

Remote stereocontrol in reactions between 4- and 5-alkoxyalk-2-enylstannanes and 1-alkoxycarbonylimines and analogues: stereoselective approaches to novel α -amino acids

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Supplementary experimental

General experimental procedures

NMR spectra were obtained using Varian Unity 500, Bruker AC 300, or Varian XL 300 spectrometers. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Low resolution MS were obtained on a Fisons VG Trio 2000 spectrometer, using electron impact (EI) and chemical ionisation (CI) modes. Fast atom bombardment (FAB) and high resolution mass measurements were acquired on a Kratos Concept spectrometer. IR spectra were measured on an ATI Mattson Genesis Series FTIR spectrometer as evaporated thin films on sodium chloride plates. Optical rotations were measured at 589 nm at ambient temperature using an Optical Activity AA-100 polarimeter.

All non-aqueous reactions were performed in oven (140 °C) or flame-dried glassware under an inert atmosphere of dry nitrogen or argon. Solvents were dried immediately prior to use by distillation under an atmosphere of dry nitrogen from sodium benzophenone ketyl (diethyl ether, tetrahydrofuran, hexane), calcium hydride (DCM, dimethyl sulfoxide) or anhydrous potassium hydroxide (triethylamine, diisopropylamine, pyridine). Analytical grade toluene and benzene were dried over sodium wire for 24 hours prior to use. Methanol was dried over magnesium turnings and then distilled. Petrol refers to that fraction of light petroleum ether which boils between 40 and 60 °C and was redistilled prior to use. Butyllithium was supplied as a solution in hexanes and was titrated against anhydrous butanol in tetrahydrofuran using 2,2'-dipyridyl as indicator. Ether refers to diethyl ether whilst brine refers to saturated aqueous sodium chloride. Preparative column chromatography was carried out using Merck silica 9385 (230-400 ASTM mesh) or Merck silica gel 60H (40-63 μ , 230-300 mesh). Analytical high performance liquid chromatography (HPLC) was carried out using a pump controlled Gilson assembly with a Dynamax 60Å silica column with (dimensions of 21.4 x 250 mm) and a guard column, monitoring at 254 nm using a Gilson 115 UV detector.

The imines were prepared following literature procedures;⁷ for the (*S*)-imine (**S**-11, $[\alpha]_D$ -48 (*c* 1.1 in CHCl₃), -24.04 (neat) [lit.⁷ -18.2 (neat)]; for the (*R*)-imine (**R**-10, $[\alpha]_D$ +46.3 (*c* 1.7 in CHCl₃), +25.9 (neat).

General procedure for the reaction of an alkoxyalk-2-enylstannane with an imine

The tin(IV) halide in DCM was cooled to -78 °C and the allylstannane (1.05 molar equivalents based on the amount of Lewis acid) in cooled (-78 °C) DCM was added. After fifteen minutes, the imine (1.05 molar equivalents based on the amount of Lewis acid) in DCM was added dropwise by syringe over five minutes whilst maintaining the reaction at -78 °C. The resulting solution or suspension was stirred at either -78 °C, -50 °C or -45 °C for the appropriate time. Saturated aqueous ammonium chloride was then added and the mixture stirred vigorously whilst being allowed to warm to ambient temperature. Water was added and the mixture extracted DCM. The aqueous phase was basified to pH 10 by the addition of aqueous sodium hydroxide (1 M) and washed with DCM. The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue gave the product.

In some cases, water (0.5 mL) was added to the reaction mixture and, after stirring to ambient temperature, silica was added (*ca.* 5 g). The solvent was then carefully removed under reduced pressure to afford a powder that was applied to a column of silica gel.

General procedure for the deprotection of nitrophenylsulfanyl amines

The nitrophenylsulfanylamine was dissolved in the minimum volume of methanol and saturated methanolic hydrogen chloride (typically 10 mL for 1 mmol of substrate) added. The resulting yellow suspension was stirred at ambient temperature for 2 h before concentration under reduced pressure. The residue was suspended in chloroform and extracted twice with aqueous hydrogen chloride (1 M). The aqueous washings were basified the addition of solid sodium hydrogen carbonate and the mixture extracted into ether. The organic phase was dried (MgSO₄) and concentrated under reduced pressure.

General procedure for the preparation of methyl carbamates

Anhydrous potassium carbonate (2 molar equivalents) and methyl chloroformate (2 molar equivalents) were added to the amine and the suspension stirred at ambient temperature for 16 h. Water was added and, after 10 min, the mixture was extracted with chloroform. The organic layer was dried (MgSO₄), absorbed on to silica and the resulting powder applied to a column of silica gel.

General procedure for the cbz-protection of α -amino esters

Anhydrous potassium carbonate (2 molar equivalents) and benzyl chloroformate (1.3 molar equivalents) were added to the α -amino ester in chloroform (typically 10 mL for a 1 mmol) and the mixture was heated under reflux for 16 h. After cooling to ambient temperature, chloroform was added and the mixture washed with water and brine. The organic extracts were dried (MgSO₄), absorbed on to silica and the resulting powder was applied to a column of silica gel.

General procedure for the ozonolysis of unsaturated α -amido esters followed by reduction using NaBH₄ and lactonisation

The α -amido ester in methanol (typically 20 mL for 1 mmol of substrate) was cooled to -78 °C and ozone bubbled through the solution for 90 min at -78 °C (a permanent blue colour appeared after *ca.* twenty minutes depending on the scale). The mixture was purged with nitrogen, methyl sulfide (3 molar equivalents based on the cbz-derivative) was added as a single portion and the reaction mixture stirred

whilst being allowed to warm to ambient temperature over 1 h. After concentration under reduced pressure, the residue was dissolved in methanol and the solution was cooled to 0 °C.

Sodium borohydride (4 molar equivalents based on the substrate) was added and the reaction mixture stirred at ambient temperature for 30 min. Saturated aqueous ammonium chloride was added and the mixture concentrated under reduced pressure. The residue was suspended in DCM, and the mixture washed with water, aqueous hydrogen chloride (0.1 M) and water and then dried (MgSO₄). Concentration under reduced pressure gave the alcohol.

The alcohol was dissolved in the minimum volume of methanol, hydrochloric acid (37% w/v) was added (typically 5 mL for a 1 mmol reaction) and the reaction mixture stirred at ambient temperature for 16 h. The resulting suspension was poured into water and solid sodium hydrogen carbonate added until neutral. The methanol was removed under reduced pressure and the aqueous residue extracted twice with ethyl acetate. The organic extracts were washed with brine, dried (MgSO₄) and absorbed on to silica. The resulting powder was applied directly to a column of silica gel and elution with hexane/ethyl acetate (4 : 1) afforded the lactones.

Alternatively, the alcohol was dissolved in chloroform (*ca.* 10 mL for a 1 mmol reaction), glacial acetic acid (catalytic) was added and the solution heated under reflux for 16 h. After cooling to ambient temperature, the mixture was washed with a saturated aqueous sodium hydrogen carbonate, dried (MgSO₄) and absorbed on to silica. The ensuing powder was applied to a column of silica gel.

General procedure for the removal of the cbz-group from homoserine lactone derivatives

Ammonium formate (5 molar equivalents based on the lactone) and 10% Pd-C (10% w/w based on the lactone) were added to the cbz-protected lactone in methanol (typically 0.05 molar concentration) and the mixture stirred at ambient temperature for 30 min. The mixture was filtered (Whatman glass microfibre filter paper GF/A) and the solution absorbed on to silica. The resulting powder was applied to a small column of silica gel. Elution with chloroform/methanol/triethylamine (99 : 0.5 : 0.5) gave the amino lactone.

General procedure for the removal of benzyl and benzhydryl groups from α-amino esters

A solution of formic acid (98%) in methanol (10% v/v) was freshly prepared and the protected amino ester was dissolved in this solution typically at ~0.075 molar concentration. 10% Pd-C (15% w/w based on the ester) was added and the reaction mixture stirred at ambient temperature for 16 h. The mixture was filtered (Whatman glass microfibre filter paper GF/A) and the solution concentrated under reduced pressure to give an oil. Any remaining formic acid was removed by adding heptane to the residue and concentrating under a high vacuum (three times).

General procedures for the acylation of α-amino esters:

The α-amino ester was dissolved in DCM (typically 10 mL for a 1 mmol reaction) and triethylamine (3 molar equivalents), acetic anhydride (1.5 molar equivalents) and DMAP (catalytic) were added. The mixture was stirred at ambient temperature for 16 h before water was added to the reaction mixture and the stirring continued for 10 min. DCM was added and the organic extract washed with a saturated aqueous sodium hydrogen carbonate and dried (MgSO₄). This solution was absorbed on to silica and the resulting powder applied to a column of silica gel.

Alternatively, the α-amino ester was dissolved in DCM (typically 10 mL for a 1 mmol reaction) and triethylamine (6 molar equivalents), acetic anhydride (3 molar equivalents) and DMAP (catalytic) were added. This mixture was stirred at ambient temperature for 16 h then worked up as above.

General procedure for the diimide reduction of alkenes

The alkene and toluene 4-sulfonylhydrazine (10 molar equivalents based on the alkene) in DME (typically 15 mL for a 1 mmol reaction) were heated under reflux. Anhydrous sodium acetate (10 molar equivalents based on the alkene) dissolved in the minimum volume of water was added over a period of two hours whilst maintaining the reaction under reflux. The heating was continued for a further 16 h and the reaction was then cooled to ambient temperature and concentrated under reduced pressure. The residue was suspended in ether and the mixture washed with saturated aqueous sodium hydrogen carbonate and water then dried (MgSO₄). The solution was absorbed on to silica and the resulting powder applied to a column of silica gel.

