New Synthetic Methodology for the Synthesis of 7-Substituted Tetrahydroazepin-2-ones

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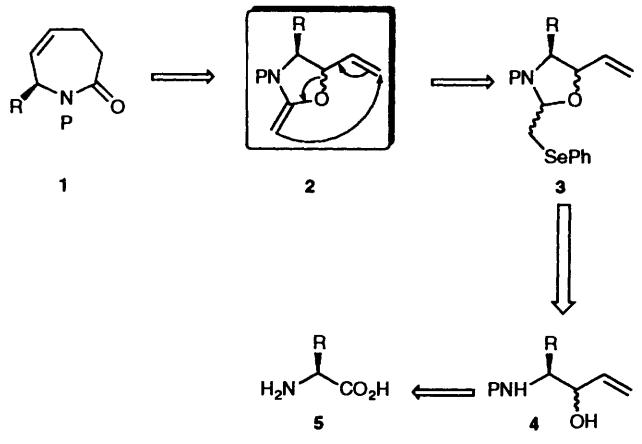
The Claisen rearrangement of the vinyl substituted ketene aminals **2** (R = CH_2CHMe_2, $CH_2OSiBu^tMe_2$) which were generated *in situ* by selenoxide elimination of the aminal precursors **3** in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) furnished the enantiomerically pure 7-substituted tetrahydroazepin-2-ones **1**.

Monocyclic medium ring nitrogen heterocycles are particularly challenging synthetic targets owing to the difficulties associated with their construction.[1,2] Despite recent work in this area,[3] the need remains for a general reliable and stereoselective method of forming the family of medium ring azacycles. The development of a new method would therefore need to fulfil the criteria of being efficient, flexible and stereoselective to overcome the problems other workers have already encountered. The Claisen rearrangement[4] has been shown to be an extremely elegant method for the preparation of unsaturated medium ring ketones[5] and lactones.[6] We recently reported our preliminary studies on the application of this methodology to the synthesis of medium ring lactams.[7] Herein, we present a complete report of our synthetic studies on the preparation of 7-substituted tetrahydroazepin-2-ones.



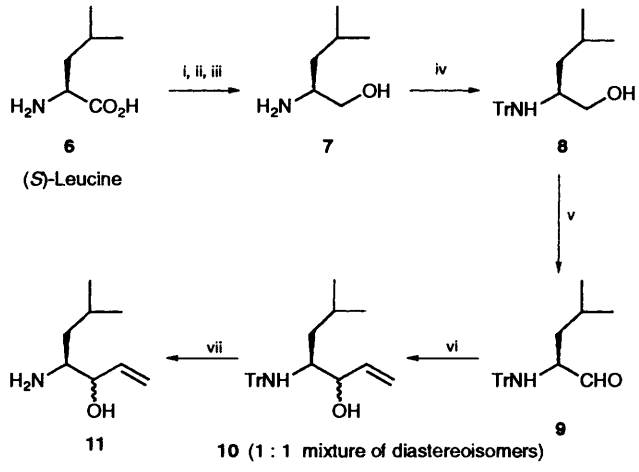
1 2 3 5 4

Scheme 1 General scheme for the preparation of 7-substituted azepin-2-ones

Results and Discussion

Our strategy for the preparation of the required medium ring lactams involves a two-carbon ring expansion as summarised in Scheme 1. The vinyl ketene aminal **2** generated *in situ* by selenoxide elimination of the aminal precursor **3** undergoes Claisen rearrangement to give the monocyclic unsaturated medium ring lactam **1**. The aminal precursors **3** would be formed from a suitably protected vinyl amino alcohol **4** derived from the chiral pool of amino acids **5**. Notably, this strategy allows the preparation of enantiomerically pure lactams with a high degree of flexibility.

(*S*)-Leucinol **7** was obtained from (*S*)-leucine **6** in 90% yield using a one-pot procedure reported for the reduction of valine to valinol (Scheme 2).[8] Tritylation with trityl chloride and



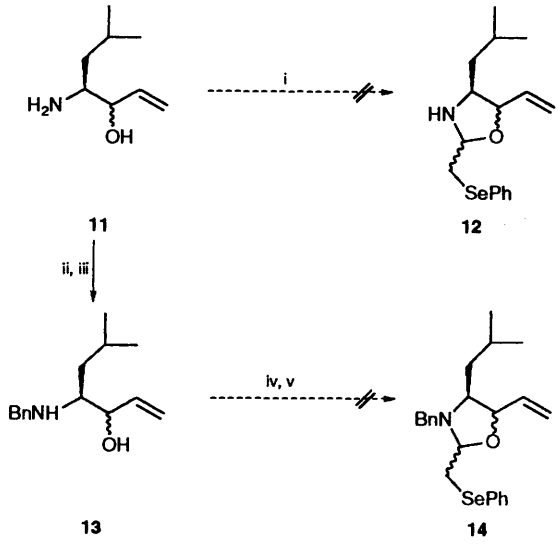
6 (*S*)-Leucine 7 8 9 10 (1 : 1 mixture of diastereoisomers) 11

Scheme 2 *Reagents and conditions:* i, BF_3OEt_2, THF, heat, 2 h (90%); ii, BH_3DMS, heat, 8 h; iii, 5 mol dm^{-3} NaOH, heat, 12 h; iv, Ph_3CCl, Et_3N, CH_2Cl_2, room temp., 90 min (87%); v, Swern oxidation; vi, vinylmagnesium bromide, THF, −30 °C, 5 min (92%); vii, DOWEX 50-X8, MeOH, room temp., 16 h (91%)

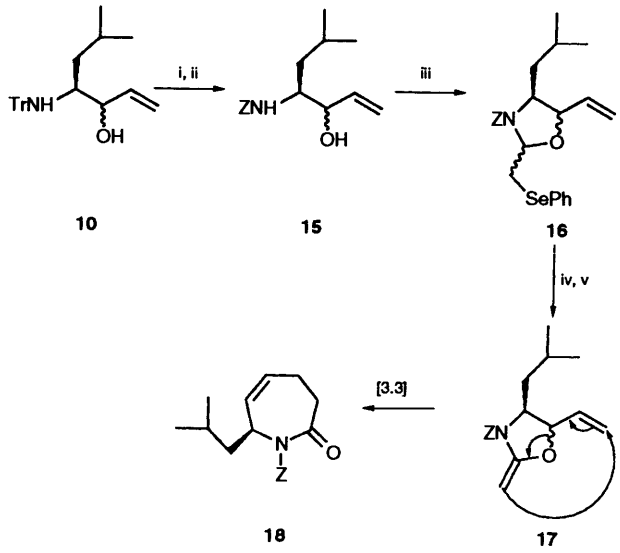
triethylamine (dichloromethane, room temp. 90 min), gave the *N*-trityl amino alcohol **8**[9] in 87% yield. This compound exhibited a consistently low optical rotation with the optical assay proving inconclusive.† Oxidation of the *N*-trityl amino alcohol **8** under Swern conditions[11] gave the amino aldehyde **9** which was used immediately without purification to minimise possible racemisation.[12] Treatment with vinylmagnesium bromide (THF, −30 °C, 5 min) afforded a nearly equal mixture of epimeric alcohols **10** in 92% overall yield. It was expected that a diastereoisomeric mixture of alcohols could be used in the Claisen ring expansion, since the uncontrolled stereocentre is lost during the transformation. Deprotection of the trityl group was achieved using DOWEX-50-X8 resin (H^+ form, RT, 16 h) to afford the vinyl amino alcohol **11** in 91% yield.

Phenylselenanylacetaldehyde diethyl acetal[13] was prepared in 80% yield by treating ethyl vinyl ether with benzeneselenenyl chloride in the presence of ethanol at room temperature. Treatment of the vinyl amino alcohol **11** with phenylselenanylacetaldehyde diethyl acetal and Amberlite IR 120 under Dean–Stark conditions (heat, 16 h), failed to afford any of the required aminal **12** (Scheme 3). This was initially attributed to hydrolysis of the aminal **12**.

† Analysis of the Mosher's ester[10] of the alcohol **8** by ^1H and ^{19}F NMR showed no signs of racemization.



Scheme 3 *Reagents and conditions:* i, $PhSeCH_2CH(OEt)_2$, toluene, Amberlite IR-120, heat 16 h; ii, PhCHO, EtOH, Na_2SO_4, heat 25 h; iii, $NaBH_4$, EtOH, 0 °C, 1 h (54%); iv, $PhSeCH_2CH(OEt)_2$, toluene, Amberlite IR-120, heat 48 h; v, $PhSeCH_2CH(OEt_2)$, benzene, toluene-*p*-sulfonic acid (TsOH), heat 16 h



Scheme 4 *Reagents and conditions:* i, Dowex 50-X8, MeOH, room temp., 16 h; ii, $PhCH_2OCOCl$, NaOH in tetrahydrofuran (THF; 2 mol dm^{-3}), room temp., 4 h (61% over two steps); iii, $PhSeCH_2CH(OEt)_2$, toluene, pyridinium toluene-*p*-sulfonate (PPTS), heat 2 h (94%); iv, $NaIO_4$ $NaHCO_3$, MeOH–H_2O, room temp., 1 h; v, heat, 16 h in *m*-xylene containing 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)

In order to suppress the hydrolysis, N-protection was deemed necessary. The hydrochloride salt of the amino **11** was formed under standard conditions, and treated with benzaldehyde and sodium sulphate (EtOH, heat 2.5 h), then reduced *in situ* with sodium borohydride (0 °C, 1 h) to afford the *N*-benzyl vinyl alcohol **13** in 54% yield. Treatment of the *N*-benzyl vinyl amino alcohol **13** with phenylselenanylacetaldehyde diethyl acetal and Amberlite IR 120 under Dean–Stark conditions (heat, 48 h) furnished none of the required aminal **14**. A modified procedure using toluene-*p*-sulfonic acid (TsOH) as the acid catalyst in benzene (heat, 16 h) also failed to afford the aminal **14**.

A recent study by Scolastico *et al.*[14] on the stereochemistry of the acid-catalysed cyclisation of *N*-protected norephedrine derivatives with α,β-unsaturated dimethyl acetals indicated that an electron-withdrawing group on nitrogen was imperative to prevent facile hydrolysis of the resulting oxazolidine. The corresponding *N*-methyloxazolidines were also reported. However, they readily undergo silica gel-promoted hydrolysis.

Therefore, based on these findings, a new strategy which employed the benzyloxycarbonyl protecting group was envisaged to eliminate the problem of hydrolysis. The benzyloxycarbonyl (*Z*)-protected vinyl amino alcohol **15** was prepared from the *N*-trityl vinyl amino alcohol **10** (Scheme 4) *via* the following two-step procedure. Deprotection of the trityl group with Dowex-50-X8 resin (H^+ form, RT, 16 h) gave the vinyl amino alcohol **11**, which was immediately *N*-protected using benzyl chloroformate and sodium hydroxide (THF, room temp., 4 h) in a 61% overall yield. Treatment of **15** with TsOH and phenylselenanylacetaldehyde diethyl acetal, under Dean–Stark conditions (heat, 15 min) furnished the aminal **16** in 51% yield. The moderate yield was improved to 94% by using the milder acid catalyst pyridinium toluene-*p*-sulfonate (PPTS). The aminal **16** was oxidised using sodium periodate to afford the selenoxides quantitatively. Refluxing in *m*-xylene with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to initiate the *syn* elimination is presumed to afford the ketene aminal **17** *in situ*. This then undergoes [3.3] sigmatropic rearrangement,[7] to furnish the Z-protected 7-substituted azepin-2-one **18**.

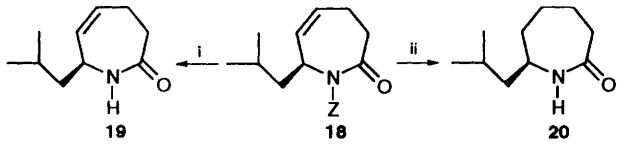
The efficiency of the *syn*-elimination process for selenoxides compared to that involving sulfoxides is the result of a greater polarisation of the Se–O bond and of the longer Se–C and Se–O bond lengths.[15] The basic oxygen atom must also be near to the proton which is to be removed. However, although selenoxide elimination usually occurs at or below room temperature in some systems, elimination of hydrogen from carbon atoms carrying electron-rich species (such as oxygen and nitrogen) is a less favourable process, and therefore requires an elevated reaction temperature.

Table 1 Claisen rearrangement of the vinyl substituted aminal **16**

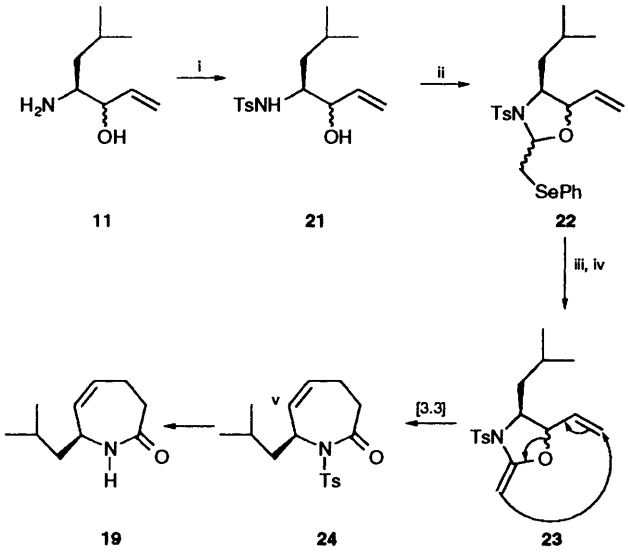
Entry	DBU (equiv.)	Solvent (heat)	Concentration	Yield of **18** (%)
1	2	*m*-Xylene	1 mmol/100 cm^3	24
2	5	*m*-Xylene	1 mmol/100 cm^3	38
3	5	*m*-Xylene	1 mmol/200 cm^3	38
4	10	*m*-Xylene	1 mmol/100 cm^3	30

In order to ascertain the optimum conditions for the cyclisation, the selenoxides were subjected to a systematic cyclisation study, as summarised in Table 1. There were deemed to be three important variables in this reaction: (1) the amount of base, (2) the temperature which is related to the boiling point of the solvent and (3) the concentration during cyclisation. Previous work by Petrizilka[5a] and Holmes[5b] gave a suitable point to begin the study. Under the reaction conditions illustrated (Entry 1) a 24% yield of the required lactam **18** was obtained. Increasing the amount of 1,8-diazabicyclo[5.4.0]undec-7-ene to 5 equiv. (Entry 2) afforded the lactam **18** in an improved 39% yield. Reducing the concentration of substrate further (Entry 3) made little difference, and it may be assumed that this was the optimum concentration to suppress deoxygenation of the selenoxide and possible polymerisation of the ketene aminal **17**. Further increases in the amount of base (10 equiv.) have detrimental effect on the yield (Entry 4). The moderate yields for the cyclisation were initially attributed to the instability of the aminal **16**.

