Supplementary Material for Organic & Biomolecular Chemistry

Supplementary Information

Asymmetric synthesis of vicinal amino alcohols: xestoaminol C, sphinganine and sphingosine

Elin Abraham, Stephen G. Davies,* Nicholas L. Millican, Rebecca L. Nicholson, Paul M. Roberts and Andrew D. Smith

Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford, OX1 3TA, UK.

E-mail: steve.davies@chem.ox.ac.uk

Experimental

General Experimental

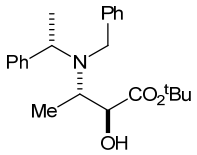
All reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen or argon atmosphere using standard vacuum line techniques and glassware that was flame dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs 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 $MgSO_4$. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Plates were visualised using UV light (254 nm), iodine, 1% aq $KMnO_4$, or 10% ethanolic phosphomolybdic acid. Flash column chromatography was performed on Kieselgel 60 silica.

Elemental analyses were recorded by the microanalysis service of the Inorganic Chemistry Laboratory, University of Oxford, UK. 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 cm^2 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. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyanaline, or a

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

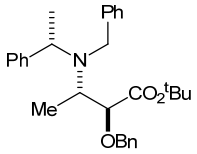
Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m × 0.25 mm) using amyl acetate as a lock mass.

tert-Butyl (2*S*,3*S*,α*S*)-2-hydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]butanoate 10



BuLi (2.5 M in hexanes, 10.9 mL, 27.3 mmol) was added dropwise *via* syringe to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (5.94 g, 28.2 mmol) in THF (50 mL) at −78 °C. After stirring for 30 min a solution of *tert*-butyl crotonate (2.5 g, 17.6 mmol) in THF (20 mL) at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with (+)-CSO (8.06 g, 35.2 mmol) and allowed to warm to rt over 12 h. Sat aq NH_4Cl (5 mL) was added and the mixture was stirred for 5 min before being concentrated *in vacuo*. The residue was partitioned between DCM (50 mL) and 10% aq citric acid (10 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 × 50 mL). The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*. The residue was dissolved in Et_2O (50 mL), the insoluble CSO residues were filtered off, and the filter cake was washed with Et_2O (2 × 20 mL). The filtrate was concentrated *in vacuo* and the process was repeated. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1) gave **10** as a white solid (4.99 g, 77%, >98% de); R_f 0.22 (30-40 °C petrol/Et_2O, 10:1); mp 87-88 °C (30-40 °C petrol/Et_2O, 10:1); $[\alpha]_D^{25}$ +34.7 (*c* 1.05 in $CHCl_3$); {lit.[2] for enantiomer $[\alpha]_D^{25}$ −33.4 (*c* 1.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.14 (3H, d, *J* 7.2, C(4)H_3), 1.38 (3H, d, *J* 6.8, C(α)*Me*), 1.42 (9H, s, CMe_3), 3.02 (1H, bs, O*H*), 3.30-3.36 (1H, m, C(3)*H*), 3.94 (1H, d, *J* 14.7, NCH_A), 4.05-4.11 (3H, m, C(2)*H*, C(α)*H*, NCH_B), 7.24-7.55 (10H, m, *Ph*).

tert-Butyl (2*S*,3*S*,α*S*)-2-benzyloxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]butanoate 11

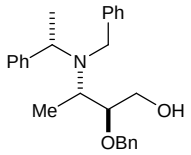


A solution of **10** (1.5 g, 4.1 mmol) in THF (5 mL) at room temperature was added dropwise *via* syringe to a stirred slurry of NaH (60% dispersion in oil, 103 mg, 4.3 mmol) in THF (5 mL) at 0 °C. The reaction

[2] M. E. Bunnage, A. N. Chernega, S. G. Davies and C. J. Goodwin, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 2373.

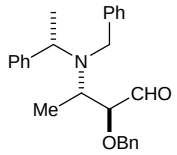
mixture was allowed to warm to rt over 1 h, after which 15-crown-5 ether (0.94 mL, 4.3 mmol) and BnBr (1.2 mL, 44.6 mmol) were sequentially added dropwise *via* syringe. Stirring was continued for 12 h before the reaction was quenched with sat aq NH_4Cl (2 mL). Brine (10 mL) was added, the organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 20:1) gave **11** as a colourless oil (1.61 g, 88%, >98% de); $[\alpha]_D^{23}$ −67.3 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 2976 (C−H), 1739 (C=O); δ_H (400 MHz, $CDCl_3$) 1.14 (3H, d, *J* 7.1, C(4)H_3), 1.30 (3H, d, *J* 6.8, C(α)*Me*), 1.40 (9H, s, CMe_3), 3.32-3.38 (1H, m, C(3)*H*), 3.80 (1H, d, *J* 3.5, C(2)*H*), 3.81 (1H, d, *J* 14.9, NCH_A), 3.94 (1H, q, *J* 6.8, C(α)*H*), 4.05 (1H, d, *J* 14.9, NCH_B), 4.30 (1H, d, *J* 11.1, OCH_A), 4.61 (1H, d, *J* 11.1, OCH_B), 7.21-7.41 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.9 (*C*(4)), 17.8 (C(α)*Me*), 28.0 (CMe_3), 50.6 (NCH_2), 54.5 (*C*(3)), 58.9 (*C*(α)), 72.3 (OCH_2), 80.9 (*C*Me_3), 82.0 (*C*(2)), 126.3, 126.6, 127.6 (*p-Ph*), 127.8, 128.01, 128.04, 128.2, 128.23 (*o-Ph*, *m-Ph*), 137.8, 142.5, 144.4 (*i-Ph*), 171.2 (*C*(1)); *m/z* (ESI^+) 460 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{30}H_{37}NO_3^+$ ($[M+H]^+$) requires 460.2852; found 460.2849.

(2*S*,3*S*,α*S*)-2-Benzyloxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]butan-1-ol 12



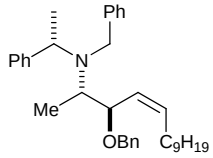
$LiAlH_4$ (1 M in THF, 1.12 mL, 1.12 mmol) was added dropwise *via* syringe to a stirred solution of **11** (250 mg, 0.56 mmol) in THF (5 mL) at 0 °C and the reaction mixture allowed to warm to rt over 6 h. The reaction was quenched with H_2O (0.5 mL) and filtered through Celite (eluent EtOAc) to give **12** as a colourless oil (200 mg, 91%, >98% de) that was used without purification. Purification of an aliquot *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 20:1) gave an analytical sample; $[\alpha]_D^{22}$ –9.5 (*c* 4.0 in $CHCl_3$); ν_{max} (film) 3413 (O−H), 2972 (C−H); δ_H (400 MHz, $CDCl_3$) 1.32 (3H, d, *J* 6.6, C(4)H_3), 1.46 (3H, d, *J* 6.8, C(α)*Me*), 3.03 (1H, app s, O*H*), 3.10-3.16 (2H, m, C(1)H_2), 3.24-3.29 (1H, m, C(2)*H*), 3.49-3.54 (1H, m, C(3)*H*), 3.82 (2H, ABq, *J* 13.4, NCH_2), 3.99 (1H, q, *J* 6.8, C(α)*H*), 4.46 (1H, d, *J* 11.1, OCH_A), 4.58 (1H, d, *J* 11.1, OCH_B), 7.24-7.42 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 13.6 (C(α)*Me*), 14.4 (*C*(4)), 50.9 (NCH_2), 54.0 (*C*(3)), 56.8 (*C*(α)), 63.0 (*C*(1)), 72.7 (OCH_2), 80.8 (*C*(2)), 127.2, 127.3, 127.7 (*p-Ph*), 128.0, 128.2, 128.22 128.4, 128.6, 129.4 (*o-Ph*, *m-Ph*), 138.2, 139.7, 143.1 (*i-Ph*); *m/z* (ESI^+) 390 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{26}H_{32}NO_2^+$ ($[M+H]^+$) requires 390.2433; found 390.2423.

(2*S*,3*S*,α*S*)-2-Benzyloxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]butanal 13



DMSO (0.04 mL, 0.57 mmol) was added dropwise *via* syringe to a stirred solution of oxaloyl chloride (0.02 mL, 0.23 mmol) in DCM (2 mL) at −78 °C. After 20 min a solution of **12** (50 mg, 0.13 mmol) in DCM (2 mL) was added dropwise *via* syringe. After a further 20 min Et_3N (0.11 mL, 0.78 mmol) was added dropwise *via* syringe and the reaction mixture was stirred for a further 30 min before being allowed to warm to rt over a further 30 min. Volatiles were removed *in vacuo* and the residue was partitioned between H_2O (10 mL) and Et_2O (10 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic extracts were dried and concentrated *in vacuo* to give **13** as a colourless oil (44 mg, 88%, >98% de) that was used without purification; δ_H (500 MHz, $CDCl_3$) 1.27 (3H, d, *J* 6.4, C(4)H_3), 1.38 (3H, d, *J* 7.0, C(α)*Me*), 3.28-3.34 (1H, m, C(3)*H*), 3.40-3.43 (1H, m, C(2)*H*), 3.77 (2H, app d, *J* 3.1, NCH_2), 3.86 (1H, q, *J* 7.0, C(α)*H*), 4.31 (1H, d, *J* 11.4, OCH_A), 4.48 (1H, d, *J* 11.4, OCH_B), 7.20-7.71 (15H, m, *Ph*), 8.59 (1H, d, *J* 4.5, C(1)*H*).

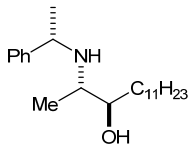
(2*S*,3*R*,4*Z*,α*S*)-2-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-3-benzyloxytetradec-4-ene (*Z*)-14



BuLi (2.5 M in hexanes, 1.84 mL, 4.5 mmol) was added dropwise *via* syringe to a stirred solution of (1-decyl)triphenylphosphonium bromide (2.5 g, 5.17 mmol) in THF (20 mL) at −78 °C. After 30 min, hexane (25 mL) was added, followed by the dropwise addition *via* syringe of a solution of **13** (400 mg, 1.03 mmol) in THF (5 mL). Stirring was continued and the reaction mixture was allowed to warm to rt over 12 h. The reaction was quenched with sat aq NH_4Cl (2 mL). Brine (10 mL) was added, the organic layer separated and the aqueous layer extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 200:1) gave (*Z*)-**14** as a colourless oil (500 mg, 95%, >98% de); $[\alpha]_D^{23}$ −26.7 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 2925 (C−H), 1644 (C=C); δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.2, C(14)H_3), 1.20-1.35 (20H, m, C(1)H_3, C(7)H_2-C(13)H_2, C(α)*Me*), 1.66-1.73 (2H, m, C(6)H_2), 2.74-2.80 (1H, m, C(2)*H*), 3.87 (1H, d, *J* 14.0, NCH_A), 3.98 (1H, q, *J* 6.8, C(α)*H*), 4.08 (1H, d, *J* 14.0, NCH_B), 4.16 (1H, dd, *J* 9.3, 4.4, C(3)*H*), 4.30 (1H, d, *J* 11.6,

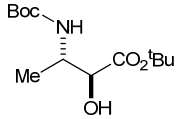
OCH_A), 4.48 (1H, d, *J* 11.6, OCH_B), 5.11 (1H, dd, *J* 10.9, 9.3, C(4)*H*), 5.40-5.47 (1H, m, C(5)*H*), 7.15-7.46 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.8 (*C*(1)), 14.1 (*C*(14)), 14.5 (C(α)*Me*), 22.7, 27.4, 29.26, 29.33, 29.6, 29.7, 31.9 (*C*(6)-*C*(13)), 51.3 (NCH_2), 55.2 (*C*(2)), 56.7 (*C*(α)), 70.2 (OCH_2), 79.6 (*C*(3)), 126.2, 126.3, 126.4 (*p*-*Ph*), 127.2, 127.7, 127.71, 128.0, 128.1, 128.6 (*o*-*Ph*, *m*-*Ph*), 129.9 (*C*(5)), 133.2 (*C*(4)), 139.0, 142.3, 145.0 (*i*-*Ph*); *m/z* (ESI^+) 512 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{36}H_{50}NO^+$ ($[M+H]^+$) requires 512.3892; found 512.3898.

(2*S*,3*R*,α*S*)-2-[*N*-(α-Methylbenzyl)amino]tetradecan-3-ol 15



Pd/C (20 mg, 50% w/w) was added to a stirred solution of (*Z*)-**14** (40 mg, 0.78 mmol) in MeOH/AcOH/H_2O (40:4:1, 5 mL) at rt. The reaction mixture was stirred under H_2 (1 atm) for 6 h. The reaction mixture was filtered through Celite (eluent MeOH) and concentrated *in vacuo* to give **15**, contaminated with an unidentified impurity, as a colourless oil (15 mg); δ_H (400 MHz, $CDCl_3$) 0.87-0.89 (6H, m, C(1)H_3, C(14)H_3), 1.23-1.33 (16H, m, C(6)H_2-C(13)H_2), 1.36-1.52 (7H, m, C(4)H_2, C(5)H_2, C(α)*Me*), 2.54 (1H, qd, *J* 6.5, 3.1, C(2)*H*), 3.62-3.66 (1H, m, C(3)*H*), 3.88 (1H, q, *J* 6.8, C(α)*H*), 7.24-7.71 (5H, m, *Ph*).

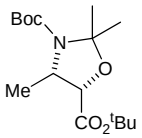
***tert*-Butyl (2*S*,3*S*)-2-hydroxy-3-(*N*-*tert*-butoxycarbonylamino)butanoate 16**



Pearlman's catalyst (250 mg, 25% w/w) was added to a vigorously stirred solution of **10** (1.0 g, 27.1 mmol) and Boc_2O (2.01 g, 92.1 mmol) in EtOAc (50 mL) and the mixture was placed under H_2 (5 atm). Stirring continued for 12 h, after which time the reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 5:1; then 30-40 °C petrol/Et_2O, 1:1) gave **16** as a colourless oil (740 mg, 98%, >98% de); R_f 0.08 (30-40 °C petrol/Et_2O, 5:1); $[\alpha]_D^{23}$ +10.8 (*c* 1.2 in $CHCl_3$); {lit.[3] $[\alpha]_D^{23}$ +10.6 (*c* 2.4 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.02 (3H, d, *J* 6.8, C(4)H_3), 1.46 (9H, s, CMe_3), 1.50 (9H, s, CMe_3), 3.03 (1H, d, *J* 5.5, O*H*), 4.07-4.14 (1H, m, C(3)*H*), 4.20-4.22 (1H, m, C(2)*H*), 4.90 (1H, d, *J* 8.9, N*H*).

