Neuraminic Acid and Related Compounds. V. Syntheses of Biologically Active Sialosyl-Glycerol Derivatives and Galactosyl-Glycerol Derivative

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New 1-acyl-sialosyl-glycerol derivatives (1α—dα, 1α—dβ, 2α, 2β, which mimic the structure of the capsular polysaccharide of group C meningococcal were synthesized by the use of a chiral glycerol derivative, and were found to have phospholipases A<sub>2</sub> and C inhibitory activities. Furthermore, syntheses of 2-palmitoyl-sialosyl-glycerol derivative (4α, 4β, 5α, 5β), galactosyl-glycerol derivative (6), and sialosyl-galactosyl-glycerol derivative (7) were carried out to examine the difference between these activities. Among these sialosyl derivatives, 3-palmitoyl-sialosyl-glycerol derivatives (1—3α, 1—3β) demonstrated the most potent inhibitory activities.

Keywords sialosyl-glycerol derivative; phospholipase A<sub>2</sub> inhibitor; phospholipase C inhibitor; galactosyl-glycerol derivative; sialosyl-galactosyl-glycerol derivative

Capsular polysaccharides are located on the surface of the bacterial cell wall. Therefore, they are important agents in bacterial pathogenesis, and they also interact directly with the host’s immune system. The capsular polysaccharide of group C meningococcal, whose structure was determined by Gotschlich and coworkers,<sup>31</sup> includes an α (2→9) linked homopolymer of sialic acid and phosphoglycerolipid. We conducted synthesis studies on biologically active new compounds by modifying the cell wall structures of gram negative bacteria.<sup>29</sup> As an extension of these studies, we have focused our attention on a polysaccharide involving sialic acid which plays important roles in various phenomena in living organisms. We synthesized sialosyl derivatives to search into a lead compound for medicines. In a recent communication, we described the novel syntheses of (S)- and (R)-3-O-acyl-1-O-sialosyl glycerol derivatives (1α—dα, 1α—dβ, 2α, 2β, 3α, 3β; Fig. 1) which were expected to produce phospholipases A<sub>2</sub> and C inhibitory activities.<sup>31</sup> This paper describes these results in detail, as well as the syntheses of new compounds, (S)- and (R)-2-O-palmitoyl-1-O-sialosyl glycerol (4α, 4β, 5α, 5β; Fig. 1), (S)-1-O-galactosyl-3-O-palmitoyl-glycerol (6; Fig. 1) and

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Synthesis of glycosyl acceptors, glycerol derivatives, was carried out in Chart 1. (S)-1-O-Acetyl-2-O-benzylglycerol (8), used as a starting material, was treated with trityl chloride and pyridine at 80°C to produce a tritylated compound (9) in 72.5% yield. Deacetylation of 9 was carried out with NH₄OH-MeOH (1:10) at room temperature to afford the 1-hydroxyl compound (10), as the intermediate of (S) and (R)-glycosyl acceptor, in 77.4% yield. Acylation of 9 with a variety of acyl groups proceeded smoothly. Compound (9) was acylated with hexadecanoyl chloride, dodacenoyl chloride, octanoyl chloride, and α-ethylhexanoyl chloride in the presence of triethylamine at room temperature to produce 11a (85.0%), 11b (93.7%), 11c (88.8%), and 11d (86.0%) respectively. The protective trityl groups of 11a-d were removed by 80% AcOH at 80°C to obtain glycosyl acceptors of (S)-3-acyl-sialosyl-(galactosyl)-glycerol derivatives (1a-4a, 1a-4β, 3a, 3β, 6, 7), 12a (74.6%), 12b (80.3%), 12c (85.8%), and 12d (73.9%), respectively. The glycosyl acceptors of (R)-sialosyl-glycerol derivatives (2x, 2β, 4x, 4β) were synthesized as follows. The 1-hydroxyl group of 10 was protected with monochloroacetyl chloride and triethylamine at room temperature to afford 13 in 91.5% yield. The trityl group of 13 was removed with 80% AcOH to produce the 3-hydroxyl compound (14), glycosyl acceptor of (R)-2-acyl-sialosyl-glycerol derivatives (4x, 4β) in a 69.0% yield.