The sequence of the reactions depicted in Scheme 5 illustrates how the *N*-benzyloxycarbonyl (Z)-protected unsaturated lactam **18** may be selectively deprotected. Removal of the benzyloxycarbonyl protecting group was achieved by treating **18** with 45% hydrobromic acid in acetic acid[16] (room temp.,



Scheme 5 *Reagents and conditions:* i, HBr (45%) in AcOH, room temp., 1 h (98%); ii, $Pd(OH)_2$, H_2, room temp., 3 h (99%)



Scheme 6 *Reagents and conditions:* i, Toluene-*p*-sulfonyl chloride (TsCl), Et_3N, 0 °C to room temp., 16 h (81%); ii, $PhSeCH_2CH(OEt)_2$, toluene, PPTS, heat 2 h (97%); iii, $NaIO_4$, $NaHCO_3$, MeOH–H_2O, room temp., 1 h; iv, heat, 16 h in solvent containing DBU; v, sodium naphthalenide, dimethoxyethane (DME), −70 °C, 30 min (87%)

Table 2 Claisen rearrangement of the vinyl substituted aminal **22**

Entry	DBU (equiv.)	Solvent (heat)	Concentration	Yield of **24** (%)
1	5	*m*-Xylene	1 mmol/100 cm^3	34
2	3	*m*-Xylene	1 mmol/100 cm^3	39
3	3	Toluene	1 mmol/100 cm^3	26
4	3	Decalin	1 mmol/100 cm^3	23

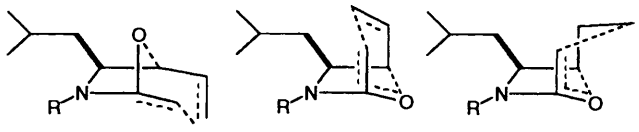
1 h), affording the required 7-substituted tetrahydroazepin-2-one **19** in 98% yield. Alternatively, the saturated lactam **20** may be prepared by direct hydrogenation of the Z-protected unsaturated lactam **18** using Pearlman's catalyst in 99% yield.

A similar Claisen rearrangement sequence was carried out on the *N*-tosyl analogue **22** (Scheme 6), prepared from **21**. It was expected that the *N*-tosyl ketene aminal **22** would be more stable under the vigorous rearrangement conditions. Treatment of the aminal **22** in an analogous manner to that described for the urethane **16** gave the *N*-7-substituted *N*-tosylazepin-2-one **24**.

A similar cyclisation study was undertaken in an attempt to obtain the optimum cyclisation conditions (see Table 2). When the cyclisation was carried out with 5 equiv. of 1,8-diazabicyclo[5.4.0]undec-7-ene (Entry 1), a 34% yield of the required lactam **24** was obtained. Decreasing the amount of base to 3 equiv. (Entry 2) afforded the lactam in an improved 38% yield. However, when a lower boiling solvent, toluene (Entry 3) was used, the yield decreased to 26%. Similarly, in the case of the higher boiling solvent decalin (Entry 4) a reduced yield was observed.

Deprotection of the toluene-*p*-sulfonyl protecting group with sodium naphthalenide[17,18] (Me_2O, −70 °C, 30 min), gave the required 7-substituted azepin-2-one **19** in 87% yield. The two unsaturated lactams prepared independently by the benzyloxycarbonyl and tosyl routes were found to be identical by spectroscopic and other physical methods.

The moderate yields of cyclisation are most likely due to steric effects in the Claisen transition state for one of the diastereoisomers. Assuming a chair-like conformation for the components of the Claisen rearrangement,[6] the *anti*-diastereoisomer *anti*-**25**, is clearly less strained than the *syn*-diastereo-

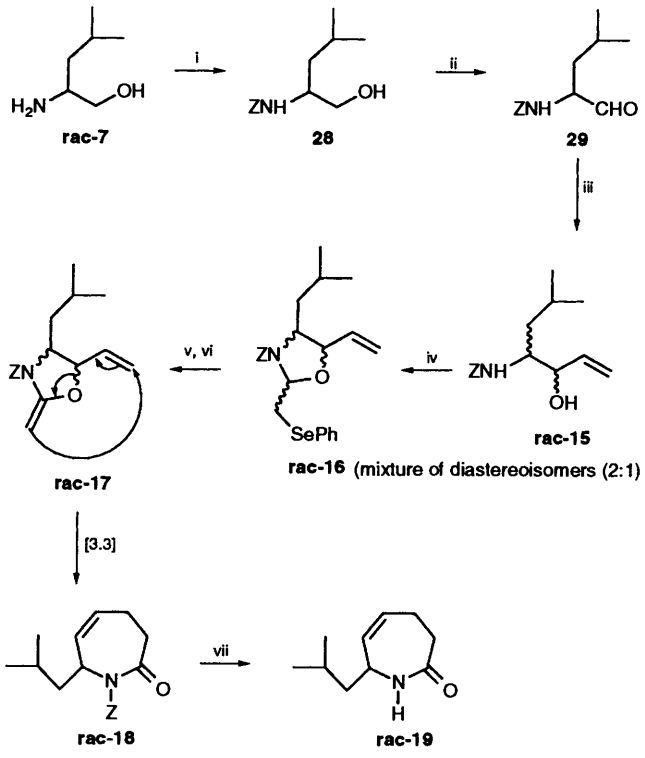


isomer, *syn*-**26**. The latter has severe 1,2-eclipsing interactions in the chair-like conformation. This could account for the moderate yields observed in the Claisen rearrangement leading to tetrahydroazepinones by this strategy. Whereas both diastereoisomeric acetals seem capable of undergoing the two-atom ring expansion in the Claisen rearrangements leading to larger rings,[6,7] only the *anti* diastereoisomer **25** is capable of rearranging to a seven-membered ring product. The boat-like conformation *syn*-**27** is disfavoured since it would produce a seven-membered lactam with an (*E*)-alkene.

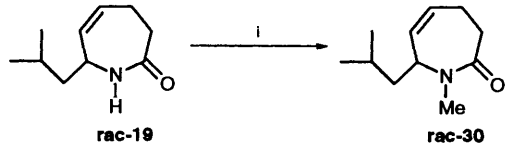
The racemic series was completed in an analogous fashion to the single enantiomeric version, using the benzyloxycarbonyl protecting group throughout. The *N*-trityl protecting group had been utilised in the asymmetric sequence to protect the chiral integrity of the α-amino aldehyde **9**. Treatment of (±)-leucinol *rac*-**7** prepared from (±)-leucine *via* the procedure reported for valinol[8] with benzyl chloroformate and triethylamine (dioxane/water, 0 °C to room temp., 16 h) afforded the required Z-protected amino alcohol **28** in 79% yield (Scheme 7). Oxidation under Swern conditions[11] furnished the amino aldehyde **29** which was used immediately without purification. Treatment of the amino aldehyde **29** with vinylmagnesium bromide (THF, −40 °C, 10 min), gave the Z-vinyl amino alcohol *rac*-**15** in 65% yield as a 2:1 mixture of epimeric alcohols. The moderate yield was attributed to enolisation of the Z-protected amino aldehyde **29**. This problem was not encountered in the asymmetric sequence with the *N*-trityl protected amino aldehyde **9**. This confirmed the inferiority of the benzyloxycarbonyl protecting group in preventing racemisation of optically pure α-amino aldehydes. The vinyl amino alcohols *rac*-**15** were converted into the racemic lactam *rac*-**18** by the Claisen sequence in an analogous fashion to the asymmetric sequence, the actual conversion of *rac*-**16** into *rac*-**18** occurring in 44% yield. Deprotection of the benzyloxycarbonyl group gave the lactam *rac*-**19** in 84% yield.

The unsaturated lactam *rac*-**19** was *N*-methylated (Scheme 8) using sodium hydride (DMF, 0 °C, 1 h) to generate the anion, followed by treatment with methyl iodide (0 °C to room temp., 3.5 h) to afford the *N*-methyl unsaturated lactam *rac*-**30** in 64% yield. The optically active derivative **30** was prepared similarly in 72% yield. ^1H NMR studies using the chiral shift reagent (+)-Eu(hfc)$_3$ did not resolve any of the signals of *rac*-**30**.

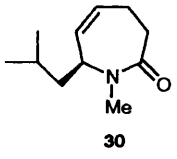
The alternative approach illustrated in Scheme 9 proved to be more successful. Catalytic reduction of the unsaturated lactam *rac*-**19** gave the saturated lactam *rac*-**20** in 96% yield. Hydrolysis with 2 mol dm^{-3} hydrochloric acid in methanol (heat, 16 h), then acylation (Ac_2O, pyridine, DMAP, room temp., 3 h) afforded the *N*-acyl amino ester *rac*-**31** in 58% yield. The saturated lactam **20** was treated similarly to afford the optically active derivative **31** in 56% yield. ^1H NMR studies



Scheme 7 *Reagents and conditions:* i, $PhCH_2OCOCl$, Et_3N dioxane–H_2O, 0 °C to room temp., 16 h (79%); ii, Swern oxidation; iii, vinylmagnesium bromide, THF, −40 °C, 10 min (65% for two steps); iv, $PhSeCH_2CH(OEt)_2$, toluene, PPTS, heat 4 h (82%); v, $NaIO_4$, $NaHCO_3$, MeOH–H_2O, room temp., 1 h; vi, heat, 16 h in *m*-xylene containing DBU (44%); vii, HBr (45%) in AcOH, 0 °C to room temp., 1 h (84%)

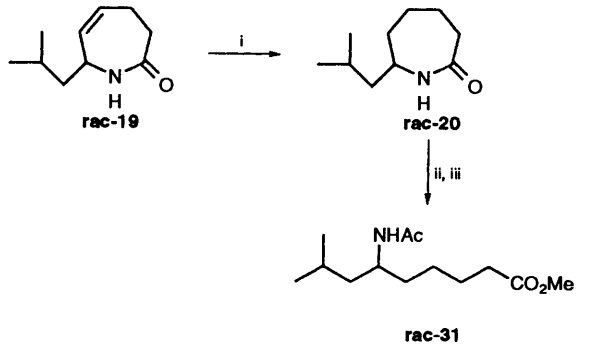


Scheme 8 *Reagents and conditions:* i, NaH, *N*,*N*-dimethylformamide (DMF) 0 °C, 45 min followed by MeI, 0 °C to room temp., 3 h (64%)

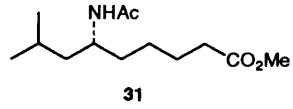


on *rac*-**31** using (+)-Eu(hfc)$_3$ as a chiral shift reagent gave baseline resolved methyl ester signals suitable for assay. The analogous assay on the optically active derivative **31** indicated an enantiomeric excess (e.e.) of ≥95%. This assay confirms the faithful transformation of (*S*)-leucine **6** into lactams **19** and **20** without loss of stereochemical integrity at the original stereocentre of the amino acid.

