Supplementary Information

Double diastereoselective conjugate addition of homochiral lithium amides to homochiral α,β-unsaturated esters containing *cis*- and *trans*-dioxolane units

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Experimental

General Experimental

All reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen 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 either on Kieselgel 60 silica on a glass column, or on a Biotage SP4 automated flash column chromatography platform.

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 a Bruker Tensor 27 FT-IR spectrometer as either a thin film on NaCl plates (film) or a KBr disc (KBr), as stated. Selected characteristic peaks are reported in cm^{-1}. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. Spectra were recorded at rt unless otherwise stated. The field was locked by external referencing to the relevant deuteron resonance. Low-resolution mass

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

spectra were recorded on either a VG MassLab 20-250 or a Micromass Platform 1 spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, 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 1: Lithium amide conjugate addition

BuLi was added dropwise to a stirred solution of the requisite amine in the solvent stated (THF or Et_2O), at the temperature stated (−78, −40 or −20 °C), and the resulting solution was stirred for 30 min. A solution of the requisite α,β-unsaturated ester in the solvent stated (THF or Et_2O), at the temperature stated (−78, −40 or −20 °C) was added dropwise *via* cannula. The reaction mixture was stirred for either 2 h (for reactions at −78 °C) or 5 h (for reactions at −40 or −20 °C) before addition of sat aq NH_4Cl. The reaction mixture was warmed to rt and concentrated *in vacuo*. The residue was dissolved in DCM and washed sequentially with 10% aq citric acid, sat aq $NaHCO_3$ and brine, dried, and concentrated *in vacuo*.

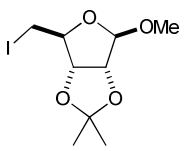
General Procedure 2: Hydrogenolysis with Pearlman's catalyst

$Pd(OH)_2/C$ (20% w/w of substrate) was added to a vigorously stirred, degassed solution of the requisite substrate in either EtOAc or MeOH, and placed under a hydrogen atmosphere (either 1 or 5 atm). Stirring was continued for 15 h at rt, after which time the reaction mixture was filtered through Celite (eluent EtOAc or MeOH) and concentrated *in vacuo*.

General Procedure 3: Tandem hydrogenolysis/reductive amination with Pearlman's catalyst

$Pd(OH)_2/C$ (50% w/w of substrate) was added to a vigorously stirred, degassed solution of the requisite substrate in EtOAc/acetone (v:v 9:1), and placed under a hydrogen atmosphere (1 atm). Stirring was continued for 16 h at rt, after which time the reaction mixture was filtered through Celite (eluent EtOAc) and concentrated *in vacuo*.

(2*R*,3*R*,4*R*,5*S*)-2-Methoxy-3,4-*O*-isopropylidene-5-iodomethyl-tetrahydrofuran 16

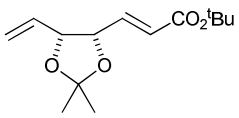


Concentrated HCl (3.50 mL) was added to a suspension of D-ribose (25.0 g, 167 mmol) in acetone/MeOH (v:v 1:1, 280 mL) and the resultant mixture heated at reflux for 1 h. After cooling to rt, the solution was neutralised with pyridine, partitioned between H_2O and Et_2O and the aqueous phase extracted with EtOAc.

The combined organic phases were washed sequentially with sat aq $CuSO_4$ solution, water and brine, dried and concentrated *in vacuo* to give methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside as a yellow oil (27.5 g, 81%);[2,3] $[\alpha]_D^{24}$ −76.6 (*c* 0.9 in $CHCl_3$); {lit.[3] $[\alpha]_D^{23}$ −73.8 (*c* 1.1 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.32 (3H, s, *Me*CMe), 1.49 (3H, s, MeC*Me*), 3.28 (1H, app dd, *J* 10.7, 2.6, C(4)*H*), 3.44 (3H, s, O*Me*), 3.62 (1H, app br td, *J* 10.8, 3.3, C(5)H_A), 3.69 (1H, app br dt, *J* 12.8, 2.8, C(5)H_B), 4.42 (1H, app t, *J* 2.8, O*H*), 4.59 (1H, app d, *J* 5.9, C(3)*H*), 4.84 (1H, app d, *J* 5.9, C(2)*H*), 4.98 (1H, s, C(1)*H*).

Methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (18.8 g, 91.9 mmol), imidazole (9.38 g, 138 mmol) and PPh_3 (28.90 g, 110 mmol) were dissolved in toluene/MeCN (v:v 5:1, 420 mL). I_2 (28.00 g, 110 mmol) was added and the resultant mixture heated to 60 °C for 1 h. After cooling to rt the solution was diluted with Et_2O (500 mL), washed sequentially with 10% $Na_2S_2O_3$ solution (1 L), water (1 L) and brine (1 L), dried and concentrated *in vacuo*. The crude product was filtered through a short plug of silica (eluent pentane/Et_2O, 19:1) to give **16** as a yellow oil (24.9 g, 86%);[2,4] $[\alpha]_D^{24}$ –63.3 (*c* 1.2 in $CHCl_3$); {lit.[4] $[\alpha]_D^{22}$ –67.3 (*c* 1.0 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.33 (3H, s, *Me*CMe), 1.49 (3H, s, MeC*Me*), 3.13-3.18 (1H, m, CH_AH_BI), 3.30 (1H, dd, *J* 10.0, 6.0, CH_AH_BI), 3.38 (3H, s, O*Me*), 4.45 (1H, app dd, *J* 10.0, 6.0, C(5)*H*), 4.63 (1H, app d, *J* 6.0, C(4)*H*), 4.77 (1H, app d, *J* 6.0, C(3)*H*), 5.06 (1H, app s, C(2)*H*).

***tert*-Butyl (2*E*,4*S*,5*R*)-4,5-*O*-isopropylidene-hepta-2,6-dienoate 18**



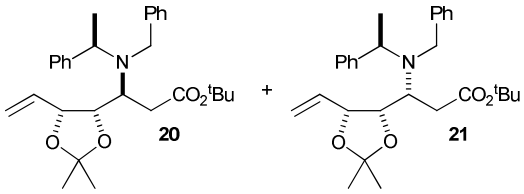
16 (387 mg, 1.23 mmol) and activated Zn dust (806 mg, 12.3 mmol) were heated at reflux in MeOH (5 mL) for 2.5 h, cooled to rt and filtered through a pad of Celite (eluent MeOH). The filtrate was concentrated *in vacuo* at 15 °C. The residue was dissolved in 30-40 °C petrol/EtOAc (v:v 3:1, 10 mL), filtered through a short plug of Florisil (eluent 30-40 °C petrol/EtOAc, 3:1), and concentrated *in vacuo*. The process was repeated to give **17** as a yellow oil (161 mg) that was used immediately without purification; δ_H (200 MHz, $CDCl_3$) 1.46 (3H, s, *Me*CMe), 1.65 (3H, s, MeC*Me*), 4.45 (1H, dd, *J* 7.3, 3.0, C(3)*H*), 4.88 (1H, app t, *J* 7.3, C(2)*H*), 5.35 (1H, dd, *J* 10.3, 1.2, C(5)H_A), 5.49 (1H, app d, *J* 16.9, C(5)H_B), 5.70-5.78 (1H, m, C(4)*H*), 9.58 (1H, d, *J* 3.1, C(1)*H*).

MeMgBr (1.6 M in Et_2O, 0.59 mL, 0.94 mmol) was added dropwise to a stirred solution of *tert*-butyl diethylphosphonoacetate (0.14 mL, 0.94 mmol) in THF (14 mL) at rt and stirred for 15 min. A solution of **17** (161 mg, ~1.03 mmol) in THF (6 mL) was then added *via* cannula and the reaction mixture heated at

[2] L. A. Paquette and S. Bailey, *J. Org. Chem.*, **1995**, *60*, 7849.
[3] A. K. Ghosh and W. Liu, *J. Org. Chem.*, **1996**, *61*, 6175.
[4] M. Ariatti and J. Žemlička, *J. Org. Chem.*, **1981**, *46*, 5204.

reflux for 2.5 h. The reaction was quenched with sat aq NH_4Cl (4 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (20 mL), dried and concentrated *in vacuo* to afford the crude product. Purification *via* flash column chromatography (eluent pentane/Et_2O, 4:1) gave **18** as a colourless oil (200 mg, 64% from **16**, >98% de); R_f 0.08 (pentane/Et_2O, 25:1); $[\alpha]_D^{24}$ −41.3 (*c* 0.5 in $CHCl_3$); ν_{max} (film) 1716 (C=O), 1661, 1650 (C=C); δ_H (400 MHz, $CDCl_3$) 1.40 (3H, s, *Me*CMe), 1.47 (9H, s, C*Me*$_3$), 1.54 (3H, s, MeC*Me*), 4.68 (1H, app t, *J* 7.3, C(5)*H*), 4.72-4.76 (1H, m, C(4)*H*), 5.25-5.28 (1H, m, C(7)H_A), 5.33-5.38 (1H, m, C(7)H_B), 5.70 (1H, ddd, *J* 17.1, 10.2, 7.3, C(6)*H*), 5.97 (1H, dd, *J* 15.6, 1.5, C(2)*H*), 6.67 (1H, dd, *J* 15.6, 5.7, C(3)*H*); δ_C (50 MHz, $CDCl_3$) 25.4, 27.8 (C*Me*$_2$), 28.1 (C*Me*$_3$), 77.5 (*C*(5)), 79.8 (*C*(4)), 80.6 (*C*Me$_3$), 109.5 (*C*Me$_2$), 119.2 (*C*(7)), 124.7 (*C*(3)), 133.5 (*C*(6)), 142.1 (*C*(2)), 165.2 (*C*(1)); *m/z* (CI^+) 272 ($[M+NH_4]^+$, 100%), 255 (17), 214 (48), 199 (31); HRMS (CI^+) $C_{14}H_{26}NO_4$ ($[M+NH_4]^+$) requires 272.1862; found 272.1863.

***tert*-Butyl (3*S*,4*S*,5*R*,α*R*)- and (3*R*,4*S*,5*R*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-hepta-6-enoate (3*S*,4*S*,5*R*,α*R*)-20 and (3*R*,4*S*,5*R*,α*R*)-21**



Method A: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.61 mL, 1.53 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (332 mg, 1.57 mmol) in THF (4 mL) at −78 °C, and **18** (200 mg, 0.79 mmol) in THF (4 mL) at −78 °C gave a 18:82 mixture of **19**:**20**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 25:1) gave **19** as a colourless oil (22 mg, 11%, >98% de); R_f 0.26 (pentane/Et_2O, 20:1); $[\alpha]_D^{24}$ −35.8 (*c* 1.15 in $CHCl_3$); ν_{max} (film) 1733 (C=O); δ_H (400 MHz, $CDCl_3$) 1.43 (3H, s, *Me*CMe), 1.45 (9H, s, C*Me*$_3$), 1.52 (3H, s, MeC*Me*), 2.98-3.12 (2H, m, C(2)H_2), 4.32 (1H, app td, *J* 7.0, 1.8, C(3)*H*), 4.94-4.97 (1H, m, C(5)*H*), 5.29 (1H, dd, *J* 10.1, 0.4, C(7)H_A), 5.38 (1H, app d, *J* 17.0, C(7)H_B), 5.74-5.83 (1H, m, C(6)*H*); δ_C (100 MHz, $CDCl_3$) 25.2, 26.8 (C*Me*$_2$), 28.1 (C*Me*$_3$), 32.0 (*C*(2)), 78.8 (*C*(5)), 80.3 (*C*Me$_3$), 88.2 (*C*(3)), 111.0 (*C*Me$_2$), 119.3 (*C*(7)), 135.3 (*C*(6)), 152.9 (*C*(4)), 171.7 (*C*(1)); *m/z* (CI^+) 272 ($[M+NH_4]^+$, 13%), 255 (16), 199 (100). Further elution gave **20** as a colourless oil (184 mg, 50%, >98% de); R_f 0.07 (pentane/Et_2O, 25:1); $[\alpha]_D^{22}$ +1.7 (*c* 0.3 in $CHCl_3$); ν_{max} (film) 1729 (C=O); δ_H (400 MHz, $CDCl_3$) 1.28 (3H, s, *Me*CMe), 1.36 (3H, d, *J* 7.0, C(α)*Me*), 1.40 (3H, s, MeC*Me*), 1.44 (9H, s, C*Me*$_3$), 2.12-2.22 (2H, m, C(2)H_2), 3.75 (2H, app d, *J* 4.2, NCH_2), 3.79 (1H, app q, *J* 6.0, C(3)*H*), 3.92 (1H, q, *J* 7.0, C(α)*H*), 4.18 (1H, app t, *J* 6.0, C(4)*H*), 4.59 (1H, app t, *J* 7.6, C(5)*H*), 5.30 (1H, app d, *J* 10.0, C(7)H_A), 5.37 (1H, app d, *J* 17.1, C(7)H_B), 5.95 (1H, ddd, *J* 17.1, 10.0, 7.6, C(6)*H*), 7.22-7.34 (10H, m, *Ph*); δ_C (50 MHz, $CDCl_3$) 15.3

(C(α)*Me*), 25.1, 27.5 (C*Me*$_2$), 28.1 (C*Me*$_3$), 36.0 (*C*(2)), 50.2 (N*C*H$_2$), 54.3 (*C*(3)), 59.1 (*C*(α)), 78.8 (*C*(4)), 79.7 (*C*(5)), 79.8 (*C*Me$_3$), 107.9 (*C*Me$_2$), 119.1 (*C*(7)), 126.6, 127.0 (*p-Ph*), 128.0, 128.1, 128.2 (*o*-, *m-Ph*), 134.7 (*C*(6)), 141.4, 142.8 (*i-Ph*), 171.5 (*C*(1)); *m/z* (APCI$^+$) 466 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{40}NO_4$ ([M+H]$^+$) requires 466.2957; found 466.2951.

