New methodology for the synthesis of unsaturated 8-, 9- and 10-membered lactams

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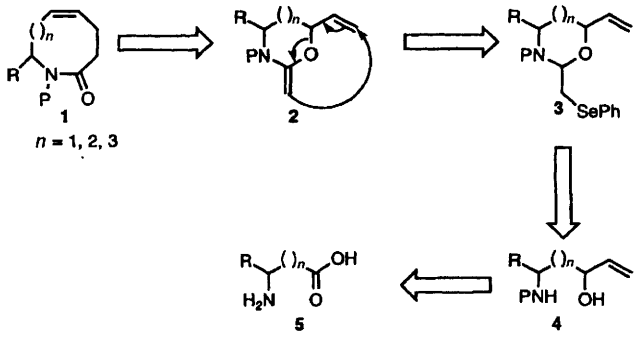
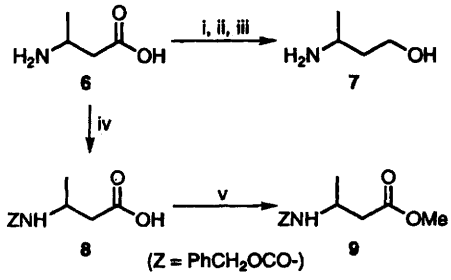
Unsaturated 8-, 9- and 10-membered medium ring lactams 1 (n = 1, 2, 3) have been prepared in good yield by the Claisen rearrangement of the vinyl-substituted precursors 3 in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

Monocyclic medium ring nitrogen heterocycles have emerged as popular synthetic targets.[1,2] Despite many recent important contributions[3] new approaches to this family of compounds remain desirable. We wished to develop a reliable stereoselective method which would enable access to the whole family of medium ring azacycles. The method therefore needed to be efficient and flexible to overcome the problems which other workers have encountered in this area. The Claisen rearrangement[4] of vinyl-substituted ketene acetals and enol ethers has been shown to be an extremely useful method for the preparation of unsaturated medium ring ketones,[5] and medium ring lactones.[6] Modification of this method would in theory allow the preparation of medium ring lactams with a high degree of latent functionality.[7]

The strategy envisaged for the preparation of the required medium ring lactams is summarised in the retrosynthetic analysis (Scheme 1). The key step would be accomplished by what is formally a two-atom ring expansion. The vinyl ketene aminal **2** generated *in situ* by selenoxide elimination of the aminal precursor **3** would undergo Claisen rearrangement to give the monocyclic unsaturated medium ring lactam **1**. The aminal precursors would be formed from a suitably protected vinyl amino alcohol **4** derived from the chiral pool of amino acids **5**.



Scheme 1 General scheme for the preparation of 8-, 9- and 10-membered azacycles



Scheme 2 *Reagents and conditions:* i, BF_3OEt_2, tetrahydrofuran (THF), heat, 2 h; ii, BH_3·SMe_2, heat, 7 h; iii, NaOH (5 mol dm^{-3}), heat, 12 h (27%); iv, BnOCOCl (ZCl), NaOH (4 mol dm^{-3}), THF, 0 °C to room temp., 16 h (97%); v, $SOCl_2$, MeOH, 0 °C to room temp., 16 h (93%)

Results and discussion

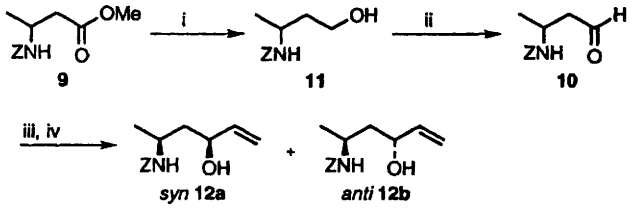
We have recently reported the synthesis of unsaturated seven-membered lactams (azepin-2-ones) by Claisen rearrangement of 2-methylene-5-vinyltetrahydroxazoles.[8] It was expected that a similar synthetic strategy could be used to prepare the more challenging azocin-2-ones, azonin-2-ones and azecin-2-ones. The synthesis of azocin-2-ones would require the preparation of the 1-vinylaminopropanol **4** (n = 1) (Scheme 1) which would be derived from either a β-amino acid or by homologation of an α-amino acid. Commercially available (±)-3-aminobutyric acid **6** was chosen to demonstrate the method.

(±)-3-Aminobutyric acid **6** was converted using the Gawley procedure[9] into (±)-3-aminobutan-1-ol **7** (Scheme 2) in 27% yield. In an alternative route, (±)-3-aminobutyric acid **6** was *N*-protected under Schotten–Baumann conditions (Scheme 2) using benzyl chloroformate and 4 mol dm^{-3} aqueous sodium hydroxide, to afford the benzyloxycarbonyl (*Z*)-amino acid **8** in 97% yield. Esterification of **8** using thionyl chloride in methanol gave the amino ester **9** in 93% yield.

Attempted reduction of the amino ester **9** to the amino aldehyde **10** using DIBAL-H at −78 °C gave a complex mixture of the amino ester **9**, the aldehyde **10** and the alcohol **11** (Scheme 3). This problem was solved by a two-step procedure; reduction of the amino ester **9** with an excess of diisobutylaluminium hydride (DIBAL-H) furnished the amino alcohol **11** in 90% yield. Problematic side reactions occurred when the reaction temperature was allowed to rise above 0 °C. The amino alcohol **11** was then oxidised using Swern conditions[10] to give the required amino aldehyde **10** in 99% yield.

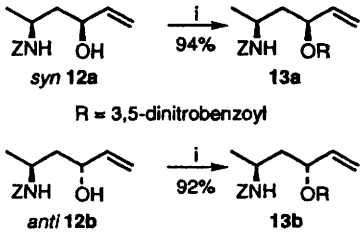
The optimum conditions for the preparation of the amino vinyl-substituted alcohol **12** required treatment of the amino aldehyde **10** in THF with vinylmagnesium bromide at −78 °C for 3 h (Scheme 3). This afforded a 1:1 mixture of epimeric alcohols **12**, separable by flash column chromatography, in 78% yield. Separation of the epimers then enabled their relative stereochemistry to be assigned, and a mechanistic study of the

Claisen rearrangement to be carried out to ascertain whether a preference for rearrangement existed between the *syn* and *anti* isomers.



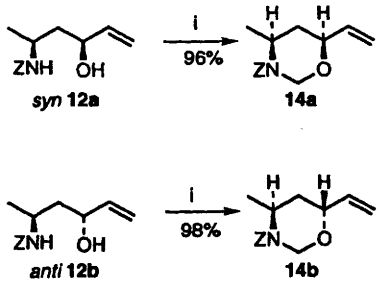
Scheme 3 *Reagents and conditions:* i, DIBAL-H, THF, −78 °C to 0 °C, 2 h (90%); ii, Swern oxidation (99%); iii, vinylmagnesium bromide, THF, −78 °C, 3 h; iv, chromatographic separation (78%)

The initial approach was to convert the vinyl amino alcohols **12** into crystalline derivatives suitable for X-ray crystallography. The *syn* and *anti* amino alcohols **12** were treated with 4-dimethylaminopyridine (DMAP) and 3,5-dinitrobenzoyl chloride in dichloromethane to afford the esters **13a** and **13b** in 94% and 92% yield, respectively, which were unfortunately obtained as oils (Scheme 4).



Scheme 4 *Reagents and conditions:* i, 3,5-dinitrobenzoyl chloride, DMAP, CH_2Cl_2, room temp., 16 h

Conversion of the vinyl amino alcohols **12** into their corresponding 1,3-oxazines **14** (Scheme 5), allowed the relative stereochemistry of the amino alcohols **12** to be assigned. The vinyl amino alcohols **12a** and **12b** were treated individually with paraformaldehyde and toluene-4-sulfonic acid (TsOH) in toluene under Dean–Stark conditions to afford the required aminals **14a** and **14b** in 96% and 98% yield, respectively.



Scheme 5 *Reagents and conditions:* i, $(CH_2O)_n$, TsOH, toluene, heat, 1 h

The ^{1}H NMR spectrum of the *syn*-1,3-oxazine **14a** shows two characteristic *trans*-diaxial vicinal coupling constants (Fig. 1: $J_{a,c} = J_{c,d} = 10.6$ Hz) (Table 1, entry 1) while the ^{1}H NMR spectrum of the *anti*-1,3-oxazine **14b** (Table 1, entry 2) does not contain two such couplings (Fig. 1). The equatorial proton H_b of **14b** resonates as a multiplet with the axial proton H_c having an axial-equatorial coupling ($J_{a,c}$ 6 Hz) and an axial-axial coupling ($J_{c,d}$ 12.2 Hz) as a result of the preference for the methyl group to be axial.

Solution conformations of the aminals **14a** and **14b** were confirmed by a series of nuclear Overhauser enhancement (NOE) experiments. Fig. 2 illustrates the observed NOEs for the *syn*-1,3-oxazine **14a**. The ring is depicted in a boat-like conformation because the coupling constants for H_a and H_d indicate that they are in a *syn*-1,3-diaxial environment. The absence of NOEs between the methylene proton H_e and both

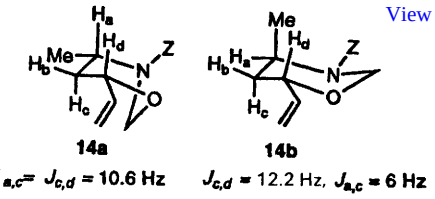


Fig. 1

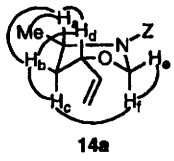


Fig. 2

Fig. 3

H_a and H_d suggests that the conformation is not that of a chair. However, the observation of an NOE between the axial proton H_c and the axial methylene proton H_f implies a boat-like conformation. The explanation for the boat-like conformation may be due to severe 1,2-eclipsing interaction (allylic strain) between the equatorial methyl and the benzyloxycarbonyl protecting group which forces the latter into a pseudo-axial environment and the ring into a boat-like conformation.

Fig. 3 illustrates the NOEs for the *anti*-1,3-oxazine **14b**. The ring is depicted in a chair-like conformation with the methyl substituent axial based on the following evidence: the coupling constants for H_b and H_c indicate that they are in an unsymmetrical environment. The presence of NOEs between the axial methyl and both H_d and the axial methylene proton H_e implies a chair-like conformation, and the absence of an NOE between the axial proton H_c and the methylene proton H_f also supports this assignment. The explanation for the chair-like conformation may be due to the absence of severe 1,2-eclipsing interactions since the methyl group is axial, allowing the benzyloxycarbonyl group to adopt a pseudo-equatorial environment.

Several other important NOEs are observed in both isomers and these are depicted in Figs. 2 and 3, and support the assignments. The effect of the bulky benzyloxycarbonyl protecting group on the conformation had not been expected, but this effect is significant and will be considered in a further discussion on the possible conformations for Claisen rearrangement.

It was then possible to investigate the Claisen cyclisation of the *syn* and *anti* vinyl amino alcohols **12** separately. This would determine whether there was a preferred conformation for rearrangement. The vinyl amino alcohols **12a** and **12b** were treated individually with phenylselenanylacetaldehyde diethyl acetal[11] and pyridinium toluene-4-sulfonate (PPTS) in toluene under Dean–Stark conditions to give the aminals **15a** and **15b** in 92% and 90% yield, respectively. The aminals **15** were quantitatively oxidised with sodium periodate to the corresponding selenoxides, which upon treatment with DBU in various solvents (see Table 2) generated the ketene aminals **16** (not isolated), which underwent [3.3] sigmatropic rearrangement[7,8] *in situ* to give the required Z-protected azocin-2-one **17** (Scheme 6).

The initial conditions were based on those previously optimised for the preparation of 7-membered lactams.[7,8] Comparison of the results obtained in refluxing *m*-xylene for the selenoxides derived from **15a** and **15b** (Table 2, entries 1 and

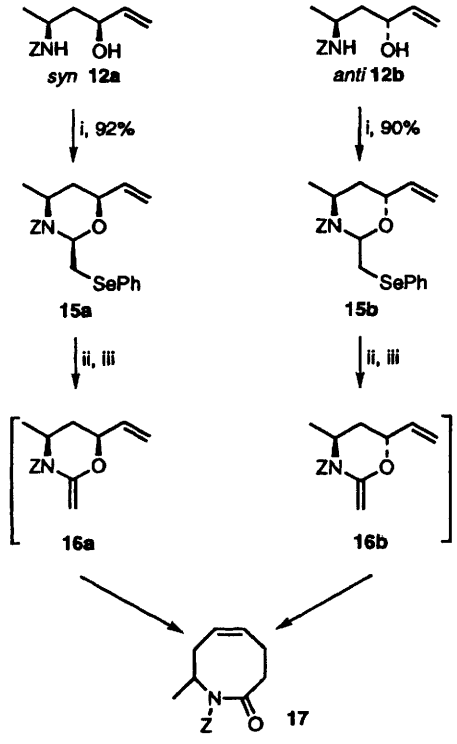
Table 1 ^{1}H NMR data for oxazines **14** (J in Hz)

Entry	Oxazine	$\delta(H_b)$	$\delta(H_c)$	$J_{a,b}$	$J_{a,c}$	$J_{b,d}$	$J_{c,d}$
1	**14a**	1.93	1.67	6	10.6	3.7	10.6
2	**14b**	1.49	1.80	m	6	m	12.2

Table 2 Claisen rearrangement of the vinyl substituted aminals **15**

Entry	Substrate*	DBU (equiv.)	Refluxing solvent	Lactam **17** (% yield)
1	**15a**	3	*m*-Xylene	48
2	**15a**	3	Toluene	51
3	**15a**	3	Benzene	4
4	**15b**	3	*m*-Xylene	43
5	**15b**	3	Toluene	58
6	**15b**	5	Toluene	49
7	**15b**	3	Pyridine	45
8	**15b**	3	Benzene	72

* At a concentration of 1 mmol 100 cm^{-3}.



Scheme 6 *Reagents and conditions:* i, $PhSeCH_2CH(OEt)_2$, PPTS, toluene, heat, 4 h; ii, $NaIO_4$, $NaHCO_3$, MeOH–H_2O, room temp., 1 h; iii, solvent, DBU, heat, 16 h

4) indicates comparable yields of the lactam **17** within the margins of experimental error (Scheme 6). The cyclisation was repeated the solvent being changed to refluxing toluene (entries 2 and 5), with similar yields again observed. When the amount of DBU was increased to 5 molar equiv. in the case of **15b** (entry 6) a decreased yield was obtained. Similarly, if the solvent was changed to pyridine (entry 7) a disappointing yield was obtained. However, when the cyclisations of the selenoxides derived from **15a** and **15b** were carried out in refluxing benzene (entries 3 and 8) there was a significant difference in the yields. Clearly a preference for the cyclisation of the *anti* isomer **15b** over the *syn* isomer **15a** is evident under these reaction conditions. Careful examination of the reaction mixture revealed the imide **22** and the ester **23**.

The vinyl ketene aminal **19** can be envisaged as reacting by

Table 3 Study of the components of the reaction mixture from the Claisen rearrangement of the vinyl substituted aminals **15**

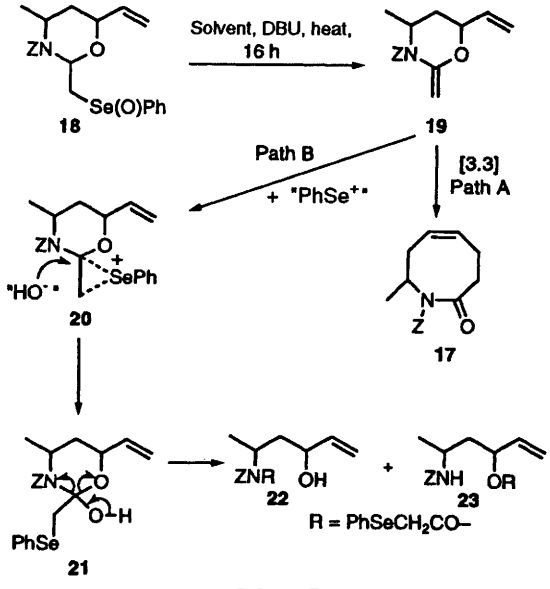
Entry	Substrate	Refluxing solvent	Lactam **17** (% yield)	Readdition products **22/23** (% yield)
1	**15a**	*m*-Xylene	48	21
2	**15a**	Toluene	51	29
3	**15a**	Benzene	4	60
4	**15b**	*m*-Xylene	43	14
5	**15b**	Toluene	58	22
6	**15b**	Benzene	72	5

two pathways (Scheme 7). It can either undergo Claisen cyclisation (path A) or readdition of phenylselenic acid (path B) *via* the episelenonium ion **20** followed by attack of hydroxide to form the 1,3-oxazin-2-ol **21**, which can open in the presence of base (DBU) to form either the imide **22** or the ester **23**. These species are fairly labile and can be hydrolysed to the original vinyl amino alcohols **12**.

Table 3 compares the amounts of lactam **17** formed *via* path A with the yield of the readdition products **22** and **23** formed *via* path B. The *syn* ketene aminal **16a** undergoes substantial readdition of benzeneselenic acid (PhSeOH) in both refluxing *m*-xylene and toluene. The vinyl amino alcohol **12a** constitutes the remainder of the isolated material. Interestingly, the ketene aminal **16a** prefers path B in refluxing benzene. This may be due to an unfavourable conformation for Claisen rearrangement which requires a higher activation energy. The results for cyclisation of the *anti* ketene aminal **16b** are essentially the same as those for the *syn* ketene aminal **16a** in refluxing *m*-xylene and toluene. However, smaller amounts of the benzeneselenic acid readdition products **22** and **23** were isolated owing to the easier hydrolysis of these materials when derived from the *anti* isomer.

