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Stereoselective Synthesis of Cytotoxic Anhydrophytosphingosine Pachastrissamine [Jaspine B]

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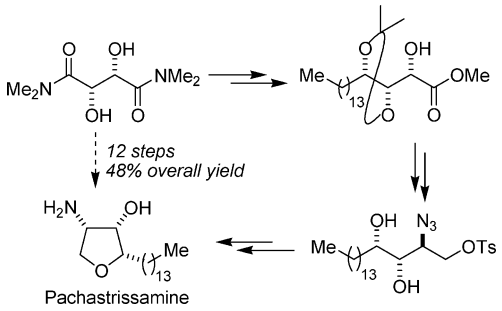

A practical stereoselective synthesis of cytotoxic anhydrophytosphingosine pachastrissamine (jaspine B) was achieved in 48% overall yield from D-(−)-tartaric acid. Key features of the sequence include the diastereoselective formation of a tetrol with three contiguous chiral centers, which was further elaborated to pachastrissamine. The synthetic route is operationally simple, diastereoselective and is amenable for the synthesis of a number of analogues of pachastrissamine.

Tetrahydrofuran backbone is ubiquitous heterocyclic unit found in a number of biologically active natural products.[1] Recently, Kuroda et al. isolated pachastrissamine **1**, a cytotoxic anhydrophytosphingosine comprising a tetrahydrofuran backbone from the Okinawan marine sponge *Pachastrissa* sp (Figure 1).[2] Subsequently, Ledroit et al. isolated the same compound from marine sponge *Jaspis* sp. (hence the name jaspine B) and another natural product jaspine A **2**.[3] **1** was found to be marginally active against the A5409 human lung carcinoma cell line and at submicromolar level against HT29, MEL28, and P388 cancer cell lines. Pachastrissamine possess three contiguous stereogenic centers and is structurally similar to the open chain sphingolipid D-*ribo*-phytosphingosine **3**. It might be very likely that **3** is the biosynthetic precursor to **1** and **2**. Interestingly, guggultetrol **4**, a naturally occurring lipid isolated from the gum-resin of the tree *Commiphoru mukul (guggulu*), known in Ayurveda, the Indian traditional system of medicine, for the treatment of arthritis, inflammation, obesity, and disorders of lipid metabolism closely resembles the sphigolipid phytosphingosine **3**.[4] The tri-substituted tetrahydrofuran structural framework and the proven bioactivity of **1** prompted extensive synthetic studies, resulting in a handful of approaches reported very recently.[5] Many of these syntheses relied on employing either carbohydrates or serine as the chiral source. For example Ramana et al.[5a] utilized D-glucose, whereas Du et al.[5c] employed D-xylose as the source of chirality in their multistep synthesis of **1**. Research groups of Datta[5d] and Rao[5e] have independently disclosed the synthesis of **1** from L-serine. Synthesis of **1** from phytosphingosine **3** has also been reported by Lee et al.[6a] and by van der Berg et al.[6b] In continuation of our successful efforts in the stereoslective synthesis of bioactive oxygenated natural products from chiral pool tartaric acid,[7] herein we report a facile stereoselective synthesis of pachastrissamine.

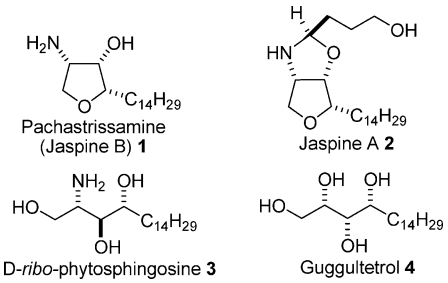

FIGURE 1. Bio-active anhydrophytosphingosine and sphingolipids.

As shown in retrosynthesis (Scheme 1), we envisaged the formation of **1**, by reduction of the azide in **14**, synthesis of which was anticipated *via* the intramolecular Williamson etherification of the tosylate **13**. The tosylate **13** can be obtained from the 3,4-protected tetrol **9**. γ-Hydroxybutyramide **7**, derived from the dimethylamide **5** obtained from tartaric acid, was identified as the appropriate precursor for the synthesis of **9**.