Method B: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.31 mL, 0.77 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in THF (2 mL) at −40 °C, and **18** (100 mg, 0.39 mmol) in THF (2 mL) at −40 °C gave an 89:11 mixture of **20**:**21**. Purification *via* flash column chromatography (eluent pentane/Et$_2$O, 25:1) gave **20** as a colourless oil (69 mg, 38%, >98% de). Further elution gave **21** as a colourless oil (5 mg, 3%, >98% de); R_f 0.03 (pentane/Et$_2$O, 25:1); $[\alpha]_D^{26}$ +22.7 (*c* 1.05 in CHCl$_3$); ν_{max} (film) 1731 (C=O), 1602 (C=C); δ_H (400 MHz, CDCl$_3$) 1.29 (3H, d, *J* 7.0, C(α)*Me*), 1.34 (3H, s, *Me*CMe), 1.50 (9H, s, C*Me*$_3$), 1.53 (3H, s, MeC*Me*), 1.95 (1H, dd, *J* 14.9, 2.8, C(2)H_A), 2.23 (1H, dd, *J* 15.0, 10.0, C(2)H_B), 3.49 (1H, app td, *J* 10.0, 2.8, C(3)*H*), 3.84 (1H, d, *J* 15.4, NCH_A), 4.05 (1H, d, *J* 15.4, NCH_B), 4.18 (1H, dd, *J* 10.0, 5.4, C(4)*H*), 4.25 (1H, dd, *J* 8.8, 5.4, C(5)*H*), 4.31 (1H, q, *J* 7.0, C(α)*H*), 5.11-5.19 (2H, m, C(7)H_2), 5.67 (1H, ddd, *J* 17.0, 9.3, 8.8, C(6)*H*), 7.20-7.33 (7H, m, *Ph*), 7.44-7.47 (3H, m, *Ph*); δ_C (100 MHz, CDCl$_3$) 20.4 (C(α)*Me*), 25.5 (*Me*CMe), 28.2 (C*Me*$_3$), 28.3 (MeC*Me*), 37.6 (*C*(2)), 50.1 (N*C*H$_2$), 55.3 (*C*(3)), 61.8 (*C*(α)), 78.8 (*C*(4)), 79.7 (*C*(5)), 80.3 (*C*Me$_3$), 108.4 (*C*Me$_2$), 119.0 (*C*(7)), 126.4, 126.7 (*p-Ph*), 127.8, 127.9, 128.0, 128.5 (*o*-, *m-Ph*), 134.2 (*C*(6)), 142.8, 145.0 (*i-Ph*), 170.7 (*C*(1)); *m/z* (ESI$^+$) 466 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{40}NO_4$ ([M+H]$^+$) requires 466.2957; found 466.2951.

Method C: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.31 mL, 0.77 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in Et$_2$O (2 mL) at −40 °C and **18** (100 mg, 0.39 mmol) in Et$_2$O (2 mL) at −40 °C gave a 4:91:5 mixture of **19**:**20**:**21**. Purification *via* flash column chromatography (eluent pentane/Et$_2$O, 25:1) gave **20** as a colourless oil (105 mg, 57%, >98% de). Further elution gave **21** as a colourless oil (9 mg, 5%, >98% de).

Method D: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.24 mL, 0.61 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (133 mg, 0.63 mmol) in THF (2 mL) at −20 °C and **18** (100 mg, 0.39 mmol) in THF (2 mL) at −20 °C gave an 84:16 mixture of **20**:**21**. Purification *via* flash column chromatography (eluent pentane/Et$_2$O, 25:1) gave **20** as a colourless oil (71 mg, 40%, >98% de). Further elution gave a mixture of **20**:**21** (32 mg, 18%).

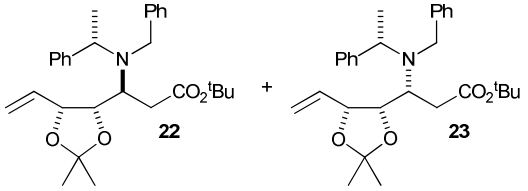
Method E: Following *General Procedure 1*, BuLi (2.2 M in hexanes, 0.35 mL, 0.77 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in Et$_2$O (2 mL) at −20 °C and **18** (100 mg, 0.39 mmol) in Et$_2$O (2 mL) at −20 °C gave a 93:7 mixture of **20**:**21**. Purification *via* flash column chromatography (eluent pentane/Et$_2$O, 25:1) gave **20** as a colourless oil (128 mg, 70%, >98% de).

X-ray crystal structure determination for 21

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.[5]

X-ray crystal structure data for **21** [$C_{29}H_{39}NO_4$]: M = 465.63, orthorhombic, space group $P\ 2_1\ 2_1\ 2_1$, a = 11.5712(2) Å, b = 13.9737(2) Å, c = 17.0380(2) Å, V = 2754.92(7) Å^3, Z = 4, μ = 0.074 mm^{-1}, colourless block, crystal dimensions = 0.2 × 0.2 × 0.2 mm^3. A total of 3491 unique reflections were measured for $5 < \theta < 27$ and 2932 reflections were used in the refinement. The final parameters were wR_2 = 0.040 and R_1 = 0.032 [$I>3\sigma(I)$]. Crystallographic data (excluding structure factors) has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 668996. 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 (3*S*,4*S*,5*R*,α*S*)- and (3*R*,4*S*,5*R*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-hepta-6-enoate (3*S*,4*S*,5*R*,α*S*)-22 and (3*R*,4*S*,5*R*,α*S*)-23**



Method A: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 2.44 mL, 6.11 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (1.33 g, 6.30 mmol) in THF (20 mL) at −78 °C, and **18** (1.00 g, 3.94 mmol) in THF (20 mL) at −78 °C gave a 40:36:24 mixture of **19**:**22**:**23**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 25:1) gave **19** as a colourless oil (351 mg, 35%, >98% de). Further elution gave **22** as a colourless oil (259 mg, 14%, >98% de); R_f 0.2 (pentane/Et_2O, 20:1); $C_{29}H_{40}NO_4$ requires C, 74.8; H, 8.4; N, 3.0%; found C, 74.65; H, 8.5; N, 3.0%; $[\alpha]_D^{26}$ −49.4 (*c* 1.25 in $CHCl_3$); ν_{max} (film) 1732 (C=O); δ_H (400 MHz, $CDCl_3$) 1.11 (3H, s, *Me*CMe), 1.31 (3H, d, *J* 7.1, C(α)*Me*), 1.36 (3H, s, MeC*Me*), 1.58 (9H, s, C*Me*$_3$), 2.20 (1H, dd, *J* 15.1, 3.5, C(2)H_A), 2.48 (1H, dd, *J* 15.1, 9.2, C(2)H_B), 3.37 (1H, dd, *J* 7.4, 2.3, C(4)*H*), 3.56 (1H, d, *J* 15.2, NCH_A), 3.74-3.77 (2H, m, C(3)*H*, C(α)*H*), 4.02 (1H, d, *J* 15.2, NCH_B), 4.17 (1H, app t, *J* 7.4, C(5)*H*), 5.28-5.38 (2H, m, C(7)H_2), 5.84-5.93 (1H, m, C(6)*H*), 7.23-7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.3 (C(α)*Me*), 24.4, 25.2 (C*Me*$_2$), 28.2 (C*Me*$_3$), 36.6 (*C*(2)), 50.5 (N*C*H$_2$), 53.5 (*C*(3)), 57.7 (*C*(α)),

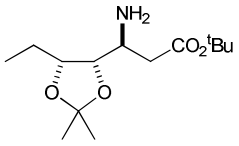
[5] P. W. Betteridge, J. R. Carruthers, R. I. Cooper, C. K. Prout and D. J. Watkin, CRYSTALS, **2001**, Issue 11, Chemical Crystallography Laboratory, University of Oxford, UK.

77.9 (*C*(4)), 79.3 (*C*(5)), 80.1 (*C*Me$_3$), 107.9 (*C*Me$_2$), 118.9 (*C*(7)), 126.6, 127.2 (*p-Ph*), 128.1, 128.6 (*o*-, *m*-*Ph*), 134.3 (*C*(6)), 141.4, 141.6 (*i-Ph*), 172.2 (*C*(1)); *m/z* (APCI$^+$) 466 ([M+H]$^+$, 100%), 410 (12). Further elution gave **23** as a colourless oil (210 mg, 11%, >98% de); R_f 0.07 (pentane/Et$_2$O, 20:1); $[\alpha]_D^{25}$ +10.0 (*c* 1.7 in CHCl$_3$); ν_{max} (film) 1732 (C=O), 1603 (C=C); δ_H (400 MHz, CDCl$_3$) 1.45 (3H, s, *Me*CMe), 1.49 (9H, s, C*Me*$_3$), 1.51 (3H, d, *J* 6.8, C(α)*Me*), 1.59 (3H, s, MeC*Me*), 1.93 (1H, dd, *J* 15.2, 2.7, C(2)H_A), 2.19 (1H, dd, *J* 15.2, 10.0, C(2)H_B), 3.69 (1H, app td, *J* 10.0, 2.7, C(3)*H*), 3.78 (1H, d, *J* 14.5, NCH_A), 3.93 (1H, d, *J* 14.5, NCH_B), 4.20 (1H, q, *J* 6.9, C(α)*H*), 4.33-4.40 (2H, m, C(4)*H*, C(5)*H*), 5.23-5.29 (2H, m, C(7)H_2), 5.88 (1H, ddd, *J* 17.1, 9.5, 8.1, C(6)*H*), 7.15-7.27 (8H, m, *Ph*), 7.43-7.45 (2H, m, *Ph*); δ_C (100 MHz, CDCl$_3$) 19.9 (C(α)*Me*), 25.5 (*Me*CMe), 28.0 (C*Me*$_3$), 28.4 (MeC*Me*), 37.6 (*C*(2)), 51.4 (N*C*H$_2$), 53.7 (*C*(3)), 59.7 (*C*(α)), 79.3, 80.1 (*C*(4), *C*(5)), 80.3 (*C*Me$_3$), 108.5 (*C*Me$_2$), 119.2 (*C*(7)), 126.4 (*p-Ph*), 128.2, 129.0 (*o*-, *m-Ph*), 134.3 (*C*(6)), 141.5, 146.2 (*i-Ph*), 170.6 (*C*(1)); *m/z* (ESI$^+$) 466 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{40}NO_4$ ([M+H]$^+$) requires 466.2957; found 466.2946.

Method B: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.31 mL, 0.77 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in THF (2 mL) at −20 °C, and **18** (100 mg, 0.394 mmol) in THF (2 mL) at −20 °C gave a 62:38 mixture of **22**:**23**. Purification *via* flash column chromatography (eluent pentane/Et$_2$O, 25:1) gave **22** as a colourless oil (45 mg, 24%, >98% de). Further elution gave **23** as a colourless oil (21 mg, 11%, >98% de).

Method C: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 3.07 mL, 7.68 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (1.66 g, 7.87 mmol) in Et$_2$O (20 mL) at −20 °C, and **18** (1.00 g, 3.94 mmol) in Et$_2$O (20 mL) at −20 °C gave a 50:50 mixture of **22**:**23**. Purification *via* flash column chromatography (eluent pentane/Et$_2$O, 25:1) gave **22** as a colourless oil (511 mg, 28%, >98% de). Further elution gave **23** as a colourless oil (540 mg, 29%, >98% de).

tert-Butyl (3*S*,4*S*,5*R*)-3-amino-4,5-*O*-isopropylidene-heptanoate 24



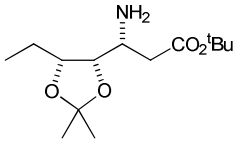
*From **20**:* Following *General Procedure 2*, **20** (200 mg, 0.43 mmol), Pd(OH)$_2$/C (50 mg) and H$_2$ (5 atm) in MeOH (5 mL) gave **24** as a colourless oil (110 mg, 94%, >98% de); $[\alpha]_D^{25}$ +19.4 (*c* 1.2 in CHCl$_3$); ν_{max} (film) 3390, 3322 (N–H), 1726 (C=O); δ_H (400 MHz, CDCl$_3$) 1.01 (3H, t, *J* 7.5, C(7)H_3), 1.31 (3H, s, *Me*CMe), 1.40 (3H, s, MeC*Me*), 1.44 (9H, s, C*Me*$_3$), 1.48-1.65 (2H, m, C(6)H_2), 2.20 (1H, dd, *J* 16.2, 9.0, C(2)H_A), 2.71 (1H, dd, *J* 16.2, 2.7, C(2)H_B), 3.20 (1H, app td, *J* 9.0, 2.7, C(3)*H*), 3.80 (1H, dd, *J* 9.0, 5.6, C(4)*H*), 4.03-4.08 (1H, m, C(5)*H*); δ_C (100 MHz, CDCl$_3$) 10.6 (*C*(7)), 22.7 (*C*(6)), 25.8 (*Me*CMe), 28.1

(C*Me*$_3$, MeC*Me*), 41.6 (*C*(2)), 47.9 (*C*(3)), 79.3 (*C*(5)), 80.6 (*C*(4)), 80.9 (*C*Me$_3$), 107.7 (*C*Me$_2$), 171.9 (*C*(1)); *m/z* (ESI$^+$) 274 ([M+H]$^+$, 100%), 218 (18); HRMS (ESI$^+$) $C_{14}H_{28}NO_4$ ([M+H]$^+$) requires 274.2018; found 274.2013.

*From **22**:* Following *General Procedure 2*, **22** (141 mg, 0.30 mmol), Pd(OH)$_2$/C (70 mg) and H$_2$ (5 atm) in MeOH (7 mL) gave **24** as a colourless oil (63 mg, 76%, >98% de).

*From **28**:* Following *General Procedure 2*, **28** (100 mg, 0.22 mmol), Pd(OH)$_2$/C (50 mg) and H$_2$ (1 atm) in MeOH (5 mL) gave **24** as a colourless oil (58 mg, 96%, >98% de).

