overnight at room temperature. After evaporation of the solvents, the residue was chromatographed on silica gel with 1:1 (v/v) ether–light petroleum. The first fractions contained syrupy **30** (0.125 g, 3%), $[\alpha]_D^{20}$ +91° (*c* 0.935, chloroform), R_F [1:1 (v/v) ether–light petroleum] 0.55; i.r. data: ν_{max}^{film} 1755 and 1250 cm^{-1} (OAc); n.m.r. data (240 MHz*, chloroform-*d*): δ 5.71 (broad d, 1 H, H-4), 3.85 (q, $J_{2,3}$ 9.5 Hz, $J_{3,4}$ 3.5 Hz, 1 H, H-3), and 2.14 (s, 3 H, OAc_{ax}).

Anal. Calc. for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81; O, 21.03. Found: C, 72.29; H, 6.73; O, 21.14.

Subsequently a mixture of **30** and **31** (1.080 g, 29%) was eluted, and finally syrupy **31** (0.900 g, 24%), $[\alpha]_D^{20}$ +109.5° (*c* 0.895, chloroform); R_F [1:1 (v/v) ether–light petroleum] 0.50; i.r. data: ν_{max}^{film} 1755 and 1250 cm^{-1} (OAc); n.m.r. data (240 MHz, chloroform-*d*): δ 5.38 (q, $J_{2,3}$ 10 Hz, $J_{3,4}$ 3.5 Hz, 1 H, H-3) and 2.01 (s, 3 H, OAc_{eq}).

Anal. Calc. for $C_{32}H_{36}O_7$: C, 72.16; H, 6.81; O, 21.03. Found: C, 72.24; H, 6.71; O, 20.92.

G.l.c. at 250° of the crude mixture of **30** and **31** before column chromatography showed one peak (27%) at 11 min corresponding to **30** and one peak (73%) at 15 min corresponding to **31**.

*Benzyl 6-*O*-allyl-2,3-di-*O*-benzyl-α-*D*-galactopyranoside* (**32**) *and benzyl 6-*O*-allyl-2,4-di-*O*-benzyl-α-*D*-galactopyranoside* (**33**). — *O*-Deacetylation of **30** in 20:2:5 (v/v) methanol–triethylamine –water for 3 days at room temperature gave syrupy **32**, $b.p._{0.01\,mm}$ 210–225°, $[\alpha]_D^{20}$ +85° (*c* 1.75, chloroform), R_F [1:1 (v/v) ether–light-petroleum] 0.25; i.r. data: ν_{max}^{film} 3500 cm^{-1} (OH).

*Spectrometer constructed in this University according to ref. 20.

Anal. Calc. for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99; O, 19.57. Found: C, 73.52; H, 6.97; O, 19.58.

O-Deacetylation under similar conditions of **31** gave syrupy **33**, b.p.$_{0.01\,mm}$ 230–240°, $[\alpha]_D^{20}$ +99° (*c* 0.786, chloroform); R_F [1:1 (v/v) ether–light petroleum] 0.25; i.r. data: ν_{max}^{film} 3500 cm^{-1} (OH).

Anal. Calc. for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99; O, 19.57. Found: C, 73.20; H, 6.88; O, 19.57.

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