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Novel synthesis of phytosphingosine from levoglucosenone

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Abstract

Phytosphingosine, (2*S*,3*S*,4*R*)-2-amino-1,3,4-octadecanetriol was prepared in 8.6% overall yield in 17 steps from levoglucosenone (1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-enopyranos-2-ulose) by reduction of the carbonyl group, selective *cis*-oxyamination of the carbon–carbon double bond, oxidation of the 2-hydroxyl group to the carbonyl group, regioselective Baeyer–Villiger oxidation, reduction of the afforded lactone to the linear amino alcohol, oxidation of the primary hydroxyl group to the aldehyde, introduction of the hydrocarbon chain using a Wittig reaction, hydrogenation of the resulting carbon–carbon double bond, and deprotection.

Keywords: Phytosphingosine; 2-Amino-1,3,4-octadecanetriol; Levoglucosenone; *cis*-Oxyamination

1. Introduction

Many phytosphingosines are quite widespread in nature as free bases or constituents of ceramides, cerebrosides, and glycosphingolipids [1–16]. Several biological investigations on phytosphingosines (and compounds containing them) have reported interesting results relating to their physiological activities [17–21]. Therefore, many synthetic approaches to phytosphingosines have been reported in the past in view of their biological and medicinal significance [14,21–31]. In this paper, we describe a novel way for the synthesis of phytosphingosine [(2*S*,3*S*,4*R*)-2-amino-1,3,4-octadecanetriol (**1**)] [22–26,28,30,31] from levoglucosenone [1,6-anhydro-3,4-dideoxy-β-D-*glycero*-hex-3-

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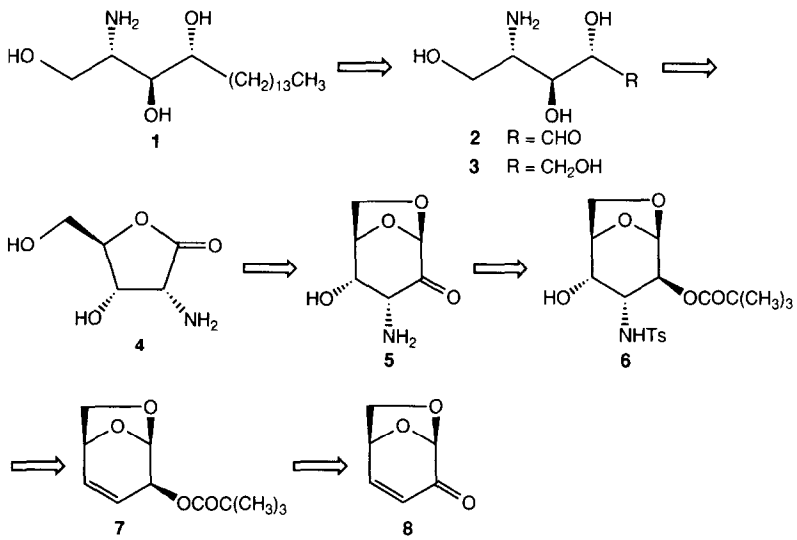


Scheme 1. Retrosynthetic plan for the preparation of phytosphingosine (**1**).

enopyranos-2-ulose (**8**)] [1], which is readily available by acidic pyrolysis of cellulose [32,33] and is used as a useful chiral building block in our various synthetic studies [34–36].

A preparation of **1** ought to satisfy the following points: (*i*) the contiguous chiral centers (2*S*,3*S*,4*R*) of the amino alcohol moiety of **1** are constructed in short steps (preferably one step) and (*ii*) a procedure is easily applicable to preparation of various derivatives of phytosphingosine. We have previously reported the synthesis of amino sugar **6** from **8** via the stereoselective *cis*-oxyamination of the carbon–carbon double bond of the pivaloate **7** (which was prepared from **8**) with the Sharpless reagent [36]. In view of point (*i*), the amino sugar **6** is a useful intermediate leading to **1** because the configurations of the 3-, 4-, and 5-positions of **6** are D-*ribo*, the same as the 2-, 3-, and 4-positions (the amino alcohol moiety) of **1**. We have designed a preparation of **1** from **8** via **6** (see Scheme 1). Phytosphingosine **1** can be prepared from aldehyde **2** via the introduction of the hydrocarbon chain using a Wittig reaction with a phosphonium alkylide. The introduction of a hydrocarbon chain into **1** was placed at the end of the process so that various phytosphingosine derivatives having different hydrocarbon chains (i.e., carbon number, linear or branching, saturated or unsaturated, presence of functional groups composed of heteroatoms, and so on) could be readily prepared, using appropriate phosphonium alkylides. The aldehyde **2** can be prepared by the oxidation of the amino alcohol **3**, which is obtainable from the lactone **4** by reduction. The formation of **4** can be expected by the selective Baeyer–Villiger oxidation of 1,6-anhydro-β-D-

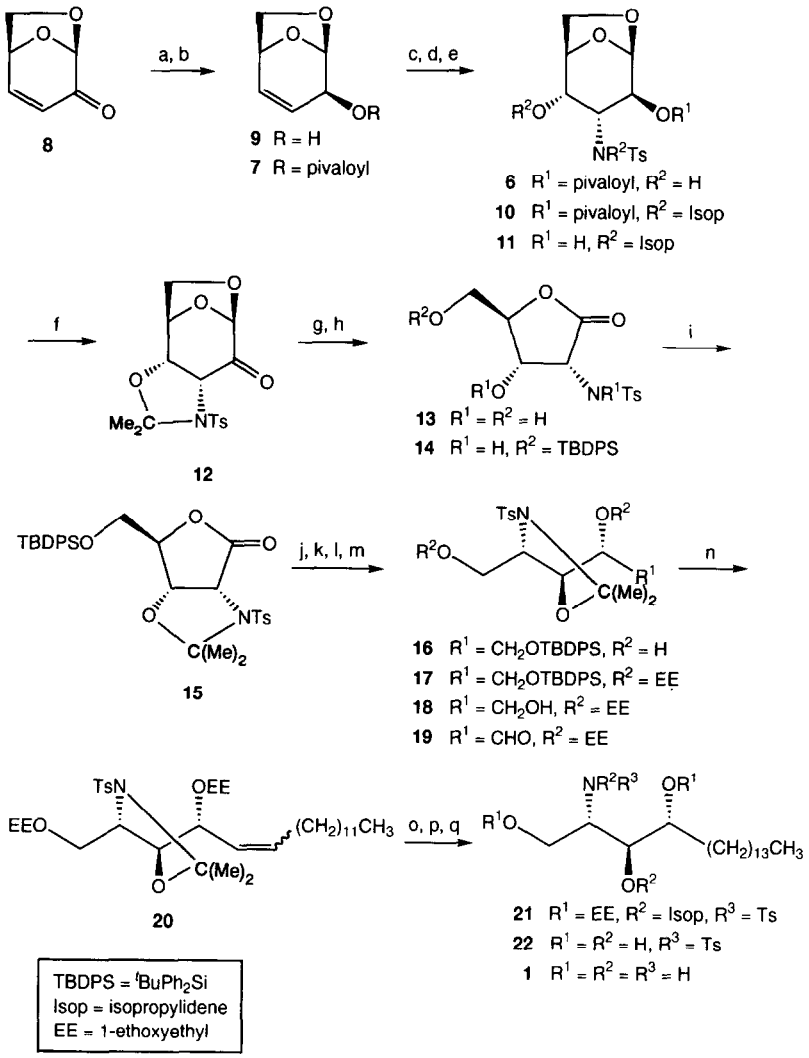
[1] Levoglucosenone (**8**) is available from Yuki Gosei Kogyo Co., Ltd; Hirakawa-cho CH BLDG. 3-24 Hirakawa-cho 2 chome, Chiyoda-ku, Tokyo 102, Japan.

hexopyranos-2-ulose (**5**) under conditions similar to those reported in our previous papers [34]. The ulose **5** can be derived from **6**.

