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Efficient and Selective Synthesis of D-*arabino*-, D-*lyxo*-, and D-*xylo*-Phytosphingosine from D-*ribo*-Phytosphingosine†

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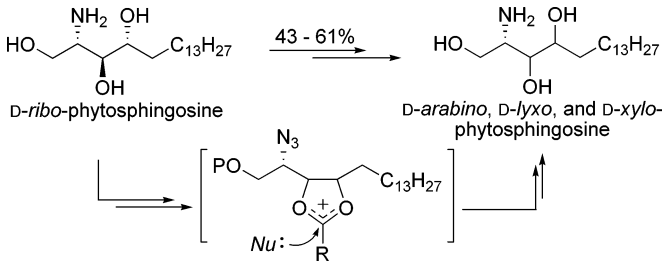
Received October 3, 2007



A new high-yield approach to the regio- and stereoselective synthesis of D-*arabino*-, D-*lyxo*-, and D-*xylo*-phytosphingosines from inexpensive D-*ribo*-phytosphingosine is described. The synthetic methodologies mainly rely on the selective configurational inversion of the stereocenter through a neighboring group participation mechanism.

Introduction

Sphingoid bases are long-chain aliphatic compounds typically possessing a 2-amino-1,3-diol functionality. They are the principal structural backbone of sphingolipids which play critical roles in many physiological processes.[1] Among the naturally occurring sphingoid bases, phytosphingosines are one of the most important and common species.[2] They are widely distributed in plants, yeasts, fungi, and even mammalian tissues. They consist mainly of an 18-carbon chain and possess a 2-amino-1,3,4-triol head group. In nature, the most predominant stereoisomer of phytosphingosines is D-*ribo*-phytosphingosine (**1**, Figure 1). Although it had been costly to isolate **1** from natural sources, it is now readily obtainable on an industrial scale from a yeast fermentation process.[3]

Because of the interesting biological properties of phytosphingosine itself and phytosphingosine-containing sphingolipids,[4] a great deal of effort has been devoted toward the synthesis of **1** as well as other stereoisomers, such as D-*lyxo*- (**2**), D-*arabino*- (**3**), and D-*xylo*- (**4**) phytosphingosines, shown in Figure 1.[2,5,6] To establish the desired stereochemistry, most syntheses rely on chiral pools such as carbohydrates and amino acids, or

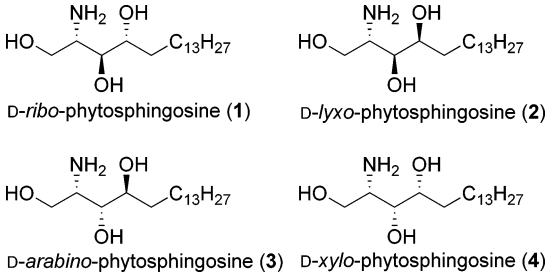


FIGURE 1. 1. D-*ribo*-Phytosphingosine (**1**) and its stereoisomers **2**−**4**.

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† Dedicated to Prof. Moon Woo Chun on the occasion of his retirement.

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10.1021/jo702147y CCC: $40.75
Published on Web 01/16/2008

asymmetric transformations such as Sharpless asymmetric dihydroxylation. The reported methodologies each have their own advantages and disadvantages, and many of them were not satisfactory in view of the stereoselective synthesis of all four possible stereoisomers of D-phytosphingosine.[6]

In the course of our ongoing sphingolipid research, all four stereoisomers of D-phytosphingosines **1**−**4** were needed as starting materials for the synthesis of certain sphingolipids. It would be medicinal-chemically interesting to examine and compare the biological activities of each of four phytosphingosine-derived sphingolipids. This is because the different configurations of one or two hydroxyl groups of phytosphingosines could elicit different biological effects of sphingolipids as a result of the different conformations and hydrogen-bonding patterns of a molecule.[7] We considered the cheap and commercially available *ribo* isomer **1** as possibly an ideal starting material[8] for the preparation of other stereoisomers **2**−**4** since they are identical except for the stereochemistries at either or both C-3 and C-4.

The selective configurational inversion of the given hydroxyl group of the diol or polyol is one of the important transformations in synthetic organic chemistry, especially in the area of carbohydrate chemistry. A number of useful methods have been developed, including protocols based on the anchimeric assistance, the Mitsunobu reaction, and sequential oxidation/reduction route as well as triflation/nitrite addition.[9] Although this type of inversion has been extensively studied in the context of cyclic systems, the regioselective inversion of the distal or proximal hydroxyl groups in an acyclic system has been less widely explored.[10]

Herein, we wish to report a concise and efficient stereoselective synthetic route to the above-mentioned three stereoisomers of phytosphingosine **2**−**4** from inexpensive *ribo* isomer **1** via a selective inversion of either of the two hydroxyl groups at C-3 and C-4. The route also provides access to the corresponding 2-azido intermediates which might be synthetically useful especially in the preparation of 1-glycosyl sphingolipids.[11] Our strategy relied mainly on the selective configurational inversion of the stereocenter through a neighboring group participation mechanism.

Results and Discussion

At the commencement of the synthesis, it occurred to us that the proper choice of protecting groups for 1,2-β-amino-alcohol functionality in D-*ribo*-phytosphingosine (**1**) was important to avoid the complication caused by the multiple anchimeric assistance during the inversion of activated hydroxyl groups. Thus, the non-nucleophilic azide was chosen as an amino protecting group, and the bulky silyl protecting group was introduced at the primary hydroxyl group. The suitably protected phytosphingosine **5** (Scheme 1) was easily prepared from **1** by a two-step sequence as described in our previous work.[12]

With multigram quantities of **5** in hand, we first examined whether the 3,4-vicinal diol of **5** would be selectively monofunctionalized with a moderately reactive leaving group such as tosylate or mesylate. We felt that the difference in the steric and electronic environment surrounding each secondary hydroxyl group of **5** would enable us to differentiate the two hydroxyl groups and introduce sulfonyl groups in a regioselective fashion.[13] After some trials, it was found that treatment of **5** with a slight excess of TsCl in pyridine provided predominantly 4-*O*-tosylate **6** (75%; 81% yield based on the recovered starting material), along with a minor amount of its regioisomer 3-*O*-tosylate (4%). The corresponding ditosylate was not detected in the crude ^{1}H NMR spectra. The minor regioisomer, 3-*O*-tosylate, could be removed by rather tedious column chromatography, although for practical reasons it is preferred to separate the isomeric mixture in the subsequent steps. The regiochemistry of **6** was determined by the ^{1}H NMR chemical shifts and splitting patterns of the protons at C-3 and C-4. To utilize the Winstein's neighboring group participation[14,15] in inverting the configuration at C-4 within **6**, the C-3 hydroxyl group was converted to its acetate **7** in 95% yield with Ac_2O/pyridine.