The ketene aminal **16b** prefers path A in refluxing benzene, indicating that this isomer can readily attain the required conformation for Claisen rearrangement. Path A is favoured over path B since the rate of cyclisation is greater than that of readdition. However, at elevated reaction temperatures the rates approach equality leading to approximately equal amounts of the lactam **17** and the readdition products **22** and **23**. Indeed, if the temperature is raised even further the readdition becomes more favourable than the cyclisation.

To explain the results obtained during the cyclisation study of **16a** and **16b**, it is appropriate to examine the various steric



Scheme 7

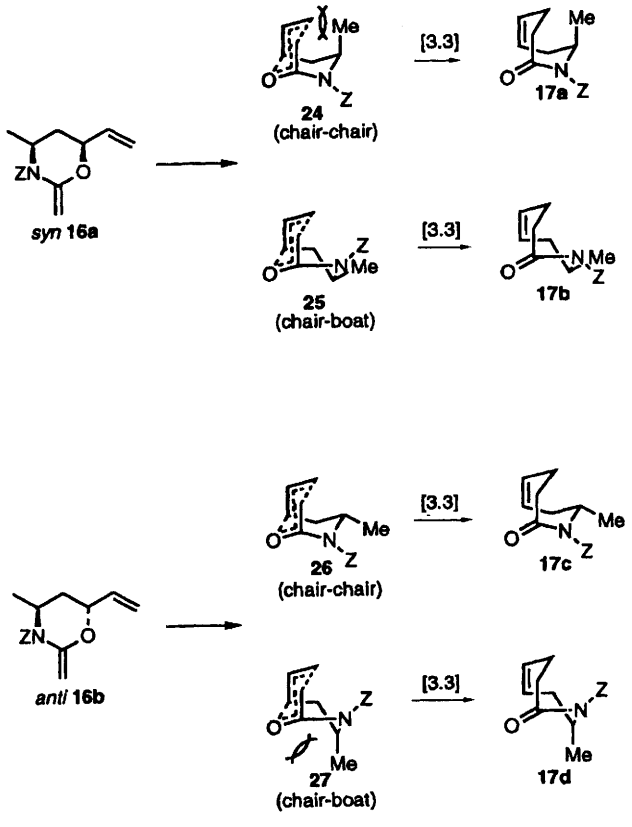
factors at play in the Claisen rearrangement chair-like[4] transition states leading to (*Z*)-alkenes (Scheme 8). The *syn* isomer **16a** has a chair–chair arrangement **24** leading to the lactam **17a**, and a chair–boat **25** leading to the lactam **17b**. Conformation **24** is presumably disfavoured owing to severe 1,3-diaxial interactions between the axial methyl and vinyl groups. Owing to these steric interactions the ketene aminal **16a** probably adopts a boat-like conformation **25**. This transition state minimises the 1,3-diaxial interactions resulting in a lactam **17b** with a pseudo-equatorial methyl group and a *transoid* lactam amide bond.

The *anti* isomer **16b** can form a favourable chair–chair conformation **26** which minimises all the steric interactions. This would produce the *cis* lactam **17c** with a pseudo-equatorial methyl group. The alternative conformation **27** is unfavourable owing to a 1,3-axial methyl interaction.

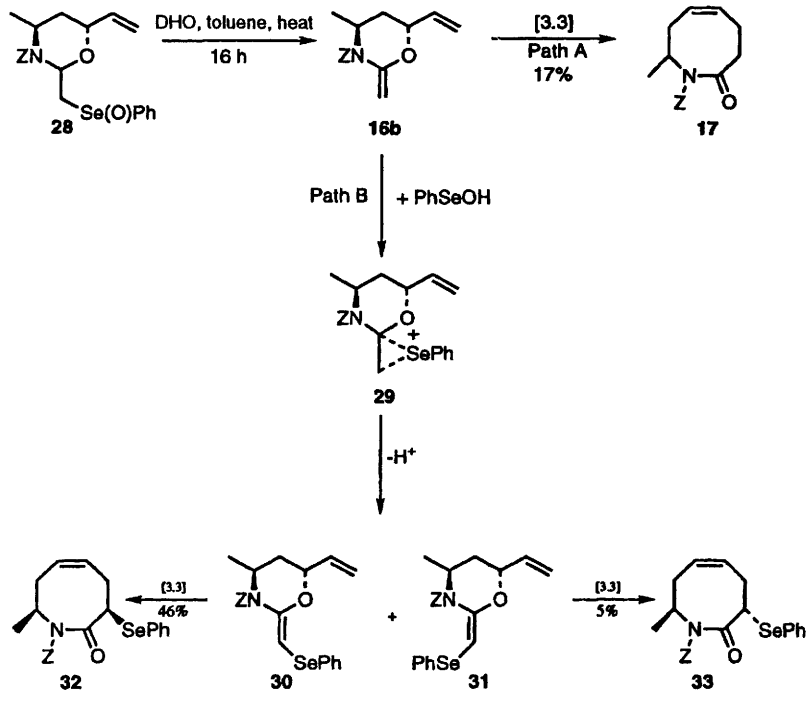
The clear preference in reactivity of the *anti* isomer **16b** over the *syn* isomer **16a** may be explained in terms of these considerations. When the cyclisation is carried out in benzene the *anti* isomer **16b** can form the favoured chair–chair conformation **26** and undergo cyclisation to **17c**. However, under these conditions the *syn* isomer **16a** undergoes readdition of PhSeOH rather than cyclisation. This may be due to the inability of this isomer to form the chair–boat conformation **25** at low temperatures.

The competing readdition of benzeneselenic acid to the electron-rich ketene aminals **16**, could possibly be suppressed with a more nucleophilic selenium scavenger than DBU. Dihydropyran (DHP) has been suggested as such a scavenger.[12] The selenoxide **28** was therefore heated in refluxing toluene in the presence of dihydropyran and yielded the lactam **17** in a disappointing 17% yield; surprisingly, the major product was the *cis*-disubstituted selanyl lactam **32** (46%) with a small quantity of the *trans*-isomer **33** (5%) (Scheme 9). The lactam **17** is formed by the usual Claisen pathway (path A). In the presence of DHP proton loss from the episelenonium ion yields the vinyl selenides **30** and **31**. The (*Z*)-vinyl selenide **30** is presumably preferred since steric interactions with the benzyloxycarbonyl protecting group are minimised. The vinyl selenides **30** and **31** then undergo Claisen rearrangement to form a 9:1 mixture of the selenanyl lactams **32** and **33**, respectively.

It is concluded that DHP does not compete effectively as a selenium trap compared with the electron-rich vinyl substituted ketene aminal **16b**. The reactions of some selenating agents with activated alkenes such as enols, enol acetates, enol ethers, and enamines have been studied. In most cases, α-arylselanyl aldehydes and ketones are obtained efficiently.[13] Therefore, the ketene acetals **34** and **35** were considered attractive candidates as selenium traps. They are electron-rich, readily undergo addition of electrophilic selenium to furnish α-phenylselanyl



Scheme 8



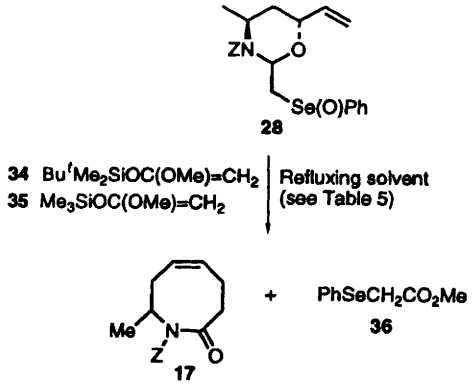
Scheme 9

Table 4 Claisen rearrangement of the vinyl substituted ketene aminal **16b** in the presence of the ketene acetals **34** and **35**

Entry	Ketene acetal	Equiv.	Lactam **17** (% yield)	Seleno ester **36** (% yield)
1	**34**	5	64	47
2	**34**	20	80	76
3	**35**	20	54	45

esters,[14] and the methodology for their preparation by silylation of ester enolates is well documented.[15]

The Claisen rearrangement of the ketene aminal **16b** in the presence of the ketene acetals **34** and **35** was examined (Scheme 10). The results from this investigation are summarised in Table



Scheme 10

4. The use of ketene acetal **34** (5 equiv., entry 1) afforded the Z-protected unsaturated lactam **17** in 64% yield. The phenylselanyl ester **36**, obtained from the addition of $PhSe^+$ to the ketene acetal **34**, was formed in 47% yield. Increasing the amount of the ketene acetal to 20 equiv. (entry 2) improved the yield of **17** to 80% and the phenylselanyl ester **36** to 76% yield. This constitutes the first use of a ketene acetal **34** as a trap for $PhSe^+$ in a selenoxide elimination reaction, and may have major synthetic utility in problematic reactions of this nature.

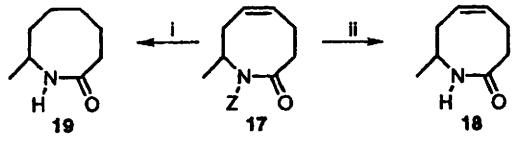
A large excess of the ketene acetal **34** was necessary in order to compete with the electron-rich ketene aminal **16b**. Use of the trimethylsilyl-derived ketene acetal **35** (entry 3) gave **17** in 54% yield and the phenylselanyl ester **36** in 45% yield. The readdition products **22** and **23** were also isolated in 15% yield. The poorer performance of the trimethylsilyl ketene acetal **35** compared with **34** was attributed to hydrolysis and possible O- to C-migration of the trimethylsilyl group under the vigorous reaction conditions.

The selanyl lactam **32** was crystallised from ether–hexane to give colourless prisms suitable for X-ray analysis.[16] The X-ray crystal structure confirmed the relative stereochemistry of the side chains in the major isomer as being *cis* and pseudo-equatorial and the alkene geometry as *Z*. The ring amide is severely twisted out of planarity, representing the most p-orbital distortion recorded in a cyclic amide. The X-ray analysis also confirmed the tentative assignment based on NOE observations in the ^1H NMR spectrum, which indicated a weak NOE between the 3-H and 8-Me.

Deprotection of the benzyloxycarbonyl group from the eight-membered lactam **17** is summarised in Table 5. The use of 45% HBr in acetic acid[17] (entry 1), afforded the unsaturated lactam **18** in 4% yield (Scheme 11). The radical anion (LiDBB) of 4,4'-di-*tert*-butylbiphenyl[18] was prepared by treatment with lithium metal under an inert atmosphere of argon to afford a dark-green solution. Sonication was found to accelerate this reaction. The Z-unsaturated lactam **17** was titrated with this solution (entry 2) to furnish the unsaturated lactam **18** in 15% yield.

Table 5 Deprotection of the Z-protected azocin-2-one **17**

Entry	Reaction conditions	Lactam **18** (% yield)
1	45% HBr in AcOH, room temp., 1 h	4
2	LiDBB, THF, −78 °C, 30 min	15
3	$AlCl_3$, $PhNO_2$, −78 °C, 30 min	15
4	TMSI, 0 °C to room temp., 16 h	73
5	BBr_3, DCM, −78 °C, 30 min	88

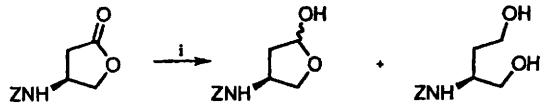


Scheme 11 *Reagents and conditions:* i, $Pd(OH)_2$, H_2, room temp., 16 h (99%); ii, see Table 5

Treatment of the Z-unsaturated lactam **17** with aluminium trichloride (entry 3) gave the unsaturated lactam **18** in 15% yield. Trimethylsilyl iodide (entry 4), afforded the unsaturated lactam **18** in 73% yield. Boron tribromide[19] was the most effective reagent (entry 5), giving the unsaturated lactam **18** in 88% yield.

Catalytic hydrogenation of the Z-protected lactam **17** using Pearlman's catalyst gave the saturated lactam **19** in 99% yield.

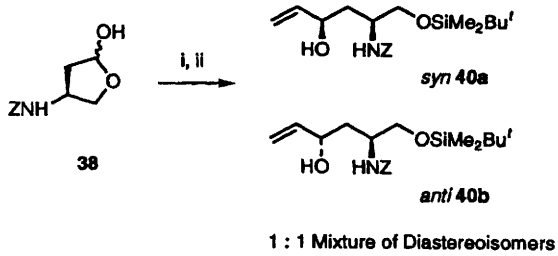
To extend the methodology to the synthesis of homochiral lactams, the preparation of the azocin-2-one **44** was investigated. The synthesis began with lactone **37**, readily derived in three steps from (*S*)-aspartic acid.[20] Reduction of the lactone **37** to the lactol **38** with DIBAL-H was found to be very sensitive to the solvent, temperature, the number of molar equivalents of DIBAL-H employed, and the manner in which the reaction was quenched. Optimum conditions for the reduction of **37** were found to be (1) the use of cold (−93 °C) dichloromethane as solvent, (2) the use of 2.0 molar equiv. of DIBAL-H and (3) the use of pre-cooled methanol as a quenching reagent (Scheme 12). Under these conditions the



Scheme 12 *Reagents and conditions:* i, DIBAL-H, CH_2Cl_2, −93 °C, 1 h (**38**: 78%; **39**: 8.7%)

lactol **38** was obtained in 78% yield, together with the over-reduced diol **39** (8.7%). Rapid mutarotation of the anomers of **38** was observed when the optical rotation was measured.

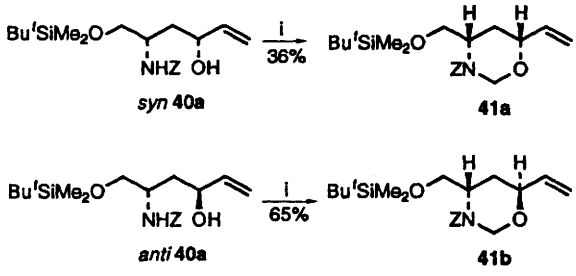
Treatment of the lactol **38** with vinylmagnesium bromide in THF gave the intermediate amino diols, which were not purified but carried directly on to the silyl ethers **40** by using *tert*-butyldimethylsilyl (TBDMS) chloride–DMAP in dichloromethane (68% yield for the two steps) (Scheme 13). The



Scheme 13 *Reagents and conditions:* i, vinylmagnesium bromide, THF, 5 °C, 4 h; ii, TBDMSCl, Et_3N, DMAP, CH_2Cl_2, 0 °C to room temp., 16 h (68%)

alcohols **40** were obtained as a 1 : 1 mixture of diastereoisomers, separable by flash chromatography.

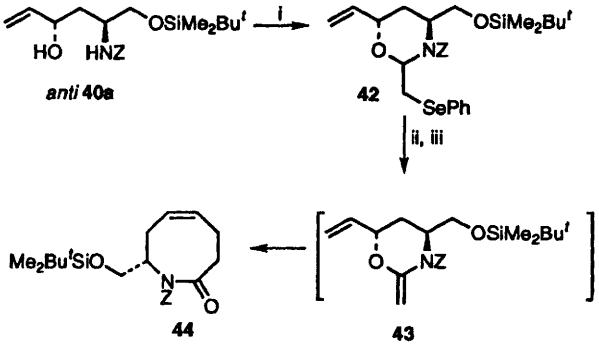
The more polar alcohol was assigned as the *syn* isomer **40a** after examination of the ^{1}H NMR coupling constants of the derived 1,3-oxazine **41a** (Scheme 14), using similar arguments



Scheme 14 *Reagents and conditions:* i, $(CH_2O)_n$, TsOH, toluene, heat, 1 h

to those used to assign the oxazine **14a**. The less polar alcohol was assigned as the *anti* isomer after conversion into the 1,3-oxazine **41b**.

Having separated and assigned the alcohols **40a** and **40b**, we examined each derived selenoxide individually. Most attention was directed towards the *anti* isomer **40a** as the selenoxide derived from this was expected to undergo more facile Claisen rearrangement by analogy with the results for **16b**. Treatment of **40a** with phenylselanylacetaldehyde diethyl acetal in refluxing toluene in the presence of acidic ion-exchange resin gave the selanyl aminal **42**, as a mixture of diastereoisomers, in 58% yield (Scheme 15). Oxidation of the selenide **42** with

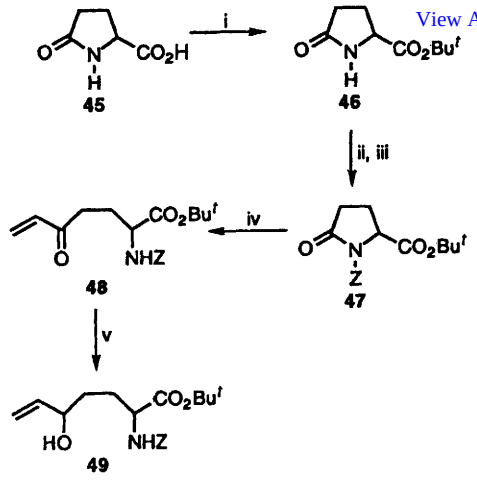


Scheme 15 *Reagents and conditions:* i, $PhSeCH_2CH(OEt)_2$, H^+ ion exchange resin, toluene, heat, 3.5 h (58%); ii, $NaIO_4$, $NaHCO_3$, MeOH–H_2O–CH_2Cl_2, room temp., 1 h; iii, **35a**, DBU, toluene, heat, 16 h (31%)

sodium periodate in a mixture of water, methanol and dichloromethane gave the corresponding selenoxide almost quantitatively.

A series of reactions was performed on the selenoxide derived from **42** in an attempt to optimise the yield of lactam **44**. The optimum conditions were found to be refluxing toluene as the solvent, in the presence of 3 molar equiv. of DBU and 5 molar equiv. of the silyl ketene acetal **34**. This afforded the lactam **44** in an optimised 31% yield. The poor yield for the final step was attributed to unfavourable steric interactions between the silyl ether group and the bulky benzyloxycarbonyl group in the transition state leading to or from the ketene aminal intermediate **43**. Indeed, when the *tert*-butyldimethylsilyloxy group was replaced with the larger *tert*-butyldiphenylsilyloxy group, the Claisen reaction completely failed.