Treatment of 14 with hexadecanoyl chloride and triethylamine afforded the acylated compound (15) in a 70.1% yield. Monochloroacetylation was carried out with disopropylethylamine and thiourea in tetrahydrofuran (THF) to give the (R)-glycosyl acceptor (16) of 2x and 2β in a 92.7% yield. The glycosyl acceptor of (S)-2-acyl-sialosyl-glycerol derivatives (5x, 5β) was obtained in two steps from the starting material (8). The 3-hydroxy group of 8 was protected with a tert-butylimidylsilyl group by use of tert-butylimidylsilyl chloride and triethylamine to obtain the silylated compound (17) in an 84.0% yield. The 1-acetyl group of 17 was removed by KOH-MeOH (1:10) to give the 1-hydroxyl derivative (18), glycosyl acceptor of 5x and 5β.

As a glycosyl donor, 5-acetamido-2-chloro-4,7,8,9-tetra-O-acetyl-d-glycero-d-galacto-2-nonulosonic acid methyl ester (19), prepared from N-acetyleneuraminic acid in three steps, was used for glycosylation of all sialosyl-glycerol derivatives except 3x and 3β. The glycosyl donor of 3x and 3β was compound (22), the benzyl ester type of 19 which could be removed by hydrogenolysis in the latter step of the synthetic route.

The synthetic route of 3-acyl-sialosyl-glycerol derivatives is shown in Chart 2. Glycosylation of the glycosyl acceptor (12a-d) with the glycosyl donor (19) in the presence of Hg(CN)₂-HgBr₂-Molecular Sieves 4A (MS4A) in CH₂Cl₂ at room temperature for 4 d produced the sialosyl-glycerol derivatives (20a-d) as a mixture of anomers. Separation by preparative thin layer chromatography (CH₂Cl₂-MeOH =
20:1 afforded 20a—dx (20az, 26.9%; 20bz, 10.8%; 20cz, 15.6%; 20dz, 27.0%) and 20a—dβ (20aβ, 32.4%; 20bβ, 11.5%; 20cβ, 17.1%; 20dβ, 23.5%). The anomic stereochemistry of 20a—dx and 20a—dβ was determined by chemical shifts of 3-H$_{eq}$ of the proton nuclear magnetic resonance ($^1$H-NMR) spectrum. It is known that for α anomers the chemical shift of 3-H$_{eq}$ varies between δ 2.6—2.8, while for β anomers that of 3-H$_{eq}$ are δ 2.1—2.5. The 3-H$_{eq}$ signals of 20a—dx were 2.62, 2.61, 2.61, 2.62 ppm, respectively (ranges of α glycoside). In the case of 20a—dβ, these signals overlapped with the methylene proton signals of fatty acids in $^1$H-NMR spectrum. Therefore, the anomeric configuration of 20a—dβ as determined by the fact that the 3-H$_{eq}$ signals of 20a—dx were not observed downfield from 2.6 ppm, and their other signals supported the structure of 20a—dβ. The protective benzyl group of 20a—dx and 20a—dβ was cleaved by hydrogenation in the presence of 30% Pd(OH)$_2$·C in MeOH to yield (S)-sialosyl-glycero derivatives, 1α—dx (1az, 71.2%; 1bz, 95%; 1cz, 95%; 1dz, 82%) and 1α—dβ (1aβ, 74.2%; 1bβ, 87%; 1cβ, 96%; 1dβ, 85%).

Glycosylation of the (R)-glycosyl acceptor (16) and the chloride (19) was carried out as described for 20a—dxβ to afford (R)-sialosyl-glycero derivatives (21α, 24.6%; 21β, 20.9%). Each of 21α and 21β were converted to debenzylated compounds (2α and 2β) by usual hydrogenolysis with yields of 86.2% and 84.8%, respectively.

