A Diastereoselective Approach to α-Allyl-β-Amino Acids using the Ireland Enolate Claisen Rearrangement

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Ireland enolate–Claisen rearrangements of the esters **11** derived from a range of *N*-alkoxycarbonyl- and related β-alanines **9** and allylic alcohols (*e.g.* **10**) generally lead to good yields of α-allyl-β-amino acid derivatives **13**, isolated for convenience as the corresponding esters **14**. The *N-tert*-butoxycarbonyl (BOC) derivatives **15** proved to be especially useful and led to good to excellent yields of the α-allyl-β-amino acid derivatives **16** and **17**, with diastereoselectivities usually in excess of 4:1. One set of optimum conditions consists of rearrangements of the *N*-BOC derivatives **15** by sequential treatment with lithium diisopropylamide and trimethylsilyl chloride [3 equiv. of each] in tetrahydrofuran at −78 °C followed by ~4 h under reflux. Isolated chemical yields of the derived methyl esters **16** and **17** were generally in the range 70–88%. The stereochemical outcome of the rearrangements was deduced by conversion of the initial silyloxymethyl derivatives **16d** and **17d**, derived from the esters (*E*)-**15d** and (*Z*)-**15d**, into the corresponding *cis*- and *trans*-butyrolactones **24** and **26**, respectively. The synthetic utility was further demonstrated by conversions of the initial hydroxyethyl derivatives **19** and **20** into the valerolactones **28** and **29** and of the *syn*-isomer **19** into the piperidine **30**. A chair-like transition state **31** is consistent with the direct relationship between the allylic alcohol geometry and the nature of the major diastereoisomer of the α-allyl-β-amino acid derivatives (**16** and **17**) obtained; the *E*-lithio enolates of the starting esters are presumably favoured due to intramolecular complexation with the enolised carbamate function.

Our recent synthesis of (−)-α-kainic acid **1**[1] featured the pyrrolidines **2** as key intermediates, obtained by a stereospecific alicyclic enolate Claisen rearrangement[2] of the azalactone **3**. The idea of utilising *O*-silyl enolates as components of Claisen rearrangements was first reported by Ireland and his colleagues[3] and has subsequently become a highly valuable and much exploited version of this classical [3.3]-sigmatropic rearrangement.[4] The extrapolation to unsaturated lactone enolates was first defined by Danishefsky[5] and has subsequently been developed in a number of directions.[2,6] Despite this, there were times during our kainic acid synthesis when problems arose which caused us to contemplate alternative strategies to this target. One of these occurred to us when considering the key intermediates **2**, the products expected[2,6] from the central enolate Claisen rearrangement of the azalactone **3**. These should also be obtainable by cyclisation of the amino alcohol derivatives **4**. These can also be regarded as α-allylated-β-amino acids and hence should be available from an acyclic enolate Claisen rearrangement of the esters **5**, which, in turn, should be readily prepared from a suitably protected β-amino acid and an allylic alcohol. By a combination of the incorporation of further substituents into one or both of these components as well as functional group manipulation of the initial products (*e.g.* **4**), this transformation could constitute a viable route to a variety of β-amino acids in general,[7] which are valuable precursors to β-lactams amongst a variety of other targets. At the same time, we realised that this methodology could find applications in the elaboration of various members of the pyrrolizidin-1-ylmethanols **6**[8] and higher homologues thereof, as the putative enolate Claisen products **7** could act as versatile precursors of these ring systems. The intermediates **7** would be available from the relatively simple homoproline esters **8**, given the success of this version of the Claisen rearrangement. We therefore undertook a series of model studies in order to define the viability, scope, stereoselectivity and limitations of this method; the outcome of these are reported herein in detail.[9]

Our first trials were conducted using the esters **11**, derived efficiently from a series of *N*-protected-β-alanines **9** and (*E*)-but-2-en-1-ol (crotyl alcohol) **10**, using the DCC–DMAP coupling method.[10] The objective was, therefore, to convert these into the corresponding *O*-silyl enolates **12**, in the expectation[2–5] that these would then rearrange when heated to 60–100 °C[4] to the silyl esters **13**, which would subsequently be converted into the methyl esters **14** for ease of characterization. The first experiments using the *N*-benzyloxycarbonyl derivative **11a** were not, however, especially encouraging. Treatment of this with a variety of non-nucleophilic bases including lithium diisopropylamide (LDA), lithium bis(trimethylsilyl)amide (LHMDS) and the potassium analogues of these, typically in

