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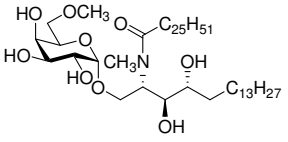
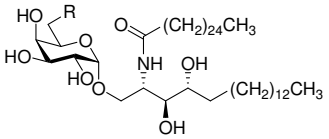
Graphical Abstract



2a



2b, R = OCH_3
2c, R = $O(CH_2)_5CH_3$
2d, R = $O(CH_2)_{11}CH_3$
2e, R = $O(CH_2)_{12}CH_3$
2f, R = $O(CH_2)_{19}CH_3$
2g, R = OPO_3H_2
2h, R = OSO_3Na
2i, R = NH_2

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ARTICLE TYPE

Design & Synthesis of Galactose-6-OH-Modified α-Galactosyl Ceramide Analogues with Th2-Biased Immune Responses

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In this study, a simple type of *O*-6 analogue of KRN7000 was synthesized starting from galactosyl iodide and D-lyxose. This transformation involve formation of a key disaccharide, the Wittig olefination on the anomeric hemiketal with simultaneous opening of furanose ring, and azido substitution of the revealed OH group, Staudinger reaction, and an amide bond formation with global deprotection, which furnished various *O*-6 substituted analogues of KRN7000. Studies of immune modulating effects of these compounds on human dendritic cells and NKT cells revealed that longer acyl chain at Gal 6' of α-GalCer induced more interleukin-4 with greater IL4/IFN-γ ratios. These new analogues may have potential applications in the field of vaccine adjuvants and Th1-dominated autoimmune disorders by skewing the immune response of CD1d reactive NKT cell toward Th2.On the other hand, modification of 6'-OH of galactose with amine might induce stronger Th1 immune response than α-GalCer. Thus, modification of 6'-OH of galactose could regulate NKT cells to modulate the immune system toward Th1 or Th2 responses.

Introduction

The α-galactosyl ceramide (α-GalCer) **1**, also known as KRN7000, is a simplified glycolipid analogue of the agelasphins originally isolated from a marine sponge *Agelas mauritianus*.[1] The isolation and the structure elucidation of **1**, was first reported by Natori et al.[2,3] The unique structure of α-GalCer **1** composed of α-linked galactose, phytosphingosine, and an acyl chain is critical for NKT-cell activation. Moreover, a clearer understanding of glycolipid-specific NKT cells and their molecular mechanism related to immunogenicity should facilitate the development of glycolipid-based vaccines adjuvant in the future.[4] Several reports are accessible in the literature for synthesis and activity of α-GalCer analogues with various diseases.[5] α-GalCer plays a crucial role in the field of glycolipids because it is the best characterized antigen for CD1d-reactive NKT-cells in mice and humans.[6,7] α-GalCer can bind with CD1d, to generate a ternary complex which is recognized by the NKT cell receptor of invariant natural killer T (iNKT) cells. Concurrently, this recognition results in the rapid secretion of Th1 (IFN-γ) and Th2 (IL-4) cytokines, which probably antagonize each other and lead to a limited outcome in clinical trials.[1c] Thus, modifications at various positions of α-GalCer have been reported to selectively induce Th1 or Th2 cytokine secretions for superior clinical effectiveness. X-ray crystallographic analysis of the binary complex of α-GalCer and CD1d molecule revealed that the long lipid chain is adapted to accommodate in a hydrophobic pocket in CD1d.[8] Moreover, the lipid chains are stabilized by hydrophobic interactions with amino acids from the β-sheet floor and helices of CD1d.[9] On the other hand, the orientation and position of the galactose ring of α-GalCer is believed to be crucial for iNKT cell recognition.[7b,7c,8e] The 2', 3', and 4'-OH of the galactose form hydrogen bonds with Gly96a, Phe29a and Ser30a, respectively, of the invariant TCR α-chain.[9] Upon removal of the 2'-OH, the cytokine response declined. The change from a galactose ring to a mannose ring weakened the binding to murine NKT TCR, indicating that 2' and

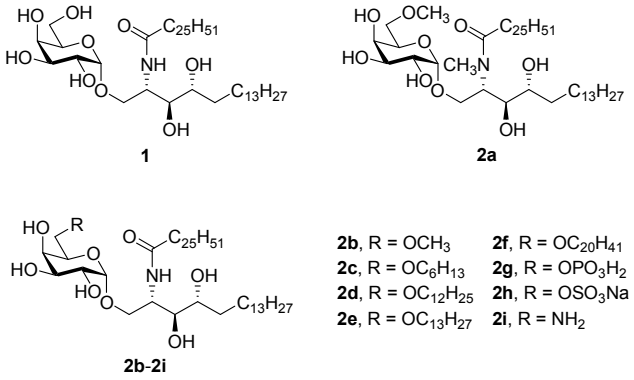
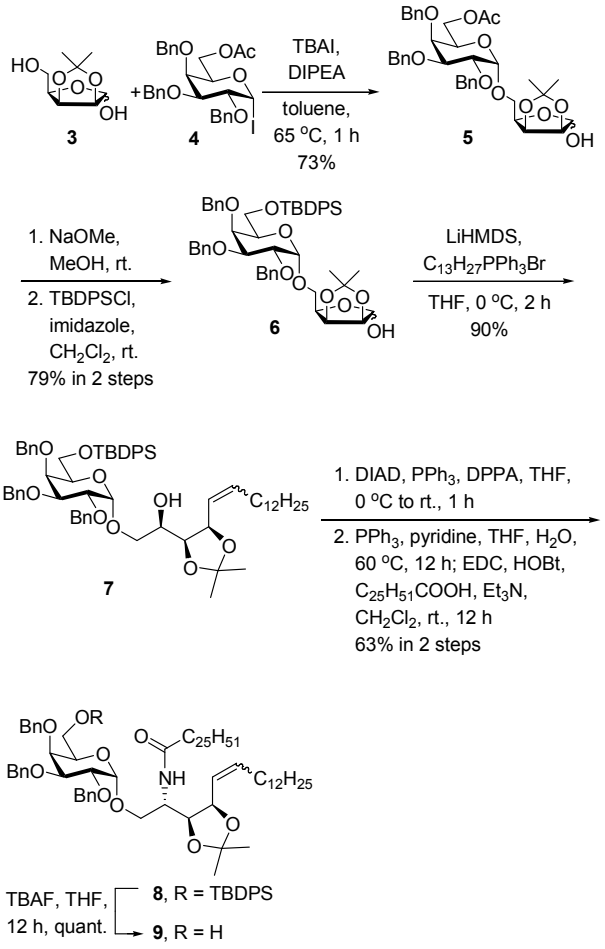


Fig. 1 Structures of α-GalCer **1** and its galactose *O*-6 analogues **2a-2i**.

4' hydroxyls of the galactose ring are important.[10] Furthermore, the binding to murine NKT TCR was slightly decrease when the galactose ring was replaced with a glucose ring[10], suggesting that the 4' hydroxyl of the galactose ring is critical. In addition, the α-GalCer analogues with 3'-deoxy of galactose showed lower activity than α-GalCer to induce IL-2 secretion by NKT hybridoma.[11] On the other hand, the X-ray crystal structure of NKT TCR-α-GalCer-CD1d complex demonstrates that the 6'-OH group of α-GalCer points toward solvent[9] and it does not direct interact with either the NKT TCR or CD1d molecules, indicating that some substituents might be introduced at this position to affect binding and activity.

For instance, α-GalCer analogues contains an extra Gal[12] or small fluorophores[13] at 6'-OH retained their ability to stimulate NKT cells. Conjugation with polyethylene glycol at 6'-amide group of α-GalCer could activate murine dendritic cells and NKT cells more efficiently than α-GalCer. When acting as an adjuvant in β-galactosidase protein vaccine, this pegylated α-GalCer induces lower production of IFN-γ when compared with α-GalCer[14].



Scheme 1 Preparation of common building block **9**.

A naphthylurea at 6'-amide of α-GalCer induced Th1 biased immune response and prevented lung metastasis of melanoma.[15] A methyl at 6' of galactose of α-GalCer induced a little higher production of IL-4 and IFN-γ in mice.[16]A triazole with PEG-tail at 6' of galactose of α-GalCer induced comparable or higher production of IFN-γ when compared with aGalCer.[17]

These reports suggests that modifications at 6-OH of galactose sugar may change the interaction between the NKT TCR and α-GalCer-CD1d complex and modulate the cytokine secretion of iNKT cells in vitro and in vivo in mice. However, most of these analogs with modifications of the 6-hydroxyl group induce Th1-biased immune responses, except that 6" triazole with aromatic group α-galactosylceramide analogous induced a small Th2 response.[18] OCH, which is an analogue of α-GalCer with a shorter phytosphingosine chain and slightly shorter acyl chain, directly stimulates NKT cells to secrete higher amounts of IL-4 than IFN-γ and triggers the immune response toward Th2. Other analogues which replaced the amide bond with a sulfonamide linkage to the acyl chain, induced less IFN-γ and comparable IL-4 when compared with α-GalCer in mice.[19] The possible molecular mechanism of OCH-induced Th2 response might result from its reduced avidity and less stable binding to CD1d when compared with α-GalCer, leading to a less sustained TCR stimulation of NKT cells.[20]

Only few glycolipids with modification of 6-OH at galactose have been shown to stimulate immune response toward Th2. To further explore this possibility, we synthesized nine *O*-6 analogues of the sugar moiety of α-GalCer (**2a-2i**), as shown in Figure 1, and evaluated their ability to stimulate iNKT cells to secrete Th1- and Th2-biased cytokines.

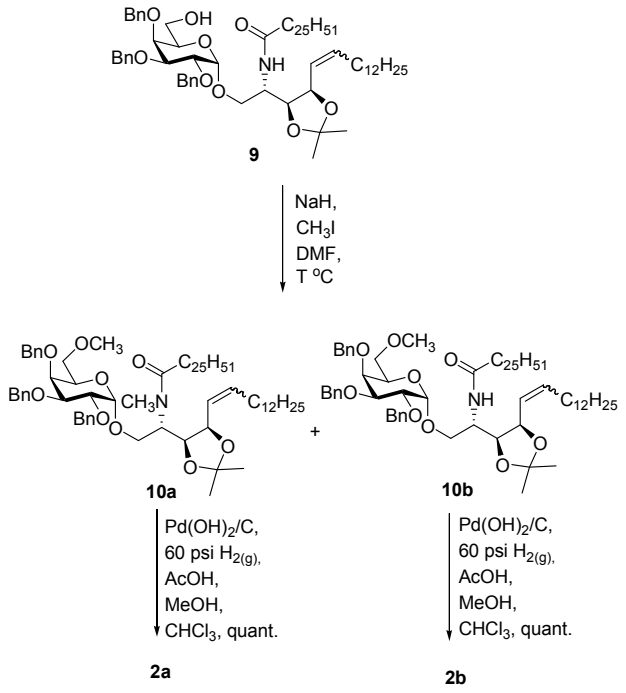
Results and discussion

Chemistry

Benzyl groups were used as the protecting groups for the sugar unit because of their ease of attachment to the galactose starting material and also important for the stereoslectivity of a-glycosylation reaction in our studies.[21a,21b] We predicted that these benzyl groups could be removed, and that the double bond of the phytosphingosine chain could be reduced in a single step.

In previous studies, we developed the five steps to synthesize α-GalCer from galactosyl iodide and D-lyxose[21a] and synthesized four interesting hydroxylated analogues of α-GalCer using galactosyl iodide and hemiacetals of selected hexopyranose.[21b] A scalable synthesis of requisite common building block **9** was designed by following the previously developed methodology. Scheme 1 summarizes the divergent route to common synthon **9** for the synthesis of eight analogues. To address the 6-OH position of a galactose sugar moiety for further modification, we choose to use the 2,3,4-tri-*O*-benzyl-6-*O*-acetyl-α-D-galactopyranosyl acetate, which was further deprotected at the C-6 position, to install the required functionalities. The regio- and stereoselective synthesis of key disaccharide **5** was prepared using the elegant Gervay-Hague glycosylation methodology, in which the galactosyl iodide **4** was generated in situ by treating 2,3,4-tri-*O*-benzyl-6-*O*-acetyl-α-D-galactopyranosyl acetate with iodotrimethylsilane.[22] Galactosyl iodide **4** was reacted with acceptor **3** in the presence of TBAI and Hünig's base to provide disaccharide **5** as the α-anomer in 73% yield.

Deacetylation of the *O*-6 position of the galactose moiety using sodium methoxide in methanol, followed by TBDPS protection[23], provided the disaccharide **6** in 79% yield over two steps. The Wittig olefination[24a] of hemiacetal **6** with $C_{13}H_{27}PPh_3Br$ produced in the presence of LiHMDS in THF at 0 °C olefin compound **7** in

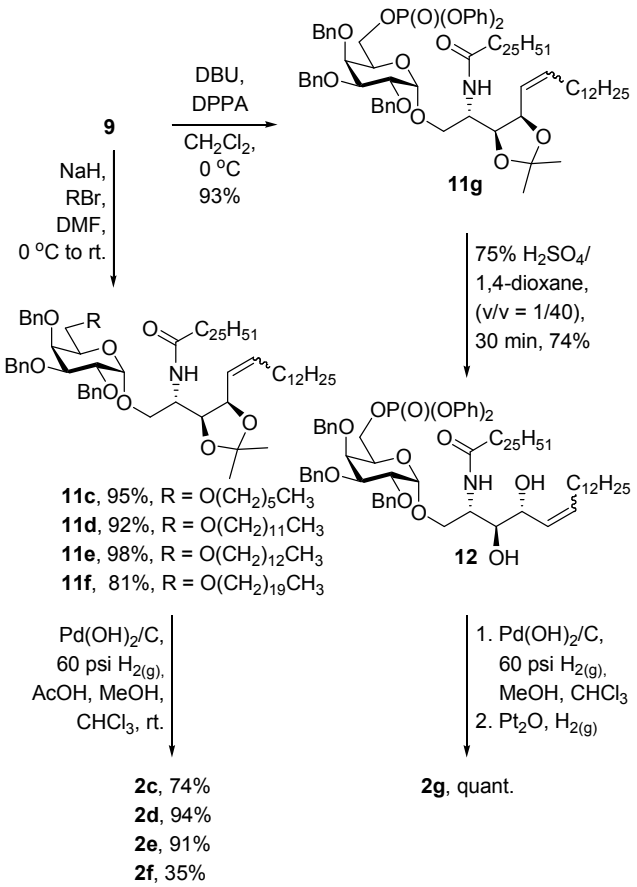


Entry	NaH (equiv)	CH_3I (equiv.)	T (°C)	t (h)	Yield (**10a**)	Yield (**10b**)
1	2	2	25	12	81%	0%
2	2	2	25	8	76%	21%
3	2	2	0	2	0%	64%

Table 1 Preparation of α-GalCer analogs **2a** and **2b**.

90% yield. The successful azido displacement of alcohol **7** by using the Mitsunobu condition[24b] produced the desired azide compound. The subsequent Staudinger reaction, followed by amide bond formation, generated an amide product **8** in 63% yields over two steps.

