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Graphical Abstract



Divergent Total Synthesis of D-*ribo*-Phytosphingosine and L-*ribo*-Phytosphingosine from D-Ribose

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Abstract

Divergent total synthesis of *D-ribo*-phytosphingosine (1) and *L-ribo*-phytosphingosine (2) was achieved from readily available *D*-ribose via cross-metathesis reaction, Wittig reaction, and diastereoselective amination reaction of allylic ethers using chlorosulfonyl isocyanate (CSI) as the key steps. As results, reactions of *anti*-1,2-dibenzyl ethers 11 and 16 with chlorosulfonyl isocyanate afforded exclusively *anti*-1,2-amino alcohols 12 and 17 with diastereoselectivity of 32:1 and 31:1 in 75% and 76% yields, respectively. These results could be explained by the neighboring group effect, leading to retention of stereochemistry.

1. Introduction

Sphingolipids (4), e.g. ceramides, cerebrosides, sphingomyelins and gangliosides, have been recognized as important elements of plasma membranes, and are composed of two nonpolar tails and one polar head group (Figure 1). In particular, these amino alcohols are known to play significant roles in many physiological processes such as cellular recognition, signal transduction, control of immune response, cell adhesion and apoptosis.¹ Therefore, these compounds have been the intensive subjects for the treatment of cancers,² diabetes,³ and diverse neurological syndromes,⁴ Phytosphingosines, one of the major components of sphingolipids, have structural features involving 2-amino-1,3,4-triol subunit and aliphatic chain. Phytosphingosines were first isolated from mushrooms in 1911.⁵ Since then, they have been found to be widely distributed in plants, yeasts, fungi, and even mammalian tissues.⁶ In nature, the phytosphingosines is *D-ribo*-phytosphingosine Unfortunately, major stereoisomer of (1). phytosphingosines are available only in limited amount from natural sources, and their isolation and purification from natural sources are expensive and difficult. Consequently, various synthetic methods for preparing these compounds have received considerable attention.^{7,8} A common approach to synthesize them involves the preparation of *anti*-1,2-amino alcohols motif from chiral starting materials, such as carbohydrates^{7b,d,i} and amino acids,^{7g,h} Recently, asymmetric synthesis for the construction of their stereogenic centers have been reported. For example, Sutherland and coworkers have described chiral MOM ether-directed palladium(II)-catalyzed Overmann rearrangement of allylic trichloroacetimidates to afford *anti*-vicinal amino alcohols.^{7a} Bittman et al. have reported the sequential strategy, involving asymmetric propagylation, epoxidation, and site-selective ring opening reaction, for the formation of *anti*-amino alcohol motif.^{7e} In addition, Castillón and coworkers have disclosed the enantioselective Pd(II)-catalyzed ring opening reaction of allylic epoxides using phthalimides to give chiral amine compounds.^{7f} Moreover, Jørgensen et al. have demonstrated the organocatalytic enantio- and diastereoselective one-pot protocol to access 4,5-disubstituted isoxazoline-*N*-oxides via α-bromination, Henry reaction and cyclization sequence.^{8b}



Figure 1. Structures of D-*ribo*-phytosphingosine (1), L-*ribo*-phytosphingosine (2), D-*erythro*-sphingosine (3), and sphingolipids (4)

In continuation of our efforts towards asymmetric synthesis of various natural products containing vicinal amino alcohol framework based on our amination methodology using chlorosulfonyl isocyanate,⁹ herein we report the construction of D-*ribo*-phytosphingosine (1) and L-*ribo*-phytosphingosine (2) using commercially available D-ribose through cross-metathesis and Wittig reaction followed by stereoselective allylic amination of 1,2-*anti*-tribenzyl ether with chlorosulfonyl isocyanate.

2. Results and discussion

The total synthesis of D-*ribo*-phytosphingosine (1) was achieved by starting with benzyl-protected lactol 5 derived from D-ribose by known procedure according to the reported literature (Scheme 1).¹⁰

Lactol **5** was readily oxidized to lactone **6** with acetic anhydride in DMSO.¹¹ Lactone **6** was then converted into alcohol **7** by treating with *N*,*O*-dimethylhydroxylamine in the presence of dimethylaluminum chloride.¹² Swern oxidation of compound **7** and subsequent Wittig reaction afforded olefinated intermediate **8** in 80% yield. Next, the installation of aliphatic chain of *D*-*ribo*-phytosphingosine (**1**) was achieved by cross-metathesis reaction between compound **8** and 1-tetradecene using Hoveyda-Grubbs second generation catalyst (5 mol %) under reflux condition in dichloromethane to afford the corresponding alkene **9** (*E*:*Z* = 7.7:1 by ¹H NMR analysis) in 68% yield. Alternatively, the olefination reaction of aldehyde compound derived from alcohol **7** using C₁₃H₂₇PPh₃Br as a Wittig reagent was performed to give compound **9**. However, this reaction did not undergo to afford the corresponding product **9**, and all starting aldehyde was recovered. Chemoselective hydrogenation of double bond on compound **9** afforded *anti,anti*-tribenzyl ether **10** in high yield (98%).



Scheme 1. Synthesis of D-ribo-Phytosphingosine (1).

After DIBAL-H reduction¹³ of Weinreb amide **10** followed by Wittig olefination, we performed diastereoselective amination reaction between 1,2-*anti*-tribenzyl ether **11** and chlorosulfonyl isocyanate (CSI) in toluene at 0 °C based on our previous reported conditions,^{9i,k} and 1,2-*anti*-amino alcohol **12** was exclusively formed with high regioselectivity and diastereoselectivity (*anti:syn* = 32:1 by HPLC analysis). Regioselective and diastereoselective substitution of compound **12** can be explained by the neighboring group effect, whereby the orientation of the NHCbz group retains its original configuration through double inversion of configuration.^{9i,14} Finally, ozonolysis of compound **12** and subsequent reduction using NaBH₄ gave alcohol product **13**, which was further hydrogenated to provide the desired product, D-*ribo*-phytosphingosine (**1**), in 80% yield. The spectroscopic data (¹H NMR and ¹³C NMR) and specific rotation of the synthesized product **1** were in full agreement with the reported values.^{7e}

