

Diastereoselective synthesis of *D*-erythro-sphingosine

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Abstract: A twelve-step, diastereoselective synthesis of *D*-erythro- C_{18} -sphingosine [(2*S*,3*R*,4*E*)-2-amino-1,3-dihydroxy-4-octadecene, **1**] is described (12 steps, 10% overall yield), starting from 2,3-*O*-isopropylidene-*D*-glyceraldehyde **3**. The first step was the crossed addition of *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsilyloxy)pyrrole (TB-SOP, **2**) to 2,3-*O*-isopropylidene-*D*-glyceraldehyde **3** (a vinylogous variant of the Mukaiyama-aldol reaction) producing a seven-carbon lactam intermediate **4**, which was then shortened by three carbon atoms to furnish the aldehyde-erythrose derivative **10**. Wittig elongation of **10** with the appropriate C_{14} ylide, followed by photoinduced *Z* to *E* double bond isomerization and removal of the protecting groups, completed the synthesis.
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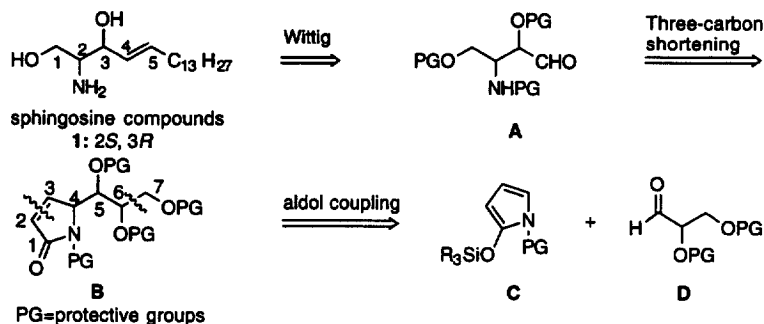
Recently, we have devised methodology to assemble chiral bioactive molecules by a homologative technique that exploits, as the key operation, the vinylogous Mukaiyama-aldol addition between furan-, pyrrole-, and thiophene-based silyloxy dienes and carbonyl precursors obtainable from the chiral pool.¹ In principle, the procedure renders the construction of a myriad of structurally diverse molecular motifs feasible by properly combining the various substituents embodied in the precursors and controlling the transmittal of the chiral information within the enantioenriched source to the emerging stereocenters.

As part of a program directed to demonstrate the viability of this method en route to densely functionalized biomolecules and collections thereof,^{2,3} we now report the diastereoselective synthesis of *D*-erythro- C_{18} -sphingosine [(2*S*,3*R*,4*E*)-2-amino-1,3-dihydroxy-4-octadecene, **1**] moving from *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsilyloxy)pyrrole (TB-SOP, **2**) and enantioenriched ($\geq 98\%$ *ee*) 2,3-*O*-isopropylidene-*D*-glyceraldehyde **3**.⁴ Compound **1** is an essential component of glycosphingolipids where the C_{18} -*D*-erythro fragment is the most commonly found.⁵ Glycosphingolipids have been shown to mediate cell-cell recognition, adhesion, and oncogenesis events,⁶ and it has been reported that sphingosine itself is a potent inhibitor of protein kinase C.⁷

From a retrosynthetic perspective (Scheme 1), a strategy that appends the C(5)–C(18) hydrocarbon portion to the four carbon aldehyde **A** by a Wittig protocol is an attractive approach to this important class of natural compounds, provided suitable stereocontrol is exerted during the construction of the key synthon **A**. **A** Can, in turn, emerge from the seven-carbon lactam **B** by oxidative extrusion of three carbon atoms [C(1), C(2), and C(7)], the synthesis of **B** being secured by regioselective aldol coupling of pyrrole-based silyloxy diene **C** to glyceraldehyde **D**.