Similarly, the glycerol derivative (12α) was glycosylated with the benzyl ester donor (22) to obtain 23α and 23β (23α, 22.2%; 23β, 17.7%). The two protective benzyl groups of 23α and 23β were removed by hydrogenolysis in the presence of 30% Pd(OH)$_2$·C to afford the free carboxylic acid derivatives (3α, quant.; 3β, 96.2%).

Syntheses of 2-acylsialosyl-glycero derivatives (4α, 4β, 5α, 5β) were shown in Chart 3. Glycosylation of the silyl derivative (18) with the chloride (19) in the presence of Hg(CN)$_2$—HgBr$_2$—MS4A afforded the sialosyl-silylglycero derivatives (24α, 11.2%; 24β, 8.8%). The benzyl groups of 24α and 24β were smoothly removed by hydrogenolysis with 30% Pd(OH)$_2$. Chemical yields of the debenzylated compounds (25α, 25β) were 77.0% and 85.5%, respectively. The 2-hydroxyl groups of 25α and 25β were acylated with palmitic acid, 1,3-dicyclohexylcarbodiimide (DCC), and 4-dimethylaminopyridine (DMAP), and then the tert-butyldimethylsilyl group was selectively removed by aqueous hydrogen fluoride in CH$_3$CN—CHCl$_3$ to 4α and 4β (4α, 24.7%; 4β, 22.5%), respectively.

The monochloroacetyl glycosyl acceptor (14) and the chloride (19) were converted to sialosyl-glycero derivatives (27α and 27β) via 26α and 26β exactly as described for 18 + 19 + 25α + 25β (14 + 19 + 26α + 26β: 26α, 2.8%; 26β, 16.4%; 26 + 27: 26α, 34.0%; 26β, 50.4%), respectively. The glycero-2-hydroxy group of 27α and 27β was acylated with palmitic acid, DCC, and DMAP, and then the monochloroacetyl group was selectively removed with diisopropylethylamine and thiolurea to yield 5α and 5β (5α, 16.9%; 5β, 14.9%; 26—5).

The synthetic routes of the galactosyl-glycero derivative (6) and the sialosyl-galactosyl-glycero derivative (7) are shown in Chart 4. Glycosylation was achieved by use of
the imidate method. With the glycosyl donor, the galactosyl imidate (28), prepared from β-galactose in three steps, was glycosylated from the glycerol derivative (12a) in the presence of BF₃·Et₂O to give the galacto-glycerol derivative (29) in a 53.9% yield. Hydrogenolysis of 29 was performed with a catalyst of Pd(OH)₂-C to obtain 6 in
93.6% yield. An α (2→6)-linked sialosyl-galactosyl derivative (30) was obtained by glycosylation of 1,2,3,4-tetra-O-benzyl-D-galactose, prepared efficiently from D-galactose with chloride (19). The disaccharide was hydrogenated in the presence of Pd(OH)₂-C to afford the tetrahydroxyl compound (31), and then acetylated with acetic anhydride and pyridine to produce a nonaacyl compound (32). Selective deacetylation at the anomeric position of the compound (32) was achieved with hydrazine acetate to produce the 1-hydroxyl compound (33). Compound (33) was transformed into the imidate (34) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene(DBU)–trichloroacetonitril as a glycosyl acceptor. Glycosylation of the glycerol derivative (12a) with 34 was performed by treatment of BF₃·Et₂O to yield the sialosyl-galactosyl-glycerol derivative (35) in a 14% yield (33–35). Hydrogenolysis of 35 was carried out with Pd(OH)₂-C to produce 7 in 81% yield. The structures of all compounds were characterized by ¹H-NMR spectroscopy, as well as infrared (IR) spectroscopy, elemental analyses, and fast-atom bombardment (FAB) mass spectroscopy.

