An Efficient Preparation of Isosteric Phosphonate Analogues of Sphingolipids by Opening of Oxirane and Cyclic Sulfamidate Intermediates with α-Lithiated Alkylphosphonic Esters

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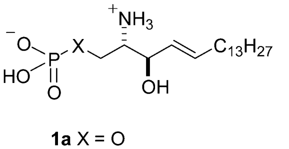
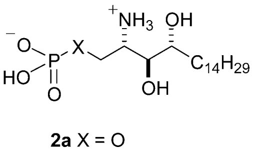
D-*erythro*-(2*S*,3*R*,4*E*)-Sphingosine-1-phosphonate (**1**), the isosteric phosphonate analogue of naturally occurring sphingosine 1-phosphate (**1a**), and D-*ribo*-phytosphingosine 1-phosphonate (**2**), the isosteric phosphonate analogue of D-*ribo*-phytosphingosine-1-phosphate (**2a**), were synthesized starting with methyl 2,3-*O*-isopropylidene-D-glycerate (**4**) and D-*ribo*-phytosphingosine (**3**), respectively. Oxirane **12** was formed in eight steps from **4**, and cyclic sulfamidate **22** was formed in five steps from **3**. The phosphonate group was introduced via regioselective ring-opening reactions of oxirane **12** and cyclic sulfamidate **22** with lithium dialkyl methylphosphonate, affording **13** and **23**, respectively. The synthesis of **1** was completed by S_N2 displacement of chloromesylate intermediate **14b** with azide ion, followed by conversion of the resulting azido group to a NHBoc group and deprotection. The synthesis of **2** was completed by cleavage of the acetal, *N*-benzyl, and alkyl phosphonate ester groups.

Introduction

Sphingolipids are ubiquitous membrane components of mammalian cells and are also implicated in the regulation of diverse cellular processes.[1] The three long-chain bases that form the backbones of sphingomyelin and glycosphingolipids are (2*S*,3*R*)-sphingosine (4-*trans*-sphingenine), 4,5-dihydrosphingosine (sphinganine), and (2*S*,3*S*,4*R*)-phytosphingosine (4D-hydroxysphinganine).[2] The roles of sphingolipids in signal transduction and lipid raft formation have received intense interest in recent years. Among the many sphingolipids that are second messengers are phosphorylated sphingolipids, such as the naturally occurring (2*S*,3*R*)-sphingosine 1-phosphate (**1a**). The latter compound induces a wide range of bioactivities, many of which involve the vascular system.[3] Compound **1a** and the 4,5-dihydro analogue of **1a** serve as extracellular ligands for a family of G-protein coupled receptors present in different cell types; they also act intracellularly, mediating calcium release and cell growth and survival.[4]



1a X = O
1 X = CH_2



2a X = O
2 X = CH_2

Compound **2a**, the phosphate ester of D-*ribo*-phytosphingosine, was recently shown to bind more tightly than **1a** to a widely distributed cell-surface G-protein coupled receptor.[5] Metabolically stable analogues of **1a** and **2a** in which the scissile O−P bond is replaced by a C−P bond are of interest in biological studies because they are resistant to phosphohydrolase action. As part of our program to study sphingolipid bioactivity,[6] the availability of isosteric 1-phosphonate derivatives **1** and **2** became a requirement; therefore, we sought to develop efficient syntheses of these phosphonolipids.

The previous synthetic efforts to prepare phosphonate derivatives of sphingolipids have all employed a Michaelis−Arbuzov reaction[7] for installation of the carbon−phosphorus bond. A major limitation of previous syntheses is low diastereoselectivity. In the first report of the preparation of sphinganine 1-phosphonate, a racemic analogue was synthesized from ethyl 2-aminohydroxy-

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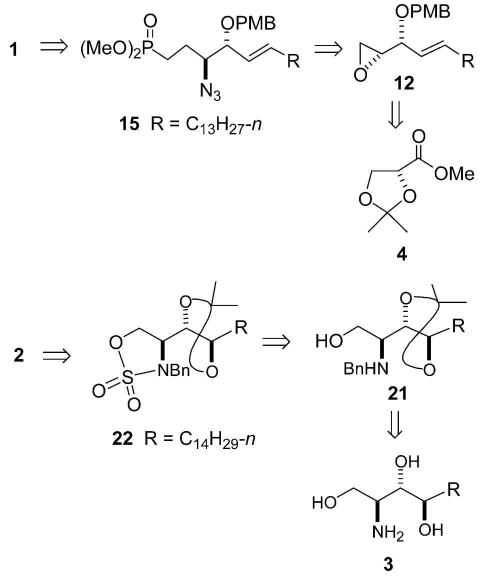
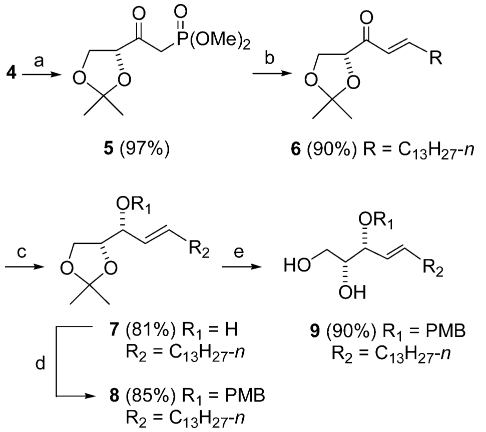
10.1021/jo0487404 CCC: $27.50

SCHEME 1. Retrosynthetic Plan



SCHEME 2. Preparation of Diol 9 from D-Glycerate 4 via HWE Reagent 5[a]



[a] Reagents and conditions: (a) $LiCH_2P(O)(OMe)_2$, THF, −78 °C; (b) $C_{13}H_{27}CHO$, Cs_2CO_3, 2-PrOH, 0 °C to rt; (c) L-Selectride, THF, −78 °C; (d) PMBCl, NaH, DMF, 0 °C to rt; (e) 3 N HCl/CH_3CN (1:4), rt.

octadecanoate in which the $CH_2OPO_3^{2-}$ headgroup of dihydro-**1a** is replaced by $CH_2PO_3^{2-}$.[8] More recently, isosteric phosphonate analogues of **1a** and sphinganine 1-phosphate were prepared as a mixture of isomers at the C4 stereocenter.[9] Sphingosine 1-phosphonate (**1**) and sphinganine 1-phosphonate were synthesized starting from D-*erythro*-sphingosine in 12 steps.[10] An isosteric phosphonate analogue of sphingomyelin was synthesized from a 2-bromoethyloxazolidinone.[11] In addition, a synthetic strategy to gain access to phosphonosphingolipids using a pentacovalent oxaphospholene has been suggested.[12] We recently reported the synthesis of the phosphonate analogue of one of the seven unnatural stereoisomers of phytosphingosine, L-*lyxo*- or 2*S*,3*S*,4*S*-phytosphingosine, via the reaction of tetramethyl methylenediphosphonate with an aldehyde derived from a threitol acetal synthon, followed by reduction of the Wittig adduct.[13] In this investigation, we report an efficient synthesis of (2*S*,3*R*)-sphingosine 1-phosphonate (**1**) and the first synthesis of D-*ribo*-phytosphingosine 1-phosphonate (**2**). These syntheses feature the use of a ring-opening reaction of an oxirane and a cyclic sulfamidate to install the phosphonate group.