2. Results and discussion

The procedures are shown in Scheme 2. A reduction of the carbonyl group of **8** with lithium aluminum hydride stereoselectively gave the allylic alcohol **9** in 70.3% yield [32,35–37]. Alcohol **9** was pivaloylated to **7** in 94.5% yield [36], and the *cis*-oxyamination of **7** with catalytic amounts of osmium tetroxide and chloramine-T in *tert*-butyl alcohol–water afforded the amino sugar **6** in 53.4% yield as a major product [36]. Treatment of **6** with 2,2-dimethoxypropane and a catalytic amount of *p*-toluenesulfonic acid in toluene gave the oxazolidine **10** in 96.5% yield. Cleavage of the pivaloyl group of **10** with sodium hydroxide in methanol and water gave **11** in 93.5% yield. Oxidation of the free hydroxyl group of **11** to **12** was achieved in 96.2% yield by using the Swern reagent [38]. Regioselective Baeyer–Villiger oxidation [34] of **12** with peracetic acid in acetic acid, followed by treatment with concd hydrochloric acid in methanol, gave the butanolide **13** in 94.0% yield. With *m*-chloroperoxybenzoic acid or magnesium monoperoxyphthalate instead of peroxyacetic acid, similar treatment to that described above could not afford butanolide. Regioselective protection of the primary hydroxyl group of **13** was carried out by *O*-silylation with *tert*-butyldiphenylsilyl chloride and imidazole in *N*,*N*-dimethylformamide to afford **14** in 93.8% yield. Protection of the secondary hydroxyl group and the sulfonamido group of **14** was effected with 2,2-dimethoxypropane and a catalytic amount of *p*-toluenesulfonic acid in toluene to give the dimethyloxazolidine **15** in 96.3% yield. Reduction of **15** with sodium borohydride in tetrahydrofuran–ethanol–water gave **16** in 97.3% yield (in contrast, the reduction of **15** with diisobutylaluminum hydride caused desilylation). The hydroxyl groups of **16** were protected by the treatment with ethyl vinyl ether and a catalytic amount of pyridinium *p*-toluenesulfonate in dichloromethane to afford **17** in 100% yield. Desilylation of **17** with tetra-*n*-butylammonium fluoride in tetrahydrofuran gave **18** in 89.3% yield. Oxidation of the free hydroxyl group of **18** to aldehyde **19** was achieved in 74.5% yield by using tetra-*n*-propylammonium perruthenate and *N*-methylmorpholine *N*-oxide in dichloromethane [39]. Aldehyde **19** was then subjected to the Wittig reaction using *n*-tridecylidenetriphenylphosphorane generated in situ from the appropriate phosphonium salt and *n*-butyllithium in tetrahydrofuran, affording a mixture of *E* and *Z* olefin **20** in 100% yield. Hydrogenation of **20** over 10% palladium-on-charcoal in ethyl acetate gave **21** in 99.5% yield. Treatment of **21** with aqueous acetic acid brought about cleavage of the 2,2-dimethyloxazolidine ring and the two 1-ethoxyethyl ether moieties to produce **22** in 81.7% yield. The photochemical detosylation [40] of **22** in the presence of 1,5-dimethoxynaphthalene and sodium borohydride in aqueous ethanol afforded phytosphingosine **1** in 62.6% yield (8.6% overall yield in 17 steps from **8**).

In conclusion, we have developed a novel method for preparing phytosphingosine [(2*S*,3*S*,4*R*)-2-amino-1,3,4-octadecanetriol (**1**)] from levoglucosenone (**8**) via the construction of the configurations of the amino alcohol moiety of **1** by using stereoselective *cis*-oxyamination with the Sharpless reagent and the introduction of the hydrocarbon



Scheme 2. Reagents and conditions: (a) $LiAlH_4$, Et_2O, r.t., 1 h, then H_2O (70.3%); (b) pivaloyl chloride, pyridine, 60–70°C, 3 h (94.5%); (c) OsO_4, chloramine-T, *t*-BuOH, H_2O, r.t., 18 h (53.4%); (d) $(MeO)_2CMe_2$, *p*-TsOH, toluene, reflux, 1 h (96.5%); (e) 10% aq NaOH, MeOH, r.t., 13.5 h (93.5%); (f) $(COCl)_2$, Me_2SO, CH_2Cl_2, −78°C, 2.5 h, then Et_3N (96.2%); (g) AcOOH, AcOH, r.t., 17 h, then Me_2S, r.t., 30 min, next concd HCl, MeOH, 40°C, 16.5 h (94.0%); (h) *t*-$BuPh_2SiCl$, imidazole, DMF, r.t., 3 h (93.8%); (i) $(MeO)_2CMe_2$, *p*-TsOH, toluene, reflux, 1 h (96.3%); (j) $NaBH_4$, THF, EtOH, H_2O, r.t., 2 h (97.3%); (k) ethyl vinyl ether, pyridinium *p*-toluenesulfonate, CH_2Cl_2, r.t., 38.5 h (100%); (l) Bu_4NF, THF, r.t. 2 h (89.3%); (m) Pr_4NRuO_4, *N*-methylmorpholine-*N*-oxide, MS 4 Å, CH_2Cl_2, r.t., 1 h (74.5%); (n) $[Ph_3P^+(CH_2)_{12}CH_3]Br^-$, BuLi, THF, hexane, −78°C to r.t., 5 h (100%); (o) H_2, 10% Pd–C, AcOEt, r.t. (99.5%); (p) 90% aq AcOH, r.t., 22.5 h (81.7%); (q) $h\nu$, 1,5-dimethoxynaphthalene, $NaBH_4$, 80% aq EtOH, r.t., 10 h (62.6%).

chain by a Wittig reaction. This method may be easily applicable to preparation of phytosphingosine derivatives that have a variety of hydrocarbon chains.

3. Experimental

General methods.—All melting points were uncorrected. Optical rotations were measured with a Jasco DIP-370 polarimeter. IR spectra were measured using a Jasco FTIR-5000 spectrophotometer. ^{1}H NMR spectra were recorded at 300 MHz, and ^{13}C NMR spectra at 75 MHz, with Me_4Si as an internal standard on a Bruker AC 300P spectrometer, unless otherwise noted. Column chromatography was performed on Silica Gel FL-100D (Fuji Silysia). TLC was performed on Silica Gel 60 F_{254} (E. Merck).

