Supplementary Information

Parallel kinetic resolution of tert-butyl (RS)-3-oxy-substituted cyclopent-1-ene-carboxylates for the
asymmetric synthesis of 3-oxy-substituted cispentacin and transpentacin derivatives

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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.

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 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. 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, and were internally calibrated with polyanaline, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m × 0.25 mm) using amyl acetate as a lock mass.

**General Procedures**

**General procedure 1a: lithium amide conjugate addition to α,β-unsaturated esters**

BuLi (as a solution in hexanes) was added dropwise *via* syringe to a stirred solution of the requisite amine in THF at −78 °C. After stirring for 30 min a solution of the requisite α,β-unsaturated ester in THF at −78 °C was added dropwise *via* cannula. After stirring for a further 4 h at −78 °C the reaction mixture was quenched with sat aq NH₄Cl, allowed to warm to rt and 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 NaHCO₃ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*.

**General procedure 1b: lithium amide conjugate addition to α,β-unsaturated esters**

BuLi (as a solution in hexanes) was added dropwise *via* syringe to a stirred solution of the requisite amine in THF at −78 °C. After stirring for 30 min a solution of the requisite α,β-unsaturated ester in THF at −78 °C was added dropwise *via* cannula. After stirring for a further 4 h at −78 °C the reaction mixture was quenched with a solution of 2,6-di-tert-butylphenol in THF and allowed to warm to rt over 1 h 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 NaHCO₃ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*.

**General Procedure 2: base catalysed epimerisation**

A catalytic amount of KO'Bu was added to the β-amino ester in 'BuOH/THF (1:1). The mixture was refluxed overnight before addition of sat aq NH₄Cl, separation and extraction of the aqueous layer with DCM. The combined organic phases were dried and concentrated *in vacuo*.
General Procedure 3: DDQ deprotection of N-3,4-dimethoxybenzyl derivatives

DDQ was added to a solution of the requisite N-3,4-dimethoxybenzyl protected β-amino ester in DCM/H2O (5:1). The reaction mixture was stirred at rt for 48 h before the addition of sat aq NaHCO3. The mixture was extracted with DCM and the combined organic extracts were washed with brine, dried and concentrated in vacuo.

General Procedure 4: hydrogenolysis

Pd(OH)2/C was added to a solution of the secondary or tertiary amine in degassed MeOH at rt and placed under a hydrogen atmosphere (5 atm). After stirring for 24 h, the reaction mixture was filtered through basic alumina (eluent MeOH) and concentrated in vacuo.

General Procedure 5: tert-butyl ester hydrolysis

TFA was added to a solution of the β-amino ester in DCM at rt and stirred for 16 h. The reaction mixture was then concentrated in vacuo. The residue was dissolved in MeOH (2 mL) and HCl in Et2O (sat, 2 mL) was added, and the mixture was concentrated in vacuo. The residue was partitioned between Et2O (4 mL) and H2O (4 mL), and the layers separated. The aqueous layer was concentrated to a quarter of its volume and subjected to ion exchange chromatography on Dowex 50WX8-200 resin.

Methyl 3-oxo-cyclopent-1-ene-carboxylate 14

CrO3 (4.82 g, 48.2 mmol) was added slowly to acetic anhydride (33 mL). When all of the CrO3 was dissolved, glacial acetic acid (250 mL) was added. The resultant solution was added dropwise to a stirred, cooled (0-5 °C) solution of 12 (13.9 g, 110 mmol) in DCM (240 mL), then a second portion of DCM (24 mL) was added to the reaction mixture and stirring was continued for a further 30 min at 0-5 °C. The reaction was neutralised with 12.5 M KOH (5 mL), then aqueous layer was separated and extracted with DCM. The combined organic extracts were washed sequentially with sat aq NaHCO3 and brine, then dried and concentrated in vacuo. The crude yellow oil was stirred in a mixture of THF/sat aq NaHCO3 overnight. Purification by chromatography (20% Et2O in pentane) gave 14 as a colourless oil (9.26 g, 60%); δH (400 MHz, CDCl3) 2.53-2.55 (2H, m, C(5)H2), 2.87-2.88 (2H, m, C(4)H2), 3.87 (3H, s, OMe), 6.76 (1H, t, J 2.3, C(2)H).
**tert-Butyl 3-oxo-cyclopent-1-ene-carboxylate 15**

Oxidation with CrO₃: CrO₃ (18.1 g, 180 mmol) was added slowly to acetic anhydride (45 mL). When all of the CrO₃ was dissolved, glacial acetic acid (90 mL) was added. The resultant solution was added dropwise to a stirred, cooled (0-5 °C) solution of 13 (10 g, 59.5 mmol) in DCM (90 mL), then a second portion of DCM (90 mL) was added to the reaction mixture and stirring was continued for a further 30 min at 0-5 °C. The reaction was neutralised with 12.5 M KOH (10 mL), then the aqueous layer was separated and extracted with DCM. The combined organic extracts were washed sequentially with sat aq NaHCO₃ and brine, then dried and concentrated in vacuo. The crude yellow oil was stirred in a mixture of THF/sat aq NaHCO₃ overnight. Purification by chromatography (20% Et₂O in pentane) gave 15 as a colourless oil (5.44 g, 50%); νmax (film) 1716 (C=O), 1613 (C=C); δH (400 MHz, CDCl₃) 1.55 (9H, s, CMe₃), 2.51-2.53 (2H, m, C(4)H₂), 2.80-2.83 (2H, m, C(5)H₂), 6.65-6.69 (1H, m, C(2)H); δC (100 MHz, CDCl₃) 27.5, 28.0, 35.7, 82.5, 137.4, 163.5, 166.5, 209.4; m/z (ESI⁺) 183 ([M+H]⁺, 100%); HRMS (ESI⁺) found 183.1023; C₁₀H₁₅O₃ ([M+H]⁺) requires 183.1021.

Oxidation with tert-butyl hydroperoxide: tert-butyl hydroperoxide (5-6 M in decane, 10.8 mL) was added dropwise to a mixture of 13 (5 g, 29.7 mmol), Pd(OH)₂/C (1.04 mg, 1.49 mmol) and K₂CO₃ (2.05 g, 14.9 mmol) in DCM (200 mL) at 0 °C and the resultant solution stirred for 4 h at 0 °C under N₂. Further tert-butyl hydroperoxide (5-6 M in decane, 43.2 mL) was added and stirring was continued for a further 18 h. The reaction mixture was filtered through a short pad of silica (elucent DCM), dried and concentrated in vacuo. Purification by chromatography (2% Et₂O in pentane) gave 15 as a colourless oil (2.0 g, 37%).

**Methyl (RS)-3-hydroxy-cyclopent-1-ene-carboxylate 16**

To a solution of 14 (5.53 g, 39.5 mmol) in MeOH (75 mL) at 0 °C was added CeCl₃·7H₂O (13.6 g, 36.6 mmol) followed by NaBH₄ (1.70 g, 45.0 mmol). The mixture was stirred for 10 min, quenched with 0.2 M aq HCl, and extracted with DCM. The combined organic extracts were washed with H₂O, dried and concentrated in vacuo. Chromatography (30% Et₂O in pentane) gave 16 as a colourless oil (5.50 g, 98%); δH (400 MHz, CDCl₃) 1.76-1.85 (1H, m, C(4)H₆), 2.36-2.55 (2H, m, C(4)H₆, C(5)H₆), 2.63-2.79 (1H, m, C(5)H₆), 3.77 (3H, s, OMe), 4.45-5.01 (1H, m, C(3)H), 6.71 (1H, app q, J 2.0, C(2)H).
**tert-Butyl (RS)-3-hydroxy-cyclopent-1-ene-carboxylate 17**

To a solution of 15 (5.50 g, 30.2 mmol) in MeOH (20 mL) at 0 °C was added CeCl₃·7H₂O (10.4 g, 28.0 mmol) followed by NaBH₄ (1.30 g, 34.4 mmol). The mixture was stirred for 10 min, quenched with 0.2 M aq HCl, and extracted with DCM. The combined organic extracts were washed with H₂O, dried and concentrated *in vacuo*. Chromatography (30% Et₂O in pentane) gave 17 as a colourless oil (5.35 g, 98%); νₘₐₓ (film) 3404 (O–H), 1711 (C=O), 1634 (C=C); δₜ (400 MHz, CDCl₃) 1.49 (9H, s, CMe₃), 1.74-1.83 (1H, m, C(4)H₄), 2.34-2.49 (2H, m, C(4)H₆, C(5)H₅), 2.62-2.73 (1H, m, C(5)H₆), 4.95 (1H, br s, C(3)H), 6.59-6.60 (1H, m, C(2)H); δₜ (100 MHz, CDCl₃) 28.1, 29.9, 33.6, 77.2, 80.7, 140.7, 141.7, 164.6; m/z (Cl⁻) 202 ([M+NH₄]⁺, 100%); HRMS (Cl⁻) found 202.1438; C₁₀H₂₀NO₃ ([M+NH₄]⁺) requires 202.1443.