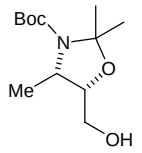
[3] M. E. Bunnage, A. J. Burke, S. G. Davies, N. L. Millican, R. L. Nicholson, P. M. Roberts and A. D. Smith, *Org. Biomol. Chem.*, **2003**, *1*, 3708.

(4*S*,5*S*)-2,2,4-Trimethyl-*N*(3),5-di-*tert*-butoxycarbonyl-oxazolidine 17



$BF_3{\cdot}Et_2O$ (1 M in Et_2O) was added dropwise to a stirred solution of **16** (1.7 g, 6.18 mmol) and 2,2-dimethoxypropane (10 mL) in acetone (50 mL) until a permanent colour change from colourless to dark orange was observed. After stirring at rt for 12 h the reaction was quenched with Et_3N until pH 7 was achieved. The reaction mixture was concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1) gave **17** as a white crystalline solid (1.72 g, 88%, >98% de); R_f 0.1 (30-40 °C petrol/Et_2O, 10:1); $C_{16}H_{29}NO_5$ requires C, 60.9; H, 9.3; N, 4.4%; found C, 60.9; H, 9.3; N, 4.4%; mp 55-57 °C (30-40 °C petrol/Et_2O); $[\alpha]_D^{21}$ −17.4 (*c* 1.2 in $CHCl_3$); ν_{max} (KBr) 2978 (C−H), 1749 (C=O), 1699 (C=O); δ_H (400 MHz, $CDCl_3$) 1.07-1.16 (3H, m, C(4)*Me*), 1.35-1.52 (21H, m, C(2)Me_A, 2 × CMe_3), 1.55-1.66 (3H, m, C(2)Me_B), 4.02-4.27 (1H, m, C(4)*H*), 4.47 (1H, d, *J* 5.8, C(5)*H*); δ_H (500 MHz, DMSO-d_6, 363 K) 1.11 (3H, d, *J* 6.4, C(4)*Me*), 1.46 (9H, s, CMe_3), 1.48 (12H, s, C(2)Me_A, CMe_3), 1.57 (3H, s, C(2)Me_B), 4.12 (1H, m, C(4)*H*), 4.60 (1H, d, *J* 5.8, C(5)*H*); δ_C (125 MHz, DMSO-d_6, 363 K) 16.0 (C(4)*Me*), 25.2 (C(2)Me_A), 28.4 (C(2)Me_B), 28.7 (CMe_3), 29.0 (CMe_3), 54.8 (*C*(4)), 76.2 (*C*(5)), 80.2 (*C*Me_3), 82.5 (*C*Me_3), 94.1 (*C*(2)), 151.7 (N*C*O), 167.5 (*C*$O_2{}^t$Bu); *m/z* (ESI^+) 316 ($[M+H]^+$, 19%), 260 (83), 204 (100); HRMS (ESI^+) $C_{16}H_{30}NO_5^+$ ($[M+H]^+$) requires 316.2124; found 316.2135.

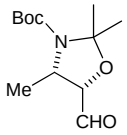
(4*S*,5*S*)-2,2,4-Trimethyl-*N*(3)-*tert*-butoxycarbonyl-5-hydroxymethyl-oxazolidine 18



$LiAlH_4$ (1 M in THF, 0.6 mL, 0.6 mmol) was added dropwise *via* syringe to a stirred solution of **17** (189 mg, 0.6 mmol) in THF (10 mL) at 0 °C. After stirring for 6 h, the reaction was quenched with H_2O (*ca* 0.5 mL) and filtered through Celite (eluent EtOAc) to give **18** as a colourless oil (152 mg, quant, >98% de) that was used without purification. Purification of an aliquot *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 20:1) gave an analytical sample; R_f 0.27 (30-40 °C petrol/Et_2O, 2:1); $C_{12}H_{23}NO_4$ requires C, 58.75; H, 9.45; N, 5.7%; found C, 58.8; H, 9.7; N, 5.5%; $[\alpha]_D^{27}$ −1.2 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 3449 (O−H), 2980 (C−H), 1698 (C=O); δ_H (400 MHz, $CDCl_3$) 1.08-1.17 (1H, m, C(4)*Me*), 1.43-1.66 (15H, m, C(2)Me_2, CMe_3), 3.66-3.83 (2H, m, C(5)CH_2), 3.89-4.10 (1H, m, C(4)*H*), 4.13-4.20 (1H, m, C(5)*H*); δ_H (500

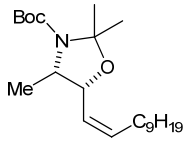
MHz, DMSO-d_6, 363 K), 1.08 (3H, d, *J* 6.4, C(4)*Me*), 1.41-1.50 (12H, m, C(2)Me_A, CMe_3), 1.52 (3H, s, C(2)Me_B), 2.99 (1H, br s, O*H*), 3.53 (1H, br dd, *J* 11.0, 6.4, C(5)CH_A), 3.58 (1H, br dd, *J* 11.0, 6.1, C(5)CH_B), 3.89-3.97 (1H, m, C(4)*H*), 4.05-4.13 (1H, m, C(5)*H*); δ_C (125 MHz, DMSO-d_6, 363 K) 14.7 (C(4)*Me*), 25.2 (C(2)Me_A), 28.5 (C(2)Me_B), 29.1 (CMe_3), 55.0 (*C*(4)), 60.3 (C(5)*C*H_2), 77.6 (*C*(5)), 79.7 (*C*Me$_3$), 93.1 (*C*(2)), 151.9 (N*C*O); *m/z* (ESI$^+$) 246 ([M+H]$^+$, 12%), 190 (100), 146 (94); HRMS (ESI$^+$) $C_{12}H_{24}NO_4^+$ ([M+H]$^+$) requires 246.1705; found 246.1714.

(4*S*,5*S*)-2,2,4-Trimethyl-*N*(3)-*tert*-butoxycarbonyl-5-formyl-oxazolidine 19



IBX (2.06 g, 7.35 mmol) was added to a solution of **18** (600 mg, 2.45 mmol) in DMSO (20 mL) at rt and stirred for 12 h. The reaction mixture was diluted with Et_2O (20 mL), washed with H_2O (5 × 20 mL), dried and concentrated *in vacuo* to give **19** as a colourless oil (600 mg, quant, >98% de) that was used without purification; δ_H (400 MHz, $CDCl_3$) 1.13-1.19 (3H, m, C(4)*Me*), 1.43-1.57 (12H, m, C(2)Me_A, CMe_3), 1.68 (3H, s, C(2)Me_B), 4.13-4.39 (1H, m, C(5)*H*), 4.40-4.66 (1H, m, C(4)*H*), 9.71 (1H, s, C*H*O).

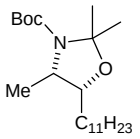
(4*S*,5*R*,1'*Z*)-2,2,4-Trimethyl-*N*(3)-*tert*-butoxycarbonyl-5-undec-1'en-1′-yl-oxazolidine (*Z*)-20



BuLi (2.5 M in hexanes, 5.74 mL, 14.3 mmol) was added dropwise *via* syringe to a stirred solution of (1-decyl)triphenylphosphonium bromide (7.95 g, 16.4 mmol) in THF (40 mL) at −78 °C. After 30 min, hexane (50 mL) was added, followed by the dropwise addition *via* cannula of a solution of **19** (800 mg, 3.29 mmol) in THF (10 mL). The reaction mixture was allowed to warm to rt over 12 h. The reaction mixture was quenched with sat aq NH_4Cl (2 mL). Brine (10 mL) was added, the organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1) gave (*Z*)-**20** as a colourless oil (1.03 g, 85%, >98% de); R_f 0.16 (30-40 °C petrol/Et_2O, 10:1); $[\alpha]_D^{21}$ −23.6 (*c* 1.3 in $CHCl_3$); ν_{max} (film) 2927 (C−H), 1700 (C=O); δ_H (400 MHz, $CDCl_3$) 0.83-0.94 (3H, m, C(11′)H_3), 1.04-1.17 (3H, m, C(4)*Me*), 1.43-1.68 (29H, m, C(2)Me_2, C(4′)H_2-C(10′)H_2, CMe_3), 1.97-2.20 (2H, m, C(3′)H_2), 3.79-4.06 (1H, m, C(4)*H*), 4.79-4.86 (1H, m, C(5)*H*), 5.39-5.48 (1H, m, C(1′)*H*), 5.63-5.73 (1H,

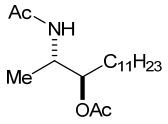
m, C(2′)*H*); δ_H (500 MHz, DMSO-d_6, 363 K) 0.90 (3H, t, *J* 6.8, C(11′)H_3), 1.07 (3H, d, *J* 6.5, C(4)*Me*), 1.25-1.57 (29H, m, C(2)Me_2, C(4′)H_2-C(10′)H_2, CMe_3), 2.04-2.21 (2H, m, C(3′)H_2), 3.91 (1H, app quintet, *J* 6.1, C(4)*H*), 4.81-4.88 (1H, m, C(5)*H*), 5.35-5.44 (1H, m, C(1′)*H*), 5.62-5.72 (1H, m, C(2′)*H*); δ_C (125 MHz, DMSO-d_6, 363 K) 14.5 (*C*(11′)), 15.7 (C(4)*Me*), 22.7, 25.2, 28.3, 28.6, 29.1, 29.3, 29.4, 29.6, 29.7, 32.0 (C(2)Me_2, *C*(3′)-*C*(10′), CMe_3), 56.3 (*C*(4)), 73.4 (*C*(5)), 79.8 (*C*Me$_3$), 92.6 (*C*(2)), 125.9 (*C*(2′)), 135.4 (*C*(1′)), 151.9 (N*C*O); *m/z* (ESI$^+$) 368 ([M+H]$^+$, 19%), 271 (100); HRMS (ESI$^+$) $C_{22}H_{42}NO_3^+$ ([M+H]$^+$) requires 368.3165; found 368.3179.

(4*S*,5*R*)-2,2,4-Trimethyl-*N*(3)-*tert*-butoxycarbonyl-5-undecan-1′-yl-oxazolidine 21



Pd/C (5 mg, 10% w/w) was added to a stirred solution of (*Z*)-**20** (50 mg, 0.14 mmol) in EtOAc (5 mL) at rt. The reaction mixture was stirred under H_2 (1 atm) for 6 h. The reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 1:1) gave **21** as a colourless oil (45 mg, 90%, >98% de); R_f 0.05 (30-40 °C petrol/Et_2O, 1:1); $[\alpha]_D^{21}$ −20.1 (*c* 1.2 in $CHCl_3$); ν_{max} (film) 2926 (C−H), 1699 (C=O); δ_H (400 MHz, $CDCl_3$) 0.88 (3H, app t, *J* 6.8, C(11')H_3), 1.04-1.14 (3H, m, C(4)*Me*), 1.22-1.67 (35H, m, C(2)Me_2, C(1')H_2-C(10')H_2, CMe_3), 3.76-4.01 (2H, m, C(4)*H*, C(5)*H*); δ_H (500 MHz, PhMe-d_8, 363 K) 0.92 (3H, t, *J* 6.9, C(11')H_3), 1.13 (3H, d, *J* 6.3 C(4)*Me*), 1.23-1.39 (18H, m, C(2')H_2-C(10')H_2), 1.46 (9H, s, CMe_3), 1.57 (3H, s, C(2)Me_A), 1.66 (3H, s, C(2)Me_B), 1.83-1.96 (2H, m, C(1')H_2), 3.84-3.90 (2H, m, C(4)*H*, C(5)*H*); *m/z* (FI$^+$) 369 ([M+H$^+$], 25%), 354 (100); HRMS (FI$^+$) $C_{22}H_{43}NO_3^+$ ([M+H$^+$]) requires 369.3243; found 369.3240.

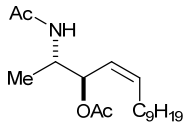
(2*S*,3*R*)-2-Acetamido-3-acetoxy-tetradecane [*N*,*O*-diacetyl xestoaminol C] 22



3 M aq HCl (1 mL) was added to a solution of **21** (50 mg, 0.14 mmol) in MeOH (10 mL) and heated at 50 °C for 3 h. The reaction mixture was concentrated *in vacuo*. The residue was dissolved in pyridine (10 mL) and Ac_2O (0.06 mL, 0.68 mmol) and DMAP (2 mg) were added sequentially. The reaction mixture was stirred for 12 h before being quenched with H_2O (2 mL). The reaction mixture was diluted with H_2O (10mL) and Et_2O (10mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10

mL). The combined organic layers were washed sequentially with sat aq $CuSO_4$ (2 × 10 mL), H_2O (10 mL) and brine (10 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/EtOAc, 1:1) gave **22** as white solid (34 mg, 80%, >98% de); R_f 0.18 (30-40 °C petrol/EtOAc, 1:1); mp 51-53 °C (30-40 °C petrol/EtOAc); $[\alpha]_D^{22}$ −22.7 (*c* 0.6 in MeOH); {lit.[4] $[\alpha]_D^{24}$ −21.8 (*c* 0.4 in MeOH), lit.[5] $[\alpha]_D^{24}$ −22.1 (*c* 0.2 in MeOH)}; ν_{max} (KBr) 3354, 2980, 2935, 1791, 1755, 1714, 1519; δ_H (400 MHz, $CDCl_3$) 0.87 (3H, t, *J* 6.8, C(14)*H*$_3$), 1.08 (3H, d, *J* 6.8, C(1)*H*$_3$), 1.20-1.37 (18H, m, C(5)*H*$_2$-C(13)*H*$_2$), 1.43-1.62 (2H, m, C(4)*H*$_2$), 1.94, (3H, s, CO*Me*), 2.08 (3H, s, CO*Me*), 4.10-4.19 (1H, m, C(2)*H*), 4.80-4.86 (1H, ddd, *J* 8.5, 5.1, 3.4, C(3)*H*), 5.90 (1H, br d, *J* 8.2, N*H*); δ_C (125 MHz, $CHCl_3$) 14.1, 14.8, 21.1, 22.7, 23.5, 25.6, 29.31, 29.34, 29.4, 29.5, 29.6, 31.3, 31.9, 47.5, 77.0, 169.3, 171.6; *m/z* (ESI^+) 336 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{18}H_{35}NNaO_3^+$ ($[M+Na]^+$) requires 336.2509; found 336.2502.