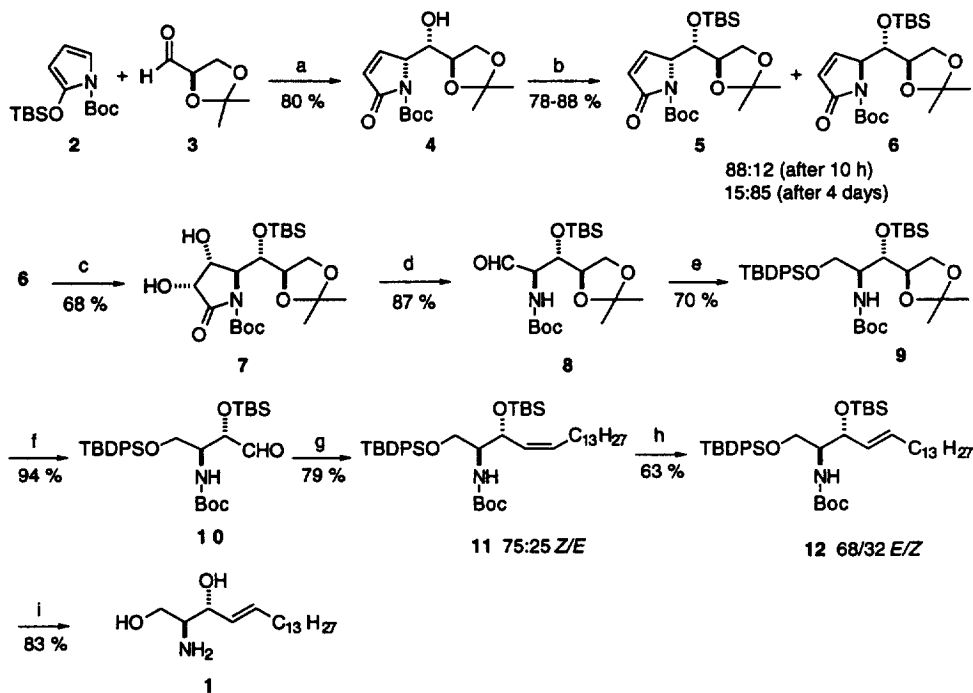
Accordingly, the chiral synthesis of *D*-erythro-sphingosine **1** (Scheme 2) commenced with the preparation of *D*-arabino-configured lactam **4**, which was accomplished in 80% isolated yield and $>95\%$ *de* by SnCl_4 -assisted coupling of *D*-glyceraldehyde **3** to TB-SOP, as previously described.^{2c} The protection of the free hydroxyl group within **4** as TBS-ether was then effected, as usual, by exposure to TBSCl in DMF in the presence of imidazole. Addition of the silylating mixture to **4** after 10 h at room temperature afforded the expected lactam **5** with only 12% loss of the chiral integrity. However,

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Scheme 1.

when the reaction mixture was left for longer (four days), only a minor amount of **5** was isolated, with the concomitant reaction being the epimerization of the stereocenter at C(4) giving rise to the *D-ribo*-configured isomer **6** in 75% isolated yield.



Scheme 2. Reagents and conditions: (a) SnCl_4 , Et_2O , -85°C ; (b) TBSCl , DMF , imidazole; (c) KMnO_4 , DCH-18-crown-6 ether, CH_2Cl_2 ; (d) 1M aq LiOH , THF ; then NaIO_4 , SiO_2 , CH_2Cl_2 ; (e) NaBH_4 , EtOH ; then TBDPSCl , DMF , imidazole; (f) 70% aq AcOH ; then NaIO_4 , SiO_2 , CH_2Cl_2 ; (g) $\text{C}_{14}\text{H}_{29}\text{PPh}_3^+\text{Br}^-$, BuLi , THF , -78°C to 20°C ; (h) $h\nu$, PhSSPh cat., cyclohexane; (i) 75% aq TFA , 20°C .