Finally, de-protection of the TBDPS group in the presence of 1 M TBAF provided the primary alcohol **9**. This common building block **9** was the key element of our study because it provided direct access to the various analogues of α-GalCer varying at the *O*-6 position of the galactose moiety. Using the common intermediate **9**, the preparation was begun by performing a methylation reaction (Table 1). The reaction of **9** with two equivalents of both NaH and methyl iodide in DMF at 25 °C produced a dimethylated product **10a** in 12 h (Table 1, Entry 1), when *O*- and *N*-methylation were observed. Interestingly, after reducing the time from 12 h to 8 h, a similar reaction produced a mixture of compounds containing the di-methylation **10a** and *O*-methylation **10b** products in 76% and 21% yields (Table 1, Entry 2), respectively. Finally, treatment of alcohol with a NaH and methyl iodide at 0 °C resulted in a O-methyl derivative **10b** in 2 h in a 64% yield (Table 1, Entry 3). Treating olefin **10a** and **10b** with palladium hydroxide in methanol and chloroform mixtures, respectively, removed all the benzyl groups and reduced the double bond, producing final analogues **2a** and **2b** in quantitative yields.[21a,21b] The synthesis of 6'-*O*-methylated analogue of α-GalCer **2b** has been previously reported by Mori et al and shown to have potent bioactivity for mouse lymphocytes to produce interferon-γ in vivo.[21c,21d]

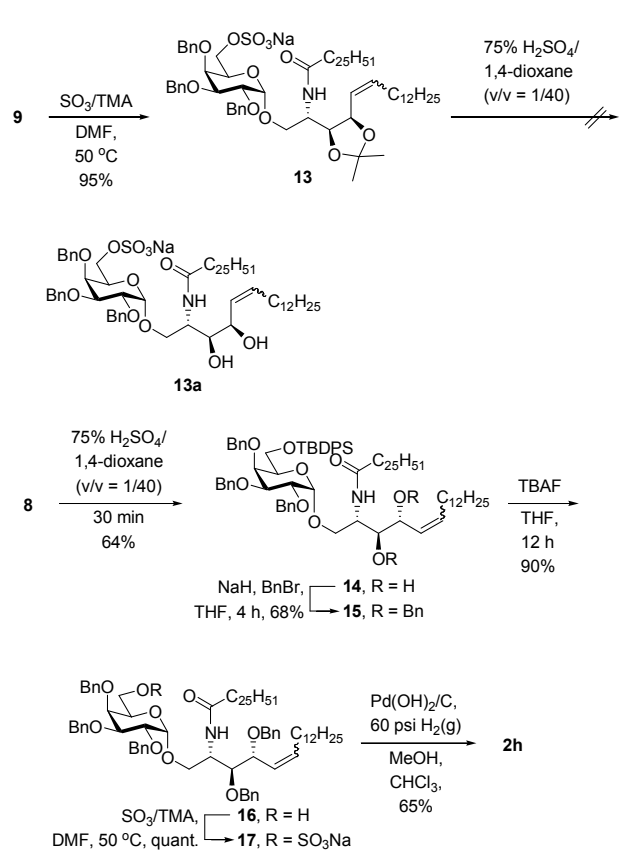


Scheme 2 Preparation of α-GalCer analogs **2c**-**2g**.

To illustrate the versatility of the common synthon **9**, we completed the synthesis of another four analogues (**2c**-**2f**), which differs in their long chains at *O*-6 positions (Scheme 2). Treating compound **9** with various alkyl halides that contain 6, 12, 13, and 20 carbons produced long chain compounds (**11c**-**11f**) with an excellent yield (**11c**: 95%, **11d**: 92%, **11e**: 98%, **11f**: 81%). Then, global de-protection using palladium hydroxide in acetic acid, MeOH, and $CHCl_3$ with hydrogen gas produced the final long-chain analogues (**2c**-**2f**) in acceptable yields (**2c**: 74%, **2d**: 94%, **2e**: 88%, **2f**: 35%).

Regarding the phosphation[25] of the 6-OH, we explored the versatility of common synthon **9** by introducing a phosphate group at the 6-OH position (Scheme 3). However, we treated the compound **9** with diphenylphosphorylazide in the presence of DBU in CH_2Cl_2 at 0 °C and obtained the diphenylphosphoryl compound **11g** in 93% yield. Direct global deprotection of the diphenylphosphoryl compound **11g** by using 75% H_2SO_4 in 1,4 dioxane produced many spots on the TLC after reaction was performed. Thus, the acetonide group in the phytosphingosine chain was hydrolyzed using 75% H_2SO_4 in 1,4-dioxane[26] and produced the diol compound **12**, which was subjected to deprotection achieving final analogue **2g** in quantitative yield. We began preparing the sulfate analogue **2h** (Scheme 3) by treating the common synthon **9** with sulfur trioxide in the

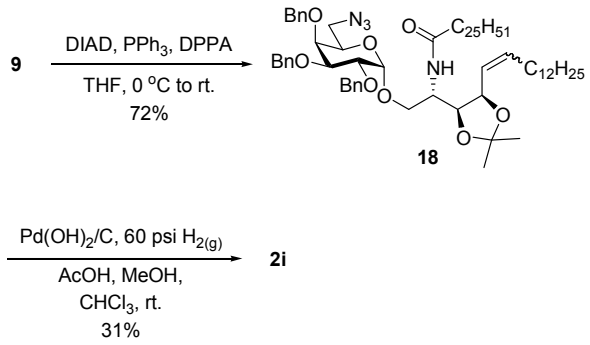
presence of trimethylamine in DMF at 50 °C, which produced sulfate **13** in 95% yield.[27] Subsequently, sulfate **13** was subjected to the hydrogenalysis conditions to deprotect the benzyl groups, but the reaction was unsuccessful because the sensitivity of the sulfate group inhibited the deprotection of the benzyl groups. Use of strongly acidic conditions was led to the cleavage of glycosidic bond. Nevertheless, an alternative approach was devised for preparing analogue **2h**.



Scheme 3 Preparation of α-GalCer analogue **2h**.

We began with the compound **8** rather than the common synthon **9** because of the problems associated with the deprotection of thecompound **13** after sulfation. Compound **8** was treated with 75% H_2SO_4 to cleave the acetonide group and produced diol **14** in 64% yield. Benzylation of diol **14** in the presence of NaH in THF produced fully protected compound **15** in 68% yield. The problems with deprotection of the sulfated compound **13** were circumvented by replacing the acetonide group in the phytosphingosine chain with the benzyl group. The TBDPS group was hydrolyzed using TBAF in THF for 12 h, producing primary alcohol **16**. Treatment of primary alcohol **16** with sulfur trioxide trimethylamine complex generated the sulfated compound **17** in quantitative yield. Finally, global deprotection was achieved by treating the benzyl compound with palladium hydroxide in a chloroform and methanol mixture with hydrogen gas, which produced the final compound **2h** in 65% yield.

We focused on the preparation of the amine compound **2i** of α-GalCer. The common synthon **9** was treated with PPh_3, DIAD, DPPA in THF to produce the azido compound **18** in 72% yield.[28] Azide **18** was then subjected to global deprotection to furnish amine analogue **2i** in a 31% yield.[21a] This amine compound **2i** was reported by Savage et al.[13] who used it to prepare the dansyl-appended glycolipids but, who in turn provided no biological evaluation.



Scheme 4. Preparation of α-GalCer analogue **2i**.

Biology

The activities of these α-GalCer analogues were assessed by induction of IL-2 production in mNK1.2 cells. A20-CD1d cells were loaded with various glycolipids and cultured with mNK1.2 cells. Three days after culture, supernatants were collected to determine the production of IL-2 by ELISA. As shown in Figure 1, the IL-2 levels induced by α-GalCer (compound **1**, 14.5 ± 0.6 ng/mL) and compound **2b** (13.3 ± 1.3 ng/mL) were significantly higher than those by other glycolipids (range: 0.17 ± 0.07-12.12 ± 1.0 ng/mL, $p < 0.05$). The findings suggest that longer acyl chain at Gal 6' of α-GalCer may diminish the activation of NKT cell. Notably, the poor activity of **2a** as shown by the low levels of IL-2 is in accord with the computing model reported by Wojno.[29]

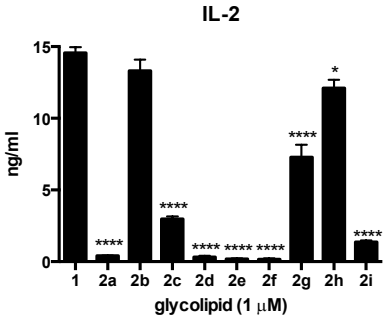


Figure 2. Induction of IL-2 by various glycolipid analogs in mNK1.2 cells. A20-CD1d cells were loaded with **1**μM of α-GalCer **1** and its analogs **2a**-**2i** and co-cultured with mNK1.2 cells. Three days after culture, supernatant was collected to determine the production of IL-2 by ELISA. Data were presented as mean ± SD and analyzed by one-way ANOVA and tukey's multiple comparison post hoc test. (* $p < 0.05$ and **** $p < 0.0001$)

A hydrogen bond can form between the NH in α-GalCer and the Thr156 in murine CD1d (Thr154 in human CD1d). This interaction is critical for guarding the glycolipid adopts an appropriate bound conformation to expose the galactose for

recognition by NKT TCRs. To evaluate the activity of these glycolipids in human NKT cells, human dendritic cell (DC) were used to present the glycolipids. Human iNKT cells were isolated with anti-TCR Vα24 antibody and cultured for 7 days in the presence of IL-2 (1 μg/mL). Meanwhile, dendritic cells were generated from CD14+ cells sorted from peripheral blood mononuclear cells (PBMC) by incubating for 7 days with GM-CSF (50 ng/mL) and IL-4 (50 ng/mL).[30]

Dendritic cells were then loaded with individual α-GalCer analogs (1 μM) and co-cultured with iNKT cells for 3 days. The supernatants were collected for analysis of the amount of cytokines by Luminex. For Th1 cytokine IFN-γ, compounds **2b** (2286 ± 344.3 pg/mL), **2g** (2704 ± 10.3 pg/mL), **2h** (2739 ± 14.52 pg/mL) and **2i** (2687 ± 89.4 pg/mL) appeared to induce comparable levels as α-GalCer (2493 ± 302.6 pg/mL), but compounds **2a** (1407 ± 31.1 pg/mL, $p < 0.0001$), **2c** (1469 ± 105.4 pg/mL, $p < 0.001$), **2d** (597.1 ± 169.2 pg/mL, $p < 0.0001$), **2e** (587.9 ± 125.7 pg/mL, $p < 0.0001$), and **2f** (800 ± 13.3 pg/mL, $p < 0.0001$) were significantly less effective than α-GalCer (Figure 3). The levels of Th2 cytokine IL-4 induced by compounds **2d** (191.5 ± 35.3 pg/mL, $p < 0.0001$), **2e** (140.4 ± 6.1 pg/mL, $p < 0.001$) and **2h** (113.9 ± 28.4 pg/mL, $p < 0.01$) were significantly higher than that by α-GalCer (46.3 ± 2.8 pg/mL). The induction of another Th1 cytokine IL-2 by glycolipid analogues was not significantly different from α-GalCer except for compound **2h** (60.3 ± 24.4 pg/mL vs. 15.6 ± 2.3 pg/mL, $p < 0.001$).

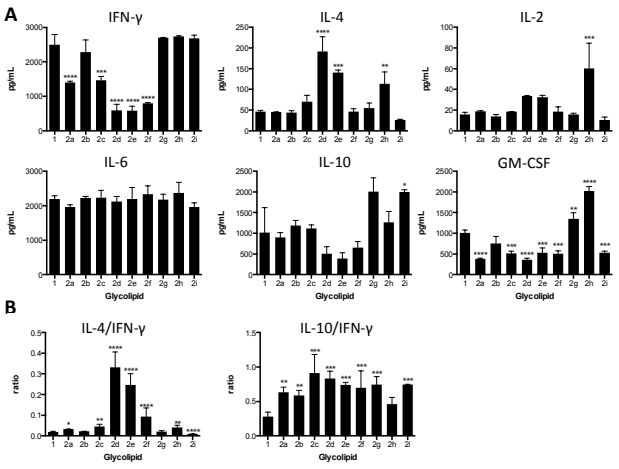


Figure 3. Cytokine levels in the supernatants of human iNKT cells co-cultured with glycolipid-loaded dendritic cells. Human $CD14^+$ cells were isolated and differentiated into dendritic cells. After loading with α-GalCer and its analogues, glycolipid-loaded dendritic cells were co-cultured with iNKT cells for 3 days. Culture supernatants were collected to determine the levels of IFN-γ, IL-2, IL-4, IL-6, IL-10 and GM-CSF by Luminex (A), and the ratio of IFN-γ/IL-4 and IFN-γ/IL-10 was calculated (B). Data were presented as mean ± SD and analyzed by one-way ANOVA and tukey's multiple comparison post hoc test. (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ and **** $p < 0.0001$.)

In addition, only compound **2i** significantly increased higher level of another Th2 cytokine IL-10 than α-GalCer (2001 ± 46.8 pg/mL vs. 1017 ± 603.4 pg/mL, $p < 0.05$), while comparable levels of IL-6 as α-GalCer (2192 ± 92.9 pg/mL) were observed in all glycolipids (range: 1963 ± 120.9-2368 ± 308.7 pg/mL). The induction of GM-CSF by compound **2g** (1350 ± 146.2 pg/mL, $p < 0.01$) and **2h** (2024 ± 108.4 pg/mL, $p < 0.0001$) was significantly higher than that in α-GalCer (1011 ± 67.1 pg/mL). It has been reported that modification of 3'-OH of galactose moiety with a sulfate group (SO_4Na_2) induced IFN-γ and IL-4 comparable to α-GalCer.[21] In this study, modification of 6'-OH of galactose moiety with sulfate group elicited not only comparable level of IFN-γ but also higher levels of IL-4, IL-2 and GM-CSF than α-GalCer, suggesting that modification at 6'-OH of galactose with sulfate group is better than at 3'-OH of galactose in stimulating NKT cells. Interestingly, modification of 6'-OH of galactose with an amine (NH_2) or phosphate group (PO_4H_2) decreased the level of IL-4, IL-2, and GM-CSF when compared with modification with sulfate group. In view of the important contribution of Th1 and Th2 immune responses to the treatment of cancer and autoimmune disorders, respectively, we used the ratio of IL-4/IFN-γ and IL-10/IFN-γ to evaluate if immune activation by these glycolipids was skewed toward Th1 or Th2 responses. Notably, the ratio of IL-4/IFN-γ and IL-10/IFN-γ (Figure 3B) was significantly higher for compound **2a** (0.032±0.0009 and 0.63± 0.07), **2c** (0.044±0.011 and 0.91 ± 0.26), **2d** (0.331± 0.074 and 0.83± 0.1), and **2e** (0.246± 0.053 and 0.73 ± 0.03) and **2f** (0.093± 0.041 and 0.69± 0.24) when compared to α-GalCer (0.018±0.003 and 0.28± 0.06), suggesting that acyl chain with length 12-13 at Gal 6'of α-GalCer may have stronger ability to trigger Th2 immune response. The cytokine production induced by **2b** is similar to α-GalCer, suggesting that modification of 6'-OH of galactose moiety with only one methyl group did not significantly change its ability to activate NKT cells. However, the production of IFN-γ was decreased and production of IL-4 was increased when the length of acyl chain increased from 6 to 12 and 13. Notably, both IFN-γ and IL-4 were decreased when the modification of 6'-OH of galactose with acyl chain reaches 20 carbons. Furthermore, in comparison to the well-known Th2-biased glycolipid, OCH, as reported in our previous study, the ratios of IL4/IFN-γ and IL-10/IFN-γ for OCH were 0.25 and 0.26. These results indicate that compound **2d** and **2e** may skew the immune responses toward Th2 response more potently than α-GalCer and at least equal to or better than OCH. In addition, when compared with α-GalCer, **2i** showed a comparable level of IFN-γ, lower level of IL-4 and lower ratio of IL-4/IFN-γ, indicating that **2i** might be more potent thanα-GalCer in inducing immune response toward Th1.