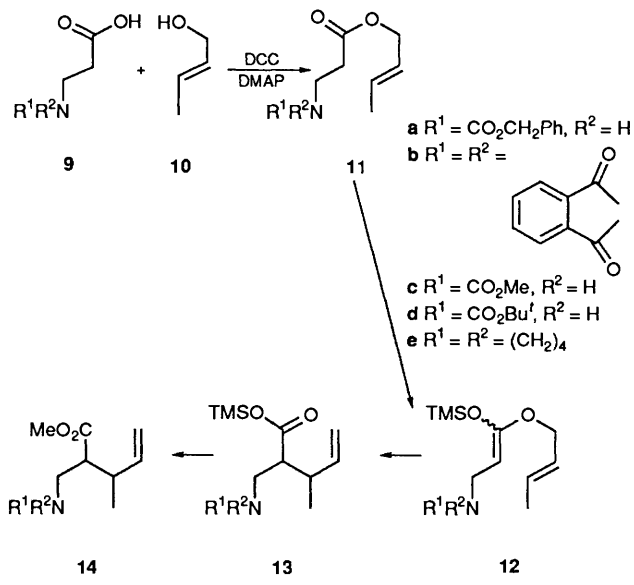
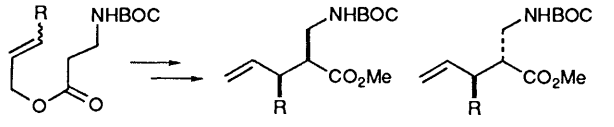


Table 1 Enolate Claisen rearrangements of (*E*)- and (*Z*)-alk-2-en-yl *N*-BOC-β-alanines **15** and **21**



		Ratios		Total yield[a] (%)
a R=Me [=**11d**]	(*E*)-isomer	86	14	88
	(*Z*)-isomer	12	88	73
b R=Ph	(*E*)-isomer	56	44	31
	(*Z*)-isomer	77	23	40
c R=Pr^i	(*E*)-isomer	80	20	84
	(*Z*)-isomer	81	19	81
d R=CH_2OTBDMS	(*E*)-isomer	92	8	77
	(*Z*)-isomer	6	94	68
e R=$(CH_2)_2$OTBDMS	(*E*)-isomer	92	8	75[b]
	(*Z*)-isomer	15	85	70[b]

[a] Total yields refer to pure products exhibiting satisfactory spectroscopic and analytical data. [b] Isolated as the corresponding hydroxy esters **19** and **20**.

tetrahydrofuran (THF) at low temperatures[2-5] followed by trimethylsilyl chloride (TMSCl) (or *tert*-butyldimethylsilyl chloride (TBDMSCl) and heating to reflux resulted in the isolation of little of the desired products **14a** but rather what appeared to be C-silylated material arising from metallation at the benzylic position and also substantial amounts of benzyl alcohol. Such problems have been observed previously in related rearrangements of prop-2-ynyl esters.[11] Perhaps not surprisingly, due to the potential for β-elimination, rearrangements of the phthalimido derivative **11b** also proved difficult. A low yield of the esters **14b** was obtained, ominously as a *ca.* 2:1 mixture of diastereoisomers, when the ester **11b** was treated with a premixed solution of LDA (3 equiv.) and TBDMSCl in THF–HMPA at −110 °C, followed by reflux. The premix method was introduced and used successfully by Ireland to prevent β-eliminations prior to enolate trapping.[12] Higher temperatures resulted in extensive or exclusive β-elimination, perhaps in both senses as substantial amounts of (*E*)-but-2-en-1-ol were also isolated. Use of less than 3 equiv. of base [LDA or KHMDS, in THF or dimethoxyethane (DME)] was unsuccessful, a feature noted previously in enolate Claisen rearrangements.[2,11] We were pleased to find however that when the *N*-methoxycarbonyl ester **11c** was treated with LDA (3 equiv.) in THF at −78 °C followed by TMSCl (3 equiv.) and the resulting mixture refluxed for ~4 h, the desired ester **14c** was isolated in 71% yield, after facile hydrolysis of the initial silyl ester **13c** and treatment with diazomethane. Equally encouraging was the diastereoisomeric ratio at 84:16, presumed on the basis of the following to be predominantly the (2*SR*,3*SR*) [2,3-*syn*] isomer (*cf.* **16**). Expected difficulties in removing the methoxycarbonyl function immediately led us to try the same procedure with the corresponding *N*-*tert*-butoxycarbonyl (BOC) ester **11d**. This was also efficiently converted into the desired ester **14d**, in a similarly good yield (87%) and with similarly useful diastereoselection (86:14). Variations in the reaction conditions including change of solvent (diethyl ether, DME), silylating agent (TBDMSCl)* and temperature (−100 °C, −20 °C *etc.*) all resulted in (greatly) reduced yields and/or stereoselectivity. For example, trapping the enolate with TBDMSCl required the addition of HMPA and gave only a 2:1 stereoselection; a similar result was obtained using premixed LDA and TMSCl. The addition of magnesium bromide to the latter did not change the stereochemical outcome but did reduce the overall yield to ~50%. Higher stereoselectivities were observed at higher temperatures [*e.g.* 91:9 at −20 °C], but at the expense of the yield (25%). At a lower temperature (−115 °C; LDA–TMSCl premix), stereoselection was essentially lost (55:45) as it was when KHMDS was used as base at −78 °C, although the good yield (80%) was maintained. It is interesting to note that the most successful conditions are related to those found by Bartlett and his colleague[15] to be the most suitable for similar rearrangements of allylic esters of α-amino acids.