The preparation of **1** called for 4,5-*erythro*-heptenonolactam **6** as the requisite precursor. According to our plan, removal of the C(1) and C(2) carbons at the left side of the molecule was required, and this was accomplished by a two-step maneuver comprising double bond dihydroxylation and oxidative fission of the C(2)–C(3) diol linkage. Thus, selective *anti-cis* dihydroxylation of the double bond within **6** was accomplished by exposure to KMnO_4 /dicyclohexano-18-crown-6 ether to give diol **7** in 68% yield, which was subjected to hydrolytic ring opening (LiOH , THF) and oxidative shortening

by two carbon atoms (NaIO₄) to generate protected aminoribose **8** in 87% yield. Aldehyde reduction (NaBH₄) and protection of the newly formed primary hydroxyl as TBDPS-ether furnished alditol **9** in 70% yield. For the advanced erythrose intermediate **10** to be prepared, additional sacrifice of the right hand terminal carbon of **9** had to be performed via selective deacetonidation (70% aq AcOH) and NaIO₄-promoted diol cleavage. In the event, the key aldehyde **10** was obtained in 94% yield for the two steps.

All that remained was the creation of the suitable unsaturated hydrocarbon appendage, and this was effected by a Wittig homologation of **10** using tetradecylidene triphenylphosphorane (C₁₄H₂₉P(C₆H₅)₃Br/BuLi).⁸ The reaction proved selective, furnishing adduct **11** as a 75:25 *Z/E* isomeric mixture (79% combined yield). Photoinduced double bond isomerization in the presence of phenyl disulfide⁸ produced the requisite *E*-disposed olefin **12** in 63% yield (93% combined yield), accompanied by a minor amount of unchanged *Z*-alkene, which was easily separated. Finally, acidic hydrolysis of **12** (75% aq TFA), followed by neutralization (NH₄OH) and chromatography, furnished pure crystalline D-erythro-sphingosine **1** in 83% yield, which corresponds to a 10% overall yield for the 12-step sequence from **3**. The ¹H and ¹³C NMR spectroscopic characteristics of our material as well as the mp value (71–74°C) were in good agreement with those in the literature, while the specific rotation [α]_D²⁰ was measured as –1.8 (*c* 0.8, CHCl₃), matching well the reported data for **1** {ref. 4g: [α]_D²⁵ –1.23 (*c* 0.5, CHCl₃), mp 72–73°C; ref. 4h: [α]_D²⁴ –1.2 (*c* 1.0, CHCl₃), mp 70–74°C}.

In conclusion, a concise and efficient total synthesis of D-erythro-C₁₈-sphingosine **1** has been completed, which served to confirm the potential and versatility of five-membered heterocyclic silyloxy dienes like **2** as functional elongation reagents. Although three carbon atoms were sacrificed throughout the synthesis, the route is direct and provides a methodology that is potentially amenable to the preparation of a variety of sphingosine-related isomers and analogs. By parallel chemistry, D-threo-C₁₈-sphingosine can virtually spring from adduct **5**, whereas representatives of the L-series can be envisioned as deriving from L-glyceraldehyde.

Experimental

General

¹H and ¹³C NMR spectra were recorded on a Varian VXR-300 instrument operating at 300.0 MHz and 75.4 MHz, respectively. Chemical shifts are related to tetramethylsilane. Optical rotations ([α]_D) were measured on a Perkin–Elmer 241 instrument and are recorded in units of 10^{–1} deg cm² g^{–1}. Column chromatography were performed on Merck silica gel 70–230 Mesh. Kieselgel 60 F₂₅₄ (from Merck) was used for TLC. Elemental analyses were performed by Microanalytical Laboratory of University of Sassari. The preparation of *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsilyloxy)pyrrole (TBSOP **2**) was carried out by the method reported in our precedent paper.^{2c} 2,3-*O*-Isopropylidene-D-glyceraldehyde (**3**) was prepared from 1,2;5,6-di-*O*-isopropylidene-D-mannitol (Fluka) by periodate fission and used immediately.⁹