*1,6-Anhydro-3-deoxy-3,4-*N,O*-isopropylidene-2-*O*-pivaloyl-3-(*p*-tolylsulfonamido)-β-*D*-altropyranose* (**10**).—A mixture of 15.1 g (37.7 mmol) of **6** [36], 25.0 mL (203 mmol) of 2,2-dimethoxypropane, and 0.11 g (0.58 mmol) of *p*-TsOH · H_2O in 180.0 mL of dry toluene was heated under reflux for 1 h under Ar (H_2O and MeOH that was produced were adsorbed on synthetic Zeolite A-4 beads (Toso) in a column that was attached between the reflux condenser and the reaction mixture). After cooling, the mixture was diluted with Et_2O and washed with satd aq $NaHCO_3$ and then satd aq NaCl. The organic layer was dried (anhyd $MgSO_4$), and the solvent was distilled off under reduced pressure. The residue was purified by column chromatography on silica gel (6:1 → 3:1 hexane–EtOAc) to afford 16.0 g (96.5%) of **10** as an amorphous solid: $[\alpha]_D^{27}$ −34.2° (*c* 0.45, $CHCl_3$); R_f 0.51 in 1:1 hexane–EtOAc; IR (KBr): 2984 (s), 1731 (s), 1601 (w), 1485 (m), 1462 (m), 1350 (s), 1286 (m), 1243 (m), 1156 (s), 1120 (s), 1100 (m), 1033 (m), 1004 (m), 942 (m), 897 (m), 874 (w), 851 (m), 816 (m), 789 (w), 768 (w), 739 (w), 719 (m), 669 (s), 603 (m), 584 (s), 551 (s), 528 (w), 464 (w), 418 cm^{-1} (w); ^{1}H NMR ($CDCl_3$): δ 7.75 (d, 2 H, *J* 8.4 Hz, Ar CH of Ts), 7.31 (d, 2 H, *J* 8.4 Hz, Ar CH of Ts), 5.39 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1), 5.00 (dd, 1 H, $J_{2,3}$ 6.2, $J_{2,1}$ 2.1 Hz, H-2), 4.69 (dbr, 1 H, $J_{5,6}$ 5.1 Hz, H-5), 3.97 (dd, 1 H, $J_{3,2}$ 6.2, $J_{3,4}$ 5.9 Hz, H-3), 3.87 (dd, 1 H, $J_{4,3}$ 5.9, $J_{4,5}$ 1.5 Hz, H-4), 3.83 (dd, 1 H, $J_{6,6'}$ 7.9, $J_{6,5}$ 5.1 Hz, H-6), 3.77 (dd, 1 H, $J_{6',6}$ 7.9, $J_{6',5}$ 1.0 Hz, H-6′), 2.43 (s, 3 H, CH_3 of Ts), 1.75 (s, 3 H, CH_3 of isopropylidene), 1.54 (s, 3 H, CH_3 of isopropylidene), 1.28 (s, 9 H, pivaloyl); ^{13}C NMR ($CDCl_3$, 77.3 ppm): δ 177.7 (1 C, CO), 143.8 (1 C, Ar C of Ts), 137.9 (1 C, Ar C of Ts), 129.9 (2 C, Ar CH of Ts), 127.5 (2 C, Ar CH of Ts), 99.1 (2 C, C-1 and $C(CH_3)_2$ of isopropylidene), 75.1 (1 C, C-4), 74.3 (1 C, C-2), 73.1 (1 C, C-5), 66.3 (1 C, C-6), 57.8 (1 C, C-3), 39.0 (1 C, $C(CH_3)_3$ of pivaloyl), 30.5 (1 C, CH_3 of isopropylidene), 27.4 (3 C, CH_3 of pivaloyl), 25.4 (1 C, CH_3 of isopropylidene), 21.7 (1 C, CH_3 of Ts). Anal. Calcd for $C_{21}H_{29}NO_7S$: C, 57.39; H, 6.65; N, 3.19; S, 7.29. Found: C, 57.25; H, 6.55; N, 2.89; S, 7.19.

*1,6-Anhydro-3-deoxy-3,4-*N,O*-isopropylidene-3-(*p*-tolylsulfonamido)-β-*D*-altropyranose* (**11**).—To a stirred and mixed solution of 420 mg (0.96 mmol) of **10** in 3.0 mL of MeOH was added 3.0 mL of 10% aq NaOH. The reaction mixture was stirred for 13.5 h at room temperature. The mixture was passed over Amberlite IR-120B (H^+). The eluting solution was added to satd aq $NaHCO_3$, and the solvents were evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (4:1 → 2:1 hexane–EtOAc) to afford 318 mg (93.5%) of **11** that was recrystallized from

hexane–$CHCl_3$: mp 179.8–182.0°C; $[\alpha]_D^{27}$ −40.3° (*c* 0.62, $CHCl_3$); R_f 0.42 in 1:1 hexane–EtOAc; IR (KBr): 3524 (m), 2944 (m), 2966 (m), 2904 (m), 2364 (m), 2344 (m), 1601 (m), 1495 (w), 1458 (w), 1377 (m), 1328 (s), 1238 (m), 1218 (m), 1147 (s), 1110 (s), 1087 (s), 1031 (m), 1013 (m), 990 (m), 949 (m), 934 (m), 876 (m), 861 (w), 822 (m), 785 (w), 745 (m), 714 (m), 669 (s), 636 (w), 623 (w), 603 (m), 584 (s), 549 (s), 528 (w), 489 (w), 443 cm^{-1} (w); ^1H NMR ($CDCl_3$): δ 7.78 (d, 2 H, *J* 8.2 Hz, Ar CH of Ts), 7.33 (d, 2 H, *J* 8.2 Hz, Ar CH of Ts), 5.48 (br, 1 H, H-1), 4.67 (d, 1 H, $J_{5,6}$ 4.9 Hz, H-5), 4.11 (d, 1 H, $J_{OH,2}$ 2.3 Hz, OH), 3.87–3.80 (m, 3 H, H-2, H-4, and H-6), 3.74 (d, 1 H, $J_{6',6}$ 7.9 Hz, H-6′), 3.60 (dd, 1 H, $J_{3,2}$ 6.0, $J_{3,4}$ 6.0 Hz, H-3), 2.45 (s, 3 H, CH_3 of Ts), 1.80 (s, 3 H, CH_3 of isopropylidene), 1.50 (s, 3 H, CH_3 of isopropylidene); ^{13}C NMR ($CDCl_3$, 77.3 ppm): δ 144.4 (1 C, Ar C of Ts), 137.0 (1 C, Ar C of Ts), 130.1 (2 C, Ar CH of Ts), 127.8 (2 C, Ar CH of Ts), 100.9 (1 C, C-1), 99.3 (1 C, $C(CH_3)_2$ of isopropylidene), 74.9 and 74.1 (2 C, C-2, and C-4), 73.3 (1 C, C-5), 66.6 (1 C, C-6), 61.6 (1 C, C-3), 30.6 (1 C, CH_3 of isopropylidene), 25.2 (1 C, CH_3 of isopropylidene), 21.8 (1 C, CH_3 of Ts). Anal. Calcd for $C_{16}H_{21}NO_6S$: C, 54.07; H, 5.96; N, 3.94; S, 9.02. Found: C, 54.01; H, 5.83; N, 3.66; S, 9.13.