**Methyl (RS)-3-methoxy-cyclopent-1-ene-carboxylate 18**

MeI (1.40 mL, 22.5 mmol) was added to a mixture of 16 (160 mg, 1.13 mmol) and silver(I) oxide (522 mg, 2.25 mmol) in MeCN (1.5 mL) and the resultant mixture refluxed at 43 °C for 20 h. The solid residue was filtered through Celite® (eluent MeCN) and filtrate was concentrated *in vacuo*. Purification by chromatography (3% Et₂O in pentane) gave 18 as a colourless oil as a colourless oil (150 mg, 88%); νₘₐₓ (film) 1723 (C=O), 1636 (C=C); δₜ (400 MHz, CDCl₃) 1.82-1.91 (1H, m, C(4)H₄), 2.25-2.33 (1H, m, C(4)H₆), 2.44-2.52 (1H, m, C(5)H₅), 2.67-2.76 (1H, m, C(5)H₆), 3.36 (3H, s, C(3)OMe), 3.76 (1H, s, CO₂Me), 4.53-4.57 (1H, m, C(3)H), 6.78-6.80 (1H, m, C(2)H); δₜ (100 MHz, CDCl₃) 29.9, 51.7, 56.4, 85.5, 139.3, 140.5, 165.5; m/z (Cl⁻) 156 ([M+H]⁺, 100%); HRMS (Cl⁻) found 157.0864; C₈H₁₂O₃ ([M+H]⁺) requires 157.0865.

**tert-Butyl (RS)-3-methoxy-cyclopent-1-ene-carboxylate 19**

MeI (16.9 mL, 272 mmol) was added to a mixture of 17 (2.50 g, 13.6 mmol) and silver(I) oxide (6.29 g, 27.2 mmol) in MeCN (20 mL) and the resultant mixture refluxed at 43 °C for 20 h. The solid residue was filtered through Celite® (eluent MeCN) and the filtrate was concentrated *in vacuo*. Purification by chromatography (3% Et₂O in pentane) gave 19 as a colourless oil (2.29 g, 85%); νₘₐₓ (film) 1713 (C=O), 1635 (C=C); δₜ (400 MHz, CDCl₃) 1.49 (9H, s, CMe₃), 1.82-1.88 (1H, m, C(4)H₄), 2.23-2.29 (1H, m,
C(4)H_10), 2.40-2.47 (1H, m, C(5)H_2), 2.58-2.69 (1H, m, C(5)H_2), 3.35 (3H, s, OMe), 4.51-4.53 (1H, m, C(3)H), 6.60 (1H, app dd, J 2.2, 1.9, C(2)H); δ_C (100 MHz, CDCl_3) 27.8, 28.0, 29.8, 56.3, 80.4, 85.5, 139.0, 141.3, 164.4; m/z (CI⁺) 199 ([M+H]^+), 100%; HRMS (CI⁺) found 199.1331; C_8H_{12}O_3 ([M+H]^+) requires 199.1334.

**Methyl (RS)-3-tert-butyldiphenylsilyloxy-cyclopent-1-ene-carboxylate 20**

TBDPSCI (1.67 g, 6.40 mmol) was added dropwise to a stirred solution of 16 (827 mg, 5.82 mmol), imidazole (495 mg, 7.27 mmol) and DMAP (~20 mg) in dry DMF (8 mL) at 0 °C. The reaction mixture was allowed to warm to rt and stirred overnight. The reaction was quenched by the addition of H_2O, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed several times with H_2O, dried and concentrated in vacuo. Purification by chromatography (5% Et_2O in pentane) gave 20 as a colourless oil (379 mg, 99%); ν_max (film) 1722 (C=O), 1630 (C=C); δ_H (400 MHz, CDCl_3) 1.07 (9H, s, CMe_3), 1.86-1.94 (1H, m, C(4)H_2), 2.13-2.21 (1H, m, C(4)H_B), 2.30-2.39 (1H, m, C(5)H_A), 2.65-2.73 (1H, m, C(5)H_B), 3.74 (3H, s, OMe), 4.93-4.98 (1H, m, C(3)H), 6.58 (1H, app q, J 2.0, C(2)H), 7.38-7.47 (5H, m, Ph), 7.68-7.70 (5H, m, Ph); δ_C (400 MHz, CDCl_3) 19.1, 26.9, 29.8, 33.9, 51.6, 78.4, 127.6, 127.7, 129.7, 133.9, 135.7, 137.3, 143.9, 165.7; m/z (CI⁺) 381 ([M+NH_4]^+); HRMS (CI⁺) found 398.2143; C_{23}H_{32}NO_3Si ([M+NH_4]^+) requires 398.2151.

