

Supplementary Information

Asymmetric synthesis of *N,O,O,O*-tetra-acetyl *D*-lyxo-phytosphingosine, jaspine B (pachastrissamine), 2-*epi*-jaspine B and deoxoprosophylline *via* lithium amide conjugate addition

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Experimental

General Experimental

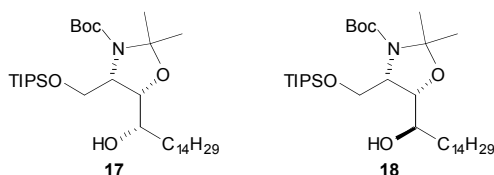
All reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.¹ Water was purified by an Elix[®] UV-10 system. All other solvents were used as supplied (analytical or HPLC grade) without prior purification. Organic layers were dried over MgSO₄. Thin layer chromatography was performed on aluminium plates coated with 60 F₂₅₄ silica. Plates were visualised using UV light (254 nm), iodine, 1% aq KMnO₄, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Melting points were recorded on a Gallenkamp Hot Stage apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter with a water-jacketed 10 cm cell. Specific rotations are reported in 10⁻¹ deg cm² g⁻¹ and concentrations in g/100 mL. IR spectra were recorded on Bruker Tensor 27 FT-IR spectrometer as either a thin film on NaCl plates (film) or a KBr disc (KBr), as stated. Selected characteristic peaks are reported in cm⁻¹. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. Spectra were recorded at rt unless otherwise stated. The field was locked by external referencing to the relevant deuteron resonance. Low-resolution mass spectra were recorded on either a VG MassLab 20-250 or a Micromass Platform 1 spectrometer. The ion [M+59]⁺ refers to

¹ A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen and F. J. Timmers, *Organometallics*, **1996**, *15*, 1518.

$[M+MeCN+NH_4]^+$. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyaniline, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m \times 0.25 mm) using amyl acetate as a lock mass.

(4*S*,5*S*,1'*S*)- and (4*S*,5*S*,1'*R*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-5-(1'-hydroxypentadecyl)oxazolidine (4*S*,5*S*,1'*S*)-17** and (4*S*,5*S*,1'*R*)-**18****



A small volume of 1-bromotetradecane (from 2.67 g, 9.65 mmol) was added *via* dropping funnel to a stirred mixture of magnesium turnings (232 mg, 9.65 mmol) and I₂ (two crystals) in degassed THF (20 mL) under argon, and the reaction mixture heated gently with a heat gun to initiate the formation of the Grignard reagent. Once the solution had decolourised, the remaining 1-bromotetradecane was diluted with THF (5 mL) and added to the reaction at such a rate so as to maintain a gentle reflux. After the addition of 1-bromotetradecane was complete, the reaction was maintained at reflux in an oil bath until all the magnesium had reacted (*ca* 2 h). The solution was then cooled to 0 °C. A solution of **16** (800 mg, 1.93 mmol) in THF (50 mL) at 0 °C was added dropwise to the Grignard reagent *via* cannula. The reaction mixture was allowed to warm to rt over 12 h and then quenched by the addition of H₂O (1 mL). The resultant slurry was filtered through a pad of Celite (eluent EtOAc), and the filtrate was dried and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/Et₂O, 10:1) gave **18** as a colourless oil (first to elute, 47 mg, 4%, >98% de) and **17** as a colourless oil (second to elute, 603 mg, 51%, >98% de).

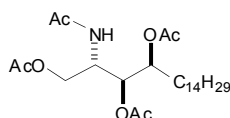
Data for **17**: R_f 0.26 (30-40 °C petrol/Et₂O, 10:1); $[\alpha]_D^{22} +7.8$ (*c* 0.5 in CHCl₃); ν_{max} (film) 3490 (O–H), 2926 (C–H), 1702 (C=O); δ_H (400 MHz, CDCl₃) [50:50 mixture of rotamers] 0.88 (3H, t J 7.0, C(15')H₃), 1.06-1.14 (21H, m, Si(CHMe₂)₃), 1.24-1.35 (24H, m, C(3')H₂-C(14')H₂), 1.47 (9H, s, CMe₃), 1.50-1.54 (3H, m, C(2)Me_A), 1.56-1.59 (3H, m, C(2)Me_B), 1.55-1.64 (2H, m, C(2')H₂), 3.36 (1H, m, OH), 3.66-3.68 (1H, m, C(4)CH_A), 3.73-3.76 (1H, m, C(4)H), 3.85-3.87 (1H, m, C(4)CH_B), 3.89-4.05 (2H, m, C(5)H, C(1')H); δ_H (500 MHz, PhMe-*d*₈, 373 K) 0.92 (3H, t J 7.1, C(15')H₃), 1.12-1.16 (21H, m, Si(CHMe₂)₃), 1.27-1.37 (22H, m, C(4')H₂-C(14')H₂), 1.45 (9H, s, CMe₃), 1.44-1.46 (2H, m, C(3')H₂), 1.54 (3H, s, C(2)Me_A), 1.63 (3H, s, C(2)Me_B), 1.67-1.71 (2H, m, C(2')H₂), 3.84-3.87 (1H, m, C(4)CH_A), 3.96-3.99 (2H, m, C(4)H, C(4')CH_B), 4.08-4.13 (2H, m, C(5)H, C(1')H); δ_C (125 MHz, PhMe-*d*₈, 373 K) 12.2, 13.6, 17.8, 22.5, 25.3, 25.9, 28.1,

29.3, 29.6, 29.7, 29.8, 29.9, 30.0, 30.1, 30.2, 30.5, 31.9, 33.9, 34.5, 60.3, 68.6, 68.8, 79.3, 79.4, 92.7, 151.4; m/z (ESI⁺) 614.5 ([M+H]⁺, 100%); HRMS (ESI⁺) C₃₅H₇₂NO₅Si⁺ ([M+H]⁺) requires 614.5174; found 614.5170.

Data for **18**: R_f 0.32 (30-40 °C petrol/Et₂O, 10:1); $[\alpha]_D^{22}$ +7.5 (*c* 2.8 in CHCl₃); ν_{\max} (film) 3491 (O–H), 2925 (C–H), 1703 (C=O); δ_H (400 MHz, CDCl₃) [50:50 mixture of rotamers] 0.89 (3H, t *J* 7.1, C(15')H₃), 1.09-1.12 (21H, m, Si(CHMe₂)₃), 1.21-1.31 (22H, m, C(4')H₂-C(14')H₂), 1.39-1.46 (2H, m, C(3')H₂), 1.46-1.48 (12H, m, CMe₃, C(2)Me_A), 1.52-1.62 (4H, m, C(2)Me_B, C(2')H_A), 1.72-1.79 (1H, m, C(2')H_B), 3.66-3.85 (3H, m, C(4)CH_A, C(1')H, OH), 3.89-3.93 (3H, m, C(4)H, C(4)CH_B), 4.04-4.19 (1H, m, C(5)H); δ_H (500 MHz, PhMe-*d*₈, 373 K) 0.89 (3H, t, *J* 7.0, C(15')H₃), 1.05-1.20 (21H, m, Si(CHMe₂)₃), 1.20-1.96 (41H, m, C(2)Me₂, C(2')H₂-C(14')H₂, CMe₃), 3.38-3.62 (1H, br s, OH), 3.80-4.30 (5H, m, C(4)HCH₂, C(5)H, C(1')H); δ_C (125 MHz, PhMe-*d*₈, 373 K) 12.6, 14.2, 18.2, 23.1, 24.4, 25.8, 28.1, 28.7, 29.8, 30.2, 30.4, 32.4, 34.5, 60.9, 61.8, 69.4, 79.9, 80.7, 93.5, 152.0; m/z (ESI⁺) 614.5 ([M+H]⁺, 100%); HRMS (ESI⁺) C₃₅H₇₂NO₅Si⁺ ([M+H]⁺) requires 614.5174; found 614.5167.