The synthetic sequence commenced with the controlled addition of *n*-tetradecylmagnesium bromide (1.5 eq) to the *bis*-dimethylamide **5**, derived from D-(−)-tartaric acid,[8] affording the keto amide **6** in 86% yield.[9] Stereoselective reduction of the ketone in **6** with $NaBH_4$ in presence of $CeCl_3 \cdot 7H_2O$ furnished

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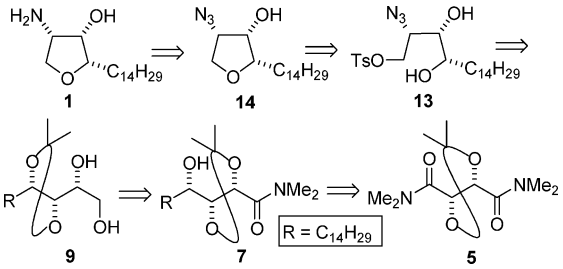
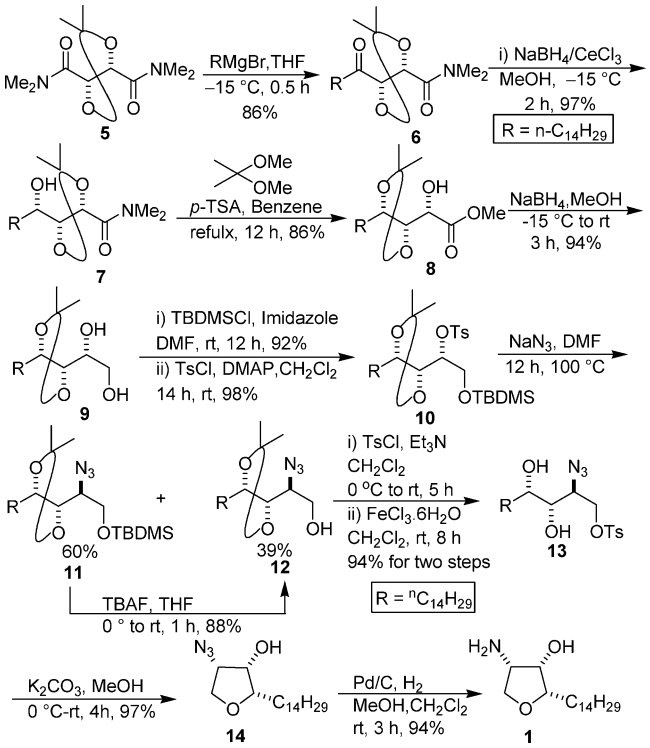
SCHEME 1. Retrosynthesis for Pachastrissamine (Jaspine B)



a mixture of diastereomeric alcohols (*dr* ≈ 95:5 by NMR,[10] **7** being the major isomer) in 97% yield. Reaction of this mixture of alcohols with excess 2,2-dimethoxypropane in presence of *p*-toluenesulphonic acid in benzene followed by column purification resulted in pure α-hydroxy ester **8** in 86% yield.[11] Reduction of the ester **8** with $NaBH_4$ produced the diol **9** in 94% yield. Primary hydroxy group in **9** was protected as the *tert*-butyldimethylsilylether in 92% yield, which on subsequent tosylation furnished the tosylate **10** in 98% yield. S_N2 displacement of the tosylate in **10** with sodium azide furnished the azide **11** in 60% yield with desilylated azidohydrin **12** in 39%. Reaction of **11** with *tetra*-butylammonium fluoride (TBAF) produced the azidohydrin **12** in 88% yield. Primary alcohol in **12** was converted to the tosylate, which on subsequent reaction with $FeCl_3{\cdot}6H_2O$[12] yielded the dihydroxy azido tosylate **13** in 94% yield for two steps. Reaction of **13** with K_2CO_3 in MeOH afforded the tetrahydrofuran **14** in 97% yield. Hydrogenation of **14** with Pd/C gave pachastrissamine **1** in 94% yield, the spectral and physical data of which are in complete agreement with that reported in literature[2,6a] (Scheme 2).

In summary, a facile and efficient stereoselective synthesis of natural phytosphingosine pachastrissamine (jaspine B) was achieved from D-(−)-tartaric acid. In the present sequence, pachastrissamine was obtained in 48% overall yield from the *bis*-dimethylamide derived from tartaric acid. The synthetic route

SCHEME 2. Stereoselective Synthesis of Pachastrissamine



is operationally simple, highly diastereoselective, and applicable for the access of different analogues of pachastrissamine.