(2*S*,3*R*,4*Z*)-2-Acetamido-3-acetoxy-tetradec-4-ene 23

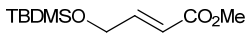


3 M aq HCl (1 mL) was added to a solution of (*Z*)-**20** (50 mg, 0.14 mmol) in MeOH (10 mL) and heated at 50 °C for 3 h. The reaction mixture was concentrated *in vacuo*. The residue was dissolved in pyridine (10 mL) and Ac_2O (0.06 mL, 0.68 mmol) and DMAP (2 mg) were added sequentially. The reaction mixture was stirred for 12 h before being quenched with H_2O (2 mL). The reaction mixture was diluted with H_2O (10mL) and Et_2O (10mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were washed sequentially with sat aq $CuSO_4$ (2 × 10 mL), H_2O (10 mL) and brine (10 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/EtOAc, 1:1) gave **23** as white solid (34 mg, 80%, >98% de); R_f 0.21 (30-40 °C petrol/EtOAc, 1:1); mp 55-57 °C (30-40 °C petrol/EtOAc); $[\alpha]_D^{22}$ −14.9 (*c* 0.8 in $CHCl_3$); ν_{max} (film) 2925, 1742, 1651, 1549; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.8, C(14)*H*$_3$), 1.13 (3H, d, *J* 6.8, C(1)*H*$_3$), 1.17-1.42 (14H, m, C(7)*H*$_2$-C(13)*H*$_2$), 1.97 (3H, s, CO*Me*), 2.07 (3H, s, CO*Me*), 2.08-2.25 (2H, m, C(6)*H*$_2$), 4.16-4.27 (1H, m, C(2)*H*), 5.29 (1H, dd, *J* 10.9, 9.2, C(3)*H*), 5.51-5.60 (2H, m, C(4)*H*, N*H*), 5.61-5.70 (1H, m, C(5)*H*); δ_C (125 MHz, $CHCl_3$) 14.5, 15.9, 21.6, 23.1, 23.9, 28.5, 29.7, 29.9, 29.95, 29.97, 32.3, 48.4, 73.2, 124.5,

[4] L. Garrido, E. Zubia, M. J. Ortega, S. Naranjo and J. Salva, *Tetrahedron*, **2001**, *57*, 4579.
[5] M. Ichihashi and K. Mori, *Biosci. Biotechnol. Biochem.*, **2002**, *67*, 329.

136.8, 169.7, 171.0; *m/z* (ESI^+) 334 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{18}H_{33}NNaO_3^+$ ($[M+Na]^+$) requires 334.2358; found 334.2354.

Methyl (*E*)-4-*tert*-butyldimethylsilyloxy-but-2-enote 26



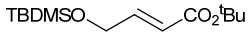
TBDMSCl (3.43 g, 22.7 mmol) was added in one portion to a stirred solution of but-2-ene-1,4-diol (0.93 mL, 11.4 mmol), imidazole (2.33 g, 34.1 mmol) and DMAP (30 mg) in DCM (30 mL) at rt. After stirring for 12 h, the reaction mixture was concentrated *in vacuo*. The residue was dissolved in Et_2O (30 mL) and washed with 1M aq HCl (30 mL), dried and concentrated *in vacuo* to give 1,4-bis-(*tert*-butyldimethylsilyloxy)but-2-ene as a colourless oil (3.5 g, 97%) that was used without purification; δ_H (400 MHz, $CDCl_3$) 0.07 (12H, s, 2 × Si*Me*$_2$), 0.90 (18H, s, 2 × SiC*Me*$_3$), 4.24 (4H, dd, *J* 2.7, 0.7, C(1)*H*$_2$, C(4)*H*$_2$), 5.56 (2H, td, *J* 2.7, 0.7, C(2)*H*, C(3)*H*).

O_3 was bubbled through a stirred solution of 1,4-bis-(*tert*-butyldimethylsilyloxy)but-2-ene (3.5 g, 11.0 mmol) in DCM (30 mL) at −78 °C until the solution turned blue. O_2 was then bubbled through the solution until it turned colourless. DMS (30 mL) was added dropwise *via* syringe and the reaction mixture stirred for 12 h. The reaction mixture was concentrated *in vacuo*. The residue was redissolved in Et_2O (30 mL) and washed with H_2O (30 mL), dried and concentrated *in vacuo* to give (*tert*-butyldimethylsilyloxy)acetaldehyde as a colourless oil (3.36 g, 86%) that was used without purification; δ_H (400 MHz, $CDCl_3$) 0.08 (6H, s, Si*Me*$_2$), 0.90 (9H, s, SiC*Me*$_3$), 4.17-4.21 (2H, m, C*H*$_2$), 9.67-9.69 (1H, m, C*H*O).

Methyl diethylphosphonoacetate (4.87 g, 23.2 mmol), LiCl (5.43 g, 129 mmol) and $^iPr_2NEt$ (3.46 mL, 21.2 mmol) were added to a stirred solution of (tri-*iso*-propylsilyloxy)acetaldehyde (3.36 g, 19.3 mmol) in MeCN (50 mL). The reaction mixture was stirred for 48 h and then quenched by addition of H_2O (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (40 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 60:1) gave **26** as a colourless oil (2.29 g, 52%, >98% de);[6] *Rf* 0.07 (30-40 °C petrol/Et_2O, 60:1); δ_H (400 MHz, $CDCl_3$) 0.09 (6H, s, Si*Me*$_2$), 0.93 (9H, s, SiC*Me*$_3$), 3.75 (3H, s, O*Me*), 4.34 (2H, dd, *J* 3.4, 2.4, C(4)*H*$_2$), 6.12 (1H, dt, *J* 15.4, 2.4, C(3)*H*), 7.01 (1H, dt, *J* 15.4, 3.4, C(2)*H*).

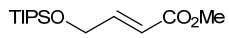
[6] E. Abraham, J. W. B. Cooke, S. G. Davies, A. Naylor, R. L. Nicholson, P. D. Price and A. D. Smith, *Tetrahedron*, **2007**, *63*, 5855.

tert-Butyl (_E_)-4-_tert_-butyldimethylsilyloxy-but-2-enote 27



tert-Butyl diethylphosphonoacetate (5.74 g, 22.8 mmol), LiCl (5.39 g, 127 mmol) and $^{i}Pr_2NEt$ (2.77 mL, 17.1 mmol) were added to a stirred solution of (*tert*-butyldimethylsilyloxy)acetaldehyde (3.30 g, 19.0 mmol) in MeCN (50 mL). The reaction mixture was stirred for 48 h and then quenched by addition of H_2O (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (40 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 60:1) gave **27** as a colourless oil (2.17 g, 67%, >98% de); R_f 0.2 (30-40 °C petrol/Et_2O, 60:1); ν_{max} (film) 1717 (C=O), 1661 (C=C); δ_H (400 MHz, $CDCl_3$) 0.06 (6H, s, Si*Me*$_2$), 0.90 (9H, s, SiC*Me*$_3$), 1.46 (9H, s, OC*Me*$_3$), 4.29 (2H, dd, *J* 3.5, 2.3, C(4)*H*$_2$), 5.97 (1H, dt, *J* 15.4, 2.3, C(2)*H*), 6.86 (1H, dt, *J* 15.4, 3.5, C(3)*H*); δ_C (100 MHz, $CDCl_3$) –5.5 (Si*Me*$_2$), 18.3 (Si*C*Me$_3$), 25.8 (SiC*Me*$_3$), 28.1 (OC*Me*$_3$), 62.1 (*C*(4)), 80.1 (O*C*Me$_3$), 121.4 (*C*(2)), 146.0 (*C*(3)), 166.0 (*C*(1)); *m/z* (CI^+) 272 ($[M]^+$, 100%); HRMS (CI^+) $C_{14}H_{28}O_3Si^+$ ($[M]^+$) requires 272.1808; found 272.1808.

Methyl (*E*)-4-tri-*iso*-propylsilyloxy- but-2-enote 28



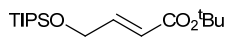
TIPSCl (4.86 mL, 22.7 mmol) was added in one portion to a stirred solution of but-2-ene-1,4-diol (0.93 mL, 11.4 mmol), imidazole (2.33 g, 34.1 mmol) and DMAP (30 mg) in DCM (30 mL) at rt. After stirring for 12 h, the reaction mixture was concentrated *in vacuo*. The residue was dissolved in Et_2O (30 mL) and washed with 1M aq HCl (30 mL), dried and concentrated *in vacuo* to give 1,4-bis-(tri-*iso*-propylsilyloxy)but-2-ene as a colourless oil (4.41 g, 97%) that was used without purification; δ_H (400 MHz, $CDCl_3$) 1.02-1.12 (42H, m, 2 × Si(C*HMe*$_2$)$_3$), 4.29-4.33 (4H, m, C(1)*H*$_2$, C(4)*H*$_2$), 5.30-5.33 (2H, m, C(2)*H*, C(3)*H*).

O_3 was bubbled through a stirred solution of 1,4-bis-(tri-*iso*-propylsilyloxy)but-2-ene (4.41 g, 11.0 mmol) in DCM (30 mL) at −78 °C until the solution turned blue. O_2 was then bubbled through the solution until it turned colourless. DMS (30 mL) was added dropwise *via* syringe and the reaction mixture stirred for 12 h. The reaction mixture was concentrated *in vacuo*. The residue was redissolved in Et_2O (30 mL) and washed with H_2O (30 mL), dried and concentrated *in vacuo* to give (tri-*iso*-propylsilyloxy)acetaldehyde as a colourless oil (4.38 g, 92%) that was used without purification; δ_H (400 MHz, $CDCl_3$) 1.02-1.10 (21H, m, Si(C*HMe*$_2$)$_3$), 4.25 (2H, d, *J* 1.0, C*H*$_2$), 9.73 (1H, t, *J* 1.0, C*H*O).

Methyl diethylphosphonoacetate (4.97 g, 23.6 mmol), LiCl (5.54 g, 132 mmol) and $^{i}Pr_2NEt$ (3.76 mL, 21.6 mmol) were added to a stirred solution of (tri-*iso*-propylsilyloxy)acetaldehyde (4.25 g, 19.7 mmol) in MeCN

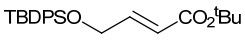
(50 mL). The reaction mixture was stirred for 48 h and then quenched by addition of H_2O (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (40 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 30:1) gave **28** as a colourless oil (2.79 g, 52%, >98% de); R_f 0.14 (30-40 °C petrol/Et_2O, 30:1); ν_{max} (film) 1728 (C=O), 1663 (C=C); δ_H (400 MHz, $CDCl_3$) 1.04-1.09 (21H, m, Si(C*H*Me_2)$_3$), 3.75 (3H, s, O*Me*), 4.38 (2H, dd, *J* 3.1, 2.4, C(4)H_2), 6.18 (1H, dt, *J* 15.4, 2.4, C(2)*H*), 7.02 (1H, dt, *J* 15.4, 3.1, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 11.9 (Si(*C*HMe$_2$)$_3$), 17.9 (Si(CH*Me*$_2$)$_3$), 51.5 (O*Me*), 62.4 (*C*(4)), 119.0 (*C*(2)), 147.8 (*C*(3)), 167.2 (*C*(1)); *m/z* (ESI^+) 273 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{14}H_{29}O_3Si^+$ ($[M+H]^+$) requires 273.1886; found 273.1880.

tert-Butyl (_E_)-4-tri-_iso_-propylsilyloxy-but-2-enoate 29



tert-Butyl diethylphosphonoacetate (6.13 g, 24.3 mmol), LiCl (4.84 g, 114 mmol) and $^iPr_2NEt$ (2.77 mL, 17.0 mmol) were added to a stirred solution of (tri-*iso*-propylsilyloxy)acetaldehyde (4.38 g, 20.3 mmol) in MeCN (50 mL). The reaction mixture was stirred for 48 h and then quenched by addition of H_2O (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (40 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 30:1) gave **29** as a colourless oil (2.94 g, 68%, >98% de); R_f 0.2 (30-40°C petrol/Et_2O, 50:1); ν_{max} (film) 1717 (C=O), 1661 (C=C); δ_H (400 MHz, $CDCl_3$) 1.03-1.16 (21H, m, Si(C*H*Me_2)$_3$), 1.49 (9H, s, CMe_3), 4.38-4.42 (2H, m, C(4)H_2), 6.02-6.08 (1H, m, C(2)*H*), 6.85-6.92 (1H, m, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 11.9 (Si(*C*HMe$_2$)$_3$), 17.9 (Si(CH*Me*$_2$)$_3$), 28.1 (C*Me*$_3$), 62.4 (*C*(4)), 80.1 (*C*Me$_3$), 121.3 (*C*(2)), 146.1 (*C*(3)), 166.1 (*C*(1)); *m/z* (CI^+) 315 ($[M+NH_4]^+$, 100%); HRMS (CI^+) $C_{17}H_{38}NO_3Si$ ($[M+NH_4]^+$) requires 332.2621; found 332.2615.

tert-Butyl (_E_)-4-_tert_-butyldiphenylsilyloxy-but-2-enoate 30

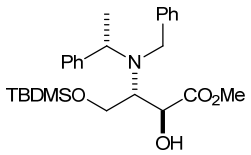


TBDPSCl (5.91 mL 22.7 mmol) was added in one portion to a stirred solution of but-2-ene-1,4-diol (0.93 mL, 11.4 mmol), imidazole (2.33 g, 34.1 mmol) and DMAP (30 mg) in DCM (30 mL) at rt. After stirring for 12 h, the reaction mixture was concentrated *in vacuo*. The residue was dissolved in Et_2O (30 mL) and washed with 1M aq HCl (30 mL), dried and concentrated *in vacuo* to give 1,4-bis-(*tert*-butyldiphenyloxy)but-2-ene as a colourless oil (6.28 g, 98%) that was used without purification; δ_H (400

MHz, $CDCl_3$) 1.01 (18H, s, 2 × SiC*Me*$_3$), 4.10-4.13 (4H, m, C(1)*H*$_2$, C(4)*H*$_2$), 5.62-5.65 (2H, m, C(2)*H*, C(3)*H*), 7.31-7.44 (12H, m, *Ph*), 7.60-7.65 (8H, m, *Ph*).

