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SYNTHESIS AND CHARACTERIZATION OF 1-*O*-β-LACTOSYL-(*R,S*)-GLYCEROLS AND 1,3-DI-*O*-β-LACTOSYLGLYCEROL*

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ABSTRACT

The synthesis of 1-*O*-β-lactosyl-(*R,S*)-glycerols was achieved by three methods: (*a*) in 25% yield by the trimethylsilyl trifluoromethanesulfonate-promoted reaction of octa-*O*-acetyl-β-lactose (**11**) with ~0.5 mol-equiv. of 2-*O*-benzylglycerol (**4**), (*b*) in ~34% yield by the coupling of **4** with an equimolar amount of hepta-*O*-acetyl-α-lactosyl bromide (**12**) in the presence of mercury(II) cyanide, and (*c*) in ~50% yield by the coupling of equimolar amounts of **12** and 1,2-di-*O*-benzyl-(*R,S*)-glycerols in the presence of mercury(II) cyanide, followed in each case by the removal of the blocking groups. 1,3-Di-*O*-β-lactosylglycerols were prepared in 21% yield by the coupling of **11** with ~0.5 mol-equivalent of **4** by method (*a*), and in 38% yield by the coupling of **12** with ~0.5 mol-equiv. of **4** by method (*b*), followed by the removal of the blocking groups. The configuration of the glycosidic linkage between the lactose units and the glycerol residue was established by high-resolution, two-dimensional ^{1}H-n.m.r. spectroscopy.

INTRODUCTION

During the past two decades, carbohydrate chemistry has been marked by major advances in the regulation, and in the understanding of the mechanisms, of the formation of glycosides[1–3]. This has led to the development of greatly improved methods for the synthesis of glycosides and complex oligosaccharides under conditions that afford a high degree of control of the configuration of the glycosidic bond[1–6]. This progress has coincided with the collateral increase in the appreciation of the functional significance of the glycan moieties of glycoproteins[7–9] as antigenic determinants[10,11], and in the mechanisms of cell adhesion[7,9,12] and receptor-site interactions[7,9,11,13].

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[*] Synthesis and Binding of D-Galatose-terminated Ligands to Human and Rabbit Asialoglycoprotein Receptor. Part I.

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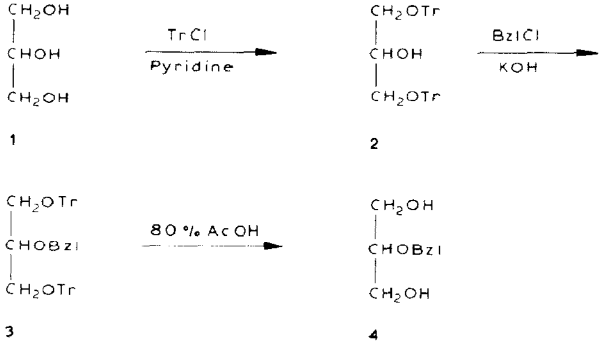
The cell surface of normal mammalian liver possesses a number of carbohydrate-specific receptors[14], of which the hepatic asialoglycoprotein receptor[14–17] has been among the most extensively studied. The hepatic-binding protein[16] contains receptor sites which exhibit a preference for terminal, nonreducing β-D-galactopyranosyl or 2-acetamido-2-deoxy-α-D-galactopyranosyl groups[17,18], and there is evidence[8,15,17–20] that the number and propinquity of the galactose termini affect the avidity with which molecules bind to the surface lectin.

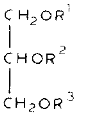
In this laboratory, we have undertaken a further study of the binding to the asialoglycoprotein receptor from the plasma membranes of normal rabbit and human hepatocytes of a series of synthetic, D-galactose-terminated oligosaccharides. We report herein the preparation and characterization of 1-*O*-β-lactosyl-(*R*,*S*)-glycerols (**20**) and 1,3-di-*O*-β-lactosylglycerol (**17**).

RESULTS AND DISCUSSION

The synthesis of **17** and **20** utilized appropriately blocked glycerol derivatives; prior, exploratory attempts to prepare glycerol-lactosides from peracetylated lactose and unprotected glycerol gave intractable mixtures of products.

2-*O*-Benzylglycerol[21] (**4**) was obtained by the reaction of glycerol (**1**) with 2.5 mol-equiv. of chlorotriphenylmethane in pyridine to produce 1,3-di-*O*-tritylglycerol[22] (**2**), which was then converted into the 2-*O*-benzyl derivative **3** by reaction with benzyl chloride and potassium hydroxide; acid-catalyzed hydrolysis of the trityl ethers afforded **4** in a yield of 50% from **1**. 1,2-Di-*O*-benzyl (*R*,*S*)-glycerols (**7**) were prepared in 38% yield (from **1**) by the same sequence of reactions, but utilizing only 0.5 mol-equiv. of chlorotriphenylmethane in the first step. Compounds **4**–**7** have been synthesized previously by several methods[21–32].

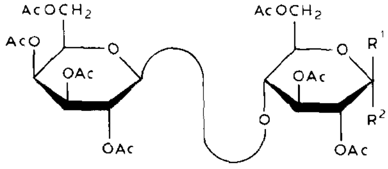




5 $R^1 = Tr,\ R^2 = R^3 = H$
6 $R^1 = Tr,\ R^2 = R^3 = Bzl$
7 $R^1 = H,\ R^2 = R^3 = Bzl$
8 $R^1 = R^3 = Tr,\ R^2 = Ac$
9 $R^1 = R^3 = H,\ R^2 = Ac$
10 $R^1 = Ac,\ R^2 = R^3 = H$

The utility of the acetyl group for the protection of the C-2 position of glycerol was investigated. The treatment of **2** with acetic anhydride in pyridine yielded 2-*O*-acetyl-1,3-di-*O*-tritylglycerol (**8**), from which the trityl groups were removed by hydrolysis using 80% acetic acid. Although the product migrated as a single component in t.l.c., the ^{1}H-n.m.r. spectrum indicated that it was composed of a mixture of the 2-*O*-acetyl (**9**) and 1-*O*-acetyl (**10**) derivatives of glycerol in the ratio 7:43 in a combined yield of 60%. Clearly, the acetyl group is much less useful as a blocking group than is the benzyl group, in this instance.