(2*S*,3*S*,4*S*)-1,3,4-Triacetoxy-2-acetamido-octadecane [*N*,*O*,*O*,*O*-tetra-acetyl *D*-lyxo-phytosphingosine]

19



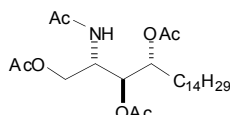
A solution of **17** (100 mg, 0.16 mmol) in 3 M aq HCl (1 mL) and MeOH (5 mL) was heated at 50 °C for 3 h. Removal of the solvent *in vacuo* gave a white solid which was redissolved in pyridine (5 mL). Ac₂O (80 mg, 0.85 mmol) and DMAP (5 mg, cat.) were added and the solution was stirred at rt for 12 h. The reaction mixture was then diluted with Et₂O (10 mL) and extracted with H₂O (10 mL). The aqueous layer was separated and extracted with Et₂O (10 mL). The combined organic layers were washed sequentially with sat aq CuSO₄ (10 mL), H₂O (10 mL) and brine (10 mL), then dried and concentrated *in vacuo* to give **19** as a pale yellow oil (58 mg, 74%, >98% de); $[\alpha]_D^{21}$ -3.1 (*c* 0.7 in CHCl₃); {lit.² $[\alpha]_D^{22}$ -3.1 (*c* 1.1 in CHCl₃); ν_{\max} (film) 2918 (C–H), 1736 (C=O), 1683 (C=O); δ_H (500 MHz, CDCl₃) 0.93 (3H, t *J* 6.6, C(18)H₃), 1.21-1.34 (24H, m, C(6)-C(17)H₂), 1.48-1.60 (2H, m, C(5)H₂), 2.03 (3H, s, COMe), 2.12 (3H, s, COMe), 2.14 (3H, s, COMe), 2.18 (3H, s, COMe), 4.00 (1H, dd *J* 11.7, 2.7, C(1)H_A), 4.29 (1H, dd *J* 11.7, 4.2, C(1)H_B), 4.57-4.61 (1H, m, C(2)H), 5.14-5.15 (2H, m, C(3)H, C(4)H), 5.80-5.82 (1H, br d *J* 9.7, NH); δ_C (125 MHz, CDCl₃)

² O. Shirota, K. Nakanishi and N. Berova, *Tetrahedron*, **1999**, *55*, 13643.

14.5 (C(18)), 20.8 (COMe), 20.9 (COMe), 21.3 (COMe), 22.7 (C(17)), 23.3 (COMe), 25.2, 25.9, 28.0, 29.4, 29.5, 29.6, 29.7, 30.9, 31.8, 32.4, 32.6 (C(5)-C(16)), 47.3 (C(2)), 63.1 (C(1)), 71.7 (C(3)), 73.0 (C(4)), 169.8 (COMe), 170.4 (COMe), 170.8 (COMe), 171.2 (COMe); m/z (ESI⁺) 508 ([M+Na]⁺, 100%), 486 (40); HRMS (ESI⁺) C₂₆H₄₈NO₇⁺ ([M+H]⁺) requires 486.3431; found 486.3439.

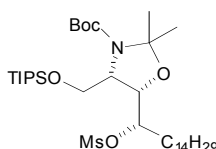
(2S,3S,4R)-1,3,4-Triacetoxy-2-acetamido-octadecane [N,O,O,O-tetra-acetyl D-ribo-phytosphingosine]

20



A solution of **18** (77 mg, 0.12 mmol) in 3 M aq HCl (1 mL) and MeOH (5 mL) was heated at 50 °C for 3 h. Removal of the solvent *in vacuo* gave a white solid which was redissolved in pyridine (5 mL). Ac₂O (80 mg, 0.85 mmol) and DMAP (5 mg, cat.) were added and the solution was stirred at rt for 12 h. The reaction mixture was then diluted with Et₂O (10 mL) and extracted with H₂O (10 mL). The aqueous layer was separated and extracted with Et₂O (10 mL). The combined organic layers were washed sequentially with sat aq CuSO₄ (10 mL), H₂O (10 mL) and brine (10 mL), then dried and concentrated *in vacuo* to give **20** as a gum (45 mg, 80%, >98% de); $[\alpha]_D^{22} +18.2$ (c 1.0 in CHCl₃); {lit.³ $[\alpha]_D^{22} +21.9$ (c 1.1 in CHCl₃)}; ν_{\max} (KBr) 2915 (C–H), 1734 (C=O), 1683 (C=O); δ_H (400 MHz, CDCl₃) 0.88 (3H, t J 7.0, C(18)H₃), 1.24-1.31 (24H, m, C(6)-C(17)H₂), 1.60-1.67 (2H, m, C(5)H₂), 2.03 (3H, s, COMe), 2.05 (6H, s, 2 × COMe), 2.08 (3H, s, COMe), 4.00 (1H, dd J 11.6, 2.9, C(1)H_A), 4.29 (1H, dd J 11.6, 4.7, C(1)H_B), 4.44-4.50 (1H, m, C(2)H), 4.93 (1H, dt J 9.7, 3.1, C(4)H), 5.1 (1H, dd J 8.3, 3.1, C(3)H), 6.01 (1H, br d J 9.4, NH); δ_C (100 MHz, CDCl₃) 14.1 (C(18)), 20.8 (COMe), 20.9 (COMe), 21.0 (COMe), 22.7 (C(17)), 23.3 (COMe), 25.5, 28.1, 29.3, 29.4, 29.5, 29.6, 29.6, 29.6, 29.7, 29.8, 29.9, 31.9 (C(5)-C(16)), 47.6 (C(2)), 62.8 (C(1)), 71.9 (C(3)), 73.0 (C(4)), 169.7 (COMe), 170.1 (COMe), 170.8 (COMe), 171.2 (COMe); m/z (ESI⁺) 508 ([M+Na]⁺, 100%), 486 (25); HRMS (ESI⁺) C₂₆H₄₈NO₇⁺ ([M+H]⁺) requires 486.3431; found 486.3436.

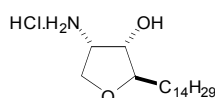
(2S,3S,1'S)-2,2-Dimethyl-N(3)-tert-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-5-[1'-(methanesulphonyloxy)pentadecyl]oxazolidine 21



³ O. Shirota, K. Nakanishi and N. Berova, *Tetrahedron*, **1999**, *55*, 13643.