**tert-Butyl (RS)-3-tert-butyldiphenylsilyloxy-cyclopent-1-ene-carboxylate 21**

TBDPSCI (3.11 mL, 12.0 mmol) was added dropwise to a stirred solution of 17 (2 g, 10.8 mmol), imidazole (924 mg, 13.6 mmol) and DMAP (~20 mg) in dry DMF (20 mL) at 0 °C. The reaction mixture was allowed to warm to rt and stirred overnight. The reaction was quenched by the addition of H_2O, and the aqueous layer was extracted with Et_2O. The combined organic layers were washed several times, with H_2O, dried and concentrated in vacuo. Purification by chromatography (1% Et_2O in pentane) gave 21 as a white crystalline solid (3.90 g, 85%); Found C, 73.7; H, 8.1%; C_{26}H_{34}O_3Si requires C, 73.9; H, 8.1%; mp 50-51°C; ν_max (film) 1712 (C=O), 1639 (C=C); δ_H (400 MHz, CDCl_3) 1.07 (9H, s, SiCMe_3), 1.48 (9H, s, OCMMe_3), 1.85-1.89 (1H, m, C(4)H_A), 2.12-2.16 (1H, m, C(4)H_B), 2.23-2.32 (1H, m, C(5)H_A), 2.59-2.67 (1H, m, C(5)H_B), 4.92-4.96 (1H, m, C(3)H), 6.44 (1H, app q, J 2.0, C(2)H), 7.38-7.78 (10H, m, Ph); δ_C (100 MHz, CDCl_3) 19.1, 26.9,
Following General Procedure 1a, BuLi (2.5 M in hexanes, 0.43 mL, 1.02 mmol), dibenzylamine (0.20 mL, 1.05 mmol) in THF (0.4 mL) and 20 (200 mg, 0.53 mmol) in THF (0.3 mL) gave a 58:42 mixture of 23:24. Purification by chromatography (1% Et₂O in pentane) gave 23 as a white crystalline solid (110 mg, 28%, >98% de); mp 118-119 °C; νmax (KBr) 1646 (C=O); δH (400 MHz, CDCl₃) 1.05 (9H, s, CMe₃), 1.41-1.54 (1H, m, C(4)H₆), 1.64-1.78 (1H, m, C(5)H₆), 1.84-1.94 (1H, m, C(4)H₆), 2.15-2.26 (1H, m, C(5)H₆), 3.15 (1H, app q, J 8.9, C(1)H), 3.43 (2H, d, J 13.0, N(CH₃)H₂Ph), 3.56 (1H, dd, J 4.4, 4.8, C(2)H), 3.83 (2H, d, J 13.0, N(CH₃)H₂Ph), 3.95 (1H, d, J 17.8, CONHC(2)H₂Ph), 4.09 (1H, d, J 14.3, CONHC(2)H₂Ph), 4.34 (1H, d, J 17.8, CONHC(2)H₂Ph), 4.92-4.96 (1H, app q, J 5.5, C(3)H), 5.25 (1H, d, J 14.3, CONHC(2)H₂Ph), 6.97-7.74 (30H, m, Ph); δC (100 MHz, CDCl₃) 19.2, 27.0, 27.5, 33.3, 44.1, 44.4, 44.9, 55.6, 69.8, 75.3, 126.1, 126.6, 127.2, 127.5, 127.7, 128.0, 128.4, 128.7, 128.8, 129.5, 129.6, 129.7, 132.9, 134.6, 135.9, 137.0, 147.1; m/z (ESI⁺) 743 ([M+H]⁺, 100%); HRMS (ESI⁺) found 743.4039; C₅₀H₅₅N₂O₂Si ([M+H]⁺) requires 743.4033. Further elution gave 24 as a colourless oil (60 mg, 21%); νmax (film) 1612 (C=O), 1581 (C=C); δH (400 MHz, CDCl₃) 1.00 (9H, s, CMe₃), 1.86-1.94 (1H, m, C(4)H₆), 2.14-2.22 (1H, m, C(4)H₆), 2.54-2.61 (1H, m, C(5)H₆), 2.72-2.80 (1H, m, C(5)H₆), 4.43-4.56 (3H, m, NCH₂Ph, NCH₃H₂Ph), 4.70 (1H, d, J 14.7, NCH₃H₂Ph), 4.89-4.92 (1H, m, C(3)H), 5.73-5.75 (1H, m, C(2)H), 7.15-7.63 (20H, m, Ph); δC (100 MHz, CDCl₃) 19.0, 26.8, 32.9, 33.3, 36.9, 50.8, 79.0, 133.9, 126.9, 127.6, 128.4, 128.6, 128.9, 129.6, 130.0, 133.5, 134.1, 135.6, 136.6, 140.0, 169.7; m/z (ESI⁺) 546 ([M+H]⁺, 100%); HRMS (ESI⁺) found 546.2849; C₃₅H₄₀NO₂Si ([M+H]⁺) requires 546.2828.

X-ray Crystal Structure Determination for 23

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-
hydrogen atoms were refined with anisotropic thermal parameters. The structure was refined using CRYSTALS.2

X-ray crystal structure data for 23 [C$_{50}$H$_{34}$N$_2$O$_2$Si]: $M = 743.08$, monoclinic, space group C 1 2/c 1, $a = 32.1772(6)$ Å, $b = 16.8013(4)$ Å, $c = 17.4982(4)$ Å, $\beta = 116.7552(8)^\circ$, $V = 8447.1(3)$ Å$^3$, $Z = 8$, $\mu = 0.097$ mm$^{-1}$, colourless block, crystal dimensions $= 0.1 \times 0.1 \times 0.1$ mm$^3$. A total of 9360 unique reflections were measured for $5 < \theta < 27$ and 5328 reflections were used in the refinement. The final parameters were $wR_2 = 0.058$ and $R_1 = 0.049$ [$D > 3\sigma(I)$]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 669233. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

tert-Butyl (1RS,2RS,3RS)- and (1RS,2SR,3SR)-2-N,N-dibenzylamino-3-methoxy-cyclopentane-carboxylate (1RS,2RS,3RS)-25 and (1RS,2SR,3SR)-26

Following General Procedure 1a, BuLi (1.6 M in hexanes, 1.56 mL, 2.50 mmol), dibenzylamine (0.49 mL, 2.52 mmol) in THF (1 mL) and 19 (100 mg, 0.51 mmol) in THF (0.4 mL) gave a 79:21 mixture of 25:26. Purification by chromatography (2% Et$_2$O in pentane) gave 25 as a colourless oil (80 mg, 40%, >98% de); $\nu_{\text{max}}$ (film) 1725 (C=O); $\delta_H$ (400 MHz, CDCl$_3$) 1.53 (9H, s, CMe$_3$), 1.57-1.61 (1H, m, C(4)H$_A$), 1.88-1.94 (2H, m, C(5)H$_2$), 2.24-2.36 (1H, m, C(4)H$_B$), 3.05-3.09 (1H, m, C(1)H), 3.17 (3H, s, OMe), 3.30-3.33 (1H, m, C(2)H), 3.73 (2H, d, J 14.1, N(CH$_2$H$_B$Ph)$_2$), 3.85 (2H, d, J 14.1, N(CH$_2$H$_B$Ph)$_2$), 4.09-4.13 (1H, m, C(3)H), 7.21-7.39 (10H, m, Ph); $\delta_C$ (100 MHz, CDCl$_3$) 25.6, 28.2, 29.2, 47.8, 55.4, 56.8, 69.1, 80.3, 82.5, 126.6, 128.0, 128.8, 139.8, 174.2; m/z (ESI$^+$) 396 ([M+H]$^+$, 100%); HRMS (ESI$^+$) found 396.2539; C$_{25}$H$_{34}$NO$_3$ ([M+H]$^+$) requires 396.2539. Further elution gave 26 as a colourless oil (20 mg, 10%, >98% de); $\nu_{\text{max}}$ (film) 1725 (C=O); $\delta_H$ (400 MHz, CDCl$_3$) 1.30 (9H, s, CMe$_3$), 1.68-2.02 (4H, m, C(4)H$_Z$, C(5)H$_Z$), 2.74-2.78 (1H, m, C(1)H), 3.29 (3H, s, OMe), 3.52-3.55 (1H, m, C(2)H), 3.67 (4H, s, N(CH$_2$Ph)$_2$), 3.78-3.86 (1H, m, C(3)H), 7.21-7.39 (10H, m, Ph); $\delta_C$ (100 MHz, CDCl$_3$) 26.9, 28.0, 30.2, 45.9, 55.1, 56.8, 70.1, 83.0,

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83.2, 126.8, 128.0, 128.8, 139.8, 174.7; m/z (ESI\(^+\)) 396 ([M+H]\(^+\), 100%); HRMS (ESI\(^+\)) found 396.2531; C\(_{25}\)H\(_{34}\)NO\(_3\) ([M+H]\(^+\)) requires 396.2539.

**tert-Butyl (1RS,2RS,3RS)- and (1RS,2SR,3SR)-2-N,N-dibenzylamino-3-tert-butylidiphenylsilyloxy-cyclopentane-carboxylate (1RS,2RS,3RS)-27 and (1RS,2SR,3SR)-28**