Conclusion

We have synthesized *O*-6 analogues **2a**-**2i** of KRN7000 and showed the *O*-6 position of sugar moiety plays a major role in the activation of iNKT cells toward more Th2-biased cytokine secretion. The length of alkyl chain at Gal 6' of α-GalCer had an impact on cytokine profiles, with longer alkyl chain inducing higher IL-4 cytokine and lower IFN-γ/IL4 ratios. These novel analogues may have potential applications in the field of vaccine adjuvants and Th1-dominated autoimmune disorders by skewing the immune responses toward Th2. Furthermore, modification of 6'-OH of galactose with amine might induce stronger Th1 immune response than does α-GalCer. In general, modification of

6'-OH of galactose could regulate NKT cell to modulate immune system toward Th1 or Th2 response.

Experimental

General Information. Some reactions were conducted in flame-dried glassware, under nitrogen atmosphere. Dichloromethane, tetrahydrofuran, toluene, methanol, and *N,N*-dimethyformamide were purified and dried from a safe purification system containing activated Al_2O_3. All reagents obtained from commercial sources were used without purification, unless otherwise mentioned. Flash column chromatography was carried out on Silica Gel 60 (230-400 mesh). TLC was performed on pre-coated glass plates of Silica Gel 60 F254 (0.25mm); detection was executed by spraying with a solution of $Ce(NH_4)_2(NO_3)_6$ (0.5 g), $(NH_4)_6Mo_7O_{24}$ (24 g) and H_2SO_4 (28 mL) in water (500 mL) and subsequent heating on a hot plate. Optical rotations were measured at 589 nm (Na) at ~ 27 °C. ^{1}H, ^{13}C NMR, DEPT, ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY, and ^{1}H-^{1}H NOESY spectra were recorded with 400 and 600 MHz instruments. Chemical shifts are in ppm from Me_4Si, generated from the $CDCl_3$ lock signal at δ7.24 ppm. IR spectra were taken with a FT-IR spectrometer using KBr plates. Mass spectra were analyzed on an Orbitrap instrument with an ESI source.

5-*O*-(6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-2,3-*O*-isopropylidene-D-lyxofuranose (5). To a solution of 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl acetate (8.23 g, 15.4 mmol) in dichloromethane (80 mL) was added iodotrimethylsilane (TMSI, 2.74 mL, 19.3 mmol) at 0 °C under nitrogen. After stirring for 30 min, the reaction was stopped by adding anhydrous toluene (80 mL). The mixture was azeotroped with toluene (80 mL) three times. The iodide residue **4** was dissolved in toluene and kept under N_2. A mixture of 2,3-*O*-isopropylidene-D-lyxofuranose **3** (3.22 g, 16.9 mmol), diisopropylethylamine (2.68 mL, 15.4 mmol), tetrabutylammonium iodide (17.1 g, 46.2 mmol) and 4 Å molecular sieves (4.00 g) was added into anhydrous toluene (50 mL) and was stirred for 10 min at 65 °C under nitrogen. Then a solution of iodo-residue **4** in toluene (80 mL) was transferred into the reaction flask by using the cannula, the mixture was kept stirring for 1 h at 65 °C, and the reaction was stopped by adding ethyl acetate. The reaction mixture was cooled to 0 °C, the white precipitate and molecular sieves was removed by filtration through Celite. The filtrate was extracted with aqueous $Na_2S_2O_3$ (80 mL) and brine (80 mL), and the organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to afford the desired disaccharide **5** as colourless oil (7.50 g) in 73% yield over two steps. R_f 0.47 (EtOAc/Hex = 1/1); $[\alpha]^{24}_D$ +3.9 (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) *v* 3404, 2925, 1742 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41-7.26 (m, 15H, ArH), 5.38 (bs, 1H, H-1), 4.97 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.87 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.86 (d, *J* = 3.0 Hz, 1H, H-1'), 4.82 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.75 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.75-4.73 (m, 1H, H-3), 4.68 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.62 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.57 (d, *J* = 6.0 Hz, 1H, H-2), 4.39-4.37 (m, 1H, H-4), 4.24-4.21 (m, 1H, H-6a'), 4.06-3.96 (m, 4H, H-2', H-3', H-5', H-6b'), 3.90-3.86 (m, 2H, H-5a, H-4'), 3.78 (dd, *J* = 11.4, 4.8 Hz, 1H, H-5b), 3.30 (bs, 1H, OH), 1.98 (s, 3H, CH_3), 1.42 (m, 3H, CH_3), 1.28 (s, 1H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.0 (C), 138.7 (C), 138.4 (C), 138.2 (C), 128.4 (CH × 2), 128.33 (CH × 2), 128.31 (CH × 2), 128.3 (CH × 2), 127.9 (CH × 2), 127.69 (CH), 127.68 (CH), 127.5 (CH), 127.4 (CH × 2), 112.4 (C), 101.0 (CH), 98.1 (CH), 85.4 (CH), 80.0 (CH), 79.0 (CH), 78.9 (CH), 76.5 (CH), 74.6 (CH), 74.5 (CH_2), 73.4 (CH_2), 73.3 (CH_2), 68.0 (CH), 67.1 (CH_2), 63.2 (CH_2), 26.0 (CH_3), 24.7 (CH_3), 20.1 (CH_3); HRMS (ESI, M+Na$^+$) calcd for $C_{37}H_{44}O_{11}Na$ 687.2776, found 687.2779.

5-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranosyl)-2,3-*O*-isopropylidene-D-lyxofuranose (6). To a solution of compound **5** (2.15 g, 3.24 mmol) and sodium methoxide (70 mg, 1.30 mmol) in methanol (25 mL) was stirred for 4 h and concentrated *in vacuo*. After the crude disaccharide was dissolved in dichloromethane (20 mL), imidazole (0.66 g, 9.71 mmol) and *tert*-butylchlorodiphenylsilane (0.9 mL, 3.40 mmol) were added to the solution, and the mixture was continuously stirred for 2 h. The reaction solution was washed by water (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of this residue via column chromatography gave the disaccharide **6** (2.20 g, 79% in 2 steps) as colorless oil. R_f 0.28 (EtOAc/Hex = 1/3); $[\alpha]^{24}_D$ +5.70 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) *v* 3406, 2932, 2857 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.72-7.29 (m, 25H, ArH), 5.50 (d, *J* = 1.8 Hz, 1H, H-1), 5.07 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.96 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.93 (d, *J* = 3.0 Hz, 1H, H-1'), 4.88 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.83 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.79-4.78 (m, 1H, H-3), 4.77 (d, *J* = 11.7 Hz, 1H, CH_2Ph), 4.69 (d, *J* = 11.7 Hz, 1H, CH_2Ph), 4.63 (d, *J* = 6.0 Hz, 1H, H-2), 4.50-4.48 (m, 1H, H-4), 4.14-4.09 (m, 3H, H-2', H-3', H-4'), 3.88 (m, 1H, H-5'), 3.90-3.75 (m, 4H, H-5a, H-5b, H-6a', H-6b'), 3.68 (bs, 1H, OH), 1.45 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.15 (s, 9H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9 (C), 138.7 (C), 138.5 (C), 135.4 (CH × 4), 133.20 (C), 133.18 (C), 129.61 (CH), 129.59 (CH), 128.24 (CH × 2), 128.18 (CH × 2), 128.0 (CH × 2), 127.9 (CH × 2), 127.8 (CH × 2), 127.7 (CH × 2), 127.6 (CH × 2), 127.5 (CH), 127.33 (CH), 127.29 (CH × 3), 112.3 (C), 100.9 (CH), 97.8 (CH), 85.3 (CH), 79.8 (CH), 78.8 (CH), 78.4 (CH), 76.4 (CH), 75.1 (CH), 74.8 (CH_2), 72.95 (CH_2), 72.92 (CH_2), 70.5 (CH), 65.9 (CH_2), 62.2 (CH_2), 26.8 (CH_3 × 3), 26.0 (CH_3), 24.7 (CH_3), 19.1 (C); HRMS (APCI, M+Na$^+$) calcd for $C_{51}H_{60}O_{10}NaSi$ 883.3848, found 883.3857.

(*2R,3S,4R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranosyl)-3,4-*O*-isopropylidene-5-octadecen-1,2,3,4-tetraol (7). A mixture of the hemiacetal **6** (2.77 g, 3.21 mmol) and tridecanyltriphenylphosphonium bromide (6.76 g, 12.9 mmol) in tetrahydrofuran (27 mL) was cooled to 0 °C under nitrogen. A 1.0 M solution of lithium hexamethyldisilamide in tetrahydrofuran (LiHMDS, 12.9 mL, 12.9 mmol) was added to the reaction mixture and stirred for another 2 h at 0 °C. Water (30 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (2 × 30 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue

was purified by column chromatography to give the olefin **7** (2.93 g, 89%) as colorless oil. R_f 0.61 (EtOAc/Hex = 1/3); $[\alpha]^{24}_D$ +3.36 (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) *v* 2926, 2855, 1456, 1104 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62-7.20 (m, 25H, ArH), 5.74-5.63 (m, 2H, H-5, H-6), 4.95 (d, *J* = 11.6 Hz, 1H, CH_2Ph), 4.96-4.92 (m, 1H, H-4), 4.86 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.80 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.77 (d, *J* = 3.6 Hz, 1H, H-1'), 4.75 (d, *J* = 11.6 Hz, 1H, CH_2Ph), 4.67 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.58 (d, *J* = 11.2 Hz, 1H, CH_2Ph), 4.13-4.09 (m, 1H, H-3), 4.03-4.00 (m, 2H, H-2', H-3'), 3.94 (dd, *J* = 10.4, 2.8 Hz, 1H, H-4'), 3.88 (t, *J* = 2.8 Hz, 1H, H-5'), 3.78-3.65 (m, 3H, H-2, H-6a', H-6b'), 3.56 (dd, *J* = 10.4, 7.2 Hz, 1H, H-1a), 3.58 (dd, *J* = 10.8, 7.2 Hz, 1H, H-1b), 2.58 (d, *J* = 6.4, 1H, OH), 2.14-1.93 (m, 2H, CH_2), 1.49 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.36-1.33 (m, 2H, CH_2), 1.28-1.24 (m, 18H, CH_2), 1.04 (s, 9H, CH_3), 0.88 (t, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8 (C), 138.7 (C), 138.5 (C), 135.5 (CH × 5), 133.22 (C), 133.21 (C), 129.69 (CH), 129.67 (CH), 128.32 (CH × 2), 128.30 (CH × 2), 128.1 (CH × 2), 128.0 (CH × 2), 127.9 (CH × 2), 127.7 (CH × 4), 127.6 (CH), 127.5 (CH), 127.38 (CH), 127.37 (CH × 2), 125.0 (CH), 108.4 (C), 97.7 (CH), 79.0 (CH), 77.3 (CH), 76.4 (CH), 74.9 (CH), 74.8 (CH_2), 73.3 (CH_2), 72.99 (CH_2), 72.97 (CH), 70.9 (CH), 69.6 (CH_2), 68.4 (CH), 62.4 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.64 (CH_2), 29.61 (CH_2), 29.57 (CH_2), 29.49 (CH_2), 29.46 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 27.7 (CH_2), 27.2 (CH_3), 26.9 (CH_3 × 3), 24.9 (CH_3), 22.7 (CH_2), 19.1 (C), 14.1 (CH_3); HRMS (ESI, M+Na^+) calcd for $C_{64}H_{86}O_9NaSi$ 1049.5933, found 1049.5954.

(*2S,3S,4R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranosyl)-2-hexacosanoylamino-3,4-*O*-isopropylidene-5-octadecen-1,3,4-triol (8). To a solution of the alcohol **7** (396 mg, 0.39 mmol) and triphenylphosphine (307 mg, 1.16 mmol) in tetrahydrofuran (4.0 mL) at 0 °C was added diisopropyl azodicarboxylate (DIAD, 235 μL, 1.16 mmol), followed by dropwise addition of diphenylphosphoryl azide (DPPA, 269 μL, 1.25 mmol). After completion of addition, the reaction was brought to room temperature and stirred for 1 h. Water (5 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (2 × 5 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to give the azide (405 mg, quant.) as colorless oil. To a solution of azide (405 mg, 0.38 mmol) and triphenylphosphine (202 mg, 0.77 mmol) in THF (4.0 mL) was added pyridine (1.3 mL). The reaction flask was warmed up to 60 °C, and the mixture was kept stirring for 12 h. The reaction was gradually cooled to room temperature, hexaeicosanoic acid (199 mg, 0.50 mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (EDC, 133 mg, 0.69 mmol), hydroxybenzotriazole (HOBt, 94 mg, 0.69 mmol) and triethylamine (54 μL, 0.39 mmol) were sequentially added to the solution, and the mixture was continuously stirred for 12 h. The reaction solution was diluted with ethyl acetate (3.0 mL), and the resulting mixture was washed by water (8.0 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of this residue via column chromatography gave the amide compound **8** (337 mg, 63%) as colorless oil. R_f 0.46 (EtOAc/Hex = 1/5);$[\alpha]^{24}_D$ +5.20 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) *v* 2923, 2853, 1680, 1537 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.61-7.23 (m, 25H, ArH), 5.98 (d, *J* = 9.0 Hz, 1H, NH), 5.59-5.54 (m, 1H, H-6), 5.43-5.40 (m, 1H, H-5), 5.02 (d, *J* = 3.6 Hz, 1H, H-1'), 4.96 (d, *J* = 10.8 Hz, 1H, CH_2Ph), 4.83 (d, *J* = 10.8 Hz, 1H, CH_2Ph), 4.83-4.81 (m, 1H, H-4), 4.80 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.78 (d, *J* = 10.8 Hz, 1H, CH_2Ph), 4.68 (d, *J* = 10.8 Hz, 1H, CH_2Ph), 4.59 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.16 (dd, *J* = 9.0, 6.0 Hz, 1H, H-3), 4.11-4.09 (m, 1H, H-2), 4.07 (d, *J* = 3.0 Hz, 1H, H-4'), 4.05 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 3.92 (dd, *J* = 10.2, 3.0 Hz, 1H, H-3'), 3.80-3.77 (m, 2H, H-5', H-6a'), 3.75 (dd, *J* = 11.4, 3.0 Hz, 1H, H-1a), 3.68 (dd, *J* = 13.2, 9.0 Hz, 1H, H-6b'), 3.58 (dd, *J* = 11.4, 3.0 Hz, 1H, H-1b), 2.07-1.86 (m, 6H, CH_2), 1.55-1.53 (m, 2H, CH_2), 1.42 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.33-1.24 (m, 62H, CH_2), 1.05 (s, 9H, CH_3), 0.88 (t, *J* = 7.2 Hz, 6H, CH_3 ×2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.1 (C), 138.7 (C), 138.6 (C), 138.3 (C), 135.5 (CH × 4), 135.0 (CH), 133.2 (C), 133.1 (C), 129.8 (CH), 129.7 (CH), 128.4 (CH × 4), 128.1 (CH × 2), 127.94 (CH × 2), 127.90 (CH × 2), 127.8 (CH), 127.74 (CH × 2), 127.71 (CH × 2), 127.6 (CH), 127.43 (CH × 2), 127.41 (CH), 124.1 (CH), 108.3 (C), 98.2 (CH), 78.9 (CH), 76.9 (CH), 76.0 (CH), 74.9 (CH_2), 74.6 (CH), 73.5 (CH_2), 73.1 (CH), 72.6 (CH_2), 70.9 (CH), 67.5 (CH_2), 62.2 (CH_2), 48.7 (CH), 36.8 (CH_2), 31.9 (CH_2 × 2), 29.7 (CH_2 × 19), 29.60 (CH_2 × 2), 29.56 (CH_2 ×3), 29.5 (CH_2 ×2), 29.4 (CH_2 ×3), 27.9 (CH_3), 27.7 (CH_2), 26.9 (CH_3 ×3), 25.7 (CH_3), 25.5 (CH_2), 22.7 (CH_2), 19.1 (C), 14.1 (CH_3 ×2); HRMS (ESI, M+H^+) calcd for $C_{90}H_{138}O_9NSi$ 1405.0135, found 1405.0104.