Heating the obtained **7** in refluxing wet ethanol (5% v/v) in the presence of 1 equiv of $CaCO_3$ for 4 days afforded a 4.3:1 mixture of inseparable acetates **8a** and **8b** in 91% combined yield. No other isomers were detected by careful ^{1}H NMR analysis of the reaction mixture. In this process, the presence

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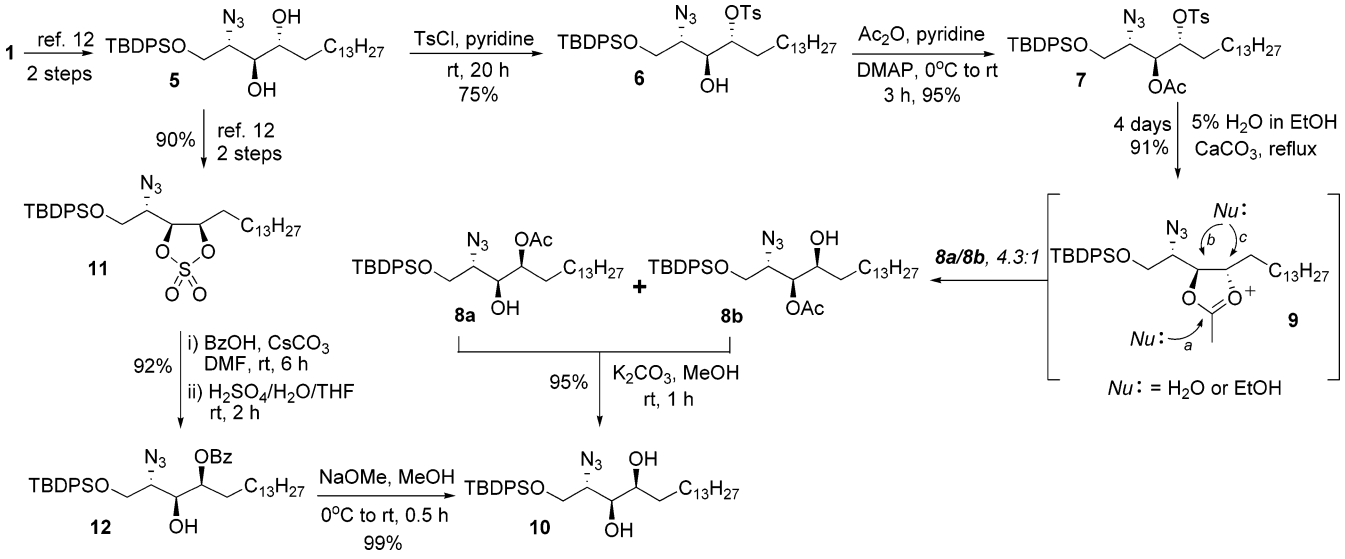
SCHEME 1. Synthesis of D-*lyxo*-Diol 10



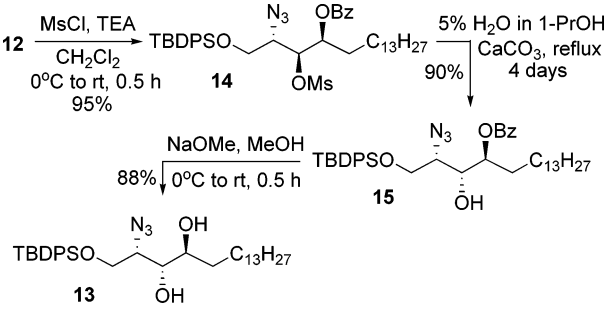
of $CaCO_3$ was essential because its absence led to very complex mixtures of unidentified products. The use of other carbonate salts such as K_2CO_3 did not afford the desired products, **8a** and **8b**, but instead gave the corresponding C3−C4 epoxide as a major product. The stereochemistry of **8a** and **8b** was determined by their conversion to the final product **2** as discussed later.

The formations of both acetates **8a** and **8b** as well as the configurational inversion of C-4 denoted the Winstein's anchimeric assistance mechanism during the process of inversion and strongly suggested this reaction proceeds via an oxonium ion intermediate **9**. From the previous observations[14,16] and the present results, it is apparent that the C-4 inverted intermediate **9** collapses via path *a* to produce **8a** and **8b**. Attack on **9** at C-3 (path *b*) or C-4 (path *c*) by oxygen nucleophiles (H_2O or EtOH) would produce the *arabino*- or *ribo*-derviatives, respectively, which were not produced during the reaction. It was seen that the formation of **8a** and **8b** would also result from the direct S_N2 displacement of the C-4 tosylate **7** with nucleophile (water) and subsequent acyl migration. However, this is quite unlikely based on literature precedents[14,16] and our result that no trace of C-4 ethyl ether was detected in the crude ^{1}H NMR spectra.

Acetate hydrolysis of a mixture of **8a** and **8b** with K_2CO_3 in methanol provided the 1,2-amino-alcohol protected D-*lyxo*-phytosphingosine **10** in 95% yield. Alternatively and more conveniently, **10** could be obtained in one-pot fashion from **7** without the isolation and purification of a mixture of **8a** and **8b**. After the displacement reaction was completed to give **8a** and **8b** as judged by TLC analysis, K_2CO_3 (3 equiv) and excess methanol were added to the reaction mixture at room temperature for the acetate hydrolysis to provide **10** in higher overall yield (94%).

The protected *lyxo* isomer **10** could be also prepared via another route. In our previous study, it was found that the nucleophilic ring opening of cyclic sulfate **11** (Scheme 1) with iodide occurred exclusively at C-4 with clean inversion.[12] This result prompted us to investigate the reaction of **11** with oxygen nucleophiles to develop a new route to *lyxo* isomer **10**. Cyclic sulfate **11** was easily prepared from **5** in high overall yield as described in our previous work. We found that the treatment of cyclic sulfate **11** with cesium benzoate[17] in DMF followed by acidic hydrolysis of the intermediate *O*-sulfate provided the 4-*O*-benzoate **12** as the only identifiable regioisomer in 92% yield, giving inversion of C-4 configuration in the product. The excellent regioselectivity could be attributed to the steric and electronic interactions between the neighboring substituents and nucleophile. Cleavage of the benzoate ester in **12** with NaOMe/MeOH furnished the 1,2-protected *lyxo* isomer **10** in 99% yield, which was identical with **10** prepared from **6** (Scheme 1).