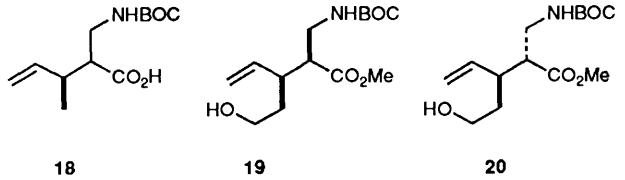
These model studies were completed by the observation that the pyrrolidino ester **11e** could also be rearranged successfully, but using premixed LDA and TMSCl, and with somewhat reduced stereoselection (62:38) in the final product **14e**. This type of substrate was not further examined as the pyrrolidino function offers limited synthetic possibilities, beyond simple elimination to the corresponding β-methylene ester.[16] This type of enolate Claisen rearrangement has literature precedent as a key step in an elegant total synthesis of the sesquiterpene lactone frullanolide,[13] although the method does not appear to have been examined further.

The effects of substituents on the rearrangement were then investigated using homologues of the ester **11d**. The results are presented in Table 1. In most cases, the mixtures of diastereoisomeric esters (**16** and **17**) obtained were not further separated. However, in the case of the ester (*E*)-**15a**, the intermediate *N*-BOC amino acid could be separated either by careful column chromatography or fractional crystallisation to give pure samples of the major *syn* (2*SR*,3*SR*)-diastereoisomer **18**. The expected involvement of a single transition state[3] is consistent with the direct relationship between the stereochemistry of the allylic alcohol component and the major diastereoisomer obtained in entries **a**, **d** and **e**. The low yields realised in the cinnamyl cases (**b**) were only obtained using a premix method and hence the poor stereoselection shown by these rearrangements cannot strictly be compared with the foregoing. Despite using this method which was specifically designed to suppress the likelihood of elimination reactions,[12] the major products were the corresponding cinnamyl alcohols,

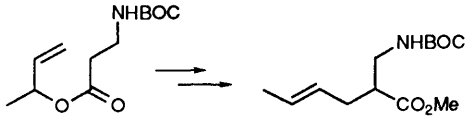
* With the exception of triethylsilyl chloride,[13] most other (bulkier) silylating reagents usually effect *C*- rather than *O*-silylation of enolates[14] and so were not investigated.

obtained with retention of geometry. The stereochemical results do, however, resemble those obtained from the methylpentenyl esters (**c**) in that all four of these examples, each of which effectively has a branch α to the alkene function, lead to a preponderance of the *syn* diastereoisomers **16**. An additional stereospecific example, the conversion of the but-3-en-2-yl ester **21** into the *E*-hexenoate **22**, suggests only that the substituent methyl group occupies, not unreasonably, an equatorial position in whatever transition state is involved in the rearrangement.

