Chapter 6

Experimental

6.1 Introduction

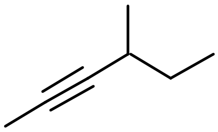
Infra-red spectra were recorded on a Perkin-Elmer FT-IR 1600 infra-red spectrometer using sodium chloride plates, and wavenumbers were measured relative to polystyrene (1630 cm^{-1}). ^{1}H and ^{13}C NMR spectra were recorded on Bruker NMR spectrometers (DRX 500, AM 400, DPX 250, AC 250 and AC 200). Chemical shifts were measured relative to tetramethylsilane (δ 0.00) or chloroform (δ 7.26). The coupling J is expressed in Hertz. In ^{13}C attached-proton test (APT) spectra, + denotes a signal in the same direction as the NMR solvent signal. Mass spectra were recorded on AE1 890, Kratos MS 50 or HP 5988A spectrometers. Melting points were measured using a *Gallenkamp* hot stage apparatus and are uncorrected.

Flash column chromatography was carried out using Merck Kieselgel 60 (230-400 mesh ASTM). Thin layer chromatography (TLC) was performed on glass plates coated to a thickness of 0.5 to 1.0 mm with Kieselgel 60 PF$_{254}$.

Tetrahydrofuran (THF) and diethyl ether (ether) were freshly distilled from lithium aluminium hydride under an argon atmosphere. Dichloromethane, carbon tetrachloride, acetonitrile, methanol, light petroleum, hexane and toluene were freshly distilled from calcium hydride under argon. Light petroleum refers to the fraction boiling in the region 40-60 °C. Other solvents and reagents where appropriate were purified before use.[312]

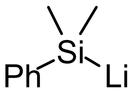
All compounds are new unless a reference is given, and recommended IUPAC names[313] have been used throughout.

6.2 Compounds for Chapter 3



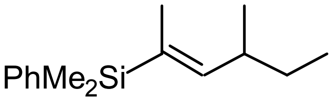
4-Methylhex-2-yne 123

One of the standard procedures for alkylation of terminal alkynes was followed.[227] n-Butyllithium (1.74 mol dm^{-3} solution in hexane, 24.5 cm^3, 43 mmol) was added to dry THF (40 cm^3) at –78 °C under an argon atmosphere with stirring. 3-Methylpent-1-yne (5.0 cm^3, 43 mmol) was added dropwise over 15 min with stirring, followed by methyl iodide (6.0 cm^3, 96 mmol), again dropwise over 15 min. The mixture was allowed to warm to room temperature as stirring was continued for 1 h and was then re-cooled to –78 °C, quenched with saturated aqueous ammonium chloride (20 cm^3) and allowed to warm to room temperature again. The layers were separated, the aqueous layer was extracted with ether (3 ∞ 10 cm^3) and the organic layers were combined, washed with brine, dried ($MgSO_4$), filtered and distilled using a Vigreux column under atmospheric pressure to give the alkyne **123**[229] (1.45 g, 35%) as a colourless liquid, bp 96-98 °C (lit.,[228] 99.5 ° C); R_f(light petroleum-ether, 1:1) 0.41; ν_{max}(film)/cm^{-1} 2205 (C+C); δ_H(400 MHz; $CDCl_3$) 2.28 (1H, sexd, *J* 5.8 and 1.0, C*H*Me), 1.78 (3H, d, *J* 2.4, MeC+C), 1.39 (2H, m, CH_2), 1.10 (3H, d, *J* 6.9, CH*Me*) and 0.95 (3H, t, *J* 7.4, CH_2*Me*); δ_C($CDCl_3$) 83.8+, 75.5+, 30.2+, 27.7–, 21.0–, 11.8– and 3.5–; *m/z* (EI) 96 (28%, M$^+$), 81 (47, M – Me), 67 (35, M – Et) and 57 (100, M – MeC+C) (Found M$^+$, 96.0940. C_7H_{12} requires *M*, 96.0939).



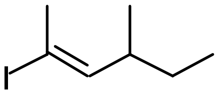
Dimethyl(phenyl)silyllithium 256

The method of Gilman was adapted.[314,315] Lithium shot (3.0 g, 0.42 mol) was washed with dry hexane under an argon atmosphere until the hexane was clear, and then the lithium was dried under high vacuum. THF (60 cm^3) was added and the mixture was cooled to 0 °C, chlorodimethyl(phenyl)silane (14 cm^3, 0.083 mol) was added with stirring and stirring was continued at 0 °C for 6 h. The resulting red-brown solution was stored in a freezer and used within a few days. Before use, the concentration of the dimethyl(phenyl)silyllithium **256** was determined by double titration[315,316] of aliquots (typically 0.50 cm^3) quenched with an excess of water and with an excess of dibromoethane. Water was added to the dibromoethane mixture and both mixtures were titrated against a standard solution of hydrochloric acid (0.10 mol dm^{-3}) using phenolphthalein as indicator. The difference between the two titres led to the molarity of the silyllithium solution, which was usually in the range 0.90-1.2 mol dm^{-3}.



***E*-2-Dimethyl(phenyl)silyl-4-methylhex-2-ene 124**

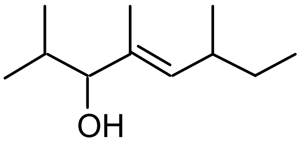
The standard method was followed.[137] Dimethyl(phenyl)silyllithium (0.9 mol dm^{-3} solution in THF, 7.8 cm^3, 7.0 mmol) was added to a stirred suspension of pre-dried copper(I) cyanide (310 mg, 3.4 mmol) at 0 °C with stirring under an argon atmosphere. After stirring at this temperature for 40 min, a solution of the alkyne **123** (560 mg, 2.3 mmol) in dry THF (0.5 cm^3) was added dropwise. The resulting solution was stirred for 1 h at 0 °C and then quenched with basic saturated aqueous ammonium chloride (10 cm^3). Ether (40 cm^3) was added, the layers separated and the ether layer washed with basic saturated aqueous ammonium chloride (2 ∞ 10 cm^3, until the aqueous layer was colourless). The combined aqueous layers were washed with ether (2 ∞ 10 cm^3) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum) gave the *vinylsilane* **124** (535 mg, 100%) as a colourless liquid; R_f(light petroleum) 0.49; ν_{max}(film)/cm^{-1} 1618 (C=C), 1248 (Si-C) and 832 (Si-C); δ_H(250 MHz; $CDCl_3$) 7.35 (5 H, m, Ph), 5.57 (1 H, dq, *J* 7.5 and 1.7, vinyl H), 2.49 (1 H, sept, *J* 7.0, C*H*MeEt), 1.65 (3 H, d, *J* 1.7, MeC=C), 1.39-1.21 (2 H, m, CH_2), 0.94 (3 H, d, *J* 6.6, CH*Me*Et), 0.85 (3 H, t, *J* 7.4, CH_2*Me*), 0.35 (3 H, s, Si$Me_A$$Me_B$) and 0.34 (3 H, s, Si$Me_A$$Me_B$); δ_C($CDCl_3$) 148.0+, 134.0–, 129.2+, 128.7–, 127.9–, 127.6–, 34.2–, 30.1+, 20.4–, 14.9–, 12.0– and –3.6–; *m/z* (EI) 232 (23%, M$^+$), 217 (22, M – Me) and 175 (20, M – MeCH_2CHMe) (Found: M$^+$, 232.1647. $C_{15}H_{24}Si$ requires *M*, 232.1647).



_E_-2-Iodo-4-methylhex-2-ene 125

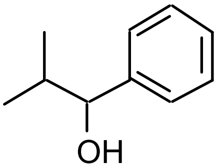
Method 1: The method of Kishi was followed.[235] Acetonitrile (3 cm^3) was added to dried vinylsilane **124** (57 mg, 0.25 mmol) with stirring, and *N*-iodosuccinimide (114 mg, 0.51 mmol) was added in one portion. The mixture was stirred for 30 min and then quenched by addition of saturated aqueous sodium sulfite (5 cm^3) and stirred vigorously until a clear colourless solution was obtained. A 1/1 (v/v) mixture of light petroleum and ethyl acetate was added, the layers separated and the organic layer washed with aqueous sodium hydroxide (1.0 mol dm^{-3}, 2 ∞ 10 cm^3) and with brine, dried ($MgSO_4$), filtered through a short pad of silica with the same light petroleum/ethyl acetate solvent mixture and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum) gave the *vinyl iodide* **125** (28 mg, 50%); R_f(light petroleum) 0.58; ν_{max}(film/cm^{-1}) 1690 (C=C); δ_H(250 MHz; $CDCl_3$) 5.93 (1 H, dq, *J* 9.9 and 1.5, vinyl H), 2.38 (3 H, d, *J* 1.5, MeC=), 2.34-2.25 (1 H, m, MeEtC*H*), 1.30 (2 H, m, MeCH_2), 0.95 (3 H, d, *J* 6.7, *Me*EtCH) and 0.86 (3 H, t, *J* 7.5, *Me*CH); δ_C(CDCl$_3$) 130.3, 127.5, 37.4, 29.8, 27.8, 20.2 and 11.7; *m/z* (EI) 209 (13%, M – Me) and 96 (21, M – I) (Found: M$^+$ – I, 96.0936. $C_7H_{13}I$ requires *M*, 96.0939).

Method 2: Iodine monochloride (1.0 mol dm^{-3} solution in dichloromethane, 0.30 cm^3, 0.30 mmol) was added to a solution of the vinylsilane **124** (34 mg, 0.15 mmol) in dry dichloromethane (4 cm^3) at –78 °C under an argon atmosphere with the reaction vessel protected from light. After stirring for 40 min, dichloromethane (5 cm^3) was added and the solution was allowed to warm to room temperature. Saturated aqueous sodium thiosulfate (10 cm^3) was added and the mixture stirred for 20 min. The layers were separated, the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3), the organic fractions combined, washed with brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give a yellow liquid. Chromatography (SiO$_2$, light petroleum) gave the *vinyl iodide* **125** (18 mg, 54%) with data identical to those given above.



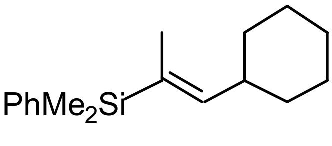
***E*-2,4,6-Trimethyloct-4-en-3-ol 127 (Attempted)**

The method of Kishi was followed.[218] Freshly-distilled isobutyraldehyde (0.025 cm^3, 0.26 mmol) was added to vinyl iodide **125** (49 mg, 0.22 mmol) and distilled dimethyl sulfoxide (2 cm^3) under an argon atmosphere. The flask was transferred to a glove box where dry chromium(II) chloride (60 mg, 0.48 mmol) was added portionwise, and a speck of pre-dried nickel(II) chloride was added to the mixture. The mixture was stirred for 23 h under an argon atmosphere and then cooled in ice and quenched with water (5 cm^3). After stirring for 10 min, the solution was extracted with ethyl acetate (3 ∞ 10 cm^3), the organic fractions combined, washed with brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give only a mixture of starting materials.



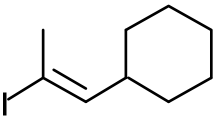
2-Methyl-1-phenylpropan-1-ol 128

The method of Kishi was followed.[218] Freshly-distilled isobutyraldehyde (0.02 cm^3, 0.22 mmol) was added to iodobenzene (0.02 cm^3, 0.18 mmol) and distilled dimethyl sulfoxide (2 cm^3) under an argon atmosphere. The flask was transferred to a glove box where dry chromium(II) chloride (49 mg, 0.40 mmol) was added portionwise, and a speck of pre-dried nickel(II) chloride was added to the mixture. The mixture was stirred for 20 h under an argon atmosphere and then cooled in ice and quenched with water (5 cm^3). After stirring for 10 min, the solution was extracted with ethyl acetate (3 ∞ 10 cm^3), the organic fractions combined, washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the alcohol **128**[239] as a yellow liquid (20 mg, 74%); R_f(light petroleum-ether, 1:1) 0.38; ν_{max}(film)/cm^{-1} 3394 (O-H), 1492-1383 (C=C); δ_H(250 MHz; $CDCl_3$) 7.32 (5 H, m, Ph), 4.36 (1 H, d, *J* 7.1, C*H*OH), 1.96 (1 H, sept, *J* 6.6, C*H*Me_2), 1.00 (3 H, d, *J* 6.7, CH$\mathit{Me}_A\mathrm{Me}_B$) and 0.80 (3 H, d, *J* 6.8, CH$\mathrm{Me}_A\mathit{Me}_B$).



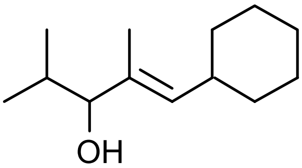
***E*-1-Cyclohexyl-2-dimethyl(phenyl)silylprop-1-ene 132**

The standard method was followed.[137] Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF, 2.5 cm^3, 2.5 mmol) was added to pre-dried copper(I) cyanide (110 mg, 1.2 mmol) at 0 °C with stirring under an argon atmosphere. After stirring at this temperature for 40 min, a solution of 1-cyclohexylprop-1-yne[240] (0.11 cm^3, 0.8 mmol) in dry THF (0.5 cm^3) was added dropwise. The resulting solution was stirred for 1 h at 0 °C and then quenched with basic saturated aqueous ammonium chloride (10 cm^3). Ether (40 cm^3) was added, the layers separated and the organic layer washed with basic saturated aqueous ammonium chloride (2 ∞ 10 cm^3, until the aqueous layer was colourless). The combined aqueous layers were extracted with ether (2 ∞ 10 cm^3) and the combined organic layers were dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum) gave the *vinylsilane* **132** (200 mg, 100%) as a colourless liquid; R_f(light petroleum) 0.52; ν_{max}(film)/cm^{-1} 1617 (C=C), 1247 (Si-C) and 831 (Si-C); δ_H(250 MHz; $CDCl_3$) 7.49 (2 H, m, *m*-Ph), 7.45 (3 H, m, *o,p*-Ph), 5.65 (1 H, dq, *J* 8.6 and 1.7, vinyl H), 2.46-2.29 (1 H, m, =C-CH), 1.67 (4 H, m, CH_2 in cyclohexyl ring), 1.66 (3 H, d, *J* 1.7, MeC=), 1.37-1.00 (6 H, m, CH_2 in cyclohexyl ring) and 0.31 (6 H, s, Me_2Si); δ_C($CDCl_3$) 147.6–, 139.1+, 133.9–, 131.4+, 128.7–, 127.6–, 37.3–, 32.7+, 26.1+, 26.0+, 14.7– and –3.4–; *m/z* (EI) 258 (10%, M$^+$), 169 (60) and 135 (71, $PhMe_2Si$) (Found: M$^+$, 258.1794. $C_{17}H_{26}Si$ requires *M*, 258.1804).



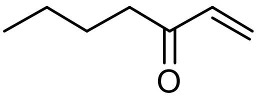
***E*-(2-Iodopropenyl)cyclohexane 133**

The method of Kishi was followed.[235] Acetonitrile (5 cm^3) was added to vinylsilane **132** (518 mg, 2.0 mmol) with stirring and *N*-iodosuccinimide (944 mg, 4.0 mmol) was added in one portion. The mixture was stirred for 30 min and then quenched by addition of saturated aqueous sodium sulfite (10 cm^3) and stirred vigorously until a clear colourless solution was obtained. A 1/1 (v/v) mixture of light petroleum and ethyl acetate was added, the layers separated and the organic layer washed with aqueous sodium hydroxide (2 ∞ 10 cm^3, 1 N), with brine, dried ($MgSO_4$), filtered through a short pad of silica with the same light petroleum/ethyl acetate solvent and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the *vinyl iodide* **133** (365 mg, 73%); R_f(light petroleum-ether; 1:1) 0.85; ν_{max}(film/cm^{-1}) 1633 (C=C); δ_H(250 MHz; $CDCl_3$) 6.02 (1 H, dq, *J* 9.4 and 1.5, vinyl H), 2.38 (3 H, d, *J* 1.5, MeC=), 2.24 (1 H, m, =CHC*H*), 1.67 (4 H, m, CH_2 in cyclohexyl ring) and 1.29-1.06 (6 H, m, CH_2 in cyclohexyl ring); $\delta_C(CDCl_3)$ 147.1–, 127.9+, 40.1–, 32.5+, 27.7–, 25.8+ and 25.7+; *m/z* (EI) 123 (1%, $M^+ - I$) (Found: $M^+ - I$, 123.1181. C_9H_{15} requires *M*, 123.1174).



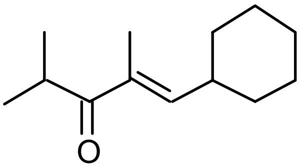
E-1-Cyclohexyl-2,4-dimethylpent-1-en-3-ol **134**

The method of Kishi was followed.[218] Freshly-distilled isobutyraldehyde (0.20 cm^3, 2.2 mmol) was added to vinyl iodide **133** (365 mg, 1.5 mmol) and distilled dimethyl sulfoxide (5 cm^3) under an argon atmosphere. The flask was transferred to a glove box where dry chromium(II) chloride (395 mg, 3.2 mmol) was added portionwise, and a speck of pre-dried nickel(II) chloride was added to the mixture. The mixture was stirred for 21 h under an argon atmosphere and then cooled in ice and quenched with water (5 cm^3). After stirring for 10 min, the solution was extracted with ethyl acetate (3 ∞ 10 cm^3), the organic fractions combined, washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a pale yellow liquid. Chromatography (SiO_2, CH_2Cl_2) gave the *alcohol* **134** (250 mg, 87%); $R_f(CH_2Cl_2)$ 0.35; $\nu_{max}(film/cm^{-1})$ 3384 (br, O-H) and 1651 (C=C); δ_H(250 MHz; $CDCl_3$) 5.18 (1 H, d, *J* 9.0, vinyl H), 3.54 (1 H, dd, *J* 8.2 and 3.1, C*H*OH), 2.20 (1 H, m, =CHC*H*), 1.70 (5 H, m), 1.59 (3 H, d, *J* 1.3, MeC=), 1.32-1.05 (6 H, m), 0.97 (3 H, d, *J* 6.6, $\mathit{Me}_A\mathrm{Me}_B$CH) and 0.77 (3 H, d, *J* 6.8, $\mathrm{Me}_A\mathit{Me}_B$CH); $\delta_C(CDCl_3)$ 134.5+, 133.8–, 84.1–, 36.6–, 33.0+, 31.1–, 26.1+, 26.0+, 19.4–, 18.6– and 11.3–; *m/z* (EI) 196 (15%, M^+), and 153 (100, M – Me_2CH) (Found: M^+, 196.1840. $C_{13}H_{24}O$ requires *M*, 196.1827).



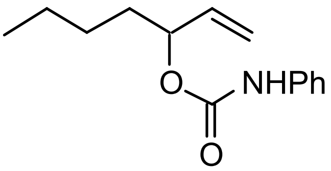
Hept-1-en-3-one 257

The standard method was followed.[317,318] Pyridinium chlorochromate (950 mg, 4.40 mmol) was suspended in dry dichloromethane (5 cm^3) and 1-hepten-3-ol (0.30 cm^3, 2.20 mmol) in dry dichloromethane (3 cm^3) was rapidly added at room temperature under an argon atmosphere. The solution became briefly homogeneous before depositing the black insoluble reduced reagent. The mixture was stirred for 48 h before being diluted with ether (10 cm^3). The solvent was decanted, the black solid washed with ether (2 ∞ 10 cm^3), the organic layers filtered through cotton wool and then through filter paper, washed with hydrochloric acid (1 mol dm^{-3}, 5 cm^3), saturated aqueous sodium hydrogen carbonate (5 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the ketone **257**[319] as a pale yellow liquid (100 mg, 41%); $R_f(CH_2Cl_2)$ 0.58; ν_{max}(film/cm^{-1}) 1680 (C=O) and 1615 (C=C);[319] δ_H(250 MHz; $CDCl_3$) 6.36 (1 H, dd, *J* 17.7 and 10.2, COCH=), 6.21 (1 H, dd, *J* 17.7 and 1.6, =C$H_{trans\text{-to-H}}$C$H_{cis\text{-to-H}}$), 5.81 (1 H, dd, *J* 10.2 and 1.6, =C$H_{trans\text{-to-H}}$C$H_{cis\text{-to-H}}$), 2.58 (2 H, t, *J* 7.4, $COCH_2$), 1.58 (2 H, m), 1.34 (2 H, m) and 0.92 (3 H, t, *J* 7.3, Me).



