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An Efficient Synthesis of the Natural Tetrahydrofuran Pachastrissamine Starting from D-*ribo*-Phytosphingosine

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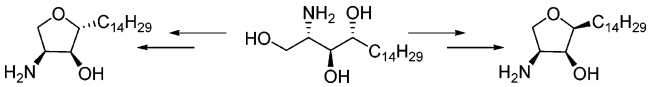

The natural product pachastrissamine, an anhydrophytosphingosine derivative isolated from various sponges and endowed with cytotoxic activity against several human carcinoma cell lines, was synthesized in three steps and with 72% overall yield from D-*ribo*-phytosphingosine.

D-*ribo*-Phytosphingosine (**1**, Figure 1) is present in large quantities in yeast and plants, as both the free sphingoid base and an integral component of (glyco)phytosphingolipids.[1] Phytosphingosine is involved in several biological processes, including heat stress response and endocytic events.[2] It is also found to be a key intermediate from which more complex metabolites are derived.[3] Apart from the phytosphingolipids, it appears that these metabolites include a number of anhydro derivatives. Several reports in recent years describe the isolation, characterization, and synthesis of a class of lipophilic pyrrolidine alkaloids termed the broussonetines,[4] which have in common with phytosphingosine (**1**) both the stereochemical sign of the three stereocenters and the number of carbon atoms, 18 in total, in the backbone of the structure. About 30 broussonetines, the general structure of which is illustrated by broussonetinine A (**2**), have been isolated, and a number of these proved to be potent inhibitors of a variety of glycosidase activities. Although the precise biosynthesis pathway toward the broussonetines has not been established unambiguously yet, labeling studies using C13-enriched glucose as the carbon source strongly suggest that at least some broussonetine pyrrolidine alkaloids are directly derived from phytosphingosine (**1**),[4] most likely through insertion of the NH in the C(5)−H bond.

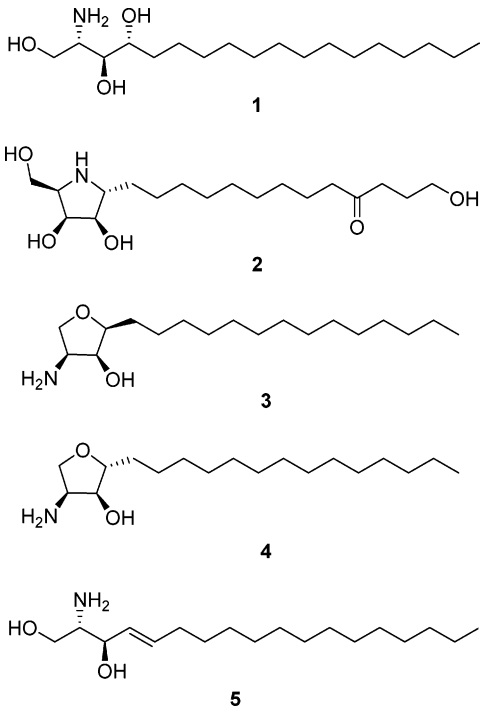

FIGURE 1. Various natural phytosphingolipids (**1**−**5**).

Very recently, another anhydrophytosphingosine analogue, pachastrissamine (jaspine B, **3**), was isolated from the marine sponges *Pachastissa sp.* and *Jaspis sp.*[5] Compound **3**, which has some interesting although as yet unspecified cytotoxic activities against several human carcinoma cell lines, highly resembles the structure of phytosphingosine (**1**). Pachastrissamine **3** has an 18-carbon backbone, it has the same functionalities and stereochemistry at C(2) and C(3) as has phytosphingosine (**1**), and it is highly likely that **3** is formed biosynthetically from **1** through intramolecular nucleophilic displacement of the alcohol functionality at C(4) by the primary alcohol at C(1), with concomitant inversion of configuration at C(4). Whether this transformation occurs in nature or not, it does represent an obvious inroad to the preparation of large quantities of **3**. This observation becomes even more true when considering the fact that phytosphingosine (**1**) can be readily obtained in highly pure form from the appropriate yeast fermentation broth and is now commercially available for a reasonable price[6] in large quantities.

