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Synthesis and characterization of 6-*O*-β-lactosyl-α,β-lactoses, 1-*O*-(6-*O*-β-lactosyl-β-lactosyl)-(*R,S*)-glycerols, and 4,6-di-*O*-β-D-galactopyranosyl-α,β-D-glucoses*

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ABSTRACT

1,2,3,2',3',4',6'-Hepta-*O*-acetyl-β-lactose (**4**) was coupled with 2,3,6,2',3',4',6'-hepta-*O*-acetyl-α-lactosyl bromide (**7**) in the presence of $Hg(CN)_2$ to afford 1,2,3,2',3',4',6'-hepta-*O*-acetyl-6-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)-β-lactose (**11**) which, upon *O*-deacetylation, gave 6-*O*-β-lactosyl-α,β-lactoses (64% from **4**). In contrast, the reaction of **7** with benzyl 2,3,2',3',4',6'-hexa-*O*-acetyl-β-lactoside in the presence of $Hg(CN)_2$ produced 3,6,2',3',4',6'-hexa-*O*-acetyl-1,2-*O*-(2,3,2',3',4',6'-hexa-*O*-acetyl-1-*O*-benzyl-β-lactos-6-yl orthoacetyl)-α-lactose (63%) and 3,6,2',3',4',6'-hexa-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-lactose (27%). The glycosidation of **4** using 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide in the presence of $Hg(CN)_2$ afforded, after deprotection, 4,6-di-*O*-β-D-galactopyranosyl-α,β-D-glucoses (66%). The reaction of **11** with 1,2-di-*O*-benzyl-(*R,S*)-glycerols and trimethylsilyl trifluoromethanesulfonate yielded, after deprotection, 1-*O*-(6-*O*-β-lactosyl-β-lactosyl)-(*R,S*)-glycerols (18%). Under the same coupling conditions **11** reacted with 2-*O*-benzylglycerol to form 3-*O*-acetyl-2-*O*-benzyl-1-*O*-{2',3',4',6'-hexa-*O*-acetyl-6-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)-β-lactosyl}-(*R,S*)-glycerols (16%).

INTRODUCTION

Normal mammalian hepatocytes possess a number of carbohydrate-specific, cell-surface receptors[1]. Among the most intensively studied of these is the hepatic asialoglycoprotein receptor (ASGP-R)[1–3], which exhibits the ability to bind preferentially molecules having terminal, non-reducing β-D-galactopyranosyl or 2-acetamido-2-deoxy-α-D-galactopyranosyl residues[2–4]. From the present evidence[2,3,5–8] it has been adduced that both the number and the proximity of the galactose termini affect the avidity with which such molecules are bound to the hepatic receptor sites.

In the course of our on-going investigation[9–12] of the binding of β-D-galactopyranosyl-terminated oligomeric compounds by the ASGP-R of normal human and rabbit hepatocytes, we have synthesized a range of mono-, di-[9–11], and tri-*O*-lactosylglycerols[11], and 6-*O*- and 2,6-di-*O*-β-lactosyl-α,β-D-mannopyranoses[12]. Because of the importance

* Synthesis and Binding of D-Galactose-terminated Ligands to Human and Rabbit Asialoglycoprotein Receptor. Part V.

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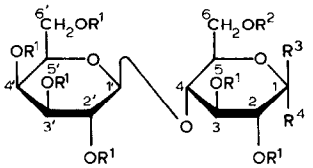
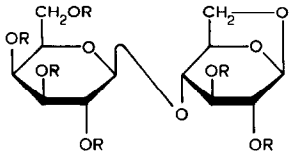
of obtaining quantitative data pertaining to the effects of variations in the number of terminal D-galactose units and their mutual propinquity[3,7,8] on the binding affinity[13,14] with ASGP-R, we have now broadened the spectrum of synthetic carbohydrates which are useful for assessing these interactions, and report herein the synthesis and characterization of 6-*O*-β-lactosyl-α,β-lactoses (**14**), 4,6-di-*O*-β-D-galactopyranosyl-α,β-D-glucoses (**15**), and 1-*O*-(6-*O*-β-lactosyl-β-lactosyl)-(*R,S*)-glycerols (**24**).

It has been noted earlier[11] that orthoesters have been obtained as side products during glycosidations under Koenigs–Knorr conditions. We now report the synthesis of a new orthoester and an orthoester-like compound, namely, 3,6,2′,3′,4′,6′-hexa-*O*-acetyl-1,2-*O*-(2,3,2′,3′,4′,6′-hexa-*O*-acetyl-1-*O*-benzyl-β-lactos-6-yl orthoacetyl)-α-lactose (**16**) and 3,6,2′,3′,4′,6′-hexa-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-lactose (**17**), respectively.

RESULTS AND DISCUSSION

The complex saccharides described in this paper necessitated the synthesis of several specifically protected derivatives of lactose. The intermediate, 1,2,3,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactose (**4**), was prepared by a slight modification of the procedure of Tejima[15]; the octa-*O*-acetyl-β-lactose (**1**) which we employed was crystalline instead of syrupy. The reaction of **1** with acetic anhydride, *p*-toluenesulfonic acid, and phenol[15] afforded the crystalline phenyl glycoside (**2**) in 63% yield (compared to a 31% yield[15] from the syrupy form of **1**). Compound **2** was converted into 2,3,2′,3′,4′,6′-hexa-*O*-





1 $R^1 = R^2 = Ac$, $R^3 = OAc$, $R^4 = H$
2 $R^1 = R^2 = Ac$, $R^3 = OPh$, $R^4 = H$
3 $R^1 = Ac$, $R^4 = Cl$, $R^2 = R^3 = H$
4 $R^1 = Ac$, $R^3 = OAc$, $R^2 = R^4 = H$
5 $R^1 = Ac$, $R^4 = Br$, $R^2 = R^3 = H$
6 $R^1 = Ac$, $R^3 = OBzl$, $R^2 = R^4 = H$
7 $R^1 = R^2 = Ac$, $R^3 = H$, $R^4 = Br$

8 R = H
9 R = Ac
10 R = Bzl

Bzl = CH_2Ph

acetyl-1,6-anhydro-β-lactose (**9**), using the method described by Tejima[15], and the latter afforded the heptaacetate **4** by way of the chloride **3**. Compound **9** was *O*-deacetylated using base[15], and the resulting lactosan (**8**) was treated with benzyl chloride and potassium hydroxide to give 1,6-anhydro-2,3,2′,3′,4′,6′-hexa-*O*-benzyl-β-lactose (**10**) in 69% yield, as a colorless oil. Compound **6**, which differed from **4** in having a benzyl

group at C-1, was prepared through the intermediacy of 2,3,2',3',4',6'-hexa-*O*-acetyl-α-lactosyl bromide (**5**) which had been produced from **9** by reaction with $TiBr_4$ in $CHCl_3$ (see ref. 16). Compound **5** was obtained as a semisolid which was used immediately without further purification. Treatment of **5** with 5 equiv. of benzyl alcohol in the presence of $Hg(CN)_2$ (ref. 17) in benzene–nitromethane for 3.5 h at 40° afforded benzyl 2,3,2',3',4',6'-hexa-*O*-acetyl-β-lactoside (**6**) in 42% yield. 2,3,6,2',3',4',6'-Hepta-*O*-acetyl-α-lactosyl bromide (**7**) was prepared by methods which have been previously described[9].

In order to confirm the assigned structures, and also to serve as aids in the analysis of the more complex saccharides described below, the 400-MHz proton nuclear magnetic resonance (^{1}H-n.m.r.) spectra of the above derivatives were acquired and the chemical shifts assigned using two-dimensional Fourier-transform, proton chemical-shift-correlation spectroscopy (COSY)[18,19] experiments. In the case of compound **9**, which exhibits numerous long-range coupling constants having magnitudes similar to those of vicinal protons, the chemical-shift assignments were made by comparing the ^{1}H-n.m.r. spectrum of **9** with that of compound **10**. A convenient summary of the diagnostic chemical shifts of the resonances of the protons in compounds **2**, **4**, **6**, **9**, and **10**, as well as the coupling constant for the proton at C-1 ($J_{1,2}$), is given in Table I. It is seen that the values for $J_{1,2}$ of compounds **2**, **4**, and **6** occur within the range 7.8–8.6 Hz and are consistent with the β-configuration[9,10] assigned at this position.