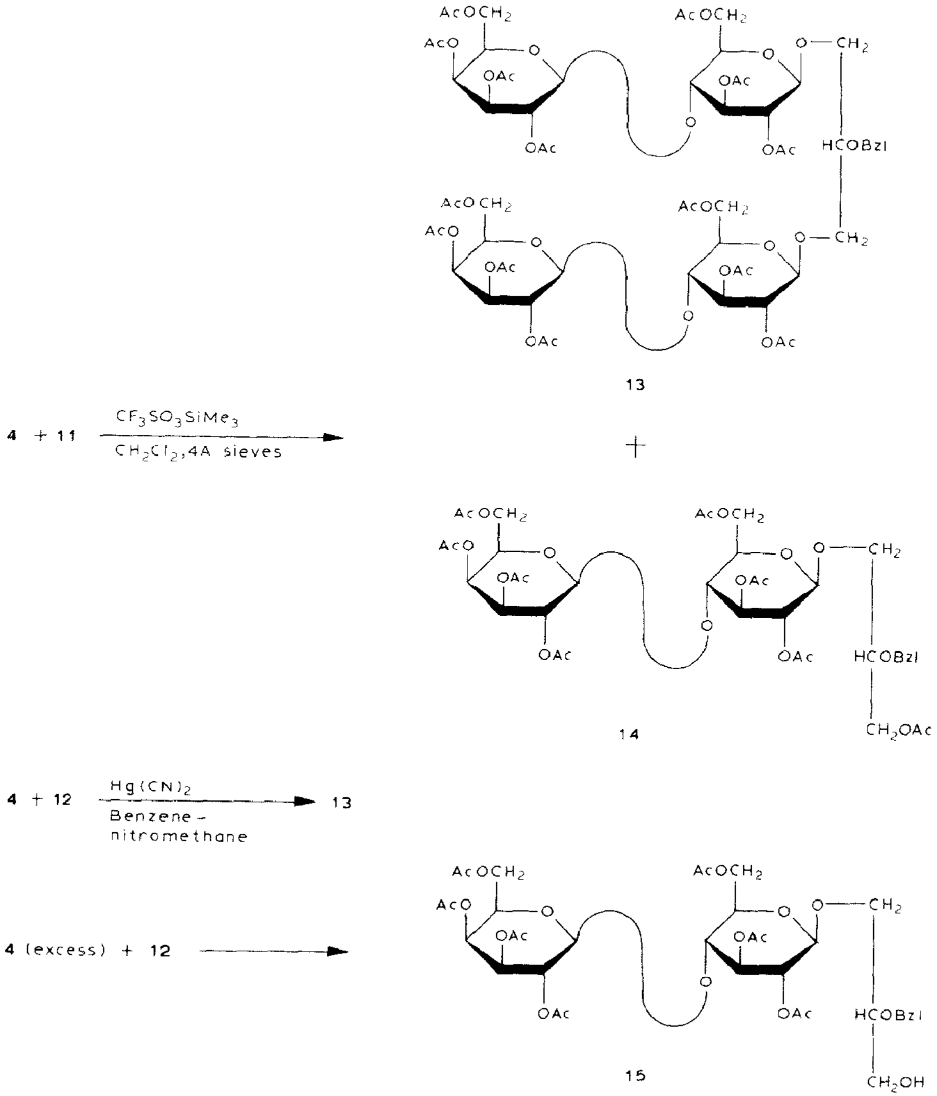
Two lactose derivatives, namely, 1,2,3,6,2′,3′,4′,6′-octa-*O*-acetyl-β-lactopyranose (**11**) and 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-α-lactopyranosyl bromide (**12**), were employed for the synthesis of glycosides of glycerol. Compound **11** was prepared from α-lactose by reaction with acetic anhydride and sodium acetate as described by Hudson and Johnson[33]. They have also described the preparation of **12**; however, in this study the application of their procedure[33] did not yield a crystalline bromide and the starting material, **11**, was recovered in crystalline form in greater than 67% yield. The procedure employed by Takeo *et al.*[34] for the preparation of 2,3,4,2′,3′,6′,2″,3″,3″,4″-deca-*O*-acetyl-α-cellotriosyl bromide was adapted to afford crystalline **12** in 82% yield (from **11**). This method involved the addition of hydrogen bromide in acetic acid to a solution of **11** in dichloromethane at room temperature.



11 R^1 = OAc, R^2 = H
12 R^1 = H, R^2 = Br

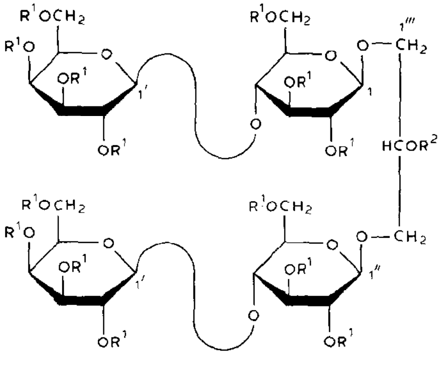
The synthesis of 2-*O*-benzyl-1,3-bis-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)glycerol (**13**) was performed by treatment of **11** with 0.5 mol-equiv. of **4** in dichloromethane, in the presence of molecular sieves (4A), with a catalytic amount of trimethylsilyl trifluoromethanesulfonate. Ogawa *et al.*[35] reported that this compound is an effective catalyst for the formation of 1,2-*trans*-glycosides; however, under the reaction conditions employed in the present work, this procedure gave a mixture of **13** (29% yield) and 3-*O*-acetyl-2-*O*-benzyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R*,*S*)-glycerols (**14**) (40% yield).

Compound **13** also has been prepared in 52% yield by the reaction of **12** with 0.5 mol-equiv. of **4** in the presence of mercury(II) cyanide[5,36] in benzene–nitromethane for 1 h at room temperature and 2.5 h at 40°. When equimolar amounts of **12** and **4** reacted under these conditions, the major isolated product (~40% yield) was 2-*O*-benzyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R*,*S*)-glycerols



(**15**). In addition, the Helferich method[36] was employed to obtain a 66% yield of 2,3-di-*O*-benzyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R*,*S*)-glycerols (**21**) by the coupling of **12** with 1,2-di-*O*-benzyl-(*R*,*S*)-glycerols (**7**).

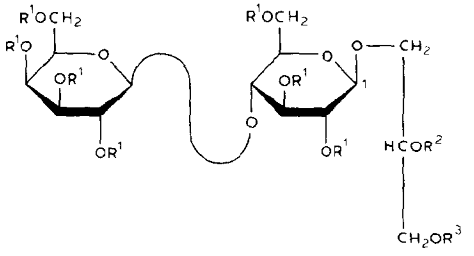
Catalytic, transfer hydrogenation[37] with 10% palladium-on-carbon in methanol containing 10% formic acid brought about complete removal of *O*-benzyl groups, thereby giving 1,3-bis-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-glycerol (**16**) from **13**, 3-*O*-acetyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R*,*S*)-glycerols (**19**) from **14**, and 1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R*,*S*)-glycerols (**22**) from each of **15** and **21**. Each product was *O*-deacetylated by the use of sodium methoxide in methanol to produce, 1,3-di-*O*-β-lactosylglycerol



16 $R^1 = Ac, R^2 = H$

17 $R^1 = R^2 = H$

18 $R^1 = R^2 = Ac$



19 $R^1 = R^3 = Ac, R^2 = H$

20 $R^1 = R^2 = R^3 = H$

21 $R^1 = Ac, R^2 = R^3 = Bzl$

22 $R^1 = Ac, R^2 = R^3 = H$

23 $R^1 = R^2 = R^3 = Ac$

(**17**) from **16**, and 1-*O*-β-lactosyl-(*R*,*S*)-glycerols (**20**) from **19** and **22**.

The ability of high resolution ¹H-n.m.r. spectroscopy to provide information about the structural details of even complex carbohydrate[38] is now established beyond question. Nevertheless, for most of the correspondent protons in the pairs of diastereomers of **14**, **15**, and **21**, and especially in the case of those of the galactosyl residues, the chemical shifts and coupling constants were very similar, and sharp signals were obtained in the ¹H-n.m.r. spectra. Furthermore, the ¹H-n.m.r. spectrum of **19** was unsuitable for the determination of the ratio of diastereomers because the carbon-bonded, glyceryl protons afforded complex, overlapping multiplets, and the chemical shifts of the correspondent glycosyl protons were virtually congruent. However, the ¹H-n.m.r. spectra of peracetylated derivatives of the lactosylglycerols proved to be particularly amenable to detailed analysis, and therefore **17** was converted into 2-*O*-acetyl-1,3-bis-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)glycerol (**18**) by treatment with acetic anhydride in pyridine[39]; this procedure was used also to obtain 2,3-di-*O*-acetyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R*,*S*)-glycerols (**23**) from **19** and **22**. In each of **22** and **23**, sufficient differences occurred in the chemical shifts of the D-glucosyl protons to allow the detection and estimation of the two diastereomers. The assignment of the signals in the ¹H-n.m.r. spectra was achieved by the use of two-dimensional, Fourier-transform, proton chemical-shift correlation spectroscopy (Cosy)[40,41] experiments.