Results and Discussion

Scheme 1 outlines our retrosynthetic analysis for the syntheses of targets **1** and **2**. Cyclic intermediates **12** and **22**, which were synthesized from methyl 2,3-*O*-isopropylidene-D-glycerate (**4**) and D-*ribo*-phytosphingosine (**3**), respectively, possess the stereochemistry needed to complete the syntheses. The preparation of target **1** via oxirane **12** involved the generation of a new chiral center at C3 and introduction of the *E* unsaturated chain at C4; the stereocenter at C2 is derived from that in D-glycerate **4**. After inversion at C2 by azide attack to provide **15**, the backbone of (2*S*,3*R*)-sphingosine 1-phosphonate was fully built. As shown in Scheme 1, we achieved an efficient preparation of target **2** by taking advantage of the chirality of **3**, a readily available lipid derived from a yeast fermentation process, to provide the requisite three stereocenters at C2, C3, and C4. Cyclic sulfamidate **22** was prepared from (2*S*,3*S*,4*R*)-**3** via *N*-benzylamino alcohol **21**[14] as a precursor. The regioselective ring-opening reaction at C1 of **12** and **22** with a phosphonate-stabilized carbanion was the key step in the synthetic strategy.

Formation of Epoxide 12. The synthesis of **12** began with the preparation of acetonide **8** from methyl 2,3-*O*-isopropylidene-D-glycerate (**4**) using a modification of published procedures. As shown in Scheme 2, acylation of the lithium salt of dimethyl methylphosphonate with **4** afforded the Horner−Wadsworth−Emmons (HWE) reagent, ketophosphonate **5**.[15] HWE reaction with tetradecanal afforded (*E*)-**6** as the sole product; no *Z* isomer was detected by NMR. Diastereoselective reduction of enone **6** with L-Selectride in THF at −78 °C gave the desired *erythro*-alcohol **7** in good yield.[16] Protection of the 3-hydroxy group as a 4-methoxybenzyl (PMB) ether afforded acetonide **8**, which was deprotected to give diol **9**.[17]

Scheme 3 shows the route we used to prepare chiral epoxide **12**. Diol **9** was converted stereoselectively to epoxide **12** in three steps. Heating at reflux with di-*n*-butyltin oxide in $CHCl_3/MeOH$ (10:1) furnished cyclic stannylene intermediate **10**. Regioselective monotosyla-

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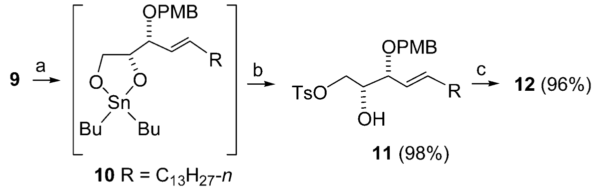
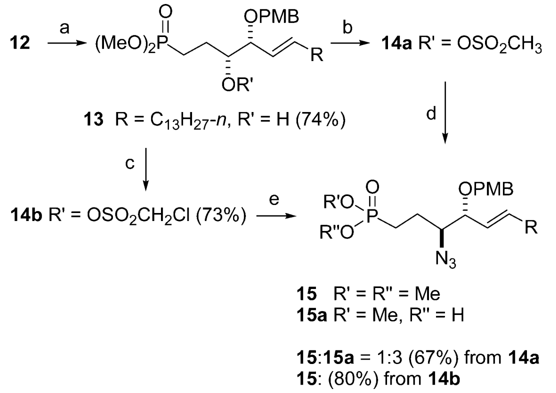
SCHEME 3. Conversion of Diol 9 to Epoxide 12[a]



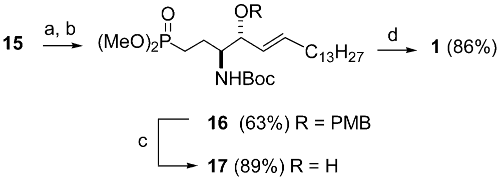
[a] Reagents and conditions: (a) Bu_2SnO, $CHCl_3$/MeOH (10:1), reflux, 2 h; (b) p-TsCl, CH_2Cl_2, rt; (c) K_2CO_3, MeOH, 0 °C.

SCHEME 4. Epoxide Opening with $LiCH_2P(O)(OMe)_2$ and Formation of Azidophosphonate 15[a]



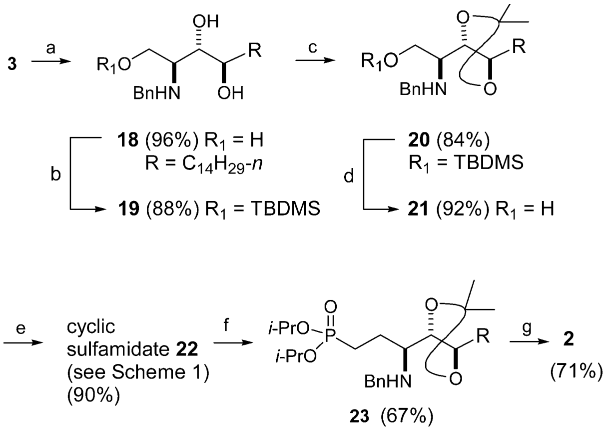
[a] Reagents and conditions: (a) $LiCH_2P(O)(OMe)_2$, $BF_3 \cdot Et_2O$ (4 equiv), THF, −78 to −20 °C; (b) MsCl, Et_3N, DMAP; (c) $ClCH_2SO_2Cl$, Py, 0 °C to rt; (d) NaN_3, DMF, 18-crown-6, reflux; (e) NaN_3, DMF, rt, overnight.

SCHEME 5. Conversion of Azidophosphonate 15 to (2*S*,3*R*)-Sphingosine 1-Phosphonate (1)[a]



[a] Reagents and conditions: (a) $HS(CH_2)_3SH$, MeOH, Et_3N, 50 °C; (b) $(Boc)_2O$, Et_3N, dioxane/water (5:2), 50 °C; (c) DDQ, CH_2Cl_2, H_2O, 0 °C; (d) TMSBr (10 equiv), CH_2Cl_2, rt.