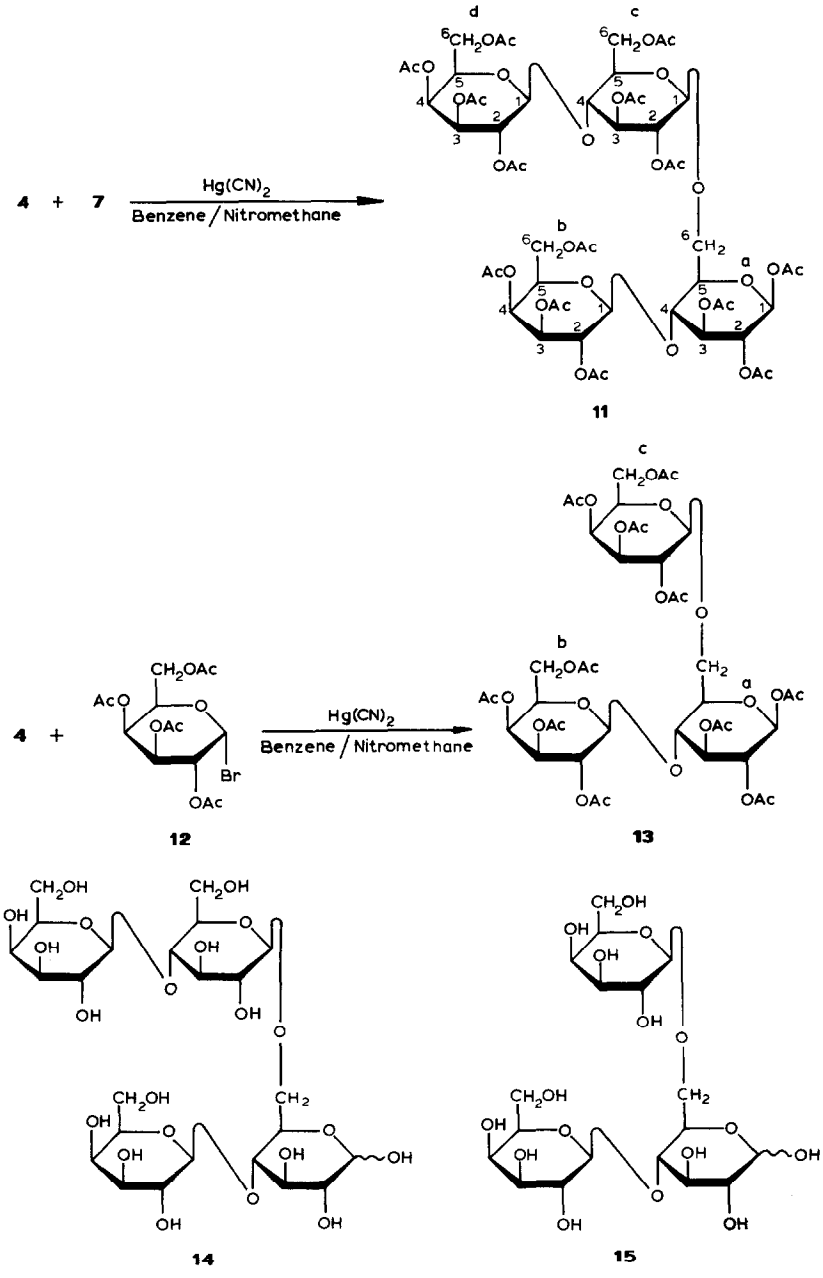
In Scheme 1 are shown the syntheses of the tetrasaccharide 1,2,3,2',3',4',6'-hepta-*O*-acetyl-6-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)-β-lactose (**11**) and the tri-

TABLE I

^{1}H-N.m.r. data[a] of **2**, **4**, **6**, **9**, and **10**

Proton	*Chemical shifts (δ) and coupling constants (Hz)*[b]				
	2	**4**	**6**	**9**	**10**
H-1($J_{1,2}$)	5.06(7.8)	5.69(8.6)	4.57(8.1)	5.46(1.6)	5.49(1.3)
H-2	5.18	5.03	4.95	4.56	3.80
H-3	5.29	5.24	5.17	5.16	3.89
H-4	3.88–3.93	4.00	3.94	3.57	3.35
H-5	3.79	3.55	3.38	4.60	4.63
H-6	4.15	3.75	3.75	3.82	3.69
H-6	4.50	3.92	3.88–3.93	3.99	3.95
H-1'	4.52	4.63	4.60	4.81	4.51
H-2'	5.13	5.12	5.10	5.29	3.90
H-3'	4.97	5.00	4.99	5.04	3.52
H-4'	5.36	5.35	5.34	5.39	3.90
H-5'	3.88–3.93	3.92	3.88–3.93	4.00	3.46–3.56
H-6'	4.10	4.08	4.05–4.15	4.06	3.46–3.56
H-6'	4.15	4.14	4.05–4.15	4.16	3.46–3.56

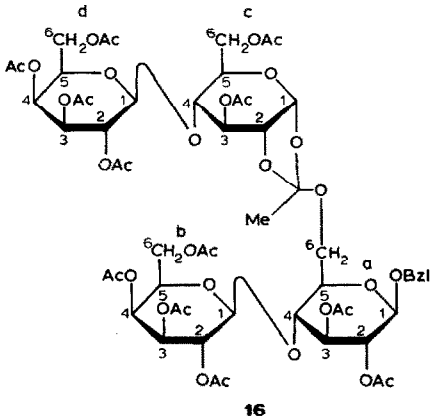
[a] For a solution in $CDCl_3$. The chemical shifts (δ) are given relative to an internal reference of Me_4Si. [b] In parentheses, $J_{1,2}$ only.


4 + 7
Hg(CN)2
Benzene / Nitromethane
11
4 +
Hg(CN)2
Benzene / Nitromethane
12
13
14
15

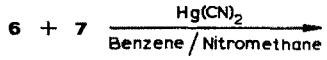
Scheme 1

saccharide 1,2,3-tri-*O*-acetyl-4,6-di-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranose (**13**). These carbohydrates were prepared by the reaction of compound **4** with hepta-*O*-acetyl-α-lactosyl bromide (**7**) and 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**12**)[20], respectively, using the Helferich method[17]. After reaction times of 11 and 12 h, respectively, compounds **11** and **13** were isolated in yields of 76 and 82%, respectively. The deprotected compounds **14** and **15** were obtained in greater than 80% yields by *O*-deacetylation of **11** and **13**, respectively, in methanol containing sodium methoxide. The value of $J_{1c,2c}$ in the ^{1}H-n.m.r. spectra of each of **11** and **13** was 8.4 Hz, thereby confirming that the anomeric linkages have the β-configuration.

The reaction of **6** with **7** (see Scheme 2) under conditions similar to those used in the preparation of **11** afforded only 3,6,2',3',4',6'-hexa-*O*-acetyl-1,2-*O*-(2,3,2',3',4',6'-hexa-*O*-acetyl-1-*O*-benzyl-β-lactos-6-yl orthoacetyl)-α-lactose (**16**) and 3,6,2',3',4',6'-hexa-*O*-acetyl-1,2-*O*-(1-cyanoethylidene)-α-lactose (**17**), together with a number of other side-reaction products. None of the expected glycoside was indicated by any of the ^{1}H-n.m.r. spectra of the isolated compounds. Compound **17** was obtained also by the reaction of **7** with $Hg(CN)_2$ in benzene–nitromethane, a result which demonstrated that **17** is the product of a competing reaction in which the cyano group from the catalyst attacks the dioxolenium intermediate. The structures of compounds **16** and **17** were



16



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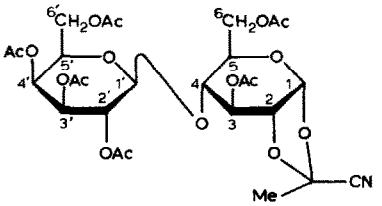


17

Scheme 2

TABLE II

^{1}H-N.m.r. data[a] for the D-glucosyl and D-galactosyl residues in **16**, **17**, and 3,6,2′,3′,4′,6′-hexa-*O*-acetyl-1,2-*O*-(ethyl orthoacetyl)-α-lactose[b]

Proton[c]	*Chemical shifts (δ) and coupling constants (Hz)*[d]		
	16[e]	**17**	[b]
H-1($J_{1,2}$)	5.68(5.1)	5.76(5.2)	5.66(5.0)
H-2($J_{2,3}$)	4.39(2.5)	4.40(2.9)	4.31(2.6)
H-3($J_{3,4}$)	5.55	5.63(1.1)	5.54(1.0)
H-4($J_{4,5}$)	3.66(9.1)	3.63(9.3)	3.66(9.5)
H-5	3.83–3.94	3.78	3.86
H-6($J_{6,5}$)	4.03–4.19	4.09(5.7)	4.10–4.17(5.7)
H-6($J_{6,5}$)	4.28(2.1)	4.23(2.7)	4.25(2.1)
Me	1.74	1.92	1.72
H-1′($J_{1',2'}$)	4.63(8.0)	4.60(8.0)	4.62(8.0)
H-2′($J_{2',3'}$)	5.20(10.3)	5.18(10.3)	5.19(10.3)
H-3′($J_{3',4'}$)	5.03(3.4)	5.01(3.4)	5.01(3.4)
H-4′($J_{4',5'}$)	5.39	5.39(1.0)	5.38(1.0)
H-5′	3.97	3.96	3.95
H-6′($J_{6',5'}$)	4.03–4.19(6.6)	4.11–4.19(6.8)	4.10–4.17(6.7)
H-6′($J_{6',5'}$)	4.03–4.19(6.6)	4.11–4.19(6.8)	4.10–4.17(6.7)

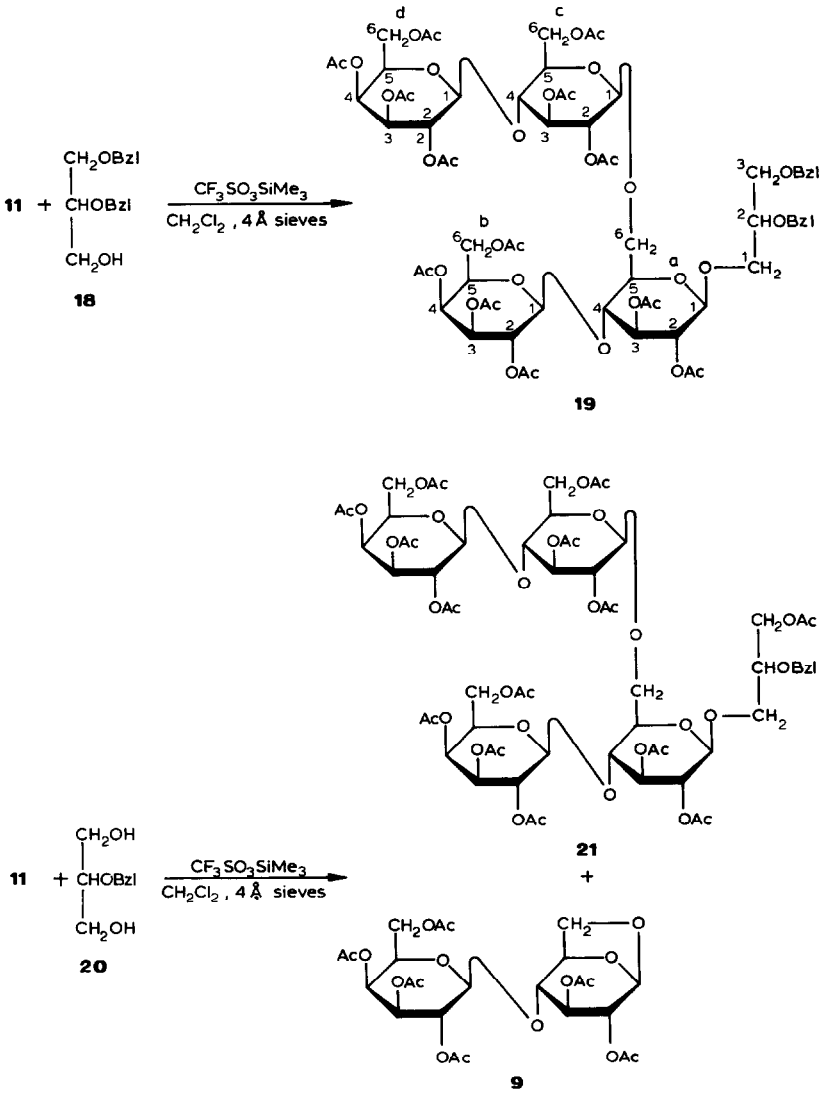
[a] For a solution in $CDCl_3$. The chemical shifts (δ) are given relative to an internal reference of Me_4Si. [b] Compound **15** in ref. 12. [c] The unprimed numbers refer to protons on the glucosyl residues and the primed ones to those on the galactosyl residues. [d] In parentheses. [e] Rings c and d.

assigned on the basis of their ^{1}H-n.m.r. spectra. A summary of the diagnostic chemical shifts of the resonance of the protons on rings c and d of compound **16**, and in the two sugar residues of compound **17** and of 3,6,2′,3′,4′,6′-hexa-*O*-acetyl-1,2-*O*-(ethyl orthoacetyl)-α-lactose (see ref. 12), is given in Table II.