The coupling constants of the anomeric protons of the D-glucosyl residues of **19**, **22**, and **23** ranged from 7.9 to 8.2 Hz, and indicated that the glycosidic linkage between the lactose units and glycerol had the β-D configuration[38,41–43]. The Cosy spectrum of **23** (Fig. 1) permitted the proton–proton connectivities to be determined readily. The assignment of the groups of chemical shifts to the diastereotopic D-glucosyl and D-galactosyl protons was based on a comparison of the ¹H-n.m.r. spectrum of **23** with that of 1,2,3,6,2′,3′,4′,6′-octa-*O*-acetyl-β-lactose (**11**). As ex-

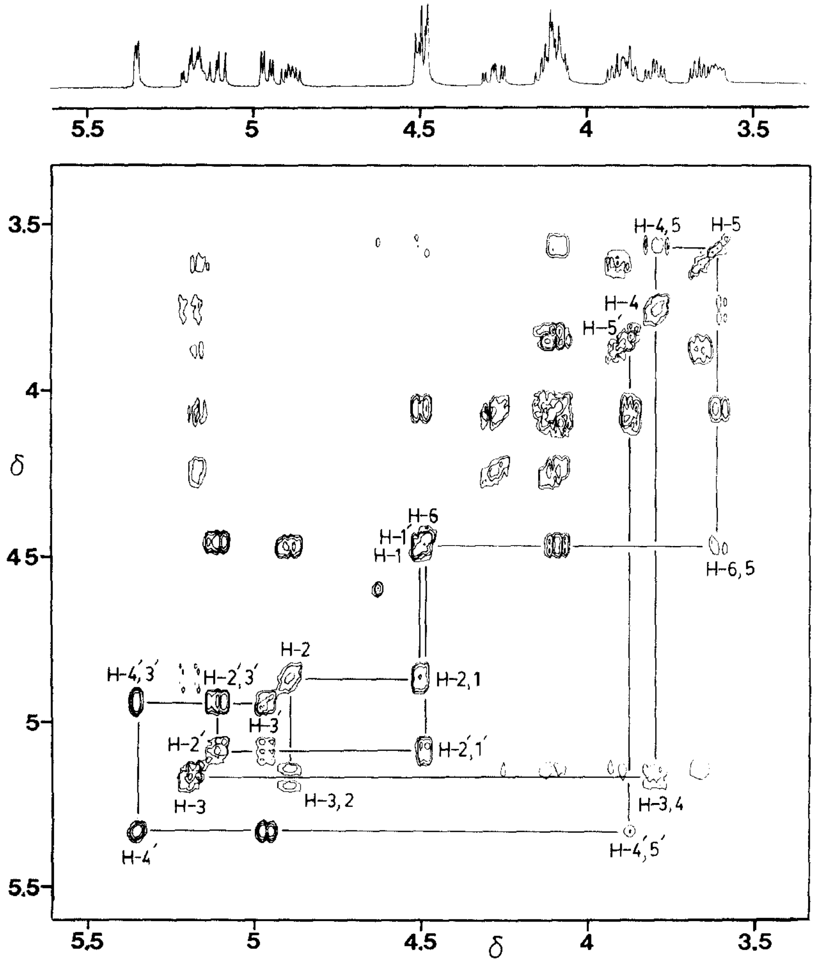


Fig. 1. 400-MHz ^{1}H-Cosy spectrum of **23** in $CDCl_3$.

pected, the similar environments of the D-galactosyl units of **11** and **23** resulted in very small differences (≦0.01 p.p.m.) in the chemical shifts of the analogous protons. In contrast, the protons of the D-glucosyl residues of **11** and **23** experience very different environments, and consequently exhibited significant differences in their chemical shifts. Thus, the anomeric proton of the D-glucosyl unit of **11** resonated at δ 5.68, whereas that of **23** resonated at δ 4.51. Similarly, the different environments of the H-4 and H-4' of **23** resulted in large differences in their chemical shifts (δ 3.794 and 3.804, H-4; δ 5.35, H-4') which assisted in the assignment of the groups of signals to particular sugar residues.

The ^{1}H-n.m.r. spectra of the dilactosylglycerol derivatives **16** and **18** revealed that the anomeric protons of the D-glucosyl units resonated in the range δ 4.45–4.85 and had coupling constants in the range 7.9–8.1 Hz. These data indicated that all

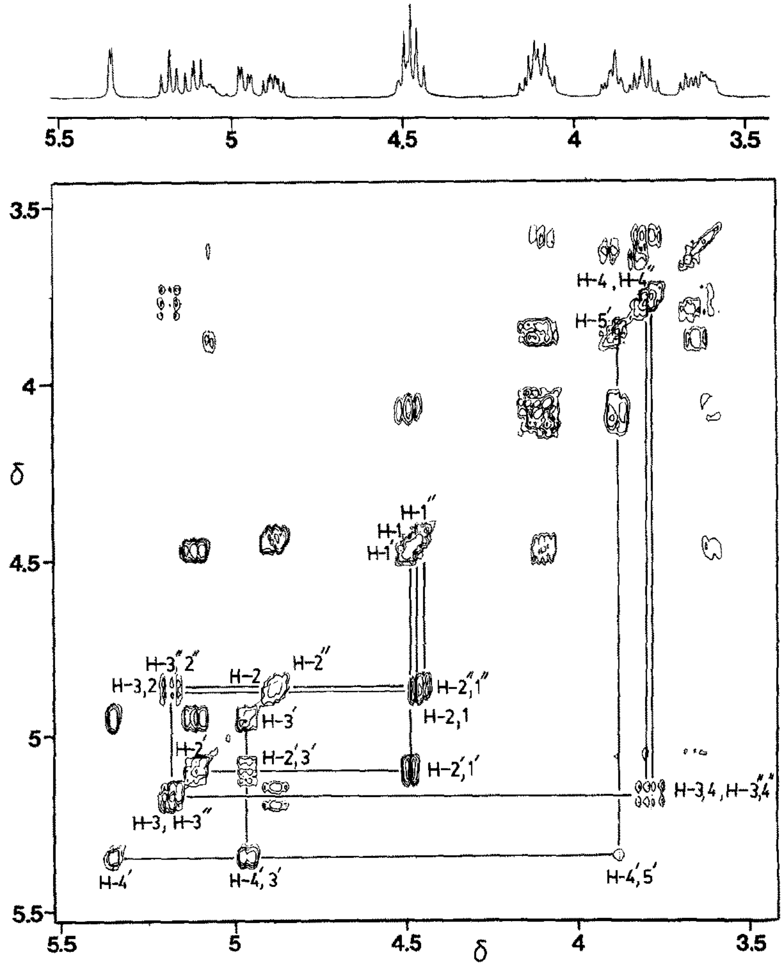


Fig. 2. 400-MHz ^{1}H-Cosy spectrum of **18** in $CDCl_3$.

of the lactosyl groups were joined to glycerol by β-D-glycosidic linkages; consequently, only one configuration is possible for each of compounds **13**, **16**, **17**, and **18**. However, the substituents at C-1 and C-3 of the glycerol residue are diastereotopic, and the correspondent protons ought to exhibit unique chemical shifts. With a 400-MHz n.m.r. spectrometer, the chemical shifts of the protons of the diastereotopic D-galactosyl units of **16** and **18** were unresolvable, but those of the D-glucosyl residues were measurably different. In addition, four distinct chemical shifts were observed for the diastereotopic CH_2-O-β-lactosyl protons in each of **16** and **18**. The integration of the signals for the acetyl protons of **13**, **16**, and **18** showed them to represent multiples of three protons in the range 3 to 18 for a total of 14 acetoxy groups in each of **13** and **16**, and 15 acetoxy groups in **18**.

