Supplementary Information

Asymmetric synthesis of β-amino-γ-substituted-γ-butyrolactones: double diastereoselective conjugate addition of homochiral lithium amides to homochiral α,β-unsaturated esters

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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), as a KBr disc (KBr), or as chloroform solutions in 0.1 mm cells ($CHCl_3$), as stated. Selected characteristic peaks are

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

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 in positive and negative modes, 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 Procedure 1a for lithium amide conjugate addition

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 carbonyl compound in THF at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with sat aq NH_4Cl and allowed to warm to rt over 15 min. The reaction mixture was concentrated *in vacuo* and the residue was partitioned between DCM and 10% aq citric acid. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ and brine, dried and concentrated *in vacuo*.

General Procedure 1b for lithium amide conjugate addition

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 carbonyl compound in THF at −78 °C was added dropwise *via* cannula. The reaction mixture was allowed to warm to −50 °C over 12 h, quenched with sat aq NH_4Cl and allowed to warm to rt over 15 min. The reaction mixture was concentrated *in vacuo* and the residue was partitioned between DCM and 10% aq citric acid. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ and brine, dried and concentrated *in vacuo*.

General Procedure 1c for lithium amide conjugate addition

BuLi (as a solution in hexanes) was added dropwise *via* syringe to a stirred solution of the requisite amine in Et_2O at −20 °C. After stirring for 30 min a solution of the requisite α,β-unsaturated carbonyl compound in Et_2O at −20 °C was added dropwise *via* cannula. After stirring for a further 6 h at −20 °C the reaction mixture was quenched with sat aq NH_4Cl and allowed to warm to rt over 15 min. The reaction mixture was

concentrated *in vacuo* and the residue was partitioned between DCM and 10% aq citric acid. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ and brine, dried and concentrated *in vacuo*.

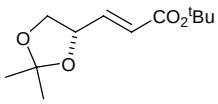
General Procedure 2 for lithium amide conjugate addition and MeI quench

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 α,-β-unsaturated carbonyl compound in THF at −78 °C was added dropwise *via* cannula. After stirring for a further 2 h at −78 °C the reaction mixture was quenched with MeI and allowed to warm to rt over 12 h, then quenched with sat aq $NaHCO_3$. The reaction mixture was concentrated *in vacuo* and the residue was partitioned between DCM and 10% aq citric acid. The organic layer was separated and the aqueous layer was extracted twice with DCM. The combined organic extracts were washed sequentially with sat aq $NaHCO_3$ and brine, dried and concentrated *in vacuo*.

General Procedure 3 for desilylation and concomitant lactonisation

TBAF was added to a solution of the requisite γ-silyloxy-β-amino ester in THF and heated at 50 °C for 24 h. The reaction mixture was then allowed to cool to rt and poured into brine. The resultant mixture was extracted with EtOAc (3 × 25 mL) and the combined organic extracts were dried and concentrated *in vacuo*. The residue was then dissolved in PhMe and TFA was added. The resultant suspension was stirred at rt for 24 h before being concentrated *in vacuo*. The residue was then partitioned between sat aq $NaHCO_3$ (50 mL) and EtOAc (25 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic extracts were dried and concentrated *in vacuo*.

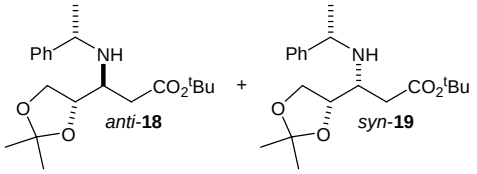
***tert*-Butyl (*S*,*E*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)propenoate (*S*,*E*)-17**



Sodium hydride (60% dispersion in mineral oil, 1.38 g, 34.5 mmol) was washed with hexane (2 × 5 mL), then suspended in THF (40 mL). The resultant suspension was cooled to 0 ºC and a solution of *tert*-butyl diethylphosphonoacetate (8.70 g, 34.5 mmol) THF (20 mL) was added. Once hydrogen evolution had ceased (*ca*. 40 min), a solution of (*R*)-isopropylidene glyceraldehyde (4.08 g, 31.4 mmol) in THF (20 mL) was added dropwise. After 15 min at 0 ºC, the reaction was allowed to warm to rt over 2 h, then quenched with

MeOH (10 mL) and the resultant mixture was concentrated *in vacuo*. The residue was poured into H_2O (150 mL), and the resultant mixture was extracted with Et_2O (3 × 50 mL). The combined organic extracts were then dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent hexane/EtOAc, 12:1) gave (*S*,*E*)-**17** as a colourless oil (4.85 g, 68%, >98% de); $C_{12}H_{20}O_4$ requires C, 63.1; H, 8.8; found: C, 63.0; H, 8.8%; $[\alpha]_D^{21}$ +37.8 (*c* 2.2 in $CHCl_3$); ν_{max} (film) 1709 (C=O), 1661 (C=C); δ_H (400 MHz, $CDCl_3$) 1.41 (3H, s, C(2′)*Me*$_A$), 1.46 (3H, s, C(2′)*Me*$_B$), 1.49 (9H, s, C*Me*$_3$), 3.68 (1H, dd, *J* 8.2, 7.3, C(5′)*H*$_A$), 4.17 (1H, dd, *J* 8.2, 6.5, C(5′)*H*$_B$), 4.61-4.68 (1H, m, C(4′)*H*), 6.02 (1H, dd, *J* 15.5, 1.4, C(2)*H*), 6.77 (1H, dd, *J* 15.5, 6.9, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 25.5 (C(2′)*Me*$_A$), 26.2 (C(2′)*Me*$_B$), 27.8 (C*Me*$_3$), 68.7 (*C*(5′)), 74.9 (*C*(4′)), 80.4 (*C*Me$_3$), 109.9 (*C*(2′)), 124.3 (*C*(2)), 143.4 (*C*(3)), 165.3 (*C*(1)); *m/z* (CI^+) 246 ($[M+NH_4]^+$, 4%), 229 (11), 213 (29), 173 (100).

tert-Butyl (3*R*,4′*S*,α*S*)- and (3*S*,4′*S*,α*S*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-[*N*-(α-methylbenzyl)amino]propanoate (3*R*,4′*S*,α*S*)-*anti*-18 and (3*S*,4′*S*,α*S*)-*syn*-19



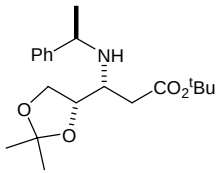
Following *general procedure 1a*, BuLi (1.60 mL, 1.00 mmol), (*S*)-α-methylbenzylamine (194 mg, 1.60 mmol) in THF (5 mL), and (*S*,*E*)-**17** (228 mg, 1.00 mmol) in THF (5 mL) gave a 17:83 mixture of *anti*-**18**:*syn*-**19**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 6:1) gave *anti*-**18** and *syn*-**19** as pale yellow oils (323 mg, 92% combined yield).

Data for *anti*-**18**: $C_{20}H_{31}NO_4$ requires C, 68.7; H, 8.9; found: C, 68.7; H, 8.75%; $[\alpha]_D^{21}$ −12.9 (*c* 1.8 in $CHCl_3$); ν_{max} (film) 1716 (C=O); δ_H (400 MHz, $CDCl_3$) 1.33 (3H, obsc d, C(α)*Me*), 1.34 (3H, s, C(2′)*Me*$_A$), 1.43 (3H, s, C(2′)*Me*$_B$), 1.44 (9H, s, C*Me*$_3$), 2.34-2.36 (2H, m, C(2)*H*$_2$), 2.96-3.01 (1H, m, C(3)*H*), 3.80 (1H, dd, *J* 8.3, 6.1, C(5′)*H*$_A$), 4.02 (1H, dd, *J* 8.3, 6.6, C(5′)*H*$_B$), 3.93 (1H, q, *J* 6.5, C(α)*H*), 4.09-4.16 (1H, m, C(4′)*H*), 7.23-7.33 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.3, 24.9, 26.4 (C(α)*Me*, C(2′)*Me*$_2$), 28.0 (C*Me*$_3$), 37.1 (*C*(2)), 54.8, 55.1 (*C*(3), *C*(α)), 67.3 (*C*(5′)), 77.7 (*C*(4′)), 80.5 (*C*Me$_3$), 109.2 (*C*(2′)), 126.8, 127.1, 128.6 (*o-Ph*, *m-Ph*, *p-Ph*), 146.3 (*i-Ph*), 172.0 (*C*(1)); *m/z* (CI^+) 350 ($[M+H]^+$, 100%), 294 (31), 248 (30), 192 (43), 105 (36).

Data for *syn*-**19**: $C_{20}H_{31}NO_4$·HCl requires C, 62.2; H, 8.4; N, 3.6; found: C, 62.3; H, 8.6; N, 3.5%; mp (HCl salt) 151-152 ºC; $[\alpha]_D^{21}$ −35.8 (*c* 1.1 in $CHCl_3$); ν_{max} 1718 (C=O); δ_H (400 MHz, $CDCl_3$) 1.32 (3H, s,

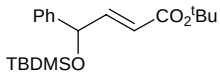
C(2′)*Me*$_A$), 1.35 (3H, d, *J* 6.6, C(α)*Me*), 1.37 (3H, s, C(2′)*Me*$_B$), 1.46 (9H, s, C*Me*$_3$), 2.31 (1H, dd, *J* 14.7, 5.1, C(2)*H*$_A$), 2.46 (1H, dd, *J* 14.7, 6.4, C(2)*H*$_B$), 2.77-2.83 (1H, m, C(3)*H*), 3.76 (1H, dd, *J* 8.0, 7.1, C(5′)*H*$_A$), 3.88 (1H, dd, *J* 8.0, 6.6, C(5′)*H*$_B$), 3.92 (1H, q, *J* 6.6 C(α)*H*), 4.08 (1H, td, *J* 6.7, 5.2, C(4′)*H*), 7.23-7.33 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.0, 25.1, 26.2 (C(α)*Me*, C(2′)*Me*$_2$), 28.0 (C*Me*$_3$), 36.9 (*C*(2)), 53.6, 55.0 (*C*(3), *C*(α)), 66.1 (*C*(5′)), 77.7 (*C*(4′)), 80.4 (*C*Me$_3$), 109.1 (*C*(2′)), 127.0, 127.1, 128.5 (*o-Ph*, *m-Ph*, *p-Ph*), 145.8 (*i-Ph*), 171.6 (*C*(1)); *m/z* (CI^+) 350 ($[M+H]^+$, 100%), 294 (37), 248 (44), 192 (54), 105 (60).

***tert*-Butyl (3*R*,4′*S*,α*R*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-[*N*-(α-methylbenzyl)amino]propanoate *syn*-21**



Following *general procedure 1a*, BuLi (1.60 mL, 1.00 mmol), (*R*)-α-methylbenzylamine (194 mg, 1.60 mmol) in THF (5 mL), and (*S*,*E*)-**17** (228 mg, 1.00 mmol) in THF (5 mL) gave a 12:88 mixture of *anti*-**20**:*syn*-**21**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 6:1) gave *syn*-**21** as a pale yellow oil (290 mg, 83%, >98% de); $C_{20}H_{31}NO_4$ requires C, 68.7; H, 8.9; N, 4.0; found: C, 68.7; H, 8.55; N, 3.7%; $[\alpha]_D^{21}$ +22.7 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1718 (C=O); δ_H (400 MHz, $CDCl_3$) 1.32 (3H, d, *J* 6.5, C(α)*Me*), 1.35 (3H, s, C(2′)*Me*$_A$), 1.40 (3H, s, C(2′)*Me*$_B$), 1.43 (9H, s, C*Me*$_3$), 2.24 (1H, dd, *J* 15.1, 6.8, C(2)*H*$_A$), 2.34 (1H, dd, *J* 15.1, 5.7, C(2)*H*$_B$), 3.09 (1H, dt, *J* 6.7, 5.5, C(3)*H*), 3.80-4.03 (3H, m, C(5′)*H*$_2$, C(α)*H*), 4.22 (1H, td, *J* 6.8, 5.1, C(4′)*H*), 7.23-7.35 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.1, 25.2, 26.4 (C(α)*Me*, C(2′)*Me*$_2$), 28.0 (C*Me*$_3$), 37.8 (*C*(2)), 53.6, 55.5 (*C*(3), *C*(α)), 66.2 (*C*(5′)), 78.0 (*C*(4′)), 80.5 (*C*Me$_3$), 109.1 (*C*(2′)), 126.6, 126.8, 128.3 (*o-Ph*, *m-Ph*, *p-Ph*), 146.1 (*i-Ph*), 171.4 (*C*(1)); *m/z* (CI^+) 350 ($[M+H]^+$, 100%), 294 (28), 248 (31), 192 (42), 105 (40).