Following General Procedure 1a, BuLi (1.6 M in hexanes, 733 \(\mu\)L, 1.17 mmol), dibenzylamine (0.23 mL, 1.18 mmol) in THF (0.6 mL) and 21 (100 mg, 0.24 mmol) in THF (0.2 mL) gave a 91:9 mixture of 27:28. Purification by chromatography (2% Et\(_2\)O in pentane) gave 27 as a colourless oil (108 mg, 74%, >98% de); \(\nu\)\(_{\text{max}}\) (film) 1723 (C=O); \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 1.08 (9H, s, SiCMe\(_3\)), 1.27-1.34 (2H, m, C(4)H\(_2\)), 1.46 (9H, s, OCMes), 1.76-1.83 (2H, m, C(5)H\(_2\)), 3.00-3.05 (1H, m, C(1)H), 3.52-3.55 (1H, m, C(2)H), 3.68 (2H, d, J 14.2, N(CH\(_A\)CH\(_B\)Ph\(_2\))), 3.82 (2H, d, J 14.2, N(CH\(_A\)CH\(_B\)Ph\(_2\))), 4.74-4.76 (1H, m, C(3)H), 7.21-7.71 (20H, m, Ph); \(\delta\)\(_C\) (100 MHz, CDCl\(_3\)) 19.0, 25.4, 26.9, 28.1, 32.4, 46.5, 55.0, 70.4, 74.9, 80.2, 126.4, 127.3, 127.4, 127.9, 128.4, 129.4, 129.5, 133.9, 134.6 135.8, 140.0, 174.2; m/z (ESI\(^+\)) 620 ([M+H]\(^+\), 100%); HRMS (ESI\(^+\)) found 620.3539; C\(_{40}\)H\(_{50}\)NO\(_3\)Si ([M+H]\(^+\)) requires 620.3560. Further elution gave 28 as a colourless oil (10 mg, 7%, >98% de); \(\nu\)\(_{\text{max}}\) (film) 1725 (C=O); \(\delta\)\(_H\) (400 MHz, CDCl\(_3\)) 1.07 (9H, s, SiCMe\(_3\)), 1.44 (9H, s, OCMes), 1.35-1.39 (1H, m, C(4)H\(_A\)), 1.56-1.67 (2H, m, C(4)H\(_B\), C(5)H\(_A\)), 1.81-1.88 (1H, m, C(5)H\(_B\)), 2.69 (1H, app q, J 7.8, C(1)H), 3.56 (2H, d, J 14.0, N(CH\(_A\)CH\(_B\)Ph\(_2\))), 3.67 (2H, d, J 14.0, N(CH\(_A\)CH\(_B\)Ph\(_2\))), 3.73 (1H, dd, J 5.7, 1.9, C(2)H), 4.34-4.38 (1H, m, C(3)H), 7.18-7.76 (20H, m, Ph); \(\delta\)\(_C\) (100 MHz, CDCl\(_3\)) 19.0, 26.3, 26.9, 27.9, 33.3, 44.2, 54.8, 72.3, 76.4, 79.9, 126.5, 127.3, 127.4, 127.9, 128.4, 128.6, 129.4, 129.5, 133.8, 134.6, 135.9, 139.8, 175.1; m/z (ESI\(^+\)) 620 ([M+H]\(^+\), 100%); HRMS (ESI\(^+\)) found 620.3558; C\(_{25}\)H\(_{34}\)NO\(_3\)Si ([M+H]\(^+\)) requires 620.3560.

**Methyl (1RS,2RS,3RS,\(\alpha\)SR)-2-[N-benzyl-N-(\(\alpha\)-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 29**

Following General Procedure 1a, BuLi (2.5 M in hexanes, 1.56 mL, 3.91 mmol), (RS)-N-benzyl-N-(\(\alpha\)-methylbenzyl)amine (835 mg, 3.95 mmol) in THF (1 mL) and 18 (123 mg, 0.79 mmol) in THF (2 mL)
gave 29 in >98% de. Purification by chromatography (1% Et₂O in pentane) gave 29 as a white crystalline solid (87 mg, 30%, >98% de); mp 70-71 °C; ν_max (KBr) 1725 (C=O); δ H (400 MHz, CDCl₃) 1.35 (3H, d, J 6.6, C(α)Me), 1.46-1.56 (1H, m, C(4)H₄), 1.74-1.91 (2H, m, C(5)H₂), 2.20-2.29 (1H, m, C(4)H₃), 2.87 (1H, dt, J 4.3, 3.8, C(1)H), 3.24 (3H, s, C(3)OMe), 3.32 (1H, app t, J 7.7, C(2)H), 3.67 (3H, s, CO₂Me), 3.94 (2H, app s, CH₂Ph), 4.02-4.07 (1H, m, C(3)H), 4.09 (1H, q, J 6.6, C(α)H), 7.22-7.45 (10H, m, Ph); δ C (100 MHz, CDCl₃) 15.1, 24.7, 28.5, 46.9, 51.3, 51.4, 57.0, 67.7, 82.0, 126.4, 126.6, 127.9, 128.1, 128.1, 141.9, 141.4, 175.6; m/z (ESI⁺) 368 ([M+H⁺], 100%); HRMS (ESI⁺) found 368.2228; C₂₃H₂₉NO₃ ([M+H⁺]) requires 368.2226.

**X-ray Crystal Structure Determination for 29**

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.³

X-ray crystal structure data for 29 [C₂₃H₂₉NO₃]: M = 734.98, orthorhombic, space group P b n 2₁, a = 13.9137(2) Å, b = 16.8715(3) Å, c = 17.2156(3) Å, V = 4041.28(11) Å³, Z = 8, μ = 0.079 mm⁻¹, colourless block, crystal dimensions = 0.2 × 0.2 × 0.2 mm³. A total of 4740 unique reflections were measured for 5 < θ < 27 and 4060 reflections were used in the refinement. The final parameters were wR₂ = 0.051 and R₁ = 0.042 [I>1.5σ(I)]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 669234. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

**Methyl (1RS,2RS,3RS,αSR)- and (1RS,2SR,3SR,αRS)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3-tert-butylidiphenylsilyloxy-cyclopentane-carboxylate (1RS,2RS,3RS,αSR)-31 and (1RS,2SR,3SR,αRS)-32**

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Following General Procedure 1a, BuLi (2.5 M in hexanes, 1.04 mL, 2.60 mmol), (RS)-N-benzyl-N-(α-methylbenzyl)amine (555 mg, 2.63 mmol) in THF (1 mL) and 20 (200 mg, 0.53 mmol) in THF (1 mL) gave a 92:8 mixture of 31:32. Purification by chromatography (1.5% Et₂O in pentane) gave 31 as a pale yellow crystalline solid (87 mg, 28%, >98% de); mp 72-73 °C; ν max (KBr) 1728 (C=O); δ H (400 MHz, CDCl₃) 1.04-1.2 (2H, m, C(4)H₂), 1.34-1.45 (2H, m, C(5)H₂), 1.73-1.82 (1H, m, C(1)H), 2.47-2.55 (1H, m, C(2)H), 3.59 (1H, s, OMe), 3.83 (1H, d, J 14.0, NCH₃), 3.96 (1H, d, J 14.0, NCH₃), 4.64 (1H, app q, J 5.5, C(3)H), 7.24-7.44 (16H, m, Ph), 7.66-7.68 (2H, m, Ph), 7.72-7.73 (2H, m, Ph); δ C (100 MHz, CDCl₃) 15.1, 19.3, 24.9, 26.9, 33.1, 45.0, 51.0, 51.4, 58.3, 71.2, 77.6, 126.4, 127.3, 127.4, 127.8, 127.9, 128.0, 129.3, 129.5, 133.8, 134.5, 135.9, 138.1, 141.5, 142.2, 176.1; m/z (ESI⁺) 592 ([M+H]+, 100%); HRMS (ESI⁺) found 592.3264; C₃₈H₄₆NO₃Si ([M+H]+) requires 592.3247.

Further elution gave 32 as a colourless oil (6.2 mg, 2%, >98% de); ν max (KBr) 1732 (C=O); δ H (400 MHz, CDCl₃) 1.04-1.2 (2H, m, C(4)H₂), 1.34-1.45 (2H, m, C(5)H₂), 1.73-1.82 (1H, m, C(1)H), 2.47-2.55 (1H, m, C(2)H), 3.59 (1H, s, OMe), 3.83 (1H, d, J 14.0, NCH₃), 3.96 (1H, d, J 14.0, NCH₃), 4.64 (1H, app q, J 5.5, C(3)H), 7.24-7.44 (16H, m, Ph), 7.65-7.68 (2H, m, Ph), 7.72-7.73 (2H, m, Ph); δ C (100 MHz, CDCl₃) 15.1, 19.3, 24.9, 26.9, 33.1, 45.0, 51.0, 51.4, 58.3, 71.2, 77.6, 126.4, 127.3, 127.4, 127.8, 127.9, 128.0, 129.3, 129.5, 133.8, 134.5, 135.9, 138.1, 141.5, 142.2, 176.1; m/z (ESI⁺) 592 ([M+H]+, 100%); HRMS (ESI⁺) found 592.3254; C₃₈H₄₆NO₃Si ([M+H]+) requires 592.3247.