In view of our interest in the application of difunctionalised seven-membered lactams as rigid 'dipeptides'[3k] this methodology was then applied to the synthesis of the hydroxymethyl derivative **41**. The differentially protected 1,2-vinylamino alcohol **38** was obtained using a modified literature procedure for the preparation of the configurationally stable amino aldehyde **36**.[19] The *N*-benzyloxycarbonyl-(*S*)-serine **32** was prepared from (*S*)-serine *via* the method of Guttmann *et al.*[20] Esterification of the amino acid **33** with thionyl chloride in methanol (0 °C to room temp., 16 h) gave the amino ester **34** in



Scheme 9 *Reagents and conditions:* i, $Pd(OH)_2$, H_2, room temp., 30 min (96%); ii, HCl (2 mol dm^{-3}) in MeOH, heat 16 h; iii, Ac_2O, pyridine, *N*,*N*-dimethylaminopyridine (DMAP), room temp., 3 h (58%)



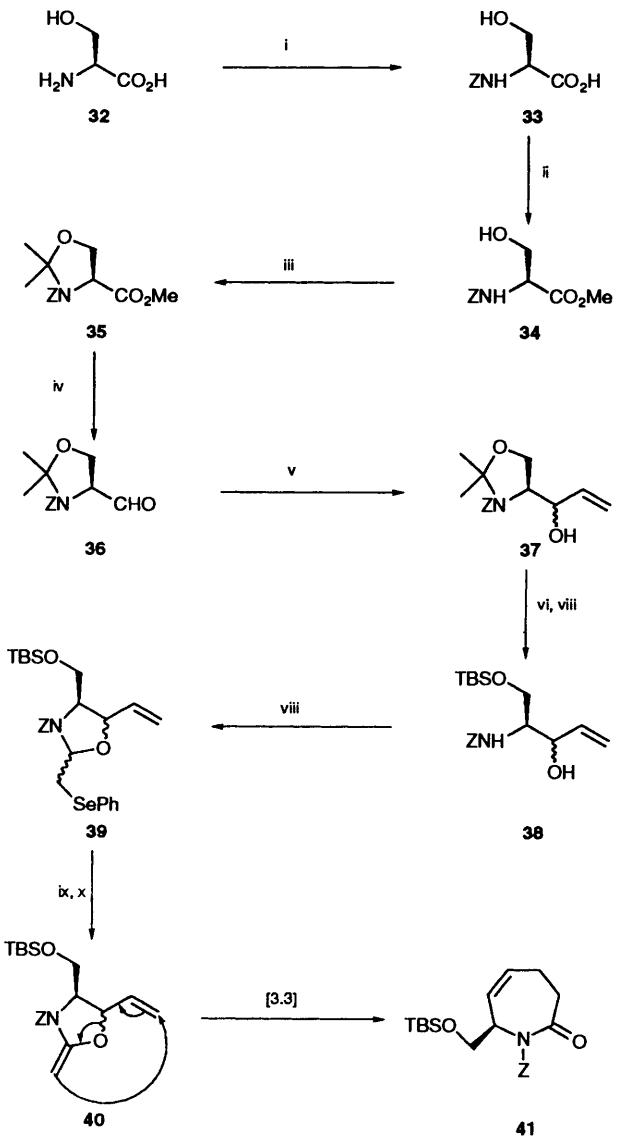
97% yield. Treatment of the amino ester **34** with 2,2-dimethoxypropane and toluene-*p*-sulfonic acid under Dean–Stark conditions (benzene, heat, 1 h), furnished the acetonide ester **35** in 91% yield. Reduction of the amino ester **35** with diisobutylaluminium hydride (THF, −78 °C, 2 h) gave the amino aldehyde **36** in 94% yield. Treatment of the amino aldehyde **36** with vinylmagnesium bromide at −78 °C gave the vinyl amino alcohol **37** in 90% yield as a 2:1 mixture of diastereoisomers. The acetonide was then cleaved with toluene-*p*-sulfonic acid in methanol (MeOH, room temp., 5 h), to afford the crude diol, which was differentially protected[21] with *tert*-butyldimethylsilyl chloride and imidazole (DMF, room temp., 16 h) furnishing the 1,2-vinylamino alcohol **38** in 88% overall yield from the acetonide **37**.

Treatment of the 1,2-vinylamino alcohol **38** with phenylselenanylacetaldehyde diethyl acetal[13] and pyridinium toluene-*p*-sulfonate under Dean–Stark conditions (toluene, heat, 2 h) furnished the aminal **39** in 68% yield as a complex mixture of diastereoisomers (Scheme 10). The aminal **39** was oxidised quantitatively using sodium periodate to afford the selenoxides. Refluxing in *m*-xylene in the presence of DBU afforded, presumably *via* the vinyl ketene aminal **40**, the *N*-benzyloxycarbonyl azepin-2-one **41** in 21% yield. The reason for the modest yield of the hydroxymethyl-substituted product **41**, compared with the isobutyl analogue **18** is not clear, but the effect may be stereoelectronic in origin.

Therefore, in conclusion, we have described a new synthetic method for the preparation of enantiomerically pure 7-substituted tetrahydroazepin-2-ones. The nature of the 4-substituent in the aminal precursor seems to have a profound affect on the efficiency of the rearrangement. This may be due to allylic strain with the *N*-benzyloxycarbonyl group forcing the ketene aminal into an unfavourable conformation in the transition state.

Experimental

^{1}H NMR spectra were recorded on Bruker WM-250 (250 MHz) and Bruker WM-400 (400 MHz) instruments, using deuteriochloroform (or other indicated solvent) as reference or internal deuterium lock. The chemical shift data for each signal is given in units of δ relative to tetramethylsilane (TMS) where δ (TMS) = 0. The multiplicity of the signal is indicated as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, *etc.* ^{13}C NMR spectra were recorded on the Bruker WM-400 (100 MHz) instrument using internal deuterium lock and proton



Scheme 10 *Reagents and conditions:* i, $PhCH_2OCOCl$, $NaHCO_3$, room temp., 4 h (93%); ii, $SOCl_2$, MeOH, 0 °C to room temp., 16 h (97%); iii, $Me_2C(OMe)_2$, TsOH, toluene, heat, 1 h (97%); iv, DIBAL-H, toluene, −78 °C, 2 h (94%); v, vinylmagnesium bromide, THF, −78 °C, 30 min (90%); vi, MeOH, TsOH, room temp., 16 h; vii, *tert*-butyl(dimethyl)silyl chloride (TBDMSCl), imidazole, DMF, room temp., 16 h (88%); viii, $PhSeCH_2CH(OEt)_2$, toluene, PPTS, heat 2 h (68%); ix, $NaIO_4$, $NaHCO_3$, MeOH–H_2O, room temp., 3 h; x, heat, 16 h in *m*-xylene containing DBU (21%)

decoupling. The chemical shift data for each signal is given in units of δ relative to tetramethylsilane (TMS), where δ (TMS) = 0. The multiplicity of the signal was determined by an APT experiment and is indicated as: o = odd (methyl or methine) and e = even (quaternary or methylene). IR spectra were recorded on a Perkin-Elmer 1310 spectrometer. The sample was prepared as a solution in the indicated solvent. Calibration in each case was made relative to polystyrene at 1603 cm^{-1}. The relative intensities are indicated as: s = strong, m = medium, w = weak, br = broad and sh = shoulder. Electron-impact (EI) mass spectra were recorded using an A.E.I. MS 902 (low resolution spectra) or an A.E.I. MS 30 (high resolution spectra) instrument in conjunction with a DS 50S data system. High resolution chemical ionisation (CI) mass spectra were performed on a VG ZAB-E instrument at the SERC Mass Spectrometry Centre, University of Swansea (Dr. J. Ballantine). CI mass spectra were recorded using NH_3 as the carrier gas. Microanalyses were carried out by the staff of the University Chemical Laboratory Microanalytical Department. Melting points were determined using a Büchi 510 melting point apparatus and are uncorrected. Optical rotations were measured using a Perkin-Elmer 241 polarimeter, in a cell of 1 dm path length. The conc (*c*) is expressed in g 100 cm^{-3} (equivalent to g 0.1 dm^{-3}). Specific rotations denoted as $[\alpha]_D^T$ imply units of $°dm^2\ g^{-1}$ (T/°C). Analytical TLC was carried out on pre-coated 0.25 mm thick Merck 60 F_{254} silica plates. Visualisation was by absorption of UV light, and spraying with either basic potassium permanganate or ethanolic phosphomolybdic acid (MPA) solution followed by thermal development. Flash chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Difficult separations were carried out using a Harrison 7924 chromatotron, using plates coated to a thickness of 1, 2 or 4 mm with Merck #7749 silica gel. Reagents were purified and dried where necessary by standard techniques.[22] THF was dried from potassium in a recycling still, using benzophenone ketyl as an indicator. Ether refers to diethyl ether. Light petroleum refers to the fraction boiling in the range 60–80 °C. Brine refers to a saturated aqueous sodium chloride. All reactions were performed under an inert atmosphere of nitrogen unless indicated to the contrary. Hydrochloride salts of amines were prepared by passing anhydrous hydrogen chloride gas through a solution of the amine in anhydrous dichloromethane at 0 °C for 10 min. Evaporation under reduced pressure gave the required hydrochloride salt.

(2S)-4-*Methyl*-2-(*triphenylmethylamino*)*pentan*-1-*ol* **8**.—(*S*)-Leucinol **7** (1.156 g, 9.87 mmol) was dissolved in anhydrous dichloromethane (10 cm^3) and triethylamine (1.51 cm^3, 11 mmol) was added to the solution followed by trityl chloride (2.75 g, 9.87 mmol) in one portion (exothermic*). The solution, which turned deep red, was stirred for 90 min after which it was poured into ethyl acetate (100 cm^3) and extracted with 50% aqueous sodium chloride (2 × 40 cm^3). The aqueous phase was then back-extracted with ethyl acetate (2 × 50 cm^3). The combined ethyl acetate layer and extracts were dried ($MgSO_4$) and evaporated under reduced pressure to afford an orange coloured oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (1:9) furnished the title compound (3.08 g, 87%) as a white foam;† R_F 0.58 (1:4 ethyl acetate–hexane); $[\alpha]_D^{22}$ +20.3 (*c* 0.29, $CHCl_3$) {lit.,[8] $[\alpha]_D^{22}$ +27 (*c* 0.27, $CHCl_3$)}; $\nu_{max}(CCl_4)/cm^{-1}$ 3745m, 3780–3360br s, 3330w, 3085m, 3065s, 3025m, 2955vs, 2925s, 2890m, 2865m; δ_H(400 MHz; $CDCl_3$) 0.55 (3 H, d, *J* 6.4, $CHCH_3$), 0.66 (3 H, d, *J* 6.3, $CHCH_3$), 1.32–1.41 [3 H, m, $CHCH_2CH(CH_3)_2$], 1.97 (2 H, br s, NH and OH), 2.62–2.67 [1 H, m, $NHCH(CH_3)_2$], 3.05 (1 H, dd, *J* 10.8, 3.6, $CHCH_2OH$), 3.21 (1 H, dd, *J* 10.9, 2.5, $CHCH_2OH$) and 7.17–7.54 (15 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.47 (o), 23.68 (o), 24.76 (o), 42.58 (e), 51.54 (o), 62.68 (e), 71.32 (e), 126.44 (o), 127.84 (o), 128.76 (o) and 146.57 (e); *m*/*z* (EI) 328 (10), 282 (5), 244 (23), 233 (100) and 165 (25) [Found: $(M - CH_3O)^+$, 328.2065. $C_{24}H_{26}N$ requires $(M - CH_3O)^+$, 328.2065].

(3R,S,4S)-6-*Methyl*-4-(*triphenylmethylamino*)*hept*-1-*en*-3-*ol* **10**.[9]—A stirred solution of oxalyl chloride (0.39 cm^3, 4.5 mmol) in anhydrous dichloromethane (9 cm^3) was cooled to −78 °C and a solution of anhydrous dimethyl sulfoxide (0.61 cm^3, 8.6 mmol in 1 cm^3 of anhydrous dichloromethane) was added to it,

* Owing to the formation of an insoluble gel a mechanical stirrer must be used.

† The procedure was modified slightly for large-scale preparative work, by pre-dissolving the trityl chloride in dichloromethane for the addition which was made at 0 °C.

the temperature being kept < −60 °C. After the complex had been allowed to form over 30 min, the amino alcohol **8** (1.277 g, 3.46 mmol) in anhydrous dichloromethane (9 cm^3) was added to it the temperature being kept at < −60 °C. The mixture was then stirred for a further 30 min before triethylamine (2.49 cm^3, 17.9 mmol) was added to it. After being stirred at this temperature for a further 10 min, the mixture was allowed to come to room temperature over *ca.* 30 min. It was then poured into water (50 cm^3) and extracted with dichloromethane (3 × 50 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (50 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude aldehyde **9** which was immediately used in the next reaction. The crude aldehyde **9** (3.46 mmol) in anhydrous THF (6.9 cm^3) was added to a solution of 1 mol dm^{-3} vinylmagnesium bromide in THF (6.9 cm^3, 6.9 mmol), and the stirred mixture cooled to −30 °C, the temperature being kept constant. After 5 min the reaction mixture was poured into stirred, ice-cold saturated aqueous ammonium chloride (20 cm^3) and allowed to warm to room temperature; it was then poured into ether (50 cm^3), shaken and separated. The aqueous phase was back-extracted with ether (2 × 25 cm^3). The organic layer and extracts were combined and then washed with saturated aqueous sodium hydrogen carbonate (20 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (1:4) afforded the title compound (1.255 g, 92%) as a lime coloured oil; R_F 0.47 (1:4 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3625m, 3550w, 3330w, 3090s, 3065vs, 3035s, 3025s, 2960vs, 2930vs and 2870vs; δ_H(400 MHz; $CDCl_3$) 0.42 (3 H, d, *J* 6.6, $CHCH_3$), 0.57 (1.5 H, d, *J* 6.4, $CHCH_3$), 0.66 (1.5 H, d, *J* 6.6, $CHCH_3$), 1.03–1.37 [3 H, m, $CHCH_2CH(CH_3)_2$], 2.46–2.50 (0.5 H, m, $NHCHCH_2$), 2.55–2.57 (0.5 H, m, $NHCHCH_2$), 3.80–3.82 [0.5 H, m, $CHCH(OH)CH$], 3.96–3.98 [0.5 H, m, $CHCH(OH)CH$], 5.06–5.38 (2 H, m, $CH{=}CH_2$), 5.06–5.38 [1 H, m, $CH(OH)$–$CH{=}CH_2$] and 7.15–7.53 (15 H, m, Ar*H*); δ_C($CDCl_3$, 100 MHz) 21.43 (o), 22.54 (o), 22.78 (o), 23.70 (o), 24.51 (o), 24.60 (o), 40.06 (e), 41.59 (e), 55.06 (o), 55.21 (o), 70.73 (e), 70.84 (e), 72.22 (o), 73.08 (o), 115.00 (e), 115.44 (e), 126.42 (o), 126.48 (o), 127.78 (o), 127.81 (o), 127.93 (o), 128.88 (o), 128.94 (o), 137.99 (o), 140.07 (o), 146.47 (e) and 146.70 (e); *m/z* 328 (5), 244 (25), 243 (100) and 165 (27); (Found: $(M - C_3H_5O)^+$, 328.2065. $C_{24}H_{26}N$ requires $(M - C_3H_5O)^+$, 328.2065).