SCHEME 6. Preparation of D-*ribo*-Phytosphingosine 1-Phosphonate (2)[a]



[a] Reagents and conditions: (a) (i) PhCHO, THF/CH_2Cl_2, $MgSO_4$, rt, (ii) $NaBH_4$, MeOH, rt; (b) TBDMSCl, imidazole (4 equiv), THF, rt; (c) $Me_2C(OMe)_2$, p-TsOH, PhH, reflux, 3 h; (d) TBAF, THF, rt; (e) (i) $SOCl_2$, Et_3N, CH_2Cl_2, −78 to −40 °C, (ii) $NaIO_4$, $RuCl_3$, CH_3CN/CCl_4 (1:1), 0 °C; (f) (i) $CH_3P(O)(OPr\text{-}i)_2$, n-BuLi, THF, −78 °C, (ii) 20% H_2SO_4/Et_2O (1:1), rt; (g) (i) TMSBr (4 equiv), CH_3CN, 60 °C, overnight, (ii) 2 N HCl/THF (2:3), rt, overnight, (iii) 20% $Pd(OH)_2$/C, H_2, MeOH, rt, overnight.

tion (*p*-TsCl, CH_2Cl_2) gave **11**, which was treated with K_2CO_3 in methanol at 0 °C to provide epoxide **12** in very high yield.

Conversion of Epoxide 12 to Sphingosine 1-Phosphonate (1). Regioselective ring opening of oxirane **12** with lithium dimethyl methylphosphonate in the presence of $BF_3 \cdot Et_2O$ (4 equiv) in THF at −78 °C furnished phosphonate **13** in good yield (Scheme 4).[18] These conditions are similar to those described to prepare phosphonolipids with a glycerol backbone,[19] but this strategy has not been used previously to produce sphingophosphonolipids. Mesylation of the hydroxy group of **13** using the usual conditions (MsCl, Et_3N, DMAP) gave **14a**; however, heating of the mesylate with sodium azide in DMF at reflux, even in the presence of a catalytic amount of 18-crown-6, gave a 1:3 mixture of **15** and **15a**, in which one of the methyl phosphonate ester groups was removed. Successful azidation, without the formation of byproduct **15a**, was achieved by chloromesylation of **13** with $ClCH_2SO_2Cl$, followed by displacement of the chloromethylsulfonyl group with NaN_3 in DMF at room temperature.

Several methods were explored for the reduction of azide **15**. We found that azide **15** was smoothly converted to the corresponding amine by using 1,3-dithiopropane[20] as the reducing agent. After the amine was protected as *N*-Boc derivative **16**, oxidative cleavage of the PMB ether group of **16** with DDQ gave alcohol **17** in high yield (Scheme 5). The methyl phosphonate ester and *N*-Boc functionalities were removed simultaneously by using an excess of bromotrimethylsilane to afford **1** in good yield.

Preparation of Acetonide 21. The synthesis of phytosphingosine 1-phosphonate (**2**) began with a readily available precursor, D-*ribo*-phytosphingosine (**3**) (Scheme 6). The amino group of **3** was protected as a *N*-benzylamine via condensation with benzaldehyde, followed by reduction of the intermediate imine. After the primary hydroxy group of **18** was selectively blocked as a TBDMS ether, the vicinal 3,4-diol of **19** was protected as an acetal with 2,2-dimethoxypropane in the presence of *p*-TsOH

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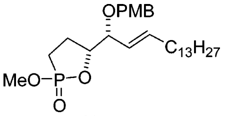
(18) A trace of cyclic phosphonate **13a** was obtained when the reaction was stirred at room temperature. However, the formation of the byproduct was avoided when the reaction was quenched at low temperature.



13a

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in benzene. After cleavage of the silyl protecting group, acetonide **21** was obtained in 65% overall yield from **3**.

Conversion of Acetonide 21 to Phytosphingosine 1-Phosphonate (2). Although lithiated dialkyl methylphosphonates have been used as nucleophiles in the regioselective opening of cyclic sulfates,[21] such a reaction has not yet been reported with a cyclic sulfamidate. Our rationale for the use of a phosphonate-stabilized anion to install the isosteric phosphonate group by opening of a cyclic sulfamidate stems from the extensive study of ring-opening reactions of five-membered cyclic sulfamidates with nucleophiles.[22] The cyclic sulfamidite precursor to sulfamidate **22** was prepared by treatment of **21** with thionyl chloride and triethylamine in CH_2Cl_2 at −40 °C. Oxidation with sodium periodate and catalytic ruthenium trichloride in $CH_3CN-H_2O-CCl_4$ at 0 °C afforded cyclic sulfamidate **22** (90% yield), which underwent reaction with lithiated diisopropyl methylphosphonate at −78 °C in THF. After the reaction was quenched at −78 °C, acid hydrolysis (20% H_2SO_4 in Et_2O) gave amine **23** in 67% yield.

The reactions for removal of the protecting groups of the isopropyl phosphate ester, *N*-benzyl group, and the acetal of **23** were conducted in one pot. First, **23** was treated with TMSBr in CH_3CN at 60 °C. After the excess TMSBr was removed, the residue was stirred with 2 N HCl, and catalytic hydrogenolysis (20% $Pd(OH)_2/C$, MeOH) gave the fully deprotected product **2** in 71% overall yield.

Conclusion

We developed a methodology to prepare nonhydrolyzable sphingolipid analogues in which the $CH_2OPO_3^{2-}$ headgroup of natural sphingosine 1-phosphate (**1a**) is replaced by the isosteric $CH_2CH_2PO_3^{2-}$ group, affording **1**. We also achieved an efficient conversion of naturally occurring (2*S*,3*S*,4*R*)-2-amino-1,3,4-octadecanetriol (D-*ribo*-phytosphingosine, **3**) to its methylenephosphonate analogue **2**. Both of these syntheses involve the ring opening of key intermediates (**12** and **22**) by $LiCH_2P(O)(OR)_2$; this is the first example of a phosphonate-stabilized carbanion attack on a cyclic sulfamidate. The phosphohydrolase-resistant phosphonate analogues **1** and **2** may be of value in understanding the pharmacology of phosphate esters **1a** and **2a** in the absence of formation of metabolites.

