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Syntheses of neoglycolipids with hexitol spacers between the saccharidic and the lipidic parts

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Abstract

Four neoglycolipids having 2-amino-2-deoxy-D-glucose or D-galactose moieties linked to the lipidic part by a glucitol or a mannitol spacer-arm have been synthesized. The key step of the synthetic strategy was the regiospecific or regioselective β-glycosylation of partially protected glucitol or mannitol acceptors by either 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl azide or 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate donors.

Keywords: Neoglycolipids; Glycosylation; Staudinger reaction; Imidate; Mannitol; Glucitol

1. Introduction

In a series of studies directed towards the understanding of self-organization of (neo)glycolipids with regard to their structures, we have recently synthesized several compounds with a carbohydrate hydrophilic head and two hydrophobic chains sometimes separated by an oligoethyleneglycol spacer. These compounds displayed thermotropic, as well as lyotropic properties, and the carbohydrate moiety could be used as a recognition signal towards lectins in supramolecular assemblies such as monolayers[1,2] or liposomes.[3] This paper deals with a synthesis of new class of neoglycolipids in which the carbohydrate head is separated from its hydrophobic alkyl chains by an hexitol spacer.

2. Results and discussion

To our knowledge, chemical glycosylation of a D-hexitol on one of its primary hydroxyl groups had never been reported in the literature; however, 1-O-glycosylated hexitols could be obtained by reduction of the reducing end of disaccharides or oligosaccharides.[4–6] In the present case, O-5 and O-6 hydroxyl groups are etherified with fatty alkyl chains prior to glycosylation, which constrained us to realize the glycosylation on the linear D-hexitol.

The first part of our syntheses was the preparation of the acceptors which is depicted in Scheme 1. Thus, in order to obtain a glucitol derivative having two fatty alkyl chains at O-5 and O-6, we started from the known 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**1**) prepared according to Fleet et al.[7] Two tetradecyl residues were incorporated on the free hydroxyl groups by reacting **1** which tetradecyl bromide at 80 °C under

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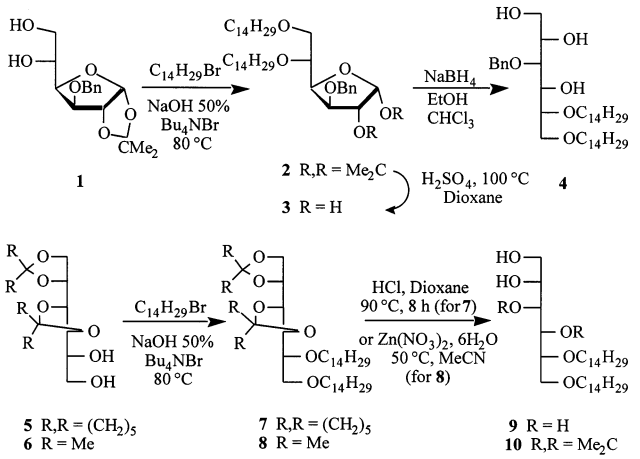


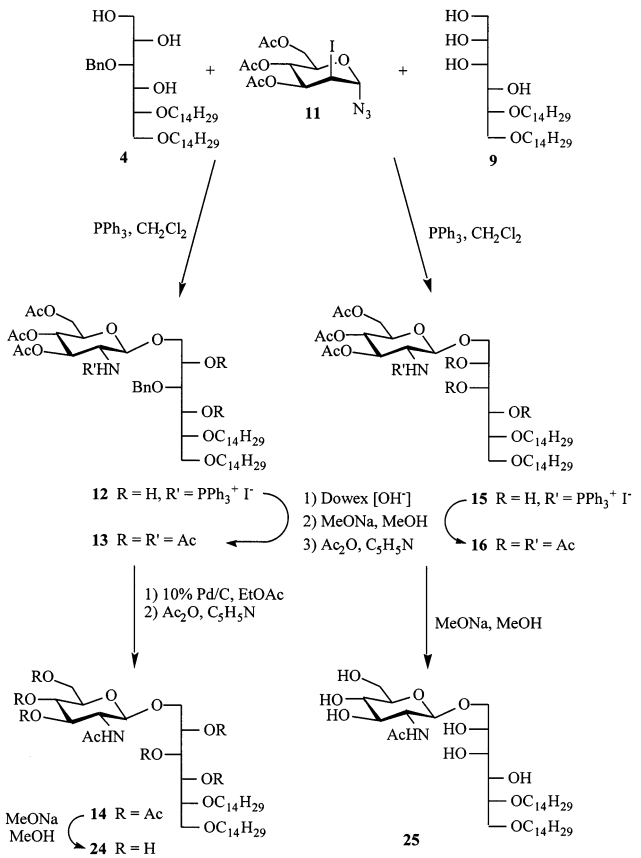
Scheme 1.

phase transfer conditions, in the presence of 50% aqueous sodium hydroxide and tetrabutylammonium bromide. Treatment of the di-*O*-tetradecyl ether (**2**) (obtained in 63% yield) with dilute sulfuric acid in refluxing dioxane afforded an α/β mixture of 3-*O*-benzyl-5,6-di-*O*-tetradecyl-D-glucose (**3**) in 93% yield. Then, the 3-*O*-benzyl-5,6-di-*O*-tetradecyl-D-glucitol (**4**) was synthesized from derivative **3** by reduction with sodium borohydride in a 1:1 chloroform–ethanol mixture (77% yield).

Analogs in the D-mannitol series were synthesized by two different routes. Thus, starting from the known 1,2:3,4-di-*O*-cyclohexylidene-D-mannitol (**5**),[8] we could obtain, as described for the preparation of **2** from **1**, the 5,6-di-*O*-tetradecyl derivative **7** in 50% yield. Cleavage of the cyclohexylidene groups was realized under harsh conditions, by treatment with 2 N hydrochloric acid in refluxing dioxane. The expected 5,6-di-*O*-tetradecyl-D-mannitol (**9**) was recovered in 40% yield. We also prepared a second acceptor, with only two free hydroxyl groups. Thus, 1,2:3,4-di-*O*-(isopropylidene)-5,6-di-*O*-tetradecyl-D-mannitol (**8**) was synthesized in 56% yield from the known 1,2:3,4-di-*O*-isopropylidene-D-mannitol (**6**)[9] as described above for **2** and **7**; selective deprotection of the terminal isopropylidene group of **8** occurred with a high regioselectivity using an excess of zinc nitrate hexahydrate in acetonitrile at 50 °C,[10] affording 3,4-*O*-isopropylidene-5,6-di-*O*-tetradecyl-D-mannitol (**10**) in 83% yield.

Glycosylation reaction was first attempted using 3-*O*-benzyl-5,6-di-*O*-tetradecyl-D-glucitol (**4**) as the acceptor, 1,3,4,6-tetra-*O*-acetyl-2-allyloxycarbonylamino-2-deoxy-β-D-glucopyranose[11] as the donor and trimethylsilyl trifluoromethanesulfonate as the promotor. Previous work in the laboratory has shown the high reactivity of this donor.[11–13] However, in the present case, this high reactivity was a disadvantage, and a complex mixture was obtained — probably mono- and di-glycosylated products — even at −30 °C. We decided to use 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl azide (**11**)[14] as the glucosamine donor: this compound reacts in the presence of triphenylphosphine with reactive alcohol, through the formation of a 1,2-aziridine intermediate, leading to β-derivatives in the 2-amino-2-deoxy-D-glucose series, after double inversion of configuration at C-1 and C-2. Furthermore, it can be prepared in high yield from 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranose[15] and trimethylsilyl azide in the presence of trimethylsilyl trifuoromethanesulfonate. Thus, the glycosylation of the alcohol **4** by the glycosyl azide **11**, in the presence of a slight excess of triphenylphosphine afforded the iodotriphenylphosphonioamino salt **12** in 76% yield (Scheme 2). The structure of this salt was ascertained by ^{1}H and ^{13}C NMR spectroscopy and comparison with literature data.[14–16] Conversion of the salt **12** to the acetamido derivative **13** was achieved by standard procedure and the overall glycosylation yield was 58%. O-Debenzylation (H_2, Pd/C, EtOAc) followed by reacetylation gave the peracetylated disaccharide **14** in 91% yield. The analogue in the mannitol series **16** was directly obtained by glycosylation of the tetraol **9** with the same donor **11** in a lower yield (53%); that could be due to the low solubility of the acceptor in methylene chloride. However, as in the glucitol series, the formation of bis(glycosylated) derivatives was not observed.