*1,6-Anhydro-3-deoxy-3,4-*N,O-*isopropylidene-3-(*p-*tolylsulfonamido)-β-*D-ribo-*hexopyranos-2-ulose* (**12**).—To a stirred solution of 3.09 mL (36.0 mmol) of oxalyl chloride in 80.0 mL of dry CH_2Cl_2 was slowly added a solution of 5.13 mL (72.3 mmol) of dry Me_2SO in 17.0 mL of dry CH_2Cl_2 at −78°C under Ar. After stirring the reaction mixture for 2 min, a solution of 10.66 g (30.0 mmol) of **11** in 72.0 mL of dry CH_2Cl_2 was slowly added, followed by stirring at −78°C for 2.5 h under Ar. Then, 21.0 mL (150.0 mmol) of dry Et_3N was slowly added to the reaction mixture, with stirring for 5 min. The temperature was then allowed to rise to room temperature. The mixture was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel (3:1 → 1:1 hexane–EtOAc) to afford 10.19 g (96.2%) of **12** that was recrystallized from hexane–$CHCl_3$: mp 200.6–202.1°C; $[\alpha]_D^{27}$ −51.0° (*c* 0.88, $CHCl_3$); R_f 0.42 in 1:1 hexane–EtOAc; IR (KBr): 3000 (m), 2964 (m), 2952 (m), 2922 (m), 1767 (s), 1601 (w), 1499 (w), 1460 (w), 1375 (w), 1336 (s), 1309 (w), 1294 (w), 1249 (m), 1220 (m), 1154 (s), 1116 (s), 1098 (s), 1033 (m), 1015 (m), 973 (m), 955 (m), 920 (m), 878 (m), 859 (m), 818 (m), 781 (w), 750 (m), 710 (m), 671 (m), 621 (m), 594 (m), 572 (m), 545 (m), 534 (m), 491 (w), 414 cm^{-1} (w); ^1H NMR ($CDCl_3$): δ 7.88 (d, 2 H, *J* 8.4 Hz, Ar CH of Ts), 7.31 (d, 2 H, *J* 8.4 Hz, Ar CH of Ts), 5.21 (s, 1 H, H-1), 4.84 (dbr, 1 H, $J_{5,6}$ 4.9 Hz, H-5), 4.79 (d, 1 H, $J_{3,4}$ 5.5 Hz, H-3), 4.48 (dd, 1 H, $J_{4,3}$ 5.5, $J_{4,5}$ 1.8 Hz, H-4), 4.02 (d, 1 H, $J_{6',6}$ 7.9 Hz, H-6), 3.96 (dd, 1 H, $J_{6',6}$ 7.9, $J_{6',5}$ 4.9 Hz, H-6′), 2.44 (s, 3 H, CH_3 of Ts), 1.68 (s, 3 H, CH_3 of isopropylidene), 1.46 (s, 3 H, CH_3 of isopropylidene); ^{13}C NMR ($CDCl_3$, 77.3 ppm): δ 195.6 (1 C, C-2), 144.2 (1 C, Ar C of Ts), 138.3 (1 C, Ar C of Ts), 129.7 (2 C, Ar CH of Ts), 128.4 (2 C, Ar CH of Ts), 101.3 (1 C, C-1), 99.2 (1 C, $C(CH_3)_2$ of isopropylidene), 78.5 (1 C, C-4), 73.5 (1 C, C-5), 66.0 (1 C, C-6), 62.2 (1 C, C-3), 28.9 (1 C, CH_3 of isopropylidene), 26.8 (1 C, CH_3 of isopropylidene), 21.9 (1 C, CH_3 of Ts). Anal. Calcd for $C_{16}H_{19}NO_6S$: C, 54.38; H, 5.42; N, 3.96; S, 9.07. Found: C, 53.90; H, 5.23; N, 3.79; S, 8.99.

*(2*R*,3*S*,4*R*)-3-Hydroxy-4-hydroxymethyl-2-(*p*-tolylsulfonamido)-4-butanolide* (**13**).—To a stirred and water-cooled solution of 337 mg (0.94 mmol) of **12** in 18.0 mL of AcOH was slowly added dropwise 1.8 mL of 40% AcOOH in AcOH. The reaction

mixture was stirred for 17 h at room temperature under Ar. To the stirred and water-cooled mixture was slowly added 10.0 mL of Me_2S. The mixture was stirred for 30 min at room temperature, and then evaporated under reduced pressure. To the residue were added 11.6 mL of MeOH and 0.5 mL of concd HCl. The mixture was stirred for 16.5 h at 40°C under Ar, and then evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (1:1 → 1:2 hexane–EtOAc) to afford 266 mg (94.0%) of **13** as a white powder: mp 157.5–159.6°C; $[\alpha]_D^{33}$ −18.6° (*c* 0.76, MeOH); R_f 0.26 in 1:5 hexane–EtOAc; IR (KBr): 3528 (m), 3404 (m), 3124 (m), 2998 (w), 2948 (m), 2906 (m), 2760 (w), 1924 (w), 1769 (s), 1657 (w), 1601 (m), 1477 (w), 1417 (m), 1363 (m), 1321 (m), 1305 (m), 1286 (m), 1265 (m), 1226 (m), 1195 (m), 1151 (s), 1089 (s), 1067 (s), 1006 (m), 982 (m), 934 (m), 903 (m), 849 (m), 810 (m), 768 (m), 710 (w), 671 (m), 632 (m), 588 (w), 572 (m), 538 (m), 480 (w), 441 cm^{-1} (w); ^1H NMR (CD_3OD): δ 7.82 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 7.35 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 4.57 (d, 1 H, $J_{2,3}$ 5.4 Hz, H-2), 4.32 (dd, 1 H, $J_{4,5}$ 2.8, $J_{4,5'}$ 2.6 Hz, H-4), 4.13 (d, 1 H, $J_{3,2}$ 5.4 Hz, H-3), 3.76 (dd, 1 H, $J_{5,5'}$ 12.6, $J_{5,4}$ 2.8 Hz, H-5), 3.69 (dd, 1 H, $J_{5',5}$ 12.6, $J_{5',4}$ 2.6 Hz, H-5′), 2.42 (s, 3 H, CH_3 of Ts); ^{13}C NMR (CD_3OD, 49.8 ppm): δ 176.6 (1 C, C-1), 145.5 (1 C, Ar C of Ts), 140.0 (1 C, Ar C of Ts), 131.3 (2 C, Ar CH of Ts), 128.9 (2 C, Ar CH of Ts), 89.0 (1 C, C-4), 71.3 (1 C, C-2), 63.0 (1 C, C-3), 58.0 (1 C, C-5), 22.2 (1 C, CH_3 of Ts). Anal. Calcd for $C_{12}H_{15}NO_6S$: C, 47.83; H, 5.02; N, 4.65; S, 10.64. Found: C, 48.01; H, 5.07; N, 4.50; S, 10.61.