Experimental Section[23]

(2*R*,3*R*,4*E*)-1,2-*O*-Propylidene-3-(4′-methoxybenzyl)-4-octadecene-1,2-diol [(−)-8]. To an ice-cold solution of **7** (3.0 g, 8.8 mmol; see the Supporting Information) in DMF (60 mL) was added NaH (0.7 g, 17.6 mmol, 60% in mineral oil) at 0 °C. After the reaction mixture was stirred at this temperature for 30 min, PMBCl (2.8 g, 17.6 mmol) was added. The mixture was warmed to room temperature, and the reaction was monitored by TLC. The reaction was quenched by addition of MeOH at 0 °C and diluted with 200 mL of Et_2O/H_2O (1:1). The aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic layers were washed with water and brine and dried ($MgSO_4$). The solvents were removed, and the residue was purified by chromatography (hexane/EtOAc 8:1) to afford **8** (2.4 g, 85%) as a colorless oil: R_f 0.44 (hexane/EtOAc 8:1); $[\alpha]^{25}_D$ −29.2 (*c* 5.75, $CHCl_3$); ^1H NMR (CD_2Cl_2) δ 0.93 (t, 3H, J = 6.8 Hz), 1.31−1.46 (m, 22H), 1.37 (s, 3H), 1.43 (s, 3H), 2.13 (dt, 2H, J = 7.2, 6.8 Hz), 3.69 (dd, 1H, J = 8.4, 6.8 Hz), 3.77 (dd, 1H, J = 7.8, 7.8 Hz), 3.83 (s, 3H), 3.92 (dd, 1H, J = 8.4, 6.4 Hz), 4.15 (dt, 1H, J = 6.8, 6.8 Hz), 4.35 (d, 1H, J = 11.4 Hz), 4.58 (d, 1H, J = 11.4 Hz), 5.35 (dd, 1H, J = 15.6, 8.4 Hz), 5.78 (dt, 1H, J = 15.6, 6.8 Hz), 6.90 (d, 2H, J = 8.4 Hz), 7.29 (d, 2H, J = 8.4 Hz); ^{13}C NMR (CD_2Cl_2) δ 14.3, 23.1, 25.7, 26.7, 29.5, 29.5, 29.8, 29.9, 30.07, 30.11, 32.3, 32.7, 55.6, 66.4, 69.8, 78.3, 81.7, 109.8, 113.9, 126.4, 129.6, 131.2, 137.7, 159.5; HR-MS (FAB, MNa^+) m/z calcd for $C_{29}H_{48}O_4Na^+$ 483.3445, found 483.3438.

(2*R*,3*R*,4*E*)-1,2-Epoxy-3-(4′-methoxybenzyl)-4-octadecene [(−)-12]. A suspension of **9** (2.2 g, 5.2 mmol) and dibutyltin oxide (1.4 g, 5.7 mmol) in 100 mL of $CHCl_3$/MeOH (10:1) was heated at reflux for 2 h. After removal of the solvents, the residue was further dried under vacuum overnight. The residue was dissolved in CH_2Cl_2 (25 mL), *p*-TsCl (1.3 g, 6.7 mmol) was added, and the reaction mixture was stirred overnight. The reaction was quenched with H_2O (0.2 mL, 11.1 mmol) and stirred for 2 h, diluted with 100 mL of hexane, and filtered through a short pad of silica gel. The pad was washed with 200 mL of hexane/EtOAc (10:1) in order to remove the excess of *p*-TsCl. The filtrate was concentrated, and the residue was purified by chromatography (hexane/EtOAc 4:1) to afford 2.9 g (98%) of **11** as a colorless oil: ^1H NMR (CD_2Cl_2) δ 0.84 (t, 3H, J = 6.8 Hz), 1.23−1.33 (m, 22H), 2.00 (dt, 2H, J = 6.8, 6.8 Hz), 2.40 (s, 3H), 2.63 (d, 1H, J = 3.2 Hz), 3.65−3.68 (m, 2H), 3.74 (s, 3H), 3.88 (dd, 1H, J = 10.0, 5.2 Hz), 4.03 (dd, 1H, J = 10.2, 3.4 Hz), 4.16 (d, 1H, J = 10.8 Hz), 4.45 (d, 1H, J = 10.8 Hz), 5.24 (dd, 1H, J = 15.2, 8.2 Hz), 5.66 (dt, 1H, J = 15.2, 6.8 Hz), 6.81 (d, 2H, J = 7.2 Hz), 7.14 (d, 2H, J = 8.6 Hz), 7.32 (d, 2H, J = 7.2 Hz), 7.71 (d, 2H, J = 8.6 Hz); ^{13}C NMR (CD_2Cl_2) δ 14.5, 22.0, 23.3, 29.6, 29.8, 29.9, 30.0, 30.22, 30.24, 30.3, 32.5, 32.9, 55.8, 70.2, 71.0, 72.3, 80.1, 114.3, 126.1, 128.5, 130.1, 130.4, 130.6, 133.3, 139.0, 145.6, 159.9. To a suspension of crude **11** in 25 mL of MeOH was added 2.86 g (20.7 mmol) of powdered K_2CO_3 at 0 °C. The reaction mixture was stirred for 2.5 h at 0 °C, diluted with 100 mL of Et_2O, and filtered through a short pad of silica gel, which was washed with 200 mL of Et_2O. The filtrate was concentrated to give **12** (1.9 g, 96%) as a colorless oil: R_f 0.43 (hexane/EtOAc 8:1); $[\alpha]^{25}_D$ −12.1 (*c* 6.14, $CHCl_3$); ^1H NMR δ 0.88 (t, 3H, J = 6.8 Hz), 1.26−1.41 (m, 22H), 2.05 (dt, 2H, J = 6.8, 6.8 Hz), 2.56 (dd, 1H, J = 4.8, 2.8 Hz), 2.76 (dd, 1H, J = 4.6, 4.6 Hz), 3.07 (m, 1H), 3.54 (dd, 1H, J = 7.0, 7.0 Hz), 3.80 (s, 3H), 4.48 (d, 1H, J = 11.6 Hz), 4.57 (d, 1H, J = 11.6 Hz), 5.43 (dd, 1H, J = 15.6, 7.6 Hz), 5.72 (dt, 1H, J = 15.6, 6.8 Hz), 6.87 (d, 2H, J = 8.4 Hz), 7.28 (d, 2H, J = 8.4 Hz); ^{13}C NMR (CD_2Cl_2) δ 14.0, 22.8, 29.15, 29.24, 29.5, 29.6, 29.70, 29.77, 29.8, 32.0, 32.4, 43.8, 54.3, 55.3, 69.7, 81.2, 113.7, 126.0, 129.4, 130.8, 136.4; HR-MS (FAB, MNa^+) m/z calcd for $C_{26}H_{42}O_3Na^+$ 425.3026, found 425.3026.

(3*R*,4*R*,5*E*)-1-(Dimethoxyphosphinyl)-3-hydroxy-4-(4′-methoxybenzyl)-5-octadecene [(−)-13]. To a solution of dimethyl methylphosphonate (1.74 g, 14.0 mmol) in THF (100 mL) was added 5.4 mL of *n*-BuLi (13.4 mmol, a 2.5 M solution in hexane) at −78 °C. After the mixture had stirred for 1 h at −78 °C, a solution of $BF_3{\cdot}Et_2O$ (13.4 mmol) and **12** (1.34 g, 3.36 mmol) in THF (10 mL) was added. The reaction mixture was warmed to −20 °C. After being stirred at −20 °C for 0.5 h, the reaction mixture was quenched with saturated aqueous NH_4Cl solution and extracted with EtOAc (2 × 100 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. Phosphonate **13** (1.31 g, 74%) was obtained as a colorless oil after purification by chromatography (hexane/EtOAc 2:5): R_f 0.41 (hexane/EtOAc 2:5); $[\alpha]^{25}_D$ −17.4 (*c* 1.72, $CHCl_3$); ^1H NMR δ 0.87 (t, 3H, J = 6.8 Hz), 1.24−1.40

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[21] For a review, see: Byun, H.-S.; He, L.; Bittman, R. *Tetrahedron* **2000**, *56*, 7051−7091.