Experimental Section

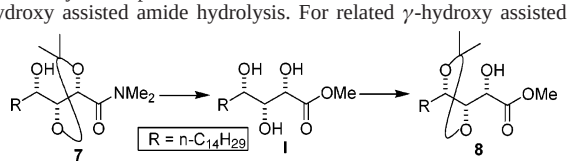
(4*S*,5*S*)-*N*,*N*,2,2-Tetramethyl-5-pentadecanoyl-1,3-dioxolane-4-carboxamide (6). In an oven-dried two-neck 100 mL, round-bottom flask equipped with a magnetic stir bar, rubber septum, and argon inlet was placed **5** (1.71 g, 7.0 mmol) dissolved in THF (20 mL). The solution was cooled to −15 °C and tetradecylmagnesium bromide (10.5 mmol, 21 mL of 0.5 M solution in THF) was added slowly and stirred for 0.5 h at the same temperature. After the reaction was complete (indicated by TLC), it was cautiously quenched by addition of ice cold solution of saturated NH_4Cl (20 mL). The reaction mixture was poured into water (25 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The residue obtained after removal of the solvent was purified by silica gel column chromatography to yield **6** (2.4 g, 86%) as white solid: R_f 0.6 (1:1 EtOAc:petroleum ether); mp 45−46 °C; $[\alpha]_D$ −14 (*c* 2, $CHCl_3$); IR ($CHCl_3$): 2925, 1719, 1659, 1373, 1155, 864 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.12 (d, 1H, J = 6 Hz), 4.78 (d, 1H, J = 6 Hz), 3.13 (s, 3H), 2.97 (s, 3H), 2.72−2.53 (m, 2H), 1.59−1.55 (m, 2H), 1.41 (s, 6H), 1.23 (brs, 24H), 0.86 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.5, 168.1, 112.0, 82.1, 74.9, 39.5, 37.0, 36.0, 31.9, 29.6, 29.5, 29.4, 29.3, 29.1, 26.3, 26.0, 23.0, 22.6, 14.1; Analysis calcd for $C_{23}H_{43}NO_4$: C 69.48; H 10.90; N 3.52. Found: C 69.28; H 10.67; N 3.67.

(4*S*,5*R*)-*N*,*N*,2,2-Tetramethyl-5-((*S*)-1-hydroxylpentadecyl)-1,3-dioxolane-4-carboxamide (7). To a solution of **6** (2.0 g, 5 mmol) in methanol (25 mL) cooled to −15 °C was added $CeCl_3{\cdot}7H_2O$ (3.72 g, 10 mmol), and the mixture was stirred for 15 min. $NaBH_4$ (0.38 g, 10 mmol) was then added portion wise at −15 °C and stirred at the same temperature for 2 h. After the reaction was complete (TLC), it was quenched by the addition of water (1 mL). Most of the volatiles were removed under reduced pressure. The solid thus obtained was triturated with diethyl ether (10 mL). The suspension was filtered through a short pad of Celite, and the Celite

(9) Formation of minor amount (4%) of diketone resulting from the addition of tetradecylmagnesium bromide to both amide groups is observed. For an optimized synthesis of γ-oxo-amides by controlled addition of Grignard reagents to **5**, see: Prasad, K. R.; Chamdrakumar, A. *Tetrahedron* **2007**, *63*, 1798.

(10) Diastereomeric ratio of the product alcohol was estimated within detectable limits by ^1H NMR. Reduction with other reducing agents such as $NaBH_4$, K-selectride produced alcohols with varied selectivity. The alcohols were inseparable at this stage. Formation of the major diastereomer can be attributed to the addition of hydride either by a Cram/Felkin open chain model or by a β-chelation, similar to that reported by Chikasita et al. Chikashita, H.; Nikaya, T.; Uemura, H.; Itoh, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2121.