SCHEME 2. Synthesis of D-*arabino*-Diol 13



With compound **12** in hand, we sought to apply it to the synthesis of *arabino* isomer **13** (Scheme 2). To invert the configuration at C-3 within **12**, the Winstein's neighboring group participation was again utilized. At first, we attempted to convert the C-3 hydroxyl group of **12** to the corresponding tosylate. The formation of the tosylate by the reaction with TsCl did not occur even at elevated temperatures, probably due to the steric crowding at C-3. On the other hand, mesylation with MsCl at room temperature proceeded effectively in 95% yield to give **14**. The resulting mesylate **14** was subjected to the same reaction conditions as described for **7** ($CaCO_3$ in refluxing wet ethanol). In this case, however, the reaction was very sluggish and did not reach completion even after one week (67% conversion). The low conversion rate might be attributed to the fact that the benzoyl group is less reactive than the acetyl counterpart to

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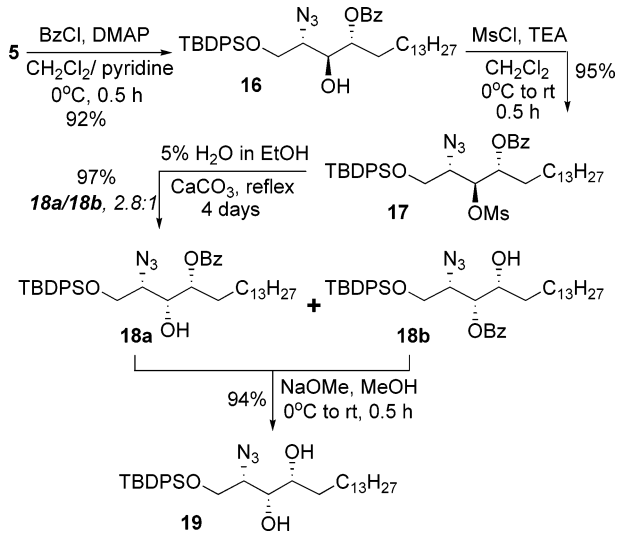
SCHEME 3. Synthesis of D-*xylo*-Diol 19

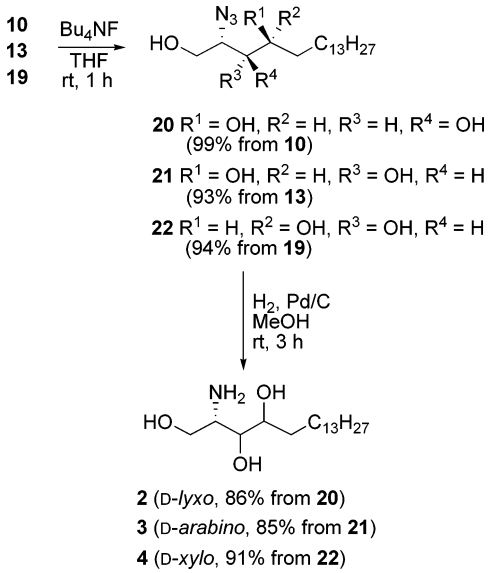


neighboring group participation.[18] Therefore, the reaction solvent was changed to a higher boiling point solvent, 1-propanol, and the reaction temperature was raised to reflux. This modification successfully led to the formation of the desired C-3 inverted product **15** as the only detectable isomer in 90% yield after 4 days refluxing. In this process, unlike the inversion reaction for the *lyxo* isomer (**7** to **8**), only a single ester was formed. Saponification of the benzoyl ester in **15** with NaOMe/MeOH produced the targeted 1,2-protected *arabino* isomer **13** in 88% yield.

For the synthesis of the *xylo*-isomer from the *ribo*-isomer using the Winstein's neighboring group participation, regioselective acylation of the hydroxyl group at C-4 was required. This was accomplished by treating diol **5** with 1 equiv of benzoyl chloride in a mixture of pyridine and CH_2Cl_2 in the presence of a catalytic amount of DMAP to furnish 4-*O*-benzoate **16** with very high yield (92%) and regioselectivity (Scheme 3). Only a trace amount (<5%) of 3-*O*-benzoate was detected in the crude mixture, and it was removed by column chromatography. Mesylation of the resulting secondary alcohol **16** gave **17** in 95% yield and set the stage for the inversion of the stereocenter at C-3. When the inversion reaction of **17** was conducted under the same reaction conditions as those for **7**, a 2.8:1 mixture of the separable benzoates **18a** and **18b** was obtained in 97% combined yield. No other isomers were detected in the crude ^{1}H NMR spectra. The ester product distribution of this inversion reaction was different from those obtained from **7** and **14**. Although the factors that determine which products are formed depend on many variables, these results could be a reflection of the relative thermodynamic preference of each system.[19] Removal of the benzoate group in **18a** and **18b** with NaOMe/MeOH afforded the 1,2-protected *xylo* isomer **19** in 94% yield.

All the obtained 1,2-protected isomers, **10**, **13**, and **19**, were completely free from any other isomers. With these compounds in hand, efforts were next directed toward the deprotection steps. Removal of the silyl protecting groups in compounds **10**, **13**, and **19** with Bu_4NF in THF furnished the corresponding 2-azidophytosphingosine **20**, **21**, and **22** in 99%, 93%, and 94% yields, respectively (Scheme 4). Finally, reduction of the azide groups of 2-azidophytosphingosines **20**, **21**, and **22** was achieved by hydrogenation with Pd/C in MeOH to give the desired target compounds D-*lyxo*- (**2**), D-*arabino*- (**3**), and D-*xylo*- (**4**) phytosphingosines in 86%, 85%, and 91% yields, respectively. For analytical reasons, the obtained phytosphingosines **2**−**4** were peracetylated with Ac_2O/pyridine to provide the corresponding tetraacetate derivatives in high yields. The analytical and spectroscopic data of both the synthetic phytosphingosine isomers **2**−**4** and their tetraacetate derivatives were identical with those reported in the literature.[5e−g,6d−g,20]

SCHEME 4. Synthesis of D-*lyxo*- (2), D-*arabino*- (3), and D-*xylo*- (4) Phytosphingosine



In conclusion, these studies provide a practical preparative route to D-*lyxo*- (**2**), D-*arabino*- (**3**), and D-*xylo*- (**4**) phytosphingosines from the low-cost D-*ribo*-phytosphingosine (**1**) in high overall yield. An important feature of this synthesis is the selective configurational inversion of the stereocenter through a neighboring group participation mechanism as well as a nucleophilic substitution of cyclic sulfate. The process is highly selective and seems to be readily amenable to multigram-scale synthesis. In addition, the synthetic methodology also provided the protected isomers of phytosphingosines which could be synthetically useful in the preparation of various sphingolipid derivatives.

Experimental Section

(2*S*,3*S*,4*R*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-hydroxyoctadecan-4-yl 4-Methylbenzenesulfonate (6). To a solution of diol **5** (610 mg, 1.05 mmol) in pyridine (5 mL) was added TsCl (240 mg, 1.26 mmol) at room temperature. After being stirred at room temperature for 20 h, this reaction mixture was diluted with CH_2Cl_2 then washed with H_2O. The aqueous phase was extracted with CH_2Cl_2 twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude

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(19) Exposure of the purified minor products **18b** to the same reaction conditions as those for starting **17** ($CaCO_3$ in refluxing wet ethanol) for 2 days led to a 2.4:1 mixture of **18a** and **18b**.