(3R,S,4S)-4-*Amino*-6-*methylhept*-1-*en*-3-*ol* **11**.—The trityl alcohol **10** (1.550 g, 4.02 mmol) was dissolved in anhydrous methanol (30 cm^3) and the solution stirred at room temperature whilst DOWEX-50-X8 resin (1.546 g) was added to it; the mixture was then stirred at this temperature overnight (16 h). After this the resin was filtered off and washed with methanol (100 cm^3) and then rewashed with methanol–ammonia (300 cm^3). The filtrate and washings were concentrated under reduced pressure and the residue was partitioned between dichloromethane–water (made basic with ammonia; 150:150 cm^3) and the mixture shaken and separated: the aqueous phase was back-extracted with dichloromethane (4 × 100 cm^3). The combined organic layer and extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give the *title compound* (0.526 g, 91%) as a light green oil; $\nu_{max}(CCl_4)/cm^{-1}$ 3725m, 3680–3050br s, 3085ms, 2955vs, 2925vs and 2865vs; δ_H(400 MHz; $CDCl_3$) 0.86 (3 H, d, *J* 6.6, $CHCH_3$), 0.91 (3 H, d, *J* 6.7, $CHCH_3$), 1.12–1.32 [2 H, m, $CHCH_2CH(CH_3)_2$], 1.65–1.73 [1 H, m, $CH_2CH(CH_3)_2$], 1.96 (3 H, br s, NH_2 and OH), 2.65–2.7 (0.5 H, m, $NH_2CHCHOH$), 2.86–2.91 (0.5 H, m, NH_2CH-$CHOH$), 3.70–3.73 [0.5 H, m, $CHCH(OH)CH$], 3.97–3.99 [0.5 H, m, $CHCH(OH)CH$], 5.15–5.31 (2 H, m, $CH{=}CH_2$) and 5.75–5.86 [1 H, m, $CH(OH)CH{=}CH_2$]; δ_C(100 MHz; $CDCl_3$) 21.58 (o), 21.74(o), 23.56 (o), 23.65 (o), 24.62 (o), 24.72 (o), 42.71 (e), 43.14 (e), 53.00 (o), 53.07 (o), 75.24 (o), 73.70 (o), 116.29 (e), 116.61 (e), 136.84 (o) and 139.16 (o); *m/z* (EI) 144 (3), 126 (2), 112 (5), 87 (16), 86 (100), 70 (8), 69 (7), 68 (12) and 65 (3) [Found: $(M + H)^+$, 144.1388. $C_8H_{18}NO$ requires $(M + H)^+$, 144.1388].

(3R,S,4S)-4-*Benzylamino*-6-*methylhept*-1-*en*-3-*ol* **13**.—Benzaldehyde (0.15 cm^3, 1.48 mmol) and anhydrous sodium sulphate (0.4 g, 2.82 mmol) were added to a solution of the vinyl amino alcohol **11** (0.201 g, 1.40 mmol) in absolute ethanol (2 cm^3). The resulting mixture was heated under reflux for 2.5 h and then cooled to room temperature, filtered and concentrated under reduced pressure to afford a crude oil. A stirred solution of the crude oil in absolute ethanol (4 cm^3) was cooled to 0 °C and sodium borohydride (0.06 g, 1.59 mmol) was added portionwise to it; the resulting solution was stirred for 1 h and then quenched at 0 °C with water (10 cm^3). The reaction mixture was extracted with dichloromethane (3 × 25 cm^3) and the combined extracts were washed with brine (25 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure to give a crude solid. Purification of this by flash chromatography over silica gel, eluting with ethyl acetate–hexane (1:4) gave the *title compound* (0.175 g, 54%) as a white crystalline solid; m.p. 86–87 °C; R_F 0.17 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3725w, 3675–3140br m, 3090w, 3065w, 3030m, 2955vs, 2925s and 2865s; δ_H(250 MHz; $CDCl_3$) 0.82 (3 H, d, *J* 6.5, $CHCH_3$), 0.90 (3 H, d, *J* 6.6, $CHCH_3$), 1.14–1.40 [2 H, m, $CHCH_2CH$-$(CH_3)_2$], 1.55–1.66 [1 H, m, $CH_2CH(CH_3)_2$], 2.70–2.77 (1 H, m, $NHCHCH_2$), 3.81 (2 H, s, $PhCH_2NH$), 4.21–4.25 [1 H, m, $CHCH(OH)CH{=}CH_2$], 5.16–5.36 (2 H, m, $CH{=}CH_2$), 5.73–5.86 [1 H, m, $CH(OH)CH{=}CH_2$] and 7.27–7.34 (5 H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$) 22.37 (o), 23.05 (o), 23.40 (o), 24.79 (o), 38.78 (e), 40.99 (e), 51.49 (e), 51.72 (e), 59.09 (o), 59.35 (o), 71.34 (o), 74.01 (o), 115.90 (e), 127.15(o), 128.12 (o), 128.72 (o), 128.47 (o), 137.07 (o), 139.66 (e) and 140.20 (e); *m/z* (EI) 177 (9), 176 (65), 92 (8), 91 (100) and 65 (7) [Found: $(M - C_3H_5O)^+$, 176.1439. $C_{12}H_{18}N$ requires $(M - C_3H_5O)^+$, 176.1439] (Found: C, 76.9; H, 9.8; N, 5.9. $C_{15}H_{23}NO$ requires C, 77.2: H, 9.9; N, 6.0%).

(3R,S,4S)-4-*Benzyloxycarbonylamino*-6-*methylhept*-1-*en*-3-*ol* **15**.—DOWEX 50-X8 (8.25 g), was added to a solution of the trityl vinylamino alcohol **10** (8.25 g, 22.9 mmol) in anhydrous methanol (150 cm^3) and the mixture was stirred at room temperature overnight. Sodium carbonate (11.16 g, 105 mmol) was added to the mixture which was then stirred for 1 h at room temperature. After this it was filtered through Celite and evaporated under reduced pressure to afford a crude oil. The crude deprotected amino alcohol was then redissolved in THF–5 mol dm^{-3} aqueous sodium hydroxide (65:65 cm^3) and the stirred solution cooled to 0 °C. Benzyl chloroformate (3.6 cm^3, 32 mmol) was added dropwise to the solution which was then allowed to warm to room temperature. After being stirred overnight, the reaction mixture was poured into water (150 cm^3) and extracted with ether (3 × 100 cm^3). The combined organic phases were washed with brine (75 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (1:9) afforded the *title compound* (3.848 g, 61%) as a colourless oil; R_F 0.46 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3625m, 3560–3165br m, 3445s, 3095w, 3070w, 3040w, 2955s, 2930m, 2865m and 1725vs; δ_H(250 MHz; $CDCl_3$) 0.91 [6 H, d, *J* 6.6, $CH(CH_3)_2$], 1.23–1.44 [2 H, m, $CHCH_2CH(CH_3)_2$], 1.60–1.70 [1 H, m, CH_2-$CH(CH_3)_2$], 1.99 (1 H, br s, OH), 3.72–3.79 (0.5 H, m, $NHCHCH_2$), 3.86–3.89 (0.5 H, m, $NHCHCH_2$), 4.07–4.09 [0.5 H, m, $CH_2CH(OH)CH{=}CH_2$], 4.20–4.22 [0.5 H, m, CH_2-

C*H*(OH)CH=CH_2], 4.75–4.86 (1 H, m, NH), 5.08 (1 H, s, PhCH_2O), 5.10 (1 H, s, PhCH_2O), 5.13–5.36 (2 H, m, CH=CH_2), 5.76–5.95 [1 H, m, CH(OH)C*H*=CH_2] and 7.27–7.39 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.65 (o), 21.93 (o), 23.28 (o), 23.45 (o), 24.64 (o), 24.73 (o), 38.79 (e), 40.85 (e), 53.27 (o), 53.84 (o), 66.69 (e), 66.92 (e), 74.88 (o), 75.48 (o), 116.36 (e), 116.74 (e), 127.93 (o), 128.03 (o), 128.14 (o), 128.45 (o), 128.50 (o), 136.30 (e), 136.55 (o), 136.00 (o), 156.73 (e), 157.01 (e); *m/z* (EI) 221 (2), 220 (10), 177 (3), 176 (20), 108 (4), 107 (3), 92 (9), 91 (100), 79 (4), 78 (2), 77 (4) and 65 (5) [Found: $(M - C_3H_5O)^+$, 220.1337. $C_{13}H_{18}NO_2$ requires $(M - C_3H_5O)^+$, 220.1337] (Found: C, 69.5; H, 8.5; N, 5.4. $C_{16}H_{23}NO_3$ requires C, 69.3; H, 8.4; N, 5.1%).

(2R,S,4S,5R,S)-3-*Benzyloxycarbonyl*-4-*isobutyl*-2-*phenylselenanylmethyl*-5-*vinyloxazolidine* **16**.—The vinyl amino alcohol **15** (1.827 g, 6.59 mmol) was dissolved in anhydrous toluene (90 cm^3) and phenylselenanylacetaldehyde diethyl acetal (1.979 g, 7.24 mmol) and PPTS (82 mg, 0.326 mmol) were added to the solution which was then heated under reflux for 1 h. Half the solvent was removed and then replaced with anhydrous toluene (45 cm^3) and the resulting mixture was heated under reflux for a further 1 h. The solution was then poured into saturated aqueous sodium hydrogen carbonate (100 cm^3) and extracted with ether (3 × 100 cm^3). The combined extracts were washed with brine (25 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give a dark orange coloured oil. Purification of this by flash chromatography on silica gel, eluting with ethyl acetate–hexane (0:1 to 1:19) afforded the *title compound* (2.850 g, 94%) as a light yellow oil; R_{F1} 0.37, R_{F2} 0.44, R_{F3} 0.48 (1:4 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3060m, 3030m, 2950s, 2920s, 2890sh, 2860s and 1705vs; δ_H(400 MHz; C_6D_6; 333 K) 0.76 (3 H, d, *J* 6.6, CHCH_3), 0.79 (3 H, d, *J* 6.6, CHCH_3), 1.27–1.34 [1 H, m, C$H_A$$H_BCH(CH_3)_2$], 1.48–1.54 [1 H, m, CH_AH_BCH$(CH_3)_2$], 1.69–1.82 [1 H, m, CH_2C*H*$(CH_3)_2$], 3.41–3.46 (1 H, m, CH_2SePh), 3.86–3.69 (1 H, m, CH_2SePh), 3.80–3.84 (1 H, m, CHN), 4.04–4.07 (1 H, m, CHO), 4.92–5.44 (5 H, m, PhCH_2O, CH=CH_2 and C*H*CH_2SePh), 5.73–5.82 (1 H, m, CHOHC*H*=CH_2), 6.94–7.22 (8 H, m, ArH) and 7.55–7.57 (2 H, m, Ar*H*); *m/z* (CI) 477 (35), 460 (100), 326 (22), 304 (37), 288 (25), 260 (74), 170 (15), 154 (11), 108 (24) and 91 (8) [Found: $(M + H)^+$, 460.1391. $C_{24}H_{30}NO_3Se$ requires $(M + H)^+$, 460.1391].

(7S)-7-1-*Benzyloxycarbonyl*-7-*isobutyl*-1,3,4,7-*tetrahydroazepin*-2-*one* **18**.—The aminal **16** (2.575 g, 5.62 mmol) was dissolved in methanol–water (6:1; 175 cm^3) and sodium periodate (3.623 g, 16.9 mmol) and sodium hydrogen carbonate (0.515 g, 6.13 mmol) were added to the solution. The mixture was then stirred for 1 h at room temperature (reaction complete by TLC) after which it was poured into brine (2 dm^3) and extracted with dichloromethane (5 × 500 cm^3). The combined extracts were dried (K_2CO_3) and evaporated under reduced pressure to furnish the crude selenoxide (2.661 g, 100%) as a light yellow oil. The crude selenoxide (0.38 g, 0.80 mmol) was dissolved in anhydrous *m*-xylene (170 cm^3) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.6 cm^3, 4.01 mmol) was added to the solution which was then heated at reflux for *ca.* 16 h. Concentration of the mixture under reduced pressure afforded a dark oil, purification of which by flash chromatography over silica gel, eluting with ethyl acetate–hexane (0:1 to 1:19) furnished the *title compound* (0.092 g, 38%) as a colourless oil; R_F 0.35 (1:4 ethyl acetate–hexane); $[\alpha]_D^{22}$ +223.9 (*c* 1.64, MeOH); $\nu_{max}(CCl_4)/cm^{-1}$ 3100w, 3070w, 3030m, 2960s, 2925s, 2865m, 2840sh and 1715vs; δ_H(250 MHz; $CDCl_3$) 0.91 [6 H, d, *J* 6.3, CH$(CH_3)_2$], 1.59–1.72 [3 H, m, CH_2C*H*$(CH_3)_2$], 2.18–2.52 (2 H, m, CH_2CH_2), 2.63–2.73 (1 H, m, CH_2CH_2), 2.88–3.01 (1 H, m, CH_2CH_2CO), 4.97–5.05 (1 H, m, CHNZ), 5.26 (2 H, s, PhCH_2O), 5.63–5.72 (1 H, m, CH_2C*H*=CH-CHNZ), 5.75–5.82 (1 H, m, CH_2CH=C*H*CHNZ) and 7.26–7.43 (5 H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$) 22.39 (o), 22.64 (o), 24.03 (e), 25.41 (o), 38.39 (e), 46.39 (e), 53.74 (o), 66.69 (e), 127.92 (o), 128.18 (o), 128.50 (o), 128.87 (o), 129.27 (o), 135.47 (e), 155.21 (e) and 175.66 (e); *m/z* (EI) 302 (4), 301 (9), 244 (23), 200 (19), 166 (10), 92 (9), 91 (100), 67 (13) and 65 (9) (Found: M^+, 301.1678. $C_{18}H_{23}NO_3$ requires M^+, 301.1678) (Found: C, 71.8; H, 8.0; N, 4.7. $C_{18}H_{23}NO_3$ requires C, 71.7; H, 7.7; N, 4.7%).