MsCl (470 mg, 4.15 mmol), DMAP (5 mg) and Et₃N (1 mL, 9.54 mmol) were added to a stirred solution of **17** (510 mg, 0.83 mmol) in DCM (20 mL) at 0 °C and stirring was continued for 3 h before the reaction was quenched with H₂O (1 mL). The aqueous phase was then separated and extracted with DCM (2 × 10 mL). The combined organic extracts were then successively washed with 1 M aq HCl (20 mL), sat aq NaHCO₃ (20 mL), and brine (20 mL), before being dried and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/Et₂O, 10:1) gave **21** as a colourless oil (433 mg, 75%, >98% de); [α]_D²² +6.1 (*c* 2.5 in CHCl₃); ν_{max} 2920 (C–H), 1703 (C=O), 1366 (S=O); δ_H (400 MHz, CDCl₃) [52:48 mixture of rotamers] 0.88 (3H, t *J* 6.4, C(15')H₃), 1.06-1.10 (21H, m, Si(CHMe₂)₃), 1.20-1.35 (24H, m, C(3')-C(14')H₂), 1.47-1.48 (9H, m, CMe₃), 1.50-1.56 (6H, m, C(2)Me₂), 1.70-1.83 (2H, m, C(2')H₂), 3.09-3.10 (3H, m, SO₂Me), 3.62-3.68 (1H, m, C(4)CH_A), 3.86-3.99 (2H, m, C(4)H, C(4)CH_B), 4.13-4.17 (1H, m, C(5)H), 5.00-5.07 (1H, m, C(1')H); δ_H (500 MHz, DMSO-*d*₆, 373 K) 0.88 (3H, t *J* 6.4, C(15')H₃), 1.09-1.16 (21H, m, Si(CHMe₂)₃), 1.23-1.35 (24H, m, C(3')-C(14')H₂), 1.45 (9H, s, CMe₃), 1.52 (6H, s, C(2)Me₂), 1.70-1.74 (1H, m, C(2')H_A), 1.77-1.83 (1H, m, C(2')H_B), 3.11 (3H, s, SMe), 3.68 (1H, m, C(4)CH_A), 3.91-3.94 (2H, m, C(4)H, C(4)CH_B), 4.24 (1H, m, C(5)H), 4.94-4.98 (1H, m, C(1')H); δ_C (125 MHz, DMSO-*d*₆, 373 K) 12.0, 14.1, 18.2, 22.4, 24.7, 28.6, 29.0-29.33, 31.7, 32.2, 39.3, 59.7, 60.5, 77.2, 80.1, 81.9, 92.9, 151.6; *m/z* (ESI⁺) 750 ([M+59]⁺, 100%); HRMS (ESI⁺) C₃₆H₇₄NO₇SSi⁺ ([M+H]⁺) requires 692.4955; found 692.4968.

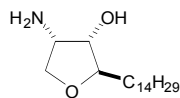
(2*R*,3*S*,4*S*)-2-Tetradecyl-4-amino-tetrahydrofuran-3-ol hydrochloride **24**



TBAF (1 M in THF, 1.4 mL, 1.4 mmol) was added to a stirred solution of **21** (236 mg, 0.34 mmol) in THF (10 mL) at rt and stirring was continued for 12 h. H₂O (10 mL) was then added, the organic layer was separated and the aqueous layer was extracted with Et₂O (10 mL). The combined organic layers were washed sequentially with H₂O (20 mL) and brine (20 mL) before being dried and concentrated *in vacuo*. The residue was dissolved in MeOH (10 mL), 3 M aq HCl (1 mL) was added and the solution was heated at 50 °C for 3 h. The reaction mixture was then allowed to cool to rt and the solvent was removed *in vacuo* to give **24** as a white solid (115 mg, quant, >98% de); mp 93-95 °C; [α]_D²¹ +15.5 (*c* 0.9 in MeOH); ν_{max} (KBr) 2917 (C–H), 3302 (O–H), 3060 (N–H); δ_H (500 MHz, MeOH-*d*₄) 0.93 (3H, t *J* 6.4, C(14')H₃), 1.26-1.46 (20H, m, (C(4')H₂-C(13')H₂), 1.46-1.68 (6H, m, C(1')H₂-C(3')H₂), 3.70-3.77 (3H, m, C(2)H, C(4)H, C(5)H_A), 4.04-4.06 (1H, m, C(3)H), 4.16-4.19 (1H, m, C(5)H_B); δ_C (125 MHz, MeOH-*d*₄) 13.1 (C(14')),

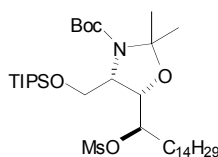
22.7, 25.5, 29.1, 29.16, 29.17, 29.28, 29.33, 29.39, 29.42, 29.45, 31.5, 31.7, 32.7 ($C(1')-C(13')$), 52.3 ($C(2)$), 68.0 ($C(5)$), 73.0 ($C(4)$), 83.8 ($C(3)$); m/z (CI^+) 300 ($[M-CI]^+$, 100%); HRMS (CI^+) $C_{18}H_{38}NO_2^+$ ($[M-CI]^+$) requires 300.2903; found 300.2902.

(2*R*,3*S*,4*S*)-2-Tetradecyl-4-amino-tetrahydrofuran-3-ol **7**



2 M aq KOH (5 mL) and DCM (5 mL) were added to **24** (31 mg, 0.09 mmol) and the mixture stirred for 1 min. The organic layer was separated and the aqueous layer extracted with DCM (3 × 5 mL). The combined organic extracts were dried and concentrated *in vacuo*. Recrystallisation of the residue from $CHCl_3$ /heptane (1:1) gave **7** as a white solid (20 mg, 70%, >98% de); mp 106-108 °C ($CHCl_3$ /heptane); $[\alpha]_D^{24} +16.4$ (c 0.85 in MeOH); {lit.⁴ $[\alpha]_D^{22} +15.0$ (c 1.0 in MeOH)}; ν_{max} 2918 (C-H); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t J 6.7, $C(14')H_3$), 1.26-1.35 (24H, m, $C(2')-C(13')H_2$), 1.37-1.49 (1H, m, $C(1')H_A$), 1.50-1.64 (1H, m, $C(1')H_B$), 2.08 (1H, br s, OH), 3.37-3.47 (1H, m, $C(5)H_A$), 3.46-3.49 (1H, m, $C(4)H$), 3.60-3.64 (2H, m, $C(2)H$, $C(3)H$), 4.11-4.15 (1H, m, $C(5)H_B$); δ_C (100 MHz, $CDCl_3$) 14.1 ($C(14')$), 22.7, 25.9, 29.4, 29.6, 29.61, 29.67, 31.9, 33.8 ($C(1')-C(13')$), 52.6 ($C(4)$), 73.2 ($C(5)$), 74.8 ($C(2)$), 85.3 ($C(3)$); m/z (ESI^+) 300 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{18}H_{38}NO_2^+$ ($[M+H]^+$) requires 300.2903; found 300.2902.

(2*S*,3*S*,1'*S*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-5-[1'-(methanesulphonyloxy)pentadecyl]oxazolidine **25**

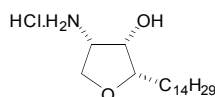


MsCl (0.8 mL) and DMAP (5 mg) were added to a stirred solution of **18** (490 mg, 0.80 mmol) in pyridine (6 mL) at 0 °C and stirring was continued for 20 h before the reaction was quenched with sat aq $NaHCO_3$ (1 mL). The mixture was then diluted with H_2O (10 mL) and extracted with DCM (3 × 10 mL). The combined organic extracts were then successively washed with 1 M aq HCl (20 mL), sat aq $NaHCO_3$ (20 mL), and brine (20 mL), before being dried and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/ Et_2O , 10:1) gave **25** as a colourless oil (402 mg, 73%, >98% de);

⁴ R. J. B. H. N. van den Berg, T. J. Boltje, C. P. Verhagen, R. E. J. N. Litjens, G. A. van der Marel and H. S. Overkleeft, **2006**, *71*, 836.