The stereochemical assignments were made largely on the basis of conversions of the silyloxymethyl products **16d** and **17d**

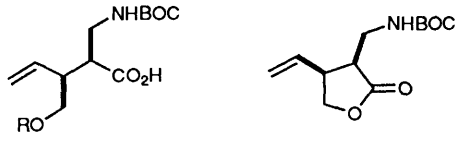


18 **19** **20**



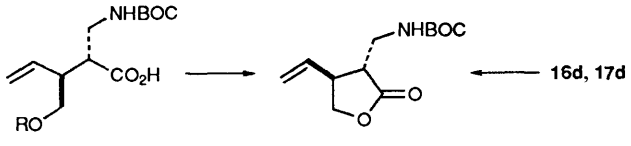
21 **22**

into the corresponding butyrolactones. Thus, the initial *N*-BOC-amino acid **23a**, the precursor to the *syn*-ester **16d** and obtained from rearrangement of (*E*)-**15d**, was converted into the hydroxy acid **23b**, by treatment with tetrabutylammonium



23 a R = TBDMS
b R = H

24 $J_{3,4}$ = 5.8 Hz
$J_{4,5\alpha}$ = 2.3 Hz
$J_{4,5\beta}$ = 5.8 Hz

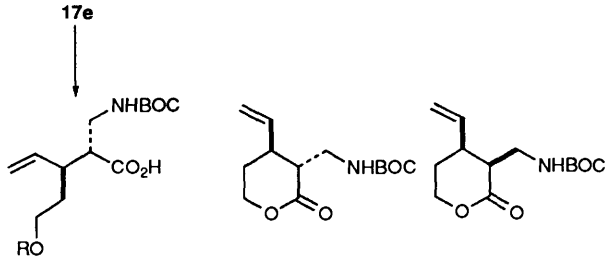


25 a R = TBDMS
b R = H(not isolated)

26 $J_{3,4}$ = 11.5 Hz
$J_{4,5\alpha}$ = 8.2 Hz
$J_{4,5\beta}$ = 10.5 Hz

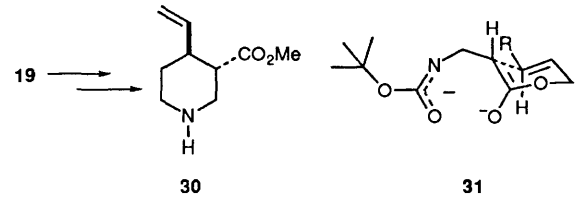
fluoride (TBAF). Subsequent lactonization using 2-chloro-1-methylpyridinium iodide (Mukaiyama's reagent)[17] then gave the butyrolactone **24** which was assigned the *cis*-stereochemistry both on the basis of the coupling constant data shown and the contrasting behaviour of the corresponding *anti*-ester **17d** and its derivatives. For example, when the silyloxy acid **25a** was similarly exposed to TBAF, the *trans*-lactone **26** was formed directly. Despite a number of attempts, the intermediate hydroxy acid **25b** (*cf.* **23b**) was not isolated. Similarly, treatment of the corresponding silyloxy ester **17d** with TBAF also led directly to the lactone **26**. By contrast, brief treatment of the *syn*-ester **16d** with TBAF did give an isolable hydroxy ester; however, and at first confusingly, prolonged treatment of the ester **16d** with TBAF also gave the *trans*-lactone **26**, presumably due to epimerisation α to the ester function caused by this somewhat basic reagent. The stereochemistries of the two lactones were deduced from the magnitudes of the coupling constants associated with each structure and comparison with established literature data.[18] The typical ranges for butyrolactones of this type are $J_{3,4}$ = 10–12 Hz for *trans*-substitution whereas in the corresponding *cis*-isomers, $J_{3,4}$ is in the range 5–8 Hz. Both values as well as the remaining coupling constants are consistent with the assigned stereochemistries. In the hope of obtaining confirmatory evidence, the homologous lactones **28** and **29** were prepared from the hydroxy esters **19** and **20**, obtained from rearrangement of the *Z*-silyloxypentenyl ester (*Z*)-**15e**. Unfortunately, a combination of flattening of the ring around the sp^2 carbonyl centre and proton coincidence precluded this. However, we were able to prepare the piperidinecarboxylate **30** from the hydroxy ester **19** by sequential mesylation, deprotection and basification. This clearly possessed the expected *trans*-stereochemistry shown from analysis of its ^1H NMR spectum.

