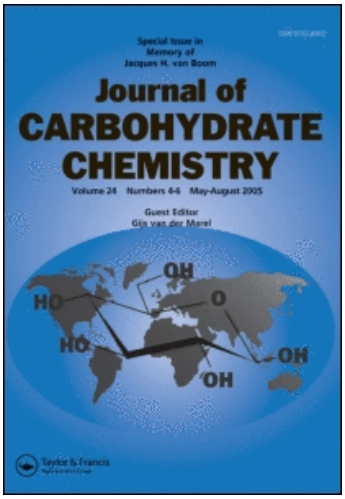

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Efficient Syntheses of a Series of Glycosphingolipids with 1,2-*trans*-Glycosidic Linkages

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Efficient Syntheses of a Series of Glycosphingolipids with 1,2-*trans*-Glycosidic Linkages

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A series of glycosphingolipids with 1,2-*trans*-glycosidic linkages were synthesized in the presence of neighboring group participation using trichloroacetimidates as glycosyl donors and an azido-sphingosine as the glycosyl acceptor. During the preparation of the target compounds, it was found that the α-L-arabinopyranosyl unit in target **7e** and intermediates **7b**–**7d** existed in the $^1C_4$ conformation and that the β-L-fucopyranosyl unit in **10e** adopted the $^4C_1$ conformation.

Keywords Glycosphingolipid with 1,2-*trans*-glycosidic linkage, Schmidt's, glycosyl trichloroacetimidate, Azido-sphingosine, Glycosylation, Conformation

INTRODUCTION

Glycosphingolipids (GSLs) are ubiquitous components of the cellular membranes of all eukaryotic cells, and nearly 300 different structures have been identified.[1] They are glycolipids composed of a long-chain amino alcohol, known as a sphingoid base, with a fatty acid residue linked to its amino group (the resulting amide is called ceramide, **1**), and a carbohydrate chain attached to the primary hydroxyl group of the ceramide.[2] The scientific interest in GSLs has increased on account of their role in various cell-surface-related processes, such as cell differentiation, transmembrane signaling, cell recognition, and toxin binding.[3–5] Such events are common to cancer, allergy, viral infection, inflammation, and autoimmune disease.[6,7]

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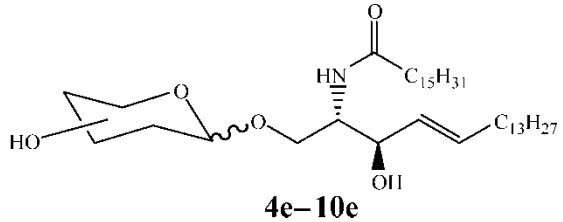
Each of these events is mediated by a specific glycosphingolipid such as a ganglioside, tumor antigen, or viral receptor.[7–9] This exquisite degree of specificity suggests that glycosphingolipid analogs could be suitable candidates for the development of new drugs.[6] Therefore, efficient synthetic routes to pure glycosphingolipids and their derivatives are in demand.[10]

The functions of some glycosphingolipids with 1,2-*trans*-glycosidic linkages have been studied extensively. For example, β-galactosyl ceramide (β-GalCer) is known to act as a ligand for the HIV-1 viral glycoprotein gp120,[11] mediating viral entry into epithelial cells. β-GalCer has also been suggested as a possible ligand for the adhesion of *Helicobacter pylori* to cells in the gastric system.[12,13] As another example, the simple monohexosyl sphingolipid glucosylceramide has been reported to have mitogenic properties that stimulate cell growth, differentiation, and DNA synthesis.[14,15]

Our interest in glycosphingolipids with 1,2-*trans*-glycosidic linkages stems from our ongoing studies of glycosphingolipid carbohydrate-carbohydrate interactions. As part of this work, we require a modular synthetic approach to obtain some glycosphingolipids with 1,2-*trans*-glycosidic linkages as shown in Figure 1, and the sugar portions in target molecules are D-lactopyranosyl, D-galactopyranosyl, D-glucopyranosyl, D-mannopyranosyl, L-arabinopyranosyl, L-rhamnopyranosyl, and L-fucopyranosyl residue, respectively.

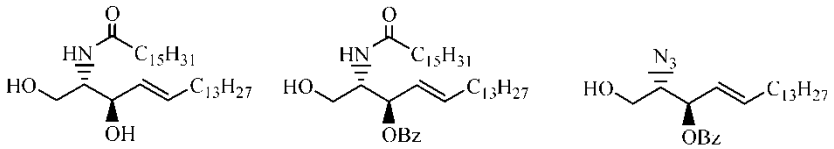
RESULTS AND DISCUSSION

Several syntheses of glycosphingolipids with 1,2-*trans*-glycosidic linkages have been reported so far. The key step is the stereoselective and regioselective coupling of the glycosyl acceptor with corresponding glycosyl donor. Among these glycosylation methods, there are two main forms of glycosyl acceptors used as shown in Figure 2, ceramide acceptor **2**[16–20] and azido-sphingosine acceptor **3**.[21–25] For the glycosyl donor, Schmidt's glycosyl trichloroacetimidates with C-2 neighboring group participation are most successfully used for the glycosphingolipids with 1,2-*trans*-glycosidic linkages. In 1986, Schmidt and coworkers smoothly glycosylated a trisaccharide trichloroacetimidate with ceramide acceptor **2** in the presence of boron trifluoride etherate



4e–10e

Figure 1: Target compounds.



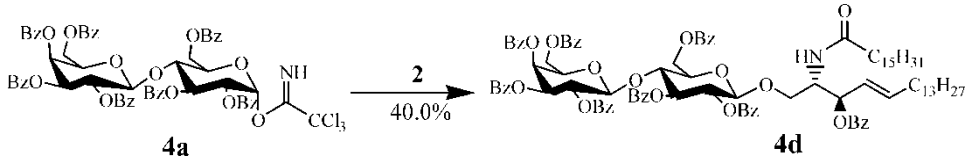
ceramide 1 **2** **3**

Figure 2: Ceramide and glycosyl acceptors.

to obtain the protected GM3 ganglioside.[20] Recently, an α-series ganglioside GM1α was efficiently synthesized by Takeda through the reaction of GM1α oligosaccharide trichloroacetimidate with an azide-C20-sphingosine acceptor.[25] Alternatively, glycosyl fluoride and glycosyl bromide donors were also used to build up the corresponding glycosphingolipids with 1,2-*trans*-glycosidic linkages.[16,17,19,23]

Taking into account the total efficiency to our target compounds and operational simpleness, we first selected Schmidt glycosyl donor and ceramide acceptor **2**,[26] and tried the glycosylation between benzoylated lactopyranosyl trichloroacetimidate (**4a**) and ceramide acceptor **2** using 1.0 molar equiv $BF_3 \cdot OEt_2$ as the catalyst at $-20^\circ C$. As a result, the desired glycoside **4d** was obtained, however, only in 40% yield (Sch. 1). Having investigated a variety of reaction conditions, including reaction solvent, promoters, reaction temperature, and the sequence of adding donor and acceptor, we found that it was very difficult to further improve the glycosylation yield. The main reason might result from the diminished nucleophilicity of the acceptor **2** due to the intramolecular hydrogen bond between the primary hydroxyl and the amide group.[27,28] Protection of the 3-OH of ceramide **1** with an electron-donating group (benzyl group) could enhance the nucleophilicity of the acceptor to some extent; however, the glycosylation yield was still unsatisfactory.[28,29]

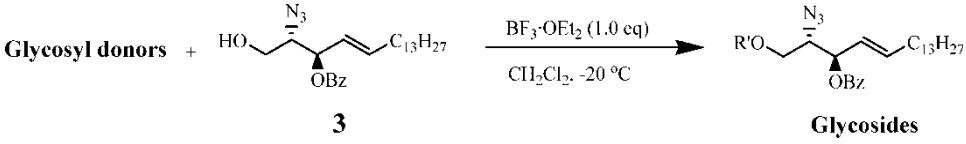
Next, the azido-sphingosine **3** was used as the glycosyl acceptor for further investigation. Thus, perbenzoylated lactopyranosyl trichloroacetimidate (**4a**) was glycosylated with **3** in the presence of $BF_3 \cdot OEt_2$ at $-20^\circ C$, and the glycoside (**4b**) was smoothly produced in 90% yield. Glycosylation of the perbenzoylated trichloroacetimidate donors (**5a**–**10a**) with acceptor **3** was undertaken next. As shown in Table 1, all donors gave the corresponding glycosides

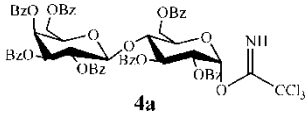
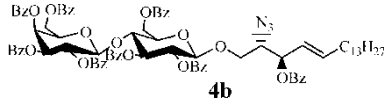
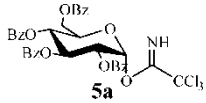
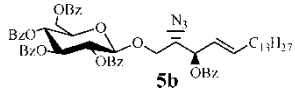
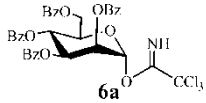
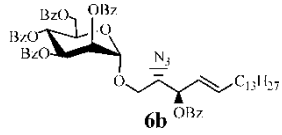
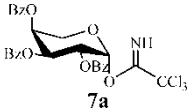
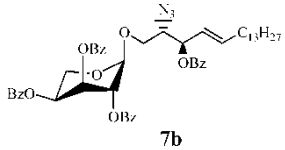
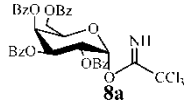
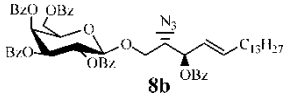
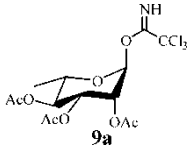
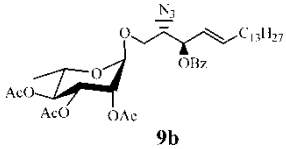
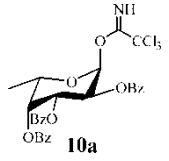
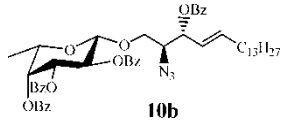


4a **4d**

Scheme 1: Synthesis of protected glycosphingolipid with 1,2-*trans*-glycosidic linkage **4d**.