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product was purified by silica gel column chromatography (hexane/EtOAc, 40:1) to give tosylate **6** (580 mg, 75%; 81% yield based on the recovered starting material) as a colorless oil as well as its regioisomer 3-*O*-tosylate (30 mg, 4% yield based on the recovered starting material), along with recovered starting material **5** (45 mg): $[\alpha]^{25}_D$ +36.7 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.6 Hz, 3H), 1.09 (s, 9H), 1.14−1.28 (m, 20H), 1.40−1.49 (m, 2H), 1.67−1.79 (m, 2H), 2.43 (s, 3H), 3.26−3.32 (m, 1H), 3.89 (dd, J = 5.4, 11.1 Hz, 1H), 3.95−3.98 (m, 1H), 4.03 (dd, J = 3.0, 10.8 Hz, 1H), 4.70 (td, J = 3.0, 9.3 Hz, 1H), 7.32 (d, J = 8.1 Hz, 1H), 7.38−7.50 (m, 6H), 7.67−7.72 (m, 4H), 7.80 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.1, 21.6, 22.6, 24.9, 26,7, 28.0, 29.1, 29.30, 29.32, 29.4, 29.60, 29.62, 29.64, 31.9, 62.7, 64.4, 71.2, 84.4, 127.79, 127.82, 127.9, 129.8, 129.87, 129.91, 132.58, 132.63, 133.6, 135.55, 135.58, 144.9; IR (CH_3Cl) υ_{max} 3493, 3073, 2926, 2855, 2101, 1177, 1113, 918 (cm^{-1}); MS (FAB) *m*/*z* 736 ($[M + 1]^+$, 6), 135 (100), 199 (55), 240 (23), 458 (10); HRMS (FAB) calcd for $C_{41}H_{62}N_3O_5SSi$ 736.4179 ($[M + H]^+$), found 736.4152.

(2*S*,3*S*,4*R*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-4-(tosyloxy)-octadecan-3-yl Acetate (7). To a solution of tosylate **6** (314 mg, 0.426 mmol) in pyridine (4 mL) were added Ac_2O (120 μL, 1.29 mmol) and DMAP (3 mg, 0.02 mmol) at 0 °C. After being stirred at room temperature for 3 h, this reaction mixture was poured into saturated $NaHCO_3$ solution and extracted with CH_2Cl_2 twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 15:1) to give acetate **7** (315 mg, 95%) as a colorless oil: $[\alpha]^{25}_D$ +15.0 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.6 Hz, 3H), 1.06 (s, 9H), 1.18−1.31 (m, 20H), 1.55−1.64 (m, 2H), 1.86 (s, 3H), 2.41 (s, 3H), 3.53−3.59 (m, 1H), 3.67 (dd, J = 6.6, 10.8 Hz, 1H), 3.79 (dd, J = 2.7, 10.8 Hz, 1H), 4.75 (ddd, J = 2.4, 5.7, 7.8 Hz, 1H), 4.95 (dd, J = 2.1, 8.1 Hz, 1H), 7.25−7.30 (m, 1H), 7.37−7.48 (m, 6H), 7.60−7.76 (m, 4H), 7.70−7.75 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.00, 19.03, 20.6. 21.6, 22.7, 25.2, 26.5, 26.6, 26.7, 29.1, 29.2, 29.4, 29.5, 29.65, 29.66, 29.67, 29.7, 29.9, 31.9, 61.9, 63.9, 71.3, 81.8, 127.7, 127.8, 127.9, 129.6, 129.7, 129.9, 132.6, 132.7, 134.0, 134.8, 135.2, 135.5, 135.55, 135.61, 135.63, 144.7, 169.3; IR (CH_3Cl) υ_{max} 3468, 3073, 2930, 2855, 2103, 1754, 1177, 1113, 910 (cm^{-1}); MS (FAB) *m*/*z* 800 ($[M + 23]^+$, 9), 135 (100), 197 (70), 353 (18); HRMS (FAB) calcd for $C_{43}H_{63}N_3O_6SSiNa$ 800.4105 ($[M + Na]^+$), found 800.4136.

(2*S*,3*S*,4*S*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-hydroxy-octadecan-4-yl Acetate (8a) and (2*S*,3*S*,4*S*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-4-hydroxyoctadecan-3-yl Acetate (8b). To a solution of acetate **7** (246 mg, 0.316 mmol) in wet EtOH (4 mL, 5% v/v) was added $CaCO_3$ (32 mg, 0.32 mmol). This reaction mixture was heated under reflex for 4 days. The reaction was filtered, and then concentrated to dryness under reduced pressure. The residue was dissolved in EtOAc and washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo to give acetate **8** (200 mg, 91%) as a mixture of acetates **8a** and **8b** in a ratio of 4.3:1. The crude mixture was used in the next step without further purification. Acetates **8a** and **8b** were separated by repeated preparative TLC on silica gel (hexane/EtOAc, 25:1) for analytical purposes.

8a: colorless oil; $[\alpha]^{24}_D$ +8.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.25 (s, 24H), 1.57−1.74 (m, 2H), 2.08 (s, 3H), 2.13 (d, J = 8.1 Hz, 1H), 3.27−3.33 (m, 1H), 3.59 (dt, J = 2.1, 8.4 Hz, 1H), 3.89 (dd, J = 6.0, 11.1 Hz, 1H), 4.01 (dd, J = 3.9, 11.1 Hz, 1H), 5.08 (ddd, J = 2.1, 7.5, 8.7 Hz, 1H), 7.36−7.49 (m, 6H), 7.64−7.72 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.1, 21.1, 22.7, 25.3, 26.8, 29.35, 29.39, 29.47, 29.52, 29.65, 29.68, 30.7, 32.0, 63.9, 64.7, 71.2, 73.4, 83.2, 127.85, 127.87, 130.0, 135.6, 170.3; IR (CH_3Cl) υ_{max} 3468, 3073, 2928, 2854, 2361, 2102, 1717, 1262, 1113 (cm^{-1}); MS (FAB) *m*/*z* 624 ($[M + 1]^+$, 6), 135 (100), 199 (48), 240 (29), 606 (10); HRMS (FAB) calcd for $C_{36}H_{58}N_3O_4Si$ 624.4197 ($[M + H]^+$), found 624.4196.

8b: colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.25 (s, 24H), 1.54−1.64 (m, 2H), 1.93 (s, 1H), 2.66 (d, J = 9.3 Hz, 1H), 3.44−3.48 (m, 1H), 3.66−3.80 (m, 3H), 4.83 (dd, J = 1.8, 7.8 Hz, 1H), 7.36−7.49 (m, 6H), 7.64−7.72 (m, 6H); MS (FAB) *m*/*z* 646 ($[M + 23]^+$, 6), 135 (100), 199 (70), 240 (40), 606 (23); HRMS (FAB) calcd for $C_{36}H_{57}N_3O_4SiNa$ 646.4016 ($[M + Na]^+$), found 646.3986.