(7S)-7-*Isobutyl*-1,3,4,7-*tetrahydroazepin*-2-*one* **19**.—45% Hydrobromic acid in acetic acid (0.69 cm^3, 5.33 mmol) was added to the Z-protected lactam **18** (0.358 g, 1.19 mmol) at room temperature, and the reaction mixture stirred at this temperature for 1 h. Ether (5 cm^3) was added to the mixture (precipitate formed) which was then stirred for a further 30 min. After this it was poured into saturated aqueous sodium carbonate (25 cm^3) and extracted with ether (3 × 25 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to afford a crude oil, purification of which by flash chromatography on silica gel eluting with ethyl acetate afforded the *title compound* (0.194 g, 98%) as a white crystalline solid; m.p. 88–90 °C; R_F 0.16 (1:1 ethyl acetate–hexane); $[\alpha]_D^{22}$ +15.3 (*c* 1.38, MeOH); $\nu_{max}(CCl_4)/cm^{-1}$ 3405m, 3300w, 3200m, 3080m, 3020m, 2950s, 2920s, 2860s and 1665vs; δ_H(250 MHz; $CDCl_3$) 0.92 (3 H, d, *J* 6.6, CHCH_3), 0.93 (3 H, d, *J* 6.6, CHCH_3), 1.37–1.46 [2 H, m, CH_2CH$(CH_3)_2$], 1.65–1.76 [1 H, m, CH_2C*H*$(CH_3)_2$], 2.34–2.46 (3 H, m, CH_2CH_2CO and CH_2CH_ACO), 2.88–3.01 (1 H, m, CH_2CH_BCO), 4.16–4.21 (1 H, m, C*H*NH), 5.47–5.53 (1 H, m, CH_2C*H*=CH) and 5.63–5.72 (1 H, m, CH_2CH=C*H*CHNH and N*H*); δ_C(100 MHz; $CDCl_3$) 21.89 (o), 22.72 (o), 24.47 (o), 24.56 (e), 33.52 (e), 44.93 (e), 47.74 (o), 129.93 (o), 130.66 (o) and 176.22 (e); *m/z* (CI) 168 (89), 154 (40), 144 (11), 126 (10), 125 (12), 112 (25), 110 (12), 108 (20), 86 (14) and 52 (100) [Found: $(M + H)^+$, 168.1388. $C_{10}H_{18}NO$ requires $(M + H)^+$, 168.1389] (Found: C, 71.4; H, 10.2; N, 8.3. $C_{10}H_{17}NO$ requires C, 71.8; H, 10.2; N, 8.4%).

(7R)-7-*Isobutylperhydroazepin*-2-*one* **20**.—The Z-protected lactam **18** (0.095 g, 0.315 mmol) was dissolved in ethyl acetate (4 cm^3) and $Pd(OH)_2$ (Pearlman's catalyst; 9.5 mg) was added to the solution. The reaction vessel was evacuated and placed under an atmosphere of hydrogen and the mixture was stirred vigorously overnight at room temperature. It was then filtered through Celite and evaporated under reduced pressure to afford a crude light brown oil. Purification of this by flash chromatography on silica gel, eluting with ethyl acetate, furnished the *title compound* (0.053 g, 99%) as a colourless oil; $[\alpha]_D^{22}$ −9.3 (*c* 0.53, MeOH); R_F 0.13 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3420m, 3305w, 3220m, 3100w, 2970s, 2940s, 2880s and 1665vs; δ_H(250 MHz; $CDCl_3$) 0.90 [6 H, d, *J* 6.5, CH$(CH_3)_2$], 1.09–2.00 (9 H, m), 2.39–2.52 (2 H, m, CH_2-CH_2CO), 3.28–3.40 (1 H, m, CH_2C*H*NH) and 5.49 (1 H, br s, NH).

(3R,S,4S)-6-*Methyl*-4-(p-*tolylsulfonylamino*)*hept*-1-*en*-3-*ol* **21**.—The vinylamino alcohol **11** (0.144 g, 1.01 mmol) was dissolved in THF (4 cm^3) and water (3 cm^3) and the stirred solution cooled to 0 °C. Triethylamine (0.16 cm^3, 1.15 mmol) was added to the solution followed by toluene-*p*-sulfonyl chloride (0.202 g, 1.06 mmol) in THF (2 cm^3) after which the reaction mixture was stirred at 0 °C for a further 30 min. It was then allowed to warm to room temperature. After being stirred at this temperature overnight, the reaction mixture was poured into brine (30 cm^3) and extracted with ethyl acetate (3 × 40 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to afford a crude yellow oil,

purification of which by flash chromatography on silica gel, eluting with 15% ethyl acetate in hexane, furnished the *title compound* (0.242 g, 81%) as a white crystalline solid; m.p. 80–82 °C; R_F 0.45 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3625w, 3500m, 3380m, 3270m, 2950s, 2920s, 2890sh and 2860m; δ_H(250 MHz; $CDCl_3$) 0.56 (1.5 H, d, *J* 6.5, $CHCH_3$), 0.67 (1.5 H, d, *J* 6.1, $CHCH_3$), 0.77 (3 H, d, *J* 6.6, $CHCH_3$), 0.78 (3 H, d, *J* 6.4, $CHCH_3$), 1.11–1.25 [2 H, m, $CH_2CH(CH_3)_2$], 1.33–1.49 [2 H, m, $CH_2CH(CH_3)_2$ and OH], 2.42 (3 H, s, $ArCH_3$), 3.25–3.41 (1 H, m, $NHCHCH_2$), 4.04–4.09 [1 H, m, $CH(OH)CH{=}CH_2$], 4.65 (1 H, dd, *J* 5.0, *J* 8.7, NH), 5.07–5.31 (2 H, m, $CH{=}CH_2$), 5.64–5.83 [1 H, m, $CH(OH)CH{=}CH_2$], 7.26–7.32 (2 H, m, ArH) and 7.72–7.80 (2 H, m, ArH); δ_H(100 MHz; $CDCl_3$) 21.21 (o), 21.46 (o), 21.80 (o), 22.85 (o), 23.15 (o), 23.96 (o), 24.16 (o), 38.87 (e), 40.66 (e), 56.11 (o), 56.40 (o), 74.16 (o), 116.95 (e), 117.23 (e), 127.12 (o), 127.17 (o), 129.48 (o), 129.62 (o), 136.18 (o), 137.18 (o), 137.51 (e), 138.11 (e), 143.25 (e) and 143.54 (e); *m/z* (CI) 315 (92), 298 (15), 280 (17), 174 (14), 144 (15) and 86 (100) [Found: $(M + NH_4)^+$, 315.1742. $C_{15}H_{27}N_2O_3S$ requires $(M + NH_4)^+$, 315.1742] (Found: C, 60.7; H, 7.8; N, 4.7; S, 10.8, $C_{15}H_{23}NO_3S$ requires C, 60.6; H, 7.8; N, 4.7; S, 10.8%).

(2R,S,4S,5R,S)-4-*Isobutyl*-2-*phenylselenanylmethyl*-3-(p-*tolylsulfonyl*)-5-*vinyloxazolidine* **22**.—The vinylamino alcohol **21** (0.061 g, 0.21 mmol) in anhydrous toluene (3 cm^3) with phenylselenoacetaldehyde diethyl acetal (0.062 g, 0.227 mmol) and pyridinium toluene-*p*-sulfonate (3 mg, 11.9 μmol) was heated under reflux for 1 h after which half the solvent was removed and replaced with anhydrous solvent. After being heated under reflux for a further 1 h, the mixture was poured into saturated aqueous sodium hydrogen carbonate (20 cm^3) and extracted with ether (3 × 20 cm^3). The combined extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give a dark orange coloured oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate in hexane (0:1 to 1:19), furnished the *title compound* (0.095 g, 97%) as a light yellow oil; R_F 0.4 (1:4 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3070sh, 3060m, 3010w, 2960s, 2925s, 2890sh and 2865s; δ_H(250 MHz; $CDCl_3$) 0.86–0.96 [6 H, m, $CH(CH_3)_2$], 1.17–1.47 [2 H, m, $CH_2CH(CH_3)_2$], 1.67–2.04 [1 H, m, $CH_2CH(CH_3)_2$], 2.42 (3 H, s, $ArCH_3$), 3.07–3.22 (1 H, m, $PhSeCH_AH_BCH$), 3.37–3.80 (2 H, m, $PhSeCH_AH_BCH$ and CHN), 3.71–3.80 (1 H, m, CHO), 4.93–5.32 (3 H, m, $PhSeCH_2CH$ and $CH{=}CH_2$), 5.51–5.65 [1 H, m, $CH(OH)CH{=}CH_2$], 7.22–7.33 (6 H, m, ArH) and 7.49–7.73 (4 H, m, ArH); *m/z* (CI) 497 (7), 480 (29), 324 (68), 280 (27), 170 (100), 154 (96), 112 (41) and 86 (21) [Found: $(M + H)^+$, 480.1111, $C_{23}H_{30}NO_3SSe$ requires $(M + H)^+$, 480.1111].

(7S)-7-*Isobutyl*-1-(p-*tolylsulfonyl*)-1,3,4,7-*tetrahydroazepin*-2-*one* **24**.—The aminal **22** (0.553 g, 1.16 mmol) was dissolved in methanol–water (6:1; 40 cm^3) and sodium periodate (0.742 g, 3.47 mmol) and sodium hydrogen carbonate (0.113 g, 1.35 mmol) were added to the solution. After the resulting mixture had been stirred for 1 h at room temperature (reaction complete by TLC) it was poured into water (400 cm^3) and extracted with dichloromethane (4 × 250 cm^3). The combined extracts were dried (K_2CO_3) and evaporated under reduced pressure to furnish the crude selenoxide (0.57 g, 100%) as a light yellow oil. The crude selenoxide (0.32 g, 0.65 mmol) was dissolved in anhydrous *m*-xylene (70 cm^3), and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.29 cm^3, 1.94 mmol) was added to the solution. After the resulting mixture had been heated at reflux for *ca.* 16 h, the solvent was removed under reduced pressure to afford a dark oil, which was purified as for **18** to afford the *title compound* (0.081 g, 39%) as a white crystalline solid; m.p. 115–117 °C; R_F 0.11 (1:4 ethyl acetate–hexane); $[\alpha]_D^{22}$ +128.1 (*c* 1.65, MeOH); $\nu_{max}(CCl_4)/cm^{-1}$ 3075w, 3030m, 2960s, 2925m, 2865m, 2840sh and 1695vs; δ_H(250 MHz; $CDCl_3$) 1.00 [3 H, d, *J* 6.3, $CH(CH_3)_2$], 1.01 [3 H, d, *J* 6.4, $CH(CH_3)_2$], 1.72–1.85 [3 H, m, $CH_2CH(CH_3)_2$], 2.14–2.22 (2 H, m, CH_2CH_2), 2.40 (3 H, s, $ArCH_3$), 2.43–2.46 (1 H, m, $CHCH_2CH_2CO$), 2.92–3.04 (1 H, m, $COCH_2CH_2$), 5.23–5.31 (1 H, m, CHNTs), 5.73–5.88 (2 H, m, $CH_2CH{=}CHCH$-NTs), 7.27 (2 H, d, *J* 8.0, ArH) and 7.79 (2 H, d, *J* 8.4, ArH); δ_C(100 MHz; $CDCl_3$) 21.62 (o), 22.35 (o), 22.83 (o), 23.68 (e), 25.62 (o), 36.72 (e), 47.63 (e), 53.29 (o), 128.01 (o), 128.34 (o), 129.16 (o), 129.53 (o), 136.74 (e), 144.26 (e) and 173.54 (e); *m/z* (EI) 321 (6), 320 (9), 306 (10), 281 (9), 264 (56), 200 (32), 172 (9), 108 (88), 91 (100) and 67 (22) (Found: M^+, 321.1399. $C_{17}H_{23}NO_3S$ requires M^+, 321.1399) (Found: C, 63.5; H, 7.2; N, 4.4, $C_{17}H_{23}NO_3S$ requires C, 63.5; H, 7.2; N, 4.4%).

(7S)-7-*Isobutyl*-1,3,4,7-*tetrahydroazepin*-2-*one* **19**.—Naphthalene (0.394 g, 3.07 mmol) and sodium (freshly cut; 0.079 g, 3.44 mmol) were suspended in freshly distilled 1,2-dimethoxyethane (10 cm^3) and the mixture was stirred at room temperature until the solution began to turn dark green.* It was then cooled to 0 °C, and stirred at this temperature for a further 2 h. A stirred solution of the *N*-tosyl lactam **24** (0.050 g, 0.155 mmol) in freshly distilled 1,2-dimethoxyethane (anhydrous; 0.65 cm^3) was cooled to −70 °C†), and the above prepared sodium naphthalenide [16] was added dropwise to it until the solution remained dark green (*ca.* 1.5 cm^3). The mixture was stirred at this temperature for a further 30 min before being quenched by the slow addition of saturated aqueous ammonium chloride (1 cm^3). After the reaction mixture had been allowed to warm to room temperature over 30 min, it was poured into water (20 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined extracts were dried ($MgSO_4$), and evaporated under reduced pressure to give a crude oil, purification of which by flash chromatography on silica gel with ethyl acetate in hexane (1:1) gave the title compound (0.023 g, 87%) as a white crystalline solid, spectroscopically identical with that formed using the benzyloxycarbonyl protecting group route; m.p. 88–90 °C; R_F 0.16 (1:1 ethyl acetate–hexane); $[\alpha]_D^{22}$ +15.8 (*c* 1.41, MeOH).