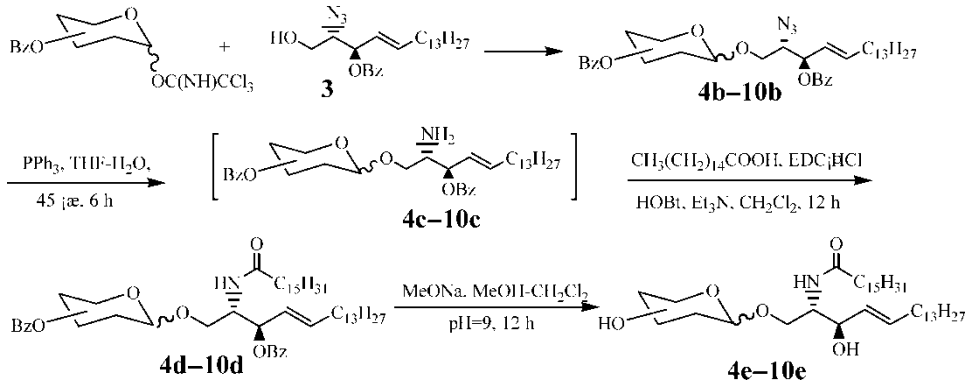
Table 1: Synthesis of Glycosides **4b**–**10b**.



Entry	Glycosyl donors	Products	Yield (%)
1	 **4a**	 **4b**	90.0
2	 **5a**	 **5b**	95.0
3	 **6a**	 **6b**	100
4	 **7a**	 **7b**	94.5
5	 **8a**	 **8b**	98.4
6	 **9a**	 **9b**	98.2
7	 **10a**	 **10b**	97.1

(**5b**–**10b**) in excellent yields. Therefore, our synthetic route to the target sphingolipids was validated (Sch. 2).

Then, following the route shown in Scheme 2, reduction of azido groups in **4b**–**10b** with triphenylphosphine was performed to produce amines (**4c**–**10c**),

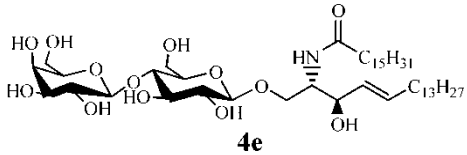
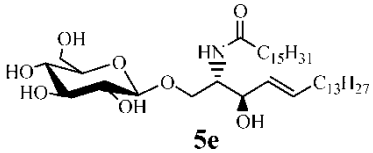
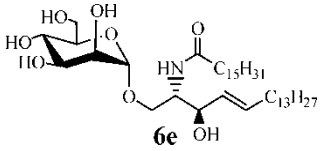
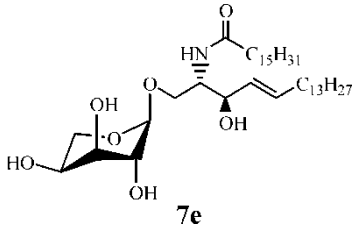
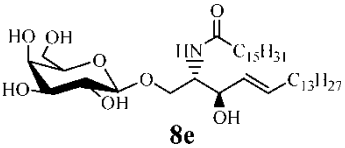
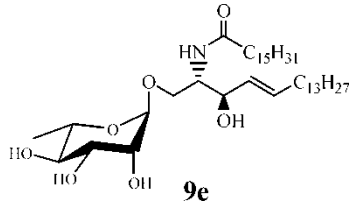
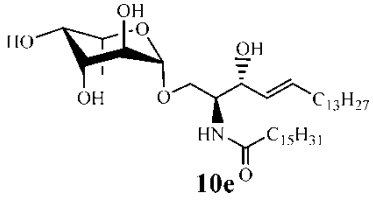


Scheme 2: The synthetic route to our target glycosphingolipids.

which were isolated without purification and immediately *N*-acylated with palmitic acid in the presence of triethylamine, EDC · HCl, and HOBt to provide amides **4d–10d** in good yields (Table 2).[10] Final removal of benzoyl groups of **4d–10d** with MeONa-MeOH readily yielded target glycosphingolipids **4e–10e** (Table 2). Overall yields for the four steps were high, ranging from 43% to 67%.

The structures of all compounds were confirmed by ^{1}H NMR, ^{13}C NMR, HMQC, HMBC, and MALDI-MS. Interestingly, the α-L-arabinopyranosyl residue in **7b** adopted a $^1C_4$ chair conformation, instead of the $^4C_1$ form. This conformational assignment was supported by the proton coupling constants observed for **7b** ($J_{1,2} = J_{2,3} = J_{3,4} = 0$ Hz) in the ^{1}H NMR spectrum. The arabinosyl C-1′ signal at δ 105.9 ppm in the ^{13}C NMR spectrum and the coupling constant $J_{C1'\text{-}H1'}$ (174.7 Hz) in the HMBC spectrum further confirmed the axial linkage.[30] After reduction of the azido group of **7b**, acylation of the amino group of **7c**, and removal of all protection to target **7e** ($J_{1,2} = 1.4$ Hz), the $^1C_4$ conformation of α-L-arabinopyranosyl residue did not reconvert into the expected ^{4}C$_1$ form. What is more interesting is that the L-fucopyranosyl ring, which adopted the expected $^1C_4$ conformation in **10b** and **10d**, adopted a $^4C_1$ conformation in deprotected **10e**. An apparent triplet for H-1′ at 4.09 ppm [$J_{1,2} = 3.72$ Hz, $J_{1,3} = 3.66$ Hz (W coupling)] and three broad singlet peaks at 3.26 (H-2′), 3.28 (H-3′), and 3.40 ppm (H-4′) for the fucopyranosyl residue in the ^{1}H NMR spectrum of **10e** clearly indicated the ^{4}C$_1$ conformation, instead of ^{1}C$_4$. The strong effect of ceramide aglycon on the chair conformations of pentopyranose and 6-deoxy-hexopyranose rings was first observed upon formation of glycosphingolipids bearing a 1,2-*trans*-diaxial glycosidic linkage. However, such conformational changes were observed previously in related series such as acetylated and benzoylated xylopyranosyl derivatives[31–35] as well as in 6-deoxy-hexopyranosyl units including 6-deoxy-L-talopyranosyl and L-rhamnopyranosyl analogs.[36]

Table 2: Synthesis of glycosphingolipids with 1,2-*trans*-glycosidic linkage **4e–10e**.

Entry	Amides	Yield (%)	Products	Yield (%)
1	**4d**	68.4	 **4e**	76.2
2	**5d**	72.4	 **5e**	86.4
3	**6d**	50.6	 **6e**	85.0
4	**7d**	71.2	 **7e**	83.0
5	**8d**	70.9	 **8e**	86.0
6	**9d**	72.2	 **9e**	95.5
7	**10d**	61.6	 **10e**	85.1

In conclusion, we have synthesized β-D-lactopyranosyl, β-D-glucopyranosyl, α-D-mannopyranosyl, β-D-galactopyranosyl, α-L-arabinopyranosyl, α-L-rhamnopyranosyl, and β-L-fucopyranosyl ceramides with 1,2-*trans*-glycosidic linkages. The results of the present investigation should be of value to synthesize other structural analogs of glycosphingolipids.

EXPERIMENTAL

General methods. All reactions were conducted under a dried argon balloon. CH_2Cl_2 was distilled from $CaH_2 \cdot BF_3 \cdot OEt_2$ was distilled. All other solvents and reagents were used without further purification. All reactions were monitored by thin-layer chromatography (TLC) on aluminum sheets, Silica Gel 60 F_{254} (E. Merck). Flash column chromatography was performed on silica gel (200-300 mesh, Qingdao, China). Optical rotations were determined with a JACSO P-1020 digital polarimeter. ^{1}H NMR, ^{13}C NMR, HMQC, and HMBC spectra were taken on a JEOL JNM-ECP 600 spectrometer with tetramethylsilane (TMS) as the internal standard, and chemical shifts are recorded in δ values. Mass spectra were measured using a HP5989A or VG Quattro MALDITOF-MS with α-cyano-4-hydroxycinnamic acid (CCA) as the matrix.

General Procedure for Forming Glycosides 4b–10b

To a solution of perbenzoylated glycosyl trichloroacetimidate donor (1.3 mmol) and acceptor **3** (1.0 mmol) in 20 mL of dry CH_2Cl_2 was added powdered molecular sieves (4 Å, 1.2 g). The mixture was stirred for 30 min at rt $BF_3 \cdot OEt_2$ (125.6 uL, 1.0 mmol) was added to the stirred mixture at −20°C. The reaction mixture was stirred at −20°C until TLC revealed full conversion of acceptor (30–45 min). The reaction was quenched with Et_3N, and the solid was then filtered off. The filtrate was concentrated under vacuum, and the syrupy residue was purified by column chromatography on silica gel.

(2S,3R,4E)-[2′,3′,6′-Tri-O-benzoyl-4-O-(2″,3″,4″,6″-Tetra-O-benzoyl-β-D-galactopyranosyl)-β-D-glucopyranosyl]-(1′ → 1)-2-azido-3-benzoyl-4-octadecene-1,3-diol (4b). Following the above-mentioned general procedure, coupling of **3** (100 mg, 0.23 mmol) with **4a** (368 mg, 0.30 mmol) afforded **4b** (310 mg, 90.0%) as a colorless oil. R_f 0.38 (3:1 petroleum ether-EtOAc); $[\alpha]_D^{20} + 22.1^\circ$ (c 1.38, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.15–8.01 (40 H, Ar-H), 5.82 (t, 1 H, $J = 9.1$ Hz, H-3″), 5.69–5.75 (m, 2 H, H-2′, H-4′), 5.69 (dt, 1 H, $J = 15.2$, 6.8 Hz, H-5), 5.49–5.53 (m, H-3, H-2″), 5.39–5.44 (m, 2 H, H-4, H-3′), 4.89 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.75 (d, 1 H, $J = 7.8$ Hz, H-1″), 4.58 (dd, 1 H, $J = 12.3$, 1.8 Hz, H-6a″), 4.48 (dd, 1 H, $J = 12.3$, 4.1 Hz, H-6b″), 4.29 (t, 1 H, $J = 9.7$ Hz, H-4″), 3.90–3.92 (m, 2 H, H-2, H-6a″), 3.85–3.87 (m, 2 H, H-5″, H-6b′), 3.70–3.75 (m, 2 H, H-1), 3.54–3.57 (m, 1 H, H-5′), 1.87–1.90

(m, 2 H, CH_2=CH-C$\underline{H}_2$), 1.32–1.34 (m, 2 H, CH_2-Alkyl), 1.20–1.25 (m, 20 H, 10 CH_2-Alkyl), 0.88 (t, 3 H, J = 6.8 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 165.8, 165.5, 165.4, 165.3, 165.2, 165.0, 164.9, 164.8 (8 C=O), 138.9 (C-5), 133.5, 133.4 (2 C), 133.3, 133.2 (3 C), 133.0 (Ar-C), 128.2–129.9 (Ar-C), 122.3 (C-4), 100.9, 100.7, 75.8, 74.7, 73.0, 72.8, 71.7, 71.5, 71.3, 69.8, 68.2, 67.5, 63.3, 62.2, 61.0, 46.3 (C-6), 32.2 (C-7), 31.9 (C-8), 22.5–29.6 (C-9, C-10, C-11, C-12, C-13, C-14, C-15, C-16), 22.6 (C-17), 14.1 (C-18). HRMS calcd. for $C_{86}H_{87}N_3O_{20}$ $[M + Na]^+$ 1504.6, found: 1504.8.