(*2S,3S,4R*)-1-*O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-2-hexacosanoylamino-3,4-*O*-iso-propylidene-5-octadecen-1,3,4-triol (9). To a solution of the silyl ether **8** (194 mg, 0.14 mmol) in tetrahydrofuran (2.0 mL) was added 1.0 M solution of tetrabutylammonium fluoride in tetrahydrofuran (280 μL, 0.28 mmol) and stirred for 12 h. Water (3 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (2 × 3 mL). The combined organic layers were washed with brine (3 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **9** (161 mg, quant.). R_f 0.19 (EtOAc/Hexane = 1/3); $[\alpha]^{25}_D$ +8.83 (*c* 0.6, $CHCl_3$); mp 65-67 °C; IR ($CHCl_3$) *v* 3424, 2918, 2850, 1644 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.41-7.26 (m, 15H, ArH), 5.98 (d, *J* = 9.0 Hz, 1H, NH), 5.64-5.60 (m, 1H, H-6), 5.46-5.43 (m, 1H, H-5), 4.98 (d, *J* = 3.6 Hz, 1H, H-1'), 4.96 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.91-4.89 (m, 1H, H-4), 4.82 (d, *J* = 11.4 Hz, 2H, CH_2Ph), 4.76 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.70 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.64 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.19-4.13 (m, 2H, H-2, H-3), 4.06 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 3.94-3.87 (m, 3H, H-1a, H-3', H-4'), 3.73-3.65 (m, 3H, H-1b, H-5', H-6a'), 3.54-3.52 (m, 1H, H-6b'), 2.21 (s, 1H, OH), 2.10-1.93 (m, 4H, CH_2), 1.54-1.53 (m, 2H, CH_2), 1.46 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.33-1.24 (m, 64H, CH_2), 0.88 (t, *J* = 7.2 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.6 (C), 138.5 (C), 138.2 (C), 138.1 (C), 135.6 (CH), 128.5 (CH × 2), 128.4 (CH × 6), 128.0 (CH × 2), 127.89 (CH), 127.85 (CH), 127.6 (CH), 127.4 (CH × 2), 123.8 (CH), 108.3 (C), 99.4 (CH), 79.1 (CH), 77.0 (CH), 76.7 (CH), 74.6 (CH), 74.6 (CH_2), 73.5 (CH_2), 73.1 (CH), 73.0 (CH_2), 70.9 (CH), 69.1 (CH_2), 62.2 (CH_2), 49.5 (CH), 36.8 (CH_2), 31.9 (CH_2 × 2), 29.7 (CH_2 ×

22), 29.50 (CH_2), 29.46 (CH_2), 29.42 (CH_2), 29.38 (CH_2), 29.3 (CH_2 × 2), 27.8 (CH_2), 27.4 (CH_3), 25.5 (CH_2), 25.4 (CH_3), 22.7 (CH_2 × 2), 14.1 (CH_3 ×2); HRMS (ESI, M+H^+) calcd for $C_{74}H_{120}O_9N$ 1166.8958, found 1166.8931.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-methyl-α-D-galacto-pyranosyl)-2-*N*-methyl-hexaco-sanoylamino-3,4-*O*-isopropyli-dene-5-octadecen-1,3,4-triol (10a). To a solution of the alcohol **9** (32 mg, 0.03 mmol) in *N*,*N*-dimethylformamide (DMF, 1 mL) were added iodomethane (4 μL, 0.06 mmol) and 60% sodium hydride (22 mg, 0.06 mmol) at 28 °C. After complete addition, the reaction mixture was stirred for 2 h. Methanol was added to quench the reaction and concentrated *in vacuo*. The mixture was extracted with ethyl acetate (3 × 5 mL) and water (5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **10a** (27 mg, 81%) as a yellow solid. R_f 0.50 (EtOAc/Hex = 1/2.5); $[\alpha]^{25}_D$ +14.3 (*c*1.0, $CHCl_3$); IR ($CHCl_3$) *v* 2924, 2853, 1651, 1370, 1057 cm^{-1}; ^1H NMR (600 MHz, C_5D_5N, 100 °C) δ 7.53-7.27 (m, 15H, ArH), 5.84 (t, *J* = 10.8 Hz, 1H, H-5), 5.79 (bs, 1H, H-6), 5.22 (bs, 2H, H-4, H-1'), 5.16 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.98 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.92 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.84-4.79 (m, 3H, $PhCH_2$), 4.36 (dd, *J* = 11.4, 3.0 Hz, 1H, H-2'), 4.25-4.23 (m, 4H, H-2, H-3', H-5', H-6a'), 4.10 (m ,1H, H-6b'), 3.84-3.80 (m, 3H, H-1a, H-3, H-4'), 3.71 (t, *J* = 6.6 Hz, 1H, H-1b), 3.39 (s, 3H, CH_3), 3.13 (s, 3H, CH_3), 2.39-2.25 (m, 3H, CH_2), 1.86 (bs, 1H, CH_2), 1.58 (s, 3H, CH_3), 1.53-1.49 (m, 4H, CH_2), 1.45 (s, 3H, CH_3), 1.40 (bs, 62H, CH_2), 0.932 (t, *J* = 6.0 Hz, 3H, CH_3), 0.928 (t, *J* = 6.0 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, C_5D_5N, 100 °C) δ 173.7 (C), 140.1 (C), 140.0 (C × 2), 135.1 (CH), 128.83 (CH × 2), 128.76 (CH × 3), 128.71 (CH × 2), 128.5 (CH × 2), 128.2 (CH × 3), 127.90 (CH), 127.86 (CH × 2), 126.6 (CH), 108.7 (C), 99.0 (CH), 79.8 (CH), 78.0 (CH), 77.8 (CH), 77.0 (CH), 75.5 (CH_2), 74.4 (CH × 2), 73.3 (CH_2), 72.4 (CH_2), 70.6 (CH), 67.5 (CH_2), 59.1 (CH_3), 34.5 (CH_2), 33.3 (CH_3), 32.3 (CH_2 × 2), 30.1 (CH_2 × 21), 30.0 (CH_2 × 2), 29.73 (CH_2 × 2), 29.69 (CH_2 × 2), 29.66 (CH_2 × 2), 28.22 (CH_2), 28.18 (CH_3), 25.80 (CH_3), 25.73 (CH_2), 23.0 (CH_2 × 2), 14.2 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{76}H_{124}O_9N$ 1194.9271, found 1194.9259.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-methyl-α-D-galacto-pyranosyl)-2-hexacosanoylamino-3,4-*O*-isopropylidene-5-oc-tadecen-1,3,4-triol (10b). To a solution of the alcohol **9** (17 mg, 0.01 mmol) in *N*,*N*-dimethylformamide (DMF, 1.0 mL) were added iodomethane (2 μL, 0.03 mmol) and 60% sodium hydride (1 mg, 0.03 mmol) at 0 °C. After complete addition, the reaction mixture was stirred for 2 h. Methanol was added to quench the reaction and concentrated *in vacuo*. The mixture was extracted with ethyl acetate (3 × 5 mL) and water (5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **10b** (11 mg, 64%) as a yellow solid. R_f 0.38 (EtOAc/Hex = 1/2.5); $[\alpha]^{25}_D$ +21.9 (*c* 0.9, $CHCl_3$); mp 59-59.6 °C; IR ($CHCl_3$) *v* 3314, 2918, 2850, 1643, 1469, 1054 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.34-7.20 (m, 15H, ArH), 6.26 (d, *J* = 9.6 Hz, 1H, NH), 5.51 (td, *J* = 10.8, 7.2 Hz, 1H, H-6), 5.35 (t, *J* = 10.2 Hz, 1H, H-5), 4.88 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.83 (d, *J* = 3.6 Hz, 1H, H-1'), 4.78 (dd, *J* = 9.6, 5.4 Hz, 1H, H-4), 4.75 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.73 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.68 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.60 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.55 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.13 (dd, *J* = 9.0, 5.4 Hz, 1H, H-3), 4.01-3.96 (m, 3H, H-2, H-1a, H-2'), 3.84-3.83 (m, 3H, H-3',H-4', H-5'), 3.55 (dd, *J* = 9.6, 2.4 Hz, 1H, H-1b), 3.38 (dd, *J* = 9.6, 7.2 Hz, 1H, H-6a'), 3.21-3.18 (m, 4H, H-6b', OCH_3), 2.05-1.81 (m, 4H, CH_2), 1.49-1.41 (m, 2H, CH_2), 1.38 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.18 (bs, 64H, CH_2), 0.81 (t, *J* = 6.6 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4 (C), 138.6 (C), 138.3 (C), 138.3 (C),134.8 (CH), 128.4 (CH× 6), 128.3 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH × 2), 124.2 (CH), 108.3 (C), 99.6 (CH), 78.8 (CH), 76.7 (CH), 75.8 (CH), 74.61 (CH_2), 74.60 (CH), 73.4 (CH_2), 72.98 (CH), 72.95 (CH_2), 72.0 (CH_2), 70.5 (CH_2), 69.7 (CH), 58.9 (CH_3), 49.0 (CH), 36.6 (CH_2), 31.9 (CH_2), 29.7 (CH_2 × 12), 29.64 (CH_2 × 5), 29.58 (CH_2 × 3), 29.52 (CH_2 × 2), 29.46 (CH_2 × 3), 29.37 (CH_2 × 2), 29.3 (CH_2 × 3), 28.0 (CH_3), 27.6 (CH_2), 25.7 (CH_3), 25.4 (CH_2), 22.7 (CH_2), 14.1 (CH_3 × 2); HRMS (ESI, M+Na^+) calcd for $C_{75}H_{121}O_9NNa$ 1202.8934, found 1202.8933.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-methyl-α-D-galactopyranosyl)-D-*ribo*-2-*N*-methyl-hexacosanoylamino-1,3,4-octadecantriol (2a). Compound **10a** (17 mg) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 2 mL) at 28 °C. The $Pd(OH)_2$/C (17 mg, Degussa type) was added to the solution and followed by addition 2-3 drops of acetic acid, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 5 h. The resulting solution was filtered through celite, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography to afford the target molecule **2a** (12 mg, quant.) as white solid. R_f 0.13 (MeOH/DCM = 1/10); $[\alpha]^{25}_D$ +46.3 (*c* 0.1, $CHCl_3$); mp 64-66 °C; IR ($CHCl_3$) *v* 3324, 2920, 2851, 1652, 1036 cm^{-1}; ^1H NMR (600 MHz, d-pyridine, 100 °C) δ 5.24 (d, *J* = 4.2 Hz, 1H, H-1'), 4.60 (dd, *J* = 10.8, 4.2 Hz, 1H, H-1a), 4.39 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2'), 4.35 (t, *J* = 6.0 Hz, 1H, H-5'), 4.31 (bs, 1H, H-4'), 4.27-4.25 (m, 2H, H-1b, H-3'), 4.21 (bs, 1H, H-3), 4.15 (dd, *J* = 6.0, 1.8 Hz, 1H, H-2), 4.05-4.03 (m, 1H, H-4), 3.97 (dd, *J* = 10.2, 5.4 Hz, 1H, H-6a'), 3.88 (dd, *J* = 9.6, 6.0 Hz, 1H, H-6b'), 3.40 (s, 3H, CH_3), 3.27 (s, 3H, CH_3), 2.50-2.36 (m, 1H, CH_2), 2.10-2.08 (m, 1H, CH_2), 1.87-1.80 (m, 4H, CH_2), 1.68-1.62 (m, 1H, CH_2), 1.52-1.44 (m, 6H, CH_2), 1.39 (bs, 30H, CH_2), 1.35 (bs, 31H, CH_2), 0.93 (t, *J* = 13.2 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, d-pyridine, 100 °C) δ 174.6 (C), 101.4 (CH), 76.8 (CH), 73.6 (CH), 73.2 (CH_2), 71.7 (CH), 71.0 (CH × 2), 70.6 (CH), 67.7 (CH, CH_2), 59.1 (CH_3), 35.0 (CH_3), 34.5 (CH_2), 34.0 (CH_2), 32.2 (CH_2 × 2), 30.4 (CH_2), 30.1 (CH_2 × 26), 29.7 (CH_2 × 2), 26.6 (CH_2), 25.7 (CH_2), 23.0 (CH_2 × 2), 14.2 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{52}H_{104}O_9N$ 886.77056, found 886.77062.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-methyl-α-D-galactopyranosyl)-D-*ribo*-2-hexacosanoylamino-1,3,4-octa-decantriol (2b). Compound **10b** (22 mg, 0.019 mmol) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 2 mL) at 28 °C. $Pd(OH)_2$/C (22 mg, Degussa type) was added to the solution followed by addition (2-