The structure of the disaccharides **14** and **16** was fully assigned on the basis of COSY $^{1}H-^{1}H$ and $^{1}H-^{13}C$ 2D experiments in chloroform-*d* at 500 MHz. ^{1}H NMR chemical shift



Scheme 2.

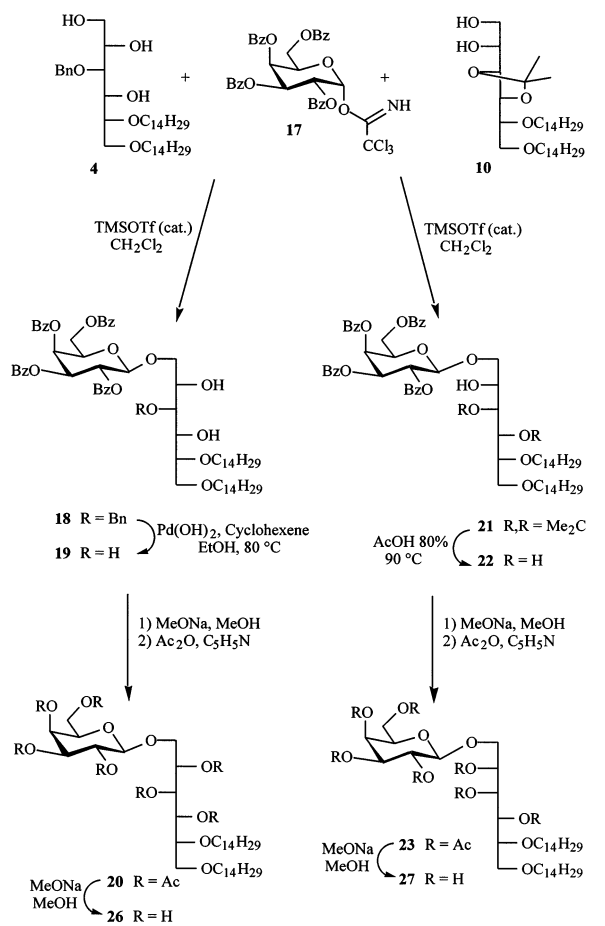
for H-2, H-3 and H-4 of the hexitol residues (δ 5.50–5.00 ppm) as well as ^{13}C chemical shift for C-1 (δ 67.00–67.50 ppm) confirmed the presence of acetyl protecting groups at C-2, C-3 and C-4 and the glycosylation at C-1.

Galactosylated derivatives were also synthesized by reacting the acceptors **4** and **10** with the known 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate **17**[17] in methylene chloride at 0 °C, using trimethylsilyl trifluoromethanesulfonate as the promotor (Scheme 3). Glycosides **18** and **21** were, respectively, obtained in 57 and 80% yield; the lower yield observed from **18** was due to the formation of bis(glycosylation) products which were not identified. Compound **18** was successively transformed into **19** by hydrogenolysis [$Pd(OH)_2$/C, cyclohexene, ethanol] followed by O-debenzoylation and O-reacetylation by standard procedures, to afford the peracetylated product **20** in good yield. Disaccharide **23** was also prepared in high yield from **21** by cleavage of the isopropylidene group in acidic medium (80% aq AcOH, 90 °C, 14 h) affording **22**, which was debenzoylated before reacetylation. As for the glucosamine derivatives, the structure of derivatives **18**, **20**, **22** and **23** was ascertained from 500 MHz NMR spectra.

O-Deacetylation of the peracetylated disaccharides **14**, **16**, **20** and **23** by the Zemplén procedure gave the fully deprotected derivatives **24**–**27** in high yields.

3. Experimental

General methods.—Pyridine was dried by boiling with CaH_2 prior to distillation. Dichloromethane was washed twice with water, dried with $CaCl_2$ and distilled from CaH_2. Pyridine and CH_2Cl_2 were stored over 4 Å molecular sieves. Melting points were determined on a Büchi apparatus and were uncorrected. Thin layer chromatography was performed on aluminum sheets coated with Silica gel 60 F_{254} (E. Merck). Compounds



Scheme 3.

were visualized by spraying the TLC plates with dilute 15% aq H_2SO_4, followed by charring at 150 °C for a few minutes. Column chromatography was performed on Silica-gel Geduran Si 60 (E. Merck). Optical rotations were recorded on a Perkin–Elmer 241 polarimeter in a 1 dm cell at 21 °C. ^1H and ^{13}C NMR spectra were recorded with Bruker AC-200 or DRX-500 spectrometers working at 200 or 500 MHz and 50 or 125 MHz, respectively, with Me_4Si as the internal standard. The assignments of ^{13}C NMR spectra for compounds **14**, **16**, **18**, **20**, **22** and **23** were based on $^1H-^{13}C$ HMQC experiments in $CDCl_3$ at 500 MHz. For compounds **4**, **7**–**9**, **10**, **12**, **13**, **15**, **19** and **21**, ^{13}C assignments were tentatives. Elemental analyses were performed by the Laboratoire Central d'Analyses du CNRS (Vernaison, France).

3-O-*Benzyl*-*1,2*-O-*isopropylidene*-*5,6*-*di*-O-*tetradecyl*-α-D-*glucofuranose* (**2**).—A suspension of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**1**)[7] (5.00 g, 16.11 mmol) in 50% NaOH solution (22.0 mL) was stirred for 1 h at 80 °C, until complete homogenization; tetradecyl bromide (20 mL, 67.2 mmol) and Bu_4NBr (2.00 g, 6.20 mmol) were then added and heating was maintained for 6 h. After cooling and addition of water, the reaction mixture was extracted three times with $CHCl_3$ (3×40 mL) and the combined organic phases were washed with water (30 mL), dried (Na_2SO_4) and concentrated. The residue was purified by silica-gel column chromatography (35:1 petroleum ether–EtOAc) affording **2** (7.14 g, 63%) as an oil. $[\alpha]_D$ −18.8° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.33 (m, 5 H, C_6H_5), 5.90 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.96 and 4.68 (2 d, 2 H, *J* 11.6 Hz, CH_2Ph), 4.59 (d, 1 H, H-2), 4.21 (dd, 1 H, $J_{3,4}$ 2.9, $J_{4,5}$ 9.1 Hz, H-4), 4.08 (d, 1 H, H-3), 3.83–3.22 (m, 7 H, H-5, H-6a, H-6b, 2 OCH_2), 1.60, 1.53 (m, 4 H, 2 OCH_2CH_2), 1.48 (2 s, 6 H, $C(CH_3)_2$), 1.34 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains). Anal. Calcd for $C_{44}H_{78}O_6$ (703.06): C, 75.16; H, 11.18. Found; C, 75.12; H, 11.04.

3-O-*Benzyl*-*5,6*-*di*-O-*tetradecyl*-D-*glucofuranose* (**3**).—3-*O*-Benzyl-1,2-*O*-isopropylidene-5,6-di-*O*-tetradecyl-α-D-glucofuranose (**2**) (3.52 g, 5.00 mmol), dioxane (60 mL) and 1 N H_2SO_4 were refluxed for 3.5 h, until TLC showed complete disappearance of the starting material. After neutralization with satd $NaHCO_3$ solution, the volatiles were evaporated and the residue was diluted with water (50 mL). The aqueous phase was extracted with CH_2Cl_2 (3×50 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated. The resulting syrup was purified by flash chromatography (2:1 petroleum ether–EtOAc) to provide **3** (3:2 α/β mixture) as an oil (3.08 g, 93%). $[\alpha]_D$ −6.2° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.33–7.26 (m, 5 H, C_6H_5), 5.49 (dd, 0.6 H, $J_{1,2}$ 4.1, $J_{1,OH}$ 6.5 Hz, H-1α), 5.11 (d, 0.4 H, $J_{1,OH}$ 12.1 Hz, H-1_β); ^{13}C NMR ($CDCl_3$): δ 103.45 (C-1_β), 96.81 (C-1_α). Anal. Calcd for $C_{41}H_{74}O_6$ (663.00): C, 74.27; H, 11.25. Found; C, 73.74; H, 11.18.