(2S,3R,4E)-2′,3′,4′,6′-Tetra-O-benzoyl-β-D-glucopyranosyl-(1′ → 1)-2-azido-3-benzoyl-4-octadecene-1,3-diol (5b). Following the above-mentioned general procedure, coupling of **3** (100 mg, 0.23 mmol) with **5a** (222 mg, 0.30 mmol) afforded **5b** (223 mg, 95.0%) as a colorless oil. R_f 0.36 (5:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ −7.39° (c 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.26–8.02 (25 H, Ar-H), 5.92 (t, 1 H, J = 9.6 Hz, H-3′), 5.73 (dt, 1 H, J = 15.1, 6.9 Hz, H-5), 5.70 (t, 1 H, J = 9.6 Hz, H-4′), 5.57–5.60 (m, 2 H, H-3, H-2′), 5.47 (dd, 1 H, J = 15.1, 8.3 Hz, H-4), 4.90 (d, 1 H, J = 7.7 Hz, H-1′), 4.62 (dd, 1 H, J = 12.1, 3.2 Hz, H-6a′), 4.48 (dd, 1 H, J = 12.1, 5.5 Hz, H-6b′), 4.16–4.19 (m, 1 H, H-5′), 3.95–3.98 (m, 2 H, H-2, H-1a), 3.66 (dd, 1 H, J = 12.8, 8.7 Hz, H-1b), 1.90–1.94 (m, 2 H, CH_2=CH-C$\underline{H}_2$), 1.22–1.30 (m, 22 H, 11 CH_2-Alkyl), 0.88 (t, 3 H, J = 6.9 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 166.0, 165.7, 165.1, 164.9 (2 C) (5 C=O), 139.0 (C-5), 133.4, 133.2 (2 C), 133.1, 133.0 (Ar-C), 128.2–129.9 (Ar-C), 122.4 (C-4), 100.9 (C-1′), 74.7, 72.7, 72.4, 71.6, 69.5, 68.2, 63.4, 63.0, 46.8 (C-6), 32.2 (C-7), 31.9 (C-8), 28.6–29.6 (C-9, C-10, C-11, C-12, C-13, C-14, C-15, C-16), 22.6 (C-17), 14.1 (C-18). HRMS calcd. for $C_{58}H_{65}N_3O_{12}$ $[M + Na]^+$ 1030.5, found: 1030.9.

(2S,3R,4E)-2′, 3′, 4′, 6′-Tetra-O-benzoyl-α-D-mannopyranosyl-(1′ → 1)-2-azido-3-benzoyl-4-octadecene-1,3-diol (6b). Following the above-mentioned general procedure, coupling of **3** (100 mg, 0.23 mmol) with **6a** (222 mg, 0.3 mmol) afforded **6b** (234 mg, 100.0%) as a colorless oil. R_f 0.38 (5:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ −43.5° (c 0.25, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.25–8.10 (25 H, Ar-H), 6.13 (t, 1 H, J = 10.1 Hz, H-4′), 5.92–5.95 (m, 2 H, H-5, H-3′), 5.76 (dd, 1 H, J = 3.2, 1.8 Hz, H-2′), 5.59–5.65 (m, 2 H, H-3, H-4), 5.17 (d, 1 H, J = 1.8, H-1′), 4.70 (dd, 1 H, J = 12.1, 2.3 Hz, H-6a′), 4.51 (dd, 1 H, J = 12.1, 4.6 Hz, H-6b′), 4.44–4.47 (m, 1 H, H-5′), 4.12–4.14 (m, 1 H, H-2), 3.99 (dd, 1 H, J = 10.5, 3.7 Hz, H-1a), 3.64 (dd, 1 H, J = 10.5, 8.2 Hz, H-1b), 2.05–2.08 (m, 2 H, CH_2=CH-C$\underline{H}_2$), 1.34–1.39 (m, 2 H, CH_2-Alkyl), 1.21–1.30 (m, 20 H, 10 CH_2-Alkyl), 0.87 (t, 3 H, J = 7.4 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 166.1, 165.5, 165.3 (3 C) (5 C=O), 139.2 (C-5), 133.5 (2 C), 133.3, 133.3, 133.1 (Ar-C), 128.3–130.0 (Ar-C), 122.8 (C-4), 98.5 (C-1′), 74.8 (C-3), 70.2 (C-2), 69.7 (C-3′), 69.3 (C-5′), 68.2 (C-1), 66.8 (C-4′), 63.9 (C-2), 62.7 (C-6′), 47.0 (C-6), 32.4 (C-7), 31.9 (C-8), 28.7–29.7 (C-9, C-10, C-11, C-12, C-13, C-14,

C-15, C-16), 22.7 (C-17), 14.1 (C-18). HRMS calcd. for $C_{58}H_{65}N_3O_{12}$ $[M + Na]^+$ 1030.5, found: 1030.6.

(2S,3R,4E)-2′,3′,4′-Tri-O-benzoyl-α-L-arabinopyranosyl-(1′ → 1)-2-azido-3-benzoyl-4-octadecene-1,3-diol (7b). Following the above-mentioned general procedure, coupling of **3** (130 mg, 0.30 mmol) with **7a** (291 mg, 0.39 mmol) afforded **7b** (300 mg, 98.4%) as a colorless oil. R_f 0.34 (5:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ −11.3° (c 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.26–8.13 (20 H, Ar-H), 5.93 (dt, 1 H, J = 15.6, 6.4 Hz, H-5), 5.69 (dd, 1 H, J = 7.3, 5.0 Hz, H-3), 5.57–5.62 (m, 2 H, H-4, H-4′), 5.55 (s, 1 H, H-3′), 5.29 (s, 1 H, H-1′), 4.81 (dd, 1 H, J = 9.6, 3.6 Hz, H-5a′), 4.66 (s, 1 H, H-2′), 4.65 (dd, 1 H, J = 9.6, 3.2 Hz, H-5b′), 3.99–4.02 (m, 1 H, H-2), 3.93 (dd, 1 H, J = 9.6, 8.2 Hz, H-1a′), 3.70 (dd, 1 H, J = 9.6, 4.1 Hz, H-1b′), 2.05–2.08 (m, 2 H, CH_2=CH-C$\underline{H}_2$), 1.35–1.37 (m, 2 H, CH_2-Alkyl), 1.23–1.29 (m, 20 H, 10 CH_2-Alkyl), 0.87 (t, 3 H, J = 6.8 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 166.2, 165.9, 165.4, 165.1 (4 C=O), 138.9 (C-5), 133.5 (2 C), 133.2, 133.0 (Ar-C), 128.3–130.0 (Ar-C), 122.9 (C-4), 105.9 (C-1′), 82.1 (C-3′), 81.4 (C-2′), 77.6 (C-4′), 74.5 (C-3), 66.7 (C-1), 63.5 (C-2, C-5′), 32.4 (C-6), 31.9 (C-7), 28.7–29.6 (C-8, C-9, C-10, C-11, C-12, C-13, C-14, C-15, C-16), 22.7 (C-17), 14.1 (C-18); HRMS calcd. for $C_{51}H_{59}N_3O_{10}$ $[M + Na]^+$ 896.4, found: 896.8.

(2S,3R,4E)-2′,3′,4′,6′-Tetra-O-benzoyl-β-D-galactopyranosyl-(1′ → 1)-2-azido-3-benzoyl-4-octadecene-1,3-diol (8b). Following the above-mentioned general procedure, coupling of **3** (130 mg, 0.30 mmol) with **8a** (291 mg, 0.39 mmol) afforded **8b** (300 mg, 98.4%) as a colorless oil. R_f 0.34 (5:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ +32.9° (c 0.52, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.23–8.11 (25 H, Ar-H), 5.99 (d, 1 H, J = 3.8, H-4′), 5.83 (dd, 1 H, J = 9.6, 7.8 Hz, H-2′), 5.73 (dt, 1 H, J = 15.1, 6.9 Hz, H-5), 5.62 (dd, 1 H, J = 9.6, 3.7 Hz, H-3′), 5.60 (dd, 1 H, J = 7.3, 4.1 Hz, H-3), 5.49 (dd, 1 H, J = 15.1, 8.3 Hz, H-4), 4.87 (d, 1 H, J = 7.7 Hz, H-1′), 4.63 (dd, 1 H, J = 11.0, 6.4 Hz, H-6a′), 4.38 (dd, 1 H, J = 11.0, 6.8 Hz, H-6b′), 4.33 (dd, 1 H, J = 6.8, 6.4 Hz, H-5′), 4.03 (dd, 1 H, J = 9.6, 6.9 Hz, H-1a), 3.98–4.00 (m, 1 H, H-2), 3.69 (dd, 1 H, J = 9.6, 5.5 Hz, H-1b), 1.92–1.94 (m, 2 H, CH_2=CH-C$\underline{H}_2$), 1.21–1.30 (m, 22 H, 11 CH_2-Alkyl), 0.88 (t, 3 H, J = 6.9 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 166.0, 165.5(2 C), 165.0 (2 C) (5 C=O), 139.0 (H-5), 133.6, 133.3 (2 C), 133.2, 133.1 (Ar-C), 128.3–130.1 (Ar-C), 122.5 (H-4), 101.2 (C-1′), 74.7, 71.6, 71.4, 69.6, 68.1, 67.9, 63.4, 61.8, 32.3 (C-6), 31.9 (C-7), 28.6–29.6 (C-8, C-9, C-10, C-11, C-12, C-13, C-14, C-15, C-16), 22.7 (C-17), 14.1 (C-18). HRMS calcd. for $C_{58}H_{65}N_3O_{12}$ $[M + Na]^+$ 1030.5, found: 1030.9.