N-(*tert*-Butoxycarbonyl)-6,7-*O*-isopropylidene-2,3-dideoxy-D-arabino-hept-2-enono-1,4-lactam **4**

This material was prepared in 80% yield from TBSOP (**2**) and aldehyde **3** according to a previously reported procedure.^{2c} Significant data: mp 138–140°C; [α]_D²⁰+197.6 (*c* 0.8, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.43 (dd, 1H, *J*=6.3, 2.1 Hz), 6.13 (dd, 1H, *J*=6.3, 1.5 Hz), 4.81 (dt, 1H, *J*=5.7, 2.4 Hz), 4.09 (ddd, 1H, *J*=6.0, 5.7, 3.9 Hz), 4.01 (q, 1H, *J*=6.0 Hz), 3.94 (dd, 1H, *J*=8.1, 6.0 Hz), 3.86 (dd, 1H, *J*=8.1, 6.0 Hz), 3.63 (d, 1H, *J*=3.9 Hz), 1.57 (s, 9H), 1.37 and 1.32 (2s, each 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 168.9, 150.9, 148.2, 126.9, 109.2, 83.8, 75.6, 72.6, 66.4, 65.6, 28.0, 26.4, 25.1.

N-(*tert*-Butoxycarbonyl)-5-*O*-(*tert*-butyldimethylsilyl)-6,7-*O*-isopropylidene-2,3-dideoxy-D-ribo-hept-2-enono-1,4-lactam **6**

To a solution of lactam **4** (2.7 g, 8.6 mmol) in dry dimethylformamide (40 ml) TBSCl (6.6 g, 43.8 mmol) and imidazole (2.9 g, 42.6 mmol) were added under argon. The mixture was stirred at room

temperature for 5 h, then further addition of TBSCl (3.9 g, 25.0 mmol) and imidazole (1.7 g, 25.9 mmol) was effected. After 4 days the reaction was quenched with 5% aqueous citric acid solution (50 mL) and the resulting slurry was extracted with AcOEt (3x30 mL). The extracts were dried (MgSO₄), filtered, and evaporated under reduced pressure to give a crude product which was purified by flash chromatography on silica gel eluting with 9:1 CH₂Cl₂/diethyl ether, to afford **6** (2.75 g, 75%) and **5** (484 mg, 13%).

Compound **6**: an oil; $[\alpha]_D^{20}$ -82.2 (*c* 2.3, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.29 (dd, 1H, *J*=6.3, 1.8 Hz), 6.12 (dd, 1H, *J*=6.3, 1.8 Hz), 4.96 (q, 1H, *J*=1.8 Hz), 4.39 (dd, 1H, *J*=7.5, 1.8 Hz), 4.15 (dd, 1H, *J*=8.1, 6.0 Hz), 4.06 (ddd, 1H, *J*=7.2, 6.0, 5.4 Hz), 3.86 (dd, 1H, *J*=8.1, 5.4 Hz), 1.59 (s, 9H), 1.49 (s, 3H), 1.40 (s, 3H), 0.89 (s, 9H), 0.04 (s, 3H), -0.01 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 169.7, 149.6, 147.5, 127.8, 109.8, 82.9, 77.4, 72.2, 68.0, 64.8, 28.2, 26.5, 25.6, 25.1, 17.9, -4.6, -4.8. Anal. Calcd for C₂₁H₃₇NO₆Si: C, 58.99; H, 8.72; N, 3.28. Found: C, 58.83; H, 8.68; N, 3.31.

Compound **5**: white solid; mp 140–142°C; $[\alpha]_D^{20}$ +180.4 (*c* 0.9, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.28 (dd, 1H, *J*=6.0, 2.1 Hz), 6.20 (dd, 1H, *J*=6.0, 1.5 Hz), 4.65 (m, 1H), 4.60 (bt, 1H, *J*=4.5 Hz), 3.60–3.80 (m, 3H), 1.58 (s, 9H), 1.35 (s, 3H), 1.24 (s, 3H), 0.93 (s, 9H), 0.21 (s, 3H), 0.16 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 169.0, 149.3, 147.4, 128.4, 109.0, 83.2, 74.7, 71.2, 66.1, 65.2, 28.2, 26.3, 25.7, 25.0, 17.9, -4.1, -5.2. Anal. Calcd for C₂₁H₃₇NO₆Si: C, 58.99; H, 8.72; N, 3.28. Found: C, 58.80; H, 8.70; N, 3.20.