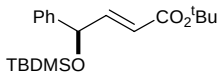
***tert*-Butyl (*RS*,*E*)-4-(*tert*-butyldimethylsilyloxy)-4-phenylbut-2-enoate (*RS*,*E*)-26**



NaH (60% dispersion in mineral oil, 920 mg, 23.0 mmol) was washed with hexane (2 × 10 mL), suspended in THF (20 mL) and cooled to 0 °C. A solution of *tert*-butyl diethylphosphonoacetate (5.54 g, 22.0 mmol) in

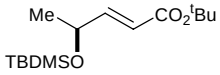
THF (20 mL) was then added dropwise. Once hydrogen evolution had ceased (*ca* 40 min), a solution of (*RS*)-**24** (5.00 g, 20.0 mmol) in THF (10 mL) was added dropwise. After 15 min at 0 °C, the reaction mixture was allowed to warm to rt over 2 h, and was then quenched with sat. aq. $NaHCO_3$ solution (5 mL) and concentrated *in vacuo*. The residue was then partitioned between H_2O (100 mL) and Et_2O (50 mL), the organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* distillation (bp 143-147 °C, 0.25 mmHg) gave (*RS*,*E*)-**26** as a colourless oil (5.21 g, 75%); $C_{20}H_{32}O_3Si$ requires C, 68.9; H, 9.25%; found C, 68.65; H, 9.5%; ν_{max} (film) 1707 (C=O), 1657 (C=C); δ_H (400 MHz, $CDCl_3$) −0.04 (3H, s, Si*Me*$_A$), 0.08 (3H, s, Si*Me*$_B$), 0.92 (9H, s, SiC*Me*$_3$), 1.47 (9H, s, OC*Me*$_3$), 5.30 (1H, dd, *J* 4.7, 1.7, C(4)*H*), 6.00 (1H, dd, *J* 15.4, 1.7, C(2)*H*), 6.86 (1H, dd, *J* 15.4, 4.7, C(3)*H*), 7.26-7.35 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.1 (Si*Me*$_2$), 18.1 (Si*C*Me$_3$), 25.7 (SiC*Me*$_3$), 28.0 (OC*Me*$_3$), 74.2 (*C*(4)), 80.3 (O*C*Me$_3$), 120.7 (*C*(2)), 126.4, 127.8, 128.6 (*o-Ph*, *m-Ph*, *p-Ph*), 142.1 (*i-Ph*), 149.3 (*C*(3)), 166.2 (*C*(1)); *m/z* (CI^+) 366 ($[M+NH_4]^+$, 5%), 349 (6), 293 (62), 235 (100), 178 (88), 161 (65).

tert-Butyl (*R*,*E*)-4-(_tert_-butyldimethylsilyloxy)-4-phenylbut-2-enoate (*R*,*E*)-26



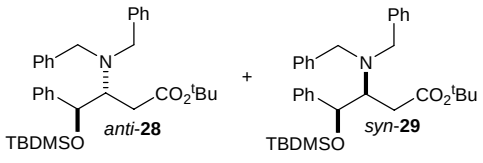
NaH (60% dispersion in mineral oil, 876 mg, 21.9 mmol) was washed with hexane (2 × 10 mL), suspended in THF (20 mL) and cooled to 0 °C. A solution of *tert*-butyl diethylphosphonoacetate (6.02 g, 23.9 mmol) in THF (20 mL) was then added dropwise. Once hydrogen evolution had ceased (*ca* 40 min), a solution of (*S*)-**24** (4.98 g, 19.9 mmol) in THF (10 mL) was added dropwise. After 15 min at 0 °C the reaction mixture was allowed to warm to rt over 2 h, quenched with sat. aq. $NaHCO_3$ solution (5 mL) and concentrated *in vacuo*. The residue was then partitioned between H_2O (100 mL) and Et_2O (50 mL), the organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* distillation (bp 132-136 °C, 0.1 mmHg) gave (*R*,*E*)-**26** as a colourless oil (5.95 g, 86%); $[\alpha]_D^{20}$ +63.3 (*c* 1.15 in $CHCl_3$).

***tert*-Butyl (*S*,*E*)-4-(*tert*-butyldimethylsilyloxy)pent-2-enoate (*S*,*E*)-27**



NaH (60% dispersion in mineral oil, 880 mg, 22.0 mmol) was washed with hexane (2 × 10 mL), suspended in THF (20 mL) and cooled to 0 °C. A solution of *tert*-butyl diethylphosphonoacetate (6.05 g, 24.0 mmol) in THF (20 mL) was then added dropwise. Once hydrogen evolution had ceased (*ca* 40 min), a solution of (*S*)-**25** (3.76 g, 20.0 mmol) in THF (10 mL) was added dropwise. After 15 min at 0 °C the reaction mixture was allowed to warm to rt over 2 h, quenched with sat. aq. $NaHCO_3$ solution (5 mL) and concentrated *in vacuo*. The residue was partitioned between H_2O (100 mL) and Et_2O (50 mL), the organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic extracts were dried and concentrated *in vacuo*. Purification *via* sequential flash column chromatography (eluent hexane/Et_2O, 6:1) and distillation (bp 86-89 °C, 0.2 mmHg) gave (*S*,*E*)-**27** as a colourless oil (5.10 g, 89%); $C_{15}H_{30}O_3Si$ requires C, 62.9; H, 10.55%; found C, 62.8; H, 10.9%; $[\alpha]_D^{20}$ +2.0 (*c* 1.3 in $CHCl_3$); ν_{max} (film) 1707 (C=O); δ_H (400 MHz, $CDCl_3$) 0.07 (6H, s, Si*Me*$_2$), 0.92 (9H, s, SiC*Me*$_3$), 1.26 (3H, d, *J* 6.5, C(5)*H*$_3$), 1.49 (9H, s, OC*Me*$_3$), 4.40-4.48 (1H, m, C(4)*H*), 5.89 (1H, dd, *J* 15.4, 1.7, C(2)*H*), 6.82 (1H, dd, *J* 15.4, 4.1, C(3)*H*); δ_C (100 MHz, $CDCl_3$) −5.1 (Si*Me*$_2$), 18.0 (Si*C*Me$_3$), 23.4 (*C*(5)), 25.7 (SiC*Me*$_3$), 28.0 (OC*Me*$_3$), 67.7 (*C*(4)), 80.1 (O*C*Me$_3$), 120.8 (*C*(2)), 150.8 (*C*(3)), 166.4 (*C*(1)); *m/z* (CI^+) 304 ($[M+NH_4]^+$, 12%), 287 (8), 248 (70), 231 (38), 173 (100).

***tert*-Butyl (3*RS*,4*SR*)- and (3*RS*,4*RS*)-3-(*N*,*N*-dibenzylamino)-4-(*tert*-butyldimethylsilyloxy)-4-phenylbutanoate (3*RS*,4*SR*)-*anti*-28 and (3*RS*,4*RS*)-*syn*-29**

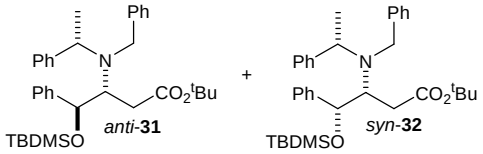


anti-**28**:*syn*-**29**, 88:12

Following *general procedure 1a*, BuLi (1.60 mL, 1.00 mmol), dibenzylamine (394 mg, 2.00 mmol) in THF (5 mL), and (*RS*,*E*)-**26** (348 mg, 1.00 mmol) in THF (5 mL) gave an 88:12 mixture of *anti*-**28**:*syn*-**29**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 20:1) gave an 88:12 mixture of *anti*-**28**:*syn*-**29** as a pale yellow oil (524 mg, 96%); $C_{34}H_{47}NO_3Si{\cdot}HCl$ requires C, 70.1; H, 8.3; N, 2.4%; found C, 70.1; H, 8.4; N, 2.3%; ν_{max} (film) 1718 (C=O); *m/z* (CI^+) 546 ($[M+H]^+$, 12%), 324 (36), 91 (100).

Data for *anti*-**28**: δ_H (400 MHz, $CDCl_3$) −0.33 (3H, s, Si*Me*$_A$), 0.04 (3H, s, Si*Me*$_B$), 0.85 (9H, s, SiC*Me*$_3$), 1.44 (9H, s, OC*Me*$_3$), 2.58 (1H, dd, *J* 15.4, 5.2, C(2)*H*$_A$), 2.70 (1H, dd, *J* 15.4, 7.4, C(2)*H*$_B$), 3.43-3.49 (1H, m, C(3)*H*), 3.70 (4H, app s, N(C*H*$_2$Ph)$_2$), 4.84 (1H, d, *J* 6.0, C(4)*H*), 7.10-7.27 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.8 (Si*Me*$_A$), −4.2 (Si*Me*$_B$), 18.1 (Si*C*Me$_3$), 26.0 (SiC*Me*$_3$), 28.2 (OC*Me*$_3$), 32.8 (*C*(2)), 54.8 (N(*C*H$_2$Ph)$_2$), 62.5 (*C*(3)), 75.2 (*C*(4)), 80.1 (O*C*Me$_3$), 127.0, 127.4, 127.5, 127.9, 128.1, 128.3, 129.0, 129.1 (*o-Ph*, *m-Ph*, *p-Ph*), 139.9, 144.3 (*i-Ph*), 172.6 (*C*(1)).

tert-Butyl (3*RS*,4*SR*,α*SR*)- and (3*RS*,4*RS*,α*SR*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(*tert*-butyldimethylsilyloxy)-4-phenylbutanoate (3*RS*,4*SR*,α*SR*)-*anti*-31 and (3*RS*,4*SR*,α*SR*)-*syn*-32



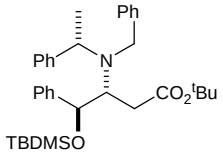
anti-**31**:*syn*-**32**, 92:8

Following *general procedure 1b*, BuLi (3.20 mL, 2.00 mmol), (*RS*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (633 mg, 3.00 mmol) in THF (10 mL), and (*RS*,*E*)-**26** (696 mg, 2.00 mmol) in THF (10 mL) gave a 92:8 mixture of *anti*-**31**:*syn*-**32**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 20:1) gave a 92:8 mixture of *anti*-**31**:*syn*-**32** as a pale yellow oil (1.01 g, 91%); $C_{35}H_{49}NO_3Si$ requires C, 75.1; H, 8.8; N, 2.5%; found C, 75.3; H, 9.1; N, 2.3%; ν_{max} (film) 1718 (C=O); *m/z* (CI^+) 560 ($[M+H]^+$, 35%), 338 (100), 282 (37), 178 (47), 105 (88), 91 (74).

Data for *anti*-**31**: δ_H (400 MHz, $CDCl_3$) −0.28 (3H, s, Si*Me*$_A$), −0.10 (3H, s, Si*Me*$_B$), 0.77 (9H, s, SiC*Me*$_3$), 0.89 (3H, d, *J* 7.1, C(α)*Me*), 1.46 (9H, s, OC*Me*$_3$), 1.76 (1H, dd, *J* 16.6, 2.3, C(2)*H*$_A$), 2.28 (1H, dd, *J* 16.6, 8.9, C(2)*H*$_B$), 3.60 (1H, q, *J* 7.1, C(α)*H*), 3.63 (1H, d, *J* 15.2, NC*H*$_A$), 3.80 (1H, d, *J* 15.2, NC*H*$_B$), 4.00-4.06 (1H, m, C(3)*H*), 4.41 (1H, d, *J* 8.1, C(4)*H*), 7.08-7.45 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.9 (Si*Me*$_A$), −4.6 (Si*Me*$_B$), 18.2 (Si*C*Me$_3$), 18.5 (C(α)*Me*), 25.9 (SiC*Me*$_3$), 28.2 (OC*Me*$_3$), 34.6 (*C*(2)), 51.2 (NCH$_2$), 57.5, 59.3 (*C*(3), C(α)), 77.8 (*C*(4)), 79.8 (O*C*Me$_3$), 127.0, 127.1, 127.4, 127.9, 128.1, 128.3, 128.6 (*o-Ph*, *m-Ph*, *p-Ph*), 141.1, 141.4, 145.4 (*i-Ph*), 172.1 (*C*(1)).

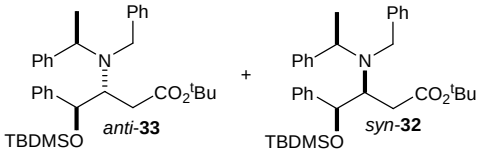
Data for *syn*-**32**: δ_H (400 MHz, $CDCl_3$) −0.26 (3H, s, Si*Me*$_A$), −0.01 (3H, s, Si*Me*$_B$), 0.65 (3H, d, *J* 7.1, C(α)*Me*), 0.81 (9H, s, SiC*Me*$_3$), 1.45 (9H, s, OC*Me*$_3$), 1.50 (1H, dd, *J* 16.7, 2.2, C(2)*H*$_A$), 2.43 (1H, dd, *J* 16.7, 10.6, C(2)*H*$_B$), 3.54-3.63 (3H, m, C(3)*H*, C(α)*H*, NC*H*$_A$), 4.39 (1H, d, *J* 14.7, NC*H*$_B$), 4.84 (1H, d, *J* 2.5, C(4)*H*), 7.09-7.49 (15H, m, *Ph*).

***tert*-Butyl (3*R*,4*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(*tert*-butyldimethylsilyloxy)-4-phenylbutanoate *anti*-31**



Following *general procedure 1b*, BuLi (0.91 mL, 0.57 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (250 mg, 1.18 mmol) in THF (2.5 mL), and (*R*,*E*)-**26** (200 mg, 0.57 mmol) in THF (2.5 mL) gave *anti*-**31** in >98% de. Purification *via* flash column chromatography (eluent hexane/EtOAc, 20:1) gave *anti*-**31** as a colourless oil (306 mg, 95%, >98% de); $C_{35}H_{49}NO_3Si$ requires C, 75.1; H, 8.8; N, 2.5%; found C, 74.9; H, 9.1; N, 2.2%; $[\alpha]_D^{20}$ +50.3 (*c* 1.1 in $CHCl_3$).