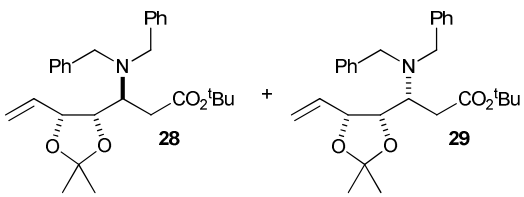
tert-Butyl (3*R*,4*S*,5*R*)-3-amino-4,5-*O*-isopropylidene-heptanoate 25



*From **23**:* Following *General Procedure 2*, **23** (52 mg, 0.11 mmol), Pd(OH)$_2$/C (25 mg) and H$_2$ (5 atm) in MeOH (5 mL) gave **25** as a colourless oil (18 mg, 61%, >98% de); $[\alpha]_D^{26}$ +20.0 (*c* 0.2 in CHCl$_3$); ν_{max} (film) 3392 (N–H), 1728 (C=O); δ_H (400 MHz, CDCl$_3$) 1.01 (3H, t, *J* 7.2, C(7)*H*$_3$), 1.34 (3H, s, *Me*CMe), 1.40-1.46 (1H, m, C(6)*H*$_A$) overlapping 1.44 (9H, s, C*Me*$_3$), 1.45 (3H, s, MeC*Me*), 1.60-1.68 (1H, m, C(6)*H*$_B$), 2.23 (1H, dd, *J* 15.9, 8.8, C(2)*H*$_A$), 2.32 (1H, dd, *J* 15.9, 4.2, C(2)*H*$_B$), 3.26 (1H, ddd, *J* 8.8, 5.8, 4.2, C(3)*H*), 3.86 (1H, app t, *J* 5.8, C(4)*H*), 3.96-4.01 (1H, m, C(5)*H*); δ_C (100 MHz, CDCl$_3$) 10.8 (*C*(7)), 22.8 (*C*(6)), 25.6, 27.8 (C*Me*$_2$), 28.1 (C*Me*$_3$), 40.8 (*C*(2)), 47.7 (*C*(3)), 78.9 (*C*(5)), 80.4 (*C*(4)), 80.8 (*C*Me$_3$), 107.7 (*C*Me$_2$), 171.2 (*C*(1)); *m/z* (ESI$^+$) 274 ([M+H]$^+$, 100%), 218 (15); HRMS (ESI$^+$) $C_{14}H_{28}NO_4$ ([M+H]$^+$) requires 274.2018; found 274.2018.

*From **29**:* Following *General Procedure 2*, **29** (83 mg, 0.18 mmol), Pd(OH)$_2$/C (40 mg) and H$_2$ (1 atm) in MeOH (5 mL) gave **25** as a colourless oil (46 mg, 92%, >98% de).

tert-Butyl (3*S*,4*S*,5*R*)- and (3*R*,4*S*,5*R*)-3-(*N*,*N*-dibenzylamino)-4,5-*O*-isopropylidene-hepta-6-enoate (3*S*,4*S*,5*R*)-28 and (3*R*,4*S*,5*R*)-29



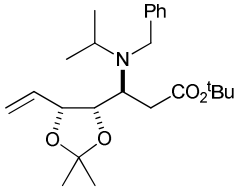
Method A: Following *General Procedure 1*, BuLi (1.6 M in hexanes, 1.91 mL, 3.05 mmol), dibenzylamine (621 mg, 3.15 mmol) in THF (10 mL) at −78 °C, and **18** (500 mg, 1.97 mmol) in THF (10 mL) at −78 °C gave a 2:65:33 mixture of **19**:**28**:**29**. Purification *via* flash column chromatography (eluent pentane/Et$_2$O, 25:1) gave **28** as a colourless oil (488 mg, 54%, >98% de); $[\alpha]_D^{24}$ +13.1 (*c* 0.4 in CHCl$_3$); ν_{max} (film) 1730

(C=O); δ_H (400 MHz, $CDCl_3$) 1.35 (3H, s, *Me*CMe), 1.46 (3H, s, MeC*Me*), 1.50 (9H, s, C*Me*$_3$), 2.33 (1H, dd, *J* 15.1, 5.9, C(2)H_A), 2.65 (1H, dd, *J* 15.1, 6.7 C(2)H_B), 3.55 (1H, dd, *J* 12.2, 6.0, C(3)*H*), 3.65 (4H, ABq, J_{AB} 13.8, N(CH_2Ph)$_2$), 4.34 (1H, app t, *J* 6.0, C(4)*H*), 4.62 (1H, app t, *J* 6.8, C(5)*H*), 5.01-5.04 (1H, m, C(7)H_A), 5.23-5.28 (1H, m, C(7)H_B), 5.61-5.70 (1H, m, C(6)*H*), 7.25-7.34 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.1, 27.3 (C*Me*$_2$), 28.1 (C*Me*$_3$), 34.4 (*C*(2)), 54.6 (N(*C*H$_2$Ph)$_2$), 55.8 (*C*(3)), 77.5 (*C*(5)), 79.2 (*C*(4)), 80.0 (*C*Me$_3$), 108.2 (*C*Me$_2$), 118.0 (*C*(7)), 127.0 (*p-Ph*), 128.1, 129.3 (*o*-, *m-Ph*), 133.9 (*C*(6)), 139.2 (*i-Ph*), 171.7 (*C*(1)); *m/z* (APCI$^+$) 452 ([M+H]$^+$, 100%), 396 (37); HRMS (ESI$^+$) $C_{28}H_{38}NO_4$ ([M+H]$^+$) requires 452.2801; found 452.2812. Further elution gave **29** as a colourless oil (84 mg, 9%, >98% de); $[\alpha]_D^{24}$ +18.3 (*c* 0.5 in $CHCl_3$); ν_{max} (film) 1730 (C=O); δ_H (400 MHz, $CDCl_3$) 1.44 (9H, s, C*Me*$_3$), 1.47 (3H, s, *Me*CMe), 1.62 (3H, s, MeC*Me*), 2.03 (1H, dd, *J* 14.3, 3.4 C(2)H_A), 2.31 (1H, dd, *J* 14.3, 10.1, C(2)H_B), 3.35-3.41 (1H, m, C(3)*H*), 3.84 (4H, app s, N(CH_2Ph)$_2$), 4.35-4.41 (2H, m, C(4)*H*, C(5)*H*), 5.17 (1H, dd, *J* 10.1, 1.4 C(7)H_A), 5.24 (1H, dd, *J* 17.0, 1.4, C(7)H_B), 5.77-5.86 (1H, m, C(6)*H*), 7.21-7.49 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 25.5 (*Me*CMe), 28.1 (C*Me*$_3$), 28.3 (MeC*Me*), 36.6 (*C*(2)), 54.4 (*C*(3)), 54.8 (N(*C*H$_2$Ph)$_2$), 79.3 (*C*(5)), 80.0 (*C*(4)), 80.3 (*C*Me$_3$), 108.7 (*C*Me$_2$), 119.2 (*C*(7)), 126.7 (*p-Ph*), 127.9, 129.5 (*o*-, *m-Ph*), 134.1 (*C*(6)), 140.1 (*i-Ph*), 170.4 (*C*(1)); *m/z* (APCI$^+$) 452 ([M+H]$^+$, 100%), 396 (27); HRMS (ESI$^+$) $C_{28}H_{38}NO_4$ ([M+H]$^+$) requires 452.2801; found 452.2795.

Method B: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.31 mL, 0.78 mmol), dibenzylamine (157 mg, 0.80 mmol) in THF (2 mL) at −20 °C, and **18** (100 mg, 0.39 mmol) in THF (2 mL) at −20 °C gave an 80:20 mixture of **28**:**29**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 25:1) gave **28** as a colourless oil (83 mg, 47%, >98% de) and **29** as a colourless oil (52 mg, 29%, >98% de).

Method C: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.31 mL, 0.78 mmol), dibenzylamine (157 mg, 0.80 mmol) in Et_2O (2 mL) at −20 °C, and **18** (100 mg, 0.39 mmol) in Et_2O (2 mL) at −20 °C gave a 68:32 mixture of **28**:**29**.

tert-Butyl (3*S*,4*S*,5*R*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-hepta-6-enoate 30



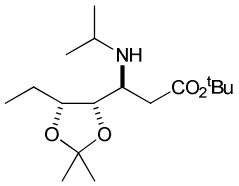
Method A: Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.48 mL, 1.22 mmol), *N*-benzyl-*N*-isopropylamine (188 mg, 1.26 mmol) in THF (5 mL) at −78 °C and **18** (200 mg, 0.79 mmol) in THF (5 mL) at −78 °C gave a 13:87 mixture of **19**:**30**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 35:1) gave a 12:88 mixture of **19**:**30** as a colourless oil (54 mg). Further elution gave **30** as a

colourless oil (174 mg, 55%, >98% de); $[\alpha]_D^{25}$ –20.2 (*c* 2.5 in $CHCl_3$); ν_{max} (film) 1730 (C=O), 1647, 1601 (C=C); δ_H (400 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.5, *Me*CHMe), 1.00 (3H, d, *J* 6.5, MeCH*Me*), 1.32 (3H, s, *Me*CMe), 1.44 (3H, s, MeC*Me*), 1.49 (9H, s, C*Me*$_3$), 2.31 (1H, dd, *J* 15.1, 4.8, C(2)H_A), 2.56 (1H, dd, *J* 15.1, 8.0, C(2)H_B), 2.93 (1H, sept, *J* 6.5, C*H*Me$_2$), 3.57-3.61 (1H, m, C(3)*H*), 3.66 (1H, d, *J* 14.9, NCH_A), 3.89 (1H, d, *J* 14.9, NCH_B), 4.29 (1H, dd, *J* 7.0, 4.3, C(4)*H*), 4.61 (1H, app t, *J* 7.0, C(5)*H*), 5.27-5.30 (1H, m, C(7)H_A), 5.36 (1H, app dt, *J* 16.8, 1.3, C(7)H_B), 5.90-5.99 (1H, m, C(6)*H*), 7.20-7.37 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 19.4, 21.4 (CH*Me*$_2$), 25.0, 27.2 (C*Me*$_2$), 28.2 (C*Me*$_3$), 36.7 (*C*(2)), 49.8 (N*C*H$_2$), 50.2 (*C*HMe$_2$), 54.1 (*C*(3)), 79.4 (*C*(5)), 79.9 (*C*Me$_3$), 108.1 (*C*Me$_2$), 118.7 (*C*(7)), 126.5 (*p*-Ph), 128.0, 128.3 (*o*-, *m-Ph*), 134.3 (*C*(6)), 141.8 (*i-Ph*), 172.1 (*C*(1)); *m/z* (ESI^+) 404 ([M+H^+], 100%); HRMS (ESI^+) $C_{24}H_{38}NO_4$ ([M+H]$^+$) requires 404.2801; found 404.2797.

Method B: Following *General Procedure 1*, BuLi (1.4 M in hexanes, 0.11 mL, 0.16 mmol), *N*-benzyl-*N*-isopropylamine (24 mg, 0.16 mmol) in THF (0.4 mL) at −20 °C, and **18** (18 mg, 0.08 mmol) in THF (0.4 mL) at −20 °C gave **30** in >98% de.

Method C: Following *General Procedure 1*, BuLi (1.4 M in hexanes, 0.16 mL, 0.22 mmol), *N*-benzyl-*N*-isopropylamine (33 mg, 0.22 mmol) in Et_2O (2 mL) at −20 °C, and **18** (25 mg, 0.11 mmol) in Et_2O (2 mL) at −20 °C gave **30** in >98% de.

***tert*-Butyl (3*S*,4*S*,5*R*)-3-(*N*-isopropylamino)-4,5-*O*-isopropylidene-heptanoate 31**



*From **24**:* Acetone (0.02 mL, 0.27 mmol) then $NaBH_3CN$ (46 mg, 0.73 mmol) were added to a solution of **24** (50 mg, 0.18 mmol) in MeOH (2 mL). The resultant solution was stirred at rt for 18 h, concentrated *in vacuo* and the reaction mixture partitioned between DCM (5 mL) and H_2O (5 mL). The organic layer was dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent pentane/Et_2O, 10:1) gave **31** as a colourless oil (35 mg, 60%, >98% de); $[\alpha]_D^{23}$ +20.5 (*c* 0.4 in $CHCl_3$); ν_{max} (film) 3330 (N–H), 1726 (C=O); δ_H (400 MHz, $CDCl_3$) 0.97-1.05 (9H, m, C(7)H_3, CH*Me*$_2$), 1.31 (3H, s, *Me*CMe), 1.41 (3H, s, MeC*Me*), 1.44 (9H, s, C*Me*$_3$), 1.45-1.52 (1H, m, C(6)H_A), 1.65-1.72 (1H, m, C(6)H_B), 2.36 (1H, dd, *J* 15.5, 5.8, C(2)H_A), 2.56 (1H, dd, *J* 15.5, 4.0, C(2)H_B), 2.91 (1H, app sept, *J* 6.2, C*H*Me$_2$), 3.08-3.12 (1H, m, C(3)*H*), 3.98-4.07 (2H, m, C(4)*H*, C(5)*H*); δ_C (100 MHz, $CDCl_3$) 10.7 (*C*(7)), 22.2 (*C*(6)), 22.4, 24.1 (CH*Me*$_2$), 25.6, 27.8 (C*Me*$_2$), 28.1 (C*Me*$_3$), 37.3 (*C*(2)), 44.8 (*C*HMe$_2$), 51.3 (*C*(3)), 79.1, 79.4 (*C*(4), *C*(5)),

80.2 (CMe_3), 107.3 (CMe_2), 171.8 (C(1)); *m/z* (ESI$^+$) 316 ([M+H]$^+$, 100%), 260 (20); HRMS (ESI$^+$) $C_{17}H_{34}NO_4$ ([M+H]$^+$) requires 316.2488; found 316.2491.

*From **30**:* Following *General Procedure 2*, **30** (89 mg, 0.22 mmol), $Pd(OH)_2/C$ (30 mg) and H_2 (1 atm) in MeOH (5 mL) gave, after purification *via* flash column chromatography (eluent pentane/Et_2O, 10:1), **31** as a colourless oil (42 mg, 61%, >98% de).

Competitive addition reactions

***26** vs **27**:* Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.31 mL, 0.77 mmol), *N*,*N*-dibenzylamine (78 mg, 0.39 mmol) and *N*-benzyl-*N*-isopropylamine (59 mg, 0.39 mmol) in THF (2.5 mL) at −78 °C, and **18** (100 mg, 0.39 mmol) in THF (2.5 mL) at −78 °C gave a 4:63:28:5 mixture of **19**:**28**:**29**:**30** (235 mg).