3-O-*Benzyl*-*5,6*-*di*-O-*tetradecyl*-D-*glucitol* (**4**).—A solution of $NaBH_4$ (1.00 g, 26.43 mmol) in water (25 mL) was added to a solution of 3-*O*-benzyl-5,6-di-*O*-tetradecyl-D-glucofuranose (**3**) (3.00 g, 4.52 mmol) in 1:2 $CHCl_3$–EtOH (75 mL) and the mixture was stirred at rt for 15 h. After neutralization with an Amberlyst IR 120 (H^+) resin, the solution was diluted with a 1:1 $CHCl_3$–EtOH mixture (200 mL); filtration and concentration of the solution provided a residue which was purified by column chromatography (1:1 petroleum ether–EtOAc) affording the pure product **4** as a solid (2.30 g, 77%). Mp 49 °C (EtOH); $[\alpha]_D$ −14.4° (*c* 1.0, $CHCl_3$); R_f 0.52 (1:1 petroleum ether–EtOAc); ^1H NMR ($CDCl_3$): δ 7.36–7.25 (m, 5 H, C_6H_5), 4.70 (s, 2 H, CH_2Ph), 3.86–3.23 (m, 13 H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, O*H*, 2 OCH_2), 2.9–32.90 (m, 2 H, 2 OH), 1.52 (m, 4 H, 2 OCH_2CH_2), 1.29 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 138.11, 128.55–128.05 (6 C, C_6H_5), 77.99, 77.55 (C-3, C-5), 74.25 ($CH_2C_6H_5$), 71.95 (OCH_2), 71.69, 71.17 (C-2,4), 70.49 (C-6), 70.28 (OCH_2), 62.48 (C-1), 31.97, 30.22, 29.74, 29.56, 29.53, 29.41, 26.27, 26.16, 22.74 (CH_2 alkyl chains), 14.15 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{41}H_{76}O_6$ (665.02): C, 74.04; H, 11.52. Found; C, 73.79; H, 11.58.

1,2:3,4-*Di*-O-*cyclohexylidene*-*5,6*-*di*-O-*tetradecyl*-D-*mannitol* (**7**).—A suspension of

1,2:3,4-di-*O*-cyclohexylidene-D-mannitol (**5**)[8] (2.50 g, 7.30 mmol) in 50% NaOH solution (8.5 mL) was stirred for 1 h at 80 °C, until complete homogenization. Tetradecyl bromide (8.8 mL, 29.6 mmol) and Bu_4NBr (0.94, 2.91 mmol) were then added and heating was maintained for 8 h at 80 °C. After cooling and addition of water, the reaction mixture was extracted three times with $CHCl_3$ (3 × 50 mL) and the combined organic phases were washed with water (30 mL), dried (Na_2SO_4) and concentrated. The residue was purified by silica-gel column chromatography (20:1 petroleum ether–EtOAc) affording **7** (2.68 g, 50%) as an oil. $[\alpha]_D$ +10.3° (*c* 1.0, $CHCl_3$); R_f 0.26 (40:1 petroleum ether–EtOAc); ^1H NMR ($CDCl_3$): δ 4.26–3.40 (m, 12 H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, 2 OCH_2), 1.58 (m, 24 H, 2 OCH_2CH_2, 10 CH_2 cyclohexyl), 1.26 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 110.18, 110.09 (2 C, 2 $C(CH_2)_2$), 79.49, 79.35, 78.32, 76.98 (C-2, C-3, C-4, C-5), 71.55, 70.38 (2 OCH_2), 70.81 (C-6), 66.59 (C-1), 37.01, 36.95, 36.21, 35.07, 31.97 (4 C, 2 C(CH_2)$_2$), 30.11–29.41, 26.21, 26.18, 25.24, 24.05, 24.00, 23.92, 22.74 (CH_2 alkyl chains and cyclohexyl), 14.14 (2 C, 2 CH_3 alkyl chains). Anal Calcd for $C_{46}H_{86}O_6$ (735.148): C, 75.15; H, 11.79. Found; C, 75.00; H, 11.61.

1,2:3,4-Di-O-*isopropylidene-5,6-di*-O-*tetradecyl*-D-*mannitol* (**8**).—Prepared from 1,2:3,4-di-*O*-isopropylidene-D-mannitol (**6**)[9] (3.00 g, 11.44 mmol) as described for **7**. The crude product was purified by silica-gel column chromatography (10:1 petroleum ether–EtOAc) affording **8** (4.75 g, 56%) as an oil. $[\alpha]_D$ +7.0° (*c* 1.0, $CHCl_3$); R_f 0.50; ^1H NMR ($CDCl_3$): δ 4.20–3.40 (m, 12 H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-6, H-6b, 2 OCH_2 alkyl chains), 1.60 (m, 4 H, 2 OCH_2CH_2), 1.43, 1.40, 1.38, 1.35 (4 s, 12 H, 2 C(CH_3)$_2$), 1.26 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 109.67, 109.46 (2 C, 2 $C(CH_3)_2$), 79.55, 79.18, 78.46, 77.03 (4 C, C-2, C-3, C-4, C-5), 71.56, 71.32 (2 C, 2 OCH_2CH_2), 70.34 (C-6), 66.58 (C-1), 31.90, 30.10–29.40 (CH_2 alkyl chains), 27.31, 27.28, 26.55, 25.42 (4 C, 2 C(CH_3)$_2$), 26.20, 26.16, 22.71 (CH_2 alkyl chains), 14.12 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{40}H_{78}O_6$ (655.02): C, 73.34; H, 12.00. Found; C, 73.53; H, 12.20.

5,6-Di-O-*tetradecyl*-D-*mannitol* (**9**).—A mixture of **7** (2.35 g, 3.20 mmol), dioxane (15 mL) and 2 N HCl (5.5 mL) was stirred for 8 h at 90 °C. After cooling to rt, the solution was neutralized with satd $NaHCO_3$ solution, and concentrated. The residue was extracted with EtOAc (3 × 30 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated again. The crude product was purified by column chromatography (EtOAc) affording a white solid which was recrystallized from EtOH: 0.74 g, 40% yield. Mp 85 °C (EtOH), $[\alpha]_D$ −5.5° (*c* 1.0, $CHCl_3$), R_f 0.55 (EtOAc); ^1H NMR ($CDCl_3$): δ 3.93–3.43 (m, 13 H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, O*H*, 2 OCH_2 alkyl chains), 3.32, 2.97, 2.52 (3 m, 3 H, 3 O*H*), 1.56 (m, 4 H, 2 OCH_2CH_2), 1.26 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 78.92 (C-5), 71.70, 70.23, 69.29 (3 C, C-2, C-3, C-4), 71.61, 70.36 (2 OCH_2), 70.96 (C-6), 63.63 (C-1), 31.65, 20.79–29.08, 25.81, 22.38 (CH_2 alkyl chains), 14.14 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{34}H_{70}O_6$ (574.90): C, 71.03; H, 12.27. Found; C, 70.92; H, 12.44.