X-ray Crystal Structure Determination for 31

Data were collected using an Enraf-Nonius χ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.⁴

X-ray crystal structure data for 31 [C₃₈H₄₅NO₃Si]: M = 591.87, monoclinic, space group C 1 2/c 1, a = 26.40(12) Å, b = 10.3877(1) Å, c = 24.6887(4) Å, β = 96.3914(6)°, V = 6728.74(16) Å³, Z = 8, μ = 0.106 mm⁻¹, colourless block, crystal dimensions = 0.1 × 0.1 × 0.1 mm³. A total of 7581 unique reflections were measured for 5 < θ < 27 and 5208 reflections were used in the refinement. The final parameters were wR₂ = 0.053 and R₁ = 0.044 [I>3σ(I)]. Crystallographic data (excluding structure factors) has been deposited with

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the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 669235. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

**tert-Butyl (1RS,2RS,3RS,αSR)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 33**

Following *General Procedure 1a*, BuLi (1.6 M in hexanes, 1.56 mL, 2.50 mmol), (RS)-N-benzyl-N-(α-methylbenzyl)amine (533 mg, 2.52 mmol) in THF (6 mL) and 19 (100 mg, 0.51 mmol) in THF (1 mL) gave 33 in >98% de. Purification by chromatography (2% Et₂O in pentane) gave 33 as a colourless oil (179 mg, 86%, >98% de); νₘₐₓ (film) 1722 (C=O); δₜₜ (400 MHz, CDCl₃) 1.37 (3H, d, J 6.9, C(α)Me), 1.52 (9H, s, CMe₃), 1.72-1.80 (2H, m, C(5)H₂), 2.18-2.29 (2H, m, C(4)H₂), 2.78-2.83 (1H, m, C(1)H), 3.10 (3H, s, OMe), 3.19 (1H, app t, J 7.6, C(2)H), 3.95-4.00 (1H, m, C(3)H), 3.99 (2H, app d, J 15.7, NCH₂), 4.24 (1H, q, J 6.9, C(α)H), 7.21-7.49 (10H, m, Ph); δ_C (100 MHz, CDCl₃) 17.3, 25.0, 28.2, 28.3, 48.4, 50.9, 56.6, 57.9, 68.8, 79.9, 82.2, 126.1, 26.7, 127.9, 128.0, 128.6, 128.7, 129.7, 142.8, 143.1, 174.9; m/z (ESI⁺) 410 ([M+H⁺], 100%); HRMS (ESI⁺) found 410.2704; C₂₀H₃₆NO₃ ([M+H⁺]) requires 410.2695.

**tert-Butyl (1RS,2SR,3SR,αRS)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 34 and (1RS,2SR,3SR,αRS)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylic acid 37**

Following *General Procedure 2*, 33 (89 mg, 0.22 mmol) and KO'Bu (3.1 mg, 0.04 mmol) in 'BuOH/THF (1:1, 6 mL) gave 34 as a colourless oil (63 mg, 71%, >98% de); νₘₐₓ (film) 1725 (C=O); δₜₜ (400 MHz, PhMe-d₈) 1.28-1.40 (1H, m, C(4)H₆), 1.39 (9H, s, CMe₃), 1.41 (3H, d, J 6.8, C(α)Me), 1.49-1.58 (1H, m, C(5)H₂), 1.58-1.67 (1H, m, C(4)H₆), 1.79-1.88 (1H, m, C(5)H₂), 2.52-2.59 (1H, m, C(1)H), 3.14 (3H, s, OMe), 3.49-3.53 (1H, m, C(3)H), 3.61 (1H, d, J 14.5, NCH₂), 3.67 (1H, d, J 14.5, NCH₂), 3.83-3.87 (1H, m, C(2)H), 4.00 (1H, q, J 6.8, C(α)H), 7.00-7.50 (10H, m, Ph); δ_C (125 MHz, PhMe-d₈) 21.2, 31.6, 32.8, 34.2,
52.8, 55.9, 61.3, 63.6, 74.3, 83.9, 88.4, 132.4, 132.5, 132.6, 132.7, 132.9, 133.0, 133.1, 133.3, 133.5, 142.0, 142.1, 178.7; m/z (ESI⁺) 410 ([M+H]⁺, 100%); HRMS (ESI⁺) found 410.2694; C₂₆H₃₆NO₃ ([M+H]⁺) requires 410.2695. Further elution gave 37 as a colourless oil (23 mg, 29%, >98% de); νmax (film) 1701 (C=O); δH (400 MHz, CDCl₃) 1.54 (3H, d, J 6.8, C(α)Me), 1.75-1.81 (2H, m, C(4)H₂A, C(5)H₂A), 1.80-1.92 (2H, m, C(4)H₂B, C(5)H₂B), 2.56-2.64 (1H, m, C(1)H), 3.39 (3H, s, OMe), 3.40-3.45 (1H, m, C(2)H), 3.85-3.94 (3H, m, C(3)H, NCH₂), 4.10 (1H, q, J 6.8, C(α)H), 7.20-7.38 (10H, m, Ph); δC (100 MHz, CDCl₃) 14.3, 27.8, 44.4, 50.6, 56.9, 57.9, 66.5, 79.9, 80.0, 127.6, 128.3, 128.4, 128.6, 128.9, 129.0, 174.4; m/z (ESI⁺) 354 ([M+H]⁺, 100%); HRMS (ESI⁺) found 354.2064; C₂₂H₂₈NO₃ ([M+H]⁺) requires 354.2069.

**tert-Butyl (1RS,2RS,3RS,αSR)- and (1RS,2SR,3SR,αRS)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3-tert-butyldiphenylsilyloxy-cyclopentane-carboxylate (1RS,2RS,3RS,αSR)-35 and (1RS,2SR,3SR,αRS)-36**

Following **General Procedure 1a**, BuLi (2.5 M in hexanes, 0.42 mL, 1.05 mmol), (RS)-N-benzyl-N-(α-methylbenzyl)amine, (225 mg, 1.07 mmol) in THF (2 mL) and 21 (90 mg, 0.21 mmol) in THF (1.5 mL) gave a 90:10 mixture of **35:36**. Purification by chromatography (1% Et₂O in pentane) gave **35** as a colourless oil (118 mg, 88%, >98% de); νmax (film) 1722 (C=O); δH (400 MHz, CDCl₃) 1.09 (9H, s, SiCMe₃), 1.33-1.34 (1H, m, C(4)H₂A), 1.35 (3H, d, J 6.6, C(α)Me), 1.41 (9H, s, OCMMe₃), 1.52-1.28 (3H, m, C(4)H₂B, C(5)H₂B), 2.48-2.49 (1H, m, C(1)H), 3.41 (1H, app t, J 7.7, C(2)H), 4.04-4.07 (3H, m, C(α)H, NCH₂), 4.65-4.70 (1H, m, C(3)H), 7.24-7.72 (20H, m, Ph); δC (100 MHz, CDCl₃) 16.5, 19.2, 25.0, 27.0, 28.1, 31.5, 47.3, 51.6, 57.2, 69.6, 76.0, 80.0, 126.4, 126.6, 127.4, 125.6, 128.0, 128.2, 128.3, 129.4, 129.5, 134.0, 134.9, 135.8, 135.9, 142.0, 144.1, 174.8; m/z (ESI⁺) 634 ([M+H]⁺, 100%); HRMS (ESI⁺) found 634.3759; C₄₁H₅₂N₂O₃Si ([M+H]⁺) requires 634.3787. Further elution gave **36** as a colourless oil (13 mg, 10%, >98% de); νmax (film) 1724 (C=O); δH (400 MHz, CDCl₃) 1.10 (9H, s, SiCMe₃), 1.35 (3H, d, J 6.8, C(α)Me), 1.41 (9H, s, OCMMe₃), 1.24-1.47 (1H, m, C(4)H₂A), 1.48-1.63 (2H, m, C(4)H₂B, C(5)H₂B), 1.69-1.78 (1H, m, C(5)H₂B), 2.45-2.55 (1H, m, C(1)H), 3.64 (1H, AB system, JAB 15.4, NCH₂), 3.85 (1H, dd, J 1.4, 5.5, C(2)H), 3.93 (1H, q, J 6.8, C(α)H), 4.26 (1H, app dd, J 5.8, 5.5, C(3)H), 7.12-7.79 (20H, m, Ph); δC (100 MHz, CDCl₃) 18.7, 19.1, 26.7, 26.9, 27.9, 33.1, 46.2, 51.0, 59.1, 71.1, 77.7, 79.7, 126.2, 126.4, 127.3, 127.4,
127.8, 127.9, 128.1, 129.3, 129.5, 133.8, 134.6, 135.7, 135.8, 135.9, 141.8 144.7, 175.0; m/z (ESI+) 634 ([M+H]+, 100%); HRMS (ESI+) found 634.3709; C₄₁H₅₂NO₅Si ([M+H]+) requires 634.3716.