The Cosy spectrum of **18** (Fig. 2) established that the chemical shifts and coupling constants of the glycosyl protons were very similar to those observed for **23**. The major differences in the spectra of **18** and **23** related to the chemical shifts of the glyceryl protons: in general, these protons resonated at higher field in **18** than in **23**, as expected from the greater number of ester groups in **23**.

These studies have established unambiguously that the synthetic routes employed have led to the preparation of the purely β-D-linked compounds **17** and **20**, unmixed with the α-D-glycosidically-linked isomers.

EXPERIMENTAL

General methods. — Melting points were determined with 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 1.0- or 0.1-dm cell at 23 ±3°. ^{1}H-N.m.r. spectra were recorded with a Bruker CXP-200 (200 MHz) or AM-400 (400 MHz) spectrometer. Tetramethylsilane (Me_4Si) was used as the internal standard, and chemical shifts (δ) are given downfield from the signal of Me_4Si. Thin-layer chromatography (t.l.c.) was performed on glass plates precoated with Merck Silica Gel 60 F-254 as the adsorbent (layer thickness: 0.25 mm). The following solvent systems (v/v) were used: (*A*) 6:1, (*B*) 5:1, and (*C*) 1:1 hexanes–ethyl acetate; (*D*) 3:2, (*E*) 1:1, (*F*) 2:3, (*G*) 1:2, and (*H*) 2:5 toluene–ethyl acetate; (*I*) 9:9:1, (*J*) 8:8:1, (*K*) 6:6:1, (*L*) 4:4:1, (*M*) 3:3:1, and (*N*) 2:2:1 toluene–ethyl acetate–2-propanol; and (*O*) 4:1 ethanol–water. The developed plates were air-dried and sprayed with a solution of 1% $Ce(SO_4)_2$ and 1.5% H_2MoO_4 in 10% aqueous H_2SO_4, and heated at 150°. Column chromatography was performed on Merck 7734 Silica Gel 60 (70–230 mesh). Solvents were evaporated under reduced pressure at <40°.

1,3-Di-O-tritylglycerol (**2**). — A mixture containing glycerol (**1**) (10.0 g, 108 mmol) and chlorotriphenylmethane (75.7 g, 272 mmol) in pyridine (225 mL) was heated[22,44] at 100° for 1 h. The mixture was cooled to room temperature, poured into ice–water (650 mL), and stirred until a semisolid mass was obtained. The supernatant solution was decanted, and the residue was washed with water (3 × 600 mL) and triturated with warm ethanol (500 mL). The resulting crystalline solid was collected by filtration, washed with ethanol (150 mL), and dried under vacuum to yield an impure sample of **2** (60.5 g, 97%) which was shown by t.l.c. (solvent *B*) to consist of a major component (R_F 0.40) and traces of minor components. This material was used in subsequent reactions without purification.

An analytical sample was prepared by purification of the reaction product on a silica gel column, followed by crystallization from ethanol to give crystalline **2**, m.p. 175–180°, lit.[22] m.p. 170–171°, lit.[23] 181–182°; ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 3.24 (dd, 2 H, J_{gem} 9.3, ^3J 5.4 Hz, H-1,3 or H-1′,3′), 3.32 (dd, 2 H, J_{gem} 9.3, ^3J 5.4 Hz, H-1′,3′ or H-1,3), 3.95 (dd, 1 H, ^3J 5.4 Hz, H-2), and 7.19–7.46 (m, 30 H, 6 C_6H_5).

Anal. Calc. for $C_{41}H_{36}O_3$: C, 85.39; H, 6.29. Found: C, 85.28; H, 6.41.

2-O-Benzyl-1,3-di-O-tritylglycerol (**3**) *and 2-O-benzyl-(*R,S*)glycerols* (**4**). —

A mixture containing **2** (25.4 g, ~44 mmol), benzyl chloride (32.8 g, 259 mmol), and KOH (25.4 g, 450 mmol)[45] in toluene (200 mL) was heated at reflux temperature for 35 min, cooled to ~50°, diluted with water (200 mL), and the liquid portion extracted with toluene (50 mL). The organic phase was washed with water (40 mL), evaporated, and the oily residue (~70 mL) diluted with ethanol (300 mL) and water (30 mL). The mixture was kept at room temperature until a red oil separated (1–2 h). The supernatant solution was decanted and the oil was triturated with warm ethanol (300 mL) to give solid **3**, R_F 0.55 (solvent *A*); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 3.23 –3.37 (m, 4 H, H-1,1′,3,3′), 3.75 (qu, 1 H, ^3J 5.4 Hz, H-2), 4.61 (s, 2 H, $CH_2C_6H_5$), and 7.16–7.47 (m, 35 H, 7 C_6H_5).

The sample of **3** was suspended in 80% acetic acid (100 mL), heated at 100° for 30 min, and cooled to room temperature. The triphenylmethanol which precipitated was removed by filtration and washed with 80% acetic acid (25 mL). The combined filtrate and wash solution was evaporated to an oil which, after column chromatography, afforded **4** as a white, crystalline solid (4.1 g, 51% from **2**), m.p. 35–36°, lit.[21] m.p. 37–39°, lit.[46] 38.5–40°; R_F 0.31 (solvent *K*); ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 3.59 (m, 1 H, ^3J 4.5 Hz, H-2), 3.71 (dd, 2 H, J_{gem} 11.8, ^3J 4.5 Hz, H-1,3 or H-1′,3′), 3.80 (dd, 2 H, J_{gem} 11.8, ^3J 4.5 Hz, H-1′,3′ or H-1,3), 4.66 (s, 2 H, $CH_2C_6H_5$), and 7.29–7.43 (m, 5 H, C_6H_5).

Anal. Calc. for **3**, $C_{48}H_{42}O_3$: C, 86.45; H, 6.35. Found: C, 85.66; H, 6.18. Calc. for **4**, $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 66.10; H, 7.75.

*1,2-Di-O-benzyl-(*R,S*)-glycerols* (**7**). — A solution containing glycerol (**1**) (17.7 g, 192 mmol) and chlorotriphenylmethane (26.3 g, 94.3 mmol) in pyridine (100 mL) was heated at 100° for 45 min, cooled to room temperature, poured into ice–water (400 mL), and stirred until a semisolid mass formed. The supernatant solution was decanted, and the residue was stirred with water (300 mL) and dried under vacuum to give a mixture which was shown by t.l.c. to consist of two components [R_F 0.52 (major) and 0.92 (minor) (solvent *I*)]. This product was used in the next step without purification. A small sample of the mixture was resolved by column chromatography and the component having R_F 0.52 crystallized from ethanol–water to give 1-*O*-trityl-(*R*,*S*)-glycerols (**5**) as fine, white needles, m.p. 108–109°, [lit.[22] m.p. 92–94° (*R*,*S* forms), lit.[24] 93–97° (*S* form), lit.[28] 94° (*S* form), lit.[27] 97–99° (*R* form), lit.[30] 98° (*S* form), lit.[29] 98–99° (*R* form), lit.[23] 109–110° (*R*,*S* forms), lit.[26] 110–112° (*R*,*S* forms)]; ^{1}H-n.m.r. [200 MHz, $(CD_3)_2SO$]: δ 2.92 (br d, 2 H, ^3J 5.6 Hz, H-3,3′), 3.3–3.5 (m, 2 H, H-1,1′), 3.67 (m, 1 H, ^3J 5.5 Hz, H-2), 4.48 (t, 1 H, ^3J 5.5 Hz, CH_2OH), 4.81 (d, 1 H, ^3J 5.4 Hz, CHO*H*), and 7.2–7.5 (m, 15 H, 3 C_6H_5).