[22] For a review, see: Meléndez, R. E.; Lubell, W. D. *Tetrahedron* **2003**, *59*, 2581−2616.

[23] See the Supporting Information for a statement describing general experimental methods. NMR spectra were recorded in $CDCl_3$ unless noted otherwise.

(m, 22H), 1.56−2.03 (m, 4H), 2.06−2.11 (m, 2H), 2.59 (br s, 1H), 3.48−3.50 (m, 2H), 3.69 (s, 3H), 3.72 (s, 3H), 3.79 (s, 3H), 4.23 (d, 1H, $J = 10.8$ Hz), 4.53 (d, 1H, $J = 10.8$ Hz), 5.28 (dd, 1H, $J = 15.2$, 8.2 Hz), 5.72 (dt, 1H, $J = 15.2$, 6.8 Hz), 6.86 (d, 2H, $J = 8.6$ Hz), 7.21 (d, 2H, $J = 8.6$ Hz); ^{13}C NMR δ 14.1, 20.6 (d, $J = 141.9$ Hz), 22.6, 25.5 (d, $J = 4.0$ Hz), 29.1, 29.2, 29.3, 29.4, 29.57, 29.60, 29.63, 31.9, 32.4, 52.2 (d, $J = 6.0$ Hz), 55.2, 69.5, 73.1 (d, $J = 16.1$ Hz), 83.3, 113.8, 126.3, 129.5, 130.1, 138.0, 159.2; ^{31}P NMR δ 35.5; HR-MS (FAB, MNa$^+$) *m/z* calcd for $C_{29}H_{51}O_6PNa^+$ 549.3315, found 549.3313.

(3*S*,4*R*,5*E*)-3-Azido-1-(dimethoxyphosphinyl)-4-(4′-methoxybenzyl)-5-octadecene [(−)-15]. Method A. To a solution of **13** (81 mg, 0.15 mmol) in CH_2Cl_2 (4 mL) at −20 °C were added MsCl (17.6 μL, 0.23 mmol), Et_3N (42.1 μL, 0.3 mmol), and DMAP (1.8 mg, 0.015 mmol). The reaction mixture was warmed to room temperature, stirred for 4 h, and then diluted with 20 mL of Et_2O/H_2O (1:1). The organic layer was separated, and the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined organic layers were washed with brine and dried ($MgSO_4$). After removal of the solvents, crude mesylate **14a** (98 mg, 108%) was obtained, which was used in the next step without purification. To a solution of **14a** in 3 mL of DMF were added 58.5 mg (0.90 mmol) of NaN_3 and 4.0 mg (0.015 mmol) of 18-crown-6. The mixture was heated overnight at 75 °C. The resulting mixture was diluted with Et_2O (50 mL) and washed with water. The ether layer was dried (Na_2SO_4), filtered, and concentrated. Compounds **15a** (40 mg, 50%) and **15** (14 mg, 17%), both colorless oils, were isolated by chromatography. For **15a**: ^{1}H NMR δ 0.88 (t, 3H, $J = 6.8$ Hz), 1.26−1.41 (m, 22H), 1.67−2.11 (m, 4H), 2.13 (br, 2H), 3.47 (br s, 1H), 3.62−3.71 (m, 4H), 3.80 (s, 3H), 4.28 (d, 1H, $J = 11.4$ Hz), 4.55 (d, 1H, $J = 11.4$ Hz), 5.41(m, 1H), 5.73 (m, 1H), 6.87 (d, 2H, $J = 7.8$ Hz), 7.23 (d, 2H, $J = 7.8$ Hz), 9.00 (br s, 1H); ^{13}C NMR δ 14.1, 22.6, 23.5 (br), 29.0, 29.2, 29.3, 29.4, 29.60, 29.62, 29.7, 31.9, 32.4, 51.6 (br), 55.2, 65.6 (br), 69.4, 81.8, 113.8, 125.8, 129.2, 130.1, 138.3, 159.1; ^{31}P NMR δ 35.6; MS (FAB, MH$^+$) *m/z* calcd for $C_{28}H_{48}N_3O_5P$ 538.3, found 538.3. **Method B.** To a solution of **13** (115 mg, 0.22 mmol) in pyridine (3 mL) at 0 °C was added chloromethylsulfonyl chloride (30 μL, 0.33 mmol). The mixture was stirred at room temperature for 2 h, diluted with water (50 mL), and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with 1 M HCl solution and brine and dried (Na_2SO_4). After removal of the solvents, the crude product was passed through a short pad of silica gel to give chloromethylsulfonate **14b** (101 mg, 73%) as a pale yellow oil. Crude **14b** was dissolved in 3 mL of DMF, and 58.5 mg (0.90 mmol) of NaN_3 was added. The mixture was stirred overnight at room temperature (if the reaction was carried out at 85 °C overnight, the yield was 46% after silica gel chromatography). The resulting mixture was diluted with Et_2O (50 mL) and washed with water. The ether layer was dried (Na_2SO_4), filtered, and concentrated. The residue was purified by chromatography (hexane/EtOAc 1:1) to give azide **15** (96 mg, 80%) as a colorless oil: R_f 0.35 (hexane/EtOAc 1:1); $[\alpha]^{25}{}_D$ −53.6 (*c* 1.38, $CHCl_3$); ^{1}H NMR δ 0.87 (t, 3H, $J = 6.8$ Hz), 1.25−1.45 (m, 22H), 1.54−1.94 (m, 4H), 2.06 (dt, 2H, $J = 6.8$, 6.8 Hz), 3.44 (m, 1H), 3.70−3.75 (m, 7H), 3.80 (s, 3H), 4.27 (d, 1H, $J = 11.6$ Hz), 4.55 (d, 1H, $J = 11.6$ Hz), 5.41 (dd, 1H, $J = 15.2$, 8.6 Hz), 5.73 (dt, 1H, $J = 15.2$, 6.8 Hz), 6.87 (d, 2H, $J = 8.6$ Hz), 7.23 (d, 2H, $J = 8.6$ Hz); ^{13}C NMR δ 14.1, 20.4 (d, $J = 141.9$ Hz), 22.7, 23.5 (d, $J = 4.0$ Hz), 29.0, 29.2, 29.3, 29.5, 29.61, 29.64, 29.7, 31.9, 32.4, 52.3 (d, $J = 6.0$ Hz), 52.4 (d, $J = 6.0$ Hz), 55.2, 65.6 (d, $J = 16.1$ Hz), 69.4, 81.8, 113.8, 125.7, 129.2, 130.1, 138.3, 159.1; ^{31}P NMR δ 34.1; HR-MS (FAB, MNa$^+$) *m/z* calcd for $C_{29}H_{50}N_3O_5PNa^+$ 574.3380, found 574.3388.