***E*-1-Cyclohexyl-2,4-dimethylpent-1-en-3-one 138**

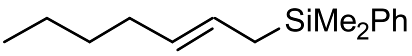
The standard method was followed.[317,318] Pyridinium chlorochromate (568 mg, 2.60 mmol) was suspended in dry dichloromethane (5 cm^3) and alcohol **134** (103 mg, 0.53 mmol) in dry dichloromethane (3 cm^3) was rapidly added at room temperature under an argon atmosphere. The solution became briefly homogeneous before depositing the black insoluble reduced reagent. The mixture was stirred for 48 h before being diluted with ether (10 cm^3). The solvent was decanted, the black solid washed with ether (2 ∞ 10 cm^3), the organic layers filtered through cotton wool and then through filter paper, washed with hydrochloric acid (1 mol dm^{-3}, 5 cm^3), saturated aqueous sodium hydrogen carbonate (5 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a pale yellow liquid. Chromatography (SiO_2, CH_2Cl_2) gave the *ketone* **138** (43 mg, 54%); R_f(CH_2Cl_2) 0.56; ν_{max}(film/cm^{-1}) 1707 (C=O) and 1665 (C=C); δ_H(250 MHz; $CDCl_3$) major isomer: 6.41 (1 H, br d, *J* 10.4, vinyl H), 3.31 (1 H, sept, *J* 6.8, CHCO), 2.77 (1 H, qn, *J* 6.9, =CHC*H*), 1.78 (3 H, d, *J* 1.3, MeC=), 1.70 (5 H, m), 1.46 (6 H, d, *J* 5.3, Me_2C) and 1.20 (5 H, m); δ_C($CDCl_3$) (both isomers present) 148.5–, 146.9–, 134.2+, 128.8+, 66.2–, 64.9–, 42.8–, 37.2–, 32.8–, 29.9–, 29.3–, 28.7–, 28.5–, 28.3–, 27.9+, 27.7–, 13.4+ and 13.2+; *m/z* (EI) 194 (15%, M^+), 151 (80, M – ^{i}Pr), 111 (66, M - Cy), 83 (91, Cy), 71 (51, ^{i}PrCO) and 43 (100, ^{i}Pr) (Found: M^+, 194.1671. $C_{13}H_{22}O$ requires *M*, 194.1671).



1-Butylprop-2-en-1-yl *N*-phenylcarbamate 140

The standard method was followed.[192,195] Phenyl isocyanate (0.95 cm^3, 8.7 mmol) was added dropwise to a stirred solution of 1-hepten-3-ol (1.20 cm^3, 8.8 mmol), 4-dimethylaminopyridine (1.07 g, 8.8 mmol) and triethylamine (1.35 cm^3, 9.8 mmol) in dry dichloromethane (10 cm^3) under an argon atmosphere at room temperature and stirred for 3 h. Water (5 cm^3) was added and the mixture was extracted with dichloromethane (3 ∞ 10 cm^3). The organic fractions were combined, washed with hydrochloric acid (1 mol dm^{-3}, 5 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, CH_2Cl_2) gave the carbamate **140**[252,253] (1.83 g, 89%) as a yellow liquid; R_f(CH_2Cl_2) 0.61; ν_{max}(film)/cm^{-1} 3320 (N-H), 1702 (C=O) and 1601 (Ph); δ_H(250

MHz; CDCl$_3$) 7.39 (2 H, d, *J* 8.3, *o*-Ph), 7.30 (2 H, t, *J* 8.0, *m*-Ph), 7.06 (1 H, tt, *J* 7.2 and 1.3, *p*-Ph), 6.58 (1 H, br s, NH), 5.84 (1 H, ddd, *J* 17.3, 10.8 and 6.6, CH$_2$=C*H*), 5.30 (1 H, dt, *J* 17.1 and 1.3, C$H_{trans\text{-to-H}}$H$_{cis\text{-to-H}}$=), 5.24-5.17 (2 H, m, CH$_{trans\text{-to-H}}$$H_{cis\text{-to-H}}$= and CHO), 1.64 (2 H, m, C*H*$_2$CHO), 1.36 (4 H, m, Me(C*H*$_2$)$_2$) and 0.91 (3 H, m, Me); δ_C(CDCl$_3$) 138.0, 136.8, 129.0, 123.3, 118.6, 116.7, 75.9, 34.1, 27.2, 22.5 and 14.0; *m/z* (EI) 233 (37%, M$^+$), 189 (3, M – CO$_2$), 97 (41, M – PhNHCO$_2$) and 93 (68, PhNH$_2$) (Found: M$^+$, 233.1417. C$_{14}$H$_{19}$NO$_2$ requires *M*, 233.1416).



_E_-1-Dimethyl(phenyl)silylhept-2-ene 141

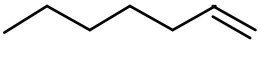
Method 1: One of the standard methods was followed.[192,195] Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF, 0.50 cm^3, 0.50 mmol) was added dropwise to a stirred slurry of dry copper(I) iodide (82 mg, 0.43 mmol) and triphenylphosphine (225 mg, 0.86 mmol) in dry ether (3 cm^3) at 0 °C under an argon atmosphere. The mixture was stirred at this temperature for 20 min. n-Butyllithium (1.7 mol dm^{-3} solution in hexane, 0.25 cm^3, 0.43 mmol) was added dropwise to a stirred solution of the carbamate **140** (100 mg, 0.43 mmol) in dry THF (2 cm^3) at 0 °C under an argon atmosphere. After stirring at this temperature for 2 min, the solution was added *via* cannula to the silylcopper reagent prepared above at 0 °C. The resulting mixture was stirred at this temperature for a further 4 h. The reaction was quenched with basic saturated aqueous ammonium chloride (10 cm^3), the mixture was filtered through celite and extracted with light petroleum (3 ∞ 10 cm^3). The organic layers were combined, washed with basic saturated aqueous ammonium chloride (10 cm^3), brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure. Chromatography (SiO$_2$, CH$_2$Cl$_2$) gave the allylsilane **141**[255] (49 mg, 49%) as a yellow liquid; R_f(CH$_2$Cl$_2$) 0.86; ν_{max}(film)/cm^{-1} 1247 (SiMe), 1113 (SiPh) and 964 (*trans*-CH=CH); δ_H(250 MHz; CDCl$_3$) 7.72-7.49 (5 H, m, Ph), 5.43-5.19 (2 H, m, CH=CH), 1.95 (2 H, m, CH$_2$C*H*$_2$CH=), 1.68 (2 H, m, CH$_2$Si), 1.30 (4 H, m, MeC*H*$_2$C*H*$_2$), 0.88 (3 H, m, Me) and 0.34 (6 H, s, SiMe$_2$);

δ_C($CDCl_3$) 139.0, 134.2, 132.1, 131.9, 129.9, 125.2, 32.4, 32.1, 22.1, 21.6, 13.9 and –3.9; *m/z* (EI) 232 (10%, M^+), and 135 (100, $PhMe_2Si$) (Found: M^+, 232.1652. $C_{15}H_{24}Si$ requires *M*, 232.1647).

Method 2: One of the standard methods was followed.[192] n-Butyllithium (1.7 mol dm^{-3} solution in hexane, 0.25 cm^3, 0.43 mmol) was added dropwise to a stirred solution of the carbamate **140** (103 mg, 0.43 mmol) in dry THF (5 cm^3) at –78 °C under an argon atmosphere. After stirring at this temperature for 1 min, the solution was added *via* cannula to a stirred slurry of dry copper(I) iodide (82 mg, 0.43 mmol) and triphenylphosphine (225 mg, 0.86 mmol) in dry ether (3 cm^3) at 0 °C under an argon atmosphere. The resulting mixture was stirred at this temperature for 30 min. Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF, 0.50 cm^3, 0.52 mmol) was added dropwise to the mixture and stirring was continued at this temperature for 2 h. The reaction was quenched with saturated aqueous ammonium chloride (10 cm^3), the layers were separated and the aqueous layer was extracted with ether (3 ∞ 10 cm^3). The organic layers were combined, washed with basic saturated aqueous ammonium chloride (10 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a mixture containing the *allylsilane* **141** with data (NMR) identical to that obtained above.

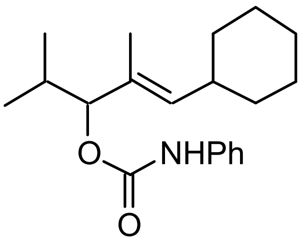
Method 3: The procedure of Singer was followed.[256] Zinc chloride (1.0 mol dm^{-3} solution in ether, 0.90 cm^3, 0.86 mmol) was placed in a dry round bottom flask and the ether removed under high vacuum. THF (4 cm^3) was added under an argon atmosphere and the solution cooled to –30 °C. Methyllithium (1.4 mol dm^{-3}, 1.20 cm^3, 1.70 mmol) was added and the mixture stirred at this temperature for 15 min. Dimethyl(phenyl)silyllithium (1.1 mol dm^{-3}, 0.80 cm^3, 0.86 mmol) was added at this temperature and the mixture stirred for another 15 min to give a dark red homogeneous solution. The solution was cooled to –78 °C. n-Butyllithium (1.5 mol dm^{-3}, 0.30 cm^3, 0.47 mmol) was added to the carbamate **140** (100 mg, 0.43 mmol) in THF (5 cm^3) at –78 °C under an argon atmosphere and stirred for 5 min before adding *via* cannula to the silylzincate reagent previously prepared. The resulting mixture was stirred for 2 h at –78 °C before being allowed to warm to 0 °C and quenched with saturated aqueous ammonium chloride (10 cm^3). The layers were separated and the aqueous layer was extracted with ether (3 ∞ 10 cm^3). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, CH_2Cl_2) gave the allylsilane **141** (102 mg, 100%) as a yellow liquid with data (NMR) identical to those obtained above.

Method 4: (Attempted) n-Butyllithium (1.5 mol dm^{-3}, 0.30 cm^3, 0.45 mmol) was added to the carbamate **140** (100 mg, 0.43 mmol) in THF (5 cm^3) at –78 °C under an argon atmosphere and stirred for 5 min. Dimethyl(phenyl)silyllithium (1.1 mol dm^{-3}, 0.80 cm^3, 0.88 mmol) was added and the mixture stirred at this temperature for 3 h before allowing to warm to 0 °C and quenching with saturated aqueous ammonium chloride (10 cm^3). The layers were separated and the aqueous layer was extracted with ether (3 ∞ 10 cm^3). The organic layers were combined, washed with brine (10 cm^3), dried ($MgSO_4$), filtered and evaporated under reduced pressure to give mainly recovered starting material.



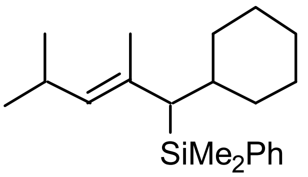
Hept-1-ene 142

One drop of trifluoroacetic acid was added to the NMR sample of the allylsilane **141** to give the alkene **142**[320] which was not isolated; R_f(CH_2Cl_2) 0.93; ν_{max}($CDCl_3$)/cm^{-1} 1639 (C=C); δ_H(250 MHz; $CDCl_3$) 5.82 (1 H, m, C*H*=CH_2), 4.96 (2 H, m, CH=CH_2), 2.05 (2 H, m, CH_2CH=), 1.35-1.26 (6 H, m) and 0.89 (3 H, br t, Me).



***E*-1-Cyclohexyl-2,4-dimethylpent-1-en-3-yl *N*-phenylcarbamate 143**

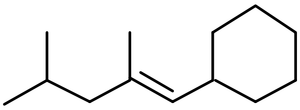
The standard method was followed.[192,195] Phenyl isocyanate (0.12 cm^3, 1.10 mmol) was added dropwise to a stirred solution of the alcohol **134** (223 mg, 1.14 mmol), 4-dimethylaminopyridine (139 mg, 1.14 mmol) and triethylamine (0.17 cm^3, 1.23 mmol) in dry dichloromethane (5 cm^3) under an argon atmosphere at room temperature and stirred for 4 h. Water (5 cm^3) was added and the mixture was extracted with dichloromethane (3 ∞ 10 cm^3). The organic fractions were combined, washed with hydrochloric acid (1 mol dm^{-3}, 5 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, CH_2Cl_2) gave the *carbamate* **143** (217 mg, 60%) as a colourless liquid; R_f(CH_2Cl_2) 0.66; ν_{max}(film)/cm^{-1} 3343 (NH), 1701 (C=O) and 1601 (C=C); δ_H(250 MHz; $CDCl_3$) 7.39 (2 H, d, *J* 8.3, *o*-Ph), 7.30 (2 H, t, *J* 7.4, *m*-Ph), 7.04 (1 H, tt, *J* 7.2 and 1.6, *p*-Ph), 6.56 (1 H, br s, NH), 5.31 (1 H, d, *J* 8.7, vinyl H), 4.78 (1 H, d, *J* 8.7, CHO), 2.17 (1 H, m, =CHC*H*), 1.92 (1 H, oct, *J* 6.7, Me_2CH), 1.65 (4 H, m, CH_2), 1.62 (3 H, d, *J* 1.3, MeC=), 1.36-1.01 (6 H, m, CH_2), 0.96 (3 H, d, *J* 6.6, Me_AMe_BCH) and 0.83 (3 H, d, *J* 6.8, Me_AMe_BCH); δ_C($CDCl_3$) 202.0, 138.2, 135.8, 130.2, 129.0, 123.1, 118.5, 85.9, 36.7, 32.8, 29.7, 26.1, 25.9, 19.1, 18.7 and 12.0; *m/z* (EI) 315 (1%, M$^+$) and 179 (34, M – $PhNHCO_2$) (Found: M$^+$, 315.2177. $C_{20}H_{29}NO_2$ requires *M*, 315.2198).



***E*-1-Cyclohexyl-1-dimethyl(phenyl)silyl-2,4-dimethylpent-2-ene 144 (Attempted)**

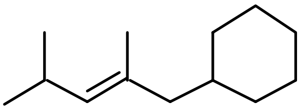
Method 1: One of the standard methods was followed.[192,195] Dimethyl(phenyl)silyllithium (0.92 mol dm^{-3} solution in THF, 1.10 cm^3, 0.99 mmol) was added dropwise to a stirred slurry of dry copper(I) iodide (94 mg, 0.50 mmol) and triphenylphosphine (260 mg, 0.99 mmol) in dry ether (6 cm^3) at 0 °C under an argon atmosphere. The mixture was stirred at this temperature for 20 min. n-Butyllithium (1.5 mol dm^{-3} solution in hexane, 0.12 cm^3, 0.19 mmol) was added dropwise to a stirred solution of the carbamate **143** (52 mg, 0.17 mmol) in dry THF (4 cm^3) at 0 °C under an argon atmosphere. After stirring at this temperature for 5 min, the solution was added *via* cannula to the silylcopper reagent prepared above at 0 °C. The resulting mixture was stirred overnight, during which time the reaction warmed to room temperature. The reaction was recooled to 0 °C and quenched with basic saturated aqueous ammonium chloride (10 cm^3), the mixture was filtered through celite and extracted with light petroleum (3 ∞ 10 cm^3). The organic layers were combined, washed with basic saturated aqueous ammonium chloride (10 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give recovered carbamate starting material only.

Method 2: The procedure of Singer was followed.[256] Zinc chloride (1.0 mol dm^{-3} solution in ether, 0.35 cm^3, 0.35 mmol) was placed in a dry round bottom flask and the ether removed under high vacuum. THF (2 cm^3) was added under an argon atmosphere and the solution cooled to –30 °C. Methyllithium (1.4 mol dm^{-3}, 0.50 cm^3, 0.68 mmol) was added and the mixture stirred at this temperature for 15 min. Dimethyl(phenyl)silyllithium (1.1 mol dm^{-3}, 0.30 cm^3, 0.34 mmol) was added at this temperature and the mixture stirred for another 15 min to give a dark red homogeneous solution. The solution was cooled to –78 °C. n-Butyllithium (1.5 mol dm^{-3}, 0.13 cm^3, 0.19 mmol) was added to the carbamate **143** (54 mg, 0.17 mmol) in THF (3 cm^3) at –78 °C under an argon atmosphere and stirred for 5 min before adding *via* cannula to the silylzincate reagent previously prepared. The resulting mixture was stirred for 2.5 h at –78 °C before being allowed to warm to 0 °C and quenched with saturated aqueous ammonium chloride (10 cm^3). The layers were separated and the aqueous layer was extracted with ether (3 ∞ 10 cm^3). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give recovered carbamate starting material only.



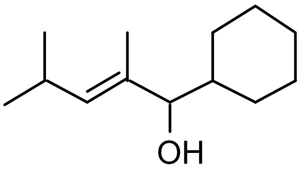
148

+



149

+



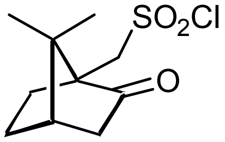
147

***E*-1-Cyclohexyl-2,4-dimethylpent-1-ene 148, *E*-1-Cyclohexyl-2,4-dimethylpent-2-ene 149, *E*-1-Cyclohexyl-2,4-dimethylpent-1-en-3-ol 134 and *E*-1-Cyclohexyl-2,4-dimethylpent-2-en-1-ol 147**

The method of Corey was followed.[245] Sulfur trioxide-pyridine complex (438 mg, 2.76 mmol) was added to alcohol **134** (180 mg, 0.92 mmol) in THF (6 cm^3) at 0 °C under an argon atmosphere and the mixture was allowed to warm to room temperature overnight. The mixture was recooled to 0 °C and lithium aluminium hydride (350 mg, 9.20 mmol) was slowly added and the mixture stirred overnight, during which time the temperature was allowed to rise to room temperature. The mixture was recooled to 0 °C and aqueous sodium hydroxide (1 mol dm^{-3}, 5 cm^3) was added slowly. Ether (10 cm^3) was added, the layers separated and the aqueous layer extracted with ether (3 ∞ 10 cm^3). The organic layers were combined, washed with hydrochloric acid (1 mol dm^{-3}, 3 ∞ 10 cm^3), saturated aqueous sodium hydrogen carbonate (10 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a yellow liquid. Chromatography (SiO_2, CH_2Cl_2) gave a mixture of alcohols **134** and **147** in a 1:1 ratio (14 mg, 8%) as a colourless liquid; R_f(CH_2Cl_2) 0.38;

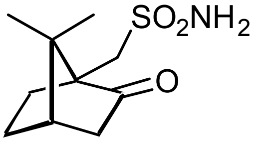
ν_{max}(CHCl$_3$)/cm^{-1} 3389 (O-H); δ_H(500 MHz; CDCl$_3$) **134** previously characterised, signals from **147** as follows: 5.14 (1 H, d, *J* 9.1, =CH), 3.58 (1 H, d, *J* 8.2, C*H*OH), 2.53 (1 H, dsept, *J* 9.0 and 6.7, C*H*Me$_2$), 1.78-1.61 (4 H, m), 1.58 (3 H, d, *J* 1.0, =CMe), 1.43-1.02 (7 H, m), 0.96 (3 H, d, *J* 6.4, *Me*$_A$Me$_B$CH) and 0.93 (3 H, d, *J* 6.7, Me$_A$*Me*$_B$CH); δ_C(CDCl$_3$) 135.7–, 134.5+, 133.5+, 133.9–, 84.2–, 83.2–, 40.6–, 36.6–, 33.0+, 31.1–, 29.6+, 29.3+, 26.8–, 26.5+, 26.2+, 26.1+, 26.0+, 22.9–, 19.5–, 18.6–, 11.3– and 11.1–; *m/z* (EI) 196 (22%, M$^+$) (Found: M$^+$, 196.1831. $C_{13}H_{24}O$ requires *M*, 196.1827) and a mixture of *alkenes* **148** and **149** in a 1:1 ratio (40 mg, 24%) as a colourless liquid; R_f(CH$_2$Cl$_2$) 0.85; ν_{max}(film)/cm^{-1} 1666 (C=C); δ_H(500 MHz; CDCl$_3$) 4.94 (1 H, d, *J* 8.9, CH= in **148**), 4.90 (1 H, d, *J* 9.0, CH= in **149**), 2.48 (1 H, dsept, *J* 8.9 and 6.7, Me$_2$C*H* in **149**), 2.16 (1 H, m, C*H*-CH= in **148**), 1.81 (2 H, d, *J* 7.1, CH$_2$C= in **149**), 1.80 (2 H, d, *J* 7.2, CH$_2$C= in **148**), 1.76-1.59 (11 H, m), 1.57 (6 H, s, MeC= in **148** and **149**), 1.36 (1 H, m, Me$_2$C*H* in **148**), 1.29-0.97 (10 H, m), 0.92 (6 H, d, *J* 6.6, CH*Me*$_2$in **149**) and 0.83 (6 H, d, *J* 6.5, CH*Me*$_2$in **148**); δ_C(CDCl$_3$) 133.9–, 132.4–, 132.2+, 131.0+, 49.6+, 48.0+, 37.0–, 35.5–, 33.4+, 33.3+, 27.1–, 26.8+, 26.5+, 26.2+, 26.1+, 25.9–, 23.3–, 22.3– and 16.0–; *m/z* (FAB) 180 (78%, M$^+$) and 123 (100, M – Me$_2$CHCH$_2$) (Found: M$^+$, 180.1869. $C_{13}H_{24}$ requires *M*, 180.1878).