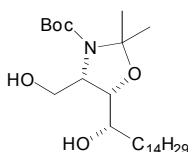
$[\alpha]_D^{23} +50.2$ (*c* 0.2 in CHCl_3); ν_{max} (film) 2926 (C–H), 1699 (C=O), 1376 (S=O); δ_{H} (400 MHz, CDCl_3) [50:50 mixture of rotamers] 0.88 (3H, t, *J* 6.8, $\text{C}(15')\text{H}_3$), 1.00-1.18 (21H, m, $\text{Si}(\text{CHMe}_2)_3$), 1.20-1.39 (24H, m, $\text{C}(3')\text{-C}(14')\text{H}_2$), 1.46-1.47 (9H, m, CMe_3), 1.50-1.58 (6H, m, $\text{C}(2)\text{Me}_2$), 1.72-2.00 (2H, m, $\text{C}(2')\text{H}_2$), 3.00-3.04 (3H, m, *SMe*), 3.80-4.10 (3H, m, $\text{C}(4)\text{H}$, $\text{C}(4)\text{CH}_2$), 4.20-4.26 (1H, m, $\text{C}(5)\text{H}$), 5.20-5.31 (1H, m, $\text{C}(1')\text{H}$); δ_{C} (100 MHz, CDCl_3) [mixture of rotamers] 11.8, 11.9, 14.1, 18.1, 22.7, 23.3, 24.5, 24.6, 24.9, 26.3, 27.0, 28.4, 28.5, 29.3, 29.5, 29.6, 29.7, 30.4, 30.8, 31.9, 38.9, 39.0, 59.3, 59.6, 60.2, 60.9, 75.8, 76.7, 80.2, 80.8, 92.7, 93.2, 151.5, 151.8; *m/z* (ESI^+) 750 ($[\text{M}+59]^+$, 100%); HRMS (ESI^+) $\text{C}_{36}\text{H}_{74}\text{NO}_7\text{SSi}^+$ ($[\text{M}+\text{H}]^+$) requires 692.4955; found 692.4953.

(2*S*,3*S*,4*S*)-2-Tetradecyl-4-amino-tetrahydrofuran-3-ol hydrochloride **28**



TBAF (1 M in THF, 1.9 mL, 1.9 mmol) was added to a stirred solution of **25** (325 mg, 0.47 mmol) in THF (10 mL) at rt and stirring was continued for 12 h. H_2O (10 mL) was then added, the organic layer was separated and the aqueous layer was extracted with Et_2O (10 mL). The combined organic layers were washed sequentially with H_2O (20 mL) and brine (20 mL) before being dried and concentrated *in vacuo*. The residue was dissolved in MeOH (10 mL), 3 M aq HCl (1 mL) was added and the solution was heated at 50 °C for 3 h. The reaction mixture was then allowed to cool to rt and the solvent was removed *in vacuo* to give **28** as a white solid (157 mg, quant, >98% de); mp 148-150 °C; $[\alpha]_D^{23} +2.6$ (*c* 0.38 in MeOH); ν_{max} (film) 3396 (O–H), 2923 (C–H); δ_{H} (400 MHz, $\text{MeOH-}d_4$) 0.91 (3H, t, *J* 6.6, $\text{C}(14')\text{H}_3$), 1.20-1.60 (24H, m, $\text{C}(2')\text{-C}(13')\text{H}_2$), 1.62-1.80 (2H, m, $\text{C}(1')\text{H}_2$), 3.73 (1H, ddd, *J* 10.0, 7.6, 3.6, $\text{C}(2)\text{H}$), 3.83 (1H, app q, *J* 4.0, $\text{C}(5)\text{H}_A$), 3.88-3.96 (2H, m, $\text{C}(4)\text{H}$, $\text{C}(5)\text{H}_B$), 4.28 (1H, dd, *J* 5.2, 3.6, $\text{C}(2)\text{H}$); δ_{C} (100 MHz, $\text{MeOH-}d_4$) 13.5, 22.8, 26.2, 28.7, 29.5, 29.7, 29.8, 29.9, 32.1, 53.4, 68.0, 69.9, 83.4; *m/z* (ESI^+) 300 ($[\text{M}-\text{Cl}]^+$, 100%).

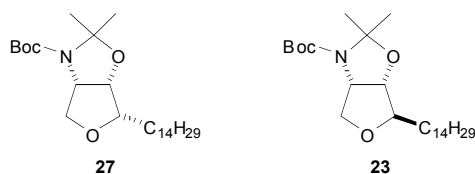
(2*S*,3*S*,1'*S*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-hydroxymethyl-5-(1'-hydroxypentadecanyl)oxazolidine **29**



TBAF (1 M in THF, 4.3 mL, 4.34 mmol) was added to a stirred solution of **17** (665 mg, 1.08 mmol) in THF (20 mL) at rt and stirring was continued for 20 min. H_2O (20 mL) was then added and the aqueous layer was

then extracted with Et₂O (3 × 50 mL). The organic layer was then successively washed with H₂O (50 mL) and brine (50 mL), before being dried and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/Et₂O, 2:1) gave **29** as a colourless oil (470 mg, 95%, >98% de); [α]_D²² +10.1 (*c* 2.2 in CHCl₃); ν_{\max} (film) 3515 (O–H), 2930 (C–H), 1705 (C=O); δ_{H} (400 MHz, CDCl₃) [50:50 mixture of rotamers] 0.88 (3H, t *J* 6.6, C(15')H₃), 1.20-1.36 (24H, m, C(2')-C(14')H₂), 1.47-1.49 (9H, m, CMe₃), 1.52-1.61 (6H, m, C(2)Me₂), 1.48-1.60 (2H, m, C(2')H₂), 2.20-3.05 (1H, br s, OH), 3.63-4.12 (6H, m, C(4)H, C(5)H, C(4)CH₂, C(1')H, OH); δ_{H} (500 MHz, DMSO-*d*₆, 373 K) 0.89 (3H, t *J* 6.9, C(15')H₃), 1.25-1.34 (24H, m, C(3')-C(14')H₂), 1.45 (9H, s, CMe₃), 1.47 (3H, s, C(2)Me_A), 1.51 (3H, s, C(2)Me_B), 1.57-1.61 (1H, m, C(2')H_A), 1.74-1.81 (1H, m, C(2')H_B), 3.47 (1H, dd *J* 10.8, 2.8, C(4)CH_A), 3.61-3.64 (1H, m, C(1')H), 3.76-3.82 (2H, m, C(4)H and C(4)CH_B), 3.87-3.89 (1H, m, C(5)H), 4.15-4.65 (2H, br s, 2 × OH); δ_{C} (125 MHz, DMSO-*d*₆, 373 K) 14.1, 22.4, 24.5, 25.7, 27.4, 28.7, 29.4, 29.5, 31.7, 34.5, 59.6, 60.5, 68.3, 79.5, 92.2, 151.7; *m/z* (ESI⁺) 516 ([M+59]⁺, 100%); HRMS (ESI⁺) C₂₆H₅₁NNaO₅⁺ ([M+Na]⁺) requires 480.3659; found 480.3643.