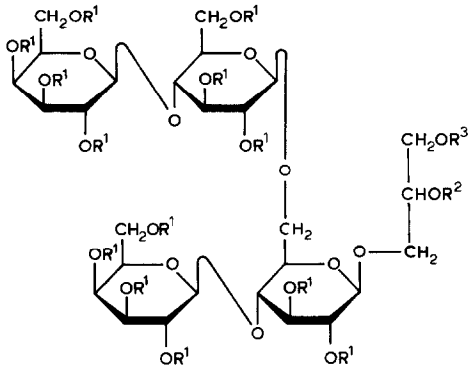
Each of compounds **16** and **17** was isolated as a single isomer. The compounds illustrated in Scheme 2 have been shown in the *exo* configuration, because the coupling constants ($J_{1,2}$ and $J_{2,3}$) of the protons, on the glucosyl residues, which are also part of the dioxolan ring, have magnitudes very similar to those reported[12] for the corresponding protons of tri-*O*-acetyl-α-D-glucopyranose 1,2-(ethyl orthoacetate). The assignment of the configuration to this last-cited compound has been previously discussed[20].

The chemical shifts of the resonances of the corresponding protons of **16**, **17**, and 3,6,2′,3′,4′,6′-hexa-*O*-acetyl-1,2-*O*-(ethyl orthoacetyl)-α-lactose (see Table II) vary relatively little, as would be expected from the very similar environments of these protons. In addition there is even less variation in the coupling constants of corresponding protons in these compounds. These results suggest that these compounds have similar conformations. The coupling constants and chemical shifts of the resonances of corresponding protons on the galactosyl residues of **16**, **17**, and 3,6,2′,3′,4′,6′-hexa-*O*-acetyl-1,2-*O*-(ethyl orthoacetyl)-α-lactose also are very similar. However, they differ significantly from those of corresponding protons of compounds in which the galactosyl residue is linked to a glucosyl residue which is also glycosidically bonded (see Table I of ref. 10).

The reaction of **11** with 1,2-di-*O*-benzyl-(*R,S*)-glycerols (**18**) (ref. 9) in methylene chloride in the presence of 4Å molecular sieves and trimethylsilyl trifluoromethanesulfonate[21] (see Scheme 3) afforded 2,3-di-*O*-benzyl-1-*O*-{2,3,2',3',4',6'-hexa-*O*-acetyl-6-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)-β-lactosyl}-(*R,S*)-glycerols (**19**) in 33% yield. In a second synthesis (see Scheme 3) compound **11** was coupled with 2-*O*-benzylglycerol (**20**) (ref. 9) under similar conditions. In this case the major isolated component consisted of a mixture of compounds **9** and **21**. It may be inferred from Scheme 3, that compound **21** resulted from a combination of glycosidation and transacetylation reactions. A similar one-pot glycosidation–transacetylation had been previously observed[9] in the coupling of octa-*O*-acetyl-β-lactose (**1**) with **20** in the presence of



Scheme 3



22 R^1 = Ac , R^2 = R^3 = H
23 R^1 = R^3 = Ac , R^2 = H
24 R^1 = R^2 = R^3 = H

trimethylsilyl trifluoromethanesulfonate. Sequential deprotection of the intermediates, **19** and **21**, provided compounds **22–24**. The benzyl groups were removed by catalytic transfer hydrogenation[22] to afford **22** in 55% yield from **19**. Similarly, *O*-debenzylation of the mixture of **9** and **21** provided **23**, which was easily separated from **9** by column chromatography. *O*-Deacetylation of **22**, using sodium methoxide in methanol[23], gave the fully deprotected glycoside (**24**) in quantitative yield.

The 400-MHz ^{1}H-n.m.r. spectra of compounds **19** and **22–24** were recorded, and chemical shifts were assigned with the aid of COSY[18,19] experiments. The values of $J_{1a,2a}$, which relate to the linkage between glycerol and the tetrasaccharide in compounds **19**, **22**, and **23**, occurred in the range 7.8–8.2 Hz, and showed that the new linkages have the *β*-configuration.

EXPERIMENTAL

General methods. — Melting points were determined on a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer model 141 or 241 automatic polarimeter for solutions in a 0.1-dm cell. Proton nuclear magnetic resonance (^{1}H-n.m.r.) spectra were recorded with a Bruker AM-400 (400 MHz) spectrometer, with tetramethylsilane (Me_4Si) as the internal standard; chemical shifts (δ) are given in p.p.m. downfield from the signal of Me_4Si. Protons have been designated in accordance with the structural formulas provided.

Thin-layer chromatography (t.l.c.) was performed using glass plates precoated with E. Merck Silica Gel 60F-254 as the adsorbent (layer thickness: 0.25 mm), using (*A*) 2:1 hexane–ethyl acetate; (*B*) 6:1, (*C*) 4:3, (*D*) 1:1, (*E*) 2:3, and (*F*) 1:2 toluene–ethyl acetate; (*G*) 9:9:1, and (*H*) 4:4:1 toluene–ethyl acetate–2-propanol; and (*I*) 4:1 ethanol–water (v/v). The developed plates were air-dried, sprayed with a solution of cerium(IV) sulfate (1%) and molybdic acid (1.5%) in 10% aqueous sulfuric acid, and heated at 150°. Column chromatography was performed using E. Merck 7734 Silica Gel 60

(70–230 mesh) as a solid phase. Solvents were evaporated under reduced pressure at ~ 40°.

Phenyl 2,3,6,2',3',4',6'-hepta-O-acetyl-β-lactoside (**2**). — Compound **2** was prepared using the procedure described by Tejima[15], except that crystalline octa-*O*-acetyl-β-lactose (**1**) (62.9 g, 92.7 mmol)[9,24] was used instead of syrupy octa-*O*-acetyl-β-lactose. Also, the benzene solvent was replaced with toluene. Crystallization from ethanol provided **2** (41.8 g, 63%) as a colorless solid, R_F 0.47 (solvent *C*); m.p. 155–158°; $[\alpha]_D^{27}$ −20.3° (*c* 3.35, chloroform) [lit.[25] m.p. 161.5°, $[\alpha]_D^{20}$ −23.2°; lit.[15] m.p. 165°, $[\alpha]_D^{25}$ −22.7° (*c* 1.58, chloroform)]; ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 3 H, OAc), 2.06 (s, 6 H, 2 OAc), 2.07 (s, 3 H, OAc), 2.08 (s, 6 H, 2 OAc), 2.16 (s, 3 H, OAc), 3.79 (ddd, 1 H, $J_{5,4}$ 9.9, $J_{5,6}$ 5.8, $J_{5,6}$ 2.0 Hz, H-5), 3.88–3.93 (m, 2 H, H-4,5'), 4.10 (dd, 1 H, J_{gem} 11.1, $J_{6',5'}$ 7.2 Hz, H-6'), 4.153 (dd, 1 H, J_{gem} 11.9, $J_{6,5}$ 5.8 Hz, H-6), 4.154 (dd, 1 H, J_{gem} 11.1, $J_{6',5'}$ 6.5 Hz, H-6'), 4.50 (dd, 1 H, J_{gem} 11.9, $J_{6,5}$ 2.0 Hz, H-6), 4.52 (d, 1 H, $J_{1',2'}$ 7.8 Hz, H-1'), 4.97 (dd, 1 H, $J_{3',2'}$ 10.4, $J_{3',4'}$ 3.4 Hz, H-3'), 5.06 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1), 5.13 (dd, 1 H, $J_{2',3'}$ 10.4, $J_{2',1'}$ 7.8 Hz, H-2'), 5.18 (dd, 1 H, $J_{2,3}$ 9.0, $J_{2,1}$ 7.8 Hz, H-2), 5.29 (t, 1 H, ^3J 9.0 Hz, H-3), 5.36 (dd, 1 H, $J_{4',3'}$ 3.4, $J_{4',5'}$ 0.7 Hz, H-4'), 6.96–7.31 (m, 5 H, Ph).