***tert*-Butyl (3*S*,4*S*,α*R*)- and (3*R*,4*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(*tert*-butyldimethylsilyloxy)-4-phenylbutanoate (3*S*,4*S*,α*R*)-*anti*-33 and (3*R*,4*S*,α*R*)-*syn*-32**

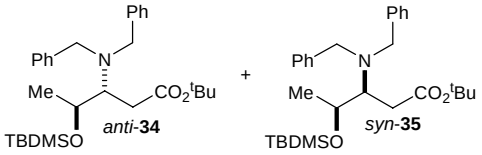


anti-**33**:*syn*-**32**, 11:89

Following *general procedure 1b*, BuLi (0.91 mL, 0.57 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (250 mg, 1.18 mmol) in THF (2.5 mL), and (*R*,*E*)-**26** (200 mg, 0.57 mmol) in THF (2.5 mL) gave an 11:89 mixture of *anti*-**33**:*syn*-**32**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 20:1) gave an 11:89 mixture of *anti*-**33**:*syn*-**32** as a colourless oil (301 mg, 94%); $C_{35}H_{49}NO_3Si$ requires C, 75.1; H, 8.8; N, 2.5%; found C, 75.05; H, 8.9; N, 2.3%; ν_{max} (film) 1714 (C=O); *m/z* (CI^+) 560 ($[M+H]^+$, 48%), 338 (100), 282 (30), 178 (37), 105 (56), 91 (45).

Data for *anti*-**33**: δ_H (400 MHz, C_6D_6) −0.17 (3H, s, Si*Me*$_A$), 0.07 (3H, s, Si*Me*$_B$), 0.79 (3H, d, *J* 7.1, C(α)*Me*), 0.88 (9H, s, SiC*Me*$_3$), 1.41 (9H, s, OC*Me*$_3$), 1.70 (1H, dd, *J* 16.8, 2.1, C(2)*H*$_A$), 2.62 (1H, dd, *J* 16.8, 10.7, C(2)*H*$_B$), 3.63 (1H, d, *J* 15.2, NC*H*$_A$), 4.58 (1H, d, *J* 15.2, NC*H*$_B$), 3.72 (1H, q, *J* 7.1, C(α)*H*), 3.90 (1H, app dt, *J* 10.7, 2.3, C(3)*H*), 5.14 (1H, d, *J* 2.3, C(4)*H*), 7.06-7.72 (15H, m, *Ph*); δ_C (100 MHz, C_6D_6) −5.5 (Si*Me*$_A$), −4.6 (Si*Me*$_B$), 18.0 (Si*C*Me$_3$), 18.5 (C(α)*Me*), 25.8 (SiC*Me*$_3$), 28.1 (OC*Me*$_3$), 33.7 (*C*(2)), 53.2 (N*C*H$_2$), 57.0, 57.1 (*C*(3), *C*(α)), 78.3 (*C*(4)), 80.1 (O*C*Me$_3$), 126.5, 127.0, 127.1, 127.4, 127.6, 128.1, 128.2, 128.4, 128.5 (*o*-*Ph*, *m*-*Ph*, *p*-*Ph*), 141.4, 141.6, 144.4 (*i*-*Ph*), 172.5 (*C*(1)).

***tert*-Butyl (3*R*,4*S*)- and (3*S*,4*S*)-3-(*N*,*N*-dibenzylamino)-4-(*tert*-butyldimethylsilyloxy)pentanoate (3*R*,4*S*)-*anti*-34 and (3*S*,4*S*)-*syn*-35**

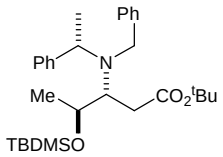


Following *general procedure 1a*, BuLi (1.60 mL, 1.00 mmol), dibenzylamine (335 mg, 1.80 mmol) in THF (5 mL), and (*S*,*E*)-**27** (286 mg, 1.00 mmol) in THF (5 mL) gave an 80:20 mixture of *anti*-**34**:*syn*-**35**. Purification *via* flash column chromatography (eluent hexane/Et_2O, 20:1) gave *anti*-**34** and *syn*-**35** as colourless oils (390 mg, 81% combined yield).

Data for *anti*-**34**: $C_{29}H_{45}NO_3Si$ requires C, 72.0; H, 9.4; N, 2.9%; found C, 72.0; H, 9.5; N, 3.0%; $[\alpha]_D^{21}$ +18.3 (*c* 1.6 in $CHCl_3$); ν_{max} (film) 1718 (C=O); δ_H (400 MHz, $CDCl_3$) 0.05 (3H, s, Si*Me*$_A$), 0.06 (3H, s, Si*Me*$_B$), 0.87 (9H, s, SiC*Me*$_3$), 1.11 (3H, d, *J* 6.2, C(5)*H*$_3$), 1.48 (9H, s, OC*Me*$_3$), 2.49 (1H, dd, *J* 15.2, 5.6, C(2)*H*$_A$), 2.55 (1H, dd, *J* 15.2, 6.9, C(2)*H*$_B$), 3.06-3.12 (1H, m, C(3)*H*), 3.66 (4H, app s, N(C*H*$_2$Ph)$_2$), 3.95-4.03 (1H, m, C(4)*H*), 7.19-7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.7 (Si*Me*$_A$), −3.9 (Si*Me*$_B$), 17.9 (Si*C*Me$_3$), 22.7 (*C*(5)), 25.9 (SiC*Me*$_3$), 28.1 (OC*Me*$_3$), 32.9 (*C*(2)), 54.8 (N(*C*H$_2$Ph)$_2$), 61.9 (*C*(3)), 68.7 (*C*(4)), 80.0 (O*C*Me$_3$), 127.0, 128.2, 129.2 (*o*-*Ph*, *m*-*Ph*, *p*-*Ph*), 140.2 (*i*-*Ph*), 173.1 (*C*(1)); *m/z* (CI^+) 484 ($[M+H]^+$, 13%), 198 (43), 91 (100).

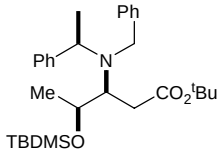
Data for *syn*-**35**: $C_{29}H_{45}NO_3Si$ requires C, 72.0; H, 9.4; N, 2.9%; found C, 71.9; H, 9.6; N, 3.2%; $[\alpha]_D^{21}$ +14.9 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 1717 (C=O); δ_H (400 MHz, $CDCl_3$) 0.01 (6H, s, Si*Me*$_2$), 0.84 (9H, s, SiC*Me*$_3$), 1.14 (3H, d, *J* 6.2, C(5)*H*$_3$), 1.47 (9H, s, OC*Me*$_3$), 2.62 (2H, app d, *J* 6.7, C(2)*H*$_2$), 2.90 (1H, td, *J* 6.7, 3.0, C(3)*H*), 3.30 (2H, app d, *J* 13.3, N(C*H*$_A$H$_B$Ph)$_2$), 3.84 (1H, qd, *J* 6.2, 3.0, C(4)*H*), 4.08 (2H, d, *J* 13.3, N(CH$_A$*H*$_B$Ph)$_2$), 7.18-7.43 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.1 (Si*Me*$_A$), −4.3 (Si*Me*$_B$), 18.0 (Si*C*Me$_3$), 21.4 (*C*(5)), 25.9 (SiC*Me*$_3$), 28.2 (OC*Me*$_3$), 31.1 (*C*(2)), 55.7 (N(*C*H$_2$Ph)$_2$), 59.4 (*C*(3)), 71.2 (*C*(4)), 80.2 (O*C*Me$_3$), 126.7, 128.0, 129.2 (*o*-*Ph*, *m*-*Ph*, *p*-*Ph*), 140.5 (*i*-*Ph*), 172.7 (*C*(1)); *m/z* (CI^+) 484 ($[M+H]^+$, 7%), 198 (55), 91 (100).

***tert*-Butyl (3*R*,4*S*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(*tert*-butyldimethylsilyloxy)pentanoate *anti*-36**



Following *general procedure 1a*, BuLi (1.60 mL, 1.00 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (422 mg, 2.00 mmol) in THF (5 mL), and (*S*,*E*)-**27** (286 mg, 1.00 mmol) in THF (5 mL) gave *anti*-**36** in >98% de Purification *via* flash column chromatography (eluent hexane/Et_2O, 30:1) gave *anti*-**36** as a colourless oil (478 mg, 96%, >98% de); $C_{30}H_{47}NO_3Si$ requires C, 72.4; H, 9.5; N, 2.8%; found C, 72.2; H, 9.8; N, 2.6%; $[\alpha]_D^{22}$ +14.2 (*c* 1.2 in $CHCl_3$); ν_{max} (film) 1726 (C=O); δ_H (400 MHz, $CDCl_3$) −0.01 (3H, s, Si*Me*$_A$), 0.03 (3H, s, Si*Me*$_B$), 0.85 (9H, s, SiC*Me*$_3$), 1.33 (3H, d, *J* 6.0, C(5)*H*$_3$), 1.38 (3H, d, *J* 7.1, C(α)*Me*), 1.43 (9H, s, OC*Me*$_3$), 1.81 (1H, dd, *J* 16.4, 3.1, C(2)*H*$_A$), 2.19 (1H, dd, *J* 16.4, 8.0, C(2)*H*$_B$), 3.49-3.82 (5H, m, C(3)*H*, C(4)*H*, C(α)*H*, NC*H*$_2$Ph), 7.22-7.43 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.7 (Si*Me*$_A$), −4.4 (Si*Me*$_B$), 18.0 (Si*C*Me$_3$), 19.5, 22.8 (C(5), C(α)*Me*), 26.0 (SiC*Me*$_3$), 28.1 (OC*Me*$_3$), 34.3 (*C*(2)), 51.4 (NCH_2), 58.2, 58.8 (*C*(3), *C*(α)), 71.2 (*C*(4)), 79.7 (O*C*Me$_3$), 126.8, 127.1, 128.1, 128.3, 128.4 (*o*-*Ph*, *m*-*Ph*, *p*-*Ph*), 141.7, 142.3 (*i*-*Ph*), 172.3 (*C*(1)); *m/z* (CI^+) 498 ($[M+H]^+$, 100%), 338 (98), 282 (38), 178 (56), 105 (48), 91 (52).

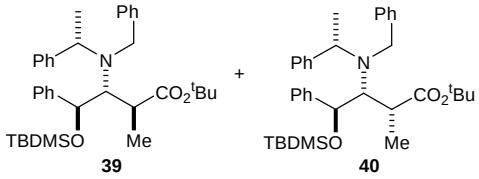
***tert*-Butyl (3*S*,4*S*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(*tert*-butyldimethylsilyloxy)pentanoate *syn*-38**



Following *general procedure 1a*, BuLi (1.60 mL, 1.00 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (422 mg, 2.00 mmol) in THF (5 mL), and (*S*,*E*)-**27** (286 mg, 1.00 mmol) in THF (5 mL) gave a 5:95 mixture of *anti*-**37**:*syn*-**38**. Purification *via* flash column chromatography (eluent hexane/Et_2O, 40:1) gave *syn*-**38** as a colourless oil (472 mg, 95%, >98% de); $C_{30}H_{47}NO_3Si$ requires C, 72.4; H, 9.5; N, 2.8%; found C, 72.4; H, 9.85; N, 2.8%; $[\alpha]_D^{21}$ +39.1 (*c* 1.3 in $CHCl_3$); ν_{max} (film) 1715 (C=O); δ_H (400 MHz, $CDCl_3$) −0.02 (3H, s, Si*Me*$_A$), 0.02 (3H, s, Si*Me*$_B$), 0.76 (9H, s, SiC*Me*$_3$), 1.33 (3H, d, *J* 7.1, C(α)*Me*), 1.39 (3H, obsc d, C(5)*H*$_3$), 1.41 (9H, s, OC*Me*$_3$), 1.48 (1H, dd, *J* 16.3, 2.0, C(2)*H*$_A$), 2.40 (1H, dd, *J* 16.3, 10.7, C(2)*H*$_B$), 3.27 (1H, app dt, *J* 10.7, 2.1, C(3)*H*), 3.43 (1H, d, *J* 14.3, NC*H*$_A$), 4.29 (1H, d, *J* 14.3, NC*H*$_B$), 3.74 (1H, q, *J* 7.1, C(α)*H*),

3.89 (1H, dq, *J* 6.1, 2.2, C(4)*H*), 7.22-7.54 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.2 (Si*Me*$_A$), −4.4 (Si*Me*$_B$), 17.9 (Si*C*Me$_3$), 20.1, 21.9 (*C*(5), C(α)*Me*), 25.7 (SiC*Me*$_3$), 28.1 (OC*Me*$_3$), 33.1 (*C*(2)), 52.9 (N*C*H$_2$), 55.9, 57.6 (*C*(3), *C*(α)), 71.5 (*C*(4)), 79.8 (O*C*Me$_3$), 126.3, 126.9, 128.0, 128.5 (*o-Ph*, *m-Ph*, *p-Ph*), 141.7, 142.1 (*i-Ph*), 172.3 (*C*(1)); *m/z* (CI$^+$) 498 ([M+H]$^+$, 100%), 338 (89), 282 (37), 178 (52), 105 (51), 91 (52).

tert-Butyl (2*S*,3*R*,4*S*,α*S*)- and (2*R*,3*R*,4*S*,α*S*)-2-methyl-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(*tert*-butyldimethylsilyloxy)-4-phenylbutanoate (2*S*,3*R*,4*S*,α*S*)-39 and (2*R*,3*R*,4*S*,α*S*)-40



Following *general procedure 2*, BuLi (4.80 mL, 3.00 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (1.27 g, 6.00 mmol) in THF (15 mL), (*R*,*E*)-**26** (1.04 g, 3.00 mmol) in THF (15 mL) and MeI (5.82 mL, 18.0 mmol) gave a 73:27 mixture of **39**:**40**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 25:1) gave a 73:27 mixture of **39**:**40** as a white solid (1.53 g, 89%). Fractional crystallisation from MeCN at 20 °C gave **39** as a colourless solid (>98% de). Concentration of the mother liquors gave a 20:80 mixture of **39**:**40** as a colourless oil.