Anal. Calc. for $C_{22}H_{22}O_3$: C, 79.02; H, 6.63. Found: C, 78.69; H, 6.86.

A mixture of **5** (31.2 g, 93.4 mmol theoretical), benzyl chloride (70 g, 553 mmol), and KOH (49.4 g, 880 mmol) in toluene (150 mL) was heated at reflux temperature for 30 min, cooled to room temperature, the supernatant solution decanted, and the solid residue dissolved in water (200 mL). The solutions were combined, and the organic phase was washed with water (50 mL) and evaporated to give a viscous oil which was dissolved in ethanol (300 mL). Water (50 mL) was added and the mixture was kept at room temperature for several hours while an oil separated. The oil was dissolved in ethanol (300 mL), water (70 mL) was added, and the mixture was stored at 2° for several days while an oil again separated. The oil was dried under vacuum to give 1,2-di-*O*-benzyl-3-*O*-trityl-(*R*,*S*)-glycerols (**6**) (28.5 g), R_F 0.46 (solvent *A*); **6** contained a trace of a second component of higher R_F value, but was used in the next step without further purification.

Anal. Calc. for $C_{36}H_{34}O_3$: C, 84.02; H, 6.66. Found: C, 84.21; H, 6.75.

A mixture of **6** (27.6 g, 54 mmol theoretical) in 80% acetic acid (125 mL) was heated at 110° for 30 min. The solid precipitate was removed by filtration and washed with 80% acetic acid (25 mL). The combined filtrate and wash solution was evaporated and the residual mixture resolved by column chromatography to give **7** (9.47 g, 38% from **1**), R_F 0.51 (solvent *D*).

Anal. Calc. for $C_{17}H_{20}O_3$: C, 74.98; H, 7.40. Found: C, 74.25; H, 7.57.

2-O-Acetyl-1,3-di-O-tritylglycerol (**8**). — A solution containing **2** (28.0 g, 48.5 mmol theoretical) and acetic anhydride (40 mL, 423 mmol) in pyridine[39] (210 mL) was stirred at room temperature for 10.5 h, poured into ice–water (1 L), and the resultant solid washed successively with water (300 mL) and ethanol (150 mL) to give **8** (26.6 g, 89%), R_F 0.37 (solvent *A*), which contained traces of other components; ^{1}H-n.m.r. (200 MHz, $CDCl_3$): δ 2.07 (s, 3 H, OAc), 3.25–3.39 (m, 4 H, H-1,1',3,3'), 5.24 (qu, 1 H, ^3J 5.2 Hz, H-2), and 7.1–7.5 (m, 30 H, 6 C_6H_5). This product was used without further purification.

2-O-Acetylglycerol (**9**) *and 1-O-acetyl-(*R,S*)-glycerols* (**10**). — A mixture of **8** (25.5 g, 41.2 mmol theoretical) in 80% acetic acid (150 mL) was heated at 110° for 1 h, and cooled to room temperature. The precipitated triphenylmethanol was removed by filtration and washed with 80% acetic acid (25 mL). The combined filtrate and wash solution was evaporated and the residual mixture purified by column chromatography to afford a colorless oil (3.28 g, 59%) which migrated as a single component in t.l.c. [R_F 0.41 (solvent *N*)] but which was found by ^{1}H-n.m.r. to be a mixture of **9** and **10** in a 7:43 ratio, respectively.

Compound **9**. ^{1}H-N.m.r. (200 MHz, $CDCl_3$): δ 2.13 (s, 3 H, OAc), 3.82 (d, 4 H, ^3J 5.0 Hz, H-1,1',3,3'), and 4.93 (qu, 1 H, ^3J 5.0 Hz, H-2).

Compound **10**. ^{1}H-N.m.r. (200 MHz, $CDCl_3$): δ 2.11 (s, 3 H, OAc), 3.60 (dd, 1 H, J_{gem} 11.7, ^3J 6.0 Hz, H-1), 3.72 (dd, 1 H, J_{gem} 11.7, ^3J 3.7 Hz, H-1'), 3.95 (m, 1 H, H-2), and 4.17 (m, 2 H, H-3,3').

1,2,3,6,2',3',4',6'-Octa-O-acetyl-β-lactose (**11**). — α-Lactose (Sigma) was heated with acetic anhydride and sodium acetate, in the manner described by Hudson and Johnson[33], to give crystalline **11**, m.p. 140–143°, $[\alpha]_D^{27}$ −4.0° (*c* 3.60, chloroform); m.p. lit.[47] 88–90°, lit.[33] 90°, lit.[48] 85–135°, lit.[49] 140–141°; lit.[33,47–49] $[\alpha]_D$ −4° (chloroform); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 3 H, OAc), 2.04 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 2.06 (s, 3 H, OAc), 2.08 (s, 3 H, OAc), 2.11 (s, 3 H, OAc), 2.13 (s, 3 H, OAc), 2.16 (s, 3 H, OAc), 3.76 (ddd, 1 H, ^3J 9.9, ^3J 4.8, $J_{5,6}$ 1.3 Hz, H-5), 3.85 (m, 1 H, H-4), 3.87 (m, 1 H, H-5'), 4.05 (m, 3 H, H-6,

H_2-6′), 4.46 (dd, 1 H, J_{gem} 12.4, $J_{6,5}$ 1.3 Hz, H-6), 4.47 (d, 1 H, $J_{1',2'}$ 7.9 Hz, H-1′), 4.95 (dd, 1 H, $J_{3',2'}$ 10.5, $J_{3',4'}$ 3.3 Hz, H-3′), 5.05 (dd, 1 H, $J_{2,1}$ 8.3, $J_{2,3}$ 9.3 Hz, H-2), 5.12 (dd, 1 H, $J_{2',1'}$ 7.9, $J_{2',3'}$ 10.5 Hz, H-2′), 5.25 (dd, 1 H, $J_{3,2}$ 9.3, $J_{3,4}$ 8.5 Hz, H-3), 5.36 (dd, 1 H, $J_{4',3'}$ 3.3, $J_{4',5'}$ 0.8 Hz, H-4′), and 5.68 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1).

2,3,6,2′,3′,4′,6′-Hepta-O-acetyl-α-lactosyl bromide (**12**). — A solution of **11** (25.0 g, 36.8 mmol) in anhydrous dichloromethane (47 mL) was treated with 30–32% HBr in acetic acid (50 mL) at room temperature for 1 h. The solution was cooled in an ice-bath, diluted with dichloromethane (100 mL), washed sequentially with ice-cold water (50 mL), an ice-cold, saturated solution of $NaHCO_3$ (2 × 50 mL), and ice-cold water (50 mL), dried (Na_2SO_4), and evaporated to give a colorless oil (~40 g) which was dissolved in dry ethyl acetate (50 mL). Dry hexanes (35 mL) were added, and after ~10 min a white, crystalline solid was collected and washed with solvent *C* to give **12** (21.12 g, 82%), m.p. 138–141°, $[\alpha]_D^{25}$ +107° (*c* 4, chloroform); lit.[48,50] m.p. 141°, $[\alpha]_D$ +105° (chloroform).