2,3,2',3',4',6'-Hexa-O-acetyl-1,6-anhydro-β-lactose (**9**). — Compound **9** was prepared from **2** (24.15 g, 33.9 mmol) in the manner described by Tejima[15]. A suspension of the crude product in hot ethanol (100 mL) was cooled to room temperature. The precipitate was collected by filtration and washed with ethanol (60 mL) to afford **9** (14.3 g, 73%) as a crystalline solid, m.p. 204–205° [lit.[26] 206–208°; lit.[15] 208°]; $[\alpha]_D^{24}$ −41.1° (*c* 1.75, chloroform) [lit.[26] $[\alpha]_D^{20}$ −40.8° (chloroform); lit.[15] $[\alpha]_D^{19}$ −39.5° (*c* 2.33, chloroform)]; ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.99 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.14 (s, 3 H, OAc), 2.15 (s, 3 H, OAc), 3.57 (m, 1 H, $^3J_{4,3}$ = $^3J_{4,5}$ = $^4J_{4,2}$ 1.2 Hz, H-4), 3.82 (dd, 1 H, J_{gem} 7.6, $J_{6,5}$ 5.7 Hz, H-6), 3.991 (dd, 1 H, J_{gem} 7.6, $J_{6,5}$ 1.0 Hz, H-6), 3.996 (td, 1 H, $J_{5',4'}$ 1.1 Hz, H-5'), 4.06 (dd, 1 H, J_{gem} 11.2, $J_{6',5'}$ 7.0 Hz, H-6'), 4.16 (dd, 1 H, J_{gem} 11.2, $J_{6',5'}$ 6.2 Hz, H-6'), 4.56 (q, 1 H, $^3J_{2,3}$ = $^3J_{2,1}$ = $^4J_{2,4}$ 1.2 Hz, H-2), 4.60 (m, 1 H, H-5), 4.81 (d, 1 H, $J_{1',2'}$ 7.9 Hz, H-1'), 5.04 (dd, 1 H, $J_{3',2'}$ 10.5, $J_{3',4'}$ 3.5 Hz, H-3'), 5.16 (quintet, 1 H, $^3J_{3,4}$ = $^3J_{3,2}$ = $^4J_{3,1}$ = $^4J_{3,5}$ 1.4 Hz, H-3), 5.29 (dd, 1 H, $J_{2',3'}$ 10.5, $J_{2',1'}$ 7.9 Hz, H-2'), 5.39 (dd, 1 H, $J_{4',3'}$ 3.5, $J_{4',5'}$ 1.1 Hz, H-4'), 5.46 (br t, 1 H, $^3J_{1,2}$ = $^4J_{1,3}$ 1.6 Hz, H-1).

1,6-Anhydro-2,3,2',3',4',6'-hexa-O-benzyl-β-lactose (**10**). — A solution of **2** (11.74 g, 16.5 mmol) in 2.6M aqueous potassium hydroxide (200 mL) was heated for 25 h at reflux temperature, cooled in an ice-bath, and neutralized using 3M sulfuric acid. The solution was concentrated as described by Tejima[15], and the residue (~ 22 g), containing 1,6-anhydro-β-lactose (**8**), was coevaporated with ethanol (20 mL) and then with toluene (25 mL). The residue was heated for 1 h at 135° in the presence of benzyl chloride (200 mL, 1.74 mol) and potassium hydroxide (75 g, 1.34 mol), cooled to room temperature, and diluted with dichloromethane (200 mL) and water (400 mL). After thorough mixing, the organic phase was separated, dried ($CaCl_2$), and concentrated under reduced pressure. The resulting oil was dissolved in ethanol (600 mL), and water (200 mL) was added slowly. A yellow oil precipitated and was treated twice more with ethanol and water as described above. The final orange oil (~ 16 g) was purified by

column chromatography to yield **10** (9.87 g, 69%) as a colorless oil, R_F 0.28 (solvent *B*); $[\alpha]_D^{27}$ −27.9° (*c* 2.35, chloroform); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 3.35 (m, 1 H, H-4), 3.46–3.56 (m, 3 H, H-5′,-6′,-6′), 3.52 (dd, 1 H, $J_{3',2'}$ 9.8, $J_{3',4'}$ 3.0 Hz, H-3′), 3.69 (dd, 1 H, J_{gem} 7.2, $J_{6,5}$ 5.7 Hz, H-6), 3.80 (m, 1 H, H-2), 3.89 (m, 1 H, H-3), 3.90 (dd, 1 H, $J_{2',3'}$ 9.8, $J_{2',1'}$ 7.5 Hz, H-2′), 3.90 (m, 1 H, H-4′), 3.95 (dd, 1 H, J_{gem} 7.2, $J_{6,5}$ 1.2 Hz, H-6), 4.36 (d, 1 H, J_{gem} 11.8 Hz, coupled to H having δ 4.39, CH_2Ph), 4.39 (d, 1 H, J_{gem} 11.8 Hz, CH_2Ph), 4.43 (d, 1 H, J_{gem} 12.0 Hz, coupled to H having δ 4.57, CH_2Ph), 4.51 (d, 1 H, $J_{1',2'}$ 7.5 Hz, H-1′), 4.55 (d, 1 H, J_{gem} 11.9 Hz, coupled to H having δ 4.61, CH_2Ph), 4.57 (d, 1 H, J_{gem} 12.0 Hz, CH_2Ph), 4.61 (d, 2 H, J_{gem} 11.7 Hz, CH_2Ph), 4.63 (m, 1 H, H-5), 4.732 (d, 1 H, J_{gem} 11.8 Hz, coupled to H having δ 4.80, CH_2Ph), 4.741 (d, 1 H, J_{gem} 10.8 Hz, coupled to H having δ 5.05, CH_2Ph), 4.80 (d, 1 H, J_{gem} 11.8 Hz, CH_2Ph), 4.99 (d, 1 H, J_{gem} 11.4 Hz, coupled to H having δ 4.61, CH_2Ph), 5.05 (d, 1 H, J_{gem} 10.8 Hz, CH_2Ph), 5.49 (br t, 1 H, *J* 1.3 Hz, H-1), 7.20–7.43 (m, 30 H, 6 Ph).

*1,2,3,2′,3′,4′,6′-Hepta-*O*-acetyl-β-lactose* (**4**). — Compound **9** (15.01 g, 26.0 mmol) was treated in the manner described by Tejima[15] to give **4** (10.51 g, 63.5%) as a crystalline solid, R_F 0.46 (solvent *G*); m.p. 194–198° (lit.[15] 191–192°); $[\alpha]_D^{19}$ −9.5° (*c* 2.35, chloroform) [lit.[15] $[\alpha]_D^{27}$ −12.5° (*c* 2.24, chloroform)]; ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.96 (dd, 1 H, ^3J 9.3, ^3J 4.5 Hz, OH), 1.97 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.05 (s, 6 H, 2 OAc), 2.07 (s, 3 H, OAc), 2.11 (s, 3 H, OAc), 2.16 (s, 3 H, OAc), 3.55 (m, 1 H, $J_{5,4}$ 9.5 Hz, H-5), 3.75 (m, 1 H, J_{gem} 12.3, ^3J 9.3, $J_{6,5}$ 2.9 Hz, H-6), 3.92 (m, 2 H, H-5′,6), 4.00 (t, 1 H, ^3J 9.5 Hz, H-4), 4.08 (dd, 1 H, J_{gem} 11.3, $J_{6',5'}$ 7.2 Hz, H-6′), 4.14 (dd, 1 H, J_{gem} 11.3, $J_{6',5'}$ 6.6 Hz, H-6′), 4.63 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 5.00 (dd, 1 H, $J_{3',2'}$ 10.4, $J_{3',4'}$ 3.4 Hz, H-3′), 5.03 (m, 1 H, H-2), 5.12 (dd, 1 H, $J_{2',3'}$ 10.4, $J_{2',1'}$ 8.0 Hz, H-2′), 5.24 (t, 1 H, ^3J 9.5 Hz, H-3), 5.35 (dd, 1 H, $J_{4',3'}$ 3.4, $J_{4',5'}$ 0.8 Hz, H-4′), 5.69 (d, 1 H, $J_{1,2}$ 8.6 Hz, H-1); the proton having a signal at δ 1.96 was exchangeable with D_2O.

*Benzyl 2,3,2′,3′,4′,6′-hexa-*O*-acetyl-β-lactoside* (**6**). — To a cold (ice-bath) solution of **9** (5.96 g, 10.3 mmol) in chloroform (30 mL) was added a solution containing $TiBr_4$ (12.87 g, 35 mmol) in chloroform (30 mL). The resultant solution was warmed in a water bath (50°) for 5 min, heated at reflux temperature for 3.5 h, stirred at room temperature for 7 h, cooled to ice-bath temperature, and poured into ice water (300 mL). The residue in the reaction flask was transferred into the ice water using chloroform (50 mL). The organic phase was separated and the aqueous phase was extracted with chloroform (25 mL). The combined chloroform extracts were washed with ice-cold water (2 × 100 mL), dried ($CaCl_2$), and the solvent was evaporated to give 2,3,2′,3′,4′,6′-hexa-*O*-acetyl-α-lactosyl bromide (**5**) (~ 8 g) as a semisolid.

A solution of benzene–nitromethane {1:1 (v/v), 50 mL}, $Hg(CN)_2$ (3.5 g, 13.9 mmol), and benzyl alcohol (7.2 g, 66.6 mmol) was added to **5** and the mixture was stirred for 3.5 h at 40°, cooled to room temperature, diluted with toluene (100 mL), and washed sequentially with a saturated aqueous solution of sodium hydrogencarbonate (2 × 50 mL), and water (50 mL). The organic phase was dried (Na_2SO_4), the solvent was evaporated, and the residue resolved by column chromatography (solvent *D*) to afford **6** (2.96 g, 42%) as a colorless, glassy solid, R_F 0.47 (solvent *G*). ^{1}H-N.m.r. spectroscopy revealed that **6** was still contaminated by trace amounts of impurities. ^{1}H-N.m.r. (400

MHz, $CDCl_3$): δ 1.89 (dd, 1 H, ^3J 9.4, ^3J 4.6 Hz, CH_2OH), 1.97 (s, 3 H, OAc), 2.01 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.054 (s, 3 H, OAc), 2.057 (s, 3 H, OAc), 2.15 (s, 3 H, OAc), 3.38 (dt, 1 H, $J_{5,4}$ 9.6, $J_{5,6}$ 2.4 Hz, H-5), 3.75 (m, 1 H, J_{gem} 12.2, $^3J_{to\ OH}$ 9.4, $J_{6,5}$ 3.0 Hz, H-6), 3.88–3.93 (m, 2 H, H-5',6), 3.94 (t, 1 H, J 9.6 Hz, H-4), 4.05–4.15 (m, 2 H, H-6',6'), 4.57 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 4.60 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1'), 4.62 (d, 1 H, J_{gem} 12.2 Hz, CH_2Ph), 4.86 (d, 1 H, J_{gem} 12.2 Hz, CH_2Ph), 4.95 (dd, 1 H, $J_{2,3}$ 9.7, $J_{2,1}$ 8.1 Hz, H-2), 4.99 (dd, 1 H, $J_{3',2'}$ 10.6, $J_{3',4'}$ 3.5 Hz, H-3'), 5.10 (dd, 1 H, $J_{2',3'}$ 10.6, $J_{2',1'}$ 7.7 Hz, H-2'), 5.17 (t, 1 H, ^3J 9.4 Hz, H-3), 5.34 (dd, 1 H, $J_{4',3'}$ 3.5, $J_{4',5'}$ 1.1 Hz, H-4'), 7.28–7.40 (m, 5 H, Ph); the proton having a signal at δ 1.89 was exchangeable with D_2O.