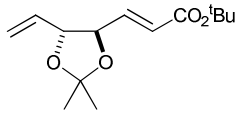
***26** vs (R)-**1**:* Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.61 mL, 1.54 mmol), *N*,*N*-dibenzylamine (155 mg, 0.79 mmol) and (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in THF (5 mL) at −78 °C, and **18** (200 mg, 0.79 mmol) in THF (5 mL) at −78 °C gave a 3:6:62:29 mixture of **19**:**20**:**28**:**29** (373 mg).

***26** vs (S)-**1**:* Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.61 mL, 1.54 mmol), *N*,*N*-dibenzylamine (155 mg, 0.79 mmol) and (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in THF (5 mL) at −78 °C, and **18** (200 mg, 0.79 mmol) in THF (5 mL) at −78 °C gave a 4:65:31 mixture of **19**:**28**:**29** (399 mg).

***27** vs (R)-**1**:* Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.61 mL, 1.54 mmol), *N*-benzyl-*N*-isopropylamine (118 mg, 0.79 mmol) and (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in THF (5 mL) at −78 °C, and **18** (200 mg, 0.79 mmol) in THF (5 mL) at −78 °C gave a 19:39:42 mixture of **19**:**20**:**30** (353 mg).

***27** vs (S)-**1**:* Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.61 mL, 1.54 mmol), *N*-benzyl-*N*-isopropylamine (118 mg, 0.79 mmol) and (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (166 mg, 0.79 mmol) in THF (5 mL) at −78 °C, and **18** (200 mg, 0.79 mmol) in THF (5 mL) at −78 °C gave a 19:6:7:68 mixture of **19**:**22**:**23**:**30** (304 mg).

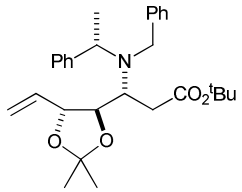
***tert*-Butyl (2*E*,4*R*,5*R*)-4,5-*O*-isopropylidene-hepta-2,6-dienoate 33**



16 (387 mg, 1.23 mmol) and activated Zn dust (806 mg, 12.3 mmol) were heated at reflux in MeOH (5 mL) for 1 h, cooled to rt and filtered through a pad of Celite (eluent MeOH). K_2CO_3 (11.4 g, 82.8 mmol) was added to the filtrate and the resultant suspension was stirred at rt for 2.5 h. AcOH (4.7 mL, 82.8 mmol) was added and the mixture was partitioned between DCM (50 mL) and H_2O (50 mL). The organic layer was dried and concentrated *in vacuo* to furnish a mixture of **32** and the corresponding methyl hemiacetal (in the ratio of ~1:3, respectively) as a colourless oil which was used without purification.

MeMgBr (1.6 M in Et_2O, 0.60 mL, 0.97 mmol) was added dropwise to a stirred solution of *tert*-butyl diethylphosphonoacetate (0.23 mL, 0.97 mmol) in THF (10 mL) at rt and stirred for 15 min. The mixture of **32** and the corresponding methyl hemiacetal was then added dropwise and the reaction mixture heated at reflux for 2 h. The reaction was quenched with sat aq NH_4Cl (2 mL) and extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with brine (10 mL), dried and concentrated *in vacuo* to give **33** in >98% de. The crude product was filtered through a short plug of silica (eluent 30-40 °C petrol/Et_2O, 25:1) to give **33** as a colourless oil (151 mg, 48% from **16**, >98% de); $[\alpha]_D^{27}$ −7.0 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 1717 (C=O), 1662 (C=C); δ_H (400 MHz, $CDCl_3$) 1.45 (3H, s, *Me*CMe), 1.46 (3H, s, MeC*Me*), 1.48 (9H, s, C*Me*$_3$), 4.13 (1H, app t, *J* 7.8, C(5)*H*), 4.20-4.24 (1H, m, C(4)*H*), 5.30 (1H, app d, *J* 10.4, C(7)H_A), 5.40 (1H, dd, *J* 17.1, 0.8, C(7)H_B), 5.78-5.87 (1H, m, C(6)*H*), 6.03 (1H, dd, *J* 15.6, 1.4, C(2)*H*), 6.75 (1H, dd, *J* 15.6, 2.7, C(3)*H*); δ_C (100 MHz, $CDCl_3$) 26.7, 26.9 (C*Me*$_2$), 28.0 (C*Me*$_3$), 79.9 (*C*(4)), 80.8 (*C*Me$_3$), 82.0 (*C*(5)), 109.8 (*C*Me$_2$), 119.6 (*C*(7)), 124.8 (*C*(2)), 133.6 (*C*(6)), 141.4 (*C*(3)), 174.6 (*C*(1)); *m/z* (CI^+) 255 ($[M+H]^+$, 5%), 199 (100); HRMS (CI^+) $C_{14}H_{23}O_4$ ($[M+H]^+$) requires 255.1596; found 255.1604.

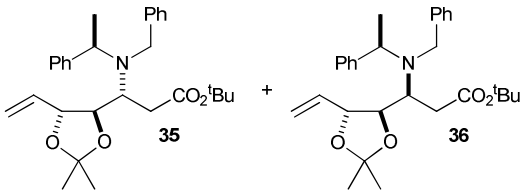
***tert*-Butyl (3*R*,4*R*,5*R*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-hepta-6-enoate 34**



Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.24 mL, 0.60 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (131 mg, 0.62 mmol) in THF (2 mL) at −78 °C, and **33** (99 mg, 0.39 mmol) in THF (2 mL) at −78 °C, gave **34** in >98% de. Purification *via* flash column chromatography (eluent pentane/Et_2O, 25:1) gave **34** as a colourless oil (138 mg, 76%, >98% de); $[\alpha]_D^{20}$ +9.4 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 1728 (C=O), 1602 (C=C); δ_H (500 MHz, $CDCl_3$) 1.39 (3H, s, *Me*CMe), 1.40 (3H, s, MeC*Me*), 1.41 (3H, obsc d, C(α)*Me*), 1.44 (9H, s, C*Me*$_3$), 2.15 (1H, dd, *J* 15.9, 4.7, C(2)H_A), 2.36 (1H, dd, *J* 15.9, 6.9, C(2)H_B), 3.66 (1H, d, *J* 14.5, NCH_A), 3.68-3.72 (1H, m, C(3)*H*), 3.82 (1H, d, *J* 14.5, NCH_B), 3.94 (1H, q, *J* 6.9, C(α)*H*),

3.97 (1H, dd, *J* 8.3, 3.9, C(4)*H*), 4.14 (1H, app t, *J* 6.9, C(5)*H*), 5.29 (1H, app d, *J* 10.3, C(7)H_A), 5.39-5.43 (1H, m, C(7)H_B), 5.88-5.95 (1H, m, C(6)*H*), 7.23-7.39 (10H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 18.8 (C(α)*Me*), 26.8, 26.9 (C*Me*$_2$), 28.0 (C*Me*$_3$), 33.9 (*C*(2)), 51.0 (N*C*H$_2$), 54.0 (*C*(3)), 57.6 (*C*(α)), 79.9 (*C*(5)), 80.8 (*C*(4)), 82.5 (*C*Me$_3$), 108.9 (*C*Me$_2$), 118.4 (*C*(7)), 126.6, 126.8 (*p-Ph*), 127.9, 128.0, 128.4, 128.5 (*o*-, *m-Ph*), 135.9 (*C*(6)), 140.8, 142.8 (*i-Ph*), 171.7 (*C*(1)); *m/z* (ESI$^+$) 466 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{40}NO_4$ ([M+H]$^+$) requires 466.2957; found 466.2953.

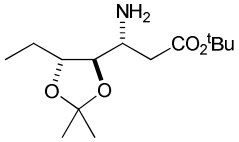
tert-Butyl (3*R*,4*R*,5*R*,α*R*)- and (3*S*,4*R*,5*R*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-hepta-6-enoate (3*R*,4*R*,5*R*,α*R*)-35 and (3*S*,4*R*,5*R*,α*R*)-36



Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.26 mL, 0.61 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (133 mg, 0.63 mmol) in THF (2 mL) at −78 °C, and **33** (100 mg, 0.39 mmol) in THF (2 mL) at −78 °C, gave a 35:65 mixture of **35**:**36**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 25:1) gave **36** as a colourless oil (39 mg, 21%, >98% de); $[\alpha]_D^{21}$ +1.2 (*c* 1.3 in $CHCl_3$); ν_{max} (film) 1726 (C=O), 1602 (C=C); δ_H (400 MHz, $CDCl_3$) 1.31 (3H, s, *Me*CMe), 1.35 (3H, s, MeC*Me*), 1.38 (3H, d, *J* 7.1, C(α)*Me*), 1.42 (9H, s, C*Me*$_3$), 1.68 (1H, dd, *J* 15.9, 2.5, C(2)H_A), 2.41 (1H, dd, *J* 15.9, 10.7, C(2)H_B), 3.53-3.58 (2H, m, C(3)*H*, NCH_A), 3.79-3.84 (2H, m, C(4)*H*, C(α)*H*), 4.35 (1H, d, *J* 14.5, NCH_B), 4.88 (1H, app t, *J* 7.2, C(5)*H*), 5.27-5.31 (1H, m, C(7)H_A), 5.39-5.44 (1H, m, C(7)H_B), 5.81-5.90 (1H, m, C(6)*H*), 7.26-7.40 (8H, m, *Ph*), 7.54 (2H, app d, *J* 7.5, *Ph*); δ_C (100 MHz, $CDCl_3$) 20.1 (C(α)*Me*), 26.3, 27.0 (C*Me*$_2$), 28.1 (C*Me*$_3$), 34.2 (*C*(2)), 49.8 (*C*(3)), 53.0 (N*C*H$_2$), 57.6 (*C*(α)), 78.4 (*C*(5)), 80.3 (*C*Me$_3$), 83.5 (*C*(4)), 108.5 (*C*Me$_2$), 118.5 (*C*(7)), 126.6, 127.2 (*p-Ph*); 128.0, 128.2, 128.3, 128.3 (*o*-, *m-Ph*), 136.2 (*C*(6)), 141.1, 141.3 (*i-Ph*), 171.5 (*C*(1)); *m/z* (ESI$^+$) 466 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{40}NO_4$ ([M+H]$^+$) requires 466.2957; found 466.2951. Further elution gave a 42:58 mixture of **35**:**36** as a colourless oil (34 mg, 19%). Further elution gave **35** as a colourless oil (26 mg, 14%, >98% de); $[\alpha]_D^{21}$ +30.5 (*c* 0.7 in $CHCl_3$); ν_{max} (film) 1727 (C=O), 1646, 1602 (C=C); δ_H (400 MHz, $CDCl_3$) 1.28 (3H, s, *Me*CMe), 1.30 (3H, s, MeC*Me*), 1.33 (3H, d, *J* 7.0, C(α)*Me*), 1.53 (9H, s, C*Me*$_3$), 2.46 (1H, dd, *J* 15.7, 5.1, C(2)H_A), 2.63 (1H, dd, *J* 15.7, 6.6, C(2)H_B), 3.52-3.59 (2H, m, C(3)*H*, C(4)*H*), 3.70-3.75 (2H, m, C(5)*H*, NCH_A), 3.88 (1H, q, *J* 7.0, C(α)*H*), 3.96 (1H, d, *J* 14.8, NCH_B), 5.14-5.17 (1H, m, C(7)H_A), 5.21-5.26 (1H, m, C(7)H_B), 5.49-5.59 (1H, m, C(6)*H*), 7.23-7.36 (8H, m, *Ph*), 7.45 (2H, app d, *J* 7.4, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.7 (C(α)*Me*), 26.9, 27.0 (C*Me*$_2$), 28.1 (C*Me*$_3$), 35.2 (*C*(2)), 51.2 (N*C*H$_2$), 53.3 (*C*(3)), 57.1 (*C*(α)), 80.3, 80.4 (*C*(5), *C*Me$_3$), 82.1

(*C*(4)), 108.9 (*C*Me$_2$), 118.4 (*C*(7)), 126.7, 126.9 (*p-Ph*), 128.0, 128.1, 128.3, 128.7 (*o-*, *m-Ph*), 135.9 (*C*(6)), 141.2, 142.9 (*i-Ph*), 172.4 (*C*(1)); *m/z* (ESI$^+$) 466 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{29}H_{40}NO_4$ ([M+H]$^+$) requires 466.2957; found 466.2952.

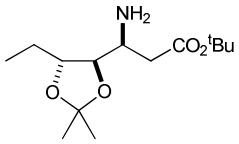
tert-Butyl (3*R*,4*R*,5*R*)-3-amino-4,5-*O*-isopropylidene-heptanoate 37



*From **34**:* Following *General Procedure 2*, **34** (75 mg, 0.16 mmol), Pd(OH)$_2$/C (35 mg) and H$_2$ (5 atm) in MeOH (5 mL) gave **37** as a colourless oil (36 mg, 83%, >98% de); $[\alpha]_D^{23}$ +27.7 (*c* 0.8 in CHCl$_3$); ν_{max} (film) 3389 (N–H), 1727 (C=O); δ_H (400 MHz, CDCl$_3$) 1.01 (3H, t, *J* 7.5, C(7)*H*$_3$), 1.37 (6H, app s, C*Me*$_2$), 1.45 (9H, s, C*Me*$_3$), 1.48-1.61 (1H, m, C(6)*H*$_A$), 1.64-1.73 (1H, m, C(6)*H*$_B$), 2.23 (1H, dd, *J* 15.8, 9.7, C(2)*H*$_A$), 2.55 (1H, app d, *J* 15.8, C(2)*H*$_B$), 3.26 (1H, br s, C(3)*H*), 3.57 (1H, app t, *J* 5.5, C(4)*H*), 3.83 (1H, app td, *J* 7.7, 3.6, C(5)*H*); δ_C (100 MHz, CDCl$_3$) 10.3 (*C*(7)), 27.2 (*C*(6)), 27.3, 27.4 (C*Me*$_2$), 28.1 (C*Me*$_3$), 40.0 (*C*(2)), 50.3 (*C*(3)), 79.7 (*C*(5)), 80.8 (*C*(4)), 83.5 (*C*Me$_3$), 108.3 (*C*Me$_2$), 171.7 (*C*(1)); *m/z* (ESI$^+$) 274 ([M+H]$^+$, 100%), 218 (75); HRMS (ESI$^+$) $C_{14}H_{28}NO_4$ ([M+H]$^+$) requires 274.2018; found 274.2013.