2-O-Benzyl-1,3-bis-O-(2,3,6,2′,3′,4′,6′-hepta-O-acetyl-β-lactosyl)glycerol (**13**) *and 3-O-acetyl-2-O-benzyl-1-O-(2,3,6,2′,3′,4′,6′-hepta-O-acetyl-β-lactosyl)-(R,S)-glycerols* (**14**). — A mixture of **11** (8.22 g, 12.1 mmol) and 4A molecular sieves (24 g) in dry dichloromethane (60 mL) was kept at room temperature overnight, treated with a solution of **4** (1.13 g, 6.20 mmol) in dichloromethane (20 mL) and trimethylsilyl trifluoromethanesulfonate (2.3 mL, 11.9 mmol), stirred at 23° for 2 h, and the solids were removed by filtration and washed with dry dichloromethane (50 mL). The combined filtrate and wash solution was washed sequentially with a saturated solution of $NaHCO_3$ (2 × 50 mL) and water (50 mL), dried (Na_2SO_4), evaporated, and the residual mixture resolved by column chromatography into two components having R_F 0.37 and 0.56 (solvent *F*), corresponding to **13** and **14**, respectively. Evaporation of the solvent afforded **13** (2.54 g, 29%) as a colorless glass, and **14** (2.10 g, 40%) as a colorless, solid foam.

Compound **13**. ^{1}H-N.m.r. (200 MHz, $CDCl_3$): δ 1.95 (s, 3 H, OAc), 1.97 (s, 6 H, 2 OAc), 2.00 (s, 3 H, OAc), 2.05–2.06 (m, 18 H, 6 OAc), 2.12 (s, 3 H, OAc), 2.12 (s, 3 H, OAc), 2.16 (s, 6 H, 2 OAc), 3.5–5.4 (33 H, a series of multiplets associated with C*H*O and C*H*$_2$O protons), 4.53–4.66 (m, 2 H, OC*H*$_2C_6H_5$), and 7.27–7.41 (m, 5 H, C_6H_5).

Anal. Calc. for $C_{62}H_{82}O_{37}$: C, 52.47; H, 5.82. Found: C, 51.87; H, 5.66.

Compound **14**. ^{1}H-N.m.r. (200 MHz, $CDCl_3$): δ 1.97 (s, 6 H, 2 OAc), 1.98 (s, 3 H, OAc), 2.02 (s, 3 H, OAc), 2.05–2.06 (m, 24 H, 8 OAc), 2.12 (s, 6 H, 2 OAc), 2.16 (s, 6 H, 2 OAc), 3.5–5.4 (38 H, a series of multiplets associated with C*H*O and C*H*$_2$O protons), 4.57–4.69 (m, 4 H, 2 $OCH_2C_6H_5$), and 7.27–7.41 (m, 10 H, 2 C_6H_5).

Preparation of **13** *from* **12** *using mercury(II) cyanide as catalyst.* — A mixture containing **12** (3.00 g, 4.29 mmol), **4** (0.392 g, 2.15 mmol), and $Hg(CN)_2$ (1.63 g, 6.45 mmol) in 1:1 (v/v) benzene–nitromethane (20 mL) was stirred at 20° for 1 h, and then at 40° for 2.5 h. The mixture was diluted with toluene (50 mL), washed sequentially with a saturated solution of $NaHCO_3$ (2 × 25 mL) and water (25 mL), dried ($MgSO_4$), evaporated, and the residual mixture resolved by column chromatography (solvent *C*) to give **13** (1.59 g, 52%) as the only major component.

*2-*O*-Benzyl-1-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)-(*R,S*)-glycerols* (**15**). — A mixture containing **12** (0.71 g, 1.02 mmol), **4** (0.187 g, 1.03 mmol), and $Hg(CN)_2$ (0.71 g, 2.81 mmol) in 1:1 (v/v) benzene–nitromethane (10 mL) was stirred at 20° for 1 h, and then at 40° for 3 h. The mixture was diluted with toluene (40 mL); washed sequentially with a saturated solution of $NaHCO_3$ (2 × 25 mL) and water (25 mL), dried ($MgSO_4$), evaporated, and the residual mixture partially resolved by column chromatography (solvent *G*) to afford **15** as the major component (0.338 g, 41%), which was shown by ^{1}H-n.m.r. spectroscopy to contain small amounts of impurities. The identity of **15** was deduced from its conversion into **22** (see below).

*1,3-Bis-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)glycerol* (**16**). — A suspension of 10% (w/w) Pd–C (1.1 g) in methanol (10 mL) was added to a solution of **13** (1.322 g, 0.93 mmol) in methanol (50 mL) containing 10% formic acid, and the mixture shaken (60 r.p.m.) under H_2 (405 kPa) at room temperature for 2 h. The solids were removed by 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 **16** (0.954 g, 77%) as a white foam, R_F 0.39 (solvent *J*); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 6 H, 2 OAc), 2.03 (s, 3 H, OAc), 2.05 (s, 15 H, 5 OAc), 2.06 (s, 6 H, 2 OAc), 2.12 (s, 3 H, OAc), 2.13 (s, 3 H, OAc), 2.15 (s, 6 H, 2 OAc), 2.93 (d, 1 H, ^3J 6.0 Hz, OH), 3.64 (ddd, 2 H, $J_{5,4(5'',4'')}$ 9.7, $J_{5,6(5'',6'')}$ 5.3, $J_{5,6(5'',6'')}$ 1.8 Hz, H-5,5''), 3.68 (d, 2 H, ^3J 5.6 Hz, H_2-1''' or H_2-3'''), 3.72 (d, 2 H, ^3J 4.6 Hz, H_2-1''' or H_2-3'''), 3.78 (t, 2 H, ^3J 9.6 Hz, H-4,4''), 3.84 (m, 1 H, H-2'''), 3.88 (br t, 2 H, $J_{5',6'}$ 6.9 Hz, 2 H-5'), 4.06–4.16 (m, 6 H, 2 H_2-6', H-6,6''), 4.477 (d, 1 H, $J_{1'',2''}$ 7.9 Hz, H-1''), 4.485 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.49 (d, 2 H, $J_{1',2'}$ 8.1 Hz, 2 H-1'), 4.51 (m, 2 H, H-6,6''), 4.88 (dd, 1 H, $J_{2'',3''}$ 9.7, $J_{2'',1''}$ 7.9 Hz, H-2''), 4.89 (dd, 1 H, $J_{2,3}$ 9.9, $J_{2,1}$ 7.9 Hz, H-2), 4.96 (br dd, 2 H, $J_{3',2'}$ 10.3, $J_{3',4'}$ 3.6 Hz, 2 H-3'), 5.11 (dd, 2 H, $J_{2',3'}$ 10.3, $J_{2',1'}$ 8.1 Hz, 2 H-2'), 5.20 (t, 2 H, ^3J 9.4 Hz, H-3,3''), and 5.35 (br d, 2 H, $J_{4',3'}$ 3.6 Hz, 2 H-4'); the proton resonating at δ 2.93 exchanged with D_2O.

Anal. Calc. for $C_{55}H_{76}O_{37}$: C, 49.70; H, 5.76. Found: C, 50.34; H, 5.87.

*1,3-Di-*O*-β-lactosylglycerol* (**17**). — A solution of **16** (2.35 g, 1.77 mmol) in absolute methanol (50 mL) was diluted with 0.1M sodium methoxide in absolute methanol (20 mL). The solution was stirred at room temperature[51] for 2 h, and then treated with Amberlite IR-120 (H^+) cation-exchange resin (10 mL) for 30 min. The resin was removed by filtration, washed with methanol (50 mL), and the combined filtrate and wash solution evaporated to give **17** (1.31 g, 95.6%) as a glassy solid, $[\alpha]_D^{21}$ +1.4° (*c* 2.60, water); R_F 0.31 (solvent *O*); ^{1}H-n.m.r. [200 MHz, $(CD_3)_2SO$]: δ 2.9–5.2 (a series of complex multiplets).