(3*S*,4*R*,5*E*)-3-*tert*-Butoxycarbonylamino-1-(dimethoxyphosphinyl)-4-(4′-methoxybenzyl)-5-octadecene [(−)-16]. To a solution of **15** (197 mg, 0.36 mmol) in MeOH (1.8 mL) were added Et_3N (0.19 mL, 1.8 mmol) and 1,3-dithiopropane (0.25 mL, 1.8 mmol). The reaction mixture was stirred overnight at 50 °C. The white precipitate was removed by filtration and washed twice with MeOH. The combined filtrates were dried, dissolved in 7 mL of dioxane/water (5:2), and cooled to 0 °C. Triethylamine (0.20 mL, 1.44 mmol) and $(Boc)_2O$ (324 mg, 1.44 mmol) were added, the ice bath was removed, and the mixture was heated overnight at 50 °C. After removal of the volatiles, the product was extracted with EtOAc, washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by chromatography ($CHCl_3$/MeOH 20:1) to afford **16** (141 mg, 63%) as a colorless oil: R_f 0.37 ($CHCl_3$/MeOH 20:1); $[\alpha]^{25}{}_D$ −37.8 (*c* 2.78, $CHCl_3$); ^{1}H NMR δ 0.84 (t, 3H, $J = 6.8$ Hz), 1.22−1.39 (m, 22H), 1.37(s, 9H), 1.59−1.92 (m, 4H), 2.01−2.06 (m, 2H), 3.57 (br s, 1H), 3.66−3.70 (m, 1H), 3.66 (s, 3H), 3.69 (s, 3H), 3.76 (s, 3H), 4.18 (d, 1H, $J = 11.4$ Hz), 4.48 (d, 1H, $J = 11.4$ Hz), 4.70 (d, 1H, $J = 9.6$ Hz), 5.32 (dd, 1H, $J = 15.6$, 7.8 Hz), 5.67 (dt, 1H, $J = 15.6$, 6.8 Hz), 6.82 (d, 2H, $J = 8.4$ Hz), 7.17 (d, 2H, $J = 8.8$ Hz); ^{13}C NMR δ 14.0, 21.3 (d, $J = 141.9$ Hz), 22.6, 28.2, 29.0 (d, $J = 4.0$ Hz), 29.2, 29.3, 29.50, 29.52, 29.6, 31.8, 32.2, 52.2 (d, $J = 7.0$ Hz), 54.5 (d, $J = 16.1$ Hz), 55.1, 69.7, 79.0, 81.3, 113.6, 126.7, 129.2, 130.2, 136.5, 155.6, 159.0; ^{31}P NMR δ 35.3; HR-MS (FAB, MNa$^+$) *m/z* calcd for $C_{34}H_{60}NO_7PNa^+$ 648.4000, found 648.3997.

(3*S*,4*R*,5*E*)-3-*tert*-Butoxycarbonylamino-1-(dimethoxyphosphinyl)-4-hydroxy-5-octadecene [(−)-17]. To a solution of **16** (60 mg, 0.10 mmol) in CH_2Cl_2 (5 mL) was added 0.5 mL of pH 7 buffer (KH_2PO_4−Na_2HPO_4). The solution was cooled to 0 °C, and DDQ (28 mg, 0.12 mmol) was added with stirring at 0 °C. After all of the starting material was consumed, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ solution and extracted with Et_2O (2 × 50 mL). The organic phases were combined, washed with brine, and dried (Na_2SO_4). After the solvents were removed, the residue was purified by chromatography (hexane/EtOAc 5:1) to give **17** (44 mg, 91%) as a colorless oil: R_f 0.14 (hexane/EtOAc 1:4); $[\alpha]^{25}{}_D$ −11.6 (*c* 1.12, $CHCl_3$); ^{1}H NMR δ 0.87 (t, 3H, $J = 6.8$ Hz), 1.25−1.37 (m, 20H), 1.44 (s, 9H), 1.59−1.88 (m, 4H), 2.03 (dt, 2H, $J = 6.8$, 6.8 Hz), 2.30 (br s, 1H), 3.63 (m, 1H), 3.72 (s, 3H), 3.74 (s, 3H), 4.13 (m, 1H), 4.82 (d, 1H, $J = 7.6$ Hz), 5.44 (dd, 1H, $J = 15.2$, 6.6 Hz), 5.73 (dt, 1H, $J = 15.2$, 6.8 Hz); ^{13}C NMR δ 14.1, 20.5 (d, $J = 142.9$ Hz), 22.7, 28.3, 29.2 (d, $J = 9.0$ Hz), 29.3, 29.5, 29.59, 29.64, 29.7, 31.9, 32.4, 52.4 (d, $J = 6.0$ Hz), 75.2, 79.8, 128.2, 134.5; ^{31}P NMR δ 35.0; HR-MS (FAB, MNa$^+$) *m/z* calcd for $C_{26}H_{52}NO_6PNa^+$ 528.3424, found 528.3427.

(3*S*,4*R*,5*E*)-3-Amino-4-hydroxynonadec-5-enyl-1-phosphonic Acid [(2*S*,3*R*,4*E*)-Sphingosine 1-Phosphonate] (1). To a solution of **17** (26 mg, 0.052 mmol) in CH_2Cl_2 (10 mL) was added TMSBr (69 μL, 0.52 mmol) at room temperature. The reaction mixture was stirred overnight at room temperature. After removal of the solvent, the residue was dissolved in 10 mL of MeOH and stirred for 1 h. The solvent was removed to give a pale yellow wax that was purified by chromatography ($CHCl_3$/MeOH/H_2O/AcOH 30:30:2:5), affording **1** (16.8 mg, 86%) as a white solid: mp 140 °C [lit.[10] mp 150 °C]; R_f 0.44 ($CHCl_3$/MeOH/H_2O/AcOH 30:30:2:5); $[\alpha]^{30}{}_D$ +4.9 (*c* 0.15, $CHCl_3$/MeOH 1:1); ^{1}H NMR (CD_3OD/CD_3CO_2D 1:1) δ 0.85 (t, 3H, $J = 6.8$ Hz), 1.26−1.39 (m, 20H), 1.87−1.99 (m, 4H), 2.06 (dt, 2H, $J = 6.8$, 6.8 Hz), 3.42 (m, 1H), 4.36 (m, 1H), 5.43 (dd, 1H, $J = 15.2$, 6.6 Hz), 5.88 (dt, 1H, $J = 15.2$, 6.8 Hz); ^{13}C NMR (CD_3OD/CD_3CO_2D 1:1) δ 12.3, 21.5, 23.9 (d, $J = 146.9$ Hz), 28.0, 28.20, 28.24, 28.4, 28.53, 28.56, 30.8, 31.3, 55.3 (d, $J = 14.1$ Hz), 70.0, 125.2, 134.8; ^{31}P NMR (CD_3OD/CD_3CO_2D 1:1) δ 28.4; MS (ESI, MH$^+$) *m/z* calcd for $C_{19}H_{41}NO_4P$ 378.3, found 378.2.