*(2R,3S,4R)-4-(*tert*-Butyldiphenylsilyloxymethyl)-3-hydroxy-2-(*p*-tolylsulfonamido)-4-butanolide* (**14**).—To a stirred, ice-cooled solution of 1.43 g (4.75 mmol) of **13** and 0.58 g (8.58 mmol) of imidazole in 9.5 mL of dry DMF was added dropwise 2.22 mL (8.54 mmol) of *tert*-butyldiphenylsilyl chloride, followed by stirring for 3 h at room temperature under Ar. The reactiom mixture was poured into ice-water and extracted three times with Et_2O. The organic layer was dried (anhyd $MgSO_4$) and then evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (1:1 → 1:2 hexane–EtOAc) to afford 2.41 g (93.8%) of **14** that was recrystallized from hexane–Et_2O: mp 132.5–134.2°C; $[\alpha]_D^{32}$ −29.3° (*c* 0.63, $CHCl_3$); R_f 0.29 in 2:1 hexane–EtOAc; IR (KBr): 3290 (br), 3046 (w), 2934 (m), 2860 (m), 2364 (m), 1796 (s), 1460 (w), 1429 (m), 1363 (m), 1330 (s), 1255 (w), 1214 (w), 1154 (s), 1114 (m), 1093 (s), 1025 (w), 988 (m), 944 (m), 907 (w), 866 (w), 824 (w), 806 (w), 768 (w), 745 (w), 704 (m), 667 (m), 627 (w), 600 (w), 561 (m), 547 (m), 514 cm^{-1} (m); ^1H NMR ($CDCl_3$): δ 7.78 (d, 2 H, *J* 8.4 Hz, Ar CH of Ts), 7.59–7.26 (m, 10 H, Ar CH of TBDPS), 7.24 (d, 2 H, *J* 8.4 Hz, Ar CH of Ts), 5.20 (br, 1 H, NH), 4.63 (d, 1 H, $J_{3,2}$ 5.3 Hz, H-3), 4.53 (dd, 1 H, $J_{4,5}$ 2.4, $J_{4,5'}$ 1.7 Hz, H-4), 4.35 (d, 1 H, $J_{2,3}$ 5.3 Hz, H-2), 3.88 (dd, 1 H, $J_{5,5'}$ 11.9, $J_{5,4}$ 2.4 Hz, H-5), 3.77 (dd, 1 H, $J_{5',5}$ 11.9, $J_{5',4}$ 1.7 Hz, H-5′), 2.98 (br, 1 H, OH), 2.38 (s, 3 H, CH_3 of Ts), 0.85 (s, 9 H, CH_3 of TBDPS); ^{13}C NMR ($CDCl_3$, 77.3 ppm) [2]: δ 173.5 (1 C, C-1), 86.0 (1 C, C-4), 70.8 (1 C, C-3), 63.8 (1 C, C-5), 56.8 (1 C, C-2), 26.9 (3 C, CH_3 of TBDPS), 21.8 (1 C, CH_3 of Ts), 19.2 (1 C, $C(CH_3)_3$ of TBDPS); HRMS: *m/z* 540.1873 (+0.3 mmu, $C_{28}H_{34}NO_6SSi$, MH^+).

[2] Only typical and assignable peaks in the ^{13}C NMR spectra of **14–16** are shown.

*(1S,5R,8R)-4-Aza-8-(*tert*-butyldiphenylsilyloxymethyl)-3,3-dimethyl-2,7-dioxa-6-oxo-4-(*p*-tolylsulfonyl)-bicyclo[3,3,0]octane* (**15**).—A mixture of 275 mg (0.51 mmol) of **14**, 0.32 mL (2.60 mmol) of 2,2-dimethoxypropane, and 1.5 mg (7.9 μmol) of *p*-TsOH · H_2O in 2.0 mL of dry toluene was heated under reflux for 1 h under Ar (H_2O and MeOH that was produced were adsorbed on synthetic Zeolite A-4 beads (Toso) in a column that was attached between the reflux condenser and the reaction mixture). After cooling, the mixture was diluted with Et_2O and washed with satd aq $NaHCO_3$ and then satd aq NaCl. The organic layer was dried (anhyd $MgSO_4$), and the solvent was distilled off under reduced pressure. The residue was purified by column chromatography on silica gel (8:1 hexane–EtOAc) to afford 285 mg (96.3%) of **15** as a white powder: mp 51.0–52.8°C; $[\alpha]_D^{27}$ +12.6° (*c* 1.56, $CHCl_3$); R_f 0.55 in 2:1 hexane–EtOAc; IR (KBr): 3076 (m), 3052 (m), 2936 (s), 2862 (s), 2304 (w), 1968 (w), 1798 (s), 1601 (m), 1570 (w), 1495 (m), 1473 (m), 1431 (m), 1354 (s), 1238 (m), 1218 (m), 1158 (s), 1114 (s), 1080 (s), 1029 (s), 1015 (s), 980 (s), 942 (m), 893 (m), 857 (s), 822 (s), 745 (s), 727 (s), 704 (s), 675 (s), 629 (m), 601 (m), 582 (s), 549 (s), 503 (s), 427 cm^{-1} (w); ^1H NMR ($CDCl_3$): δ 7.83 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 7.65–7.36 (m, 10 H, Ar CH of TBDPS), 7.28 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 4.89 (d, 1 H, $J_{5,1}$ 5.3 Hz, H-5), 4.59 (d, 1 H, $J_{1,5}$ 5.3 Hz, H-1), 4.46 (br, 1 H, H-8), 3.91 (dd, 1 H, $J_{8-gem-CH_2O-TBDPS}$ 11.6, $J_{8-CH_2O-TBDPS,8}$ 2.4 Hz, 8-CH_2O-TBDPS), 3.73 (dd, 1 H, $J_{8-gem-CH_2O-TBDPS}$ 11.6, $J_{8-CH_2O-TBDPS,8}$ 1.4 Hz, 8-CH_2O-TBDPS), 2.43 (s, 3 H, CH_3 of Ts), 1.71 (s, 3 H, 3-CH_3), 1.62 (s, 3 H, 3-CH_3), 1.06 (s, 9 H, CH_3 of TBDPS); ^{13}C NMR ($CDCl_3$, 77.3 ppm) [3]: δ 172.8 (1 C, C-6), 100.8 (1 C, C-3), 81.1 (1 C, C-8), 77.9 (1 C, C-1), 63.6 (1 C, 8-CH_2O-TBDPS), 60.9 (1 C, C-5), 28.4 (1 C, 3-CH_3), 27.1 (3 C, CH_3 of TBDPS), 25.8 (1 C, 3-(CH_3)), 21.9 (1 C, CH_3 of Ts), 19.3 (1 C, $C(CH_3)_3$ of TBDPS). Anal. Calcd for $C_{31}H_{37}NO_6SSi$: C, 64.22; H, 6.43; N, 2.42; S, 5.53. Found: C, 63.97; H, 6.44; N, 2.40; S, 5.51.

*5-O-(*tert*-Butyldiphenylsilyl)-2-deoxy-2,3-*N,O*-isopropylidene-2-(*p*-tolylsulfonamido)-*D*-ribitol* (**16**).—To a stirred and ice-cooled solution of 298 mg (0.51 mmol) of **15** in a mixed solvent of 3.8 mL of THF, 0.5 mL of EtOH, and 0.7 mL of water was added portionwise 39.0 mg (1.03 mmol) of $NaBH_4$. The mixture was stirred for 2 h at room temperature, and the excess amount of reductant was decomposed by the addition of acetone with ice-cooling. Saturated aq NaCl was added to the mixture, and it was extracted five times with Et_2O. The combined organic layers were dried (anhyd $MgSO_4$) and then evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (4:1 hexane–EtOAc) to afford 292 mg (97.3%) of **16** as an amorphous solid: mp 48.0–52.0°C; $[\alpha]_D^{29}$ −15.5° (*c* 0.50, $CHCl_3$); R_f 0.36 in 2:1 hexane–EtOAc; IR (KBr): 3390 (br), 3074 (w), 3010 (w), 2934 (m), 2870 (w), 2862 (m), 1601 (w), 1475 (w), 1431 (w), 1371 (w), 1344 (m), 1241 (w), 1220 (w), 1160 (s), 1112 (s), 1031 (w), 946 (w), 886 (w), 822 (m), 743 (m), 706 (s), 661 (m), 596 (s), 551 (m), 503 cm^{-1} (m); ^1H NMR ($CDCl_3$): δ 7.78 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 7.64–7.60 (m, 4 H, Ar CH), 7.46–7.30 (m, 8 H, Ar CH), 3.95–3.69 (m, 7 H, H-1, H-2, H-3, H-4, and H-5), 3.12 (d, 1 H, *J* 4.8 Hz, 4-OH), 2.93 (dd, 1 H, *J* 6.7, *J* 4.6 Hz,

[3] Only typical and assignable peaks in the ^{13}C NMR spectra of **14–16** are shown.