tert-Butyl (1RS,2SR,3SR,αRS)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3-tert-butyldiphenylsilyloxy-cyclopentane-carboxylate 36

Following General Procedure 2, 35 (81 mg, 0.13 mmol) and KO'Bu (2.3 mg, 0.03 mmol) in 'BuOH/THF (1:1, 6 mL) gave 36 as a colourless oil (81 mg, quant, >98% de).

tert-Butyl (1RS,2RS,3RS,αSR)-2-[N-3,4-dimethoxybenzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 39

Following General Procedure 1a, BuLi (2.5 M in hexanes, 1 mL, 2.5 mmol), (RS)-N-3,4-dimethoxybenzyl-N-(α-methylbenzyl)amine (684 mg, 2.52 mmol) in THF (70 mL) and 19 (100 mg, 0.5 mmol) in THF (4.2 mL) gave 39 in >98% de. Purification by chromatography (15% Et₂O in pentane) gave 39 as a pale yellow oil (208 mg, 89%, >98% de); νmax (film) 1721 (C=O); δH (400 MHz, CDCl₃) 1.37 (3H, d, J 6.8, C(α)Me), 1.48 (9H, s, CMe₃), 1.67-1.77 (2H, m, C(5)H₂), 2.17-2.26 (2H, m, C(4)H₂), 2.74-2.78 (1H, m, C(1)H), 3.14 (3H, s, C(OMe)), 3.16-3.20 (1H, m, C(2)H), 3.83-3.98 (2H, m, NCH₂), 3.87 (3H, s, ArOMe), 3.91 (3H, s, ArOMe), 4.01-4.06 (1H, m, C(3)H), 4.21 (1H, q, J 6.8, C(α)H), 6.80-7.42 (8H, m, Ar, Ph); δC (100 MHz, CDCl₃) 16.7, 24.9, 28.0, 28.1, 48.2, 50.7, 55.7, 55.8, 57.6, 68.7, 79.9, 82.0, 110.6, 111.3, 119.5, 126.5, 127.9, 135.2, 143.4, 147.3, 148.6, 174.6; m/z (ESI+) 470 ([M+H]+, 100%); HRMS (ESI+) found 470.2903; C₄₃H₅₆NO₅Si ([M+H]+) requires 470.2906.
Methyl (1RS,2SR,3SR,αRS)-2-[N-3,4-dimethoxybenzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 40

Following General Procedure 2, 39 (60 mg, 0.13 mmol) and KOtBu (2.3 mg, 0.03 mmol) in tBuOH/THF (1:1, 6 mL) gave 40 as a pale yellow oil (60 mg, quant, >98% de); νmax (film) 1722 (C=O); δH (400 MHz, PhMe-d8) 1.34 (3H, d, J 6.8, C(α)Me), 1.44 (9H, s, CMe3), 1.45-1.49 (1H, m, C(4)H3), 1.55-1.62 (1H, m, C(5)H5), 1.62-1.68 (1H, m, C(4)H3), 1.82-1.87 (1H, m, C(5)H5), 2.57-2.63 (1H, m, C(1)H), 3.15 (3H, s, C(3)OMe), 3.52-3.56 (1H, m, C(3)H), 3.52 (3H, s, ArOMe), 1.07 (9H, s, SiCMe3), 1.21-1.47 (13H, m, C(4)H4, C(α)Me, OCMes), 1.52-1.60 (2H, m, C(5)H5), 1.61-1.68 (2H, m, C(4)H4), 2.46-2.49 (1H, m, C(1)H), 3.38-3.41 (1H, m, C(2)H), 3.86 (3H, s, ArOMe), 3.88 (3H, s, ArOMe), 3.95 (2H, AB system, JAB 14.3, NCH2), 4.05 (1H, q, J 6.7, C(α)H), 4.66-4.70 (1H, m, C(3)H), 6.76-7.71 (18H, m, Ar, Ph); δC (100 MHz, CDCl3) 15.5, 19.1, 24.8, 26.9, 28.0, 31.5, 47.7, 51.1, 55.5, 55.6, 56.4, 69.3,

tert-Butyl (1RS,2RS,3RS,αSR)-2-[N-3,4-dimethoxybenzyl-N-(α-methylbenzyl)amino]-3-tert-butyldiphenylsilyloxy-cyclopentane-carboxylate 41

Following General Procedure 1a, BuLi (2.5 M in hexanes, 0.47 mL, 1.17 mmol), (RS)-N-3,4-dimethoxybenzyl-N-(α-methylbenzyl)amine (321 mg, 1.18 mmol) in THF (33 mL) and 21 (100 mg, 0.24 mmol) in THF (2 mL) gave a 94:6 mixture of 41:42. Purification by chromatography (20% Et2O in pentane) gave 41 as a yellow oil (130 mg, 79%, >98% de); νmax (film) 1721 (C=O); δH (400 MHz, CDCl3) 1.07 (9H, s, SiCMe3), 1.21-1.47 (13H, m, C(4)H4, C(α)Me, OCMes), 1.52-1.60 (2H, m, C(5)H5), 1.61-1.68 (2H, m, C(4)H4), 2.46-2.49 (1H, m, C(1)H), 3.38-3.41 (1H, m, C(2)H), 3.86 (3H, s, ArOMe), 3.88 (3H, s, ArOMe), 3.95 (2H, AB system, JAB 14.3, NCH2), 4.05 (1H, q, J 6.7, C(α)H), 4.66-4.70 (1H, m, C(3)H), 6.76-7.71 (18H, m, Ar, Ph); δC (100 MHz, CDCl3) 15.5, 19.1, 24.8, 26.9, 28.0, 31.5, 47.7, 51.1, 55.5, 55.6, 56.4, 69.3,
75.9, 79.7, 110.6, 111.4, 119.9, 126.4, 129.4, 133.9, 135.8, 143.9, 147.5, 148.7, 174.9; m/z (ESI\(^{+}\)) 694 ([M+H]\(^{+}\), 100%); HRMS (ESI\(^{-}\)) found 694.3920; C\(_{43}\)H\(_{56}\)NO\(_{5}\)Si ([M+H]\(^{+}\)) requires 694.3928.

tert-Butyl (1RS,2SR,3SR,aRS)-2-[N-3,4-dimethoxybenzyl-N-(\(\alpha\)-methylbenzyl)amino]-3-tert-butyldiphenylsilyloxy-cyclopentane-carboxylate 42