(3a*S*,6*S*,6a*S*)- and (3a*S*,6*R*,6a*S*)-2,2-dimethyl-*N*(3)-*tert*-butoxycarbonyl-6-tetradecyl-hexahydrofuro[3,4-*d*]oxazole (3a*S*,6*S*,6a*S*)-27** and (3a*S*,6*R*,6a*S*)-**23****



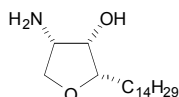
TsCl (162 mg, 0.85 mmol) was added to a stirred solution of **29** (130 mg, 0.28 mmol) and DMAP (5 mg) in pyridine (3 mL) and the reaction mixture was heated at 80 °C for 8 h. The reaction was then quenched with sat aq NaHCO₃ solution (1 mL), and H₂O (10 mL) was added. The resultant mixture was extracted with DCM (3 × 10 mL). The combined organic extracts were then sequentially washed with 1 M aq HCl (20 mL), sat aq NaHCO₃ solution (20 mL) and brine (20 mL) before being dried and concentrated *in vacuo* to give an 82:18 mixture of **27**:**23**. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/Et₂O, 50:1) gave **27** as a white solid (65 mg, 52%, >98% de) and **23** as a white solid (19 mg, 15%, >98% de).

Data for **23**: δ_{H} (400 MHz, CDCl₃) [50:50 mixture of rotamers] 0.88 (3H, t, *J* 7.0, C(14')H₃), 1.21-1.32 (24H, m, C(2')H₂-C(13')H₂), 1.45-1.49 (9H, m, CMe₃), 1.50-1.67 (8H, m, C(2)Me₂, C(1')H₂), 3.71-3.84 (1H, m, C(4)H_A), 4.00-4.07 (2H, m, C(6)H, C(3a)H), 4.32-4.47 (2H, m, C(4)H_B, C(6a)H); δ_{C} (100 MHz, CDCl₃) [mixture of rotamers] 14.2, 22.7, 24.3, 25.6, 25.7, 26.9, 27.6, 27.7, 28.4, 28.5, 29.3, 29.4, 29.5, 29.6, 29.7,

29.8, 29.9, 31.1, 31.5, 31.9, 61.7, 62.1, 72.6, 73.1, 80.6, 80.8, 82.8, 83.2, 84.3, 84.4, 97.3, 97.5, 151.3, 151.7.

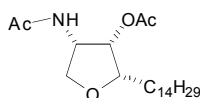
Data for **27**: mp 54-56 °C; $[\alpha]_{\text{D}}^{23}$ +66.0 (*c* 1.1 in CHCl₃); ν_{max} (film) 2926 (C–H), 1709 (C=O); δ_{H} (400 MHz, CDCl₃) [50:50 mixture of rotamers] 0.88 (3H, t, *J* 6.8, C(14')H₃), 1.20-1.40 (24H, m, C(2')H₂-C(13')H₂), 1.45-1.48 (9H, m, CMe₃), 1.57-1.62 (6H, m, C(2)Me₂), 1.69-1.77 (2H, m, C(1')H₂), 3.40 (1H, dt, *J* 6.8, 3.2, C(6)H), 3.57-3.60 (1H, m, C(4)H_A), 3.97-4.06 (1H, m, C(4)H_B), 4.31-4.47 (1H, m, C(3a)H), 4.48-4.53 (1H, m, C(6a)H); δ_{C} (100 MHz, CDCl₃) [mixture of rotamers] 14.1, 22.7, 24.5, 25.6, 26.2, 26.3, 27.1, 28.1, 28.3, 28.4, 29.3, 29.5, 29.6, 29.7, 31.9, 62.3, 62.7, 73.4, 73.8, 79.2, 79.6, 79.9, 80.5, 83.0, 83.1, 95.7, 96.5, 151.6, 152.4; *m/z* (ESI⁺) 440 ([M+H]⁺, 100%); HRMS (ESI⁺) C₂₆H₄₉NNaO₄⁺ ([M+Na]⁺) requires 462.3554; found 462.3567.

(2*S*,3*S*,4*S*)-2-Tetradecyl-4-amino-tetrahydrofuran-3-ol [jaspine B (pachastrissamine)] **6**



2 M aq KOH (5 mL) and DCM (5 mL) were added to **28** (157 mg, 0.47 mmol) and the mixture stirred for 1 min. The organic layer was separated and the aqueous layer extracted with DCM (3 × 5 mL). The combined organic extracts were dried and concentrated *in vacuo*. Recrystallisation of the residue from Et₂O/heptane (1:1) gave **6** as a white solid (110 mg, 79%, >98% de); mp 90-92 °C (Et₂O/heptane); $[\alpha]_{\text{D}}^{23}$ +17.5 (*c* 0.3 in EtOH); {lit.⁵ $[\alpha]_{\text{D}}^{25}$ +18.0 (*c* 0.1 in EtOH)}; ν_{max} (KBr) 3340 (N–H), 3074 (O–H), 2921 (C–H), 2849 (C–H); δ_{H} (400 MHz, CDCl₃) 0.87 (3H, t, *J* 6.7, C(14')H₃), 1.18-1.50 (24H, m, C(2')H₂-C(13')H₂), 1.55-1.70 (2H, m, C(1')H₂), 3.50 (1H, dd, *J* 8.4, 7.2, C(5)H_A), 3.61-3.69 (1H, m, C(4)H), 3.74 (1H, td, *J* 7.2, 4.0, C(2)H), 3.87 (1H, t, *J* 4.0, C(3)H), 3.91 (1H, t, *J* 7.7, C(5)H_B); δ_{C} (100 MHz, CDCl₃) 14.1, 22.7, 26.3, 29.3, 29.4, 29.5, 29.6, 29.7, 29.8, 31.9, 54.4, 71.8, 72.4, 83.1; *m/z* (ESI⁺) 300 ([M+H]⁺, 100%); HRMS (ESI⁺) C₁₈H₃₈NO₂⁺ ([M+H]⁺) requires 300.2897; found 300.2900.

(2*S*,3*S*,4*S*)-2-Tetradecyl-3-acetoxy-4-acetamido-tetrahydrofuran [*N*,*O*-diacetyl-jaspine B] **30**

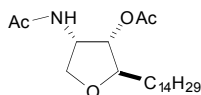


Ac₂O (1 mL) and DMAP (2 mg) were added sequentially to a stirred solution of **6** (67 mg, 0.22 mmol) in pyridine (5 mL) at rt. After 12 h the reaction mixture was quenched with H₂O (2 mL). The reaction mixture

⁵ I. Kuroda, M. Musman, I. I. Ohtani, T. Ichiba, J. Tanaka, D. Garcia-Gravalos and T. Higa, *J. Nat. Prod.*, **2002**, 65, 1505.