(2*S*,3*S*,4*R*)-2-(*N*,*N*-Benzylamino)-1-(*tert*-butyldimethylsilyl)octadecane-3,4-diol [(+)-19]. To a cooled (0 °C) solution of **18** (see the Supporting Information) (2.0 g, 4.91 mmol) in THF (100 mL) were added imidazole (1.30 g, 19.6 mmol) and TBDMSCl (1.48 g, 9.82 mmol). The reaction mixture was warmed to room temperature and stirred overnight. The reaction was diluted with water and extracted with CH_2Cl_2. The layers were separated, the aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue (elution with $CHCl_3$/MeOH 20:1) gave **19** (2.3 g, 88%) as a colorless oil: R_f 0.50 ($CHCl_3$/MeOH 9:1); $[\alpha]^{25}_{D}$ +23.4 (*c* 7.6, $CHCl_3$); ^{1}H NMR δ 0.08 (s, 3H), 0.09 (s, 3H), 0.88 (t, 3H, *J* = 6.8 Hz), 0.90 (s, 9H), 1.40−1.71 (m, 26H), 2.81 (m, 1H), 3.43 (dd, 1H, *J* = 7.6, 7.6 Hz), 3.63 (dt, 1H, *J* = 2.8, 8.0 Hz), 3.76−3.86 (m, 4H), 7.25−7.30 (m, 5H); ^{13}C NMR δ −5.5, 14.1, 18.2, 22.7, 25.3, 25.8, 29.4, 29.65, 29.68, 29.8, 31.9, 33.9, 51.4, 60.2, 61.7, 72.2, 74.5, 127.4, 128.3, 128.6, 139.1; HR-MS (FAB, MH$^+$) *m*/*z* calcd for $C_{31}H_{59}NO_3SiH^+$ 522.4337, found 522.4323.

(2*S*,3*S*,4*R*)-Benzyl-[2-(*tert*-butyldimethylsilanyloxy)-1-(2,2-dimethyl-5-tetradecyl[1,3]dioxolan-4-yl)ethyl]-amine [(+)-20]. 2,2-Dimethoxypropane (4.9 mL, 38.3 mmol) and *p*-TsOH (134 mg, 7.0 mmol) were added to a solution of **19** (2.0 g, 3.83 mmol) in benzene (100 mL) at room temperature. The mixture was stirred at reflux for 3 h, and the solvent was removed. The residue was extracted with 150 mL of Et_2O/H_2O (2:1), and the organic phase was separated. The aqueous phase was extracted with Et_2O (50 mL), and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated. Purification of the residue by chromatography (hexane/EtOAc 20:1) afforded 2.2 g (84%) of **20** as a colorless oil: R_f 0.36 (hexane/EtOAc 10:1); $[\alpha]^{25}_{D}$ +46.7 (*c* 5.8, $CHCl_3$); ^{1}H NMR δ 0.08 (s, 3H), 0.09 (s, 3H), 0.89 (t, 3H, *J* = 6.8 Hz), 0.91 (s, 9H), 1.27−1.38 (m, 26H), 1.32 (s, 3H), 1.41 (s, 3H), 2.68 (d, 1H, *J* = 9.6 Hz), 3.65 (d, 1H, *J* = 12.4 Hz), 3.77 (dd, 1H, *J* = 10.0, 2.2 Hz), 3.89−3.41 (m, 2H), 4.01−4.05 (m, 1H), 4.15 (m, 1H), 7.24−7.29 (m, 5H); ^{13}C NMR δ −4.4, 14.1, 18.3, 22.7, 25.9, 26.0, 28.5, 29.4, 29.5, 29.60, 29.64, 29.66, 29.7, 31.9, 51.0, 57.1, 59.3, 76.1, 78.2, 107.3, 126.9, 128.3, 128.4, 129.2, 140.6; HR-MS (FAB, MH$^+$) *m*/*z* calcd for $C_{34}H_{63}NO_3SiH^+$ 562.4650, found 562.4651.

(2*S*,3*S*,4*R*)-2-(*N*-Benzylamino)-2-(2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)ethanol [(+)-21]. A solution of (*n*-Bu)$_4$NF (4.0 mL, 4.0 mmol, a 1 M solution in THF) was added to a solution of **20** (1.90 g, 3.38 mmol) in THF (70 mL) and stirred for 1 h at room temperature. The reaction was monitored by TLC ($CHCl_3$/MeOH 20:1). After water (20 mL) was added, most of the solvents were removed. The residue was extracted with Et_2O (2 × 50 mL), and the extract was dried ($MgSO_4$) and concentrated. The residue was purified by chromatography ($CHCl_3$/MeOH 20:1) to give **21** (1.26 g, 92%) as a colorless oil: R_f 0.47 ($CHCl_3$/MeOH 20:1); $[\alpha]^{25}_{D}$ +30.1 (*c* 6.3, $CHCl_3$); ^{1}H NMR δ 0.88 (t, 3H, *J* = 6.8 Hz), 1.26−1.51 (m, 26H), 1.33 (s, 3H), 1.42 (s, 3H), 2.83 (m, 1H), 3.74−3.84 (m, 3H), 3.92 (d, 1H, *J* = 12.8 Hz), 4.09−4.13 (m, 1H), 4.15−4.20 (m, 1H), 7.25−7.31 (m, 5H); ^{13}C NMR δ 14.1, 22.7, 25.6, 26.4, 27.9, 29.4, 29.56, 29.61, 29.66, 29.69, 31.9, 51.1, 57.1, 61.3, 77.9, 78.1, 107.8, 127.2, 128.3, 128.4, 140.0; HR-MS (FAB, MNa$^+$) *m*/*z* calcd for $C_{28}H_{49}NO_3Na^+$ 470.3604, found 470.3604.