(11) The reaction proceeds through the intermediacy of trihydroxy ester **I**, formed by the deprotection of the acetonide in alcohol **7**, followed by γ-hydroxy assisted amide hydrolysis. For related γ-hydroxy assisted hydrolysis of butyramides (a) Martin, R. B.; Hedrick, R.; Parcell, A. *J. Org. Chem.* **1964**, *29*, 158. (b) Hauser, C. R.; Adams, T. C., Jr. *J. Org. Chem.* **1977**, *42*, 3029. (c) Vedejs, E.; Kruger, A. W. *J. Org. Chem.* **1999**, *64*, 4790.



(12) For $FeCl_3$ mediated deprotection of acetals see: (a) Sen, S. E.; Roach, S. L.; Boggs, J. K.; Ewing, G. J.; Magrath, J. *J. Org. Chem.* **1997**, *62*, 6684. (b) Prasad, K. R.; Chandrakumar, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1897. (c) Reference 7.

pad was washed with diethyl ether (25 mL). The ethereal layers were combined and evaporation of solvent followed by silica gel column chromatography of the resultant crude residue afforded the alcohol **7** (1.94 g, 97%) (*dr* ~95 : 5) as a white solid: R_f 0.4 (1:1 EtOAc:petroleum ether); mp 42−44 °C; $[\alpha]_D$ +10 (*c* 1.5, $CHCl_3$); IR ($CHCl_3$): 3447, 2924, 2854, 1653, 1380, 1069 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.60−4.53 (m, 2H), 3.66−3.58 (m, 1H), 3.15 (s, 3H), 2.97 (s, 3H), 2.05 (d, 1H, J = 9.3 Hz), 1.54−1.26 (m, 26H), 1.45 (s, 3H), 1.39 (s, 3H), 0.88 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 110.1, 80.2, 74.2, 70.0, 37.0, 35.7, 34.8, 31.9, 29.7, 29.6, 29.5, 29.3, 26.8, 26.1, 25.8, 22.7, 14.1; Analysis calcd for $C_{23}H_{45}NO_4$: C 69.13; H 11.35; N 3.51. Found: C 69.00; H 11.21; N 3.49.

(*S*)-methyl 2-hydroxy-2-((4*S*,5*S*)-2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)acetate (8). To a solution of **7** (0.9 g, 2.3 mmol) in benzene (10 mL), *p*-toluenesulphonic acid (0.64 g, 3.38 mmol) and 2,2-dimethoxypropane (0.5 mL, 4.5 mmol) were added and refluxed for 12 h. The reaction mixture was cooled to room temperature, and K_2CO_3 (0.75 g) was added. After stirring for 15 min, it was filtered through a short pad of Celite, and the Celite pad was washed with diethyl ether (20 mL). Evaporation of solvent followed by silica gel column chromatography of the resultant residue gave **8** (0.76 g, 86%) as a colorless oil: R_f 0.6 (3:7 EtOAc: petroleum ether); $[\alpha]_D$ −29 (*c* 1.2, $CHCl_3$); IR (neat): 3508, 2925, 1750, 1466, 1131, 899 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.15−4.07 (m, 2H), 3.88−3.80 (m, 1H), 3.84 (s, 3H), 3.00 (d, 1H, J = 9.0 Hz), 1.68−1.18 (m, 26H), 1.40 (s, 6H), 0.88 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 109.1, 81.4, 76.4, 68.8, 52.7, 32.6, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 27.0, 26.5, 26.0, 22.6, 14.1; HRMS for $C_{22}H_{42}O_5$ + Na calcd: 409.2930; found: 409.2920.

((*R*)-1-((4*S*,5*S*)-2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)-ethane-1,2-diol (9). In a single-neck round-bottom flask equipped with magnetic stir bar and guard tube was placed a solution of **8** (0.68 g, 1.75 mmol) in MeOH (10 mL). $NaBH_4$ (0.13 g, 3.5 mmol) was then introduced portion wise at 0 °C. The reaction mixture was slowly warmed up to room temperature and stirred for 3 h at the same temperature. After the reaction was complete (TLC), most of the methanol was removed under reduced pressure and water (20 mL) was added to the reaction mixture and extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the crude residue furnished **9** (0.59 g, 94%) as a white solid: R_f 0.3 (1:1 EtOAc: petroleum ether); mp 48−49 °C; $[\alpha]_D$ −31.2 (*c* 0.8, $CHCl_3$); IR ($CHCl_3$): 3414, 2924, 2854, 1467, 1216, 1038, 689 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.07−4.00 (m, 1H), 3.70−3.63 (m, 4H), 2.66 (brs, 1H), 2.48 (brs, 1H), 1.58−1.19 (m, 26H), 1.41 (s, 6H), 0.88 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.1, 82.0, 77.2, 69.5, 65.3, 32.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 27.4, 26.8, 26.0, 22.7, 14.1; Analysis calcd for $C_{21}H_{42}O_4$: C 70.34; H 11.81. Found: C 69.98; H 11.56.