The biological effects (7) (phospholipases A₂ and C inhibitions) of all compounds (1a→d, 1a→dβ, 2→5a, 2→5f, 6, 7) were tested. 3-Palmitoyl-sialosyl-glycerol derivatives (1→3β, 1→3β) and 2-palmitoyl derivative (4β) possessed the strongest activities, while the 2-palmitoyl derivatives (4β, 5β, 5f) the galactosyl-glycerol derivative (6), and the sialosyl-galactosyl-glycerol derivative (7) showed little or no inhibitory activity.

Experimental
All melting points were determined with a micro-melting point apparatus (Yanagimoto) and are uncorrected. Optical rotations were measured on a JASCO-DIP-140 digital polarimeter. IR spectra were measured on JASCO A-202 and JASCO IR-810 infrared spectrophotometers. ¹H-NMR spectra were recorded on JEOL JNM-FX90Q (90 MHz), JEOL JNM-270GX (270 MHz), and JEOL JNM-500GX (500 MHz) spectrophotometers using tetramethylsilane (TMS) as an internal standard. Chemical shifts were recorded in values (δ) downfield from TMS, and the abbreviations of signal patterns are as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. Thin layer chromatography (TLC) was performed on silica gel (Kieselgel 60F₂₅₄ on aluminum sheet, Merck). All compounds were located by spraying with sulfuric acid and heating on a hot plate. Preparative TLC was performed on the preparative layer chromatography plate (Kieselgel 60F₂₅₄ and 0.5 mm, Merck). Column chromatography was performed on silica gel (Kieselgel 60, 70→230 mesh, Merck).

(S)-1-O-Acetyl-2-O-benzyl-3-O-tritylglucor (9) Trityl chloride (8.76 g, 3.14 × 10⁻² mol) was added to a solution of (S)-1-O-acetyl-2-O-benzylglycerol (8, 4.70 g, 2.09 × 10⁻³ mol) in dry pyridine (50 ml). The mixture was heated at 80°C for 3 h, diluted with CHCl₃ (200 ml), and washed with saturated aqueous CuSO₄ and brine. The organic phase was concentrated to dryness and the residue was purified on a column of silica gel (CHCl₃, n-hexane = 10:1) to produce 9 (7.09 g, 72.5% as colorless oil. [α]D₂ = +11.3° (c 1.98, CHCl₃). IR (neat): 1740, 700 cm⁻¹. ¹H-NMR (CDCl₃): δ 1.97 (3H, s, -COCH₃), 4.60 (2H, s, -CH₂CH₃), 7.20→7.53 (20H, m, phenyl x 4).

(R)-2-O-Benzyl-1-O-tritylglucor (10) (753 mg, 1.61 × 10⁻² mol) in NH₄OH-MeOH (1:10) (50 ml) was stirred at room temperature for 15 h. The resulting mixture was evaporated to dryness and subjected to column chromatography on silica gel (CHCl₃) to afford 10 (530 mg, 77.4%) as a colorless solid. [α]D₂ = +22.5° (c 0.58, IR): 3450, 700 cm⁻¹. ¹H-NMR (CDCl₃): δ 3.24→3.28 (2H, s, -CH₂OCH₃), 4.57 (2H, d, J = 4.4 Hz, -CH₂Ph), 7.06→7.54 (20H, m, phenyl x 4).

General Procedure for Syntheses of (S)-1-O-Acetyl-2-O-benzyl-3-O-tritylglucor (11a→d) Acetyl chloride (8.69 × 10⁻² mol) was added to a solution of 10 (30.8 g, 7.25 × 10⁻² mol) and triethylamine (11.0 g, 1.09 × 10⁻¹ mol) in dry CH₂Cl₂ (200 ml) at 0°C, and then stirred at room temperature for 15 h. The solution was washed with brine, dried (MgSO₄), and purified on silica gel (CHCl₃, n-hexane = 10:1) to produce 11a→d (11a, 85.0%; 11b, 93.8%; 11c, 88.8%; 11d, 86.0%) as colorless oils.