O_3 was bubbled through a stirred solution of 1,4-bis-(*tert*-butyldiphenylsilyloxy)but-2-ene (6.28 g, 11.1 mmol) in DCM (30 mL) at −78 °C until the solution turned blue. O_2 was then bubbled through the solution until it turned colourless. DMS (30 mL) was added dropwise *via* syringe and the reaction mixture stirred for 12 h. The reaction mixture was concentrated *in vacuo*. The residue was redissolved in Et_2O (30 mL) and washed with H_2O (30 mL), dried and concentrated *in vacuo* to give (*tert*-butyldiphenylsilyloxy)acetaldehyde as a colourless oil (5.77 g, 87%) that was used without purification; δ_H (400 MHz, $CDCl_3$) 1.10 (9H, s, SiC*Me*$_3$), 4.22 (2H, d, *J* 0.7, C*H*$_2$), 7.38-7.49 (6H, m, *Ph*), 7.63-7.69 (4H, m, *Ph*), 9.73 (1H, t, *J* 0.7, C*H*O). *tert*-Butyl diethylphosphonoacetate (6.72 g, 26.7 mmol), LiCl (5.25 g, 124 mmol) and $^{i}Pr_2NEt$ (3.0 mL, 18.5 mmol) were added to a stirred solution of (*tert*-butyldiphenylsilyloxy)acetaldehyde (5.60 g, 22.2 mmol) in MeCN (50 mL). The reaction mixture was stirred for 48 h and then quenched by addition of H_2O (5 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (40 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 50:1) gave **30** as a white solid (3.89 g, 68%, >98% de); R_f 0.2 (30-40 °C petrol/Et_2O, 50:1); $C_{24}H_{32}O_3Si$ requires C, 72.7; H, 8.1%; found C, 72.6; H, 8.1%; mp 73-75 °C (30-40 °C petrol/Et_2O); ν_{max} (KBr) 1709 (C=O), 1652 (C=C); δ_H (400 MHz, $CDCl_3$) 1.18 (9H, s, SiC*Me*$_3$), 1.59 (9H, s, OC*Me*$_3$), 4.41 (2H, app t, *J* 2.4, C(4)*H*$_2$), 6.26-6.34 (1H, m, C(2)*H*), 6.95-7.02 (1H, m, C(3)*H*), 7.42-7.51 (6H, m, *Ph*), 7.73-7.78 (4H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.3 (Si*C*Me$_3$), 26.9 (SiC*Me*$_3$), 28.2 (OC*Me*$_3$), 63.0 (*C*(4)), 80.2 (*C*Me$_3$), 121.6 (*C*(2)), 127.9, 129.9, 133.1, 135.5 (*Ph*), 145.6 (*C*(3)), 166.0 (*C*(1)); *m/z* (CI^+) 414 ($[M+NH_4]^+$, 100%); HRMS (CI^+) $C_{24}H_{36}NO_3Si$ ($[M+NH_4]^+$) requires 414.2464; found 414.2454.

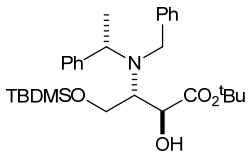
Methyl (2*S*,3*S*,α*S*)-2-hydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(*tert*-butyldimethylsilyloxy)butanoate 31



BuLi (2.5 M in hexanes, 2.7 mL, 6.74 mmol) was added dropwise *via* syringe to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (1.47 g, 6.96 mmol) in THF (20 mL) at −78 °C. After stirring for 30 min a solution of **26** (1.0 g, 4.35 mmol) in THF (10 mL) at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with (+)-CSO (4.2 g, 18.4 mmol) and

allowed to warm to rt over 12 h. Sat aq NH_4Cl (5 mL) was added and the mixture was stirred for 5 min before being concentrated *in vacuo*. The residue was partitioned between DCM (50 mL) and 10% aq citric acid (10 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 × 50 mL). The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*. The residue was dissolved in Et_2O (50 mL), the insoluble CSO residues were filtered off, and the filter cake was washed with Et_2O (2 × 20 mL). The filtrate was concentrated *in vacuo* and the process was repeated. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 20:1) gave **31** as a colourless oil (1.55 g, 78%, >98% de); R_f 0.25 (30-40 °C petrol/Et_2O 20:1); $[\alpha]_D^{21}$ +26.2 (*c* 1.0 in $CHCl_3$); {lit.[7] $[\alpha]_D^{21}$ +25.0 (*c* 1.2 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 0.02 (3H, s, Si*Me*$_A$), 0.03 (3H, s, Si*Me*$_B$), 0.88 (SiC*Me*$_3$), 1.37 (3H, d, *J* 6.8, C(α)*Me*), 2.98 (1H, d, *J* 6.5, O*H*), 3.55-3.62 (1H, m, C(3)*H*), 3.68 (3H, s, O*Me*), 3.70-3.76 (1H, m, C(4)H_A), 3.83 (1H, d, *J* 15.2, NCH_B), 3.87-4.02 (3H, m, C(2)*H*, C(4)H_B, C(α)*H*,), 4.14 (1H, d, *J* 15.2, NCH_B), 7.16-7.48 (10H, m, *Ph*).

tert-Butyl (2*S*,3*S*,α*S*)-2-hydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-_tert_-butyldimethylsilyloxy-butanoate 32

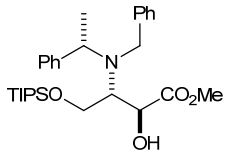


BuLi (2.5 M in hexanes, 5.7 mL, 14.2 mmol) was added dropwise *via* syringe to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (3.1 g, 14.7 mmol) in THF (50 mL) at −78 °C. After stirring for 30 min a solution of **27** (2.5 g, 9.19 mmol) in THF (20 mL) at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with (+)-CSO (4.2 g, 18.4 mmol) and allowed to warm to rt over 12 h. Sat aq NH_4Cl (5 mL) was added and the mixture was stirred for 5 min before being concentrated *in vacuo*. The residue was partitioned between DCM (50 mL) and 10% aq citric acid (10 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 × 50 mL). The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*. The residue was dissolved in Et_2O (50 mL), the insoluble CSO residues were filtered off, and the filter cake was washed with Et_2O (2 × 20 mL). The filtrate was concentrated *in vacuo* and the process was repeated. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 30:1)

[7] E. Abraham, J. W. B. Cooke, S. G. Davies, A. Naylor, R. L. Nicholson, P. D. Price and A. D. Smith, *Tetrahedron*, **2007**, *63*, 5855.

gave **32** as a colourless oil (3.33 g, 91%, >98% de); R_f 0.05 (30-40 °C petrol:Et_2O, 30:1); $[\alpha]_D^{22}$ +58.7 (*c* 1.05 in $CHCl_3$); ν_{max} (film) 3491 (O−H), 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 0.01 (3H, s, Si*Me*$_A$), 0.04 (3H, s, Si*Me*$_B$), 0.90 (9H, s, SiC*Me*$_3$), 1.35 (3H, d, *J* 7.0, C(α)*Me*), 1.43 (9H, s, OC*Me*$_3$), 3.04 (1H, d, *J* 6.1, O*H*), 3.51-3.56 (1H, m, C(3)*H*), 3.73-3.83 (3H, m, C(4)H_2, NCH_A), 3.92 (1H, dd, *J* 6.3, 1.8, C(2)*H*), 4.00 (1H, q, *J* 6.8, C(α)*H*), 4.21 (1H, d, *J* 15.2, NCH_B), 7.20-7.47 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.6 (Si*Me*$_A$), −5.5 (Si*Me*$_B$), 18.5 (Si*C*Me$_3$), 18.8 (C(α)*Me*), 26.1 (SiC*Me*$_3$), 28.1 (OC*Me*$_3$), 51.2 (N*C*H$_2$), 58.0 (*C*(α)), 59.9 (*C*(3)), 61.9 (*C*(4)), 71.7 (*C*(2)), 82.0 (O*C*Me$_3$), 126.4, 126.8 (*p-Ph*), 127.8, 127.9, 128.1, 128.2 (*o-Ph, m-Ph*), 142.2, 143.5 (*i-Ph*), 173.7 (*C*(1)); *m/z* (ESI$^+$) 500 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{45}NO_4Si^+$ ([M+H]$^+$) requires 500.3196; found 500.3209.

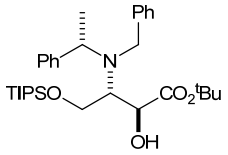
Methyl (2*S*,3*S*,α*S*)-2-hydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-tri-*iso*-propylsilyloxy-butanoate 33



BuLi (2.5 M in hexanes, 8.14 mL, 11.4 mmol) was added dropwise *via* syringe to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (2.48 g, 11.8 mmol) in THF (50 mL) at −78 °C. After stirring for 30 min a solution of **28** (2.0 g, 7.35 mmol) in THF (20 mL) at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with (+)-CSO (3.37 g, 14.7 mmol) and allowed to warm to rt over 12 h. Sat aq NH_4Cl (5 mL) was added and the mixture was stirred for 5 min before being concentrated *in vacuo*. The residue was partitioned between DCM (50 mL) and 10% aq citric acid (10 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 × 50 mL). The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*. The residue was dissolved in Et_2O (50 mL), the insoluble CSO residues were filtered off, and the filter cake was washed with Et_2O (2 × 20 mL). The filtrate was concentrated *in vacuo* and the process was repeated. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 20:1) gave **33** as a colourless oil (2.75 g, 75%, >98% de); R_f 0.18 (30-40 °C petrol/Et_2O, 20:1); $C_{29}H_{45}NO_4Si$ requires C, 69.7; H, 9.1; N, 2.8%; found C, 69.6; H, 9.1; N, 2.8%; $[\alpha]_D^{22}$ +37.0 (*c* 2.3 in $CHCl_3$); ν_{max} (film) 3515 (O−H), 1737 (C=O); δ_H (400 MHz, $CDCl_3$) 1.02-1.06 (21H, m, Si(C*HMe*$_2$)$_3$), 1.36 (3H, d, *J* 6.8, C(α)*Me*), 3.03 (1H, d, *J* 6.2, O*H*), 3.55-3.61 (1H, m, C(3)*H*), 3.67 (3H, s, O*Me*), 3.82 (1H, d, *J* 15.0, NCH_A), 3.79-3.85 (1H, m, C(4)H_A), 3.93-4.02 (2H, m, C(4)H_B, C(α)*H*), 4.05-4.10 (1H, m, C(2)*H*),

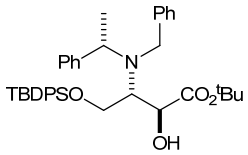
4.14 (1H, d, *J* 15.0, NCH_B), 7.20-7.46 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 11.9 (Si(*C*HMe$_2$)$_3$), 17.9 (Si(CH*Me*$_2$)$_3$), 18.1 (C(α)*Me*), 51.4 (N*C*H$_2$), 52.1 (O*Me*), 58.0 (*C*(α)), 60.1 (*C*(3)), 62.2 (*C*(4)), 71.0 (*C*(2)), 126.6, 127.0 (*p-Ph*), 127.9, 128.1, 128.2, 128.3 (*o-Ph*, *m-Ph*), 141.7, 143.1 (*i-Ph*), 174.7 (*C*(1)); *m/z* (ESI$^+$) 522 ([M+Na]$^+$, 28%), 500 (100); HRMS (ESI$^+$) $C_{29}H_{46}NO_4Si^+$ ([M+H]$^+$) requires 500.3196; found 500.3194.

tert-Butyl (2*S*,3*S*,α*S*)-2-hydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-tri-*iso*-propylsilyloxy-butanoate 34



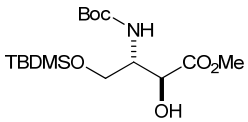
BuLi (2.5 M in hexanes, 4.9 mL, 12.3 mmol) was added dropwise *via* syringe to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (2.70 g, 12.7 mmol) in THF (50 mL) at −78 °C. After stirring for 30 min a solution of **29** (2.5 g, 8.0 mmol) in THF (20 mL) at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with (+)-CSO (3.64 g, 16.0 mmol) and allowed to warm to rt over 12 h. Sat aq NH_4Cl (5 mL) was added and the mixture was stirred for 5 min before being concentrated *in vacuo*. The residue was partitioned between DCM (50 mL) and 10% aq citric acid (10 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 × 50 mL). The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*. The residue was dissolved in Et_2O (50 mL), the insoluble CSO residues were filtered off, and the filter cake was washed with Et_2O (2 × 20 mL). The filtrate was concentrated *in vacuo* and the process was repeated. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1) gave **34** as a colourless oil (3.56 g, 82%, >98% de); R_f 0.24 (30-40 °C petrol/Et_2O, 10:1); $[\alpha]_D^{28}$ +37.4 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 3505 (O−H), 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 0.98-1.14 (21H, m, Si(C*HMe*$_2$)$_3$), 1.35 (3H, d, *J* 6.8, C(α)*Me*), 1.42 (9H, s, C*Me*$_3$), 3.48-3.54 (1H, m, C(3)*H*), 3.80 (1H, d, *J* 15.2, NCH_A), 3.84-3.88 (2H, m, C(4)H_2), 3.97-4.00 (1H, m, C(2)*H*), 4.02 (1H, q, *J* 6.8, C(α)*H*), 4.20 (1H, d, *J* 15.2, NCH_B), 7.20-7.47 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 12.0 (Si(*C*HMe$_2$)$_3$), 18.1 (Si(CH*Me*$_2$)$_3$), 18.2 (C(α)*Me*), 28.1 (C*Me*$_3$), 51.2 (N*C*H$_2$), 58.3 (*C*(α)), 60.6 (*C*(3)), 62.0 (*C*(4)), 71.8 (*C*(2)), 82.1 (*C*Me$_3$), 126.5, 126.8 (*p-Ph*), 128.0, 128.1, 128.2, 128.3 (*o-Ph*, *m-Ph*), 142.2, 144.0 (*i-Ph*), 173.7 (*C*(1)); *m/z* (ESI$^+$) 542 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{32}H_{52}NO_4Si$ ([M+H]$^+$) requires 542.3666; found 542.3676.