(2S,3R,4E)-2′,3′,4′-Tri-O-acetyl-α-L-rhamnopyranosyl-(1′ → 1)-2-azido-3-benzoyl-4-octadecene-1,3-diol (9b). Following the above-mentioned general procedure, coupling of **3** (100 mg, 0.23 mmol) with **9a** (130 mg, 0.30 mmol)

afforded (160 mg, 98.2%) as a colorless oil. R_f 0.24 (5:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ −45.9° (c 0.82, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.05–8.06 (m, 2 H, Ar-H), 7.57–7.60 (m, 1 H, Ar-H), 7.45–7.48 (m, 2 H, Ar-H), 5.95 (dt, 1 H, J = 14.6, 6.8 Hz, H-5), 5.54–5.60 (m, 2 H, H-3, H-4), 5.30 (dd, 1 H, J = 10.1, 3.2 Hz, H-3′), 5.28 (dd, 1 H, J = 3.2, 1.4 Hz, H-2′), 5.08 (t, 1 H, J = 10.1 Hz, H-4′), 4.75 (d, 1 H, J = 1.4 Hz, H-1′), 3.95–3.98 (m, 1 H, H-2), 3.88–3.93 (m, 1 H, H-5′), 3.76 (dd, 1 H, J = 10.1, 8.2 Hz, H-1a), 3.62 (dd, 1 H, J = 10.1, 4.1 Hz, H-1b), 2.15 (s, 3 H, CH_3-Acetyl), 2.06–2.10 (m, 2 H, CH_2=CH-C$\underline{H}_2$), 2.06 (s, 3 H, CH_3-Acetyl), 2.00 (s, 3 H, CH_3-Acetyl), 1.37–1.39 (m, 2 H, CH_2-Alkyl), 1.24–1.30 (m, 20 H, 10 CH_2-Alkyl), 1.18 (d, 3 H, J = 5.9 Hz, H-6′), 0.88 (t, 3 H, J = 6.8 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 170.1 (2 C), 169.8, 165.1 (4 C=O), 138.9 (C-5), 133.3, 129.7 (3 C), 128.5 (2 C) (Ar-C), 123.0 (C-4), 97.5 (C-1′), 74.4, 70.7, 69.6, 68.9, 67.3, 66.8, 63.5, 32.3, 31.9, 28.6–29.6 (C-8, C-9, C-10, C-11, C-12, C-13, C-14, C-15, C-16), 22.7 (C-17), 20.7, 20.8, 20.7, 17.3 (C-6′), 14.1 (C-18). HRMS calcd. for $C_{37}H_{59}N_3O_{10}$ $[M + Na]^+$ 724.4, found: 724.5.

(2S,3R,4E)-2′,3′,4′-Tri-O-benzoyl-β-L-fucopyranosyl-(1′ → 1)-2-azido-3-benzoyl-4-octadecene-1,3-diol (10b). Following the above-mentioned general procedure, coupling of **3** (100 mg, 0.23 mmol) with **10a** (186 mg, 0.30 mmol) afforded **10b** (200 mg, 97.1%) as a colorless oil. R_f 0.13 (5:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ −108.8° (c 0.40, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.23–8.10 (20 H, Ar-H), 5.84–5.88 (m, 1 H, H-5), 5.78 (dd, 1 H, J = 10.6, 7.8 Hz, H-2′), 5.72 (d, 1 H, J = 3.5 Hz, H-4′), 5.53 (dd, 1 H, J = 10.6, 3.5 Hz, H-3′), 5.51–5.53 (m, 1 H, H-5′), 5.51 (dd, 1 H, J = 14.1, 7.7 Hz, H-4), 4.85 (d, 1 H, J = 7.8 Hz, H-1′), 4.08–4.12 (m, 2 H, H-2, H-1a), 3.95–3.98 (m, 1 H, H-3), 3.59 (dd, 1 H, J = 11.0, 8.3 Hz, H-1b), 2.01–2.05 (m, 2 H, CH_2=CH-C$\underline{H}_2$), 1.35 (d, 3 H, J = 6.4 Hz, H-6′), 1.23–1.30 (m, 22 H, 11 CH_2-Alkyl), 0.88 (t, 3 H, J = 6.9 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 166.0, 165.7, 165.3, 165.1 (4 C=O), 138.7 (C-5), 133.4, 133.2 (2 C), 133.1 (Ar-C), 128.2–130.0 (Ar-C), 122.9 (C-4), 101.6 (C-1′), 74.6, 72.1, 70.9, 69.9, 69.5, 68.9, 64.3, 32.3, 31.9, 28.6–29.2 (C-8, C-9, C-10, C-11, C-12, C-13, C-14, C-15, C-16), 22.7 (C-17), 16.3 (C-6′), 14.1 (C-18′). HRMS calcd. for $C_{52}H_{61}N_3O_{10}$ $[M + Na]^+$ 910.4, found: 910.7.

General Procedure for the Syntheses of Amides 4d–10d

PPh_3 (3.0 mol) and water (0.02 mol) were added to a stirred solution of azide (1.0 mol) in THF (60 mL), and the mixture was heated at 45°C until TLC indicated the complete transformation of the starting azide into corresponding amine (**4c–10c**, about 6 h). After rotary evaporation, the amine residue was redissolved in dry CH_2Cl_2 (60 mL), and Et_3N (1.5 mol), EDC · HCl (1.3 mol), HOBt (1.3 mol), and palmitic acid (1.0 mol) were added.

The reaction mixture was stirred at rt for 10 h. The solution was concentrated under vacuum, and the syrupy residue was purified by column chromatography on silica gel.

(2S,3R,4E)-[2′,3′,6′-Tri-O-benzoyl-4-O-(2″,3″,4″,6″-tetra-O-benzoyl-β-D-galactopyanosyl)-β-D-glucopyranosyl]-(1′ → 1)-2-(hexadecanoylamido)-3-benzoyl-4-octadecene-1,3-diol (4d). **4b** (518 mg, 0.35 mmol) was treated accordingly to the corresponding general procedure to afford **4d** (405 mg, 68.4% for two steps) as a colorless oil. R_f 0.14 (5:1 petroleum ether-EtOAc); $[\alpha]_D^{20} + 27.8^\circ$ (c 0.60, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.16–8.00 (m, 40 H, Ar-H), 5.80 (t, 1 H, $J = 9.6$ Hz, H-3′), 5.78 (dt, 1 H, $J = 15.1$, 6.9 Hz, H-5), 5.73 (d, 1H, $J = 3.5$ Hz, H-4″), 5.69 (dd, 1 H, $J = 10.1$, 7.8 Hz, H-2″), 5.63 (d, 1 H, $J = 9.7$ Hz, N-H), 5.49 (t, 1 H, $J = 7.8$ Hz, H-3), 5.43 (dd, 1 H, $J = 9.6$, 7.8 Hz, H-2′), 5.41 (dd, 1 H, $J = 15.1$, 7.3 Hz, H-4), 5.36 (dd, 1 H, $J = 10.1$, 3.5 Hz, H-3″), 4.83 (d, 1 H, $J = 7.8$ Hz, H-1″), 4.65 (d, 1 H, $J = 7.8$ Hz, H-1″), 4.39–4.21 (m, 2 H, H-1), 4.36–4.38 (m, 1 H, H-2), 4.21 (t, 1 H, $J = 9.6$ Hz, H-4′), 4.09 (dd, 1 H, $J = 9.7$, 2.8 Hz, H-6a′), 3.87 (t, 1 H, $J = 6.8$ Hz, H-5″), 3.74–3.78 (m, 2 H, H-5′, H-6a″), 3.67 (dd, 1 H, $J = 11.5$, 6.8 Hz, H-6b″), 3.57 (dd, 1 H, $J = 9.6$, 3.7 Hz, H-6b′), 1.92–1.96 (m, 2 H, CH_2-CO), 1.76–1.79 (m, 2 H, CH = CH-C$\underline{H}_2$), 1.33–1.39 (m, 2 H, CH_2-Alkyl), 1.16–1.26 (m, 44 H, 22 CH_2-Alkyl), 1.08–1.11 (m, 2 H, CH_2-Alkyl), 0.86–0.89 (m, 6 H, 2 CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 172.6 (NC═O), 165.7, 165.5, 165.4, 165.3, 165.2 (2 C), 165.1, 164.8 (8 C═O), 137.3 (C-5), 133.5, 133.4 (2 C), 133.3 (2 C), 133.2 (2 C), 132.8 (Ar-C), 128.2–130.1 (Ar-C), 124.8 (C-4), 100.9 (2 C) (C-1′, C-1″), 75.7, 74.0, 73.0, 72.5, 72.1, 71.7, 71.3, 69.8, 67.6, 67.4, 65.9, 62.2, 61.0, 50.4, 36.4, 32.3, 31.9, 28.9–29.7 (21 C), 25.5, 22.7, 14.1. HRMS calcd. for $C_{102}H_{119}NO_{21}$ $[M + Na]^+$ 1716.8, found: 1717.6.