We recently reported a number of facile and efficient synthetic strategies for the transformation of D-*ribo*-phytosphingosine (**1**) into D-*erythro*-sphingosine (**5**).[7] In the course of these studies, we inadvertently, but with high efficiency, synthesized 4-*epi*-pachastrissamine (**4**) as its *N*-benzoyl derivative. This transfor-

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(6) Phytosphingosine [(2*S*,3*S*,4*R*)-2-amino-1,3,4-octadecanetriol] was a gift from Degussa Cosmoferm B.V., The Netherlands. For more information see the Supporting Information.

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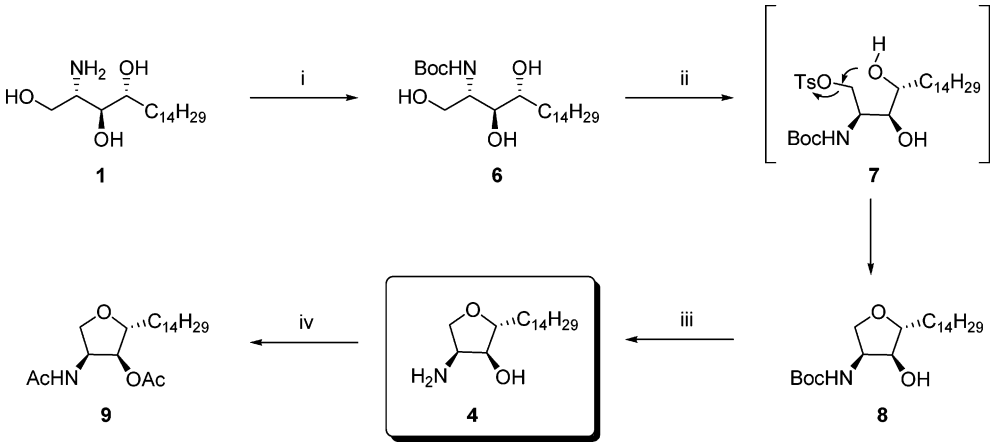
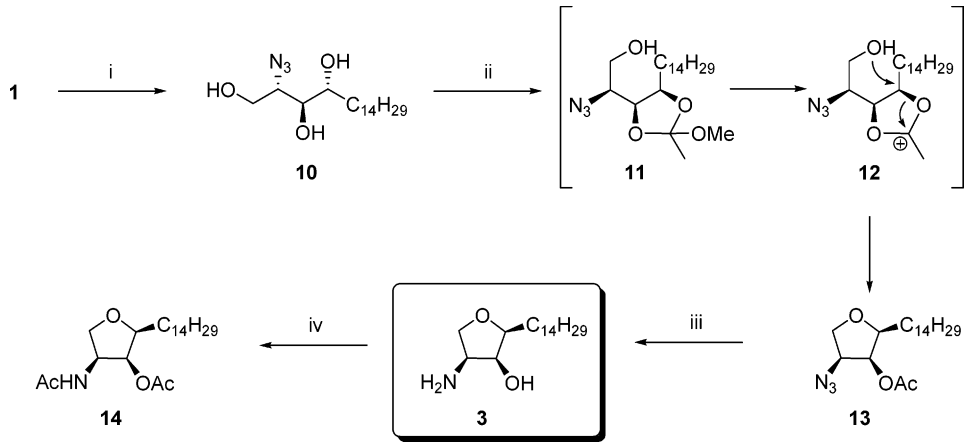
SCHEME 1. Preparation of 4-*epi*-Pachastrissamine (4)[a]



[a] Reagents and conditions: (i) Boc_2O, TEA, THF, rt, 30 min, 92%; (ii) TsCl, pyridine/DCM (1:1), rt, 16 h, 83%; (iii) TFA (3 equiv), DCM, rt, 3 h, 95%; (iv) Ac_2O, pyridine, rt, 16 h, 98%.