The foregoing results are consistent with the predominant intermediacy of a chair-like transition state **31**, in which the



27 a R = TBDMS
b R = H

28 **29**



30 **31**

enolate oxygen and the ionized *N*-BOC group are *cis* to each other, a configuration which suggests chelation between these two functions, and which imposes an *E* geometry on the initially formed lithioenolate. A significant drawback associated with the Ireland enolate Claisen rearrangement is the selective generation of a single enolate geometry. This can be achieved by using an appropriate solvent system;[3] in the present case, it would appear that because of the chelation control, solvents other than THF compete with this and reduce the stereoselectivities obtained, as does exchange of the lithium counter cation to potassium. This is also consistent with the results of the initial studies where it was found that rearrangements of the corresponding phthalimido and pyrrolidino derivatives (**11b**, **e**) showed little stereoselectivity. In the 'α-branched' examples (**15b**, **c**), perhaps the extra, proximate steric bulk forces rearrangements of the *Z*-isomers to proceed largely through a boat-like transition state, in order to avoid excessive $A_{1,3}$ interactions, and hence, in the case of esters **15c** lead to predominantly the same diastereoisomer, independent of the initial alkene geometry.

The present study has gone some way to establishing the viability of this type of Claisen rearrangement leading to β-amino acid derivatives. The synthetic utility of the initial products appears to be considerable. In the present work, we have shown that these can act as precursors to 5- and 6-membered lactones and to piperidinecarboxylates. Other possibilities include a number of different saturated *O*- and

N-heterocyclic ring systems, the most obvious of which are examples of β-lactams. Further studies will be required to fully define the scope of these possibilities.

Experimental

General.—^{1}H NMR spectra were obtained using a Perkin–Elmer R32a instrument operating at 90 MHz (90), a Bruker WM-250 instrument operating at 250 MHz (250) or a Bruker WM-400 spectrometer operating at 400 MHz (400). The latter instrument was also used to measure ^{13}C NMR spectra. All spectra were recorded using dilute solutions in deuteriochloroform unless otherwise stated, with tetramethylsilane as the internal standard. Mass spectra were obtained using either an AEI MS 902 or a VG 7070E instrument operating at 70 eV, unless otherwise stated.

All reactions were performed under dry nitrogen and all organic solutions from aqueous work-ups were dried by brief exposure to anhydrous magnesium sulfate followed by filtration. SG chromatography refers to column chromatography using silica gel (Merck 9385) and the eluents specified. Petroleum refers to light petroleum with b.p. 60–80 °C.

General Esterification Procedure—(E)-*But*-2-*enyl* 3-(tert-*butoxycarbonylamino*)-*propanoate* **11d**.—A solution of *N*-*tert*-butoxycarbonyl-3-aminopropanoic acid (*N*-BOC-β-alanine) **9d** (7.00 g, 37 mmol) [from β-alanine and 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile (BOC-ON)] [19] in dry tetrahydrofuran (100 cm^3) was treated sequentially with (*E*)-but-2-en-1-ol **10** (3.10 g, 43 mmol), 4-dimethylaminopyridine (DMAP; ~20 mg) [10] and a solution of *N*,*N*-dicyclohexylcarbodiimide (DCC) (8.00 g, 38.8 mmol) in THF (10 cm^3), the latter added dropwise during 10 min. The resulting white suspension was stirred at ambient temperature overnight and then filtered. The solid residue was washed with ether (3 × 50 cm^3) and the combined filtrates evaporated. The resulting residue was purified by SG chromatography (short column) [15% ethyl acetate in petroleum] and distillation [Kugelrohr; ~140 °C (oven temp.) at 0.05 mmHg] to give the *ester* **11d** as a colourless oil (7.91 g, 88%); ν_{max}/cm^{-1} 3380, 1718, 1512, 1252, 1172 and 970; δ_H(90) 1.43 (9 H, s, Bu^t), 1.73 (3 H, br d, *J* 7, CH_3C=), 2.53 (2 H, t, *J* 7.5, CH_2C=O), 3.39 (2 H, app. q, *J* 7.5, NCH_2), 4.53 (br d, *J* 7, OCH_2C=), 4.99–5.19 (1 H, br, NH) and 5.55–5.91 (2 H, m, 2 × =CH); *m*/*z* 187 [$M^+ - (CH_3)_2C{=}CH_2$), 31%], 133 (17), 132 (16), 116 (67), 98 (20), 88 (39), 70 (10), 57 (100) and 55 (75) (Found: C, 59.3; H, 8.8; N, 5.6%; M^+-$(CH_3)_2C{=}CH_2$, 187.0840. $C_{12}H_{21}NO_4$ requires C, 59.3; H, 8.7; N, 5.8%; $C_8H_{13}NO_4$ requires *M*, 187.0844).