was then diluted with H₂O (10 mL) and extracted with Et₂O (3 × 10 mL). The combined organic extracts were washed sequentially with sat aq CuSO₄ solution (2 × 20 mL), H₂O (20 mL) and brine (20 mL), then dried and concentrated *in vacuo* to give **30** as a white solid (80 mg, 95%, >98% de); mp 100-102 °C (Et₂O/heptane); [α]_D²³ -26.4 (*c* 0.5 in CHCl₃); {lit.⁶ [α]_D²⁵ -22.6 (*c* 1.0 in CHCl₃)}; ν_{max} (KBr) 3295 (N-H), 2921 (C-H), 1733 (C=O), 1653 (C=O); δ_H (400 MHz, CDCl₃) 0.88 (3H, t, *J* 6.0, C(14')H₃), 1.20-1.32 (24H, m, C(2')-C(13')H₂), 1.35-1.57 (2H, m, C(1')H₂), 2.00 (3H, s, COMe), 2.19 (3H, s, COMe), 3.60 (1H, t, *J* 8.1, C(5)H_A), 3.91 (1H, ddd, *J* 7.6, 5.2, 3.6, C(2)H), 4.10 (1H, t, *J* 8.1, C(5)H_B), 4.82 (1H, ddd, *J* 13.2, 7.6, 5.6, C(4)H), 5.38 (1H, dd, *J* 5.6, 3.6, C(3)H), 5.60 (1H, br d, *J* 7.9, NH); δ_C (100 MHz, CDCl₃) 14.1 (C(14')), 20.8 (COMe), 22.7 (C(13')), 23.2 (COMe), 26.0, 28.4, 28.5, 29.2, 29.3, 29.4, 29.5, 29.6, 29.7, 31.9 (C(1')-C(12')), 51.3 (C(4)), 69.8 (C(5)), 73.5 (C(3)), 81.2 (C(2)), 169.9 (COMe), 170.0 (COMe); *m/z* (ESI⁺) 442 ([M+59]⁺, 100%); HRMS (ESI⁺) C₂₂H₄₁NNaO₄⁺ ([M+Na]⁺) requires 406.2933; found 406.2929.

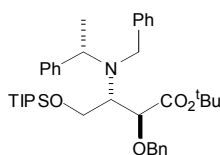
(2*R*,3*S*,4*S*)-2-Tetradecyl-3-acetoxy-4-acetamido-tetrahydrofuran **31**



Ac₂O (1 mL) and DMAP (5 mg) were added sequentially to a stirred solution of **7** (25 mg, 0.08 mmol) in pyridine (5 mL) at rt. After 12 h the reaction mixture was quenched with H₂O (2 mL). The reaction mixture was then diluted with H₂O (10 mL) and extracted with Et₂O (3 × 10 mL). The combined organic extracts were washed sequentially with sat aq CuSO₄ solution (2 × 20 mL), H₂O (20 mL) and brine (20 mL), then dried and concentrated *in vacuo* to give **31** as a white solid (23 mg, 81%, >98% de); mp 65-67 °C; [α]_D²¹ -14.6 (*c* 0.5 in CHCl₃); {lit.⁶ [α]_D²² -15.4 (*c* 1.0 in CHCl₃)}; ν_{max} (KBr) 2915 (C-H), 1730 (C=O), 1685 (C=O); δ_H (500 MHz, CDCl₃) 0.93 (3H, t, *J* 7.1, C(14')H₃), 1.26-1.35 (24H, m, C(2')H₂-C(13')H₂), 1.34-1.68 (2H, m, C(1')H₂), 2.06 (3H, s, COMe), 2.18 (3H, s, COMe), 3.55-3.58 (1H, m, C(5)H_A), 3.90-3.93 (1H, m, C(2)H), 4.21-4.24 (1H, m, C(5)H_B), 4.67-4.73 (1H, m, C(4)H), 4.95-4.97 (1H, m, C(3)H), 5.69 (1H, d *J* 8.2, NH); δ_C (125 MHz, CDCl₃) 14.2 (C(14')), 21.1 (COMe), 22.8 (C(13')), 23.2 (COMe), 25.6, 29.4, 29.51, 29.55, 29.60, 29.65, 29.67, 29.70, 29.72, 29.80, 32.0, 33.6 (C(1')C(12')), 49.9 (C(4)), 69.9 (C(5)), 77.1 (C(3)), 84.2 (C(2)); *m/z* (ESI⁺) 442 ([M+59]⁺, 100%); HRMS (ESI⁺) C₂₂H₄₂NO₄⁺ ([M+H]⁺) requires 384.2114; found 384.3112.

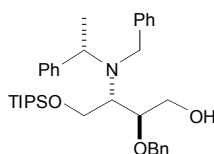
⁶ R. J. B. H. N. van den Berg, T. J. Boltje, C. P. Verhagen, R. E. J. N. Litjens, G. A. van der Marel and H. S. Overkleeft, **2006**, *71*, 836.

tert*-Butyl (2*S*,3*S*, α *S*)-2-benzyloxy-3-[*N*-benzyl-*N*-(α -methylbenzyl)amino]-4-(tri-*iso*-propylsilyloxy)butanoate **37*



A solution of **36** (1.00 g, 1.85 mmol) in THF (30 mL) was added dropwise to a stirred slurry of NaH (100 mg, 2.78 mmol) in THF (5.0 mL) at 0 °C. The reaction mixture was allowed to warm to rt over 1 h before successive addition of 15-crown-5-ether (0.55 mL) and BnBr (0.26 mL, 2.22 mmol). Stirring was continued for 12 h where upon the reaction was quenched with sat aq NH₄Cl solution (1 mL). Brine (2 mL) was added and the organic layer was separated. The aqueous layer was extracted with Et₂O (3 × 10 mL) and the combined organic extracts were dried and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/Et₂O, 100:1) gave **37** as a colourless oil (940 mg, 83%, >98% de); [α]_D²⁰ –33.1 (*c* 0.7 in CHCl₃); ν_{\max} (film) 1738 (C=O); δ_{H} (400 MHz, CDCl₃) 1.04-1.10 (21H, m, Si(CHMe₂)₃), (3H, d, *J* 7.0, C(α)Me), 1.43 (9H, s, CMe₃), 3.49-3.56 (1H, m, C(3)H), 3.66 (1H, d, *J* 15.3, NCH_A), 3.76 (1H, d, *J* 2.7, C(2)H), 3.84 (1H, dd, *J* 11.0, 3.7, C(4)H_A), 3.95-4.09 (2H, m, C(4)H_B, C(α)H), 4.19 (1H, d, *J* 11.1, OCH_AH_BPh), 4.28 (1H, d, *J* 15.3, NCH_B), 4.55 (1H, d, *J* 11.1, OCH_AH_BPh), 7.17-7.45 (15H, m, Ph); δ_{C} (100 MHz, CDCl₃) 11.9, 18.2, 19.5, 28.1, 51.1, 58.6, 60.8, 61.1, 72.5, 80.1, 81.2, 126.2, 126.6, 127.6, 128.0, 128.3, 128.4, 142.6, 144.2, 170.9; *m/z* (ESI⁺) 632 ([M+H]⁺, 100%); HRMS (ESI⁺) C₃₉H₅₈NO₄Si ([M+H]⁺) requires 632.4129; found 632.4130.