(2*S*,3*S*,4*R*)-*N*-Benzyl-2-(2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)-1,2-cyclic Sulfamidate [(+)-22]. To a solution of **21** (1.0 g, 2.46 mmol) in CH_2Cl_2 (55 mL) was added Et_3N (1.40 mL, 9.84 mmol), and the solution was cooled to −78 °C. After $SOCl_2$ (0.24 mL, 3.20 mmol) was added over a 5-min period, the solution was warmed to −40 °C and stirred at this temperature for 0.5 h. The reaction was quenched by addition of cold Et_2O, and the mixture was washed with water and brine, dried ($MgSO_4$), and concentrated. After the residue was dried thoroughly using a vacuum pump, 1.22 g (100%) of crude cyclic sulfamidite was obtained as a colorless oil. To a cooled (0 °C) mixture of cyclic sulfamidite in 60 mL of CH_3CN/CCl_4 (1:1) was added a solution of 1.05 g (4.92 mmol) of $NaIO_4$ and 6.75 mg (0.030 mmol) of $RuCl_3{\cdot}H_2O$ in 12 mL of water. After the purple suspension was stirred at 0 °C for 20 min, 100 mL of Et_2O and 50 mL of H_2O were added. The layers were separated, and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined ether layer was dried ($MgSO_4$) and concentrated. The residue was purified by filtration through a short pad of silica gel (hexane/EtOAc 4:1) to afford 1.13 g (90%) of **22** as a colorless oil: R_f 0.61 (hexane/$CHCl_3$ 4:1); $[\alpha]^{25}_{D}$ +2.31 (*c* 5.2, $CHCl_3$); ^{1}H NMR δ 0.88 (t, 3H, *J* = 6.8 Hz), 1.26−1.47 (m, 26H), 1.32 (s, 3H), 1.40 (s, 3H), 2.61 (m, 1H), 4.03 (m, 1H), 4.19 (dd, 1H, *J* = 7.5, 7.5 Hz), 4.28 (dd, 1H, *J* = 12.0, 8.6 Hz), 4.42 (s, 2H), 4.51 (dd, 1H, *J* = 8.0, 4.0 Hz), 7.32−7.40 (m, 5H); ^{13}C NMR δ 14.1, 22.7, 25.1, 26.5, 27.4, 29.40, 29.47, 29.52, 29.60, 29.65, 29.68, 30.0, 31.9, 52.2, 58.5, 68.1, 75.7, 108.3, 128.6, 128.8, 128.9, 134.5; HR-MS (FAB, MNa$^+$) *m*/*z* calcd for $C_{28}H_{47}NO_5SNa^+$ 532.3067, found 532.3073.

(2*S*,3*S*,4*R*)-Diisopropyl 3-(*N*-Benzylamino)-3-(2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)propylphosphonate [(+)-23]. To a solution of diisopropyl methylphosphonate (487 mg, 2.70 mmol) in 10 mL of THF was added dropwise *n*-BuLi (1.35 mL, 2.70 mmol, a 2.0 M solution in THF) at −78 °C. After the reaction was stirred at −78 °C for 1 h, a solution of cyclic sulfamidate **22** (360 mg, 0.71 mmol) in THF (15 mL) was added via cannula. The reaction mixture was stirred for 2 h at −78 °C and then quenched with H_2O (1 mL) at −78 °C and allowed to warm to room temperature. After removal of the volatiles, 40 mL of Et_2O/20% H_2SO_4 (1:1) was added. The mixture was neutralized with Na_2CO_3 in an ice bath, extracted with EtOAc, washed with brine, dried (Na_2SO_4), and concentrated. Purification of the residue by chromatography ($CHCl_3$/MeOH 40:1) afforded **23** as a colorless oil (290 mg, 67%): R_f 0.38 ($CHCl_3$/MeOH 20:1); $[\alpha]^{25}_{D}$ +14.7 (*c* 1.8, $CHCl_3$); ^{1}H NMR δ 0.87 (t, 3H, *J* = 6.8 Hz), 1.25−1.43 (m, 24H), 1.31 (s, 3H), 1.33 (s, 3H), 1.78−1.98 (m, 4H), 2.78 (m, 1H), 3.70 (d, 1H, *J* = 12.8 Hz), 3.84 (d, 1H, *J* = 12.8 Hz), 3.95 (m, 1H), 4.12 (m, 1H), 4.70 (m, 2H), 7.23−7.28 (m, 5H); ^{13}C NMR δ 14.1, 21.9 (d, *J* = 141.8 Hz), 22.7, 23.0 (br), 24.0 (d, *J* = 4.5 Hz), 24.1 (d, *J* = 4.5 Hz), 26.0 (d, *J* = 56.0 Hz), 27.9, 29.3, 29.5, 29.60, 29.63, 29.7, 31.9, 50.4, 55.4 (d, *J* = 17.0 Hz), 69.9 (d, *J* = 6.0 Hz), 77.9, 78.1, 107.5, 127.1, 128.3, 128.4; ^{31}P NMR δ 31.3; HR-MS (FAB, MNa$^+$) *m*/*z* calcd for $C_{35}H_{64}NO_5PNa^+$ 632.4414, found 632.4424.

(3*S*,4*S*,5*R*)-3-Amino-4,5-dihydroxynonadecyl-1-phosphonic Acid (D-*ribo*-Phytosphingosine 1-Phosphonate) (2). To a solution of **23** (59 mg, 0.10 mmol) in CH_3CN (3 mL) was added TMSBr (54 μL, 0.40 mmol) at room temperature. After the mixture was heated overnight at 60 °C, the volatiles were removed with an oil pump. To the crude product was added 5 mL of 2 N HCl/THF (2:3). The mixture was stirred overnight at room temperature and then pumped to dryness. A mixture of the dry residue and 20% Pd(OH)$_2$/C (12.1 mg) in dry MeOH (10 mL) was stirred under H_2 atmosphere overnight. The black suspension was passed through a short pad of Celite, which was washed twice with MeOH. Concentration and purification of the residue by chromatography ($CHCl_3$/MeOH/H_2O 65:25:4) provided 28 mg (71%) of **2** as a white powder: mp 180 °C dec; R_f 0.18 ($CHCl_3$/MeOH/H_2O 65:25:4); $[\alpha]^{25}_{D}$ +3.0 (*c* 0.56, $CHCl_3$/MeOH 3:1); ^{1}H NMR ($CDCl_3$/CD_3OD 3:1) δ 0.84 (t, 3H, *J* = 6.8 Hz), 1.22−1.52 (m, 26H), 1.78−2.08 (m, 4H), 3.45 (m, 3H); ^{13}C NMR ($CDCl_3$/CD_3OD 3:1) δ 13.5, 20.1, 22.2, 24.8, 28.9, 29.16, 29.20, 31.4, 33.8, 54.2 (*J* = 11.0 Hz), 71.8, 72.9; ^{31}P NMR (CD_3OD/CD_3CO_2D 1:1) δ 27.6; HR-MS (FAB, MNa$^+$) *m*/*z* calcd for $C_{19}H_{42}NO_3PNa^+$ 418.2693, found 418.2707.

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Supporting Information Available: General experimental information, preparation of compounds **5**−**9** and **18**, and copies of ^{1}H and ^{13}C NMR spectra for compounds **1**, **2**, **5**−**9**, **11**−**14**, **15a**, **15**−**17**, and **19**−**23** and ^{31}P NMR spectra for compounds **1**, **2**, **5**, **13**, **15a**, **15**−**17**, and **23**. This material is available free of charge via the Internet at http://pubs.acs.org..

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