The synthetic strategy for the nine-membered lactams (azonin-2-ones) required the preparation of a 4-amino-1-vinylbutanol. This could be derived from either a γ-amino acid or by a two-carbon homologation of an α-amino acid. (±)-Pyroglutamic acid **45** was esterified, using *tert*-butyl acetate and sulfuric acid to afford the *tert*-butyl amino ester **46** in 91% yield

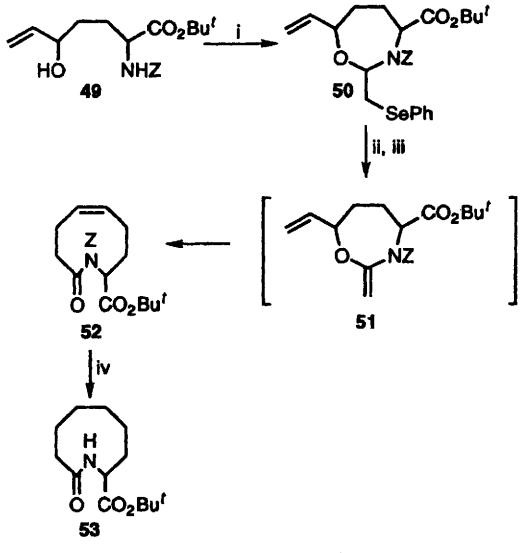


Scheme 16 *Reagents and conditions:* i, Bu^{t}OAc, H_2SO_4, room temp., 16 h (91%); ii, Bu^{t}OK, THF, room temp., 15 min; iii, BnOCOCl, room temp., 30 min (89%); iv, vinylmagnesium bromide, THF, −78 °C, 2 h (61%); v, $NaBH_4$, $CeCl_3 \cdot 7H_2O$, −20 °C, 15 min (95%)

(Scheme 16). *N*-Alkylation, using sodium hydride [21] and benzyl chloroformate in THF afforded the Z-protected lactam **47** in 77% yield. However, this method was found to be quite capricious (especially on a large scale), since the anion was insoluble and complete anion formation was difficult to assess. Using a modified literature procedure involving treatment of the lactam **46** with potassium *tert*-butoxide in THF to generate a soluble anion substantially improved the yield of **47** (89%).[22]

Treatment of the imide **47** with vinylmagnesium bromide afforded the enone **48** in 61% yield.[23] Some loss of product arising from attack of the Grignard reagent at the benzyloxycarbonyl protecting group was observed, giving rise to benzyl acrylate as a side product. Luché reduction [24] of the enone **48** with sodium boranuide and cerium(III) chloride heptahydrate furnished the vinyl amino alcohol **49** in 95% yield as a mixture of epimers. The original publication [23] does not describe the reduction in detail, nor the outcome. This may be explained by the fact that the epimeric mixture is only detectable by ^{13}C NMR which was not reported in the original work.

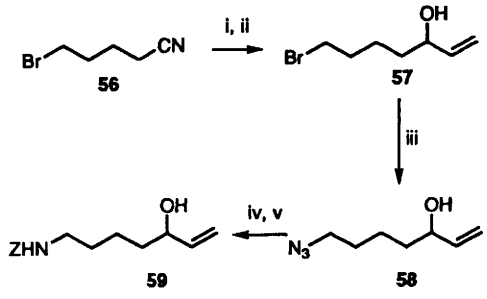
The vinyl amino alcohol **49** was converted into the aminal **50** in 72% yield as a complex mixture of diastereoisomers (Scheme 17). The aminal **50** was oxidised to the selenoxide and



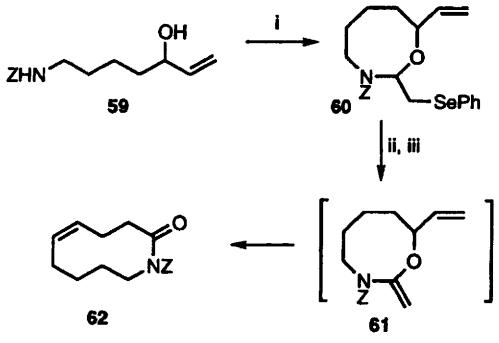
Scheme 17 *Reagents and conditions:* i, $PhSeCH_2CH(OEt)_2$, PPTS, toluene, heat, 2 h (72%); ii, $NaIO_4$, $NaHCO_3$, MeOH–H_2O, room temp., 1 h; iii, DBU, toluene, heat, 16 h (75%); iv, $Pd(OH)_2$, H_2, room temp., 16 h (96%)

then heated in refluxing toluene with DBU to give the Z-protected 9-substituted azonin-2-one **52**, presumably *via* **51**, in 75% yield. The saturated lactam **53** was prepared by hydrogenation of the Z-protected unsaturated lactam **52** using Pearlman's catalyst, in 96% yield. The saturated lactam **53** exists as a 1:1 mixture of (*Z*)- and (*E*)-amides at room temperature in deuteriated chloroform. This is particularly apparent in the ^{13}C NMR spectrum which exhibits a duplicate set of signals. It can be assumed that the cyclisation proceeds through a chair-like transition state[4] (Fig. 4). The transition state **54** is clearly energetically favoured. The alternative conformation **55** is more strained and would produce a nine-membered lactam with a (*Z*)-alkene and a (*Z*)-imide bond (carbonyl oxygen and Z group *cis*).

The route to the ten-membered lactam **62** is outlined in Schemes 18 and 19. Reduction of 5-bromovaleronitrile **56** with



Scheme 18 *Reagents and conditions:* i, DIBAL-H, CH_2Cl_2, −68 °C, 2 h; ii, vinylmagnesium bromide, THF, −78 °C, 20 min (58%); iii, tetramethylguanidinium azide, CH_2Cl_2, room temp., 19 h, 99%; iv, $SnCl_2$, MeOH, 0 °C, 3 h; v, BnOCOCl, $NaHCO_3$, dioxane, room temp., 19 h, 88%



Scheme 19 *Reagents and conditions:* i, $PhSeCH_2CH(OEt)_2$, PPTS, toluene, heat, 1 h (58%); ii, $NaIO_4$, $NaHCO_3$, MeOH–H_2O, 30 min, room temp.; iii, DBU, xylene, heat, 19 h (78%)

DIBAL-H,[25] followed by treatment of the crude aldehyde solution with vinylmagnesium bromide gave the 1,5-bromo alcohol **57** in 58% yield. Displacement of the bromide using tetramethylguanidinium azide[26] gave the corresponding hydroxy azide **58**.

Reduction of the azido group of **58** with methanolic tin(II) chloride, followed by protection of the resulting amine as its benzyloxycarbamate gave **59** in 88% yield. Formation of the eight-membered selanyl aminal **60** (Scheme 19) was achieved in an unoptimised yield of 58% by refluxing the amino alcohol **59** with phenylselanylacetaldehyde diethyl acetal and a catalytic amount of pyridine toluene-*p*-sulfonate (PPTS) in toluene, to give the product **60** as a mixture of diastereoisomers. Oxidation of the selenide **60** with sodium periodate in aqueous methanol gave the selenoxide in quantitative yield, which upon being heated in refluxing xylene with 5 molar equiv. of DBU gave the protected lactam **62**, *via* the ketene aminal **61**, as a single product in 78% yield. The improved yield presumably reflects decreasing strain in the Claisen transition state. Only one double bond isomer was observed by TLC, HPLC and NMR. The ^1H NMR spectrum of **62** at room temperature indicated a

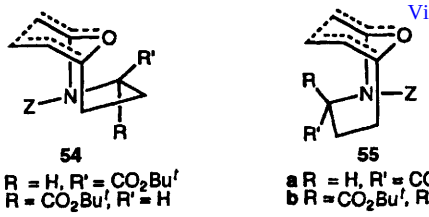


Fig. 4

mixture of rotamers, but by recording the spectrum at 60 °C in C_6D_6 with ^1H decoupling at the frequency of the allylic protons, the olefinic protons could be observed as sharp doublets (δ 5.16, *J* 10.9; δ 5.40, *J* 10.9). By comparison of the value of the olefinic coupling constant with those obtained by Malherbe and Bellus[27] for the unsaturated ten-membered lactones (*Z*)-phoracantholide J (*J* 11.3 Hz) and the (*E*) isomer (*J* 15.5 Hz), the geometry of the double bond in **62** could confidently be assigned as (*Z*).

In conclusion, the Claisen rearrangement route has been demonstrated to be an effective ring expansion route for the synthesis of medium ring lactams. The use of the ketene acetal **34** has been demonstrated as a novel selenium trap to minimise selenium re-addition to nucleophilic species generated during selenoxide eliminations.

Experimental

^1H 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 multiplicity of the signal is indicated as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets, *etc.* and *J* values are expressed in Hz. ^{13}C NMR spectra were recorded on Bruker WM-400 (100 MHz) or Bruker AC-250 (62.5 MHz) instruments using internal deuterium lock and proton 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 attached proton test experiment (APT) and is indicated as: e = methylene and quaternary carbons and o = methine and methyl carbons. IR spectra were recorded either as KBr discs or as solutions in the indicated solvents using a Perkin-Elmer 1310 spectrometer. 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 concentration (*c*) is expressed in g 100 cm^{-3}. Specific rotations denoted as $[\alpha]_D^T$ imply units of ° dm^2 g^{-1} (*T* = temp °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 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.[28] 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 between 60 and 80 °C. Brine refers to saturated aqueous sodium chloride. All reactions were performed under an atmosphere of dry nitrogen unless indicated to the contrary.

(±)-3-Aminobutan-1-ol 7

A dry flask was charged with the amino acid **6** (4.22 g, 41 mmol) and anhydrous THF (20 cm^3) and the slurry was stirred whilst boron trifluoride–diethyl ether (5 cm^3, 41 mmol) was added to it during 30 min. The resulting solution was refluxed for 2 h to give a heterogeneous reaction mixture. Borane–dimethyl sulfide complex (10 mol dm^{-3}; 4.5 cm^3, 45 mmol) was added **CAUTIOUSLY** during 60 min to the **VIGOROUSLY** refluxing mixture. During the course of the addition there was a continuous evolution of dimethyl sulfide together with dissolution of the amino acid. The mixture was refluxed for an additional 5 h (TLC chloroform, methanol, ammonia solution; 5:5:1), after which further borane–dimethyl sulfide complex (10 mol dm^{-3}; 0.45 cm^3, 4.5 mmol) was added. After the solution had been refluxed for a further 1 h, it was cooled to ambient temperature and quenched by the slow addition of a 1:1 THF–water mixture (5 cm^3) followed by aqueous sodium hydroxide (5 mol dm^{-3}; 30 cm^3). The resulting two-phase mixture was refluxed for 12 h, cooled to room temperature and filtered through a coarse frit. The residual solid was washed with THF (3 × 20 cm^3), and the filtrate was concentrated on the rotary evaporator to remove most of the THF. The resulting slurry was extracted with dichloromethane (4 × 50 cm^3), dried (Na_2SO_4), filtered, and concentrated on a rotary evaporator to give an orange oil which was distilled under reduced pressure to furnish the title compound **7**[29] as a colourless oil (0.973 g, 27%); bp 55 °C/5 mmHg (lit.,[30] 82–85 °C/19 mmHg); $\nu_{max}(CCl_4)/cm^{-1}$ 3635m, 3580–3030br s, 2955s, 2920s and 2860s; δ_H(250 MHz; $CDCl_3$) 1.13 (3 H, d, *J* 6.4, CH_3), 1.40–1.69 (2 H, m, CH_2CH_2OH), 2.54 (3 H, br s, NH_2 and OH), 3.05–3.17 (1 H, m, H_2NCH) and 3.72–3.86 (2 H, m, CH_2OH); δ_C(100 MHz; $CDCl_3$) 25.43 (o), 29.65 (e), 47.33 (o) and 61.73 (e); *m/z* (EI) 89 (M^+, 3%), 88 (8), 87 (6), 86 (17), 85 (54), 84 (63), 74 (39), 72 (16), 71 (15), 70 (28), 61 (45) and 58 (100) (Found: M^+, 89.0841. $C_4H_{11}NO$ requires *M*, 89.0841).

(±)-3-[(Benzyloxycarbonyl)amino]butan-1-oic acid 8

A solution of the amino acid **6** (20.6 g, 200 mmol) dissolved in aqueous sodium hydroxide (4 mol dm^{-3}; 50 cm^3) and THF (110 cm^3) was cooled and stirred to 0 °C whilst aqueous sodium hydroxide solution (4 mol dm^{-3}; 60 cm^3) and benzyl chloroformate (42.8 cm^3, 300 mmol) were added alternatively, the reaction mixture being kept basic and the temperature constant, over *ca.* 30 min. The reaction mixture was allowed to warm to room temperature and stirred overnight after which it was poured into ether (200 cm^3), shaken and separated. The aqueous phase was stirred and cooled to 0 °C and then acidified to Congo Red with 5 mol dm^{-3} hydrochloric acid. The aqueous phase was extracted with ethyl acetate (6 × 250 cm^3) and the combined organic phases were dried ($MgSO_4$) and evaporated to furnish the title compound **8**[30] as a white crystalline solid (45.93 g, 97%); mp 129 °C (from EtOAc–hexane) (lit.,[30] 120–123 °C); $\nu_{max}(CHCl_3)/cm^{-1}$ 3645w, 3570–2300br m, 3425s, 2920s, 2890sh and 1705vs; δ_H(250 MHz; [$^2H_6$]-DMSO) 1.08 (3 H, d, *J* 6.6, CH_3), 2.36 (2 H, ABX, *J* 15.4, 7.3 and 6.7, CH_2CO_2), 3.34 (1 H, br s, NH), 3.86 (1 H, septet, *J* 7.0, ZNHC*H*), 5.00 (2 H, s, $PhCH_2O$), 7.23–7.40 (5 H, m, ArH) and 12.17 (1 H, br s, OH); δ_C(100 MHz; [$^2H_6$]-DMSO) 20.60 (o), 40.99 (e), 43.91 (o), 65.22 (e), 127.85 (o), 128.46 (o), 137.30 (e), 155.34 (e) and 172.52 (e); *m/z* (EI) 237 (M^+, 47%), 219 (6), 193 (5), 178 (4), 143 (6), 134 (5), 108 (79), 91 (100), 84 (14) and 65 (8) (Found: M^+, 237.1001. $C_{12}H_{15}NO_4$ requires *M*, 237.1001).

Methyl (±)-3-[(benzyloxycarbonyl)amino]butanoate 9

A solution of the amino acid **8** (15.12 g, 63.7 mmol) in anhydrous methanol (120 cm^3) was stirred and cooled to 0 °C after which thionyl chloride (7.2 cm^3, 98 mmol) was added to it dropwise over *ca.* 15 min. The solution was allowed to warm to room temperature and stirred overnight after which it was evaporated to afford an oil. This was dissolved in dichloromethane (400 cm^3) and the solution washed with aqueous sodium hydroxide (2 mol dm^{-3}; 2 × 100 cm^3) and brine (100 cm^3), dried ($MgSO_4$) and evaporated to give a crude oil. Purification of this by flash chromatography (3:7, EtOAc–hexane) gave the title compound **9**[31] as a white crystalline solid (14.89 g, 93%); mp 43–46 °C (lit.,[31] 40–43 °C); R_F 0.45 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3440s, 3115sh, 3095w, 3070m, 3035m, 2975s, 2950s, 2895m, 2870m, 2840w and 1720vs; δ_H(250 MHz; $CDCl_3$) 1.23 (3 H, d, *J* 6.8, CH_3), 2.53 (2 H, d, *J* 5.5, CH_2CO_2), 3.66 (3 H, s, CO_2CH_3), 4.07–4.69 (1 H, m, ZNHC*H*), 5.08 (2 H, s, $PhCH_2O$), 5.20 (1 H, s, NH) and 7.29–7.35 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 20.34 (o), 40.29 (e), 43.96 (o), 51.64 (o), 66.57 (e), 128.07 (o), 128.49 (o), 136.52 (e), 155.53 (e) and 171.83 (e); *m/z* (EI) 251 (M^+, 23%), 144 (9), 134 (11), 108 (70), 107 (24), 92 (9), 91 (100), 79 (10), 78 (8) and 65 (10) (Found: M^+, 251.1158. $C_{13}H_{17}NO_4$ requires *M*, 251.1158).

(±)-3-[(Benzyloxycarbonyl)amino]butan-1-ol 11

A solution of the amino ester **9** (30.19 g, 120 mmol) in anhydrous THF (500 cm^3) was stirred and cooled to −78 °C after which DIBAL-H (1.5 mol dm^{-3} in toluene; 240 cm^3, 360 mmol) was added dropwise to it, the temperature being kept constant. The reaction mixture was stirred at −78 °C for 1 h before being allowed to warm to 0 °C at which temperature it was stirred for 1 h. After this the mixture was cooled to −78 °C and quenched by the slow addition of hydrochloric acid (2 mol dm^{-3}; 5 cm^3, **CAUTION** effervescence). The reaction mixture was allowed to warm to room temperature and poured into saturated aqueous Rochelle salt (sodium potassium tartrate) (100 cm^3) and extracted with ethyl acetate (1 × 500 cm^3 and 3 × 250 cm^3). The combined extracts were washed with brine (250 cm^3), dried ($MgSO_4$) and evaporated to afford an oil, purification of which by flash chromatography (1:1 EtOAc–hexane) furnished the *title compound* **11** as a white crystalline solid (24.22 g, 90%); mp 58–60 °C (Found: C, 64.6; H, 7.6; N, 6.3. $C_{12}H_{17}NO_3$ requires C, 64.6; H, 7.7; N, 6.3%); R_F 0.17 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3635w, 3500br m, 3440s, 3090w, 3070w, 3035m, 2960s, 2925s, 2890m, 2870m and 1705vs; δ_H(250 MHz; $CDCl_3$) 1.20 (3 H, d, *J* 6.7, CH_3), 1.29–1.44 (1 H, m, 2-H_A), 1.74–1.85 (1 H, m, 2-H_B), 2.69 (1 H, br s, OH), 3.64 (2 H, dd, *J* 7.7 and 3.6, CH_2OH), 3.94–3.96 (1 H, m, CH_3CH), 4.72 (1 H, br s, NH), 5.10 (2 H, s, $PhCH_2O$) and 7.28–7.40 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.29 (o), 40.11 (e), 43.96 (o), 58.94 (e), 66.83 (e), 128.06 (o), 128.16 (o), 128.51 (o), 136.34 (e) and 156.87 (e); *m/z* (EI) 223 (M^+, 13%), 178 (20), 134 (46), 108 (51), 92 (10), 91 (100), 79 (10) and 65 (8) (Found: M^+, 223.1208. $C_{12}H_{17}NO_3$ requires *M*, 223.1208).

