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 $MgSO_4$. 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. 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

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

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 NH_4Cl, 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 $NaHCO_3$ (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 $NaHCO_3$ (50 mL) and brine (50 mL), dried and concentrated *in vacuo*.

General Procedure 2: base catalysed epimerisation

A catalytic amount of KO^tBu was added to the β-amino ester in ^tBuOH/THF (1:1). The mixture was refluxed overnight before addition of sat aq NH_4Cl, 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/H_2O (5:1). The reaction mixture was stirred at rt for 48 h before the addition of sat aq $NaHCO_3$. The mixture was extracted with DCM and the combined organic extracts were washed with brine, dried and concentrated *in vacuo*.

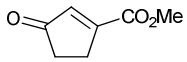
General Procedure 4: hydrogenolysis

$Pd(OH)_2/C$ 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

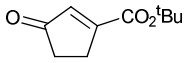
TFA was added to a solution of the β-amino ester in DCM at rt and stirred for 16 h. The reaction mixture was then concentrated *in vacuo*. The residue was dissolved in MeOH (2 mL) and HCl in Et_2O (sat, 2 mL) was added, and the mixture was concentrated *in vacuo*. The residue was partitioned between Et_2O (4 mL) and H_2O (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



CrO_3 (4.82 g, 48.2 mmol) was added slowly to acetic anhydride (33 mL). When all of the CrO_3 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 $NaHCO_3$ and brine, then dried and concentrated *in vacuo*. The crude yellow oil was stirred in a mixture of THF/sat aq $NaHCO_3$ overnight. Purification by chromatography (20% Et_2O in pentane) gave **14** as a colourless oil (9.26 g, 60%); δ_H (400 MHz, $CDCl_3$) 2.53-2.55 (2H, m, C(5)H_2), 2.87-2.88 (2H, m, C(4)H_2), 3.87 (3H, s, O*Me*), 6.76 (1H, t, *J* 2.3, C(2)*H*).

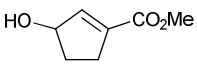
tert-Butyl 3-oxo-cyclopent-1-ene-carboxylate 15



Oxidation with CrO_3: CrO_3 (18.1 g, 180 mmol) was added slowly to acetic anhydride (45 mL). When all of the CrO_3 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 $NaHCO_3$ and brine, then dried and concentrated *in vacuo*. The crude yellow oil was stirred in a mixture of THF/sat aq $NaHCO_3$ overnight. Purification by chromatography (20% Et_2O in pentane) gave **15** as a colourless oil (5.44 g, 50%); ν_{max} (film) 1716 (C=O), 1613 (C=C); δ_H (400 MHz, $CDCl_3$) 1.55 (9H, s, C*Me*$_3$), 2.51-2.53 (2H, m, C(4)*H*$_2$), 2.80-2.83 (2H, m, C(5)*H*$_2$), 6.65-6.69 (1H, m, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 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; $C_{10}H_{15}O_3$ ($[M+H]^+$) requires 183.1021.

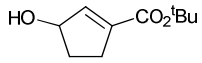
Oxidation with tert-butyl hydroperoxide: tert-butyl hydroperoxide (5-6 M in decane, 10.8 mL) was added dropwise to a mixture of **13** (5 g, 29.7 mmol), $Pd(OH)_2/C$ (1.04 mg, 1.49 mmol) and K_2CO_3 (2.05 g, 14.9 mmol) in DCM (200 mL) at 0 °C and the resultant solution stirred for 4 h at 0 °C under N_2. 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 (eluent DCM), dried and concentrated *in vacuo*. Purification by chromatography (2% Et_2O in pentane) gave **15** as a colourless oil (2.0 g, 37%).

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



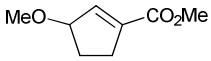
To a solution of **14** (5.53 g, 39.5 mmol) in MeOH (75 mL) at 0 °C was added $CeCl_3 \cdot 7H_2O$ (13.6 g, 36.6 mmol) followed by $NaBH_4$ (1.70 g, 45.0 mmol). The mixture was stirred for 10 min, quenched with 0.2 M aq HCl, and extracted with DCM. The combined organic extracts were washed with H_2O, dried and concentrated *in vacuo*. Chromatography (30% Et_2O in pentane) gave **16** as a colourless oil (5.50 g, 98%); δ_H (400 MHz, $CDCl_3$) 1.76-1.85 (1H, m, C(4)*H*$_A$), 2.36-2.55 (2H, m, C(4)*H*$_B$, C(5)*H*$_A$), 2.63-2.79 (1H, m, C(5)*H*$_B$), 3. 77 (3H, s, O*Me*), 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**



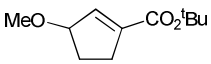
To a solution of **15** (5.50 g, 30.2 mmol) in MeOH (20 mL) at 0 °C was added $CeCl_3 \cdot 7H_2O$ (10.4 g, 28.0 mmol) followed by $NaBH_4$ (1.30 g, 34.4 mmol). The mixture was stirred for 10 min, quenched with 0.2 M aq HCl, and extracted with DCM. The combined organic extracts were washed with H_2O, dried and concentrated *in vacuo*. Chromatography (30% Et_2O in pentane) gave **17** as a colourless oil (5.35 g, 98%); ν_{max} (film) 3404 (O−H), 1711 (C=O), 1634 (C=C); δ_H (400 MHz, $CDCl_3$) 1.49 (9H, s, CMe_3), 1.74-1.83 (1H, m, C(4)H_A), 2.34-2.49 (2H, m, C(4)H_B, C(5)H_A), 2.62-2.73 (1H, m, C(5)H_B), 4.95 (1H, br s, C(3)*H*), 6.59-6.60 (1H, m, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 28.1, 29.9, 33.6, 77.2, 80.7, 140.7, 141.7, 164.6; *m/z* (CI^+) 202 ($[M+NH_4]^+$, 100%); HRMS (CI^+) found 202.1438; $C_{10}H_{20}NO_3$ ($[M+NH_4]^+$) 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% Et_2O in pentane) gave **18** as a colourless oil as a colourless oil (150 mg, 88%); ν_{max} (film) 1723 (C=O), 1636 (C=C); δ_H (400 MHz, $CDCl_3$) 1.82-1.91 (1H, m, C(4)H_A), 2.25-2.33 (1H, m, C(4)H_B), 2.44-2.52 (1H, m, C(5)H_A), 2.67-2.76 (1H, m, C(5)H_B), 3.36 (3H, s, C(3)O*Me*), 3.76 (1H, s, CO_2*Me*), 4.53-4.57 (1H, m, C(3)*H*), 6.78-6.80 (1H, m, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 29.9, 51.7, 56.4, 85.5, 139.3, 140.5, 165.5; *m/z* (CI^+) 156 ($[M+H]^+$, 100%); HRMS (CI^+) found 157.0864; $C_8H_{12}O_3$ ($[M+H]^+$) requires 157.0865.