Data for **39**: $C_{36}H_{51}NO_3Si$ requires C, 75.3; H, 9.0; N, 2.7%; found C, 75.4; H, 9.2; N, 2.7%; mp 95-97 °C; $[\alpha]_D^{21}$ +66.5 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1718 (C=O); δ_H (400 MHz, $CDCl_3$) −0.33 (3H, s, Si*Me*$_A$), −0.04 (3H, s, Si*Me*$_B$), 0.68 (9H, s, SiC*Me*$_3$), 0.86 (3H, d, *J* 7.1, C(2)*Me*), 1.26 (3H, d, *J* 7.1, C(α)*Me*), 1.55 (9H, s, OC*Me*$_3$), 2.79 (1H, qd, *J* 7.1, 1.8, C(2)*H*), 3.64 (1H, q, *J* 7.1, C(α)*H*), 3.75 (1H, d, *J* 14.8, NC*H*$_A$), 4.16 (1H, d, *J* 14.8, NC*H*$_B$), 4.43 (1H, dd, *J* 9.5, 1.8, C(3)*H*), 4.65 (1H, d, *J* 9.5, C(4)*H*), 7.07-7.44 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.7 (Si*Me*$_A$), −4.6 (Si*Me*$_B$), 12.6, 18.4 (C(2)*Me*, C(α)*Me*), 18.2 (Si*C*Me$_3$), 25.9 (SiC*Me*$_3$), 28.4 (OC*Me*$_3$), 40.1 (*C*(2)), 52.3 (N*C*H$_2$), 57.0, 61.7 (*C*(3), *C*(α)), 75.0 (*C*(4)), 79.8 (O*C*Me$_3$), 126.8, 127.0, 127.7, 127.8, 128.0, 128.3, 128.5, 129.2 (*o-Ph*, *m-Ph*, *p-Ph*), 141.1, 141.7, 145.3 (*i-Ph*), 174.5 (*C*(1)); *m/z* (CI$^+$) 574 ([M+H]$^+$, 32%), 352 (100), 296 (39), 192 (55), 105 (87), 91 (96).

X-ray Crystal Structure Determination for 39

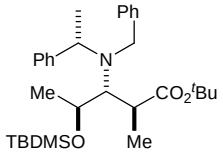
Data were collected using an Enraf-Nonius κ-CCD diffractometer with graphite monochromated Mo-Kα radiation using standard procedures at 190 K. The structure was solved by direct methods (SIR92), all non-

hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were added at idealised positions. The structure was refined using CRYSTALS.[2]

X-ray crystal structure data for **39** [$C_{36}H_{51}NO_3Si$]: M = 1147.78, triclinic, space group $P1$, a = 11.4449(2), b = 11.8000(2), c = 14.6478(2) Å, V = 1722.68(5) Å^3, Z = 2, μ = 0.10 mm^{-1}, colourless block, crystal dimensions = 0.1 × 0.1 × 0.1 mm. A total of 7805 unique reflections were measured for $5 < \theta < 27$ and 6098 reflections were used in the refinement. The final parameters were wR_2 = 0.082 and R_1 = 0.066 [$I>3.0\sigma(I)$]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 634215. 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].

Data for **40**: ν_{max} (film) 1714 (C=O); δ_H (400 MHz, $CDCl_3$) −0.33 (3H, s, Si*Me*$_A$), −0.02 (3H, s, Si*Me*$_B$), 0.79 (9H, s, SiC*Me*$_3$), 1.11 (3H, d, *J* 7.3, C(2)*Me*), 1.17 (3H, d, *J* 6.9, C(α)*Me*), 1.38 (9H, s, OC*Me*$_3$), 2.79 (1H, app quintet, *J* 7.2, C(2)*H*), 3.63 (1H, app t, *J* 6.5, C(3)*H*), 3.89 (1H, q, *J* 6.9, C(α)*H*), 3.96 (1H, d, *J* 15.6, NC*H*$_A$), 4.09 (1H, d, *J* 15.6, NC*H*$_B$), 4.90 (1H, d, *J* 6.2, C(4)*H*), 7.02-7.37 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −4.8 (Si*Me*$_A$), −4.4 (Si*Me*$_B$), 16.5, 20.4 (C(2)*Me*, C(α)*Me*), 18.2 (Si*C*Me$_3$), 26.0 (SiC*Me*$_3$), 28.0 (OC*Me*$_3$), 42.0 (*C*(2)), 52.4 (N*C*H$_2$), 60.0, 65.6 (*C*(3), *C*(α)), 77.8 (*C*(4)), 79.5 (O*C*Me$_3$), 126.5, 126.9, 127.3, 127.9, 128.1, 128.4, 128.7 (*o-Ph*, *m-Ph*, *p-Ph*), 142.4, 144.2, 144.9 (*i-Ph*), 175.5 (*C*(1)); *m/z* (CI^+) 574 ([M+H]$^+$, 63%), 352 (100), 296 (44), 192 (83), 105 (46), 91 (84).

tert-Butyl (2*S*,3*R*,4*S*,α*S*)-2-methyl-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(_tert_-butyldimethylsilyloxy)pentanoate 41

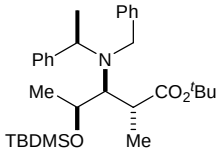


Following *general procedure 2*, BuLi (1.60 mL, 1.00 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (422 mg, 2.00 mmol) in THF (5 mL), (*S*,*E*)-**27** (286 mg, 1.00 mmol) in THF (5 mL) and MeI (1.94 mL, 6.00 mmol) gave a 93:7 mixture of **41**:**42**. Purification *via* flash column chromatography (eluent hexane/Et_2O, 30:1) gave **41** as a colourless oil (397 mg, 78%, >98% de); $C_{31}H_{49}NO_3Si$ requires C, 72.75; H, 9.65; N, 2.7; found: C, 72.6; H, 9.9; N, 2.65%; $[\alpha]_D^{21}$ +36.1 (*c* 1.2 in $CHCl_3$), ν_{max} (film) 1718 (C=O); δ_H (400 MHz,

[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.

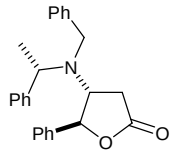
$CDCl_3$) 0.03 (3H, s, Si*Me*$_A$), 0.05 (3H, s, Si*Me*$_B$), 0.85 (9H, s, SiC*Me*$_3$), 1.21 (3H, d, *J* 7.0, C(2)*Me*), 1.24 (3H, d, *J* 7.2, C(5)*H*$_3$), 1.27 (3H, d, *J* 6.7, C(α)*Me*), 1.51 (9H, s, OC*Me*$_3$), 2.70 (1H, dq, *J* 8.6, 7.0, C(2)*H*), 3.31 (1H, dd, *J* 8.6, 2.6, C(3)*H*), 3.68 (1H, d, *J* 14.9, NC*H*$_A$), 4.08 (1H, d, *J* 14.9, NC*H*$_B$), 3.92-4.02 (2H, m, C(4)*H*, C(α)*H*), 7.17-7.41 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) –4.8, –3.7 (Si*Me*$_2$), 15.4, 18.9, 24.6 (*C*(5), C(2)*Me*, C(α)*Me*), 18.0 (Si*C*Me$_3$), 26.0 (SiC*Me*$_3$), 28.2 (OC*Me*$_3$), 43.0 (*C*(2)), 51.0 (N*C*H$_2$), 60.8, 65.7 (*C*(3), *C*(α)), 68.9 (*C*(4)), 79.5 (O*C*Me$_3$), 126.5, 127.0, 127.9, 128.0, 128.6, 128.7 (*o-Ph*, *m-Ph*, *p-Ph*), 142.5, 143.4 (*i-Ph*), 176.0 (*C*(1)); *m/z* (CI^+) 512 ($[M+H]^+$, 7%), 352 (29), 192 (31), 148 (31), 120 (41), 105 (62), 91 (100).

tert-Butyl (2*R*,3*S*,4*S*,α*R*)-2-methyl-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4-(_tert_-butyldimethylsilyloxy)pentanoate 43



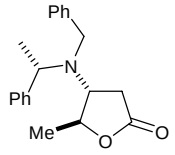
Following *general procedure 2*, BuLi (1.60 mL, 1.00 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (422 mg, 2.00 mmol) in THF (5 mL), (*S*,*E*)-**27** (286 mg, 1.00 mmol) in THF (5 mL) and MeI (1.94 mL, 6.00 mmol) gave a 95:5 mixture of **43**:**44**. Purification *via* flash column chromatography (eluent hexane/Et_2O, 30:1) gave **43** as a colourless oil (468 mg, 92%, >98% de); $C_{31}H_{49}NO_3Si$ requires C, 72.75; H, 9.65; N, 2.7%; found C, 72.5; H, 10.0; N, 2.7%; $[\alpha]_D^{21}$ −30.3 (*c* 1.45 in $CHCl_3$); ν_{max} (film) 1714 (C=O); δ_H (400 MHz, $CDCl_3$) 0.00 (3H, s, Si*Me*$_A$), 0.01 (3H, s, Si*Me*$_B$), 0.77 (9H, s, SiC*Me*$_3$), 1.12 (6H, app d, *J* 6.6, C(5)*H*$_3$, C(2)*Me*), 1.25 (3H, d, *J* 6.9, C(α)*Me*), 1.51 (9H, s, OC*Me*$_3$), 2.85 (1H, dq, *J* 8.9, 6.8, C(2)*H*), 2.95 (1H, dd, *J* 8.9, 2.3, C(3)*H*), 3.98-4.05 (2H, m, C(4)*H*, NC*H*$_A$,), 4.19 (1H, q, *J* 6.9, C(α)*H*), 4.33 (1H, d, *J* 15.1, NC*H*$_B$), 7.14-7.45 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) –5.2 (Si*Me*$_A$), –3.8 (Si*Me*$_B$), 16.8, 20.1, 21.9 (*C*(5), C(2)*Me*, C(α)*Me*), 17.8 (Si*C*Me$_3$), 25.7 (SiC*Me*$_3$), 28.0 (OC*Me*$_3$), 41.5 (*C*(2)), 52.7 (N*C*H$_2$), 61.3, 64.1 (*C*(3), *C*(α)), 70.4 (*C*(4)), 80.0 (O*C*Me$_3$), 126.1, 126.7, 127.8, 128.1, 128.5, 128.6 (*o-Ph*, *m-Ph*, *p-Ph*), 144.0, 146.1 (*i-Ph*), 177.0 (*C*(1)); *m/z* (CI^+) 512 ($[M+H]^+$, 7%), 352 (27), 148 (34), 120 (37), 105 (56), 91 (100).

(4*R*,5*S*,α*S*)-4-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-5-phenyltetrahydro-2-furanone 45



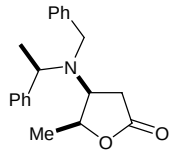
Following *general procedure 3*, TBAF (868 mg, 2.75 mmol) and *anti*-**31** (280 mg, 0.50 mmol) in THF (10 mL) gave the crude reaction product. Purification *via* sequential flash column chromatography (eluent hexane/EtOAc, 6:1) and recrystallisation from hexane/DCM (1:1) at −30 ºC gave **45** as a white crystalline solid (123 mg, 66%, >98% de); $C_{25}H_{25}NO_2$ requires C, 80.8; H, 6.8; N, 3.8; found: C, 80.45; H, 6.8; N, 3.5%; mp 122-124 ºC; $[\alpha]_D^{21}$ –124.0 (*c* 0.6 in $CHCl_3$). ν_{max} (KBr) 1780 (C=O); δ_H (400 MHz, $CDCl_3$) 1.15 (3H, d, *J* 7.0, C(α)*Me*), 2.05 (2H, dd, *J* 18.1, 8.6, C(2)H_A), 2.29 (2H, dd, *J* 18.1, 8.2, C(2)H_B), 3.73-3.93 (4H, m, C(4)*H*, C(α)*H*, NCH_2), 5.25 (1H, d, *J* 6.9, C(5)*H*), 7.15-7.49 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.2 (C(α)*Me*), 29.6 (*C*(3)), 50.6 (N*C*H_2), 57.4, 62.0 (*C*(4), *C*(α)), 84.1 (*C*(5)), 126.1, 127.6, 127.8, 128.5, 128.8, 129.0 (*o-Ph*, *m-Ph*, *p-Ph*), 139.0, 139.7, 141.4 (*i-Ph*), 176.0 (*C*(2)); *m/z* (CI^+) 372 ($[M+H]^+$, 89%), 268 (97), 237 (54), 146 (84), 105 (77), 91 (100).