3 drops) of acetic acid, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 5 h. The resulting solution was filtered through Celite, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography to afford the target molecule **2b** (16 mg, quant.) as a white solid. R_f 0.31 (MeOH/CH_2Cl_2 = 1/10); $[\alpha]^{25}_D$ +25.0 (*c* 0.04, $CHCl_3$); mp 86-88 °C; IR ($CHCl_3$) *v* 3274, 2918, 2850, 1641 cm^{-1}; ^1H NMR (600 MHz, d-pyridine) δ 8.47 (d, *J* = 9.0 Hz, 1H, NH), 6.48 (bs, 1H, OH), 5.52 (d, *J* = 3.6 Hz, 1H, H-1'), 5.27-5.23 (m, 1H, H-2), 4.64 (dd, *J* = 10.8, 5.4 Hz, 1H, H-1a), 4.61 (dd, *J* = 10.2, 4.2 Hz, 1H, H-2'), 4.46 (t, *J* = 6.0 Hz, 1H, H-5'), 4.40-4.36 (m, 3H, H-1b, H-3', H-4'), 4.34-4.30 (m, 2H, H-3, H-4), 3.97 (dd, *J* = 9.6, 5.4 Hz, 1H, H-6a'), 3.94 (dd, *J* = 10.2, 6.6 Hz, 1H, H-6b'), 3.33 (s, 3H, CH_3), 2.43-2.42 (m, 2H, CH_2), 2.30-2.25 (m, 1H, CH_2), 1.95-1.86 (m, 2H, CH_2), 1.84-1.78 (m, 2H, CH_2), 1.71-1.62 (m, 2H, CH_2), 1.30 (bs, 26H, CH_2), 1.23 (bs, 39H, CH_2), 0.850 (t, *J* = 7.2 Hz, 3H, CH_3), 0.847 (t, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, d-pyridine) δ 173.1 (C), 101.5 (CH), 76.5 (CH), 73.0 (CH_2), 72.5 (CH), 71.3 (CH), 70.8 (CH), 70.7 (CH), 70.1 (CH), 68.8 (CH_2), 58.7 (CH_3), 51.2 (CH), 36.8 (CH_2), 34.2 (CH_2), 32.1 (CH_2 × 2), 30.3 (CH_2), 30.1 (CH_2), 30.0 (CH_2 × 20), 29.92 (CH_2 × 3), 29.86 (CH_2 × 2), 29.82 (CH_2), 29.75 (CH_2), 29.6 (CH_2 × 2), 26.5 (CH_2), 26.4 (CH_2), 22.9 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{51}H_{102}O_9N$ 872.7549, found 872.7536.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-hexyl-α-D-galacto-pyranosyl)-2-hexacosanoylamino-3,4-*O*-isopropylidene-5-octadecen-1,3,4-triol (11c). To a solution of the alcohol **9** (33 mg, 0.03 mmol) in *N*,*N*-dimethylformamide (1 mL) were added 1-bromohexane (8 μL, 0.06 mmol) and 60% sodium hydride (2 mg, 0.06 mmol) at 28 °C. After complete addition, the reaction mixture was stirred for 8 h. Methanol was added to quench the reaction and concentrated *in vacuo*. The mixture was extracted with ethyl acetate (3 × 5 mL) and water (5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **11c** (34 mg, 95%) as a yellow solid. R_f 0.64 (EtOAc/Hex = 1/2.5); $[\alpha]^{25}_D$ +26.3 (*c* 0.6, $CHCl_3$); mp 43-44 °C; IR ($CHCl_3$) *v* 3317, 2920, 2851, 1646, 1537, 1468, 1055 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ7.34-7.19 (m, 15H, ArH), 6.17 (d, *J* = 9.6 Hz, 1H, NH), 5.51 (td, *J* = 10.8, 7.2 Hz, 1H, H-6), 5.35 (t, *J* = 9.6 Hz, 1H, H-5), 4.87 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.87 (d, *J* = 3.6 Hz, 1H, H-1'), 4.78 (dd, *J* = 9.6, 6.0 Hz, 1H, H-4), 4.73 (d, *J*= 10.8 Hz, 2H, $PhCH_2$), 4.68 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.61 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.55 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.14 (dd, *J* = 9.0, 6.0 Hz, 1H, H-3), 4.02-3.96 (m, 2H, H-2, H-2'), 3.91 (dd, *J* = 11.4, 3.0 Hz, 1H, H-1a), 3.87 (bs, 1H, H-4'), 3.85-3.81 (m, 2H, H-3', H-5'), 3.56 (dd, *J* = 10.8, 2.4 Hz, 1H, H-1b), 3.38 (dd, *J* = 9.0, 6.0 Hz, 1H, H-6a'), 3.33 (td, *J* = 10.2, 6.6 Hz, 1H, CH_2), 3.29 (dd, *J* = 9.0, 6.0 Hz, 1H, H-6b'), 3.22 (td, *J* = 9.6, 7.2 Hz, 1H, CH_2), 2.00 (dddd, *J* = 15.0, 7.2, 7.2, 7.2 Hz, 1H, CH_2), 1.97-1.88 (m, 2H, CH_2), 1.38 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.18 (bs, 70H, CH_2), 0.82 (t, *J* = 6.6 Hz, 3H, CH_3), 0.81 (t, *J* = 7.2 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4 (C), 138.6 (C), 138.4 (C), 138.3 (C), 135.0 (CH), 128.4 (CH × 2), 128.34 (CH × 2), 128.30 (CH × 2), 128.2 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.7 (CH), 127.54 (CH), 127.46 (CH × 2), 124.1 (CH), 108.3 (C), 99.2 (CH), 78.8 (CH), 76.7 (CH), 75.8 (CH), 74.7 (CH_2), 74.5 (CH), 73.4 (CH_2), 73.0 (CH), 72.8 (CH_2), 71.6 (CH_2), 69.57 (CH_2), 69.56 (CH), 69.45 (CH_2), 49.0 (CH), 36.7 (CH_2), 34.7 (CH_2), 31.9 (CH_2 × 2), 29.72 (CH_2 × 5), 29.68 (CH_2 × 8), 29.64 (CH_2 × 3), 29.59 (CH_2), 29.55 (CH_2), 29.48 (CH_2 × 2), 29.4 (CH_2 × 2), 29.3 (CH_2 × 2), 28.0 (CH_3), 27.7 (CH_2), 25.71 (CH_2), 25.68 (CH_3), 25.4 (CH_2), 22.7 (CH_2 × 2), 22.6 (CH_2), 14.1 (CH_3 × 2), 14.0 (CH_3); HRMS (ESI, M+H^+) calcd for $C_{80}H_{132}O_9N$ 1250.98966, found 1250.98974.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-dodecyl-α-D-galacto-pyranosyl)-2-hexacosanoylamino-3,4-*O*-isopropylidene-5-octadecen-1,3,4-triol (11d). To a solution of the alcohol **9** (33 mg, 0.03 mmol) in *N*,*N*-dimethylformamide (1 mL) were added 1-bromododecane (14 μL, 0.06 mmol) and 60% sodium hydride (2 mg, 0.06 mmol) at 28 °C. After complete addition, the reaction mixture was stirred for 8 h. Methanol was added to quench the reaction and concentrated *in vacuo*. The mixture was extracted with ethyl acetate (3 × 5 mL) and water (5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **11d** (35 mg, 93%) as a yellow solid. R_f 0.64 (EtOAc/Hex = 1/2.5); $[\alpha]^{25}_D$ +28.5 (*c* 0.4, $CHCl_3$); mp 49-50 °C; IR ($CHCl_3$) *v* 3353, 2918, 2860, 1662, 1531, 1468, 1043 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.41-7.28 (m, 15H, ArH), 6.16 (d, *J* = 8.4 Hz, 1H, NH), 5.58 (td, *J* = 10.8, 7.2 Hz, 1H, H-6), 5.42 (d, *J* = 10.2 Hz, 1H, H-5), 4.94 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.92 (d, *J* = 3.6 Hz, 1H, H-1'), 4.85 (dd, *J* = 9.0, 6.0 Hz, 1H, H-4), 4.81 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.80 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.75 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.68 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.62 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.21 (dd, *J* = 9.6, 6.0 Hz, 1H, H-3), 4.07 (td, *J* = 9.0, 3.0 Hz, 1H, H-2), 4.05 (dd, *J* = 9.6, 3.0 Hz, 1H, H-2'), 4.50 (dd, *J* = 11.4, 3.0Hz, 1H, H-1a), 3.94 (bs, 1H, H-4'), 3.92-3.89 (m, 2H, H-3', H-5'), 3.64 (dd, *J* = 11.4, 2.4 Hz, 1H, H-1b), 3.46 (dd, *J* = 9.6, 6.6 Hz, 1H, H-6a'), 3.40 (dt, *J* = 9.0, 6.6 Hz, 1H, CH_2), 3.35 (dd, *J* = 9.0, 6.0 Hz, 1H, H-6b'), 3.29 (dt, *J* = 9.6, 7.2 Hz, 1H, CH_2), 2.11-1.88 (m, 4H, CH_2), 1.55-1.49 (m, 4H, CH_2), 1.45 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.25 (bs, 82H, CH_2), 0.88 (t, *J* = 10.8 Hz, 9H, CH_3 × 3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4 (C), 138.6 (C), 138.4 (C), 138.3 (C), 135.0 (CH), 128.34 (CH × 3), 128.32 (CH × 3), 128.2 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH × 2), 124.2 (CH), 108.3 (C), 99.3 (CH), 78.8 (CH), 75.9 (CH), 74.7 (CH_2), 74.6 (CH), 73.4 (CH_2), 73.0 (CH), 72.8 (CH_2), 71.7 (CH_2), 69.8 (CH_2), 69.6 (CH), 69.5 (CH), 49.0 (CH), 36.7 (CH_2), 31.9 (CH_2), 30.0 (CH_2), 29.7 (CH_2 × 28), 29.61 (CH_2 × 2), 29.60 (CH_2 × 2), 29.55 (CH_2 × 2), 29.49 (CH_2), 29.47 (CH_2), 29.40 (CH_2), 29.37 (CH_2 × 2), 28.0 (CH_3), 27.7 (CH_2), 26.1(CH_2), 25.7 (CH_3), 25.4 (CH_2), 22.7 (CH_2), 14.1 (CH_3 × 3); HRMS (ESI, M+Na^+) calcd for $C_{86}H_{143}O_9NNa$ 1357.0655, found 1357.0661.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-tridecyl-α-D-galacto-pyranosyl)-2-hexacosanoylamino-3,4-*O*-isopropylidene-5-octadecen-1,3,4-triol (11e). To a solution of the alcohol **9** (149 mg, 0.13 mmol) in *N*,*N*-dimethylformamide (2 mL) were added 1-bromotridecane (65 μL, 0.25 mmol) and 60% sodium hydride

(10 mg, 0.26 mmol) at 28 °C. After complete addition, the reaction mixture was stirred for 8 h. Methanol was added to quench the reaction and concentrated *in vacuo*. The mixture was extracted with ethyl acetate (3 × 5 mL) and water (5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **11e** (151 mg, 87%) as a yellow solid. R_f0.52 (EtOAc/Hex = 1/2.5); $[\alpha]^{25}_D$ +23.6 (*c* 0.1, $CHCl_3$); mp 49-50 °C; IR ($CHCl_3$) *v* 3591, 2919, 2851, 1660, 1511, 1467, 1043 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ7.41-7.27 (m, 15H, ArH), 6.20 (d, *J* = 9.0 Hz, 1H, NH), 5.58 (td, *J* = 10.8, 7.8 Hz, 1H, H-6), 5.42 (dd, *J* = 10.8, 9.6 Hz, 1H, H-5), 4.94 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.92 (d, *J* = 3.6 Hz, 1H, H-1'), 4.85 (dd, *J* = 9.0, 6.0 Hz, 1H, H-4), 4.81 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.80 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.75 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.68 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.62 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.21 (dd, *J* = 9.0, 5.4 Hz, 1H, H-3), 4.08-4.03 (m, 2H, H-2, H-2'), 4.00 (dd, *J* = 10.8, 3.0 Hz, 1H, H-1a), 3.94 (bs, 1H, H-4'), 3.92-3.88 (m, 2H, H-3', H-5'), 3.63 (dd, *J* = 11.4, 2.4 Hz, 1H, H-1b), 3.45 (dd, *J* = 9.6, 6.6 Hz, 1H, H-6a'), 3.39 (td, *J* = 9.6, 7.2 Hz, 1H, CH_2), 3.34 (dd, *J* = 9.0, 6.0 Hz, 1H, H-6b'), 3.29 (td, *J* = 9.0, 7.2 Hz, 1H, CH_2), 2.10-1.87 (m, 4H, CH_2), 1.55-1.47 (m, 6H, CH_2), 1.45 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.25 (bs, 82H, CH_2), 0.88 (t, *J* = 6.6 Hz, 9H, CH_3 × 3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4 (C), 138.6 (C), 138.4 (C), 138.3 (C), 135.0 (CH), 129.5 (CH), 128.4 (CH × 3), 128.3 (CH × 3), 128.2 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH × 2), 124.1 (CH), 108.3 (C), 99.3 (CH), 78.8 (CH), 76.8 (CH), 75.8 (CH), 74.7 (CH_2), 74.5 (CH), 73.4 (CH_2), 73.0 (CH), 72.8 (CH_2), 71.7 (CH_2), 69.8 (CH_2), 69.6 (CH), 69.5 (CH_2), 49.0 (CH), 36.7(CH_2), 31.9 (CH_2), 29.7 (CH_2 × 26), 29.6 (CH_2 × 2), 29.56 (CH_2 × 2), 29.50 (CH_2), 29.48 (CH_2), 29.42 (CH_2), 29.38 (CH_2 × 2), 28.0 (CH_3), 27.7 (CH_2), 26.1 (CH_2), 25.7 (CH_3), 25.4 (CH_2), 22.7 (CH_2), 14.1 (CH_3 × 3); HRMS (ESI, M+Na^+) calcd for $C_{87}H_{145}O_9NNa$ 1371.0812, found 1371.0806.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-eicosyl-α-D-galacto-pyranosyl)-2-hexacosanoylamino-3,4-*O*-isopropylidene-5-oc-tadecen-1,3,4-triol (11f). To a solution of the alcohol **9** (33 mg, 0.028 mmol) in *N*,*N*-dimethylformamide (1 mL) were added 1-bromoeicosane (20 mg, 0.06 mmol) and 60% sodium hydride (2 mg, 0.06 mmol) at 28 °C. After complete addition, the reaction mixture was stirred for 12 h. Methanol was added to quench the reaction and concentrated *in vacuo*. The mixture was extracted with ethyl acetate (3 × 5 mL) and water (5 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **11f** (37 mg, 91%) as a yellow solid. R_f 0.68 (EtOAc/Hex = 1/2.5); $[\alpha]^{25}_D$ +23.0 (*c* 0.4, $CHCl_3$); mp 56-58 °C; IR ($CHCl_3$) *v* 3342, 2919, 2851, 1649, 1538, 1468, 1056 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.41 (m, 15H, ArH), 6.22 (d, *J* = 9.0 Hz, 1H, NH), 5.58 (td, *J* = 10.8, 7.2 Hz, 1H, H-6), 5.42 (t, *J* = 9.6 Hz, 1H, H-5), 4.94 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.93 (d, *J* = 4.2 Hz, 1H, H-1'), 4.85 (dd, *J* = 9.0, 6.0 Hz, 1H, H-4), 4.81 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.80 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.75 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.68 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.62 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.21 (dd, *J* = 9.6, 6.0 Hz, 1H, H-3), 4.08-4.03 (m, 2H, H-2, H-2'), 3.99 (dd, *J* = 12.0, 3.6 Hz, 1H, H-1a), 3.95 (bs, 1H, H-4'), 3.92-3.88 (m, 2H, H-3', H-5'), 3.63 (dd, *J* = 12.0, 2.4 Hz, 1H, H-1b), 3.45 (dd, *J* = 6.6, 3.6 Hz, 1H, H-6a'), 3.39 (td, *J* = 9.6, 7.2 Hz, 1H, CH_2), 3.34 (dd, *J* = 9.0, 6.0 Hz, 1H, H-6b'), 3.30 (td, *J* = 9.6, 7.2 Hz, 1H, CH_2), 2.11-1.87 (m, 4H, CH_2), 1.56-1.49 (m, 4H, CH_2), 1.45 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.25 (bs, 98H, CH_2), 0.88 (t, *J* = 6.6 Hz, 9H, CH_3 × 3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4 (C), 138.6 (C), 138.4 (C), 138.3 (C), 135.0 (CH), 128.37 (CH × 2), 128.5 (CH × 2), 128.3 (CH × 2), 128.2 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.7 (CH), 127.54 (CH), 127.45 (CH × 2), 124.1 (CH), 108.3 (C), 99.3 (CH), 78.8 (CH), 76.8 (CH), 75.8 (CH), 74.7 (CH_2), 74.6 (CH), 73.4 (CH_2), 73.0 (CH), 72.8 (CH_2), 71.7 (CH_2), 69.8 (CH_2), 69.6 (CH), 69.5 (CH_2), 49.0 (CH), 36.7 (CH_2), 31.9 (CH_2), 29.7 (CH_2 × 38), 29.6 (CH_2 × 2), 29.58 (CH_2 × 2), 29.50 (CH_2), 29.48 (CH_2), 29.41 (CH_2), 29.36 (CH_2 × 2), 28.0 (CH_3), 27.7 (CH_2), 26.1 (CH_2), 25.7 (CH_3), 25.4 (CH_2), 22.7 (CH_2), 14.1 (CH_3 × 3); HRMS (ESI, M+Na^+) calcd for $C_{94}H_{159}O_9NNa$ 1469.1907, found 1469.1926.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-hexyl-α-D-galactopyranosyl)-D-*ribo*-2-hexacosanoylamino-1,3,4-octa-decantriol (2c). Compound **11c** (49 mg) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 4 mL) at 28 °C. The $Pd(OH)_2$/C (49 mg, Degussa type) was added to the solution and followed by addition 2-3 drops of acetic acid, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 5 h. The resulting solution was filtered through celite, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography to afford the target molecule **2c** (27 mg, 74%) as white solid. R_f 0.3 (MeOH/DCM = 1/10); $[\alpha]^{25}_D$ +36.3 (*c* 0.1, $CHCl_3$); mp 70-72 °C; IR ($CHCl_3$) *v* 3279, 2920, 2851, 1642, 1036 cm^{-1}; ^1H NMR (600 MHz, C_5D_5N) δ 8.49 (d, *J* = 8.4 Hz, 1H, NH), 5.53 (d, *J* = 3.0 Hz, 1H, H-1'), 5.27-5.23 (m, 1H, H-2), 4.66 (dd, *J* = 10.8, 5.4 Hz, 1H, H-1a), 4.63 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2'), 4.49 (t, *J* = 6.6 Hz, 1H, H-5'), 4.42 (d, *J* = 2.4 Hz, 1H, H-4'), 4.39 (dd, *J* = 9.6, 3.6 Hz, 1H, H-1b), 4.38 (t, *J* = 5.4 Hz, 1H, H-3'), 4.35-4.30 (m, 2H, H-3, H-4), 4.10 (dd, *J* = 10.2, 6.6 Hz, 1H, H-6a'), 4.00 (dd, *J* = 10.2, 6.6 Hz, 1H, H-6b'), 3.54-3.47 (m, 2H, CH_2), 2.46-2.43 (m, 2H, CH_2), 2.29-2.25 (m, 1H, CH_2), 1.94-1.86 (m, 2H, CH_2), 1.85-1.80 (m, 2H, CH_2), 1.71-1.67 (m, 2H, CH_2), 1.60-1.57(m, 2H, CH_2), 1.30 (bs, 48H, CH_2), 1.23 (bs, 23H, CH_2), 0.85 (t, *J* = 6.6 Hz, 6H, CH_3 × 2), 0.82 (t, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, C_5D_5N) δ 173.1 (C), 100.5 (CH), 76.5 (CH), 72.4 (CH), 71.6 (CH_2), 71.4 (CH), 71.0 (CH_2), 70.8 (CH), 70.7 (CH), 70.1 (CH), 68.7 (CH_2), 51.3 (CH), 36.8 (CH_2), 34.2 (CH_2), 32.1 (CH_2), 31.9 (CH_2), 30.44 (CH_2), 30.36 (CH_2), 30.2 (CH_2 × 2), 30.00 (CH_2 × 19), 29.92 (CH_2 × 4), 29.83 (CH_2), 29.77 (CH_2), 29.6 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 26.1 (CH_2 × 2), 22.93 (CH_2 × 2), 22.87 (CH_2), 14.3 (CH_3 × 2), 14.2 (CH_3); HRMS (ESI, M+Na^+) calcd for $C_{56}H_{111}O_9NNa$ 964.8151, found 964.8160.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-dodecyl-α-D-galactopyranosyl)-D-*ribo*-2-hexacosanoylamino-1,3,4-octa-decantriol (2d). Compound **11d** (17 mg) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 2 mL) at 28 °C. The $Pd(OH)_2$/C (17 mg, Degussa type) was added to the solution and followed by addition 2-3 drops of acetic acid, the reaction vessel was purged with hydrogen, and the