(2S,3R,4E)-2′,3′,4′,6′-Tetra-O-benzoyl-β-D-glucopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-3- benzoyl-4-octadecene-1,3-diol (5d). **5b** (182 mg, 0.18 mmol) was treated accordingly to the corresponding general procedure to afford **5d** (160 mg, 72.4% for two steps) as a white solid. R_f 0.15 (3:1 petroleum ether-EtOAc); $[\alpha]_D^{20} + 5.98^\circ$ (c 0.31, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.27–8.01 (25 H, Ar-H), 5.92 (t, 1 H, $J = 9.6$ Hz, H-3′), 5.84 (dt, 1 H, $J = 15.1$, 6.9 Hz, H-5), 5.74 (d, 1 H, $J = 9.1$ Hz, N-H), 5.64 (t, 1 H, $J = 9.6$ Hz, H-4′), 5.56 (t, 1 H, $J = 7.3$ Hz, H-3), 5.49 (dd, 1 H, $J = 9.6$, 7.8 Hz, H-2′), 5.46 (dd, 1 H, $J = 15.1$, 7.8 Hz, H-4), 4.81 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.44–4.48 (m, 2 H, H-2, H6a′), 4.33 (dd, 1 H, $J = 12.4$, 5.0 Hz, H-6b′), 4.18 (dd, 1 H, $J = 9.6$, 3.2 Hz, H-1a), 4.09–4.11 (m, 1 H, H-5′), 3.69 (dd, 1 H, $J = 9.6$, 4.4 Hz, H-1b), 1.96–1.99 (m, 2 H, CH_2-CO), 1.81–1.84 (m, 2 H, CH═CH-C$\underline{H}_2$), 1.38–1.42 (m, 2 H, CH_2-Alkyl), 1.22–1.30 (m, 44 H, 22 CH_2-Alkyl), 1.09–1.14 (2 H, m, CH_2-Alkyl), 0.86–0.89 (m, 6 H, 2 CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 172.7 (NC═O), 166.0, 165.7, 165.2 (2 C), 165.1 (C═O), 137.4 (C-5), 133.5, 133.4,

133.3, 133.1, 132.9 (Ar-C), 128.3–130.2 (25 C), 124.8 (C-4), 100.9 (C-1′), 74.1, 72.5, 72.3, 72.2, 69.5, 67.5, 62.9, 50.5, 36.5, 32.3, 31.9, 28.9–29.7 (22 C), 25.5, 22.7, 14.1. HRMS S calcd. for $C_{75}H_{97}NO_{13}$ $[M + Na]^+$ 1242.7, found: 1242.8.

(2S,3R,4E)-2′,3′,4′,6′-Tetra-O-benzoyl-α-D-mannopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-3-benzoyl-4-octadecene-1,3-diol (6d). **6b** (217 mg, 0.22 mmol) was treated accordingly to the corresponding general procedure to afford **6d** (133 mg, 50.6% for two steps) as a colorless oil. R_f 0.15 (3:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ −23.2° (c 0.33, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.26–8.09 (25 H, Ar-H), 6.08 (t, 1 H, J = 9.9 Hz, H-4′), 6.00 (d, 1 H, J = 9.2 Hz, N-H), 5.95 (dt, 1 H, J = 15.2, 6.6 Hz, H-5), 5.88 (dd, 1 H, J = 9.9, 3.3 Hz, H-3′), 5.71 (dd, 1 H, J = 3.3, 1.5 Hz, H-2′), 5.68 (t, 1 H, J = 6.8 Hz, H-3), 5.59 (dd, 1 H, J = 15.2, 6.8 Hz, H-4), 5.08 (d, 1 H, J = 1.5 Hz, H-1′), 4.63–4.66 (m, 2 H, H-2, H-6a′), 4.42–4.48 (m, 2 H, H-5′, H-6b′), 4.02 (dd, 1 H, J = 10.4, 4.4 Hz, H-1a), 3.82 (dd, 1 H, J = 10.4, 4.3 Hz, H-1b), 2.26–2.33 (m, 2 H, CH_2-CO), 2.06–2.09 (m, 2 H, CH=CH-C$\underline{H}_2$), 1.66–1.71 (m, 2 H, CH_2-Alkyl), 1.32–1.38 (m, 2 H, CH_2-Alkyl), 1.19–1.25 (m, 44 H, 22 CH_2-Alkyl), 0.88 (t, 3 H, J = 7.0 Hz, CH_3-Alkyl), 0.87 (t, 3 H, J = 7.3 Hz, CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 173.0 (NC=O), 166.1, 165.5, 165.4 (2 C), 165.2 (C=O), 137.6 (C-5), 133.5 (2 C), 133.2 (2 C), 133.1, 128.3–129.9 (25 C), 124.5 (C-4), 98.4 (C-1), 74.8, 70.1, 69.9, 69.2, 67.2, 66.8, 62.6, 51.3, 37.0, 32.4, 31.9, 28.9–29.7 (22 C), 25.8, 22.7, 14.1. HRMS calcd. for $C_{75}H_{97}NO_{13}$ $[M + Na]^+$ 1242.7, found: 1242.9.

(2S,3R,4E)-2′,3′,4′-Tri-O-benzoyl-α-L-arabinopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-3-benzoyl-4-octadecene-1,3-diol (7d). **7b** (133 mg, 0.15 mmol) was treated accordingly to the corresponding general procedure to afford **7d** (133 mg, 71.2% for two steps) as a yellow powder. R_f 0.35 (3:1 petroleum ether-EtOAc); $[\alpha]_D^{20}$ + 7.32° (c 0.32, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.26–8.18 (20 H, Ar-H), 6.00 (d, 1 H, J = 9.6 Hz, N-H), 5.83 (dt, 1 H, J = 15.1, 6.9 Hz, H-5), 5.63 (t, 1 H, J = 8.2 Hz, H-3), 5.60 (dd, 1 H, J = 5.0, 1.4 Hz, H-3′), 5.53 (dd, 1 H, J = 15.1, 8.2 Hz, H-4), 5.51 (d, 1 H, J = 1.4 Hz, H-2′), 5.20 (s, 1 H, H-1′), 4.59–4.61 (m, 1 H, H-2), 4.58 (dd, 1 H, J = 11.9, 3.7 Hz, H-5a′), 4.53 (dd, 1 H, J = 8.7, 4.6 Hz, H-4′), 4.49 (dd, 1 H, J = 11.5, 4.6 Hz, H-5b′), 4.13 (dd, 1 H, J = 10.1, 2.3 Hz, H-1a), 3.55 (dd, 1 H, J = 10.1, 3.2 Hz, H-1b), 2.15–2.24 (m, 2 H, CH_2-CO), 1.98–2.02 (m, 2 H, CH=CH-C$\underline{H}_2$), 1.58–1.64 (m, 2 H, CH_2-Alkyl), 1.23–1.32 (m, 46 H, 23 CH_2-Alkyl), 0.88 (t, 6 H, J = 6.9 Hz, 2 CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 172.8 (NC=O), 166.1, 165.8, 165.7, 165.3 (C=O), 138.0 (C-5), 133.6, 133.5, 133.1, 133.0 (Ar-C), 128.3–130.2 (20 C, Ar-C), 125.2 (C-4), 106.2 (C-1′), 82.5, 80.3, 77.4, 73.9, 66.3, 63.2, 50.4, 36.9, 32.3, 31.9, 28.9–29.7 (22 C), 25.8, 22.7, 14.1. HRMS calcd. for $C_{67}H_{91}NO_{11}$ $[M + Na]^+$ 1108.7, found: 1109.0.

(2S,3R,4E)-2′,3′,4′,6′-Tetra-O-benzoyl-β-D-galactopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-3-benzoyl-4-octadecene-1,3-diol (8d). **8b** (270 mg, 0.27 mmol) was treated accordingly to the corresponding general procedure to afford **8d** (232 mg, 70.9% for two steps) as a colorless oil. $\boldsymbol{R}_f$ 0.29 (3:1 petroleum ether-EtOAc); $[\alpha]_D^{20} + 40.2^\circ$ (c 0.72, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.23–8.13 (25 H, Ar-H), 5.94 (d, 1 H, $J = 3.5$ Hz, H-4′), 5.88 (dt, 1 H, $J = 15.1$, 6.8 Hz, H-5), 5.74 (dd, 1 H, $J = 9.7$, 7.8 Hz, H-2′), 5.73 (d, 1 H, $J = 8.7$ Hz, N-H), 5.63 (dd, 1 H, $J = 9.7$, 3.5 Hz, H-3′), 5.59 (t, 1 H, $J = 7.5$ Hz, H-3), 5.50 (dd, 1 H, $J = 15.1$, 7.5 Hz, H-4), 4.79 (d, 1 H, $J = 7.8$ Hz, H-1′), 4.49–4.53 (m, 1 H, H-2), 4.34 (dd, 1 H, $J = 11.0$, 6.4 Hz, H-6a′), 4.27 (dd, 1 H, $J = 9.1$, 3.5 Hz, H-1a), 4.24 (t, 1 H, $J = 6.4$ Hz, H-5′), 4.18 (dd, 1 H, $J = 11.0$, 6.4 Hz, H-6b′), 3.69 (dd, 1 H, $J = 9.1$, 3.5 Hz, H-1b), 1.99–2.02 (m, 2 H, CH_2-CO), 1.80–1.83 (m, 2 H, CH=CH-C$\underline{H}_2$), 1.37–1.45 (m, 2 H, CH_2-Alkyl), 1.23–1.32 (m, 46 H, 23 CH_2-Alkyl), 0.88 (t, 6 H, $J = 6.8$ Hz, 2 CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 172.6 (NC=O), 165.8, 165.4 (2 C), 165.4, 165.1 (C=O), 137.4 (C-5), 133.6, 133.5, 133.3, 133.2, 132.9, 128.2–130.3 (25 C), 124.9 (C-4), 101.0 (C-1′), 74.0, 71.3, 71.2 (3 C), 67.8, 67.3, 61.6, 50.5, 36.5, 32.3, 31.9, 28.9–29.7 (21 C), 25.5, 22.7, 14.1. HRMS calcd. for $C_{75}H_{97}NO_{13}$ $[M + Na]^+$ 1242.7, found: 1242.8.