(±)-2-(*Benzyloxycarbonylamino*)-4-*methylpentan*-1-*ol* **28**.—(±)-Leucinol *rac*-**7** (10.0 g, 85.3 mmol) was dissolved in THF–dioxane (1:1; 500 cm^3) and the stirred solution cooled to 0 °C. Triethylamine (14.9 cm^3, 106.9 mmol) was added to the solution, followed by the dropwise addition of benzyl chloroformate (15.8 cm^3, 105 mmol). After the reaction mixture had been allowed to warm to room temperature, it was stirred overnight to give a colourless homogeneous solution. This was poured into brine (400 cm^3) and extracted with ether (4 × 250 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude oil, purification of which by flash chromatography on silica gel, eluting with 50% ethyl acetate in hexane, afforded the *title compound* (16.897 g, 79%) as a waxy white solid; m.p. 29–32 °C; R_F 0.23 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3645m, 3565–3120br m, 3445s, 3095w, 3070w, 3035m, 2955s, 2925s, 2895sh, 2865m and 1720vs; δ_H(250 MHz; $CDCl_3$) 0.92 [6 H, d, *J* 6.6, $CH(CH_3)_2$], 1.30–1.37 [2 H, m, $CH_2CH(CH_3)_2$], 1.58–1.74 [1 H, m, $CH_2CH(CH_3)_2$], 1.59–2.10 (1 H, bs, OH), 3.53 (1 H, dd, *J* 11, 5.7, $CHCH_2OH$), 3.69 (1 H, dd, *J* 11, 3.4, $CHCH_2OH$), 3.75–3.83 (1 H, m, CHNH), 4.79 (1 H, d, *J* 6.9, NH), 5.10 (2 H, s, $PhCH_2O$) and 7.30–7.37 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 22.15 (o), 22.04 (o), 24.77 (o), 40.48 (e), 51.45 (o), 66.09 (e), 66.88 (e), 128.09 (o), 128.16 (o), 128.54 (o), 136.38 (e) and 156.80 (e);

* Sonication was found to accelerate the reaction.

† The solution must be kept at −70 °C since it freezes below this temperature.

m/z (EI) 251 (24), 234 (10), 220 (16), 176 (21), 91 (100) and 65 (5) (Found: M^+, 251.1521, $C_{14}H_{21}NO_3$ requires M^+, 251.1521).

4-(*Benzyloxycarbonylamino*)-6-*methylhept*-1-*en*-3-*ol* rac-**15**.—To a stirred solution of oxalyl chloride (0.13 cm^3, 1.45 mmol) in anhydrous dichloromethane (3 cm^3) cooled to −78 °C was added anhydrous dimethyl sulfoxide (0.2 cm^3, 2.78 mmol in 1 cm^3 of anhydrous dichloromethane) the temperature being kept < −60 °C. The complex was allowed to form over 30 min, after which the amino alcohol **28** (0.281 g, 1.12 mmol) in anhydrous dichloromethane (3 cm^3) was added to the mixture the temperature being kept < −60 °C. After the mixture had been stirred for a further 30 min at this temperature triethylamine (0.81 cm^3, 5.81 mmol) was added to it. The mixture was stirred at the same temperature for a further 10 min before being allowed to come to room temperature over *ca.* 30 min. It was then poured into water (50 cm^3) and extracted with dichloromethane (3 × 50 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (40 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to give the crude aldehyde **29**. The crude aldehyde **29** (1.12 mmol) in anhydrous THF (2.3 cm^3) was added to a solution of vinylmagnesium bromide in THF (1 mol dm^{-3}; 2.25 cm^3), at −30 °C over *ca.* 5 min. The reaction mixture was then poured into stirred, ice-cold saturated aqueous ammonium chloride (50 cm^3). After 5 min the reaction mixture was allowed to warm to room temperature and extracted with ether (3 × 50 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (40 cm^3) and brine (40 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure to give a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (1:4) gave the *title compound* (0.202 g, 65%) as a lime coloured oil; R_F 0.51 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3625m, 3560–3160br s, 3440s, 3090w, 3065w, 3035m, 2955s, 2925s, 2895sh, 2865s and 1720vs; δ_H(250 MHz; $CDCl_3$) 0.84–0.98 [6 H, m, $CH(CH_3)_2$], 1.24–1.44 [2 H, m, $CH_2CH(CH_3)_2$], 1.60–1.72 [1 H, m, $CH_2CH(CH_3)_2$], 3.70–3.83 (0.67 H, m, CHNH), 3.83–3.95 (0.33 H, m, CHNH), 4.04–4.15 (0.67 H, m, CHCHOH), 4.20–4.26 (0.33 H, m, CHCHOH), 4.71–4.90 (1 H, br m, NH), 5.09–5.35 (4 H, m, $PhCH_2O$ and $CH{=}CH_2$), 5.81–5.91 [1 H, m, $CH(OH)CH{=}CH_2$] and 7.27–7.38 (5 H, m, ArH).

3-*Benzyloxycarbonyl*-4-*isobutyl*-2-*phenylselenanylmethyl*-5-*vinyloxazolidine* rac-**16**.—The amino alcohol *rac*-**15** (1.34 g, 4.83 mmol) was dissolved in anhydrous toluene (70 cm^3) and phenylselenanylacetaldehyde diethyl acetal (1.45 g, 5.31 mmol) and pyridinium toluene-*p*-sulfonate (60 mg, 0.239 mmol) were added to the solution. This was then heated under reflux for 2 h after which half the solvent was removed. This was replaced with anhydrous solvent and the mixture refluxed for a further 2 h. The mixture was then poured into saturated aqueous sodium hydrogen carbonate (100 cm^3) and extracted with ether (3 × 75 cm^3). The combined extracts were washed with brine (50 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to give a dark orange coloured oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (0:1 to 1:19) furnished the *title compound* (1.82 g, 82%) as a light yellow oil; R_{F1} 0.37, R_{F2} 0.44, R_{F3} 0.48 (1:4 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3070w, 3035w, 2955s, 2925m, 2900sh, 2865m and 1705vs; δ_H(250 MHz; $CDCl_3$) 0.70–1.02 [6 H, m, $CH(CH_3)_2$], 1.12–1.57 [3 H, m, $CH_2CH(CH_3)_2$], 3.09–3.33 (1 H, m, $PhSeCH_2CH$), 3.49–3.67 (1 H, m, $PhSeCH_2CH$), 3.79–3.86 (1 H, m, CHN), 4.27 (0.66 H, dd, *J* 6.9, 4.2, CHO), 4.40 (0.33 H, dd, *J* 6.4, 5.3, CHO), 4.98–5.46 (5 H, m, $PhCH_2O$, $CH{=}CH_2$ and $PhSeCH_2CH$), 5.73–5.96 (1 H, m, $CH{=}CH_2$), 7.18–7.22 (3 H, m, ArH), 7.27–7.40 (5 H, m, ArH) and 7.49–7.52 (2 H, m, ArH).

(±)-1-*Benzyloxycarbonyl*-7-*isobutyl*-1,3,4,7-*tetrahydroazepin*-2-*one* rac-**18**.—The aminal *rac*-**16** (2.01 g, 4.38 mmol) was dissolved in methanol–water (6:1; 140 cm^3) and sodium periodate (2.811 g, 13.14 mmol) and sodium hydrogen carbonate (0.402 g, 4.79 mmol) were added to the solution. The mixture was then stirred for 1 h at room temperature (reaction complete by TLC) after which it was poured into water (1.5 dm^3) and extracted with dichloromethane (7 × 150 cm^3). The combined extracts were dried (K_2CO_3) and evaporated under reduced pressure to furnish the crude selenoxide (1.975 g, 95%) as a light yellow oil. The crude selenoxide (1.74 g, 3.67 mmol) was dissolved in anhydrous *m*-xylene (175 cm^3), and 1,8-diazabicyclo[5.4.0]undec-7-ene (1.67 cm^3, 11.2 mmol) was added to the solution. The reaction mixture was then heated at reflux for *ca.* 16 h* after which it was evaporated under reduced pressure to afford a dark oil. Purification by flash chromatography over silica gel, eluting with ethyl acetate–hexane (0:1 to 1:19) gave a crude oil, which was repurified using the chromatotron, eluting with ethyl acetate in hexane (1:19) to afford the *title compound* (0.481 g, 44%) as a colourless oil; R_F 0.35 (1:4 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3095sh, 3070w, 3030m, 2960s, 2930s, 2865m, 2840sh and 1715vs; δ_H(250 MHz; $CDCl_3$) 0.91 [6 H, d, *J* 6.3, $CH(CH_3)_2$], 1.61–1.72 [3 H, m, $CH_2CH(CH_3)_2$], 2.18–2.30 (1 H, m, $CHCH_2CH_2CO$), 2.38–2.52 (1 H, m, $CHCH_2CH_2CO$), 2.64–2.73 (1 H, m, $CHCH_2CH_2CO$), 2.88–3.01 (1 H, m, CH_2CH_2CO), 4.97–5.05 (1 H, m, CHNZ), 5.26 (2 H, s, $PhCH_2O$), 5.63–5.72 (1 H, m, $CH_2CH{=}CH$), 5.75–5.82 (1 H, m, $CH{=}CHCHNZ$) and 7.27–7.43 (5 H, m, ArH).

(±)-7-*Isopropyl*-1,3,4,7-*tetrahydroazepin*-2-*one* rac-**19**.—45% Hydrobromic acid in acetic acid (0.33 cm^3, 2.55 mmol) was added to the Z-protected lactam *rac*-**18** (0.154 g, 0.51 mmol) at 0 °C after which the reaction mixture was allowed to warm to room temperature. It was stirred for 90 min at this temperature after which it was diluted with ether (5 cm^3) (precipitate formed) and stirred for a further 30 min. The reaction mixture was then poured into saturated aqueous sodium carbonate (25 cm^3) and extracted with ether (3 × 25 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate, furnished the *title compound* (0.072 g, 84%) as a white crystalline solid, m.p. 88–90 °C; R_F 0.16 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3410w, 3300w, 3210m, 3080m, 3020m, 2960s, 2925s, 2910sh, 2865s, 2840sh and 1670vs; δ_H(250 MHz; $CDCl_3$) 0.93 (3 H, d, *J* 6.5, $CHCH_3$), 0.94 (3 H, d, *J* 6.6, $CHCH_3$), 1.32–1.51 [2 H, m, $CH_2CH(CH_3)_2$], 1.62–1.76 [1 H, m, $CH_2CH(CH_3)_2$], 2.33–2.47 (3 H, m, CH_2CH_2CO and $CH_2CH_AH_BCO$), 2.88–3.01 (1 H, m, $CH_2CH_AH_BCO$), 4.17–4.24 (1 H, m, CHNH), 5.47–5.53 (1 H, m, $CH_2CH{=}CH$) and 5.63–5.72 (2 H, m, $CH{=}CHCHNH$ and NH).

(±)-7-*Isobutyl*-1-*methyl*-1,3,4,7-*tetrahydroazepin*-2-*one* rac-**30**.—Sodium hydride (50% dispersion in oil washed twice with anhydrous hexane; 16 mg, 0.33 mmol) was suspended in anhydrous dimethylformamide (1 cm^3) and the stirred suspension cooled to 0 °C under an atmosphere of argon. The unsaturated lactam *rac*-**19** (51.5 mg, 0.31 mmol) in anhydrous dimethylformamide (0.5 cm^3) was added dropwise at 0 °C to the suspension and the anion allowed to form over 45 min. Methyl iodide (0.021 cm^3, 0.34 mmol) was added to the mixture which was then allowed to warm to room temperature. The mixture was stirred for 3 h at this temperature after which it was diluted

* The selenoxide was converted into the lactam *rac*-**18** in two almost equal batches, which were combined after the overnight reflux and purified together.

with ether (10 cm^3), filtered and evaporated under reduced pressure to give a crude oil. Purification of this by flash chromatography on silica gel, eluting with ethyl acetate–hexane (3:7), furnished the *title compound* (35.9 mg, 64%) as a colourless oil; R_F 0.24 (1:1 ethyl acetate–hexane); ν_{max}(CCl_4)/cm^{-1} 3020m, 2955s, 2925s, 2905sh, 2865m, 2835m and 1640vs; δ_H(250 MHz; $CDCl_3$) 0.92 [3 H, d, *J* 6.0, $CH(CH_3)_2$], 0.93 [3 H, d, *J* 5.9, $CH(CH_3)_2$], 1.57–1.69 [3 H, m, $CH_2CH(CH_3)_2$], 2.14–2.45 (2 H, m), 2.55–2.64 (1 H, m), 2.71–2.82 (1 H, m, CH_2CO), 2.95 (3 H, s, CH_3N), 3.79–3.87 (1 H, m, CH_2CHNCH_3), 5.55–5.64 (1 H, m, CH=$CHCH_2$) and 5.68–5.76 (1 H, m, CH=$CHCHNH$).