***tert*-Butyl (2*S*,3*S*,α*S*)-2-hydroxy-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-*tert*-butyldiphenylsilyloxy-butanoate 35**



BuLi (2.5 M in hexanes, 3.9 mL, 9.8 mmol) was added dropwise *via* syringe to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (2.12 g, 10.1 mmol) in THF (50 mL) at −78 °C. After stirring for 30 min a solution of **30** (2.5 g, 6.3 mmol) in THF (20 mL) at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with (+)-CSO (2.9 g, 12.6 mmol) and allowed to warm to rt over 12 h. Sat aq NH_4Cl (5 mL) was added and the mixture was stirred for 5 min before being concentrated *in vacuo*. The residue was partitioned between DCM (50 mL) and 10% aq citric acid (10 mL). The organic layer was separated and the aqueous layer was extracted with DCM (2 × 50 mL). The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*. The residue was dissolved in Et_2O (50 mL), the insoluble CSO residues were filtered off, and the filter cake was washed with Et_2O (2 × 20 mL). The filtrate was concentrated *in vacuo* and the process was repeated. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1) gave **35** as a colourless oil (3.5 g, 89%, >98% de); R_f 0.2 (30-40 °C petrol/Et_2O, 10:1); $[\alpha]_D^{28}$ +40.1 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 3499 (O−H), 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 1.06 (9H, s, SiC*Me*$_3$), 1.27 (3H, d, *J* 6.8, C(α)*Me*), 1.31 (9H, s, OC*Me*$_3$), 3.03 (1H, d, *J* 5.6, O*H*), 3.59 (1H, td, *J* 6.8, 1.8, C(3)*H*), 3.80 (1H, d, *J* 15.2, NCH_A), 3.84 (2H, d, *J* 7.3, C(4)H_2), 4.00 (1H, q, *J* 6.8, C(α)*H*), 4.02-4.06 (1H, m, C(2)*H*), 4.13 (1H, d, *J* 14.9, NCH_B), 7.20-7.76 (20H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.4 (Si*C*Me$_3$), 19.2 (C(α)*Me*), 27.0 (SiC*Me*$_3$), 28.0 (OC*Me*$_3$), 51.2 (N*C*H$_2$), 58.0 (*C*(α)), 60.4 (*C*(3)), 62.5 (*C*(4)), 71.6 (*C*(2)), 82.2 (O*C*Me$_3$), 126.5, 126.9, 127.6, 127.72, 127.74, 127.9, 128.2, 128.3, 129.6, 129.7, 133.4, 134.8, 135.56, 135.59, 141.9, 143.9 (*Ph*), 173.5 (*C*(1)); *m/z* (ESI$^+$) 625 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{39}H_{50}NO_4Si$ ([M+H]$^+$) requires 624.3509; found 624.3514.

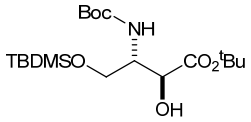
Methyl (2*S*,3*S*)-2-hydroxy-3-[*N*-(*tert*-butoxycarbonyl)amino]-4-*tert*-butyldimethylsilyloxy-butanoate 36



Pearlman's catalyst (125 mg, 25% w/w) was added to a vigorously stirred solution of **31** (500 mg, 1.09 mmol) and Boc_2O (262 mg, 1.20 mmol) in EtOAc (15 mL) and the mixture was placed under H_2 (5 atm).

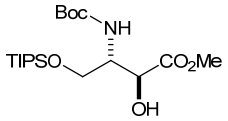
Stirring continued for 12 h, after which time the reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 5:1; then 30-40 °C petrol/Et_2O, 1:1) gave **36** as a colourless oil (270 mg, 68%, >98% de); R_f 0.08 (30-40 °C petrol/Et_2O, 5:1); $C_{16}H_{33}NO_6Si$ requires C, 52.9; H, 9.15; N, 3.85%; found C, 52.9; H, 9.2; N, 4.0%; $[\alpha]_D^{21}$ +26.8 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3452 (O−H), 1719 (C=O); δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, Si*Me*$_2$), 0.87 (9H, s, SiC*Me*$_3$), 1.43 (9H, s, C*Me*$_3$), 3.38-3.49 (1H, br s, O*H*), 3.64-3.78 (2H, m, C(4)*H*$_2$), 3.75 (3H, s, O*Me*), 3.97-4.06 (1H, m, C(3)*H*), 4.21-4.28 (1H, m, C(2)*H*), 5.12 (1H, d, *J* 8.9, N*H*); δ_C (100 MHz, $CDCl_3$) −5.7 (Si*Me*$_A$), −5.7 (Si*Me*$_B$), 18.3 (Si*C*Me$_3$), 25.8 (SiC*Me*$_3$), 28.3 (OC*Me*$_3$), 52.4 (O*Me*), 53.4 (*C*(3)), 62.0 (*C*(4)), 71.6 (*C*(2)), 79.7 (O*C*Me$_3$), 155.3 (N*C*O), 173.2 (*C*(1)); *m/z* (ESI$^+$) 386 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{16}H_{33}NNaO_6Si$ ([M+Na$^+$]) requires 386.1975; found 386.1962.

tert-Butyl (2*S*,3*S*)-2-hydroxy-3-[*N*-(_tert_-butoxycarbonyl)amino]-4-_tert_-butyldimethylsilyloxy-butanoate 37



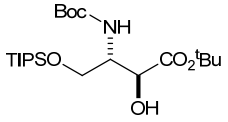
Pearlman's catalyst (62.5 mg, 25% w/w) was added to a vigorously stirred solution of **32** (250 mg, 0.50 mmol) and Boc_2O (120 mg, 0.55 mmol) in EtOAc (10 mL) and the mixture was placed under H_2 (5 atm). Stirring continued for 12 h, after which time the reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 5:1; then 30-40 °C petrol/Et_2O, 1:1) gave **37** as a colourless oil (175 mg, 86%, >98% de); R_f 0.18 (30-40 °C petrol/Et_2O, 5:1); $[\alpha]_D^{17}$ +22.0 (*c* 0.8 in $CHCl_3$); ν_{max} (film) 3447 (O−H), 1722 (C=O), 1716 (C=O); δ_H (400 MHz, $CDCl_3$) 0.065 (3H, s, Si*Me*$_A$), 0.068 (3H, s, Si*Me*$_B$), 0.90 (9H, s, SiC*Me*$_3$), 1.46 (9H, s, OC*Me*$_3$), 1.50 (9H, s, OC*Me*$_3$), 3.41 (1H, d, *J* 8.9, O*H*), 3.76 (2H, dq, *J* 13.7, 3.8, C(4)*H*$_2$), 3.91-4.00 (1H, m, C(3)*H*), 4.18 (1H, dd, *J* 8.9, 4.4, C(2)*H*), 5.20 (1H, d, *J* 8.9, N*H*); δ_C (100 MHz, $CDCl_3$) −6.6 (Si*Me*$_2$), 17.3 (Si*C*Me$_3$) 24.8 (SiC*Me*$_3$) 27.0 (OC*Me*$_3$), 27.4 (OC*Me*$_3$), 52.1 (*C*(3)), 62.1 (C(4)), 71.7 (*C*(2)), 78.6 (O*C*Me$_3$), 81.5 (O*C*Me$_3$), 154.4 (N*C*O), 170.6 (*C*(1)); *m/z* (ESI$^+$) 406 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{19}H_{40}NO_6Si$ ([M+H$^+$]) requires 406.2625; found 406.2633.

Methyl (2*S*,3*S*)-2-hydroxy-3-[*N*-(*tert*-butoxycarbonyl)amino]-4-tri-*iso*-propylsilyloxy-butanoate 38



Pearlman's catalyst (1.25 g, 25% w/w) was added to a vigorously stirred solution of **33** (5.0 g, 10.0 mmol) and Boc_2O (2.4 g, 11.0 mmol) in EtOAc (50 mL) and the mixture was placed under H_2 (5 atm). Stirring continued for 12 h, after which time the reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1; then 30-40 °C petrol/Et_2O, 1:1) gave **38** as a colourless oil (3.81 g, 94%, >98% de); R_f 0.08 (30-40 °C petrol/Et_2O, 10:1); $C_{19}H_{39}NO_6Si$ requires C, 56.3; H, 9.7; N, 3.45%; found C, 56.2; H, 9.7; N, 3.5%; $[\alpha]_D^{21}$ +17.3 (*c* 0.4 in $CHCl_3$); ν_{max} (film) 3453 (O−H), 1732 (C=O), 1720 (C=O); δ_H (400 MHz, $CDCl_3$) 1.01-1.09 (21H, m, Si(C*H*Me$_2$)$_3$), 1.45 (9H, s, C*Me*$_3$), 3.54 (1H, br s, O*H*), 3.74-3.91 (2H, m, C(4)H_2), 3.78 (3H, s, O*Me*), 3.95-4.05 (1H, m, C(3)*H*), 4.26-4.34 (1H, m, C(2)*H*), 5.19 (1H, d *J* 8.5, N*H*); δ_C (100 MHz, $CDCl_3$) 11.8 (Si(*C*HMe$_2$)$_3$), 17.8 (Si(CH*Me*$_2$)$_3$), 28.3 (C*Me*$_3$), 52.5 (O*Me*), 53.5 (*C*(3)), 62.9 (*C*(4)), 72.1 (*C*(2)), 79.7 (*C*Me$_3$), 155.4 (N*C*O), 173.1 (*C*(1)); *m/z* (ESI$^+$) 428 ([M+Na]$^+$, 44%), 406 (100); HRMS (ESI$^+$) $C_{19}H_{40}NO_6Si^+$ ([M+H]$^+$) requires 406.2625; found 406.2615.

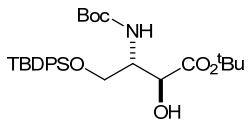
***tert*-Butyl (2*S*,3*S*)-2-hydroxy-3-[*N*-(*tert*-butoxycarbonyl)amino]-4-tri-*iso*-propylsilyloxy-butanoate 39**



Pearlman's catalyst (250 mg, 25% w/w) was added to a vigorously stirred solution of **34** (1.0 g, 1.85 mmol) and Boc_2O (443 mg, 2.03 mmol) in EtOAc (20 mL) and the mixture was placed under H_2 (5 atm). Stirring continued for 12 h, after which time the reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 9:1; then 30-40 °C petrol/Et_2O, 1:1) gave **39** as a colourless oil (744 mg, 90%, >98% de); R_f 0.08 (30-40 °C petrol/Et_2O, 9:1); $C_{22}H_{45}NO_6Si$ requires C 59.0, H 10.1, N 3.1%; found C 59.0, H 10.15, N 3.1%; $[\alpha]_D^{18}$ +36.9 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3452 (O−H), 1721 (C=O); δ_H (400 MHz, $CDCl_3$) 1.03-1.16 (21H, m, Si(C*H*Me$_2$)$_3$), 1.45 (9H, s, C*Me*$_3$), 1.49 (9H, s, C*Me*$_3$), 3.54 (1H, d, *J* 9.6, O*H*), 3.82-3.98 (3H, m, C(3)*H*, C(4)H_2), 4.22 (1H, dd, *J* 9.6, 4.3, C(2)*H*), 5.31 (1H, d, *J* 8.8, N*H*); δ_C (100 MHz, $CDCl_3$) 11.6 (Si(*C*HMe$_2$)$_3$), 17.8 (Si(CH*Me*$_2$)$_3$), 27.9 (C*Me*$_3$), 28.3 (C*Me*$_3$), 53.1 (*C*(3)), 63.4 (*C*(4)), 72.8 (*C*(2)), 79.4 (*C*Me$_3$), 82.3

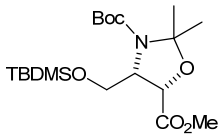
(*C*Me$_3$), 155.3 (N*C*O), 171.5 (*C*(1)); *m/z* (ESI$^+$) 448 ([M+H]$^+$, 100%]; HRMS (ESI$^+$) $C_{22}H_{46}NO_6Si$ ([M+H$^+$]) requires 448.3094; found 448.3088.

tert-Butyl (2*S*,3*S*)-2-hydroxy-3-[*N*-(_tert_-butoxycarbonyl)amino]-4-_tert_-butyldiphenylsilyloxy-butanoate 40



Pearlman's catalyst (500 mg, 25% w/w) was added to a vigorously stirred solution of **35** (1.00 g, 1.60 mmol) and Boc_2O (350 mg, 1.76 mmol) in EtOAc (50 mL) and the mixture was placed under H_2 (5 atm). Stirring continued for 12 h, after which time the reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 9:1; then 30-40 °C petrol/Et_2O, 1:1) gave **40** as a colourless oil (696 mg, 82%, >98% de); R_f 0.05 (30-40 °C petrol/Et_2O, 9:1); $[\alpha]_D^{18}$ +17.2 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 3452 (O−H), 1720 (C=O); δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, SiC*Me*$_3$), 1.41 (9H, s, OC*Me*$_3$), 1.47 (9H, s, OC*Me*$_3$), 3.40 (1H, d, *J* 8.8, O*H*), 3.68-3.83 (2H, m, C(4)H_2), 3.97-4.08 (1H, m, C(3)*H*), 4.24 (1H, dd, *J* 8.6, 4.3, C(2)*H*), 5.24 (1H, d, *J* 8.8, N*H*), 7.34-7.48 (6H, m, *Ph*), 7.63-7.71 (4H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.1 (Si*C*Me$_3$), 26.8 (SiC*Me*$_3$), 27.9 (OC*Me*$_3$), 28.4 (OC*Me*$_3$), 53.5 (*C*(3)), 63.7 (*C*(4)), 72.6 (*C*(2)), 79.6 (O*C*Me$_3$), 82.7 (O*C*Me$_3$), 127.8, 129.9, 132.5, 132.6 (*Ph*), 155.5 (N*C*O), 171.6 (*C*(1)); *m/z* (ESI$^+$) 552 ([M+Na]$^+$, 100%), 530 (11); HRMS (ESI$^+$) $C_{29}H_{43}NNaO_6Si$ ([M+Na]$^+$) requires 552.2757; found 552.2758.