(4*R*,5*S*,α*S*)-4-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-5-methyltetrahydro-2-furanone 46



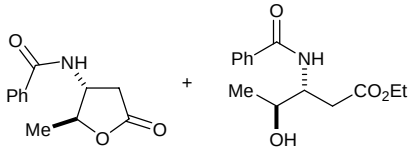
Following *general procedure 3*, TBAF (432 mg, 1.37 mmol) and *anti*-**36** (340 mg, 0.68 mmol) in THF (10 mL) gave the crude reaction product. Purification *via* flash column chromatography (eluent hexane/EtOAc, 4:1) gave **46** as a white crystalline solid (180 mg, 86%, >98% de); $C_{20}H_{23}NO_2$ requires C, 77.6; H, 7.5; found: C, 77.9; H, 7.3%; mp 124-125 ºC; $[\alpha]_D^{21}$ –189.4 (*c* 0.9 in $CHCl_3$); ν_{max} (KBr) 1778, 1758 (C=O); δ_H (400 MHz, $CDCl_3$) 1.39 (3H, d, *J* 7.0, C(α)*Me*), 1.48 (3H, d, *J* 6.2, C(5)*Me*), 1.94 (1H, dd, *J* 18.0, 8.5, C(3)H_A), 2.20 (1H, dd, *J* 18.0, 8.6, C(3)H_B), 3.48-3.56 (1H, m, C(4)*H*), 3.66 (1H, d, *J* 14.8, NCH_A), 3.76 (1H, d, *J* 14.8, NCH_B), 3.83 (1H, q, *J* 7.0, C(α)*H*), 4.33-4.42 (1H, m, C(5)*H*), 7.25-7.44 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 18.6, 19.2 (C(5)*Me*, C(α)*Me*), 29.6 (*C*(3)), 50.6 (N*C*H_2), 57.7, 60.3 (*C*(4), *C*(α)), 79.4 (*C*(5)), 127.5, 127.7, 128.2, 128.8 (o-*Ph*, *m-Ph*, *p-Ph*), 139.8, 141.6 (*i-Ph*), 176.1 (*C*(2)); *m/z* (CI^+) 310 ($[M+H]^+$, 7%), 212 (100), 196 (55), 116 (43), 106 (66), 105 (39), 91 (70).

(4*S*,5*S*,α*R*)-4-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-5-methyltetrahydro-2-furanone 47



Following *general procedure 3*, TBAF (331 mg, 1.05 mmol) and *syn*-**38** (260 mg, 0.52 mmol) in THF (10 mL) gave the crude reaction product. Purification *via* flash column chromatography (eluent hexane/EtOAc, 4:1) gave **47** as a white crystalline solid (104 mg, 65%, >98% de); $C_{20}H_{23}NO_2$ requires C, 77.6; H, 7.5; N, 4.5; found: C, 77.6; H, 7.6; N, 4.45%; mp 129-131 °C; $[\alpha]_D^{21}$ +116.0 (*c* 0.85 in $CHCl_3$); ν_{max} (KBr) 1774 (C=O); δ_H (400 MHz, $CDCl_3$) 1.43 (3H, d, *J* 7.0, C(α)*Me*), 1.54 (3H, d, *J* 6.6, C(5)*Me*), 1.85 (1H, dd, *J* 17.9, 5.8, C(3)H_A), 2.12 (1H, dd, *J* 17.9, 7.9, C(3)H_B), 3.62 (1H, d, *J* 14.6, NCH_A), 3.72 (1H, d, *J* 14.6, NCH_B), 3.86-3.93 (2H, m, C(4)*H*, C(α)*H*), 4.78 (1H, app quintet, *J* 6.6, C(5)*H*), 7.26-7.46 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 15.1, 15.7 (C(5)*Me*, C(α)*Me*), 31.9 (*C*(3)), 52.2 (N*C*H_2), 56.2 (*C*(4), *C*(α)), 80.7 (*C*(5)), 127.4, 127.7, 127.8, 128.2, 128.6, 128.9 (*o-Ph*, *m-Ph*, *p-Ph*), 139.5, 141.3 (*i-Ph*), 176.7 (*C*(2)); *m/z* (CI^+) 310 ($[M+H]^+$, 28%), 212 (52), 206 (100), 204 (41), 196 (30), 105 (44), 91 (60).

(4*R*,5*S*)-4-(*N*-Benzoylamino)-5-methyltetrahydro-2-furanone 48 and ethyl (3*R*,4*S*)-3-(*N*-benzoylamino)-4-hydroxypentanoate 49



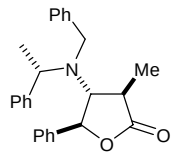
46 (120 mg, 0.35 mmol) and Pd/C (10%, 24 mg), in EtOH (4.0 mL) were stirred vigorously at 60 ºC under an atmosphere of hydrogen (6 atm). After 48 h the solution was allowed to cool to rt and filtered through Celite® and the solvent was removed *in vacuo*. The residue was redissolved in DCM (10 mL), treated with pyridine (85 μL, 1.05 mmol) and benzoyl chloride (82 μL, 0.70 mmol) and stirred at 20 ºC for 48 h. The reaction mixture was then poured into sat aq $NaHCO_3$ solution (50 mL), extracted with DCM (3 × 20 mL), and the combined organic extracts were dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent hexane/EtOAc, 2:3) gave **48** as a white solid and **49** as a colourless oil (10 mg, 11%, >98% de). Further purification of **48** by recrystallisation from $CHCl_3$/hexane (1:1) gave a white crystalline solid (49 mg, 64%, >98% de).

Data for **48**: $C_{12}H_{13}NO_3$ requires C, 65.7; H, 6.0; N, 6.4; found: C, 65.5; H, 5.9; N, 6.1%; mp 116-117 ºC; $[\alpha]_D^{21}$ +28.0 (*c* 0.6 in $CHCl_3$); ν_{max} (KBr) 1779 (C=O, ester), 1667 (C=O, amide), 1514 (C=O, amide); δ_H (400 MHz, $CDCl_3$) 1.53 (3H, d, *J* 6.3, C(5)*Me*), 2.59 (1H, dd, *J* 18.2, 4.6, C(3)H_A), 3.09 (1H, dd, *J* 18.2, 8.0, C(3)H_B), 4.54-4.66 (2H, m, C(4)*H*, C(5)*H*), 6.49 (1H, br s, N*H*), 7.28-7.58 (3H, m, *Ph*), 7.77-7.80 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.4 (C(5)*Me*), 34.2 (*C*(3)), 52.2 (*C*(4)), 83.3 (*C*(5)), 127.4, 128.8, 132.2 (*o-Ph*, *m-Ph*, *p-Ph*), 133.5 (*i-Ph*), 168.1 (*C*OPh), 176.2 (*C*(2)); *m/z* (CI^+) 220 ($[M+H]^+$, 100%).

Data for **49**: δ_H (400 MHz, $CDCl_3$) 1.24-1.28 (6H, m, CH_2Me, C(5)H_3), 2.70 (1H, dd, *J* 15.9, 4.7, C(2)H_A), 2.82 (2H, dd, *J* 15.9, 6.3, C(2)H_B), 4.06 (1H, qd, *J* 6.4, 4.5, C(4)*H*), 4.16 (2H, q, *J* 7.1, CH_2Me), 4.28-4.34 (1H, m, C(3)*H*), 7.32 (1H, br d, *J* 7.8, N*H*), 7.41-7.54 (3H, m, *Ph*), 7.78-7.82 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.1, 20.1 (CH_2Me, *C*(5)), 33.7 (*C*(2)), 52.7 (*C*(3)), 61.0 (*C*H_2Me), 69.5 (*C*(4)), 127.0, 128.6, 131.7 (*o-Ph*, *m-Ph*, *p-Ph*), 134.2 (*i-Ph*), 167.5 (*C*OPh), 172.8 (*C*(1)); *m/z* (CI^+) 238 (24), 220 (100), 122 (25), 105 (20).

49 (64 mg, 0.29 mmol) was subsequently dissolved in PhMe (1 mL) and the solution treated with TFA (3 drops) and allowed to stand for 16 h. The solvent was then removed *in vacuo* and the residue was dissolved in Et_2O and filtered through a plug of silica gel (eluent Et_2O). The filtrate was concentrated *in vacuo* to afford lactone **48** (57 mg, 74%, >98% de) as a white solid.

(3*R*,4*R*,5*S*,α*S*)-3-Methyl-4-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-5-phenyl-tetrahydro-2-furanone 50



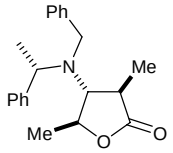
*From **39**:* Following *general procedure 3*, TBAF (678 mg, 2.15 mmol) and **39** (410 mg, 0.72 mmol) in THF (10 mL) gave the crude reaction product. Purification *via* flash column chromatography (eluent hexane/EtOAc, 6:1) gave **50** as a colourless oil (235 mg, 85%, >98% de).

*From **40**:* Following *general procedure 3*, TBAF (678 mg, 2.15 mmol) and **40** (283 mg, 0.49 mmol) in THF (10 mL) gave the crude reaction product. Purification *via* flash column chromatography (eluent hexane/EtOAc, 6:1) gave **50** as a yellow oil (129 mg, 68%, >98% de).

Data for **50**: $[\alpha]_D^{21}$ −42.5 (*c* 0.55 in $CHCl_3$); $C_{26}H_{27}NO_2$ requires C, 81.0; H, 7.1; N, 3.6; found: C, 81.05; H, 7.2; N, 3.5%; mp 109-110 ºC, ν_{max} (KBr) 1767 (C=O); δ_H (400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 7.1, C(3)*Me*), 1.08 (3H, d, *J* 6.9, C(α)*Me*), 2.77 (1H, dq, *J* 10.2, 7.1, C(3)*H*), 3.45 (1H, dd, *J* 10.2, 8.4, C(4)*H*), 3.86 (1H, d,

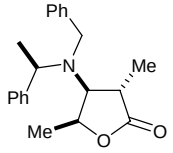
J 14.6, NCH_A), 3.94 (1H, d, *J* 14.6, NCH_B), 3.98 (1H, q, *J* 6.9, C(α)*H*), 5.07 (1H, d, *J* 8.4, C(5)*H*), 7.15-7.49 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.0, 18.3 (C(3)*Me*, C(α)*Me*), 37.8 (*C*(3)), 50.6 (N*C*H_2), 58.2, 69.9 (*C*(4), *C*(α)), 81.9 (*C*(5)H), 127.3, 127.4, 127.9, 128.3, 128.5, 128.7 (*o-Ph*, *m-Ph*, *p-Ph*), 138.2, 140.2, 143.3 (*i-Ph*), 177.8 (*C*(2)); *m/z* (CI^+) 386 ($[M+H]^+$, 100%), 282 (61), 251 (31), 105 (37), 91 (42).

(3*R*,4*R*,5*S*,α*S*)-3,5-Dimethyl-4-[*N*-benzyl-*N*-(α-methylbenzyl)amino]tetrahydro-2-furanone 51



Following *general procedure 3*, TBAF (544 mg, 1.72 mmol) and **39** (440 mg, 0.86 mmol) in THF (10 mL) gave the crude reaction product. Purification *via* flash column chromatography (eluent hexane/EtOAc, 4:1) gave **51** as a white crystalline solid (236 mg, 85%, >98% de); $C_{21}H_{25}NO_2$ requires C, 78.0; H, 7.8; N, 4.3; found: C, 78.3; H, 8.1; N, 4.1%; mp 107-109 ºC, $[\alpha]_D^{21}$ –56.3 (*c* 1.1 in $CHCl_3$), ν_{max} (KBr) 1764 (C=O); δ_H (400 MHz, $CDCl_3$) 1.01 (3H, d, *J* 7.2, C(3)*Me*), 1.38 (3H, d, *J* 6.9, C(α)*Me*), 1.42 (3H, d, *J* 6.2, C(5)*Me*), 2.65 (1H, dq, *J* 9.7, 7.2, C(3)*H*), 3.05 (1H, dd, *J* 9.7, 8.1, C(4)*H*), 3.84 (1H, d, *J* 14.8, NCH_A), 3.91 (1H, d, *J* 14.8, NCH_B), 4.07 (1H, q, *J* 6.9, C(α)*H*), 4.26 (1H, dq, *J* 8.0, 6.2, C(5)*H*), 7.25-7.41 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.6, 19.4, 19.8 (C(3)*Me*, C(5)*Me*, C(α)*Me*), 37.6 (*C*(3)), 51.0 (N*C*H_2), 59.0, 68.6 (*C*(4), *C*(α)), 77.0 (*C*(5)), 127.4, 127.6, 127.9, 128.1, 128.7 (*o-Ph*, *m-Ph*, *p-Ph*), 140.8, 143.9 (*i-Ph*), 178.4 (*C*(2)); *m/z* 324 ($[M+H]^+$, 82%), 220 (100), 212 (62), 130 (31), 91 (46).