Anal. Calc. for $C_{27}H_{48}O_{23} \cdot 2\ H_2O$: C, 41.75; H, 6.75. Found: C, 41.60; H, 6.87.

*2-*O*-Acetyl-1,3-bis-*O*-(2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-lactosyl)glycerol* (**18**).

— Compound **16** (0.187 g, 0.14 mmol) was treated with acetic anhydride (5 mL) in pyridine (15 mL) at room temperature[39] for 46 h. The solution was evaporated and the residual mixture was resolved by column chromatography to yield **18** (0.132 g, 68%) as a colorless, glassy solid, $[\alpha]_D^{22}$ −15.0° (*c* 2.43, chloroform); R_F 0.38 (solvent *H*); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 6 H, 2 OAc), 2.03 (s, 3 H, OAc), 2.05 (s, 18 H, 6 OAc), 2.06 (s, 6 H, 2 OAc), 2.13 (s, 3 H, OAc), 2.14 (s, 3 H, OAc), 2.15 (s, 6 H, 2 OAc), 3.61 (m, 2 H, $J_{5,4(5'',4'')}$ 9.7 $J_{5,6(5'',6'')}$ 4.8, $J_{5,6(5'',6'')}$ 2.5 Hz, H-5,5″), 3.65 (dd, 1 H, J_{gem} 11.4, ^{3}J 6.9 Hz, H-1‴ or H-3‴), 3.67 (dd, 1 H, J_{gem} 11.3, ^{3}J 6.2 Hz, H-1‴ or H-3‴), 3.78 (t, 1 H, ^{3}J 9.2 Hz, H-4 or H-4″), 3.80 (t, 1 H, ^{3}J 9.1 Hz, H-4 or H-4″), 3.82 (dd, 1 H, J_{gem} 11.2, ^{3}J 5.2 Hz, H-1‴ or H-3‴), 3.88 (br t, 2 H, *J* 6.6 Hz, 2 H-5′), 3.90 (1 H, dd, J_{gem} 11.3, ^{3}J 4.0 Hz, H-1‴ or H-3‴), 4.06–4.16 (m, 6 H, H-6,6″ and 4 H-6′), 4.45 (d, 1 H, $J_{1'',2''}$ 8.0 Hz, H-1″), 4.47 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 4.49 (d, 2 H, $J_{1',2'}$ 7.8 Hz, 2 H-1′), 4.49 (m, 2 H, H-6,6″), 4.87 (dd, 1 H, $J_{2'',1''}$ 8.0, $J_{2'',3''}$ 9.4 Hz, H-2″), 4.88 (dd, 1 H, $J_{2,1}$ 8.1, $J_{2,3}$ 9.3 Hz, H-2), 4.96 (dd, 2 H, $J_{3',2'}$ 10.4, $J_{3',4'}$ 3.3 Hz, 2 H-3′), 5.07 (m, 1 H, H-2‴), 5.11 (dd, 2 H, $J_{2',1'}$ 7.8, $J_{2',3'}$ 10.4 Hz, 2 H-2′), 5.18 (t, 2 H, $J_{3,2(3'',2'')}$ 9.3 Hz, H-3,3″), and 5.35 (br d, 2 H, $J_{4',3'}$ 3.3 Hz, 2 H-4′).

Anal. Calc. for $C_{57}H_{78}O_{38}$: C, 49.93; H, 5.73. Found: C, 50.04; H, 5.71.

*1-*O*-β-Lactosyl-(*R,S*)-glycerols* (**20**). — (*a*) *From* **14**. A suspension of 10% (w/w) Pd–C (1.3 g) in methanol (13 mL) was added to a solution of **14** (1.81 g, 2.15 mmol) in methanol (70 mL) containing 10% formic acid, and the mixture was shaken (60 r.p.m.) under H_2 (405 kPa) at room temperature for 2 h. The solids were removed by filtration, washed with methanol (50 mL), the combined filtrate and wash solution was evaporated, and the residual mixture resolved by column chromatography to give *3-*O*-acetyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R,S*)-glycerols* (**19**; 1.12 g, 69%) as an amorphous solid, R_F 0.42 (solvent *J*); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 6 H, 2 OAc), 2.05 (s, 18 H, 6 OAc), 2.07 (s, 6 H, 2 OAc), 2.09 (s, 6 H, 2 OAc), 2.13 (s, 6 H, 2 OAc), 2.15 (s, 6 H, 2 OAc), 2.75 (d, 1 H, ^{3}J 6.1 Hz, OH), 2.91 (d, 1 H, ^{3}J 4.1 Hz, OH), 3.66 (ddd, 2 H, ^{3}J 9.9, ^{3}J 5.7, ^{3}J 2.0 Hz, 2 H-5), 3.7–4.1 (m, 12 H, 2 H-4, 4 H-1″, 2 H-2″, and 4 H-3″), 3.88 (m, 2 H, 2 H-5′), 4.06–4.16 (m, 6 H, 2 H-6 and 4 H-6′), 4.50 (d, 2 H, $J_{1',2'}$ 8.0 Hz, 2 H-1′), 4.50–4.55 (m, 2 H, 2 H-6), 4.51 (d, 2 H, $J_{1,2}$ 8.2 Hz, 2 H-1), 4.91 (dd, 2 H, $J_{2,1}$ 8.2, $J_{2,3}$ 9.4 Hz, 2 H-2), 4.97 (dd, 2 H, $J_{3',2'}$ 10.5, $J_{3',4'}$ 3.4 Hz, 2 H-3′), 5.11 (dd, 2 H, $J_{2',1'}$ 8.0, $J_{2',3'}$ 10.5 Hz, 2 H-2′), 5.20 (t, 2 H, ^{3}J 9.4 Hz, 2 H-3); and 5.35 (br d, 2 H, $J_{4',3'}$ 3.4 Hz, 2 H-4′). The protons resonating at δ 2.75 and 2.91 exchanged with D_2O.

Anal. Calc. for $C_{31}H_{44}O_{21}$: C, 49.47; H, 5.89. Found: C, 49.64; H, 5.87.

To a solution of **19** (1.13 g, 1.50 mmol) in absolute methanol (25 mL) was added 0.1M sodium methoxide in methanol. The solution was stirred for 2 h at room temperature, and treated with Amberlite IR-120 (H^+) cation-exchange resin (5 mL) for 30 min. The resin was removed by filtration, washed with methanol (30 mL), and the combined filtrate and wash solution evaporated to afford **20** (0.569 g, 91%) as an amorphous solid, $[\alpha]_D^{23}$ 0° (*c* 2.5, water), R_F 0.59 (solvent *O*): ^{1}H-n.m.r. [200 MHz, $(CD_3)_2SO$]: δ 2.9–5.2 (a series of complex multiplets).

Anal. Calc. for $C_{15}H_{28}O_{13} \cdot 0.5\ H_2O$: C, 42.35; H, 6.87. Found: C, 42.42; H, 6.97.

(*b*) *From* **21**. A solution containing **12** (3.55 g, 5.08 mmol), **7** (1.384 g, 5.08 mmol), and $Hg(CN)_2$ (2.03 g, 8.04 mmol) in 1:1 (v/v) benzene–nitromethane (20 mL) was stirred at 40° for 2.5 h, and at room temperature for 17 h, diluted with toluene (40 mL), and washed sequentially with a saturated solution of $NaHCO_3$ (2 × 30 mL) and water. The organic phase was dried (Na_2SO_4), evaporated, and the residual mixture resolved by column chromatography to give *2,3-di-*O*-benzyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R,S*)-glycerols* (**21**; 2.98 g, 66%) as a colorless, glassy solid, R_F 0.46 (solvent *E*).