(R)-2-O-Benzyl-1-O-tritylglucor (16) A mixture of 15 (1.72 g, 3.47 × 10⁻² mol), disopropylpropylamine (538 mg, 4.16 × 10⁻² mol) and tiourea (317 mg, 4.16 × 10⁻² mol) in dry THF (30 ml) was refluxed for 2 h. The resulting mixture was filtered and the filtrate was concentrated to dryness. The residue was chromatographed on silica gel (CHCl₃) to produce 16 (1.35 g, 92.7%) as a colorless oil. [α]D₂ = +4.7° (c 4.13, CHCl₃). IR (neat): 3445, 1740, 700 cm⁻¹. ¹H-NMR (CDCl₃): δ 0.88 (3H, t, J = 6.1 Hz, -COCH₂CH₂CH₃), 1.26 (26H, s, -COCH₂CH₂CH₂CH₃), 2.32 (2H, t, J = 6.1 Hz, -COCH₂CH₂CH₂CH₃), 7.07→7.45 (20H, m, phenyl x 4).

(R)-1-O-Acetyl-2-O-benzyl-3-O-tert-butyldimethylsilylglucor (17) tert-Butyldimethylsilyle chloride was added to a solution of 8 (6.04 g, 2.69 × 10⁻² mol) and triethylamine (3.39 g, 3.35 × 10⁻² mol) in dry CH₂Cl₂
(50 ml) at 0°C under argon. The mixture was stirred at room temperature for 3h, washed with brine, and dried (MgSO4). The organic phase was evaporated to dryness and the residue was chromatographed on a column of silica gel (CH3ClO2) to afford 17 (6.75, 84.0%) as a colorless oil. [α]D2 = 15.6° (c = 1.78, CHCl3), IR (neat): 1745, 700 cm⁻¹. H-NMR (CDCl3) δ: 0.075 (6H, s, -Si(CH3)2), 0.89 (9H, s, -Si(CH3)CH2), 2.04 (3H, s, -CH3Ph), 4.65 (2H, s, -CH2Ph), 7.32–7.34 (5H, m, phenyl).

(R)-(2)-Benzy I-o-t er-hyldimethylglycerol (18) 17 (6.93 g, 2.02 × 10⁻² mol, as described for 10) gave 18 (5.62, 92.7%) as a colorless oil. [α]D2 = +17.3° (c = 1.00, CHCl3), IR (neat): 3450, 3400, 1750, 700 cm⁻¹. H-NMR (CDCl3) δ: 0.090 (6H, s, -Si(CH3)2), 0.90 (9H, s, -Si(CH3)CH2), 4.60, 4.68 (2H, d, J = 11.9 Hz, -CH2Ph), 7.29 (5H, s, phenyl).

General Procedure for the Synthesis of 2-O-Benzyl-3-O-acetyl-1-(meth yl-5-acet amido-4,7,8,9-tetra-O-acetyl-3,5-dioxyo-glycero-a-galacto-2-nonulopyranosyl)glycerolates (1aα–dα, 1aβ–dβ, 2a, 2β). A solution of (2a–dα, 2a–dβ, 2a, 2β) Glyceryl-derivatives (12a–dα, 16), pulverized MSMA (3g), Hg(CH3CN)2 (1.26g, 4.99 × 10⁻³ mol), and HgBr2 (771 mg, 2.14 × 10⁻³ mol) were dried by means of a high vacuum-pump for 2h. The mixture was dissolved in dry CH2Cl2 (30 ml) and stirred at room temperature for 1h under argon. 5-Acetamido-2-chloro-4,7,8,9-tetra-O-acetyl-2,3-trideoxy-a-galacto-a-galacto-2-nonalopyranosyl nonulopyranosic acid methyl ester (19, 3.64g, 7.13 × 10⁻³ mol) in dry CH2Cl2 (20 ml) was added by drops to the mixture within 1h at room temperature, and the suspension was then stirred for 4d. The resulting mixture was diluted with CH2Cl2, filtered, and the filtrate was washed with aqueous 10% KI and brine. The organic phase was dried (MgSO4) concentrated to dryness, and purified on a column of silica gel (CH3ClO2 to yield 20α and 21β). The anomeric mixture was further purified on preparative TLC (CH3ClO2 : MeOH = 20:1) to afford 20α–dα, 20α (26.9%), 20β (10.8%), 20c (15.6%), 20d (27.0%), 20a–dβ (20αβ, 32.4%, 20ββ, 11.5%, 20cβ, 17.1%, 20dβ, 23.5%), 21 (24.6%), and 21β (20.9%) as colorless, amorphous powders.