1-OH), 2.43 (s, 3 H, CH_3 of Ts), 1.63 (s, 3 H, CH_3 of isopropylidene), 1.47 (s, 3 H, CH_3 of isopropylidene), 1.02 (s, 9 H, CH_3 of TBDPS); ^{13}C NMR ($CDCl_3$, 77.3 ppm) [4]: δ 97.7 (1 C, $C(CH_3)_2$ of isopropylidene), 30.6 (1 C, CH_3 of isopropylidene), 27.0 (3 C, CH_3 of TBDPS), 24.9 (1 C, CH_3 of isopropylidene), 21.8 (1 C, CH_3 of Ts), 19.5 (1 C, $C(CH_3)_3$ of TBDPS); HRMS: m/z 584.2469 (+3.3 mmu, $C_{31}H_{42}NO_6SSi$, MH^+).

*5-O-(*tert*-Butyldiphenylsilyl)-1,4-di-O-(1'-ethoxyethyl)-2-deoxy-2,3-*N,O*-isopropylidene-2-(*p*-tolylsulfonamido)-*D*-ribitol* (**17**).—To a stirred and mixed solution of 155 mg (0.27 mmol) of **16** in 3.0 mL of dry CH_2Cl_2 were added 0.63 mL (6.59 mmol) of ethyl vinyl ether and 6.0 mg (0.02 mmol) of pyridinium *p*-toluenesulfonate, followed by stirring for 38.5 h at room temperature under Ar. Then 60.0 μL of Et_3N was added to the reaction mixture that was then diluted with CH_2Cl_2 and washed with satd aq $NaHCO_3$ and satd aq NaCl. The organic layer was dried (anhyd Na_2SO_4) and then evaporated under reduced pressure (< 30°C). The residue was purified by column chromatography on silica gel (4:1 hexane–EtOAc) to afford 215 mg (100%) of **17** as a mixture of four stereoisomers: $[\alpha]_D^{28}$ +6.2° (*c* 0.69, $CHCl_3$); R_f 0.58 in 2:1 hexane–EtOAc; IR (neat): 3076 (w), 2984 (s), 2936 (s), 2894 (s), 2862 (s), 2250 (w), 1601 (w), 1475 (m), 1462 (m), 1446 (m), 1431 (m), 1381 (m), 1344 (s), 1307 (w), 1290 (w), 1241 (m), 1218 (m), 1152 (s), 1114 (s), 1067 (s), 1017 (m), 955 (m), 911 (m), 861 (w), 822 (m), 795 (w), 758 (s), 706 (s), 687 (m), 667 (m), 590 (m), 551 (m), 505 cm^{-1} (m); ^1H NMR ($CDCl_3$): δ 7.77 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 7.69–7.62 (m, 4 H, Ar CH), 7.44–7.29 (m, 8 H, Ar CH), 4.87 (q, *J* 5.2 Hz) and 4.83 (q, *J* 5.2 Hz) (1 H, CH of EE), 4.68 (q, *J* 5.3 Hz), 4.65 (q, *J* 5.3 Hz), 4.56 (q, *J* 5.3 Hz), and 4.54 (q, *J* 5.3 Hz) (1 H, CH of EE), 4.22–4.15 (m), 4.12–4.07 (m), 4.01–3.37 (m), and 3.34–3.23 (m) (11 H, H-1, H-2, H-3, H-4, H-5, and CH_2 of EE), 2.42 (s, 3 H, CH_3 of Ts), 1.68 (br), and 1.66 (s) (3 H, CH_3 of isopropylidene), 1.50 (s), 1.48 (br), and 1.47 (s) (3 H, CH_3 of isopropylidene), 1.29–1.07 (m, 12 H, CH_3 of EE), 1.00 (s, 9 H, CH_3 of TBDPS). Anal. Calcd for $C_{39}H_{57}NO_8SSi$: C, 64.34; H, 7.89; N, 1.92. Found: C, 63.79; H, 7.88; N, 1.76.

*2-Deoxy-1,4-di-O-(1'-ethoxyethyl)-2,3-*N,O*-isopropylidene-2-(*p*-tolylsulfonamido)-*D*-ribitol* (**18**).—To a stirred solution of 112 mg (154 μmol) of **17** in 3.8 mL of THF was added 560 μL (560 μmol) of a 1.0 M solution of tetra-*n*-butylammonium fluoride in THF. The reaction mixture was stirred for 2 h at room temperature under Ar. In order to trap F^-, Amberlite IRA-410 (OH^-) was added to this solution, and the resin was filtered off. Then $NaHCO_3$ (powder) was added to the filtrate, and the mixture was dried (anhyd Na_2SO_4). The solvent was distilled off under reduced pressure (< 30°C). The residue was purified by column chromatography on silica gel (2:1 hexane–EtOAc) to afford 67 mg (89.3%) of **18** as a colorless oil which is a mixture of four stereoisomers: $[\alpha]_D^{28}$ +60.1° (*c* 1.09, $CHCl_3$); R_f 0.35 and 0.23 in 2:1 hexane–EtOAc; IR (neat): 3440 (br), 2986 (s), 2938 (s), 2888 (s), 1601 (w), 1495 (w), 1448 (m), 1383 (s), 1344 (s), 1307 (m), 1243 (s), 1220 (s), 1154 (br), 1093 (br), 1056 (s), 1017 (m), 946 (m), 903 (w), 861 (w), 816 (w), 756 (s), 710 (m), 667 (s), 594 (s), 553 (s), 516 cm^{-1} (w); ^1H NMR ($CDCl_3$): δ 7.76 (d, *J* 8.2 Hz) and 7.75 (d, *J* 8.2 Hz) (2 H, Ar CH of Ts), 7.30 (d, *J*

[4] Only typical and assignable peaks in the ^{13}C NMR spectra of **14–16** are shown.

8.2 Hz) and 7.29 (d, *J* 8.2 Hz) (2 H, Ar CH of Ts), 4.89–4.83 (m, 1 H, CH of EE), 4.78–4.55 (m, 1 H, CH of EE), 4.14–4.08 (m) and 3.95–3.41 (m) (11 H, H-1, H-2, H-3, H-4, H-5, and CH_2 of EE), 2.92 (dd, *J* 6.3, *J* 6.3 Hz) and 2.84 (dd, *J* 6.7, *J* 6.7 Hz) (1 H, OH), 2.42 (s, 3 H, CH_3 of Ts), 1.68 (s), 1.67 (s), 1.64 (s), and 1.62 (s) (3 H, CH_3 of isopropylidene), 1.51 (s), 1.49 (s), 1.47 (s), and 1.44 (s) (3 H, CH_3 of isopropylidene), 1.36–1.28 (m, 6 H, CH_3 of EE), 1.24–1.14 (m, 6 H, CH_3 of EE).