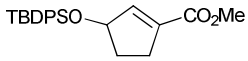
***tert*-Butyl (*RS*)-3-methoxy-cyclopent-1-ene-carboxylate 19**



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% Et_2O in pentane) gave **19** as a colourless oil (2.29 g, 85%); ν_{max} (film) 1713 (C=O), 1635 (C=C); δ_H (400 MHz, $CDCl_3$) 1.49 (9H, s, CMe_3), 1.82-1.88 (1H, m, C(4)H_A), 2.23-2.29 (1H, m,

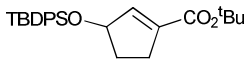
C(4)H_B), 2.40-2.47 (1H, m, C(5)H_A), 2.58-2.69 (1H, m, C(5)H_B), 3.35 (3H, s, O*Me*), 4.51-4.53 (1H, m, C(3)*H*), 6.60 (1H, app dd, *J* 2.2, 1.9, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 27.8, 28.0, 29.8, 56.3, 80.4, 85.5, 139.0, 141.3, 164.4; *m/z* (CI^+) 199 ($[M+H]^+$, 100%); HRMS (CI^+) found 199.1331; $C_8H_{12}O_3$ ($[M+H]^+$) requires 199.1334.

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



TBDPSCl (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, C*Me*$_3$), 1.86-1.94 (1H, m, C(4)H_A), 2.13-21.21 (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, O*Me*), 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, CDCl3) 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.

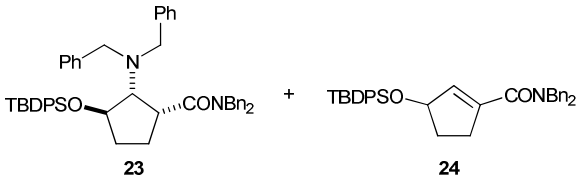
***tert*-Butyl (*RS*)-3-*tert*-butyldiphenylsilyloxy-cyclopent-1-ene-carboxylate 21**



TBDPSCl (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 crystaline 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, SiC*Me*$_3$), 1.48 (9H, s, OC*Me*$_3$), 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,

28.1, 29.8, 34.0, 78.5, 80.4, 127.7, 127.9, 129.7, 130.3, 132.5, 134.0, 135.2, 135.7, 135.8, 139.3, 142.7, 164.7; *m/z* (ESI^+) 440 ($[M+H]^+$, 100%); HRMS (ESI^+) found 440.2622; $C_{26}H_{35}O_3Si$ ($[M+H]^+$) requires 440.2621.

_N_,_N_-Dibenzyl (1*RS*,2*RS*,3*RS*)-2-_N_,_N_-dibenzylamino-3-*tert*-butyldiphenylsilyloxy-cyclopentane-carboxamide 23 and _N_,_N_-dibenzyl (*RS*)-3-*tert*-butyldiphenylsilyloxy-cyclopent-1-ene-carboxamide 24



23 **24**

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% Et_2O in pentane) gave **23** as a white crystalline solid (110 mg, 28%, >98% de); mp 118-119 °C; ν_{max} (KBr) 1646 (C=O); δ_H (400 MHz, $CDCl_3$) 1.05 (9H, s, C*Me*$_3$), 1.41-1.54 (1H, m, C(4)H_A), 1.64-1.78 (1H, m, C(5)H_A), 1.84-1.94 (1H, m, C(4)H_B), 2.15-2.26 (1H, m, C(5)H_B), 3.15 (1H, app q, *J* 8.9, C(1)*H*), 3.43 (2H, d, *J* 13.0, N(CH_AH$_B$Ph)$_2$), 3.56 (1H, dd, *J* 4.4, 4.8, C(2)*H*), 3.83 (2H, d, *J* 13.0, N(CH$_A$$H_B$Ph)$_2$), 3.95 (1H, d, *J* 17.8, CONCH_AH$_B$Ph), 4.09 (1H, d, *J* 14.3, CONCH_CH$_D$Ph), 4.34 (1H, d, *J* 17.8, CONCH$_A$$H_B$Ph), 4.92-4.96 (1H, app q, *J* 5.5, C(3)*H*), 5.25 (1H, d, *J* 14.3, CONCH$_C$$H_D$Ph), 6.97-7.74 (30H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.2, 27.0, 27.5, 33.3, 44.1, 44.4, 44.9, 55.6, 69.8, 75.3, 126.1, 126.6, 127.2, 127.5, 127.7, 128.0, 128.4, 128.7, 128.8, 129.5, 129.6, 129.7, 132.9, 134.6, 135.9, 137.0, 174.1; *m/z* (ESI^+) 743 ($[M+H]^+$, 100%); HRMS (ESI^+) found 743.4039; $C_{50}H_{55}N_2O_2Si$ ($[M+H]^+$) requires 743.4033. Further elution gave **24** as a colourless oil (60 mg, 21%); ν_{max} (film) 1612 (C=O), 1581 (C=C); δ_H (400 MHz, $CDCl_3$) 1.00 (9H, s, C*Me*$_3$), 1.86-1.94 (1H, m, C(4)H_A), 2.14-2.22 (1H, m, C(4)H_B), 2.54-2.61 (1H, m, C(5)H_A), 2.72-2.80 (1H, m, C(5)H_B), 4.43-4.56 (3H, m, NCH_2Ph, NCH_AH$_B$Ph), 4.70 (1H, d, *J* 14.7, NCH$_A$$H_B$Ph), 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*); δ_C (100 MHz, $CDCl_3$) 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; $C_{36}H_{40}NO_2Si$ ($[M+H]^+$) requires 546.2828.