General Procedure for the Synthesis of 3-O-Benzyl-2-O-acetyl-1-(m ethyl-5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dioxyo-glycero-a-galacto-2-nonulopyranosyl)glycerolates (1aα–dα, 1aβ–dβ, 2a, 2β). A solution of (2a–dα, 2a–dβ, 2a, 2β) Glyceryl-derivatives (12α–dα, 16), pulverized MSMA (3g), Hg(CH3CN)2 (1.26g, 4.99 × 10⁻³ mol), and HgBr2 (771 mg, 2.14 × 10⁻³ mol) were dried by means of a high vacuum-pump for 2h. The mixture was dissolved in dry CH2Cl2 (30 ml) and stirred at room temperature for 1h under argon. 5-Acetamido-2-chloro-4,7,8,9-tetra-O-acetyl-2,3-trideoxy-a-galacto-a-galacto-2-nonalopyranosyl nonulopyranosic acid methyl ester (19, 3.64g, 7.13 × 10⁻³ mol) in dry CH2Cl2 (20 ml) was added by drops to the mixture within 1h at room temperature, and the suspension was then stirred for 4d. The resulting mixture was diluted with CH2Cl2, filtered, and the filtrate was washed with aqueous 10% KI and brine. The organic phase was dried (MgSO4) concentrated to dryness, and purified on a column of silica gel (CH3ClO2 : MeOH = 20:1) to yield 20α and 21β. The anomeric mixture was further purified on preparative TLC (CH3ClO2 : MeOH = 20:1) to afford 20α–dα, 20α (26.9%), 20β (10.8%), 20c (15.6%), 20d (27.0%), 20a–dβ (20αβ, 32.4%, 20ββ, 11.5%, 20cβ, 17.1%, 20dβ, 23.5%), 21 (24.6%), and 21β (20.9%) as colorless, amorphous powders.
2.67 (1H, dd, J = 4.6 Hz, 3-H\textsubscript{a}), 5.18 (2H, s, -COOH\textsubscript{Ph}), 7.31, 7.34 (10H, s, x, 2 phenyl x), 2.84 (positive lab FAB-(M + H)\textsuperscript{+} m/z: 790. 23F\textsubscript{2}:[x\textsubscript{D}] = -6.4 (c = 1.00, CHCl\textsubscript{3}). IR (neat): 3395, 1740, 1650, 1500, 1400 cm\textsuperscript{-1}.

(5)-O-(5-Acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-\textit{D}-glycero-\textit{D}-galacto-2-nonulopyranosyl)-\textit{O}-hexadeccanamyl glycerol (32, 3\textbf{f}) A solution of 12\textbf{a} and 3\textbf{f} (33 mg, 3.40 \times 10\textsuperscript{-5} mol) in MeOH (1 ml) was hydrogenated in the presence of 30\% Pd(OH\textsubscript{2})-C at room temperature. The catalyst was filtered off and the filtrate was concentrated to dryness.

The residue was chromographed on silica gel (CHCl\textsubscript{3}: MeOH = 30:1) to give 3\textbf{a} (27 mg, quant.) and 3\textbf{b} (23 mg, 96.2\%, respectively).