6.3 Compounds for Chapter 4



(1*R*)-(–)-Camphorsulfonyl chloride 164

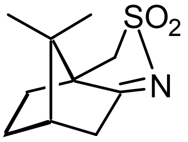
Pre-dried (1R)-(–)-camphorsulfonic acid (49.57 g, 0.214 mol) was dissolved in distilled chloroform (300 cm^3) which had been filtered through silica. Freshly-distilled thionyl chloride (20 cm^3, 0.274 mol) was added dropwise over 1 h while the mixture was heated to reflux. Refluxing was continued for a further 18 h before the dark brown solution[279,280] was allowed to cool and was kept under an argon atmosphere to be used immediately in the next reaction without isolation or purification.



(1*R*)-(–)-Camphorsulfonamide 165

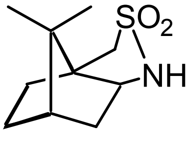
Crude (–)-camphorsulfonyl chloride **164** in chloroform (prepared from 49.57 g (–)-camphorsulfonic acid, 0.214 mol) was added slowly by cannula over 30 min to concentrated aqueous ammonia (600 cm^3) at 0 °C with vigorous stirring. The resulting mixture was allowed to warm to room temperature and was stirred for a further 4 h. The layers were separated and the aqueous layer was extracted with dichloromethane (3 ∞ 100 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the (–)-sulfonamide **165**[279,280] (40.0 g, 81% over two steps) as cream needles, mp 105-110 °C (lit.,[321] 131-132 °C); $R_f(CH_2Cl_2)$ 0.37, mixed with the sulfonimine **166** (about 70% present); ν_{max}(Nujol)/cm^{-1} 3302 (NH_2), 1733 (C=O), 1321 (SO_2N) and 1134 (SO_2N); δ_H(250 MHz; $CDCl_3$) 5.39 (2 H, br s, NH_2), 3.46 (1 H, d, *J* 15.1,

$CH_AH_BSO_2$), 3.11 (1 H, d, *J* 15.5, $CH_AH_BSO_2$), 0.99 (3 H, s, CMe_AMe_B) and 0.91 (3 H, s, CMe_AMe_B).



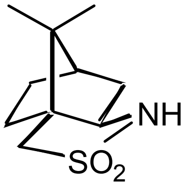
(7*R*)-(+)-Camphorsulfonimine 166

(–)-Camphorsulfonamide **165** (39.80 g, 0.172 mol) and Amberlyst 15 ion-exchange resin[288] (4.95 g) in dry toluene (500 cm^3) were stirred and heated to reflux under an argon atmosphere for 4 h in a round bottom flask fitted with a Dean Stark trap. The mixture was allowed to cool to about 50 °C and dichloromethane (50 cm^3) was added. The warm solution was filtered and the filtrate evaporated under reduced pressure to give the (+)-sulfonimine **166**[279,280] (31.12 g, 85%) as a white solid, mp 220-221 °C (from EtOH) (lit.,[279,280] 225-228 °C); $R_f(CH_2Cl_2)$ 0.30 (lit.,[321] 0.28); ν_{max}(Nujol)/cm^{-1} 1639 (C=N), 1312 (SO_2N) and 1170 (SO_2N); δ_H(250 MHz; $CDCl_3$) 3.18 (1 H, d, *J* 13.3, $CH_AH_BSO_2$), 2.97 (1 H, d, *J* 13.3, $CH_AH_BSO_2$), 2.82-2.72 (1 H, m), 2.38 (1 H, d, *J* 19.3), 2.26 (1 H, t, *J* 4.3), 2.12-1.98 (2 H, m), 1.78 (1 H, t, *J* 9.0), 1.47 (1 H, t, *J* 8.8), 1.08 (3 H, s, CMe_AMe_B) and 0.87 (3 H, s, CMe_AMe_B).



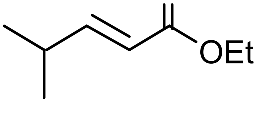
(7*R*)-(+)-2,10-Camphorsultam 161

(+)-Camphorsulfonimine **166** (7.70 g, 0.033 mol) was added to a suspension of lithium aluminium hydride (1.49 g, 0.039 mol) in dry THF (100 cm^3). The mixture was stirred under an argon atmosphere for 5 d. The reaction was quenched by cautiously adding distilled water dropwise while cooling in ice, and the mixture was then stirred overnight and allowed to settle before filtering. The layers were separated and the aqueous layer extracted with dichloromethane (2 ∞ 50 cm^3). The organic layers were separately washed with brine and then combined, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the (+)-sultam **161**[279,280] (5.02 g, 65%) as white needles, mp 180-181 °C (from EtOH) (lit.,[279,280] 183-184 °C); R_f(light petroleum-ether, 1:1) 0.17; ν_{max}(Nujol)/cm^{-1} 3289 (N-H), 1337 (SO_2N) and 1163 (SO_2N); δ_H(250 MHz; $CDCl_3$) 4.10 (1 H, br s, NH), 3.41 (1 H, m, CHN), 3.13 (1 H, d, J 13.8, $CH_AH_BSO_2$), 3.05 (1 H, d, J 13.8, $CH_AH_BSO_2$), 2.02-1.78 (5 H, m), 1.41 (1 H, m), 1.28 (1 H, m), 1.11 (3 H, s, CMe_AMe$_B$) and 0.92 (3 H, s, CMe$_A$$Me_B$).



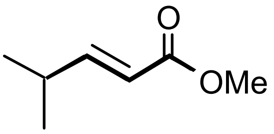
(7*S*)-(–)-2,10-Camphorsultam 174

This was synthesised from (1*S*)-(+)-camphorsulfonic acid as described above to give a sample with data identical (mp, NMR) to the enantiomer **161**.[279,280]



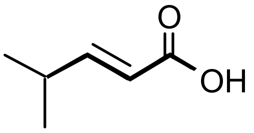
Ethyl (4-methyl)pent-2-enoate 168 (Attempted)

Following Williams,[137] sodium hydride (60% dispersion in oil, pre-washed with hexane and dried under reduced pressure, 4.25 g, 106 mmol) in dry ether (120 cm^3) under an argon atmosphere was cooled to 0 °C. Triethyl phosphonoacetate (21.3 cm^3, 107 mmol) was added dropwise. After 5 min, freshly-distilled isobutyraldehyde (9.7 cm^3, 107 mmol) was added dropwise and the resulting thick mixture was allowed to warm to room temperature as it was stirred overnight. Water (60 cm^3) was added slowly to dissolve the solid, the layers were separated and the aqueous layer was extracted with ether (2 ∞ 50 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a pale yellow liquid. This liquid was distilled at water pump pressure, but NMR showed that only a small amount of product had formed and the liquid was mainly starting material (triethyl phosphonoacetate).



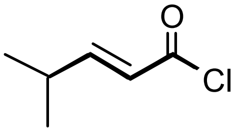
Methyl (4-methyl)pent-2-enoate 170

Isobutyraldehyde (5.50 cm^3, 61 mmol) (freshly distilled over $CaSO_4$ under an argon atmosphere) was slowly added to a stirred solution of carbomethoxymethylene triphenylphosphorane[292] (25.07 g, 74 mmol) in dichloromethane (100 cm^3) at 0 °C under an argon atmosphere. The mixture was stirred for 3 h and then allowed to warm to room temperature and evaporated under reduced pressure. The residue was triturated with light petroleum (200 cm^3), the triphenylphosphine oxide filtered off and the filtrate evaporated under reduced pressure to give the unsaturated ester **170** (6.98 g, 89%); R_f(light petroleum-ether, 10:1) 0.71; ν_{max}(film)/cm^{-1} 1724 (C=O) and 1657 (C=C); δ_H(250 MHz; $CDCl_3$) 6.94 (1 H, dd, *J* 15.7 and 6.7, C*H*CHMe$_2$), 5.76 (1 H, dd, *J* 15.7 and 1.5, COCH), 3.71 (3 H, s, OMe), 2.44 (1 H, octetd, *J* 6.8 and 1.4, C*H*Me$_2$) and 1.04 (6 H, d, *J* 6.7, CH*Me*$_2$).



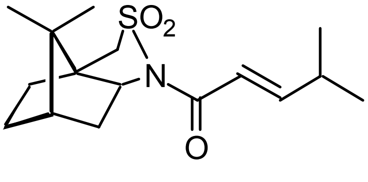
4-Methylpent-2-enoic acid 171

The unsaturated ester **170** (2.84 g, 0.022 mol) in THF (100 cm^3) and water (33 cm^3) was treated with lithium hydroxide monohydrate (6.32 g, 0.166 mol) and the resulting mixture was stirred vigorously for 5 d. More lithium hydroxide (6.05 g) was added and stirring was continued for a further 2 d. The mixture was acidified to pH 1 by adding concentrated hydrochloric acid slowly while cooling in ice. The layers were separated and the aqueous layer was extracted with ether (3 ∞ 50 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the acid **171** (2.19 g, 87%), R_f(light petroleum-ether, 1:1) 0.29; ν_{max}(film)/cm^{-1} 3500-2500 (O-H), 1694 (C=O) and 1652 (C=C); δ_H(250 MHz; $CDCl_3$) 10.63 (1 H, br s, OH), 7.05 (1 H, dd, *J* 15.7 and 6.6, C*H*CHMe$_2$), 5.77 (1 H, dd, *J* 15.7 and 1.3, COCH), 2.48 (1 H, octetd, *J* 6.8 and 1.2, C*H*Me$_2$) and 1.07 (6 H, d, *J* 6.8, CH*Me*$_2$).



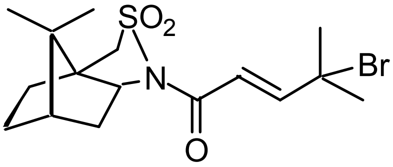
4-Methylpent-2-enyl chloride 162

Oxalyl chloride (2.5 cm^3, 0.028 mol) was added to a solution of the dry acid **171** (2.19 g, 0.019 mol) in dry dichloromethane (40 cm^3) at 0 °C under an argon atmosphere. The resulting solution was stirred at 0 °C for 1 h and then at room temperature for 2 h. The solvent was evaporated on a high vacuum pump until bubbling had ceased, giving the acid chloride **162** which was used immediately without purification or characterisation.



***N*-(4-Methylpent-2-enoyl)-(7*R*)-2,10-camphorsultam 160**

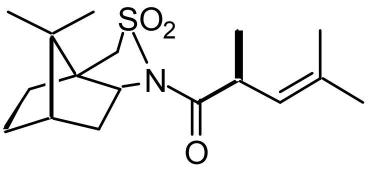
(+)-Camphorsultam **161** (13.19 g, 61 mmol) in dry toluene (50 cm^3) was added *via* cannula to a stirred suspension of sodium hydride (60% dispersion in oil, pre-washed with light petroleum and dried under reduced pressure, 2.89 g, 0.64 mol) in dry toluene (50 cm^3) under an argon atmosphere. The resulting mixture was stirred for 3 h, before addition of a solution of the acid chloride **162** (freshly made from acid **171**, 9.03 g, 79 mmol) in toluene (50 cm^3). The mixture was stirred for 2 h before careful addition of water. The layers were separated and the aqueous layer was extracted with ether (2 ∞ 50 cm^3). The combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate (2 ∞ 50 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1.5:1) gave the sultam **160**[281,284] (13.65 g, 72%) as white needles, mp 154-155 °C (lit.,[284] 161 °C); R_f(light petroleum-ether, 1:1) 0.36; ν_{max}(Nujol)/cm^{-1} 1672 (C=O), 1636 (C=C) and 1328 (SO_2N); δ_H(400 MHz; $CDCl_3$) 7.03 (1 H, dd, *J* 15.1 and 7.0, C*H*CHMe$_2$), 6.48 (1 H, dd, *J* 15.1 and 1.3, COCH), 3.91 (1 H, dd, *J* 7.5 and 5.1, CHN), 3.50 (1 H, d, *J* 13.8, C*H*$_A$H$_B$SO$_2$), 3.43 (1 H, d, *J* 13.8, CH$_A$*H*$_B$SO$_2$), 2.51 (1 H, octd, *J* 6.8 and 1.3, C*H*Me$_2$), 2.16-2.05 (2 H, m), 1.95-1.84 (3 H, m), 1.44-1.31 (2 H, m), 1.16 (3 H, s, C*Me*$_A$Me$_B$), 1.07 (6 H, d, *J* 6.8, CH*Me*$_2$) and 0.96 (3 H, s, CMe$_A$*Me*$_B$).



N-(4-Bromo-4-methylpent-2-enoyl)-(7*R*)-2,10-camphorsultam **159**

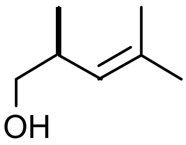
N-Bromosuccinimide (0.92 g, 5.2 mmol) was added to a solution of the sultam **160** (1.61 g, 5.2 mmol) in dry carbon tetrachloride (15 cm^3) under an argon atmosphere. The resulting suspension was heated to reflux for 18 h and then allowed to cool. The mixture was filtered through celite and the residue washed with carbon tetrachloride (20 cm^3). The filtrate was evaporated under reduced pressure to give the bromide **159**[284] as a white solid (1.31 g, 65%), mp 146 °C (dec.) (from EtOH) (lit.,[284] 146 °C); R_f(light petroleum-ether, 1:1) 0.34; ν_{max}(Nujol)/cm^{-1} 1687 (C=O), 1639 (C=C), 1321 (SO_2N) and 1163 (SO_2N); δ_H(250 MHz; $CDCl_3$) 7.25 (1 H, d, *J* 15.1, vinyl H), 6.58 (1 H, d, *J* 15.2, vinyl H), 3.92 (1 H, dd, *J* 7.1 and

5.6, CHN), 3.51 (1 H, d, *J* 13.8, $\mathrm{C}H_{\mathrm{A}}\mathrm{H}_{\mathrm{B}}\mathrm{SO}_2$), 3.44 (1 H, d, *J* 13.8, $\mathrm{CH}_{\mathrm{A}}H_{\mathrm{B}}\mathrm{SO}_2$), 2.13 (2 H, m), 1.93 (3 H, m), 1.93 (3 H, s, $\mathrm{CBr}Me_{\mathrm{A}}\mathrm{Me}_{\mathrm{B}}$), 1.92 (3 H, s, $\mathrm{CBrMe}_{\mathrm{A}}Me_{\mathrm{B}}$), 1.43-1.35 (2 H, m), 1.16 (3 H, s, $\mathrm{C}Me_{\mathrm{C}}\mathrm{Me}_{\mathrm{D}}$) and 0.97 (3 H, s, $\mathrm{CMe}_{\mathrm{C}}Me_{\mathrm{D}}$).



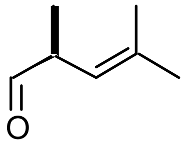
N-[(2*R*)-2,4-dimethylpent-3-enoyl]-(7*R*)-2,10-camphorsultam 158

Methyllithium (1.6 mol dm^{-3} solution in ether, 17.0 cm^3, 27 mmol) was added to a stirred suspension of dry copper(I) cyanide (2.50 g, 28 mmol) in dry THF (20 cm^3) at –20 °C under an argon atmosphere. After 5 min, boron trifluoride diethyletherate (3.40 cm^3, 27 mmol) was added, the solution stirred for 15 min and then cooled to –78 °C. A solution of the bromide **159** (3.68 g, 9.4 mmol) in dry THF (5 cm^3) was added slowly and the resulting solution stirred for 1.5 h. Basic saturated aqueous ammonium chloride (10 cm^3) was added and the mixture was allowed to warm to room temperature and stirred for 30 min until the lower layer became a deep blue. The layers were separated and the deep blue aqueous layer was extracted with ether (3 ∞ 10 cm^3). The combined organic fractions were washed with basic saturated aqueous ammonium chloride (repeated until the aqueous layer was colourless) and brine, dried ($\mathrm{MgSO_4}$), filtered and evaporated under reduced pressure. Chromatography ($\mathrm{SiO_2}$, light petroleum-ether, 2:1) gave the methylated product **158**[284] (1.96 g, 64%) as white needles, mp 94-96 °C (from EtOH-water) (lit.,[137] 102-104 °C); R_{f}(light petroleum-ether, 2:1) 0.25; ν_{max}(Nujol)/cm^{-1} 1693 (C=O), 1321 ($\mathrm{SO_2N}$) and 1164 ($\mathrm{SO_2N}$); δ_{H}(400 MHz; $\mathrm{CDCl_3}$) 5.28 (1 H, dq, *J* 9.0 and 1.4, vinyl H), 3.94 (1 H, dq, *J* 8.8 and 7.0, $\mathrm{COC}H\mathrm{Me}$), 3.86 (1 H, t, *J* 6.4, CHN), 3.50 (1 H, d, *J* 13.8, $\mathrm{C}H_{\mathrm{A}}\mathrm{H}_{\mathrm{B}}\mathrm{SO}_2$), 3.42 (1 H, d, *J* 13.8, $\mathrm{CH}_{\mathrm{A}}H_{\mathrm{B}}\mathrm{SO}_2$), 2.04 (2 H, br d, *J* 5.5, $\mathrm{C}H_2\mathrm{CHN}$), 1.94-1.85 (3 H, m), 1.71 (3 H, d, *J* 1.1, vinyl Me_{A}), 1.67 (3 H, d, *J* 1.2, vinyl Me_{B}), 1.41-1.34 (2 H, m), 1.26 (3 H, d, *J* 6.9, $\mathrm{COCH}Me$), 1.15 (3 H, s, $\mathrm{C}Me_{\mathrm{A}}\mathrm{Me}_{\mathrm{B}}$) and 0.96 (3 H, s, $\mathrm{CMe}_{\mathrm{A}}Me_{\mathrm{B}}$).



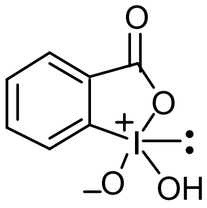
(2*S*),4-Dimethylpent-3-enol 172

A solution of the sultam derivative **158** (250 mg, 0.77 mmol) in dry ether (10 cm^3) was added to a stirred suspension of lithium aluminium hydride (88 mg, 2.32 mmol) in dry ether (10 cm^3) at –78 °C under an argon atmosphere. The resulting mixture was stirred and allowed to warm to room temperature over 45 min before being recooled to –78 °C and quenched slowly with aqueous potassium hydrogen sulfate (3.50 g in 100 cm^3). The mixture was again allowed to warm to room temperature and stirred for 45 min. Dilute hydrochloric acid (3 mol dm^{-3}, 10 cm^3) was added, the layers were separated and the aqueous layer was extracted with dichloromethane (2 ∞ 20 cm^3). The organic fractions were combined, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the regained sultam auxiliary **161** [(155 mg, 94%); R_f(light petroleum-ether, 1:1) 0.19, previously characterised], and the alcohol **172**[284] (79 mg, 90%); R_f(light petroleum-ether, 1:1) 0.40; ν_{max}(film)/cm^{-1} 3339 (O-H) and 1672 (C=O); δ_H(400 MHz; $CDCl_3$) 4.87 (1 H, dqn, *J* 9.5 and 1.4, vinyl H), 3.46 (1 H, dd, *J* 14.1 and 7.0, CH_AH_BOH), 3.29 (1 H, dd, *J* 10.3 and 8.4, CH_AH_BOH), 2.60 (1 H, m, C*H*Me), 1.72 (3 H, d, *J* 1.3, vinyl Me), 1.65 (3 H, d, *J* 1.3, vinyl Me), 1.43 (1 H, br s, OH) and 0.90 (3 H, d, *J* 6.8, CH*Me*).