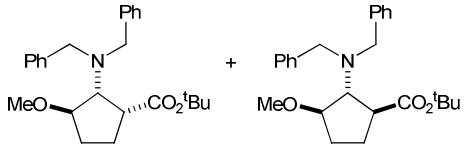
X-ray Crystal Structure Determination for 23

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-$K\alpha$ 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.[2]

X-ray crystal structure data for **23** [$C_{50}H_{54}N_2O_2Si$]: 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, β = 116.7552(8)°, V = 8447.1(3) Å^3, Z = 8, μ = 0.097 mm^{-1}, colourless block, crystal dimensions = 0.1 × 0.1 × 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 [$I>3\sigma(I)$]. 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 (1*RS*,2*RS*,3*RS*)- and (1*RS*,2*SR*,3*SR*)-2-*N*,*N*-dibenzylamino-3-methoxy-cyclopentane-carboxylate (1*RS*,2*RS*,3*RS*)-25 and (1*RS*,2*SR*,3*SR*)-26



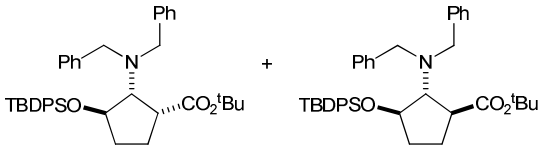
25 **26**

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_2O in pentane) gave **25** as a colourless oil (80 mg, 40%, >98% de); ν_{max} (film) 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.53 (9H, s, C*Me*$_3$), 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, O*Me*), 3.30-3.33 (1H, m, C(2)*H*), 3.73 (2H, d, *J* 14.1, N(C*H*$_A$H$_B$Ph)$_2$), 3.85 (2H, d, *J* 14.1, N(CH$_A$*H*$_B$Ph)$_2$), 4.09-4.13 (1H, m, C(3)*H*), 7.21-7.39 (10H, m, *Ph*); δ_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); ν_{max} (film) 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.30 (9H, s, C*Me*$_3$), 1.68-2.02 (4H, m, C(4)*H*$_2$, C(5)*H*$_2$), 2.74-2.78 (1H, m, C(1)*H*), 3.29 (3H, s, O*Me*), 3.52-3.55 (1H, m, C(2)*H*), 3.67 (4H, s, N(C*H*$_2$Ph)$_2$), 3.78-3.86 (1H, m, C(3)*H*), 7.21-7.39 (10H, m, *Ph*), δ_C (100 MHz, $CDCl_3$) 26.9, 28.0, 30.2, 45.9, 55.1, 56.8, 70.1, 83.0,

[2] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, **2001**, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

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.

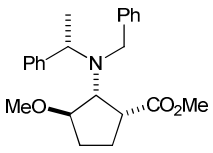
***tert*-Butyl (1*RS*,2*RS*,3*RS*)- and (1*RS*,2*SR*,3*SR*)-2-*N*,*N*-dibenzylamino-3-*tert*-butyldiphenylsilyloxy-cyclopentane-carboxylate (1*RS*,2*RS*,3*RS*)-27 and (1*RS*,2*SR*,3*SR*)-28**



27 **28**

Following *General Procedure 1a*, BuLi (1.6 M in hexanes, 733 μL, 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_2O in pentane) gave **27** as a colourless oil (108 mg, 74%, >98% de); ν_{max} (film) 1723 (C=O); δ_H (400 MHz, $CDCl_3$) 1.08 (9H, s, SiC*Me*$_3$), 1.27-1.34 (2H, m, C(4)*H*$_2$), 1.46 (9H, s, OC*Me*$_3$), 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_AH$_B$Ph)$_2$), 3.82 (2H, d, *J* 14.2, N(CH$_A$CH_BPh)$_2$), 4.74-4.76 (1H, m, C(3)*H*), 7.21-7.71 (20H, m, *Ph*); δ_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; $C_{40}H_{50}NO_3Si$ ($[M+H]^+$) requires 620.3560. Further elution gave **28** as a colourless oil (10 mg, 7%, >98% de); ν_{max} (film) 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, SiC*Me*$_3$), 1.44 (9H, s, OC*Me*$_3$), 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_ACH$_B$Ph)$_2$), 3.67 (2H, d, *J* 14.0, N(CH$_A$CH_BPh)$_2$), 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*); δ_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; $C_{25}H_{34}NO_3Si$ ($[M+H]^+$) requires 620.3560.

Methyl (1*RS*,2*RS*,3*RS*,α*SR*)-2-[*N*-benzyl-*N*-(α-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*-(α-methylbenzyl)amine (835 mg, 3.95 mmol) in THF (1 mL) and **18** (123 mg, 0.79 mmol) in THF (2 mL)

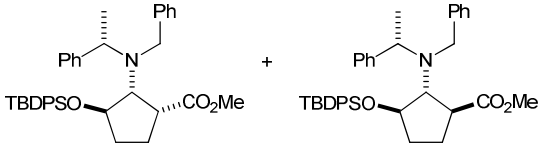
gave **29** in >98% de. Purification by chromatography (1% Et_2O in pentane) gave **29** as a white crystalline solid (87 mg, 30%, >98% de); mp 70-71 °C; ν_{max} (KBr) 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.35 (3H, d, *J* 6.6, C(α)*Me*), 1.46-1.56 (1H, m, C(4)H_A), 1.74-1.91 (2H, m, C(5)H_2), 2.20-2.29 (1H, m, C(4)H_B), 2.87 (1H, dt, *J* 4.3, 3.8, C(1)*H*), 3.24 (3H, s, C(3)O*Me*), 3.32 (1H, app t, *J* 7.7, C(2)*H*), 3.67 (3H, s, CO_2Me), 3.94 (2H, app s, CH_2Ph), 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, $CDCl_3$) 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; $C_{23}H_{29}NO_3$ ($[M+H]^+$) requires 368.2226.