To further extend the scope of our above protocol, we envisioned the synthesis of L-*ribo*-phytosphingosine (**2**) from lactol **5** via an eight-step synthesis (Scheme 2). Firstly, olefination of lactol **5** with freshly prepared *n*-tridecyltriphenylphosphonium bromide $(C_{13}H_{27}PPh_3Br)^{15}$ in the presence of NaHMDS provided an inseparable mixture of alkene **14** (*Z*:*E* = 8:1 by ¹H NMR analysis) in 75% yield.¹⁶ Sequential hydrogenation, oxidation and Wittig reaction gave 1,2-*anti*-tribenzyl ether **16** (*Z*:*E* = 6.8:1 by ¹H NMR analysis). The spectroscopic data (¹H NMR and ¹³C NMR) of compound **16** were found to be identical to those of compound **11**, an enantiomeric isomer. Stereoselective amination of **16** with CSI furnished 1,2-*anti*-amino alcohol **17** with high level of diastereoselectivity (*anti:syn* = 31:1 by HPLC analysis) in 76% yield. Ozonolysis and subsequent reduction of compound **17** afforded compound **18** in 82% yield. Finally, both benzyl and Cbz groups were easily removed under hydrogenation conditions to afford L-*ribo*-phytosphingosine (**2**) with specific rotation and spectral data (¹H and ¹³C NMR) identical to those reported in the literature.^{8b}



3. Conclusions

We described the total synthesis of D-*ribo*-phytosphingosine and L-*ribo*-phytosphingosine starting from readily available D-ribose via cross-metathesis reaction, Wittig reaction, and diastereoselective amination reaction of allylic ethers using chlorosulfonyl isocyanate (CSI) as the key steps. We believe that this synthetic protocol can be applied to the preparation of a wide range of 1,2-amino alcohol compounds and phytosphingosine analogues.

4. Experimental Section

4.1. General

Commercially available reagents were used without additional purification, unless otherwise stated. All reactions were performed under an inert atmosphere of nitrogen or argon. Nuclear magnetic resonance spectra (¹H and ¹³C NMR) were recorded on a Varian Unit 400 MHz or 500 MHz instrument with CDCl₃ or CD₃OD as solvent and residual CHCl₃ (δ 7.26 ppm) or CH₃OH (δ 3.31 ppm) as internal standard for ¹H and CDCl₃ (δ 77.0 ppm) or CD₃OD (δ 49.0 ppm) as internal standard for ¹³C. Resonance patterns are reported with the notations s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). In addition, the notation br is used to indicate a broad signal. Coupling constants (*J*) are reported in hertz (Hz). IR spectra were recorded on a JASCO FT/IR-4600 and reported as cm⁻¹. Optical rotations were measured with a JASCO P1020 polarimeter and are reported as [α]^{*t*}_{*D*} (concentration g/100 mL, solvent). Thin layer chromatography was carried out using plates coated with Kieselgel 60F₂₅₄ (Merck). For flash column chromatography, E. Merck Kieselgel 60 (230-400 mesh) was used. High-performance liquid chromatography (HPLC) was recorded on an Agilent 1260 series. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700 mass spectrometer.

4.2. 3,4,5-Tri-benzyloxy-tetrahydro-pyran-2-ol (5): To a stirred solution of D-ribose (10 g, 66.61 mmol) in anhydrous MeOH (100 mL), thionyl chloride (1.93 mL, 26.64 mmol) was carefully added at 0 °C. The resulting solution was refluxed for 4 h and allowed to cool at 0 °C. The resulting solution was neutralized by the addition of solid NaHCO₃ (3.92 g, 46.63 mmol) and stirred at room temperature for 1 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The residue was dissolved in EtOH (100 mL), and the solution was concentrated to one half of the original volume. Then toluene (50 mL) was added and the mixture was concentrated to dryness. The residual viscous oil was used without

further purification in the next step. To a stirred solution of NaH (13.32 g, 333.04 mmol, 60% in mineral oil) in DMF (65 mL) was added droppwise a solution of methyl lyxoside from the previous step in anhydrous THF (65 mL) over 30 min at 0 °C. After the H₂ gas evolution was completed, the reaction mixture was treated with BnBr (31.7 mL, 266.44 mmol) and then stirred for 12 h at room temperature. The reaction mixture was carefully quenched with cold aqueous solution of 10% NH₄Cl (100 mL). The aqueous layer was extracted with EtOAc (2 x 100 mL) and the organic layer was washed with H₂O (3 x 100 mL) and brine (100 mL), dried over MgSO₄ and concentrated in vacuo. The residual oil (about 40 g) was subjected to the next step without purification. Finally, the crude mixture of lyxoside from the previous step was refluxed for 6 h with 1 M H₂SO₄ (88 mL), AcOH (88 mL) and 1,4-dioxane (88 mL). The reaction mixture was cooled to 0 °C and diluted with EtOAc (220 mL) and H₂O (110 mL). The organic layer was separated and the aqueous layer was back-extracted with EtOAc (110 mL). The combined organic layer was washed with H₂O (2 x 110 mL), aqueous 5% NaHCO₃ (3 x 110 mL) and brine solution (110 mL). The combined layer was dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 6:1 to 4:1) to afford 21.18 g (50.37 mmol, 76 % yield for 3 steps) of **5** as a colorless oil. $R_f = 0.27$ (hexane/EtOAc = 2:1); $[\alpha]_D^{25} = -1.6$ (c 1.0, CHCl₃); IR (neat) 3435, 3029, 2294, 1736, 1693, 1455, 1093, 1051 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.40 (br s, 0.4H), 3.47–3.57 (m, 2.6H), 3.69–3.73 (m, 1H), 3.99–4.08 (m, 1H), 4.51–4.94 (m, 6H), 5.16– 5.20 (br, 0.4H), 5.36 (br s, 0.6H); 13 C NMR (125 MHz, CDCl₃) δ 56.49 (two carbons), 69.90, 70.33, 70.85, 71.56, 72.57, 72.75, 73.10, 73.75, 73.78, 74.69, 74.85, 75.54, 77.08, 78.03, 78.09, 81.12, 81.15, 81.32, 92.24, 96.51, 127.70, 127.73, 127.84, 127.91, 127.98, 128.05, 128.07, 128.11, 128.14, 128.17, 128.19, 128.23, 128.25, 128.39, 128.43, 128.64, 128.67, 128.71, 128.74, 128.75, 128.77, 137.78, 137.81, 137.97, 138.05, 138.11, 138.18; HRMS (CI) Calcd for C₂₆H₂₉O₅ [M+H]⁺421.2015, found 421.2009.