(±)-3-[(Benzyloxycarbonyl)amino]butan-1-al 10

A solution of oxalyl chloride (0.15 cm^3, 1.7 mmol) in anhydrous dichloromethane (4 cm^3) was stirred and cooled to −78 °C after which anhydrous DMSO (0.23 cm^3 in 0.5 cm^3 of anhydrous dichloromethane) was added to it, the temperature being kept < −60 °C. The complex was allowed to form over 30 min then the amino alcohol **11** (0.282 g, 1.26 mmol) in anhydrous dichloromethane (4 cm^3) was added, the temperature being kept < −60 °C. Stirring was continued for a further 30 min after which triethylamine (0.92 cm^3, 6.6 mmol) was added to the mixture and stirring at −60 °C continued for a further 10 min. The mixture was then allowed to come to room temperature during *ca.* 30 min when it was 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 solution (20 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and evaporated to give an oil. Purification of this by flash chromatography (3:7, EtOAc–hexane) afforded the *title compound* **10** as an off-white crystalline solid (0.279 g, 99%), mp 50–51 °C (from ether–hexane) (Found: C, 64.8; H, 6.9; N, 6.1. $C_{12}H_{15}NO_3$ requires C, 65.1; H, 6.8; N, 6.3%); R_F 0.42 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3440s, 3095w, 3070w, 3040w, 2970m, 2935sh, 2890w, 2825m, 2725w and 1720vs; δ_H(250 MHz; $CDCl_3$) 1.23 (3 H, d, *J* 6.8, CH_3), 2.53–2.69 (2 H, m, CH_2CHO), 4.10–4.23 (1 H, m, ZNHC*H*), 5.07 (3 H, br s, $PhCH_2O$ and NH), 7.26–7.40 (5 H, m, ArH) and 9.73 (1 H, s, CHO); δ_C(100 MHz; $CDCl_3$) 20.79 (o), 42.85 (o), 50.07 (e), 66.72 (e), 128.08 (o), 128.16 (o), 128.52 (o), 136.30 (e), 155.60 (e) and 200.80 (o); *m/z* (EI) 222 [$(M + H)^+$, 3%], 221 (17), 152 (3), 151 (20), 134 (9), 130 (20), 109 (5), 108 (59), 107 (17), 92 (9), 91 (100), 79 (11) and 65 (12) (Found: M^+, 221.1052. $C_{12}H_{15}NO_3$ requires *M*, 221.1052).

(3*S,5*S**)-5-[(Benzyloxycarbonyl)amino]hex-1-en-3-ol 12a and (3*R**,5*S**)-5-[(benzyloxycarbonyl)amino]hex-1-en-3-ol 12b**

Vinylmagnesium bromide (1 mol dm^{-3} solution in THF; 38.1 cm^3, 38.1 mmol) was stirred and cooled to −78 °C after which the amino aldehyde **10** (3.371 g, 15.2 mmol) in anhydrous THF (45 cm^3) was added dropwise to it over *ca.* 45 min the temperature being kept < −70 °C. The reaction mixture was stirred at this temperature for 2 h after which it was quenched by the addition of saturated aqueous ammonium chloride (250 cm^3) and then allowed to warm to room temperature when it was extracted with ether (3 × 250 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (250 cm^{-3}) and brine (250 cm^{-3}), dried ($MgSO_4$) and evaporated to furnish an oil. Purification of this by flash chromatography (1:1, EtOAc–hexane) gave an epimeric mixture of the *title compounds* **12** (2.943 g, 78%). (Note: The overall yield was assessed from the ^1H NMR spectrum of the crude reaction mixture.) Yield of **12a** = 1.389 g, 37%, which crystallised when stored at −20 °C; yield of **12b** = 1.918 g, 51%, which was contaminated with the unchanged amino aldehyde **10**. [Note: The contaminated amino alcohol *anti*-**12b** was purified as in (a) to afford the pure amino alcohol *anti*-**12b** (0.973 g, 27%)].

Data for *syn*-**12a**: mp 40–43 °C (Found: C, 67.4; H, 7.8; N, 5.5. $C_{14}H_{19}NO_3$ requires C, 67.5; H, 7.7; N, 5.6%); R_F 0.27 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3610m, 3565–3160br s, 3435s, 3085w, 3065m, 3030m, 2960s, 2925s, 2865m, 2845sh and 1715vs; δ_H(250 MHz; $CDCl_3$) 1.19 (3 H, d, *J* 6.6, CH_3), 1.64–1.75 (2 H, m, 4,4-H), 2.37 (1 H, br s, OH), 3.81–3.89 (1 H, m, NHC*H*), 4.20 (1 H, dd, *J* 12.4 and 6.0, 3-H), 4.89 (1 H, br s, NH), 5.05–5.26 (4 H, m, $PhCH_2O$ and $CH{=}CH_2$), 5.86 (1 H, ddd, *J* 16.6, 10.4 and 5.8, $CH{=}CH_2$) and 7.29–7.39 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.67 (o), 44.07 (e), 45.03 (o), 66.62 (e), 70.92 (o), 114.57 (e), 128.10 (o), 128.50 (o), 136.49 (e), 140.76 (o) and 155.97 (e); *m/z* (CI, NH_3) 267 [$(M + NH_4)^+$, 100%], 251 (11), 250 (73), 232 (15), 206 (3) and 108 (2) [Found: $(M + H)^+$, 250.1443. $C_{14}H_{20}NO_3$ requires *M*, 250.1443].

Data for *anti*-**12b**: R_F 0.32 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3610w, 3565–3160br s, 3435s, 3085sh, 3065m, 3030m, 2965s, 2925s, 2885s, 2865m and 1705vs; δ_H(250 MHz; $CDCl_3$) 1.20 (3 H, d, *J* 6.7, CH_3), 1.46 (1 H, ddd, *J* 13.8, 10.2 and 3.2, 4-H_A), 1.64 (1 H, ddd, *J* 14.0, 10.5 and 3.4, 4-H_B), 3.96–4.04 (1 H, m, NHC*H*), 4.14–4.20 (1 H, m, 3-H), 4.82 (1 H, br d, *J* 9.1, NH), 5.05–5.28 (2 H, m, $CH{=}CH_2$), 5.10 (2 H, s, $PhCH_2O$), 5.89 (1 H, ddd, *J* 16.3, 10.7 and 5.7, $CH{=}CH_2$) and 7.27–7.36 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.36 (o), 44.07 (o), 45.17 (e), 66.98 (e), 68.85 (o), 114.17 (e), 128.22 (o), 128.54 (o), 136.28 (e), 140.18 (o) and 156.99 (e); *m/z* (CI, NH_3) 267 [$(M + NH_4)^+$, 10%], 250 (100), 232 (66), 222 (4), 206 (23), 188 (2), 178 (3), 159 (7), 142 (22), 134 (7), 125 (2), 116 (5), 108 (14), 96 (2), 91 (15), 82 (3) and 58 (3) [Found: $(M + H)^+$, 250.1443. $C_{14}H_{20}NO_3$ requires *M*, 250.1443].

(3*S,5*S**)-5-[(Benzyloxycarbonyl)amino]-3-(3,5-dinitrobenzoyloxy)hex-1-ene 13a**

To a stirred solution of the amino alcohol *syn*-**12a** (72 mg, 0.29 mmol) in anhydrous dichloromethane (3 cm^3) was added DMAP (81 mg, 0.66 mmol), followed by 3,5-dinitrobenzoyl chloride (133 mg, 0.58 mmol). The solution turned a yellow colour and after being stirred at room temperature overnight, was poured into water (40 cm^3) and extracted with dichloromethane (3 × 25 cm^3). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (20 cm^3), water (20 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and evaporated to afford an oil. Purification of this by flash chromatography (3:7, EtOAc–hexane) furnished the *title compound* **13a** as a lime-coloured oil (120 mg, 94%) (Found: C, 57.2; H, 5.1; N, 9.6. $C_{21}H_{21}N_3O_8$ requires C, 56.9; H, 4.8; N, 9.5%); R_F 0.6 (1:1, EtOAc–hexane); $\nu_{max}(CHCl_3)/cm^{-1}$ 3680m, 3620–3200br m, 3435s, 3100–2900br m and 1720vs; δ_H(250 MHz; $CDCl_3$) 1.24 (3 H, d, *J* 6.6, CH_3), 1.82–1.92 (1 H, m, 4-H_A), 2.04–2.16 (1 H, m, 4-H_B), 3.84–3.92 (1 H, m, C*H*NHZ), 4.70 (1 H, br d, *J* 9.3, NH), 5.01 (2 H, s, $PhCH_2O$), 5.29–5.44 (2 H, m, $CH{=}CH_2$), 5.64 (1 H, q, *J* 6.7, 3-H), 5.85–5.96 (1 H, m, $CH{=}CH_2$), 7.22–7.35 (5 H, m, ArH) and 9.13 (3 H, s, ArH); δ_C(100 MHz; $CDCl_3$) 21.63 (o), 41.48 (e), 44.49 (o), 66.59 (e), 75.84 (o), 119.17 (e), 122.37 (o), 127.90 (o), 128.13 (o), 128.48 (o), 129.37 (o), 133.89 (e), 134.65 (o), 136.27 (e), 148.58 (e), 155.51 (e) and 161.71 (e); *m/z* (CI, NH_3) 461 [$(M + NH_4)^+$, 100%], 444 (30), 431 (7), 400 (6), 310 (5), 249 (18), 232 (100), 188 (10), 159 (21), 142 (16) and 108 (30) [Found: $(M + NH_4)^+$, 461.1672. $C_{21}H_{25}N_4O_8$ requires *M*, 461.1672].

(3*R,5*S**)-5-[(Benzyloxycarbonyl)amino]-3-(3,5-dinitrobenzoyloxy)hex-1-ene 13b**

To a solution of the amino alcohol *anti*-**12b** (780 mg, 0.31 mmol) in anhydrous dichloromethane (3 cm^3) was added DMAP (88 mg, 0.72 mmol), followed by 3,5-dinitrobenzoyl chloride (144 mg, 0.63 mmol). The solution turned a yellow colour and after being stirred overnight at room temperature, was worked up and purified as above to afford the *title compound* **13b** as a colourless oil (0.128 g, 92%); R_F 0.6 (1:1, EtOAc–hexane); $\nu_{max}(CHCl_3)/cm^{-1}$ 3615–3200br m, 3430s, 3100–2800br m and 1720vs; δ_H(250 MHz; $CDCl_3$) 1.25 (3 H, d, *J* 6.7, CH_3), 1.76–1.87 (1 H, m, 4-H_A), 2.03–2.14 (1 H, m, 4-H_B), 3.95–4.09 (1 H, m, C*H*NHZ), 4.56 (1 H, d, *J* 8.9, NH), 4.99 (2 H, s, $PhCH_2O$), 5.26–5.42 (2 H, m, $CH{=}CH_2$), 5.59–5.67 (1 H, m, 3-H), 5.84–5.95 (1 H, m, $CH{=}CH_2$), 7.30–7.35 (5 H, m, ArH), 9.14 (2 H, s, ArH) and 9.18 (1 H, s, ArH); δ_C(100 MHz; $CDCl_3$) 21.72 (o), 41.48 (e), 43.63 (o), 66.71 (e), 74.49 (o), 118.60 (e), 122.81 (o), 127.99 (o), 128.12 (o), 128.49 (o), 129.39 (o), 134.25 (e), 134.97 (o), 136.32 (e), 148.56 (e), 155.61 (e) and 161.82 (e); *m/z* (CI, NH_3) 461 [$(M + NH_4)^+$, 38%], 444 (16), 431 (6), 414 (4), 384 (2), 310 (2), 269 (2), 249 (3), 232 (100), 178 (2), 159 (12), 142 (11), 108 (19) and 91 (6) [Found: $(M + NH_4)^+$, 461.1672. $C_{21}H_{25}N_4O_8$ requires *M*, 461.1672].

(4*S,6*S**)-3-Benzyloxycarbonyl-4-methyl-6-vinyl-2,4,5,6-tetrahydro-1,3-oxazine 14a**

To a solution of the amino alcohol *syn*-**12a** (73 mg, 0.29 mmol) in anhydrous toluene (5 cm^3) was added paraformaldehyde (26 mg, 0.90 mmol) and toluene-4-sulfonic acid (6 mg, 31.5 μmol). The resulting mixture was heated under Dean–Stark conditions for 1 h after which it was poured into saturated aqueous sodium hydrogen carbonate (25 cm^3) and extracted with ether (3 × 25 cm^3). The combined extracts were washed with water (20 cm^3) and brine (20 cm^3), dried (Na_2SO_4) and evaporated to afford a crude oil. Purification of this by flash chromatography (1:9, ether–hexane) furnished the *title compound* **14a** as a colourless oil (73 mg, 96%) (Found: C, 68.7; H, 7.3; N, 5.6. $C_{15}H_{19}NO_3$

requires C, 68.9; H, 7.3; N, 5.4%); R_F 0.29 (1:4, EtOAc–hexane); $\nu_{max}(CHCl_3)/cm^{-1}$ 3100w, 3075w, 3040m, 2965s, 2925s, 2880m and 1710vs; δ_H(400 MHz; CD_2Cl_2) 1.30 (3 H, d, *J* 6.5, CH_3), 1.67 (1 H, dt, *J* 14.3 and 10.6, 5-H_A), 1.93 (1 H, ddd, *J* 14.3, 6.0 and 3.7, 5-H_B), 3.99–4.08 (1 H, m, ZNCH), 4.21–4.27 (1 H, m, 6-H), 4.99 (2 H, q, *J* 10.2, $ZNCH_2O$), 5.08–5.28 (2 H, m, $CH{=}CH_2$), 5.14 (2 H, s, $PhCH_2O$), 5.85 (1 H, ddd, *J* 16.0, 10.5 and 5.5, $CH{=}CH_2$) and 7.26–7.78 (5 H, m, ArH); δ_C(100 MHz; CD_2Cl_2) 20.43 (o), 35.71 (e), 49.05 (o), 67.18 (e), 69.61 (e), 73.87 (o), 115.11 (e), 128.00 (o), 128.18 (o), 128.69 (o), 137.11 (e), 138.64 (o) and 155.39 (e); *m/z* (CI, NH_3) 279 [$(M + NH_4)^+$, 29%], 262 (59), 246 (2), 232 (6), 219 (27), 218 (100), 192 (6), 148 (5), 126 (10), 108 (28), 91 (17) and 58 (32) [Found: $(M + H)^+$, 262.1442. $C_{15}H_{20}NO_3$ requires *M*, 262.1443].

(4*S,6*R**)-3-Benzyloxycarbonyl-4-methyl-6-vinyl-2,4,5,6-tetrahydro-1,3-oxazine 14b**

To a solution of the amino alcohol *anti*-**12b** (72 mg, 0.29 mmol) in anhydrous toluene (5 cm^3) was added paraformaldehyde (26 mg, 1.0 mmol) and toluene-4-sulfonic acid (6 mg, 31.5 μmol). The resulting mixture was heated under Dean–Stark conditions for 1 h after which it was worked up and purified as above to afford the *title compound* **14b** as a colourless oil (0.074 g, 98%); R_F 0.29 (1:4, EtOAc–hexane); $\nu_{max}(CHCl_3)/cm^{-1}$ 3100w, 3075w, 3040m, 2980s, 2950s, 2920sh, 2860m and 1705vs; δ_H(400 MHz; CD_2Cl_2) 1.30 (3 H, d, *J* 7.1, CH_3), 1.47–1.50 (1 H, m, 5-H_A), 1.80 (1 H, dt, *J* 13.3 and 6.0, 5-H_B), 4.21–4.25 (1 H, m, 6-H), 4.50–4.61 (2 H, br m, ZNCH and 2-H_A), 5.11–5.28 (2 H, m, $CH{=}CH_2$), 5.14 (2 H, s, $PhCH_2O$), 5.46–5.49 (1 H, br m, 2-H_B), 5.81 (1 H, ddd, *J* 16.2, 10.6 and 5.3, $CH{=}CH_2$) and 7.30–7.41 (5 H, m, ArH); δ_C(100 MHz; CD_2Cl_2) 16.26 (o), 16.71 (o), 35.77 (e), 45.25 (o), 45.26 (o), 67.28 (e), 71.19 (e), 73.05 (o), 115.33 (e), 128.03 (o), 128.21 (o), 128.69 (o), 137.10 (e), 138.40 (o) and 154.56 (e); *m/z* (CI, NH_3) 279 [$(M + NH_4)^+$, 24%], 262 (38), 246 (1), 232 (4), 218 (100), 206 (2), 192 (3), 146 (4), 126 (4), 108 (19), 96 (3), 91 (9) and 58 (14) [Found: $(M + H)^+$, 262.1443. $C_{15}H_{20}NO_3$ requires *M*, 262.1443].