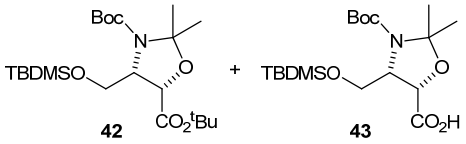
(4*S*,5*S*)-2,2-Dimethyl-*N*(3)-_tert_-butoxycarbonyl-4-_tert_-butyldimethylsilyloxymethyl-5-methoxycarbonyl-oxazolidine 41



$BF_3{\cdot}Et_2O$ (1 M in Et_2O) was added dropwise to a stirred solution of **36** (240 mg, 0.66 mmol) and 2,2-dimethoxypropane (5 mL) in acetone (10 mL) until a permanent colour change from colourless to dark orange was observed. After stirring at rt for 12 h Et_3N was added dropwise until pH 7 was achieved and the reaction mixture was concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1; then 30-40 °C petrol/Et_2O, 2:1) gave **41** as a colourless oil (first to elute, 132 mg, 48%, >98% de) and unreacted **36** as a colourless oil (second to elute, 93 mg, 39%, >98% de).

Data for **41**: R_f 0.4 (30-40 °C petrol/Et_2O, 2:1); $C_{19}H_{37}NO_6Si$ requires C, 56.5; H, 9.2; N, 3.5%; found C, 56.7; H, 9.25; N, 3.5%; $[\alpha]_D^{22}$ +18.9 (*c* 0.2 in $CHCl_3$); ν_{max} (film) 1770 (C=O), 1704 (C=O); δ_H (400 MHz, $CDCl_3$) 0.03-0.05 (6H, m, Si*Me*$_2$), 0.86-0.90 (9H, m, SiC*Me*$_3$), 1.46-1.50 (9H, s, OC*Me*$_3$), 1.50-1.56 (3H, m, C(2)*Me*$_A$), 1.61-1.67 (3H, m, C*Me*$_B$), 3.59-3.87 (2H, m, C(4)C*H*$_2$), 3.77 (3H, s, O*Me*), 4.08-4.26 (1H, m, C(4)*H*), 4.61-4.67 (1H, m, C(5)*H*); *m/z* (ESI$^+$) 404 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{19}H_{38}NO_6Si^+$ ([M+H]$^+$) requires 404.2468; found 404.2463.

(4*S*,5*S*)-2,2-Dimethyl-*N*(3),5-di-*tert*-butoxycarbonyl-4-*tert*-butyldimethylsilyloxymethyl-oxazolidine 42 and (4*S*,5*S*)-2,2-dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-*tert*-butyldimethylsilyloxymethyl-oxazolidine-5-carboxylic acid 43



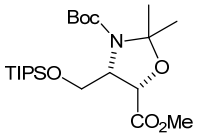
$BF_3{\cdot}Et_2O$ (1 M in Et_2O) was added dropwise to a stirred solution of **37** (1.20 g, 2.96 mmol) and 2,2-dimethoxypropane (25 mL) in acetone (100 mL) until a permanent colour change from colourless to dark orange was observed. After stirring at rt for 12 h Et_3N was added dropwise until pH 7 was achieved and the reaction mixture was concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1; then 30-40 °C petrol/Et_2O, 2:1) gave **42** as a colourless oil (first to elute, 686 mg, 52%, >98% de) and **43** as a pale yellow oil (second to elute, 230 mg, 20%, >98% de).

Data for **42**: R_f 0.54 (30-40 °C petrol/Et_2O, 2:1); $[\alpha]_D^{22}$ +10.5 (*c* 1.6 in $CHCl_3$); ν_{max} (film) 1759 (C=O), 1699 (C=O); δ_H (400 MHz, $CDCl_3$) 0.03-0.08 (6H, m, Si*Me*$_2$), 0.86-0.91 (9H, m, SiC*Me*$_3$), 1.42-1.67 (24H, m, , C(2)*Me*$_2$, 2 × OC*Me*$_3$), 3.58-3.76 (1H, m, C(4)C*H*$_A$), 3.82-3.99 (1H, m, C(4)C*H*$_B$), 4.03-4.23 (1H, m, C(4)*H*), 4.49-4.56 (1H, m, C(5)*H*); δ_H (250 MHz, DMSO-d_6, 363 K) 0.04 (6H, s, Si*Me*$_2$), 0.88 (9H, s, SiC*Me*$_3$), 1.45 (9H, s, OC*Me*$_3$), 1.47 (9H, s, OC*Me*$_3$), 1.54 (6H, s, C(2)*Me*$_2$), 3.66 (1H, dd, *J* 10.4, 3.4, C(4)C*H*$_A$), 3.87 (1H, dd, *J* 10.4, 5.2, C(4)C*H*$_B$), 4.05 (1H, ddd, *J* 6.4, 5.2, 3.4, C(4)*H*), 4.59 (1H, d, *J* 6.4, C(5)*H*); *m/z* (ESI$^+$) 446 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{44}NO_6Si^+$ ([M+H]$^+$) requires 446.2938; found 446.2937.

Data for **43**: R_f 0.38 (30-40 °C petrol/Et_2O, 2:1); $[\alpha]_D^{22}$ +7.56 (*c* 1.6 in $CHCl_3$); ν_{max} (film) 1801 (C=O), 1716 (C=O); δ_H (250 MHz, $CDCl_3$) 0.03 (6H, s, Si*Me*$_2$), 0.85 (9H, s, SiC*Me*$_3$), 1.39 (9H, s, OC*Me*$_3$), 1.52 (3H, s, C(2)*Me*$_A$), 1.55 (3H, s, C(2)*Me*$_B$), 3.59-3.65 (1H, m, C(4)C*H*$_A$), 3.71-3.78 (1H, m, C(4)C*H*$_B$), 3.93-3.97 (1H, m, C(4)*H*), 4.56 (1H, d, *J* 2.7, C(5)*H*); δ_C (62.5 MHz, $CDCl_3$) –5.1 (Si*Me*$_2$), 18.6 (Si*C*Me$_3$), 26.2 (SiC*Me*$_3$),

26.8 (C(2)*Me*$_A$), 27.3 (C(2)*Me*$_B$), 28.7 (OC*Me*$_3$), 53.1 (*C*(4)), 61.5 (C(4)*C*H$_2$), 73.8 (*C*(5)), 80.4 (O*C*Me$_3$), 111.2 (*C*(2)), 155.6 (N*C*O), 171.2 (*C*O$_2$H); *m/z* (ESI$^+$) 390 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{18}H_{36}NO_6Si$ ([M+H]$^+$) requires 390.2312; found 390.2300.

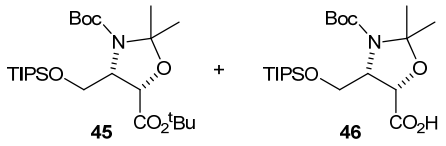
(4*S*,5*S*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-5-methoxycarbonyl-oxazolidine 44



$BF_3{\cdot}Et_2O$ (1 M in Et_2O) was added dropwise to a stirred solution of **38** (1.10 g, 2.72 mmol) and 2,2-dimethoxypropane (10 mL) in acetone (20 mL) until a permanent colour change from colourless to dark orange was observed. After stirring at 50 °C for 12 h the reaction mixture was allowed to cool to rt and Et_3N was added dropwise until pH 7 was achieved. The reaction mixture was then concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1; then 30-40 °C petrol/Et_2O, 2:1) gave **44** as a colourless oil (first to elute, 907 mg, 75%, >98% de) and unreacted **38** as a colourless oil (second to elute, 218 mg, 20%, >98% de).

Data for **44**: R_f 0.53 (30-40 °C petrol/Et_2O, 2:1); $[\alpha]_D^{22}$ +15.2 (*c* 1.8 in $CHCl_3$); ν_{max} (film) 1739 (C=O), 1699 (C=O); δ_H (400 MHz, $CDCl_3$) 1.01-1.10 (21H, m, Si(C*H*Me$_2$)$_3$), 1.47 (9H, s, C*Me*$_3$), 1.50-1.57 (3H, m, C(2)*Me*$_A$), 1.63-1.69 (3H, m, C(2)*Me*$_B$), 3.70-3.98 (2H, m, C(4)C*H*$_2$), 3.77 (3H, s, O*Me*), 4.12-4.29 (1H, m, C(4)*H*), 4.62-4.69 (1H, m, C(5)*H*); δ_H (500 MHz, DMSO-d_6, 363 K) 1.02-1.10 (21H, m, Si(C*H*Me$_2$)$_3$), 1.45 (9H, s, C*Me*$_3$), 1.50 (3H, s, C(2)*Me*$_A$), 1.56 (3H, s, C(2)*Me*$_B$), 3.70 (3H, s, O*Me*), 3.73 (1H, dd, *J* 10.1, 3.0, C(4)C*H*$_A$), 3.84 (1H, dd, *J* 10.1, 6.7, C(4)C*H*$_B$), 4.12 (1H, dt, *J* 6.3, 3.0, C(4)*H*), 4.76 (1H, d, C(5)*H*); δ_C (125 MHz, DMSO-d_6, 363 K) 12.4 (Si(*C*HMe$_2$)$_3$), 18.6 (Si(CH*Me*$_2$)$_3$), 25.1 (C(2)*Me*$_A$), 27.6 (C(2)*Me*$_B$), 28.9 (C*Me*$_3$), 52.2 (O*Me*), 60.7 (C(4)*C*H$_2$), 61.3 (*C*(4)), 74.0 (*C*(5)), 80.6 (*C*Me$_3$), 94.1 (*C*(2)), 151.8 (N*C*O), 168.5 (*C*O$_2$Me); *m/z* (ESI$^+$) 468 ([M+Na]$^+$, 54%), 446 (100); HRMS (ESI$^+$) $C_{22}H_{44}NO_6Si^+$ ([M+H]$^+$) requires 446.2938; found 446.2934.

(4*S*,5*S*)-2,2-Dimethyl-*N*(3),5-di-*tert*-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-oxazolidine 45 and (4*S*,5*S*)-2,2-dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-oxazolidine-5-carboxylic acid 46

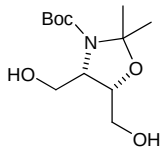


$BF_3 \cdot Et_2O$ (1 M in Et_2O) was added dropwise *via* syringe to a stirred solution of **39** (400 mg, 0.89 mmol) and 2,2-dimethoxypropane (10 mL) in acetone (50 mL) until a permanent colour change from colourless to dark orange was observed. After stirring at rt for 12 h Et_3N was added dropwise until pH 7 was achieved and the reaction mixture was concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 2:1) gave **45** as a colourless oil (first to elute, 328 mg, 75%, >98% de) and **46** as a colourless oil (second to elute, 96 mg, 25%, >98% de).

Data for **45**: R_f 0.53 (30-40 °C petrol/Et_2O, 2:1); $C_{25}H_{49}NO_6Si$ requires C, 61.6; H, 10.1; N, 2.9%; found C, 61.7; H, 10.1; N, 2.9%; $[\alpha]_D^{22}$ +8.1 (*c* 1.8 in $CHCl_3$); ν_{max} (film) 1759 (C=O), 1701 (C=O); δ_H (400 MHz, $CDCl_3$) 1.06-1.11 (21H, m, Si(C*H*M*e*$_2$)$_3$), 1.48 (9H, s, C*Me*$_3$), 1.49-1.59 (12H, m, C(2)*Me*$_A$, C*Me*$_3$), 1.61-1.69 (3H, s, C(2)*Me*$_B$), 3.70-4.04 (2H, m, C(4)C*H*$_2$), 4.07-4.31 (1H, m, C(4)*H*), 4.50-4.56 (1H, m, C(5)*H*); δ_H (500 MHz, PhMe-*d*$_8$, 363 K) 1.16-1.20 (21H, m, Si(C*H*M*e*$_2$)$_3$), 1.44 (9H, s, C*Me*$_3$), 1.45 (9H, s, C*Me*$_3$), 1.67 (6H, s, C(2)*Me*$_2$), 4.02 (1H, dd, *J* 10.1, 3.8, C(4)C*H*$_A$), 4.19 (1H, dd, *J* 10.1, 5.7, C(4)C*H*$_B$), 4.24-4.30 (1H, m, C(4)*H*), 4.45 (1H, d, *J* 6.3, C(5)*H*); δ_C (500 MHz, PhMe-*d*$_8$, 363 K) 12.3 (Si(*C*HMe$_2$)$_3$), 17.9 (Si(CH*Me*$_2$)$_3$), 27.0 (C(2)*Me*$_A$), 27.9 (C(2)*Me*$_B$), 28.0 (C*Me*$_3$), 29.2 (C*Me*$_3$), 60.6 (C(4)*C*H$_2$), 61.6 (*C*(4)), 74.9 (*C*(5)), 79.3 (*C*Me$_3$), 80.8 (*C*Me$_3$), 94.7 (*C*(2)), 151.5 (N*C*O), 166.1 (C(5)*C*O$_2$^{t}Bu); *m/z* (ESI$^+$) 510 ([M+Na]$^+$, 32%), 488 (100); HRMS (ESI$^+$) $C_{25}H_{50}NO_6Si^+$ ([M+H]$^+$) requires 488.3407; found 488.3427.