*From **39**:* Following *General Procedure 2*, **39** (56 mg, 0.13 mmol), Pd(OH)$_2$/C (25 mg) and H$_2$ (1 atm) in MeOH (5 mL) gave **37** as a colourless oil (21 mg, 61%, >98% de).

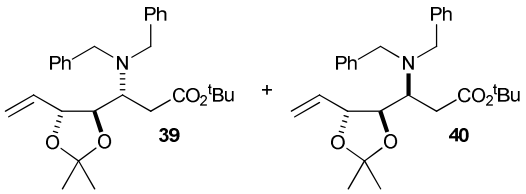
tert-Butyl (3*S*,4*R*,5*R*)-3-amino-4,5-*O*-isopropylidene-heptanoate 38



*From **36**:* Following *General Procedure 2*, **36** (52 mg, 0.11 mmol), Pd(OH)$_2$/C (25 mg) and H$_2$ (5 atm) in MeOH (5 mL) gave, after purification *via* flash column chromatography (eluent pentane/Et$_2$O, 1:2), **38** as a colourless oil (16 mg, 52%, >98% de); $[\alpha]_D^{23}$ +9.4 (*c* 0.5 in CHCl$_3$); ν_{max} (film) 3395 (N–H), 1727 (C=O); δ_H (400 MHz, CDCl$_3$) 1.02 (3H, app t, *J* 7.4, C(7)*H*$_3$), 1.39 (3H, s, *Me*CMe), 1.40 (3H, s, MeC*Me*), 1.46 (9H, s, C*Me*$_3$), 1.53-1.67 (2H, m, C(6)*H*$_2$), 2.34 (1H, dd, *J* 15.8, 9.1, C(2)*H*$_A$), 2.43 (1H, dd, *J* 15.8, 4.4, C(2)*H*$_B$), 3.14-3.18 (1H, m, C(3)*H*), 3.55 (1H, dd, *J* 7.7, 3.8, C(4)*H*), 3.92 (1H, app td, *J* 7.7, 4.2, C(5)*H*); δ_C (100 MHz, CDCl$_3$) 10.2 (*C*(7)), 26.5, 27.1, 27.4 (*C*(6), C*Me*$_2$), 28.1 (C*Me*$_3$), 41.8 (*C*(2)), 49.2 (*C*(3)), 78.8 (*C*(5)), 80.8 (*C*(4)), 83.4 (*C*Me$_3$), 108.4 (*C*Me$_2$), 171.4 (*C*(1)); *m/z* (ESI$^+$) 274 ([M+H]$^+$, 95%), 218 (100); HRMS (ESI$^+$) $C_{14}H_{28}NO_4$ ([M+H]$^+$) requires 274.2018; found 274.2016.

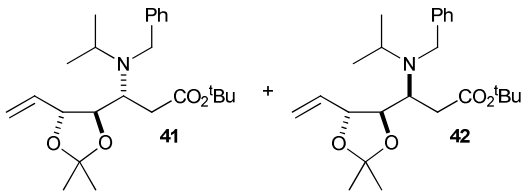
*From **40**:* Following *General Procedure 2*, a 45:55 mixture of **39**:**40** (78 mg, 0.17 mmol), $Pd(OH)_2/C$ (35 mg) and H_2 (1 atm) in MeOH (5 mL) gave a 45:55 mixture of **37**:**38** as a colourless oil (35 mg, 74%).

tert-Butyl (3*R*,4*R*,5*R*)- and (3*S*,4*R*,5*R*)-3-(*N*,*N*-dibenzylamino)-4,5-*O*-isopropylidene-hepta-6-enoate (3*R*,4*R*,5*R*)-39 and (3*S*,4*R*,5*R*)-40



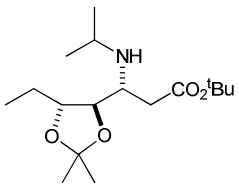
Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.24 mL, 0.61 mmol), *N*,*N*-dibenzylamine (124 mg, 0.63 mmol) in THF (2 mL) at −78 °C, and **33** (100 mg, 0.39 mmol) in THF (2 mL) at −78 °C gave a 65:35 mixture of **39**:**40**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 25:1) gave a 45:55 mixture of **39**:**40** as a colourless oil (78 mg, 44%). Data for **40**: δ_H (500 MHz, $CDCl_3$) 1.36 (3H, s, *Me*CMe), 1.39 (3H, s, MeC*Me*), 1.48 (9H, s, C*Me*$_3$), 2.60 (1H, dd, *J* 14.2, 9.2, C(2)H_A), 2.80 (1H, dd, *J* 14.2, 4.5, C(2)H_B), 3.20 (1H, ddd, *J* 9.2, 4.5, 3.4, C(3)*H*), 3.37 (2H, d, *J* 13.4, N(CH_AH$_B$Ph)$_2$), 3.73 (1H, dd, *J* 8.3, 2.7, C(4)*H*), 4.10 (2H, d, *J* 13.4, N(CH$_A$$H_B$Ph)$_2$), 4.54 (1H, dd, *J* 8.3, 6.9, C(5)*H*), 4.59-4.63 (1H, m, C(7)H_A), 4.88-4.90 (1H, m, C(7)H_B), 5.38-5.45 (1H, m, C(6)*H*), 7.22-7.40 (10H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 26.2, 27.0 (C*Me*$_2$), 28.0 (C*Me*$_3$), 32.6 (*C*(2)), 52.6 (*C*(3)), 55.7 (N(*C*H$_2$Ph)$_2$), 78.3 (*C*(5)), 80.5 (*C*Me$_3$), 83.2 (*C*(4)), 108.6 (*C*Me$_2$), 117.5 (*C*(7)), 126.8 (*p-Ph*), 128.1, 129.3 (*o*-, *m-Ph*), 135.7 (*i-Ph*), 139.8 (*C*(6)), 171.7 (*C*(1)). Further elution gave **39** as a colourless oil (56 mg, 32%, >98% de); R_f 0.21 (pentane/Et_2O, 20:1); $[\alpha]_D^{20}$ +6.5 (*c* 1.6 in $CHCl_3$); ν_{max} (film) 1728 (C=O), 1603 (C=C); δ_H (500 MHz, $CDCl_3$) 1.35 (3H, s, *Me*CMe), 1.42 (3H, s, MeC*Me*), 1.47 (9H, s, C*Me*$_3$), 2.47 (1H, dd, *J* 15.2, 5.7, C(2)H_A), 2.68 (1H, dd, *J* 15.2, 6.8, C(2)H_B), 3.35-3.40 (1H, m, C(3)*H*), 3.63 (4H, app s, N(CH_2Ph)$_2$), 3.95 (1H, app t, *J* 8.2, C(5)*H*), 4.03 (1H, dd, *J* 8.2, 3.3, C(4)*H*), 5.21 (1H, dd, *J* 10.3, 0.5, C(7)H_A), 5.26-5.30 (1H, m, C(7)H_B), 5.79-5.86 (1H, m, C(6)*H*), 7.21-7.34 (10H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 26.8, 27.0 (C*Me*$_2$), 28.0 (C*Me*$_3$), 32.7 (*C*(2)), 54.4 (N(*C*H$_2$Ph)$_2$), 55.5 (*C*(3)), 80.1, 80.4 (*C*(4), *C*(5)), 80.5 (*C*Me$_3$), 109.2 (*C*Me$_2$), 118.2 (*C*(7)), 126.8 (*p-Ph*), 127.9, 129.0 (*o*-, *m-Ph*), 135.5 (*C*(6)), 139.3 (*i-Ph*), 171.9 (*C*(1)); *m/z* (ESI^+) 452 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{28}H_{38}NO_4$ ($[M+H]^+$) requires 452.2801; found 452.2808.

***tert*-Butyl (3*R*,4*R*,5*R*)- and (3*S*,4*R*,5*R*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-hepta-6-enoate (3*R*,4*R*,5*R*)-41 and (3*S*,4*R*,5*R*)-42**



Following *General Procedure 1*, BuLi (2.5 M in hexanes, 0.44 mL, 0.92 mmol), *N*-benzyl-*N*-isopropylamine (141 mg, 0.95 mmol) in THF (5 mL) at −78 °C, and **33** (150 mg, 0.59 mmol) in THF (5 mL) at −78 °C gave a 91:9 mixture of **41**:**42**. Purification *via* flash column chromatography (eluent pentane/Et_2O, 25:1) gave a 94.5:5.5 mixture of **41**:**42** as a colourless oil (171 mg, 72%); ν_{max} (film) 1729 (C=O), 1659, 1603 (C=C); *m/z* (ESI^+) 404 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{24}H_{38}NO_4$ ($[M+H]^+$) requires 404.2801; found 404.2813. Data for **41**: δ_H (400 MHz, $CDCl_3$) 1.02 (6H, app t, *J* 6.5, CH*Me*$_2$), 1.37 (3H, s, *Me*CMe), 1.40 (3H, s, MeC*Me*), 1.50 (9H, s, C*Me*$_3$), 2.42 (1H, dd, *J* 15.4, 5.0, C(2)H_A), 2.61 (1H, dd, *J* 15.4, 7.1, C(2)H_B), 2.95 (1H, app sept, *J* 6.5, C*H*Me$_2$), 3.47-3.51 (1H, m, C(3)*H*), 3.66 (1H, d, *J* 14.6, NCH_A), 3.82 (1H, d, *J* 14.6, NCH_B), 3.94 (1H, dd, *J* 8.4, 3.1, C(4)*H*), 4.03 (1H, app t, *J* 7.5, C(5)*H*), 5.27 (1H, app d, *J* 10.3, C(7)H_A), 5.41 (1H, dd, *J* 17.2, 0.8, C(7)H_B), 5.84-5.92 (1H, m, C(6)*H*), 7.20-7.37 (5H, m, *Ph*); δ_C (125 MHz, $CDCl_3$) 19.8, 20.0 (CH*Me*$_2$), 27.0 (C*Me*$_2$), 28.0 (C*Me*$_3$), 35.2 (*C*(2)), 48.6 (*C*HMe$_2$), 50.0 (N*C*H$_2$), 53.7 (*C*(3)), 80.0 (*C*Me$_3$), 80.9 (*C*(5)), 82.3 (*C*(4)), 109.0 (*C*Me$_2$), 118.3 (*C*(7)), 126.4 (*p-Ph*), 127.8, 128.5 (*o*-, *m-Ph*), 136.0 (*C*(6)), 141.1 (*i-Ph*), 172.2 (*C*(1)).

***tert*-Butyl (3*R*,4*R*,5*R*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-heptanoate 43**

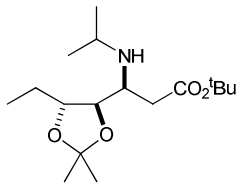


*From **37**:* Acetone (0.02 mL, 0.2 mmol) then $NaBH_3CN$ (33 mg, 0.53 mmol) were added to a solution of **37** (36 mg, 0.13 mmol) in MeOH (2 mL). The resultant solution was stirred at rt for 18 h before being concentrated *in vacuo*. The residue was partitioned between DCM (5 mL) and H_2O (5 mL). The organic layer was dried and concentrated *in vacuo* to give **43** as a colourless oil (16 mg, 38%, >98% de); $[\alpha]_D^{23}$ +12.5 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 1725 (C=O); δ_H (400 MHz, $CDCl_3$) 0.96-1.04 (9H, m, C(7)H_3, CH*Me*$_2$), 1.36 (6H, app s, C*Me*$_2$), 1.44 (9H, s, C*Me*$_3$), 1.52-1.59 (1H, m, C(6)H_A), 1.70-1.76 (1H, m, C(6)H_B), 2.34 (1H, dd, *J* 15.4, 6.2, C(2)H_A), 2.49 (1H, dd, *J* 15.4, 4.9, C(2)H_B), 2.89 (1H, app quint, *J* 6.0, C*H*Me$_2$), 3.05-3.09 (1H, m, C(3)*H*), 3.65-3.72 (2H, m, C(4)*H*, C(5)*H*); δ_C (100 MHz, $CDCl_3$) 10.3 (*C*(7)), 22.9, 23.6 (CH*Me*$_2$), 27.0, 27.1, 27.3 (*C*(6), C*Me*$_2$), 28.0 (C*Me*$_3$), 37.1 (*C*(2)), 45.5 (*C*HMe$_2$), 53.7 (*C*(3)), 80.4, 82.3 (*C*(4), *C*(5),

*C*Me$_3$), 108.2 (*C*Me$_2$), 171.9 (*C*(1)); *m/z* (ESI$^+$) 316 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{34}NO_4$ ([M+H]$^+$) requires 316.2488; found 316.2486.