Using the foregoing esterification procedure, the following aminoesters were prepared.

(E)-*But*-2-*enyl*-3-*phthalimidopropanoate* **11b**. 3-Phthalimidopropanoic acid **9b** [20] and (*E*)-but-2-en-1-ol **10** by the general procedure on a 10-mmol scale gave, after SG chromatography (20% ethyl acetate in petroleum) the *ester* **11b** as a colourless oil (2.43 g, 89%); ν_{max}/cm^{-1} 1769, 1734, 1711, 1610, 1466, 1440, 1392, 1381, 1173, 1000, 964 and 707; δ_H(90) 1.71 (3 H, br d, *J* 7, CH_3C=), 2.77 (2 H, t, *J* 7.5, CH_2C=O), 4.05 (2 H, t, *J* 7.5, NCH_2), 4.57 (br d, *J* 7, OCH_2C=), 5.43–6.06 (2 H, m, 2 × =CH) and 7.74–8.02 and (5 H, m, Ph); *m*/*z* 273 (M^+, 2%), 218 (7), 203 (59), 202 (39), 175 (44), 174 (13), 173 (15), 161 (25), 160 (100), 130 (21), 105 (15), 77 (23), 76 (28), 55 (49) and 54 (66) (Found: C, 66.0; H, 5.8; N, 5.0%; M^+, 273.0988. $C_{15}H_{15}NO_4$ requires C, 65.9; H, 5.5; N, 5.1%; *M*, 273.1001).

(E)-*But*-2-*enyl* 3-(*methoxycarbonylamino*)*propanoate* **11c**. 3-Methoxycarbonylaminopropanoic acid **9a** and (*E*)-but-2-en-1-ol **10** (52.7 mmol), after SG chromatography (20% ethyl acetate in petroleum), gave the *ester* **11c** (7.35 g, 76%) as a colourless oil; ν_{max}/cm^{-1} 3345, 1730br, 1530 and 1260; δ_H(90) 1.70 (3 H, br d, *J* 7, CH_3C=), 2.52 (2 H, t, *J* 7, CH_2C=O), 3.41 (2 H, app. q, *J* 7, NCH_2), 3.63 (3 H, s, OMe), 4.49 (br d, *J* 7, OCH_2C=), 5.22–5.52 (1 H, br, NH) and 5.36–6.00 (2 H, m, 2 × =CH); *m*/*z* 201 (M^+, 3%), 146 (22), 130 (54), 103 (11), 101 (14), 98 (14), 88 (100), 71 (11), 59 (15), 55 (48) and 54 (24) (Found: C, 53.7; H, 7.7; N, 7.0%; M^+, 201.1006. $C_9H_{15}NO_4$ requires C, 53.7; H, 7.5; N, 7.0%; *M*, 201.1001).

(E)-3-*Phenylprop*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*E*)-**15b**. *N*-BOC-β-Alanine **9d** and (*E*)-cinnamyl alcohol (10 mmol) gave the *ester* (*E*)-**15b** (2.59 g, 85%) as a colourless solid, m.p. 49 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3380 and 1710br; δ_H(90) 1.42 (9 H, s Bu^t), 2.53 [2 H, t, *J* 7, CH_2C(O)], 3.41 (2 H, app. q, *J* 7, NCH_2), 4.74 (2 H, d, *J* 7, OCH_2), 5.05–5.36 (1 H, br, NH), 6.26 (1 H, dt, *J* 16 and 7, CH_2CH=), 6.68 (1 H, br d, *J ca.* 16, PhCH=) and 7.23–7.48 (5 H, m, Ph); *m*/*z* 249 [M^+–$(CH_3)_2C{=}CH_2$, 22%], 134 (46), 133 (45), 117 (82), 116 (72), 115 (18), 98 (21), 91 (10) and 57 (100) [Found: C, 67.0; H, 7.5; N, 4.8; $M^+ - (CH_3)_2C{=}CH_2$, 249.1014. $C_{17}H_{23}NO_4$ requires C, 66.9; H, 7.6; N, 4.6%; $C_{13}H_{15}NO_4$ *M*, 249.1001].