Butyl (2*S*,6*S*,*E*)- and butyl (2*R*,6*S*,*E*)-6-(*tert*-butyldimethylsilyloxy)-2-[(*S*)-(1-phenylethyl)amino]hept-4-enoates **53** and **54**

Following the general procedure, tin(IV) chloride (128 mg, 491 μmol) in DCM (3 mL), the 4-silyloxy-pentenylstannane **52** (253 mg, 514 μmol) in DCM (3 mL) and the imine (**S**)-**11** (120 mg, 514 μmol) in DCM (3 mL) after 12 h at -45 °C and chromatography using petrol/ether/triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **53** and **54** (162 mg, 76%) as a colourless oil. A sample of each isomer as a colourless oil was obtained using preparative scale HPLC (LCDIOL column, UV at 215 nm, eluent heptane/*tert*-butyl dimethyl ether 98 : 2, flow rate 0.5 mL min⁻¹): (2*S*)-epimer **53** (less polar, 66% of the mixture) (Found: M⁺ + H, 434.3088. C₂₅H₄₄NO₃Si requires M, 434.3090; [α]_D -42.2 (*c* 0.8 in CHCl₃); δ_H (250 MHz, CDCl₃) -0.01 and 0.00 (each 3 H, s, SiCH₃), 0.83, [9 H, s, SiC(CH₃)₃], 0.88 (3 H, t, *J* 7.3, CH₃CH₂), 1.11 (3 H, d, *J* 6.2, 7-H₃), 1.28 (3 H, d, *J* 6.4, CHCH₃), 1.31 (2 H, hex, *J* 7.3, CH₃CH₂), 1.56 (2 H, qn, *J* 7.4, CH₂CH₂O), 1.90 (1 H, br s, NH), 2.20-2.28 (2 H, m, 3-H₂), 3.00 (1 H, t, *J* 6.3, 2-H), 3.65 (1 H, q, *J* 6.4, CHCH₃), 3.98-4.11 (2 H, m, CH₂CH₂O), 4.18 (1 H, m, 6-H), 5.32-5.51 (2 H, m, 4-H and 5-H) and 7.18-7.26 (5 H, m, ArH); δ_H (500 MHz, acetone-*d*₆) 5.53 (1 H, dd, *J* 15.4 and 5.1, 5-H), 5.60 (1 H, dt, *J* 15.4 and 6.4, 4-H); δ_C (63 MHz, CDCl₃) -4.88, -4.66, 13.58, 18.19, 19.06, 24.41, 25.01, 25.82, 30.64, 36.38, 56.36, 58.58, 64.36, 68.93, 123.51, 126.83, 126.99, 128.33, 138.15, 144.72 and 175.20; *m/z* (CI) 434 (M⁺ + 1, 100%); (2*R*)-epimer **54** (more polar, 34% of the mixture) (Found: M⁺ + H, 434.3081. C₂₅H₄₄NO₃Si requires M, 434.3090); [α]_D -19.4 (*c* 1.0 in CHCl₃); δ_H (250 MHz, CDCl₃) -0.01 and 0.01 (each 3 H, s, SiCH₃), 0.83, [9 H, s, SiC(CH₃)₃], 0.86 (3 H, t, *J* 7.6, CH₃CH₂), 1.12 (3 H, d, *J* 6.4, 7-H₃), 1.20-1.38 (2 H, m, CH₃CH₂), 1.28 (3 H, d, *J* 6.6, CHCH₃), 1.50 (2 H, qn, *J* 7.3, CH₂CH₂O), 1.76 (1 H, br s, NH), 2.27-2.40 (2 H, m, 3-H₂), 3.29 (1 H, t, *J* 6.3, 2-H), 3.72 (1 H, q, *J* 6.6, CHCH₃), 3.92 (2 H, t, *J* 6.8, CH₂CH₂O), 4.20 (1 H, m, 6-H), 5.42-5.57 (2 H, m, 4-H and 5-H) and 7.16-7.30 (5 H, m, ArH); δ_H (500 MHz, C₆D₆) 5.62 (1 H, dd, *J* 15.6 and 5.7, 5-H), 5.75 (1 H, dt, *J* 15.6 and 6.9, 4-H); δ_C (63 MHz, CDCl₃) -4.80, -4.60, 13.68, 18.04, 19.11, 23.14, 24.54, 25.88, 30.62, 35.73, 56.15, 58.92, 64.41, 68.99, 123.52, 126.99, 127.08, 128.37, 138.30, 145.24 and 174.53; *m/z* (CI) 434 (M⁺ + 1, 100%).

Butyl (2*S*,6*S*,*E*)- and butyl (2*R*,6*S*,*E*)-6-(*tert*-butyldimethylsilyloxy)-2-[(*R*)-(1-phenylethyl)amino]hept-4-enoates **55** and **56**

Following the general procedure, tin(IV) chloride (128 mg, 0.491 mmol) in DCM (3 mL), the 4-silyloxy-pentenylstannane **52** (253 mg, 0.514 mmol) in DCM (3 mL) and imine (**R**)-**11** (120 mg, 0.514 mmol) in DCM (3 mL) after chromatography using petrol/ether/triethylamine (90 : 9.5 : 0.5) the *title compounds* **55** and **56** (198 mg, 93%) as a colourless oil. Samples of each isomer as colourless oils were obtained preparative scale HPLC (LCDIOL column, UV at 215 nm, eluent heptane/*tert*-butyl dimethyl ether 98 : 2, flow rate 1 mL min⁻¹): (2*R*)-epimer **56** (less polar, 27% of the mixture) (Found: M⁺ + H, 434.3092. C₂₅H₄₄NO₃Si requires M, 434.3090; [α]_D +34.4 (c 0.7 in CHCl₃); δ_H (250 MHz, CDCl₃) 0.01 (6 H, s, 2 x SiCH₃), 0.83, [9 H, s, SiC(CH₃)₃], 0.89 (3 H, t, J 7.3, CH₃CH₂), 1.13 (3 H, d, J 6.4, 7-H₃), 1.27-1.40 (2 H, m, CH₃CH₂), 1.28 (3 H, d, J 6.4, CHCH₃), 1.50-1.61 (2 H, m, CH₂CH₂O), 1.70 (1 H, br s, NH), 2.20-2.27 (2 H, m, 3-H₂), 3.01 (1 H, t, J 6.1, 2-H), 3.67 (1 H, q, J 6.4, CHCH₃), 4.02-4.10 (2 H, m, CH₂CH₂O), 4.19 (1 H, m, 6-H), 5.32-5.52 (2 H, m, 4-H and 5-H), and 7.16-7.27 (5 H, m, ArH); δ_H (500 MHz, C₆D₆) 5.56 (1 H, dd, J 15.2 and 5.6, 5-H), 5.64 (1 H, dt, J 15.2 and 7.0, 4-H); δ_C (63 MHz, CDCl₃) -4.78, -4.55, 13.66, 18.30, 19.13, 24.48, 25.29, 25.89, 30.73, 36.53, 56.52, 58.74, 64.33, 68.94, 123.58, 126.89, 126.98, 128.35, 138.15, 145.04 and 175.20; m/z (CI) 434 (M⁺ + 1, 100%) and 120 (70): (2*S*)-epimer **55** (more polar, 73% of the mixture) (Found: M⁺ + H, 434.3090. C₂₅H₄₄NO₃Si requires M, 434.3090; [α]_D +17.69 (c 0.8 in CHCl₃); δ_H (250 MHz, CDCl₃) 0.01 (6 H, s, 2 x SiCH₃), 0.85, [9 H, s, SiC(CH₃)₃], 0.88 (3 H, t, J 7.3, CH₃CH₂), 1.14 (3 H, d, J 6.2, 7-H₃), 1.21-1.36 (2 H, m, CH₃CH₂), 1.29 (3 H, d, J 6.6, CHCH₃), 1.45-1.59 (2 H, m, CH₂CH₂O), 1.80 (1 H, br s, NH), 2.24-2.34 (2 H, m, 3-H₂), 3.29 (1 H, t, J 6.1, 2-H), 3.72 (1 H, q, J 6.6, CHCH₃), 3.93 (2 H, t, J 6.8, CH₂CH₂O), 4.20 (1 H, m, 6-H), 5.40-5.57 (2 H, m, 4-H and 5-H) and 7.16-7.30 (5 H, m, ArH); δ_H (500 MHz, C₆D₆) 5.61 (1 H, dd, J 15.3 and 5.7, 5-H), 5.75 (1 H, dt, J 15.3 and 7.0, 4-H); δ_C (63 MHz, CDCl₃) -4.82, -4.59, 13.67, 18.80, 19.10, 23.12, 24.56, 25.88, 30.62, 35.84, 56.08, 58.93, 64.39, 68.93, 123.52, 126.79, 127.06, 128.36, 138.29, 145.25 and 174.57; m/z (CI) 434 (M⁺ + 1, 40%) and 120 (100).

The (2*S*)-amino-ester **55** (90 mg, 0.208 mmol) in THF (4 mL) was treated with potassium *tert*-butoxide in THF (1 M, 225 μL, 0.225 mmol) and the mixture stirred at -78 °C for ten minutes before adding water (500 μL). The mixture was allowed to warm to ambient temperature and was then diluted with ether (10 mL) and absorbed on to silica. The powder was applied to a column of silica gel and elution with hexane/ether/triethylamine (90 : 9.5 : 0.5) gave the esters **55** and **56** (77 mg, 86%) as a colourless oil, **55** : **56** = 15 : 85 (¹H NMR and HPLC).

Butyl (2*S*,6*S*,*E*)-2-{benzyloxycarbonyl-[(*R*)-(1-phenyl)ethyl]-amino}-6-(*tert*-butyldimethylsilyloxy)hept-4-enoate **57**

The general procedure using the 2-amino-ester **55** (370 mg, 0.853 mmol), anhydrous potassium carbonate (236 mg, 1.71 mmol) and benzyl chloroformate (160 μL, 1.12 mmol) after chromatography using hexane/ether (12 : 1) as eluent gave the *title compound* **57** (385 mg, 79%) as a colourless oil (Found: M⁺ - C₄H₉, 510.2679. C₂₉H₄₀NO₅Si requires M, 510.2676; ν_{max}/cm⁻¹ 700, 774, 834, 1077, 1210, 1254, 1308, 1428, 1451, 1706, 1742, 2931 and 2957; δ_H (300 MHz, toluene-*d*₈, 90 °C) 0.06 (6 H, s, 2 x SiCH₃), 0.82 (3 H, t, J 7.3, CH₃CH₂), 0.97 [9 H, s, SiC(CH₃)₃], 1.15 (3 H, d, J 6.3, 7-H₃), 1.17-1.30 (2 H, m, CH₃CH₂), 1.42 (2 H, qn, J 6.8, CH₂CH₂O), 1.56 (3 H, d, J 7.1, CH₃CHN), 2.05 and 2.93 (each 1 H, m, 3-H), 3.67 (1 H, m), 3.90-4.02 (2 H, m), 4.10 (1 H, m), 5.08-5.18 (3 H, m), 5.41 (1 H, m), 5.60 (1 H, m) and 7.06-7.37 (10 H, m, ArH); δ_C (75 MHz, CDCl₃, major rotamer) -4.63, -4.50, 13.71, 18.30, 19.14, 23.16, 24.26, 25.95, 30.47, 30.65, 54.64, 64.43, 65.02, 67.40, 68.97, 126.83, 127.11, 127.92, 128.06, 128.25, 128.40, 128.47, 128.56, 137.17, 140.23, 155.72 and 171.50; m/z (CI) 585 (M⁺ + 18, 1%), 510 (4) and 436 (100).

Following the general procedure, the cbz-protected amino-ester **57** (360 mg, 0.634 mmol), ozone, methyl sulfide (140 μL, 1.90 mmol) and sodium borohydride (96 mg, 2.54 mmol) gave alcohol **20** that was cyclised using hydrogen chloride in methanol to give the cbz-protected amino-lactone **21** (104 mg, 48%) as a white powder. A single recrystallisation from DCM/hexane gave the lactone **21** as colourless needles, m.p. 152-153 °C; [α]_D +24 (c 0.4 in CHCl₃).