4.3. 3,4,5-Tri-benzyloxy-tetrahydro-pyran-2-one (6): To a stirred solution of **5** (18.88 g, 44.9 mmol) in DMSO (84 mL) was added acetic anhydride (84.34 mL, 897.98 mmol) at room temperature. After stirring for 17 h, the reaction mixture was treated with H₂O (95 mL) and extracted with EtOAc (190 mL). The organic layer was extracted with H₂O (2 x 95 mL) and brine solution (95 mL). The combined organic layer was dried over MgSO₄ and concentrated in vacuo. The residue was dissolved with isopropyl ether (38 mL), concentrated in vacuo and again dissolved with isopropyl ether (190 mL). The solution was stirred at room temperature for 1 h and cooled at 0 °C. The precipitate **6** as a white solid was filtered and washed with isopropyl ether. Then the filtrate was concentrated in vacuo and purified by flash column chromatography (hexane/EtOAc = 8:1) to afford 12.59 g (30.08 mmol, 67 % yield) of **6** as a white solid. *R_f* = 0.5 (hexane/acetone = 3:1); mp = 94–96 °C; $[\alpha]_{D}^{25}$ +74.05 (*c* 1.02, CHCl₃); IR (neat) 3027, 2873, 1755, 1496, 1454, 1380, 1339, 1173, 1050 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.40–7.23 (m, 15H), 5.07

(d, J = 12.0 Hz, 1H), 4.95 (d, J = 12.0 Hz, 1H), 4.86 (d, J = 12.0 Hz, 1H), 4.66 (d, J = 12.0 Hz, 1H), 4.50 (d, J = 11.6 Hz, 1H), 4.47–4.40 (m, 2H), 4.27 (dd, J = 6.4, 6.0 Hz, 1H), 4.22–4.21 (m, 1H), 3.83 (d, J = 2.4 Hz, 1H), 3.80–3.75 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 169.97, 138.31, 137.62, 137.37, 128.82, 128.74, 128.46, 128.37, 128.29, 128.19, 128.10, 127.86, 127.79, 76.10, 74.32, 73.85, 73.46, 72.92, 71.79, 67.26; HRMS (EI) Calcd for C₂₆H₂₆O₅ [M]⁺ 418.1780, found 418.1777.

4.4. (*2R*,*3R*,*4R*)-2,3,4-Tri-benzyloxy-5-hydroxy-pentanoic acid methoxy-methyl-amide (7): To a stirred solution of *N*,*O*-dimethylhydroxyamine hydrochloride (0.47 g, 4.78 mmol) in CH₂Cl₂ (10 mL) was added droppwise 1 M solution of dimethylaluminum chloride in hexane (4.8 mL, 4.78 mmol) at 0 °C. The reaction mixure was stirred for 1 h at room temperature and cooled to 0 °C. The dissolving solution of **6** (1 g, 2.39 mmol) in CH₂Cl₂ (10 mL) was added droppwise to the reaction mixture. The mixture was stirred for 1 h at room temperature, quenched with pH 8.0 phosphate buffer solution (14.4 mL) and filtered over celite pad. The organic layer was separated, washed with brine (10 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 4:1) to afford 0.91 g (1.89 mmol, 79 %) of **7** as a colorless oil. $R_f = 0.2$ (hexane/EtOAc = 2:1); $[\alpha]_{\rm p}^{25}$ +37.58 (*c* 0.82, CHCl₃); IR (neat) 3441, 3062, 3030, 2935, 2870, 1858, 1454, 1089 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.22 (m, 15H), 4.70–4.62 (m, 4H), 4.58 (d, *J* = 11.2 Hz, 1H), 4.52 (d, *J* = 11.2 Hz, 1H), 4.43 (d, *J* = 11.6 Hz, 1H), 4.13–4.11 (m, 1H), 3.89–3.86 (m, 1H), 3.82–3.72 (m, 2H), 3.39 (s, 3H), 3.07 (s, 3H), 2.47 (br s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 171.30, 138.58, 138.20, 137.40, 129.97, 128.61, 128.57, 128.51, 128.33, 128.23, 128.17, 127.98, 127.90, 80.09, 79.03, 74.39, 73.80, 72.22, 72.10, 61.74, 61.38, 32.54; HRMS (EI) calcd for C₂₈H₃₃NO₆ [M]⁺ 479.2308, found 479.2309.

4.5. (*2R*,*3R*,*4R*)-2,3,4-Tri-benzyloxy-hex-5-enoic acid methoxy-methyl-amide (8): To a stirred solution of oxalyl chloride (3.03 mL, 35.84 mmol) in CH₂Cl₂ (50 mL) was added droppwise dimethyl sulfoxide (5.09 mL, 71.69 mmol) in CH₂Cl₂ (50 mL) at -78 °C. The reaction mixture was stirred for 1 h at -78 °C and treated with **7** (11.46 g, 23.9 mmol) in CH₂Cl₂ (100 mL). After stirring for 1 h at same temperature, Et₃N (16.65 mL, 119.48 mmol) was added droppwise. The reaction mixture was further stirred for 0.5 h at -78 °C, heated to 0 °C and carefully quenched with H₂O (100 mL). Then the organic layer was separated, washed with H₂O (100 mL) and brine solution (100 mL), dried over MgSO₄ and concentrated in vacuo. The residual oil was used without purification in the next step. To a stirred solution of methyltriphenylphosphonium bromide (17.07 g, 47.79 mmol) in THF (50 mL) was slowly added 1 M sodium bis(trimethylsilyl)amide solution in THF (47.79 mL, 47.79 mmol) at 0 °C under N₂ atmosphere. The reaction mixture was stirred for 2 h at room temperature, and a solution of the former aldehyde (23.9 mmol) in THF (100 mL) was added at 0 °C. The reaction mixture was stirred for 1 h at 0 °C. After stirring