((*R*)-1-((4*R*,5*S*)-2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)-2-*O*-*tert*-butyldimethylsilyl-1-*O*-*p*-toluenesulphonyl-ethane-1,2-diol (10). To a solution of **9** (0.55 g, 1.55 mmol) in DMF (2 mL) was added imidazole (0.16 g, 2.32 mmol) and TBDMSCl (0.36 g, 2.32 mmol) at room temperature and stirred for 12 h. The reaction mixture was then poured into water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent followed by silica gel column chromatography of the crude residue afforded the silyl ether (0.68 g, 92%) as a colorless oil: R_f 0.6 (1:9 EtOAc/ petroleum ether); $[\alpha]_D$ −18.6 (*c* 1.5, $CHCl_3$); IR (neat): 3495, 2927, 1464, 1256, 1109, 837, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.04−3.97 (m, 1H), 3.74−3.55 (m, 4H), 2.36 (brs, 1H), 1.56−1.25 (m, 26H), 1.47 (s, 6H), 0.88 (t, 3H, J = 6.9 Hz), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.6, 80.2, 77.0, 70.1, 64.6, 33.0, 31.9, 29.7, 29.6, 29.5, 29.4, 27.4, 26.9, 26.0,25.8, 22.7, 18.2, 14.1, −5.4, −5.5; HRMS for $C_{27}H_{56}O_4Si$ + Na calcd: 495.3846; found: 495.3860.

To a solution of the silyl ether obtained above (0.59 g, 1.3 mmol) in CH_2Cl_2 (10 mL) was added DMAP (0.31 g, 2.5 mmol) and *p*-toluenesulphonyl chloride (0.36 g, 1.9 mmol) at room temperature, and the mixture was stirred for 4 h at the same temperature. It was then poured into water (10 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine (15 mL) and dried (Na_2SO_4). Evaporation of solvent followed by silica gel column chromatography of the crude residue afforded **10** (0.80 g, 98%) as a colorless oil: R_f 0.7 (1:9 EtOAc: petroleum ether); $[\alpha]_D$ −16.6 (*c* 0.6, $CHCl_3$); IR (neat): 2926, 2855, 1371, 1096, 835 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, 2H, J = 7.8 Hz), 7.30 (d, 2H, J = 7.8 Hz), 4.40−4.35 (m, 1H), 3.85−3.67 (m, 4H), 2.41 (s, 3H), 1.59−1.20 (m, 26H), 1.29 (s, 3H), 1.16 (s, 3H), 0.86 (t, 3H, J = 6.9 Hz), 0.82 (s, 9H), 0.00 (s, 3H), −0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 133.9, 129.7, 127.9, 108.6, 79.4, 78.2, 76.3, 61.7, 32.6, 31.9, 29.7, 29.6, 29.5, 29.4, 27.3, 26.4, 25.9, 25.7, 22.7, 21.6, 18.2, 14.1, −5.6; HRMS for $C_{34}H_{62}O_6SSi$ + Na calcd: 649.3934; found: 649.3962.