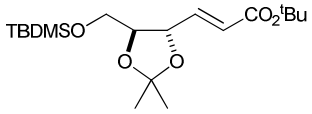
*From **41**:* Following *General Procedure 2*, **41** (85 mg, 0.21 mmol), Pd(OH)$_2$/C (25 mg) and H_2 (1 atm) in MeOH (5 mL) gave **43** as a colourless oil (65 mg, 98%, 89% de).

tert-Butyl (3*S*,4*R*,5*R*)-3-*N*-isopropylamino-4,5-*O*-isopropylidene-heptanoate 44



Following *General Procedure 3*, **36** (27 mg, 0.21 mmol), Pd(OH)$_2$/C (14 mg) and H_2 (1 atm) in MeOH/acetone (9:1, 2 mL) gave **44** as a colourless oil (18 mg, 98%, >98% de); $[\alpha]_D^{23}$ +21.0 (*c* 0.5 in $CHCl_3$); ν_{max} (film) 1728 (C=O); δ_H (400 MHz, $CDCl_3$) 0.98-1.07 (9H, m, C(7)*H*$_3$, CH*Me*$_2$), 1.38 (3H, s, *Me*CMe) 1.40 (3H, s, MeC*Me*), 1.46 (9H, s, C*Me*$_3$), 1.56-1.66 (2H, m, C(6)*H*$_2$), 2.41-2.45 (2H, m, C(2)*H*$_2$), 2.90 (1H, app quint, *J* 6.0, C*H*Me$_2$) 3.10 (1H, dt, *J* 6.4, 2.9, C(3)*H*), 3.70 (1H, dd, *J* 7.8, 2.9, C(4)*H*), 3.99 (1H, dt, *J* 7.8, 4.6, C(5)*H*); δ_C (100 MHz, $CDCl_3$) 10.2 (*C*(7)), 22.5, 23.9 (CH*Me*$_2$), 26.4 (*C*(6)), 27.1, 27.4 (C*Me*$_2$), 28.1 (C*Me*$_3$), 38.7 (*C*(2)), 45.5 (*C*HMe$_2$), 51.8 (*C*(3)), 78.4 (*C*(4)), 80.9 (*C*Me$_3$), 82.7 (*C*(5)), 108.1 (*C*Me$_2$), 171.7 (*C*(1)); *m/z* (ESI$^+$) 316 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{17}H_{34}NO_4$ ([M+H]$^+$) requires 316.2481; found 316.2482.

tert-Butyl (2*E*,4*S*,5*R*)-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hex-2-enoate 46



TsOH (2.5 g) was added to a stirred solution of dimethyl L-tartrate (50 g, 281 mmol) in 2,2-dimethoxypropane (250 mL), and the resultant solution heated at reflux for 16 h. After cooling to rt the reaction mixture was diluted with Et_2O (250 mL), washed with sat aq $NaHCO_3$ (250 mL), dried, and concentrated *in vacuo* to give dimethyl (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate as an orange oil (54 g, 89%) which was used without purification; δ_H (400 MHz, $CDCl_3$), 1.49 (6H, s, C*Me*$_2$), 3.83 (6H, s, O*Me*), 4.81 (2H, s, C*H*).

$NaBH_4$ (30.4 g, 798 mmol) was added portionwise to a stirred solution of dimethyl (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (54 g, 266 mmol) in MeOH (650 mL) at 0 °C, and the resultant solution stirred at rt for 16 h. The reaction mixture was concentrated *in vacuo*, diluted with H_2O (500 mL), extracted with EtOAc (3 × 250 mL) and dried. The aqueous layer was evaporated to dryness and soxhlet extracted

with Et_2O for 8 h. The combined organic extracts were concentrated *in vacuo* to give (4*R*,5*R*)-2,2-dimethyl-4,5-bis(hydroxymethyl)-1,3-dioxolane as a colourless oil (29 g, 67%) which was used without purification; δ_H (400 MHz, $CDCl_3$) 1.44 (6H, s, C*Me*$_2$), 3.67-3.85 (4H, m, C*H*$_2$), 4.00-4.30 (2H, m, C*H*).

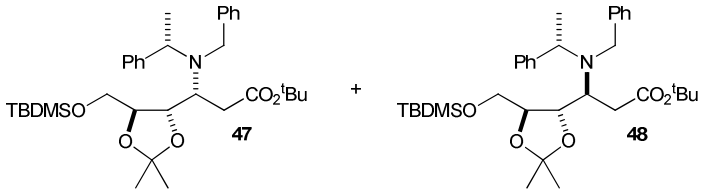
NaH (60% in mineral oil, 1.23 g, 30.8 mmol) was washed with hexane (30 mL), then vigorously stirred in THF (30 mL) at 0 °C. (4*R*,5*R*)-2,2-dimethyl-4,5-bis(hydroxymethyl)-1,3-dioxolane (5.0 g, 30.8 mmol) in THF (20 mL) was added dropwise *via* cannula and the resulting solution stirred at rt for 45 min before addition of TBDMSCl (4.6 g, 30.8 mmol) in a single portion. The resulting solution was stirred at rt for 16 h. The mixture was diluted with Et_2O (50 mL) and washed with 5% aq $NaHCO_3$ (3 × 50 mL). The combined aqueous washings were extracted with Et_2O (3 × 50 mL) and the combined organic extracts were dried and concentrated *in vacuo* to give (4*R*,5*R*)-2,2-dimethyl-4-hydroxymethyl-5-(*tert*-butyldimethylsilyl-oxy)methyl-1,3-dioxolane as an orange oil (8.52 g, quant) which was used without purification; δ_H (400 MHz, $CDCl_3$), 0.09 (6H, s, Si*Me*$_2$), 0.91 (9H, s, SiC*Me*$_3$), 1.41 (3H, s, *Me*CMe), 1.42 (3H, s, MeC*Me*), 3.70-4.10 (6H, m, C*H*$_2$, C*H*).

DMSO (0.31 mL, 4.36 mmol) was added dropwise to a stirred solution of oxalyl chloride (0.19 mL, 2.18 mmol) in DCM (7.5 mL) at −78 °C. After 15 min a solution of (4*R*,5*R*)-2,2-dimethyl-4-hydroxymethyl-5-(*tert*-butyldimethylsilyloxy)methyl-1,3-dioxolane (300 mg, 1.09 mmol) in DCM (1.75 mL) was added dropwise *via* cannula. After a further 15 min a solution of Et_3N (0.92 mL, 6.6 mmol) in DCM (1.75 mL) was added dropwise *via* cannula. The resultant solution was stirred at −78 °C for 20 min and then allowed to warm to rt. After stirring for 30 min at rt the reaction mixture was concentrated *in vacuo* and the residue was triturated with Et_2O (6 × 2.5 mL). The combined organic extracts were washed sequentially with H_2O (3 × 2.5 mL), and brine (3 × 2.5 mL), dried and concentrated *in vacuo* to give **45** as a colourless oil that was used without purification.

MeMgBr (1.7 M in Et_2O, 0.58 mL, 1.00 mmol) was added dropwise to a stirred solution of *tert*-butyl diethylphosphonoacetate (0.24 mL, 1.00 mmol) in THF (13 mL) at rt and stirred for 15 min. A solution of **45** in THF (3 mL) was then added *via* cannula and the reaction mixture heated at reflux for 2.5 h. The reaction was quenched with sat aq NH_4Cl (5 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried and concentrated *in vacuo*. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 10:1) gave **46** as a colourless oil (160 mg, 24% from dimethyl L-tartrate, >98% de); $[\alpha]_D^{24}$ −3.9 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1716 (C=O), 1662 (C=C); δ_H (400 MHz, $CDCl_3$) 0.08 (6H, m, Si*Me*$_2$), 0.90 (9H, s, SiC*Me*$_3$), 1.46 (6H, s, C*Me*$_2$), 1.49 (9H, s, OC*Me*$_3$), 3.74-3.84 (3H, m, C(5)*H*, C(6)*H*$_2$), 4.49 (1H, m, C(4)*H*), 6.04 (1H, d, *J* 15.6, C(2)*H*), 6.82 (1H, dd, *J* 15.6, 5.4, C(3)*H*); δ_C (100 MHz, $CDCl_3$) −5.5, −5.4 (Si*Me*$_2$), 18.3 (Si*C*Me$_3$), 25.8 (SiC*Me*$_3$), 26.8, 26.9 (C*Me*$_2$), 28.0

(OC*Me*$_3$), 62.6 (*C*(6)), 77.7, 80.5 (*C*(4), *C*(5)), 80.7 (O*C*Me$_3$), 109.7 (*C*Me$_2$), 124.0 (*C*(2)), 143.3 (*C*(3)), 165.3 (*C*(1)); *m/z* (CI$^+$) 390 ([M+NH$_4$]$^+$, 40%), 335 (75), 318 (100); HRMS (CI$^+$) $C_{19}H_{40}NO_5Si$ ([M+NH$_4$]$^+$) requires 390.2676; found 390.2666.

tert-Butyl (3*R*,4*S*,5*R*,α*S*)- and (3*S*,4*S*,5*R*,α*S*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hexanoate (3*R*,4*S*,5*R*,α*S*)-47 and (3*S*,4*S*,5*R*,α*S*)-48

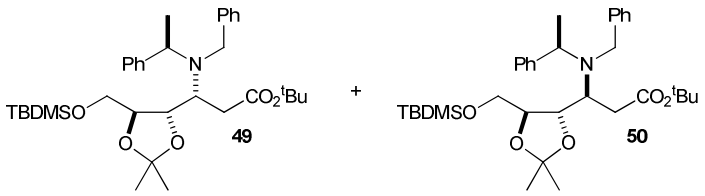


Method A: Following *General Procedure 1*, BuLi (1.6 M in hexanes, 0.56 mL, 0.41 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (89 μL, 0.43 mmol) in THF (10 mL) at −78 °C, and **46** (100 mg, 0.27 mmol) in THF (5 mL) at −78 °C gave **47** in >98% de. Purification *via* flash column chromatography (eluent 30-40°C petrol, increased to 30-40 °C petrol/Et$_2$O, 50:1) gave **47** as a colourless oil that solidified on standing (107 mg, 69%, >98% de); mp 44-45 °C; $[\alpha]_D^{21}$ −1.5 (*c* 1.1 in CHCl$_3$); ν_{max} (film) 1728 (C=O); δ_H (400 MHz, CDCl$_3$), 0.10 (6H, s, Si*Me*$_2$), 0.94 (9H, s, SiC*Me*$_3$), 1.25-1.39 (9H, m, C*Me*$_2$, C(α)*Me*), 1.45 (9H, s, OC*Me*$_3$), 1.70 (1H, dd, *J* 15.2, 2.8, C(2)*H*$_A$), 2.44 (1H, dd, *J* 15.2, 10.6, C(2)*H*$_B$), 3.50-3.58 (2H, m, C(3)*H*, NC*H*$_A$), 3.63 (1H, dd, *J* 10.9, 2.1, C(6)*H*$_A$), 3.81-3.85 (2H, m, C(6)*H*$_B$, C(α)*H*), 4.07 (1H, dd, *J* 7.9, 2.8 C(4)*H*), 4.34 (1H, d, *J* 14.7, NC*H*$_B$), 4.53-4.55 (1H, m, C(5)*H*), 7.22-7.40 (8H, m, *Ph*), 7.51 (2H, d, *J* 7.5, *Ph*); δ_C (100 MHz, CDCl$_3$) −5.5, −5.3 (Si*Me*$_2$), 18.5 (Si*C*Me$_3$), 19.9 (C(α)*Me*), 25.9 (SiC*Me*$_3$), 26.3, 27.1 (C*Me*$_2$), 28.1 (OC*Me*$_3$), 34.2 (*C*(2)), 50.8 (*C*(α)), 53.0 (N*C*H$_2$), 57.6 (*C*(3)), 63.2 (*C*(6)), 77.7, 80.0 (*C*(4), *C*(5)), 80.2 (O*C*Me$_3$), 108.2 (*C*Me$_2$), 126.5, 127.1 (*p-Ph*), 128.0, 128.1, 128.2, 128.2 (*o-*, *m-Ph*), 141.5, 141.3 (*i-Ph*), 171.5 (*C*(1)); *m/z* (ESI$^+$) 584 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{34}H_{54}NO_5Si$ ([M+H]$^+$) requires 584.3771; found 584.3776.

Method B: Following *General Procedure 1*, BuLi (1.6 M in hexanes, 0.52 mL, 0.83 mmol), (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (0.18 mL, 0.86 mmol) in Et$_2$O (5 mL) at −20 °C, and **46** (200 mg, 0.54 mmol) in Et$_2$O (5 mL) at −20 °C gave a 63:37 mixture of **47**:**48**. Purification *via* flash column chromatography (eluent 30-40 °C petrol, increased to 30-40 °C petrol/Et$_2$O, 50:1) gave **47** as a colourless oil (187 mg, 60%, >98% de). Further elution gave **48** as a colourless oil (64 mg, 11%, >98% de); $[\alpha]_D^{22}$ −51.0 (*c* 0.5 in CHCl$_3$); ν_{max} (film) 1730 (C=O); δ_H (400 MHz, CDCl$_3$) 0.08 (3H, s, *Me*SiMe), 0.12 (3H, s, MeSi*Me*), 0.94 (9H, s, SiC*Me*$_3$), 1.24 (3H, s, *Me*CMe), 1.29 (3H, s, MeC*Me*), 1.37 (3H, d, *J* 7.07, C(α)*Me*), 1.51 (9H, s, OC*Me*$_3$), 2.47 (1H, dd, *J* 15.7, 6.1, C(2)*H*$_A$), 2.64 (1H, dd, *J* 15.7, 5.4, C(2)*H*$_B$), 3.11-3.18 (1H, m, C(5)*H*), 3.41-3.57 (3H, m, C(3)*H*, C(6)*H*$_2$), 3.75 (1H, d, *J* 14.2, NC*H*$_A$), 3.88 (1H, d, *J* 14.2, NC*H*$_B$), 3.92-4.00 (2H, m, C(4)*H*,

C(α)*H*), 7.19-7.37 (8H, m, *Ph*), 7.44-7.47 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.2, −5.1 (Si*Me*$_2$), 15.5 (Si*C*Me$_3$), 18.5 (C(α)*Me*), 26.1 (SiC*Me*$_3$), 26.9, 27.1 (C*Me*$_2$), 29.2 (OC*Me*$_3$), 35.5 (*C*(2)), 51.3 (N*C*H$_2$), 54.9 (*C*(3)), 57.3 (*C*(α)), 63.0 (*C*(6)), 77.7 (*C*(4)), 80.2 (*C*(5)), 80.4 (O*C*Me$_3$), 108.5 (*C*Me$_2$), 126.8, 127.0 (*p-Ph*), 128.0, 128.2, 129.0 (*o-*, *m-Ph*), 141.2, 143.7 (*i-Ph*), 172.2 (*C*(1)); *m/z* (ESI$^+$) 548 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{34}H_{54}NO_5Si$ ([M+H]$^+$) requires 584.3771; found 584.3776.