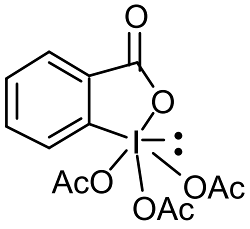
(2*S*),4-Dimethylpent-3-enal 155

The Swern procedure was followed.[171,293] Freshly-distilled (from CaH_2) dimethyl sulfoxide (0.15 cm^3, 2.1 mmol) in dry dichloromethane (2 cm^3) was added dropwise to a stirred solution of oxalyl chloride (0.10 cm^3, 1.2 mmol) in dry dichloromethane (7 cm^3) at –78 °C. After 10 min, the alcohol **172** (0.047 g, 0.42 mmol) in dry dichloromethane (2 cm^3) was added dropwise. The resulting solution was stirred at –78 °C for 30 min before addition of freshly-distilled triethylamine (0.80 cm^3, 5.7 mmol). After stirring for 10 min, the solution was allowed to warm to room temperature, water (7 cm^3) was added and the resulting mixture was stirred for a further 10 min. The layers were separated, the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3) and the combined organic fractions were washed with hydrochloric acid (3 mol dm^{-3}, 2 ∞ 10 cm^3), saturated aqueous sodium hydrogen carbonate (2 ∞ 10 cm^3) and brine, dried ($MgSO_4$), filtered and quickly evaporated under reduced pressure (without heating) to concentrate the aldehyde **155**,[322] which was not isolated but was used immediately in the next step without purification or characterisation.



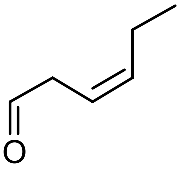
1-Hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide 181

The standard procedure was followed.[297] Caution must be exercised in this preparation as the compound or some impurity has been reported to be explosive under excessive heating or impact.[298,299] Potassium bromate(V) (7.60 g, 45 mmol) was added over 30 min to a vigorously stirred mixture of 2-iodobenzoic acid (8.50 g, 34 mmol) and sulfuric acid (0.73 mol dm^{-3}, 70 cm^3) in a 55 °C oil bath. The mixture turned orange-red and was stirred for 3.5 h at 68 °C and then cooled in an ice bath. The mixture was filtered and then washed with water (100 cm^3) and ethanol (2 ∞ 10 cm^3) to give the oxide **181** as a pale yellow solid (7.51 g, 78%), mp 236-237 °C (dec.) (lit.,[298] 233 °C).



1,1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one **182** (Attempted)

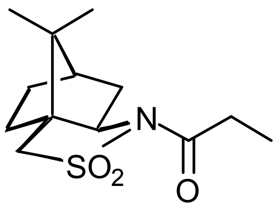
The standard procedure was followed.[297] Caution must be exercised in this preparation as hydrolysis converts the periodinane **182** to the oxide **181**, which has been reported to be explosive under excessive heating or impact.[298,299] A slurry of small crystals of oxide **181** (7.51 g, 27 mmol) in a mixture of acetic anhydride (25 cm^3, 270 mmol) and acetic acid (27 cm^3, 451 mmol) was stirred at room temperature under an argon atmosphere for 24 h and then filtered in an argon atmosphere to give recovered starting material only (mp).



Z-Hex-3-en-1-al **180**

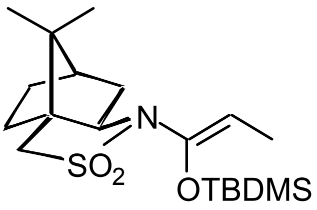
Method 1: The Swern procedure was followed.[171,293] Freshly-distilled (from CaH_2) dimethyl sulfoxide (0.20 cm^3, 2.7 mmol) in dry dichloromethane (2 cm^3) was added dropwise to a stirred solution of oxalyl chloride (0.15 cm^3, 1.6 mmol) in dry dichloromethane (7 cm^3) at –78 °C. After 10 min, *Z*-hex-3-en-1-ol (0.06 cm^3, 0.50 mmol) in dry dichloromethane (2 cm^3) was added dropwise. The resulting solution was stirred at –78 °C for 30 min before addition of freshly-distilled triethylamine (1.00 cm^3, 6.9 mmol). After stirring for 10 min, the solution was allowed to warm to room temperature, water (7 cm^3) was added and the resulting mixture was stirred for a further 10 min. The layers were separated, the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3) and the combined organic fractions were washed with hydrochloric acid (3 mol dm^{-3}, 2 ∞ 10 cm^3), saturated aqueous sodium hydrogen carbonate solution (2 ∞ 10 cm^3) and brine, dried ($MgSO_4$), filtered and quickly evaporated under reduced pressure (without heating) to concentrate the aldehyde **180**.[323,324] A crude NMR was quickly taken which showed a complicated mixture of compounds.

Method 2: A solution of *Z*-hex-3-en-1-ol (0.06 cm^3, 0.5 mmol) in dry dichloromethane (2 cm^3) was added to a stirred suspension of the Dess-Martin periodinane[300] (weighed out in a glove box) (250 mg, 0.6 mmol) in dry dichloromethane (4 cm^3) at 0 °C under an argon atmosphere. The resulting solution was allowed to warm to room temperature and was stirred for 2 h (a white precipitate appeared). Ether (9 cm^3) was added and the mixture cooled to 0 °C prior to addition of sodium thiosulfate (2 g) dissolved in saturated aqueous sodium hydrogen carbonate (10 cm^3). The mixture was allowed to warm to room temperature during which time the precipitate dissolved. The aqueous layer was extracted with ether (3 ∞ 5 cm^3) and the combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate solution (5 cm^3) and brine, dried ($MgSO_4$), filtered and quickly evaporated under reduced pressure (without heating) to give the aldehyde **180**;[323,324] R_f(light petroleum-ether, 1:1) 0.57; ν_{max}(film)/cm^{-1} 1726 (C=O) and 1654 (C=C); δ_H(250 MHz; $CDCl_3$) 9.67 (1 H, t, *J* 2.0, HCO), 5.70 (1 H, m, vinyl H), 5.51 (1 H, m, vinyl H), 3.18 (2 H, br t, *J* 9.0, CH_2CO), 2.06 (2 H, br qn, *J* 7.5, MeCH_2) and 0.99 (3 H, t, *J* 7.5, MeCH$_2$).



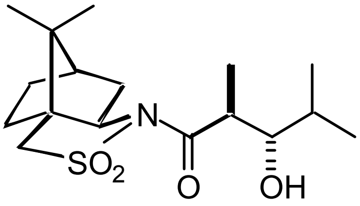
N-Propionyl-(7S)-2,10-camphorsultam 175

A solution of dry (–)-camphorsultam **174** (4.75 g, 0.022 mol) in dry toluene (50 cm^3) was added *via* cannula to a stirred suspension of sodium hydride (60% dispersion in oil, pre-washed with light petroleum and dried under reduced pressure, 1.34 g, 0.034 mol) in dry toluene (50 cm^3) under an argon atmosphere. The resulting mixture was stirred overnight before addition of propionyl chloride (3.9 cm^3, 0.044 mol). After stirring for 4 h, the reaction was quenched by adding water (50 cm^3). The layers were separated, the aqueous layer was extracted with ether (2 ∞ 50 cm^3), the combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate (2 ∞ 50 cm^3) and brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the sultam **175**[282] (4.95 g, 83%), mp 154-155 °C (from MeOH) (lit.,[282] 153-155 °C); R_f(light petroleum-ether, 2:1) 0.22; ν_{max}(Nujol)/cm^{-1} 1687 (C=O), 1331 (SO$_2$N) and 1164 (SO$_2$N); δ_H(250 MHz; CDCl$_3$) 3.85 (1 H, dd, *J* 7.4 and 5.3, CHN), 3.49 (1 H, d, *J* 13.8, C*H*$_A$H$_B$SO$_2$), 3.41 (1 H, d, *J* 13.8, CH$_A$*H*$_B$SO$_2$), 2.74 (1 H, q, *J* 7.4, C*H*$_C$H$_D$Me), 2.73 (1 H, q, *J* 7.3, CH$_C$*H*$_D$Me), 2.14-2.04 (2 H, m), 1.93-1.83 (3 H, m), 1.44-1.34 (2 H, m), 1.15 (3 H, t, *J* 7.3, CH$_2$*Me*), 1.14 (3 H, s, C*Me*$_E$Me$_F$) and 0.96 (3 H, s, CMe$_E$*Me*$_F$).



N-Propionyl-(7*S*)-2,10-camphorsultam-*O*-t-butyldimethylsilyl-*N*,*O*-ketene acetal 173

The method of Oppolzer was used.[283] The propionated sultam **175** (0.399 g, 1.47 mmol) in dry dichloromethane (6 cm^3) was treated with t-butyldimethylsilyltrifluoromethane sulfonate (0.80 cm^3, 3.54 mmol) and freshly-distilled triethylamine (0.60 cm^3, 4.28 mmol) at room temperature under an argon atmosphere. The resulting yellow solution was stirred for 7 d (became a deep red colour). The solvent was removed on a high vacuum pump and the dark red solid residue was treated with dry hexane (8 cm^3) to give a pale orange solution over a dark red liquid residue. The solution was removed by syringe (residues washed once more with hexane) and evaporated on the pump to give the silylketene acetal **173**[283] as a creamy solid which was redissolved in dry dichloromethane (2.5 cm^3) to be used immediately without purification or characterisation.

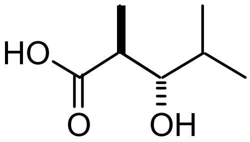


N-[(2*S*,3*S*)-2,4-Dimethyl-3-hydroxypentanoyl]-(7*S*)-2,10-camphorsultam 176

Method 1: The method of Oppolzer was used.[283] Freshly-distilled isobutyraldehyde (0.40 cm^3, 4.3 mmol) was dissolved in dry dichloromethane (4 cm^3) under an argon atmosphere and cooled to –78 °C before addition of titanium tetrachloride (1.0 mol dm^{-3} solution in dichloromethane, 4 cm^3, 4 mmol). The resulting mixture was stirred at this temperature for 3 min before addition of the solution of silylketene acetal **173** (made from 0.447 g of sultam **175**, 1.60 mmol) in dry dichloromethane (2.5 cm^3) *via* cannula. After 5 min the reaction was quenched at –78 °C by addition of saturated aqueous ammonium chloride (3 cm^3) and was allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 2:1) gave recovered sultam **175** (0.041 g, 9%) and the aldol product **176** (0.340 g, 62%) as needles, mp 149-150 °C (lit.[283] 147-148 °C); R_f(light petroleum-ether, 2:1) 0.12; ν_{max}(Nujol)/cm^{-1} 3515 (O-H), 1679 (C=O), 1323 (SO_2N) and 1164 (SO_2N); δ_H(400 MHz; $CDCl_3$) 3.89 (1 H, dd, *J* 7.8 and 5.0, CHN), 3.52 (1 H, d, *J* 13.8, $CH_AH_BSO_2$), 3.45 (1 H, d, *J* 13.9, $CH_AH_BSO_2$), 3.40 (1 H, m, C*H*OH), 3.27 (1 H, qn, *J* 6.7, COC*H*Me), 2.43 (1 H, d, *J* 10.3, OH), 2.17 (2 H, m), 2.06 (1 H, dd, *J* 13.9 and 7.8), 1.96-1.85 (3 H, m), 1.71 (1 H, doct, *J* 6.6 and 1.9, $CHMe_2$), 1.42-1.31 (2 H, m), 1.20 (3 H, d, *J* 6.7, COCH*Me*), 1.18 (3 H, s, CMe_AMe_B), 0.97 (3 H, d, *J* 7.0, $CHMe_CMe_D$), 0.96 (3 H, s, CMe_AMe_B) and 0.91 (3 H, d, *J* 6.8, $CHMe_CMe_D$).

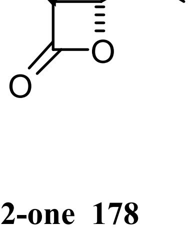
Method 2: (Attempted) The procedure of Oppolzer was followed.[283] The propionated sultam **175** (100 mg, 0.37 mmol) in dry dichloromethane (6 cm^3) was treated with t-butyldimethyl-silyltrifluoromethane sulfonate (0.20 cm^3, 0.89 mmol) and freshly-distilled triethylamine (0.15 cm^3, 1.07 mmol) at room temperature under an argon atmosphere. The resulting yellow solution was stirred for 16 h (became a deep red colour) before cooling to –40 °C and addition of isobutyraldehyde (0.50 cm^3, 5.4 mmol). The mixture was stirred at this temperature for 30 min before quenching with saturated aqueous ammonium chloride (3 cm^3) and allowing to warm to room temperature. The layers were separated and the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a mixture of unidentifiable products.

Method 3: (Attempted) The method of Oppolzer was used.[283] Zinc chloride (1.0 mol dm^{-3} solution in ether, 0.50 cm^3, 0.50 mmol) was placed in a dry round bottom flask and the ether removed under high vacuum. Dry dichloromethane (2 cm^3) was added under an argon atmosphere and the solution cooled to –78 °C. Freshly-distilled isobutyraldehyde (0.05 cm^3, 0.54 mmol) was added and the mixture stirred for 5 min before addition of a solution of silylketene acetal **173** (made from 50 mg of sultam **175**, 0.19 mmol) in dry dichloromethane (2 cm^3) *via* cannula. After 1 h the reaction was quenched at –78 °C by addition of saturated aqueous ammonium chloride (3 cm^3) and was allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give mainly recovered starting material.



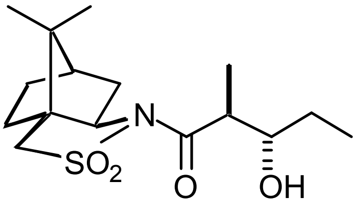
(2*S*,3*S*)-2,4-Dimethyl-3-hydroxypentanoic acid **177**

A solution of the aldol adduct **176** (340 mg, 0.99 mmol) in THF (12 cm^3) and water (4 cm^3) at 0 °C was treated with lithium hydroxide monohydrate (74.2 mg, 1.77 mmol) and hydrogen peroxide (30% solution in water, 0.55 cm^3, 5.4 mmol). The resulting solution was stirred at this temperature for 3 h before addition of sodium sulfite (1.21 g, 11.7 mmol) in water (12 cm^3). The THF was removed by evaporation under reduced pressure and the residue extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic layers were washed with brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the recovered (–)-sultam **174** (133 mg, 63%) (previously characterised). The aqueous layers were acidified to pH 1 (hydrochloric acid) and extracted with ethyl acetate (3 ∞ 15 cm^3). The combined organic layers were washed with brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the hydroxy acid **177**[295,296] (77 mg, 53%); R_f(light petroleum-ether, 1:1) 0.11; ν_{max}(film)/cm^{-1} 3396 (O-H), 3300-2500 (CO$_2$H) and 1710 (C=O); δ_H(250 MHz; CDCl$_3$) 3.43 (1 H, t, *J* 6.2, C*H*OH), 2.69 (1 H, qn, *J* 6.9, C*H*Me), 1.81 (1 H, oct, *J* 6.7, C*H*Me$_2$) 1.26 (3 H, d, *J* 7.2, CH*Me*), 0.99 (3 H, d, *J* 6.8, CH*Me*$_A$Me$_B$) and 0.95 (3 H, d, *J* 6.7, CHMe$_A$*Me*$_B$).



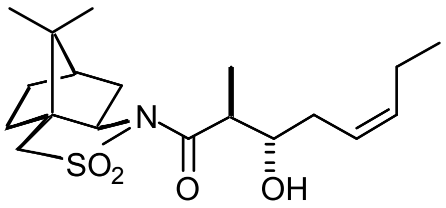
(3*S*,4*S*)-4-Isopropyl-3-methyloxetan-2-one **178**

The method of Adam was used.[78] Freshly-distilled benzenesulfonyl chloride (0.30 cm^3, 2.4 mmol) was added to a solution of the hydroxy acid **177** (77 mg, 0.53 mmol) in dry pyridine (10 cm^3) at 0 °C under an argon atmosphere. The resulting solution was stirred for 5 min and then put in the freezer for 7 d. Ice (10 g) was added, the mixture was stirred for 5 min and dichloromethane (10 cm^3) was added. The layers were separated and the aqueous layer was extracted with dichloromethane (4 ∞ 10 cm^3), the combined organic fractions were washed with hydrochloric acid (3 mol dm^{-3}, 4 ∞ 20 cm^3), saturated aqueous sodium hydrogen carbonate (2 ∞ 20 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *lactone* **178** (197 mg, mixed with pyridine); R_f(light petroleum-ether, 1:1) 0.51; ν_{max}(film)/cm^{-1} 1824 (C=O); δ_H(400 MHz; $CDCl_3$) 3.83 (1 H, dd, *J* 8.4 and 4.2, CHO), 3.24 (1 H, dq, *J* 4.1 and 3.4, C*H*Me), 1.93 (1 H, br oct, *J* 6.7, C*H*Me_2), 1.37 (3 H, d, *J* 7.5, CH*Me*), 1.03 (3 H, d, *J* 6.6, $CH\mathit{Me}_A Me_B$) and 0.95 (3 H, d, *J* 6.8, $CHMe_A\mathit{Me}_B$); δ_C($CDCl_3$) 172.1, 84.3, 48.8, 32.4, 18.1, 16.8 and 12.9; *m/z* (EI) 84 (52%, M – CO_2), 69 (100, $CHCHCHMe_2$) and 56 (54, CH_2CHMe_2) (Found: M – CO_2, 84.0942. C_6H_{12} requires *M*, 84.0939).



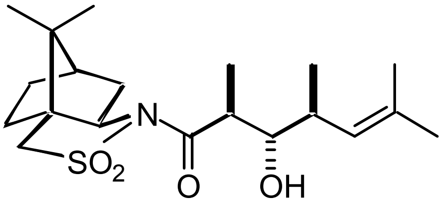
N-[(2S,3S)-2-Methyl-3-hydroxypentanoyl]-(7S)-2,10-camphorsultam 184

The method of Oppolzer was adapted.[283] Freshly-distilled propionaldehyde (0.10 cm^3, 1.4 mmol) was dissolved in dry dichloromethane (3 cm^3) under an argon atmosphere and was cooled to –78 °C before addition of titanium tetrachloride (1.0 mol dm^{-3} solution in dichloromethane, 1.4 cm^3, 1.4 mmol). The resulting mixture was stirred at this temperature for 10 min before addition of the solution of silylketene acetal **173** (made from 0.100 g of sultam **175**, 0.36 mmol) in dry dichloromethane (4 cm^3). The reaction was allowed to warm gradually to room temperature overnight and was then cooled to 0 °C and quenched by addition of saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the *aldol product* **184** (33 mg, 27%) as a pale yellow liquid; R_f(light petroleum-ether, 1:1) 0.20; ν_{max}(Nujol)/cm^{-1} 3518 (O-H), 1694 (C=O), 1332 (SO_2N) and 1166 (SO_2N); δ_H(250 MHz; $CDCl_3$) 3.90 (1 H, dd, *J* 7.5 and 5.2, CHN), 3.56 (1 H, m, C*H*OH), 3.53 (1 H, d, *J* 13.8, C*H*$_A$H$_B$SO$_2$), 3.44 (1 H, d, *J* 13.8, CH$_A$*H*$_B$SO$_2$), 3.19 (1 H, qn, *J* 6.7, C*H*Me), 2.15 (2 H, m), 1.87 (3 H, m), 1.63 (2 H, m), 1.35 (2 H, m), 1.22 (3 H, d, *J* 6.7, CH*Me*), 1.18 (3 H, s, C*Me*$_A$Me$_B$), 0.99 (3 H, t, *J* 7.4, CH$_2$*Me*) and 0.97 (3 H, s, CMe$_A$*Me*$_B$); δ_C($CDCl_3$) 175.5+, 65.4–, 64.5+, 53.2+, 48.3+, 47.8+, 45.1–, 44.7–, 38.5+, 33.0+, 28.5+, 26.4+, 20.7–, 19.9–, 14.3– and 9.8–; *m/z* (EI) 330 (20%, MH$^+$), 300 (46, M – Et) and 271 (45, M – EtCO) (Found: MH$^+$, 330. 1746. $C_{16}H_{27}NSO_4$ requires *M*, 330.1739).



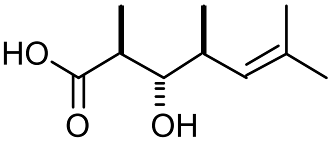
***Z-N*-[(2*S*,3*S*)-2-Methyl-3-hydroxyoctan-5-enoyl]-(7*S*)-2,10-camphorsultam 183 (Attempted)**

The method of Oppolzer was adapted.[283] A solution of crude aldehyde **180** (assuming 100% yield from the Swern oxidation, 1.0 mmol) in dry dichloromethane (5 cm^3) was cooled to –78 °C before addition of titanium tetrachloride (1.0 mol dm^{-3} solution in dichloromethane, 1.0 cm^3, 1.0 mmol). The resulting mixture was stirred at this temperature for 10 min before addition of the solution of silylketene acetal **173** (made from 100 mg of sultam **175**, 0.36 mmol) in dry dichloromethane (4 cm^3). The reaction was allowed to warm gradually to room temperature overnight and was then cooled to 0 °C and quenched by addition of saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer was extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give recovered starting material.