(2*S*,3*S*,4*S*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-hydroxy-octadecan-4-yl Benzoate (12). To a solution of cyclic sulfate **11** (4.25 g, 6.60 mmol) in DMF (33 mL) were added BzOH (1.37 g, 11.2 mmol) and $CsCO_3$ (3.23 g, 9.91 mmol). This reaction mixture was stirred at room temperature for 6 h, and to it were added concentrated H_2SO_4 (5 mL), H_2O (6 mL), and THF (11.5 mL). The mixture was stirred for 2 h at room temperature, and then diluted with EtOAc. It was then washed with saturated aqueous $NaHCO_3$ solution and brine. The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 10:1) to give benzoate **12** (4.17 g, 92%) as a colorless oil: $[\alpha]^{27}_D$ +7.4 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.20−1.40 (m, 24H), 1.64−1.94 (m, 2H), 2.30 (d, J = 8.1 Hz, 1H), 3.33−3.39 (m, 1H), 3.71 (td, J = 2.1, 8.4 Hz, 1H), 3.92 (dd, J = 6.3, 11.1 Hz, 1H), 4.04 (dd, J = 3.9, 10.8 Hz, 1H), 5.35 (ddd, J = 2.1, 6.3, 8.1 Hz, 1H), 7.32−7.50 (m, 9H), 7.56−7.72 (m, 4H), 8.02−8.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.0, 22.6, 25.4, 26.7, 29.28, 29.34, 29.38, 29.44, 29.54, 29.58, 29.60, 29.62, 30.7, 31.8, 63.9, 64.6, 71.4, 74.2, 127.73, 127.75, 128.3, 129.7, 129.8, 129.9, 132.6, 132.7, 133.0, 135.5, 135.51, 165.9; IR ($CHCl_3$) υ_{max} 3493, 2926, 2863, 2100, 1711, 1271, 1111 (cm^{-1}); MS (FAB) *m*/*z* 708 ($[M + 23]^+$, 3), 105 (100), 135 (45), 199 (23), 240 (15); HRMS (FAB) calcd for $C_{41}H_{59}N_3O_4SiNa$ 708.4173 ($[M + Na]^+$), found 708.4181.

(2*S*,3*S*,4*S*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)octadecane-3,4-diol (10). Method A: To a solution of the crude acetate **8** (174 mg, 0.279 mmol) in MeOH (3 mL) was added K_2CO_3 (58 mg, 0.42 mmol) at room temperature. After being stirred at room temperature for 1 h, this reaction mixture was poured into saturated NH_4Cl solution and extracted with EtOAc twice. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 8:1) to give *lyxo*-diol **10** (154 mg, 95%) as a colorless oil.

Method B: To a solution of benzoate **12** (1.03 g, 1.50 mmol) in MeOH (15 mL) was added NaOMe (1.5 equiv, 25 wt % solution in MeOH) at 0 °C. After being stirred at room temperature for 1 h, this reaction mixture was poured into saturated NH_4Cl solution and MeOH was evaporated under reduced pressure. The residue was extracted with EtOAc and washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 8:1) to give *lyxo*-diol **10** (865 mg, 99%) as a colorless oil: $[\alpha]^{27}_D$ +1.8 (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.26 (s, 24H), 1.40−1.52 (m, 2H), 2.08 (d, J = 5.7 Hz, 1H), 2.60 (d, J = 7.2 Hz, 1H), 3.48 (dt, J = 1.8, 7.2 Hz, 1H), 3.55−3.63 (m, 1H), 3.70−3.78 (m, 1H), 3.88 (dd, J = 5.7, 10.5 Hz, 1H), 3.97 (dd, J = 4.5, 10.8 Hz, 1H), 7.37−7.50 (m, 6H), 7.66−7.72 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.1, 22.7, 25.7, 26.7, 29.3, 29.5, 29.6, 29.63, 29.7, 31.9, 33.8, 64.3, 64.5, 70.4, 72.5, 127.8, 129.9, 132.6, 135.5; IR (CH_3Cl) υ_{max} 3418, 2926, 2849, 2361, 2098, 1113 (cm^{-1}); MS (FAB) *m*/*z* 604 ($[M + 23]^+$, 13), 135 (100), 199 (65); HRMS (FAB) calcd for $C_{34}H_{55}N_3O_3SiNa$ 604.3910 ($[M + Na]^+$), found 604.3907.

(2*S*,3*S*,4*S*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-(methylsulfonyloxy)octadecan-4-yl Benzoate (14). To a solution of benzoate **12** (1.56 g, 2.27 mmol) in CH_2Cl_2 (22 mL) were added TEA (1.60 mL) and MsCl (350 μL, 4.54 mmol) at 0 °C. After being stirred at room temperature for 30 min, this reaction mixture

was diluted with CH_2Cl_2 then washed with H_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 10:1) to give benzoate **14** (1.65 g, 95%) as a colorless oil: $[\alpha]^{27}_D$ −3.4 (*c* 0.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.3 Hz, 3H), 1.07 (s, 9H), 1.18−1.37 (m, 24H), 1.62−1.78 (m, 2H), 2.93 (s, 3H), 3.77−3.93 (m, 3H), 4.90 (t, J = 4.2 Hz, 1H), 5.37−5.45 (m, 1H), 7.32−7.49 (m, 9H), 7.54−7.70 (m, 4H), 8.01−8.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.0, 22.7, 24.9, 26.5, 26.7, 29.3, 29.32, 29.34, 29.5, 29.54, 29.6, 29.63, 29.64, 31.2, 31.9, 38.8, 63.4, 63.44, 71.4, 80.3, 127.7, 127.8, 128.4, 129.5, 129.6, 129.8, 130.0, 132.4, 132.5, 133.2, 134.8, 135.5, 135.6, 165.6; IR ($CHCl_3$) υ_{max} 3430, 3073, 2928, 2855, 2110, 1725, 1369, 1267, 1179, 708 (cm^{-1}); MS (FAB) *m*/*z* 786 ($[M + 23]^+$, 1), 105 (100), 135 (33), 197 (15), 303 (12); HRMS (FAB) calcd for $C_{42}H_{61}N_3O_6SSiNa$ 786.3948 ($[M + Na]^+$), found 786.3943.

(2*S*,3*R*,4*S*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-hydroxyoctadecan-4-yl Benzoate (15). To a solution of benzoate **14** (1.31 g, 1.71 mmol) in wet 1-PrOH (17 mL, 5% v/v) was added $CaCO_3$ (171 mg, 1.71 mmol). This reaction mixture was heated under reflex for 4 days. The reaction was filtered, and then concentrated to dryness under reduced pressure. The residue was dissolved in EtOAc and washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 10:1) to give benzoate **15** (1.06 g, 90%) as a colorless oil: $[\alpha]^{27}_D$ +5.1 (*c* 1.6, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.20−1.45 (m, 24H), 1.68−1.92 (m, 2H), 2.46 (d, J = 8.1 Hz, 1H), 3.52−3.58 (m, 1H), 3.80−3.88 (m, 1H), 3.88−4.00 (m, 2H), 5.22 (dt, J = 3.6, 7.5 Hz, 1H), 7.31−7.51(m, 9H), 7.56−7.72 (m, 4H), 8.02−8.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.0, 22.7, 24.9, 26.7, 29.3, 29.4, 29.5, 29.6, 30.6, 31.9, 63.1, 64.9, 71.8, 74.6, 127.8, 128.4, 129.7, 129.9, 129.94, 132.5, 133.1, 135.5, 166.0; IR ($CHCl_3$) υ_{max} 3480, 3073, 2926, 2855, 2110, 1723, 1271, 1113, 708 (cm^{-1}); MS (FAB) *m*/*z* 708 ($[M + 23]^+$, 3), 105 (100), 135 (49), 199 (22), 240 (19); HRMS (FAB) calcd for $C_{41}H_{59}N_3O_4$-SiNa 708.4173 ($[M + Na]^+$), found 708.4181.