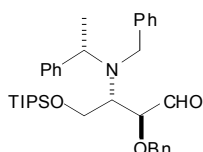
(2*S*,3*S*, α *S*)-2-Benzyloxy-3-[*N*-benzyl-*N*-(α -methylbenzyl)amino]-4-(tri-*iso*-propylsilyloxy)butan-1-ol **38**



DIBAL-H (1 M in DCM, 2.85 mL, 2.85 mmol) was added to a stirred solution of **37** (900 mg, 1.42 mmol) in DCM (100 mL) at 0 °C. After stirring for 18 h, the reaction mixture was quenched with sat aq NH₄Cl solution (*ca* 0.5 mL) and stirred for a further 1 h. The resultant mixture was filtered through Celite (eluent DCM) and the filtrate was dried and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/Et₂O, 20:1) gave **38** as a colourless oil (456 mg, 83%, >98% de); [α]_D²² –30.2 (*c* 0.7 in CHCl₃); ν_{\max} (film) 3389 (O–H); δ_{H} (400 MHz, CDCl₃) 1.06-1.18 (21H, m,

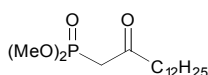
Si(CHMe₂)₃, 1.43 (3H, d, *J* 6.8, C(α)Me), 3.07 (1H, app t, *J* 5.3, OH), 3.18 (1H, app q, *J* 6.1, C(3)H), 3.37-3.53 (3H, m, C(2)H, C(1)H₂), 3.88-4.08 (4H, m, NCH₂, C(α)H, C(4)H_A), 4.16 (1H, dd, *J* 10.2, 5.1, C(4)H_B), 4.36 (1H, d, *J* 11.5, OCH_AH_BPh), 4.55 (1H, d, *J* 11.5, OCH_AH_BPh), 7.22-7.38 (15H, m, Ph); δ_C (100 MHz, CDCl₃) 12.0, 17.3, 18.1, 52.1, 58.0, 60.0, 62.2, 62.7, 71.4, 77.9, 126.9, 127.0, 127.5, 127.8, 127.9, 128.3, 128.8, 138.4, 141.0, 144.2; *m/z* (ESI⁺) 562 ([M+H]⁺, 100%); HRMS (ESI⁺) C₃₅H₅₂NO₃Si, ([M+H]⁺) requires 562.3711; found 562.3711.

(2*S*,3*S*,α*S*)-2-Benzoyloxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(tri-*iso*-propylsilyloxy)butanal **39**



IBX (230 mg, 0.81 mmol) was added to a solution of **38** (150 mg, 0.27 mmol) in DMSO (10 mL) at rt and stirred for 18 h. The reaction mixture was diluted with Et₂O (50 mL), washed with H₂O (3 × 50 mL), dried and concentrated *in vacuo* to give **39** as a colourless oil (149 mg, quant, >98% de) that was used immediately; δ_H (400 MHz, CDCl₃) 1.01-1.12 (21H, m, Si(CHMe₂)₃), 1.38 (3H, d, *J* 7.1, C(α)Me), 3.45-3.51 (1H, m, C(3)H), 3.56 (1H, dd, *J* 4.0, 2.7, C(2)H), 3.78 (1H, d, *J* 14.8, NCH_A), 3.81-3.92 (2H, m, C(4)H_A, C(α)H), 4.06 (1H, dd, *J* 9.6, 7.6, C(4)H_B), 4.12 (1H, d, *J* 14.8, NCH_B), 4.34 (1H, d, *J* 11.4, OCH_AH_BPh), 4.48 (1H, d, *J* 11.4, OCH_AH_BPh), 7.16-7.40 (15H, m, Ph), 9.19 (1H, d, *J* 2.7, C(1)H).

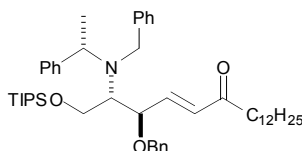
Dimethyl 2-oxotetradecylphosphonate **40**



BuLi (2.5 M in hexanes, 4.8 mL, 12 mmol) was added to a solution of dimethyl methylphosphonate (1.5 g, 12 mmol) in THF (30 mL) at -78 °C. The reaction mixture was stirred for 30 min before a solution of methyl tridecanoate (2.4 g, 10.5 mmol) in THF (10 mL) was added dropwise. The resultant mixture was stirred at -78 °C for a further 1 h then allowed to warm to 0 °C over 1 h. The reaction was quenched with sat aq NH₄Cl solution and extracted with CHCl₃ (3 × 30 mL). The combined organic extracts were then dried, filtered and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/EtOAc, 2:1) gave **40** as a white solid (1.46 g, 40%); mp 41-43 °C; δ_H (400 MHz, CDCl₃) 0.88 (3H, t, *J* 7.0, C(14)H₃), 1.20-1.31 (20H, m, C(4)H₂-C(13)H₂), 2.61 (2H, t, *J* 7.4, C(3)H₂), 3.10 (2H, d, *J* 22.8, C(1)H₂), 3.76 (6H, d, *J* 11.2, P(OMe)₂); δ_C (100 MHz, CDCl₃) 13.7, 22.7, 28.9, 29.3, 29.4,

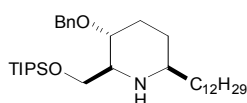
29.6, 29.7, 31.9, 41.2 (d, J 128), 44.2, 53.5, 202.1 (d, J 6.3); m/z (ESI⁺) 343 ([M+Na]⁺, 100%), 321 (70); HRMS (ESI⁺) C₁₆H₃₄NO₄P ([M+H]⁺) requires 321.2186; found 321.2189.

(2*S*,3*R*,4*E*, α *S*)-1-(Tri-*iso*-propylsilyloxy)-2-[*N*-benzyl-*N*-(α -methylbenzyl)amino]-3-benzyloxy-octadec-4-en-6-one **41**



BuLi (2.5 M in hexanes, 1.1 mL, 2.75 mmol) was added to a stirred solution of **40** (880 mg, 2.75 mmol) in THF (40 mL) at -78 °C, and the resultant solution was stirred for 30 min at -78 °C. A solution of **39** (750 mg, 1.37 mmol) in THF (80 mL) at -78 °C was then added *via* cannula with stirring continued for a further 30 min at -78 °C. The reaction mixture was then allowed to warm to rt over 16 h before being quenched with sat aq NH₄Cl solution (2 mL) and left to stir for a further 15 min. The resultant mixture was diluted with brine (30 mL) and the organic layer was separated. The aqueous layer was then extracted with Et₂O (3 × 30 mL) and the combined organic extracts were dried, filtered and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent 30-40 °C petrol/Et₂O, 50:1) gave **41** (630 mg, 61%, >98% de) as a colourless oil; $[\alpha]_D^{20}$ -6.6 (c 0.5 in CHCl₃); ν_{\max} (film) 1676 (C=O), 1454 (C=C); δ_H (400 MHz, CDCl₃) 0.89 (3H, t, J 6.7, C(18)H₃), 1.06-1.10 (21H, m, Si(CH(CH₃)₂)₃), 1.24-1.31 (20H, m, C(8)H₂-C(17)H₂), 1.38 (3H, d, J 6.8, C(α)Me), 2.44 (2H, app t, J 7.5, C(7)H₂), 3.01-3.21 (1H, m, C(2)H), 3.76-3.89 (2H, m, NCH_APh, C(3)H), 3.95-4.07 (3H, m, C(α)H, C(1)H₂), 4.13 (1H, d, J 14.8, NCH_BPh), 4.16 (1H, d, J 11.7, OCH_AH_BPh), 4.36 (1H, d, J 11.7, OCH_AH_BPh), 5.90, (1H, d, J 16.2, C(5)H), 6.54 (1H, dd, J 16.2, 7.0, C(4)H), 7.16-7.39 (15H, m, Ph); δ_C (100 MHz, CDCl₃) 12.0, 14.1, 17.5, 17.5, 18.1, 22.7, 29.3, 29.5, 29.6, 29.7, 29.9, 40.0, 51.9, 57.3, 61.8, 62.0, 71.1, 79.3, 126.6, 126.8, 127.6, 127.8, 127.9, 128.1, 128.2, 128.6, 130.6, 137.8, 141.5, 144.0, 200.5; m/z (ESI⁺) 754 ([M+H]⁺, 100%), 650 (59); HRMS (ESI⁺) C₄₉H₇₆NO₃Si, ([M+H]⁺) requires 754.5622; found 754.5589.