for 10 h at room temperature, the mixture was quenched with H₂O (100 mL) and the aqueous layer was extracted with EtOAc (2 x 100 mL). The organic layer was washed with H₂O (2 x 100 mL) and brine (100 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 6:1) to afford 9.09 g (19.11 mmol, 80%) of **8** as a colorless oil. R_f = 0.5 (hexane/EtOAc = 2:1); $[\alpha]_D^{25}$ +5.77 (*c* 1.17, CHCl₃); IR (neat) 3441, 3063, 3029, 2937, 2866, 1663, 1454, 1071 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.20 (m, 15H), 5.98–5.89 (m, 1H), 5.26 (dd, *J* = 10.4, 2.0 Hz, 1H), 5.02 (dd, *J* = 17.2, 1.2 Hz, 1H), 4.82 (d, *J* = 11.2 Hz, 1H), 4.63–4.58 (m, 2H), 4.53 (d, *J* = 11.2 Hz, 1H), 4.43–4.40 (m 2H), 4.33 (d, *J* = 11.6 Hz, 1H), 4.16–4.11 (m, 2H), 3.41 (s, 3H), 3.40 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.96, 137.63, 134.94, 128.52, 128.48, 128.45, 128.28, 128.25, 128.03, 127.77, 127.59, 127.51, 119.65, 81.69, 74.87, 73.68, 71.99, 70.49, 61.47, 32.29; HRMS (EI) calcd for C₂₉H₃₃NO₅ [M]⁺ 475.2359, found 475.2357.

4.6. (*2R*,*3R*,*4R*)-*2*,*3*,4-Tri-benzyloxy-octadec-5-enoic acid methoxy-methyl-amide (9): To a stirred solution of **8** (0.48 g, 1 mmol) in CH₂Cl₂ (15 mL) was added Hoveyda-Grubbs 2^{nd} generation catalyst (0.031 g, 0.05 mmol) and 1-tetradecene (0.55 mL, 2 mmol). The reaction mixture was refluxed for 20 h, cooled to room temperature and filtered through a pad of celite. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (hexane/EtOAc = 10:1) to afford 0.44 g (0.68 mmol, 68%) of **9** as a colorless oil. $R_f = 0.4$ (hexane/EtOAc = 3:1); $[\alpha]_D^{25} + 3.14$ (*c* 0.9, CHCl₃); IR (neat) 3063, 3030, 2921, 2854, 1667, 1454, 1091 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.35–7.22 (m, 15H), 5.55 (dd, *J* = 15.6, 8.8 Hz, 1H), 5.39–5.33 (m,1H), 4.83 (d, *J* = 11.2 Hz, 1H), 4.62–4.52 (m, 4H), 4.38 (d, *J* = 12 Hz, 1H), 4.31 (d, *J* = 12 Hz, 1H), 4.12 (dd, *J* = 8.8, 2.0 Hz, 1H), 4.05 (dd, *J* = 8.8, 2.0 Hz, 1H), 3.42 (s, 3H), 3.11 (s, 3H), 2.03–1.99 (m, 2H), 1.29–1.19 (m, 20H), 0.88 (t, *J* = 6.0, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.91, 138.79, 137.37, 137.16, 128.46, 128.38, 128.23, 128.19, 128.05, 127.99, 127.79, 127.54, 127.50, 127.32, 127.19, 126.92, 125.80, 81.58, 81.06, 74.72, 73.27, 71.72, 69.76, 61.19, 32.48, 31.91, 29.70, 29.65, 29.63, 29.54, 29.37, 29.28, 29.25, 22.69, 14.14; HRMS (EI) calcd for C₄₁H₅₇NO₅ [M]⁺ 643.4237, found 643.4235.

4.7. (*2R*,*3R*,*4R*)-2,*3*,*4*-**Tri-benzyloxy-octadecanoic acid methoxy-methyl-amide** (**10**): To a stirred solution of **9** (0.37 g, 0.57 mmol) in MeOH (4 mL) was added platinum (IV) oxide (7 mg, 0.03 mmol). The reaction mixture was degassed, stirred for 1 h under H₂ atmosphere and filtered through a pad of celite. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (hexane/EtOAc = 9:1) to afford 0.36 g (0.56 mmol, 98%) of **10** as a colorless oil. $R_f = 0.4$ (hexane/EtOAc = 3:1); $[\alpha]_D^{25}$ +97.23 (*c* 1.03, CHCl₃); IR (neat) 3063, 3030, 2921, 2852, 1667, 1454, 1092 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.21 (m, 15H), 4.73 (t, *J* = 10.8, 11.6 Hz, 2H), 4.64 (d, *J* o

= 12.4 Hz, 1H), 4.49 (dd, J = 10.8, 11.6 Hz, 3H), 4.36 (d, J = 12.0 Hz, 1H), 4.12 (d, J = 8.4 Hz, 1H), 3.68 (d, J = 8.8 Hz, 1H), 3.45 (s, 3H), 3.15 (s, 3H), 1.69–1.65 (m, 1H), 1.42–1.38 (m, 1H), 1.32–1.22 (m, 24H), 0.88 (t, J = 6.0, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.70, 138.50, 137.29, 128.49, 128.29, 128.27, 128.21, 128.11, 128.07, 128.03, 127.87, 127.51, 127.43, 126.93, 79.85, 79.35, 74.21, 73.06, 71.73, 71.57, 61.17, 31.93, 29.73, 29.70, 29.68, 29.47, 29.38, 26.02, 22.71, 14.15; HRMS (EI) calcd for C₄₁H₅₉NO₅ [M]⁺ 645.4393, found 645.4387.