mixture was stirred under 60 psi pressure at the same temperature for 5 h. The resulting solution was filtered through celite, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography to afford the target molecule **2d** (11 mg, 94%) as white solid. R_f 0.21 (MeOH/DCM = 1/10); $[\alpha]^{25}_D$ +46.7 (*c* 0.05, $CHCl_3$); mp 92-93 °C; IR ($CHCl_3$) *v* 3308, 2920, 2851, 1647, 1036 cm^{-1}; ^1H NMR (600 MHz, C_5D_5N) δ 8.51 (d, *J* = 9.0 Hz, 1H, NH), 6.49 (bs, 1H, OH), 6.44 (bs, 1H, OH), 6.12 (bs, 1H, OH), 5.53 (d, *J* = 3.0 Hz, 1H, H-1'), 5.26-5.23 (m, 1H, H-2), 4.67-4.62 (m, 2H, H-1a, H-2'), 4.50 (t, *J* = 6.0 Hz, 1H, H-5'), 4.42-4.38 (m, 3H, H-1b, H-3', H-4'), 4.34-4.31 (m, 2H, H-3, H-4), 4.11 (dd, *J* = 10.2, 6.0 Hz, 1H, H-6a'), 4.02 (dd, *J* = 9.6, 6.0 Hz, 1H, H-6b'), 3.57-3.50 (m, 2H, CH_2), 2.46-2.43 (m, 2H, CH_2), 2.28-2.27 (m, 1H, CH_2), 1.92-1.81 (m, 6H, CH_2), 1.71-1.61 (m, 8H, CH_2), 1.30-1.24 (bs, 77H, CH_2), 0.86 (t, *J* = 6.6 Hz, 9H, CH_3 × 2); ^{13}C NMR (150 MHz, C_5D_5N) δ 173.1 (C), 101.5 (CH), 76.5 (CH), 72.4 (CH), 71.7 (CH_2), 71.4 (CH), 71.0 (CH_2), 70.8 (CH), 70.7 (CH), 70.1 (CH), 68.8 (CH_2), 37.6 (CH_2), 37.3 (CH_2), 36.8 (CH_2), 34.2 (CH_2), 33.9 (CH_2), 33.0 (CH), 32.1 (CH_2 × 3), 30.5 (CH_2), 30.4 (CH_2), 30.3 (CH_2 × 2), 30.2 (CH_2), 30.0 (CH_2 × 16), 29.92 (CH_2 × 4), 29.85 (CH_2 × 2), 29.8 (CH_2 × 2), 29.6 (CH_2 × 3), 29.4 (CH_2), 27.0 (CH_2), 26.6 (CH_2), 26.4 (CH_2), 22.9 (CH_2 × 3), 14.3 (CH_3 × 3); HRMS (ESI, M+H^+) calcd for $C_{62}H_{124}O_9N$ 1026.9271, found 1026.9285.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-tridecyl-α-D-galactopyranosyl)-D-*ribo*-2-hexacosanoylamino-1,3,4-octa-decantriol (2e). Compound **11e** (22 mg) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 2 mL) at 28 °C. The $Pd(OH)_2$/C (22 mg, Degussa type) was added to the solution and followed by addition 2-3 drops of acetic acid, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 5 h. The resulting solution was filtered through celite, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography to afford the target molecule **2e** (15.7 mg, 91%) as white solid. R_f 0.24 (MeOH/DCM = 1/10); $[\alpha]^{25}_D$ +20.6 (*c* 0.4, $CHCl_3$); mp 88-90 °C; IR ($CHCl_3$) *v* 3331, 2920, 2851, 1648, 1032 cm^{-1}; ^1H NMR (600 MHz, C_5H_5N) δ 8.53 (d, *J* = 8.4 Hz, 1H, NH), 6.50 (bs, 1H, OH), 6.12 (bs, 1H, OH), 5.52 (d, *J* = 3.6 Hz, 1H, H-1'), 5.25-5.21 (m, 1H, H-2), 4.65 (dd, *J* = 10.8, 4.8 Hz, 1H, H-1a), 4.62 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2'), 4.49 (t, *J* = 6.6 Hz, 1H, H-5'), 4.41-4.38 (m, 3H, H-1b, H-3', H-4'), 4.36-4.30 (m, 2H, H-3, H-4), 4.10 (dd, *J* = 10.2, 6.6 Hz, 1H, H-6a'), 4.01 (dd, *J* = 10.2, 6.6 Hz, 1H, H-6b'), 3.57-3.50 (m, 2H, CH_2), 2.46-2.43 (m, 2H, CH_2), 2.30-2.24 (m, 1H, CH_2), 2.07-1.80 (m, 8H, CH_2), 1.71-1.60 (m, 7H, CH_2), 1.30 (bs, 23H, CH_2), 1.25 (bs, 23H, CH_2), 1.24 (bs, 32H, CH_2), 0.85 (t, *J* = 6.6 Hz, 9H, CH_3 × 3); ^{13}C NMR (150 MHz, C_5H_5N) δ 173.1 (C), 101.4 (CH), 76.4 (CH), 72.4 (CH), 71.7 (CH_2), 71.4 (CH), 71.0 (CH_2), 70.8 (CH), 70.7 (CH), 70.1 (CH), 68.7 (CH_2), 51.3 (CH), 37.3 (CH_2), 36.8 (CH_2), 34.1 (CH_2), 32.1 (CH_2 × 2), 30.4 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 30.0 (CH_2 × 29), 29.85 (CH_2 × 2), 29.77 (CH_2), 29.6 (CH_2 × 2), 27.4 (CH_2), 27.0 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 22.9 (CH_2 × 2), 14.3 (CH_3 × 3); HRMS (ESI, M+Na^+) calcd for $C_{63}H_{125}O_9NNa$ 1062.92466, found 1062.92475.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-eicosanyl-α-D-galactopyranosyl)-D-*ribo*-2-hexacosanoylamino-1,3,4-octa-decantriol (2f). Compound **11f** (81 mg) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 4 mL) at 28 °C. The $Pd(OH)_2$/C (81 mg, Degussa type) was added to the solution and followed by addition 2-3 drops of acetic acid, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 5 h. The resulting solution was filtered through celite, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography to afford the target molecule **2f** (23 mg, 35%) as white solid. R_f0.38 (MeOH/DCM = 1/10); $[\alpha]^{25}_D$ +50.0(*c* 0.12, $CHCl_3$); mp 98-100 °C; IR ($CHCl_3$) 3272, 2918, 2850, 1649, 1033 cm^{-1}; ^1H NMR (600 MHz, C_5H_5N) δ 8.46 (d, *J* = 8.4 Hz, 1H, NH), 5.53 (d, *J* = 4.2 Hz, 1H, H-1'), 5.23-5.21 (m Hz, 1H, H-2), 4.66 (dd, *J* = 10.8, 5.4 Hz, 1H, H-1a), 4.63 (dd, *J* = 9.6, 4.2 Hz, 1H, H-2'), 4.51 (t, *J* = 6.6 Hz, 1H, H-5'), 4.43-4.39 (m, 3H, H-1b, H-3', H-4'), 4.35-4.31 (m, 2H, H-3, H-4), 4.11 (dd, *J* = 9.6, 6.0 Hz, 1H, H-6a'), 4.03 (dd, *J* = 9.6, 6.0 Hz, 1H, H-6b'), 3.59-3.51 (m, 2H, CH_2), 2.48-2.43 (m, 2H, CH_2), 2.31-2.26 (m, 1H, CH_2), 1.95-1.81 (m, 5H, CH_2), 1.72-1.63 (m, 5H, CH_2), 1.31 (bs, 36H, CH_2), 1.28 (bs, 21H, CH_2), 1.25 (bs, 40H, CH_2), 0.87-0.84 (m, 9H, CH_3 × 3); ^{13}C NMR (150 MHz, C_5H_5N) δ 173.1 (C), 101.5 (CH), 76.5 (CH), 72.5 (CH), 71.7 (CH_2), 71.4 (CH), 71.0 (CH_2), 70.8 (CH), 70.7 (CH), 70.2 (CH), 68.8 (CH_2), 51.3 (CH), 36.7 (CH_2), 34.2 (CH_2), 32.1 (CH_2 × 4), 30.4 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 30.0 (CH_2 × 27), 29.94 (CH_2 × 6), 29.86 (CH_2), 29.8 (CH_2), 29.6 (CH_2 × 4), 26.6 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 22.9 (CH_2 × 4), 14.3 (CH_3 × 3); HRMS (CI, M + H^+) calcd for $C_{70}H_{140}O_9N$ 1139.0523, found 1139.0511.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-diphenylphospho-ryl-α-D-galactopyranosyl)-2-hexa-cosanoylamino-3,4-*O*-iso-propylidene-5-octadecen-1,3,4-triol (11g). To a solution of compound **9** (200 mg, 0.17 mmol) and diphenylphosphoryl azide (222 μL, 1.03 mmol) in dichloromathane (2.0 mL) at 0 °C was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 146 μL, 0.98 mmol), the reaction mixture was stirred at the same temperature for 2 h. Water (3.0 mL) was added to quench the reaction and the mixture was extracted with dichloromathane (2 × 3 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **11g** (224 mg, 93%) as white solid. R_f 0.53 (EtOAc/Hex = 1/3);$[\alpha]^{25}_D$ +27.3 (*c* 1.0, $CHCl_3$); mp 58-60 °C; IR ($CHCl_3$) *v* 3318, 2919, 2850, 1645 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.40-7.17 (m, 25H, ArH), 6.01-5.99 (m, 1H, NH), 5.59-5.55 (m, 1H, H-6), 5.43-5.39 (m, 1H, H-5), 5.03 (d, *J* = 3.0 Hz, 1H, H-1'), 4.93 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.86-4.83 (m, 1H, H-4), 4.80 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.78 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.74 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.68 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.52 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.33-4.29 (m, 1H, H-6a'), 4.22-4.16 (m, 2H, H-3, H-6b'), 4.08-4.04 (m, 2H, H-2, H-2'), 4.00 (t, *J* = 6.6 Hz, 1H, H-5'), 3.90-3.89 (m, 2H, H-3', H-4'), 3.81 (dd, *J* =11.4, 2.4 Hz, 1H, H-1a), 3.62 (dd, *J* =10.8, 1.8 Hz, 1H, H-1b), 2.08-1.86 (m, 6H, CH_2), 1.53-1.49 (m, 2H, CH_2), 1.43 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.31-1.23 (m, 62H, CH_2), 0.88 (t, *J* = 7.2 Hz, 6H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.2 (C), 150.4 (t, C × 2), 138.4 (C), 138.2 (C), 138.1 (C), 135.1 (CH), 129.80 (d, CH × 4), 128.40 (CH × 2), 128.39 (CH × 2), 128.3