(2*S,4*S**,6*S**)-3-Benzyloxycarbonyl-4-methyl-2-phenylselanylmethyl-6-vinyl-2,4,5,6-tetrahydro-1,3-oxazine 15a**

The vinyl amino alcohol *syn*-**12a** (0.94 g, 3.77 mmol) was dissolved in anhydrous toluene (45 cm^3) and phenylselanylacetaldehyde diethyl acetate (1.14 g, 4.17 mmol) and PPTS (40 mg, 0.16 mmol) were added to the solution which was then heated under Dean–Stark conditions for 4 h. After this, the reaction mixture was poured into saturated aqueous sodium hydrogen carbonate (75 cm^3) and extracted with ether (1 × 50 cm^3 and 3 × 20 cm^3). The combined extracts were washed with water (25 cm^3) and brine (25 cm^3), dried (Na_2SO_4) and evaporated to afford a yellow oil. Purification of this by flash chromatography (0:1 to 1:19, EtOAc–hexane) furnished the *title compound* **15a** as a light yellow oil (1.495 g, 92%) (Found: C, 61.6; H, 5.9; N, 3.2. $C_{22}H_{25}NO_3Se$ requires C, 61.4; H, 5.9; N, 3.3%); R_F 0.32 (1:4, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3095w, 3065m, 3035w, 2945m, 2925m, 2865w and 1700vs; δ_H(250 MHz; $CDCl_3$) 1.35 (3 H, d, *J* 6.9, CH_3), 1.58 (1 H, ddd, *J* 13.6, 10.6 and 4.8, 5-H_A), 2.20 (1 H, ddd, *J* 13.7, 9.2 and 5.2, 5-H_B), 3.26 (2 H, ddd, *J* 12.4, 8.1 and 4.3, $PhSeCH_2$), 4.02–4.09 (1 H, m, 4-H), 4.40–4.48 (1 H, m, 6-H), 5.08–5.25 (2 H, m, $CH{=}CH_2$), 5.13 (2 H, s, $PhCH_2O$), 5.55 (1 H, dd, *J* 8.1 and 4.2, $PhSeCH_2CH$), 5.82 (1 H, ddd, *J* 16.0, 10.6 and 5.4, $CH{=}CH_2$), 7.15–7.22 (2 H, m, ArH), 7.27–7.37 (6 H, m, ArH) and 7.47–7.54 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 24.48 (o), 33.88 (e), 35.99 (e), 45.42 (o), 67.24 (e), 73.11 (o), 85.10 (o), 115.33 (e), 126.82 (o), 128.00 (o), 128.14 (o), 128.58 (o), 128.99 (o), 130.55 (e), 132.60 (o), 136.34 (e), 137.69 (o) and 154.54 (e); *m/z* (CI, NH_3) 432 [$(M + H)^+$, 2%], 276 (17), 232 (84), 218 (65), 200 (11), 191 (7), 174 (17), 159 (16), 142 (15), 134 (4), 126 (4), 116 (4), 108 (11), 94 (7), 78 (8), 61 (8) and 52 (100) [Found: $(M + H)^+$, 432.1078. $C_{22}H_{26}NO_3Se$ requires *M*, 432.1078].

(2*R or *S**,4*S**,6*R**)-3-Benzyloxycarbonyl-4-methyl-2-phenylselanylmethyl-6-vinyl-2,4,5,6-tetrahydro-1,3-oxazine 15b**

To a solution of the vinyl amino alcohol *anti*-**12b** (0.78 g, 3.13 mmol) in anhydrous toluene (40 cm^3) was added phenylselanylacetaldehyde diethyl acetal (0.95 g, 3.46 mmol) and PPTS (33 mg, 0.13 mmol). The resulting solution was heated under Dean–Stark conditions for 4 h after which it was worked up and purified as above to furnished the *title compound* **15b** as a light yellow oil (1.215 g, 90%); R_F 0.36 (1:4, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3065m, 3030m, 2965s, 2945s, 2920m, 2865w and 1700vs; δ_H(250 MHz; $CDCl_3$) 1.34 (3 H, d, *J* 7.1, CH_3), 1.49–1.65 (1 H, m, 5-H_A), 1.83 (1 H, ddd, *J* 17.9, 11.5 and 6.5, 5-H_B), 3.13 (1 H, dd, *J* 12.6 and 4.4, $PhSeCHH$), 3.56 (1 H, dd, *J* 12.6 and 10.1, $PhSeCHH$), 4.30–4.36 (1 H, m, 4-H), 4.39–4.59 (1 H, m, 6-H), 5.05–5.32 (4 H, m, $PhCH_2O$ and $CH{=}CH_2$), 5.75 (1 H, ddd, *J* 15.6, 10.5 and 5.1, $CH{=}CH_2$), 5.87 (1 H, dd, *J* 10.0 and 4.6, $PhSeCH_2CH$), 7.15–7.38 (8 H, m, ArH) and 7.49–7.54 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.48 (o), 30.63 (e), 34.29 (e), 44.63 (o), 64.85 (o), 67.22 (e), 81.39 (o), 116.00 (e), 127.09 (o), 127.94 (o), 128.08 (o), 128.51 (o), 129.04 (o), 129.92 (e), 133.10 (o), 136.34 (e), 137.38 (o) and 153.89 (e); *m/z* (CI, NH_3) 432 [$(M + H)^+$, 3%)], 274 (3), 260 (9), 232 (100), 216 (2), 142 (2), 108 (9) and 91 (6) [Found: $(M + H)^+$, 432.1078. $C_{22}H_{26}NO_3Se$ requires *M*, 432.1078].

General procedure for the preparation of the selenoxides

The aminal **15a** (1.105 g, 2.57 mmol) was dissolved in methanol–water (6:1; 75 cm^3) and sodium periodate (1.65 g, 7.7 mmol) and sodium hydrogen carbonate (0.24 g, 2.8 mmol) were added to the solution to provide a heterogeneous mixture which was stirred for 1 h at room temperature. It was then poured into water (500 cm^3) and extracted with dichloromethane (4 × 250 cm^3). The organic phases were combined, dried (K_2CO_3) and evaporated to furnish the crude selenoxide (1.117 g, 98%) as a light yellow oil.

(±)-Benzyloxycarbonyl-8-methyl-3,4,7,8-tetrahydroazocin-2(1*H*)-one 17

(a) From the *syn* aminal 15a. A solution of the selenoxide derived from **15a** (401 mg, 0.898 mmol) and DBU (0.4 cm^3, 2.7 mmol) in anhydrous toluene (100 cm^3) was heated under reflux overnight. The mixture was evaporated to give a dark oil which was purified by flash chromatography (0:1 to 1:9, EtOAc–hexane) to furnish the title lactam **17** (124 mg, 51%) and the readdition products **22** and **23** (116 mg, 29%) as colourless oils.

(b) From the *anti* aminal 15b. A solution of the selenoxide derived from **15b** (273 mg, 0.612 mmol) and DBU (0.28 cm^3, 1.84 mmol) in anhydrous benzene (65 cm^3) was heated under reflux overnight. The mixture was evaporated to give a dark oil, which was purified as in (a) to furnish the *title compound* **17** (121 mg, 72%) and the *readdition products* **22** and **23** (0.013 g, 5%) as colourless oils. The lactam **17** crystallised to form a waxy solid upon storage at −20 °C for several weeks.

Data for the lactam **17**: mp 30–31 °C (Found: C, 70.1; H, 7.2; N, 5.1. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%); R_F 0.36 (1:4, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3095w, 3065w, 3025m, 2990sh, 2930s, 2895sh, 2865m, 1740s and 1700vs; δ_H(400 MHz; $CDCl_3$) 1.39 (3 H, d, *J* 6.8, CH_3), 2.10 (1 H, ddd, *J* 14.1, 6.6 and 3.7, 7-H_A), 2.18–2.33 (3 H, m, 7-H_B and 4,4-H), 2.54 (1 H, ddd, *J* 11.6, 6.1 and 3.0, 3-H_A), 2.83 (1 H, dd, *J* 11.7 and 4.3, 3-H_B), 4.05–4.14 (1 H, m, 8-H), 5.18 (2 H, q, *J* 12.3, $PhCH_2$), 5.71–5.83 (2 H, m, CH=CH) and 7.30–7.37 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 20.52 (o), 24.76 (e), 32.21 (e), 42.07 (e), 50.28 (o), 67.75 (e), 128.07 (o), 128.36 (o), 128.59 (o), 130.24 (o), 130.61 (o), 135.58 (e), 154.16 (e) and 182.58 (e); *m/z* (EI) 274 [$(M + H)^+$, 5%], 273 (27), 260 (8), 258 (9), 214 (8), 178

(43), 139 (23), 138 (13), 134 (57), 108 (19), 107 (42), 92 (12), 91 (100) and 65 (7) (Found: M^+, 273.1365. $C_{16}H_{19}NO_3$ requires *M*, 273.1365).

Data for the readdition products **22** and **23**: inseparable mixture of the ester and imide; R_F 0.19 (1:4, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3620w, 3575–3200br m, 3450s, 3100m, 3075m, 3040s, 2975s, 2935s, 2875m and 1725vs; δ_H(250 MHz; $CDCl_3$) 1.14 (1.5 H, d, *J* 6.7, CH_3), 1.18 (1.5 H, d, *J* 6.7, CH_3), 1.61–1.80 (2 H, m, ZNCHCH_2), 2.05 (1 H, br s, PhSeCH_2), 3.44–3.63 (1 H, br m, PhSeCH_2), 3.71–3.93 (1 H, m, CH_3CHNH), 4.56–4.81 (1 H, m, C*H*CH=CH_2), 5.05–5.33 (5 H, m, PhCH_2O and CH=CH_2), 5.64–5.77 (1 H, m, C*H*=CH_2), 7.23–7.39 (8 H, m, ArH) and 7.53–7.58 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.21 (o), 21.40 (o), 27.56 (e), 41.01 (e), 41.22 (e), 44.25 (o), 44.30 (o), 66.55 (e), 72.45 (o), 73.41 (o), 117.33 (e), 117.75 (e), 127.82 (o), 128.08 (o), 128.51 (o), 129.19 (o), 133.31 (o), 135.24 (o), 135.76 (o), 136.53 (e), 155.53 (e), 170.07 (e) and 170.31 (e); *m/z* (CI, NH_3) 465 [(M + NH_4), 2%], 448 (4), 357 (10), 340 (8), 309 (5), 233 (17), 232 (100), 156 (8), 142 (14) and 108 (8) [Found: $(M + H)^+$, 448.1027. $C_{22}H_{26}NO_4Se$ requires *M*, 448.1027].

(±)-8-Methyl-3,4,7,8-tetrahydroazocin-2(1*H*)-one 18

A solution of the Z-protected lactam **17** (34.5 mg, 0.126 mmol) in anhydrous dichloromethane (2 cm^3) was stirred and cooled to −78 °C whilst a solution of boron tribromide (1 mol dm^{-3} solution in dichloromethane; 0.13 cm^3, 0.13 mmol) was added dropwise. The reaction mixture was stirred for *ca.* 30 min after which it was treated with saturated aqueous sodium hydrogen carbonate (1 cm^3) to quench the reaction and allowed to warm to room temperature. The reaction mixture was then poured into saturated aqueous sodium hydrogen carbonate (20 cm^3) and extracted with dichloromethane (1 × 20 cm^3 and 3 × 10 cm^3). The combined extracts were washed with brine (15 cm^3), dried ($MgSO_4$), and evaporated to afford an oil. Purification of this by flash chromatography on silica gel (EtOAc) furnished the *title compound* **18** as a white crystalline solid (15.6 mg, 88%); mp 89–91 °C; R_F 0.13 (EtOAc); $\nu_{max}(CCl_4)/cm^{-1}$ 3400w, 3300sh, 3205m, 3080m, 3035m, 2980s, 2940m, 2900m, 2830w and 1660vs; δ_H(250 MHz; $CDCl_3$) 1.19 (3 H, d, *J* 6.5, CH_3), 2.04–2.30 (2 H, m, allylic CH_2), 2.46–2.79 (4 H, m, 2 × CH_2), 3.96–4.03 (1 H, m, CH_3CH), 5.46–5.56 (1 H, m, C*H*=CH), 5.66–5.74 (1 H, m, CH=C*H*) and 6.18 (1 H, br s, NH); δ_C(100 MHz; $CDCl_3$) 22.61 (o), 24.51 (e), 34.80 (e), 37.90 (e), 47.34 (o), 127.37 (o), 128.95 (o) and 175.91 (e); *m/z* (EI) 140 [(M + $H)^+$, 92%], 124 (82), 110 (14), 96 (13), 82 (14), 68 (70) and 54 (100) [Found: $(M + H)^+$, 140.1075. $C_8H_{14}NO$ requires *M*, 140.1075].

(±)-8-Methyl-3,4,5,6,7,8-hexahydroazocin-2(1*H*)-one 19

$Pd(OH)_2$ (3 mg, Pearlman's catalyst) was added to a solution of the Z-protected lactam **17** (26.6 mg, 97.3 μmol) dissolved in ethyl acetate (3 cm^3) after which the reaction vessel was evacuated and placed under an atmosphere of hydrogen. After being stirred vigorously overnight at room temperature, the reaction mixture was filtered through Celite and evaporated to afford a crude light brown solid. Purification of this by flash chromatography (EtOAc) gave the *title compound* **19** as a white crystalline solid (13.6 g, 99%); mp 74–76 °C (Found: C, 67.8; H, 10.9; N, 9.6. $C_8H_{15}NO$ requires C, 68.1; H, 10.7; N, 9.9%); R_F 0.13 (EtOAc); $\nu_{max}(CCl_4)/cm^{-1}$ 3395w, 3285sh, 3200m, 3070m, 2975s, 2935s, 2860m and 1660vs; δ_H(250 MHz; $CDCl_3$) 1.19 (3 H, d, *J* 6.7, CH_3), 1.30–1.46 (3 H, m), 1.58–1.88 (5 H, m), 2.28 (1 H, ddd, *J* 12.6, 4.3 and 3.5, 3-H_A), 2.50 (1 H, dd, *J* 12.6 and 3.8, 3-H_B), 3.62–3.66 (1 H, m, CH_3CH) and 5.46 (1 H, br s, NH); δ_C(100 MHz; $CDCl_3$) 22.11 (o), 24.66 (e), 26.09 (e), 28.20 (e), 33.35 (e), 40.24 (e), 47.98 (o) and 176.81 (e); *m/z* (EI) 142 [(M + $H)^+$, 76%], 113 (3), 98 (16), 81 (4), 70 (6) and 55 (100) [Found: $(M + H)^+$, 142.1232. $C_8H_{16}NO$ requires *M*, 142.1232].

(3*S**,8*R**)-1-Benzyloxycarbonyl-8-methyl-3-phenylselanyl-3,4,7,8-tetrahydroazocin-2(1 *H*)-one and (3*S**,8*S**)-1-benzyloxycarbonyl-8-methyl-3-phenylselanyl-3,4,7,8-tetrahydroazocin-2(3*H*)-one 32 and 33

A solution of the selenoxide (302 mg, 0.677 mmol) derived from **15b**, and dihydropyran (1.54 cm^3, 16.9 mmol) in anhydrous toluene (70 cm^3) was heated under reflux overnight after which it was evaporated to give a light orange oil. Purification of this by flash chromatography (1:1 to 1:0, CH_2Cl_2–hexane) furnished the cis-*selanyl lactam* **32** (134 mg, 46%) as a white crystalline solid, the trans-*selanyl lactam* **33** (15 mg, 5%) as a colourless oil, and the *Z-protected lactam* **17** (31 mg, 17%) as a colourless oil which was spectroscopically identical with that prepared earlier.

Data for the major (*cis*) isomer **32**: mp 69–70 °C (Found: C, 61.5; H, 5.3; N, 3.0. $C_{22}H_{23}NO_3Se$ requires C, 61.7; H, 5.4; N, 3.3%); R_F 0.49 (1:4, hexane–CH_2Cl_2); $\nu_{max}(CCl_4)/cm^{-1}$ 3075m, 3030s, 3000sh, 2975s, 2940s, 2900m, 2875m, 1745vs and 1700vs; δ_H(400 MHz; $CDCl_3$) 1.42 (3 H, d, *J* 6.7, CH_3), 2.08 (1 H, ddd, *J* 13.8, 6.8 and 3.7, 7-H_A), 2.17–2.26 (1 H, m, 7-H_B), 2.40 (1 H, ddd, *J* 13.7, 8.4 and 3.5, 4-H_A), 2.56 (1 H, dd, *J* 13.7 and 7.7, 4-H_B), 4.04–4.13 (1 H, m, 8-H), 4.24 (1 H, br d, *J* 10.7, C*H*SePh), 5.14 (2 H, q, *J* 12.2, PhCH_2), 5.60–5.67 (1 H, m, C*H*=CH), 5.72–5.79 (1 H, m, CH=C*H*) and 7.17–7.38 (10 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 20.62 (o), 32.00 (e), 33.81 (e), 49.74 (o), 51.71 (o), 68.01 (e), 128.00 (o), 128.24 (o), 128.47 (o), 128.61 (o), 129.02 (o), 129.36 (o), 131.41 (o), 135.26 (o), 153.82 (e) and 181.34 (e); *m/z* (CI, NH_3) 430 [$(M + H)^+$, 44%], 386 (3), 296 (15), 274 (100), 272 (89), 174 (2), 155 (6), 140 (43), 138 (38), 108 (10) and 52 (4) [Found: $(M + H)^+$, 430.0921. $C_{22}H_{24}NO_3Se$ requires *M*, 430.0921].