4.8. (3S,4R,5R)-3,4,5-Tri-benzyloxy-1-phenylnonadec-1-ene (11): To a solution of 10 (3.66 g, 5.59 mmol) in THF (30 mL) at -78 °C was added DIBAL-H (22.35 mL, 22.35 mmol, 1 M solution in THF). The reaction mixture was stirred for 0.5 h at -78 °C, guenched with 0.5 M tartaric acid (112 mL) at 0 °C and further stirred for 0.5 h. The aqueous layer was extracted with CH₂Cl₂ (2 x 100 mL). The organic layer was washed with H₂O (100 mL) and brine (100 mL), dried over MgSO₄ and concentrated in vacuo. The residual oil was used without purification in the next step. To a stirred solution of benzyltriphenylphosphonium chloride (3.26 g, 8.38 mmol) in THF (30 mL) was slowly added sodium bis(trimethylsilyl)amide solution (8.38 mL, 8.38 mmol, 1 M solution in THF) at 0 °C under N₂ atmosphere. The reaction mixture was stirred for 2 h at room temperature, and a solution of the former aldehyde (5.59 mmol) in THF (30 mL) was added droppwise at 0 °C. The reaction mixture was stirred for 0.5 h at 0 °C. After stirring for 2 h at room temperature, the mixture was quenched with H₂O (60 mL) and the aqueous layer was extracted with EtOAc (2 x 100 mL). The organic layer was washed with H₂O (2 x 100 mL) and brine (100 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 50:1) to afford 3.39 g (5.14 mmol, 92%, Z:E = 6.4:1) of 11 as a colorless oil. $R_f = 0.5$ (hexane/EtOAc = 19:1); $[\alpha]_{D}^{25} + 87.95$ (c 1.0, CHCl₃); IR (neat) 3062, 3029, 2922, 2852, 1495, 1454, 1089, 1063, 1027 cm⁻¹; **Z-isomer:** ¹H NMR (400 MHz, CDCl₃) δ 7.38–6.99 (m, 20H), 6.88 (d, J = 12.0 Hz, 1H), 5.75 (dd, J = 12.0, 10.4 Hz, 1H), 4.78 (s, 2H), 4.51–4.46 (m, 2H), 4.39 (s, 2H), 4.12 (d, J = 11.6 Hz, 1H), 3.85 (dd, J = 8.4, 3.6 Hz, 1H), 3.61–3.59 (m, 1H), 1.69–1.64 (m, 1H), 1.42–1.37 (m, 1H), 1.26–1.13 (m, 24H), 0.88 (t, J = 6.0, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.90, 138.74, 137.97, 136.74, 134.38, 130.26, 128.94, 128.30, 128.23, 128.17, 128.14, 128.10, 127.96, 127.85, 127.40, 127.32, 127.27, 127.09, 80.33, 79.62, 73.88, 73.44, 71.22, 69.74, 31.93, 29.81, 29.72, 29.68, 29.38, 29.28, 25.56, 22.70, 14.15; HRMS (EI) calcd for $C_{46}H_{60}O_3$ [M]⁺ 660.4542, found 660.4538.

4.9. (2*S*,3*S*,4*R*)-(2,3-Bis-benzyloxy-1-styryl-heptadecyl)-carbamic acid benzyl ester (12): To a stirred solution of **11** (3.15 g, 4.77 mmol) and Na₂CO₃ (6.06 g, 57.19 mmol) in anhydrous toluene (24 mL) was added droppwise chlorosulfonyl isocyanate (3.32 mL, 38.13 mmol) at -20 °C under N₂ atmosphere. The reaction mixture was stirred for 24 h at 0 °C and quenched with aqueous 5% NaCl (30 mL). The aqueous 10

layer was extracted with EtOAc (2 x 10 mL). The organic layer was added to a saturated solution of Na₂SO₃ (20 mL), and the reaction mixture was stirred for 24 h at room temperature. The organic layer was separated, washed with H₂O (20 mL) and brine (20 mL), dried over MgSO₄, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 15:1) to afford 2.52 g (3.57 mmol, 75%, *Z:E* = 8:1, *anti:syn* = 32:1) of **12** as a white solid. R_f = 0.2 (hexane/EtOAc = 14:1); mp = 54–56 °C; $[\alpha]_D^{25}$ -52.66 (*c* 1.03, CHCl₃); IR (neat) 3338, 3062, 3029, 2932, 2852, 1707, 1495, 1454, 1213, 1060, 1027 cm⁻¹; **Z-isomer:** ¹H NMR (400 MHz, CDCl₃) δ 7.38–7.12 (m, 20H), 6.58 (d, *J* = 12.0 Hz, 1H), 5.79 (t, *J* = 10.4, 10.8 Hz, 1H), 5.19 (d, *J* = 8.4 Hz, 1H), 5.10–5.04 (m, 3H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.54 (d, *J* = 9.2 Hz, 1H), 4.32 (d, *J* = 11.6 Hz, 1H), 4.23 (d, *J* = 11.6 Hz, 1H), 3.69 (br s, 1H), 3.40 (d, *J* = 4.0 Hz, 1H), 1.69–1.59 (m, 2H), 1.26–1.22 (m, 24H), 0.88 (t, *J* = 6.0, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.42, 138.21, 136.33, 132.27, 128.59, 128.52, 128.45, 128.39, 128.36, 128.19, 127.98, 127.81, 127.71, 127.58, 127.38, 127.27, 126.46, 81.67, 79.93, 73.75, 71.71, 66.56, 50.33, 31.92, 30.47, 29.79, 29.71, 29.67, 29.62, 29.37, 25.26, 22.70, 14.15; HRMS (EI) calcd for C₄₇H₆₁NO₄ [M]⁺ 703.4601, found 703.4600; HPLC (Chiralpak AD column, *n*-hexane:*i*-PrOH = 90:10, 0.3 mL/min, 254 nm) R_t (minor) = 6.17 min, R_t (major) = 6.76 min, dr = 32:1.

4.10. (2*S*,3*S*,4*R*)-(2,3-Bis-benzyloxy-1-hydroxymethyl-heptadecyl)-carbamic acid benzyl ester (13): Compound 12 (2.28 g, 3.24 mmol) was dissolved with CH₂Cl₂ (32 mL) and MeOH (32 mL). The solution was bubbled with ozone for 1 h at -78 °C, flushed with argon gas for 1 h, and slowly treated with NaBH₄ (1.22 g, 32.39 mmol) at the same temperature. The reaction mixture was stirred for 3 h at 0 °C, quenched with a saturated solution of NH₄Cl (30 mL), and extracted with CH₂Cl₂ (2 x 30 mL). The organic layer was separated, washed with H₂O (20 mL) and brine (20 mL), dried over MgSO₄, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 7:1) to afford 1.71 g (2.7 mmol, 83%) of 13 as a colorless oil. *R*_f = 0.3 (hexane/EtOAc 3:1); $[\alpha]_{\rm D}^{25}$ -26.23 (*c* 0.96, CHCl₃); IR (neat) 3392, 3064, 3031, 2961, 2923, 2852, 1705, 1454, 1262, 1213, 1102, 1060, 1027 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.44–7.28 (m, 15H), 5.46 (d, *J* = 8.4 Hz, 1H), 5.05 (s, 2H), 4.69 (d, *J* = 11.6 Hz, 1H), 4.61 (d, *J* = 11.6 Hz, 1H), 4.51 (t, *J* = 14.8, 11.6 Hz, 2H), 3.93–3.90 (m, 2H), 3.74 (s, 1H), 3.65–3.64 (m, 2H), 2.99 (br s, 1H), 1.68–1.60 (m, 2H), 1.42–1.27 (m, 24H), 0.88 (t, *J* = 6.0, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 156.01, 138.12, 137.81, 136.53, 129.64, 128.55, 128.52, 128.46, 128.39, 128.06, 127.98, 127.95, 127.74, 81.55, 78.95, 73.28, 72.57, 66.65, 62.49, 52.50, 31.92, 30.45, 29.71, 29.67, 29.63, 29.60, 29.46, 29.37, 25.88, 22.69, 14.14; HRMS (EI) calcd for C₄₀H₅₇NO₅ [M]⁺ 631.4237, found 631.4241.