(2S,3R,4E)-2′,3′,4′-Tri-O-acetyl-α-L-rhamnopyranosyl-(1′ → 1)-2-(hexadecaneoylamido)-3-benzoyl-4-octadecene-1,3-diol (9d). **9b** (140 mg, 0.20 mmol) was treated accordingly to the corresponding general procedure to afford **9d** (168 mg, 72.2% for two steps) as a colorless oil. $\boldsymbol{R}_f$ 0.40 (3:1 petroleum ether-EtOAc); $[\alpha]_D^{20} -15.3^\circ$ (c 0.33, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.03–8.04 (m, 2 H, Ar-H), 7.55–7.58 (m, 1 H, Ar-H), 7.43–7.46 (m, 2 H, Ar-H), 5.94 (dt, 1 H, $J = 15.1$, 7.3 Hz, H-5), 5.84 (d, 1 H, $J = 9.7$ Hz, N-H), 5.48–5.56 (m, 2 H, H-3, H-4), 5.33 (dd, 1 H, $J = 3.7$, 1.8 Hz, H-2′), 5.21 (dd, 1 H, $J = 10.1$, 3.7 Hz, H-3′), 5.00 (t, 1 H, $J = 10.1$ Hz, H-4′), 4.67 (d, 1 H, $J = 1.8$ Hz, H-1′), 4.56–4.59 (m, 1 H, H-2), 3.99 (dd, 1 H, $J = 10.1$, 2.3 Hz, H-1a), 3.61–3.65 (m, 1 H, H-5′), 3.44 (dd, 1 H, $J = 10.1$, 3.2 Hz, H-1b), 2.18–2.26 (m, 2 H, CH_2-CO), 2.13 (s, 3 H, CH_3-Acetyl), 2.06 (s, 3 H, CH_3-Acetyl), 2.01–2.05 (m, 2 H, CH=CH-C$\underline{H}_2$), 2.00 (s, 3 H, CH_3-Acetyl), 1.62–1.65 (m, 2 H, CH_2-Alkyl), 1.23–1.34 (m, 46 H, 23 CH_2-Alkyl), 0.88 (t, 6 H, $J = 4.8$ Hz, 2 CH_3-Alkyl), 0.85 (d, 3 H, $J = 6.4$ Hz, H-6′). ^{13}C NMR ($CDCl_3$): δ 172.9 (NC=O), 170.1, 170.0 (2 C), 165.1, 138.6 (C-5), 133.2, 129.6, 128.4, 124.9, 97.7 (C-1′), 73.7, 70.4, 69.4, 69.3, 66.7, 66.6, 50.1, 36.9, 33.8, 32.3, 31.9, 28.9–29.7 (17 C), 25.8, 24.7, 22.7, 20.8 (2 C), 20.7, 16.9 (C-6′), 14.1.

(2S,3R,4E)-2′,3′,4′-Tri-O-benzoyl-β-L-fucopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-3-benzoyl-4-octadecene-1,3-diol (10d). **10b** (400 mg, 0.45 mmol) was treated accordingly to the corresponding general procedure to afford **10d** (309 mg, 61.6% for two steps) as a white solid. $\boldsymbol{R}_f$ 0.40 (3:1 petroleum

ether-EtOAc); $[\alpha]_D^{20}$ −64.9° (c 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.23–8.19 (20 H, Ar-H), 5.88 (d, 1 H, J = 9.2 Hz, N-H), 5.75 (dd, 1 H, J = 10.1, 7.8 Hz, H-2′), 5.70 (d, 1 H, J = 3.2 Hz, H-4′), 5.59 (dd, 1 H, J = 10.1, 3.2 Hz, H-3′), 5.33–5.39 (m, 2 H, H-3, H-4), 5.19 (dt, 1 H, J = 14.2, 6.9 Hz, H-5), 4.75 (d, 1 H, J = 7.8 Hz, H-1′), 4.40–4.44 (m, 1 H, H-2), 4.00–4.03 (m, 2 H, H-1a, H-5′), 3.79 (dd, 1 H, J = 10.5, 1.8 Hz, H-1b), 2.06–2.17 (m, 2 H, CH_2-CO), 1.78–1.80 (m, 2 H, CH═CH-C$\underline{H}_2$), 1.55–1.57 (m, 2 H, CH_2-Alkyl), 1.14–1.29 (m, 49 H, 23 CH_2-Alkyl, H-6′), 0.88 (t, 6 H, J = 6.8 Hz, 2 CH_3-Alkyl). ^{13}C NMR ($CDCl_3$): δ 172.7 (NC═O), 165.9, 165.7, 165.5, 165.1 (C═O), 137.7 (C-5), 133.4, 133.3, 133.2, 133.0, 128.2–130.2 (20 C), 124.8 (C-4), 101.7 (C-1′), 73.9, 71.7, 71.0, 69.9, 69.8, 67.8, 50.5, 36.9, 32.1, 31.9, 28.7–29.7 (22 C), 25.7, 22.7, 16.2, 14.1. HRMS calcd. for $C_{68}H_{93}NO_{11}$ $[M + Na]^+$ 1122.7, found: 1123.2.

General Procedure for the Syntheses of Target Glycolipids 4e–10e

The amide was dissolved in MeOH-CH_2Cl_2 (2:1, 6 mL), and then NaOMe in MeOH was added until pH was 9. After stirring at rt for 12 h, the solution was neutralized with ion-exchange resin (H^+) and then filtered. To the filtrate was added silica gel (100 mg), and the solvent was removed under vacuum. The resulting silica powder was loaded into a column and purified.

(2S,3R,4E)-[4-O-(β-D-Galactopyanosyl)-β-D-glucopyranosyl]-(1′ → 1)-2-(hexadecanoylamido)-4-octadecene-1,3-diol (4e). **4d** (100 mg, 0.06 mmol) was treated according to the general procedure for obtaining the target glycolipid to provide **4e** (39 mg, 76.2%) as a white solid. $\boldsymbol{R}_f$ 0.20 (5:1 $CHCl_3$-MeOH); $[\alpha]_D^{22}$ −5.4° (c 1.0, Pyridine); ^{1}H NMR (DMSO-d_6, 21.9°C): δ 7.54 (d, 1 H, J = 9.2 Hz, N-H), 5.52 (dt, 1 H, J = 15.1, 6.4 Hz, H-5), 5.35 (dd, 1 H, J = 15.1, 6.8 Hz, H-4), 5.16 (d, 1 H, J = 2.3 Hz, 2′-OH), 5.13 (d, 1 H, J = 2.2 Hz, 2″-OH), 4.90 (d, 1 H, J = 5.5 Hz, 3-OH), 4.84 (d, 1 H, J = 3.2 Hz, 3″-OH), 4.68–4.69 (m, 2 H, 3′-OH, 6″-OH), 4.60 (t, 1 H, J = 5.0 Hz, 6′-OH), 4.56 (d, 1 H, J = 4.1 Hz, 4″-OH), 4.20 (d, 1 H, J = 6.4 Hz, H-1″), 4.16 (d, 1 H, J = 7.8 Hz, H-1′), 3.98–4.00 (m, 1 H, H-1), 3.86–3.88 (m, 1 H, H-3), 3.73–3.78 (m, 2 H, H-2, H-6a′), 4.59–4.62 (m, 2 H, H-4′, H-6b′), 3.52–3.54 (m, 1 H, H-6a″), 3.48–3.50 (m, 1 H, H-6b″), 3.45–3.47 (m, 1 H, H-5″), 3.39–3.41 (m, 2 H, H-1, H-4″), 3.28–3.11 (m, 4 H, H-3″, H-5′, H-3′, H-2″), 3.03–3.05 (m, 1 H, H-2′), 2.01–2.03 (m, 2 H, CH_2-CO), 1.92–1.94 (m, 2 H, CH═CH-C$\underline{H}_2$), 1.43–1.45 (m, 2 H, CH_2-Alkyl), 1.28–1.31 (m, 46 H, 23 CH_2-Alkyl), 0.84–0.86 (m, 6 H, 2 CH_3-Alkyl). ^{13}C NMR (DMSO-d_6, 21.9°C): δ 171.8, 131.4 (2 C), 103.8, 103.5, 80.7, 79.2, 75.5, 74.8, 74.6, 73.2, 70.8, 70.7, 70.5, 69.2, 68.1, 62.8, 60.4, 60.3, 53.0, 45.7, 40.4, 35.6, 31.7, 31.3, 28.7–29.1 (18 C), 25.4, 22.1, 13.9. HRMS calcd. for $C_{46}H_{87}NO_{13}$ $[M + Na]^+$ 884.6034, found: 884.6070.

(2S,3R,4E)-β-D-Glucopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-4-octadecene-1,3-diol (5e). **5d** (50 mg, 0.04 mmol) was treated according to the general procedure for obtaining the target glycolipid to provide **5e** (25 mg, 86.4%) as a white solid. R_f 0.40 (3:1 $CHCl_3$-MeOH); $[\alpha]_D^{22}$ −9.1° (c 1, Pyridine), {Ref. [22] $[\alpha]_D^{22}$ −9.5° (c 1.0, Pyridine)}; ^{1}H NMR (DMSO-d_6, 22.3°C): δ 7.50 (d, 1 H, J = 9.2 Hz, N-H), 5.53 (dt, 1 H, J = 15.1, 6.8 Hz, H-5), 5.35 (dd, 1 H, J = 15.1, 7.3 Hz, H-4), 5.04 (d, 1 H, J = 1.9 Hz, 2′-OH), 4.95 (d, 1 H, J = 3.2 Hz, 3′-OH), 4.90 (d, 1 H, J = 4.1 Hz, 4′-OH), 4.88 (d, 1 H, J = 5.0 Hz, 3-OH), 4.51 (t, 1 H, J = 5.5 Hz, 6′-OH), 4.07 (d, 1 H, J = 7.8 Hz, H-1′), 3.97 (dd, 1 H, J = 10.5, 4.6 Hz, H-1a), 3.87 (d, 1 H, J = 13.3, 7.3 Hz, H-3), 3.75–3.79 (m, 1 H, H-2), 3.66 (dd, 1 H, J = 11.4, 5.0 Hz, H-6a′), 3.43 (dd, 1 H, J = 11.4, 5.9 Hz, H-6b′), 3.40 (dd, 1 H, J = 10.5, 3.7 Hz, H-1b), 3.13 (m, 1 H, H-3′), 3.04–3.09 (m, 2 H, H-4′, H-5′), 2.97 (m, 1 H, H-2′), 2.00–2.03 (m, 2 H, CH_2-CO), 1.90–1.95 (m, 2 H, CH=CH-C$\underline{H}_2$), 1.41–1.46 (m, 2 H, CH_2-Alkyl), 1.22–1.28 (m, 46 H, 23 CH_2-Alkyl), 0.83–0.86 (m, 6 H, 2 CH_3-Alkyl). ^{13}C NMR (DMSO-d_6, 22.3°C): δ 171.8 (NC=O), 131.5 (C-5), 131.4 (C-4), 103.8 (C-1′), 76.9 (C-5′), 76.3 (C-3′), 73.5 (C-2′), 70.7 (C-3), 70.0 (C-4′), 69.1 (C-1), 61.0 (C-6′), 53.0 (C-2), 35.6 ($\underline{C}H_2$-NCO), 31.8 (C-6), 31.3 (CH_2-Alkyl), 28.7–29.1 (22 C) (CH_2-Alkyl), 25.4 (CH_2-Alkyl), 22.1 (CH_3-Alkyl), 13.9 (CH_3-Alkyl). HRMS calcd. for $C_{40}H_{77}NO_8$ $[M + Na]^+$ 722.5518, found: 722.5541. Physical data of compound **5e** were in agreement with those reported in Ref. [37].