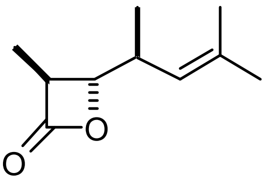
***N*-[(2*S*,3*S*,4*S*)-3-Hydroxy-2,4,6-timethylhept-5-enoyl]-(7*S*)-2,10-camphorsultam 185**
The method of Oppolzer was used.[283] A solution of crude aldehyde **155** (assuming 100% yield from the Swern oxidation, 0.9 mmol) in dry dichloromethane (10 cm^3) was cooled to –78 °C before addition of titanium tetrachloride (1.0 mol dm^{-3} solution in dichloromethane, 0.5 cm^3, 0.5 mmol) under an argon atmosphere. The resulting mixture was stirred at this temperature for 2 min before addition of the solution of silylketene acetal **173** (made from 0.470 g of sultam **175**, 1.70 mmol) in dry dichloromethane (2.5 cm^3) *via* cannula. After 5 min the reaction was quenched at –78 °C by addition of saturated aqueous ammonium chloride (10 cm^3) and was allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted with dichloromethane (3 ∞ 40 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 2:1) gave recovered sultam **175** (0.212 g, 45%) (previously characterised) and the aldol product **185** (0.271 g, 42%) as needles, mp 133-134 °C (from EtOH) (lit.,[137] 155-158 °C); R_f(light petroleum-ether, 2:1) 0.11; ν_{max}(Nujol)/cm^{-1} 3600 (O-H), 1688 (C=O), 1325 (SO_2N) and 1125 (SO_2N); δ_H(250 MHz; $CDCl_3$) 5.10 (1 H, br d, *J* 9.9, CH=), 3.90 (1 H, dd, *J* 8.0 and 5.2, CHN), 3.52 (1 H, d, *J* 13.9, $CH_AH_BSO_2$), 3.49 (1 H, m, C*H*OH), 3.43 (1 H, d, *J* 13.9, $CH_AH_BSO_2$), 3.19 (1 H, m, COC*H*Me), 2.55 (1 H, m, C*H*MeC=), 2.33 (1 H, d, *J* 10.0, OH), 2.17 (1 H, m), 2.06 (1 H, dd, *J* 13.6 and 7.9, $CH_{endo}HCHN$), 1.92-1.86 (3 H, m), 1.74 (3 H, d, *J* 1.1, $=CMe_AMe_B$), 1.63 (3

H, d, *J* 1.1, =CMe$_A$*Me*$_B$), 1.36 (2H, m), 1.20 (3 H, s, C*Me*$_A$Me$_B$), 1.16 (3 H, d, *J* 6.6, COCH*Me*), 1.03 (3H, d, *J* 6.9, =CCH*Me*) and 0.97 (3 H, s, CMe$_A$*Me*$_B$).



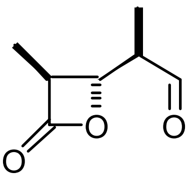
(2*S*,3*S*,4*S*)-3-Hydroxy-2,4,6-trimethylhept-5-enoic acid 186

A solution of the aldol adduct **185** (39 mg, 0.10 mmol) in THF (6 cm^3) and water (2 cm^3) at 0 °C was treated with lithium hydroxide monohydrate (21 mg, 0.51 mmol) and hydrogen peroxide (6% solution in water, 0.83 cm^3, 1.53 mmol). The resulting solution was stirred at this temperature for 3 h and allowed to warm to room temperature overnight. The mixture was recooled to 0 °C and saturated aqueous sodium sulfite (10 cm^3) was added. The THF was removed by evaporation under reduced pressure and the residue extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic layers were washed with brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the recovered (–)-sultam **174** (19 mg, 89%) (previously characterised). The aqueous layer was acidified to pH 1 (hydrochloric acid) and extracted with ethyl acetate (3 ∞ 15 cm^3), the combined organic layers were washed with brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the hydroxy acid **186** (15 mg, 78%); *R*$_f$(light petroleum-ether, 1:1) baseline; ν_{max}(film)/cm^{-1} 3500-2500 (O-H) and 1713 (C=O); δ_H(400 MHz; CDCl$_3$) 5.06 (1 H, br d, *J* 9.9, vinyl H), 3.50 (1 H, t, *J* 5.8, C*H*OH), 2.65-2.53 (2 H, m), 1.71 (3 H, d, *J* 0.9, vinyl Me$_A$), 1.63 (3 H, d, *J*1.1, vinyl Me$_B$), 1.23 (3 H, d, *J* 7.2, HO$_2$CCH*Me*) and 1.01 (3 H, d, *J* 6.8, CH*Me*C=).



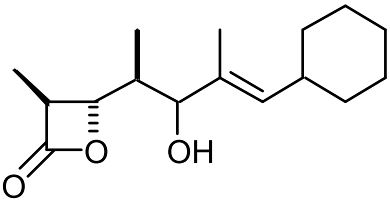
(3*S*,4*S*,5*S*)-4-(1,3-Dimethylbut-2-enyl)-3-methyloxetan-2-one 187

The method of Adam was used.[78] Freshly-distilled benzenesulfonyl chloride (0.30 cm^3, 2.15 mmol) was added to a solution of the hydroxy acid **186** (100 mg, 0.54 mmol) in dry pyridine (10 cm^3) at 0 °C under an argon atmosphere. The resulting solution was stirred for 5 min and then put in the freezer for 5 d. Ice (10 g) was added, the mixture was stirred for 5 min and dichloromethane (10 cm^3) was added. The layers were separated and the aqueous layer was extracted with dichloromethane (4 ∞ 10 cm^3), the combined organic fractions were washed with hydrochloric acid (3 mol dm^{-3}, 4 ∞ 20 cm^3), saturated aqueous sodium hydrogen carbonate (2 ∞ 20 cm^3) and brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give the lactone **187** (50 mg, 55%); R_f(light petroleum-ether, 1:1) 0.56; ν_{max}(film)/cm^{-1} 1822 (C=O); δ_H(400 MHz; CDCl$_3$) 4.95 (1 H, dt, *J* 9.4 and 1.4, vinyl H), 4.00 (1 H, dd, *J* 6.5 and 4.1, CHO), 3.27 (1 H, qd, *J* 7.6 and 4.1, C*H*Me in lactone), 2.74 (1 H, sex, *J* 6.8, C*H*Me in side chain), 1.71 (3 H, d, *J* 1.2, vinyl Me$_A$), 1.64 (3 H, d, *J* 1.3, vinyl Me$_B$), 1.36 (3 H, d, *J* 7.6, CH*Me* in lactone) and 1.01 (3 H, d, *J* 6.8, CH*Me* in side chain).



(2*S*,3*S*,4*S*)-2-(3-Methyl-4-oxo-oxetan-2-yl)-propionaldehyde 20

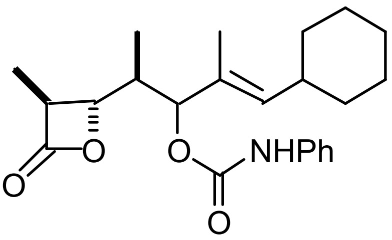
The method of Williams was adapted.[137] A solution of the lactone **187** (50 mg, 0.30 mmol) in dry dichloromethane (50 cm^3) was cooled to –78 °C under an argon atmosphere and ozone was bubbled through the solution for about 3 min until a blue coloration (due to excess ozone) was observed. Argon was then blown over the surface of the liquid for 2 min and dimethyl sulfide (2 drops) was added. The resulting solution was stirred for 20 min at –78 °C and then for 30 min as it was allowed to warm to room temperature. The solution was washed with water (10 cm^3), brine, dried (MgSO$_4$), filtered and cautiously evaporated under reduced pressure to give the aldehyde **20**[137] (364 mg, containing dichloromethane) as a pale yellow liquid; R_f(light petroleum-ether, 1:1) 0.09; ν_{max}(film)/cm^{-1} 1825 (C=O in lactone) and 1724 (C=O in aldehyde);[137] δ_H(250 MHz; CDCl$_3$) 9.77 (1 H, d, *J* 1.1, HC=O), 4.37 (1 H, dd, *J* 7.7 and 4.1, CHO), 3.45 (1 H, qd, *J* 7.5 and 4.1, C*H*Me in the ring), 2.91 (1 H, qnd, *J* 7.1 and 1.0, C*H*Me in the side chain), 1.46 (3 H, d, *J* 7.5, CH*Me* in the ring) and 1.22 (3 H, d, *J* 7.3, CH*Me* in the side chain).



E-(3S,4S,5S,6RS)-4-(4-Cyclohexyl-1,3-dimethyl-2-hydroxy-but-3-enyl)-3-methyl-oxetan-2-ones 188 and 189

The method of Kishi was followed.[218] Freshly-prepared aldehyde **20** (made from 50 mg of lactone **187**, 100% yield would be 0.30 mmol) was added to vinyl iodide **133** (203 mg, 0.81 mmol) and distilled dimethyl sulfoxide (3 cm^3) in a round bottom flask under an argon atmosphere. The flask was transferred to a glove box where dry chromium(II) chloride (219 mg, 1.78 mmol) was added portionwise, and a speck of pre-dried nickel(II) chloride was added to the mixture. The mixture was stirred for 20 h under an argon atmosphere and then cooled in ice and quenched with water (5 cm^3). After stirring for 10 min, the solution was extracted with ethyl acetate (3 ∞ 10 cm^3), the organic fractions combined, washed with brine (10 cm^3), dried (MgSO$_4$), filtered and evaporated under reduced pressure to give a pale yellow liquid. Chromatography (SiO$_2$, light petroleum-ether, 1:1) gave an inseparable mixture of *alcohols* **188** and **189** in the ratio 2:3 (23 mg, 29%); R_f(light petroleum-ether, 1:1) 0.36; ν_{max}(film)/cm^{-1} 3330 (br, O-H) and 1811 (C=O); δ_H(400 MHz; CDCl$_3$) 5.28 (1 H, d, *J*

9.2, =CH in **188**), 5.23 (1 H, d, *J* 9.0, =CH in **189**), 4.32 (1 H, dd, *J* 6.4 and 4.3, CHO in the ring in **189**), 4.21 (1 H, dd, *J* 8.4 and 4.1, CHO in the ring in **188**), 4.11 (1 H, d, *J* 3.6, C*H*OH in **188**), 3.84 (1 H, d, *J* 8.0, C*H*OH in **189**), 3.46 (1 H, dd, *J* 7.3 and 4.2, C*H*Me in the ring in **189**), 3.29 (1 H, dd, *J* 7.5 and 4.1, C*H*Me in the ring in **188**), 2.18 (3 H, m, C*H*Me in the side chain in **189** and =CHC*H*), 1.98 (1 H, m, C*H*Me in the side chain in **188**), 1.79-1.56 (10 H, m), 1.62 (3 H, d, *J* 1.0, =CMe in **189**), 1.58 (3 H, s, =CMe in **188**), 1.38 (3 H, d, *J* 7.5, CH*Me* in the ring), 1.29-0.99 (10 H, m), 0.88 (3 H, d, *J* 6.8, CH*Me* in the side chain in **188**) and 0.82 (3 H, d, *J* 7.0, CH*Me* in the side chain in **189**); δ_C($CDCl_3$) 135.2–, 132.0–, 81.3–, 80.7–, 74.8–, 49.0–, 48.2–, 38.6–, 36.6–, 33.0+, 32.9+, 26.0+, 25.9+, 13.5–, 12.7–, 11.4– and 11.0–; *m/z* (EI) 266 (7%, M^+), 249 (32, M – OH) and 205 (38, M – OH – CO_2) (Found: M^+, 266.1874. $C_{16}H_{26}O_3$ requires *M*, 266.1882).

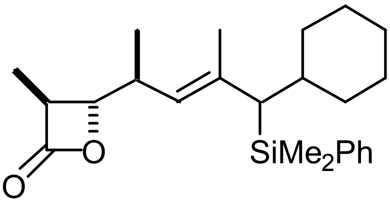


***E*-(3*S*,4*S*,5*S*,6*RS*)-Phenylcarbamic acid 1-(3-cyclohexylpropen-2-yl)-2-(3-methyl-4-oxo-oxetan-2-yl)propyl esters 190 and 191**

The standard method was followed.[192,195] Phenyl isocyanate (0.05 cm^3, 0.46 mmol) was added dropwise to a stirred solution of the alcohols **188** and **189** (103 mg, 0.39 mmol), 4-dimethylaminopyridine (57 mg, 0.46 mmol) and triethylamine (0.07 cm^3, 0.50 mmol) in dry dichloromethane (3 cm^3) under an argon atmosphere at room temperature and stirred for 3.5 h. Water (5 cm^3) was cautiously added and the mixture was extracted with dichloromethane

(3 ∞ 10 cm^3). The organic fractions were combined, washed with hydrochloric acid (1 mol dm^{-3}, 5 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave an inseparable mixture of the

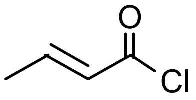
carbamates **190** and **191** in the ratio 2:3 (41 mg, 27%) as a colourless liquid; R_f(light petroleum-ether, 1:1) 0.45; ν_{max}($CDCl_3$)/cm^{-1} 3336 (N-H), 1826 (C=O in lactone), 1731 (C=O in carbamate), 1601 (C=C) and 1538 (Ph); δ_H(400 MHz; $CDCl_3$) 7.53 (2 H, d, *J* 7.7, *o*-H), 7.35 (2 H, m, *m*-H), 7.06 (1 H, m, *p*-H), 6.64 (1 H, br s, NH in **190**), 6.60 (1 H, br s, NH in **191**), 5.35 (1 H, d, *J* 9.0, =CH in **191**), 5.27 (1 H, d, *J* 9.1, =CH in **190**), 5.13 (1 H, d, *J* 5.8, CHO in the side chain in **190**), 5.02 (1 H, d, *J* 9.0, CHO in the side chain in **191**), 4.24 (1 H, dd, *J* 7.0 and 4.3, CHO in the ring in **191**), 4.08 (1 H, dd, *J* 7.6 and 4.1, CHO in the ring in **190**), 3.36 (1 H, m, C*H*Me in the ring), 2.37 (1 H, sex, *J* 7.0, C*H*Me in the side chain), 2.18 (1 H, m, =CH-C*H*), 1.71-1.54 (5 H, m), 1.65 (3 H, d, *J* 1.2, =CMe in **191**), 1.57 (3 H, s, =CMe in **190**), 1.36 (3 H, d, *J* 7.7, CH*Me* in the ring), 1.29-0.98 (5 H, m) and 0.86 (3 H, d, *J* 7.1, CH*Me* in the side chain); δ_C($CDCl_3$) 171.8+, 152.4+, 137.7+, 137.4–, 134.8–, 133.0–, 129.1–, 129.0–, 128.8–, 128.6–, 127.7–, 124.1–, 123.6–, 120.0–, 118.7–, 82.1–, 80.3–, 79.5–, 78.8–, 48.3–, 48.1–, 39.4–, 38.9–, 38.0–, 36.7–, 32.9+, 32.8+, 32.6+, 26.0+, 25.9+, 25.8+, 13.1–, 12.8–, 12.6–, 11.8–, 10.6– and 8.9–; *m/z* (EI) 385 (30%, M^+) and 249 (14, M – $PhNHCO_2$) (Found: M^+, 385.2277. $C_{23}H_{31}NO_4$ requires *M*, 385.2253).



_E_-(3_S_,4_S_,5_S_,8_RS_)-4-[4-Cyclohexyl-4-dimethyl(phenyl)silyl-1,3-dimethylbut-2-enyl]-3-methyloxetan-2-ones 192 (Attempted)

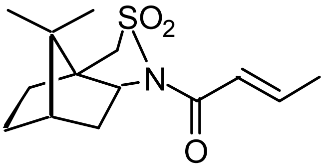
One of the standard methods was followed.[192,195] Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF, 0.42 cm^3, 0.42 mmol) was added dropwise to a stirred slurry of dry copper(I) iodide (40 mg, 0.21 mmol) in dry ether (4 cm^3) at 0 °C under an argon atmosphere. The mixture was stirred at this temperature for 20 min. n-Butyllithium (1.6 mol dm^{-3} solution in hexane, 0.07 cm^3, 0.11 mmol) was added dropwise to a stirred solution of the carbamates **190** and **191** (40 mg, 0.10 mmol) in dry THF (3 cm^3) at 0 °C under an argon atmosphere. After stirring at this temperature for 5 min, the solution was added *via* cannula to the silylcopper reagent prepared above at 0 °C. The resulting mixture was stirred overnight, during which time the reaction warmed to room temperature. The reaction was recooled to 0 °C and quenched with basic saturated aqueous ammonium chloride (10 cm^3) and extracted with light petroleum (3 ∞ 5 cm^3). The organic layers were combined, washed with basic saturated aqueous ammonium chloride (5 cm^3), brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a mixture containing no identifiable products (besides fast-running silicon-containing impurities).

6.4 Compounds for Chapter 5



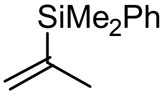
_E_-But-2-enyl chloride 217

Oxalyl chloride (3.80 cm^3, 40.7 mmol) was added to a solution of crotonic acid (1.75 g, 20.3 mmol) in dry dichloromethane (8 cm^3) at 0 °C under argon. The resulting solution was stirred at 0 °C for 1 h and then at room temperature for 2 h. The solvent was removed briefly on a high vacuum pump (to remove the dichloromethane and excess oxalyl chloride but not the product) to give the crude acid chloride **217** which was used immediately without purification or characterisation.



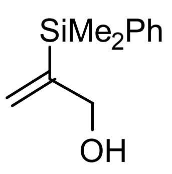
_N_-(_E_-But-2-enoyl)-(7_R_)-2,10-camphorsultam 218

(+)-Camphorsultam **161** (875 mg, 4.1 mmol) in dry toluene (10 cm^3) was added *via* cannula to a stirred suspension of sodium hydride (60% dispersion in oil, pre-washed with light petroleum and dried under reduced pressure, 330 mg, 8.2 mmol) in dry toluene (10 cm^3) under an argon atmosphere. The resulting mixture was stirred for 1.5 h before addition of a solution of the acid chloride **217** (freshly made from crotonic acid, 1.75 g, 20.3 mmol) in toluene (10 cm^3). The mixture was stirred for 1.5 h before careful addition of water. The layers were separated and the aqueous layer was extracted with dichloromethane (2 ∞ 20 cm^3). The combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate (2 ∞ 20 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Recrystallisation from methanol gave crotonylsultam **218**[277] (821 mg, 71%) as white needles, mp 189-191 °C (from MeOH) (lit.,[277] 186-187 °C); R_f(light petroleum-ether, 1:1) 0.29; ν_{max}(Nujol)/cm^{-1} 1674 (C=O), 1634 (C=C), 1324 (SO_2N) and 1163 (SO_2N); δ_H(250 MHz; $CDCl_3$) 7.10 (1 H, dq, *J* 15.0 and 7.1, C*H*Me), 6.59 (1 H, dq, *J* 15.0 and 1.7, COCH), 3.94 (1 H, m, CHN), 3.47 (1 H, d, *J* 13.8, $CH_AH_BSO_2$), 3.43 (1 H, d, *J* 13.7, $CH_AH_BSO_2$), 2.13 (2 H, m), 1.93 (3 H, dd, *J* 6.9 and 1.7, *Me*CH), 1.89 (3 H, m), 1.43-1.36 (2 H, m), 1.18 (3 H, s, CMe_AMe_B) and 0.98 (3 H, s, CMe_AMe_B).

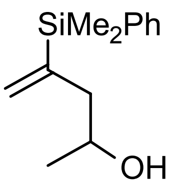


2-Dimethyl(phenyl)silylpropene 203

The method of Pulido was followed.[303] Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF, 1.7 cm^3, 1.7 mmol) was added to pre-dried copper(I) cyanide (150 mg, 1.7 mmol) in THF (10 cm^3) at 0 °C under an argon atmosphere. After stirring at this temperature for 20 min, the mixture was cooled to –40 °C and allene (40 cm^3, 1.7 mmol) in THF (10 cm^3) was added dropwise. The mixture was stirred for 1 h. The solution was cooled to –78 °C and a mixture of methanol with a small quantity of saturated aqueous ammonium chloride (10 cm^3) was slowly added dropwise. The solution was allowed to warm to –40 °C and stirred for 10 min, then to 0 °C and stirred for a further 1 h. Ether (20 cm^3) was added, the layers separated and the aqueous layer extracted with ether (3 ∞ 10 cm^3). The combined organic layers were washed with basic saturated aqueous ammonium chloride (2 ∞ 10 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a yellow liquid (360 mg) containing the vinylsilane **203**;[139] R_f(CH_2Cl_2) 0.26; ν_{max}(film)/cm^{-1} 1590 (Ph), 1249 ($SiMe_2$) and 1112 (SiPh); δ_H(250 MHz; $CDCl_3$) 7.60-7.50 (5 H, m, Ph), 5.68 (1 H, m, C=$CH_{\textit{trans}\text{-to-Si}}$), 5.33 (1 H, m, C=$CH_{\textit{cis}\text{-to-Si}}$), 1.81 (3 H, m, Me) and 0.36 (6 H, s, $SiMe_2$).