4.11. p-*ribo*-Phytosphingosine (1): A solution of **13** (0.4 g, 0.63 mmol) and 20% palladium hydroxide on carbon (0.2 g, 50% w/w) in MeOH (6 mL) was shaken for 2 day under 50-psi hydrogen pressure using 11

Parr hydrogenator. The reaction mixture was filtered through a pad of celite and concentrated in vacuo. The residue was treated with EtOAc (10 mL), refluxed for 1 h, and cooled to 0 °C. The precipitate **1** as a white solid was filtered and washed with EtOAc. Then the filtrate was concentrated in vacuo and purified by flash column chromatography (CH₂Cl₂/MeOH/NH₄OH = 80:20:1) to afford 0.16g (0.51 mmol, 80%) of **1** as a white solid. $R_f = 0.10$ (CH₂Cl₂/MeOH/HCO₂H = 85:15:0.2); mp = 98–101 °C [lit.^{7e} mp = 99–101 °C]; $[\alpha]_D^{25}$ +8.91 (*c* 0.87, pyridine) [lit.^{7e} $[\alpha]_D^{25}$ +8.0 (*c* 0.8, pyridine)]; IR (neat) 3385, 3064, 3031, 2962, 2917, 2848, 1455, 1262, 1103, 1063, 1032 cm⁻¹; ¹H NMR (400 MHz, CD₃OD) δ 3.78 (dd, *J* = 10.8, 4.0 Hz, 1H), 3.61–3.54 (m, 2H), 3.39–3.34 (m, 1H), 2.99–2.95 (m, 1H), 1.80–1.75 (m, 1H), 1.60–1.58 (m, 1H), 1.32 (m, 24H), 0.93 (t, *J* = 6.4, 6.8 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 76.55, 74.48, 64.29, 55.83, 34.75, 33.07, 30.95, 30.81, 30.77, 30.48, 26.62, 23.74, 14.46; HRMS (EI) calcd for C₁₈H₃₉NO₃ [M]⁺ 317.2930, found 317.2928.

4.12. (2R,3S,4S)-(2,3,4-Tri-benzyloxy-octadec-5-en-1-ol (14): A mixture of 1-bromotridecane (3.33 g, 12.66 mmol) and triphenylphosphine (3.32 g, 12.66 mmol) was heated at 140 °C under N₂ atmosphere for 5 h. The reaction mixture was cooled to 60 °C, and the formed solid gel was dissolved with THF (30 mL). To a solution of C₁₃H₂₇PPh₃Br in THF at 0 °C was added droppwise sodium bis(trimethylsilyl)amide solution (12.66 mL, 12.66 mmol, 1 M solution in THF). The reaction mixture was stirred at 0 °C for 1.5 h and cooled to -78 °C. To a stirred solution was added a solution of 5 (2.66 g, 6.33 mmol) in THF (20 mL) for 0.5 h under N₂ atmosphere at -78 °C. The reaction mixture was stirred at -78 °C for 0.5 h, and then at room temperature for 10 h. The mixture was quenched with a saturated solution of NH₄Cl (40 mL), and extracted with EtOAc (2 x 50 mL). The organic layer was washed with H₂O (40 mL) and brine (40 mL), dried over MgSO₄, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 10:1) to afford 2.78 g (4.74 mmol, 75%) of alkene 14 (Z:E = 8:1 by ¹H NMR analysis), as a colorless oil. $R_f = 0.40$ (hexane/EtOAc = 5:1); $[\alpha]_D^{25} + 34.65$ (c 1.13, CHCl₃); IR (neat) 3367, 3064, 3031, 2961, 2923, 2852, 1454, 1262, 1101, 1063, 1028 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.31–7.24 (m, 15H), 5.76–5.70 (m, 1H), 5.50 (t, J = 10.4, 10.0 Hz, 1H), 4.81–4.69 (m, 2H), 4.59 (dd, J = 12.0, 11.6 Hz, 2H), 4.49–4.45 (m, 2H), 4.35 (d, J = 12.4 Hz, 1H), 3.85 (t, J = 5.2, 4.4 Hz, 1H), 3.84–3.80 (m, 2H), 3.61– 3.58 (m, 1H), 2.56 (br s, 1H), 2.00–1.85 (m, 2H), 1.25–1.19 (m, 20H), 0.88 (t, J = 5.6, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.46, 138.39, 138.21, 136.16, 128.39, 128.36, 128.29, 128.09, 127.66, 127.62, 127.58, 127.46, 127.44, 126.27, 81.34, 79.21, 74.58, 74.16, 71.56, 70.01, 61.02, 31.92, 29.70, 29.66, 29.61, 29.51, 29.43, 29.36, 28.07, 22.69, 14.14; HRMS (EI) calcd for C₃₉H₅₄O₄ [M]⁺ 586.4022, found 586.4018.