tert-Butyl (3*R*,4*S*,5*R*,α*R*)- and (3*S*,4*S*,5*R*,α*R*)-3-[*N*-benzyl-*N*-(α-methylbenzyl)amino]-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hexanoate (3*R*,4*S*,5*R*,α*R*)-49 and (3*S*,4*S*,5*R*,α*R*)-50

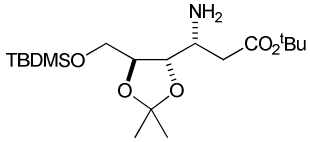


Following *General Procedure 1*, BuLi (1.6 M in hexanes, 0.26 mL, 0.41 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (0.09 mL, 0.43 mmol) in THF (5 mL) at −78 °C, and **46** (100 mg, 0.27 mmol) in THF (5 mL) at −78 °C gave a 30:70 mixture of **49**:**50**. Purification *via* flash column chromatography (eluent 30-40 °C petrol, increased to 30-40 °C petrol/Et_2O, 50:1) gave **49** as a colourless oil (38 mg, 24%, >98% de); $[\alpha]_D^{21}$ +19.5 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 1728 (C=O); δ_H (400 MHz, $CDCl_3$) −0.07 (3H, s, *Me*SiMe), −0.06 (3H, s, MeSi*Me*), 0.82 (9H, s, SiC*Me*$_3$), 1.27 (3H, s, *Me*CMe), 1.34-1.44 (6H, m, C(α)*Me*, MeC*Me*), 1.49 (9H, s, OC*Me*$_3$), 2.05 (1H, dd, *J* 12.0, 1.4, C(6)H_A), 2.74 (1H, dd, *J* 14.5, 3.0, C(2)H_A), 2.85 (1H, dd, *J* 14.5, 10.0, C(2)H_B), 3.15-3.25 (2H, m, C(3)*H*, C(6)H_B), 3.67 (1H, d, *J* 13.4, NCH_A), 3.86-3.96 (3H, m, C(4)*H*, C(5)*H*, C(α)*H*), 4.37 (1H, d, *J* 13.4, NCH_B), 7.15-7.31 (6H, m, *Ph*), 7.38 (2H, t, *J* 7.5 *Ph*), 7.51 (2H, d, *J* 7.5 *Ph*); δ_C (100 MHz, $CDCl_3$) −5.4, −5.2 (Si*Me*$_2$), 18.4 (Si*C*Me$_3$), 25.9, 26.0, 27.3 (C(α)*Me*, C*Me*$_2$), 28.1 (SiC*Me*$_3$), 28.1 (OC*Me*$_3$), 36.5 (*C*(2)), 49.8 (*C*(α)), 52.9 (N*C*H$_2$), 56.1 (*C*(3)), 59.7 (*C*(6)), 77.3, 78.0 (*C*(4), *C*(5)), 80.5 (O*C*Me$_3$), 107.5 (*C*Me$_2$), 126.8, 126.9 (*p-Ph*), 127.9, 128.3, 128.6, 129.1 (*o-*, *m-Ph*), 141.1, 143.3 (*i-Ph*), 171.8 (*C*(1)); *m/z* (ESI$^+$) 584 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{34}H_{54}NO_5Si$ ([M+H]$^+$) requires 584.3771; found 584.3768. Further elution gave **50** as a colourless oil (66 mg, 42%, >98% de); $[\alpha]_D^{21}$ −20.2 (*c* 1.45 in $CHCl_3$); ν_{max} (film) 1728 (C=O); δ_H (400 MHz, C_6D_6) 0.14 (3H, s, *Me*SiMe), 0.15 (3H, s, MeSi*Me*), 1.02 (9H, s, SiC*Me*$_3$), 1.32-1.44 (18H, m, C(α)*Me*, C*Me*$_2$, OC*Me*$_3$), 2.23 (1H, dd, *J* 15.9, 4.3, C(2)H_A), 2.49 (1H, dd, *J* 15.9, 7.3, C(2)H_B), 3.55 (1H, d, *J* 14.7, NCH_A), 3.75-3.77 (1H, m, C(6)H_A), 3.82-3.91 (4H, m, C(3)*H*, C(5)*H*, C(6)H_B, NCH_B), 3.96 (1H, q, *J* 7.0 C(α)*H*), 4.37 (1H, dd, *J* 8.4, 4.6, C(4)*H*), 7.06-7.17 (2H, m, *Ph*), 7.18-7.28 (4H, m, *Ph*), 7.37-7.47 (4H, m, *Ph*); δ_C (100 MHz, C_6D_6) −4.8, −4.7 (Si*Me*$_2$), 18.9 (Si*C*Me$_3$), 20.0 (C(α)*Me*), 26.5 (SiC*Me*$_3$), 27.5, 27.7 (C*Me*$_2$), 28.4 (OC*Me*$_3$), 34.5 (*C*(2)), 51.9 (N*C*H$_2$), 55.7 (*C*(α)), 58.3 (*C*(3)), 63.5 (*C*(6)), 78.6 (*C*(4)), 79.7 (O*C*Me$_3$), 81.5 (*C*(5)), 109.1 (*C*Me$_2$), 127.3,

127.5 (*p-Ph*), 128.6, 128.8, 128.8, 129.2 (*o*-, *m-Ph*), 141.7, 143.8 (*i-Ph*), 172.1 (*C*(1)); *m/z* (CI^+) 584 ($[M+H]^+$, 100%); HRMS (CI^+) $C_{34}H_{54}NO_5Si$ ($[M+H]^+$) requires 584.3771; found 584.3766.

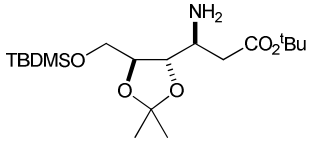
Method B: Following *General Procedure 1*, BuLi (1.6 M in hexanes, 0.52 mL, 0.83 mmol), (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (0.18 mL, 1.86 mmol) in Et_2O (5 mL) at −20 °C, and **46** (200 mg, 0.54 mmol) in Et_2O (5 mL) at −20 °C gave a 15:85 mixture of **49**:**50**. Purification *via* flash column chromatography (eluent 30-40 °C petrol, increased to 30-40 °C petrol/Et_2O, 50:1) gave **49** as a colourless oil (26 mg, 8%, >98% de). Further elution gave **50** as a colourless oil (190 mg, 60%, >98% de).

tert-Butyl (3*R*,4*S*,5*R*)-3-amino-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hexanoate 51



Following *General Procedure 2*, $Pd(OH)_2/C$ (30 mg) and **47** (60 mg, 0.1 mmol) in EtOAc (2 mL) under H_2 (1 atm) gave **51** as a colourless oil (35 mg, 90%, >98% de); $[\alpha]_D^{19}$ + 2.5 (*c* 1.1 in $CHCl_3$); ν_{max} (film) 1732 (C=O); δ_H (400 MHz, $CDCl_3$) 0.08 (6H, s, Si*Me*$_2$), 0.90 (9H, s, SiC*Me*$_3$), 1.38 (3H, s, *Me*CMe), 1.42 (3H, MeC*Me*), 1.46 (9H, s, OC*Me*$_3$), 2.29 (1H, dd, *J* 15.8, 10.0, C(2)H_A), 2.51 (1H, dd, *J* 15.8, 3.7, C(2)H_B), 3.21-3.28 (1H, m, C(3)*H*), 3.66-3.72 (1H, m, C(6)H_A), 3.75-3.84 (2H, m, C(4)*H*, C(6)H_B), 3.98-1.04 (1H, m, C(5)*H*); δ_C (100 MHz, $CDCl_3$) −5.4 (Si*Me*$_2$), 15.3 (Si*C*Me$_3$), 25.9 (SiC*Me*$_3$), 27.2, 27.3 (C*Me*$_2$), 28.1 (OC*Me*$_3$), 41.4 (*C*(2)), 49.8 (*C*(3)), 64.0 (*C*(6)), 78.9 (*C*(5)), 80.7 (O*C*Me$_3$), 82.0 (*C*(4)), 109.0 (*C*Me$_2$), 171.8 (*C*(1)); *m/z* (ESI^+) 390 ($[M+H]^+$, 18%), 334 (100); HRMS (ESI^+) $C_{19}H_{40}NO_5Si$ ($[M+H]^+$) requires 390.2627; found 390.2672.

tert-Butyl (3*S*,4*S*,5*R*)-3-amino-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hexanoate 52

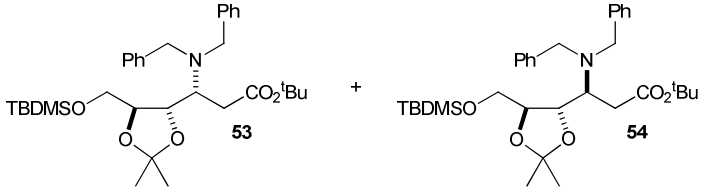


*From **48**:* Following *General Procedure 2*, $Pd(OH)_2/C$ (18 mg) and **48** (35 mg, 0.06 mmol) in EtOAc (1 mL) under H_2 (1 atm) gave **52** as a colourless oil (26 mg, quant, >98% de); $[\alpha]_D^{19}$ −5.3 (*c* 0.9 in $CHCl_3$); ν_{max} (film) 1730 (C=O); δ_H (500 MHz, $CDCl_3$) 0.09 (6H, s, Si*Me*$_2$), 0.90 (9H, s, SiC*Me*$_3$) 1.36 (3H, s, *Me*CMe), 1.39 (3H, s, MeC*Me*), 1.46 (9H, s, OC*Me*$_3$), 2.25 (1H, dd, *J* 16.1, 9.8, C(2)H_A), 2.61 (1H, dd, *J* 16.1, 3.2, C(2)H_B), 3.26-3.32 (1H, m, C(3)*H*), 3.71-3.82 (3H, m, C(4)*H*, C(6)H_2), 3.90-3.94 (1H, m, C(5)*H*); δ_C (125 MHz, $CDCl_3$) −5.5, −5.4 (Si*Me*$_2$), 18.4 (Si*C*Me$_3$), 26.0 (SiC*Me*$_3$), 27.0, 27.2 (C*Me*$_2$), 28.1 (OC*Me*$_3$), 40.1 (*C*(2)), 50.6 (*C*(3)), 64.5 (*C*(6)), 79.6 (*C*(5)), 80.0 (O*C*Me$_3$), 82.0 (*C*(4)), 109.0 (*C*Me$_2$), 172.0 (*C*(1)); *m/z*

(ESI$^+$) 390 ([M+H]$^+$, 55%), 334 (100); HRMS (ESI$^+$) $C_{19}H_{40}NO_5Si$ ([M+H]$^+$) requires 390.2676; found 390.2670.

*From **50**:* Following *General Procedure 2*, $Pd(OH)_2$/C (35 mg) and **50** (66 mg, 0.11 mmol) in EtOAc (2 mL) under H_2 (1 atm) gave **52** as a colourless oil (30 mg, 72%, >98% de).

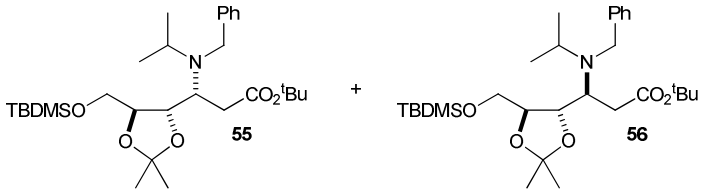
tert-Butyl (3*R*,4*S*,5*R*)- and (3*S*,4*S*,5*R*)-3-(*N*,*N*-dibenzylamino)-4,5-*O*-isopropylidene-6-(_tert_-butyldimethylsilyloxy)hexanoate (3*R*,4*S*,5*R*)-53 and (3*S*,4*S*,5*R*)-54



Following *General Procedure 1*, BuLi (1.6 M in hexanes, 1.3 mL, 2.08 mmol), dibenzylamine (0.41 mL, 2.14 mmol) in THF (10 mL) at −78 °C, and **46** (500 mg, 1.34 mmol) in THF (10 mL) at −78 °C gave a 50:50 mixture of **53**:**54**. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 100:1, increased to 50:1) gave **53** as a colourless oil (322 mg, 50%, >98% de); $[\alpha]_D^{20}$ +4.8 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1725 (C=O); δ_H (400 MHz, $CDCl_3$) −0.05 (6H, s, Si*Me*$_2$), 0.83 (9H, s, SiC*Me*$_3$), 1.32 (3H, s, *Me*CMe), 1.36 (3H, s, MeC*Me*), 1.48 (9H, s, OC*Me*$_3$), 2.61 (1H, dd, *J* 14.3, 8.7 C(2)H_A), 2.73-2.79 (2H, m, C(2)H_B, C(6)H_A), 3.12-3.18 (1H, m, C(3)*H*), 3.38 (2H, d, *J* 3.4, N(CH_AH$_B$Ph)$_2$), 3.47 (1H, dd, *J* 11.8, 2.9, C(6)H_B), 3.99-4.03 (3H, m, C(4)*H*, N(CH$_A$$H_B$Ph)$_2$), 4.23-4.25 (1H, m, C(5)*H*), 7.20-7.24 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$), −5.3, −5.1 (Si*Me*$_2$), 18.5 (Si*C*Me$_3$), 26.1 (SiC*Me*$_3$), 27.1, 27.3 (C*Me*$_2$), 28.2 (OC*Me*$_3$), 32.9 (*C*(2)), 54.6 (N(*C*H$_2$Ph)$_2$), 56.6 (*C*(3)), 62.6 (*C*(6)), 75.6 (*C*(4)), 80.5 (O*C*Me$_3$), 80.6 (*C*(5)), 108.9 (*C*Me$_2$), 126.2, 127.0, 129.2 (*o*-, *m*-, *p*-*Ph*), 140.0 (*i*-*Ph*), 172.2 (*C*(1)); *m/z* (ESI$^+$) 570 ([M+H]$^+$, 100%), 514 (44); HRMS (ESI$^+$) $C_{33}H_{52}NO_5Si$ ([M+H]$^+$) requires 570.3615; found 570.3609.