219

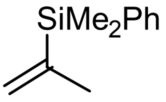


220

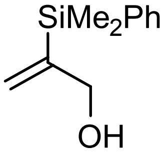
2-Dimethyl(phenyl)silanylprop-2-en-1-ol 219 and 4-Dimethyl(phenyl)-silanylpent-4-en-2-ol 220

The method of Pulido was followed.[303] Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF, 1.70 cm^3, 1.70 mmol) was added to pre-dried copper(I) cyanide (150 mg, 1.70 mmol) in THF (10 cm^3) at 0 °C under an argon atmosphere. After stirring at this temperature for 20 min, the mixture was cooled to –40 °C and allene (40 cm^3, 1.70 mmol) in THF (10 cm^3) was added dropwise. The mixture was stirred for 1 h and then ethylaluminium dichloride (1.0 mol dm^{-3} solution in hexanes) was added and the mixture stirred for 10 min. Crotonylsultam **218** (46 mg, 0.16 mmol) in THF (5 cm^3) was added and the mixture stirred for 15 min. The mixture was allowed to warm to 0 °C and stirred for 1 h, allowed to warm to room temperature and stirred for 2 h before recooling to 0 °C and addition of water (10 cm^3). Basic saturated aqueous ammonium chloride (10 cm^3) was added, followed by ether (20 cm^3), the layers were separated and the aqueous layer extracted with ether (3 ∞ 10 cm^3). The combined organic layers were washed with basic saturated aqueous ammonium chloride (2 ∞ 10 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a yellow liquid. Chromatography (SiO_2, CH_2Cl_2) gave an inseparable mixture of alcohol **219** (previously characterised) and *alcohol* **220**[325] (6 mg, 20%); R_f(CH_2Cl_2) 0.22; ν_{max}(CH_2Cl_2)/cm^{-1} 3383 (O-H), 1595 (Ph), 1250 ($SiMe_2$) and 1111 (SiPh); δ_H(500 MHz; $CDCl_3$) 7.51 (2 H, m, aromatic-$H_{ortho\text{-to-Si}}$), 7.37 (3 H, m, aromatic-$H_{meta/para\text{-to-Si}}$), 5.80 (1 H, t, *J* 1.4, =$CH_{cis\text{-to-Si}}H_{trans\text{-to-Si}}$), 5.59 (1 H, d, *J* 2.9, =$CH_{cis\text{-to-Si}}H_{trans\text{-to-Si}}$), 3.73 (1 H, m, C*H*OH), 2.35 (1 H, dd, *J* 13.6 and 3.7, =CCH_AH_B), 2.20 (1 H, dd, *J* 13.8 and 8.9, =CCH_AH_B), 1.11 (3

H, d, *J* 6.1, *Me*CH) and 0.40 (6 H, s, $SiMe_2$); *m/z* (EI) 205 (30%, M – Me) and 135 (82, $PhMe_2Si$) (Found: M – Me, 205.1050. $C_{12}H_{17}SiO$ requires *M*, 205.1049).



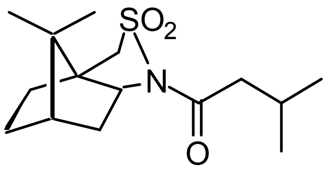
203



219

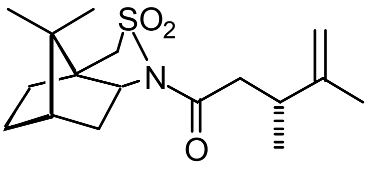
2-Dimethyl(phenyl)silylpropene 203 and 2-Dimethyl(phenyl)silanylprop-2-en-1-ol 219

The method of Pulido was followed.[303] Dimethyl(phenyl)silyllithium (1.1 mol dm^{-3} solution in THF, 0.40 cm^3, 0.44 mmol) was added to pre-dried copper(I) cyanide (40 mg, 0.44 mmol) in THF (10 cm^3) at 0 °C under an argon atmosphere. After stirring at this temperature for 20 min, the mixture was cooled to –40 °C and allene (10 cm^3, 0.43 mmol) in THF (10 cm^3) was added dropwise. The mixture was stirred for 1 h, allowed to warm to 0 °C and stirred for another 1 h, and finally allowed to warm to room temperature. The solution was stirred for 2 h before addition of water (5 cm^3). Ether (20 cm^3) was added, the layers separated and the aqueous layer extracted with ether (3 ∞ 10 cm^3). The combined organic layers were washed with basic saturated aqueous ammonium chloride (2 ∞ 10 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give a yellow liquid (86 mg) containing the vinylsilane **203** (previously characterised) and the alcohol **219**;[326] $R_f(CH_2Cl_2)$ 0.22; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3383 (O-H), 1595 (Ph), 1250 ($SiMe_2$) and 1111 (SiPh); δ_H(500 MHz; $CDCl_3$) 7.51 (2 H, aromatic-$H_{ortho\text{-to-Si}}$), 7.37 (3 H, m, aromatic-$H_{meta/para\text{-to-Si}}$), 5.92 (1 H, m, =$C\mathit{H}_AH_B$), 5.50 (1 H, m, =$CH_A\mathit{H}_B$), 4.24 (2 H, t, *J* 1.5, $C\mathit{H}_2OH$) and 0.41 (6 H, s, $SiMe_2$).



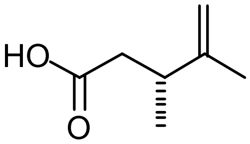
***N*-(3-Methylbutyryl)-(7*R*)-2,10-camphorsultam 222**

Following Buckle,[150,304] methyllithium (1.4 mol dm^{-3} solution in ether, 5.00 cm^3, 7.04 mmol) was added slowly to a stirred suspension of copper(I) iodide (670 mg, 3.52 mmol) in dry ether (9 cm^3) under an argon atmosphere at –20 °C to give a colourless solution. The solution was stirred for 20 min before being transferred *via* cannula to a solution of crotonylsultam **218** (100 mg, 0.350 mmol) in dry THF (1 cm^3) which had been pre-mixed for 20 min at –78 °C with ethylaluminium dichloride (1.0 mol dm^{-3} solution in hexanes, 3.50 cm^3, 3.52 mmol) under an argon atmosphere. The resulting mixture was stirred at –78 °C for 2 h and then allowed to warm gradually to room temperature overnight before being cooled to 0 °C and quenched with saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer was extracted with ether (2 ∞ 20 cm^3). The combined organic fractions were washed with saturated aqueous ammonium chloride (2 ∞ 10 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *sultam* **222** (57 mg, 54%) as white needles, mp 110-111 °C (from MeOH); R_f(light petroleum-ether, 1:1) 0.43; ν_{max}(CH_2Cl_2)/cm^{-1} 1694 (C=O), 1329 (SO_2N) and 1165 (SO_2N); δ_H(250 MHz; $CDCl_3$) 3.88 (1 H, t, *J* 6.4, CHN), 3.50 (1 H, d, *J* 13.8, $C\mathit{H}_AH_BSO_2$), 3.41 (1 H, d, *J* 13.8, $CH_A\mathit{H}_BSO_2$), 2.67 (1 H, dd, *J* 15.8 and 7.2, $COC\mathit{H}_AH_B$), 2.51 (1 H, dd, *J* 15.8 and 6.7, $COCH_A\mathit{H}_B$), 2.23 (1 H, m, $C\mathit{H}Me_2$), 2.09 (2 H, m), 1.89 (3 H, m), 1.45-1.32 (2 H, m), 1.16 (3 H, s, $C\mathit{Me}_AMe_B$), 0.98 (3 H, d, *J* 6.6, $CH\mathit{Me}_AMe_B$), 0.97 (3 H, s, $CMe_A\mathit{Me}_B$) and 0.96 (3 H, d, *J* 6.6, $CHMe_A\mathit{Me}_B$); δ_C($CDCl_3$) 172.0+, 65.3–, 53.1+, 48.3–, 47.8–, 44.7–, 44.3+, 42.5+, 38.6+, 32.9+, 26.5+, 25.6+, 22.3–, 20.8– and 19.9–; *m/z* (EI) 299 (37%, M^+), 284 (21, M – Me), 85 (100, Me_2CHCH_2CO) and 57 (92, Me_2CHCH_2) (Found: M^+, 299.1557. $C_{15}H_{25}NSO_3$ requires *M*, 299.1555).



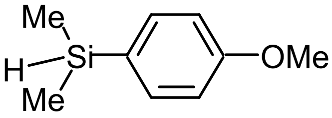
N-(3*R*)-(3,4-Dimethylpent-4-enoyl)-(7*R*)-2,10-camphorsultam 224

Following Buckle,[150,304] t-butyllithium (1.7 mol dm^{-3} solution in pentane, 4.20 cm^3, 7.04 mmol) was added dropwise to a stirred solution of 2-bromopropene (0.35 cm^3, 3.52 mmol) in ether (5 cm^3) at –78 °C under an argon atmosphere. The solution was stirred for 2 h before being added *via* cannula to a suspension of copper(I) iodide (670 mg, 3.52 mmol) in dry ether (5 cm^3) under an argon atmosphere at –20 °C. The solution was stirred for 20 min before being transferred *via* cannula to a solution of crotonylsultam **218** (100 mg, 0.350 mmol) in dry THF (2 cm^3) which had been pre-mixed for 20 min at –78 °C with ethylaluminium dichloride (1.0 mol dm^{-3} solution in hexanes, 3.50 cm^3, 3.52 mmol) under an argon atmosphere. The resulting mixture was stirred at –78 °C for 2 h and then allowed to warm gradually to room temperature overnight before being cooled to 0 °C and quenched with saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer was extracted with ether (2 ∞ 20 cm^3). The combined organic fractions were washed with saturated aqueous ammonium chloride (2 ∞ 5 cm^3) and brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure. Chromatography (SiO$_2$, light petroleum-ether, 1:1) gave the *sultam* **224** (103 mg, 91%) as a pale yellow liquid; R_f(light petroleum-ether, 1:1) 0.35; ν_{max}(CH$_2$Cl$_2$)/cm^{-1} 1698 (CO), 1645 (C=C), 1331 (SO$_2$N) and 1165 (SO$_2$N); δ_H(250 MHz; CDCl$_3$) 4.75 (1 H, m, =CH_AH$_B$), 4.69 (1 H, m, =CH$_A$$H_B$), 3.87 (1 H, t, *J* 6.3, CHN), 3.49 (1 H, d, *J* 13.7, CH_AH$_B$SO$_2$), 3.41 (1 H, d, *J* 13.7, CH$_A$$H_BSO_2$), 2.98 (1 H, dd, *J* 15.2 and 7.7, CH_AH$_B$CO), 2.77 (1 H, m, C*H*Me), 2.55 (1 H, dd, *J* 15.1 and 6.4, CH$_A$$H_B$CO), 2.07 (2 H, m), 1.87 (3 H, m), 1.73 (3 H, s, =CMe), 1.44-1.34 (2 H, m), 1.14 (3 H, s, CMe_AMe$_B$), 1.08 (3 H, d, *J* 4.1, CH*Me*) and 0.96 (3 H, s, CMe$_A$$Me_B$); δ_C(CDCl$_3$) 171.1+, 148.5+, 109.9+, 65.2–, 53.1+, 43.3+, 44.7–, 41.0+, 38.5+, 37.5–, 32.9+, 29.7+, 26.5+, 22.5–, 20.7–, 19.9– and 19.7–; *m/z* (EI) 325 (39%, M$^+$) (Found: M$^+$, 325.1714. C$_{17}$H$_{27}$NSO$_3$ requires *M*, 325.1712).



(3*R*)-3,4-Dimethylpent-4-enoic acid 227

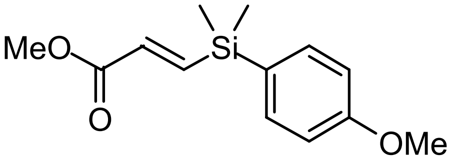
A solution of the sultam **224** (100 mg, 0.31 mmol) in THF (12 cm^3) and water (4 cm^3) at 0 °C was treated with lithium hydroxide monohydrate (65 mg, 1.54 mmol) and hydrogen peroxide (6% solution in water, 2.50 cm^3, 4.62 mmol). The resulting solution was stirred at this temperature for 1 d and allowed to warm to room temperature before recooling to 0 °C and addition of saturated aqueous sodium sulfite. The THF was removed by evaporation under reduced pressure and the residue extracted with dichloromethane (3 ∞ 10 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the recovered (+)-sultam **161** (46 mg, 69%) (previously characterised). The aqueous layers were acidified to pH 1 (hydrochloric acid) and extracted with ethyl acetate (3 ∞ 15 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the acid **227**[327] (12 mg, 30%); R_f(light petroleum-ether, 1:1) 0.10; ν_{max}(film)/cm^{-1} 2968 (O-H, broad), 1710 (C=O) and 1647 (C=C); δ_H(250 MHz; $CDCl_3$) 4.75 (2 H, m, =CH_2), 2.66 (1 H, m, C*H*Me), 2.52 (1 H, dd, *J* 15.1 and 6.8, $COCH_AH_B$), 2.32 (1 H, dd, *J* 14.9 and 7.9, $COCH_AH_B$), 1.73 (3 H, s, =CMe) and 1.11 (3 H, d, *J* 6.8, CH*Me*); δ_C($CDCl_3$) 148.1+, 109.9+, 39.7+, 37.4–, 19.9– and 19.4–; *m/z* (EI) 129 (12%, M^+) (Found: MH^+, 129.0921. $C_7H_{12}O_2$ requires *M* + H, 129.0916).



(4-Methoxyphenyl)dimethylsilane 232

Method 1: The Method of Zwicky was followed.[328,329,199a] 4-Bromoanisole (5.3 cm^3, 42 mmol) in dry ether (20 cm^3) was added slowly to magnesium turnings (1.0 g, 42 mmol) in dry ether (10 cm^3) at room temperature under an argon atmosphere with stirring. The mixture was cautiously heated until it became exothermic, and then once the reaction had subsided the mixture was heated under reflux for a further 2 h and allowed to cool to room temperature. Chlorodimethylsilane (4.69 cm^3, 42 mmol) in dry ether (10 cm^3) was slowly added dropwise as the mixture was stirred, and refluxing was then continued for 45 h. After cooling, the mixture was carefully poured into distilled water (50 cm^3), the layers were separated and the aqueous layer was extracted with ether (3 ∞ 20 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the pure silane **232**[310] as a pale yellow liquid (4.06 g, 58%); R_f(light petroleum) 0.12; ν_{max}(film)/cm^{-1} 2113 (Si-H), 1594 (Ar), 1247 ($SiMe_2$), 1114 (SiAr); δ_H(250 MHz; $CDCl_3$) 7.45 (2 H, d, *J* 8.6, aromatic-H), 6.92 (2 H, d, *J* 8.6, aromatic-H), 4.41 (1 H, sept, *J* 3.7, SiH), 3.82 (3 H, s, MeO) and 0.32 (6 H, d, *J* 3.8, $SiMe_2$).

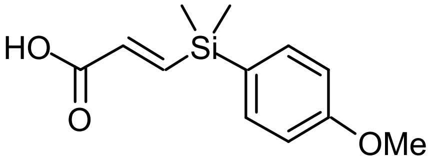
Method 2: The method of Hiyama was adapted.[310] 4-Bromoanisole (5.3 cm^3, 42 mmol) in dry THF (10 cm^3) was added slowly to magnesium turnings (1.0 g, 42 mmol) in dry THF (20 cm^3) at 0 °C under an argon atmosphere with stirring. The mixture was allowed to warm to room temperature until it became exothermic and was then cooled in ice until the reaction had subsided before being stirred for a further 2 h at room temperature. The mixture was recooled to 0 °C and chlorodimethylsilane (4.7 cm^3, 42 mmol) in dry THF (10 cm^3) was slowly added dropwise with stirring, and then stirring was continued overnight. The mixture was carefully poured into distilled water (50 cm^3), the layers were separated and the aqueous layer was extracted with ether (3 ∞ 20 cm^3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the pure silane **232** as a pale yellow liquid (4.85 g, 70%) with data (TLC, IR, NMR) identical to those obtained above.



E-Methyl 3-[(4-methoxyphenyl)dimethylsilanyl]acrylate **231**

The Method of Zwicky was followed.[328,130] Dicobalt octacarbonyl (100 mg, 0.3 mmol) was added cautiously to crude silane **232** (999 mg, 6.0 mmol) in a glove box. Dry toluene (10 cm^3) was added under an argon atmosphere and the mixture was cooled in ice. Freshly-distilled (from CaH_2) methyl acrylate (2.75 cm^3, 30.1 mmol) was added dropwise and the mixture was stirred at room temperature for 22 h under an argon atmosphere. The mixture was recooled to 0 °C and water (20 cm^3) was added slowly with vigorous stirring. Stirring was continued for 24 h and the mixture was then filtered through celite and washed through with ether (20 cm^3). The layers were separated and the aqueous layer was extracted with ether

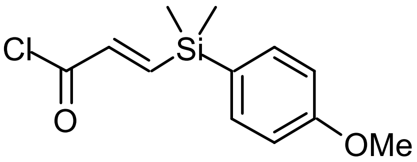
(3 ∞ 20 cm^3), the combined organic layers washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *acrylate* **231** as a pale yellow liquid (1.09 g, 72%); R_f(light petroleum-ether, 1:1) 0.56; ν_{max}(film)/cm^{-1} 1728 (C=O), 1594 (Ar), 1248 ($SiMe_2$) and 1113 (SiAr); δ_H(250 MHz; $CDCl_3$) 7.43 (2 H, d, *J* 8.3, aromatic-H), 7.36 (1 H, d, *J* 18.9, =CHSi), 6.93 (2 H, d, *J* 8.4, aromatic-H), 6.25 (1 H, d, *J* 18.8, CHCO), 3.82 (3 H, s, ArOMe), 3.75 (3 H, s, MeOCO) and 0.39 (6 H, s, Me_2Si); δ_C($CDCl_3$) 166.3+, 160.8+, 148.3–, 135.3–, 134.6–, 127.1+, 113.8–, 55.1–, 51.7– and –3.0–; *m/z* (EI) 250 (41%, M^+), 235 (100, M – Me), 219 (37, M – MeO), 165 [45, *p*-MeO-(C_6H_4)-$SiMe_2$], 135 [18, *p*-MeO-(C_6H_4)-Si] and 59 (8, MeOCO) (Found: M^+, 250.1029. $C_{13}H_{18}O_3Si$ requires *M*, 250.1025).



E-3-[(4-Methoxyphenyl)dimethylsilanyl]acrylic acid 233

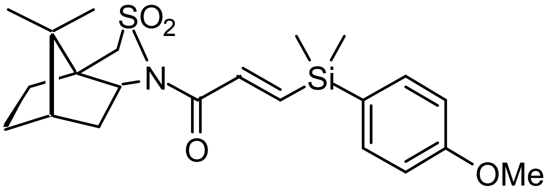
The unsaturated ester **231** (5.26 g, 21 mmol) in THF (90 cm^3) and water (30 cm^3) was treated with lithium hydroxide monohydrate (4.40 g, 105 mmol) and the resulting mixture was stirred vigorously for 1 d. More lithium hydroxide monohydrate (4.00 g) was added and stirring was continued for a further 6 d. The THF was removed by evaporating under reduced pressure, and the remaining aqueous solution was washed with ether (3 ∞ 50 cm^3) to remove remaining starting material and non-acidic impurities and then acidified to pH 1 by adding concentrated hydrochloric acid slowly while cooling in ice. The solution was then extracted with ether

(3 ∞ 50 cm^3) and the combined organic fractions washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *acid* **233** (1.97 g, 37%) as white cubes, mp 77-78 °C (from light petroleum); R_f(light petroleum-ether, 1:1) 0.11; ν_{max}(film)/cm^{-1} 3500-2500 (O-H), 1699 (C=O), 1595 (Ar), 1249 ($SiMe_2$) and 1116 (SiAr); δ_H(250 MHz; $CDCl_3$) 7.47 (1 H, d, J 18.8, =CHSi), 7.43 (2 H, d, J 8.5, aromatic-H), 6.93 (2 H, d, J 8.5, aromatic-H), 6.25 (1 H, d, J 18.8, CHCO), 3.82 (3 H, s, ArOMe) and 0.41 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 170.2+, 160.9+, 151.3–, 135.3–, 134.1–, 126.7+, 113.9–, 55.1– and –3.1–; *m/z* (EI) 236 (21%, M$^+$), 221 (100, M – Me), 165 [58, *p*-MeO-(C_6H_4)-$SiMe_2$] and 135 [29, *p*-MeO-(C_6H_4)-Si] (Found: M$^+$, 236.0869. $C_{12}H_{16}O_3Si$ requires *M*, 236.0869).