Data for **46**: R_f 0.38 (30-40 °C petrol/Et_2O, 2:1); $C_{21}H_{41}NO_6Si$ requires C, 58.4; H, 9.6; N, 3.25%; found C, 58.5; H, 9.6; N, 3.3%; $[\alpha]_D^{21}$ +11.1 (*c* 1.9 in $CHCl_3$); ν_{max} (film) 3358 (O−H), 1802 (C=O), 1721 (C=O); δ_H (400 MHz, $CDCl_3$) 1.01-1.08 (21H, m, Si(C*H*M*e*$_2$)$_3$), 1.43 (9H, s, C*Me*$_3$), 1.53 (3H, s, C(2)*Me*$_A$), 1.60 (3H, s, C(2)*Me*$_B$), 3.82 (2H, d, *J* 5.8, C(4)C*H*$_2$), 4.10-4.21 (1H, m, C(4)*H*), 4.48-4.61 (1H, m, C(5)*H*), 4.75 (1H, d, *J* 9.2, N*H*); δ_C (100 MHz, $CDCl_3$) 11.8 (Si(*C*HMe$_2$)$_3$), 17.8 (Si(CH*Me*$_2$)$_3$), 26.2 (C(2)*Me*$_A$), 26.9 (C(2)*Me*$_B$), 28.2 (C*Me*$_3$), 52.8 (*C*(4)), 61.5 (C(4)*C*H$_2$), 73.1 (*C*(5)), 79.7 (*C*Me$_3$), 110.6 (*C*(2)), 155.2 (N*C*O), 170.7 (*C*O$_2$H); *m/z* (ESI$^+$) 454 ([M+Na]$^+$, 45%) 432 (100); HRMS (ESI$^+$) $C_{21}H_{41}NNaO_6Si^+$ ([M+Na]$^+$) requires 454.2595; found 454.2587.

(4*S*,5*S*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4,5-bis(hydroxymethyl)oxazolidine 47

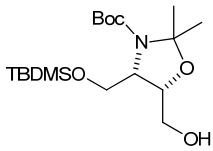


*From **42***: $LiAlH_4$ (1 M in THF, 0.11 mL, 0.11 mmol) was added dropwise *via* syringe to a stirred solution of **42** (50 mg, 0.11 mmol) in THF (2 mL) at 0 °C. After stirring for 12 h, the reaction was quenched with crushed ice, diluted with EtOAc (5 mL), and stirred for a further 3 h. The resultant mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo* to give **47** as a colourless oil (29 mg, quant, >98% de).

*From **45***: $LiAlH_4$ (1 M in THF, 0.4 mL, 0.4 mmol) was added dropwise *via* syringe to a stirred solution of **45** (50 mg, 0.10 mmol) in THF (5 mL) at 0 °C. After stirring for 12 h, the reaction was quenched with crushed ice, diluted with EtOAc (10 mL), and stirred for a further 3 h. The resultant mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo* to give **47** as a colourless oil (27 mg, quant, >98% de).

Data for **47**: $[\alpha]_D^{21}$ +0.9 (*c* 0.9 in $CHCl_3$); ν_{max} (film) 3425 (O−H), 1669 (C=O); δ_H (400 MHz, $CDCl_3$) 1.48 (9H, s, C*Me*$_3$), 1.49-1.60 (6H, m, C(2)*Me*$_2$), 3.18 (2H, br s, 2 × O*H*), 3.62-3.80 (2H, m, C(4)C*H*$_2$), 3.81-4.16 (3H, m, C(4)*H*, C(5)C*H*$_2$), 4.19-4.34 (1H, m, C(5)*H*); *m/z* (ESI^+) 262 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{12}H_{24}NO_5$ ($[M+H]^+$) requires 262.1654; found 262.1656.

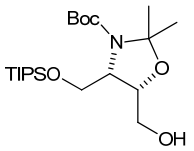
(4*S*,5*S*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-*tert*-butyldimethylsilyloxymethyl-5-hydroxymethyl-oxazolidine 48



DIBAL-H (1 M in DCM, 0.47 mL, 0.47 mmol) was added dropwise *via* syringe to a stirred solution of **42** (50 mg, 0.12 mmol) in DCM (5 mL) at 0 °C. After stirring for 12 h the reaction was quenched with sat aq NH_4Cl (0.1 mL) and stirred for a further 1 h. The resultant mixture was filtered through Celite (eluent DCM) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40°C petrol/Et_2O, 1:1) gave **48** as a colourless oil (first to elute, 24 mg, 51%, >98% de) and **47** as a colourless oil (second to elute, 8 mg, 24%, >98% de).

Data for **48**: R_f 0.09 (30-40°C petrol/Et_2O, 1:1); $[\alpha]_D^{22}$ +12.4 (*c* 0.9 in $CHCl_3$); ν_{max} (film) 3501 (O−H), 1703 (C=O); δ_H (400 MHz, $CDCl_3$) 0.06-0.16 (6H, m, Si*Me*$_2$), 0.88-0.94 (9H, m, SiC*Me*$_3$), 1.45-1.56 (12H, m, C(2)*Me*$_2$, OC*Me*$_3$), 3.10-3.30 (1H, m, O*H*), 3.59-3.76 (2H, m, C(4)C*H*$_2$), 3.79-3.88 (2H, m, C(5)C*H*$_2$), 3.93-4.09 (1H, m, C(4)*H*), 4.23-4.31 (1H, m, C(5)*H*); δ_H (250 MHz, DMSO-d_6, 363 K) 0.07 (3H, s, Si*Me*$_A$), 0.08 (3H, s, Si*Me*$_B$), 0.91 (9H, s, SiC*Me*$_3$), 1.45 (9H, s, OC*Me*$_3$), 1.47 (3H, s, C(2)*Me*$_A$), 1.50 (3H, s, C(2)*Me*$_B$), 3.06 (1H, br s, O*H*), 3.55-3.85 (4H, m, C(4)C*H*$_2$, C(5)C*H*$_2$), 4.17 (1H, dt, *J* 7.3, 5.5 C(4)*H*), 4.33 (1H, t, *J* 5.5, C(5)*H*); *m/z* (ESI^+) 376 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{18}H_{38}NO_5Si$ ($[M+H]^+$) requires 376.2519; found 376.2520.

(4*S*,5*S*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-5-hydroxymethyl-oxazolidine 49

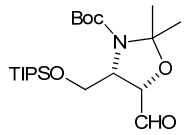


*From **44***: DIBAL-H (1 M in DCM, 5.38 mL, 5.38 mmol) was added dropwise *via* syringe to a stirred solution of **44** (1.2 g, 2.69 mmol) in DCM (20 mL) at 0 °C. After stirring for 6 h, the reaction mixture was quenched with sat aq NH_4Cl (0.5 mL), filtered through Celite (eluent DCM) and concentrated *in vacuo* to give **49** as a colourless oil (1.1 g, 98%, >98% de) that was used without purification. Purification of an aliquot *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 2:1) gave an analytical sample; R_f 0.09 (30-40 °C petrol/Et_2O, 2:1); $[\alpha]_D^{22}$ +9.8 (*c* 0.8 in $CHCl_3$); ν_{max} (film) 3495 (O−H), 1700 (C=O); δ_H (400 MHz, $CDCl_3$) 1.04-1.44 (21H, m, Si(C*HMe*$_2$)$_3$), 1.44-1.57 (15H, m, C(2)*Me*$_2$, C*Me*$_3$), 3.09-3.33 (1H, br m, O*H*), 3.67-3.82 (2H, m, C(5)C*H*$_2$), 3.84-3.92 (2H, m, C(4)C*H*$_2$), 3.98-4.16 (1H, m, C(4)*H*), 4.25-4.33 (1H, m, C(5)*H*); δ_H (500 MHz, DMSO-d_6, 363 K) 1.05-1.12 (21H, m, Si(C*HMe*$_2$)$_3$), 1.45 (9H, s, C*Me*$_3$), 1.48 (3H, s, C(2)*Me*$_A$), 1.50 (3H, s, C(2)*Me*$_B$), 3.72-3.91 (4H, m, C(4)C*H*$_2$, C(5)C*H*$_2$), 4.12-4.22 (1H, m, C(4)*H*), 4.35 (1H, app t, *J* 5.8, C(5)*H*); δ_C (125 MHz, DMSO-d_6, 363 K) 12.5 (Si(*C*HMe$_2$)$_3$), 18.7 (Si(CH*Me*$_2$)$_3$), 29.0 (C*Me*$_3$), 32.2 (C(2)*Me*$_2$), 60.2 (*C*(4)), 60.7 (C(4)*C*H$_2$, C(5)*C*H$_2$), 79.8 (*C*(5)), 80.8 (*C*Me$_3$), 93.1 (*C*(2)), 152.0 (N*C*O); *m/z* (ESI^+) 440 ($[M+Na]^+$, 14%), 418 (100); HRMS (ESI^+) $C_{21}H_{44}NO_5Si^+$ ($[M+H]^+$) requires 418.2989; found 418.2997.

*From **45***: DIBAL-H (1 M in DCM, 0.80 mL, 0.80 mmol) was added dropwise *via* syringe to a stirred solution of **45** (200 mg, 0.40 mmol) in DCM (5 mL) at 0 °C. After stirring for 18 h, the reaction was quenched with sat aq NH_4Cl (0.1 mL) and stirred for a further 1 h. The resultant mixture was filtered

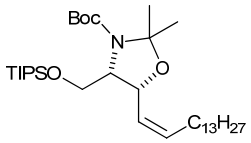
through Celite (eluent DCM) and concentrated *in vacuo* to give **49** as a colourless oil (157 mg, 92%, >98% de) that was used without purification.

(4*S*,5*S*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsilyloxymethyl-5-carbonylmethyl-oxazolidine 50



IBX (2.21 g, 7.89 mmol) was added to a solution of **49** (1.10 g, 2.63 mmol) in DMSO (20 mL) at rt and stirred for 12 h. The reaction mixture was diluted with Et_2O (20 mL), washed with H_2O (5 × 20 mL), dried and concentrated *in vacuo* to give **50** as a colourless oil (1.09 g, quant, >98% de) that was used without purification; δ_H (400 MHz, $CDCl_3$) 1.00-1.10 (21H, m, Si(C*H*Me_2)$_3$), 1.43-1.57 (12H, m, C(2)Me_A, CMe_3), 1.63-1.69 (3H, m, C(2)Me_B), 3.67-3.97 (2H, m, C(4)CH_2), 4.20-4.36 (1H, m, C(4)*H*), 4.44-4.54 (1H, m, C(5)*H*), 9.72-9.82 (1H, m, C*H*O).

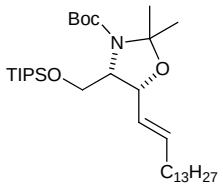
(4*S*,5*R*,1′*Z*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsiloxymethyl-5-pentadec-1′-en-1′-yl-oxazolidine (*Z*)-51



BuLi (2.5M in hexanes, 2.1 mL, 5.29 mmol) was added dropwise *via* syringe to a stirred solution of (1-tetradecyl)triphenylphosphonium bromide (3.25 g, 6.01 mmol) in THF (60 mL) at −78 °C. After 30 min hexane (75 mL) was added, followed by the dropwise addition of a solution of **50** (500 mg, 1.20 mmol) in THF (15 mL) *via* cannula. The reaction mixture was allowed to warm to rt over 12 h and quenched with sat aq NH_4Cl (10 mL). Brine (100 mL) was added, the organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 200:1; increased to 30-40 °C petrol/Et_2O, 10:1) gave (*Z*)-**51** as a colourless oil (645 mg, 90%, >98% de); R_f 0.16 (30-40 °C petrol/Et_2O, 10:1); $[\alpha]_D^{22}$ −7.8 (*c* 1.7 in $CHCl_3$); ν_{max} (film) 2926 (C−H), 1702 (C=O); δ_H (400 MHz, $CDCl_3$) 0.89-0.91 (3H, m, C(15')*H*$_3$), 1.02-1.09 (21H, m, Si(C*H*Me_2)$_3$), 1.20-1.65 (37H, m, C(2)Me_2, C(4')H_2-C(14')H_2, CMe_3,), 1.99-2.20 (2H, m, C(3')H_2), 3.64 (1H, dd, *J* 10.2, 2.0, C(4)CH_A), 3.71-3.93 (1H, m, C(4)*H*), 4.00 (1H, dd, *J* 10.2, 4.6, C(4)CH_B), 4.88-4.95 (1H, m, C(5)*H*), 5.62-5.77 (2H, m, C(1')*H*, C(2')*H*); δ_H (500 MHz,

PhMe-d_8, 363 K) 0.92 (3H, t, *J* 6.9, C(15')H_3), 1.08-1.20 (21H, m, Si(CHMe_2)$_3$), 1.27-1.46 (22H, m, C(4')H_2-C(14')H_2), 1.47 (9H, s, CMe_3), 1.62 (3H, s, C(2)Me_A), 1.70 (3H, s, C(2)Me_B), 2.04-2.20 (2H, m, C(3')H_2), 3.86 (1H, dd, *J* 9.8, 2.5, C(4)CH_A), 4.01 (1H, br s, C(4)*H*), 4.12 (1H, dd, *J* 9.8, 6.4, C(4)CH_B), 4.96-4.99 (1H, m, C(5)*H*), 5.62-5.67 (1H, m, C(2')*H*), 5.91-5.96 (1H, m, C(1')*H*); δ_C (125 MHz, PhMe-d_8, 363 K) 12.2 (Si(*C*HMe$_2$)$_3$), 13.6 (*C*(15′)), 17.9 (Si(CHMe_2)$_3$), 22.5, 27.8, 28.2, 29.15, 29.23, 29.5, 29.55, 29.59, 29.61, 29.64, 29.7, 31.9 (C(2)Me_2, *C*(3′)-*C*(14′), CMe_3), 61.3 (*C*(4)) 61.8 (C(4)*C*H$_2$), 72.3 (*C*(5)), 79.0 (*C*Me$_3$), 92.0 (*C*(2)), 125.7 (*C*(2′)), 133.9 (*C*(1′)), 151.5 (N*C*O); *m/z* (CI$^+$) 596.5 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{35}H_{70}NO_4Si^+$ ([M+H]$^+$) requires 596.5074; found 596.5054.