N-(*tert*-Butoxycarbonyl)-5-*O*-(*tert*-butyldimethylsilyl)-6,7-*O*-isopropylidene-*D*-glycero-*D*-allo-heptono-1,4-lactam **7**

To a stirring solution of unsaturated lactam **6** (1.28 g, 3.0 mmol) in CH₂Cl₂ (20 mL), KMnO₄ (572 mg, 3.6 mmol) and *cis*-dicyclohexano-18-crown-6 ether (46 mg, 0.12 mmol) were added under nitrogen. The reaction mixture was stirred at room temperature for 2 h, then a saturated aqueous Na₂SO₃ solution was added. After neutralization with a 5% aqueous citric acid solution, the mixture was extracted with CH₂Cl₂ (3x30 mL) and AcOEt (3x30 mL). The collected organic extracts were dried with MgSO₄ and evaporated under reduced pressure to give crude lactam **7** (940 mg, 68%) which was used as such in the next reaction: $[\alpha]_D^{20}$ -1.5 (*c* 3.6, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 4.56–4.49 (m, 2H), 4.40 (s, 1H), 4.20–4.12 (m, 3H), 3.90–3.84 (m, 2H), 3.45 (bs; 1H), 1.57 (s, 9H), 1.49 (s, 3H), 1.39 (s, 3H), 0.87 (s, 9H), 0.09 (s, 3H), 0.01 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 174.0, 149.5, 109.8, 83.7, 76.9, 72.2, 71.7, 67.2, 66.0, 65.5, 28.0, 26.4, 25.7, 25.0, 17.9, -4.3, -5.1.

2-(*tert*-Butoxycarbonylamino)-3-*O*-(*tert*-butyldimethylsilyl)-4,5-*O*-isopropylidene-2-*deoxy*-*D*-ribose **8**

The diol **7** (940 mg, 2.0 mmol) was directly dissolved in THF (20 mL) and 1 M aqueous LiOH solution (2.3 mL) was added to the stirred solution at 0°C. After 1 h the solvent was removed and the residue was dissolved in CH₂Cl₂ (35 mL). SiO₂ (4 g) was added to the solution and the resulting slurry was treated with 0.65 M aq NaIO₄ (4.2 mL) at room temperature. The suspension was stirred for 2 h and then filtered. The organic layers were dried with MgSO₄ and evaporated under reduced pressure to give **8** (715 mg, 87%): a glass; $[\alpha]_D^{20}$ -17.5 (*c* 0.6, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 9.71 (s, 1H), 5.37 (d, 1H, *J*=6.0 Hz), 4.54 (1H, bd, *J*=6.0 Hz), 4.20–4.13 (m, 3H), 3.90 (m, 1H), 1.45 (s, 9H), 1.43 (s, 3H), 1.35 (s, 3H), 0.85 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ¹³C NMR (75.4 MHz, CDCl₃) δ 198.3, 154.9, 110.1, 79.9, 76.3, 75.0, 67.7, 63.0, 28.3, 26.3, 25.6, 25.0, 17.9, -4.6, -4.8. Anal. Calcd for C₁₉H₃₇NO₆Si: C, 56.54; H, 9.24; N, 3.47. Found: C, 56.43; H, 9.13; N, 3.51.