Following the general procedure for transfer hydrogenolysis, the cbz-protected amino-lactone **21** (40 mg, 0.118 mmol), ammonium formate (37 mg, 0.587 mmol) and 10% Pd-C (4 mg) gave the amino-lactone **22** (16 mg, 66%) as a colourless oil, [α]_D +33 (c 0.5 in CHCl₃).

Methyl (2*S*,6*S*,*E*)- and (2*R*,6*S*,*E*)-6-(*tert*-butyldimethylsilyloxy)-2-(2-nitrophenylsulfanyl)aminohept-4-enoate **58** and **60**

Following the general procedure, tin(IV) chloride (391 mg, 1.50 mmol) in DCM (5 mL), the 5-silyloxy-pentenylstannane **52** (771 mg, 1.58 mmol) in DCM (5 mL) and the imine **29** (379 mg, 1.58 mmol) in DCM (5 mL) after 12 h at -45 °C and chromatography using hexane/ether/triethylamine (60 : 39.5 : 0.5) as eluent gave the *title compounds* **58** and **60** (562 mg, 85%) as a yellow oil, **58** : **60** = 75 : 25 (¹H NMR) (Found: M⁺ + H, 441.1888. C₂₀H₃₃N₂O₅SiS requires M, 441.1879; ν_{max}/cm⁻¹ 736, 777, 836, 971, 1097, 1148, 1209, 1255, 1306, 1338, 1512, 1591, 1741, 2954 and 3339; δ_H (300 MHz, CDCl₃) major isomer 0.10 and 0.11 (3 H, s, 2 x SiCH₃), 0.94 [9 H, s, SiC(CH₃)₃], 1.25 (3 H, d, J 6.3, 7-H₃), 2.54-2.66 (2 H, m, 3-H₂), 3.29 (1 H, d, J 8.6, NH), 3.64 (1 H, m, 2-H), 3.80 (3 H, s, CH₃O), 4.35 (1 H, m, 6-H), 5.59 (1 H, dt, J 15.3 and 6.4, 4-H), 5.70 (1 H, dd, J 15.3 and 4.5, 5-H), 7.30 (1 H, ddd, J 8.3, 8.3 and 1.1, ArH), 7.68 (1 H, ddd, J 7.7, 7.7 and 1.0, ArH), 8.13 (1 H, dd, J 8.2 and 1.0, ArH), 8.30 (1 H, dd, J 8.3 and 1.2, ArH); minor isomer 3.31 (d, J 8.6, NH) and 5.62 (1 H, dt, J 15.3 and 6.4, 4-H); δ_C (75 MHz, CDCl₃) major isomer -4.70, -4.56, 18.30, 24.52, 25.90, 36.20, 52.33, 63.46, 68.57, 121.98, 124.64, 124.77, 125.78, 133.85, 139.67, 142.60, 145.01 and 173.62; minor isomer 63.75, 68.76 and 122.20; m/z (CI) 441 (M⁺ + 1, 100%).

Methyl (2*S*,6*S*,*E*)- and (2*R*,6*S*,*E*)-6-hydroxy-2-(2-nitrophenyl-sulfanyl)aminohept-4-enoate **59** and **61**

Tetra-*n*-butylammonium fluoride in THF (1 M, 708 μL, 0.708 mmol) was added to the silyl ethers **58** and **60** (260 mg, 0.590 mmol, 3 : 1) in THF (2 mL) at 0 °C and the mixture was stirred at 0 °C for 12 h. Methanol (1 mL) was added followed by water (5 mL) and the mixture concentrated under reduced pressure. The aqueous residue was extracted with ethyl acetate and the organic extracts dried (MgSO₄) then concentrated under reduced pressure then dissolved in DCM and absorbed on to silica. The resulting powder was applied to a column of silica gel eluting with hexane/ethyl acetate/triethylamine (60 : 39.5 : 0.5) to give the *title compounds* **59** and **61** (153 mg, 79%) as a viscous, yellow oil. Samples of each isomer as yellow oils were obtained by preparative scale HPLC (Silica Resolve cartridge, UV at 255 nm, eluent hexane / ethyl acetate 3 : 1, flow rate 2 mL min⁻¹): (2*R*)-epimer **61** (less polar, 28% of the mixture) (Found: M⁺ + H, 327.1006. C₁₄H₁₉N₂O₅S requires M, 327.1015; [α]_D +1.4 (c 1.1 in CHCl₃); ν_{max}/cm⁻¹ 737, 789, 852, 973, 1058, 1099, 1211, 1306, 1338, 1447, 1511, 1566, 1593, 1738, 2970 and 3334; δ_H (500 MHz, CDCl₃) 1.26 (3 H, d, J 6.4, 7-H₃), 1.75 (1 H, br s, OH), 2.50 (1 H, m, 3-H), 2.59 (1

H, m, 3-H), 3.305 (1 H, d, *J* 8.5, NH), 3.58 (1 H, m, 2-H), 3.76 (3 H, s, CH₃O), 4.30 (1 H, qn, *J* 6.4, 6-H), 5.61 (1 H, dt, *J* 16.0 and 7.4, 4-H), 5.68 (1 H, dd, *J* 16.0 and 5.8, 5-H), 7.23 (1 H, ddd, *J* 8.3, 8.3 and 1.2, ArH), 7.62 (1 H, td, *J* 8.3 and 1.3, ArH), 8.05 (1 H, dd, *J* 8.3 and 1.3, ArH) and 8.24 (1 H, dd, *J* 8.3 and 1.2, ArH); δ_{C} (75 MHz, CDCl₃) 23.41, 36.17, 52.44, 63.54, 68.42, 124.07, 124.60, 124.84, 125.81, 133.86, 139.06, 142.59, 144.91 and 173.62; *m/z* (CI) 344 (M⁺ + 18, 40%), 327 (M⁺ + 1, 60) and 309 (100); (2*S*)-epimer **59** (more polar, 72% of the mixture) (Found: M⁺ + H, 327.1019. C₁₄H₁₉N₂O₅S requires *M*, 327.1015); [α]_D -1.50 (*c* 0.8 in CHCl₃); ν_{max} /cm⁻¹ 699, 737, 850, 973, 1059, 1099, 1210, 1308, 1338, 1446, 1511, 1566, 1597, 1733, 2970 and 3334; δ_{H} (500 MHz, CDCl₃) 1.25 (3 H, d, *J* 6.4, 7-H₃), 1.86 (1 H, br s, OH), 2.50 (1 H, m, 3-H), 2.59 (1 H, m, 3-H), 3.31 (1 H, d, *J* 8.6, NH), 3.58 (1 H, m, 2-H), 3.75 (3 H, s, CH₃O), 4.29 (1 H, qn, *J* 6.4, 6-H), 5.62 (1 H, dt, *J* 15.4 and 6.4, 4-H), 5.67 (1 H, dd, *J* 15.4 and 5.6, 5-H), 7.23 (1 H, ddd, *J* 8.2, 8.2 and 1.2, ArH), 7.62 (1 H, td, *J* 8.3 and 1.2, ArH), 8.05 (1 H, dd, *J* 8.4 and 1.3, ArH) and 8.23 (1 H, dd, *J* 8.3 and 1.3, ArH); δ_{C} (75 MHz, CDCl₃) 23.39, 36.16, 52.44, 63.55, 68.31, 123.95, 124.61, 124.84, 125.78, 133.88, 139.06, 142.56, 144.89 and 173.67; *m/z* (CI) 344 (M⁺ + 18, 55%), 327 (M⁺ + 1, 70) and 309 (100).

Butyl (2*S*,6*S*,*E*)- and (2*R*,6*S*,*E*)-2-[(diphenylmethyl)-amino]-6-(*tert*-butyldimethylsilyloxy)hept-4-enoates **62** and **63**

The general procedure using tin(IV) chloride (145 mg, 0.557 \square mol) in DCM (4 mL), 4-silyloxy-pentenylstannane **52** (286 mg, 0.584 \square mol) in DCM (4 mL) and the imine **32** (173 mg, 0.586 mmol) in DCM (4 mL) after 12 h at -45 °C and chromatography using petrol/ether/triethylamine (90 : 9.5 : 0.5) gave the *title compounds* **62** and **63** (251 mg, 91%) as a colourless oil, **62** : **63** = 75 : 25 (¹H NMR) (Found: M⁺ + H, 496.324122. C₃₀H₄₆NO₃Si requires *M*, 496.324698); [α]_D -4.4 (*c* 1.2 in CHCl₃); ν_{max} /cm⁻¹ 837, 970, 1079, 1150, 1187, 1361, 1454, 1472, 1600, 1725, 2931 and 3334; δ_{H} (500 MHz, C₆D₆) major isomer 0.11 and 0.14 (each 3 H, s, SiCH₃), 0.79 (3 H, t, *J* 7.4, CH₃CH₂), 1.04 [9 H, s, SiC(CH₃)₃], 1.16-1.23 (2 H, m, CH₃CH₂), 1.20 (3 H, d, *J* 6.7, 7-H₃), 1.38-1.44 (2 H, m, CH₂CH₂O), 2.34-2.51 (3 H, m, 3-H₂ and NH), 3.51 (1 H, m, 2-H), 4.02-4.10 (2 H, m, CH₂O), 4.20 (1 H, m, 6-H), 5.10 (1 H, s, Ph₂CH), 5.58 (1 H, dd, *J* 15.3 and 5.5, 5-H), 5.69 (1 H, dt, *J* 15.3 and 6.9, 4-H), 7.02-7.12 (2 H, m, ArH), 7.14-7.24 (4 H, m, ArH) and 7.52-7.58 (4 H, m, ArH); minor isomer 0.10 (s, SiCH₃), 1.02 [s, SiC(CH₃)₃], 1.23 (d, *J* 6.7, 7-H₃), 5.09 (s, Ph₂CH), 5.60 (1 H, dd, *J* 15.3 and 5.5, 5-H) and 5.71 (1 H, dt, *J* 15.3 and 6.9, 4-H); δ_{C} (63 MHz, CDCl₃) major isomer -4.80, -4.60, 13.66, 18.20, 19.13, 24.54, 25.88, 30.71, 36.37, 58.98, 64.42, 65.22, 68.93, 123.50, 123.58, 127.10, 127.30, 127.58, 128.43, 138.24, 142.79, 144.26 and 174.86; minor isomer 65.33; *m/z* (CI) 496 (M⁺ + 1, 100%).