(2*S*,3*R*,4*S*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)octadecane-3,4-diol (13). To a solution of benzoate **15** (1.03 g, 1.50 mmol) in MeOH (15 mL) was added NaOMe (1.5 equiv, 25 wt % solution in MeOH) at 0 °C. After being stirred at room temperature for 1 h, this reaction mixture was poured into saturated NH_4Cl solution and MeOH was evaporated under reduced pressure. The residue was extracted with EtOAc and washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 8:1) to give *arabino*-diol **13** (769 mg, 88%) as a colorless oil: $[\alpha]^{27}_D$ +10.7 (*c* 2.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.26 (s, 24H), 1.48−1.86 (m, 2H), 2.48 (br s, 1H), 3.44−3.52 (m, 1H), 3.56−3.66 (m, 1H), 3.74−3.82 (m, 1H), 3.90 (dd, J = 4.5, 10.5 Hz, 1H), 3.96 (dd, J= 6.9, 10.8 Hz, 1H), 7.36−7.50 (m, 6H), 7.64−7.73 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.0, 22.7, 25.5, 26.7, 29.3, 29.6, 29.63, 29.7, 31.9, 33.3, 63.0, 65.6, 72.5, 73.7, 127.9, 129.9, 130.0, 132.5, 132.6, 135.5, 135.6; IR (CH_3Cl) υ_{max} 3424, 3073, 2920, 2855, 2361, 2110, 1111 (cm^{-1}); MS (FAB) *m*/*z* 604 ($[M + 23]^+$, 20), 135 (100), 199 (65), 240 (30); HRMS (FAB) calcd for $C_{34}H_{55}N_3O_3SiNa$ 604.3910 ($[M + Na]^+$), found 604.3907.

(2*S*,3*S*,4*R*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-hydroxyoctadecan-4-yl Benzoate (16). To a solution of diol **5** (1.69 g, 2.90 mmol) in pyridine/CH_2Cl_2 (1:1, 29 mL) were added BzCl (0.34 mL, 2.9 mmol) and DMAP (18 mg, 0.15 mmol) at 0 °C. After being stirred at room temperature for 30 min, this reaction mixture was diluted with CH_2Cl_2 then washed with H_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 40:1) to give benzoate **16** (1.93 g, 97%) as a colorless oil: $[\alpha]^{26}_D$ +19.5 (*c* 0.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.16−1.48 (m, 24H), 1.68−1.94 (m, 2H), 2.78 (br s, 1H), 3.47 (dt, J = 3.3, 6.3 Hz, 1H), 3.88−4.08 (m, 3H), 5.25 (dt, J = 4.2, 8.7 Hz, 1H), 7.33−7.48 (m, 9H), 7.54−7.72 (m, 4H), 7.98−8.04 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.1, 22.7, 25.4, 26.5, 26.6, 26.7, 29.31, 29.38, 29.40, 29.51, 29.53, 29.57, 29.61, 29.64, 31.9, 63.4, 64.6, 72.5, 76.0, 127.6, 127.77, 127.80, 128.4, 129.5, 129.66, 129.8, 129.9, 132.5, 133.2, 134.8, 135.6, 166.3; IR ($CHCl_3$) υ_{max} 3486, 3073, 2928, 2855, 2101, 1721, 1273, 1113, 708 (cm^{-1}); MS (FAB) *m*/*z* 708 ($[M + 23]^+$, 2), 105 (100), 135 (50), 199 (25), 240 (17); HRMS (FAB) calcd for $C_{41}H_{59}N_3O_4SiNa$ 708.4173 ($[M + Na]^+$), found 708.4181.

(2*S*,3*S*,4*R*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-(methylsulfonyloxy)octadecan-4-yl Benzoate (17). To a solution of benzoate **16** (1.69 g, 2.42 mmol) in CH_2Cl_2 (24 mL) were added TEA (1.69 mL) and MsCl (380 μL, 4.84 mmol) at 0 °C. After being stirred at room temperature for 30 min, this reaction mixture was diluted with CH_2Cl_2 then washed with H_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 10:1) to give benzoate **17** (1.76 g, 95%) as a colorless oil: $[\alpha]^{26}_D$ +7.8 (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.3 Hz, 3H), 1.09 (s, 9H), 1.20−1.38 (m, 24H), 1.66−1.82 (m, 2H), 2.92 (s, 3H), 3.80−3.90 (m, 2H), 4.0−4.09 (m, 1H), 4.91 (dd, J = 3.9, 5.4 Hz, 1H), 5.40 (ddd, J = 3.9, 7.8, 9.0 Hz, 1H), 7.35−7.48 (m, 9H), 7.52−7.72 (m, 4H), 7.94−8.00 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.0, 22.7, 25.3, 26.7, 29.18, 29.2, 29.3, 29.35, 29.47, 29.54, 29.61, 29.62, 29.64, 31.9, 38.9, 63.1, 63.8, 72.6, 80.1, 127.8, 128.5, 129.5, 129.7, 129.92, 129.94, 132.4, 132.6, 133.2, 135.6, 165.6; IR ($CHCl_3$) υ_{max} 3410, 3073, 2928, 2855, 2359, 2110, 1725, 1366, 1179, 1109, 708 (cm^{-1}); MS (FAB) *m*/*z* 786 ($[M + 23]^+$, 2), 105 (100), 135 (33), 197 (16), 277 (11), 303 (11); HRMS (FAB) calcd for $C_{42}H_{61}N_3O_6$-SSiNa 786.3948 ($[M + Na]^+$), found 786.3943.

(2*S*,3*R*,4*R*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-3-hydroxyoctadecan-4-yl Benzoate (18a) and (2*S*,3*R*,4*R*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)-4-hydroxyoctadecan-3-yl Benzoate (18b). To a solution of benzoate **17** (1.53 g, 2.00 mmol) in wet EtOH (20 mL, 5% v/v) was added $CaCO_3$ (20 mg, 2.0 mmol). This reaction mixture was heated under reflex for 4 days. The reaction was filtered, and then concentrated to dryness under reduced pressure. The residue was dissolved in EtOAc and washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo to give benzoate **18** (1.33 g, 97%) as a mixture of benzoates **18a** and **18b** in a ratio of 2.8:1. The crude mixture was used in the next step without further purification. Benzoates **18a** and **18b** were isolated by column chromatography on silica gel (hexane/EtOAc, 15:1) for analytical purposes.