((*S*)-2-Azido-2-((4*S*,5*S*)-2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)ethoxy)(*tert*-butyl)dimethylsilane (11). To a solution of **10** (0.44 g, 0.7 mmol) in DMF (10 mL) was added NaN_3 (0.09 g, 1.4 mmol) and was heated to 100 °C and stirred at the same temperature for 12 h (CAUTION: Care should be taken when manipulating sodium azide due to its toxicity and explosive nature). The reaction mixture was cooled to room temperature and poured into water (20 mL). It was then extracted with diethyl ether (3 × 10 mL), and the combined organic layers was washed with brine (15 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the crude residue afforded **11** (0.21 g, 60%) as a colorless oil and **12** (0.10 g, 39%). Compound **11**: R_f 0.7 (1:9 EtOAc: petroleum ether); $[\alpha]_D$ −9.4 (*c* 1.8, $CHCl_3$); IR (neat): 2927, 2855, 2099, 1464, 1256, 1101, 838, 777 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.01−3.93 (m, 2H), 3.73 (dd, 1H, J = 10.5, 7.2 Hz), 3.57 (t, 1H, J = 7.2 Hz), 3.49−3.43 (m, 1H), 1.73−1.26 (m, 26H), 1.26 (s, 6H), 0.92 (s, 9H), 0.88 (t, 3H, J = 6.9 Hz), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.0, 79.8, 78.7, 65.3, 64.3, 34.0, 31.9, 29.7, 29.6, 29.5, 29.4, 27.4, 27.0, 26.1, 25.8, 22.7, 18.2, 14.1, −5.4; HRMS for $C_{27}H_{55}N_3O_3Si$ + Na calcd: 520.3910; found: 520.3911.

(*S*)-2-Azido-2-((4*S*,5*S*)-2,2-dimethyl-5-tetradecyl-1,3-dioxolan-4-yl)ethanol (12). To a solution of **11** (0.20 g, 0.4 mmol) in THF (2.5 mL) was added TBAF (0.8 mL of 1 M solution in THF, 0.8 mmol) at 0 °C and stirred at room temperature for 1 h. It was then poured into water (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the crude residue afforded **12** (0.14 g, 88%) as a colorless oil: R_f 0.4 (2:8 EtOAc: petroleum ether); $[\alpha]_D$ −15 (*c* 0.4, $CHCl_3$); IR (neat): 3446, 2925, 2854, 2103, 1219, 1070, 877 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.98−3.96 (m, 1H), 3.89−3.87 (m, 1H), 3.77−3.74 (m, 1H), 3.67 (t, 1H, J = 7.2 Hz), 3.57−3.54 (m, 1H), 2.25 (t, 1H, J = 6.0 Hz), 1.67−1.26 (m, 26H), 1.40 (s, 6H), 0.88 (t, 3H, J = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.3, 80.1, 79.6, 64.8, 63.1, 33.9, 31.9, 29.7, 29.6, 29.5, 29.4, 27.4, 26.9, 26.1, 22.7, 14.1; HRMS for $C_{21}H_{41}N_3O_3$ + Na calcd: 406.3046; found: 406.3027.

(2*S*,3*S*,4*S*)-2-Azido-3,4-dihydroxyoctadecyl-4-methylbenzenesulfonate (13). To a solution of **12** (0.20 g, 0.5 mmol) in CH_2Cl_2 (2 mL) was added Et_3N (0.2 mL) and *p*-toluenesulphonyl chloride (0.15 g, 0.8 mmol) at 0 °C and stirred at room temperature for 4 h. The reaction mixture was quenched by addition of water (10 mL), extracted with diethyl ether (3 × 10 mL) and dried (Na_2SO_4). Residue obtained after evaporation of the solvent was used as such without further purification in the next step.

To a solution of the crude tosylate (obtained above) in CH_2Cl_2 (10 mL) was added $FeCl_3 \cdot 6H_2O$ (0.49 g, 1.8 mmol) at room

temperature. The resulting yellow colored suspension was stirred for 8 h at room temperature. After the reaction was complete (monitored by TLC), it was quenched by the addition of saturated solution of $NaHCO_3$. It was then extracted with EtOAc (3 × 10 mL), and the combined organic layers were washed with brine (15 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the residue afforded **13** (0.24 g, 94% for two steps) as a white solid: R_f 0.5 (4:6 EtOAc:petroleum ether); mp 63−64 °C; $[\alpha]_D$ +15 (*c* 0.4, $CHCl_3$); IR ($CHCl_3$): 3374, 2920, 2101, 1467, 1190, 1178, 814 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, 2H, J = 8.4 Hz), 7.37 (d, 2H, J = 8.4 Hz), 4.44 (dd, 1H, J = 11.1, 3.0 Hz), 4.31−4.19 (m, 1H), 3.78−3.73 (m, 2H), 3.37 (m, 1H), 2.46 (s, 3H), 1.59−1.19 (m, 26H), 0.88 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 132.4, 130.0, 128.0, 71.6, 70.0, 69.8, 61.6, 34.0, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 25.6, 22.7, 21.7, 14.1; Analysis calcd for $C_{25}H_{43}N_3O_5S$: C 60.33; H 8.71; N 8.44; S 6.44. Found: C 60.29; H 8.66; N 8.49; S 6.68.