7(S)-*Isobutyl*-1-*methyl*-1,3,4,7-*tetrahydroazepin*-2-*one* **30**.—Sodium hydride (50% dispersion in oil washed twice with anhydrous hexane; 12 mg, 0.25 mmol) was suspended in anhydrous dimethylformamide (0.8 cm^3) and the stirred suspension cooled to 0 °C under an atmosphere of argon. The unsaturated lactam **19** (40 mg, 0.24 mmol) in anhydrous dimethylformamide (0.4 cm^3) was added dropwise at 0 °C, to the suspension and the anion allowed to form over 1 h. Methyl iodide (0.016 cm^3, 0.26 mmol) was added to the mixture which was then allowed to warm to room temperature. The mixture was stirred for 2 h at this temperature after which it was diluted with ether (10 cm^3), filtered and evaporated under reduced pressure to afford a crude oil. Purification of this as above gave the *title compound* (31.3 mg, 72%) as a colourless oil; R_F 0.24 (1:1 ethyl acetate–hexane); $[\alpha]_D^{22}$ +189.5 (*c* 1.39, MeOH); ν_{max}(CCl_4)/cm^{-1} 3025m, 2955s, 2925s, 2900sh, 2865m, 2835w and 1640vs; δ_H(250 MHz; $CDCl_3$) 0.94 [3 H, d, *J* 6.2, $CH(CH_3)_2$], 0.95 [3 H, d, *J* 6.2, $CH(CH_3)_2$], 1.59–1.71 [3 H, m, $CH_2CH(CH_3)_2$], 2.20–2.37 (2 H, m), 2.58–2.67 (1 H, m), 2.73–2.84 (1 H, m, CH_2CO), 2.97 (3 H, s, CH_3N), 3.81–3.89 (1 H, m, CH_2CHNCH_3), 5.57–5.66 (1 H, m, CH=$CHCH_2$) and 5.70–5.78 (1 H, m, CH=$CHCHNH$); δ_C(100 MHz; $CDCl_3$) 22.22 (o), 22.90 (o), 24.57 (e), 25.26 (o), 35.24 (e), 35.95 (o), 45.17 (e), 58.09 (o), 128.63 (o), 129.73 (o) and 174.21 (e); *m/z* (EI) 181 (3), 125 (8), 124 (97), 98 (5), 68 (8), 67 (100) and 58 (37) (Found: M^+, 181.1466, $C_{11}H_{19}NO$ requires M^+, 181.1466).

(±)-7-*Isobutylperhydroazepin*-2-*one* rac-**20**.—The unsaturated lactam *rac*-**19** (0.214 g, 1.28 mmol) was dissolved in ethyl acetate (4 cm^3) and $Pd(OH)_2$ (21.4 mg, Pearlman's catalyst) was added to the solution. The reaction vessel was then evacuated, placed under an atmosphere of hydrogen and stirred vigorously at room temperature for 30 min. The reaction mixture was then filtered through Celite and evaporated under reduced pressure to afford a light yellow solid, purification of which by flash chromatography on silica gel, eluting with ethyl acetate, gave the *title compound* (0.207 g, 96%) as a white crystalline solid; m.p. 80–81 °C; R_F 0.13 (1:1 ethyl acetate–hexane); ν_{max}(CCl_4)/cm^{-1} 3405m, 3290w, 3200m, 3080w, 2955s, 2925s, 2860m and 1665vs; δ_H(250 MHz; $CDCl_3$) 0.88 [6 H, d, *J* 6.6, $CH(CH_3)_2$], 1.17–1.99 (9 H, m), 2.37–2.50 (2 H, m, CH_2CH_2CO), 3.26–3.38 (1 H, m, $CHNH$) and 5.61 (1 H, br s, NH); δ_C(100 MHz; $CDCl_3$) 21.90 (o), 22.89 (o), 23.22 (e), 24.62 (o), 29.71 (e), 36.03 (e), 36.81 (e), 45.38 (e), 51.65 (o) and 177.78 (e); *m/z* (EI) 170 (2), 169 (8), 126 (5), 113 (7), 112 (100), 86 (39), 85 (9), 84 (16), 70 (5), 69 (23) and 67 (10) (Found: M^+, 169.1467, $C_{10}H_{19}NO$ requires M^+, 169.1467) (Found: C, 71.2; H, 11.3; N, 8.0, $C_{10}H_{19}NO$ requires C, 71.0; H, 11.3; N, 8.3%).

(±)-*Methyl* 6-(*Acetylamino*)-8-*methylnonanoate* rac-**31**.—The saturated lactam *rac*-**20** (36.1 mg, 0.213 mmol) was dissolved in 2 mol dm^{-3} hydrochloric acid–methanol (3 cm^3) and the solution heated under reflux for 16 h. The mixture was then evaporated under reduced pressure to give a crude oil, which was further dried under high vacuum. The resulting amino ester was redissolved in pyridine (0.5 cm^3, 6.2 mmol) and the solution stirred at room temperature whilst acetic anhydride (0.2 cm^3, 2.12 mmol) followed by DMAP (2.6 mg, 2.0 μmol) were added to it; the mixture was then stirred at the same temperature for a further 3 h. After this the reaction mixture was poured into water (10 cm^3) and extracted with ethyl acetate (4 × 10 cm^3). The combined extracts were washed with 1 mol dm^{-3} hydrochloric acid (10 cm^3) and brine (10 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to afford a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate, furnished the *title compound* (30.3 mg, 58%) as a white crystalline solid which was recrystallised from ether–hexane; m.p. 53–55 °C; R_F 0.13 (1:1 ethyl acetate–hexane); ν_{max}(CCl_4)/cm^{-1} 3440m, 3390–3260br w, 2955s, 2865m, 2840sh, 1740vs and 1675vs; δ_H(250 MHz; $CDCl_3$) 0.86 (3 H, d, *J* 6.6, $CHCH_3$), 0.87 (3 H, d, *J* 6.5, $CHCH_3$), 1.20–1.63 (11 H, m), 1.94 (3 H, s, $NHCOCH_3$), 2.27 (2 H, t, *J* 7.5, $CH_2CH_2CO_2CH_3$), 3.63 (3 H, s, CO_2CH_3), 3.95–4.05 (1 H, m, $CHNHAc$) and 5.28 (1 H, br d, *J* 6.5, NH); δ_C(100 MHz; $CDCl_3$) 22.14 (o), 23.17 (o), 23.42 (o), 24.84 (e), 24.91 (o), 25.30 (e), 33.89 (e), 35.60 (e), 44.66 (e), 47.25 (o), 51.42 (o), 169.50 (e) and 174.05 (e); *m/z* (EI) 244 (4), 243 (18), 228 (7), 212 (8), 200 (36), 187 (14), 186 (48), 170 (29), 169 (8), 144 (14), 128 (43), 112 (79), 86 (100) and 69 (15) (Found: M^+, 243.1834, $C_{13}H_{25}NO_3$ requires M^+, 243.1834) (Found: C, 63.9; H, 10.6; N, 5.5; $C_{13}H_{25}NO_3$ requires C, 64.2; H, 10.4; N, 5.8%).

(6R)-*Methyl* 6-(*Acetylamino*)-8-*methylnonanoate* **31**.—A solution of the saturated lactam **20** (158 mg, 0.933 mmol) in 2 mol dm^{-3} hydrochloric acid–methanol (6 cm^3) was heated under reflux for 5 h and then evaporated under reduced pressure to give a crude oil, which was further dried under high vacuum. The resulting amino ester was redissolved in pyridine (2 cm^3, 24.7 mmol) and the solution stirred at room temperature whilst acetic anhydride (0.9 cm^3, 9.54 mmol) followed by DMAP (11.4 mg, 93 μmol) were added to it; the mixture was then stirred at the same temperature for a further 3 h. After this the reaction mixture was poured into water (10 cm^3) and extracted with ethyl acetate (4 × 10 cm^3). The combined extracts were washed with 1 mol dm^{-3} hydrochloric acid (10 cm^3) and brine (10 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure to afford a crude oil, purification of which as above furnished the *title compound* (0.127 g, 56%) as a white waxy solid; m.p. 60–63 °C; R_F 0.13 (1:1 ethyl acetate–hexane); $[\alpha]_D^{22}$ −24.9 (*c* 1.02, MeOH); ν_{max}(CCl_4)/cm^{-1} 3445m, 2960s, 2940sh, 2920sh, 2870m, 2850sh, 1740vs and 1680vs; δ_H(250 MHz; $CDCl_3$) 0.89 (6 H, d, *J* 6.5, CH_3CH), 1.21–1.70 (9 H, m), 1.96 (3 H, s, $NHCOCH_3$), 2.29 (2 H, t, *J* 7.4, $CH_2CH_2CO_2CH_3$), 3.65 (3 H, s, CO_2CH_3), 3.94–4.03 (1 H, m, $CHNHAc$), 5.12 (1 H, br d, *J* 9.1, NH).

(2S)-*Methyl* 2-(*Benzyloxycarbonylamino*)-3-*hydroxypropanoate* **34**.[19]—A stirred solution of the amino acid **33** (43.53 g, 182 mmol) in anhydrous methanol (350 cm^3) was cooled to 0 °C and thionyl chloride (20.5 cm^3, 281 mmol) was added dropwise to it. The mixture was then stirred at 0 °C for *ca.* 30 min, before being allowed to warm to room temperature. It was stirred at this temperature overnight after which it was evaporated under reduced pressure to afford a crude oil which was redissolved in dichloromethane (250 cm^3) and the solution washed with saturated aqueous sodium hydrogen carbonate (2 × 250 cm^3). The aqueous phase was back-extracted with dichloromethane (3 × 150 cm^3) after which the combined organic phase and extracts were washed with water (150 cm^3) and brine (150 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude oil. Purification of this by flash chromatography on silica gel, eluting with ethyl acetate–hexane (1:1) furnished the title compound (44.52 g, 97%) as a colourless oil which

crystallized with time. The solid was triturated with hexane to give the product as a white crystalline solid; m.p. 38–40 °C; R_F 0.53 (ethyl acetate); $[\alpha]_D^{22}$ +6.2 (*c* 6.42, $CHCl_3$) {lit.,[18] $[\alpha]_D^{23}$ +7.2 (*c* 6.36, $CHCl_3$)}; $\nu_{max}(CCl_4)/cm^{-1}$ 3700–3200br s, 3505m, 3425s, 3105sh, 3095w, 3065w, 3035m, 2950s, 2885m, 2845sh and 1725vs; δ_H(250 MHz; $CDCl_3$) 3.77 (3 H, s, CO_2CH_3), 3.88–4.02 (2 H, ABX, J_{AB} 11.2, J_{AX} 3,2, J_{BX} 3.4, $CHCH_2OH$), 4.43–4.46 (1 H, m, $ZNHCHCH_2OH$), 5.12 (2 H, s, $PhCH_2O$), 5.74 (1 H, d, *J* 6.7, NH) and 7.30–7.35 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 52.66 (o), 55.99 (o), 63.10 (e), 67.14 (e), 128.06 (o), 128.19 (o), 128.49 (o), 135.99 (e), 156.24 (e) and 171.04 (e); *m/z* (EI) 254 (3), 253 (19), 223 (8), 194 (35), 164 (13), 163 (10), 162 (82), 151 (9), 150 (80), 146 (8), 108 (44), 92 (14), 91 (100) and 65 (10) (Found: M^+, 253.0951, $C_{12}H_{15}NO_5$ requires M^+, 253.0951).

(4S-)*Methyl* 3-*Benzyloxycarbonyl*-2,2-*dimethyloxazolidine*-4-*carboxylate* **35**.[19]—A solution of the amino ester **34** (2.755 g, 10.9 mmol) in anhydrous benzene (150 cm^3) with 2,2-dimethoxypropane (2.0 cm^3, 16.3 mmol) and TsOH (0.104 g, 0.547 mmol) was heated under Dean–Stark conditions for 1 h (reaction monitored by TLC). The reaction mixture was poured into saturated aqueous sodium hydrogen carbonate (150 cm^3) and extracted with ether (1 × 150 cm^3 and 2 × 50 cm^3). The organic phases were combined, washed with water (50 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (1:9), furnished the title compound (3.094 g, 97%) as a light orange coloured oil;*† R_F 0.57 (1:1 ethyl acetate–hexane); $[\alpha]_D^{22}$ −52.1 (*c* 1.31, $CHCl_3$); $\nu_{max}(CCl_4)/cm^{-1}$ 3115sh, 3090w, 3065w, 3035m, 2995s, 2950s, 2880m, 2840w, 1765vs, 1740s and 1714vs; δ_H(250 MHz; $CDCl_3$) 1.48 (1 H, s, CCH_3), 1.55 (2 H, s, CCH_3), 1.63 (1 H, s, CCH_3), 1.70 (2 H, s, CCH_3), 3.62 (2 H, s, CO_2CH_3), 3.76 (1 H, s, CO_2CH_3), 4.05–4.19 (2 H, m, $CHCH_2OH$), 4.47 (0.67 H, dd, *J* 6.7, 2.8, $ZNCHCH_2OH$), 4.55 (0.33 H, dd, *J* 6.4, 2.8, $ZNCHCH_2OH$), 5.09 (1.33 H, AB quartet, J_{AB} 12.4, $PhCH_2O$), 5.18 (0.67 H, AB quartet, J_{AB} 12.4, $PhCH_2O$) and 7.27–7.36 (5 H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$) 24.04 (o), 24.87 (o), 25.10 (o), 25.97 (o), 52.32 (o), 52.45 (o), 58.79 (o), 59.48 (o), 66.09 (e), 66.51 (e), 66.69 (e), 67.50 (e), 94.74 (e), 95.40 (e), 127.68 (o), 127.94 (o), 128.11 (o), 128.36 (o), 128.48 (o), 135.95 (e), 136.25 (e), 151.69 (e), 152.77 (e), 170.90 (e) and 171.17 (e); *m/z* (EI) 293 (8), 279 (10), 278 (61), 235 (24), 234 (60), 190 (9), 186 (4), 139 (5), 128 (8), 107 (5), 92 (8), 91 (100) and 65 (5) (Found: M^+, 293.1264, $C_{15}H_{19}NO_5$ requires M^+, 293.1264).