3,4-O-*Isopropylidene-5,6-di*-O-*tetradecyl*-D-*mannitol* (**10**).—To a solution of 1,2:3,4-di-*O*-isopropylidene-5,6-di-*O*-tetradecyl-D-mannitol (**8**) (0.655 g, 1.00 mmol) in MeCN (5 mL) was added $Zn(NO_3)_2 \cdot 6\ H_2O$ (1.49 g, 5.00 mmol) and the mixture was stirred at 50 °C for 8 h. After cooling, the solution was concentrated and the oily residue, diluted with CH_2Cl_2 (15 mL), washed with water and dried (Na_2SO_4). Evaporation of the volatiles and purification of the crude product by column chromatography (3:1 petroleum ether–EtOAc) afforded **10** (0.510 g, 83%) as a solid. An analytical sample was recrystallized from EtOH. Mp 55 °C; $[\alpha]_D$ −3.0° (*c* 1.0, $CHCl_3$); R_f 0.55; ^1H NMR ($CDCl_3$): δ 4.15 (d, 1 H, O*H*), 3.74–3.38 (m, 12 H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, 2 OCH_2), 2.35 (dd, 1 H, CH_2OH), 1.58 (m, 4 H, 2 OCH_2CH_2), 1.39, 1.38 (2 s, 6 H, C(CH_3)$_2$), 1.26 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 109.28 ($C(CH_3)_2$), 80.39,

80.18, 78.50 (3 C, C-3, C-4, C-5), 73.07 (C-2), 71.62, 71.08 (2 C, 2 O*C*H$_2$), 70.87 (C-6), 63.91 (C-1), 31.92, 29.70–29.36 (*C*H$_2$ alkyl chains), 26.78 (2 C, C(*C*H$_3$)$_2$), 26.14, 25.93, 22.66 (*C*H$_2$ alkyl chains), 14.06 (2 C, 2 *C*H$_3$ alkyl chains). Anal Calcd for $C_{37}H_{74}O_6$ (614.96): C, 72.26; H, 12.13. Found; C, 72.51; H, 12.34.

*3,4,6-Tri-*O*-acetyl-2-deoxy-2-iodo-α-*D*-mannopyranosyl azide* (**11**).—Trimethysilyl azide (1.00 mL, 7.60 mmol) and Me_3SiOTf (250 μL, 0.98 mmol) were successively added to a solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-iodo-α-D-mannopyranose[15] (2.05 g, 4.47 mmol) in CH_2Cl_2 (10 mL); the mixture was stirred for 15 h, and then poured into a satd $NaHCO_3$ solution (15 mL). The product was extracted with CH_2Cl_2 (3 × 25 mL), and the combined organic phases were washed with water (20 mL), dried (Na_2SO_4) and concentrated. The residue was purified on a short column of silica-gel (1:1 petroleum ether–AcOEt) to afford the pure product **11** as an oil (1.88 g, 95%); $[\alpha]_D^{20}$ +81.2° (*c* 2, $CHCl_3$); lit.[14] $[\alpha]_D^{20}$ +80.4° (*c* 3, $CHCl_3$).

*1-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-*D*-glucopyranosyl)-2,4-di-*O*-acetyl-3-*O*-benzyl-5,6-di-*O*-tetradecyl-*D*-glucitol* (**13**).—Triphenylphosphine (0.288 g, 1.10 mmol) was added quickly to a cooled solution (0 °C) of 3,4,6-tri-*O*-acetyl-2-iodo-2-deoxy-α-D-mannopyranosyl azide (**11**) (0.441 g, 1.00 mmol) and 3-*O*-benzyl-5,6-di-*O*-tetradecyl-D-glucitol (**4**) (0.652 g, 0.98 mmol) in CH_2Cl_2 (5 mL); the mixture was allowed to reach rt and stirring was maintained for 15 h. After concentration, the residue was applied to the top of a short column of silica-gel and eluted first with 1:1 petroleum ether–EtOAc, then with pure EtOAc and finally with 4:1 EtOAc–EtOH affording 1-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodotriphenylphosphonioamino-β-D-glucopyranosyl)-3-*O*-benzyl-5,6-di-*O*-tetradecyl-D-glucitol (**12**) (0.990 g, 76%) containing traces of triphenylphospine oxide. Yellow amorphous solid; R_f 0.76 (4:1 EtOAc–EtOH); ^{1}H NMR ($CDCl_3$): δ 7.87–7.42 (m, 20 H, $CH_2C_6H_5$ and 3 PC_6H_5), 5.84 (dd, 1 H, $J_{2',3'}$ 9.5, $J_{3',4'}$ 9.5 Hz, H-3′), 5.71 (d, 1 H, $J_{1',2'}$ 8.4 Hz, H-1′), 4.79 (dd, 1 H, $J_{4',5'}$ 9.5 Hz, H-4′), 4.65 (dd, 2 H, *J* 11.7 Hz, CH_2C$_6$H$_5$), 4.26–3.03 (m, 16 H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, H-2′, H-5′, H-6′a, H-6′b, 2 O*C*H_2), 2.05, 1.90, 1.70 (3 s, 9 H, 3 CH_3COO), 1.28 (m, 48 H, 24 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 170.57, 170.10, 169.10 (3 C, 3 CH_3*C*OO), 138.21, 135.00, 134.23, 134.00, 132.07–127.85 (21 C, 3 PC_6H_5 and $CH_2C_6H_5$), 121.42 (d, 3 C, $J_{C,P}$ 103.5 Hz, 3 C-*ipso* PC_6H_5), 100.21 (C-1′), 78.13 (C-5), 77.39 (C-3), 74.73 (C-3′), 74.24 (*C*H$_2$C$_6$H$_5$), 72.19 (C-1), 71.86 (O*C*H$_2$), 71.69, 71.29 (3 C, C-2, C-4, C-5′), 70.53 (C-6), 70.28 (O*C*H$_2$), 69.32 (C-4′), 62.03 (C-6′), 57.98 (C-2′), 31.93, 30.31, 29.72, 29.56, 29.37, 26.26, 26.18, 22.70 (*C*H$_2$ alkyl chains), 20.70, 20.67, 20.46 (3 C, 3 *C*H$_3$COO), 14.14 (2 C, 2 *C*H$_3$ alkyl chains).

Compound **12** was dissolved in a minimum amount of EtOH, and the solution was applied on the top of a column packed with Dowex 2X8 [OH$^-$] resin and eluted with EtOH. After concentration of the eluate, the residue was treated overnight with a catalytic amount of MeONa in MeOH (15 mL). Concentration followed by acetylation of the residue with a 2:1 pyridine–Ac_2O mixture (10 mL) afforded a crude compound which was purified by column chromatography (1:5 petroleum ether–AcOEt) to provide the pure product **13** as an oil (0.625 g, 58%). $[\alpha]_D$ −18.9° (*c* 1.0, $CHCl_3$); R_f 0.77; ^{1}H NMR ($CDCl_3$): δ 7.33 (m, 5 H, $CH_2C_6H_5$), 5.24–5.10 (m, 3 H, H-3′, H-2, H-4), 5.08 (dd, 1 H, $J_{3',4''}$ 9.5, $J_{4',5''}$ 9.5 Hz, H-4′), 4.69 (s, 2 H, CH_2C$_6$H$_5$), 4.50 (d, 1 H, $J_{1',2'}$ 8.4 Hz, H-1′), 4.29 (dd, 1 H, $J_{5',6'a}$ 4.4, $J_{6'a,6'b}$ 12.4 Hz, H-6′a), 4.15–3.30 (m, 13 H, H-1a, H-1b, H-3, H-5, H-6a, H-6b, H-2′, H-5′, H-6′b, 2 OCH_2 alkyl chains), 2.11, 2.08, 2.05, 2.02, 2.00, 1.92 (6 s, 18 H, 5 CH_3COO, 1 CH_3CON), 1.52 (m, 4 H, 2 OCH$_2$CH_2), 1.28 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 170.88, 170.79, 170.72, 170.38, 170.18, 169.32 (6 C, 6 CH_3*C*O), 138.23, 128.46–127.59 (6 C, $CH_2C_6H_5$), 99.07 (C-1′), 76.48 (C-5), 75.78 (C-3), 74.72 (*C*H$_2$C$_6$H$_5$), 73.10 (C-3′), 71.92 (C-5′), 71.74 (O*C*H$_2$), 71.31, 71.00 (C-2, C-4), 70.23 (C-6), 69.50 (O*C*H$_2$), 68.47 (C-4′), 66.98 (C-1), 61.89 (C-6′), 54.10 (C-2′), 31.92, 30.08-29.35, 26.16, 26.08 (*C*H$_2$ alkyl chains), 23.17 (*C*H$_3$CON), 21.14, 21.06, 20.90, 20.72, 20.60 (5 C, 5

CH_3COO), 14.14 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{59}H_{99}NO_{16}$ (1078.39): C, 65.71; H, 9.25; N 1.30. Found; C, 65.44; H, 9.02; N, 1.37.