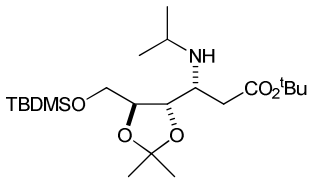
Further elution gave **54** as a colourless oil (256 mg, 40%, >98% de); $C_{33}H_{51}NO_5Si$ requires C, 69.55; H, 9.0; N, 2.5%; found C, 69.6; H, 8.9; N, 2.5%; $[\alpha]_D^{20}$ −23.4 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1729 (C=O); δ_H (400 MHz, $CDCl_3$), 0.13 (3H, s, Si*Me*), 0.14 (3H, s, Si*Me*), 0.99 (9H, s, SiC*Me*$_3$), 1.34 (3H, s, *Me*CMe), 1.43 (3H, s, MeC*Me*), 1.52 (9H, s, OC*Me*$_3$), 2.50 (1H, dd, *J* 15.7, 5.8, C(2)H_A), 2.74 (1H, dd, *J* 15.7, 6.6, C(2)H_B), 3.37-3.39 (1H, m, C(3)*H*), 3.57-3.59 (1H, m, C(5)*H*), 3.51-3.52 (5H, m, C(6)H_A, N(CH_2Ph)$_2$), 3.81-3.84 (1H, m, C(6)H_B), 4.39 (1H, dd, *J* 8.3, 4.0, C(4)*H*), 7.02-7.04 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$), −5.3, −5.1 (Si*Me*$_2$), 18.5 (Si*C*Me$_3$), 26.1 (SiC*Me*$_3$), 27.1, 27.3 (C*Me*$_2$), 28.2 (OC*Me*$_3$), 32.9 (*C*(2)), 54.6 (N(*C*H$_2$Ph)$_2$), 56.6 (*C*(3)), 62.6 (*C*(6)), 75.6 (*C*(4)), 80.2 (O*C*Me$_3$), 80.7 (*C*(5)), 108.9 (*C*Me$_2$), 126.2 (*p*-*Ph*), 127.0, 129.2 (*o*-, *m*-*Ph*), 140.0 (*i*-*Ph*), 172.2 (*C*(1)); *m/z* (ESI$^+$) 570 ([M+H]$^+$, 100%), 514 (62); HRMS (ESI$^+$) $C_{33}H_{52}NO_5Si$ ([M+H]$^+$) requires 570.3615; found 570.3611.

***tert*-Butyl (3*R*,4*S*,5*R*)- and (3*S*,4*S*,5*R*)-3-(*N*-benzyl-*N*-isopropylamino)-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hexanoate (3*R*,4*S*,5*R*)-55 and (3*S*,4*S*,5*R*)-56**



Following *General Procedure 1*, BuLi (1.6 M in hexanes, 1.3 mL, 2.08 mmol), *N*-benzyl-*N*-isopropylamine (3.53 mL, 2.14 mmol) in THF (10 mL) at −78 °C, and **46** (500 mg, 1.34 mmol) in THF (10 mL) at −78 °C gave a 25:75 mixture of **55**:**56**. Purification *via* flash column chromatography (eluent 30-40 °C petrol/Et_2O, 100:1, increased to 50:1) gave **55** as a colourless oil (102 mg, 15%, >98% de); $[\alpha]_D^{18}$ +4.8 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1726 (C=O); δ_H (400 MHz, $CDCl_3$) 0.03 (6H, s, Si*Me*$_2$), 0.88 (9H, s, SiC*Me*$_3$), 1.01 (3H, d, *J* 6.6, *Me*CHMe), 1.08 (3H, d, *J* 6.6, MeCH*Me*), 1.32 (6H, s, C*Me*$_2$), 1.48 (9H, s, OC*Me*$_3$), 2.62-2.74 (2H, m, C(2)*H*$_2$), 3.07-3.18 (1H, m, C*H*Me$_2$), 3.22-3.32 (2H, m, C(3)*H*, C(6)*H*$_A$), 3.65 (1H, d, *J* 13.9, NC*H*$_A$), 3.64 (1H, dd, *J* 11.4, 3.8, C(6)*H*$_B$), 4.01 (1H, dd, *J* 8.1, 3.3, C(4)*H*), 4.09 (1H, d, *J* 13.9, NC*H*$_B$), 4.21-4.29 (1H, m, C(5)*H*), 7.17-7.39 (5H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.5, −5.4 (Si*Me*$_2$), 17.3 (Si*C*Me$_3$), 18.5, 22.5 (CH*Me*$_2$), 26.0 (SiC*Me*$_3$), 26.3, 27.2 (C*Me*$_2$), 28.1 (OC*Me*$_3$), 36.0 (*C*(2)), 49.0 (*C*HMe$_2$), 52.0 (N*C*H$_2$), 52.0 (*C*(3)), 62.5 (*C*(6)), 77.8 (*C*(5)), 79.7 (O*C*Me$_3$), 80.3 (*C*(4)), 107.9 (*C*Me$_2$), 126.5 (*p-Ph*), 128.0, 128.7 (*o*-, *m-Ph*), 141.5 (*i-Ph*), 172.0 (*C*(1)); *m/z* (ESI$^+$) 522 ([M+H]$^+$, 100%), 466 (98); HRMS (ESI$^+$) $C_{33}H_{52}NO_5Si$ ([M+H]$^+$) requires 522.3615; found 522.3609. Further elution gave **56** as a colourless oil (331 mg, 48%, >98% de); $[\alpha]_D^{18}$ −124 (*c* 1.0 in $CHCl_3$); ν_{max} (film) 1728 (C=O); δ_H (400 MHz, $CDCl_3$) 0.10 (6H, s, Si*Me*$_2$), 0.93 (9H, s, SiC*Me*$_3$), 1.02-1.09 (6H, m, CH*Me*$_2$), 1.34 (3H, s, *Me*CMe), 1.37 (3H, s, MeC*Me*), 1.50 (9H, s, OC*Me*$_3$), 2.41 (1H, dd, *J* 15.4, 5.3, C(2)*H*$_A$), 2.63 (1H, dd, *J* 15.4, 7.2, C(2)*H*$_B$), 2.98-2.99 (1H, m, C*H*Me$_2$), 3.46-3.48 (1H, m, C(3)*H*), 3.63-3.71 (2H, m, C(5)*H*, NC*H*$_A$), 3.73-3.86 (3H, m, C(6)*H*$_2$, NC*H*$_B$), 4.22 (1H, dd, *J* 8.1, 4.1, C(4)*H*), 7.19-7.24 (1H, m, *Ph*), 7.29 (2H, t, *J* 7.5 *Ph*), 7.34-7.39 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) −5.3, −5.2 (Si*Me*$_2$), 18.5 (Si*C*Me$_3$), 19.8, 20.2 (CH*Me*$_2$), 26.0 (SiC*Me*$_3$), 27.1, 27.2 (C*Me*$_2$), 28.2 (OC*Me*$_3$), 35.5 (*C*(2)), 48.4 (*C*HMe$_2$), 50.1 (N*C*H$_2$), 55.0 (*C*(3)), 63.2 (*C*(6)), 78.1 ((*C*(4)), 80.0 (O*C*Me$_3$), 80.7 (*C*(5)), 108.7 (*C*Me$_2$), 126.6 (*p-Ph*), 128, 128.7 (*o*-, *m-Ph*), 141.2 (*i-Ph*), 172.4 (*C*(1)); *m/z* (ESI$^+$) 522 ([M+H]$^+$, 100%), 466 (92); HRMS (ESI$^+$) $C_{33}H_{52}NO_5Si$ ([M+H]$^+$) requires 522.3615; found 522.3609.

***tert*-Butyl (3*R*,4*S*,5*R*)-3-(*N*-isopropylamino)-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hexanoate 57**



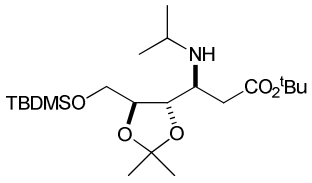
*From **47**:* Following *General Procedure 3*, $Pd(OH)_2$/C (40 mg) and **47** (78 mg, 0.12 mmol) in MeOH/acetone (v:v 9:1, 2 mL) under H_2 (1 atm) gave **57** as a colourless oil (42 mg, 74%, >98% de); $[\alpha]_D^{19}$ −20.5 (*c* 0.9 in $CHCl_3$); ν_{max} (film) 1729 (C=O); δ_H (500 MHz, $CDCl_3$) 0.08 (6H, s, Si*Me*$_2$), 0.91 (9H, s, SiC*Me*$_3$), 1.00 (3H, d, *J* 6.0, *Me*CHMe), 1.05 (3H, d, *J* 6.3, MeCH*Me*), 1.38 (3H, s, *Me*CMe), 1.41 (3H, s, MeC*Me*), 1.46 (9H, s, OC*Me*$_3$), 2.35 (1H, dd, *J* 14.8, 6.6, C(2)H_A), 2.48-2.51 (1H, m, C(2)H_B), 2.87-2.94 (1H, m, C*H*Me$_2$), 3.19-3.22 (1H, m, C(3)*H*), 3.75 (2H, app t, *J* 4.4, C(6)H_2), 3.96 (1H, dd, *J* 7.7, 3.3, C(4)*H*), 4.07-4.10 (1H, m, C(5)*H*); δ_C (125 MHz, $CDCl_3$) −5.4, −5.3 (Si*Me*$_2$), 18.4 (Si*C*Me$_3$), 22.8, 24.0 (CH*Me*$_2$), 26.0 (SiC*Me*$_3$), 27.2 (C*Me*$_2$), 28.1 (OC*Me*$_3$), 38.8 (*C*(2)), 45.6 (*C*HMe$_2$), 52.2 (*C*(3)), 64.1 (*C*(6)), 77.8 (*C*(4)), 80.3 (O*C*Me$_3$), 80.4 (*C*(5)), 108.7 (*C*Me$_2$), 171.1 (*C*(1)); *m/z* (ESI^+) 432 ($[M+H]^+$, 26%), 376 (82), 318 (100); HRMS (ESI^+) $C_{26}H_{45}NO_5Si$ ($[M+H]^+$) requires 432.3145; found 432.3141.

*From **49**:* Following *General Procedure 3*, $Pd(OH)_2$/C (25 mg) and **49** (38 mg, 0.07 mmol) in MeOH/acetone (v:v 9:1, 2 mL) under H_2 (1 atm) gave **57** as a colourless oil (24 mg, 86%, >98% de).

*From **53**:* Following *General Procedure 3*, $Pd(OH)_2$/C (20 mg) and **53** (43 mg, 0.08 mmol) in MeOH/acetone (v:v 9:1, 2 mL) under H_2 (1 atm) gave **57** as a colourless oil (30 mg, 90%, >98% de).

*From **55**:* Following *General Procedure 2*, $Pd(OH)_2$/C (42 mg) and **55** (83 mg, 0.16 mmol) in EtOAc (5 mL) under H_2 (1 atm) gave **57** as a colourless oil (64 mg, 93%, >98% de).

***tert*-Butyl (3*S*,4*S*,5*R*)-3-(*N*-isopropylamino)-4,5-*O*-isopropylidene-6-(*tert*-butyldimethylsilyloxy)hexanoate 58**



*From **48**:* Following *General Procedure 3*, $Pd(OH)_2$/C (40 mg) and **48** (26 mg, 0.12 mmol) in MeOH/acetone (v:v 9:1, 2 mL) under H_2 (1 atm) gave **58** as a colourless oil (15 mg, 79%, >98% de); $[\alpha]_D^{19}$ −3.8 (*c* 3.2 in $CHCl_3$); ν_{max} (film) 1729 (C=O); δ_H (500 MHz, $CDCl_3$) 0.08 (6H, s, Si*Me*$_2$), 0.90 (9H, s, SiC*Me*$_3$), 1.03 (6H, app t, *J* 6.3, CH*Me*$_2$), 1.38 (3H, s, *Me*CMe), 1.39 (3H, s, MeC*Me*), 1.46 (9H, s, OC*Me*$_3$), 2.38 (1H, dd, *J* 15.1, 6.6, C(2)H_A), 2.53 (1H, dd, *J* 15.1, 4.4, C(2)H_B), 2.89-3.98 (1H, m, C*H*Me$_2$), 3.11-3.16

(1H, m, C(3)*H*), 3.76-3.86 (3H, m, C(4)*H*, C(6)H_2), 3.91-3.96 (1H, m, C(5)*H*); δ_C (125 MHz, $CDCl_3$) −5.4, −5.3 (SiMe_2), 18.5 (Si*C*Me_3), 22.9, 23.7 (CHMe_2), 26.0 (SiCMe_3), 27.1, 27.2 (CMe_2), 28.2 (OCMe_3), 36.6 (*C*(2)), 45.6 (*C*HMe_2), 54.3 (*C*(3)), 64.5 (*C*(6)), 79.4 (*C*(4)), 80.1 (*C*(5)), 80.1 (O*C*Me_3), 108.9 (*C*Me_2), 171.9 (*C*(1)); *m/z* (ESI^+) 432 ($[M+H]^+$, 10%), 376 (58), 318 (100); HRMS (ESI^+) $C_{26}H_{45}NO_5Si$ ($[M+H]^+$) requires 432.3145; found 432.3142.

*From **50**:* Following *General Procedure 3*, $Pd(OH)_2$/C (70 mg) and **50** (140 mg, 0.24 mmol) in MeOH/acetone (v:v 9:1, 2 mL) under H_2 (1 atm) gave **58** as a colourless oil (82 mg, 80%, >98% de).

*From **54**:* Following *General Procedure 3*, $Pd(OH)_2$/C (25 mg) and **54** (50 mg, 0.09 mmol) in MeOH/acetone (v:v 9:1, 2 mL) under H_2 (1 atm) gave **58** as a colourless oil (72 mg, 94%, >98% de).

*From **56**:* Following *General Procedure 2*, $Pd(OH)_2$/C (77 mg) and **56** (153 mg, 0.29 mmol) in EtOAc (5 mL) under H_2 (1 atm) gave **58** as a colourless oil (82 mg, 65%, >98% de).