X-ray Crystal Structure Determination for 29

Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-$K\alpha$ 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** [$C_{23}H_{29}NO_3$]: M = 734.98, orthorhombic, space group $P\ b\ n\ 2_1$, a = 13.9137(2) Å, b = 16.8715(3) Å, c = 17.2156(3) Å, V = 4041.28(11) Å^3, Z = 8, μ = 0.079 mm^{-1}, colourless block, crystal dimensions = 0.2 × 0.2 × 0.2 mm^3. A total of 4740 unique reflections were measured for $5 < \theta < 27$ and 4060 reflections were used in the refinement. The final parameters were wR_2 = 0.051 and R_1 = 0.042 [$I>1.5\sigma(I)$]. 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 (1*RS*,2*RS*,3*RS*,α*SR*)- and (1*RS*,2*SR*,3*SR*,α*RS*)-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-3-*tert*-butyldiphenylsilyloxy-cyclopentane-carboxylate (1*RS*,2*RS*,3*RS*,α*SR*)-31 and (1*RS*,2*SR*,3*SR*,α*RS*)-32



31 **32**

[3] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, **2001**, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

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% Et_2O 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, $CDCl_3$) 1.08 (9H, s, C*Me*$_3$), 1.21-1.35 (4H, m, C(4)H_A, C(α)*Me*), 1.45-1.52 (1H, m, C(4)H_B), 1.67-1.82 (2H, m, C(5)H_2), 2.80-2.86 (1H, m, (C(1)*H*), 3.47-3.52 (1H, m, C(2)*H*), 3.59 (1H, s, O*Me*), 3.83 (1H, d, *J* 14.0, NCH_A), 3.91 (1H, q, *J* 6.8, C(α)*H*), 3.96 (1H, d, *J* 14.0, NCH_B), 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, $CDCl_3$) 14.4, 19.2, 24.9, 27.0, 32.6, 46.3, 51.4, 51.8, 56.2, 68.8, 95.7, 126.5, 126.6, 127.5, 127.6, 127.7, 128.2, 128.5, 129.5, 129.7, 135.9, 133.9, 134.7, 141.2, 143.9, 175.4; *m/z* (ESI$^+$) 592 ([M+H]$^+$, 100%); HRMS (ESI$^+$) found 592.3264; $C_{38}H_{46}NO_3Si$ ([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, $CDCl_3$) 1.10 (9H, s, C*Me*$_3$), 1.30-1.33 (1H, m, C(4)H_A), 1.34 (3H, d, *J* 6.9, C(α)*Me*), 1.51-1.64 (2H, m, C(5)H_2), 1.73-1.81 (1H, m, C(4)H_B), 2.54-2.62 (1H, m, (C(1)*H*), 3.55 (3H, s, O*Me*), 3.67 (2H, dd, *J* 14.9, 9.2, NCH_2), 3.78 (1H, dd, *J* 5.4, 1.3, C(2)*H*), 3.90 (1H, q, *J* 6.9, C(α)*H*), 4.27 (1H, q, *J* 5.6, C(3)*H*), 7.16-7.76 (20H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 15.1, 19.1, 26.3, 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, 135.8, 135.9, 141.5, 144.2, 176.1; *m/z* (ESI$^+$) 592 ([M+H]$^+$, 100%); HRMS (ESI$^+$) found 592.3254; $C_{38}H_{46}NO_3Si$ ([M+H]$^+$) requires 592.3247.

X-ray Crystal Structure Determination for 31

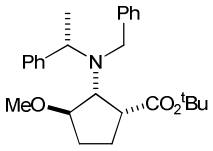
Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-$K\alpha$ radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92); all non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added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

X-ray crystal structure data for **31** [$C_{38}H_{45}NO_3Si$]: M = 591.87, monoclinic, space group *C 1 2/c 1*, a = 26.4012(4) Å, b = 10.3877(1) Å, c = 24.6887(4) Å, β = 96.3914(6)°, V = 6728.74(16) Å^3, Z = 8, μ = 0.106 mm^{-1}, colourless block, crystal dimensions = 0.1 × 0.1 × 0.1 mm^3. A total of 7581 unique reflections were measured for $5 < \theta < 27$ and 5208 reflections were used in the refinement. The final parameters were wR_2 = 0.053 and R_1 = 0.044 [$I>3\sigma(I)$]. Crystallographic data (excluding structure factors) has been deposited with

[4] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, **2001**, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

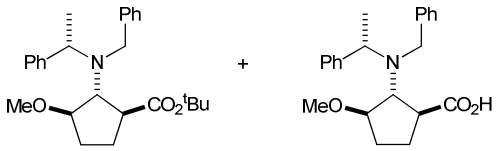
the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 669235. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

tert-Butyl (1*RS*,2*RS*,3*RS*,α*SR*)-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% Et_2O in pentane) gave **33** as a colourless oil (179 mg, 86%, >98% de); ν_{max} (film) 1722 (C=O); δ_H (400 MHz, $CDCl_3$) 1.37 (3H, d, *J* 6.9, C(α)*Me*), 1.52 (9H, s, C*Me*$_3$), 1.72-1.80 (2H, m, C(5)*H*$_2$), 2.18-2.29 (2H, m, C(4)*H*$_2$), 2.78-2.83 (1H, m, C(1)*H*), 3.10 (3H, s, O*Me*), 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, NC*H*$_2$), 4.24 (1H, q, *J* 6.9, C(α)*H*), 7.21-7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 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; $C_{26}H_{36}NO_3$ ($[M+H]^+$) requires 410.2695.