(CH × 2), 128.2 (CH × 2), 127.92 (CH × 2), 127.87 (CH), 127.74 (CH), 127.65 (CH), 127.4 (CH × 2), 125.5 (d, CH × 2), 124.0 (CH), 120.0 (d, CH × 4), 108.3 (C), 98.6 (CH), 78.6 (CH), 76.6 (CH), 76.0 (CH), 74.7 (CH_2), 74.0 (CH), 73.6 (CH_2), 73.1 (CH), 72.8 (CH_2), 69.3 (d, CH), 68.4 (CH_2), 67.3 (t, CH_2), 48.9 (CH), 36.7 (CH_2), 31.9 (CH_2 × 2), 29.7 (CH_2 × 22), 29.6 (CH_2 × 2), 29.5 (CH_2 × 2), 29.4 (CH_2 × 2), 27.9 (CH_3), 27.7 (CH_2), 25.6 (CH_3), 25.4 (CH_2), 22.7 (CH_2 × 2), 14.1 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{86}H_{129}O_{12}NP$ 1398.9247, found 1398.9257.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-diphenylphospho-ryl-α-D-galactopyranosyl)-2-hexacosanoylamino-5-octadecen-1,3,4-triol (12).To a solution of compound **11g** (41 mg, 0.03 mmol) in 1,4-dioxane (800 μL) was added 75% H_2SO_4 (20 μL) and stirred for 30 min. Saturated sodium bicarbonate was added to quench the reaction, and the reaction was extracted with ethyl acetate (2 × 2 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography to get the diol **12** (30 mg, 74%) as white solid. R_f 0.24 (EtOAc/Hex = 1/2);$[\alpha]^{25}_D$ +20.3 (*c* 0.9, $CHCl_3$); mp 52 °C; IR ($CHCl_3$) *v* 3337, 2919, 2850, 1614, 1543, 1191, 1026 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$)δ 7.38-7.15 (m, 25H, ArH), 6.23 (d, *J* = 8.4 Hz, 1H, NH), 5.62-5.58 (m, 1H, H-6), 5.43-5.39 (m, 1H, H-5), 4.91 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.89 (d, *J* = 3.6 Hz, 1H, H-1'), 4.85 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.78 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.72 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.71 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.50 (d, *J* = 11.4 Hz, 1H, CH_2Ph), 4.46-4.45 (m, 1H, H-4), 4.31-4.26 (m, 1H, H-6a'), 4.22-4.18 (m, 1H, H-2), 4.16-4.11 (m, 1H, H-6b'), 4.06-4.03 (m, 2H, H-2', H-5'), 3.86-3.84 (m, 2H, H-3', H-4'), 3.79 (dd, *J* =10.8, 4.2 Hz, 1H, H-1a), 3.70 (dd, *J* =10.8, 3.6 Hz, 1H, H-1b), 3.57-3.54 (m, 1H, H-3), 3.44 (bs, 1H, OH), 3.04 (bs, 1H, OH), 2.12-1.98 (m, 4H, CH_2), 1.58-1.56 (m, 2H, CH_2), 1.34-1.24 (m, 64H, CH_2), 0.88 (t, 6H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.0 (C), 150.3 (t, C × 2), 138.1 (C), 138.0 (C), 137.6 (C), 134.9 (CH), 129.8 (CH × 4), 128.5 (CH × 2), 128.4 (CH × 2), 128.3 (CH × 2), 128.22 (CH × 2), 128.18 (CH × 2), 128.1 (CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH × 2), 125.5 (d, CH × 2), 120.0 (d, CH × 4), 98.8 (CH), 78.8 (CH), 75.7 (CH), 75.3 (CH), 74.6 (CH_2), 74.0 (CH_2), 73.8 (CH), 73.0 (CH_2), 69.4 (d, CH), 68.9 (CH_2), 68.8 (CH), 67.3 (CH_2), 49.8 (CH), 36.6 (CH_2), 31.9 (CH_2 × 2), 29.7 (CH_2 × 16), 29.62 (CH_2 × 4), 29.57 (CH_2), 29.5 (CH_2), 29.4 (CH_2 × 2), 29.3 (CH_2 × 4), 28.0 (CH_2), 25.6 (CH_2), 22.7 (CH_2 × 2), 14.1 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{83}H_{125}O_{12}NP$ 1358.8934, found 1358.8967.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-phospho-α-D-galactopyranosyl)-D *ribo*-2-hexacosanoylamino-1,3,4-octa-decantriol, phosphoric acid (2g). Compound **12** (140 mg) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 2.0 mL) at room temperature. $Pd(OH)_2$/C (100 mg, Degussa type) was added to the solution, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 1 d. The resulting solution was filtered through celite, the filtrate was concentrated *in vacuo*. The residue was dissolved in MeOH/$CHCl_3$ (3/1 ratio, 2.0 mL), Adam's catalyst (PtO_2, 70 mg) was added, and the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 1 d. The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo*, filtered, and washed the solid to afford the crude product **2g** as white solid. $[\alpha]^{22}_D$ +39.9 (*c* 0.4, $CHCl_3$/MeOH); mp 182 °C; IR (KBr) *v* 2918, 2849, 1742, 1466, 1173 cm^{-1}; ^1H NMR (600 MHz, d-pyridine) δ 8.61 (d, *J* = 8.4 Hz, 1H, NH), 5.46 (d, *J* = 3.6 Hz, 1H, H-1'), 5.22-5.20 (m, 1H, H-2), 4.94 (dd, *J* = 16.2, 9,6 Hz, 1H, H-6a'), 4.76 (dd, *J* = 15.6, 9,0 Hz, 1H, H-6b'), 4.70 (t, *J* = 6.0 Hz, 1H, H-5'), 4.63 (dd, *J* = 10.8, 4.8 Hz, 1H, H-1a), 4.58 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 4.52 (bs, 1H, H-3'), 4.38-4.24 (m, 4H, H-1b, H-3, H-4, H-4'), 2.46 (t, *J* = 7.2 Hz, 2H, CH_2), 2.28-2.23 (m, 1H, H-5a), 1.94-1.87 (m, 1H, H-5b), 1.83-1.76 (m, 2H, CH_2), 1.71-1.67 (m, 2H, CH_2), 1.39-1.12 (m, 66H, CH_2), 0.84 (m, 6H, CH_3); ^{13}C NMR (150 MHz, C_5D_5N) δ 173.4 (C), 101.4 (CH), 76.5 (CH), 72.3 (CH), 71.1 (CH), 71.0 (CH), 70.2 (CH), 69.9 (CH), 68.5 (CH_2), 65.3 (CH_2), 51.6 (CH), 36.8 (CH_2), 34.2 (CH_2), 32.09 (CH_2 × 2), 32.08 (CH_2 × 2), 30.4 (CH_2), 30.2 (CH_2), 30.0 (CH_2 × 19), 29.83 (CH_2), 29.75 (CH_2), 29.60 (CH_2 × 2), 29.58 (CH_2 × 2), 26.5 (CH_2), 26.4 (CH_2), 22.9 (CH_2 × 2), 14.3 (CH_3 × 2); HRMS (ESI, M-H^+) calcd for $C_{50}H_{99}O_{12}NP$ 936.6899, found 936.6869.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-sulfo-α-D-galacto-pyranosyl)-2-hexacosanoylamino-5-octadecen-1,3,4-triol, sodium salt (13). To a solution of compound **9** (92 mg, 0.08 mmol) and SO_3/TMA (55 mg, 0.40 mmol) in DMF (1.5 mL), and the mixture was kept stirring for 12 h. Sodium bicarbonate (100 mg, 1.19 mmol) in water (3.0 mL) was added to the solution and stirred for 30 min., filtered to afford the product **13** (100 mg, quant.) as white solid. R_f 0.36 (EtOAc); $[\alpha]^{24}_D$ +32.1 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) *v* 3312, 2919, 2851, 1644, 1543, 1219 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.18 (m, 15H, ArH), 6.06 (d, *J* = 9.0 Hz, 1H, NH), 5.54 (td, *J* = 10.8, 7.2 Hz, 1H, H-6), 5.37 (t, *J* = 10.2 Hz, 1H, H-5), 5.04 (d, *J* = 3.6 Hz, 1H, H-1'), 4.87 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.86-4.85 (m, *J* = 5.4 Hz, 1H, H-4), 4.73-4.71 (m, 3H, $PhCH_2$), 4.66 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.60 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.19-4.13 (m, 3H, H-3, H-6a', H-6b'), 4.10-4.06 (m, 2H, H-2, H-5'), 4.03-4.01 (m, 2H, H-2', H-4'), 3.86 (dd, *J* = 10.2, 2.4 Hz, 1H, H-3'), 3.82-3.80 (m, 1H, H-1a), 3.70-3.68 (m, 1H, H-1b), 2.11-2.04 (m, 1H, H-7a), 1.98-1.88 (m, 3H, H-7b, CH_2), 1.46-1.45 (m, 2H, CH_2), 1.44 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.29-1.20 (m, 64H, CH_2), 0.88 (t, *J* = 6.6 Hz, 6 H, CH_3); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.7 (C), 138.6 (C), 138.32 (C), 138.25 (C), 135.4 (CH), 128.3 (CH × 8), 127.9 (CH × 2), 127.7 (CH), 127.6 (CH), 127.50 (CH × 2), 127.45 (CH), 123.8 (CH), 108.5 (C), 97.4 (CH), 78.6 (CH), 76.5 (CH), 75.6 (CH), 74.7 (CH_2), 74.6 (CH), 73.0 (CH_2), 72.9 (CH), 72.4 (CH_2), 69.0 (CH), 67.6 (CH_2), 66.7 (CH_2), 48.8 (CH), 36.8 (CH_2), 31.9 (CH_2 × 2), 29.8 (CH_2 × 8), 29.7 (CH_2 × 12), 29.66 (CH_2), 29.63 (CH_2), 29.59 (CH_2), 29.56 (CH_2), 29.5 (CH_2 × 2), 29.38 (CH_2), 29.36 (CH_2), 28.0 (CH_3), 27.7 (CH_2), 25.7 (CH_3), 25.5 (CH_2), 22.7 (CH_2 × 2), 14.1 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{74}H_{119}O_{12}NNaS$ 1268.8345 found 1268.8296.

(*2S,3S,4R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsi-lyl-α-D-galactopyranosyl)-2-hexacosanoylamino-5-octadecen-1,3,4-triol (14). To a solution of compound **8** (690 mg, 0.49 mmol) in 1,4-dioxane (1.3 mL) was added 75% H_2SO_4 (345 μL) and was kept stirring for 30 min. Saturated sodium bicarbonate

was added to quench the reaction, and the reaction was extracted with ethyl acetate (3 × 3 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography to get the diol **14** (432 mg, 64%) as colorless oil. R_f 0.21 (EtOAc/Hex = 1/3); $[\alpha]^{25}_D$ +21.2 (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) *v* 3411, 2924, 2853, 1650, 1464, 1091 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.60-7.20 (m, 25H, ArH), 6.24 (d, *J* = 8.4 Hz, 1H, NH), 5.62-5.58 (m, 1H, H-6), 5.43-5.40 (m, 1H, H-5), 4.93 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.89 (d, *J* = 3.6 Hz, 1H, H-1'), 4.87 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.82 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.77 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.71 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.57 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.46 (t, *J* = 6.0 Hz, 1H, H-4), 4.25-4.22 (m, 1H, H-2), 4.02 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 4.02 (d, 1H, *J* = 2.4 Hz, H-4'), 3.88 (dd, *J* = 10.2, 2.4 Hz, 1H, H-3'), 3.82 (dd, *J* = 10.2, 4.2 Hz, 1H, H-1a), 3.76-3.71 (m, 3H, H-1b, H-5',H-6a'), 3.68 (dd, *J* = 9.6, 5.4 Hz, 1H, H-6b'), 3.55 (dd, *J* = 10.8, 6.6 Hz, 1H, H-3), 3.50 (d, *J* = 7.6 Hz, 1H, 3-OH), 2.80 (s, 1H, 4-OH), 2.14-1.98 (m, 4H, CH_2), 1.60-1.55 (m, 2H, CH_2), 1.34-1.25 (m, 64H, CH_2), 1.04 (s, 9H, CH_3), 0.88 (t, *J* = 7.2 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.7 (C), 138.41 (C), 138.35 (C), 137.6 (C), 135.4 (CH × 4), 135.0 (CH), 133.2 (C), 130.0 (C), 129.8 (CH), 129.7 (CH), 128.5 (CH × 2), 128.4 (CH × 2), 128.3 (CH × 2), 128.2 (CH × 2), 128.0 (CH), 127.9 (CH × 3), 127.73 (CH × 2), 127.71 (CH × 2), 127.6 (CH), 127.5 (CH), 127.4 (CH × 2), 98.7 (CH), 79.3 (CH), 75.9 (CH), 75.5 (CH), 74.8 (CH_2), 74.4 (CH), 74.2 (CH_2), 72.7 (CH_2), 71.5 (CH), 69.1 (CH), 68.7 (CH_2), 62.3 (CH_2), 49.3 (CH), 36.7 (CH_2), 31.9 (CH_2 × 2), 29.7 (CH_2 × 17), 29.64 (CH_2 ×2), 29.61 (CH_2), 29.58 (CH_2), 29.57 (CH_2), 29.5 (CH_2), 29.38 (CH_2 ×2), 29.35 (CH_2 × 3), 28.0 (CH_2), 26.8 (CH_3 × 3), 25.7 (CH_2), 22.7 (CH_2 × 2), 19.1 (C), 14.1 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{87}H_{134}O_9NSi$ 1364.9822, found 1364.9845.

(*2S,3S,4R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranosyl)-3,4-di-*O*-benzyl-2-hexacosanoylamino-5-octadecen-1,3,4-triol (15). To a solution of compound **14** (80.5 mg, 0.06 mmol) and benzyl bromide (18 μL, 0.15 mmol) in tetrahydrofuran (1.0 mL) at 0 °C was added 60% sodium hydride (6.0 mg, 0.15 mmol). After completion of addition, the reaction mixture was brought to room temperature and stirred for 4 h. Water (3 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (2 × 3 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the product **21** (62 mg, 68%) as colorless oil. R_f 0.43 (EtOAc/Hex = 1/7); $[\alpha]^{25}_D$ +15.4 (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) *v* 2924 2853, 1680, 1498, 1456, 1095 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.61-7.20 (m, 35H, ArH), 5.96 (d, *J* = 8.4 Hz, 1H, NH), 5.75-5.70 (m, 1H, H-6), 5.47 (t, *J* = 10.2 Hz, 1H, H-5), 4.95 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.84 (d, *J* = 3.6 Hz, 1H, H-1'), 4.82 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.75 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.74 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.72 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.63 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.564 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.558 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.51 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.31-4.26 (m, 2H, H-2, H-4), 4.27 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.05-4.01 (m, 2H, H-2', H-4'), 3.92 (dd, *J* = 10.2, 3.0 Hz, 1H, H-3'), 3.84-3.81 (m, 1H, H-3), 3.78-3.65 (m, 5H, H-1a, H-1b, H-5', H-6a', H-6b'), 2.00-1.81 (m, 6H, CH_2), 1.49-1.45 (m, 2H, CH_2), 1.30-1.20 (m, 62H, CH_2), 1.04 (s, 9H, CH_3), 0.88 (t, *J* = 7.2 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.6 (C), 138.70 (C), 138.66 (C), 138.60 (C), 138.57 (C), 138.3 (C), 136.7 (CH), 135.5 (CH × 4), 133.2 (C), 133.0 (C), 129.73 (CH), 129.67 (CH), 128.33 (CH × 2), 128.29 (CH × 2), 128.2 (CH × 4), 128.1 (CH × 2), 127.9 (CH × 4), 127.73 (CH × 2), 127.70 (CH × 4), 127.6 (CH × 3), 127.5 (CH), 127.44 (CH), 127.39 (CH), 127.37 (CH × 3), 126.0 (CH), 98.6 (CH), 80.1 (CH), 79.1 (CH), 76.7 (CH), 74.9 (CH), 74.85 (CH), 74.83 (CH_2), 73.6 (CH_2), 73.4 (CH_2), 72.8 (CH_2), 71.1 (CH), 69.7 (CH_2), 67.1 (CH_2), 62.2 (CH_2), 50.2 (CH), 36.8 (CH_2), 31.9 (CH_2 × 2), 29.7 (CH_2 × 19), 29.64 (CH_2 × 2), 29.61 (CH_2 × 2), 29.5 (CH_2 × 2), 29.41 (CH_2), 29.36 (CH_2), 29.35 (CH_2), 28.0 (CH_2), 26.9 (CH_3 × 3), 25.7 (CH_2), 22.7 (CH_2 × 2), 19.1 (C), 14.1 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{101}H_{146}O_9NSi$ 1545.0761, found 1545.0786.