Following General Procedure 2, 41 (50 mg, 0.07 mmol) and KO\(^{1}\)Bu (1.2 mg, 0.01 mmol) in \(^{1}\)BuOH/THF (1:1, 6 mL) gave 42 as a viscous yellow oil (49 mg, 98%, >98% de); \(\nu\)\(_{\max}\) (film) 1721 (C=O); \(\delta\)\(_{\text{H}}\) (400 MHz, PhMe-\(d_{8}\)) 1.23-1.24 (1H, m, C(4)H\(_{\alpha}\)), 1.24 (9H, s, SiCMe\(_{3}\)), 1.29-1.37 (1H, m, C(5)H\(_{\alpha}\)), 1.40 (9H, s, OCMe\(_{3}\)), 1.46 (3H, d, J 6.8, C(\(\alpha\))Me), 1.72-1.77 (1H, m, C(4)H\(_{\beta}\)), 1.87-1.92 (1H, m, C(5)H\(_{\beta}\)), 2.57-2.65 (1H, m, C(1)H), 3.46-3.53 (2H, m, NCH\(_{2}\)), 3.50 (3H, s, ArOMe), 3.63 (3H, s, ArOMe), 4.03 (1H, q, J 6.8, C(\(\alpha\))H), 4.12-4.16 (1H, m, C(2)H), 4.36-4.44 (1H, m, C(3)H), 6.42-7.90 (18H, m, Ar, Ph); \(\delta\)\(_{\text{C}}\) (100 MHz, PhMe-\(d_{8}\)) 20.7, 21.0, 21.3, 26.7, 27.2, 28.1, 47.0, 50.9, 55.5, 55.6, 58.9, 71.7, 78.6, 79.3, 112.1, 112.7, 120.5, 124.7, 137.4, 145.3, 149.0, 150.2, 174.6; m/z (ESI\(^{-}\)) 694 ([M+H]\(^{+}\), 100%); HRMS (ESI\(^{-}\)) found 694.3914; C\(_{43}\)H\(_{56}\)NO\(_{5}\)Si ([M+H]\(^{+}\)) requires 694.3928.

Parallel kinetic resolution of 19: tert-butyl (1R,2R,3R,\(\alpha\)S)-2-[N-benzyl-N-(\(\alpha\)-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 33 and tert-butyl (1S,2S,3S,\(\alpha\)R)-2-[N-3,4-dimethoxybenzyl-N-(\(\alpha\)-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 39

Following General Procedure 1b, BuLi (750 \(\mu\)L, 1.87 mmol), (S)-N-benzyl-N-(\(\alpha\)-methylbenzyl)amine (200 mg, 0.95 mmol), (R)-N-3,4-dimethoxybenzyl-N-(\(\alpha\)-methylbenzyl)amine (257 mg, 0.95 mmol) in THF (52 mL) and 19 (75 mg, 0.38 mmol) in THF (3.2 mL) gave a 50:50 mixture of 33:39. Purification by chromatography (3% Et\(_{2}\)O in pentane) gave (1R,2R,3R,\(\alpha\)S)-33 as a colourless oil (39 mg, 25%, >98% de);
Further elution gave (1S,2S,3S,αR)-39 as a pale yellow oil (53 mg, 30%, >98% de); [α]$_D^{24}$ +67.4 (c 1.2 in CHCl$_3$).

tert-Butyl (1S,2R,3R,αS)-[N-benzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 34 and (1S,2R,3R,αS)-2-[N-benzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylic acid 37

Following General Procedure 2, (1R,2R,3R,αS)-33 (190 mg, 0.46 mmol) and KO'Bu (7.1 mg, 0.09 mmol) in $^3$BuOH/THF (1:1, 10 mL) gave (1S,2R,3R,αS)-34 as a colourless oil (160 mg, 85%, >98% de); [α]$_D^{24}$ +46.7 (c 0.7 in CHCl$_3$). Further elution gave (1S,2R,3R,αS)-37 as a colourless oil (24 mg, 15%, >98% de); [α]$_D^{24}$ +12.6 (c 1.0 in CHCl$_3$).

tert-Butyl (1R,2S,3S,αR)-2-[N-3,4-dimethoxybenzyl-N-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 40

Following General Procedure 2, (1S,2S,3S,αR)-39 (348 mg, 0.74 mmol) and KO'Bu (12 mg, 0.15 mmol) in $^3$BuOH/THF (1:1, 18 mL) gave (1R,2S,3S,αR)-40 (210 mg, 61%, >98% de) as a pale yellow oil; [α]$_D^{24}$ −36.0 (c 1.0 in CHCl$_3$).

Following General Procedure 1b, BuLi (2.5 M in hexanes, 469 µL, 1.17 mmol), (S)-N-benzyl-N-(α-methylbenzyl)amine (125 mg, 0.59 mmol), (R)-N-3,4-dimethoxybenzyl-N-(α-methylbenzyl)amine (161 mg, 0.59 mmol) in THF (16 mL) and 21 (100 mg, 0.24 mmol) in THF (2 mL) gave a 45:5:45:5 mixture of 35:36:41:42. Purification by chromatography (1% Et₂O in pentane) gave (1*R,2*R,3*R,αS)-35 as a colourless oil (60 mg, 40%, >98% de); [α]²⁴D −22.6 (c 1.0 in CHCl₃). Further elution gave (1*S,2*S,3*S,αR)-41 as a colourless oil (59 mg, 36%, >98% de); [α]²⁴D +13.1 (c 1.0 in CHCl₃).

*tert*-Butyl (1*S,2*S,3*S,αR)-2-N-(α-methylbenzyl)amino-3-methoxy-cyclopentane-carboxylate 43

Following General Procedure 3, (1*S,2*S,3*S,αR)-39 (310 mg, 0.66 mmol) and DDQ (295 mg, 1.32 mmol) in DCM:H₂O (5:1, 6 mL) gave, after purification by chromatography (7% Et₂O in pentane), 43 as a pale yellow oil (207 mg, 98%, >98% de); Found C, 71.2; H, 9.2; N, 4.4%; C₁₉H₂₉NO₃ requires C, 71.4; H, 9.2; N, 4.4%; [α]²⁴D +25.8 (c 1.0 in CHCl₃); νₘₐₓ (film) 1719 (C=O); δₜ (400 MHz, CDCl₃) 1.33 (3H, d, J 6.5, C(α)Me), 1.39-1.49 (1H, m, C(4)H₄), 1.52 (9H, s, CMe₃), 1.75-1.93 (2H, m, C(5)H₂), 2.05-2.09 (1H, m, C(4)H₃), 2.93-2.96 (1H, m, C(1)H), 3.03-3.05 (1H, m, C(2)H), 3.20 (3H, s, OMe), 3.61 (1H, app dd, J 6.5, 5.1, C(3)H), 3.87 (1H, q, J 6.5, C(α)H), 7.19-7.34 (5H, m, Ph); δₚ (100 MHz, CDCl₃) 23.4, 23.8, 27.1, 27.2, 45.5, 55.9, 56.0, 64.8, 79.3, 85.0, 125.7, 125.9, 127.4, 144.6, 173.2; m/z (ESI⁺) 320 ([M+H]⁺, 100%); HRMS (ESI⁺) found 320.2223; C₁₉H₃₀NO₃ ([M+H]⁺) requires 320.2226.
**tert-Butyl (1R,2S,3S,αR)-2-N-(α-methylbenzyl)amino-3-methoxy-cyclopentane-carboxylate 44**

Following General Procedure 3, (1R,2S,3S,αR)-40 (210 mg, 0.45 mmol) and DDQ (203 mg, 0.90 mmol) in DCM/H₂O (5:1, 6 mL) gave, after purification by chromatography (15% Et₂O in pentane), 44 as a pale yellow oil (141 mg, 98%, >98% de); [α]²⁴D +8.8 (c 1.0 in CHCl₃); νmax (film) 1720 (C=O); δH (400 MHz, CDCl₃) 1.37 (3H, d, J 6.6, C(α)Me), 1.43 (9H, s, CMe₃), 1.62-1.71 (1H, m, C(4)H₄), 1.77-1.94 (3H, m, C(4)H₆, C(5)H₂), 2.44-2.50 (1H, m, C(1)H), 3.12 (3H, s, OMe), 3.20-3.22 (1H, m, C(2)H), 3.35-3.41 (1H, m, C(3)H), 3.91 (1H, q, J 6.6, C(α)H), 7.20-7.35 (5H, m, Ph); δC (100 MHz, CDCl₃) 24.7, 25.6, 28.0, 29.1, 51.0, 56.5, 56.6, 65.5, 80.3, 87.6, 126.6, 126.7, 128.3, 145.8, 174.2; m/z (ESI⁺) 320 ([M+H]+, 100%); HRMS (ESI⁺) found 320.2220; C₁₉H₃₀NO₃ ([M+H]+) requires 320.2226.