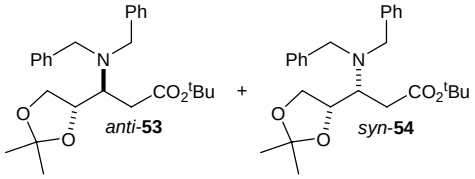
(3*S*,4*S*,5*S*,α*R*)-3,5-dimethyl-4-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]tetrahydro-2-furanone 52



Following *general procedure 3*, TBAF (453 mg, 1.43 mmol) and **43** (366 mg, 0.72 mmol) in THF (10 mL) gave the crude reaction product. Purification *via* sequential flash column chromatography (eluent hexane/EtOAc, 4:1) and recrystallisation from $CHCl_3$/hexane (1:1) gave **52** as a white solid (204 mg, 88%, >98% de); $C_{21}H_{25}NO_2$ requires C, 78.0; H, 7.8; N, 4.3; found: C, 78.0; H, 7.7; N, 4.1%; mp 138-139 °C; $[\alpha]_D^{21}$ +66.9 (*c* 1.15 in $CHCl_3$); ν_{max} (KBr) 1767 (C=O); δ_H (400 MHz, $CDCl_3$) 0.94 (3H, d, *J* 7.4, C(3)*Me*), 1.41 (3H, d, *J* 7.1, C(α)*Me*), 1.53 (3H, d, *J* 6.7, C(5)*Me*), 2.18-2.28 (1H, m, C(3)*H*), 3.44-3.49 (1H, m, C(4)*H*), 3.84 (1H, obsc d, *J* 15.2, NCH_A), 3.90 (1H, obsc d, *J* 15.2, NCH_B), 3.93 (1H, q, *J* 7.1, C(α)*H*), 4.74

(1H, app quintet, *J* 6.7, C(5)*H*), 7.23-7.50 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.6, 15.8, 17.8 (C(3)*Me*, C(5)*Me*, C(α)*Me*), 36.4 (*C*(3)), 51.7 (N*C*H_2), 56.2, 61.8 (*C*(4), *C*(α)), 79.2 (*C*(5)), 127.4, 127.8, 128.0, 128.2, 128.6, 128.9 (*o-Ph*, *m-Ph*, *p-Ph*), 139.7 141.5 (*i-Ph*), 179.5(*C*(2)); *m/z* (CI^+) 324 ($[M+H]^+$, 30%), 220 (100).

tert-Butyl (3*R*,4′*S*)- and (3*S*,4′*S*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-(*N*,*N*-dibenzylamino)propanoate (3*R*,4′*S*)-*anti*-53 and (3*S*,4′*S*)-*syn*-54

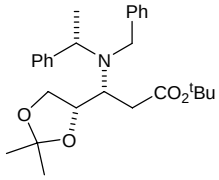


Following *general procedure 1a*, BuLi (0.80 mL, 0.50 mmol), dibenzylamine (197 mg, 1.00 mmol) in THF (2.5 mL), and (*S*,*E*)-**17** (114 mg, 0.50 mmol) in THF (2.5 mL) gave a 29:71 mixture of *anti*-**53**:*syn*-**54**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 12:1) gave *anti*-**53** and *syn*-**54** as colourless oils (121 mg, 57% combined yield).

Data for *anti*-**53**: $C_{26}H_{35}NO_4$ requires C, 73.4; H, 8.3; N, 3.3; found: C, 73.4; H, 7.9; N, 3.4%; $[\alpha]_D^{21}$ +8.9 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 1719 (C=O); δ_H (400 MHz, $CDCl_3$) 1.23 (3H, s, C(2′)*Me*$_A$), 1.30 (3H, s, C(2′)*Me*$_B$), 1.50 (9H, s, C*Me*$_3$), 2.46 (1H, dd, *J* 14.8, 6.7, C(2)*H*$_A$), 2.68 (1H, dd, *J* 14.8, 5.7, C(2)*H*$_B$), 3.22-3.29 (1H, m, C(3)*H*), 3.46 (1H, dd, *J* 8.2, 7.0, C(5′)*H*$_A$), 4.07 (1H, dd, *J* 8.2, 6.4, C(5′)*H*$_B$), 3.51 (2H, d, *J* 13.6, N(C*H*$_A$H$_B$Ph)$_2$), 3.70 (2H, d, *J* 13.6, N(CH$_A$*H*$_B$Ph)$_2$), 4.13-4.20 (1H, m, C(4′)*H*), 7.23-7.35 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.5 (C(2′)*Me*$_A$), 26.1 (C(2′)*Me*$_B$), 28.0 (C*Me*$_3$), 33.3 (*C*(2)), 54.7 (N(*C*H$_2$Ph)$_2$), 58.6 (*C*(3)), 68.7 (*C*(5′)), 76.7 (*C*(4′)), 80.3 (*C*Me$_3$), 109.4 (*C*(2′)), 127.3, 128.4, 129.2 (*o-Ph*, *m-Ph*, *p-Ph*), 139.6 (*i-Ph*), 172.4 (*C*(1)); *m/z* (CI^+) 426 ($[M+H]^+$, 54%), 324 (37), 268 (45), 91 (100).

Data for *syn*-**54**: $C_{26}H_{35}NO_4$ requires C, 73.4; H, 8.3; N, 3.3; found: C, 73.0; H, 8.5; N, 3.0%; $[\alpha]_D^{21}$ +22.3 (*c* 0.8 in $CHCl_3$); ν_{max} (film) 1719 (C=O); δ_H (400 MHz, $CDCl_3$) 1.34 (3H, s, C(2′)*Me*$_A$), 1.39 (3H, s, C(2′)*Me*$_B$), 1.46 (9H, s, C*Me*$_3$), 2.37 (1H, dd, *J* 14.6, 7.4, C(2)*H*$_A$), 2.63 (1H, dd, *J* 14.6, 6.2, C(2)*H*$_B$), 3.19-3.25 (1H, m, C(3)*H*), 3.52 (2H, d, *J* 13.4, N(C*H*$_A$H$_B$Ph)$_2$), 3.94 (2H, d, *J* 13.4, N(CH$_A$*H*$_B$Ph)$_2$), 3.83 (2H, d, *J* 7.1, C(5′)*H*$_2$), 4.23 (1H, td, *J* 7.1, 5.3, C(4′)*H*), 7.20-7.40 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.9 (C(2′)*Me*$_A$), 26.3 (C(2′)*Me*$_B$), 28.0 (C*Me*$_3$), 33.8 (*C*(2)), 55.3 (N(*C*H$_2$Ph)$_2$), 55.9 (*C*(3)), 66.5 (*C*(5′)), 77.5 (*C*(4′)), 80.6 (*C*Me$_3$), 108.9 (*C*(2′)), 127.1, 128.3, 129.4 (*o-Ph*, *m-Ph*, *p-Ph*), 140.2 (*i-Ph*), 171.9 (*C*(1)); *m/z* (CI^+) 426 ($[M+H]^+$, 24%), 198 (100), 91 (53).

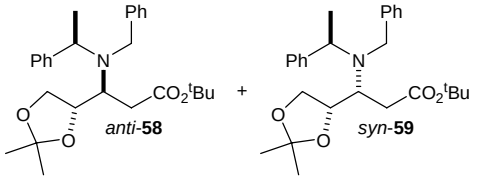
***tert*-Butyl (3*R*,4′*S*,α*S*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]propanoate *syn*-57**



Method A: Following *general procedure 1a*, BuLi (1.6 mL, 1.00 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (338 mg, 1.60 mmol) in THF (5 mL), and (*S*,*E*)-**17** (228 mg, 1.00 mmol) in THF (5 mL) gave a 5:95 mixture of *anti*-**56**:*syn*-**57**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 10:1) gave *syn*-**57** as a pale yellow oil (230 mg, 52%, >98% de); $C_{27}H_{37}NO_4$ requires C, 73.8; H, 8.5; N, 3.2; found: C, 73.5; H, 8.8; N, 3.0%; $[\alpha]_D^{21}$ –0.7 (*c* 1.2 in $CHCl_3$); ν_{max} (film) 1718 (C=O); δ_H (400 MHz, $CDCl_3$) 1.32 (3H, s, C(2′)*Me*$_A$), 1.32 (3H, s, C(2′)*Me*$_B$), 1.38 (3H, d, *J* 7.0, C(α)*Me*), 1.42 (9H, s, C*Me*$_3$), 1.77 (1H, dd, *J* 16.0, 3.6, C(2)*H*$_A$), 2.29 (1H, dd, *J* 16.0, 9.3, C(2)*H*$_B$), 3.53-3.59 (1H, obsc m, C(3)*H*), 3.57 (1H, d, *J* 14.6, NC*H*$_A$), 4.14 (1H, d, *J* 14.6, NC*H*$_B$), 3.84 (1H, q, *J* 7.0, C(α)*H*), 3.96-4.11 (2H, m, C(5′)*H*$_2$), 4.21-4.28 (1H, m, C(4′)*H*), 7.22-7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.5 (C(α)*Me*), 24.8 (C(2′)*Me*$_A$), 26.3 (C(2′)*Me*$_B$), 28.0 (C*Me*$_3$), 34.5 (*C*(2)), 52.3 (N*C*H$_2$), 52.9, 57.8 (*C*(3), *C*(α)), 66.3 (*C*(5′)), 78.2 (*C*(4′)), 80.2 (*C*Me$_3$), 108.5 (*C*(2′)), 126.5, 126.9, 127.9, 128.1, 128.1, 128.3 (*o-Ph*, *m-Ph*, *p-Ph*), 141.3, 142.2 (*i-Ph*), 171.5 (*C*(1)); *m/z* (CI^+) 440 ($[M+H]^+$, 27%), 212 (100), 108 (40), 105 (22), 91 (43).

Method B: Following *general procedure 1c*, BuLi (0.34 mL, 0.86 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (185 mg, 0.88 mmol) in Et_2O (2 mL), and (*S*,*E*)-**17** (100 mg, 0.44 mmol) in Et_2O (2 mL) gave a 27:73 mixture of *anti*-**56**:*syn*-**57**. Purification *via* flash column chromatography (eluent hexane/EtOAc 10:1) gave a 27:73 mixture of *anti*-**56**:*syn*-**57** as a pale yellow oil (135 mg, 70%).

***tert*-Butyl (3*R*,4′*S*,α*R*)- and (3*S*,4′*S*,α*R*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]propanoate (3*R*,4′*S*,α*R*)-*anti*-58 and (3*S*,4′*S*,α*R*)-*syn*-59**



Method A: Following *general procedure 1a*, BuLi (1.6 mL, 1.00 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (338 mg, 1.60 mmol) in THF (5 mL), and (*S*,*E*)-**17** (228 mg, 1.00 mmol) in THF (5

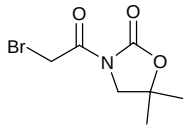
mL) gave a 62:38 mixture of *anti*-**58**:*syn*-**59**. Purification *via* flash column chromatography (eluent hexane/EtOAc, 10:1) gave *anti*-**58** and *syn*-**59** as pale yellow oils (246 mg, 56% combined yield).

Data for *anti*-**58**: $C_{27}H_{37}NO_4$ requires C, 73.8; H, 8.5; N, 3.2; found: C, 73.5; H, 8.7; N, 2.9%; ν_{max} (film) 1719 (C=O); δ_H (400 MHz, $CDCl_3$) 1.34 (6H, app s, C(2′)*Me*$_2$), 1.41 (3H, d, *J* 7.1, C(α)*Me*), 1.44 (9H, s, C*Me*$_3$), 1.94 (1H, dd, *J* 15.6, 2.8, C(2)*H*$_A$), 2.17 (1H, dd, *J* 15.6, 8.6, C(2)*H*$_B$), 3.47-4.22 (7H, m, C(3)*H*, C(4′)*H*, C(5′)*H*$_2$, C(α)*H*, NC*H*$_2$), 7.23-7.51 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.8 (C(α)*Me*), 25.5 (C(2′)*Me*$_A$), 26.3 (C(2′)*Me*$_B$), 28.1 (C*Me*$_3$), 35.3 (*C*(2)), 50.9 (N*C*H$_2$), 56.5, 58.5 (*C*(3), *C*(α)), 68.9 (*C*(5′)), 78.1 (*C*(4′)), 79.8 (*C*Me$_3$), 109.3 (*C*(2′)), 126.8, 127.1, 128.0, 128.1, 128.3, 128.7 (*o-Ph*, *m-Ph*, *p-Ph*), 140.9, 142.0 (*i-Ph*), 171.5 (*C*(1)); *m/z* (CI^+) 440 ($[M+H]^+$, 71%), 338 (39), 212 (39), 178 (61), 105 (93), 91 (100).

Data for *syn*-**59**: δ_H (400 MHz, $CDCl_3$) 1.30 (6H, app s, C(2′)*Me*$_2$), 1.37 (3H, d, *J* 7.0, C(α)*Me*), 1.50 (9H, s, C*Me*$_3$), 2.53 (1H, dd, *J* 15.0, 6.2, C(2)*H*$_A$), 2.61 (1H, dd, *J* 15.0, 4.4, C(2)*H*$_B$), 3.47-4.22 (7H, m, C(3)*H*, C(4′)*H*, C(5′)*H*$_2$, C(α)*H*, NC*H*$_2$), 7.23-7.51 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 14.7 (C(α)*Me*), 24.7 (C(2′)*Me*$_A$), 26.3 (C(2′)*Me*$_B$), 28.1 (C*Me*$_3$), 36.0 (*C*(2)), 51.8 (N*C*H$_2$), 53.5, 57.4 (*C*(3), *C*(α)), 65.8 (*C*(5′)), 77.5 (*C*(4′)), 80.5 (*C*Me$_3$), 108.0 (*C*(2′)), 126.8, 127.1, 128.0, 128.1, 128.3, 128.7 (*o-Ph*, *m-Ph*, *p-Ph*), 141.1, 143.4 (*i-Ph*), 171.7 (*C*(1)); *m/z* (CI^+) 440 ($[M+H]^+$, 85%), 338 (52), 212 (54), 178 (64), 105 (91), 91 (100).