*4-Deoxy-2,5-di-*O*-(1'-ethoxyethyl)-3,4-*N,O*-isopropylidene-4-(*p*-tolylsulfonamido)-*L*-ribose* (**19**).—The suspension of 936 mg (1.91 mmol) of **18**, 620 mg (97%, 5.13 mmol) of *N*-methylmorpholine-*N*-oxide, and 1.00 g of molecular sieves 4 Å in 60.0 mL of dry CH_2Cl_2 was stirred for 30 min at room temperature under Ar. To the mixture was added 90 mg (97%, 0.25 mmol) of tetra-*n*-propylammonium perruthenate, followed by stirring for 1 h at room temperature under Ar. The reaction mixture was diluted with 300 mL of Et_2O, and then it was washed with 120 mL of satd aq Na_2SO_3, 120 mL of satd aq NaCl, and 120 mL of satd aq $CuSO_4$. The organic layer was dried (anhyd Na_2SO_4), and the solvent was distilled off under reduced pressure ($< 30°C$). The residue was purified by column chromatography on silica gel (4:1 → 2:1 hexane–EtOAc) to afford 694 mg (74.5%) of **19** as a colorless oil that is a mixture of four stereoisomers: R_f 0.47 in 2:1 hexane–EtOAc; IR (neat): 2984 (m), 2936 (m), 2890 (m), 1740 (m), 1601 (w), 1448 (w), 1383 (m), 1348 (s), 1307 (w), 1295 (w), 1241 (w), 1220 (w), 1154 (s), 1093 (s), 1058 (s), 1020 (w), 949 (w), 930 (w), 861 (w), 816 (w), 710 (w), 665 (m), 594 (m), 553 cm^{-1} (m); ^1H NMR ($CDCl_3$): δ 9.60 (d, *J* 1.7 Hz), 9.59 (d, *J* 1.9 Hz), 9.54 (d, *J* 2.5 Hz), 9.53 (d, *J* 2.9 Hz) (1 H, CHO), 7.76 (2 H, d, *J* 8.2 Hz, Ar CH of Ts), 7.30 (2 H, d, *J* 8.2 Hz, Ar CH of Ts), 4.79–4.71 (m, 1 H, CH of EE), 4.70–4.58 (m, 1 H, CH of EE), 4.50–4.47 (m), 4.22 (dd, *J* 7.1, *J* 2.5 Hz), and 4.17 (dd, *J* 7.7, *J* 2.9 Hz) (1 H, 2-H), 4.11–4.02 (1 H, m) and 3.95–3.40 (7 H, m) (H-3, H-4, H-5, and CH_2 of EE), 2.44 (s, 3 H, CH_3 of Ts), 1.67 (s), 1.66 (s), 1.65 (s), and 1.64 (s) (3 H, CH_3 of isopropylidene), 1.50 (s), 1.48 (br), and 1.45 (s) (3 H, CH_3 of isopropylidene), 1.34–0.90 (m, 12 H, CH_3 of EE).

*(2S,3S,4R)-1,4-Di-*O*-(1'-ethoxyethyl)-2,3-*N,O*-isopropylidene-2-(p-tolylsulfonamido)-5-octadecene-1,3,4-triol* (**20**).—To a stirred and ice-cooled solution of 21.0 g (40.0 mmol) of *n*-tridecyltriphenylphosphonium bromide was slowly added dropwise 19.0 mL (31.5 mmol) of a solution (1.66 mol dm^{-3}) of *n*-butyllithium in hexane under Ar. After stirring for 3 h at ca. 0°C under Ar, the mixture was slowly added to a solution of 694 mg (1.42 mmol) of **19** in 20.0 mL of dry THF at −78°C under Ar. The reaction mixture was stirred for 5 h at room temperature under Ar. Then it was poured into ice-water and extracted with Et_2O. The organic layer was washed with satd aq NaCl and then dried (anhyd Na_2SO_4). The solvent was distilled off under reduced pressure ($< 30°C$). The residue was purified by column chromatography on silica gel (5:1 hexane–EtOAc) to afford 936 mg (100%) of **20** as a colorless oil that is a mixture of stereoisomers: $[\alpha]_D^{28}$ +2.4° (*c* 2.36, $CHCl_3$); R_f 0.42 in 5:1 hexane–EtOAc; IR (neat): 2950 (s), 2922 (s), 2858 (s), 1738 (w), 1657 (w), 1601 (w), 1562 (w), 1543 (w), 1495 (w), 1460 (m), 1383 (m), 1344 (m), 1305 (m), 1243 (m), 1218 (m), 1093 (br), 948 (m), 857 (m), 816 (m), 758 (m), 710 (m), 685 (m), 665 (m), 590 (m), 553 cm^{-1} (m); ^1H NMR ($CDCl_3$): δ 7.76 (d, 2 H, *J* 8.1 Hz, Ar CH of Ts), 7.28 (d, 2 H, *J* 8.1 Hz, Ar CH of Ts), 5.77–5.63 (m, 1 H, H-6), 5.31–5.12 (m, 1 H, H-5), 4.86–4.56 (m, 3

H, H-4, and CH of EE), 3.97–3.31 (m, 8 H, H-1, H-2, H-3, and CH_2 of EE), 2.42 (s, 3 H, CH_3 of Ts), 2.08 (br, 2 H, H-7), 1.67 (br), 1.65 (s), and 1.64 (s) (3 H, CH_3 of isopropylidene), 1.49 (s), 1.47 (br), and 1.45 (s) (3 H, CH_3 of isopropylidene), 1.35–1.11 (br, 32 H, H-8–H-17, and CH_3 of EE), 0.88 (t, 3 H, $J_{18,17}$ 6.4 Hz, H-18). Anal. Calcd for $C_{36}H_{63}NO_7S$: C, 66.12; H, 9.71; N, 2.14; S, 4.90. Found: C, 66.06; H, 9.73; N, 1.98; S, 4.98.

(2S,3S,4R)-1,4-Di-O-(1'-ethoxyethyl)-2,3-N,O-isopropylidene-2-(p-tolylsulfonamido)-1,3,4-octadecanetriol (**21**).—A vigorously stirred solution of 760 mg (1.16 mmol) of **20** in 40.0 mL of AcOEt was hydrogenated over 300 mg of 10% Pd–C at room temperature under H_2. The catalyst was removed by filtration through Celite, and then the solvent was distilled off under reduced pressure (< 30°C). The residue was purified by column chromatography on silica gel (5:1 hexane–EtOAc) to afford 758 mg (99.5%) of **21** as a colorless oil which is a mixture of four stereoisomers: $[\alpha]_D^{27}$ +29.5° (*c* 0.93, $CHCl_3$); R_f 0.42 in 5:1 hexane–EtOAc; IR (neat): 2984 (m), 2928 (s), 2858 (s), 1738 (w), 1601 (w), 1460 (m), 1381 (m), 1346 (m), 1307 (w), 1243 (m), 1218 (m), 1154 (s), 1096 (s), 1058 (m), 1017 (w), 948 (w), 864 (w), 816 (w), 758 (s), 710 (w), 665 (m), 594 (m), 551 cm^{-1} (m); ^1H NMR ($CDCl_3$): δ 7.76 (d, 2 H, *J* 7.6 Hz, Ar CH of Ts), 7.28 (d, *J* 7.6 Hz) and 7.27 (d, *J* 7.6 Hz) (2 H, Ar CH of Ts), 4.91–4.82 (m) and 4.74–4.56 (m) (2 H, CH of EE), 4.02–3.40 (m, 9 H, H-1, H-2, H-3, H-4, and CH_2 of EE), 2.41 (s, 3 H, CH_3 of Ts), 1.69 (br), 1.65 (s), and 1.64 (s) (3 H, CH_3 of isopropylidene), 1.52 (s), 1.50 (br), and 1.48 (s) (3 H, CH_3 of isopropylidene), 1.43–1.11 (br, 38 H, H-5–H-17, and CH_3 of EE), 0.88 (t, 3 H, $J_{18,17}$ 6.6 Hz, H-18). Anal. Calcd for $C_{36}H_{65}NO_7S$: C, 65.92; H, 9.99; N, 2.14; S, 4.89. Found: C, 65.77; H, 10.03; N, 2.00; S, 4.97.