18a: colorless oil; $[\alpha]^{26}_D$ +17.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.3 Hz, 3H), 1.07 (s, 9H), 1.20−1.40 (m, 24H), 1.69−1.80 (m, 2H), 2.32 (br s, 1H), 3.52−3.62 (m, 1H), 3.79 (t, J = 3.9 Hz, 1H), 3.91 (dd, J = 5.7, 5.7 Hz, 2H), 5.23 (m, 1H), 7.34−7.49 (m, 9H), 7.53−7.71 (m, 4H), 8.00−8.07 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.1, 22.7, 25.3, 26.7, 29.3, 29.4, 29.50, 29.59, 29.63, 30.7, 31.9, 64.5, 64.9, 71.4, 75.3, 127.81, 127.84, 128.4, 129.7, 129.9, 129.94, 132.67, 132.70, 133.1, 135.5, 135.6, 166.5; IR (CH_3Cl) υ_{max} 3474, 3073, 2932, 2855, 2106, 1719, 1271, 1111, 708 (cm^{-1}); MS (FAB) *m*/*z* 708 ($[M + 23]^+$, 4), 105 (100), 135 (49), 197 (23), 240 (15); HRMS (FAB) calcd for $C_{41}H_{59}N_3O_4SiNa$ 708.4173 ($[M + Na]^+$), found 708.4181.

18b: colorless oil; $[\alpha]^{26}_D$ +25.6 (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.6 Hz, 3H), 1.08 (s, 9H), 1.20−1.32 (m, 24H), 1.39−1.51 (m, 2H), 1.93 (d, J = 7.8 Hz, 1H), 3.77−3.87 (m, 2H), 3.91 (dd, J = 1.2, 5.1 Hz, 2H), 5.30 (dd, J = 3.3, 5.7 Hz, 1H), 7.30−7.50 (m, 9H), 7.56−7.70 (m, 4H), 8.02−8.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.1, 22.6, 25.4, 26.7, 29.3, 29.4, 29.47, 29.51, 29.61, 29.64, 31.9, 33.7, 63.4, 63.6, 70.9, 74.9, 127.77, 127.81, 128.4, 129.4, 129.9, 132.5, 132.6, 133.3, 135.50, 135.54, 165.9; IR (CH_3Cl) υ_{max} 3437, 3073, 2928, 2855, 2101, 1726,

1267, 1113, 708 (cm^{-1}); MS (FAB) *m*/*z* 708 ($[M + 23]^+$, 4), 105 (100), 135 (49), 197 (23), 240 (15); HRMS (FAB) calcd for $C_{41}H_{59}N_3O_4SiNa$ 708.4173 ($[M + Na]^+$), found 708.4181.

(2*S*,3*R*,4*R*)-2-Azido-1-(*tert*-butyldiphenylsilyloxy)octadecane-3,4-diol (19). To a solution of benzoate **18** (1.32 g, 1.92 mmol) in MeOH (22 mL) was added NaOMe (1.5 equiv, 25 wt % solution in MeOH) at 0 °C. After being stirred at room temperature for 1 h, this reaction mixture was poured into saturated NH_4Cl solution and MeOH was evaporated under reduced pressure. The residue was extracted with EtOAc and washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 8:1) to give *xylo*-diol **19** (1.05 g, 94%) as a waxy oil: $[\alpha]^{25}_D$ +19.9 (*c* 3.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, $J = 6.3$ Hz, 3H), 1.08 (s, 9H), 1.26 (s, 24H), 1.48−1.51 (m, 2H), 2.32 (d, $J = 4.8$ Hz, 1H), 2.48 (d, $J = 6.0$ Hz, 1H), 3.49−3.52 (m, 2H), 3.52−3.54 (m, 1H), 3.89 (dd, $J = 4.2$, 10.8 Hz, 1H), 3.95 (dd, J= 6.0, 10.8 Hz, 1H), 7.36−7.50 (m, 6H), 7.62−7.72 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 19.1, 22.7, 25.5, 26.7, 29.3, 29.56, 29.58, 29.65, 29.7, 31.9, 33.5, 64.5, 65.1, 71.8, 72.8, 127.9, 130.0, 132.6, 135.5, 135.6; IR (CH_3Cl) υ_{max} 3395, 3073, 2926, 2855, 2106, 1265, 1113, 702 (cm^{-1}); MS (FAB) *m*/*z* 604 ($[M + 23]^+$, 43), 73 (98), 199 (49); HRMS (FAB) calcd for $C_{34}H_{55}N_3O_3SiNa$ 604.3910 ($[M + Na]^+$), found 604.3904.

General Procedure for Removal of the Silyl Protecting Groups in Compounds 10, 13, and 19. To a solution of **10**, **13**, or **19** (300 mg, 0.520 mmol) in THF (0.1 M) was added TBAF (2 equiv, 1.0 M solution in THF) at room temperature. After being stirred for 1 h at room temperature, the reaction mixture was diluted with EtOAc and washed with brine. The organic layer was dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (hexane/EtOAc, 2:1) to give **20**, **21**, or **22**.

(2*S*,3*S*,4*S*)-2-Azidooctadecane-1,3,4-triol (**20**) (175 mg, 99%) was obtained as a white solid: mp 77−78 °C; $[\alpha]^{26}_D$ +9.6 (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, $J = 6.3$ Hz, 3H), 1.16−1.36 (m, 22H), 1.38−1.50 (m, 2H), 1.50−1.66 (m, 2H), 2.48 (br d, $J = 6.9$ Hz, 3H), 3.50−3.64 (m, 2H), 3.77 (t, $J = 6.0$ Hz, 1H), 3.88 (dd, $J = 4.5$, 11.7 Hz, 1H), 3.97 (dd, $J = 4.2$, 11.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 22.7, 25.7, 29.3, 29.52, 29.55, 29.64, 29.66, 29.68, 31.9, 34.1, 62.6, 64.2, 70.7, 73.2; IR (KBr) υ_{max} 3329, 2917, 2847, 2357, 2091, 1472 (cm^{-1}); MS (FAB) *m*/*z* 366 ($[M + 23]^+$, 38), 176 (64), 413 (28), 717 (29), 739 (58); HRMS (FAB) calcd for $C_{18}H_{37}N_3O_3Na$ 366.2733 ($[M + Na]^+$), found 366.2733.

(2*S*,3*R*,4*S*)-2-Azidooctadecane-1,3,4-triol (**21**) (165 mg, 93%) was obtained as a white solid: mp 77.0−78.2 °C; $[\alpha]^{27}_D$ +16.5 (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, $J = 6.9$ Hz, 3H), 1.20−1.40 (m, 22H), 1.40−1.75 (m, 4H), 3.60 (dd, $J = 2.4$, 6.3 Hz, 1H), 3.63−3.70 (m, 2H), 3.81 (dt, $J = 2.7$, 5.4 Hz, 1H), 3.96 (dd, $J = 5.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 22.7, 25.5, 29.3, 29.6, 29.7, 31.9, 33.4, 62.9, 63.9, 72.7, 74.3; IR (KBr) υ_{max} 3405, 3291, 2917, 2851, 2128, 1267, 1086 (cm^{-1}); MS (FAB) *m*/*z* 366 ($[M + 23]^+$, 18), 136 (80), 154 (100), 717 (15), 739 (8); HRMS (FAB) calcd for $C_{18}H_{37}N_3O_3Na$ 366.2733 ($[M + Na]^+$), found 366.2734.