Method B: Following *general procedure 1c*, BuLi (0.34 mL, 0.86 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (185 mg, 0.88 mmol) in Et_2O (2 mL), and (*S*,*E*)-**17** (100 mg, 0.44 mmol) in Et_2O (2 mL) gave a 72:28 mixture of *anti*-**58**:*syn*-**59**. Purification *via* flash column chromatography (eluent hexane/EtOAc 10:1) gave a 27:73 mixture of *anti*-**58**:*syn*-**59** as a pale yellow oil (141 mg, 73%).

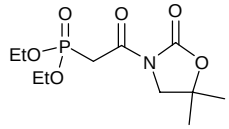
_N_(3)-Bromoacetyl-5,5-dimethyl-oxazolidin-2-one 61



BuLi (19.1 mL, 47.8 mmol) was added dropwise to a stirred solution of 5,5-dimethyl-oxazolidin-2-one **60** (5.00 g, 43.5 mmol) in THF (100 mL) at −78 °C. After 30 min, bromoacetyl bromide (4.9 mL, 56.6 mmol) was added dropwise *via* syringe and the resultant mixture was left stirring at −78 °C for 10 min before being allowed to warm to rt. After 1.5 hours, the reaction mixture was quenched with sat. aq. NH_4Cl, extracted with DCM (3 × 100 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent pentane/Et_2O, 2:1) gave **61** as a white crystalline solid (9.06 g, 88%); mp 46-48 °C (pentane/Et_2O); ν_{max} (KBr) 1711 (C=O, exocyclic), 1769 (C=O, endocyclic); δ_H (200 MHz, $CDCl_3$) 1.54 (6H, s, C(5)*Me*$_2$),

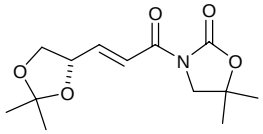
3.80 (2H, s, C(4)H_2), 4.54 (2H, s, C(2')H_2); δ_C (50 MHz, $CDCl_3$) 27.2 (C(5)Me_2), 28.1 (*C*(4)), 54.5 (*C*(2')), 79.7 (*C*(5)), 152.2 (*C*(2)), 166.3 (*C*(1')); *m/z* (APCI$^+$) 236 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_7H_{11}{}^{81}BrNO_3$ ([M+H]$^+$) requires 236.9824; found 236.9835; $C_7H_{11}{}^{79}BrNO_3$ ([M+H]$^+$) requires 234.9844; found 234.9843.

Diethyl 2-(5′,5′-dimethyl-oxazolidin-2′-one-3′-yl)-2-oxophosphonoacetate 62



A mixture of **61** (950 mg, 4.01 mmol) and $P(OEt)_3$ (0.77 mL, 4.41 mmol) in PhMe (10 mL) was refluxed for 3 h, then allowed to cool to rt and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent Et_2O) gave **62** as a pale yellow oil (600 mg, 50%); ν_{max} (film) 1698 (C=O, exocyclic), 1770 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 1.33 (6H, t, *J* 7.1, P(OCH$_2$CH_3)$_2$), 1.52 (6H, s, C(5')Me_2), 3.78 (2H, s, C(4')H_2), 3.80 (2H, d, *J* 22.1, C(1)H_2), 4.15-4.23 (4H, m, P(OCH_2CH$_3$)$_2$); δ_C (100 MHz, $CDCl_3$) 16.3 (d, *J* 7.0, P(OCH$_2$*C*H$_3$)$_2$), 27.0 (C(5')Me_2), 34.2 (d, *J* 131.8, *C*(1)), 54.4 (*C*(4')), 62.7 (d, *J* 6.0, P(O*C*H$_2$CH$_3$)$_2$), 78.8 (*C*(5')), 152.6 (*C*(2')), 165.3 (d, *J* 7.0, *C*(2)); *m/z* (APCI$^+$) 316 ([M+Na]$^+$, 7%), 294 (42), 179 (100),116 (51); HRMS (CI$^+$) $C_{11}H_{21}NO_6P$ ([M+H]$^+$) requires 294.1107; found 294.1108.

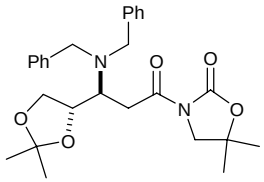
(*S*,*E*)-*N*(3)-[3′-(2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)propenyl]-5,5-dimethyloxazolidin-2-one (*S*,*E*)-63



A solution of (*R*)-isopropylidine glyceraldehyde (0.74 g, 5.69 mmol) in MeCN (10 mL) and $^iPr_2NEt$ (0.49 mL, 2.79 mmol) were added sequentially to a solution of **62** (1.10 g, 3.77 mmol) and anhydrous LiCl (1.08 g, 25.5 mmol) in MeCN (10 mL) at rt. After stirring for 48 h the reaction mixture was diluted with brine, extracted with Et_2O (2 × 20 mL), then dried and concentrated *in vacuo.* Purification *via* flash column chromatography (eluent hexane/Et_2O, 2:1) gave (*S*,*E*)-**63** as a white solid (725 mg, 72%, >98% de); $C_{13}H_{19}NO_5$ requires C, 57.8; H, 7.3; N 5.1; found C, 57.8; H, 7.1; N, 5.2%; mp 73-75 °C (pentane/Et_2O); $[\alpha]_D^{25}$ +21.7 (*c* 1.0 in $CHCl_3$); ν_{max} (KBr) 1642 (C=C), 1684 (C=O, exocyclic), 1773 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 1.42 (3H, s, C(2″)Me_A), 1.48 (3H, s, C(2″)Me_B), 1.51 (3H, s, C(5)Me_A), 1.52 (3H, s, C(5)Me_B), 3.70-3.74 (1H, m, C(5″)H_A), 3.80 (1H, app s, C(4)H_A), 3.80 (1H, app s, C(4)H_B), 4.19-4.29 (1H, m, C(5″)H_B), 4.73-4.78 (1H, m, C(4″)*H*), 7.05 (1H, app ddd, *J* 15.4, 6.0, 2.0, C(3')*H*), 7.53 (1H, dt, *J* 15.4,

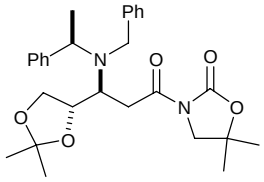
1.6, C(2')*H*); δ_C (50 MHz, $CDCl_3$) 25.7 (C(2″)*Me*$_A$), 26.4 (C(2″)*Me*$_B$), 27.2 (C(5)*Me*$_2$), 54.4 (*C*(4)), 68.7 (*C*(5″)), 75.3 (*C*(4″)), 78.7 (*C*(5)), 110.3 (*C*(2″)), 121.4 (*C*(3')), 146.5 (*C*(2')), 152.5 (*C*(2)), 164.9 (*C*(1')); *m/z* (APCI$^+$) 270 ([M+H]$^+$, 20%), 212 (71); HRMS (CI$^+$) $C_{13}H_{20}NO_5$ ([M+H]$^+$) requires 270.1341; found 270.1337.

(3′*S*,4″*S*)-*N*(3)-[3′-(2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)-3′-(*N*′,*N*′-dibenzylamino)propenyl]-5,5-dimethyloxazolidin-2-one *anti*-64



Following *general procedure 1a*, BuLi (0.58 mL, 1.45 mmol), dibenzylamine (293 mg, 1.49 mmol) in THF (5 mL), and (*S*,*E*)-**17** (200 mg, 0.74 mmol) in THF (5 mL) gave a 72:28 mixture of *anti*-**64**:*syn*-**65**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 2:1) gave *anti*-**64** as a yellow oil (96 mg, 28%, >98% de); $[\alpha]_D^{22}$ +15.4 (*c* 4.8 in $CHCl_3$); ν_{max} (film) 1698 (C=O, exocyclic), 1775 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 1.18 (3H, s, C(2″)*Me*$_A$), 1.25 (3H, s, C(2″)*Me*$_B$), 1.48 (3H, s, C(5)*Me*$_A$), 1.51 (3H, s, C(5)*Me*$_B$), 3.02 (1H, dd, *J* 14.2, *J* 5.1, C(2')*H*$_A$), 3.33-3.38 (1H, m, C(3')*H*), 3.56-3.79 (8H, m, C(4)*H*$_2$, C(2')*H*$_B$, C(5″)*H*$_A$, N′(C*H*$_2$Ph)$_2$), 4.08 (1H, dd, *J* 8.4, 6.6, C(5″)*H*$_B$), 4.30 (1H, dd, *J* 14.4, 6.6, C(4″)*H*), 7.22-7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.6 (C(2″)*Me*$_A$), 26.2 (C(2″)*Me*$_B$), 27.3 (C(5)*Me*$_2$), 31.3 (*C*(2')), 54.7 (N′(*C*H$_2$Ph)$_2$), 54.8 (*C*(4)), 59.4 (*C*(3')), 68.5 (*C*(5″)), 76.3 (*C*(4″)), 78.0 (*C*(5)), 109.1 (*C*(2″)), 127.1 (*p*-*Ph*), 128.3, 129.0 (*o*-*Ph*, *m*-*Ph*), 139.3 (*i*-*Ph*), 152.8 (*C*(2)), 172.8 (*C*(1')); *m/z* (APCI$^+$) 467 ([M+H]$^+$, 100%); HRMS (CI$^+$) $C_{27}H_{35}N_2O_5$ ([M+H]$^+$) requires 467.2546; found 467.2529.

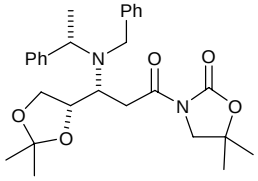
(3′*S*,4″*S*,α*R*)-*N*(3)-[3′-(2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)-3′-(*N*′-benzyl-*N*′-(α-methylbenzyl)amino)propenyl]-5,5-dimethyloxazolidin-2-one *anti*-66



Following *general procedure 1a*, BuLi (2.3 mL, 5.79 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (1.20 g, 5.95 mmol) in THF (15 mL), and (*S*,*E*)-**63** (800 mg, 2.97 mmol) in THF (15 mL) gave *anti*-**66** in >98% de. Purification *via* flash column chromatography (eluent hexane/Et_2O, 2:1) gave *anti*-**66** as a viscous

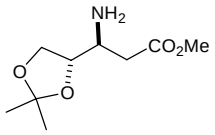
yellow oil (857 mg, 60%, >98% de); $[\alpha]_D^{24}$ +7.3 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1694 (C=O, exocyclic), 1770 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 1.26 (3H, s, C(2″)*Me*$_A$), 1.28 (3H, s, C(2″)*Me*$_B$), 1.43 (3H, d, *J* 6.3, C(α)*Me*), 1.46 (3H, s, C(5)*Me*$_A$), 1.47 (3H, s, C(5)*Me*$_B$), 2.15 (1H, dd, *J* 14.9, *J* 3.1, C(2')*H*$_A$), 3.49 (1H, dd, *J* 14.9, *J* 9.1, C(2')*H*$_B$), 3.56-3.88 (6H, m, C(4)*H*$_2$, C(3')*H*, C(α)*H*, N′C*H*$_2$), 3.94-3.98 (1H, m, C(5″)*H*$_A$), 4.11-4.20 (2H, m, C(4″)*H*, C(5″)*H*$_B$), 7.22-7.39 (10H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 19.4 (C(α)*Me*), 25.5 (C(2″)*Me*$_A$), 26.4 (C(2″)*Me*$_B$), 27.1 (C(5)*Me*$_A$), 27.2 (C(5)*Me*$_B$), 33.1 (*C*(2')), 51.2 (N′*C*H$_2$), 54.5 (*C*(4)), 57.1, (*C*(3')), 57.9 (*C*(α)), 68.7 (*C*(5″)), 77.8 (*C*(5)), 77.9 (*C*(4″)), 109.2 (*C*(2″)), 126.7, 126.9 (*p-Ph*), 127.3, 128.2, 128.5, 128.5 (*o-Ph*, *m-Ph*), 140.7, 141.6 (*i-Ph*), 152.7 (*C*(2)), 172.4 (*C*(1′)); *m/z* (APCI$^+$) 481 ([M+H]$^+$, 9%), 116 (15), 105 (100); HRMS (ESI$^+$) $C_{28}H_{37}N_2O_5$ ([M+H]$^+$) requires 481.2702; found 481.2687.