(*2S,3S,4R*)-1-*O*-(2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl)-3,4-di-*O*-benzyl-2-hexacosanoylamino-5-octadecen-1,3,4-triol (16). To a solution of compound **15** (111 mg, 0.07 mmol) in tetrahydrofuran (1.1 mL) was added 1.0 M solution of tetrabutylammonium fluoride in tetrahydrofuran (140 μL, 0.14 mmol) and stirred for 12 h. Water (2 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (2 × 2 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to afford the alcohol **16** (84 mg, 90%) as white solid. R_f 0.31 (EtOAc/Hex = 1/3); $[\alpha]^{25}_D$ -18.1 (*c* 1.0, $CHCl_3$); mp 64 °C; IR ($CHCl_3$) *v* 3334, 2921, 2851, 1639, 1538, 1455, 1056 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.25 (m, 25H, ArH), 5.82 (d, *J* = 9.2 Hz, 1H, NH), 5.78-5.72 (m, 1H, H-6), 5.46 (t, *J* = 10.0 Hz, 1H, H-5), 4.94 (d, *J* = 11.2 Hz, 1H, $PhCH_2$), 4.84 (d, *J* = 3.8 Hz, 1H, H-1'), 4.81 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.79 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.71 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.67 (d, *J* = 11.2 Hz, 1H, $PhCH_2$), 4.64 (d, *J* = 11.2 Hz, 1H, $PhCH_2$), 4.63 (d, *J* = 11.6 Hz, 1H, $PhCH_2$), 4.59 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.50-4.45 (m, 1H, H-2), 4.45 (d, *J* = 11.8 Hz, 1H, $PhCH_2$), 4.29 (d, *J* = 11.8 Hz, 1H, $PhCH_2$), 4.28-4.25 (m, 1H, H-4), 4.02 (dd, *J* = 9.6, 3.6 Hz, 1H, H-2'), 3.93 (dd, *J* = 11.6, 8.0 Hz, 1H, H-1a), 3.85-3.82 (m, 2H, H-3', H-4'), 3.78 (dd, *J* = 11.6, 3.8 Hz, 1H, H-1b), 3.73-3.65 (m, 2H, H-5', H-6a'), 3.58 (t, *J* = 4.4 Hz, 1H, H-3), 3.50-3.45 (m, 1H, H-6b'), 2.59 (bs, 1H, OH), 2.01-1.84 (m, 6H, CH_2), 1.48-1.40 (m, 2H, CH_2), 1.32-1.25 (m, 62H, CH_2), 0.88 (t, *J* = 6.8 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.1 (C), 138.6 (C), 138.39 (C), 138.35 (C), 138.2 (C × 2), 136.7 (CH), 128.4 (CH × 2), 128.3 (CH × 10), 128.0 (CH × 2), 127.91 (CH × 2), 127.86 (CH × 2), 127.8 (CH), 127.7 (CH), 127.62 (CH), 127.57 (CH), 127.5 (CH), 127.4 (CH × 2), 126.5 (CH), 100.0 (CH), 81.3 (CH), 79.2 (CH), 76.6 (CH), 74.8 (CH), 74.5 (CH_2), 74.2 (CH), 73.5 (CH_2), 73.4 (CH_2), 73.1 (CH_2), 71.1 (CH), 69.7 (CH_2), 69.5 (CH_2), 62.3 (CH_2), 50.8 (CH), 36.8 (CH_2), 31.9 (CH_2 × 2), 29.7 (CH_2 × 17), 29.63 (CH_2 × 3), 29.56 (CH_2 × 3), 29.42 (CH_2), 29.41 (CH_2), 29.3 (CH_2 × 3), 28.0 (CH_2), 25.7 (CH_2), 22.7 (CH_2 × 2), 14.1 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{85}H_{128}O_9N$ 1306.9584, found 1306.9567.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-sulfo-α-D-galacto-pyranosyl)-3,4-di-*O*-benzyl-2-hexacosanoylamino-5-octadecen-1,3,4-triol, sodium salt (17). To a solution of the alcohol **16** (245 mg, 0.19 mmol) and SO_3/TMA (130 mg, 0.94 mmol) in DMF (4.0 mL). The reaction flask was warmed up to 50 °C, and the mixture was kept stirring for 12 h. After sodium bicarbonate (236 mg, 2.81 mmol) and water (7.5 mL) were added to the solution and stirred for 30 minutes, filtered product **17** (258 mg, quant.) was afforded. R_f 0.36 (EtOAc); $[\alpha]^{25}_D$ -4.88 (*c* 0.9, $CHCl_3$); mp 70 °C; IR ($CHCl_3$) *v* 3422, 2923, 2853, 1653, 1455, 1149 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35-7.18 (m, 25H, ArH), 6.07 (d, *J* = 8.4 Hz, 1H, NH), 5.71-5.67 (m, 1H, H-6), 5.42 (t, *J* = 10.2 Hz, 1H, H-5), 4.86 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.80 (d, *J* = 3.6 Hz, 1H, H-1'), 4.74 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.70-4.61 (m, 6H, $PhCH_2$), 4.39 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.33-4.30 (m, 1H, H-2), 4.27 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.21 (d, *J* = 6.0 Hz, 2H, H-6a', H-6b'), 4.07-4.04 (m, 3H, H-4, H-4', H-5'), 3.99 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 3.85 (dd, *J* = 10.2, 2.4 Hz, 1H, H-3'), 3.77-3.72 (m, 2H, H-1a, H-3), 3.62 (dd, *J* = 10.2, 3.0 Hz, 1H, H-1b), 2.05-1.76 (m, 6H, CH_2), 1.40-1.38 (m, 2H, CH_2), 1.31-1.15 (m, 62H, CH_2), 0.88 (t, *J* = 7.2 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.3 (C), 138.6 (C), 138.4 (C × 2), 138.3 (C), 137.5 (C), 137.2 (CH), 128.6 (CH × 2), 128.4 (CH × 2), 128.28 (CH × 4), 128.25 (CH × 4), 128.2 (CH × 2), 127.9 (CH × 2), 127.8 (CH), 127.63 (CH × 2), 127.57 (CH), 127.5 (CH × 2), 127.4 (CH × 3), 126.5 (CH), 98.7 (CH), 80.4 (CH), 78.8 (CH), 76.0 (CH), 74.87 (CH_2), 74.84 (CH), 74.5 (CH_2), 73.5 (CH_2), 73.2 (CH), 72.4 (CH_2), 69.38 (CH), 69.35 (CH_2), 67.0 (CH_2), 66.2 (CH_2), 50.8 (CH), 36.8 (CH_2), 31.9 (CH_2 × 2), 29.8 (CH_2 × 8), 29.7 (CH_2 × 12), 29.6 (CH_2), 29.5 (CH_2 × 2), 29.40 (CH_2), 29.38 (CH_2 × 2), 29.35 (CH_2 × 2), 28.1 (CH_2), 25.9 (CH_2), 22.7 (CH_2 × 2), 14.1 (CH_3 × 2); HRMS (ESI, M+Na^+) calcd for $C_{85}H_{126}O_{12}NNa_2S$ 1430.8791, found 1430.8770.

(2*S*,3*S*,4*R*)-1-*O*-(6-*O*-sulfo-α-D-galactopyranosyl)-D-*ribo*-2-hexacosanoylamino-1,3,4-octadecantriol, sodium salt (2h). Compound **17** (38.4 mg, 0.027 mmol) was dissolved in a mixed solvent of H_2O/MeOH/$CHCl_3$ (6/3/1 ratio, 1 mL) at room temperature. $Pd(OH)_2$/C (58.0 mg, Degussa type) was added to the solution, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 1 d. The resulting solution was filtered through celite, then saturated sodium bicarbonate (3.0 mL) was added to stir at room temperature for 0.5 h, filtered, and washed the solid to afford the crude product **2h** (17.1 mg, 65%) as white solid. $[\alpha]^{24}_D$ +200.5 (*c* 0.2, $CHCl_3$); IR (KBr) *v* 3350, 2923, 2853, 1639, 1542, 1455, 1257, 1056 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.95 (d, *J* = 8.4 Hz, 1H, NH), 5.44 (d, *J* = 3.6 Hz, 1H, H-1'), 5.17-5.13 (m, 1H, H-2), 5.04-4.97 (m, 2H, H-6a', H-6b'), 4.76 (t, *J* = 6.0 Hz, 1H, H-5'), 4.64-4.58 (m, 2H, H-1a, H-2'), 4.49-4.39 (m, 3H, H-3, H-3', H-4'), 4.34-4.29 (m, 2H, H-1b, H-4), 2.62-2.56 (m, 2H, CH_2), 2.20-2.15 (m, 1H, H-5a), 1.89-1.73 (m, 3H, H-5b, CH_2), 1.64-1.59 (m, 2H, CH_2), 1.36-1.17 (m, 66H, CH_2), 0.88 (m, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.3 (C), 100.8 (CH), 75.9 (CH), 72.4 (CH), 71.0 (CH), 70.55 (CH), 70.52 (CH), 69.9 (CH), 68.0 (CH_2), 67.6 (CH_2), 51.5 (CH), 36.8 (CH_2), 33.9 (CH_2), 32.07 (CH_2 × 2), 32.05 (CH_2 × 2), 30.4 (CH_2), 30.1 (CH_2), 30.0 (CH_2 × 16), 29.7 (CH_2), 29.59 (CH_2 × 2), 29.56 (CH_2 × 2), 26.4 (CH_2 × 2), 22.9 (CH_2 × 4), 14.3 (CH_3 × 2); HRMS (ESI, M+Na^+) calcd for $C_{50}H_{98}O_{12}NNa_2S$ 982.6600 found 982.6610.

(2*S*,3*S*,4*R*)-1-*O*-(2,3,4-Tri-*O*-benzyl-6-azido-α-D-galactopy-ranosyl)-2-hexacosanoylamino-3,4-*O*-isopropylidene-5-octa-decen-1,3,4-triol (18). To a solution of alcohol **9** (98 mg, 0.08 mmol) and triphenylphosphine (66 mg, 0.25 mmol) in tetrahydrofurane (1 mL) at 0 °C was added diisopropylazodicarboxylate (51 μL, 0.25 mmol), followed by the dropwise addition of diphenylphosphorylazide (63 μL, 0.29 mmol). After completion of addition, the temperature of the reaction mixture was brought to 28 °C and stirred for 1 h. Water (5 mL) was added to quench the reaction and the mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo* to give a residue. The residue was purified by column chromatography to give the azide **18** (100 mg, 99%) as white solid. R_f 0.71 (EtOAc/Hex = 1/2.5); $[\alpha]^{25}_D$ +17.0 (*c* 0.6, $CHCl_3$); mp 80-82 °C; IR ($CHCl_3$) *v* 3309, 2918, 2850, 2095, 1641, 1546, 1469, 1042 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.42-7.25 (m, 15H, ArH), 8.89 (d, *J* = 9.0 Hz, 1H, NH), 5.60 (td, *J* = 10.8, 7.2 Hz, 1H, H-6), 5.44 (t, *J* = 9.6 Hz, 1H, H-5), 5.02-4.98 (m, 2H, H-1', $PhCH_2$), 4.88 (dd, *J* = 9.6, 6.6 Hz, 1H, H-4), 4.85 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.81 (d, *J* = 10.8 Hz, 1H, $PhCH_2$), 4.77 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.69 (d, *J* = 11.4 Hz, 1H, $PhCH_2$), 4.60 (d, *J* = 12.0 Hz, 1H, $PhCH_2$), 4.18 (dd, *J* = 7.8, 5.4 Hz, 1H, H-3), 4.14-4.10 (m, 1H, H-2), 4.05 (dd, *J* = 10.2, 3.6 Hz, 1H, H-2'), 3.91 (dd, *J* = 12.0, 2.4 Hz, 1H, H-3'), 3.89 (dd, *J* = 11.4, 3.6 Hz, 1H, H-1a), 3.83-3.81 (m, 2H, H-4', H-5'), 3.69 (dd, *J* = 11.4, 7.8 Hz, 1H, H-1b), 3.52 (dd, *J* = 12.0, 7.8 Hz, 1H, H-6a'), 3.04 (dd, *J* = 12.0, 4.8 Hz, 1H, H-6b'), 2.11-1.90 (m, 2H, CH_2), 1.56-1.51 (m, 2H, CH_2), 1.46 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.25 (bs, 64H, CH_2), 0.88 (t, *J* = 7.2 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.3 (C), 138.4 (C), 138.2 (C), 138.0 (C), 135.1 (CH), 130.0 (CH × 3), 128.4 (CH × 3), 127.94 (CH), 127.89 (CH), 127.87 (CH), 127.7 (CH), 127.5 (CH), 126.1 (CH × 2), 124.0 (CH), 120.22 (CH), 120.18 (CH), 108.4 (C), 98.8 (CH), 78.7 (CH), 76.6 (CH), 76.3 (CH), 74.65 (CH_2), 74.63 (CH), 73.4 (CH_2), 73.12 (CH_2), 73.06 (CH), 69.8 (CH), 68.9 (CH_2), 51.4 (CH_2), 49.0 (CH), 36.8 (CH_2), 31.9 (CH_2), 29.7 (CH_2 × 24), 29.6 (CH_2), 29.5 (CH_2), 29.45 (CH_2), 29.42 (CH_2), 29.3 (CH_2 × 2), 27.8 (CH_3), 27.7 (CH_2), 25.6 (CH_2), 25.5 (CH_3), 22.7 (CH_2), 14.1 (CH_3 × 2); HRMS (ESI, M+H^+) calcd for $C_{74}H_{119}O_8N_4$ 1191.9022, found 1191.9016.

(2*S*,3*S*,4*R*)-1-*O*-(6-amine-α-D-galactopyranosyl)-D-*ribo*-2-hexacosanoylamino-1,3,4-octadecantriol (2i). Compound **18** (73 mg, 0.061 mmol) was dissolved in a mixed solvent of MeOH/$CHCl_3$ (3/1 ratio, 4 mL) at 28 °C. $Pd(OH)_2$/C (73 mg, Degussa type) was added to the solution and added 2-3 drop acetic acid, the reaction vessel was purged with hydrogen, and the mixture was stirred under 60 psi pressure at the same temperature for 5 h. The resulting solution was filter through celite, the filtrate was concentrated *in vacuo*, and the residue was purified by column chromatography to afford the target molecule **2i** (17 mg, 31%) as white solid. R_f 0.2 (MeOH/DCM = 1/4); the poor solubility of this amine compound at room temperature prevented

us from obtaining reliable optical rotation data. Mp 187-188 °C; IR (KBr) ν 3417, 2920, 2851, 1645, 1072 cm^{-1}; ^1H NMR (600 MHz, d-pyridine, 100 °C) δ 8.02 (bs, 1H, NH), 5.35 (d, J = 2.4 Hz, 1H, H-1'), 5.02 (bs, 1H, H-2), 4.87 (d, J = 3.0 Hz, 1H, H-5'), 4.64 (dd, J = 10.2, 4.8 Hz, 1H, H-1a), 4.39 (dd, J = 9.0, 3.6 Hz, 1H, H-2'), 4.34-4.33 (m, 2H, H-3', H-4'), 4.19-4.16 (m, 3H, H-1b, H-3, H-4), 3.85 (dd, J = 13.2, 7.8 Hz, 1H, H-6a'), 3.65 (dd, J = 12.6, 2.4 Hz, 1H, H-6b'), 2.46 (t, J = 7.2 Hz, 2H, CH_2), 2.40 (t, J = 7.8 Hz, 1H, CH_2), 2.20-2.15 (m, 1H, CH_2), 1.84-1.83(m, 4H, CH_2), 1.75-1.65 (m, 3H, CH_2), 1.40 (bs, 34H, CH_2), 1.35 (bs, 29H, CH_2), 0.93 (t, J = 6.6 Hz, 6H, CH_3 × 2); ^{13}C NMR (150 MHz, d-pyridine, 100 °C) δ 174.0 (C), 101.8 (CH), 77.3 (CH), 73.0 (CH), 71.6 (CH), 71.2 (CH), 70.2 (CH), 69.8 (CH_2), 68.5 (CH), 52.9 (CH), 42.0 (CH_2), 37.2 (CH_2), 34.84 (CH_2), 34.78 (CH_2), 34.6 (CH_2), 32.3 (CH_2 × 3), 31.2 (CH_2), 30.6 (CH_2), 30.5 (CH_2 × 2), 30.2 (CH_2 × 2), 30.1 (CH_2 × 7), 29.94 (CH_2 × 3), 29.91 (CH_2 × 2), 29.7 (CH_2 × 3), 29.52 (CH_2), 29.46 (CH_2), 27.4 (CH_2), 26.5 (CH_2 × 2), 24.6 (CH_2), 23.0 (CH_2 × 3), 14.2 (CH_3 × 2); HRMS (ESI, M + H^+) calcd for $C_{50}H_{101}O_8N_2$ 857.7552, found 857.7558.

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