Butyl (2*S*,6*S*,*E*)- and (2*R*,6*S*,*E*)-6-(*tert*-butyldimethylsilyloxy)-2-[(1-methyl-1-phenyl)ethyl]aminohept-4-enoates **64** and **65**

The general procedure using tin(IV) chloride (128 mg, 0.491 \square mol) in DCM (4 mL), 4-silyloxy-pentenylstannane **52** (253 mg, 0.517 \square mol) in DCM (4 mL) and the imine **35** (128 mg, 0.518 \square mol) in DCM (5 mL) after 12 h at -45 °C and chromatography using petrol/ether/triethylamine (95 : 4.5 : 0.5) gave the *title compounds* **64** and **65** (163 mg, 74%) as a colourless oil, **64** : **65** = 75 : 25 (¹H NMR) (Found: M⁺ + H, 448.325042. C₂₆H₄₆NO₃Si requires *M*, 448.324698); [α]_D -8.8 (*c* 0.8 in CHCl₃); ν_{max} /cm⁻¹ 812, 836, 908, 940, 971, 996, 1077, 1179, 1364, 1383, 1472, 1602, 1725, 2931 and 3338; δ_{H} (250 MHz, CDCl₃) 0.03 and 0.05 (each 3 H, s, SiCH₃), 0.88 [9 H, s, SiC(CH₃)₃], 0.91 (3 H, t, *J* 7.6, CH₃CH₂), 1.17 (3 H, d, *J* 6.6, 7-H₃), 1.32 (2 H, hex, *J* 7.6, CH₃CH₂), 1.40 and 1.42 (each 3 H, s, CH₃), 1.53 (2 H, qn, *J* 7.6, CH₂CH₂O), 1.77 (1 H, br s, NH), 2.19-2.26 (2 H, m, 3-H₂), 3.03 (1 H, t, *J* 6.6, 2-H), 3.88-3.96 (2 H, m, CH₂O), 4.24 (1 H, m, 6-H), 5.39-5.54 (2 H, m, 4-H and 5-H), 7.16-7.24 (1 H, m, ArH), 7.26-7.34 (2 H, m, ArH) and 7.43-7.48 (2 H, m, ArH); δ_{C} (63 MHz, CDCl₃) major isomer -4.70, -4.50, 13.71, 18.28, 19.14, 22.42, 24.54, 25.93, 28.17, 30.58, 31.21, 38.24, 56.27, 64.42, 68.98, 123.98, 126.14, 126.32, 127.94, 138.02, 147.45 and 176.41; minor isomer 56.20, 65.39, 68.04, 70.32, 124.06 and 137.91; *m/z* (CI) 448 (M⁺ + 1, 100%).

Butyl (2*S*,6*S*,*E*)-2-(diphenylmethyl)amino-6-hydroxyhept-4-enoate **66**

Tetrabutylammonium fluoride in THF (1 M, 580 μ L, 580 \square mol) was added to a mixture of the silyl ethers **62** and **63** (240 mg, 0.484 \square mol, **62** : **63** = 75 : 25) in THF (1 mL) and the reaction mixture stirred at ambient temperature for 6 h. Methanol (1 mL) was added followed by water (5 mL) and the mixture concentrated under reduced pressure. The aqueous residue was extracted twice with ether and the organic extracts dried (MgSO₄) and absorbed on to silica. The resulting powder was applied to a column of silica gel and after chromatography using hexane/ether/triethylamine (50 : 49.5 : 0.5) as eluent gave the *title compound* **66** (177 mg, 96%) a colourless oil containing *ca.* 25% of its (2*R*)-epimer (¹H NMR) (Found: M⁺ + H, 382.2385. C₂₄H₃₂NO₃ requires *M*, 382.2382); [α]_D -7.1 (*c* 0.8 in CHCl₃); ν_{max} /cm⁻¹ 668, 705, 727, 972, 1063, 1121, 1189, 1208, 1453, 1580, 1725, 2963, 3335 and 3596; δ_{H} (250 MHz, CDCl₃) major isomer 0.93 (3 H, t, *J* 7.1, CH₃CH₂), 1.235 (3 H, d, *J* 6.2, 7-H₃), 1.38 (2 H, hex, *J* 7.3, CH₃CH₂), 1.60 (2 H, qn, *J* 7.2, CH₂CH₂O), 2.08 (2 H, br s, NH and OH), 2.37-2.41 (2 H, m, 3-H₂), 3.26 (1 H, t, *J* 6.2, 2-H), 4.11 (2 H, t, *J* 6.5, CH₂O), 4.25 (1 H, m, 6-H), 4.81 (1 H, s, Ph₂CH), 5.56-5.68 (2 H, m, 4-H and 5-H) and 7.19-7.46 (10 H, m, ArH); minor isomer 1.24 (d, *J* 6.2, 7-H₃); δ_{C} (63 MHz, CDCl₃) major isomer 13.69, 19.17, 23.27, 30.73, 36.33, 59.10, 64.53, 65.36, 68.55, 125.49, 127.12, 127.15, 127.22, 127.55, 128.40, 128.44, 137.54, 142.67, 144.06 and 174.75; *m/z* (CI) 382 (M⁺ + 1, 100%).

Butyl (2*S*,6*R*,*E*)-2-(diphenylmethyl)amino-6-(4-oxopentanoyl-oxy)hept-4-enoate **67**

Diethyl azodicarboxylate (60 mg, 0.345 \square mol) in THF (2 mL) was added dropwise over 1 min to the alcohol **66** [100 mg, 0.262 \square mol, containing *ca.* 25% of its (2*R*)-epimer], triphenylphosphine (90 mg, 0.343 \square mol) and levulinic acid (33 mg, 0.284 \square mol) in THF (2 mL) and the mixture stirred at ambient temperature for 1 h. More triphenylphosphine (45 mg, 0.172 \square mol), levulinic acid (16 mg, 0.138 \square mol) and diethyl azodicarboxylate were then added dropwise to give a permanent orange colour and the mixture was stirred at ambient temperature for 16 h. After concentration under reduced pressure, the residue was suspended in ether, washed with water, saturated aqueous sodium hydrogen carbonate, water, then dried (MgSO₄) and absorbed on to silica. The resulting powder was applied to a column of silica gel to give, after chromatography using hexane/ether (65 : 35) as eluent the *title compound* **67** (104 mg, 83%) $\square\square\square\square\square\square\square\square\square\square\square\square\square\square\square\square$ containing *ca.* 25% of its (2*R*)-epimer (¹H NMR) (Found: M⁺ + H, 480.274729. C₂₉H₃₈NO₅ requires *M*, 480.274999); [α]_D +19 (*c* 0.5 in CHCl₃); ν_{max} /cm⁻¹ 600, 838, 970, 1040, 1162, 1188, 1363, 1454, 1600, 1723, 2935 and 3336; δ_{H} (250 MHz, CDCl₃) major isomer 0.94 (3 H, t, *J* 7.3, CH₃CH₂), 1.30 (3 H, d, *J* 6.4, 7-H₃), 1.37 (2 H, hex, *J* 7.5, CH₃CH₂), 1.54-1.67 (2 H, m, CH₂CH₂O), 2.13 (1 H, br, s, NH), 2.16 (3 H, s, H₃CO), 2.32-2.42 (2 H, m, 3-H₂), 2.50-2.58 and 2.67-2.75 (each 2 H, m, CH₂CO), 3.26 (1 H, m, 2-H), 4.11 (2 H, t, *J* 6.6, CH₂O), 4.80 (1 H, s, Ph₂CH), 5.30 (1 H, qn, *J* 6.4, 6-H), 5.54 (1 H, dd, *J* 15.0 and 6.0, 5-H), 5.69 (1 H, dt, *J* 15.0 and 6.5, 4-H) and 7.16-7.44 (10 H,

m, ArH); minor isomer 1.28 (d, J 6.4, 7-H₃); δ_C (63 MHz, CDCl₃) major isomer 13.69, 19.17, 20.19, 28.34, 29.87, 30.74, 36.48, 37.99, 58.86, 64.53, 65.36, 70.92, 127.11, 127.14, 127.23, 127.55, 128.10, 128.42, 128.45, 132.64, 142.67, 144.13, 171.82 and 174.66; minor isomer 20.23 and 70.99; m/z (CI) 480 ($M^+ + 1$, 100%).

Butyl (2*S*,6*R*,*E*)-2-(diphenylmethyl)amino-6-hydroxyhept-4-enoate **68**

Sodium borohydride (13 mg, 0.344 mmol) was added to the levulinate **67** [80 mg, 0.167 mmol, containing *ca.* 25% of its (2*R*)-epimer] in methanol (5 mL) at 0 °C and the reaction was stirred at ambient temperature for 30 min. Saturated aqueous ammonium chloride (1 mL) was added and the mixture concentrated under reduced pressure. The residue was suspended in ether, washed with water, dried (MgSO₄) and concentrated under reduced pressure to give an oil that was dissolved in chloroform (10 mL). Glacial acetic acid (catalytic) was added and the mixture heated under reflux for 16 h. After cooling to ambient temperature, the mixture was washed with saturated aqueous sodium hydrogen carbonate, dried (MgSO₄) and absorbed on to silica. The ensuing powder was applied to a column of silica gel and elution using hexane/ether/triethylamine (60 : 39.5 : 0.5) gave the *title compound* **68** (57 mg, 90%) as a colourless oil containing *ca.* 25% of its (2*R*)-epimer **ent-66** (¹H NMR) (Found: $M^+ + H$, 382.2386. C₂₄H₃₂NO₃ requires M , 382.2382); $[\alpha]_D$ -1.31 (c 0.2 in CHCl₃); $\nu_{\max}/\text{cm}^{-1}$ 972, 1028, 1063, 1147, 1189, 1304, 1454, 1494, 1725, 2935, 3331 and 3601; δ_H (250 MHz, CDCl₃) major isomer 0.92 (3 H, t, J 7.2, CH₃CH₂), 1.22 (3 H, d, J 6.4, 7-H₃), 1.38 (2 H, hex, J 7.4, CH₃CH₂), 1.60 (2 H, qn, J 7.1, CH₂CH₂O), 2.10 (2 H, br s, NH and OH), 2.35-2.41 (2 H, m, 3-H₂), 3.26 (1 H, t, J 6.2, 2-H), 4.12 (2 H, t, J 6.9, CH₂O), 4.25 (1 H, m, 6-H), 4.80 (1 H, s, Ph₂CH), 5.53-5.70 (2 H, m, 4-H and 5-H) and 7.18-7.44 (10 H, m, ArH); minor isomer 1.21 (d, J 6.4, 7-H₃); δ_C (63 MHz, CDCl₃) major isomer 13.63, 19.11, 23.20, 30.69, 36.29, 59.06, 64.52, 65.38, 68.52, 125.52, 127.16, 127.19, 127.26, 127.59, 128.43, 128.49, 137.59, 142.74, 144.10 and 174.81; m/z (CI) 382 ($M^+ + 1$, 100%).