1,2,3,2',3',4',6'-Hepta-O-*acetyl-6*-O-*(2,3,6,2',3',4',6'-hepta*-O-*acetyl-β-lactosyl)-β-lactose* (**11**). — A mixture containing 2,3,6,2',3',4',6'-hepta-*O*-acetyl-α-lactosyl bromide[9] (**7**) (2.62 g, 3.75 mmol), 1,2,3,2',3',4',6'-hepta-*O*-acetyl-β-lactose (**4**) (2.384 g, 3.75 mmol), and $Hg(CN)_2$ (0.95 g, 3.76 mmol) in benzene–nitromethane {1:1 (v/v), 40 mL} was stirred for 11 h at 40°. Further additions of compound **7** (1.3 g, 1.86 mmol) and $Hg(CN)_2$ (0.5 g, 1.98 mmol) were made after 6 and 9 h. The reaction mixture was diluted with toluene (100 mL) and washed sequentially with a saturated aqueous solution of sodium hydrogencarbonate (2 × 50 mL), and water (50 mL). The organic phase was dried ($CaCl_2$), evaporated, and the residual mixture resolved by column chromatography to give **11** (3.593 g, 76%) as a colorless, glassy solid, R_F 0.25 (solvent *E*); $[\alpha]_D^{27}$ − 11.2° (*c* 2.00, chloroform); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 6 H, 2 OAc), 2.02 (s, 6 H, 2 OAc), 2.04 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.07 (s, 6 H, 2 OAc), 2.08 (s, 3 H, OAc), 2.10 (s, 3 H, OAc), 2.14 (s, 3 H, OAc), 2.16 (s, 6 H, 2 OAc), 3.61 (m, 1 H, H-5c), 3.62 (m, 1 H, H-5a), 3.81 (dd, 1 H, J_{gem} 12.0, $J_{6a,5a}$ 4.5 Hz, H-6a), 3.84 (t, 2 H, ^3J 9.6 Hz, H-4a,4c), 3.88 (t, 1 H, ^3J 7.1 Hz, H-5d), 3.95 (m, 1 H, H-6a), 3.97 (m, 1 H, H-5b), 4.06–4.16 (m, 5 H, H-6b,-6b,-6c,-6d,-6d), 4.47 (dd, 1 H, J_{gem} 12.2, $J_{6c,5c}$ 1.5 Hz, H-6c), 4.50 (d, 1 H, $J_{1d,2d}$ 7.9 Hz, H-1d), 4.54 (d, 1 H, $J_{1b,2b}$ 7.4 Hz, H-1b), 4.58 (d, 1 H, $J_{1c,2c}$ 7.7 Hz, H-1c), 4.91 (dd, 1 H, $J_{2c,3c}$ 9.3, $J_{2c,1c}$ 7.7 Hz, H-2c), 4.96 (dd, 1 H, $J_{3d,2d}$ 10.5, $J_{3d,4d}$ 3.3 Hz, H-3d), 4.99 (dd, 1 H, $J_{2a,3a}$ 9.3, $J_{2a,1a}$ 8.4 Hz, H-2a), 5.01–5.11 (m, 2 H, H-2b,3b), 5.11 (dd, 1 H, $J_{2d,3d}$ 10.5, $J_{2d,1d}$ 7.9 Hz, H-2d), 5.20 (t, 1 H, ^3J 9.1 Hz, H-3c), 5.21 (t, 1 H, ^3J 9.2 Hz, H-3a), 5.36 (m, 2 H, H-4b,4d), 5.62 (d, 1 H, $J_{1a,2a}$ 8.4 Hz, H-1a).

Anal. Calc. for $C_{52}H_{70}O_{35}$: C, 49.76; H, 5.62. Found: C, 49.75; H, 5.60.

1,2,3-Tri-O-*acetyl-4,6-di*-O-*(2',3',4',6'-tetra*-O-*acetyl-β*-D-*galactopyranosyl)-β*-D-*glucopyranose* (**13**). — A mixture containing 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**12**)[20] (2.17 g, 5.28 mmol), 1,2,3,2',3',4',6'-hepta-*O*-acetyl-β-lactose (**4**) (3.36 g, 5.28 mmol), and $Hg(CN)_2$ (1.33 g, 5.26 mmol) in benzene–nitromethane [1:1 (v/v), 60 mL] was stirred for 12 h at 40°. Further additions of compound **12** (1.2 g, 2.9 mmol) and $Hg(CN)_2$ (0.7 g, 2.8 mmol) were made after 6 and 9 h. The reaction mixture was diluted with toluene (100 mL) and washed sequentially with a saturated aqueous solution of sodium hydrogencarbonate (2 × 50 mL), and water (50 mL). The organic phase was dried ($CaCl_2$), evaporated, and the residual mixture resolved by column chromatography to give **13** (4.19 g, 82%) as a colorless, glassy solid, R_F 0.42 (solvent *F*); $[\alpha]_D^{27}$ − 11.4° (*c* 2.35, chloroform); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 3 H, OAc), 2.00 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 2.04 (s, 6 H, 2 OAc), 2.05 (s, 3 H, OAc), 2.07 (s, 3

H, OAc), 2.10 (s, 3 H, OAc), 2.11 (s, 3 H, OAc), 2.16 (s, 3 H, OAc), 2.18 (s, 3 H, OAc), 3.63 (ddd, 1 H, $J_{5a,4a}$ 9.9, $J_{5a,6a}$ 4.4, $J_{5a,6a}$ 1.1 Hz, H-5a), 3.84 (t, 1 H, ^3J 9.3 Hz, H-4a), 3.86 (dd, 1 H, J_{gem} 12.1, $J_{6a,5a}$ 4.4 Hz, H-6a), 3.90 (td, 1 H, ^3J 6.7, $J_{5c,4c}$ 1.1 Hz, H-5c), 3.99 (m, 1 H, H-6a), 3.99 (m, 1 H, H-5b), 4.08–4.21 (m, 4 H, H-6b,-6b,-6c,-6c), 4.54 (d, 1 H, $J_{1b,2b}$ 7.3 Hz, H-1b), 4.58 (d, 1 H, $J_{1c,2c}$ 7.5 Hz, H-1c), 5.02 (dd, 1 H, $J_{2a,3a}$ 9.1, $J_{2a,1a}$ 8.4 Hz, H-2a), 5.03 (dd, 1 H, $J_{3c,2c}$ 10.8, $J_{3c,4c}$ 3.6 Hz, H-3c), 5.05 (dd, 1 H, $J_{3b,2b}$ 10.5, $J_{3b,4b}$ 3.3 Hz, H-3b), 5.10 (dd, 1 H, $J_{2b,3b}$ 10.5, $J_{2b,1b}$ 7.3 Hz, H-2b), 5.19 (dd, 1 H, $J_{2c,3c}$ 10.8, $J_{2c,1c}$ 7.5 Hz, H-2c), 5.22 (t, 1 H, ^3J 9.1 Hz, H-3a), 5.36 (dd, 1 H, $J_{4b,3b}$ 3.3, $J_{4b,5b}$ 0.9 Hz, H-4b), 5.40 (dd, 1 H, $J_{4c,3c}$ 3.6, $J_{4c,5c}$ 1.1 Hz, H-4c), 5.62 (d, 1 H, $J_{1a,2a}$ 8.4 Hz, H-1a).

Anal. Calc. for $C_{40}H_{54}O_{27}$: C, 49.69; H, 5.63. Found: C, 50.74; H, 5.70.

6-O-β-Lactosyl-α,β-lactoses (**14**). — To a solution of **11** (0.556 g, 0.443 mmol) in absolute methanol (15 mL) was added 0.1M sodium methoxide in methanol (5 mL). After stirring for 5 min, a white solid precipitated; the stirring was continued for an additional 2.5 h. Amberlite IR-120 (H^+) cation-exchange resin (5 mL) was added, and the mixture was stirred for 30 min at room temperature, during which time the white precipitate dissolved. The resin was removed by filtration and washed with methanol (20 mL). The combined filtrate and wash solution was evaporated, and the residue was dried under vacuum. The dried residue was treated once more with sodium methoxide as described above and, after drying under vacuum, afforded **14** (0.250 g, 85%) as a glassy solid, R_F 0.44 (solvent *I*); $[\alpha]_D^{25}$ + 38° (*c* 2.45, water).

Anal. Calc. for $C_{24}H_{42}O_{21}\cdot 2H_2O$: C, 41.02; H, 6.60. Found: C, 40.80; H, 6.76.

4,6-Di-O-β-D-galactopyranosyl-α,β-D-glucoses (**15**). — To a solution of **13** (0.577 g, 0.597 mmol) in absolute methanol (15 mL) was added 0.1M sodium methoxide in methanol (5 mL). After ~ 5 min a white solid precipitated. The mixture was stirred at room temperature for 2.5 h and treated with Amberlite IR-120 (H^+) cation-exchange resin (5 mL). The *O*-deacetylation was repeated as described above, and, after removal of the resin and evaporation of the solvents, **15** was obtained as a colorless, glassy solid (0.240 g, 80%), R_F 0.46 (solvent *I*); $[\alpha]_D^{25}$ + 51° (*c* 2.2, water).