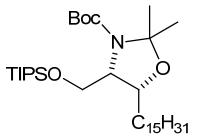
(4*S*,5*R*,1′*E*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsiloxymethyl-5-pentadec-1′-en-1′-yl-oxazolidine (*E*)-52



BuLi (2.5M in hexanes, 2.1 mL, 5.29 mmol) was added dropwise *via* syringe to a stirred solution of (1-tetradecyl)triphenylphosphonium bromide (3.25 g, 6.01 mmol) in THF (60 mL) at −78 °C. After 30 min hexane (75 mL) was added, followed by the dropwise addition of a solution of **50** (500 mg, 1.20 mmol) in THF (15 mL) *via* cannula. The reaction mixture was stirred at −78 °C for 2 h before the addition of MeOH (50 mL). The reaction mixture was allowed to warm to rt over a further 12 h and quenched with sat aq NH_4Cl (10 mL). Brine (100 mL) was added, the organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1) gave (*E*)-**52** as a colourless oil (523 mg, 73%, (*E*):(*Z*) 94:6); R_f 0.16 (30-40 °C petrol/Et_2O, 10:1); $[\alpha]_D^{20}$ +3.5 (*c* 2.2 in $CHCl_3$); ν_{max} (film) 2926 (C−H), 1703 (C=O); δ_H (400 MHz, $CDCl_3$) 0.95-0.99 (3H, m, C(15')H_3), 1.10-1.23 (21H, m, Si(CHMe_2)$_3$), 1.31-1.72 (37H, m, C(2)Me_2, C(4')H_2-C(14')H_2, CMe_3), 2.10-2.19 (2H, m, C(3')H_2), 3.70-3.78 (1H, m, C(4)CH_A), 3.84-4.12 (2H, m, C(4)*H*, C(4)CH_B), 4.59-4.64 (1H, m, C(5)*H*), 5.80-5.96 (2H, m, C(1')*H*, C(2')*H*); δ_H (500 MHz, PhMe-d_8, 363 K) 0.92 (3H, t, *J* 6.9, C(15')H_3), 1.11-1.18 (21H, m, Si(CHMe_2)$_3$), 1.26-1.50 (31H, m, C(4')H_2-C(14')H_2, CMe_3), 1.58 (3H, s, C(2)Me_A), 1.68 (3H, s, C(2)Me_B), 2.10-2.14 (2H, m, C(3')H_2), 3.80-3.86 (1H, m, C(4)CH_A), 3.93 (1H, br s, C(4)*H*), 4.04 (1H, dd, *J* 9.8, 7.6, C(4)CH_B), 4.50-4.52 (1H, m, C(5)*H*), 5.77-5.85 (1H, m, C(2')*H*), 5.87-5.93 (1H, m, C(1')*H*); δ_C (125 MHz,

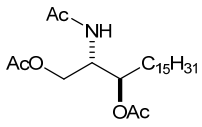
PhMe-d_8, 363 K) 12.2 (Si(*C*HMe$_2$)$_3$), 13.6 (*C*(15′)), 17.9 (Si(CH*Me*$_2$)$_3$), 22.5, 24.1, 27.3, 28.1, 29.2, 29.27, 29.30, 29.53, 29.57, 29.61, 29.7, 31.9 (C(2)*Me*$_2$, *C*(3′)-*C*(14′), C*Me*$_3$), 61.3 (*C*(4)), 62.0 (C(4)*C*H$_2$), 77.2 (*C*(5)), 79.0 (*C*Me$_3$), 92.4 (*C*(2)), 125.7 (*C*(2′)), 134.1 (*C*(1′)), 151.5 (N*C*O); *m/z* (CI$^+$) 596.5 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{35}H_{70}NO_4Si^+$ ([M+H]$^+$) requires 596.5074; found 596.5084.

(4*S*,5*R*)-2,2-Dimethyl-*N*(3)-*tert*-butoxycarbonyl-4-tri-*iso*-propylsiloxymethyl-5-pentadecan-1′-yl-oxazolidine 53



Pd/C (5 mg, 10% w/w) was added to a stirred solution of (*Z*)-**51** (50 mg, 0.08 mmol) in EtOAc (5 mL) at rt. The reaction mixture was stirred under H_2 (1 atm) for 6 h. The reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et$_2$O, 2:1) gave **53** as a colourless oil (43 mg, 86%, >98% de); R_f 0.8 (30-40 °C petrol/Et$_2$O, 2:1); $[\alpha]_D^{17}$ +10.0 (*c* 2.2 in CHCl$_3$); ν_{max} (film) 2925 (C−H), 1702 (C=O); δ_H (400 MHz, CDCl$_3$) 0.85-0.91 (3H, m, C(15')*H*$_3$), 1.02-1.12 (21H, m, Si(C*HMe*$_2$)$_3$), 1.20-1.37 (26H, m, C(2')*H*$_2$-C(14')*H*$_2$), 1.45-1.54 (15H, m, C(2)*Me*$_2$, C*Me*$_3$), 1.55-1.85 (2H, m, C(1')*H*$_2$), 3.59-3.89 (3H, m, C(4)*H*, C(4)*H*$_2$), 4.00-4.06 (1H, m, C(5)*H*); δ_H (500 MHz, PhMe-d_8, 363 K) 0.88-1.68 (65H, m, C(2)*Me*$_2$, C(2')-C(13')*H*$_2$, C(14')*H*$_3$, C*Me*$_3$, Si(C*HMe*$_2$)$_3$), 1.80-1.92 (2H, m, C(1')*H*$_2$), 3.78-4.05 (4H, m, C(4)*HCH*$_2$, C(5)*H*); δ_C (125 MHz, PhMe-d_8, 363 K) 12.2, 13.5, 17.8, 22.5, 23.9, 26.8, 27.4, 28.0, 28.1, 29.2, 29.3, 29.6, 29.7, 31.8, 61.2, 76.7, 78.9, 92.0, 151.5; *m/z* (ESI$^+$) 598.5 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{35}H_{72}NO_4Si^+$ ([M+H]$^+$) requires 598.5231; found 598.5252.

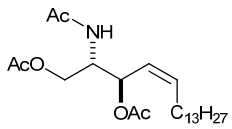
(2*S*,3*R*)-1,3-Diacetoxy-2-acetamido-octadecane [*N*,*O*-diacetyl sphinganine] 54



3 M aq HCl (1 mL) was added to a solution of **53** (30 mg, 0.05 mmol) in MeOH (10 mL) and heated at 50 °C for 3 h. The reaction mixture was concentrated *in vacuo*. The residue was dissolved in pyridine (10 mL) and Ac$_2$O (0.1 mL, excess) and DMAP (2 mg) were added sequentially. The reaction mixture was stirred for 12 h before being quenched with H$_2$O (2 mL). The reaction mixture was diluted with H$_2$O (10 mL) and Et$_2$O (10 mL) and the layers were separated. The aqueous layer was extracted with Et$_2$O (2 × 10 mL). The combined organic layers were washed sequentially with sat aq CuSO$_4$ (2 × 10 mL), H$_2$O (10 mL) and brine

(10 mL), dried and concentrated *in vacuo*. Recrystallisation from $CHCl_3$/pentane (1:1) gave **54** as a white solid (11 mg, 75%, >98% de); mp 83-85 °C ($CHCl_3$/pentane); $[\alpha]_D^{22}$ +18.4 (*c* 0.25 in $CHCl_3$); {lit.[8] $[\alpha]_D^{22}$ +19.2 (*c* 1.0 in $CHCl_3$); lit.[9] $[\alpha]_D^{24}$ +17.2 (*c* 0.2 in $CHCl_3$)}; ν_{max} (KBr) 3306, 2912, 2853, 1732, 1649, 1545, 1232; δ_H (400 MHz, $CDCl_3$) 0.87 (3H, t, *J* 6.7, C(18)H_3), 1.21-1.38 (22H, m, C(7)H_2-C(17)H_2), 1.52-1.70 (2H, m, C(6)H_2), 2.01 (3H, s, CO*Me*), 2.07 (3H, s, CO*Me*), 2.08 (3H, s, CO*Me*), 4.07 (1H, dd, *J* 11.6, 3.9, C(1)H_A), 4.26 (1H, dd, *J* 11.6, 6.1, C(1)H_B), 4.34-4.45 (1H, m, C(2)*H*), 4.88-4.95 (1H, m, C(3)*H*), 5.85 (1H, d, *J* 8.9 N*H*); δ_C (100 MHz, $CDCl_3$) 14.1, 20.8, 21.0, 22.7, 23.3, 25.3, 29.3, 29.4, 29.5, 29.60, 29.63, 29.7, 31.5, 31.9, 50.5, 62.6, 73.9, 169.8, 170.9, 171.0; *m/z* (ESI^+) 450 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{24}H_{45}NNaO_5^+$ ($[M+Na]^+$) requires 450.3190; found 450.3180.

(2*S*,3*R*,4*Z*)-1,3-Diacetoxy-2-acetamido-octadec-4-ene [*N*,*O*,*O*-triacetyl-(*Z*)-sphingosine] 55



3 M aq HCl (1 mL) was added to a solution of (*Z*)-**51** (30 mg, 0.05 mmol) in MeOH (10 mL) and heated at 50 °C for 3 h. The reaction mixture was concentrated *in vacuo*. The residue was dissolved in pyridine (10 mL) and Ac_2O (0.1 mL, excess) and DMAP (2 mg) were added sequentially. The reaction mixture was stirred for 12 h before being quenched with H_2O (2 mL). The reaction mixture was diluted with H_2O (10 mL) and Et_2O (10 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were washed sequentially with sat aq $CuSO_4$ (2 × 10 mL), H_2O (10 mL) and brine (10 mL), dried and concentrated *in vacuo*. Recrystallisation from $CHCl_3$/pentane (1:1) gave **55** as a white solid (13 mg, 87%, >98% de); mp 83-85 °C ($CHCl_3$/pentane); $[\alpha]_D^{22}$ +6.6 (*c* 0.9 in $CHCl_3$); {lit.[10] $[\alpha]_D^{24}$ +4.3 (*c* 0.9 in $CHCl_3$)}; ν_{max} (KBr) 3336, 2926, 2851, 1734, 1655, 1539, 1236; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.8, C(18)H_3), 1.14-1.43 (22H, m, C(7)H_2-C(17)H_2), 1.99 (3H, s, CO*Me*), 2.05 (3H, s, CO*Me*), 2.08 (3H, s, CO*Me*), 2.00-2.27 (2H, m, C(6)H_2), 4.04 (1H, dd, *J* 11.6, 3.9, C(1)H_A), 4.34 (1H, dd, *J* 11.6, 6.5, C(1)H_B), 4.39-4.47 (1H, m, C(2)*H*), 5.28-5.36 (1H, m, C(3)*H*), 5.60-5.73 (2H, m, C(4)*H*, C(5)*H*); δ_C (125 MHz, $CDCl_3$) 14.1, 20.8, 21.1, 22.7, 23.4, 28.0, 29.3, 29.35, 29.42, 29.5, 29.6, 29.64, 29.66, 29.67, 31.9, 51.1, 62.6, 69.6, 77.2, 123.8, 137.0, 169.8, 170.0, 171.0; *m/z* (ESI^+) 448 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{24}H_{43}NNaO_5^+$ ($[M+Na]^+$) requires 448.3033; found 448.3030.

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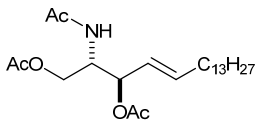
[9] R. A. Fernandes and P. Kumar, *Tetrahedron: Asymmetry*, **1999**, *10*, 4797.
[10] H. Shibuya, K. Kawashima, N. Narita, M. Ikeda and I. Kitagawa, *Chem. Pharm. Bull.*, **1992**, *40*, 1154.

(2*S*,3*R*,4*E*)-1,3-Diacetoxy-2-acetamido-octadec-4-ene [*N*,*O*,*O*-triacetyl sphingosine] 56



3 M aq HCl (1 mL) was added to a solution of (*E*)-**52** (50 mg, 0.05 mmol, (*E*):(*Z*) 94:6) in MeOH (10 mL) and heated at 50 °C for 3 h. The reaction mixture was concentrated *in vacuo*. The residue was dissolved in pyridine (10 mL) and Ac_2O (0.1 mL, excess) and DMAP (2 mg) were added sequentially. The reaction mixture was stirred for 12 h before being quenched with H_2O (2 mL). The reaction mixture was diluted with H_2O (10 mL) and Et_2O (10 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were washed sequentially with sat aq $CuSO_4$ (2 × 10 mL), H_2O (10 mL) and brine (10 mL), dried and concentrated *in vacuo*. Recrystallisation from $CHCl_3$/pentane (1:1) gave **56** as a white solid (29 mg, 80%, >98% de); mp 99-101 °C ($CHCl_3$/pentane); $[\alpha]_D^{20}$ −12.0 (*c* 1.0 in $CHCl_3$); {lit.[11] $[\alpha]_D^{24}$ −13.0 (*c* 1.6 in $CHCl_3$)}; ν_{max} (KBr) 3287, 2919, 2850, 1734, 1656, 1552, 1232; δ_H (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.8, C(18)H_3), 1.19-1.40 (22H, m, C(7)-C(17)H_2), 1.95-2.09 (2H, m, C(6)H_2) overlapping 1.99 (3H, s, CO*Me*) and 2.07 (6H, s, 2 × CO*Me*), 4.04 (1H, dd, *J* 11.6, 4.1, C(1)H_A), 4.30 (1H, dd, *J* 11.6, 6.1, C(1)H_B), 4.39-4.48 (1H, m, C(2)*H*), 5.26-5.28 (1H, m, C(3)*H*), 5.39 (1H, dd, *J* 15.4, 7.5, C(4)*H*), 5.68 (1H, d, *J* 9.2, N*H*), 5.79 (1H, dd, *J* 15.4, 6.8, C(5)*H*); δ_C (100 MHz, $CDCl_3$) 14.1, 20.8, 21.1, 22.7, 23.4, 28.9, 29.2, 29.3, 29.4, 29.6, 29.7, 31.9, 32.3, 50.6, 60.4, 62.6, 73.8, 124.1, 137.5, 169.7, 170.0, 171.0; *m/z* (ESI^+) 448 ($[M+Na]^+$, 100%); HRMS (ESI^+) $C_{24}H_{43}NNaO_5^+$ ($[M+Na]^+$) requires 448.3033; found 448.3023.

[11] W. Disadee and T. Ishikawa, *J. Org. Chem.*, **2005**, *70*, 9399.