Data for the minor (*trans*) isomer **33**: R_F 0.25 (1:4, hexane–CH_2Cl_2); $\nu_{max}(CCl_4)/cm^{-1}$ 3070m, 3030s, 3000sh, 2975s, 2940s, 2880m, 2860sh, 1740vs and 1700vs; δ_H(250 MHz; $CDCl_3$) 1.36 (3 H, d, *J* 6.9, CH_3), 2.16 (1 H, ddd, *J* 14.6, 6.3 and 3.5, 7-H_A), 2.28–2.35 (1 H, m, 7-H_B), 2.59–2.74 (2 H, m, 4,4-H), 4.19–4.28 (1 H, m, 8-H), 4.65 (1 H, dd, *J* 7.4 and 5.7, C*H*SePh), 5.23 (2 H, q, *J* 12.1, PhCH_2), 5.73–5.83 (2 H, m, C*H*=C*H*), 7.21–7.38 (8 H, m, ArH) and 7.50–7.52 (2 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 19.35 (o), 31.27 (e), 33.53 (e), 51.15 (o), 54.46 (o), 68.36 (e), 127.98 (o), 128.16 (o), 128.56 (o), 128.59 (o), 128.65 (o), 129.20 (o), 130.03 (o), 135.01 (e), 135.06 (o), 153.99 (e) and 177.81 (e); *m/z* (CI, NH_3) 430 [$(M + H)^+$, 61%], 386 (15), 296 (3), 274 (100), 232 (13), 134 (6), 109 (26) and 91 (15) [Found: $(M + H)^+$, 430.0921. $C_{22}H_{24}NO_3Se$ requires *M*, 430.0921].

(±)-Benzyloxycarbonyl-8-methyl-3,4,7,8-tetrahydroazocin-2(1*H*)-one 17

A solution of the selenoxide (207 mg, 0.464 mmol) derived from **15b** and DBU (0.21 cm^3, 1.4 mmol) and the ketene acetal **34**[18] (1.746 g, 9.27 mmol) in anhydrous toluene (50 cm^3) was heated under reflux overnight and then evaporated to give a light orange oil. Purification of this by flash chromatography (0:1 to 1:0, CH_2Cl_2–hexane) furnished the title compound (0.101 g, 80%) as a colourless oil which was spectroscopically identical with that prepared earlier, and the *phenylselanyl ester* **36** (0.081 g, 76%) as a colourless oil.

Data for methyl 2-phenylselanylethanoate **36**; $\nu_{max}(CCl_4)/cm^{-1}$ 3080sh, 3065s, 3025m, 3005m, 3055s, 2900w, 2845w, 1735vs and 1700s; δ_H(250 MHz; $CDCl_3$) 3.52 (2 H, s, PhSeCH_2), 3.67 (3 H, s, CH_3), 7.24–7.34 (3 H, m, ArH) and 7.54–7.60 (2 H, m, ArH); *m/z* (EI) 230 [$(M + H)^+$, 29%], 171 (22), 157 (16), 105 (2), 91 (100), 77 (32), 65 (11) and 51 (24) (Found: M^+, 229.9846. $C_9H_{10}O_2Se$ requires *M*, 229.9846).

(±) 5-(*tert*-Butoxycarbonyl)pyrrolidin-2-one 46[23]

To a stirred suspension of the amino acid **45** (1.210 g, 9.37 mmol) in anhydrous *tert*-butyl acetate (25 cm^3) at room temperature was slowly added concentrated H_2SO_4 (1.5 cm^3). The resulting mixture was stirred at room temperature

overnight to afford a homogeneous solution which was poured into aqueous sodium hydroxide (2 mol dm^{-3}; 50 cm^3) and extracted with dichloromethane (4 × 50 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated to afford a solid. Purification of this by flash chromatography (EtOAc) furnished the title compound **46**[23] as a white crystalline solid (1.581 g, 91%); mp 91–92 °C; R_F 0.32 (EtOAc); $\nu_{max}(CCl_4)/cm^{-1}$ 3450w, 3400–3150br s, 3350w, 3210s, 3110m, 2990s, 2940s, 2890m and 1710vs; δ_H(250 MHz; $CDCl_3$) 1.46 (9 H, s, CMe_3), 2.10–2.49 (4 H, m, 2 × CH_2), 4.08–4.14 (1 H, m, 4-H) and 6.22 (1 H, br s, NH); δ_C(100 MHz; $CDCl_3$) 24.78 (e), 27.88 (o), 29.43 (e), 56.17 (o), 82.10 (e), 171.20 (e) and 178.25 (e); *m/z* (CI, NH_3) 186 [$(M + H)^+$, 100%], 147 (8), 130 (12), 101 (3) and 84 (10) [Found: $(M + H)^+$, 186.1130. $C_9H_{16}NO_3$ requires *M*, 186.1130].

(±)-1-Benzyloxycarbonyl-5-(*tert*-butoxycarbonyl)pyrrolidin-2-one 47[23]

A solution of potassium *tert*-butoxide (768 mg, 6.84 mmol) in anhydrous THF (14 cm^3) was stirred at room temperature whilst the amino ester **46** (1.046 g, 5.65 mmol) in anhydrous THF (7 cm^3) was added dropwise to it. The resulting solution was stirred for 15 min after which benzyl chloroformate (0.91 cm^3, 6.37 mmol) was added dropwise to it and stirring continued at room temperature for 1 h. The reaction mixture was poured into water (30 cm^3) and extracted with ethyl acetate (3 × 20 cm^3) and the combined extracts were washed with water (20 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and evaporated to afford an oil. Purification of this by flash chromatography (3:7, EtOAc–hexane) furnished the title compound **47**[23] as a white crystalline solid (1.602 g, 89%); mp 87–89 °C; R_F 0.41 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3120w, 3075w, 3080sh, 2980s, 2940m, 2880m, 1805s, 1765vs and 1730vs; δ_H(250 MHz; $CDCl_3$) 1.38 (9 H, s, CMe_3), 1.97–2.08 (1 H, m, 4-H_A), 2.22–2.71 (3 H, m, 3,3-H and 4-H_B), 4.54 (1 H, dd, *J* 9.2 and 2.5, 5-H), 5.26 (2 H, q, *J* 12.4, PhCH_2O) and 7.29–7.41 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 21.87 (e), 27.76 (o), 30.99 (e), 59.36 (o), 68.19 (e), 82.53 (e), 128.18 (o), 128.38 (o), 128.52 (o), 135.05 (e), 150.89 (e), 170.06 (e) and 173.11 (e); *m/z* (CI, NH_3) 337 [$(M + NH_4)^+$, 80%], 320 (68), 276 (33), 237 (25), 220 (100), 186 (2), 174 (5), 108 (15) and 91 (9) [Found: $(M + H)^+$ 320.1498. $C_{17}H_{22}NO_5$ requires *M*, 320.1498].

(±)-2-[(Benzyloxycarbonyl)amino]-1-(*tert*-butoxycarbonyl)-hept-6-en-5-one 48[23]

Vinylmagnesium bromide (1 mol dm^{-3} solution in THF; 1.2 cm^3, 1.2 mmol) was added dropwise to a stirred, chilled (−78 °C) solution of the lactam **47** (320 mg, 1.0 mmol) in anhydrous THF (6 cm^3). The mixture was stirred at this temperature for a further 2 h after which it was treated with methanol–acetic acid (1:1; 0.5 cm^3) to quench the reaction and diluted with ether (25 cm^3). The mixture was then washed with water (25 cm^3), dried ($MgSO_4$) and evaporated to afford an oil. Purification of this by flash chromatography (3:7, EtOAc–hexane) furnished the title compound **48**[23] (0.213 g, 61%) and benzyl acrylate (0.057 g, 35%) as colourless oils (Note: The enone **48** is prone to polymerisation and must, therefore, be used immediately); R_F 0.55 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3430m, 3355w, 3310sh, 3100sh, 3070w, 3040w, 2980s, 2880sh and 1725vs; δ_H(250 MHz; $CDCl_3$) 1.45 (9 H, s, CMe_3), 1.88–2.01 (1 H, m, 3-H_A), 2.13–2.22 (1 H, m, 3-H_B), 2.62–2.72 (2 H, m, 4,4-H), 4.21–4.30 (1 H, m, 2-H), 5.09 (2 H, s, PhCH_2), 5.37 (1 H, d, *J* 7.7, NH), 5.81 (1 H, dd, *J* 10.2 and 1.5, C*H*H=CH), 6.18 (1 H, q, *J* 16.7, CH*H*=CH), 6.33 (1 H, dd, *J* 17.6 and 10.1, CH_2=C*H*) and 7.26–7.36 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 26.78 (e), 27.94 (o), 35.36 (e), 53.92 (o), 66.89 (e), 82.36 (e), 128.08 (o), 128.14 (o), 128.46 (e), 128.49 (o), 136.22 (o), 136.29 (e), 155.97 (e), 171.12 (e) and 199.38 (e); *m/z* (CI, NH_3) 365 [$(M + NH_4)^+$, 15%], 348 (24), 330 (100), 309 (31), 292 (77), 274 (23), 248 (24), 230 (45), 202 (16), 140 (4) and 108 (6) [Found: $(M + H)^+$, 348.1811. $C_{19}H_{26}NO_5$ requires *M*, 348.1811].

Data for benzyl acrylate: R_F 0.67 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3100m, 3080s, 3045s, 2995sh, 2960s, 2900w and 1725vs; δ_H(250 MHz; $CDCl_3$) 5.20 (2 H, s, PhCH_2), 5.85 (1 H, dd, *J* 10.4 and 1.4, C*H*H=CH), 6.30 (2 H, ddd, *J* 17.3, 10.4 and 1.4, CH*H*=C*H*) and 7.32–7.40 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 66.31 (e), 128.25 (o), 128.27 (o), 128.34 (o), 128.45 (o), 128.59 (o), 131.08 (e), 135.91 (e) and 165.98 (e); *m/z* (EI) 162 (M^+, 27%), 144 (16), 117 (55), 107 (20), 91 (100), 79 (23), 65 (20), 55 (92) and 51 (14) (Found: M^+, 162.0681. $C_{10}H_{10}O_2$ requires *M*, 162.0681).

***tert*-Butyl 2-[(benzyloxycarbonyl)amino]-5-hydroxyhept-6-enoate 49**[23]

Cerium(III) chloride heptahydrate (1.34 g, 3.6 mmol) was added to a stirred solution of the enone **48** (1.251 g, 3.6 mmol) in methanol (9 cm^3) cooled to −20 °C after which the mixture was stirred at this temperature for *ca.* 10 min. Sodium borohydride (136 mg, 3.6 mmol) was then added portionwise to the mixture which, after being stirred at −20 °C for a further 15 min, was poured into water (20 cm^3) and extracted with ether (3 × 20 cm^3). The combined extracts were washed with brine (20 cm^3), dried ($MgSO_4$) and evaporated to afford an oil. Purification of this by flash chromatography (3:7, EtOAc–hexane) furnished the epimeric amino alcohols **49**[23] as a colourless oil (1.191 g, 95%); R_F 0.52 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3620w, 3580–3200br s, 3440s, 3340sh, 3100sh, 3075w, 3040w, 3010sh, 2980s, 2940s, 2870m and 1725vs; δ_H(250 MHz; $CDCl_3$) 1.45 (9 H, s, CMe_3), 1.49–1.94 (5 H, m, CH_2CH_2 and OH), 4.06–4.19 (1 H, m, 2-H), 4.23–4.36 (1 H, m, C*H*OH), 5.09 (2 H, s, PhCH_2), 5.13–5.25 (2 H, m, CH=CH_2), 5.36–5.43 (1 H, m, NH), 5.83 (1 H, ddd, *J* 16.9, 10.3 and 6.1, C*H*=CH_2) and 7.29–7.36 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 27.97 (o), 28.66 (e), 29.02 (e), 32.14 (e), 32.19 (e), 54.03 (o), 54.08 (o), 66.88 (e), 72.39 (o), 72.59 (o), 82.15 (e), 115.02 (e), 128.13 (o), 128.50 (o), 136.29 (e), 140.59 (o), 140.64 (o), 155.93 (e) and 171.43 (e); *m/z* (CI, NH_3) 350 [$(M + H)^+$, 44%], 311 (6), 294 (100), 276 (27), 250 (8), 232 (14), 203 (32), 186 (5), 142 (76), 106 (8) and 96 (5) [Found: $(M + H)^+$, 350.1967. $C_{19}H_{28}NO_5$ requires *M*, 350.1967].

3-Benzyloxycarbonyl-4-(*tert*-butoxycarbonyl)-2-phenylselanyl-7-vinyl-hexamethylhydro-1,3-oxazepine 50

A mixture of the vinyl amino alcohol **49** (857 mg, 2.45 mmol), phenylselanylacetaldehyde diethyl acetal (734 mg, 2.69 mmol) and PPTS (31 mg, 0.123 mmol) in anhydrous toluene (40 cm^3) was heated under Dean–Stark conditions for 2 h after which it was poured into saturated aqueous sodium hydrogen carbonate (30 cm^3) and extracted with ether (3 × 25 cm^3). The combined extracts were washed with water (25 cm^3) and brine (25 cm^3), dried ($MgSO_4$) and evaporated to afford an oil. Purification of this by flash chromatography (1:9, EtOAc–hexane) furnished a diastereoisomeric mixture of the *title compounds* **50** as a light yellow oil (0.937 g, 72%); R_F 0.31 (1:4, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3070w, 3040w, 3010sh, 2980s, 2940m, 2870sh, 1740s and 1705vs; δ_H(250 MHz; $CDCl_3$) 1.31–1.46 (9 H, s, CMe_3), 1.59–1.83 (3 H, m, C*H*HCH_2), 2.25–2.33 (1 H, m, CH*H*CH_2), 3.06–3.21 (2 H, m, PhSeCH_2), 3.77–4.00 (2 H, m, 4-H and 7-H), 4.99–5.70 (5 H, m, PhCH_2, NCHO and CH=CH_2), 5.73–5.84 (1 H, m, C*H*=CH_2) and 7.11–7.62 (10 H, m, ArH); *m/z* (EI) 531 (M^+, 4%), 374 (4), 332 (8), 318 (38), 304 (10), 276 (16), 260 (19), 232 (10), 214 (6), 186 (7), 169 (8), 91 (100), 78 (6) and 57 (21) (Found: M^+, 531.1524. $C_{27}H_{33}NO_5Se$ requires *M*, 531.1524).

(±)-1-Benzyloxycarbonyl-9-(*tert*-butoxycarbonyl)-1,3,4,7,8,9-hexahydro-2*H*-azonin-2-one 52

A solution of the selenoxide (418 mg, 0.764 mmol) derived from **50** and DBU (0.34 cm^3, 2.274 mmol) in anhydrous toluene (80 cm^3) was heated under reflux overnight and then

evaporated to give a dark oil. Purification of this by flash chromatography (0:1 to 1:19, EtOAc–hexane) furnished the *title compound* **52** as a colourless oil (213 mg, 75%); R_F 0.32 (1:4, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3120sh, 3100w, 3080w, 3045m, 3020s, 2985s, 2945s, 2910sh, 2880m, 1735vs and 1700vs; δ_H(250 MHz; $CDCl_3$) 1.35 (9 H, s, CMe_3), 1.77–2.34 (7 H, m, 2 × CH_2 and CH_2CHHCO), 3.53–3.76 (1 H, br m, $CHHCO$), 4.82–5.06 (1 H, br m, $CHCO_2$), 5.18 (2 H, q, J 12.0, $PhCH_2$), 5.36–5.45 (2 H, m, CH=CH) and 7.32–7.39 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 23.30 (e), 25.15 (e), 27.86 (o), 29.69 (e), 37.35 (e), 57.54 (o), 68.42 (e), 81.54 (e), 128.11 (o), 128.45 (o), 128.61 (o), 128.68 (o), 128.75 (o), 134.81 (e), 153.82 (e), 169.77 (e) and 179.85 (e); m/z (CI, NH_3) 391 [$(M + NH_4)^+$, 43%], 374 (96), 335 (86), 318 (100), 293 (6), 274 (63), 240 (4), 184 (5), 108 (18) and 91 (2) [Found: $(M + H)^+$, 374.1967. $C_{21}H_{28}NO_5$ requires M, 374.1967].

(±)-9-(*tert*-Butoxycarbonyl)heptahydroazonin-2-one 53

$Pd(OH)_2$ (51 mg, Pearlman's catalyst) was added to a solution of the Z-protected lactam **52** (102 mg, 0.273 mmol) in ethyl acetate (4 cm^3) after which the reaction vessel was evacuated and placed under an atmosphere of hydrogen. The reaction mixture was stirred vigorously overnight at room temperature after which it was filtered through Celite and evaporated to afford a crude light brown solid. Purification of this by flash chromatography (EtOAc) furnished the *title compound* **53** as a white crystalline solid (63 mg, 96%); mp 84–85 °C; R_F 0.26 (1:1, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 3440m, 3380w, 3100sh, 3070w, 3040sh, 2970vs, 2940vs, 2870s, 2825sh, 1740vs, 1700sh and 1685vs; δ_H(250 MHz; $CDCl_3$) 1.43 (4.5 H, s, CMe_3), 1.44 (4.5 H, s, CMe_3), 1.16–4.43 (12 H, m, 2 × CH_2), 4.05–4.22 (0.5 H, m, $CHCO_2Bu^t$), 4.45–4.59 (0.5 H, m, $CHCO_2Bu^t$) and 5.89–6.05 (1 H, m, NH); δ_C(100 MHz; $CDCl_3$) 22.02 (e), 22.55 (e), 24.10 (e), 25.87 (e), 26.07 (e), 27.24 (e), 27.91 (o), 29.72 (e), 32.50 (e), 34.06 (e), 34.22 (e), 38.32 (e), 53.51 (o), 56.61 (o), 81.91 (e), 82.54 (e), 170.87 (e), 171.88 (e), 174.89 (e) and 175.96 (e); m/z (CI, NH_3) 242 [$(M + H)^+$, 56%], 203 (4), 186 (100), 168 (1), 157 (3), 140 (31), 112 (3), 98 (2) and 56 (4) [Found: $(M + H)^+$, 242.1756. $C_{13}H_{24}NO_3$ requires M, 242.1756].