4.13. (2*R*,3*S*,4*S*)-(2,3,4-Tri-benzyloxy-octadecan-1-ol (15): To a stirred solution of 14 (0.84 g, 1.43 12

mmol) in MeOH (7 mL) was added platinum (IV) oxide (16 mg, 0.071 mmol) at room temperature. The reaction mixture was degassed, stirred for 1 h under H₂ atmosphere and filtered through a pad of celite. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (hexane/EtOAc = 10:1) to afford 0.8 g (1.36 mmol, 95%) of **15** as colorless oil. $R_f = 0.3$ (hexane/EtOAc = 5:1); $[\alpha]_D^{25} -2.72$ (*c* 1.16, CHCl₃); IR (neat) 3393, 3064, 3031, 2961, 2922, 2852, 1454, 1262, 1099, 1063, 1028 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.21 (m, 15H), 4.77 (d, *J* = 11.6 Hz, 1H), 4.70 (d, *J* = 11.2 Hz, 1H), 4.62 (t, *J* = 11.2, 9.6 Hz, 2H), 4.51 (d, *J* = 3.6 Hz, 1H), 4.48 (d, *J* = 2.4 Hz, 1H), 3.86–3.81 (m, 3H), 3.63–3.61 (m, 1H), 3.59–3.55 (m, 1H), 2.54 (br s, 1H), 1.65–1.63 (m, 1H), 1.44–1.41 (m, 1H), 1.26 (m, 24H), 0.88 (t, *J* = 6.0, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.37, 138.23, 137.87, 128.45, 128.40, 128.32, 128.10, 128.01, 127.85, 127.75, 127.61, 79.90, 79.46, 78.51, 73.79, 72.04, 71.80, 61.27, 31.93, 30.03, 29.75, 29.71, 29.67, 29.65, 29.38, 25.73, 22.70, 14.15; HRMS (EI) calcd for C₃₉H₅₆O₄ [M]⁺ 588.4179, found 588.4174.

4.14. (3R,4S,5S)-3,4,5-Tri-benzyloxy-1-phenylnonadec-1-ene (16): To a stirred solution of oxalyl chloride (0.18 mL, 2.13 mmol) in CH₂Cl₂ (3 mL) was added dropwise dimethyl sulfoxide (0.3 mL, 4.25 mmol) in CH₂Cl₂ (3 mL) at -78 °C. The reaction mixture was stirred for 1 h at -78 °C and treated with 15 (0.83 g, 1.42 mmol) in CH₂Cl₂ (7 mL). After stirring for 1 h at same temperature, Et₃N (0.99 mL, 7.09 mmol) was added droppwise. The reaction mixture was further stirred for 0.5 h at -78 °C, heated to 0 °C and carefully quenched with H₂O (10 mL). Then, the organic layer was separated, washed with H₂O (10 mL) and brine (10 mL), dried over MgSO₄ and concentrated in vacuo. The residual oil was used without purification in the next step. To a stirred solution of benzyltriphenylphosphonium chloride (0.83 g, 2.13 mmol) in THF (6 mL) was slowly added sodium bis(trimethylsilyl)amide solution (2.13 mL, 2.13 mmol, 1 M solution in THF) at 0 °C under N₂ atmosphere. The reaction mixture was stirred for 2 h at room temperature, and a solution of the former aldehyde (1.42 mmol) in THF (6 mL) was added droppwise at 0 °C. The reaction mixture was stirred for 0.5 h at 0 °C. After stirring for 2 h at room temperature, the mixture was quenched with H₂O (7 mL) and the aqueous layer was extracted with EtOAc (2 x 14 mL). The organic layer was washed with H₂O (10 mL) and brine (10 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 60:1) to afford 0.84 g (1.27 mmol, 90%, Z:E = 6.8:1) of **16** as colorless oil. $R_f = 0.5$ (hexane/EtOAc = 19:1); $[\alpha]_{D}^{25}$ -98.62 (c 1.07, CHCl₃); IR (neat) 3063, 3031, 2922, 2852, 1496, 1454, 1100, 1062, 1027 cm⁻¹; **Z-isomer:** ¹H NMR (400 MHz, CDCl₃) δ 7.37–6.99 (m, 20H), 6.89 (d, J = 11.6 Hz, 1H), 5.75 (t, J = 11.2, 10.4 Hz, 1H), 4.78 (s, 2H), 4.50–4.47 (m, 2H), 4.39 (s, 2H), 4.12 (d, J = 11.6 Hz, 1H), 3.85 (dd, J = 6.4, 3.6 Hz, 1H), 3.61-3.59 (m, 1H), 1.69-1.64 (m, 1H), 1.42-1.37 (m, 1H), 1.26-1.13 (m, 24H), 0.88 (t, J = 6.4, 7.2Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 138.96, 138.82, 138.06, 136.78, 134.35, 130.31, 128.96, 128.31, 13

128.17, 128.13, 128.10, 127.95, 127.86, 127.84, 127.40, 127.31, 127.27, 127.10, 80.52, 79.69, 73.91, ACCEPTED MANUSCRIPT 73.57, 71.27, 69.79, 31.94, 29.83, 29.73, 29.72, 29.69, 29.38, 29.36, 25.59, 22.70, 14.14; HRMS (EI) calcd for $C_{46}H_{60}O_3$ [M]⁺ 660.4542, found 660.4542.