Butyl (2*S*,6*R*,*E*)- and (2*R*,6*R*,*E*)-2-(diphenylmethyl)-amino-6-(*tert*-butyldimethylsilyloxy)hept-4-enoate **ent-63** and **ent-62**

Imidazole (9 mg, 0.132 mmol) and *tert*-butyldimethylsilyl chloride (15 mg, 0.100 mmol) were added to the alcohol **68** (25 mg, 66 μmol, containing *ca.* 25% of its (2*R*)-epimer) in DCM (1 mL) and the suspension stirred at ambient temperature for 16 h. Water (10 mL) and DCM (10 mL) were added and the organic phase was washed with brine, dried (MgSO₄) then absorbed on to silica. The resulting powder was applied to a column of silica gel and elution using hexane/ether (98 : 2 to 9 : 1) gave the *title compounds* **ent-63** and **ent-62** (32 mg, 100%) as a colourless oil, **ent-63** : **ent-62** = 75 : 25 (NMR) (Found: $M^+ + H$, 496.324537. C₃₀H₄₆NO₃Si requires M , 496.324698); $[\alpha]_D$ -1.20 (c 1.0 in CHCl₃); $\nu_{\max}/\text{cm}^{-1}$ 702, 744, 776, 835, 968, 1081, 1148, 1182, 1255, 1356, 1468, 1590, 1731, 2956 and 3334; δ_H (250 MHz, CDCl₃) major isomer -0.02 and 0.00 (each 3 H, s, SiCH₃), 0.83 [9 H, s, SiC(CH₃)₃], 0.90 (3 H, t, J 7.3, CH₃CH₂), 1.14 (3 H, d, J 6.4, 7-H₃), 1.32 (2 H, hex, J 7.4, CH₃CH₂), 1.58 (2 H, qn, J 7.3, CH₂CH₂O), 2.10 (1 H, br s, NH), 2.30-2.40 (2 H, m, 3-H₂), 3.23 (1 H, t, J 6.2, 2-H), 4.08 (2 H, t, J 6.8, CH₂O), 4.21 (1 H, m, 6-H), 4.79 (1 H, s, Ph₂CH), 5.46-5.59 (2 H, m, 4-H and 5-H) and 7.11-7.41 (10 H, m, ArH); minor isomer 3.22 (t, J 6.2, 2-H); δ_C (63 MHz, CDCl₃) major isomer, -4.72, -4.53, 13.70, 18.25, 19.18, 24.57, 25.91, 30.76, 36.40, 59.02, 64.42, 65.36, 68.94, 123.48, 123.55, 127.05, 127.27, 127.55, 128.40, 138.21, 142.80, 144.24 and 174.72; minor isomer 65.25; m/z (CI) 496 ($M^+ + 1$, 100%).

Methyl (2*S*,6*S*,*E*)-2-(diphenylmethyl)amino-6-(*tert*-butyldimethylsilyloxy)hept-4-enoate **69**

Anhydrous potassium carbonate (293 mg, 2.12 mmol) was added to the esters **62** and **63** (200 mg, 0.40 mmol, **62** : **63** = 75 : 25) in methanol (5.6 mL) and water (1.4 mL) and the mixture was heated under reflux for 16 h. After cooling to ambient temperature and concentration under reduced pressure, the residue was dissolved in saturated aqueous sodium hydrogen carbonate. The solution was washed ether and the aqueous layer acidified with hydrogen chloride (1 M) then extracted with ether. The organic phase was dried (MgSO₄), filtered and concentrated to *ca.* 10 mL under reduced pressure. An excess of diazomethane in ether was added and the yellow solution stirred at ambient temperature for 30 min before glacial acetic acid was added dropwise until a colourless solution was obtained. Water (20 mL) was then added and the organic phase was washed with saturated aqueous sodium hydrogen carbonate then dried (MgSO₄). Silica (*ca.* 1 g) was added and the mixture dried under reduced pressure. The ensuing powder was applied to a column of silica gel to give, after chromatography using hexane/ether (9 : 1) as eluent, the *title compound* **69** (179 mg, 98%) as a colourless oil containing *ca.* 25% of its (2*R*)-epimer (Found: $M^+ + H$, 454.2767. C₂₇H₄₀NO₃Si requires M , 454.2777); $\nu_{\max}/\text{cm}^{-1}$ 701, 744, 777, 834, 970, 1000, 1082, 1150, 1199, 1254, 1453, 1468, 1493, 1738, 2856, 2953 and 3331; δ_H (300 MHz, CDCl₃) major isomer 0.09 and 0.11 (each 3 H, s, SiCH₃), 0.95 [9 H, s, SiC(CH₃)₃], 1.22 (3 H, d, J 6.5, 7-H₃), 2.18 (1 H, br s, NH), 2.40-2.46 (2 H, m, 3-H₂), 3.34 (1 H, t, J 6.2, 2-H), 3.72 (3 H, s, CH₃O), 4.30 (1 H, m, 6-H), 4.86 (1 H, s, Ph₂CH), 5.54-5.65 (2 H, m, 4-H and 5-H) and 7.21-7.50 (10 H, m, ArH); minor isomer 0.93 [s, SiC(CH₃)₃] and 1.225 (d, J 6.5, 7-H₃); δ_C (75 MHz, CDCl₃) major isomer -4.75, -4.56, 18.30, 24.63, 25.93, 36.42, 51.62, 59.01, 65.28, 68.94, 123.43, 127.18, 127.36, 127.59, 128.51, 138.38, 142.80, 144.21 and 175.34; minor isomer 59.07 and 65.38; m/z (CI) 454 ($M^+ + 1$, 100%).

Methyl (2*S*,6*S*,*E*)-2-(diphenylmethyl)amino-6-hydroxyhept-4-enoate **70**

Tetrabutylammonium fluoride in THF (1 M, 2.2 mL, 2.2 mmol) was added to the silyl ether **69** [660 mg, 1.45 mmol containing *ca.* 25% of its (2*R*)-epimer] in THF (5 mL) and the mixture stirred at ambient temperature for 16 h. Methanol (1 mL) was added followed by water (20 mL) and the mixture concentrated under reduced pressure. The residue was extracted twice with ether and the organic extracts dried (MgSO₄) then absorbed on to silica. The resulting powder was applied to a column of silica gel to give after chromatography using hexane/ether/triethylamine (60 : 39.5 : 0.5) as eluent, the *title compound* **70** (479 mg, 97%) as a colourless oil containing *ca.* 25% of its (2*R*)-epimer (Found: $M^+ + H$, 340.1907. C₂₁H₂₆NO₃ requires M , 340.1913); $\nu_{\max}/\text{cm}^{-1}$ 702, 746, 971, 1062, 1202, 1452, 1492, 1734, 2969, 3336 and 3453; δ_H (300 MHz, CDCl₃) major isomer 1.28 (3 H, d, J 6.4, 7-H₃), 1.75 (1 H, br, OH), 2.20 (1 H, br s, NH), 2.40-2.44 (2 H, m, 3-H₂), 3.33 (1 H, t, J 6.2, 2-H), 3.73 (3 H, s, CH₃O), 4.29 (1 H, qn, J 5.9, 6-H), 4.85 (1 H, s, Ph₂CH), 5.60-5.70 (2 H, m, 4-H and 5-H) and 7.20-7.50 (10 H, m, ArH); minor isomer 1.29 (d, J 6.4, 7-H₃); δ_C (75 MHz, CDCl₃) major isomer 23.31, 36.32, 51.71, 59.11, 65.40, 68.55, 125.40, 127.26, 127.32, 127.61, 128.52, 128.56, 137.78, 142.73, 144.09 and 175.29; m/z (CI) 340 ($M^+ + 1$, 100%).

Methyl (2*S*,6*S*,*E*)-6-acetoxy-2-(diphenylmethyl)aminohept-4-enoate **71**

Following the general procedure, the hydroxyl-ester **70** [390 mg, 1.15 mmol containing *ca.* 25% of its (2*R*)-epimer], triethylamine (480 μ L, 3.44 mmol), acetic anhydride (163 μ L, 1.72 mmol) and DMAP (5 mg, 41 μ mol) after chromatography using hexane/ether (3 : 1) as eluent gave the *title compound* **71** (436 mg, 99%) as a colourless oil containing *ca.* 25% of its (2*R*)-epimer (Found: $M^+ + H$, 382.2013. $C_{23}H_{28}NO_4$ requires M , 382.2018); ν_{max}/cm^{-1} 703, 746, 1044, 1200, 1242, 1370, 1452, 1493, 1758, 2950, 3027 and 3336; δ_H (300 MHz, $CDCl_3$) major isomer 1.33 (3 H, d, J 6.4, 7-H₃), 2.07 (3 H, s, CH_3CO), 2.19 (1 H, br s, NH), 2.43 (2 H, t, J 6.8, 3-H₂), 3.32 (1 H, t, J 6.6, 2-H), 3.74 (3 H, s, CH_3O), 4.84 (1 H, s, Ph_2CH), 5.37 (1 H, qn, J 6.4, 6-H), 5.59 (1 H, dd, J 15.5 and 6.2, 5-H), 5.74 (1 H, dt, J 15.5 and 6.9, 4-H) and 7.20-7.49 (10 H, m, ArH); minor isomer 1.34 (d, J 6.4, 7-H₃), 2.06 (s, CH_3CO), 3.33 (t, J 6.4, 2-H); δ_C (75 MHz, $CDCl_3$) major isomer 20.30, 21.39, 36.51, 51.68, 58.91, 65.38, 70.67, 127.22, 127.25, 127.30, 127.60, 127.97, 128.51, 128.54, 132.94, 142.70, 144.12, 170.29 and 175.20; m/z (CI) 382 ($M^+ + 1$, 100%) and 322 (30).

Methyl (2*S*,6*S*,*E*)-6-acetoxy-2-(diphenylmethyl)aminoheptanoate **72**

The general procedure for diimide reduction of alkenes using the heptenoate **71** [220 mg, 0.577 μ mol containing *ca.* 25% of its (2*R*)-epimer], toluene 4-sulfonylhydrazine (1.07 g, 5.75 mmol) and anhydrous sodium acetate (473 mg, 5.77 mmol) after chromatography using hexane/ether (70 : 30) as eluent gave the *title compound* **72** (220 mg, 99%) as a colourless oil containing about 25% of its (2*R*)-epimer (Found: $M^+ + H$, 384.2172. $C_{23}H_{30}NO_4$ requires M , 384.2175); ν_{max}/cm^{-1} 702, 747, 790, 1025, 1148, 1199, 1245, 1372, 1453, 1492, 1732, 2865, 2948 and 3325; δ_H (300 MHz, $CDCl_3$) major isomer 1.24 (3 H, d, J 6.3, 7-H₃), 1.40-1.70 (6 H, m, 3-H₂, 4-H₂ and 5-H₂), 2.06 (3 H, s, CH_3CO), 2.13 (1 H, br s, NH), 3.22 (1 H, t, J 6.5, 2-H), 3.75 (3 H, s, CH_3O), 4.81 (1 H, s, Ph_2CH), 4.92 (1 H, hex, J 5.9, 6-H) and 7.20-7.50 (10 H, m, ArH); minor isomer 2.07 (s, CH_3CO); δ_C (75 MHz, $CDCl_3$) major isomer 19.96, 21.38, 21.73, 33.61, 35.54, 51.70, 58.86, 65.57, 70.78, 127.21, 127.23, 127.28, 127.64, 128.49, 128.54, 142.79, 144.28, 170.75 and 176.15; minor isomer 70.54; m/z (CI) 384 ($M^+ + 1$, 100%) and 324 (10).