1-O-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2,3,4-tri-O-acetyl-5,6-di-O-tetradecyl-D-glucitol (**14**).—Compound **13** (0.600 g, 0.56 mmol) in EtOAc (15 mL) was hydrogenated at rt under atmospheric hydrogen pressure in the presence of 10% Pd/C (60 mg). The suspension was stirred overnight. After filtration and concentration, the crude residue was acetylated for 18 h in a 1:2 Ac_2O–pyridine mixture (15 mL). The pure compound **14** was obtained by concentration of the solution, coevaporation from toluene and column chromatography (1:5 petroleum ether–EtOAc): 0.513 g, 91% yield. An analytical sample was recrystallized from EtOH; mp 73–74 °C; $[\alpha]_D$ −15.4° (*c* 1.0, $CHCl_3$); R_f 0.65; ^{1}H NMR ($CDCl_3$): δ 5.90 (d, 1 H, $J_{2',NH}$ 8.5 Hz, N*H*), 5.47 (dd, 1 H, $J_{2,3}$ 5.6, $J_{3,4}$ 5.5 Hz, H-3), 5.25 (dd, 1 H, $J_{2',3'}$ 10.0, $J_{3',4'}$ 9.7 Hz, H-3′), 5.23 (ddd, 1 H, $J_{1a,2}$ 7.0, $J_{1b,2}$ 4.5 Hz, H-2), 5.20 (dd, 1 H, $J_{4,5}$ 10.4 Hz, H-4), 5.11 (dd, 1 H, $J_{4',5'}$ 9.4 Hz, H-4′), 4.58 (d, 1 H, $J_{1',2'}$ 8.4 Hz, H-1′), 4.31 (dd, 1 H, $J_{5',6'a}$ 4.5, $J_{6'a,6'b}$ 12.3 Hz, H-6′a), 4.12 (dd, 1 H, $J_{5',6'b}$ 1.2 Hz, H-6′b), 3.89 (ddd, 1 H, H-2′), 3.86 (ddd, 1 H, $J_{1a,1b}$ 11.7 Hz, H-1a), 3.75 (dd, 1 H, H-1b), 3.71 (ddd, 1 H, H-5′), 3.55 (dd, 1 H, $J_{5,6a}$ 4.6, $J_{6a,6b}$ 10.0 Hz, H-6a), 3.50–3.37 (m, 6 H, H-5, H-6b, 2 OCH_2), 2.10, 2.09, 2.09, 2.08, 2.02, 2.01, 1.96 (7 s, 21 H, 6 CH_3COO, 1 CH_3CON), 1.52 (m, 4 H, 2 OCH_2CH_2), 1.26 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 170.64, 170.61, 170.32, 170.32, 170.00, 169.90, 169.26 (7 C, 7 CH_3CO), 99.85 (C-1′), 76.83 (C-5), 73.37 (C-3′), 72.23 (C-5′), 72.15 (OCH_2), 71.44 (OCH_2), 70.65 (C-4), 69.80 (C-3), 69.69 (C-6), 69.54 (C-2), 68.80 (C-4′), 67.16 (C-1), 62.19 (C-6′), 54.59 (C-2′), 31.88, 29.82, 29.65-29.35, 26.00, 25.96 (CH_2 alkyl chains), 23.40 (CH_3CON), 21.12, 20.90, 20.90, 20.60, 20.60, 20.60 (6 C, 6 CH_3COO), 14.06 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{54}H_{95}NO_{17}$ (1030.31): C, 62.95; H, 9.29; N 1.36. Found; C, 62.96; H, 9.40; N, 1.63.

1-O-(2-Acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-glucopyranosyl)-2,3,4-tri-O-acetyl-5,6-di-O-tetradecyl-D-mannitol (**16**).—A solution of 3,4,6-tri-*O*-acetyl-2-deoxy-2-iodo-α-D-mannopyranosyl azide (**11**) (0.441 g, 1.00 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise to a suspension of 5,6-di-*O*-tetradecyl-D-mannitol (**9**) (0.470 g, 0.82 mmol) and PPh_3 (0.288 g, 1.10 mmol) in CH_2Cl_2 (20 mL) and the mixture was stirred overnight. After concentration, the residue was applied to the top of a short column of silica-gel and eluted first with pure EtOAc, then with 4:1 EtOAc–EtOH affording 1-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-iodotriphenylphosphonioamino-β-D-glucopyranosyl)-5,6-di-*O*-tetradecyl-D-mannitol (**15**) containing approximately 10% of starting alcohol **9** and traces of triphenylphospine oxide. Yellow amorphous solid; R_f 0.70 (4:1 EtOAc–EtOH); ^{1}H NMR ($CDCl_3$): δ 5.83 (dd, 1 H, $J_{2',3'}$ 9.8, $J_{3',4'}$ 9.3 Hz, H-3′), 5.78 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 4.79 (dd, 1 H, $J_{4',5'}$ 9.2 Hz, H-4′), 4.25–2.95 (m, 19 H, H-1a, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, H-2′, H-5′, H-6′a, H-6′b, 3 O*H*, 2 OCH_2 alkyl chains), 2.03, 1.99, 1.68 (3 s, 9 H, 3 CH_3COO), 1.28 (m, 48 H, 24 CH_2 alkyl chains, 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 170.62, 169.88, 169.28 (3 C, 3 CH_3COO), 135.02, 134.18, 133.96, 132.01-128.58 (15 C, 3 PC_6H_5), 120.95 (d, 3 C, $J_{C,P}$ 104.1 Hz, 3 C-*ipso* PC_6H_5), 100.82 (C-1′), 79.09 (C-5), 74.52 (C-3′), 71.80, 71.18 (2 C, C-6, OCH_2), 71.11 (C-5′), 71.05, 70.13, 69.78, 69.35 (4 C, C-2, C-3, C-4, C-4′), 68.21 (OCH_2), 66.51 (C-1), 61.83 (C-6′), 57.87 (C-2′), 31.83, 30.09, 29.62–29.27, 26.02, 22.59 (CH_2 alkyl chains), 20.68, 20.61, 20.37 (3 C, 3 CH_3COO), 14.14 (2 C, 2 CH_3 alkyl chains).

The salt **15** was treated as described for **12**, and the crude compound was purified by column chromatography (1:5 petroleum ether–AcOEt) to provide the pure product **16** as a solid (0.446 g, 53%). Mp 101–102 °C (EtOH); $[\alpha]_D$ −4.7° (*c* 1.0, $CHCl_3$); R_f 0.65; ^{1}H NMR ($CDCl_3$): δ 6.13 (d, 1 H, $J_{2,NH}$ 8.3 Hz, NH), 5.47 (dd, 1 H, $J_{2,3}$ 9.1, $J_{3,4}$ 2.0 Hz, H-3), 5.22 (dd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 5.20 (dd, 1 H, $J_{2',3'}$ 10.1, $J_{3',4'}$ 9.6 Hz, H-3′), 5.08 (dd, 1 H, $J_{4',5'}$ 9.8 Hz, H-4′), 4.98 (ddd, 1 H, $J_{1a,2}$ 2.7, $J_{1b,2}$ 3.2 Hz, H-2), 4.42 (d, 1 H, $J_{1',2'}$ 8.4 Hz, H-1′), 4.27 (dd, 1 H, $J_{5',6'a}$ 4.9, $J_{6'a,6'b}$ 12.3 Hz, H-6′a), 4.08 (m, 2 H, H-1a, H-6′b), 3.98 (ddd, 1 H, H-2′), 3.57 (ddd, 1 H, $J_{5',6'b}$ 2.3