1\textsuperscript{H}-NMR (CDCl\textsubscript{3}) \delta: 0.38 (3H, s, -COOH\textsubscript{Ph}), 1.26 (26H, s, -CO-CH\textsubscript{2}(CH\textsubscript{3})\textsubscript{12}CH\textsubscript{3}), 1.92-2.16 (15H, m, -COCH\textsubscript{2}X), 2.35 (2H, t, J = 7.3 Hz, -COCH\textsubscript{2}(CH\textsubscript{3})\textsubscript{12}CH\textsubscript{3}), 5.97 (1H, d, J = 9.6 Hz, -NH-). Positive FAB-MS (M + H\textsuperscript{+}) m/z: 790.

3\textbf{f}: [x\textsubscript{D}] = -13.3 (c = 0.36, CHCl\textsubscript{3}). IR (neat): 3480, 1740, 1650, 1500 cm\textsuperscript{-1}.

1\textsuperscript{H}-NMR (CDCl\textsubscript{3}) \delta: 0.38 (3H, s, -COOH\textsubscript{Ph}), 1.26 (26H, s, -CO-CH\textsubscript{2}(CH\textsubscript{3})\textsubscript{12}CH\textsubscript{3}), 1.92-2.16 (15H, m, -COCH\textsubscript{2}X), 2.35 (2H, t, J = 7.3 Hz, -COCH\textsubscript{2}(CH\textsubscript{3})\textsubscript{12}CH\textsubscript{3}), 5.97 (1H, d, J = 9.6 Hz, -NH-). Positive FAB-MS (M + H\textsuperscript{+}) m/z: 790.

(5)-O-(2-Benzyl-1-O-[\textit{methyl}(5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-\textit{D}-glycero-\textit{D}-galacto-2-nonulopyranosyl)-\textit{O}-hexadeccanamyl glycerol (27a, 2\textbf{b}) A solution of 26\textbf{a} (50 mg, 6.51 \times 10\textsuperscript{-5} mol in MeOH (1 ml) was hydrogenated in the presence of 30\% Pd(OH\textsubscript{2})-C (5 mg) at room temperature. The catalyst was filtered off and the filtrate was concentrated to dryness. The residue was chromographed in a column of silica gel (CHCl\textsubscript{3}: MeOH = 20:1) to give 27a (25 mg, 30\% yield). Positive FAB-MS (M + H\textsuperscript{+}) m/z: 732.

26\textbf{a}: [x\textsubscript{D}] = -10.8 (c = 0.48). IR (neat): 3400, 1750, 1670, 1540, 700 cm\textsuperscript{-1}. 1\textsuperscript{H}-NMR (CDCl\textsubscript{3}) \delta: 1.85-2.09 (15H, m, -COCH\textsubscript{2}X), 2.41 (1H, d, J = 4.9, 12.9 Hz, 3-H\textsubscript{a}), 3.77 (3H, s, -COOH\textsubscript{Ph}), 4.15 (2H, s, -COCH\textsubscript{2}Cl), 4.65 (2H, s, -CH\textsubscript{2}Ph), 7.31-7.50 (5H, m, phenyl). Positive FAB-MS (M + H\textsuperscript{+}) m/z: 732.

(5)-O-[\textit{Methyl}(5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-\textit{D}-glycero-\textit{D}-galacto-2-nonulopyranosyl)-\textit{O}-hexadeccanamyl glycerol (27a, 2\textbf{b}) A solution of 26\textbf{a} (50 mg, 6.51 \times 10\textsuperscript{-5} mol in MeOH (1 ml) was hydrogenated in the presence of 30\% Pd(OH\textsubscript{2})-C (5 mg) at room temperature. The catalyst was filtered off and the filtrate was concentrated to dryness.

The residue was chromographed in a column of silica gel (CHCl\textsubscript{3}: MeOH = 20:1) to give 27a (25 mg, 30\% yield). Positive FAB-MS (M + H\textsuperscript{+}) m/z: 732.