E-3-[(4-Methoxyphenyl)dimethylsilanyl]acryloyl chloride 234

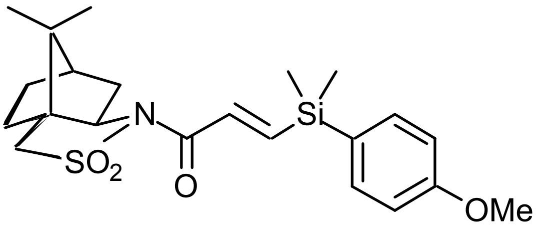
Oxalyl chloride (0.60 cm^3, 7.1 mmol) was added to a solution of the dry acid **233** (1.10 g, 4.7 mmol) in dry dichloromethane (10 cm^3) at 0 °C under an argon atmosphere. The resulting solution was stirred at 0 °C for 1 h and then at room temperature for 2 h. The solvent was evaporated on a high vacuum pump until bubbling had ceased, giving the *acid chloride* **234** which was used immediately without purification or characterisation.



N-{*E*-3-[(4-Methoxyphenyl)dimethylsilanyl]acryloyl}-(7*R*)-2,10-camphorsultam 212

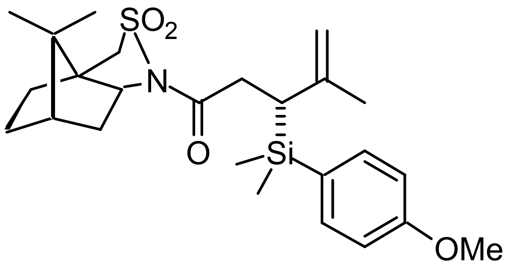
(+)-Camphorsultam **161** (91 mg, 0.42 mmol) in dry toluene (5 cm^3) was added *via* cannula to a stirred suspension of sodium hydride (60% dispersion in oil, pre-washed with light petroleum and dried under reduced pressure, 21 mg, 0.47 mmol) in dry toluene (5 cm^3) under an argon atmosphere. The resulting mixture was stirred for 3 h before addition of a solution of the acid chloride **234** (freshly made from acid **233**, 100 mg, 0.42 mmol) in toluene (5 cm^3). The mixture was stirred for 1.5 h before careful addition of water. The layers were separated and the aqueous layer was extracted with ether (2 ∞ 5 cm^3). The combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate (2 ∞ 5 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the *sultam* **212** (57 mg, 32%) as white needles, mp 102-104 °C (from MeOH); R_f(light petroleum-ether, 1:1) 0.26; ν_{max}(CH_2Cl_2)/cm^{-1} 1679 (C=O), 1594 (Ar), 1165 (SO_2N) and 1113 (SiAr); δ_H(250 MHz;

$CDCl_3$) 7.50 (1 H, d, *J* 18.3, =CHSi), 7.44 (2 H, d, *J* 8.8, aromatic-H), 7.00 (1 H, d, *J* 18.2, CHCO), 6.92 (2 H, d, *J* 8.6, aromatic-H), 3.93 (1 H, dd, *J* 7.2 and 5.5, CHN), 3.81 (3 H, s, ArOMe), 3.51 (1 H, d, *J* 13.7, $CH_AH_BSO_2$), 3.43 (1 H, d, *J* 13.7, $CH_AH_BSO_2$), 2.12 (2 H, m), 1.89 (3 H, m), 1.47-1.32 (2 H, m), 1.18 (3 H, s, CMe_AMe_B), 0.98 (3 H, s, CMe_AMe_B) and 0.41 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 161.2+, 149.2–, 135.4–, 134.0–, 127.1+, 113.8–, 110.0+, 65.2–, 55.1–, 53.2+, 48.6+, 47.8+, 44.7–, 38.5+, 33.0+, 26.5+, 20.9–, 19.9– and –3.0–; *m/z* (EI) 433 (72%, M^+) and 418 (24, M – Me) (Found: M^+, 433.1734. $C_{22}H_{31}O_4SNSi$ requires *M*, 433.1743) (Found: C, 60.6; H, 7.10; N, 3.1; S, 7.6. $C_{22}H_{31}O_4SNSi$ requires C, 60.9; H, 7.20; N, 3.2; S, 7.4%).



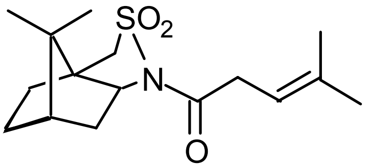
***N*-{*E*-3-[(4-Methoxyphenyl)dimethylsilanyl]acryloyl}-(7*S*)-2,10-camphorsultam 249**

This was synthesised from (7*S*)-(–)-2,10-camphorsultam **174** as described above to give a sample with data identical (mp, NMR) to the enantiomer **212**.



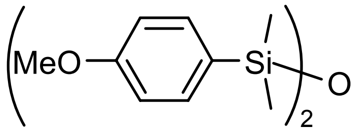
N-(3*R*)-{3-[(4-Methoxyphenyl)dimethylsilanyl]-4-methylpent-4-enoyl}-(7*R*)-2,10-camphorsultam **236**

Following Buckle,[150,304] t-butyllithium (1.7 mol dm^{-3} solution in pentane, 3.40 cm^3, 5.73 mmol) was added dropwise to a stirred solution of 2-bromopropene (0.25 cm^3, 2.86 mmol) in ether (5 cm^3) at –78 °C under an argon atmosphere. The solution was stirred for 2 h before being added *via* cannula to a suspension of copper(I) iodide (544 mg, 2.86 mmol) in dry ether (5 cm^3) under an argon atmosphere at –20 °C. The solution was stirred for 20 min before being transferred *via* cannula to a solution of sultam **212** (124 mg, 0.29 mmol) in dry THF (2 cm^3) which had been pre-mixed for 20 min at –78 °C with ethylaluminium dichloride (1.0 mol dm^{-3} solution in hexanes, 2.90 cm^3, 2.86 mmol) under an argon atmosphere. The resulting mixture was stirred at –78 °C for 2 h and then allowed to warm gradually to room temperature overnight before being cooled to 0 °C and quenched with basic saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer was extracted with ether (2 ∞ 20 cm^3). The combined organic fractions were washed with basic saturated aqueous ammonium chloride (2 ∞ 5 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the *sultam* **236** (60 mg, 44%) as a pale yellow liquid; R_f(light petroleum-ether, 1:1) 0.39; δ_H(250 MHz; $CDCl_3$) the following diagnostic signals were observed: 4.67 (1 H, m, $=\mathrm{C}\mathit{H}_\mathrm{A}\mathrm{H}_\mathrm{B}$), 4.54 (1 H, s, $=\mathrm{CH}_\mathrm{A}\mathit{H}_\mathrm{B}$), 3.81 (3 H, s, OMe), 3.14 (1 H, dd, *J* 16.1 and 12.2, $\mathrm{COC}\mathit{H}_\mathrm{A}\mathrm{H}_\mathrm{B}$), 2.58 (1 H, dd, *J* 16.3 and 3.8, $\mathrm{COCH}_\mathrm{A}\mathit{H}_\mathrm{B}$), 2.37 (1 H, dd, *J* 12.1 and 3.6, CHSi), 1.57 (3 H, s, =CMe), 0.32 (3 H, s, $\mathrm{Si}\mathit{Me}_\mathrm{A}\mathrm{Me}_\mathrm{B}$) and 0.29 (3 H, s, $\mathrm{SiMe}_\mathrm{A}\mathit{Me}_\mathrm{B}$); the compound protodesilylated (to give sultam **237**) too rapidly for any further data to be obtained.



237

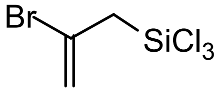
+



238

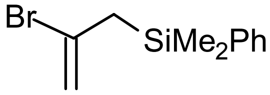
N-(4-Methylpent-3-enoyl)-(7*R*)-2,10-camphorsultam 237 and di-4-methoxyphenyl(tetramethyl)disiloxane 238

On standing at room temperature for 10 d, sultam **236** was converted entirely into a pale yellow liquid. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the *sultam* **237** (60 mg, 67%), as a pale yellow liquid; R_f(light petroleum-ether, 1:1) 0.35; ν_{max}(CH_2Cl_2)/cm^{-1} 1700 (C=O), 1674 (C=C), 1328 (SO_2N) and 1197 (SO_2N); δ_H(250 MHz; $CDCl_3$) 5.33 (1 H, tsept, *J* 5.5 and 1.4, HC=), 3.87 (1 H, dd, *J* 7.5 and 5.2, CHN), 3.50 (1 H, d, *J* 13.9, $CH_AH_BSO_2$ with H_A italic: C*H*$_A$H$_B$SO$_2$), 3.45 (2 H, m, $COCH_2$), 3.42 (1 H, d, *J* 13.8, CH$_A$*H*$_B$SO$_2$), 2.11 (2 H, m), 1.89 (3 H, m), 1.75 (3 H, d, *J* 1.1, =*Me*$_{trans\text{-to-H}}$Me$_{cis\text{-to-H}}$), 1.65 (3 H, s, =Me$_{trans\text{-to-H}}$*Me*$_{cis\text{-to-H}}$), 1.37 (2 H, m), 1.16 (3 H, s, C*Me*$_A$Me$_B$) and 0.97 (3 H, s, CMe$_A$*Me*$_B$); δ_C($CDCl_3$) 170.7+, 136.2+, 114.9–, 65.4–, 53.0+, 48.5+, 47.8+, 44.7–, 38.5+, 34.9+, 32.9+, 26.5+, 25.7–, 20.8–, 19.9– and 18.2–; *m/z* (EI) 311 (52%, M$^+$) and 69 (100, $Me_2C{=}CHCH_2$) (Found: M$^+$, 311.1555. $C_{16}H_{25}NSO_3$ requires *M*, 325.1555) and *disiloxane* **238** (16 mg, 16%), a pale yellow liquid; R_f(light petroleum-ether, 1:1) 0.63; ν_{max}(film)/cm^{-1} 1596 (Ar), 1249 ($SiMe_2$), 1117 (SiAr) and 1036 (SiO); δ_H(250 MHz; $CDCl_3$) 7.47 (2 H, d, *J* 6.6, aromatic-H), 6.90 (2 H, m, aromatic-H), 3.82 (3 H, s, MeO) and 0.29 (6 H, s, $SiMe_2$); δ_C($CDCl_3$) 160.5+, 134.5–, 113.4–, 55.0– and 1.0–; *m/z* (EI) 346 (42%, M$^+$), 331 (100, M – Me) and 165 (86, *p*-MeO-(C_6H_4)-$SiMe_2$) (Found: M$^+$, 346.1413. $C_{18}H_{26}Si_2O_3$ requires *M*, 346.1420).



2-Bromo-3-trichlorosilylprop-1-ene 225

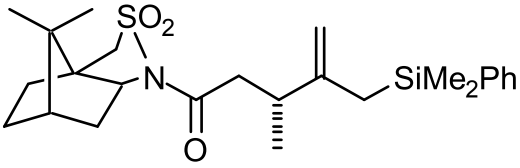
A mixture of 2,3-dibromopropene (4.14 cm^3, 40 mmol) and trichlorosilane (4.43 cm^3, 44 mmol) was added dropwise under an argon atmosphere over 1 h to a suspension of copper(I) chloride in dry ether (20 cm^3) and triethylamine (5.56 cm^3) at room temperature. The reaction mixture was stirred at room temperature overnight after which time the white solid was filtered off and washed with dry ether (10 cm^3). The orange filtrate was evaporated under reduced pressure to give the silyl chloride **225**[308] (7.64 g, 75%) as a pale brown liquid; ν_{max}($CHCl_3$)/ cm^{-1} 1623 (C=C); δ_H(250 MHz; $CDCl_3$) 5.71 (1 H, m, $=CH_{cis\text{-to-Br}}$), 5.60 (1 H, d, *J* 2.1, $=CH_{trans\text{-to-Br}}$) and 2.90 (2 H, d, *J* 0.9, CH_2Si).



2-Bromo-3-dimethyl(phenyl)silylprop-1-ene 223

Phenylmagnesium bromide (3.0 mol dm^{-3} solution in ether, 12 cm^3, 36 mmol) was added slowly to a solution of the silyl chloride **225** (7.64 g, 30 mmol) in ether (20 cm^3) and heated under reflux under an argon atmosphere for 20 h. The solution was allowed to cool to room temperature and methylmagnesium iodide (3.0 mol dm^{-3} solution in ether, 22 cm^3, 66 mmol) was added dropwise and the mixture stirred for a further 20 h. The reaction mixture was poured cautiously into saturated aqueous ammonium chloride (100 cm^3), the layers were separated and the aqueous layer extracted with ether (3 ∞ 20 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give an orange liquid. Chromatography (SiO_2, light petroleum) gave the vinyl bromide **223**[308] (4.74 g, 62%) as a colourless liquid; R_f(light petroleum) 0.41; ν_{max}(film)/

cm^{-1} 1618 (C=C), 1250 (SiMe$_2$) and 1114 (SiPh); δ_H(250 MHz; CDCl$_3$) 7.54 (2 H, m, Ph), 7.38 (3 H, m, Ph), 5.28 (1 H, m, =C$H_{cis\text{-to-Br}}$H$_{trans\text{-to-Br}}$), 5.23 (1 H, d, *J* 1.6, =CH$_{cis\text{-to-Br}}$$H_{trans\text{-to-Br}}$), 2.33 (2 H, d, *J* 0.9, CH$_2$Si) and 0.42 (6 H, s, SiMe$_2$).



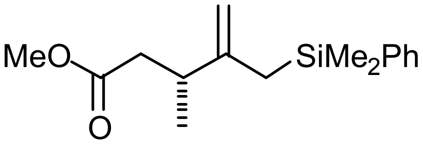
N-(3*R*)-3-Methyl-4-[dimethyl(phenyl)silanyl]methylpent-4-enoyl-(7*R*)-2,10-camphorsultam **221**

Method 1: (Attempted) The method of Pulido was followed.[303]

Dimethyl(phenyl)silyllithium (1.0 mol dm^{-3} solution in THF, 0.20 cm^3, 0.20 mmol) was added to pre-dried copper(I) cyanide (20 mg, 0.22 mmol) in THF (2 cm^3) at 0 °C under an argon atmosphere. After stirring at this temperature for 20 min, the mixture was cooled to –40 °C and allene (10 cm^3, 0.43 mmol) in THF (4 cm^3) was added dropwise. The mixture was stirred for 1 h. The solution was then added slowly to a solution of crotonylsultam **218** (24 mg, 0.08 mmol) in dry THF (2 cm^3), pre-mixed at –40 °C for 5 min with ethylaluminium dichloride (1.0 mol dm^{-3}, 0.10 cm^3, 0.10 mmol). The solution was allowed to warm to 0 °C and stirred for a further 1 h. Basic saturated aqueous ammonium chloride (10 cm^3) was added, followed by ether (20 cm^3), the layers were separated and the aqueous layer extracted with ether (3 ∞ 10 cm^3). The combined organic layers were washed with basic saturated aqueous ammonium chloride (2 ∞ 10 cm^3) and brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure to give a yellow liquid (360 mg) containing only the starting material crotonylsultam **218** and the vinylsilane **203** (both previously characterised).

Method 2: Following Buckle,[150,304] t-butyllithium (1.7 mol dm^{-3} solution in pentane, 4.20 cm^3, 7.04 mmol) was added dropwise to a stirred solution of vinyl bromide **223** (898 mg, 3.52 mmol) in ether (5 cm^3) at –78 °C under an argon atmosphere. The solution was stirred for 2 h before being added *via* cannula to a suspension of copper(I) iodide (670 mg, 3.52 mmol) in dry ether (5 cm^3) under an argon atmosphere at –20 °C. The solution was stirred for 20 min before being transferred *via* cannula to a solution of crotonylsultam **218** (100 mg, 0.350 mmol) in dry THF (2 cm^3) which had been pre-mixed for 20 min at –78 °C with ethylaluminium dichloride (1.0 mol dm^{-3} solution in hexanes, 3.50 cm^3, 3.52 mmol) under an argon atmosphere. The resulting mixture was stirred at –78 °C for 2 h and then allowed to warm gradually to room temperature overnight before being cooled to 0 °C and quenched with basic saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer extracted with ether (2 ∞ 20 cm^3). The combined organic fractions were washed with basic saturated aqueous ammonium chloride (2 ∞ 5 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the allylsilane **211** and vinylsilane **203** as an inseparable mixture (431 mg); R_f(light petroleum-ether, 1:1) 0.81; ν_{max}(film)/cm^{-1} 1630 (C=C), 1584 (Ph), 1248 ($SiMe_2$) and 1113 (SiPh); δ_H(250 MHz; $CDCl_3$) vinylsilane **203** (previously characterised), allylsilane **211**[330] signals as follows: 7.50 (2 H, m, Ph), 7.36 (3 H, m, Ph), 5.91-5.73 (1 H, m, *H*C=CH$_2$), 4.90 (2 H, m, HC=C*H*$_2$), 1.76 (2 H, dt, *J* 8.1 and 1.1, CH$_2$Si) and 0.29 (6 H, s, Me$_2$Si); and the *sultam* **221** (90 mg, 56%) as a pale yellow liquid; R_f(light petroleum-ether, 1:1) 0.42; ν_{max}(film)/cm^{-1} 1698 (C=O), 1633 (C=C), 1331 (SO_2N), 1250 ($SiMe_2$), 1165 (SO_2N) and 1117 (SiPh); δ_H(400 MHz; $CDCl_3$) 7.59 (2 H, m, Ph), 7.51 (3 H, m, Ph), 4.67 (1 H, s, =C*H*$_A$H$_B$), 4.50 (1 H, s, =CH$_A$*H*$_B$), 3.85 (1 H, t, *J* 6.3, CHN), 3.48 (1 H, d, *J* 14.0, C*H*$_A$H$_B$SO$_2$), 3.41 (1 H, d, *J* 13.8, CH$_A$*H*$_B$SO$_2$), 2.97 (1 H, dd, *J* 15.3 and 6.2, COC*H*$_A$H$_B$), 2.55 (1 H, m, C*H*Me), 2.48 (1 H, dd, *J* 15.2 and 7.6, COCH$_A$*H*$_B$), 2.03 (2 H, m), 1.92-1.82 (3 H, m), 1.79 (1 H, s, SiC*H*$_A$H$_B$), 1.77 (1 H, s, SiCH$_A$*H*$_B$), 1.38 (2 H, m), 1.09 (3 H, s, C*Me*$_A$Me$_B$), 1.00 (3 H, d, *J* 6.7, CH*Me*), 0.97 (3 H, s, CMe$_A$*Me*$_B$) and 0.41 (6 H, s, SiMe$_2$); δ_C($CDCl_3$) 171.0+, 150.3+, 133.7–, 133.0–, 129.6–, 128.9–, 127.9–, 127.7–, 106.9+, 65.2–, 53.0+, 48.3+, 47.8+, 44.7–, 41.6+, 38.6+, 37.0–, 32.9+, 26.5+, 24.9+, 20.8–, 19.9–, 19.5–, 0.0– and –2.8–; *m/z* (EI) 459 (42%, M$^+$), 444 (57, M – Me) and 135 (100, PhMe$_2$Si) (Found: M$^+$, 459.2276. $C_{25}H_{37}SiNSO_3$ requires *M*, 459.2263).

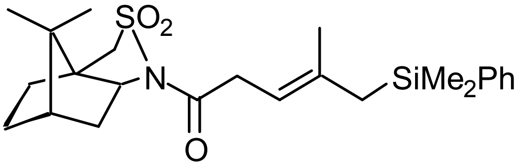
On standing at room temperature for 30 d, sultam **221** was converted entirely into sultam **224** (previously characterised).