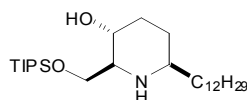
(2*R*,3*S*,6*S*)-2-[(Tri-*iso*-propylsilyloxy)methyl]-3-benzyloxy-6-dodecylpiperidine **42**



Pd(OH)₂/C (50 mg) was added to a degassed, vigorously stirred solution of **41** (70 mg, 0.09 mmol) in EtOAc (2 mL) at rt. Stirring was continued under H₂ (1 atm) for 24 h, before filtration through Celite (eluent

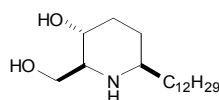
EtOAc). Concentration of the filtrate *in vacuo* gave **42** as a colourless oil (51 mg, quant, >98% de); δ_{H} (400 MHz, CDCl_3) 0.89 (3H, t, J 6.9, $\text{C}(12')\text{H}_3$), 1.00-1.17 (22H, m, $\text{Si}(\text{CH}(\text{CH}_3)_2)_3$, $\text{C}(5)\text{H}_A$), 1.20-1.38 (23H, m, $\text{C}(1')\text{H}_2$ - $\text{C}(11')\text{H}_2$), $\text{C}(4)\text{H}_A$), 1.70-1.75 (1H, m, $\text{C}(5)\text{H}_B$), 1.99-2.11 (1H, m, $\text{C}(4)\text{H}_B$), 2.44-2.55 (1H, m, $\text{C}(6)\text{H}$), 2.64-2.72 (1H, m, $\text{C}(2)\text{H}$), 3.14 (1H, ddd, J 10.7, 8.9, 4.7, $\text{C}(3)\text{H}$), 3.57 (1H, dd, J 9.5, 6.2, $\text{C}(2)\text{CH}_A\text{H}_B\text{OH}$), 4.12 (1H, dd, J 9.5, 6.8, $\text{C}(2)\text{CH}_A\text{H}_B\text{OH}$), 4.49 (1H, d, J 11.8, $\text{OCH}_A\text{H}_B\text{Ph}$), 4.60 (1H, d, J 11.8, $\text{OCH}_A\text{H}_B\text{Ph}$), 7.21-7.39 (5H, m, *Ph*).

(2*S*,3*R*,6*R*)-2-[(Tri-*iso*-propylsilyloxy)methyl]-6-tetradecylpiperidin-3-ol **43**



$\text{Pd}(\text{OH})_2/\text{C}$ (50 mg) was added to a degassed, vigorously stirred solution of **41** (70 mg, 0.09 mmol) in EtOAc (2 mL) and AcOH (0.25 mL) at rt. Stirring was continued under H_2 (5 atm) for 48 h, before filtration through Celite (eluent EtOAc). Concentration of the filtrate *in vacuo* gave **43** as a colourless oil (43 mg, quant, >98% de); $[\alpha]_{\text{D}}^{20}$ -4.0 (c 0.3 in CHCl_3); ν_{max} (film) 3287 (O–H); δ_{H} (400 MHz, CDCl_3) 0.89 (3H, t, J 6.9, $\text{C}(12')\text{H}_3$), 1.00-1.17 (22H, m, $\text{Si}(\text{CH}(\text{CH}_3)_2)_3$, $\text{C}(5)\text{H}_A$), 1.20-1.38 (23H, m, $\text{C}(1')\text{H}_2$ - $\text{C}(11')\text{H}_2$, $\text{C}(4)\text{H}_A$), 1.70-1.75 (1H, m, $\text{C}(5)\text{H}_B$), 1.99-2.11 (1H, m, $\text{C}(4)\text{H}_B$), 2.44-2.55 (1H, m, $\text{C}(6)\text{H}$), 2.56-2.67 (1H, m, $\text{C}(2)\text{H}$), 3.43 (1H, ddd, J 10.7, 8.9, 4.7, $\text{C}(3)\text{H}$), 3.78 (1H, dd, J 9.5, 6.2, $\text{C}(2)\text{CH}_A\text{H}_B\text{OH}$), 3.93 (1H, dd, J 9.5, 6.8, $\text{C}(2)\text{CH}_A\text{H}_B\text{OH}$); δ_{C} (100 MHz, CDCl_3) 11.8, 14.1, 17.7, 17.9, 22.3, 26.2, 29.4, 29.6, 29.7, 29.8, 31.2, 31.9, 33.6, 36.7, 55.7, 62.5, 67.5, 72.5; m/z (ESI^+) 456 ($[\text{M}+\text{H}]^+$, 100%); HRMS (ESI^+) found 456.4231; $\text{C}_{27}\text{H}_{58}\text{NO}_2\text{Si}$ ($[\text{M}+\text{H}]^+$) requires 456.4232.

(2*R*,3*S*,6*S*)-2-Hydroxymethyl-6-dodecylpiperidin-3-ol [deoxoprosophylline] **32**



TBAF (1 M in THF, 0.16 mL, 0.16 mmol) was added to a stirred solution of **43** (50 mg, 0.11 mmol) in THF (5 mL) at rt and the resultant solution was stirred for 12 h. The mixture was then diluted with Et_2O (10 mL) and H_2O (10 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3×10 mL). The combined organic extracts were successively washed with H_2O (10 mL) and brine (10 mL) before being dried and concentrated *in vacuo*. Recrystallization from acetone gave **32** as a white solid (25 mg, 76%, >98% de); mp 84-85 °C; {lit.⁷ mp 90-91 °C; lit.⁸ mp 83 °C}; $[\alpha]_{\text{D}}^{22}$ $+13.5$ (c 0.3 in CHCl_3); {lit.⁷ for

⁷ Y. Saitoh, Y. Moriyama, T. Takahashi and Q. Khuong-Huu, *Tetrahedron Lett.*, **1980**, 21, 75.

enantiomer $[\alpha]_D -14.0$ (c 0.2 in CHCl_3); lit.⁸ $[\alpha]_D^{20} +13.0$ (c 0.2 in CHCl_3); ν_{max} (KBr) 3267 (O–H); δ_{H} (400 MHz, CDCl_3) 0.89 (3H, t, J 6.9, C(12') H_3), 1.20-1.32 (24H, m, C(1') H_2 -C(11') H_2 , C(4) H_A , C(5) H_A), 1.66-1.79 (1H, m, C(5) H_B), 1.96-2.2 (1H, m, C(4) H_B), 2.40-2.70 (2H, m, C(2) H , C(6) H), 3.39-3.53 (1H, ddd, J 10.9, 9.1, 4.7, C(3) H), 3.71 (1H, dd, J 10.8, 5.2, C(2) CH_AH_BOH), 3.85 (1H, dd, J 10.8, 4.8, C(2) CH_AH_BOH); δ_{C} (100 MHz, CDCl_3) 14.1, 22.6, 26.2, 29.3, 29.6, 29.8, 31.2, 31.9, 34.0, 36.6, 55.9, 63.2, 65.0, 70.1.

⁸ C. Herdeis and J. Telsler, *Eur. J. Org. Chem.*, **1999**, 1407.