Anal. Calc. for $C_{18}H_{32}O_{16}\cdot 1.5H_2O$: C, 40.68; H, 6.64. Found: C, 40.57; H, 6.82.

3,6,2',3',4',6'-Hexa-O-acetyl-1,2-O-(2,3,2',3',4',6'-hexa-O-acetyl-1-O-benzyl-β-lactos-6-yl orthoacetyl)-α-lactose (**16**) *and 3,6,2',3',4',6'-hexa-O-acetyl-1,2-O-(1-cyanoethylidene)-α-lactose* (**17**). — A mixture of **7** (4.06 g, 5.80 mmol), **6** (1.98 g, 2.90 mmol), and $Hg(CN)_2$ (1.47 g, 5.8 mmol) in benzene–nitromethane {1:1 (v/v), 75 mmol} was stirred for 5 h at 40°. Further additions of compound **7** (1 g, 1.43 mmol) and $Hg(CN)_2$ (0.4 g, 1.58 mmol) were made after 3 h. The reaction mixture was diluted with toluene (60 mL) and washed sequentially with a saturated aqueous solution of sodium hydrogencarbonate (2 × 50 mL), and water (50 mL). The organic phase was dried (Na_2SO_4), evaporated, and the residual mixture was resolved by column chromatography to give three main components having R_F 0.35, 0.25, and 0.17 (solvent *D*). The component having R_F 0.25 was shown by ^{1}H-n.m.r. spectroscopy to be starting material, **6** (0.642 g, 32% recovery). The component having R_F 0.17 was a colorless, glassy solid, which was identified by ^{1}H-n.m.r. spectroscopy as **16** (2.392 g, 63%) containing small amounts of impurities; ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.74 (s, 3 H, Me), 1.97 (s, 3 H,

OAc), 1.98 (s, 3 H, OAc), 2.00 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 2.06 (s, 6 H, 2 OAc), 2.07 (s, 3 H, OAc), 2.09 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.15 (s, 3 H, OAc), 2.17 (s, 3 H, OAc), 3.44 (ddd, 1 H, $J_{5a,4a}$ 9.5, $J_{5a,6a}$ 3.8, $J_{5a,6a}$ 1.7 Hz, H-5a), 3.66 (m, 1 H, $J_{4c,5c}$ 9.1 Hz, H-4c), 3.68 (dd, 1 H, J_{gem} 10.8, $J_{6a,5a}$ 3.8 Hz, H-6a), 3.82 (t, 1 H, ^3J 9.3 Hz, H-4a), 3.83–3.94 (m, 2 H, H-5c,6a), 3.91 (br t, 1 H, ^3J 6.6 Hz, H-5b), 3.97 (br t, 1 H, ^3J 6.6 Hz, H-5d), 4.03–4.19 (m, 5 H, H-6b,-6b,-6c,-6d,-6d), 4.28 (dd, 1 H, J_{gem} 12.0, $J_{6c,5c}$ 2.1 Hz, H-6c), 4.39 (br dd, 1 H, $J_{2c,1c}$ 5.1, $J_{2c,3c}$ 2.5 Hz, H-2c), 4.48 (d, 1 H, $J_{1a,2a}$ 8.1 Hz, H-1a), 4.572 (d, 1 H, $J_{1b,2b}$ 7.7 Hz, H-1b), 4.583 (d, 1 H, J_{gem} 12.5 Hz, CH_2Ph), 4.63 (d, 1 H, $J_{1d,2d}$ 8.0 Hz, H-1d), 4.84 (d, 1 H, J_{gem} 12.5 Hz, CH_2Ph), 4.92 (dd, 1 H, $J_{2a,3a}$ 9.3, $J_{2a,1a}$ 8.1 Hz, H-2a), 4.95 (dd, 1 H, $J_{3b,2b}$ 10.5, $J_{3b,4b}$ 3.6 Hz, H-3b), 5.03 (dd, 1 H, $J_{3d,2d}$ 10.3, $J_{3d,4d}$ 3.4 Hz, H-3d), 5.09 (dd, 1 H, $J_{2b,3b}$ 10.5, $J_{2b,1b}$ 7.7 Hz, H-2b), 5.13 (t, 1 H, ^3J 9.2 Hz, H-3a), 5.20 (dd, 1 H, $J_{2d,3d}$ 10.3, $J_{2d,1d}$ 8.0 Hz, H-2d), 5.36 (m, 1 H, H-4b), 5.39 (br d, 1 H, $J_{4d,3d}$ 3.4 Hz, H-4d), 5.55 (m, 1 H, H-3c), 5.68 (d, 1 H, $J_{1c,2c}$ 5.1 Hz, H-1c), 7.17–7.40 (m, 5 H, Ph).

The component having R_F 0.35 was identified as **17** (1.265 g, 27% based on **7**). This product was obtained as a crystalline solid and had a ^{1}H-n.m.r. spectrum which was identical to that of the sample of **17**, prepared as described below.

Preparation of **17** *from* **7**. — A mixture of **7** (1.08 g, 1.54 mmol) and $Hg(CN)_2$ (0.78 g, 3.08 mmol) in benzene–nitromethane (1:1, 10 mL) was stirred for 6.5 h at 40°, diluted with toluene (15 mL), and washed sequentially with a saturated aqueous solution of sodium hydrogencarbonate (2 × 10 mL), and water (10 mL). The organic phase was dried (Na_2SO_4), evaporated, and the residual mixture was partially resolved by column chromatography to give an oil (0.443 g) consisting of **17** and an unidentified disaccharide. ^{1}H-N.m.r. spectroscopy indicated that **17** accounted for ~ 75% of the oily mixture (33% yield). The oil was crystallized from absolute ethanol (15 mL), and the crystals were collected by suction and washed with ethanol (6 mL) to give **17** (0.231 g, 23%) as a white crystalline solid, m.p. 190–191°; $[\alpha]_D^{25}$ −0.7° (*c* 2.35, chloroform); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.92 (s, 3 H, Me), 1.98 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.14 (s, 3 H, OAc), 2.17 (s, 3 H, OAc), 3.63 (m, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 3.78 (ddd, 1 H, $J_{5,4}$ 9.3, $J_{5,6}$ 5.7, $J_{5,6}$ 2.7 Hz, H-5), 3.96 (td, 1 H, $J_{5',6'}$ 6.8, $J_{5',4'}$ 1.0 Hz, H-5'), 4.09 (dd, 1 H, J_{gem} 12.0, $J_{6,5}$ 5.7 Hz, H-6), 4.11–4.19 (m, 2 H, H-6',-6'), 4.23 (dd, 1 H, J_{gem} 12.0, $J_{6,5}$ 2.7 Hz, H-6), 4.40 (ddd, 1 H, $J_{2,1}$ 5.2, $J_{2,3}$ 2.9, $^4J_{2,4}$ 1.1 Hz, H-2), 4.60 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1'), 5.01 (dd, 1 H, $J_{3',2'}$ 10.3, $J_{3',4'}$ 3.4 Hz, H-3'), 5.18 (dd, 1 H, $J_{2',3'}$ 10.3, $J_{2',1'}$ 8.0 Hz, H-2'), 5.39 (dd, 1 H, $J_{4',3'}$ 3.4, $J_{4',5'}$ 1.0 Hz, H-4'), 5.63 (dd, 1 H, $J_{3,2}$ 2.9, $J_{3,4}$ 1.1 Hz, H-3), 5.76 (d, 1 H, $J_{1,2}$ 5.2 Hz, H-1).

Anal. Calc. for $C_{27}H_{35}O_{17}N$: C, 50.23; H, 5.46; N, 2.17. Found: C, 50.31; H, 4.85; N, 2.15.

*2,3-Di-*O*-benzyl-1-*O*-{2,3,2',3',4',6'-hexa-*O*-acetyl-6-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)-β-lactosyl}-(*R,S*)-glycerols* (**19**). — A mixture of **11** (1.18 g, 0.94 mmol), 1,2-di-*O*-benzyl-(*R,S*)-glycerols (**18**) (ref. 9) (0.272 g, 1.00 mmol), 4 Å molecular sieves (4.5 g), and trimethylsilyl trifluoromethanesulfonate (0.18 mL, 0.93 mmol) in dichloromethane (8.0 mL) was stirred for 2.5 h at room temperature. The solids were removed by filtration and washed with dry dichloromethane (10 mL). The combined filtrate and wash solution was washed sequentially with a saturated aqueous solution of