(S)-4-[(Benzyloxycarbonyl)amino]tetrahydrofuran-2-ol 38

DIBAL-H (1.0 mol dm^{-3} in hexanes; 50 cm^3, 50 mmol) was added dropwise during 30 min to a stirred, chilled solution of the lactone **37**[20] (5.88 g, 25.0 mmol) in dry dichloromethane (100 cm^3) at such a rate as to maintain the temperature between −93 and −95 °C. Stirring was continued at this temperature for 60 min, after which pre-cooled methanol (15 cm^3) was added dropwise to the mixture. The cooling bath was removed and the solution was stirred for a further 30 min and then treated with saturated aqueous sodium hydrogen carbonate (50 cm^3). It was then extracted with dichloromethane (4 × 150 cm^3) and the combined extracts were dried ($MgSO_4$) and evaporated. The resulting pale yellow semi-solid was subjected to flash chromatography (EtOAc) to yield the title *lactol* **38**, a 2:1 mixture of diastereoisomers, as colourless crystals (4.61 g, 78%); mp 60.5–76.5 °C (Found: C, 60.8; H, 6.3; N, 5.7. $C_{12}H_{15}NO_4$ requires C, 60.75; H, 6.4; N, 5.9%); R_F 0.44 (EtOAc); $[\alpha]_D^{22}$ −20.7→+2.96 (*c* 1.015 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3598m, 3431br s, 1713s and 1602w; δ_H(400 MHz; $CDCl_3$) 1.82–2.22 (2 H, m, 3,3-H), 3.84–4.20 (2 H, m, 5,5-H), 4.20–4.43 (1 H, m, 4-H), 4.47 (1 H, br s, OH), 5.06 (2 H, s, $PhCH_2$), 5.47–5.58 (1 H, m, 2-H), 5.93 (1 H, d, J 8.8, NH) and 7.26–7.34 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) (major diastereoisomer): 39.71 (e), 50.23 (o), 66.93 (e), 74.36 (e), 98.39 (o), 128.31 (o), 128.37 (o), 128.67 (o), 136.47 (e) and 156.11 (e); δ_C(100 MHz; $CDCl_3$) (minor diastereoisomer): 40.96 (e), 51.45 (o), 66.93 (e), 74.36 (e), 98.07 (o), 128.31 (o), 128.37 (o), 128.67 (o), 136.38 (e) and 156.11 (e); m/z (CI, NH_3) 238 [$(M + H)^+$, 3%], 220 (100), 162 (3), 147 (17), 130 (94), 108 (31), 91 (47), 84 (4), 78 (3), 69 (4), 56 (6) and 44 (5) [Found: $(M + H)^+$, 238.1080. $C_{12}H_{16}NO_4$ requires M, 238.1079].

Further elution of the column with EtOAc yielded (*S*)-2-[(benzyloxycarbonyl)amino]butane-1,4-diol **39** (521 mg, 8.7%); mp 49–50.5 °C (Found: C, 60.0; H, 7.4; N, 5.9. $C_{12}H_{17}NO_4$ requires C, 60.2; H, 7.2; N, 5.85%); R_F 0.31 (EtOAc); $[\alpha]_D^{22}$ −13.14 (*c* 1.035 in $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3688w, 3601w, 3234br s, 1702s and 1602w; δ_H(400 MHz; $CDCl_3$) 1.53–1.61 (1 H, m, 3-H_A), 1.70–1.78 (1 H, m, 3-H_B), 3.50–3.67 (4 H, m, 1,1-H and 4,4-H), 3.75–3.98 (3 H, m, 2-H and 2 × OH), 5.02 (1 H, d, J 12.4, $PhCHH$), 5.06 (1 H, d, J 12.2, $PhCHH$), 5.65 (1 H, d, J 8.5, NH) and 7.25–7.33 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 34.61 (e), 50.42 (o), 58.88 (e), 64.91 (e), 67.16 (e), 128.24 (o), 128.41 (o), 128.75 (o), 136.47 (e) and 157.44 (e); m/z (CI, NH_3) 240 [$(M + H)^+$, 100%], 196 (62), 149 (35), 132 (38), 108 (15) and 91 (11) [Found: $(M + H)^+$, 240.1236. $C_{12}H_{18}NO_4$ requires M, 240.1236].

***syn*- and *anti*-Amino diols 40a and 40b**

Vinylmagnesium bromide (1.0 mol dm^{-3} in THF; 50.0 cm^3, 50.0 mmol) was added dropwise during 60 min to a stirred, chilled (ice-bath) solution of the lactol **38** (2.970 g, 12.52 mmol) in anhydrous THF (20 cm^3), at such a rate as to maintain the temperature < 5 °C. The resulting mixture was stirred at this temperature for a further 1 h and then at room temperature for 3 h. The reaction was cautiously quenched by the dropwise addition of saturated aqueous ammonium chloride (50 cm^3) to the mixture after which the layers were separated and the aqueous phase was extracted with diethyl ether (3 × 200 cm^3). The combined organic layer and extracts were washed with brine (100 cm^3), dried ($MgSO_4$) and evaporated to give the crude amino diols **40** as a viscous yellow oil. To a solution of this in dry dichloromethane (20 cm^3) was added 4-dimethylaminopyridine (50 mg) and triethylamine (1.38 g, 13.6 mmol). The solution was chilled in ice and then treated with *tert*-butyl(chloro)dimethylsilane (2.07 g, 13.7 mmol). The resulting yellow solution was stirred overnight at room temperature after which it was poured into brine (20 cm^3) and extracted with dichloromethane (3 × 50 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated to a yellow oil. Flash chromatography (25–33% EtOAc in hexane) of this first gave the *anti*-isomer **40b** (1.265 g), a mixed fraction (275 mg) and then the *syn*-isomer **40a** (1.472 g), each as colourless oils (total yield: 3.012 g, 63% for two steps). Further elution of the column with ethyl acetate gave the starting lactol **38** (247 mg).

anti-(3S,5S)-5-(*Benzyloxycarbonyl*)*amino*-6-[(tert-*butyldimethyl*)*siloxy*]*hex*-1-*en*-3-*ol* **40b** (Found: C, 63.5; H, 8.85; N, 3.9. $C_{20}H_{33}NO_4Si$ requires C, 63.3; H, 8.8; N, 3.7%); R_F 0.49 (1:1, EtOAc–hexane); $[\alpha]_D^{22}$ −16.8 (*c* 1.36 in CCl_4); $\nu_{max}(CCl_4)/cm^{-1}$ 3617w, 3443br s, 3068w, 3034w, 3015w, 2954s, 2930s, 2884m, 2858s, 2739w, 2362w, 1946w and 1703s; δ_H(400 MHz; $CDCl_3$) 0.04 (6 H, s, $SiMe_2$), 0.87 (9 H, s, CMe_3), 1.52 (1 H, ddd, J 3.2, 10.7 and 13.9, 4-H_A), 1.74 (1 H, ddd, J 2.6, 10.7 and 13.9, 4-H_B), 3.59 (1 H, dd, J 3.1 and 10.0, 6-H_A), 3.72 (1 H, dd, J 4.2 and 10.0, 6-H_B), 3.87 (1 H, br s, OH), 3.93 (1 H, m, 5-H), 4.16 (1 H, m, 3-H), 5.03–5.15 (3 H, m) and 5.25 (1 H, d, J 17.2, $PhCH_2$ and $CH=CH_2$), 5.31 (1 H, d, J 8.7, NH), 5.87 (1 H, ddd, J 5.3, 10.5 and 17.2, $CH=CH_2$) and 7.27–7.36 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) −5.28 (o), 18.46 (e), 26.06 (o), 40.28 (e), 49.65 (o), 65.59 (e), 67.23 (e), 68.97 (o), 114.19 (e), 128.38 (o), 128.43 (o), 128.75 (o), 136.50 (e), 140.55 (o) and 157.49 (e); m/z (CI, NH_3) 380 [$(M + H)^+$, 16%], 273 (20), 272 (100), 220 (15), 116 (18), 108 (12) and 91 (15) [Found: $(M + H)^+$], 380.2257. $C_{20}H_{34}NO_4Si$ requires M, 380.2257].

syn-(3R,5S)-5-(*Benzyloxycarbonyl*)*amino*-6-[(tert-*butyldimethyl*)*siloxy*]*hex*-1-*en*-3-*ol* **40a** (Found: C, 63.4; H, 8.8; N, 3.7. $C_{20}H_{33}NO_4Si$ requires C, 63.3; H, 8.8; N, 3.7%); R_F 0.44 (1:1, EtOAc–hexane); $[\alpha]_D^{22}$ −20.4 (*c* 1.01 in CCl_4); $\nu_{max}(CCl_4)/cm^{-1}$ 3616w, 3445br m, 3090w, 3068w, 3034w,

2954s, 2929s, 2884m, 2857m, 2740w, 1724s and 1645w; δ_H(400 MHz; $CDCl_3$) 0.03 (6 H, s, $SiMe_2$), 0.87 (9 H, s, CMe_3), 1.69–1.84 (2 H, m, 4,4-H), 2.90 (1 H, br s, OH), 3.65 (2 H, br s, 6,6-H), 3.80–3.90 (1 H, m, 5-H), 4.18–4.22 (1 H, m, 3-H), 5.05–5.27 (5 H, m, NH, $PhCH_2$ and $CH{=}CH_2$), 5.86 (1 H, ddd, *J* 17.1, 10.4 and 5.6, $CH{=}CH_2$) and 7.27–7.36 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) −5.48 (o), −5.46 (o), 18.29 (e), 25.88 (o), 39.21 (e), 49.95 (o), 65.02 (e), 66.79 (e), 70.31 (o), 114.51 (e), 128.16 (o), 128.54 (o), 136.49 (e), 140.76 (o) and 156.17 (e); *m*/*z* (CI, NH_3) 380 [(M + H)$^+$, 100%], 362 (20), 273 (11), 272 (51), 246 (22), 108 (16) and 91 (15) [Found: (M + H)$^+$, 380.2257. $C_{20}H_{34}NO_4Si$ requires *M*, 380.2257].

(4*S*,6*S*)-3-Benzyloxycarbonyl-4-[(*tert*-butyldimethylsiloxy)-methyl]-6-vinyl-2,4,5,6-tetrahydro-1,3-oxazine 41b

A mixture of the *anti*-amino alcohol **40b** (190 mg, 0.501 mmol), paraformaldehyde (53.1 mg, 1.77 mmol) and toluene-4-sulfonic acid (5.1 mg) in toluene (30 cm^3) was heated in a flask fitted with a Dean–Stark trap for 3 h after which it was poured into saturated aqueous sodium hydrogen carbonate (30 cm^3) and extracted with diethyl ether (3 × 50 cm^3). The combined extracts were washed with brine (50 cm^3), dried (K_2CO_3) and evaporated to give a yellow oil which, purified by flash chromatography (1:9, EtOAc–hexane), afforded the title *oxazine* **41b** as a viscous colourless oil (128 mg, 65%) (Note: compound **41b** exists as a mixture of rotamers in $CDCl_3$ at room temperature) (Found: C, 64.15; H, 8.75; N, 3.7. $C_{21}H_{33}NO_4Si$ requires C, 64.4; H, 8.5; N, 3.6%); R_F 0.48 (1:4, EtOAc–hexane); $[\alpha]_D^{22}$ −66.2 (*c* 1.14 in $CHCl_3$); ν_{max}(CCl_4)/cm^{-1} 3090w, 3068w, 3034w, 2955s, 2929s, 2883m, 2857s and 1711s; δ_H(400 MHz; $CDCl_3$) −0.04–0.09 (6 H, m, $SiMe_2$), 0.83–0.92 (9 H, m, CMe_3), 1.68–1.89 (2 H, m, 5,5-H), 3.70–3.90 (2 H, m, CH_2OSi), 4.19–4.46 (2 H, m, 4-H and 6-H), 4.65 (d, *J* 10.3) and 4.55 (d, *J* 10.0, 1 H, 2-H_A), 5.10–5.28 (4 H, m, $PhCH_2$ and $CH{=}CH_2$), 5.63 (d, *J* 9.9) and 5.52 (d, *J* 10.3, 1 H, 2-H_B), 5.80 (1 H, ddd, *J* 17.3, 10.7 and 5.4, $CH{=}CH_2$) and 7.28–7.37 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) −5.45 (o), 18.22 (e), 25.86 (o), 30.52 (e), 50.00 (o), 50.62 (o), 62.26 (e), 62.64 (e), 67.40 (e), 72.71 (e), 73.01 (e), 73.79 (o), 73.99 (o), 115.77 (e), 128.04 (o), 128.12 (o), 128.52 (o), 136.39 (e), 137.98 (o) and 154.48 (e); *m*/*z* (CI, NH_3) 392 [(M + H)$^+$, 100%], 334 (16), 108 (16), 100 (95), 91 (33) and 56 (22) [Found: (M + H)$^+$, 392.2278. $C_{21}H_{34}NO_4Si$ requires *M*, 392.2257].

(4*S*,6*R*)-3-Benzyloxycarbonyl-4-[(*tert*-butyldimethylsiloxy)-methyl]-6-vinyl-2,4,5,6-tetrahydro-1,3-oxazine 41a

A mixture of the *syn*-amino alcohol **40a** (248 mg, 0.654 mmol), paraformaldehyde (68.3 mg, 2.27 mmol) and toluene-4-sulfonic acid (7.2 mg) in toluene (30 cm^3) was heated in a flask fitted with a Dean–Stark trap for 3 h after which it was poured into saturated aqueous sodium hydrogen carbonate (30 cm^3) and extracted with diethyl ether (3 × 50 cm^3). The combined extracts were washed with brine (50 cm^3), dried (K_2CO_3) and evaporated to give a yellow oil which, purified by flash chromatography (1:4, EtOAc–hexane), afforded the title *oxazine* **41a** as a colourless oil (92 mg, 36%) (Found: C, 64.4; H, 8.6; N, 3.6. $C_{21}H_{33}NO_4Si$ requires C, 64.4; H, 8.5; N, 3.6%); R_F 0.39 (1:4, EtOAc–hexane); $[\alpha]_D^{22}$ −79.5 (*c* 1.11 in $CHCl_3$); ν_{max}(CCl_4)/cm^{-1} 3035w, 2955m, 2929m, 2884w, 2857w and 1713s; δ_H(400 MHz; $CDCl_3$) 0.00 (3 H, s, SiMe), 0.01 (3 H, s, SiMe), 0.86 (9 H, s, CMe_3), 1.93 (1 H, ddd, *J* 14.4, 6.5 and 4.2, 5-H_{eq}), 1.99 (1 H, dt, *J* 14.4 and 10.6, 5-H_{ax}), 3.70–3.97 (2 H, m, CH_2OSi), 3.96–4.05 (1 H, m, 4-H), 4.25–4.30 (1 H, m, 6-H), 4.86 (1 H, d, *J* 10.0, 2-H_A), 5.13–5.15 (3 H, m, $PhCH_2$ and $CH{=}CHH$), 5.20 (1 H, d, *J* 10.0, 2-H_B), 5.28 (2 H, dt, *J* 17.2 and 1.3, $CH{=}CHH$), 5.85 (1 H, ddd, *J* 17.2, 10.5 and 5.6, $CH{=}CH_2$) and 7.28–7.35 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) −5.47 (o), −5.48 (o), 18.23 (e), 25.87 (o), 29.72 (e), 53.69 (o), 64.09 (e), 67.33 (e), 72.99 (e), 73.40 (o), 115.58 (e), 127.99 (o), 128.12 (o), 128.53 (o), 136.32 (e), 138.22 (o) and 155.33 (e); *m*/*z* (CI, NH_3) 393 [(M + H)$^+$, 100%], 260 (15), 130 (10), 108 (32) and 91 (31) [Found: (M + H)$^+$, 392.2257. $C_{21}H_{34}NO_4Si$ requires *M*, 392.2257].

(2*RS*,4*S*,6*S*)-3-Benzyloxycarbonyl-4-[(*tert*-butyldimethylsiloxy)-methyl]-2-(phenylselanylmethyl)-6-vinyl-2,4,5,6-tetrahydro-1,3-oxazine 42

Amberlite™ IR-120 (plus) (233 mg) was suspended in a solution of the *anti*-amino alcohol **40a** (500 mg, 1.32 mmol) and phenylselanylacetaldehyde diethyl acetal (433 mg, 1.59 mmol) in anhydrous toluene (20 cm^3), in a flask fitted with a Dean–Stark trap. The mixture was heated under reflux for 3.5 h after which the resin was filtered off and the filtrate was evaporated to give a yellow oil which, purified by flash chromatography (1:19→1:9, EtOAc–hexane), afforded the title *oxazines* **42**, a mixture of diastereoisomers, as a pale yellow oil (427 mg, 58%); R_F 0.32 and 0.36 (1:4, EtOAc–hexane); ν_{max}(CCl_4)/cm^{-1} 3069w, 3034w, 2955s, 2929s, 2884m, 2857m, 1702s, 1648w, 1579w, 1558w, 1551w, 1539w and 1523w; δ_H(400 MHz; $CDCl_3$) 0.00–0.09 (6 H, m, $SiMe_2$), 0.87 and 0.86 (9 H, CMe_3), 1.65–1.77 (1 H, m, 5-H_A), 1.91 (1 H, br d, *J* 13.9, 5-H_B), 3.42–3.81 (4 H, m, $PhSeCH_2$ and CH_2OSi), 4.21–4.46 (2 H, m, 4-H and 6-H), 5.03–5.31 (4 H, m, $PhCH_2$ and $CH{=}CH_2$), 5.75 (1 H, ddd, *J* 17.3, 10.6 and 5.3, $CH{=}CH_2$), 5.83–5.93 (1 H, m, 2-H) and 7.13–7.61 (10 H, m, ArH); δ_C(100 MHz; $CDCl_3$) −5.26 (o), −5.19 (o), 18.41 (e), 26.05 (o), 33.26 (e), 36.98 (e), 50.34 (o), 52.43 (o), 62.49 (e), 64.70 (e), 67.41 (e), 67.56 (e), 72.77 (o), 81.06 (e), 84.23 (e), 115.93 (e), 116.19 (e), 127.06 (o), 127.22 (o), 128.25 (o), 128.35 (o), 128.45 (o), 128.74 (o), 129.19 (o), 129.23 (o), 129.39 (o), 129.63 (o), 132.96 (o), 133.22 (o), 133.84 (o), 136.39 (e), 137.72 (o), 138.87 (o), 154.44 (e) and 154.61 (e); *m*/*z* (CI, NH_3) 562 [(M + H)$^+$, 3%] and 362 (100) [Found: (M + H)$^+$, 562.1890. $C_{28}H_{40}NO_4SeSi$ requires *M*, 562.1890].