(E)-4-*Methylpent*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*E*)-**15c**. *N*-BOC-β-Alanine **9d** and (*E*)-4-methylpent-2-en-1-ol (8.5 mmol) gave the *ester* (*E*)-**15c** (1.96 g, 84%) as a colourless oil, ν_{max}/cm^{-1} 3390, 1723br, 1612, 1178 and 981; δ_H(90) 0.98 [6 H, d, *J* 7, $(CH_3)_2CH$], 1.44 (9 H, s, Bu^t), 2.08–2.45 [partly obscured, 1 H, m, $(CH_3)_2)CH$], 2.52 [2H, t, *J* 7, CH_2C(O)], 3.41 (2 H, app. q, *J* 7, CH_2N), 4.54 (2 H, d, *J* 7, CH_2O), 4.95–5.22 (1 H, br, NH) and 5.35–5.94 (2 H, m, CH=CH); *m*/*z* 215 [$M^+ - (CH_3)_2C{=}CH_2$, 5%], 134 (31), 133 (12), 132 (10), 116 (68), 98 (18) 88 (31), 83 (58), 82 (94), 74 (10), 70 (11), 67 (19), 59 (15), 57 (100) and 55 (42) (Found: C, 62.0; H, 9.5; N, 5.0%; $M^+ - (CH_3)_2C{=}CH_2$, 215.1149. $C_{14}H_{25}NO_4$ requires C, 62.0; H, 9.3; N, 5.2%; $C_{10}H_{17}NO_4$ requires *M*, 215.1157).

(E)-4-[(1,1-*Dimethylethyl*)*dimethylsilyloxy*]*but*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*E*)-**15d**. *N*-BOC-β-Alanine **9d** and (*E*)-4-[(1,1-dimethylethyl)dimethylsilyloxy]but-2-en-1-ol (6 mmol) gave the *ester* (*E*)-**15d** (2.06 g, 92%) as a colourless oil, ν_{max}/cm^{-1} 3380 and 1720br; δ_H(90) 0.01 (6 H, s, Me_2Si), 0.86 (9 H, s, Bu^{t}Si), 1.39 (9 H, s, Bu^{t}O), 2.47 [2 H, t *J* 7, CH_2C(O)], 3.35 (2 H, app. q, *J* 7, NCH_2), 4.11–4.22 (2 H, m, CH_2OSi), 4.49–4.61 [2 H, m, CH_2OC(O)], 4.79–5.09 (1 H, br, NH) and 5.71–5.85 (2 H, m, CH=CH) (Found: C, 57.7; H, 9.4; N, 3.6. $C_{18}H_{35}NO_5Si$ requires C, 57.9; H, 9.4; N, 3.8%).

(E)-5-[(1,1-*Dimethylethyl*)*dimethylsilyloxy*]*pent*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*E*)-**15e**. *N*-BOC-β-Alanine **9d** and (*E*)-5-[(1,1-dimethylethyl)dimethylsilyloxy]pent-2-en-1-ol (3 mmol) gave the *ester* (*E*)-**15e** (1.00 g, 86%) as a colourless oil, ν_{max}/cm^{-1} 3375 and 1720br; δ_H(90) 0.00 (6 H, s, Me_2Si), 0.83 (9 H, s, Bu^{t}Si), 1.36 (9 H, s, Bu^{t}O), 2.04–2.33 (2 H, m, CH_2C=), 2.47 [2 H, t, *J* 7, CH_2C(O)], 3.35 (2 H, app. q, *J* 7, NCH_2), 3.60 (2 H, d, *J* 7, CH_2OSi), 4.48 [2 H, d, *J* 6, CH_2OC(O)], 5.00–5.30 (1 H, br, NH) and 5.55–5.79 (2 H, m, CH=CH) (Found: C, 58.8; H, 9.8; N, 3.8. $C_{19}H_{37}NO_5Si$ requires C, 58.9; H, 9.6; N, 3.6%).