(2S,3R,4E)-α-D-Mannopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-4-octadecene-1,3-diol (6e). **6d** (40 mg, 0.03 mmol) was treated according to the general procedure for obtaining the target glycolipid to provide **6e** (20 mg, 85.0%) as a white solid. R_f 0.19 (10:1 $CHCl_3$-MeOH); $[\alpha]_D^{22}$ + 10.5° (c 0.65, Pyridine); ^{1}H NMR (DMSO-d_6, 22.3°C): δ 7.50 (d, 1 H, J = 8.7 Hz, N-H), 5.53 (dt, 1 H, J = 15.1, 6.4 Hz, H-5), 5.35 (dd, 1 H, J = 15.1, 6.8 Hz, H-4), 4.86 (d, 1 H, J = 6.4 Hz, 3-OH), 4.67 (brs, 2 H, 2′-OH, 3′-OH), 4.57 (brs, 1 H, H-1′), 4.52 (brs, 1 H, 4′-OH), 4.38 (m, 1 H, 6′-OH), 3.83–3.86 (m, 1 H, H-3), 3.74–3.79 (m, 1 H, H-2), 3.96 (dd, 1 H, J = 10.1, 4.1 Hz, H-1a), 3.58–3.61 (m, 2 H, H-2′, H-6a′), 3.35–3.50 (m, 4 H, H-3′, H-6b′, H-1b, H-4′), 3.26–3.29 (m, 1 H, H-5′), 2.00–2.02 (m, 2 H, CH-CO), 1.90–1.94 (m, 2 H, CH=CH-C$\underline{H}_2$), 1.40–1.46 (m, 2 H, CH_2-Alkyl), 1.18–1.30 (m, 46 H, 23 CH_2-Alkyl), 0.83–0.85 (m, 6 H, 2 CH_3-Alkyl). ^{13}C NMR (DMSO-*d*6, 22.3°C): δ 171.9 (NC=O), 131.2 (2 C), 100.6, 73.8, 71.0, 70.8, 70.3, 69.8, 66.9, 66.3, 61.1, 53.4, 35.5, 31.8, 31.3, 28.6–29.1 (19 C), 26.5, 25.4, 24.6, 22.1, 13.9. HRMS calcd. for $C_{40}H_{77}NO_8$ $[M + Na]^+$ 722.5521, found: 722.5541.

(2S,3R,4E)-α-L-Arabinopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-4-octadecene-1, 3-diol (7e). **7d** (60 mg, 0.06 mmol) was treated according to the general procedure for obtaining the target glycolipid to provide **7e** (31 mg, 83.0%) as a white solid. R_f 0.31 (15:1 $CHCl_3$-MeOH); $[\alpha]_D^{22}$ −6.9° (c 0.1,

Pyridine); ^{1}H NMR (DMSO-d_6-D_2O, 60°C): δ 5.55 (dt, 1 H, $J = 15.5$, 6.4 Hz, H-5), 5.38 (dd, 1 H, $J = 15.6$, 6.8 Hz, H-4), 4.71 (d, 1 H, $J = 1.4$ Hz, H-1′), 3.89 (t, 1 H, $J = 6.8$ Hz, H-3), 3.76–3.84 (m, 3 H, H-2, H-2′, H-4′), 3.65–3.68 (m, 2 H, H-1a, H-3′), 3.54 (dd, 1 H, $J = 11.5$, 3.7 Hz, H-5a′), 3.42–3.46 (m, 2 H, H-1b, H-5b′), 2.03–2.06 (m, 2 H, CH_2-CO), 1.92–1.96 (m, 2 H, CH = CH-C<u>H</u>$_2$), 1.44–1.49 (m, 2 H, CH_2-Alkyl), 1.19–1.31 (m, 46 H, 23 CH_2-Alkyl), 0.84–0.86 (m, 6 H, 2 CH_3-Alkyl). ^{13}C NMR (DMSO-d_6, 60°C): δ 171.8 (NC═O), 131.1 (C-5), 130.9 (C-4), 107.7 (C-1′), 84.0 (C-4′), 81.5 (C-2′), 76.9 (C-3′), 71.2 (C-3), 66.2 (C-1), 61.3 (C-5′), 52.9 (C-2), 35.5, 31.6, 31.2, 28.6–30.0 (22 C), 25.2, 21.9, 13.7. HRMS calcd. for $C_{39}H_{75}NO_7$ $[M + Na]^+$ 692.5418, found: 692.5436.

(2S,3R,4E)-β-D-Galactopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-4-octadecene-1, 3-diol (8e). **8d** (40 mg, 0.03 mmol) was treated according to the general procedure for obtaining the target glycolipid to provide **8e** (20 mg, 85.0%) as a white solid. R_f 0.31 (5:1 $CHCl_3$-MeOH); $[\alpha]_D^{22}$ −4.4° (c 1.0, Pyridine), Ref. [22] $[\alpha]_D^{22}$ −5.2° (c 1.0, Pyridine)}; ^{1}H NMR (DMSO-d_6-D_2O, 50°C): δ5.55 (1 H, dt, $J = 15.1$, 6.9 Hz, H-5), 5.38 (dd, 1 H, $J = 15.1$, 7.3 Hz, H-4), 4.05 (d, 1 H, $J = 7.3$ Hz, H-1′), 3.91–3.95 (m, 2 H, H-1a, H-3), 3.77–3.80 (m, 1 H, H-2), 3.65 (d, 1 H, $J = 3.2$ Hz, H-4′), 3.55 (dd, 1 H, $J = 11.0$, 5.9 Hz, H-6a′), 3.49 (dd, 1 H, $J = 11.0$, 6.0 Hz, H-6b′), 3.44 (dd, 1 H, $J = 10.1$, 4.1 Hz, H-1b), 3.31–3.34 (m, 2 H, H-2′, H-5′), 3.28 (dd, 1 H, $J = 9.2$, 3.2 Hz, H-3′), 2.02–2.04 (m, 2 H, CH_2-CO), 1.92–1.96 (m, 2 H, CH═CH-C<u>H</u>$_2$), 1.45–1.48 (m, 2 H, CH_2-Alkyl), 1.20–1.30 (m, 46 H, 23 CH_2-Alkyl), 0.86 (t, 6 H, $J = 6.9$ Hz, 2 CH_3-Alkyl). ^{13}C NMR (DMSO-d_6, 50°C): δ 171.7 (NC═O), 131.4, 131.3, 104.4, 75.2, 72.9, 70.6 (2 C), 70.5, 68.9, 68.0, 67.9, 60.3, 60.2, 52.9 (2 C), 35.5, 31.7, 31.2, 28.7–29.0 (18 C), 25.3, 22.1, 13.8. HRMS calcd. for $C_{40}H_{77}NO_8$ $[M + Na]^+$ 722.5551, found: 722.5541. Physical data of compound **8e** were in agreement with those reported in Ref. 23.

(2S,3R,4E)-α-L-Rhamnopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-4-octadecene-1, 3-diol (9e). **9d** (42 mg, 0.05 mmol) was treated according to the general procedure for obtaining the target glycolipid to provide **9e** (30 mg, 95.5%) as a white solid. R_f 0.13 (15:1 $CHCl_3$-MeOH); $[\alpha]_D^{22}$ −2.1° (c 0.25, Pyridine); ^{1}H NMR (DMSO-d_6, 26.3°C): δ 7.47 (d, 1 H, $J = 8.3$ Hz, N-H), 5.52 (dt, 1 H, $J = 15.1$, 6.9 Hz, H-5), 5.35 (dd, 1 H, $J = 15.1$, 6.4 Hz, H-4), 4.81 (dd, 1 H, $J = 5.0$ Hz, 3-OH), 4.67 (d, 1 H, $J = 4.6$ Hz, 2′-OH), 4.64 (d, 1 H, $J = 2.8$ Hz, 4′-OH), 4.48 (d, 1 H, $J < 1$ Hz, H-1′), 4.43 (d, 1 H, $J = 4.6$ Hz, 3′-OH), 3.79–3.82 (m, 2 H, H-2, H-3), 3.59–3.63 (m, 2 H, H-1a, H-2′), 3.43–3.45 (m, 1 H, H-1b), 3.38–3.40 (m, 1 H, H-5′), 3.37–3.38 (m, 1 H, H-3′), 3.15–3.18 (m, 1 H, H-4′), 1.99–2.04 (m, 2 H, CH_2-CO), 1.89–1.94 (m, 2 H, CH═CH-C<u>H</u>$_2$), 1.22–1.30 (m, 48 H, 24 CH_2-Alkyl), 1.11 (d, 3 H, $J = 6.4$ Hz, H-6′), 0.83–0.86 (m, 6 H, 2 CH_3-Alkyl). ^{13}C NMR (DMSO-d_6, 26.3°C): δ 171.7

(NC═O), 131.4, 131.1, 99.5, 72.0, 71.2, 70.7, 68.2, 65.7, 52.5, 52.4, 35.5 (2 C), 31.7, 31.3, 28.7–29.1 (20 C), 25.4, 22.1, 17.9, 13.9. HRMS calcd. for $C_{40}H_{77}NO_7$ $[M + Na]^+$ 706.5571, found: 706.5592.