1-*O*-(*tert*-Butyldiphenylsilyl)-2-(*tert*-butoxycarbonylamino)-3-*O*-(*tert*-butyldimethylsilyl)-4,5-*O*-isopropylidene-2-*deoxy*-*D*-ribo-pentitol **9**

To a solution of aldehyde **8** (700 mg, 1.73 mmol) in EtOH (40 mL) NaBH₄ (266 mg, 7.0 mmol) was added at room temperature. The reaction was stirred at this temperature for 4 h and then methanol and water were added. The mixture was extracted with CH₂Cl₂ (3x15 mL) and AcOEt (3x15 mL), the combined organic extracts were dried with MgSO₄, filtered, and evaporated under reduced pressure. The crude product obtained was then purified by flash chromatography on silica gel eluting with 7:3

hexanes/ethyl acetate to afford 563 mg (80%) of the corresponding carbinol: a glass; $[\alpha]_{\text{D}}^{20} +3.1$ (c 2.8, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 5.17 (d, 1H, $J=6.6$ Hz), 4.12–4.05 (m, 2H), 4.03 (dd, 1H, $J=11.7, 3.0$ Hz), 3.98–3.96 (m, 1H), 3.88–3.78 (m, 2H), 3.74–3.66 (m, 1H), 2.86 (bs, 1H), 1.45 (s, 9H), 1.43 (s, 3H), 1.33 (s, 3H), 0.89 (s, 9H), 0.15 (s, 3H), 0.10 (s, 3H); $^{13}\text{C NMR}$ (75.4 MHz, CDCl_3) δ 155.4, 109.5, 79.4, 76.2, 75.6, 67.5, 62.5, 53.0, 29.6, 28.4, 26.6, 25.8, 25.3, 18.0, –4.3, –4.7. To a solution of this carbinol (540 mg, 1.33 mmol) in dry DMF (15 mL), imidazole (272 mg, 3.99 mmol) and TBDPSCI (450 μL , 1.73 mmol) were added under argon. The mixture was stirred at room temperature for 2 h and then further addition of TBDPSCI (450 μL , 1.73 mmol) and imidazole (181 mg, 2.66 mmol) was effected. After 2 h the reaction was quenched with water and the resulting mixture was extracted with CH_2Cl_2 (3x 20 mL). The combined organic extracts were dried with MgSO_4 , filtered, and evaporated under reduced pressure to give a crude product which was purified by flash chromatography eluting with 9:1 hexanes/ethyl acetate to afford **9** (754 mg, 88%): an oil; $[\alpha]_{\text{D}}^{20} +14.8$ (c 2.3, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.70–7.60 (m, 4H), 7.45–7.35 (m, 6H), 4.52 (bs, 1H), 4.02–3.76 (m, 5H), 3.73 (dd, 1H, $J=7.5, 6.6$ Hz), 3.63 (bt, 1H, $J=9.3$ Hz), 1.44 (s, 9H), 1.37 (s, 3H), 1.27 (s, 3H), 1.06 (s, 9H), 0.80 (s, 9H), 0.09 (s, 6H). $^{13}\text{C NMR}$ (75.4 MHz, CDCl_3) δ 155.4, 135.6, 134.7, 133.3, 129.7, 127.7, 108.8, 79.0, 76.3, 73.0, 66.7, 62.3, 55.0, 28.4, 26.8, 26.4, 25.8, 25.1, 19.2, 18.0, –4.3, –4.4. Anal. Calcd for $\text{C}_{35}\text{H}_{57}\text{NO}_6\text{Si}_2$: C, 65.28; H, 8.92; N, 2.17. Found: C, 65.32; H, 8.80; N, 2.23.