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

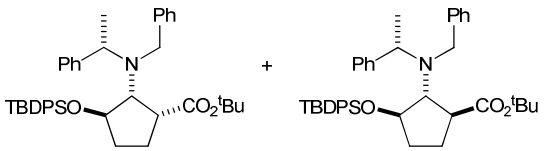


34 **37**

Following *General Procedure 2*, **33** (89 mg, 0.22 mmol) and KO^{t}Bu (3.1 mg, 0.04 mmol) in ^{t}BuOH/THF (1:1, 6 mL) gave **34** as a colourless oil (63 mg, 71%, >98% de); ν_{max} (film) 1725 (C=O); δ_H (400 MHz, PhMe-d_8) 1.28-1.40 (1H, m, C(4)H_A), 1.39 (9H, s, C*Me*$_3$), 1.41 (3H, d, *J* 6.8, C(α)*Me*), 1.49-1.58 (1H, m, C(5)H_A), 1.58-1.67 (1H, m, C(4)H_B), 1.79-1.88 (1H, m, C(5)H_B), 2.52-2.59 (1H, m, C(1)*H*), 3.14 (3H, s, O*Me*), 3.49-3.53 (1H, m, C(3)*H*), 3.61 (1H, d, *J* 14.5, NCH_A), 3.67 (1H, d, *J* 14.5, NCH_B), 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-d_8) 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; $C_{26}H_{36}NO_3$ ($[M+H]^+$) requires 410.2695. Further elution gave **37** as a colourless oil (23 mg, 29%, >98% de); ν_{max} (film) 1701 (C=O); δ_H (400 MHz, $CDCl_3$) 1.54 (3H, d, *J* 6.8, C(α)*Me*), 1.75-1.81 (2H, m, C(4)H_A, C(5)H_A), 1.80-1.92 (2H, m, C(4)H_B, C(5)H_B), 2.56-2.64 (1H, m, C(1)*H*), 3.39 (3H, s, O*Me*), 3.40-3.45 (1H, m, C(2)*H*), 3.85-3.94 (3H, m, C(3)*H*, NCH_2), 4.10 (1H, q, *J* 6.8, C(α)*H*), 7.20-7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 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; $C_{22}H_{28}NO_3$ ($[M+H]^+$) requires 354.2069.

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

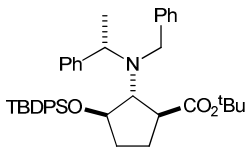


35 **36**

Following *General Procedure 1a*, BuLi (2.5 M in hexnaes, 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% Et_2O in pentane) gave **35** as a colourless oil (118 mg, 88%, >98% de); ν_{max} (film) 1722 (C=O); δ_H (400 MHz, $CDCl_3$) 1.09 (9H, s, SiCMe_3), 1.33-1.34 (1H, m, C(4)H_A), 1.35 (3H, d, *J* 6.6, C(α)*Me*), 1.41 (9H, s, OCMe_3), 1.52-1.28 (3H, m, C(4)H_B), C(5)H_2), 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*, NCH_2), 4.65-4.70 (1H, m, C(3)*H*), 7.24-7.72 (20H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 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; $C_{41}H_{52}NO_3Si$ ($[M+H]^+$) requires 634.3787. Further elution gave **36** as a colourless oil (13 mg, 10%, >98% de); ν_{max} (film) 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 1.10 (9H, s, SiCMe_3), 1.35 (3H, d, *J* 6.8, C(α)*Me*), 1.41 (9H, s, OCMe_3), 1.24-1.47 (1H, m, C(4)H_A), 1.48-1.63 (2H, m, C(4)H_B, C(5)H_A), 1.69-1.78 (1H, m, C(5)H_B), 2.45-2.55 (1H, m, C(1)*H*), 3.64 (1H, AB system, J_{AB} 15.4, NCH_2), 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*); δ_C (100 MHz, $CDCl_3$) 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,

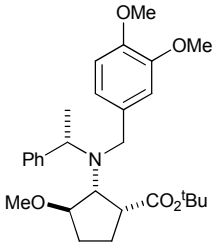
127.8, 127.9, 128.1, 129.3, 129.5, 133.8, 134.6, 135.7, 135.8, 135.9, 141.8 144.7, 175.0; *m/z* (ESI^+) 634 ($[M+H]^+$, 100%); HRMS (ESI^+) found 634.3709; $C_{41}H_{52}NO_3Si$ ($[M+H]^+$) requires 634.3716.

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



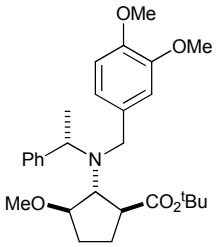
Following *General Procedure 2*, **35** (81 mg, 0.13 mmol) and KO^tBu (2.3 mg, 0.03 mmol) in ^{t}BuOH/THF (1:1, 6 mL) gave **36** as a colourless oil (81 mg, quant, >98% de).

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



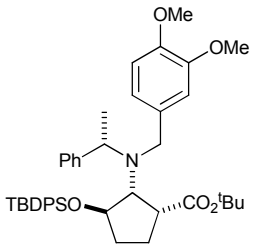
Following *General Procedure 1a*, BuLi (2.5 M in hexanes, 1 mL, 2.5 mmol), (*RS*)-*N*-3,4-dimethoxybenzyl-*N*-(α-methylbenzyl)amine (684 mg, 2.52 mmol) in THF (70 mL) and **19** (100 mg, 0.5 mmol) in THF (4.2 mL) gave **39** in >98% de. Purification by chromatography (15% Et_2O in pentane) gave **39** as a pale yellow oil (208 mg, 89%, >98% de); ν_{max} (film) 1721 (C=O); δ_H (400 MHz, $CDCl_3$) 1.37 (3H, d, *J* 6.8, C(α)*Me*), 1.48 (9H, s, C*Me*$_3$), 1.67-1.77 (2H, m, C(5)*H*$_2$), 2.17-2.26 (2H, m, C(4)*H*$_2$), 2.74-2.78 (1H, m, C(1)*H*), 3.14 (3H, s, C(3)O*Me*), 3.16-3.20 (1H, m, C(2)*H*), 3.83-3.98 (2H, m, NC*H*$_2$), 3.87 (3H, s, ArO*Me*), 3.91 (3H, s, ArO*Me*), 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*); δ_C (100 MHz, $CDCl_3$) 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; $C_{43}H_{56}NO_5Si$ ($[M+H]^+$) requires 470.2906.