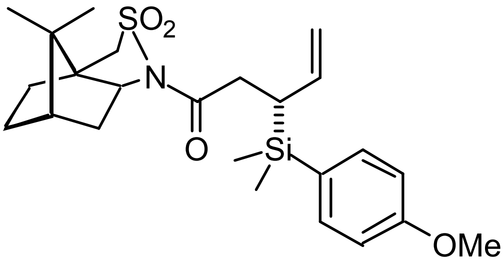
(3*R*)-Methyl 3-methyl-4-[dimethyl(phenyl)silanyl]methylpent-4-enoate 228

Following Williams,[137] methylmagnesium iodide (3.0 mol dm^{-3} solution in ether, 0.25 cm^3, 0.66 mmol) was added slowly to a stirred solution of dry methanol (0.04 cm^3, 0.88 mmol) in dry THF (2 cm^3) under an argon atmosphere at 0 °C. After 10 min, the sultam **221** (100 mg, 0.22 mmol) in dry THF (2 cm^3) was added at 0 °C. The mixture was stirred for 18 h at room temperature before addition of light petroleum (5 cm^3) followed by saturated aqueous ammonium chloride (8 cm^3). The layers were separated and the aqueous layer was extracted with light petroleum (2 ∞ 10 cm^3). The combined organic fractions were washed with brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure. Chromatography (SiO$_2$, light petroleum-ether, 1:1) gave the recovered sultam **161** (12 mg, 25%) (previously characterised) together with the *ester* **228** (38 mg, 63%); R_f(light petroleum-ether, 1:1) 0.72; ν_{max}(CDCl$_3$)/cm^{-1} 1739 (C=O), 1633 (C=C), 1248 (SiMe$_2$) and 1113 (SiPh); δ_H(400 MHz; CDCl$_3$) 7.50 (2 H, m, Ph), 7.34 (3 H, m, Ph), 4.63 (1 H, s, =C*H*$_A$H$_B$), 4.54 (1 H, br s, =CH$_A$*H*$_B$), 3.63 (3 H, s, OMe), 2.44 (1 H, dd, *J* 14.5 and 5.6, COC*H*$_A$H$_B$), 2.37 (1 H, m, C*H*Me), 2.17 (1 H, dd, *J* 14.3 and 8.3, COCH$_A$*H*$_B$), 1.75 (2 H, br s, CH$_2$Si), 0.99 (3 H, d, *J* 6.7, *Me*CH), 0.31 (3 H, s, Si*Me*$_A$Me$_B$) and 0.30 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(CDCl$_3$) 173.2+, 150.4+, 133.6–, 129.0–, 127.7–, 106.9+, 51.4–, 40.6+, 37.5–, 24.8+, 19.5–, –2.9– and –2.9–;

m/z (EI) 276 (16%, M$^+$), 261 (8, M – Me), 202 (4, M – MeCO$_2$Me) and 135 (100, PhMe$_2$Si) (Found: M$^+$, 276.1546. $C_{16}H_{24}SiO_2$ requires *M*, 276.1546).

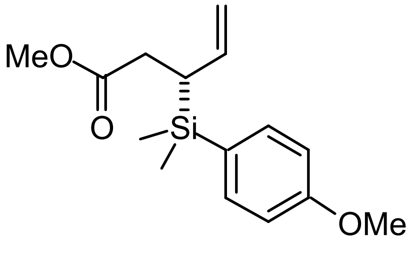


***N*-*E*-4-Methyl-5-[dimethyl(phenyl)silanyl]pent-3-enoyl-(7*R*)-2,10-camphorsultam 239** Following Buckle,[150,304] t-butyllithium (1.7 mol dm^{-3} solution in pentane, 2.04 cm^3, 3.50 mmol) was added dropwise to a stirred solution of vinyl bromide **223** (442 mg, 1.73 mmol) in ether (5 cm^3) at –78 °C under an argon atmosphere. The solution was stirred for 2 h before being added *via* cannula to a suspension of copper(I) iodide (329 mg, 1.73 mmol) in dry ether (5 cm^3) under an argon atmosphere at –20 °C. The solution was stirred for 20 min before being transferred *via* cannula to a solution of sultam **212** (150 mg, 0.35 mmol), in dry THF (5 cm^3), which had been pre-mixed for 20 min at –78 °C with ethylaluminium dichloride (1.0 mol dm^{-3} solution in hexanes, 3.50 cm^3, 3.52 mmol) under an argon atmosphere. The resulting mixture was stirred at –78 °C for 2 h and then allowed to warm gradually to room temperature overnight before being cooled to 0 °C and quenched with basic saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer extracted with ether (2 ∞ 20 cm^3). The combined organic fractions were washed with basic saturated aqueous ammonium chloride (2 ∞ 5 cm^3) and brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the starting sultam **212** (30 mg, 20%) (previously characterised) and the *sultam* **239** [46 mg, 30% (37% accounting for recovered starting material)] as a colourless liquid; R_f(light petroleum-ether, 1:1) 0.42; ν_{max}(film)/cm^{-1} 1698 (C=O), 1591 (Ph), 1329 (SO$_2$N), 1248 (SiMe$_2$), 1164 (SO$_2$N) and 1114 (SiPh); δ_H(250 MHz; CDCl$_3$) 7.50 (2 H, m, Ph), 7.41 (3 H, m, Ph), 5.16 (1 H, br t, *J* 6.4, =CH), 3.85 (1 H, m, CHN), 3.50 (1 H, d, *J* 13.8, CH_AH$_B$SO$_2$), 3.46 (2 H, m, COCH$_2$), 3.42 (1 H, d, *J* 13.7, CH$_A$*H*$_B$SO$_2$), 2.10 (2 H, m), 1.94-1.82 (3 H, m), 1.78 (2 H, br s, CH$_2$Si), 1.54 (3 H, br s, =CMe), 1.38 (2 H, m), 1.16 (3 H, s, C*Me*$_A$Me$_B$), 0.97 (3 H, s, CMe$_A$*Me*$_B$) and 0.29 (6 H, s, SiMe$_2$); δ_C(CDCl$_3$) 170.7+, 137.3+, 133.6–, 128.9–, 127.7–, 113.3–, 65.3–, 53.0+, 48.4+, 47.8+, 44.7–, 38.5+, 35.2+, 32.9+, 29.3+, 26.5+, 20.9–, 19.9–, 19.2– and –2.9–; *m/z* (EI) 445 (38%, M$^+$) and 135 (100, PhMe$_2$Si) (Found: M$^+$, 445.2103. $C_{24}H_{35}SiNSO_3$ requires *M*, 445.2107).



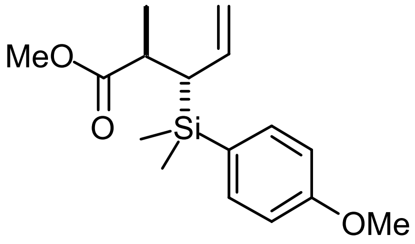
N-(3*R*)-{3-[(4-Methoxyphenyl)dimethylsilanyl]pent-4-enoyl}-(7*R*)-2,10-camphorsultam 251

Following Buckle,[150,304] t-butyllithium (1.7 mol dm^{-3} solution in pentane, 3.29 cm^3, 5.59 mmol) was added dropwise to a stirred solution of vinyl bromide (1.0 mol dm^{-3} solution in THF, 2.79 cm^3, 2.79 mmol) in ether (4 cm^3) at –78 °C under an argon atmosphere. The solution was stirred for 2 h before being added *via* cannula to a suspension of copper(I) iodide (531 mg, 2.79 mmol) in dry ether (5 cm^3) under an argon atmosphere at –20 °C. The solution was stirred for 20 min before being transferred *via* cannula to a solution of sultam **212** (121 mg, 0.28 mmol) in dry THF (2 cm^3) which had been pre-mixed for 20 min at –78 °C with ethylaluminium dichloride (1.0 mol dm^{-3} solution in hexanes, 2.79 cm^3, 2.79 mmol) under an argon atmosphere. The resulting mixture was stirred at –78 °C for 2 h and then allowed to warm gradually to room temperature overnight before being cooled to 0 °C and quenched with basic saturated aqueous ammonium chloride (5 cm^3). The layers were separated and the aqueous layer was extracted with ether (2 ∞ 20 cm^3). The combined organic fractions were washed with basic saturated aqueous ammonium chloride (2 ∞ 5 cm^3) and brine, dried (MgSO$_4$), filtered and evaporated under reduced pressure. Recrystallisation from methanol gave the *sultam* **251** (85 mg, 66%) as white needles, mp 172-173 °C (from MeOH); R_f(light petroleum-ether, 1:1) 0.33; ν_{max}(CH_2Cl_2)/cm^{-1} 1696 (C=O), 1591 (Ar), 1328 (SO_2N) and 1112 (SiAr); δ_H(250 MHz; $CDCl_3$) 7.43 (2 H, d, *J* 8.6, aromatic-H), 6.91 (2 H, d, *J* 8.6, aromatic-H), 5.76 (1 H, m, C*H*=CH_2), 4.85 (1 H, d, *J* 10.8, =C$H_{cis\text{-to-H}}$$H_{trans\text{-to-H}}$), 4.84 (1 H, d, *J* 16.3, =C$H_{cis\text{-to-H}}$$H_{trans\text{-to-H}}$), 3.82 [1 H, m (detail obscured by OMe), CHN], 3.81 (3 H, s, OMe), 3.48 (1 H, d, *J* 13.7, C$H_A$$H_B$$SO_2$), 3.39 (1 H, d, *J* 13.8, C$H_A$$H_B$$SO_2$), 2.99 (1 H, dd, *J* 15.5 and 11.4, COC$H_A$$H_B$), 2.55 (1 H, dd, *J* 15.5 and 3.4, COC$H_A$$H_B$), 2.46 (1 H, m, CHSi), 2.03 (2 H, br d, *J* 6.6, CH_2CHN), 1.89-1.83 (3 H, m), 1.38-1.26 (2 H, m), 1.13 (3 H, s, C$Me_A$$Me_B$), 0.95 (3 H, s, C$Me_A$$Me_B$), .0.29 (3 H, s, Si$Me_A$$Me_B$) and 0.28 (3 H, s, Si$Me_A$$Me_B$); δ_C($CDCl_3$) 172.0+, 160.6+, 137.9–, 135.5–, 127.4+, 113.6–, 112.6+, 65.4–, 55.0–, 53.1+, 48.3+, 47.7+, 44.7–, 38.5+, 34.0+, 32.9+, 30.8–, 26.5+, 20.8–, 19.9–, –4.6– and –5.1–; *m/z* (EI) 461 (9%, M^+) and 165 [43, MeO(C_6H_4)$SiMe_2$] (Found: M^+, 461.2043. $C_{24}H_{35}NSiSO_4$ requires *M*, 461.2056) (Found: C, 62.1; H, 7.65; N, 2.6. $C_{24}H_{35}NSiSO_4$ requires C, 62.4; H, 7.64; N, 3.0%. This was the best microanalysis data that could be obtained.).



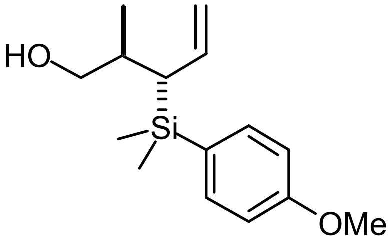
Methyl (3*R*)-3-dimethyl(4-methoxyphenyl)silylpent-4-enoate 252

Following Williams,[137] methylmagnesium iodide (3.0 mol dm^{-3} solution in ether, 1.16 cm^3, 3.49 mmol) was added slowly to a stirred solution of dry methanol (0.19 cm^3, 4.66 mmol) in dry THF (3 cm^3) under an argon atmosphere at 0 °C. After 10 min, the sultam derivative **251** (179 mg, 0.39 mmol) in dry THF (5 cm^3) was added at 0 °C. The mixture was stirred for 18 h at room temperature before addition of light petroleum (5 cm^3) followed by saturated aqueous ammonium chloride (8 cm^3). The layers were separated and the aqueous layer was extracted with light petroleum (2 ∞ 10 cm^3). The combined organic fractions were washed with brine, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, light petroleum-ether, 1:1) gave the *ester* **252** (94 mg, 87%); R_f(light petroleum-ether, 1:1) 0.59; ν_{max}(CH_2Cl_2)/cm^{-1} 1738 (C=O), 1638 (C=C), 1594 (Ar), 1248 ($SiMe_2$) and 1112 (SiAr); δ_H(250 MHz; $CDCl_3$) 7.41 (2 H, d, *J* 8.6, aromatic-H), 6.91 (2 H, d, *J* 8.6, aromatic-H), 5.72 (1 H, ddd, *J* 18.3, 10.5 and 7.8, C*H*=CH_2), 4.91 (1 H, d, *J* 10.6, =C$H_{cis\text{-to-H}}$$\mathrm{H}_{trans\text{-to-H}}$), 4.84 (1 H, d, *J* 18.2, =C$\mathrm{H}_{cis\text{-to-H}}$$H_{trans\text{-to-H}}$), 3.82 (3 H, s, OMe on aromatic ring), 3.59 (3 H, s, OMe in ester), 2.34 (3 H, m, $COCH_2CHSi$), 0.27 (3 H, s, Si$Me_A$$Me_B$) and 0.27 (3 H, s, Si$Me_A$$Me_B$); δ_C($CDCl_3$) 173.9+, 160.7+, 138.0–, 135.5–, 127.3+, 113.6–, 112.7+, 55.0–, 51.5–, 33.7+, 30.5–, –4.5– and –5.3–; *m/z* (FAB) 278 (3%, M^+) and 165 [100, MeO(C_6H_4)$SiMe_2$] (Found: M^+, 278.1346. $C_{15}H_{22}SiO_3$ requires *M*, 278.1338).



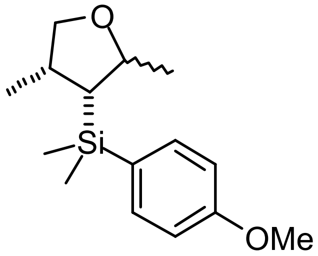
Methyl (2*R*,3*R*)-3-dimethyl(4-methoxyphenyl)silyl-2-methylpent-4-enoate 253

Following Archibald,[157] n-butyllithium (1.5 mol dm^{-3} solution in hexane, 0.20 cm^3, 0.29 mmol) was added dropwise to a solution of distilled diisopropylamine (0.04 cm^3, 0.32 mmol) in dry THF (1 cm^3) at 0 °C under an argon atmosphere. The solution was stirred at 0 °C for 20 min before cooling to –78 °C and adding ester **252** (68 mg, 0.24 mmol) in THF (3 cm^3) dropwise under an argon atmosphere. After 2 h, methyl iodide (0.30 cm^3, 4.89 mmol) was added slowly and the reaction mixture stirred for a further 3 h at –78 °C before allowing the mixture to warm to room temperature overnight. The solution was cooled to 0 °C, saturated aqueous ammonium chloride (10 cm^3) was added, the layers separated and the aqueous layer extracted with dichloromethane (3 ∞ 10 cm^3). The organic fractions were separately washed with brine, combined, dried ($MgSO_4$), filtered and evaporated under reduced pressure. Chromatography (SiO_2, hexane-ethyl acetate, 9:1) gave the *ester* **253** (49 mg, 70%); R_f(hexane-ethyl acetate, 9:1) 0.27; ν_{max}($CDCl_3$)/cm^{-1} 1737 (C=O), 1594 (Ar), 1248 ($SiMe_2$) and 1112 (SiAr); δ_H(400 MHz; $CDCl_3$) 7.42 (2 H, d, *J* 8.6, aromatic-H), 6.90 (2 H, d, *J* 8.6, aromatic-H), 5.59 (1 H, dt, *J* 16.9 and 10.5, C*H*=CH_2), 4.95 (1 H, dd, *J* 10.1 and 2.0, =$CH_{cis\text{-}to\text{-}H}H_{trans\text{-}to\text{-}H}$), 4.86 (1 H, dd, *J* 16.9 and 1.7, =$CH_{cis\text{-}to\text{-}H}H_{trans\text{-}to\text{-}H}$), 3.80 (3 H, s, aromatic-OMe), 3.47 (3 H, s, OMe in ester), 2.56 (1 H, qn, *J* 7.1, C*H*Me), 2.17 (1 H, dd, *J* 10.8 and 7.3, CHSi), 1.07 (3 H, d, *J* 7.0, CH*Me*), 0.28 (3 H, s, $SiMe_AMe_B$) and 0.24 (3 H, s, $SiMe_AMe_B$); δ_C($CDCl_3$) 176.6+, 160.5+, 135.8–, 135.2–, 127.9+, 115.1+, 113.5–, 55.0–, 51.4–, 39.6–, 15.9–, 14.1–, –3.4– and –4.3–; *m/z* (ESI) 315 (MNa^+) (Found: MNa^+, 315.1387. $C_{16}H_{24}SiO_3Na$ requires *M*, 315.1392).



3-Dimethyl(4-methoxyphenyl)silanyl-2-methylpent-4-en-1-ol 254

A solution of the ester **253** (30 mg, 0.10 mmol) in dry ether (3 cm^3) was added to a stirred suspension of lithium aluminium hydride (20 mg, 0.50 mmol) in dry ether (2 cm^3) at –78 °C under an argon atmosphere. The resulting mixture was stirred and allowed to warm to room temperature overnight before being cooled to 0 °C and quenched slowly with aqueous potassium hydrogen sulfate (0.35 g in 10 cm^3). The mixture was again allowed to warm to room temperature and stirred for 45 min. Dilute hydrochloric acid (3 mol dm^{-3}, 2 cm^3) was added, the layers were separated and the aqueous layer was extracted with dichloromethane (2 ∞ 10 cm^3). The organic fractions were combined, dried ($MgSO_4$), filtered and evaporated under reduced pressure to give the *alcohol* **254** (15 mg, 57%) as a colourless liquid; R_f(light petroleum-ether, 1:1) 0.32; δ_H(250 MHz; $CDCl_3$) 7.44 (2 H, d, *J* 8.6, aromatic-H), 6.91 (2 H, d, *J* 8.6, aromatic-H), 5.78 (1 H, dt, *J* 16.7 and 10.6, C*H*=CH$_2$), 4.97 (1 H, dd, *J* 10.2 and 2.2, CH=C$H_{cis\text{-to-H}}$H$_{trans\text{-to-H}}$), 4.91 (1 H, dd, *J* 16.8 and 2.3, CH=CH$_{cis\text{-to-H}}$$H_{trans\text{-to-H}}$), 3.82 (3 H, s, OMe), 3.38 (2 H, m, CH$_2$O), 2.03 (1 H, dd, *J* 11.0 and 3.5, CHSi), 1.82 (1 H, m, C*H*Me), 0.86 (3 H, d, *J* 7.0, CH*Me*), 0.31 (3 H, s, Si*Me*$_A$Me$_B$) and 0.28 (3 H, s, SiMe$_A$*Me*$_B$); the compound isomerised (to give the tetrahydrofuran **255**) too rapidly for any further data to be obtained.



(2,4-Dimethyltetrahydrofuran-3-yl)dimethyl(4-methoxyphenyl)silane 255

On standing at room temperature for 7 d, alcohol **254** was converted entirely into *tetrahydrofuran* **255**; R_f(light petroleum-ether, 1:1) 0.51; ν_{max}(CDCl$_3$)/cm^{-1} 1595 (Ar), 1248 (SiMe$_2$) and 1109 (SiAr); δ_H(400 MHz; CDCl$_3$) 7.43 (2 H, d, *J* 8.6, aromatic-H), 6.90 (2 H, d, *J* 8.6, aromatic-H), 4.08 (1 H, dq, *J* 11.8 and 5.9, MeC*H*O), 3.82 (1 H, m, CH_AH$_B$O, detail obscured by OMe), 3.80 (3 H, s, OMe), 3.39 (1 H, dd, *J* 7.8 and 2.2, CH$_A$$H_B$O), 2.44 (1 H, m, CH$_2$C*H*Me), 1.78 (1 H, dd, *J* 12.5 and 8.2, CHSi), 1.10 (3 H, d, *J* 6.0, *Me*CHO), 0.94 (3 H, d, *J* 7.1, CH$_2$CH*Me*), 0.34 (3 H, s, Si*Me*$_A$Me$_B$) and 0.32 (3 H, s, SiMe$_A$*Me*$_B$); *m/z* (EI) 264 (1%, M$^+$) and 165 (100, SiMe$_2$(C$_6$H$_4$)OMe) (Found: M$^+$, 264.1528. C$_{15}$H$_{24}$SiO$_2$ requires *M*, 264.1546).