Hz, H-5′), 3.57 (dq, 1 H, 0.5 OCH_2), 3.49–3.33 (m, 6 H, H-5, H-6a, H-6b, 1.5 OCH_2), 3.31 (dd, 1 H, $J_{1a,1b}$ 11.6 Hz, H-1b), 2.14, 2.08, 2.05, 2.05, 2.02, 2.01, 1.97 (7 s, 21 H, 6 CH_3COO, 1 CH_3CON), 1.52 (m, 4 H, 2 OCH$_2$CH_2), 1.26 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 170.40, 170.30, 170.30, 170.06, 170.06, 169.82, 169.30 (7 C, 7 CH$_3$*C*O), 101.15 (C-1′), 77.01 (C-5), 73.55 (C-3′), 72.43 (C-5′), 72.18, 71.64 (2 C, 2 O*C*H$_2$), 71.16 (C-6), 70.04 (C-4), 68.87 (C-2, C-4′), 68.67 (C-3), 67.58 (C-1), 62.47 (C-6′), 54.58 (C-2′), 32.36, 30.32–29.69, 26.44, 26.30 (*C*H$_2$ alkyl chains), 23.45 (*C*H$_3$CON), 21.32, 21.15, 21.03, 20.90, 20.60, 20.60 (6 C, 6 *C*H$_3$COO), 14.44 (2 C, 2 *C*H$_3$ alkyl chains). Anal. Calcd for $C_{54}H_{95}NO_{17}$ (1030.31): C, 62.95; H, 9.29; N 1.36. Found; C, 62.78; H, 9.56; N, 1.51.

1-O-*(2,3,4,6-Tetra*-O-*benzoyl-β*-D-*galacto-pyranosyl)-3*-O-*benzyl-5,6-di*-O-*tetradecyl*-D-*glucitol* (**18**).—To a suspension of 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate (**17**)[17] (0.700 g, 0.94 mmol), alcohol **4** (0.780 g, 1.18 mmol) and crushed activated 4 Å molecular sieves in CH_2Cl_2 (10 mL) at 0 °C, was added in 1 h a solution of Me_3SiOTf (15 μL) in CH_2Cl_2 (0.5 mL). The mixture was stirred overnight, then neutralized with triethylamine (20 μL), diluted with CH_2Cl_2 (50 mL) and filtrated over celite. After concentration, the residue was purified by column chromatography (5:3 petroleum ether–EtOAc) to afford the pure galactoside **18** (0.660 g, 57%) as an oil. $[\alpha]_D$ +51.6° (*c* 1.0, $CHCl_3$); R_f 0.55 (2:1 petroleum ether–EtOAc); ^{1}H NMR ($CDCl_3$): δ 8.12–7.18 (m, 25 H, 5 C$_6H_5$), 6.02 (dd, 1 H, $J_{3',4'}$ 3.4, $J_{4',5'}$ 0.5 Hz, H-4′), 5.84 (dd, 1 H, $J_{1',2'}$ 7.9, $J_{2',3'}$ 10.4 Hz, H-2′), 5.63 (dd, 1 H, H-3′), 4.87 (d, 1 H, H-1′), 4.62 (dd, 1 H, $J_{5',6'a}$ 7.2, $J_{6'a,6'b}$ 11.4 Hz, H-6′a), 4.60 and 4.54 (2 d, 2 H, *J* 11.0 Hz, CH_2C$_6H_5$), 4.53 (dd, 1 H, $J_{5',6'b}$ 6.0 Hz, H-6′b), 4.37 (ddd, 1 H, H-5′), 4.14 (m, 1 H, H-2), 4.00 (bd, 1 H, $J_{1a,2}$ 7.0, $J_{1a,1b}$ 10.9 Hz, H-1a), 3.97 (dd, 1 H, $J_{1b,2}$ 5.0 Hz, H-1b), 3.85 (m, 1 H, H-4), 3.83 (m, 1 H, H-3), 3.68 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 10.2 Hz, H-6a), 3.61 (dq, 1 H, 0.5 OCH_2), 3.59 (dd, 1 H, $J_{5,6b}$ 4.7 Hz, H-6b), 3.49–3.40 (m, 4 H, H-5, O*H*, OCH_2), 3.39 (dq, 1 H, 0.5 OCH_2), 2.93 (d, 1 H, $J_{4,OH}$ 6.3 Hz, OH), 1.55 (m, 4 H, 2 OCH$_2$CH_2), 1.27 (m, 44 H, 22 CH_2 alkyl chains), 0.90 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 166.12, 165.63, 165.6, 165.34 (4 C, 4 C$_6H_5$*C*OO), 138.23, 133.67–133.27, 130.09-127.84 (30 C, 5 *C*$_6$H$_5$), 102.26 (C-1′), 78.35 (C-5), 76.91 (C-3), 74.28 (*C*H$_2$C$_6$H$_5$), 72.63 (C-1), 71.82 (O*C*H$_2$), 71.79–71.72 (4 C, C-2, C-4, C-3′, C-5′), 70.59 (C-6), 70.31 (O*C*H$_2$), 69.92 (C-2′), 68.29 (C-4′), 62.35 (C-6′), 32.00, 30.24–29.45, 26.23, 22.77 (*C*H$_2$ alkyl chains), 14.18 (2 C, 2 *C*H$_3$ alkyl chains). Anal. Calcd for $C_{75}H_{102}NO_{15}$ (1243.57): C, 72.43; H, 8.27. Found; C, 72.34; H, 8.46.

1-O-*(2,3,4,6-Tetra*-O-*benzoyl-β*-D-*galacto-pyranosyl)-5,6-di*-O-*tetradecyl*-D-*glucitol* (**19**).—Palladium hydroxide (0.100 g) was added to a solution of the galactoside **18** (0.635 g, 0.51 mmol) in EtOH (8 mL) and freshly distilled cyclohexene (4 mL) and the suspension was stirred for 8 h at 80 °C. After filtration over celite, the solution was concentrated and the residue was purified on a short column of silica-gel (2:1 petroleum ether–EtOAc) to provide the pure galactoside **19** (0.524 g, 89%) as an oil. $[\alpha]_D$ +55.6° (*c* 1.0, $CHCl_3$); R_f 0.50 (2:1 petroleum ether–EtOAc; ^{1}H NMR ($CDCl_3$): δ 8.12–7.18 (m, 20 H, 4 C$_6H_5$), 6.01 (dd, 1 H, $J_{3',4'}$ 3.4, $J_{4',5'}$ 0.6 Hz, H-4′), 5.82 (dd, 1 H, $J_{1',2'}$ 7.8, $J_{2',3'}$ 10.4 Hz, H-2′), 5.62 (dd, 1 H, H-3′), 4.91 (d, 1 H, H-1′), 4.63 (dd, 1 H, $J_{5',6'a}$ 7.3, $J_{6'a,6'b}$ 11.4 Hz, H-6′a), 4.61 (dd, 1 H, $J_{5',6'b}$ 6.0 Hz, H-6′b), 4.39 (ddd, 1 H, H-5′), 3.99 (m, 2 H, H-1a, H-1b), 3.80–3.41 (m, 12 H, H-2, H-3, H-4, H-5, H-6a, H-6b, 2 O*H*, 2 OCH_2), 2.98 (d, 1 H, *J* 6.7 Hz, O*H*), 1.52 (m, 4 H, 2 OCH$_2$CH_2), 1.26 (m, 44 H, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 166.05, 165.58, 165.55, 165.46 (4 C, 4 C$_6$H$_5$*C*OO), 133.65-133.34, 130.08–128.32 (24 C, 4 *C*$_6$H$_5$), 102.51 (C-1′), 78.58 (C-5), 73.56, 73.29 (C-2, C-4), 73.19 (C-1), 71.90 (O*C*H$_2$), 71.75 (C-3′, C-5′), 71.27 (O*C*H$_2$), 70.57 (C-6), 69.93 (C-2′), 68.84 (C-3), 68.24 (C-4′), 62.33 (C-6′), 30.09–29.45, 26.15, 26.12, 22.75 (*C*H$_2$ alkyl chains), 14.19 (2 C, 2 *C*H$_3$ alkyl chains). Anal. Calcd for $C_{68}H_{96}NO_{15}$ (1153.43): C, 70.80; H, 8.39. Found; C, 70.56; H, 8.47.