Methyl (1*RS*,2*SR*,3*SR*,α*RS*)-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 KO^{t}Bu (2.3 mg, 0.03 mmol) in ^{t}BuOH/THF (1:1, 6 mL) gave **40** as a pale yellow oil (60 mg, quant, >98% de); ν_{max} (film) 1722 (C=O); δ_H (400 MHz, PhMe-d_8) 1.34 (3H, d, *J* 6.8, C(α)*Me*), 1.44 (9H, s, C*Me*$_3$), 1.45-1.49 (1H, m, C(4)*H*$_A$), 1.55-1.62 (1H, m, C(5)*H*$_A$), 1.62-1.68 (1H, m, C(4)*H*$_B$), 1.82-1.87 (1H, m, C(5)*H*$_B$), 2.57-2.63 (1H, m, C(1)*H*), 3.15 (3H, s, C(3)O*Me*), 3.52-3.56 (1H, m, C(3)*H*), 3.52 (3H, s, ArO*Me*), 3.63 (2H, dd , *J* 14.7, 8.5, NC*H*$_2$), 3.75 (3H, s, ArO*Me*), 3.85-3.88 (1H, m, C(2)*H*), 4.04 (1H, q, *J* 6.8, C(α)*H*), 6.68-7.50 (8H, m, *Ar*, *Ph*); δ_C (125 MHz, PhMe-d_8) 16.1, 27.0, 28.1, 29.5, 48.5, 50.8, 55.6, 55.7, 56.7, 58.6, 69.5, 79.3, 83.9, 112.0, 112.2, 113.1, 127.8, 127.9, 134.8, 137.2, 137.5, 145.0, 149.3, 150.5, 174.0; *m/z* (ESI$^+$) 470 ([M+H]$^+$, 100%); HRMS (ESI$^+$) found 470.2903; $C_{43}H_{56}NO_5Si$ ([M+H]$^+$) requires 470.2906.

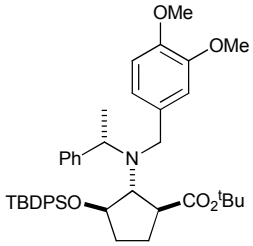
***tert*-Butyl (1*RS*,2*RS*,3*RS*,α*SR*)-2-[*N*-3,4-dimethoxybenzyl-*N*-(α-methylbenzyl)amino]-3-*tert*-butyldiphenylsilyloxy-cyclopentane-carboxylate 41**



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% Et_2O in pentane) gave **41** as a yellow oil (130 mg, 79%, >98% de); ν_{max} (film) 1721 (C=O); δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, SiC*Me*$_3$), 1.21-1.47 (13H, m, C(4)*H*$_A$, C(α)*Me*, OC*Me*$_3$), 1.52-1.60 (2H, m, C(5)*H*$_2$), 1.61-1.68 (2H, m, C(4)*H*$_B$), 2.46-2.49 (1H, m, C(1)*H*), 3.38-3.41 (1H, m, C(2)*H*), 3.86 (3H, s, ArO*Me*), 3.88 (3H, s, ArO*Me*), 3.95 (2H, AB system, J_{AB} 14.3, NC*H*$_2$), 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*); δ_C (100 MHz, $CDCl_3$) 15.5, 19.1, 24.8, 26.9, 28.0, 31.5, 47.7, 51.1, 55.5, 55.6, 56.4, 69.3,

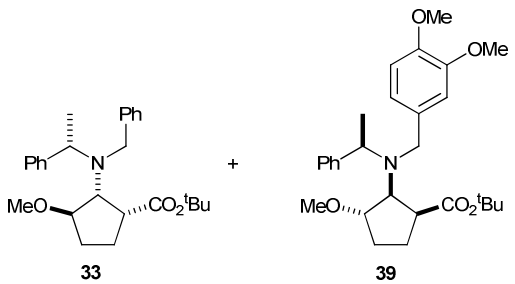
75.9, 79.7, 110.6, 111.4, 119.9, 126.4, 129.4, 133.9, 135.8, 143.9, 147.5, 148.7, 174.9; *m/z* (ESI^+) 694 ($[M+H]^+$, 100%); HRMS (ESI^+) found 694.3920; $C_{43}H_{56}NO_5Si$ ($[M+H]^+$) requires 694.3928.

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



Following *General Procedure 2*, **41** (50 mg, 0.07 mmol) and KO^{t}Bu (1.2 mg, 0.01 mmol) in ^{t}BuOH/THF (1:1, 6 mL) gave **42** as a viscous yellow oil (49 mg, 98%, >98% de); ν_{max} (film) 1721 (C=O); δ_H (400 MHz, PhMe-d_8) 1.23-1.24 (1H, m, C(4)H_A), 1.24 (9H, s, SiCMe_3), 1.29-1.37 (1H, m, C(5)H_A), 1.40 (9H, s, OCMe_3), 1.46 (3H, d, *J* 6.8, C(α)*Me*), 1.72-1.77 (1H, m, C(4)H_B), 1.87-1.92 (1H, m, C(5)H_B), 2.57-2.65 (1H, m, C(1)*H*), 3.46-3.53 (2H, m, NCH_2), 3.50 (3H, s, ArO*Me*), 3.63 (3H, s, ArO*Me*), 4.03 (1H, q, *J* 6.8, C(α)*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*); δ_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; $C_{43}H_{56}NO_5Si$ ($[M+H]^+$) requires 694.3928.

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

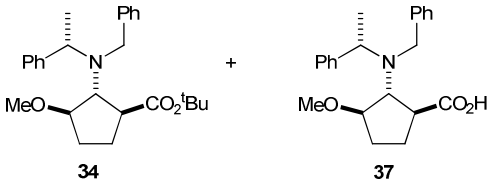


33 39

Following *General Procedure 1b*, BuLi (750 μL, 1.87 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (200 mg, 0.95 mmol), (*R*)-*N*-3,4-dimethoxybenzyl-*N*-(α-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_2O in pentane) gave (1*R*,2*R*,3*R*,α*S*)-**33** as a colourless oil (39 mg, 25%, >98% de);

$[\alpha]_D^{24}$ −91.1 (*c* 1.0 in $CHCl_3$). Further elution gave (1*S*,2*S*,3*S*,α*R*)-**39** as a pale yellow oil (53 mg, 30%, >98% de); $[\alpha]_D^{24}$ +67.4 (*c* 1.2 in $CHCl_3$).