4.15. (2R,3R,4S)-(2,3-Bis-benzyloxy-1-styryl-heptadecyl)-carbamic acid benzyl ester (17): To a stirred solution of **16** (0.8 g, 1.21 mmol) and Na₂CO₃ (1.54 g, 14.52 mmol) in anhydrous toluene (6 mL) was added droppwise chlorosulfonyl isocyanate (0.84 mL, 9.68 mmol) at -20 °C under N₂ atmosphere. The reaction mixture was stirred for 24 h at 0 °C and quenched with aqueous 5% NaCl (6 mL). The aqueous layer was extracted with EtOAc (2 x 3 mL). The organic layer was added to a saturated solution of Na₂SO₃ (5 mL), and the reaction mixture was stirred for 24 h at room temperature. The organic layer was separated, washed with H₂O (5 mL) and brine (5 mL), dried over MgSO₄, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 15:1) to afford 0.65 g (0.92) mmol, 76%, Z:E = 7.7:1, *anti:syn* = 31:1) of **17** as a white solid. $R_f = 0.2$ (hexane/EtOAc = 14:1); mp = 54–56 °C; [α]²⁵_D+59.98 (*c* 1.11, CHCl₃); IR (neat) 3365, 3064, 3031, 2962, 2918, 2849, 1697, 1517, 1453, 1261, 1104, 1063, 1027 cm⁻¹; **Z-isomer:** ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.12 (m, 20H), 6.59 (d, J = 12.0 Hz, 1H), 5.79 (t, J = 10.0, 11.6 Hz, 1H), 5.18 (d, J = 8.0 Hz, 1H), 5.10–5.04 (m, 3H), 4.61 (d, J = 10.0, 11.6 Hz, 1H), 5.18 (d, J = 10.0, 1H), 5.10–5.04 (m, 3H), 4.61 (d, J = 10.0, 1H), 5.18 (d, J = 10.0, 1H), 5.10 (d, J = 10.0, 1H), 5.18 (d, J = 10.0, 1H), 12.0 Hz, 1H), 4.55-4.52 (m, 1H), 4.32 (d, J = 11.2 Hz, 1H), 4.23 (d, J = 11.2 Hz, 1H), 3.68 (br s, 1H), 3.40 (d, J = 4.0 Hz, 1H), 1.68–1.54 (m, 2H), 1.25–1.21 (m, 24H), 0.88 (t, J = 6.8, 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.40, 138.29, 136.37, 132.25, 128.59, 128.49, 128.42, 128.36, 128.33, 128.17, 127.95, 127.91, 127.80, 127.77, 127.66, 127.55, 127.34, 127.24, 126.46, 81.74, 80.00, 73.75, 71.72, 66.52, 50.38, 31.92, 30.49, 29.77, 29.70, 29.66, 29.61, 29.59, 29.36, 25.28, 22.69, 14.14; HRMS (EI) calcd for $C_{47}H_{61}NO_4 [M]^+$ 703.4601, found 703.4600; HPLC (Chiralpak AD column, *n*-hexane:*i*-PrOH = 90:10, 0.3 mL/min, 254 nm) R_t (minor) = 6.98 min, R_t (major) = 7.55 min, dr = 31:1.

4.16. (*2R*,*3R*,*4S*)-(*2*,*3*-Bis-benzyloxy-1-hydroxymethyl-heptadecyl)-carbamic acid benzyl ester (18): Compound **17** (5.8 g, 8.24 mmol) was dissolved with CH₂Cl₂ (80 mL) and MeOH (80 mL). The solution was bubbled with ozone for 1 h at -78 °C, flushed with argon gas for 1 h, and slowly treated with NaBH₄ (3.12 g, 82.39 mmol) at the same temperature. The reaction mixture was stirred for 3 h at 0 °C, quenched with a saturated solution of NH₄Cl (80 mL), and extracted with CH₂Cl₂ (2 x 80 mL). The organic layer was separated, washed with H₂O (80 mL) and brine (80 mL), dried over MgSO₄, and concentrated in vacuo. The residue was purified by flash column chromatography (hexane/EtOAc = 7:1) to afford 4.27 g (6.76 mmol, 82%) of **18** as a colorless oil. $R_f = 0.3$ (hexane/EtOAc = 3:1); $[\alpha]_D^{25} + 28.66$ (*c* 1.16, CHCl₃); IR (neat) 3367, 3064, 3031, 2961, 2923, 2862, 1706, 1454, 1262, 1213, 1106, 1061, 1027 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.44–7.26 (m, 15H), 5.44 (d, *J* = 8.8 Hz, 1H), 5.05 (s, 2H), 4.69 (d, *J* = 11.6 Hz, 1H), 14 4.61 (d, J = 11.2 Hz, 1H), 4.56–4.48 (m, 2H), 3.92–3.89 (m, 2H), 3.74 (s, 1H), 3.66–3.65 (m, 2H), 2.95 (br s, 1H), 1.61–1.60 (m, 2H), 1.42–1.27 (m, 24H), 0.88 (t, J = 6.0, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 156.00, 138.11, 137.78, 136.52, 129.65, 128.57, 128.54, 128.47, 128.40, 128.07, 128.00, 127.95, 127.75, 81.68, 78.92, 73.28, 72.61, 66.67, 62.53, 52.47, 31.93, 30.49, 29.71, 29.67, 29.63, 29.60, 29.56, 29.46, 29.37, 25.89, 22.69, 14.14; HRMS (EI) calcd for C₄₀H₅₇NO₅ [M]⁺ 631.4237, found 631.4242.

4.17. L-*ribo*-Phytosphingosine (2): A solution of compound **18** (3.0 g, 4.75 mmol) and 20% palladium hydroxide on carbon (1.5 g, 50% w/w) in MeOH (50 mL) was shaken for 3 day under 50-psi hydrogen pressure using Parr hydrogenator. The reaction mixture was filtered through a pad of celite and concentrated in vacuo. The residue was treated with EtOAc (70 mL), refluxed for 1 h, and cooled to 0 °C. The precipitate **2** as a white solid was filtered and washed with EtOAc. Then the filtrate was concentrated in vacuo and purified by flash column chromatography (CH₂Cl₂/MeOH/NH₄OH = 80:20:1) to afford 1.24g (3.9 mmol, 82%) of **2** as a white solid. $R_f = 0.1$ (CH₂Cl₂/MeOH/HCO₂H = 85:15:0.2); mp = 99–102 °C [lit.^{8b} mp = 99–101 °C]; $[\alpha]_D^{25}$ –8.21 (*c* 0.8, pyridine) [lit.^{8b} $[\alpha]_D^{25}$ –7.7 (*c* 0.74, pyridine)]; IR (neat) 3365, 3064, 3031, 2962, 2917, 2848, 1455, 1262, 1103, 1063, 1032 cm⁻¹; ¹H NMR (400 MHz, CD₃OD) δ 3.78 (dd, *J* = 10.8, 4.0 Hz, 1H), 3.61–3.54 (m, 2H), 3.39–3.34 (m, 1H), 2.99–2.95 (m, 1H), 1.80–1.75 (m, 1H), 1.60–1.58 (m, 1H), 1.32 (m, 24H), 0.93 (t, *J* = 6.4, 7.2 Hz, 3H); ¹³C NMR (100 MHz, CD₃OD) δ 76.55, 74.48, 64.29, 55.83, 34.75, 33.07, 30.95, 30.81, 30.77, 30.48, 26.62, 23.74, 14.46; HRMS (EI) calcd for C₁₈H₃₉NO₃ [M]⁺ 317.2930, found 317.2932.

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Supplementary data

Supplementary data available: ¹H NMR and ¹³C NMR copies of all compounds. Supplementary data associated with this article can be found in the online version, at http://

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