(2*S*,3*S*,4*S*)-4-Azido-2-tetradecyl-tetrahydrofuran-3-ol (14). To a solution of **13** (0.12 g, 0.24 mmol) in MeOH (2 mL) was added K_2CO_3 (0.07 g, 0.50 mmol) at 0 °C and allowed to warm to room temperature and stirred for 4 h. The volatiles were removed under reduced pressure and the solid thus obtained was triturated with diethyl ether (10 mL) and filtered through a short pad of Celite. The Celite pad was washed with diethyl ether (20 mL). Evaporation of solvent followed by silica gel column chromatography of the crude residue obtained gave **14** (0.08 g, 97%) as a white solid: R_f 0.6 (1:6 EtOAc:petroleum ether); mp 99−100 °C (lit[6a] mp 99.4−100.1 °C); $[\alpha]_D$ +17 (*c* 1.0, $CHCl_3$), lit[6a] $[\alpha]_D$ +16.7 (*c* 1.0, CHCl3); IR ($CHCl_3$): 3333, 2917, 2849, 2104, 1469, 1019, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.21−4.19 (m, 1H), 4.14−4.01 (m, 1H), 3.97 (dd, 1H, J = 9.2, 7.6 Hz), 3.85 (dd, 1H, J = 9.2, 6.8 Hz), 3.76 (m, 1H), 2.10 (brs, 1H), 1.66−1.59 (m, 2H), 1.43−1.25 (m, 24H), 0.88 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 82.1, 72.5, 68.5, 63.7, 31.9, 29.7, 29.66, 29.6, 29.5, 29.4, 28.9, 26.1, 22.7, 14.1; Analysis calcd for $C_{18}H_{35}N_3O_2$: C 66.42; H 10.84; N 12.91. Found: C 66.53; H 10.69; N 12.79.

Pachastrissamine (Jaspine B) (1). To a solution of **14** (32 mg, 0.1 mmol) in MeOH (1 mL) and CH_2Cl_2 (0.5 mL) was added 10% Pd/C (16 mg). The reaction mixture was stirred for 3 h under H_2 balloon at room temperature. The reaction mixture was then filtered through a short pad of Celite and the Celite pad was washed with CH_2Cl_2/MeOH (1:1, 10 mL). Evaporation of solvent followed by silica gel column chromatography of the crude residue with CH_2Cl_2/MeOH (9:1) containing 1% NH_4OH as an eluent gave pachastrissamine (Jaspine B) (28 mg, 94%) as a white solid: R_f 0.2 (1:9 MeOH:$CHCl_3$ containing 1% NH_4OH); mp 96−97 °C (lit[6a] mp 96.6−97.2 °C); $[\alpha]_D$ +17.5 (*c* 0.4, EtOH), (lit[2] $[\alpha]_D$ +18 (*c* 0.1, EtOH); IR ($CHCl_3$): 3289, 2921, 1467, 1036, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.95−3.91 (m, 1H), 3.88−3.86 (m, 1H), 3.76−3.71 (m, 1H), 3.53−3.50 (m, 1H), 1.96 (brs, 3H),1.71−1.62 (m, 2H), 1.43−1.25 (m, 24H), 0.88 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 84.3, 70.9, 68.9, 54.4, 33.1, 30.9, 30.8, 30.74, 30.71, 30.69, 30.5, 29.7, 27.2, 23.7, 14.1; HRMS for $C_{18}H_{37}NO_2$ + H calcd: 300.2902; found: 300.2901.

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Supporting Information Available: General experimental procedures and spectroscopic data for the compounds and copies of ^1H NMR, ^{13}C NMR spectra are provided. This material is available free of charge via the Internet at http://pubs.acs.org

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