1-O-*(2,3,4,6-Tetra*-O-*acetyl-β*-D-*galacto-pyranosyl)-2,3,4-tri*-O-*acetyl-5,6-di*-O-*tetra-*

decyl-D-*glucitol* (**20**).—The glycoside **19** (0.440 g, 0.50 mmol) was treated overnight in MeOH (30 mL) containing a catalytic amount of MeONa. After concentration, the residue was acetylated for 16 h at rt in a 2:1 pyridine–Ac_2O mixture (40 mL). After a new concentration, the crude product was purified by column chromatography (2:1 petroleum ether–EtOAc) to afford the pure peracetylated glycoside **20** (0.360 g, 92%) as an oil. $[\alpha]_D$ −6.8° (*c* 1.0, $CHCl_3$); R_f 0.58; ^{1}H NMR ($CDCl_3$): δ 5.46 (dd, 1 H, $J_{2,3}$ 5.0, $J_{3,4}$ 5.7 Hz, H-3), 5.40 (dd, 1 H, $J_{3',4'}$ 3.4, $J_{4',5'}$ 0.7 Hz, H-4′), 5.23 (m, 1 H, H-4), 5.22 (ddd, 1 H, $J_{1a,2}$ 7.0, $J_{1b,2}$ 3.9 Hz, H-2), 5.17 (dd, 1 H, $J_{1',2'}$ 7.9, $J_{2',3'}$ 10.4 Hz, H-2′), 5.02 (dd, 1 H, H-3′), 4.47 (d, 1 H, H-1′), 4.17 (d, 2 H, *J* 6.9 Hz, H-6′a, H-6′b), 3.93 (dd, 1 H, $J_{1a,1b}$ 11.5 Hz, H-1a), 3.91 (ddd, 1 H, H-5′), 3.71 (dd, 1 H, H-1b), 3.58-3.38 (m, H-5, H-6a, H-6b, 2 OCH_2), 2.17, 2.11, 2.11, 2.09, 2.07, 2.07, 1.99 (7s, 21 H, 7 CH_3CO), 1.55 (m, 4 H, 2 OCH_2CH_2), 1.29 (m, 44 H, 22 CH_2 alkyl chains), 0.89 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 170.10, 170.04, 169.85, 169.61, 169.73, 169.45, 169.30 (7 C, 7 CH_3COO), 100.92 (C-1′), 76.53 (C-5), 71.59 (OCH_2), 70.79 (C-6), 70.64 (C-3′), 70.20 (C-5′), 70.16 (C-2, C-4), 69.66 (OCH_2), 69.11 (C-3), 68.42 (C-2′), 67.15 (C-1), 66.96 (C-4′), 61.05 (C-6′), 31.85, 29.75, 29.60, 29.50, 29.41, 29.37, 29.27, 26.03, 25.91, 22.58 (CH_2 alkyl chains), 20.67, 20.65, 20.60, 20.47, 20.47, 20.47, 20.37 (7 C, 7 CH_3COO), 14.00 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{54}H_{94}O_{18}$ (1031.29): C, 62.88; H, 9.19. Found; C, 62.93; H, 9.37.

1-O-*(2,3,4,6-Tetra*-O-*benzoyl-β*-D-*galacto-pyranosyl)*-*3,4*-O-*isopropylidene*-*5,6*-*di*-O-*tetradecyl*-D-*mannitol* (**21**).—To a suspension of 2,3,4,6-tetra-*O*-benzoyl-α-D-galactopyranosyl trichloroacetimidate (**17**)[17] (741 mg, 1.00 mmol), alcohol **10** (0.615 g, 1.00 mmol) and crushed activated 4 Å molecular sieves in CH_2Cl_2 (5 mL) at 0 °C, was added in 1 h a solution of Me_3SiOTf (10 μL) in CH_2Cl_2 (0.5 mL). The mixture was stirred overnight, then neutralized with triethylamine (20 μL), diluted with CH_2Cl_2 (50 mL) and filtrated over celite. After concentration, the residue was purified by column chromatography (3:1 petroleum ether–EtOAc) to afford the pure glycoside **21** (0.955 g, 80%) as an oil. $[\alpha]_D$ +54.3° (*c* 1.0, $CHCl_3$); R_f 0.64; ^{1}H NMR ($CDCl_3$): δ 8.12–7.21 (m, 20 H, 4 C_6H_5), 6.01 (dd, 1 H, $J_{3',4'}$ 3.3, $J_{4',5'}$ 0.7 Hz, H-4′), 5.85 (dd, 1 H, $J_{1',2'}$ 7.9, $J_{2',3'}$ 10.3 Hz, H-2′), 5.62 (dd, 1 H, H-3′), 4.98 (d, 1 H, H-1′), 4.70 (dd, 1 H, $J_{5',6'a}$ 5.9, $J_{6'a,6'b}$ 10.6 Hz, H-6′a), 4.44 (dd, 1 H, $J_{5',6'b}$ 6.8 Hz, H-6′b), 4.35 (ddd, 1 H, H-5′), 4.24 (bd, 1 H, $J_{1a,2}$ 0.8, $J_{1a,1b}$ 10.3 Hz, H-1a), 3.88–3.15 (m, 12 H, H-1b, H-2, H-3, H-4, H-5, H-6a, H-6b, 1 O*H*, 2 OCH_2), 1.54 (m, 4 H, 2 OCH_2CH_2), 1.26 (m, 50 H, $C(CH_3)_2$, 22 CH_2 alkyl chains), 0.88 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 166.05, 165.61, 165.61, 165.19 (4 C, 4 C_6H_5COO), 133.56–133.26, 129.84–128.29 (24 C, 4 C_6H_5), 109.39 ($C(CH_3)_2$), 102.34 (C-1′), 80.11 (C-5), 78.80 (2 C, C-3, C-4), 72.76 (C-2), 71.90 (C-3′), 71.76, 71.63 (2 C, C-1, OCH_2), 71.32 (C-5′), 71.23 (OCH_2), 70.84 (C-6), 70.06 (C-2′), 68.20 (C-4′), 62.02 (C-6′), 31.98, 29.77-29.42 (CH_2 alkyl chains), 26.84 (2 C, $C(CH_3)_2$), 26.21-25.89, 22.74 (CH_2 alkyl chains), 14.18 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{71}H_{100}NO_{15}$ (1193.51): C, 71.44; H, 8.44. Found; C, 71.28; H, 8.47.

1-O-*(2,3,4,6-Tetra*-O-*benzoyl-β*-D-*galacto-pyranosyl)*-*5,6*-*di*-O-*tetradecyl*-D-*mannitol* (**22**).—A solution of the pure glycoside **21** (0.478 g, 0.40 mmol) in 80% aq AcOH was heated for 14 h at 90 °C. After concentration and coevaporation from toluene (2 × 10 mL), the residue was purified on a short column of silica-gel (5:4 petroleum ether–EtOAc) to afford the pure glycoside **22** (0.410 g, 89%) as an oil. $[\alpha]_D$ +48.9° (*c* 1.0, $CHCl_3$); R_f 0.35 (2:1 petroleum ether–EtOAc); ^{1}H NMR ($CDCl_3$): δ 8.13–7.26 (m, 20 H, 4 C_6H_5), 6.02 (dd, 1 H, $J_{3',4'}$ 3.4, $J_{4',5'}$ 0.6 Hz, H-4′), 5.82 (dd, 1 H, $J_{1',2'}$ 7.8, $J_{2',3'}$ 10.5 Hz, H-2′), 5.65 (dd, 1 H, H-3′), 4.94 (d, 1 H, H-1′), 4.67 (dd, 1 H, $J_{5',6'a}$ 6.6, $J_{6'a,6'b}$ 11.4 Hz, H-6′a), 4.48 (dd, 1 H, $J_{5',6'b}$ 6.4 Hz, H-6′b), 4.38 (ddd, 1 H, H-5′), 4.22 (bd, 1 H, $J_{1a,2}$ 2.4, $J_{1a,1b}$ 10.0 Hz, H-1a), 3.94–3.89 (m, 2 H, H-2, H-4), 3.87 (dd, 1 H, $J_{1b,2}$ 6.6 Hz, H-1b), 3.67 (ddd, 1 H, $J_{2,3}$ 6.3, $J_{3,4}$ 2.4, $J_{3,OH}$ 6.0 Hz, H-3), 3.59 (dq, 1 H, 0.5 OCH_2), 3.55–3.50 (m, 3 H, H-5, H-6a, H-6b), 3.46 (dq, 1 H, 0.5 OCH_2), 3.42 (dq, 2 H, 1 OCH_2), 3.16 (d, 1 H, *J* 5.7 Hz, O*H*), 3.14 (d, 1 H, *J* 6.3 Hz, O*H*), 2.78 (d, 1 H, *J* 6.0 Hz, O*H*), 1.54 (m, 4 H, 2 OCH_2CH_2), 1.27 (m, 44 H, 22