SCHEME 2. Preparation of Pachastrissamine (3)[a]



[a] Reagents and conditions: (i) TfN_3, Na_2CO_3, $CuSO_4$, DCM, MeOH, H_2O, rt, 16 h, 96%; (ii) TMOA (1.2 equiv), $BF_3{\cdot}OEt_2$, (0.1 equiv), DCM, 0 °C → rt, 16 h, 92%; (iii) (a) KO*t*Bu, MeOH; (b) Me_3P, toluene/H_2O (24:1), rt, 16 h, 82%; (iv) Ac_2O, pyridine, rt, 16 h, 98%.

mation was effected in 80% yield by treatment of *N*-benzoyl-**1** with *p*-toluenesulfonyl chloride in pyridine and proceeded through tosylation of the primary alcohol function, followed by tetrahydrofuran formation. By adapting this synthesis protocol and by manipulating the functional groups in **1** in a way that cyclization proceeds selectively either O(4) → C(1) or O(1) → C(4), both 4-*epi*-pachastrissamine (**4**) and pachastrissamine (**3**) can be readily prepared as follows. Phytosphingosine (**1**, see Scheme 1) was transformed into its *N*-Boc protected derivative **6** (Boc_2O, triethylamine, THF, room temperature, 30 min, 92%), which was treated with 1.1 equiv of *p*-toluenesulfonyl chloride in a 1:1 mixture of dichloromethane and pyridine. As we observed before, ring closure was readily effected, presumably via reaction intermediate **7** that will be formed after selective tosylation of the primary alcohol in **6**. *N*-Boc-4-*epi*-pachastrissamine **8** was obtained in 83% after running the reaction overnight at room temperature. Removal of the temporary Boc protective group (3 equiv of trifluoroacetic acid in dichloromethane) provided target compound **4**[8] (95%), which was peracetylated (acetic anhydride, pyridine, 16 h, 98%) for analytical purposes.

The title compound was prepared with equal efficiency via the following sequence of reactions. Treatment of phytosphingosine (**1**, see Scheme 2) with trifluoromethanesulfonyl azide (TfN_3) in the presence of cupric sulfate[9] in a mixture of methanol and water resulted in an efficient diazotransfer to produce azide **10** in 96% yield. At this stage, O(1) → C(4) cyclization was readily effected by adopting the recently reported one-pot cyclization of 1,2,*n*-triols by Borhan and co-workers[10] under Lewis acidic conditions. Accordingly, azide **10** was reacted with trimethylorthoacetate (TMOA, 1.2 equiv) and a catalytic (0.1 equiv) amount of borontrifluoride diethyl etherate in dichloromethane for 16 h at room temperature to cleanly and efficiently furnish tetrahydrofuran **13** (92% yield). In analogy

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(10) Zheng, T.; Narayan, R. S.; Schomaker, J. M.; Borhan, B. *J. Am. Chem. Soc.* **2005**, *127*, 6946−6947.

to the Borhan report, the reaction is presumed to proceed through initial ortho ester formation (**10** → **11**) followed by in situ generation of oxonium ion species **12**, which undergoes nucleophilic displacement selectively at C(4) to give acetate **13**. Base catalyzed (KOtBu, MeOH) removal of the acetate group was followed by Staudinger reduction (2 equiv of Me_3P, wet toluene, 16 h) of the azide in **13** to give pachastrissamine (**3**) in 82% yield over the two steps. For analytical purposes,[11] compound **3** was peracetylated (acetic anhydride, pyridine, 16 h, 98%).

In conclusion, this Note describes a fast and efficient synthesis of the cytotoxic natural agent, pachastrissamine (**3**), and its unnatural 4-*epi*-congener, starting from phytosphingosine (**1**). Our strategy nicely complements the two synthetic strategies reported previously in the literature,[12] which are based on the elaboration of serine based building blocks.