Anal. Calc. for $C_{43}H_{54}O_{20}$: C, 57.97; H, 6.11. Found: C, 57.39; H, 6.02.

A suspension of 10% (w/w) Pd–C (2.0 g) in methanol (10 mL) was added to a solution of **21** (2.806 g, 3.15 mmol) in methanol (50 mL) containing 10% formic acid, and the mixture shaken (60 r.p.m.) under H_2 (405 kPa) at room temperature for 1.25 h. An additional portion (0.6 g) of catalyst was added and the shaking continued for 0.5 h. The solids were removed by filtration and washed with methanol (25 mL), the combined filtrate and wash solution was evaporated, and the residual mixture resolved by column chromatography to give *1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R,S*)-glycerols* (**22**; 1.666 g, 74%) as a colorless, glassy solid, R_F 0.34 (solvent *L*); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 6 H, 2 OAc), 2.05 (s, 12 H, 4 OAc), 2.06 (s, 6 H, 2 OAc), 2.07 (s, 6 H, 2 OAc), 2.14 (s, 6 H, 2 OAc), 2.16 (s, 6 H, 2 OAc), 3.52–3.85 (m, 10 H, 2 H_2-1″, H_2-2″, and 2 H_2-3″), 3.63–3.68 (m, 2 H, 2 H-5), 3.73–3.84 (m, 2 H, 2 H-4), 3.89 (br t, 2 H, ^3J 6.8 Hz, 2 H-5′), 4.06–4.16 (m, 6 H, 2 H-6 and 2 H_2-6′), 4.51 (d, 2 H, $J_{1',2'}$ 7.8 Hz, 2 H-1′), 4.52 (d, 2 H, $J_{1,2}$ 8.0 Hz, 2 H-1), 4.56 (dd, 1 H, J_{gem} 12.0, $J_{6,5}$ 2.0 Hz, H-6), 4.57 (dd, 1 H, J_{gem} 11.8, $J_{6,5}$ 2.0 Hz, H-6), 4.91 (dd, 1 H, $J_{2,1}$ 8.0, $J_{2,3}$ 9.0 Hz, H-2), 4.91 (dd, 1 H, $J_{2,1}$ 8.0, $J_{2,3}$ 9.3 Hz, H-2), 4.97 (dd, 2 H, $J_{3',2'}$ 10.4, $J_{3',4'}$ 3.4 Hz, 2 H-3′), 5.11 (dd, 2 H, $J_{2',1'}$ 7.8, $J_{2',3'}$ 10.4 Hz, 2 H-2′), 5.21 (t, 1 H, ^3J 9.3 Hz, H-3), 5.21 (t, 1 H, ^3J 9.2 Hz, H-3), and 5.35 (br d, 2 H, $J_{4',3'}$ 3.4 Hz, 2 H-4′).

Anal. Calc. for $C_{29}H_{42}O_{20}$: C, 49.01; H, 5.96. Found: C, 49.23; H, 5.92.

To a solution of **22** (0.377 g, 0.53 mmol) in absolute methanol (15 mL) was added 0.1M sodium methoxide in methanol (5 mL), the solution stirred at room temperature for 2 h, and treated with Amberlite IR-120 (H^+) cation-exchange resin (5 mL) for 35 min. The resin was removed by filtration, washed with methanol (20 mL), and the combined filtrate and wash solution evaporated to afford **20** (0.221 g, 100%) as a glassy solid; ^{1}H-n.m.r. [400 MHz, $(CD_3)_2SO$]: δ 3.00–3.82 and 4.19–4.22 (19 H, a series of multiplets associated with C*H*O and C*H*$_2$O protons), and 4.47–5.14 (9 H, a series of multiplets associated with CHO*H* and CH$_2$O*H* protons). All of the protons resonating in the range δ 4.47–5.14 exchanged with D_2O.

(*c*) *From* **15**. Compounds **15** (0.304 g, 0.38 mmol) were debenzylated in the manner described for the preparation of **16**, and the product was purified by column chromatography to give **22** (0.124 g, 46%) as an amorphous solid, R_F 0.44 (solvent *M*), the ^{1}H-n.m.r. spectrum of which was indistinguishable from that described above for **22** obtained from **21**. Compounds **22** (0.086 g, 0.121 mmol) were *O*-

deacetylated as described above to afford **20** (0.042 g, 84%) as a colorless, glassy solid, R_F 0.54 (solvent *O*).

*2,3-Di-*O*-acetyl-1-*O*-(2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-lactosyl)-(*R,S*)-glycerols* (**23**). —Compounds **22** (0.302 g, 0.424 mmol) were acetylated, in the manner described above for the preparation of **18**, to give **23** (0.187 g) as a colorless, glassy solid, $[\alpha]_D^{22}$ −13.9° (*c* 2.42, chloroform), R_F 0.46 (solvent *G*); ^{1}H-n.m.r. (400 MHz, $CDCl_3$): δ 1.97 (s, 6 H, 2 OAc), 2.05–2.08 (m, 36 H, 12 OAc), 2.13 (s, 6 H, 2 OAc), 2.15 (s, 6 H, 2 OAc), 3.61 (ddd, 2 H, $J_{5,4}$ 9.6, $J_{5,6}$ 4.6, $J_{5,6}$ 1.4 Hz, 2 H-5), 3.64–3.69 (m, 2 H, 2 H-1″), 3.79 (t, 1 H, ^3J 9.4 Hz, H-4), 3.80 (t, 1 H, ^3J 9.4 Hz, H-4), 3.88 (br t, 2 H, *J* 7.0 Hz, 2 H-5′), 3.89–3.94 (m, 2 H, 2 H-1″), 4.06–4.16 (m, 8 H, 2 H-6, 2 H_2-6′, and 2 H-3″), 4.25–4.31 (m, 2 H, 2 H-3″), 4.49 (d, 2 H, $J_{1',2'}$ 8.0 Hz, 2 H-1′), 4.49 (m, 2 H, 2H-6), 4.51 (d, 2 H, $J_{1,2}$ 7.9 Hz, 2 H-1), 4.88 (dd, 1 H, $J_{2,1}$ 7.9, $J_{2,3}$ 9.4 Hz, H-2), 4.90 (dd, 1 H, $J_{2,3}$ 9.5, $J_{2,1}$ 7.9 Hz, H-2), 4.96 (dd, 2 H, $J_{3',2'}$ 10.3 $J_{3',4'}$ 3.3 Hz, 2 H-3′), 5.11 (dd, 2 H, $J_{2',1'}$ 8.0, $J_{2',3'}$ 10.3 Hz, 2 H-2′), 5.14–5.20 (m, 2 H, 2 H-2″), 5.18 (t, 1 H, ^3J 9.2 Hz, H-3), 5.19 (t, 1 H, ^3J 9.3 Hz, H-3), 5.35 (br d, 2 H, $J_{4',3'}$ 3.3 Hz, 2 H-4′).

Anal. Calc. for $C_{33}H_{46}O_{22}$: C, 49.88; H, 5.83. Found: C, 49.76; H, 5.72.

Treatment of **19** with acetic anhydride in pyridine in the manner described for the preparation of **18** afforded a product, the ^{1}H-n.m.r. spectrum of which was indistinguishable from that of **23**.

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