CH_2 alkyl chains), 0.90 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 166.02, 165.60, 165.53, 165.53 (4 C, 4 C_6H_5COO), 133.56–133.25, 130.50–128.28 (24 C, 4 C_6H_5), 102.22 (C-1′), 79.96 (C-5), 72.46 (C-1), 71.84 (OCH_2), 71.75 (C-3′), 71.56 (C-5′), 71.36 (OCH_2), 70.82 (C-6), 70.77 (C-2), 70.50 (C-3), 70.13 (C-2′, C-4), 68.34 (C-4′), 62.20 (C-6′), 31.97, 30.11–29.41, 26.14, 22.73 (CH_2 alkyl chains), 14.17 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{68}H_{96}NO_{15}$ (1153.44): C, 70.80; H, 8.39. Found; C, 70.64; H, 8.45.

1-O-*(2,3,4,6-Tetra*-O-*acetyl-β*-D-*galactopyranosyl)-2,3,4-tri*-O-*acetyl-5,6-di*-O-*tetradecyl*-D-*mannitol* (**23**).—The glycoside **22** (0.577 g, 0.50 mmol) was treated overnight in MeOH (30 mL) containing a catalytic amount of MeONa. After concentration, the residue was acetylated for 16 h at rt in a 2:1 pyridine–Ac_2O mixture (40 mL). After a new concentration, the residue was purified by column chromatography (2:1 petroleum ether–EtOAc) to afford the pure peracetylated glycoside **23** (0.480 g, 93%) as a solid. Mp 60 °C (EtOH); $[\alpha]_D$ +42.5° (*c* 1.0, $CHCl_3$); R_f 0.58; ^1H NMR ($CDCl_3$): δ 5.47 (dd, 1 H, $J_{2,3}$ 8.4, $J_{3,4}$ 2.3 Hz, H-3), 5.39 (dd, 1 H, $J_{3',4'}$ 3.4, $J_{4',5'}$ 0.8 Hz, H-4′), 5.20 (dd, 1 H, $J_{1',2'}$ 7.9, $J_{2',3'}$ 10.4 Hz, H-2′), 5.18 (dd, 1 H, $J_{4,5}$ 7.8 Hz, H-4), 5.14 (ddd, 1 H, $J_{1a,2}$ 3.2, $J_{1b,2}$ 6.7 Hz, H-2), 5.00 (dd, 1 H, H-3′), 4.48 (d, 1 H, H-1′), 4.18 (dd, 1 H, $J_{5',6'a}$ 6.6, $J_{6'a,6'b}$ 11.2 Hz, H-6′a), 4.13 (dd, 1 H, $J_{5',6'b}$ 6.9 Hz, H-6′b), 3.99 (dd, 1 H, $J_{1a,1b}$ 11.3 Hz, H-1a), 3.90 (ddd, 1 H, H-5′), 3.60 (dq, 1 H, 0.5 OCH_2), 3.57 (dd, 1 H, H-1b), 3.50 (dd, 1 H, $J_{5,6a}$ 3.5, $J_{6a,6b}$ 9.8 Hz, H-6a), 3.44 (m, 1 H, H-5), 3.43–3.36 (m, 3 H, H-6b, OCH_2), 3.31 (dq, 1 H, 0.5 OCH_2), 2.16, 2.14, 2.09, 2.08, 2.07, 2.05, 1.99 (7s, 21 H, 7 CH_3COO), 1.53 (m, 4 H, 2 OCH_2CH_2), 1.27 (m, 44 H, 22 CH_2 alkyl chains), 0.90 (t, 6 H, 2 CH_3 alkyl chains); ^{13}C NMR ($CDCl_3$): δ 170.10, 170.02, 169.85, 169.85, 169.68, 169.68, 169.68 (7 C, 7 CH_3COO), 100.91 (C-1′), 76.35 (C-5), 71.58, 71.13 (2 C, 2 OCH_2), 70.80 (C-3′), 70.63 (C-5′), 70.46 (C-6), 69.46 (C-4), 69.14 (C-2), 68.98 (C-3), 68.40 (C-2′), 67.48 (C-1), 66.97 (C-4′), 62.10 (C-6′), 31.82, 29.83–29.26, 26.01, 25.90, 22.57 (CH_2 alkyl chains), 13.99 (2 C, 2 CH_3 alkyl chains). Anal. Calcd for $C_{54}H_{94}O_{18}$ (1031.29): C, 62.88; H, 9.19. Found; C, 62.58; H, 9.20.

1-O-*(2-Acetamido-2-deoxy-β*-D-*glucopyranosyl)-5,6-di*-O-*tetradecyl*-D-*glucitol* (**24**).—Compound **14** (0.402 g, 0.39 mmol) in MeOH (15 mL) was stirred for 24 h in the presence of a catalytic amount of MeONa. The solubilization occurred after a few minutes, and the deacetylated product started to crystallize some minutes later. The product **24** (0.175 g, 90%) was obtained by filtration and washed with MeOH (3 × 5 mL): solid, mp 193 °C (MeOH). Anal. Calcd for $C_{42}H_{83}NO_{11}$ (778.09): C, 64.83; H, 10.75; N 1.80. Found; C, 64.76; H, 11.13; N, 1.92.

1-O-*(2-Acetamido-2-deoxy-β*-D-*glucopyranosyl)-5,6-di*-O-*tetradecyl*-D-*mannitol* (**25**).—Compound **16** (0.360 g, 0.35 mmol) in MeOH (15 mL) was treated as described for **14**. The product **25** was recovered as a solid (0.253 g, 93%); mp 191 °C (MeOH). Anal. Calcd for $C_{42}H_{83}NO_{11}\cdot H_2O$ (796.11): C, 63.36; H, 10.76; N 1.76. Found; C, 63.17; H, 10.61; N, 1.86.

1-O-*β*-D-*Galactopyranosyl-5,6-di*-O-*tetradecyl*-D-*glucitol* (**26**).—The glycoside **20** (0.300 g, 0.29 mmol) was treated overnight in MeOH (10 mL) containing a catalytic amount of sodium methylate. After neutralization with an Amberlyst IR 120 (H^+) resin, the solution was concentrated to afford a solid which was just washed with deionized water, recovered by filtration and crystallized from abs EtOH (0.195 g, 89% yield). Mp 192 °C (EtOH). Anal. Calcd. for $C_{40}H_{80}O_{11}\cdot H_2O$ (755.06): C, 63.62; H, 10.95. Found; C, 63.47; H, 10.85.

1-O-*β*-D-*Galactopyranosyl-5,6-di*-O-*tetradecyl*-D-*mannitol* (**27**).—The glycoside **23** (0.343 g, 0.42 mmol) was treated as described for **16** to afford **27** as a solid (0.291 g, 92% yield). Mp 199 °C (MeOH). Anal. Calcd. for $C_{40}H_{80}O_{11}\cdot H_2O$ (755.06): C, 63.62; H, 10.95. Found; C, 63.47; H, 10.84.

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