Experimental Section

(2*S*,3*S*,4*R*)-2-*N*-*tert*-Butoxycarbonylamino-1,3,4-octadecanetriol (6). To a stirred emulsion of d-*ribo*-phytosphingosine (10.0 g, 31.5 mmol) in THF (250 mL) were added TEA (5.3 mL, 37.8 mmol) and di-*tert*-butyl dicarbonate (7.6 g, 33.0 mmol). The mixture was stirred for 18 h at ambient temperature. The solvent was evaporated, and the residue was dissolved in EtOAc (250 mL). Cooling to 0 °C afforded **2** (12.1 g, 92%) as white crystals. TLC: 10%MeOH/DCM R_f 0.40; mp 86 °C; $[\alpha]^{22}_D$ +7.9° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}): 650, 806, 1012, 1056, 1164, 1205, 1238, 1544, 1668, 1778, 2918; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, CH_3), 1.28 (s, 24H, 12 × CH_2), 1.48 (s, 9H, *t*Bu Boc), 1.52−1.74 (m, 2H, CH_2), 2.78 (br s, 1H, OH), 3.31 (br s, 1H, OH), 3.39 (br s, 1H, OH), 3.63 (br s, 1H, H-3) (m, 1H, H-4), 3.75 (dd, 1H, H-1a, $J_{1a,1b}$ = 11.2 Hz, $J_{1a,2}$ = 5.6 Hz), 3.85 (m, 1H, H-2), 3.90 (dd, 1H, H-1b, $J_{1a,1b}$ = 11.2 Hz, $J_{1b,2}$ = 2.4 Hz), 5.34 (d, 1H, NH, $J_{2,NH}$ = 8.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1 (CH_3), 22.6, 25.9 (CH_2), 28.3 (*t*Bu Boc), 29.3, 29.6, 31.9, 32.9 (CH_2), 52.8 (C-2), 61.8 (C-1), 72.9 (C-4), 75.9 (C-3), 80.0 (Cq Boc), 156.4 (C═O Boc); ES-MS: *m*/*z* 418.4 $[M + H]^+$, 440.4 $[M + Na]^+$, 835.8 $[2M + H]^+$, 857.7 $[2M + Na]^+$; HRMS: (M + H) calcd for $C_{23}H_{47}NO_5$ + H 418.35270, found 418.35273.

1,4-Anhydro-(2*S*,3*S*,4*R*)-2-*N*-*tert*-butoxycarbonylamino-1,3,4-octadecanetriol (8). To a solution of **6** (0.517 g, 1.00 mmol) in pyridine/DCM (5 mL, 1:1 v/v) was added *p*-toluenesulfonyl chloride (0.210 g, 1.10 mmol). The mixture was stirred for 18 h at ambient temperature. MeOH (0.5 mL) and EtOAc (50 mL) were added to the mixture, and the solution was extensively washed with aqueous saturated $CuSO_4$ solution (5 × 25 mL), dried ($MgSO_4$), and concentrated. Column chromatography of the residue over silica gel with petroleum ether/EtOAc (100:0 → 60:40, v/v) gave **8** (0.331 g, 83%) as a white solid. TLC: 40% EtOAc/PE R_f 0.7; mp 79−81 °C; $[\alpha]^{22}_D$ 5.2° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}): 781, 819, 848, 862, 1006, 1041, 1168, 1245, 1334, 1467, 1525, 1689, 2846, 2916; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, 3H, CH_3), 1.25 (s, 24H, 12 × CH_2), 1.45 (s, 9H, *t*Bu Boc), 1.54 (m, 2H, CH_2), 3.03 (br s, 1H, OH-3), 3.51 (t, 1H, H-1a, *J* = 7.7 Hz), 3.70 (m, 1H, H-4), 3.91, (br t, 1H, H-3), 4.12 (m, 2H, H-1b, H-2), 5.17 (br s, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (CH_3), 22.6, 25.7, (CH_2), 28.3 (*t*Bu Boc), 29.3, 29.6, 31.8, 33.5 (CH_2), 52.8 (C-2), 70.3 (C-1), 74.6 (C-3), 79.9 (Cq Boc), 85.1 (C-4), 156.0 (C═O Boc); ES-MS: *m*/*z* 400.4 $[M + H]^+$, 422.2 $[M + Na]^+$, 799.7 $[2M + H]^+$, 821.8 $[2M + Na]^+$; HRMS: (M + H) calcd for $C_{23}H_{45}NO_4$ + H 400.34214, found 400.34238.