Methyl (2*S*,6*S*)-6-acetoxy-2-acetamidoheptanoate **73**

The general procedure for transfer hydrogenolysis using the 2-(diphenylmethyl)aminoheptanoate **72** [120 mg, 0.314 μ mol containing *ca.* 25% of its (2*R*)-epimer] gave an oil. Acetylation using triethylamine (131 μ L, 0.940 μ mol), acetic anhydride (44 μ L, 0.465 μ mol) and DMAP (1 mg, 8 μ mol) after chromatography using chloroform then chloroform/methanol (99 : 1) as eluent gave the *title compound* **73** (69 mg, 85%) as a colourless oil containing *ca.* 25% of its (2*R*)-epimer (decoupled 1H NMR) (Found: $M^+ + H$, 260.1500. $C_{12}H_{22}NO_5$ requires M , 260.1498); ν_{max}/cm^{-1} 803, 1026, 1091, 1150, 1250, 1376, 1438, 1540, 1656, 1733, 2866, 2953 and 3290; δ_H (500 MHz, $CDCl_3$) major isomer 1.17 (3 H, d, J 6.4, 7-H₃), 1.26-1.85 (6 H, m, 3-H₂, 4-H₂ and 5-H₂), 1.99 (6 H, s, 2 x CH_3CO), 3.73 (3 H, s, CH_3O), 4.58 (1 H, m, 2-H), 4.84 (1 H, m, 6-H) and 6.01 (1 H, d, J 6.9, NH); δ_C (75 MHz, $CDCl_3$) major isomer 20.01, 21.26, 21.42, 23.23, 32.37, 35.40, 51.95, 52.38, 70.54, 169.57, 170.54 and 172.79; minor isomer 20.10, 32.17, 52.05, 70.26 and 170.60; m/z (CI) 277 ($M^+ + 18$, 70%) and 260 ($M^+ + 1$, 100).

Butyl (2*S*,6*S*,*E*)-6-hydroxy-2-(1-methyl-1-phenylethyl)amino-hept-4-enoate **74**

Tetrabutylammonium fluoride in THF (1 M, 500 μ L, 0.500 μ mol) was added to a mixture of the 6-silyloxyheptenoates **64** and **65** (160 mg, 0.357 μ mol, **64** : **65** = 75 : 25) in THF (1 mL) and the mixture was stirred at ambient temperature for 4 h. Methanol (1 mL) was added followed by water (5 mL) and the mixture concentrated under reduced pressure. The residue was extracted with ether and the organic extracts dried ($MgSO_4$) then absorbed on to silica. The resulting powder was applied to a column of silica gel to give, after chromatography using hexane/ether/triethylamine (70 : 29.5 : 0.5) as eluent, the *title compound* **74** (102 mg, 86%) as a colourless oil (Found: $M^+ + H$, 334.2377. $C_{20}H_{32}NO_3$ requires M , 334.2382); ν_{max}/cm^{-1} 702, 766, 970, 1064, 1177, 1365, 1383, 1446, 1731, 2874, 2965 and 3428; δ_H (500 MHz, $CDCl_3$) major isomer 0.89 (3 H, t, J 7.4, CH_3CH_2), 1.19 (3 H, d, J 6.2, 7-H₃), 1.31 (2 H, hex, J 7.7, CH_3CH_2), 1.38 and 1.40 (each 3 H, s, CH_3), 1.52 (2 H, qn, J 7.3, CH_2CH_2O), 1.84 (2 H, br s, NH and OH), 2.18-2.21 (2 H, m, 3-H₂), 3.01 (1 H, t, J 6.5, 2-H), 3.94 (2 H, t, J 6.6, CH_2O), 4.21 (1 H, m, 6-H), 5.47-5.51 (2 H, m, 4-H and 5-H), 7.12-7.20 (1 H, m, ArH), 7.27-7.30 (2 H, m, ArH) and 7.43-7.45 (2 H, m, ArH); minor isomer 3.00 (t, J 6.5, 2-H) and 3.95 (t, J 6.6, CH_2O); δ_C (75 MHz, $CDCl_3$) 13.70, 19.14, 23.22, 27.93, 30.58, 31.41, 38.23, 56.25, 56.36, 64.57, 68.57, 126.02, 126.25, 126.49, 128.01, 137.27, 147.38 and 176.50; m/z (CI) 334 ($M^+ + 1$, 100%).

Butyl (2*S*,6*S*,*E*)-6-acetoxy-2-(1-methyl-1-phenylethyl)amino-hept-4-enoate **75**

The general procedure for acetylation using the 6-hydroxyhept-2-enoate **74** (50 mg, 0.150 μ mol), triethylamine (63 μ L, 0.452 μ mol), acetic anhydride (23 mg, 0.225 μ mol) and DMAP (0.5 mg, 4 μ mol) after chromatography using hexane/ether (4 : 1) as eluent gave the *title compound* **75** (53 mg, 94%) as a colourless oil; any minor (2*R*)-epimer could not be distinguished (Found: $M^+ + H$, 377.2569. $C_{22}H_{34}NO_4$ requires M , 377.2566); ν_{max}/cm^{-1} 702, 766, 952, 969, 1043, 1175, 1241, 1370, 1735, 2963 and 3329; δ_H (500 MHz, $CDCl_3$) 0.89 (3 H, t, J 7.3, CH_3CH_2), 1.24 (3 H, d, J 6.3, 7-H₃), 1.30 (2 H, hex, J 7.4, CH_3CH_2), 1.37 and 1.41 (each 3 H, s, CH_3), 1.51 (2 H, qn, J 7.3, CH_2CH_2O), 2.00 (3 H, s, CH_3CO), 2.01 (1 H, br s, NH), 2.16-2.22 (2 H, m, 3-H₂), 2.99 (1 H, t, J 6.8, 2-H), 3.90-3.96 (2 H, m, CH_2O), 5.26 (1 H, qn, J 7.4, 6-H), 5.46 (1 H, dd, J 15.3 and 6.2, 5-H), 5.55 (1 H, dt, J 15.3 and 7.2, 4-H), 7.18 (1 H, tt, J 7.2 and 0.9, ArH), 7.26-7.29 (2 H, m, ArH) and 7.43 (2 H, dd, J 7.5 and 1.0, ArH); δ_C (75 MHz, $CDCl_3$) 13.69, 19.14, 20.22, 21.40, 27.94, 30.56, 31.37, 38.32, 56.18, 56.23, 64.54, 70.71, 126.25, 126.47, 128.01, 128.38, 132.54, 147.37, 170.29 and 176.45; m/z (CI) 377 ($M^+ + 1$, 100%).

Butyl (2*S*,6*R*,*E*)- and (2*R*,6*R*,*E*)-7-(*tert*-butyldimethyl silyloxy)-6-methyl-2-[(*R*)-(1-phenylethyl)amino]hept-4-enoate **97** and **98**

The general procedure using tin(IV) chloride (332 mg, 1.27 mmol) in DCM (5 mL), the 5-silyloxy-pentenylstannane **82** (674 mg, 1.34 mmol) in DCM (5 mL) and the imine (**R**)-**11** (312 mg, 1.34 mmol) in DCM (5 mL) after chromatography using hexane/ether/triethylamine (90 : 9.5 : 0.5) gave the *title compounds* **97** and **98** (423 mg, 74%) as a colourless oil, **97** : **98** = 95 : 5 (1H NMR) (Found: $M^+ + H$, 448.3243. $C_{26}H_{46}NO_3Si$ requires M , 448.3247); $[\alpha]_D^{+28}$ (*c* 2.7 in $CHCl_3$); ν_{max}/cm^{-1} 667, 701, 776, 838, 971, 1087, 1178, 1254, 1468, 1735, 2958 and 3336; δ_H (500 MHz, C_6D_6) major isomer 0.15 (6 H, s, 2 x $SiCH_3$), 0.86 (3 H, t, J 7.4, CH_3CH_2), 1.08 [9 H, s, $Si(CH_3)_3$], 1.14 (3 H, d, J 7.1, 6- CH_3), 1.26 (2 H, hex, J 7.4, CH_3CH_2), 1.38 (3 H, d, J 6.5, $PhCHCH_3$), 1.43-1.49 (2 H, m, CH_2CH_2O), 2.15 (1 H, br s, NH), 2.43 (1 H, sep, J 6.6, 6-H), 2.50-2.59 (2 H, m, 3-H₂), 3.45 (1 H, dd, J 9.5 and 7.2, 7-H), 3.58 (1 H, t, J 6.1, 2-H), 3.59 (1 H, dd, J 9.5 and 5.7, 7-H), 3.94 (1 H, q, J 6.3, $PhCHCH_3$), 4.02 and 4.08 (each 1 H, m, CH_2HCH), 5.60 (1 H, dd, J 15.3 and 7.0, 5-H), 5.68 (1 H, dt, J 15.3 and

6.9, 4-H), 7.18 (1 H, tt, *J* 7.5 and 1.0, ArH), 7.28 (2 H, tt, *J* 7.9 and 1.0, ArH) and 7.42 (2 H, dd, *J* 7.5 and 0.9, ArH); δ_{H} (200 MHz, CDCl_3) minor isomer 3.05 (t, *J* 6.3, 2-H) and major isomer 3.35 (1 H, t, *J* 6.3, 2-H); δ_{C} (75 MHz, CDCl_3 , major isomer, 2S) -5.29, 13.71, 17.10, 18.38, 19.15, 23.22, 25.96, 30.67, 36.49, 39.39, 56.19, 59.10, 64.36, 68.13, 124.59, 126.83, 127.09, 128.40, 136.62, 145.50 and 174.90; *m/z* (CI) 448 ($\text{M}^+ + 1$, 100%).