(4S)-3-*Benzyloxycarbonyl* 2,2-*dimethyloxazolidine*-4-*carbaldehyde* **36**.[19]—A stirred solution of the amino ester **35** (16.221 g, 55.3 mmol) in anhydrous toluene (135 cm^3) was cooled to −78 °C and diisobutylaluminium hydride (1.5 mol dm^{-3} solution in toluene; 64.5 cm^3, 96.8 mmol) was added dropwise to it, the internal temperature being kept < −70 °C. After the mixture had been stirred at −78 °C for a further 2 h, methanol (25 cm^3) was slowly added to it, the internal temperature being kept < −70 °C, in order to quench the reaction. The reaction mixture was then poured into ice-cold 1 mol dm^{-3} hydrochloric acid (300 cm^3) and extracted with ethyl acetate (1 × 200 cm^3 and 3 × 150 cm^3). The combined extracts were washed with brine (150 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to afford a crude oil. This was distilled under reduced pressure to give the title compound (13.687 g, 94%) as a colourless oil; b.p. 160–163 °C at 0.2 mmHg (lit.,[18] 174–180 °C at 0.8 mmHg)†; R_F 0.46 (1:1 ethyl acetate–hexane); $[\alpha]_D^{22}$ +67.2 (*c* 1.02, $CHCl_3$) {lit.,[18] $[\alpha]_D^{25}$ +70.1 (*c* 1.01, $CHCl_3$)}; $\nu_{max}(CCl_4)/cm^{-1}$ 3120sh, 3100w, 3080w, 3045m, 2995m, 2940m, 2885m, 2805m, 2715w, 1740sh and 1720vs; δ_H(250 MHz; $CDCl_3$) 1.50 (1.2 H, s, CCH_3), 1.57 (1.8 H, s, CCH_3), 1.59 (1.2 H, s, CCH_3), 1.67 (1.8 H, s, CCH_3), 3.53–4.47 (3 H, m, $ZNCHCH_2O$), 5.07–5.20 (2 H, m, $PhCH_2O$), 7.30–7.36 (5 H, m, ArH), 9.56 (0.6 H, br s, $CHCHO$) and 9.62 (0.4 br s, $CHCHO$); δ_C(100 MHz; $CDCl_3$) 23.58 (o), 24.73 (o), 25.71 (o), 26.66 (o), 63.59 (e), 64.17 (e), 64.46 (o), 65.12 (o), 67.16 (e), 67.87 (e), 94.79 (e), 95.54 (e), 127.95 (o), 128.14 (o), 128.25 (o), 128.36 (o), 128.58 (o), 135.90 (e), 151.92 (e) and 198.93 (o); *m/z* (EI) 248 (7), 235 (8), 234 (48), 191 (5), 190 (32), 186 (8), 170 (4), 144 (14), 128 (14), 108 (6), 107 (8), 92 (8), 91 (100) and 65 (5) [Found: $(M - CH_3)^+$, 248.0923. $C_{13}H_{14}NO_4$ requires $(M - CH_3)^+$, 248.0923].

(4S)-*Benzyl* 4-[(1R,S)-1′-*Hydroxyallyl*]-2,2-*dimethyloxazolidine*-3-*carboxylate* **37**.—A solution of the amino aldehyde **36** (1.407 g, 5.34 mmol) in anhydrous THF (10 cm^3) was added dropwise over 30 min to vinylmagnesium bromide (1 mol dm^{-3} solution in THF; 10.7 cm^3, 10.7 mmol) at −78 °C; the reaction was then quenched by the slow addition of saturated aqueous ammonium chloride (5 cm^3) to the mixture. After this the reaction mixture was poured into saturated aqueous ammonium chloride (50 cm^3) and extracted with ether (1 × 50 cm^3 and 3 × 25 cm^3). The combined extracts were washed with brine (40 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to afford a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (3:7), furnished the *title compound* (1.395 g, 90%) as a colourless oil;‡ R_F 0.48 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3620w, 3560w, 3590–3200br m, 3095sh, 3070w, 3040w, 2985s, 2955sh, 2935m, 2880m, 1705vs and 1670s; δ_H(250 MHz; $CDCl_3$) 1.37–1.62 [6 H, m, $C(CH_3)_2$], 3.54–4.31 (4 H, m, $ZNCHCH_2O$ and $CHOHCH{=}CH_2$), 5.01–5.35 (4 H, m, $PhCH_2O$ and $CH{=}CH_2$), 5.65–5.82 [1 H, m, $CH(OH)CH{=}CH_2$] and 7.21–7.29 (5 H, m, Ar*H*); *m/z* (CI) 292 (100), 281 (9), 264 (20), 248 (6), 234 (82), 220 (11), 206 (11), 190 (15), 158 (11), 108 (34), 91 (20) and 58 (11) [Found: $(M + H)^+$, 292.1549. $C_{16}H_{22}NO_4$ requires $(M + H)^+$, 292.1549].

(3R,S,4S)-4-(*Benzyloxycarbonylamino*)-5-[tert-*butyl*(*dimethyl*)*siloxy*]*pent*-1-*en*-3-*ol* **38**.—The oxazolidine **37** (0.149 g, 0.51 mmol) was dissolved in anhydrous methanol (6 cm^3) and toluene-*p*-sulfonic acid (9.7 mg, 51 μmol) was added to the solution. The reaction mixture was stirred at room temperature for 5 h (TLC control) after which imidazole (77 mg, 1.13 mmol) was added to it and the solvent removed under reduced pressure to afford a crude oil; this was further dried under high vacuum. The crude oil was redissolved in anhydrous dimethylformamide (25 cm^3) and *tert*-butyl(dimethyl)silyl chloride (96 mg, 0.637 mmol) was added to the solution and the mixture stirred at room temperature overnight. It was then poured into water (25 cm^3) and extracted with dichloromethane (3 × 25 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (20 cm^3), dried ($MgSO_4$) and evaporated under reduced pressure to afford a crude oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (1:9), afforded the crude amino alcohol. This was further purified by preparative TLC, eluting with ethyl acetate–hexane (1:4) to furnish the *title compound* (0.165 g, 88%) as a colourless oil; R_F 0.69 (1:1 ethyl acetate–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3625w, 3660–3300br s, 3485m, 3440s, 3095w, 3070w, 3040w, 2955s, 2925s, 2885m, 2855s and 1725vs; δ_H(250 MHz; $CDCl_3$) 0.02–0.09 [6 H, m, $Si(CH_3)_2$], 0.85–0.93 [9 H, m,

* The product may also be distilled b.p. 156–158 °C at 0.3 mmHg.
† The product exists at room temperature as a mixture of rotamers.
‡ The amino alcohol **37** was obtained as a 2:1 mixture of diastereoisomers and exists at room temperature as a mixture of rotamers.

$C(CH_3)_3$], 3.60–4.02 (4 H, m, $CHCH_2O$, $NHCHCH_2$ and O*H*), 4.18–4.34 (0.67 H, m, $CHCH(OH)CH{=}CH_2$), 4.45–4.50 (0.33 H, m, $CHCH(OH)CH{=}CH_2$), 5.04–5.42 (4 H, m, $PhCH_2O$ and $CH{=}CH_2$), 5.53 (1 H, bd, *J* 8.3, NH), 5.77–5.99 [1 H, m, $CH(OH)CH{=}CH_2$] and 7.30–7.37 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) −5.76 (o), −5.70 (o), −5.66 (o), 18.05 (e), 25.75 (o), 54.34 (o), 54.72 (o), 63.36 (e), 65.07 (e), 66.81 (e), 73.28 (o), 74.60 (o), 116.11 (e), 116.32 (e), 128.01 (o), 128.08 (o), 128.13 (o), 128.51 (o), 136.37 (e), 137.14 (o), 137.59 (o), 156.15 (e) and 156.50 (e); *m/z* (CI) 366 (100), 338 (12), 322 (8), 275 (25), 258 (88), 232 (28), 174 (12), 108 (31), 91 (34) and 70 (17) [Found: $(M + H)^+$, 366.2101, $C_{19}H_{32}NO_4Si$ requires $(M + H)^+$, 366.2101] (Found: C, 62.6; H, 8.5; N, 5.2; $C_{19}H_{32}NO_4Si$ requires C, 62.4; H, 8.5; N, 5.1%).

(2R,S,4S,5R,S)-*Benzyl* 4-[tert-*Butyl(dimethyl)siloxymethyl*]-2-*phenylselenanylmethyl*-5-*vinyloxazolidine* **39**.—The vinyl amino alcohol **38** (0.629 g, 1.72 mmol) in anhydrous toluene (25 cm^3) with phenylselenanylacetaldehyde diethyl acetal (0.516 g, 1.89 mmol) and pyridinium toluene-*p*-sulfonate (21 mg, 0.836 μmol) was heated under Dean–Stark conditions for 2 h. The reaction mixture was then poured into saturated aqueous sodium hydrogen carbonate (50 cm^3) and extracted with ether (1 × 50 cm^3 and 3 × 30 cm^3). The combined extracts were washed with water (25 cm^3) and brine (25 cm^3), dried (Na_2SO_4) and evaporated under reduced pressure to afford a crude yellow oil, purification of which by flash chromatography on silica gel, eluting with ethyl acetate–hexane (0:1 to 1:24), furnished the *title compound* (0.643 g, 68%) as a light yellow oil, and a mixture of diastereoisomers;* $\nu_{max}(CCl_4)/cm^{-1}$ 3065w, 3025w, 2945s, 2920s, 2850m, 2840s and 1705vs; δ_H(250 MHz; $CDCl_3$) −0.11–0.09 [6 H, m, $Si(CH_3)_2$], 0.81–0.90 [9 H, m, $C(CH_3)_3$], 3.20–3.96 (5 H, m, $PhSeCH_2CH$ and CH_2CHNZ), 4.48 (0.27 H, t, *J* 6.4, $CHCH(O)CH{=}CH_2$), 4.55 (0.33 H, t, *J* 6.5, $CHCHOCH{=}CH_2$), 4.79 (0.15 H, t, *J* 6.1, $CHCHOCH{=}CH_2$), 4.87 (0.45 H, t, *J* 6.4, $CHCHOCH{=}CH_2$), 4.95–5.50 (5 H, m, $PhSeCH_2CH$, $PhCH_2O$ and $CH{=}CH_2$), 5.82–6.01 (1 H, m, $CHOCH{=}CH_2$), 7.18–7.23 (3 H, m, ArH), 7.27–7.43 (5 H, m, ArH) and 7.46–7.59 (2 H, m, ArH); *m/z* (CI) 548 (17), 414 (3), 392 (8), 376 (3), 348 (100), 275 (4), 258 (11), 242 (4), 200 (4), 160 (4), 108 (16), 91 (3) and 70 (2) [Found: $(M + H)^+$ 548.1736, $C_{27}H_{38}NO_4SeSi$ requires $(M + H)^+$ 548.1736] (Found: C, 59.1; H, 6.9; N, 2.6; $C_{27}H_{37}NO_4SeSi$ requires C, 59.3; H, 6.8; N, 2.6%).

(7S)-*Benzyl* 7-[tert-*Butyl(dimethyl)siloxymethyl*]-2-*oxo*-1,3,4,7-*tetrahydroazepine*-1-*carboxylate* **41**.—The aminal **39** (15.43 g, 28.2 mmol) was dissolved in methanol–water (6:1; 1 dm^3) and sodium periodate (18.077 g, 84.5 mmol) and sodium hydrogen carbonate (2.602 g, 30.97 mmol) were added to the solution. The mixture was then stirred for 3 h at room temperature (TLC control) after which it was poured into brine (3 dm^3) and extracted with dichloromethane (5 × 500 cm^3). The combined extracts were dried (K_2CO_3) and evaporated under reduced pressure to furnish the crude selenoxide (15.557 g, 98%) as a light yellow oil. The crude selenoxide (0.332 g, 0.59 mmol) in anhydrous *m*-xylene (60 cm^3) with DBU (0.27 cm^3, 1.81 mmol) was heated under reflux overnight after which evaporation of the mixture afforded a dark oil. Purification of this by flash chromatography on silica gel, eluting with ethyl acetate–hexane (0:1 to 1:19), furnished the crude product. The crude oil was rechromatographed using the chromatotron, eluting with acetone–hexane (1:9), to furnish the *title compound* (0.049 g, 21%) as a colourless oil; R_F 0.35 (1:4 ethyl acetate–hexane); $[\alpha]_D^{20}$ +145.6 (*c* 1.9, MeOH); $\nu_{max}(CCl_4)/cm^{-1}$ 3095sh, 3065w, 3030m, 2945s, 2925s, 2885m, 2850s and 1715vs; δ_H(400 MHz; $CDCl_3$) 0.01–0.06 [6 H, m, $Si(CH_3)_2$], 0.84–0.87 [9 H, s, $C(CH_3)_3$], 2.19–2.25 (1 H, m, $CHCH_AH_BCO$), 2.37–2.47 (1 H, m, $CHCH_AH_BCO$), 2.62–2.67 (1 H, m, $CHCH_AH_BCO$), 3.04–3.12 (1 H, m, $CHCH_AH_BCO$), 3.82 (2 H, d, *J* 5.8, $CHCH_2OSi$), 5.06–5.12 (1 H, m, CH_2CHNZ), 5.25 (2 H, s, $PhCH_2O$), 5.59–5.64 (1 H, m, $CH{=}CHCH_2$), 5.89–5.94 (1 H, m, $CHCH{=}CH$) and 7.27–7.43 (5 H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$) −5.56 (o), 18.30 (e), 23.66 (e), 25.83 (o), 38.08 (e), 57.75 (o), 65.60 (e), 68.79 (e), 125.51 (o), 127.94 (o), 128.17 (o), 128.54 (o), 131.22 (o), 135.50 (e), 155.63 (e) and 175.43 (e); *m/z* (CI) 390 (100), 366 (9), 346 (23), 332 (6), 288 (8), 256 (2), 224 (4) and 108 (7) [Found: $(M + H)^+$, 390.2101. $C_{21}H_{32}NO_4Si$ requires $(M + H)^+$ 390.2101] (Found: C, 64.8; H, 7.8; N, 3.8. $C_{21}H_{31}NO_4Si$ requires C, 64.8; H, 8.0; N, 3.6%).

* The product was obtained as a mixture of four diastereoisomers R_{F1} = 0.15, R_{F2} = 0.18, R_{F3} = 0.23, R_{F4} = 0.29 (1:4 ethyl acetate–hexane).

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