2-Amino-1,4-anhydro-(2*S*,3*S*,4*R*)-1,3,4-octadecanetriol (4). To a solution of **8** (0.199 g, 0.500 mmol) in DCM (2.0 mL) was added TFA (0.55 mmol, 0.063 mg, 41 μL). The mixture was stirred for 1 h at ambient temperature. The solvent was evaporated to afford **4** as a white solid (0.195 g, 95% yield). TLC: 1% NH_4OH/10% MeOH/EtOAc R_f 0.3; mp 85−87 °C; $[\alpha]^{22}_D$ +15.0° (*c* 1.0, MeOH); IR (neat, cm^{-1}): 720, 802, 846, 1055, 1103, 1130, 1154, 1173, 1211, 1444, 1468, 1502, 1606, 1668, 2847, 2919; ^{1}H NMR (300 MHz, $CDCl_3$/CD_3OD): δ 0.88 (t, 3H, CH_3), 1.25 (s, 24H, 12 × CH_2), 1.54 (m, 2H, CH_2), 3.67 (quin, 1H, H-2, $J_{1a,2}$ = 12.6 Hz, $J_{1b,2}$ = 6.4 Hz, $J_{2,3}$ = 5.4 Hz), 3.74 (m, 1H, H-4), 3.75 (dd, H-1a, $J_{1a,1b}$ = 9.8 Hz, $J_{1a,2}$ = 12.7 Hz), 4.04 (t, 1H, H-3, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 6.1 Hz), 4.13 (dd, 1H, H-1b, $J_{1a,1b}$ = 9.8 Hz, $J_{1b,2}$ = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$/CD_3OD): δ 14.0 (CH_3), 22.6, 25.6, 29.2, 29.5, 29.6, 31.8, 32.8, (CH_2), 52.0 (C-2), 68.0 (C-1), 73.1 (C-3), 84.4 (C-4); ES-MS: *m*/*z* ES-MS: *m*/*z* 302.0 $[M + H]^+$, 599.6 $[2M + H]^+$, 900.0 $[3M + H]^+$; HRMS: (M + H) calcd for $C_{18}H_{37}NO_2$ + H 300.28971, found 300.28975.

2-Acetamido-3-*O*-acetyl-1,4-anhydro-(2*S*,3*S*,4*R*)-1,3,4-octadecanetriol (9). To a solution of **4** (0.063 g, 0.15 mmol) in pyridine (2 mL) was added acetic anhydride (1.0 mL, 11 mmol). The mixture was stirred for 18 h at ambient temperature. MeOH (0.5 mL) and EtOAc (50 mL) were added, and the mixture was extensively washed with an aqueous saturated $CuSO_4$ solution (5 × 10 mL), dried ($MgSO_4$), and concentrated. Column chromatography of the residue over silica gel with toluene/EtOAc (1:0 → 4:1, v/v) gave **9** (0.056 g, 98%) as a white solid. TLC: 90% EtOAc/PE R_f 0.2; mp 72−73 °C; $[\alpha]^{22}_D$ −15.4° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}): 718, 1036, 1104, 1233, 1374, 1554, 1651, 1733, 2847, 2914; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, CH_3), 1.25 (s, 24H, 12 × CH_2), 1.58 (m, 2H, CH_2-5), 2.01 (s, 3H, CH_3, NHAc), 2.13 (s, 3H, CH_3 Ac), 3.52 (dd, 1H, H-1a, $J_{1a,1b}$ = 8.4 Hz, $J_{1a,2}$ = 8.8 Hz), 3.86 (m, 1H, H-4, $J_{3,4}$ = 2.6 Hz, $J_{4,5a}$ = 5.6 Hz, $J_{4,5b}$ = 8.0 Hz), 4.17 (dd, 1H, H-1b, $J_{1a,1b}$ = 8.4 Hz, $J_{1b,2}$ = 6.8 Hz), 4.65 (m, H-2, $J_{1a,2}$ = 8.8 Hz, $J_{1b,2}$ = 6.8 Hz, $J_{2,3}$ = 5.8 Hz, $J_{2,NH}$ = 8.4 Hz), 4.91 (dd, 1H, H-3, $J_{2,3}$ = 5.8 Hz, $J_{3,4}$ = 2.6 Hz), 5.72 (d, 1H, NH, $J_{2,NH}$ = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (CH_3), 20.9 (CH_3 Ac), 23.1 (CH_3 NHAc), 22.6, 25.4, 25.9, 29.3, 29.4, 29.5, 29.6, 31.8, 33.4 (CH_2), 49.8 (C-2), 69.7 (C-1), 76.6 (C-3), 84.0 (C-4), 169.8 (2 × C═O Ac); ES-MS: *m*/*z* ES-MS: *m*/*z* 384.2 $[M + H]^+$, 406. 3 $[M + Na]^+$, 767.8 $[2M + H]^+$, 789.8 $[2M + Na]^+$; HRMS: (M + Na) calcd for $C_{22}H_{41}NO_4Na$ 406.29278, found 406.29329.