(3′*R*,4″*S*,α*S*)-*N*(3)-[3′-(2″,2″-dimethyl-1″,3″-dioxolan-4″-yl)-3′-(*N*′-benzyl-*N*′-(α-methylbenzyl)amino)propenyl]-5,5-dimethyloxazolidin-2-one *syn*-68



Following *general procedure 1a*, BuLi (0.29 mL, 0.73 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (100 mg, 0.37 mmol) in THF (5 mL), and (*S*,*E*)-**63** (156 mg, 0.73 mmol) in THF (5 mL) gave a 12:88 mixture of *anti*-**67**:*syn*-**68**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 2:1) gave *syn*-**68** as a yellow oil (121 mg, 68%, >98% de); $[\alpha]_D^{22}$ –27.9 (*c* 0.6 in $CHCl_3$); ν_{max} (film) 1697 (C=O, exocyclic), 1778 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 1.30 (6H, app s, C(2″)*Me*$_2$), 1.39 (3H, d, *J* 10.0, C(α)*Me*), 1.46 (3H, s, C(5)*Me*$_A$), 1.48 (3H, s, C(5)*Me*$_B$), 2.34 (1H, dd, *J* 18.0, 3.3, C(2')*H*$_A$), 3.00 (1H, dd, *J* 18.0, 8.7, C(2')*H*$_B$), 3.62 (1H, d, *J* 10.8, N′C*H*$_A$), 3.64 (1H, d, *J* 10.8, N′C*H*$_B$), 3.69-3.74 (3H, m, C(4)*H*$_2$, C(3')*H*), 3.80-3.85 (1H, m, C(α)*H*), 4.01-4.04 (1H, m, C(5″)*H*$_A$), 4.19-4.22 (1H, m, C(4″)*H*), 4.26-4.31 (1H, m, C(5″)*H*$_B$), 7.20-7.40 (8H, m, *Ph*), 7.53-7.55 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.1 (C(α)*Me*), 25.4 (C(2″)*Me*$_A$), 26.2 (C(2″)*Me*$_B$), 27.2 (C(5)*Me*$_A$), 27.3 (C(5)*Me*$_B$), 33.6 (*C*(2′)), 51.1 (*C*(3′)), 52.7 (N′*C*H$_2$), 54.4 (*C*(4)), 57.1 (*C*(α)), 66.1 (*C*(5″)), 77.2 (*C*(5)), 78.6 (*C*(4″)), 108.6 (*C*(2″)), 126.9, 127.1 (*p-Ph*), 127.8, 128.0, 128.2, 128.5, 128.8 (*o-Ph*, *m-Ph*), 140.3, 141.6 (*i-Ph*), 152.2 (*C*(2)), 172.1 (C(1')); *m/z* (APCI$^+$) 481 ([M+H]$^+$, 30%), 377 (21), 105 (100); HRMS (CI$^+$) $C_{28}H_{37}N_2O_5$ ([M+H]$^+$) requires 481.2702; found 481.2703.

Methyl (3*S*,4'*S*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-amino-propanoate *anti*-69

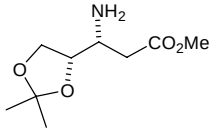


Method A: anti-**64** (94 mg, 0.20 mmol) and Pearlman's catalyst (50 mg) were dissolved in MeOH (5 mL). The resultant solution was degassed, placed under an atmosphere of H_2 (5 atm) and stirred vigorously for 15 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give a mixture of **60** and *anti*-**69** as a colourless oil (47 mg).

Method B: anti-**66** (400 mg, 0.83 mmol) and Pearlman's catalyst (200 mg) were dissolved in MeOH (2 mL). The resultant solution was degassed, placed under an atmosphere of H_2 (5 atm) and stirred vigorously for 15 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give a mixture of **60** and *anti*-**69** as a colourless oil (228 mg).

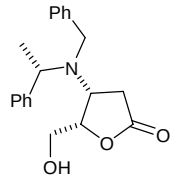
Data for *anti*-**69**: δ_H (400 MHz, $CDCl_3$) 1.35 (3H, s, C(2′)*Me*$_A$), 1.42 (3H, s, C(2′)*Me*$_B$), 2.02 (2H, br s, N*H*$_2$), 2.36 (1H, dd, *J* 16.2, 9.2, C(2)*H*$_A$), 2.70 (1H, dd, *J* 16.2, 3.5, C(2)*H*$_B$), 3.28-3.29 (1H, m, C(3)*H*), 3.71 (3H, s, O*Me*), 3.88 (1H, dd, *J* 8.1, *J* 5.8, C(5′)*H*$_A$), 4.01 (1H, app q, *J* 6.2, C(4′)*H*), 4.09 (1H, dd, *J* 8.1, 6.4, C(5′)*H*$_B$); δ_C (100 MHz, $CDCl_3$) 25.1 (C(2′)*Me*$_A$), 26.7 (C(2′)*Me*$_B$), 38.1 (*C*(2)), 50.7 (*C*(3)), 51.8 (O*Me*), 66.5 (*C*(5′)), 78.4 (*C*(4′)), 81.0 (*C*(2′)), 109.5 (*C*(1)).

Methyl (3*R*,4'*S*)-3-(2′,2′-dimethyl-1′,3′-dioxolan-4′-yl)-3-amino-propenoate *syn*-70



syn-**68** (300 mg, 0.62 mmol) and Pearlman's catalyst (150 mg) were dissolved in MeOH (10 mL). The resultant solution was degassed, placed under an atmosphere of H_2 (5 atm) and stirred vigorously for 15 h. The reaction mixture was then filtered through Celite® (eluent MeOH) and the filtrate was concentrated *in vacuo* to give a mixture of **60** and *syn*-**70** as a colourless oil (137 mg).

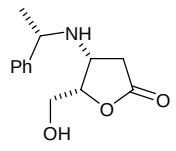
(4*R*,5*S*,α*S*)-4-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-5-(hydroxymethyl)dihydrofuran-2-one 71



Method A: syn-**68** (400 mg, 0.83 mmol) was dissolved in 60% aqueous TFA (4 mL) at rt and the solution allowed to stir for 3 h. The reaction mixture was then diluted with H_2O (4 mL) then extracted with EtOAc (3 × 15 mL). The combined organic extracts were then washed with sat aq Na_2CO_3 (30 mL) and brine (30 mL), then dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent pentane/Et_2O, 1:2) gave **71** as a colourless oil (105 mg, 39%, >98% de); ν_{max} (film) 1776 (C=O), 3401 (O–H); δ_H (400 MHz, $CDCl_3$) 1.45 (3H, d, *J* 6.9, C(α)*Me*), 1.92 (1H, dd, *J* 18.1, 5.8, C(3)H_A), 2.14 (1H, dd, *J* 18.1, 8.6, C(3)H_B), 3.69 (1H, d, *J* 14.7, NCH_A), 3.77 (1H, d, *J* 14.7, NCH_B), 3.90 (1H, q, *J* 6.9, C(α)*H*), 4.03-4.15 (3H, m, C(4)*H*, C(1')H_2), 4.67 (1H, app q, *J* 6.1, C(5)*H*), 7.24-7.41 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.9 (C(α)*Me*), 32.2 (*C*(3)), 52.9 (NCH_2), 55.3 (*C*(4)), 57.1 (*C*(α)), 62.2 (*C*(1')), 83.1 (*C*(5)), 125.6, 127.3, 128.0, 128.1, 128.3, 128.4, 128.7, 129.1, 129.3, 129.4 (*o-Ph*, *m-Ph*, *p-Ph*), 138.4, 140.0 (*i-Ph*), 176.1 (*C*(2)); *m/z* (APCI$^+$) 222 ([M–C_8H_8]$^+$, 40%), 105 (100); HRMS (CI$^+$) $C_{20}H_{24}NO_3$ ([M+H]$^+$) requires 326.1756; found 326.1757.

Method B: syn-**57** (200 mg, 0.456 mmol) was dissolved in TFA (8 mL) and the resultant solution was stirred for 3 h at rt, then diluted with H_2O (5 mL) and stirred for 1 h. The reaction mixture was then partitioned between EtOAc (20 mL) and sat aq Na_2CO_3 (20 mL). The organic layer was dried and concentrated *in vacuo*. Purification of the residue *via* flash column chromatography (eluent pentane/Et_2O, 1:2) gave **71** as a colourless oil (39 mg, 26%, >98% de).

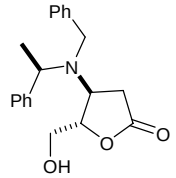
(4*R*,5*S*,α*S*)-4-[*N*-(α-Methylbenzyl)amino]-5-(hydroxymethyl)dihydrofuran-2-one 72



CAN (350 mg, 0.65 mmol) was added to a stirred solution of **71** (94 mg, 0.29 mmol) in MeCN/H_2O (v:v 5:1, 24 mL) at rt. After stirring for 2 h, the reaction mixture was partitioned between sat aq $NaHCO_3$ (50 mL) and Et_2O (50 mL). The organic layer was dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent pentane/Et_2O, 1:1) gave **72** as a colourless oil (21 mg, 29%, >98% de); $[\alpha]_D^{24}$ –67.8

(*c* 0.35 in $CHCl_3$), {lit.[3] $[\alpha]_D^{20}$ −78.6 (*c* 1.85 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.39 (3H, d, *J* 6.5, C(α)*Me*), 2.58 (1H, dd, *J* 17.4, 7.2, C(3)H_A), 2.70 (1H, dd, *J* 17.4, 8.2, C(3)H_B), 3.51 (1H, app q, *J* 7.4, C(4)*H*), 3.80 (1H, q, *J* 6.5, C(α)*H*), 3.93 (1H, dd, *J* 12.6, 3.9, C(1')H_A), 4.00 (1H, dd, *J* 12.6, 3.3, C(1')H_B), 4.36-4.40 (1H, m, C(5)*H*), 7.21-7.40 (5H, m, *Ph*).

(4*S*,5*S*,α*R*)-4-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-5-(hydroxymethyl)dihydrofuran-2-one 73

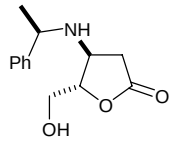


Method A: anti-**66** (1.35 g, 2.81 mmol) was dissolved in 60% aqueous TFA (12 mL) at rt and the solution allowed to stir for 3 h. The reaction mixture was then diluted with H_2O (12 mL) and extracted with EtOAc (3 × 30 mL). The combined organic extracts were then washed sequentially with sat aq Na_2CO_3 (50 mL) and brine (50 mL), dried, and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent pentane/Et_2O, 1:2) gave **73** as a colourless oil (571 mg, 63%, >98% de); $[\alpha]_D^{23}$ +151 (*c* 0.5 in $CHCl_3$); ν_{max} (film) 3434 (O−H), 1778 (C=O); δ_H (500 MHz, $CDCl_3$) 1.49 (3H, d, *J* 6.8, C(α)*Me*), 2.08 (1H, dd, *J* 18.4, 9.1, C(3)H_A), 2.20 (1H, dd, *J* 18.4, 7.3, C(3)H_B), 3.71 (1H, d, *J* 14.7, NCH_A), 3.79 (1H, d, *J* 14.7, NCH_B), 3.84 (1H, dd, *J* 12.7, 3.5, C(1')H_A), 3.87-3.90 (1H, m, C(α)*H*), 4.03 (1H, dd, *J* 12.7, 2.5, C(1')H_B), 4.07-4.10 (1H, m, C(4)*H*), 4.40-4.42 (1H, m, C(5)*H*), 7.29-7.49 (10H, m, *Ph*); δ_C (100 MHz, C_6D_6) 18.9 (C(α)*Me*), 30.6 (*C*(3)), 50.7 (N*C*H_2), 53.7 (*C*(4)), 57.7 (*C*(α)), 62.1 (*C*(1')), 84.4 (*C*(5)), 127.7, 127.9 (*p-Ph*), 128.1, 128.3, 128.4, 128.6, 128.7, 128.9, 129.1 (*o-Ph*, *m-Ph*), 140.4, 141.6 (*i-Ph*), 176.7 (*C*(2)); *m/z* ($APCI^+$) 348 ($[M+Na]^+$, 56%), 326 (69), 222 (100); HRMS (CI^+) $C_{20}H_{24}NO_3$ ($[M+H]^+$) requires 326.1756; found 326.1765.

Method B: anti-**58** (200 mg, 0.456 mmol) was dissolved in TFA (8 mL) and the resultant solution stirred for 3 h at rt, then diluted with H_2O (5 mL) and stirred for 1 h. The reaction mixture was then partitioned between EtOAc (20 mL) and sat aq Na_2CO_3 (20 mL) and the organic layer was dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent pentane:Et_2O, 1:2) gave **73** as a colourless oil (58 mg, 39%, >98% de).

[3] N. Sewald, K. D. Hiller, M. Körner and M. Findeisen, *J. Org. Chem.*, **1998**, *63*, 7263.

(4*S*,5*S*,α*R*)-4-[*N*-(α-Methylbenzyl)amino]-5-(hydroxymethyl)dihydrofuran-2-one 74



CAN (334 mg, 0.61 mmol) was added to a stirred solution of **73** (94 mg, 0.29 mmol) in MeCN/H_2O (v:v 5:1, 18 mL) at rt. After stirring for 2 h, the reaction mixture was partitioned between sat aq $NaHCO_3$ (40 mL) and Et_2O (40 mL), and the organic layer was dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent pentane/Et_2O, 1:3) gave **74** as a colourless oil (61 mg, 89%, >98% de); $[\alpha]_D^{22}$ +47.9 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 3309 (O–H), 1775 (C=O); δ_H (400 MHz, $CDCl_3$) 1.36 (3H, d, *J* 6.4, C(α)*Me*), 2.41 (1H, dd, *J* 17.7, 6.4, C(3)H_A), 2.79 (1H, d, *J* 17.7, 7.8, C(3)H_B), 3.25-3.30 (1H, m, C(4)*H*), 3.55 (1H, dd, *J* 12.3, 4.4, C(1')H_A), 3.74 (1H, dd, *J* 12.3, 3.5, C(1')H_B), 3.80 (1H, q, *J* 6.4, C(α)*H*), 4.18-4.20 (1H, m, C(5)*H*), 7.25-7.36 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 24.8 (C(α)*Me*), 36.6 (*C*(3)), 53.6 (*C*(4)), 56.5 (*C*(α)), 62.6 (*C*(1')), 85.8 (*C*(5)), 126.5, 127.5, 128.6 (*o-Ph*, *m-Ph*, *p-Ph*), 144.0 (*i-Ph*), 178.9 (*C*(2)); *m/z* ($APCI^+$) 236 ($[M+H]^+$, 3%), 132 (69), 105 (100); HRMS (CI^+) $C_{13}H_{18}NO_5$ ($[M+H]^+$) requires 236.1287; found 236.1281.