**tert-Butyl (1S,2S,3S)-2-amino-3-methoxy-cyclopentane-carboxylate (1S,2S,3S)-45**

Following General Procedure 4, Pd(OH₂)/C (50 mg, 50% w/w) and 43 (100 mg, 0.31 mmol) in MeOH (5 mL) gave (1S,2S,3S)-45 as a colourless oil (60 mg, 90%, >98% de); [α]²⁴D +42.4 (c 0.7 in CHCl₃); νmax (film) 1724 (C=O); δH (400 MHz, CDCl₃) 1.47 (9H, s, CMe₃), 1.55-1.60 (1H, m, C(4)H₄), 1.88-2.01 (2H, m, C(5)H₂), 2.08-2.16 (1H, m, C(4)H₉), 2.89-2.95 (1H, m, C(1)H), 3.35 (3H, s, OMe), 3.40-3.45 (1H, m, C(2)H), 3.54-3.57 (1H, m, C(3)H); δC (100 MHz, CDCl₃) 23.5, 28.0, 28.3, 48.2, 56.9, 58.6, 80.4, 88.3, 173.5; m/z (ESI⁺) 216 ([M+H]+, 100%); HRMS (ESI⁺) found 216.1596; C₁₁H₂₁NO₃ ([M+H]+) requires 216.1599.

**tert-Butyl (1R,2R,3R)-2-amino-3-methoxy-cyclopentane-carboxylate (1R,2R,3R)-45**

Following General Procedure 4, Pd(OH₂)/C (124 mg, 50% w/w) and (1R,2R,3R,αS)-33 (248 mg, 0.60 mmol) in MeOH (10 mL) gave (1R,2R,3R)-45 as a colourless oil (115 mg, 89%, >98% de); [α]²⁴D −60.5 (c 1.0 in CHCl₃).
**tert-Butyl (1R,2S,3S)-2-amino-3-methoxy-cyclopentane-carboxylate (1R,2S,3S)-46**

Following *General Procedure 4*, Pd(OH₂)/C (64 mg, 50% w/w) and 44 (127 mg, 0.40 mmol) in MeOH (5 mL) gave (1R,2S,3S)-46 as a colourless oil (83 mg, 96%, >98% de); [α]D24⁻¹0.0 (c 1.0 in CHCl₃); νₘₐₓ (film) 3400-3300 (N–H), 1725 (C=O); δH (400 MHz, CDCl₃) 1.44 (9H, s, CMe₃), 1.55-1.59 (1H, m, C(4)H₄), 1.81-2.01 (3H, m, C(4)H₄, C(5)H₂), 2.32-2.40 (1H, m, C(1)H), 3.29-3.23 (1H, m, C(2)H), 3.34 (3H, s, OMe), 3.36-3.41 (1H, m, C(3)H); δC (100 MHz, CDCl₃) 23.7, 28.1, 27.8, 28.1, 50.8, 57.3, 60.8, 80.5, 95.7, 173.7; m/z (ESI⁺) 216 ([M+H]+, 100%); HRMS (ESI⁺) found 216.1590; C₁₁H₂₁NO₃ ([M+H]+) requires 216.1600.

**tert-Butyl (1S,2R,3R)-2-amino-3-methoxy-cyclopentane-carboxylate (1S,2R,3R)-46**

Following *General Procedure 4*, Pd(OH₂)/C (80 mg, 50% w/w) and (1S,2R,3R,αS)-34 (160 mg, 0.39 mmol) in MeOH (5 mL) gave (1S,2R,3R)-46 as a colourless oil (79 mg, 94%, >98% de); [α]D24⁺10.4 (c 1.0 in CHCl₃).

**(1S,2S,3S)-2-Amino-3-methoxy-cyclopentane-carboxylic acid (1S,2S,3S)-47**

Following *General Procedure 5*, (1S,2S,3S)-45 (60 mg, 0.28 mmol) and TFA (1 mL) in DCM (1 mL) gave (1S,2S,3S)-47 as a white crystalline solid (27 mg, 75%); mp 187-188 °C; [α]D24⁺77.1 (c 1.0 in H₂O); νₘₐₓ (film) 3500-3300 (O–H, N–H), 1710 (C=O); δH (400 MHz, D₂O) 1.51-1.59 (1H, m, C(4)H₄), 1.75-1.85 (1H, m, C(5)H₄), 2.03-2.14 (2H, m, C(4)H₄, C(5)H₄), 2.87-2.92 (1H, m, C(1)H), 3.28 (3H, s, OMe), 3.45-3.48 (1H, m, C(2)H), 3.91-3.96 (1H, m, C(3)H); δC (125 MHz, D₂O) 26.5, 28.0, 45.1, 57.1, 57.3, 84.2, 180.4; m/z (ESI⁻) 158 ([M–H]⁻, 100%); HRMS (ESI⁻) found 158.0817; C₇H₁₂NO₃ ([M–H]⁻) requires 158.0817.

**(1R,2R,3R)-2-Amino-3-methoxy-cyclopentane-carboxylic acid (1R,2R,3R)-47**
Following General Procedure 5, (1R,2R,3R)-45 (115 mg, 0.53 mmol) and TFA (1 mL) in DCM (1 mL) gave (1R,2R,3R)-47 as a colourless crystalline solid (52 mg, 77%, >98% de); $[\alpha]_{D}^{24} = -76.4$ (c 1.0 in H$_2$O).

(1R,2S,3S)-2-Amino-3-methoxy-cyclopentane-carboxylic acid (1R,2S,3S)-48

Following General Procedure 5, (1R,2S,3S)-46 (83 mg, 0.38 mmol) and TFA (1 mL) in DCM (1 mL) gave (1R,2S,3S)-48 as a white crystalline solid (30 mg, 60%, >98% de); mp 171-172 °C; $[\alpha]_{D}^{24} = -16.9$ (c 1.0 in H$_2$O); $\nu_{\text{max}}$ (film) 3500-3300 (O–H, N–H), 1710 (C=O); $\delta_H$ (400 MHz, D$_2$O) 1.56-1.65 (1H, m, C(4)H$_A$), 1.69-1.80 (1H, m, C(5)H$_A$), 1.98-2.05 (2H, m, C(4)H$_B$, C(5)H$_B$), 2.59-2.66 (1H, m, C(1)H), 3.29 (3H, s, OMe), 3.50-3.56 (1H, m, C(2)H), 3.75-3.83 (1H, m, C(3)H); $\delta_C$ (100 MHz, D$_2$O) 25.8, 28.1, 49.0, 57.2, 59.6, 84.6, 180.8; $m/z$ (ESI$^-$) 158 ([M–H]$^-$, 100%), HRMS (ESI$^-$) found 158.0819; C$_7$H$_{12}$NO$_3$ ([M–H]$^-$) requires 158.0817.

(1S,2R,3R)-2-Amino-3-methoxy-cyclopentane-carboxylic acid (1S,2R,3R)-48

Following General Procedure 5, (1S,2R,3R)-46 (79 mg, 0.37 mmol) and TFA (1 mL) in DCM (1 mL) gave (1S,2R,3R)-48 as a colourless solid (31 mg, 65%, >98% de); $[\alpha]_{D}^{24} = +17.0$ (c 1.0 in H$_2$O).