(2*S*,3*S*,4*R*)-2-Azido-1,3,4-octadecanetriol (10). To a stirred suspension of d-*ribo*-phytosphingosine (9.80 g, 30.9 mmol) in MeOH (300 mL) was added a solution of K_2CO_3 (6.4 g, 60 mmol) and $CuSO_4$ (47 mg, 0.29 mmol) in water (100 mL) and a solution of triflyl azide in DCM (∼60 mmol, 100 mL). Stirring was continued for 18 h, after which the white crystals were collected, washed with aqueous MeOH (2 × 100 mL, 1:1, v/v), and dried to afford **10** (10.20 g, 96%). TLC: 10% MeOH/DCM R_f 0.4; $[\alpha]^{22}_D$ +15.1° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}): 657, 819, 918, 1014, 1056, 1209, 1240, 1278, 1299, 1417, 1774, 2102; mp 97−98 °C; ^{1}H NMR (400 MHz, CD_3OD): δ 0.89 (t, 3H, CH_3), 1.28 (s, 24H, 12 × CH_2), 1.55−1.67 (m, 2H, CH_2), 3.52 (m, 2H, H-3, H-4), 3.58 (ddd, 1H, H-2, $J_{1b,2}$ = 4.0 Hz, $J_{2,3}$ = 6.0 Hz, $J_{1a,2}$ = 10.0 Hz), 3.75 (dd, 1H, H-1a, $J_{1a,1b}$ = 14.5 Hz, $J_{1a,2}$ = 10.0 Hz), 3.91 (dd, 1H, H-1b, $J_{1b,2}$ = 4.20 Hz, $J_{1a,1b}$ = 14.5 Hz); ^{13}C NMR (100 MHz, CD_3OD): δ 14.4 (CH_3), 23.7, 26.7, 30.4, 30.7, 30.8, 33.0, 33.8 (CH_2), 62.4 (C-1), 66.6 (C-2), 72.8, 75.9 (C-3/C-4); ES-MS: *m*/*z* 344.2 $[M + H]^+$, 366.2 $[M + Na]^+$, 709.8 $[2M + Na]^+$; HRMS: (M + H) calcd for $C_{18}H_{37}N_3O_3$ + H 344.29077, found 344.31624.

1,4-Anhydro-(2*S*,3*S*,4*S*)-2-azido-1,3,4-octadecanetriol (13). To a solution of **10** (0.343 g, 1.00 mmol) in DCM (15 mL) were successively added trimethyl orthoacetate (1.20 mmol, 0.144 g, 0.152 mL) and BF_3·OEt_2 (0.028 g, 25 μL). After 16 h, the reaction was quenched by the addition of acetone (0.5 mL) and the volatiles were evaporated. Column chromatography of the residue over silica gel with petroleum ether/EtOAc (10:0 → 9:1, v/v) gave **13** (0.338

(11) The spectral and analytical data of compounds **3** and **14** are in complete accordance with the reported data; see refs 5b and 12a.