(2*S*,3*R*,4*R*)-2-Azidooctadecane-1,3,4-triol (**22**) (166 mg, 94%) was obtained as a white solid: mp 76.0−76.6 °C; $[\alpha]^{25}_D$ +16.2 (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, $J = 6.3$ Hz, 3H), 1.26 (s, 22H), 1.08−1.52 (m, 4H), 2.44 (br s, 1H), 2.50 (br s, 1H), 2.78 (d, $J = 5.4$, Hz, 1H), 3.50−3.53 (m, 2H), 3.74 (br s, 1H), 4.09 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 22.7, 25.6, 29.3, 29.6, 29.7, 31.9, 33.5, 62.3, 64.4, 71.5, 73.7; IR (KBr) υ_{max} 3372, 2919, 2851, 2103, 1717, 1466, 1265 (cm^{-1}); MS (FAB) *m*/*z* 366 ($[M + 23]^+$, 25), 414 (18), 717 (17), 739 (34); HRMS (FAB) calcd for $C_{18}H_{37}N_3O_3Na$ 366.2733 ($[M + Na]^+$), found 366.2744.

General Procedure for Azide Reduction. A solution of azide **20**, **21**, or **22** (100 mg, 0.290 mmol) in MeOH (0.1 M) was added to 10% Pd/C (50 wt %) and the mixture was hydrogenated for 3 h at room temperature. The suspension was diluted with MeOH and filtered through a pad of Celite. The solvent was removed, and the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH/NH_4OH, 40:10:1) to give D-phytosphingosine **2**, **3**, or **4**.

(2*S*,3*S*,4*S*)-2-Aminooctadecane-1,3,4-triol (D-*lyxo*-phytosphingosine, **2**) (79.1 mg, 86%) was obtained as a white solid: mp 104−105 °C (lit.[6d] mp 104.8−106.0 °C, lit.[20a] mp 92−95 °C, lit.[20e] mp 95 °C); $[\alpha]^{25}_D$ −6.7 (*c* 0.9, pyridine) {lit.[5e] $[\alpha]^{25}_D$ −7.5 (*c* 1.0, pyridine), lit.[6d] $[\alpha]^{25}_D$ −7.4 (*c* 0.9, pyridine), lit.[20a] $[\alpha]^{24}_D$ −2.6 (*c* 0.2, pyridine), lit.[6f] $[\alpha]^{20}_D$ −7.1 (*c* 0.4, pyridine)}; ^1H NMR (pyridine-d_5, 300 MHz) δ 0.85 (t, $J = 6.6$ Hz, 3H), 1.12−1.45 (m, 22H), 1.49−1.66 (m, 1H), 1.69−1.84 (m, 1H), 1.85−2.08 (m, 2H), 3.67 (ddd, $J = 4.8$, 6.6, 11.4 Hz, 1H), 4.00 (dd, $J = 2.7$, 6.9 Hz, 1H), 4.19 (dd, $J = 6.6$, 10.5 Hz, 1H), 4.26−4.36 (m, 2H); ^{13}C NMR (pyridine-d_5, 75 MHz) δ 14.3, 22.9, 26.8, 29.6, 29.9, 30.1, 30.3, 32.1, 34.6, 56.5, 65.2, 72.3, 75.1; IR (KBr) υ_{max} 3358, 2924, 2853, 2361, 1645, 1468, 1119 (cm^{-1}); MS (FAB) *m*/*z* 318 ($[M + 1]^+$, 25), 43 (100), 60 (97), 81 (22), 282 (17); HRMS (FAB) calcd for $C_{18}H_{40}NO_3$ 318.3008 ($[M + H]^+$), found 318.3011.

(2*S*,3*R*,4*S*)-2-Aminooctadecane-1,3,4-triol (D-*arabino*-phytosphingosine, **3**) (78.2 mg, 85%) was obtained as a white solid: mp 86−88 °C (lit.[6e] mp 86 °C, lit.[6g] mp 75 °C); $[\alpha]^{23}_D$ −2.76 (*c* 1.0, pyridine) {lit.[6e] $[\alpha]^{26}_D$ −3.7 (*c* 1.0, pyridine), lit.[6g] $[\alpha]^{20}_D$ −12.3 (*c* 0.6, pyridine), lit.[20c] $[\alpha]^{23}_D$ −4.5 (*c* 0.6, pyridine)}; ^1H NMR (pyridine-d_5, 300 MHz) δ 0.84 (t, $J = 6.3$ Hz, 3H), 1.14−1.48 (m, 22H), 1.54−1.70 (m, 1H), 1.74−1.94 (m, 2H), 1.98−2.12 (m, 1H), 3.84 (t, $J = 5.4$ Hz, 1H), 4.06 (dd, $J = 1.8$, 6.6 Hz, 1H), 4.10−4.16 (m, 1H), 4.16−4.29 (m, 2H); ^{13}C NMR (pyridine-d_5, 75 MHz) δ 14.3, 22.9, 26.5, 29.6, 29.9, 30.0, 30.1, 30.3, 32.1, 35.2, 54.4, 65.8, 73.8, 74.0; IR (KBr) υ_{max} 3353, 2922, 2853, 1591, 1468, 1053, 760 (cm^{-1}); MS (FAB) *m*/*z* 318 ($[M + 1]^+$, 54), 60 (100), 154 (97), 643 (48); HRMS (FAB) calcd for $C_{18}H_{40}NO_3$ 318.3008 ($[M + H]^+$), found 318.3007.

(2*S*,3*R*,4*R*)-2-Aminooctadecane-1,3,4-triol (D-*xylo*-phytosphingosine, **4**) (83.7 mg, 91%) was obtained as a white solid: mp 99−100 °C (lit.[5g] mp 98−99 °C); $[\alpha]^{25}_D$ +14.2 (*c* 1.0, pyridine) {lit.[5g] $[\alpha]^{27}_D$ +11.8 (*c* 0.45, pyridine)}; ^1H NMR (pyridine-d_5, 300 MHz) δ 0.85 (t, $J = 6.6$ Hz, 3H), 1.24 (s, 22H), 1.47−1.62 (m, 1H), 1.64−1.78 (m, 1H), 1.78−1.90 (m, 1H), 1.90−2.04 (m, 1H), 3.46 (dt, $J = 3.0$, 6.3 Hz, 1H), 4.0−4.07 (m, 2H), 4.08−4.18 (m, 2H); ^{13}C NMR (pyridine-d_5, 75 MHz) δ 14.3, 22.9, 26.5, 29.6, 29.9, 30.0, 30.1, 30.3, 32.1, 34.8, 57.3, 65.6, 72.8, 74.6; IR (KBr) υ_{max} 3372, 2920, 2851, 2361, 1734, 1470, 1057 (cm^{-1}); MS (FAB) *m*/*z* 318 ($[M + 1]^+$, 25), 60 (93), 154 (38), 643 (53); HRMS (FAB) calcd for $C_{18}H_{40}NO_3$ 318.3008 ($[M + H]^+$), found 318.3007.

Acknowledgment. This work was supported by the Korea Science and Engineering Foundation (KOSEF) through the National Research Laboratory Program funded by the Ministry of Science and Technology (M10500000055-06J0000-05510).

Supporting Information Available: Experimental procedures for peracetylation of phytosphingosines **2**−**4** and copies of NMR spectra for compounds **2**−**4**, **6**−**8**, **10**, and **12**−**25**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO702147Y