sodium hydrogencarbonate (10 mL), and water (10 mL). The organic phase was dried (Na_2SO_4) and evaporated, and the residual mixture was resolved by column chromatography to give **19** (0.451 g, 33%) as a colorless, glassy solid, R_F 0.36 (solvent *E*); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.923 (s, 3 H, OAc), 1.935 (s, 3 H, OAc), 1.97 (br s, 12 H, 4 OAc), 2.006 (s, 3 H, OAc), 2.014 (s, 3 H, OAc), 2.024 (s, 6 H, 2 OAc), 2.028 (s, 6 H, 2 OAc), 2.038 (s, 6 H, 2 OAc), 2.046 (s, 6 H, 2 OAc), 2.059 (s, 12 H, 4 OAc), 2.108 (s, 3 H, OAc), 2.113 (s, 3 H, OAc), 2.140 (s, 3 H, OAc), 2.144 (s, 3 H, OAc), 2.16 (s, 6 H, 2 OAc), 3.46–3.61 (m, 7 H, H-5a,-5a,-5c,-5c, and 3 of H-1 and/or H-3), 3.65 (dd, 1 H, J_{gem} 10.9, ^3J 7.2 Hz, H-1 or H-3), 3.688 (t, 1 H, ^3J 9.4 Hz, H-4c), 3.701 (t, 1 H, ^3J 9.3 Hz, H-4c), 3.71–4.03 {m, 14 H, (H-1 and/or H-3)(4), H-2,-2,-5b,-5b,-5d,-5d,-6a(4)}, 3.806 (t, 1 H, ^3J 9.4 Hz, H-4a), 3.813 (t, 1 H, ^3J 9.4 Hz, H-4a), 4.05–4.15 {m, 10 H, H-6b(4),-6c,-6c,-6d (4)}, 4.46 (m, 1 H, H-6c), 4.46–4.51 (m, 1 H, H-6c), 4.465 (d, 1 H, $J_{1a,2a}$ 8.0 Hz, H-1a), 4.475 (br d, 2 H, ^3J 8.2 Hz, 2 of H-1b and/or H-1d), 4.480 (d, 1 H, ^3J 8.0 Hz, H-1b or H-1d), 4.488 (d, 1 H, ^3J 7.6 Hz, H-1b or H-1d), 4.515 (d, 1 H, J_{gem} 12.0 Hz, CH_2Ph), 4.52 (d, 1 H, H-1a), 4.53 (s, 2 H, CH_2Ph), 4.55 (d, 1 H, J_{gem} 12.0 Hz, CH_2Ph), 4.608 (d, 1 H, $J_{1c,2c}$ 7.8 Hz, H-1c), 4.635 (s, 2 H, CH_2Ph), 4.638 (d, 1 H, $J_{1c,2c}$ 7.8 Hz, H-1c), 4.653 (s, 2 H, CH_2Ph), 4.873 (dd, 1 H, $J_{2a,3a}$ 9.8, $J_{2a,1a}$ 8.0 Hz, H-2a), 4.901 (dd, 3 H, ^3J 9.3, ^3J 7.8 Hz, H-2a,-2c,-2c), 4.95 (dd, 2 H, ^3J 10.4, ^3J 3.4 Hz, 2 of H-3b and/or H-3d), 5.015 (dd, 1 H, ^3J 10.6, ^3J 3.4 Hz, H-3b or H-3d), 5.019 (dd, 1 H, ^3J 10.4, ^3J 3.4 Hz, H-3b or H-3d), 5.086 (dd, 2 H, ^3J 10.3, ^3J 7.6 Hz, 2 of H-2b and/or H-2d), 5.11 (m, 2 H, 2 of H-2b and/or H-2d), 5.152 (t, 1 H, ^3J 9.3 Hz, H-3c), 5.159 (t, 1 H, ^3J 9.4 Hz, H-3c), 5.168 (t, 1 H, ^3J 9.1 Hz, H-3a), 5.183 (t, 1 H, ^3J 9.3 Hz, H-3a), 5.34–5.36 (m, 4 H, H-4b,-4b,-4d,-4d), 7.24–7.37 (m, 20 H, 4 Ph).

Anal. Calc. for $C_{67}H_{86}O_{36}$: C, 54.84; H, 5.91. Found: C, 54.82; H, 5.95.

3-O-Acetyl-2-O-benzyl-1-O-{2,3,2',3',4',6'-hexa-O-acetyl-6-O-(2,3,6,2',3',4',6'-hepta-O-acetyl-β-lactosyl)-β-lactosyl}-(R,S)-glycerols (**21**). — A mixture of **11** (2.01 g, 1.60 mmol), 2-*O*-benzylglycerol (**20**) (ref. 9) (0.133 g, 0.73 mmol), 4 Å molecular sieves (4.3 g), and trimethylsilyl trifluoromethanesulfonate (0.31 mL, 1.60 mmol) in dichloromethane (12 mL) was stirred for 2 h at room temperature. The reaction mixture was treated as described above for the preparation of **19** and, after resolution by column chromatography, two components were obtained having R_F 0.30 and 0.23 (solvent *E*). The component having R_F 0.23 (0.258 g) lacked resonances for the benzyl protons in its ^{1}H-n.m.r. spectrum and was discarded. The less-polar component (R_F 0.30) (0.330 g) was shown by ^{1}H-n.m.r. spectroscopy to be a mixture (~ 1:1) of compounds **21** and **9**. Compound **21** was obtained in ~ 16% yield. The ^{1}H-n.m.r. spectrum ($CDCl_3$) showed the presence of a 5-proton multiplet at δ 7.2–7.4 attributable to CH_2Ph.

1-O-{2,3,2',3',4',6'-Hexa-O-acetyl-6-O-(2,3,6,2',3',4',6'-hepta-O-acetyl-β-lactosyl)-β-lactosyl}-(R,S)-glycerols (**22**). — A suspension of 10% (w/w) palladium-on-carbon (1.0 g) in methanol (6.0 mL)* was added to a solution of **19** (0.403 g, 0.275 mmol) in methanol (50 mL) containing 10% formic acid[22]. The reaction mixture was shaken (60 c.p.m.) under H_2 (60 p.s.i.g.) for 2 h at room temperature. The solids were removed by

* It should be noted that the combination of palladium-on-carbon in methanol is particularly pyrophoric.

filtration and washed with methanol (25 mL). The combined filtrate and wash solution was evaporated, and the residual mixture was resolved by column chromatography to give **22** (0.196 g, 55%) as a colorless, glassy solid, R_F 0.38 (solvent *H*); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.970 (s, 6 H, 2 OAc), 1.973 (s, 6 H, 2 OAc), 2.032 (s, 12 H, 4 OAc), 2.048 (s, 3 H, OAc), 2.052 (s, 9 H, 3 OAc), 2.058 (s, 6 H, 2 OAc), 2.070 (s, 6 H, 2 OAc), 2.072 (s, 6 H, 2 OAc), 2.09 (s, 6 H, 2 OAc), 2.16 (s, 18 H, 6 OAc), 2.61 (t, 1 H, ^3J 5.9 Hz, CH_2OH), 2.65 (t, 1 H, ^3J 5.7 Hz, CH_2OH), 3.05 (d, 1 H, ^3J 6.5 Hz, CHO*H*), 3.19 (d, 1 H, ^3J 2.6 Hz, CHO*H*), 3.54 (m, 2 H, J_{gem} 11.7, $J_{3,2}$ 5.1 Hz, H-3,3), 3.54–3.60 (m, 2 H, H-5a,5a), 3.65–3.73 (m, 6 H, H-1,-1,-3,-3,-5c,-5c), 3.70 (t, 2 H, ^3J 9.6 Hz, H-4a,4a), 3.79–4.01 (m, 10 H, H-1,-1,-2,-2,-5b,-5b,-5d,-5d,-6a,-6a), 3.86 (t, 2 H, ^3J 9.4 Hz, H-4c,4c), 3.985 (dd, 1 H, J_{gem} 11.7, $J_{6a,5a}$ 2.2 Hz, H-6a), 3.990 (dd, 1 H, J_{gem} 11.9, $J_{6a,5a}$ 1.9 Hz, H-6a), 4.05–4.17 {m, 10 H, H-6b(4),-6c,-6c,-6d(4)}, 4.469 (d, 1 H, ^3J 7.8 Hz, H-1b or H-1d), 4.473 (d, 1 H, $J_{1a,2a}$ 8.2 Hz, H-1a), 4.477 (d, 1 H, $J_{1a,2a}$ 7.9 Hz, H-1a), 4.480 (d, 1 H, ^3J 7.5 Hz, H-1b or H-1d), 4.485 (d, 1 H, ^3J 8.0 Hz, H-1b or H-1d), 4.494 (d, 1 H, ^3J 8.0 Hz, H-1b or H-1d), 4.514 (dd, 2 H, J_{gem} 12.2, $J_{6c,5c}$ 2.2 Hz, H-6c,-6c), 4.754 (d, 1 H, $J_{1c,2c}$ 7.5 Hz, H-1c), 4.767 (d, 1 H, $J_{1c,2c}$ 7.5 Hz, H-1c), 4.882 (dd, 1 H, $J_{2a,3a}$ 9.5, $J_{2a,1a}$ 7.9 Hz, H-2a), 4.897 (dd, 1 H, $J_{2a,3a}$ 10.0, $J_{2a,1a}$ 8.2 Hz, H-2a), 4.924 (dd, 2 H, $J_{2c,3c}$ 9.3, $J_{2c,1c}$ 7.5 Hz, H-2c,-2c), 4.972 (dd, 1 H, ^3J 10.5, ^3J 3.4 Hz, H-3b or H-3d), 4.983 (dd, 1 H, ^3J 10.5, ^3J 3.4 Hz, H-3b or H-3d), 5.016 (dd, 1 H, ^3J 10.5, ^3J 3.4 Hz, H-3b or H-3d), 5.021 (dd, 1 H, ^3J 10.5, ^3J 3.4 Hz, H-3b or H-3d), 5.08 (dd, 2 H, ^3J 10.5, ^3J 7.5 Hz, 2 of H-2b and/or H-2d), 5.093 (dd, 1 H, ^3J 10.5, ^3J 7.9 Hz, H-2b or H-2d), 5.100 (dd, 1 H, ^3J 10.5, ^3J 7.9 Hz, H-2b or H-2d), 5.17 (t, 2 H, ^3J 9.4 Hz, H-3a,-3a), 5.249 (t, 1 H, ^3J 9.2 Hz, H-3c), 5.282 (t, 1 H, ^3J 9.3 Hz, H-3c), 5.35–5.36 (m, 4 H, H-4b,-4b,-4d,-4d); the protons exhibiting resonances at δ 2.61, 2.65, 3.05, and 3.19 p.p.m. were exchangeable with D_2O.

Anal. Calc. for $C_{53}H_{74}O_{36}\cdot H_2O$: C, 48.77; H, 5.87. Found: C, 48.77; H, 5.71.