(8*S*)-1-Benzyloxycarbonyl-8-[(*tert*-butyldimethylsiloxy)-methyl]-3,4,7,8-tetrahydroazocin-2(1*H*)-one 44

Sodium hydrogen carbonate (36 mg, 0.43 mmol) and sodium periodate (245 mg, 0.115 mmol) were added to a stirred solution of the selenide **42** (204 mg, 0.359 mmol) in methanol (17 cm^3), dichloromethane (4 cm^3) and water (3.0 cm^3) to give a thick white precipitate within a few min. Stirring was continued for 60 min after which the mixture was poured into brine (100 cm^3) and extracted with dichloromethane (3 × 100 cm^3). The combined extracts were dried (K_2CO_3) and evaporated to give the crude selenoxide as a yellow viscous oil (205 mg, 99%). A solution of this, 1,8-diazabicyclo[5.4.0]undec-7-ene (161 mg, 1.06 mmol) and the silyl ketene acetal **35a** (336 mg, 1.79 mmol) in dry toluene (36 cm^3) was heated under reflux overnight. The mixture was then evaporated and the residue dissolved in a little dichloromethane and the solution filtered through a plug of silica. The filtrate was evaporated to give a brown oil which was subjected to flash chromatography (1:1→0:1, CH_2Cl_2–hexane) to yield the title *lactam* **44** as a colourless oil (45 mg, 31%); R_F 0.36 (2:1, CH_2Cl_2–hexane); $[\alpha]_D^{24}$ +19.2 (*c* 0.53 in CCl_4); ν_{max}(CCl_4)/cm^{-1} 3068w, 3011w, 2955m, 2929m, 2858m, 1718s, 1559w, 1552w, 1544w and 1500m; δ_H(400 MHz; $CDCl_3$) 0.02 (3 H, s, SiMe), 0.03 (3 H, s, SiMe), 0.86 (9 H, s, CMe_3), 2.23–2.32 (3 H, m) and 2.03–2.12 (4 H, m, 4-H_A, 4-H_B, 7-H_A and 7-H_B), 2.55 (1 H, ddd, *J* 3.2, 5.8 and 11.4, 3-H_A), 2.85 (1 H, dt, *J* 4.6 and 11.6, 3-H_B), 3.76 (1 H, dd, *J* 8.0 and 10.0, $SiOCH_A$), 3.87 (1 H, dd, *J* 6.0 and 9.9, $SiOCH_B$), 3.99–4.05 (1 H, m, 8-H), 5.15 (1 H, d, *J* 12.3, $PhCHH$), 5.20 (1 H, d, *J* 12.3, $PhCHH$), 5.72–5.85 (2 H, m, 5-H and 6-H) and 7.30–7.38 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) −5.41 (o), −5.37 (o), 18.21 (e), 25.05 (e), 25.85 (o), 27.62 (e), 41.91 (e), 55.27 (o), 64.89 (e), 67.90 (e), 128.12 (o), 128.38 (o), 128.60 (o), 130.02 (o), 130.92 (o), 135.54 (e), 154.54 (e) and 182.38 (e); *m*/*z* (CI, NH_3) 404 [(M + H)$^+$, 100%], 364 (13), 362 (15), 312 (11), 289 (20), 279 (32), 270 (20), 108 (24) and 91 (39) [Found: (M + H)$^+$, 404.2257. $C_{22}H_{34}NO_4Si$ requires *M*, 404.2257].

7-Bromohept-1-en-3-ol 57[25]

A solution of DIBAL-H (1.0 mol dm^{-3} in CH_2Cl_2; 37 cm^3, 37 mmol) was added dropwise during 90 min to a stirred solution of 5-bromovaleronitrile **56** (5.0 g, 31 mmol) in dry dichloromethane (15 cm^3) cooled to −78 °C, the temperature being kept < −68 °C. The mixture was stirred for an additional 1 h, after which it was quenched with the addition of methanol (1.0 cm^3). The reaction mixture was allowed to warm to room temp. and then poured into ice-cold dilute aqueous sulfuric acid (1 mol dm^{-3}; 120 cm^3) and stirred vigorously. The aqueous phase was separated and extracted with ether (3 × 50 cm^3), and each extract was successively washed with brine (2 × 100 cm^3). The combined organic phase and extracts were dried ($MgSO_4$) and evaporated to yield crude 5-bromopentanal as a pale yellow oil. This was dissolved in THF (10 cm^3) and added to a pre-cooled (−78 °C) solution of vinylmagnesium bromide (1.0 mol dm^{-3} in THF; 74 cm^3, 0.074 mol) in THF (15 cm^3). The reaction mixture was stirred for 20 min and then quenched by the addition of saturated aqueous ammonium chloride. After this it was allowed to warm to room temperature, when it was poured into saturated aqueous ammonium chloride (100 cm^3) and extracted with ether (3 × 50 cm^3). The combined organic phases were dried ($MgSO_4$) and evaporated to give a pale yellow oil, purification of which by flash column chromatography (1:5, ether–hexane) gave *title compound* **57** as a colourless oil (3.46 g, 58% for two steps) (Found: C, 43.4; H, 6.9; Br, 41.1. $C_7H_{13}BrO$ requires C, 43.5; H, 6.8; Br, 41.4%); R_F 0.33 (1:1, hexane–ether); ν_{max}(KBr)/cm^{-1} 3400m and 1643w; δ_H(250 MHz; $CDCl_3$) 1.43–1.62 (4 H, m, $CH_2CH_2CH_2Br$), 1.84–1.95 (2 H, m, CH_2CHOH), 3.42 (2 H, t, *J* 6.7, CH_2Br), 4.12 (1 H, apparent q, *J* 6.1, C*H*OH), 5.18 (2 H, m, CH=CH_2) and 5.81–5.94 (1 H, m, C*H*=CH_2); δ_C(100 MHz; $CDCl_3$) 24.3 (e), 32.9 (e), 33.9 (e), 36.3 (e), 73.1 (o), 115.2 (o) and 141.3 (o); *m/z* (EI) 191 [(M − H)$^+$ (^{79}Br), 1%], 175 (67), 163 (3), 149 (1), 135 (14), 121 (1), 113 (8), 96 (20), 95 (100), 85 (46) and 83 (37) [Found: (M − OH)$^+$, 175.0124. $C_7H_{12}Br$ requires *M*, 175.0123].

7-Azidohept-1-en-3-ol 58

Tetramethylguanidinium azide[26] (6.39 g, 40 mmol) was added to a solution of the bromo alcohol **57** in dry dichloromethane (70 cm^3) at room temperature and the reaction mixture stirred under argon for *ca.* 70 h. It was then poured into water (100 cm^3) and extracted with ether (3 × 150 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated to give a pale yellow oil, purification of which by flash column chromatography (1:3, ether–hexane) gave the title *hydroxy-azide* **58** as a colourless oil which slowly turned brown when stored in air at room temperature (2.10 g, 99%); R_F 0.33 (1:1, hexane–ether); ν_{max}(KBr)/cm^{-1} 3400m and 2101s; δ_H(250 MHz; $CDCl_3$) 1.36–1.69 (6 H, m, $CH_2CH_2CH_2Br$), 3.29 (2 H, t, *J* 6.8, CH_2N_3), 4.11 (1 H, m, C*H*OH), 5.10–5.28 (2 H, m, CH=CH_2) and 5.80–5.93 (1 H, m, C*H*=CH_2); δ_C(100 MHz; $CDCl_3$) 22.3 (e), 29.0 (e), 36.6 (e), 51.6 (e), 73.1 (o), 115.0 (e) and 141.3 (o); *m/z* (CI, NH_3) 173 [(M + NH_4)$^+$, 100%], 156 (21), 142 (8), 130 (5), 128 (65), 126 (3), 111 (6), 110 (80), 108 (5) and 97 (4) [Found: (M + NH_4)$^+$, 173.1387. $C_7H_{17}N_4O$ requires *M*, 173.1402].

7-(Benzyloxycarbonyl)aminohept-1-en-3-ol 59

A solution of tin(II) chloride, prepared by dissolving $SnCl_2{\cdot}2H_2O$ (1.163 g, 5.15 mmol) in methanol (15 cm^3) and water (1 drop), was stirred at room temperature for 15 min and then cooled to 0 °C and treated with a solution of the azide **58** (200.0 mg, 1.289 mmol) in methanol (2 cm^3 + 2 × 1 cm^3 rinse). The reaction mixture was warmed to room temperature and stirred overnight. The mixture was evaporated, taken up in dioxane (10 cm^3) and saturated aqueous sodium hydrogen carbonate (10 cm^3) and treated with benzyl chloroformate (0.30 cm^3, 2.10 mmol). After being stirred at room temperature for 5 h, the reaction mixture was poured into brine (50 cm^3) and extracted with ether (4 × 50 cm^3). The combined organic extracts were dried ($MgSO_4$) and evaporated to give a yellow oil, purification of which by flash column chromatography (7:3, ether–hexane) gave the *carbamate* **59** as a very pale yellow oil (298 mg, 88% for 2 steps) (Found: C, 68.1; H, 8.1; N, 5.6. $C_{15}H_{21}NO_3$ requires C, 68.4; H, 8.0; N, 5.3%); R_F 0.05 (1:1, hexane–ether); ν_{max}(KBr)/cm^{-1} 3335 and 1702; δ_H(400 MHz; $CDCl_3$) 1.25–1.54 (6 H, m, $CH_2CH_2CH_2$), 1.78 (1 H, br s, OH), 3.17–3.20 (2 H, m, CH_2N), 4.08 (1 H, apparent q, *J* 5.9, C*H*OH), 4.83 (1 H, br s, NH), 5.08–5.22 (4 H, m, CH=CH_2 and PhCH_2), 5.80–5.89 (1 H, m, C*H*=CH_2) and 7.28–7.37 (5 H, m, ArH); δ_C(100 MHz; $CDCl_3$) 22.5 (e), 29.9 (e), 36.5 (e), 41.0 (e), 66.7 (e), 73.0 (o), 114.7 (e), 128.1 (o), 128.6 (o), 136.7 (e), 141.2 (o) and 156.5 (e); *m/z* (CI, NH_3) 281 [(M + NH_4)$^+$, 100%], 264 (52), 246 (78), 233 (11), 220 (11), 202 (52), 185 (6), 173 (8), 156 (4), 139 (4) and 130 (16) [Found: (M + H)$^+$, 264.1600. $C_{15}H_{22}NO_3$ requires *M*, 264.1600].

3-Benzyloxycarbonyl-2-phenylselanylmethyl-8-vinyl-2,4,5,6,7,8-hexahydro-1,3-oxazocine 60

Toluene (75 cm^3) was refluxed under argon for 1 h in a flask fitted with a Dean–Stark trap and then cooled to room temperature. The amino alcohol **59** (700 mg, 2.658 mmol), phenylselanylacetaldehyde diethyl acetal (944.2 mg, 3.455 mmol) and pyridinium toluene-4-sulfonate (33 mg, 0.133 mmol) were added to the flask and the mixture was refluxed for 1.25 h. It was then cooled to room temperature and poured into saturated aqueous sodium hydrogen carbonate (100 cm^3). The aqueous phase was separated and extracted with ether (3 × 100 cm^3) and the combined organic phases were dried ($MgSO_4$) and evaporated. Purification of the residue by flash column chromatography (9:1 to 6:1, hexane–EtOAc, then ether) gave recovery of starting material **59** (79.1 mg, 11%), followed by the title selanylacetal **60** as an inseparable mixture of diastereoisomers (639 mg, 54%) (Found: C, 62.3; H, 6.2; N, 3.4. $C_{23}H_{27}NO_3Se$ requires C, 62.2; H, 6.1; N, 3.15%); R_F 0.39 (4:1, hexane–EtOAc); ν_{max}(CCl_4)/cm^{-1} 1701s; δ_H(250 MHz; $CDCl_3$) 1.50–1.76 (6 H, m, $CH_2CH_2CH_2$), 2.93–3.25 (3 H, m, CH*H*N and CH_2SePh), 3.49 (0.56 H, br dt, *J* 11.4 and 3.0, CH*H*N), 3.62 (0.44 H, br dt, *J* 14.0 and 3.6, C*H*HN), 3.92–4.02 (1 H, br m, CHO), 5.08–5.33 (4 H, m, CH_2OPh and CH=CH_2), 5.45 (0.56 H, dd, *J* 8.0 and 5.0, NCH′O), 5.58 (0.44 H, dd, *J* 7.7 and 5.2, NCHO), 5.77 (1 H, ddd, *J* 17.2, 10.6 and 4.6, C*H*=CH_2) and 7.13–7.56 (10 H, m, ArH); δ_C(50 MHz; $CDCl_3$) 21.9 (e), 26.7 (e), 27.6 (e), 30.8 (e), 31.0 (e), 32.6 (e), 32.7 (e), 40.6 (e), 41.3 (e), 66.8 (e), 66.9 (e), 79.4 (o), 79.8 (o), 85.2 (o), 85.5 (o), 114.6 (e), 126.8 (o), 126.9 (o), 127.7 (o), 127.9 (o), 128.4 (o), 128.9 (o), 130.3 (e), 132.55 (o), 132.61 (o), 136.49 (e), 136.55 (e), 138.5 (o), 138.6 (o), 154.4 (e) and 156.2 (e); *m/z* (CI, NH_3) 446 [(M + H)$^+$, 95%], 444 (7), 307 (10), 291 (25), 290 (100), 274 (2), 263 (3), 246 (7), 218 (1), 198 (1), 174 (4), 158 (5) and 156 (37) [Found: (EI) M$^+$, 445.1160. $C_{23}H_{27}NO_3{}^{80}Se$ requires *M*, 445.1156].

(*Z*)-1-Benzyloxycarbonyl-1,2,3,4,7,8,9,10-octahydroazecin-2-one 62

A solution of the selanylacetal **60** (51 mg, 0.114 mmol) in methanol (6 cm^3) and water (1 cm^3) was treated with sodium periodate (74 mg, 0.35 mmol) and sodium hydrogen carbonate (11.2 mg, 0.133 mmol). The mixture was stirred at room temperature for 1 h after which it was poured into brine (40 cm^3) and extracted with dichloromethane (4 × 20 cm^3). The combined organic phases were dried (K_2CO_3) and evaporated to give a colourless oil. This was taken up in dry xylene (18 cm^3), treated with DBU (0.5 cm^3, 0.33 mmol) and refluxed in a flask fitted with a Dean–Stark trap for 19 h. The resulting brown–black reaction mixture was evaporated to give a brown solid. Purification of this by flash column chromatography (0:100 to 1:10, EtOAc–hexane) gave the *title lactam* **62** as a colourless oil, which solidified to a white solid after refrigeration for several weeks (24.4 mg, 78%); mp 41–42 °C

(hexane) (Found: C, 71.1; H, 7.3; N, 4.8. $C_{17}H_{22}NO_3$ requires C, 71.1; H, 7.4; N, 4.9%); R_F 0.53 (1:4, EtOAc–hexane); $\nu_{max}(CCl_4)/cm^{-1}$ 1732s, 1707s and 1686w (Note: the product exists as a mixture of rotamers in $CDCl_3$ at room temperature); δ_H(250 MHz; $CDCl_3$) 1.51–1.67 (4 H, m, CH_2CH_2), 2.1 (2 H, br m, $CH_2C{=}C$), 2.2 (2 H, br m, $CH_2C{=}C$), 3.0 (2 H, br m, CH_2CO), 3.86–3.90 (2 H, br m, CH_2N), 5.22–5.32 (3 H, m, $CH{=}CH$ and $PhCH_2O$), 5.42–5.53 (1 H, m, $CH{=}CH$) and 7.35–7.43 (5 H, m, ArH); δ_C(50 MHz; C_6D_6) 22.6 (e), 23.2 (e), 25.7 (e), 26.6 (e), 38.9 (e), 46.0 (e), 68.4 (e), 127.5 (o), 128.0 (o), 128.4 (o), 128.7 (o), 131.5 (o), 135.8 (o), 154.8 (e) and 175.7 (e); *m/z* (CI, NH_3) 305 [$(M + NH_4)^+$, 14%], 290 (67), 288 (100), 263 (2), 246 (4), 222 (2), 171 (10), 154 (20), 152 (6), 138 (2), 125 (2), 110 (2) and 108 (8) [Found: $(M + H)^+$, 288.1596. $C_{17}H_{22}NO_3$ requires *M*, 288.1600].

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