(12) (a) Sudhakar, N.; Ravi Kumar, A.; Prabhakar, A.; Jagadeesh, B.; Venkateswara Rao, B. *Tetrahedron Lett.* **2005**, *46*, 328−327. (b) Bhaket, P.; Morris, K.; Stauffer, C. S.; Datta, A. *Org. Lett.* **2005**, *7*, 875−876.

g, 92%) as a white solid. TLC: 15% EtOAc/PE R_f 0.5; mp 43−44 °C; $[\alpha]^{22}_D$ +8.4° (*c* 1.0, $CHCl_3$); IR (neat, cm^{-1}): 615, 663, 715, 931, 1051, 1085, 1234, 1344, 1471, 1735, 2133; ^1H NMR (600 MHz, $CDCl_3$): δ 0.87 (t, 3H, CH_3), 1.25 (s, 23H, CH_2), 1.41 (m, 1H, CH-6), 1.51 (m, 1H, CH-5a), 1.62 (m, 1H, CH-5b), 2.18 (s, 3H, CH_3 Ac), 3.83 (dd, 1H, H-1a, $J_{1a,1b}$ = 9.1 Hz, $J_{1a,2}$ = 6.6 Hz), 3.92 (quin, 1H, H-4, $J_{3,4}$ = 4.9 Hz, $J_{4,5a}$ = 5.1 Hz, $J_{4,5a}$ = 7.8 Hz), 3.99 (dd, 1H, H-1b, $J_{1a,1b}$ = 9.1 Hz, $J_{1b,2}$ = 7.4 Hz), 4.09 (app. ddd, H-2, $J_{1a,2}$ = 6.6 Hz, $J_{1b,2}$ = 7.3 Hz, $J_{2,3}$ = 5.4 Hz), 5.41 (app. dd, 1H, H-3, $J_{2,3}$ = 4.5 Hz, $J_{3,4}$ = 4.9 Hz); ^{13}C NMR (150 MHz, $CDCl_3$): δ 14.0 (CH_3), 20.5 (CH_3 Ac), 22.6, 25.8, 29.0, 29.3, 29.4, 29.5, 29.6, 29.7, 31.8 (CH_2), 61.4 (C-2), 68.6 (C-1), 73.7 (C-4), 80.4 (C-3), 170.2 (C═O Ac); ES-MS: *m*/*z* 368.3 $[M + H]^+$, 390.3 $[M + Na]^+$, 735.5 $[2M + H]^+$; HRMS: (M + H) calcd for $C_{20}H_{37}N_3O_3$ + H 368.29077, found 368.29051.

2-Amino-1,4-anhydro-(2*S*,3*S*,4*S*)-1,3,4-octadecanetriol (Jaspine B, 3). To a solution of **13** (0.073 g, 0.20 mmol) in MeOH (1.0 mL) was added a catalytic amount of KO*t*Bu. After 1 h, the mixture was neutralized by the addition of Amberlite IR-120 H^+, filtrated, and concentrated. The residue was dissolved in aqueous THF (10%, 1.0 mL), and trimethyl phosphine (0.40 mL, 0.40 mmol) was added. The mixture was stirred for 4 h at ambient temperature, after which the solvent was evaporated. Column chromatography of the residue over silica gel with petroleum ether/EtOAc (1:1, v/v), MeOH/DCM (1:9, v/v), and MeOH/EtOAc/NH_4OH (10:89:1, v/v/v) gave **3** (0.049 g, 82%) as an off-white solid. TLC: 50% EtOAc/petroleum ether R_f 0.0; mp 89−91 °C; $[\alpha]^{22}_D$ +4.8° (*c* 1.0, MeOH); IR (neat, cm^{-1}): 719, 798, 831, 852, 877, 960, 987, 1031, 1070, 1151, 1353, 1456, 1471, 1583, 1631, 1654, 2848, 2916; ^1H NMR (600 MHz, $CDCl_3$): δ 0.88 (t, 3H, CH_3), 1.25 (s, 24H, 12 × CH_2), 1.65 (m, 2H, CH_2-5), 2.66 (br s, 3H, NH_2, OH), 3.53 (dd, 1H, H-1a, $J_{1a,1b}$ = 8.5 Hz, $J_{1a,2}$ = 7.3 Hz), 3.59 (br m, 1H, H-2), 3.75 (ddd, 1H, H-4, $J_{3,4}$ = 4.4 Hz, $J_{4,5a}$ = 6.3 Hz, $J_{4,5b}$ = 7.5 Hz), 3.87 (dd, H-3, $J_{2,3}$ = 4.9 Hz, $J_{3,4}$ = 3.4 Hz), 3.92 (dd, 1H, H-1b, $J_{1a,1b}$ = 8.5 Hz, $J_{1b,2}$ = 7.5 Hz); ^{13}C NMR (150 MHz, $CDCl_3$/CD_3OD): δ 14.0 (CH_3), 22.5, 26.0, 29.2, 29.3, 29.4, 29.5, 29.6, 29.7, 31.8 (CH_2), 54.3 (C-2), 71.7 (C-3), 71.8 (C-1), 82.9 (C-4); ES-MS: *m*/*z* 300.0 $[M + H]^+$, 599.6 $[2M + H]^+$, 899.0 $[3M + H]^+$; HRMS: (M + H) calcd for $C_{18}H_{37}NO_2$ + H 300.28971, found 300.29001.