(2S,3S,4R)-2-(p-Tolylsulfonamido)-1,3,4-octadecanetriol (**22**).—A solution of 509 mg (0.78 mmol) of **21** in 20.0 mL of 90% aq AcOH was stirred for 22.5 h at room temperature. The rection mixture was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (1:3 hexane–EtOAc) to afford 299 mg (81.7%) of **22** as a white powder: mp 120.5–123.3°C; $[\alpha]_D^{28}$ −2.7° (*c* 0.26, $CHCl_3$); R_f 0.10 in 1:1 hexane–EtOAc; IR (KBr): 3416 (s), 3292 (s), 3048 (w), 2922 (s), 2854 (s), 2530 (w), 2456 (w), 1920 (w), 1603 (w), 1468 (m), 1437 (m), 1377 (w), 1303 (m), 1189 (w), 1154 (s), 1093 (s), 1064 (m), 1042 (m), 1027 (m), 994 (m), 980 (m), 911 (w), 859 (w), 812 (m), 723 (w), 706 (w), 675 (m), 574 (m), 534 cm^{-1} (m); ^1H NMR (CD_3OD–$CDCl_3$): δ 7.77 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 7.33 (d, 2 H, *J* 8.3 Hz, Ar CH of Ts), 3.68–3.35 (m, 5 H, H-1, H-2, H-3, and H-4), 2.44 (s, 3 H, CH_3 of Ts), 1.46 (m, 2 H, H-5), 1.27 (br, 24 H, H-6–H-17), 0.89 (t, 3 H, $J_{18,17}$ 6.6 Hz, H-18); ^{13}C NMR (CD_3OD–$CDCl_3$, CD_3OD; 49.8 ppm): δ 144.8 (1 C, Ar C of Ts), 139.2 (1 C, Ar C of Ts), 130.9 (2 C, Ar CH of Ts), 128.2 (2 C, Ar CH of Ts), 76.8 (1 C), 73.4 (1 C), 62.2 (1 C), 56.6 (1 C), 33.9 (1 C), 33.1 (1 C), 30.9 (7 C), 30.6 (1 C), 26.9 (1 C), 23.9 (1 C), 22.4 (1 C, CH_3 of Ts), 15.1 (1 C, C-18). Anal. Calcd for $C_{25}H_{45}NO_5S$: C, 63.66; H, 9.62; N, 2.97; S, 6.80. Found: C, 63.91; H, 9.73; N, 2.80; S, 6.59.

(2S,3S,4R)-2-Amino-1,3,4-octadecanetriol (**1**).—A solution of 182 mg (0.39 mmol) of **22**, 46 mg (0.24 mmol) of 1,5-dimethoxynaphthalene, and 93 mg (2.46 mmol) of $NaBH_4$ in 74.0 mL of 80% EtOH solution was irradiated under Ar with a 100-W high-pressure mercury lamp (λ 365 nm) for 10 h. After the addition of acetone to

decompose the excess $NaBH_4$, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on Iatrobeads (40:10:1 $CHCl_3$–MeOH–25% aq NH_4OH) to afford 77 mg (62.6%) of **1** as a white powder: mp 95.4–98.5°C; $[\alpha]_D^{27}$ +7.3° (*c* 0.99, pyridine) (lit. [41], mp 95–97°C; $[\alpha]_{578}^{23}$ +7.7°, pyridine, lit. [26], mp 95°C; $[\alpha]_{578}^{23}$ +8.5°, *c* 1, pyridine, lit. [24], mp 98–100°C, lit. [42], mp 97–101°C, lit. [28], mp 98–101°C, $[\alpha]_D^{24}$ +8.7°, *c* 0.80, pyridine, lit. [22], mp 103°C, $[\alpha]_D^{20}$ +7.9°, *c* 1, pyridine, lit. [43], mp 103°C, $[\alpha]_D^{20}$ +10.3°, pyridine, lit. [44], mp 104–108°C, $[\alpha]_D^{20}$ +8.2°, pyridine); R_f 0.33 in 40:10:1 $CHCl_3$–MeOH–25% aq NH_4OH; IR (KBr): 3360 (br), 2922 (s), 2854 (s), 1603 (w), 1520 (w), 1468 (s), 1323 (w), 1191 (m), 1129 (m), 1079 (br), 953 (w), 919 (w), 849 (w), 816 (w), 721 (m), 688 (m), 669 (m), 569 cm^{-1} (m); ^1H NMR (Me_2SO-d_6) [22] [5]: δ 3.55 (dd, 1 H, $J_{1,1'}$ 10.5, $J_{1,2}$ 3.5 Hz, H-1), 3.40–3.32 (m, 2 H, H-1′ and H-4), 3.09 (dd, 1 H, $J_{3,2}$ 7.2, $J_{3,4}$ 7.2 Hz, H-3), 2.76 (br, 1 H, H-2), 1.61 (br, 1 H, H-5), 1.44 (br, 1 H) and 1.24 (br, 24 H) (H-5′ and H-6–H-17), 0.86 (t, 3 H, $J_{18,17}$ 6.2 Hz, H-18); ^1H NMR (pyridine-d_5): δ 4.38 (dd, 1 H, $J_{1,1'}$ 10.6, $J_{1,2}$ 4.4 Hz, H-1), 4.29 (dd, 1 H, $J_{1',1}$ 10.6, $J_{1',2}$ 6.1 Hz, H-1′), 4.19 (ddd, 1 H, *J* 8.0, $J_{3,4}$ 7.8, *J* 2.1 Hz, H-4), 4.07 (dd, 1 H, $J_{3,4}$ 7.8, $J_{3,2}$ 6.4 Hz, H-3), 3.67 (ddd, 1 H, $J_{2,3}$ 6.4, $J_{2,1'}$ 6.1, $J_{2,1}$ 4.4 Hz, H-2), 2.29–2.19 (m, 1 H, H-5), 1.92–1.81 (m, 2 H), 1.67 (br, 1 H), and 1.25 (br, 22 H) (H-5′ and H-6–H-17), 0.87 (t, 3 H, $J_{18,17}$ 6.3 Hz, H-18); ^{13}C NMR (Me_2SO-d_6, 39.5 ppm) [22]: δ 74.2 (1 C, C-3), 73.5 (1 C, C-4), 63.2 (1 C, C-1), 56.3 (1 C, C-2), 33.7, 31.6, 29.7, 29.5, 29.4, 29.3, 29.0, 25.3, 22.4, 14.3 (1 C, C-18); ^{13}C NMR (pyridine-d_5, 124.0 ppm): δ 76.3 (1 C, C-3), 75.4 (1 C, C-4), 65.2 (1 C, C-1), 58.1 (1 C, C-2), 35.3 (1 C, C-5), 32.6, 30.9, 30.7, 30.5, 30.4, 30.1, 26.7, 23.4, 14.8 (1 C, C-18); HRMS: *m/z* 318.3019 (−1.1 mmu, $C_{18}H_{40}NO_3$, MH^+).

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[5] The ^1H NMR spectral data given for **1** do not entirely accord with those reported in ref. [35]; however, our data were undoubtedly and correctly assigned by decoupling.

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