(2S,3R,4E)-β-L-Fucopyranosyl-(1′ → 1)-2-(hexadecanoylamido)-4-octadecene-1,3- diol (10e). **10d** (75 mg, 0.07 mmol) was treated according to the general procedure for obtaining the target glycolipid to provide **10e** (40 mg, 85.1%) as a white solid. $\boldsymbol{R}_f$ 0.36 (10:1 $CHCl_3$-MeOH); $[\alpha]_D^{22}$ −7.4° (c 0.1, Pyridine); ^{1}H NMR (DMSO-d_6, 40°C): δ 7.30 (d, 1 H, $J = 8.7$ Hz, N-H), 5.54 (dt, 1 H, $J = 15.1$, 6.4 Hz, H-5), 5.36 (dd, 1 H, $J = 15.5$, 6.9 Hz, H-4), 4.77 (d, 1 H, $J = 5.0$ Hz, 3-OH), 4.60 (brs, 1 H, 3′-OH), 4.55 (brs, 1 H, 2′-OH), 4.30 (brs, 1 H, 4′-OH), 4.09 (apparent t, 1 H, $J = 3.7$ Hz, H-1′), 3.96 (dd, 1 H, $J = 12.4$, 6.4 Hz, H-3), 3.72–3.74 (m, 1 H, H-2), 3.66–2.68 (m, 2 H, H-1), 3.50 (q, 1 H, $J = 6.4$ Hz, H-5′), 3.40 (brs, 1 H, H-4′), 3.28 (brs, 1 H, H-3′), 3.26 (brs, 1 H, H-2′), 2.02–2.04 (m, 2 H, CH_2-CO), 1.91–1.94 (m, 2 H, CH═CH-C$\underline{H}_2$), 1.20–1.30 (m, 48 H, 24 CH_2-Alkyl), 1.13 (d, 3 H, $J = 6.4$ Hz, H-6), 0.85 (t, 6 H, $J = 6.4$ Hz, 2 CH_3-Alkyl). ^{13}C NMR (DMSO-d_6, 40°C): δ 171.6 (NC═O), 131.1, 130.9, 103.8, 73.3, 70.9, 70.6, 70.3, 69.9, 67.9, 53.3, 31.6, 31.2, 28.5–28.9 (22 C), 25.2, 21.9, 16.4, 13.7. HRMS calcd. for $C_{40}H_{77}NO_7$ $[M + Na]^+$ 706.5564, found: 706.5592.

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REFERENCES

[1] Butters, T.D.; Dwek, R.A.; Platt, F.M. Inhibition of glycosphingolipid biosynthesis: application to lysosomal storage disorders. Chem. Rev. **2000**, *100*, 4683–4696.

[2] Costantino, V.; Fattorusso, E.; Imperatore, C.; Mangoni, A. Glycolipids from sponges. Clarhamnoside, the first rhamnosylated α-galactosylceramide from *agelas clathrodes*. Improving spectral strategies for glycoconjugate structure determination. J. Org. Chem. **2004**, *69*, 1174–1179.

[3] Rao, C.S.; Lin, X.; Pike, H.M.; Molotkovsky, J.G.; Brown, R.E. Glycolipid transfer protein mediate transfer of glycosphingolipids between membranes: a model for action based on kinetic thermodynamic analyses. Biochemistry **2004**, *43*, 13805–13815.

[4] Kakugawa, Y.; Wada, T.; Yamaguchi, K.; Yamanami, H.; Oucho, I.; Miyagi, T. Up-regulation of plasma membrane-associated ganglioside sialidase (Neu3) in human colon cancer and its involvement in apoptosis suppression. Proc. Natl. Sat Acad. Sci. U.S.A. **2002**, *99*, 10718–10723.

[5] Nakajima, H.; Kiyokawa, N.; Katagiri, Y.U.; Taguchi, T.; Suzuki, T.; Sekino, T.; Mimori, K.; Ebata, T.; Saito, M.; Nakao, H.; Takeda, T.; Fujimoto, J. Kinetic

analysis of binding between Shiga toxin and receptor glycolipid Gb3Cer by surface plasmon resonance. J. Biol. Chem. **2001**, *276*, 42915–42922.

[6] Hannun, Y.A.; Bell, R.M. Functions of sphingolipids and sphingolipid breakdown products in cellular regulation. Science **1989**, *243*, 500–507.

[7] Karlsson, K.A. Glycobiology: a growing field for drug design. Trends Pharm. Sci. **1991**, *12*, 265–272.

[8] Kanemitsu, K.; Sweeley, C.C. Synthesis of double-labeled lactosylceramide. Glycoconjugate J. **1986**, *3*, 143–151.

[9] Lemieux, R.U. Haworth memorial lecture human blood groups and carbohydrate chemistry. Chem. Soc. Rev. **1978**, *7*, 423.

[10] Barrett, G.M.; Beall, J.C.; Braddock, D.C.; Flack, K. Asymmetric allylboration and ring closing alkene metathesis: a novel strategy for synthesis of glucosphingolipids. J. Org. Chem. **2000**, *65*, 6508–6514.

[11] Nolting, B.; Yu, J.J.; Liu, G.; Cho, S.J.; Kauzlarich, S.; Gervay, H.J. Synthesis of gold glyconanoparticles and biological evaluation of recombinant Gp120 interactions. Langmuir **2003**, *19*, 6465.

[12] Tang, W.; Seino, K.; Ito, M.; Konishi, T.; Senda, H.; Makuuchi, M.; Kojima, N.; Mizuochi, T. Requirement of ceramide for adhesion of helicobacter pylori to glycosphingolipids. FEBS Lett. **2001**, *504*, 31–35.

[13] Rai, A.N.; Basu, A. Synthesis of glycosphingolipid β-galactosyl ceramide and analogues *via* olefin cross metathesis. J. Org. Chem. **2005**, *70*, 8228–8230.

[14] Radin, N.S.; Inokuchi, J. Glucosphingolipids as sites of action in the chemotherapy of cancer. Biochem. Pharmacol. **1988**, *37*, 2879–2886.

[15] Mattjus, P.; Pike, H.M.; Molotkovsky, J.G.; Brown, R.E. Charged membrane surfaces impede the protein-mediated transfer of glycosphingolipids between phospholipid bilayers. Biochemistry **2000**, *39*, 1067–1075.

[16] Ohashi, K.; Kosai, S.; Arizuka, M.; Watanabe, T.; Fukunaga, M.; Monden, K.; Uchikoda, T.; Yamagiwa, Y.; Kamikawa, T. Synthesis of phosphonosphingoglycolipid found in marine snail turbo cornutus. Tetrahedron Lett. **1988**, *29*, 1189.

[17] Koike, K.; Sugimoto, M.; Sato, S.; Ito, Y.; Nakahara, Y.; Ogawa, Tomoya. Total synthesis of globotriaosyl-*E* and *Z*-ceramides and isoglobotriaosyl-*E*-ceramide. Carbohydr. Res. **1987**, *163*, 189–208.

[18] Duclos, R.I. Jr. The total synthesis of ganglioside GM3. Carbohydr. Res. **2000**, *328*, 489–507.

[19] Murakami, T.; Hirono, R.; Furusawa, K. Efficient stereocontrolled synthesis of sphingadienine derivatives. Tetrahedron **2005**, *61*, 9233–9241.

[20] Schmidt, R.R. New methods for the synthesis of glycosides and oligosaccharides—are there alternatives to the Koenigs-Knorr method? Angew. Chem. Int. Ed. Engl. **1986**, *25*, 212–235.

[21] Schmidt, R.R.; Zimmermann, P. Syntheses of glycosphingolipids and psychosinen. Angew. Chem. Int. Ed. Engl. **1986**, *25*, 725–726.

[22] Zimmermann, P.; Bommer, R.; Schmidt, R.R. Azido-sphingosine glycosylation in glycosphingolipid synthesis. J. Carbohydr. Chem. **1988**, *7*, 435–452.

[23] Nicolaou, K.C.; Caulfield, T.J.; Katoaka, H. Total synthesis of globotriaosylceramide (Gb_3) and lysoglobotriaosylceramide (lysoGb$_3$). Carbohydr. Res. **1990**, *202*, 177–191.

[24] Hansen, H.C.; Magnusson, G. Synthesis of selected aminodeoxy analogues of galabiose and globotriose. Carbohydr. Res. **1999**, *322*, 166–180.

[25] Takeda, Y.; Horito, S. Synthesis of α-series ganglioside GM1α containing C20-sphingosine. Carbohydr. Res. **2005**, *340*, 211–220.

[26] Li, Y.L.; Wu, Y.L. A facile stereoselective synthesis of sphingosine and ceramide. Liebigs Ann. **1996**, 2079–2082.

[27] Szabo, L.; Li, Y.; Polt, R. O-Glycopeptides: a simple β-stereoselective glycosidation of serine and threonine *via* a favorable hydrogen bonding pattern. Tetrahedron Lett. **1991**, *32*, 585–588.

[28] Du, W.; Gervay, H.J. Efficient synthesis of α-galactosyl ceramide analogues using glycosyl iodide donors. Organic Lett. **2005**, *7*, 2063–2065.

[29] Xing, G.; Wu, D.; Poles, M.A.; Horowitz, A.; Tsuji, M.; Ho, D.D.; Wong, C. Synthesis and human NKT cell stimulating properties of 3-O-sulfo-α/β-galactosyl ceramides. Bio. Med. Chem. **2005**, *13*, 2907–2916.

[30] Gu, G.; Du, Y.; Linhardt, R.J. Facile synthesis of saponins containing 2,3-branched oligosaccharides by using partially protected glycosyl donors. J. Org. Chem. **2004**, *69*, 5497–5500.

[31] Holland, C.V.; Horton, D.; Jewell, J.S. The favored conformation of tri-O-acetyl-β-D-xylopyranosyl chloride. An all-axial tetrasubstituted six-menber ring. J. Org. Chem. **1967**, *32*, 1818–1821.

[32] Paulsen, H.; Espinosa, F.G.; Trautwein, W.; Heyns, K. Acetoxonium-umlagerungen der D-xylose. Chem. Ber. **1968**, *101*, 179–185.

[33] Hall, L.D.; Manville, J.F. The favored conformation of 2, 3, 4-tri-O-acetyl-β-D-xylopyranosyl fluoride and other pentopyranosyl fluorides: the anomeric effect of a fluorine substituent. Carbohyd. Res. **1967**, *4*, 512–513.

[34] Hall, L.D.; Manville, J.F.; Tracey, A. The stereospecificity of long-range coupling constants of saturated carbohydrate derivatives. Carbohyd. Res. **1967**, *4*, 514–515.

[35] Kerekgyarto, J.; Kamerling, J.P.; Liptak, A.; Vliegenthart, J.F.G. Synthesis of a selectively protected trisaccharide building block that is part of xylose-containing carbohydrate chains from N-glycoproteins. Carbohyd. Res. **1993**, *238*, 135–145.

[36] Aniko, T.; Judit, R.; Istvan, B.; Andras, L. Synthesis of the methyl ethers of methyi 6-deoxy-3-C-methyl-α-L-talopyranoside and α-L-mannopyranoside. Examination of the conformation and chromatographic properties of the compounds. Arkivoc **2003**, *5*, 28–45.

[37] Richard, I.; Duclous, Jr. The total synthesis of D-*erythro*-sphingosine, N-palmitoylsphingosine (ceramide), and glucosylceramide (cerebroside) *via* an azido-sphingosine analog. Chemistry and Physics of Lipids **2001**, *111*, 111–138.