3-(tert-Butoxycarbonylamino)-2-O-(tert-butyldimethylsilyl)-4-O-(tert-butyldiphenylsilyl)-3-deoxy-L-erythrose 10

Compound **9** (680 mg, 1.05 mmol), dissolved in THF (10 mL), was treated with a 70% aqueous acetic acid solution (10 mL) at 0°C. After being stirred at this temperature for 3 h, the solution was heated at 50°C for 24 h. A saturated aqueous NaHCO_3 solution was then added and the mixture was extracted with CH_2Cl_2 (3x15 mL), dried with MgSO_4 , and evaporated under reduced pressure to give a crude product which was chromatographed on silica gel eluting with 7:3 hexanes/ethyl acetate giving 605 mg (95%) of a pure diol: $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.68–7.62 (m, 4H), 7.45–7.35 (m, 6H), 4.66 (bd, 1H, $J=7.5$ Hz), 3.98–3.82 (m, 3H), 3.78–3.56 (m, 4H), 3.45–3.30 (bs, 2H), 1.41 (s, 9H), 1.06 (s, 9H), 0.80 (s, 9H), 0.06 (s, 3H), –0.02 (s, 3H). $^{13}\text{C NMR}$ (75.4 MHz, CDCl_3) δ 155.7, 135.6, 132.8, 129.8, 127.8, 116.0, 79.5, 73.5, 72.9, 63.4, 62.2, 54.0, 28.3, 26.8, 25.8, 19.1, 18.0, –4.6. The entire material was dissolved in 5 mL of CH_2Cl_2 and SiO_2 (2 g) was added. The resulting slurry was treated with 0.65 M aq NaIO_4 (2 mL). The suspension was stirred vigorously for 30' and then filtered. The organic layer was dried with MgSO_4 and evaporated under reduced pressure to give crude aldehyde **10** (567 mg, 99%) which was used as such for the next reaction: $[\alpha]_{\text{D}}^{20} +4.2$ (c 3.4, CHCl_3); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 9.66 (s, 1H), 7.67–7.62 (m, 4H), 7.49–7.37 (m, 6H), 4.53 (bd, 1H, $J=9.6$ Hz), 4.25–4.16 (m, 2H), 3.67 (dd, 1H, $J=9.6, 8.1$ Hz), 3.61–3.54 (m, 1H), 1.40 (s, 9H), 1.02 (s, 9H), 0.92 (s, 9H), 0.12 (s, 3H), 0.05 (s, 3H). $^{13}\text{C NMR}$ (75.4 MHz, CDCl_3) δ 200.4, 155.2, 135.5, 132.5, 129.8, 127.8, 79.7, 78.0, 61.1, 53.8, 28.2, 26.7, 25.7, 19.0, 18.1, –4.6, –5.2. Anal. Calcd for $\text{C}_{31}\text{H}_{49}\text{NO}_5\text{Si}_2$: C, 65.11; H, 8.64; N, 2.45. Found: C, 65.09; H, 8.56; N, 2.47.

(2S,3R,4E)-1-O-(tert-Butyldiphenylsilyl)-2-(tert-butoxycarbonylamino)-3-O-(tert-butyldimethylsilyl)-1,3-dihydroxy-4-octadecene 12

To a suspension of tetradecyltriphenylphosphonium bromide (1.6 g, 3.0 mmol) in THF (10 mL), *n*-butyllithium (1.6 M in hexane, 1.8 mL, 2.88 mmol) was added at –78°C under nitrogen. The red suspension was stirred at this temperature for 2 h and then a solution of crude aldehyde **10** (550 mg, 0.96 mmol) in THF (8 mL) was added. After 2h, the temperature was raised to 20°C and maintained at this temperature for 1 day; then the mixture was concentrated under reduced pressure and water was added. The mixture was extracted with CH_2Cl_2 (3x10 mL), the organic layers were dried with MgSO_4 , filtered, and concentrated *in vacuo* to give a crude product which was purified by flash chromatography eluting with 9.5:0.5 hexanes/ethyl acetate to afford **11** (570 mg, 79%) as a 75/25

Z/E mixture. A cyclohexane solution (2 mL) of the isomer mixture (570 mg, 0.76 mmol) and phenyl disulphide (50 mg) was irradiated with a 100-W high pressure mercury lamp under argon for 12 h. The solution was concentrated under reduced pressure and chromatographed on silica gel eluting with 96:4 cyclohexane/ethyl acetate to give **12** (359 mg, 63%) and **11** (171 mg, 30%).