2-Acetamido-3-*O*-acetyl-1,4-anhydro-(2*S*,3*S*,4*S*)-1,3,4-octadecanetriol (14). To a solution of **3** (0.062 g, 0.21 mmol) in pyridine (2 mL) was added acetic anhydride (1.0 mL, 11 mmol). The mixture was stirred for 18 h at ambient temperature. MeOH (0.5 mL) and EtOAc (50 mL) were added, and the mixture was extensively washed with an aqueous saturated $CuSO_4$ solution (5 × 10 mL), dried ($MgSO_4$), and concentrated. Column chromatography of the residue over silica gel with toluene/EtOAc (1:0 → 4:1, v/v) gave **14** (0.078 g, 98%) as a white solid. TLC: 90% EtOAc/PE R_f 0.3; mp 95−98 °C; $[\alpha]^{22}_D$ −22.6° (*c* 1.0, $CDCl_3$); IR (neat, cm^{-1}): 719, 947, 1051, 1082, 1234, 1375, 1469, 1550, 1652, 1739, 2848, 2916; ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, CH_3), 1.25 (s, 24H, 12 × CH_2), 1.51 (m, 2H, CH_2-5), 1.98 (s, 3H, CH_3 Ac), 2.16 (s, 3H, CH_3 Ac), 3.59 (dd, 1H, H-1a, $J_{1a,1b}$ = 8.8 Hz, $J_{1a,2}$ = 7.5 Hz), 3.90 (m, 1H, H-4, $J_{3,4}$ = 3.4 Hz), 4.07 (dd, 1H, H-1b, $J_{1a,1b}$ = 8.5 Hz, $J_{1b,2}$ = 8.2 Hz), 4.81 (ddd, 1H, H-2, $J_{1a,2}$ = 8.0 Hz, $J_{1b,2}$ = 8.2 Hz, $J_{2,3}$ = 5.3 Hz, $J_{2,NH}$ = 7.9 Hz), 5.38 (dd, H-3, $J_{2,3}$ = 5.4 Hz, $J_{3,4}$ = 3.4 Hz), 5.57 (d, 1H, NH, $J_{2,NH}$ = 7.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (CH_3), 20.6 (CH_3 Ac), 22.5 (CH_2), 23.0 (CH_3 Ac), 25.9, 29.2, 29.3, 29.4, 29.5, 29.6, 29.7, 31.8 (CH_2), 51.2 (C-2), 69.7 (C-1), 71.4 (C-3), 81.1 (C-4), 169.8 (2 × C═O Ac); HRMS: (M + H) calcd for $C_{22}H_{41}NO_4$ + H 384.31084, found 384.31136.

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Supporting Information Available: ^1H, $^1H-^1H$ COSY, and ^{13}C NMR spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

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