26\textbf{a}: [x\textsubscript{D}] = -10.8 (c = 0.48). IR (neat): 3400, 1750, 1670, 1540, 700 cm\textsuperscript{-1}. 1\textsuperscript{H}-NMR (CDCl\textsubscript{3}) \delta: 1.85-2.09 (15H, m, -COCH\textsubscript{2}X), 2.41 (1H, d, J = 4.9, 12.9 Hz, 3-H\textsubscript{a}), 3.77 (3H, s, -COOH\textsubscript{Ph}), 4.15 (2H, s, -COCH\textsubscript{2}Cl), 4.65 (2H, s, -CH\textsubscript{2}Ph), 7.31-7.50 (5H, m, phenyl). Positive FAB-MS (M + H\textsuperscript{+}) m/z: 732.
was dissolved in dry CH₂Cl₂ (5 ml) and stirred at −20 °C under argon. BF₃·Et₂O (0.08 ml) was added to the mixture, −20 °C, stirred for 3 h and further at room temperature for 15 h. The resulting mixture was filtered and the filtrate was washed with saturated aqueous NaHCO₃ and brine. The organic phase was dried (MgSO₄) and concentrated. The residue was purified on a column of silica gel (CHCl₃: MeOH = 50:1) to afford 29 (184 mg, 53.9%) as a colorless, amorphous powder. [d]₂₉ +5.0° (c = 0.20, CHCl₃) [1] R (neat) = 1400, 1790, 245, 2495, 3451 cm⁻¹. 1H-NMR: (CDCl₃) δ: 1.88 (8H, t, J = 6.2 Hz, -COCH₂CH₂CH₂CH₂CH₂CH₂CH₃), 2.15 (26H, s, -COCH₂CH₂CH₂CH₂CH₂CH₂CH₃), 2.95 (171H, m, -COCH₂CH₃), 2.24 (24H, J = 7.8 Hz, -COCH₂CH₂CH₂CH₃), 2.34 (24H, J = 7.8 Hz, -COCH₂CH₂CH₂CH₃), 1.98–2.16 (12H, m, - COCH₂CH₃x5), 5.30 (2H, s, -CH₂Ph), 7.33–7.35 (5H, m, phenyl). Positive FAB-MS (M + H)⁺ m/z: 751.

(5S)-3-Hexadecanoyl-1-O-(2,3,4,6-tetra-O-acetyl-5,6,7,8-tetradecyloxy-γ-glycerol-β-galacto-2-nonulopyranosyl)-2,3,4,6-tetra-O-acetyl-5,6,7,8-tetradecyloxy-γ-glycerol-β-galacto-2-nonulopyranosyloylglycerol (6) A solution of 29 (295 mg, 3.93 × 10⁻4 mol) in MeOH (2 ml) was hydrogenated in the presence of Pd(OH)₂·C (50 mg) at room temperature for 2 h. The catalyst was filtered off and the filtrate was chromatographed on a silica gel column to give 6 (248 mg, 93.6%) as a colorless, amorphous powder. [d]₂₉ +18.3° (c = 0.24, CHCl₃) [1] R (neat) = 3470, 1750 cm⁻¹. 1H-NMR (CDCl₃): δ: 0.88 (3H, t, J = 6.2Hz, -COCH₂CH₂CH₂CH₂CH₂CH₂CH₃), 1.23 (26H, s, - COCH₂CH₂CH₂CH₂CH₂CH₂CH₃), 1.95–2.17 (12H, m, -COCH₂CH₃), 2.34 (24H, J = 7.8 Hz, -COCH₂CH₂CH₂CH₃), 2.43 (24H, J = 7.8 Hz, -COCH₂CH₂CH₂CH₃), 1.88–2.13 (24H, m, -COCH₂CH₃x5), 2.58 (1H, dd, J = 4.8, 12.8 Hz, 3-H₃), 3.82 (3H, s, - COOCH₂CH₃), 7.29–7.37 (5H, m, phenyl). Positive FAB-MS (M + H)⁺ m/z: 1182.

References