Compound **12**: [α]_D²⁰ -9.1 (*c* 2.8, CHCl₃); ¹H NMR (300 MHz, C₆D₆) δ 7.81–7.68 (m, 4H), 7.51–7.42 (m, 6H), 5.72–5.61 (m, 1H), 5.51–5.47 (m, 1H), 4.74 (d, 1H, *J*=8.7 Hz), 4.50 (bt, 1H, *J*=6.0 Hz), 4.18–4.06 (m, 2H), 4.02–3.98 (m, 1H), 1.98–1.92 (m, 2H), 1.52 (s, 9H), 1.45–1.28 (m, 22H), 0.98 (s, 9H), 0.96 (s, 9H), 0.91 (m, 3H), 0.14 (s, 6H). ¹³C NMR (75.4 MHz, C₆D₆) δ 151.7, 137.9, 136.6, 135.6, 130.5, 127.3, 79.0, 74.5, 63.5, 58.0, 32.8, 30.7, 30.3, 29.1, 28.1, 27.7, 26.6, 23.6, 20.5, 20.0, 14.9, -3.4, -4.2.

Compound **11**: ¹H NMR (300 MHz, C₆D₆) δ 7.80–7.66 (m, 4H), 7.48–7.42 (m, 6H), 5.51–5.34 (m, 2H), 4.97 (bt, 1H, *J*=5.7 Hz), 4.80 (d, 1H, *J*=8.4 Hz), 4.02–3.89 (m, 3H), 2.26–2.18 (m, 2H), 1.52 (s, 9H), 1.45–1.28 (m, 22H), 0.97 (s, 9H), 0.96 (s, 9H), 0.91 (m, 3H), 0.13 (s, 6H). ¹³C NMR (75.4 MHz, C₆D₆) δ 152.0, 137.9, 136.0, 136.1, 130.3, 127.3, 79.0, 70.0, 63.0, 58.5, 32.8, 30.7, 30.0, 29.1, 28.1, 27.7, 26.6, 23.6, 20.5, 20.0, 14.9, -3.4, -4.2.

(2S,3R,4E)-2-Amino-1,3-dihydroxy-4-octadecene [D-erythro-sphingosine] **1**

A solution of **12** (310 mg, 0.41 mmol) in 75% aqueous trifluoroacetic acid (15 mL) was stirred at room temperature for 16 h thereafter aqueous ammonia was added until neutral. The resulting mixture was extracted with CH₂Cl₂, the organic layers were dried with MgSO₄, filtered, and evaporated under reduced pressure to afford a crude material which was purified by flash chromatography on silica gel eluting with 1:9:1 MeOH/ CH₂Cl₂/ Et₃N to give pure sphingosine **1** (102 mg, 83%): waxy solid; mp 71–74°C; [α]_D²⁰ -1.8 (*c* 0.80, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 5.77 (dt, 1H, *J*=15.3, 7.5 Hz), 5.49 (dd, 1H, *J*=15.3, 7.5 Hz), 4.09 (t, 1H, *J*=6.0 Hz), 3.68 (m, 2H), 2.83 (m, 1H), 1.9–2.2 (brs, 4H), 2.05 (q, 2H, *J*=6.2 Hz), 1.2–1.5 (m, 22H), 0.88 (t, 3H, *J*=6.7 Hz). ¹³C NMR (75.4 MHz, CDCl₃) δ 135.2, 128.5, 76.3, 64.0, 55.7, 32.4, 31.2, 30.3, 29.7, 29.5, 29.3, 29.2, 29.0, 23.0, 14.1. Anal. Calcd for C₁₈H₃₇NO₂: C, 72.17; H, 12.46; N, 4.68. Found: C, 72.01; H, 12.43; N, 4.70.

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9. An *ee* value of $\geq 98\%$ was determined by NaBH₄ reduction to the corresponding glycerol derivative and subsequent Mosher ester analysis.

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