Butyl (2S,6R,E)- and (2R,6R,E)-7-(tert-butylidimethyl silyloxy)-6-methyl-2-[(S)-(1-phenylethyl)amino]hept-4-enoate **99** and **100**

The general procedure using tin(IV) chloride (285 mg, 1.09 mmol) in DCM (5 mL), 5-silyloxy-pentenylstannane **82** (578 mg, 1.15 mmol) in DCM (5 mL) and the imine (**S**-**11**) (268 mg, 1.15 mmol) in DCM (5 mL) after chromatography using hexane/ether/triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **99** and **100** (391 mg, 80%) as a colourless oil. Samples of each epimer as colourless oils were obtained by preparative scale HPLC (Silica Resolve cartridge, UV at 255 nm, eluent hexane/ethyl acetate 15 : 1, flow rate 2 mL min⁻¹); (2S)-epimer **99** (less polar, 75% of the mixture) (Found: $\text{M}^+ + \text{H}$, 448.3254. $\text{C}_{26}\text{H}_{46}\text{NO}_3\text{Si}$ requires *M*, 448.3247); $[\alpha]_{\text{D}} -37$ (*c* 1.7 in CHCl_3); $\nu_{\text{max}}/\text{cm}^{-1}$ 701, 776, 838, 970, 1026, 1088, 1180, 1254, 1468, 1734, 2958 and 3333; δ_{H} (500 MHz, CDCl_3) 0.00 (6 H, s, 2 x SiCH_3), 0.86 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.91 (3 H, t, *J* 7.4, CH_3CH_2), 0.94 (3 H, d, *J* 6.6, 6- CH_3), 1.30 (3 H, d, *J* 6.5, PhCHCH_3), 1.35 (2 H, hex, *J* 7.6, CH_3CH_2), 1.58 (2 H, qn, *J* 7, $\text{CH}_2\text{CH}_2\text{O}$), 1.71 (1 H, br s, NH), 2.21-2.28 (3 H, m, 3- H_2 and 6-H), 3.01 (1 H, t, *J* 6.6, 2-H), 3.30 (1 H, dd, *J* 9.5 and 7.6, 7-H), 3.45 (1 H, dd, *J* 9.5 and 5.9, 7-H), 3.68 (1 H, q, *J* 6.5, PhCHCH_3), 4.04-4.12 (2 H, m, $\text{CH}_2\text{CH}_2\text{O}$), 5.32 (1 H, dt, *J* 15.5 and 6.5, 4-H), 5.39 (1 H, dd, *J* 15.5 and 6.7, 5-H) and 7.20-7.30 (5 H, m, ArH); δ_{C} (75 MHz, CDCl_3) -5.29, 13.70, 16.72, 18.38, 19.15, 23.17, 25.95, 30.67, 36.51, 39.42, 56.12, 59.11, 64.35, 68.12, 124.60, 126.82, 127.09, 128.40, 136.63, 145.26 and 174.70; *m/z* (CI) 448 ($\text{M}^+ + 1$, 100%); (2R)-epimer **100** (more polar, 25% of the mixture) $[\alpha]_{\text{D}} -15$ (*c* 0.85 in CHCl_3); δ_{H} (500 MHz, CDCl_3) 0.00 (6 H, s, 2 x SiCH_3), 0.86 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 0.89 (3 H, t, *J* 7.3, CH_3CH_2), 0.94 (3 H, d, *J* 6.7, 6- CH_3), 1.31 (3 H, d, *J* 6.7, PhCHCH_3), 1.31 (2 H, hex, *J* 7.6, CH_3CH_2), 1.53 (2 H, qn, *J* 7.5, $\text{CH}_2\text{CH}_2\text{O}$), 1.66 (1 H, br s, NH), 2.26 (1 H, sep, *J* 6.6, 6-H), 2.30-2.34 (2 H, m, 3- H_2), 3.29 (1 H, t, *J* 6.3, 2-H), 3.32 (1 H, dd, *J* 9.9 and 7.6, 7-H), 3.45 (1 H, dd, *J* 9.9 and 6.0, 7-H), 3.76 (1 H, q, *J* 6.6, PhCHCH_3), 3.91-3.99 (2 H, m, $\text{CH}_2\text{CH}_2\text{O}$), 5.36 (1 H, dt, *J* 15.6 and 6.5, 4-H), 5.42 (1 H, dd, *J* 15.6 and 6.3, 5-H) and 7.20-7.30 (5 H, m, ArH); δ_{C} (75 MHz, CDCl_3) -5.28, 13.70, 16.59, 18.39, 19.17, 25.30, 25.96, 30.77, 37.20, 39.29, 56.61, 59.01, 64.32, 68.15, 124.84, 126.91, 127.02, 128.37, 136.23, 145.11 and 175.40.

Methyl (2S,6R,E)- and (2R,6R,E)-7-(tert-butylidimethylsilyloxy)-6-methyl-2-(2-nitrophenylsulfanyl)aminohept-4-enoate **101** and **102**

The general procedure using tin(IV) chloride (508 mg, 1.95 mmol) in DCM (6 mL), 5-silyloxy-pentenylstannane **82** (1.03 g, 2.05 mmol) in DCM (6 mL) and the imine **29** (492 mg, 2.05 mmol) in DCM (6 mL) after chromatography hexane/ether/triethylamine (90 : 9.5 : 0.5) as eluent gave the *title compounds* **101** and **102** (682 mg, 77%) as a yellow oil, **101** : **102** = 80 : 20 (¹H NMR). Partial separation was achieved using preparative HPLC (the Silica Resolve cartridge, UV at 255 nm, eluent hexane/ethyl acetate 30 : 1, flow rate 2 mL min⁻¹); (2R)-epimer **102** (less polar, 20% of the mixture), containing 40% of the (2S)-epimer **101**; δ_{H} (500 MHz, C_6D_6) 1.00 (d, *J* 6.5, 6- CH_3), 3.07 (1 H, d, *J* 9, NH); δ_{C} (75 MHz, CDCl_3) 39.37, 123.45 and 138.20; (2S)-epimer **101** (more polar, 80% of the mixture) (Found: $\text{M}^+ + \text{H}$, 455.2033. $\text{C}_{21}\text{H}_{35}\text{N}_2\text{O}_5\text{SiS}$ requires *M*, 455.2036; $[\alpha]_{\text{D}} +19$ (*c* 1.8 in CHCl_3); $\nu_{\text{max}}/\text{cm}^{-1}$ 736, 778, 838, 1097, 1208, 1254, 1305, 1338, 1513, 1566, 1593, 1742, 2857, 2954 and 3337; δ_{H} (300 MHz, CDCl_3) 0.07 (6 H, s, 2 x SiCH_3), 0.92 [9 H, s, $\text{SiC}(\text{CH}_3)_3$], 1.04 (3 H, d, *J* 6.7, 6- CH_3), 2.38 (1 H, sep, *J* 6.7, 6-H), 2.48-2.67 (2 H, m, 3- H_2), 3.30 (1 H, d, *J* 8.9, NH), 3.42-3.55 (2 H, m, 7- H_2), 3.61 (1 H, m, 2-H), 3.80 (3 H, s, CH_3O), 5.45 (1 H, dt, *J* 15.4 and 6.7, 4-H), 5.59 (1 H, dd, *J* 15.4 and 6.9, 5-H), 7.29 (1 H, ddd, *J* 7.7, 7.7 and 1.1, ArH), 7.66 (1 H, ddd, *J* 7.7, 7.7 and 1.2, ArH), 8.15 (1 H, dd, *J* 8.3 and 1.0, ArH) and 8.30 (1 H, dd, *J* 8.3 and 1.1, ArH); δ_{H} (500 MHz, C_6D_6) 1.06 (3 H, d, *J* 6.5, 6- CH_3), 3.04 (1 H, d, *J* 9.0, NH); δ_{C} (75 MHz, CDCl_3) -5.28, 16.60, 18.39, 25.95, 36.91, 39.52, 52.31, 63.73, 68.00, 123.50, 124.68, 124.74, 125.78, 133.79, 138.36, 142.54, 145.16 and 173.77; *m/z* (CI) 472 ($\text{M}^+ + 18$, 2%), 455 ($\text{M}^+ + 1$, 85) and 302 (100).

Methyl (2S,7S,4E)- and (2R,7S,4E)-7-methoxy-2-[(2-nitrophenyl)sufanylamino]oct-4-enoates **130** and **134**

The general procedure using the (S)-methoxyhexenylstannane (**S**)-**123** (55 mg, 0.136 mmol) in DCM (1.5 mL), the 2-nitrophenylsulfanylamine **29** (31 mg, 0.130 mmol) in DCM (1 mL) and tin(IV) bromide in DCM (1 M, 136 μL , 0.136 mmol) after 9 h at -50 °C and chromatography using DCM/ether/triethylamine (70 : 29.5 : 0.5) as eluent gave a mixture of the *title compounds* **130** and **134** (24.5 mg, 58%) as a pale yellow oil, $[\alpha]_{\text{D}} -7.4$ (*c* 2.29 in DCM) (Found: $\text{M}^+ + \text{H}$, 355.1326. $\text{C}_{16}\text{H}_{23}\text{O}_5\text{N}_2\text{S}$ requires *M*, 355.1328); $\nu_{\text{max}}/\text{cm}^{-1}$ 736, 1095, 1206, 1337, 1511, 1592, 1739, 2929 and 3328; δ_{H} (500 MHz, CDCl_3) 1.11 (3 H, d, *J* 6.5, 8- H_3), 2.17 and 2.24 (each 1 H, dt, *J* 14 and 7, 6-H), 2.49 and 2.57 (each 1 H, dt, *J* 14 and 7, 3-H), 3.27 (1 H, d, *J* 8.5, NH), 3.29 (3 H, s, 7- OCH_3), 3.33 (1 H, hex, *J* 6.5, 7-H), 3.55 (1 H, dt, *J* 8.5 and 6.5, 2-H), 3.74 (3 H, s, CH_3O), 5.43 (1 H, dt, *J* 15 and 7.5, 5-H), 5.59 (1 H, dt, *J* 15 and 7.5, 4-H), 7.22 (1 H, ddd, *J* 8, 8 and 1.5, ArH), 7.60 (1 H, ddd, *J* 8, 8 and 1.5, ArH), 8.06 (1 H, dd, *J* 8 and 1, ArH) and 8.23 (1 H, dd, *J* 8 and 1.5, ArH); δ_{C} (125 MHz, CDCl_3) major epimer 18.80, 36.70, 39.17, 52.29, 55.97, 63.51, 76.25, 124.57, 124.68, 125.70, 126.08, 131.53, 133.75, 142.48, 145.01 and 173.63; minor epimer 18.82, 126.14, 131.50, 144.99; *m/z* (CI) 356 ($\text{M}^+ + 2$, 10%), 355 ($\text{M}^+ + 1$, 62), 202 (100) and 126 (20).

Methyl (2S,7S,4E)- and (2R,7S,4E)-2-amino-7-methoxyoct-4-enoates **131** and **135**

A mixture of the 2-nitrophenylsulfanylamine **130** and **134** (185 mg, 0.521 mmol) was dissolved in the minimum volume of anhydrous methanol and hydrogen chloride in methanol (5 M, 13 mL) was added. After stirring for 2 h at ambient temperature, the mixture was concentrated under reduced pressure. The residue was dissolved in DCM (10 mL) and the solution extracted with hydrogen chloride (1 M, 3 x 5 mL). The aqueous phases were combined and basified by the addition of solid sodium hydrogen carbonate until the solution had pH~10. The solution was extracted with ether (6 x 10 mL) and the organic extracts were dried (MgSO_4) and concentrated under reduced pressure to leave a mixture of the *title compounds* **131** and **135** (92 mg, 92%) as a pale yellow oil, $[\alpha]_{\text{D}} -6.4$ (*c* 1.8 in DCM) (Found: $\text{M}^+ + \text{H}$, 202.1440. $\text{C}_{10}\text{H}_{20}\text{O}_3\text{N}$ requires *M*, 202.1443); $\nu_{\text{max}}/\text{cm}^{-1}$ 722, 974, 1093, 1200, 1438, 1593, 1739, 2971 and 3379; δ_{H} (300 MHz, CDCl_3) 1.15 (3 H, d, *J* 6.5, 8- H_3), 2.19 and 2.29 (each 1 H, m, 6-H), 2.45 (2 H, m, 3- H_2), 3.31-3.36 (2 H, m, 2-H and 7-H), 3.34 and 3.75 (each 3 H, s, CH_3O), 5.43 (1 H, dt, *J* 15 and 7.5, 5-H) and 5.58 (1 H, dt, *J* 15 and 7.5, 4-H); *m/z* (CI) 203 ($\text{M}^+ + 2$, 14%) and 202 ($\text{M}^+ + 1$, 100).

Methyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-methoxy-2-[(*R*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl]amino-oct-4-enoates **132** and **136**

(*S*)-Mosher's acid chloride (24 μ L, 0.137 mmol), triethylamine (74 μ L, 0.542 mmol) and 4-dimethylaminopyridine (3 mg, cat.) were added to a mixture of the 2-amino-octenoates **131** and **135** (22 mg, 0.108 mmol) in dry DCM (1.5 mL) at room temperature and the mixture stirred for 15 h before being poured into water. The mixture was diluted with DCM and the aqueous phase extracted with DCM (3 x 7 mL). The organic extracts were washed with brine, dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue using petrol/ether (3 : 1) as eluent afforded the *title compounds* **132** and **136** (35 mg, 74%) as a pale yellow oil, **132** : **136** = 70 : 30 (¹H NMR). Preparative HPLC using hexane/ethyl acetate (88 : 12) as the eluent gave the less polar, major (2*S*)-epimer **132** as a colourless oil, [α]_D -11 (*c* 0.97 in DCM) (Found: M⁺ + H, 418.1839. C₂₀H₂₇O₅NF₃ requires *M*, 418.1842); δ_{H} (300 MHz, CDCl₃) 1.17 (3 H, d, *J* 6.5, 8-H₃), 2.21 and 2.29 (each 1 H, dt, *J* 14 and 7, 6-H), 2.62 (2 H, m, 3-H₂), 3.35 (1 H, m, 7-H), 3.35 (3 H, s, 7-OCH₃), 3.41 and 3.78 (each 3 H, s, CH₃O), 4.73 (1 H, dt, *J* 8 and 6.5, 2-H), 5.39 (1 H, dt, *J* 15 and 7.5, 5-H), 5.63 (1 H, dt, *J* 15 and 7.5, 4-H), 7.43-7.45 (4 H, m, ArH and NH) and 7.59 (2 H, d, *J* 8, ArH); δ_{C} (75 MHz, CDCl₃) 18.67, 35.03, 39.04, 51.79, 52.35, 54.81, 55.87, 76.22, 125.37, 127.97, 128.47, 129.45, 131.79, 162.90 and 171.56; *m/z* (CI) 435 (M⁺ + 18, 28%), 419 (M⁺ + 2, 20) and 418 (M⁺ + 1, 100); δ_{F} -70.7; followed by the more polar, minor (*R*)-epimer **136** as a colourless oil, [α]_D -20 (*c* 0.22 in DCM) (Found: M⁺ + H, 418.1840. C₂₀H₂₇O₅NF₃ requires *M*, 418.1841); δ_{H} (300 MHz, CDCl₃) 1.09 (3 H, d, *J* 6.5, 8-H₃), 2.06 and 2.19 (each 1 H, dt, *J* 14 and 7, 6-H), 2.55 (2 H, t, *J* 6.5, 3-H₂), 3.26 (1 H, hex, *J* 6.5, 7-H), 3.32 (3 H, s, 7-OCH₃), 3.57 (3 H, d, *J* 1.5, CH₃O), 3.81 (3 H, s, CH₃O), 4.76 (1 H, dt, *J* 8 and 6.5, 2-H), 5.24 (1 H, dt, *J* 15 and 7.5, 5-H), 5.41 (1 H, dt, *J* 15 and 7.5, 4-H), 7.15 (1 H, br d, *J* 5, NH), 7.43-7.45 (3 H, m, ArH) and 7.57-7.60 (2 H, m, ArH); *m/z* (CI) 435 (M⁺ + 18, 24%), 419 (M⁺ + 2, 20) and 418 (M⁺ + 1, 100); δ_{F} -70.4.

Methyl (2*S*,7*S*,4*E*)- and (2*R*,7*S*,4*E*)-7-methoxy-2-[(*S*)-2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl]amino-oct-4-enoates **133** and **137**

Following the procedure outlined above, the (*R*)-Mosher's chloride (24 μ L, 0.125 mmol), triethylamine (80 μ L, 0.567 mmol) and 4-dimethylaminopyridine (3 mg, cat.) were added to a mixture of the 2-amino-octenoates **131** and **135** (23 mg, 0.113 mmol) in dry DCM (1.5 mL), at room temperature and the mixture stirred for 15 h to afford after chromatography using petrol/ether (3 : 1) as the eluent, the *title compounds* **133** and **137** (36 mg, 77%) as a pale yellow oil, **133** : **137** = 70 : 30 (¹H NMR). Preparative HPLC using hexane/ethyl acetate (88 : 12) as the eluent gave the less polar, major (2*S*)-epimer **133** as a colourless oil, [α]_D +11 (*c* 1.34 in DCM) (Found: M⁺ + H, 418.1843. C₂₀H₂₇O₅NF₃ requires *M*, 418.1841); $\nu_{\text{max}}/\text{cm}^{-1}$ 720, 996, 1105, 1167, 1271, 1355, 1441, 1514, 1696, 1746, 2971 and 3416; δ_{H} (300 MHz, CDCl₃) 1.09 (3 H, d, *J* 6.5, 8-H₃), 2.07 and 2.18 (each 1 H, dt, *J* 13 and 6.5, 6-H), 2.55 (2 H, t, *J* 6.5, 3-H₂), 3.26 (1 H, hex, *J* 6.5, 7-H), 3.31 (3 H, s, 7-OCH₃), 3.56 (3 H, d, *J* 1.5, CH₃O), 3.80 (3 H, s, CH₃O), 4.74 (1 H, dt, *J* 8 and 6.5, 2-H), 5.25 (1 H, dt, *J* 15 and 7, 5-H), 5.42 (1 H, dt, *J* 15 and 7, 4-H), 7.17 (1 H, d, *J* 8, NH), 7.42-7.44 (3 H, m, ArH) and 7.58-7.61 (2 H, m, ArH); δ_{C} (75 MHz, CDCl₃) 18.65, 34.95, 38.96, 51.59, 52.42, 55.13, 55.85, 76.08, 125.27, 127.33, 128.36, 129.40, 131.66, 132.80, 165.95 and 171.50; *m/z* (CI) 419 (M⁺ + 2, 20%), 418 (M⁺ + 1, 100), 386 (10), 359 (4) and 236 (4); δ_{F} -70.4; followed by the more polar, minor (*R*)-epimer **137** as a colourless oil, [α]_D -1.9 (*c* 0.62 in DCM) (Found: M⁺ + H, 418.1838. C₂₀H₂₇O₅NF₃ requires *M*, 418.1841); $\nu_{\text{max}}/\text{cm}^{-1}$ 721, 977, 1104, 1166, 1270, 1355, 1440, 1512, 1697, 1746, 2973 and 3415; δ_{H} 1.17 (3 H, d, *J* 6.5, 8-H₃), 2.18 and 2.30 (each 1 H, dt, *J* 13 and 6.5, 6-H), 2.63 (2 H, m, 3-H₂), 3.33 (1 H, m, 7-H), 3.35 (3 H, s, 7-OCH₃), 3.40 (3 H, d, *J* 1.5, CH₃O), 3.78 (3 H, s, CH₃O), 4.73 (1 H, dt, *J* 7.5 and 6.5, 2-H), 5.39 (1 H, dt, *J* 15 and 7.5, 5-H), 5.63 (1 H, dt, *J* 15 and 7.5, 4-H), 7.42-7.47 (4 H, m, NH, ArH) and 7.59 (2 H, m, ArH); *m/z* (CI) 419 (M⁺ + 2, 20%), 418 (M⁺ + 1, 100), 386 (6) and 359 (4); δ_{F} -70.7.

Methyl (2*S*,7*S*,4*E*)-7-methoxy-2-(methoxycarbonyl)amino-oct-4-enoate **138**

Methyl carbamate (66 μ L, 0.85 mmol) and anhydrous potassium carbonate (118 mg, 0.850 mmol) were added to the amino-octenoates **131** and **135** (86 mg, 0.425 mmol) in chloroform (4 mL) at room temperature. After 16 h, water was added and the stirring continued for 10 min. Chloroform was added and the aqueous phase was extracted with DCM (3 x 7 mL). The organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Chromatography of the residue using DCM/ether (5 : 1) as the eluent gave the *title compound* **138** (91 mg, 83%) as a pale yellow oil, [α]_D -3.6 (*c* 0.9 in DCM) (Found: M⁺ + H, 260.1500. C₁₂H₂₂O₅N requires *M*, 260.1498); $\nu_{\text{max}}/\text{cm}^{-1}$ 780, 973, 1060, 1211, 1353, 1442, 1529, 1729, 2979 and 3336; δ_{H} (300 MHz, CDCl₃) 1.12 (3 H, d, *J* 6.5, 8-H₃), 2.14 and 2.25 (each 1 H, dt, *J* 14 and 7, 6-H), 2.51 (2 H, m, 3-H₂), 3.33 (1 H, m, 7-H), 3.32 (3 H, s, 7-OCH₃), 3.69 and 3.75 (each 3 H, s, CH₃O), 4.43 (1 H, m, 2-H), 5.30 (1 H, d, *J* 6, NH), 5.35 (1 H, dt, *J* 15 and 7.5, 5-H) and 5.56 (1 H, dt, *J* 15 and 7.5, 4-H); δ_{C} (75 MHz, CDCl₃) 18.67, 35.48, 38.87, 39.09, 52.22, 53.30, 55.84, 76.19, 125.60, 131.55, 156.27 and δ_{N} 172.28; *m/z* (CI) 277 (M⁺ + 18, 4%), 261 (M⁺ + 2, 12), 260 (M⁺ + 1, 100), 228 (36) and 196 (24).

The general procedures using the 2-methoxycarbonylamino-octenoate **138** (91 mg, 0.349 mmol), ozone and dimethyl sulfide (77 μ L, 1.048 mmol) then sodium borohydride (53 mg, 1.397 mmol) gave an alcohol (70 mg) that was lactonised using chloroform (4 mL) and glacial acetic acid (2 drops) to give, after chromatography using hexane/ethyl acetate/triethylamine (60 : 39.5 : 0.5) as eluent, the (*S*)-methoxycarbonylaminolactone (**S**)-**39** (33 mg, 58% from **135**) as a colourless oil, [α]_D -29 (*c* 0.9 in MeOH) lit.¹⁴ -39.5 (*c* 1 in MeOH) (Found: M⁺ + H, 160.0611. C₆H₁₀O₄N requires *M*, 160.0610).