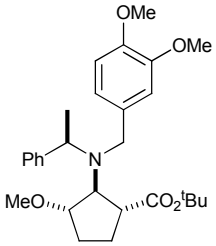
***tert*-Butyl (1*S*,2*R*,3*R*,α*S*)-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylate 34 and (1*S*,2*R*,3*R*,α*S*)-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-3-methoxy-cyclopentane-carboxylic acid 37**



34 **37**

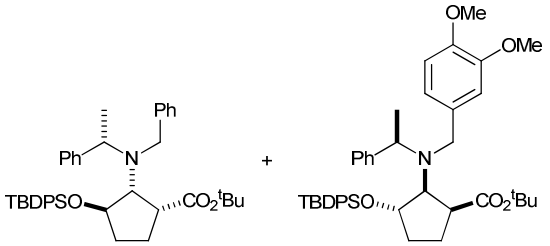
Following *General Procedure 2*, (1*R*,2*R*,3*R*,α*S*)-**33** (190 mg, 0.46 mmol) and KO^{t}Bu (7.1 mg, 0.09 mmol) in ^{t}BuOH/THF (1:1, 10 mL) gave (1*S*,2*R*,3*R*,α*S*)-**34** as a colourless oil (160 mg, 85%, >98% de); $[\alpha]_D^{24}$ +46.7 (*c* 0.7 in $CHCl_3$). Further elution gave (1*S*,2*R*,3*R*,α*S*)-**37** as a colourless oil (24 mg, 15%, >98% de); $[\alpha]_D^{24}$ +12.6 (*c* 1.0 in $CHCl_3$).

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



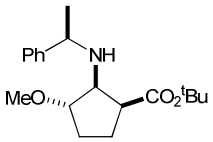
Following *General Procedure 2*, (1*S*,2*S*,3*S*,α*R*)-**39** (348 mg, 0.74 mmol) and KO^{t}Bu (12 mg, 0.15 mmol) in ^{t}BuOH/THF (1:1, 18 mL) gave (1*R*,2*S*,3*S*,α*R*)-**40** (210 mg, 61%, >98% de) as a pale yellow oil; $[\alpha]_D^{24}$ −36.0 (*c* 1.0 in $CHCl_3$).

Parallel kinetic resolution of 21: *tert*-butyl (1*R*,2*R*,3*R*,α*S*)-2-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-3-*tert*-butyldiphenylsilyloxy-cyclopentane-carboxylate 35 and *tert*-butyl (1*S*,2*S*,3*S*,α*R*)-2-[*N*-3,4-dimethoxybenzyl-*N*-(α-methylbenzyl)amino]-3-*tert*-butyldiphenylsilyloxy-cyclopentane-carboxylate 41



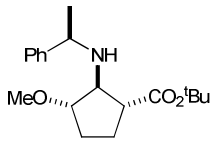
Following *General Procedure 1b*, BuLi (2.5 M in hexanes, 469 μL, 1.17 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (125 mg, 0.59 mmol), (*R*)-*N*-3,4-dimethoxybenzyl-*N*-(α-methylbenzyl)amine (161 mg, 0.59 mmol) in THF (16 mL) and **21** (100 mg, 0.24 mmol) in THF (2 mL) gave a 45:5:45:5 mixture of **35**:**36**:**41**:**42**. Purification by chromatography (1% Et_2O in pentane) gave (1*R*,2*R*,3*R*,α*S*)-**35** as a colourless oil (60 mg, 40%, >98% de); $[\alpha]_D^{24}$ −22.6 (*c* 1.0 in $CHCl_3$). Further elution gave (1*S*,2*S*,3*S*,α*R*)-**41** as a colourless oil (59 mg, 36%, >98% de); $[\alpha]_D^{24}$ +13.1 (*c* 1.0 in $CHCl_3$).

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



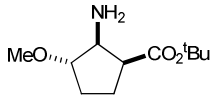
Following *General Procedure 3*, (1*S*,2*S*,3*S*,α*R*)-**39** (310 mg, 0.66 mmol) and DDQ (295 mg, 1.32 mmol) in DCM:H_2O (5:1, 6 mL) gave, after purification by chromatography (7% Et_2O in pentane), **43** as a pale yellow oil (207 mg, 98%, >98% de); Found C, 71.2; H, 9.2; N, 4.4%; $C_{19}H_{29}NO_3$ requires C, 71.4; H, 9.2; N, 4.4%; $[\alpha]_D^{24}$ +25.8 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1719 (C=O); δ_H (400 MHz, $CDCl_3$) 1.33 (3H, d, *J* 6.5, C(α)*Me*), 1.39-1.49 (1H, m, C(4)H_A), 1.52 (9H, s, CMe_3), 1.75-1.93 (2H, m, C(5)H_2), 2.05-2.09 (1H, m, C(4)H_B), 2.93-2.96 (1H, m, C(1)*H*), 3.03-3.05 (1H, m, C(2)*H*), 3.20 (3H, s, O*Me*), 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*); δ_C (100 MHz, $CDCl_3$) 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; $C_{19}H_{30}NO_3$ ($[M+H]^+$) requires 320.2226.

***tert*-Butyl (1*R*,2*S*,3*S*,α*R*)-2-*N*-(α-methylbenzyl)amino-3-methoxy-cyclopentane-carboxylate 44**



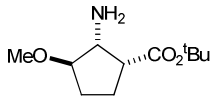
Following *General Procedure 3*, (1*R*,2*S*,3*S*,α*R*)-**40** (210 mg, 0.45 mmol) and DDQ (203 mg, 0.90 mmol) in DCM/H_2O (5:1, 6 mL) gave, after purification by chromatography (15% Et_2O in pentane), **44** as a pale yellow oil (141 mg, 98%, >98% de); $[\alpha]_D^{24}$ +8.8 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1720 (C=O); δ_H (400 MHz, $CDCl_3$) 1.37 (3H, d, *J* 6.6, C(α)*Me*), 1.43 (9H, s, C*Me*$_3$), 1.62-1.71 (1H, m, C(4)H_A), 1.77-1.94 (3H, m, C(4)H_B, C(5)H_2), 2.44-2.50 (1H, m, C(1)*H*), 3.12 (3H, s, O*Me*), 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*); δ_C (100 MHz, $CDCl_3$) 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 320.2230; $C_{19}H_{30}NO_3$ ($[M+H]^+$) requires 320.2226.