3-O-Acetyl-1-O-{2,3,2',3',4',6'-hexa-O-acetyl-6-O-(2,3,6,2',3',4',6'-hepta-O-acetyl-β-lactosyl)-β-lactosyl}-(R,S)-glycerols (**23**). — A suspension of 10% (w/w) palladium-on-carbon (0.6 g) in methanol (6 mL)* was added to a solution of the mixture of **21** and **9** (0.309 g) in methanol (25 mL) containing 10% (v/v) formic acid[22] and stirred for 1 h at room temperature. The solids were removed by filtration and washed with methanol (20 mL). The combined filtrate and wash solution was evaporated, and the residual mixture was resolved by column chromatography to give two components having R_F 0.30 and 0.46 (solvent *G*). The less-polar component (R_F 0.46) was shown by ^{1}H-n.m.r. spectroscopy to be **9** (0.081 g). The more-polar component (R_F 0.30) was **23** (0.093 g) which was obtained as a colorless, glassy solid, $[\alpha]_D^{27}$ −15.5° (*c* 0.90, chloroform); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.968 (s, 3 H, OAc), 1.969 (s, 9 H, 3 OAc), 2.026 (s, 3 H, OAc), 2.029 (s, 3 H, OAc), 2.031 (s, 3 H, OAc), 2.032 (s, 3 H, OAc), 2.046 (s, 3 H, OAc), 2.050 (s, 9 H, 3 OAc), 2.057 (s, 3 H, OAc), 2.059 (s, 3 H, OAc), 2.069 (s, 12 H, 4 OAc), 2.083 (s, 3 H, OAc), 2.090 (s, 3 H, OAc), 2.096 (s, 6 H, 2 OAc), 2.152 (s, 3 H, OAc), 2.154 (s, 3 H, OAc), 2.157 (s, 12 H, 4 OAc), 2.96 (d, 1 H, ^3J 6.2 Hz, OH), 3.17 (d, 1 H, ^3J 3.8 Hz, OH), 3.540 (ddd, 1 H, $J_{5a,4a}$ 9.8, $J_{5a,6a}$ 5.8, $J_{5a,6a}$ 1.6 Hz, H-5a), 3.544 (ddd, 1 H, $J_{5a,4a}$ 9.8,

* It should be noted that the combination of palladium-on-carbon in methanol is particularly pyrophoric.

$J_{5a,6a}$ 5.7, $J_{5a,6a}$ 1.4 Hz, H-5a), 3.66 (ddd, 2 H, $J_{5c,4c}$ 9.8, $J_{5c,6c}$ 4.9, $J_{5c,6c}$ 2.0 Hz, H-5c,-5c), 3.68 (dd, 1 H, J_{gem} 10.7, $J_{1,2}$ 5.2 Hz, H-1), 3.72–3.76 (m, 3 H, H-1,-1,-1), 3.750 (t, 1 H, H-4a), 3.758 (t, 1 H, ^3J 9.5 Hz, H-4a), 3.811 (dd, 1 H, J_{gem} 11.7, $J_{6a,5a}$ 5.7 Hz, H-6a), 3.818 (dd, 1 H, J_{gem} 11.8, $J_{6a,5a}$ 5.7 Hz, H-6a), 3.863 (t, 1 H, H-4c), 3.869 (t, 1 H, H-4c), 3.87–3.91 (m, 2 H, 2 of H-5b and/or H-5d), 3.93–4.04 (m, 6 H, H-2,-2,-6a,-6a, and 2 of H-5b and/or H-5d), 4.05–4.16 {m, 14 H, H-3(4),-6b(4),-6c,-6c,-6d(4)}, 4.464 (d, 1 H, $J_{1a,2a}$ 7.9 Hz, H-1a), 4.476 (d, 1 H, $J_{1a,2a}$ 7.9 Hz, H-1a), 4.504 (br d, 2 H, ^3J 7.9 Hz, 2 of H-1b and/or H-1d), 4.511 (br d, 2 H, ^3J 7.2 Hz, 2 of H-1b and/or H-1d), 4.522 (dd, 1 H, J_{gem} 11.8, $J_{6c,5c}$ 2.0 Hz, H-6c), 4.538 (dd, 1 H, J_{gem} 12.2, $J_{6c,5c}$ 2.0 Hz, H-6c), 4.639 (d, 1 H, $J_{1c,2c}$ 7.6 Hz, H-1c), 4.658 (d, 1 H, $J_{1c,2c}$ 7.7 Hz, H-1c), 4.867 (dd, 1 H, $J_{2a,3a}$ 9.7, $J_{2a,1a}$ 7.9 Hz, H-2a), 4.872 (dd, 1 H, $J_{2a,3a}$ 9.8, $J_{2a,1a}$ 7.9 Hz, H-2a), 4.921 (dd, 1 H, $J_{2c,3c}$ 9.4, $J_{2c,1c}$ 7.4 Hz, H-2c), 4.925 (dd, 1 H, $J_{2c,3c}$ 9.5, $J_{2c,1c}$ 7.3 Hz, H-2c), 4.962 (dd, 1 H, ^3J 10.3, ^3J 3.4 Hz, H-3b or H-3d), 4.968 (dd, 1 H, ^3J 10.4, ^3J 3.4 Hz, H-3b or H-3d), 5.02–5.08 (m, 4 H, 2 of H-2b and/or H-2d, and 2 of H-3b and/or H-3d), 5.10 (dd, 2 H, ^3J 10.4, ^3J 7.8 Hz, 2 of H-2b and/or H-2d), 5.160 (t, 1 H, ^3J 9.4 Hz, H-3a), 5.164 (t, 1 H, ^3J 9.4 Hz, H-3a), 5.204 (t, 1 H, ^3J 9.2 Hz, H-3c), 5.212 (t, 1 H, ^3J 9.2 Hz, H-3c), 5.35–5.36 (m, 4 H, H-4b,-4b,-4d,-4d); the protons exhibiting resonances at δ 2.96 and 3.17 were exchangeable with D_2O.

1-O-(6-O-β-Lactosyl-β-lactosyl)-(R,S)-glycerols (**24**). — To a solution of **22** (0.174 g, 0.135 mmol) in absolute methanol (15 mL) was added 0.1 M sodium methoxide in methanol (2.0 mL). The solution was stirred for 2 h at room temperature, treated with Amberlite IR-120 (H^+) cation-exchange resin (4 mL) for 30 min, and the resin was removed by filtration and washed with methanol (20 mL). The combined filtrate and wash solution was evaporated, and the residue was dried under vacuum to give **24** (0.100 g, 100%) as a glassy solid, R_F 0.39 (solvent *I*); ^{1}H-n.m.r. (400 MHz, Me_2SO-d_6): δ 3.01–4.41 (a series of multiplets corresponding to C*H*O and CH_2O protons, 33 H), 4.47–5.29 (a series of multiplets corresponding to CHO*H* and CH_2OH protons, 15 H); all of the multiplets in the 4.47–5.29 p.p.m. region were extinguishable in the presence of D_2O.

Anal. Calc. for $C_{27}H_{48}O_{23}\cdot 2H_2O$: C, 41.75; H, 6.75. Found: C, 41.49; H, 6.77.

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REFERENCES

1 G. Ashwell and J. Harford, *Annu. Rev. Biochem.*, 51 (1982) 531–554.
2 J. Harford and G. Ashwell, in M. I. Horowitz (Ed.), *The Glycoconjugates*, Vol. 4, Academic Press, New York, 1982, pp. 27–55.
3 A. L. Schwartz, *CRC Crit. Rev. Biochem.*, 16 (1984) 207–233, and references cited therein.
4 C. P. Stowell, R. T. Lee, and Y. C. Lee, *Biochemistry*, 19 (1980) 4904–4908.
5 J. Montreuil, *Adv. Carbohydr. Chem. Biochem.*, 37 (1980) 157–223.
6 R. J. Stockert and A. G. Morell, *Hepatology*, 3 (1983) 750–757.
7 Y. C. Lee, R. R. Townsend, M. R. Hardy, J. Lönngren, J. Arnarp, M. Haraldsson, and H. Lönn, *J. Biol. Chem.*, 258 (1983) 199–202, and references cited therein.

8 R. T. Lee, P. Lin, and Y. C. Lee, *Biochemistry*, 23 (1984) 4255–4261.
9 L. J. J. Hronowski, W. A. Szarek, G. W. Hay, A. Krebs, and W. T. Depew, *Carbohydr. Res.*, 190 (1989) 203–218.
10 L. J. J. Hronowski, W. A. Szarek, G. W. Hay, A. Krebs, and W. T. Depew, *Carbohydr. Res.*, 193 (1989) 91–103.
11 L. J. J. Hronowski, W. A. Szarek, G. W. Hay, A. Krebs, and W. T. Depew, *Carbohydr. Res.*, 219 (1991) 33–49, and references cited therein.
12 L. J. J. Hronowski, W. A. Szarek, G. W. Hay, E. R. Ison, A. Krebs, and W. T. Depew, *Carbohydr. Res.*, 219 (1991) 51–69.
13 R. L. Hudgin, W. E. Pricer, Jr., and G. Ashwell, *J. Biol. Chem.*, 249 (1974) 5536–5543.
14 D. T. Connolly, R. R. Townsend, K. Kawaguchi, W. R. Bell, and Y. C. Lee, *J. Biol. Chem.*, 257 (1982) 939–945.
15 S. Tejima, *Carbohydr. Res.*, 20 (1971) 123–132.
16 M. Mori, M. Haga, and S. Tejima, *Chem. Pharm. Bull.*, 22 (1974) 1331–1338.
17 B. Helferich and K. Weis, *Chem. Ber.*, 89 (1956) 314–321.
18 A. Bax, R. Freeman, and G. Morris, *J. Magn. Reson.*, 42 (1981) 164–168; R. Benn and H. Günther, *Angew. Chem. Int. Ed. Engl.*, 22 (1983) 350–380; S. L. Patt, *J. Carbohydr. Chem.*, 3 (1984) 493–511.
19 A. Bax, W. Egan, and P. Kováč, *J. Carbohydr. Chem.*, 3 (1984) 593–611.
20 R. U. Lemieux and A. R. Morgan, *Can. J. Chem.*, 43 (1965) 2199–2204.
21 T. Ogawa, K. Beppu, and S. Nakabayashi, *Carbohydr. Res.*, 93 (1981) c6–c9.
22 V. S. Rao and A. S. Perlin, *Carbohydr. Res.*, 83 (1980) 175–177.
23 A. Thompson and M. L. Wolfrom, *Methods Carbohydr. Chem.*, 2 (1963) 215–220, and references cited therein.
24 C. S. Hudson and J. M. Johnson, *J. Am. Chem. Soc.*, 37 (1915) 1270–1275.
25 B. Helferich and R. Griebel, *Ann.*, 544 (1940) 191–205.
26 E. M. Montgomery, N. K. Richtmyer, and C. S. Hudson, *J. Am. Chem. Soc.*, 65 (1943) 1848–1854.