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



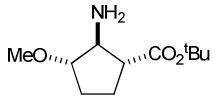
Following *General Procedure 4*, $Pd(OH_2)$/C (50 mg, 50% w/w) and **43** (100 mg, 0.31 mmol) in MeOH (5 mL) gave (1*S*,2*S*,3*S*)-**45** as a colourless oil (60 mg, 90%, >98% de); $[\alpha]_D^{24}$ +42.4 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 1724 (C=O); δ_H (400 MHz, $CDCl_3$) 1.47 (9H, s, C*Me*$_3$), 1.55-1.60 (1H, m, C(4)H_A), 1.88-2.01 (2H, m, C(5)H_2), 2.08-2.16 (1H, m, C(4)H_B), 2.89-2.95 (1H, m, C(1)*H*), 3.35 (3H, s, O*Me*), 3.40-3.45 (1H, m, C(2)*H*), 3.54-3.57 (1H, m, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 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; $C_{11}H_{21}NO_3$ ($[M+H]^+$) requires 216.1599.

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



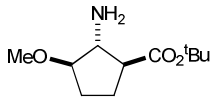
Following *General Procedure 4*, $Pd(OH_2)$/C (124 mg, 50% w/w) and (1*R*,2*R*,3*R*,α*S*)-**33** (248 mg, 0.60 mmol) in MeOH (10 mL) gave (1*R*,2*R*,3*R*)-**45** as a colourless oil (115 mg, 89%, >98% de); $[\alpha]_D^{24}$ −60.5 (*c* 1.0 in $CHCl_3$).

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



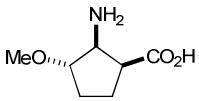
Following *General Procedure 4*, $Pd(OH_2)/C$ (64 mg, 50% w/w) and **44** (127 mg, 0.40 mmol) in MeOH (5 mL) gave (1*R*,2*S*,3S)-**46** as a colourless oil (83 mg, 96%, >98% de); $[\alpha]_D^{24}$ −10.0 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3400-3300 (N−H), 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 1.44 (9H, s, C*Me*$_3$), 1.55-1.59 (1H, m, C(4)H_A), 1.81-2.01 (3H, m, C(4)H_B, C(5)H_2), 2.32-2.40 (1H, m, C(1)*H*), 3.29-3.23 (1H, m, C(2)*H*), 3.34 (3H, s, O*Me*), 3.36-3.41 (1H, m, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 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; $C_{11}H_{21}NO_3$ ($[M+H]^+$) requires 216.1600.

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



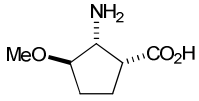
Following *General Procedure 4*, $Pd(OH_2)/C$ (80 mg, 50% w/w) and (1*S*,2*R*,3*R*,α*S*)-**34** (160 mg, 0.39 mmol) in MeOH (5 mL) gave (1*S*,2*R*,3*R*)-**46** as a colourless oil (79 mg, 94%, >98% de); $[\alpha]_D^{24}$ +10.4 (*c* 1.0 in $CHCl_3$).

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



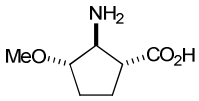
Following *General Procedure 5*, (1*S*,2*S*,3*S*)-**45** (60 mg, 0.28 mmol) and TFA (1 mL) in DCM (1 mL) gave (1*S*,2*S*,3*S*)-**47** as a white crystalline solid (27 mg, 75%); mp 187-188 °C; $[\alpha]_D^{24}$ +77.1 (*c* 1.0 in H_2O); ν_{max} (film) 3500-3300 (O−H, N−H), 1710 (C=O); δ_H (400 MHz, D_2O) 1.51-1.59 (1H, m, C(4)H_A), 1.75-1.85 (1H, m, C(5)H_A), 2.03-2.14 (2H, m, C(4)H_B, C(5)H_B), 2.87-2.92 (1H, m, C(1)*H*), 3.28 (3H, s, O*Me*), 3.45-3.48 (1H, m, C(2)*H*), 3.91-3.96 (1H, m, C(3)*H*); δ_C (125 MHz, D_2O) 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; $C_7H_{12}NO_3$ ($[M-H]^-$) requires 158.0817.

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



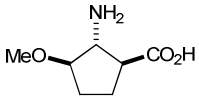
Following *General Procedure 5*, (1*R*,2*R*,3*R*)-**45** (115 mg, 0.53 mmol) and TFA (1 mL) in DCM (1 mL) gave (1*R*,2*R*,3*R*)-**47** as a colourless crystalline solid (52 mg, 77%, >98% de); $[\alpha]_D^{24}$ −76.4 (*c* 1.0 in H_2O).

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



Following *General Procedure 5*, (1*R*,2*S*,3*S*)-**46** (83 mg, 0.38 mmol) and TFA (1 mL) in DCM (1 mL) gave (1*R*,2*S*,3*S*)-**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_2O); ν_{max} (film) 3500-3300 (O−H, N−H), 1710 (C=O); δ_H (400 MHz, D_2O) 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, O*Me*), 3.50-3.56 (1H, m, C(2)*H*), 3.76-3.83 (1H, m, C(3)*H*); δ_C (100 MHz, D_2O) 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; $C_7H_{12}NO_3$ ([M−H]$^-$) requires 158.0817.

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



Following *General Procedure 5*, (1*S*,2*R*,3*R*)-**46** (79 mg, 0.37 mmol) and TFA (1 mL) in DCM (1 mL) gave (1*S*,2*R*,3*R*)-**48** as a colourless solid (31 mg, 65%, >98% de); $[\alpha]_D^{24}$ +17.0 (*c* 1.0 in H_2O).