But-2-*ynyl* 3-(tert-*butoxycarbonylamino*)*propanoate*. *N*-BOC-β-Alanine **9d** and but-2-yn-1-ol (15 mmol) gave the expected *ester* (2.96 g, 82%) as a colourless oil, ν_{max}/cm^{-1} 3390, 2244, 1740 and 1712; δ_H(90) 1.42 (9 H, s, Bu^t), 1.83 (3 H, t, *J* 3, MeC=), 2.54 [2 H, t, *J* 7, CH_2C(O)], 3.38 (2 H, app. q, *J* 7, NCH_2), 4.64 (2 H, q, *J* 3, CH_2O) and 4.89–5.12 (1 H, br, NH); *m*/*z* 185 [$M^+ - (CH_3)_2C{=}CH_2$, 32%], 184 (10), 116 (50), 98 (25), 88 (29), 70 (19), 69 (10), 59 (35) and 57 (100) [Found: C, 59.5; H, 7.8; N, 5.8%; $M^+ - (CH_3)_2C{=}CH_2$, 185.0695. $C_{12}H_{19}NO_4$ requires C, 59.7; H, 7.9; N, 5.8%; $C_8H_{11}NO_4$ requires M, 185.0688].

(Z)-3-*Phenylprop*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*Z*)-**15b**.–*N*-BOC-β-Alanine **9d** and (*Z*)-cinnamyl alcohol (5 mmol) gave the *ester* (*Z*)-**15b** (1.37 g, 90%) as a

colourless oil; ν_{max}/cm^{-1} 3370 and 1715; $\delta_H(250)$ 1.44 (9 H, s, Bu^t), 2.52 [2 H, t, *J* 7, $CH_2C(O)$], 3.47 (2 H, app. q, *J* 7, CH_2N), 4.87 (2 H, dd, *J* 7.5 and 1.5, CH_2O), 5.12–5.40 (1 H, br, NH), 5.79 (1 H, dt, *J* 10.5 and 7.5, $=CHCH_2$), 6.66 (1 H, dt, *J* 10.5 and 1.5, PhCH=) and 7.18–7.39 (5 H, Ph); *m/z* 249 [M^+–$(CH_3)_2C{=}CH_2$, 29%], 134 (49), 133 (45), 117 (85), 116, (69), 98 (26) and 57 (100) [Found: M^+–$(CH_3)_2C{=}CH_2$, 249.1008].

(Z)-4-*Methylpent*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*Z*)-**15c.** *N*-BOC-β-Alanine **9d** and (*Z*)-4-methylpent-2-en-1-ol (5 mmol) gave the *ester* (*Z*)-**15c** (1.15 g, 85%) as a colourless oil; ν_{max}/cm^{-1} 3400 and 1730; $\delta_H(90)$ 0.96 [6 H, d, *J* 7, $(CH_3)_2CH$], 1.42 (9 H, s, Bu^t), 2.50 [2 H, t, *J* 7, $CH_2C(O)$], 2.45–2.69 [obscured, 1 H, $(CH_3)_2CH$], 3.37 (2 H, app. q, *J* 7, CH_2N), 4.64 (2 H, br d, *J* ~ 6, CH_2O), 5.02–5.24 (1 H, br, NH) and 5.33–5.51 (2 H, m, CH=CH); *m/z* 215 [M^+–$(CH_3)_2C{=}CH_2$, 2%], 134 (37), 116 (79), 88 (35), 83 (65), 82 (89) and 57 (100) [Found: M^+–$(CH_3)_2C{=}CH_2$, 215.1151].

(Z)-4-[(1,1-*Dimethylethyl*)*dimethylsilyloxy*]*but*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*Z*)-**15d**. *N*-BOC-β-Alanine **9d** and (*Z*)-4-[(1,1-dimethylethyl)dimethylsilyoxy]but-2-en-1-ol (5 mmol) gave the *ester* (*Z*)-**15d** (1.58 g, 89%) as a colourless oil; ν_{max}/cm^{-1} 3390 and 1725; $\delta_H(90)$ 0.00 (6 H, s, Me_2Si), 9.81 (9 H, s, Bu^{t}Si), 1.36 (9 H, s, Bu^{t}O), 2.42 [2 H, t, *J* 7, $CH_2C(O)$], 3.28 (2 H, app. q, *J* 7, NCH_2), 4.16 (2 H, d, *J* 6, CH_2OSi), 4.55 [2 H, d, *J* 7, $CH_2OC(O)$], 4.94–5.21 (1 H, br, NH) and 5.27–5.78 (2 H, m, CH=CH) (Found: C, 57.6; H, 9.6; N, 3.9%).

(Z)-5-[(1,1-*Dimethylethyl*)*dimethylsilyloxy*]*pent*-2-*enyl* 3-(tert-*butoxycarbonyl-amino*)*propanoate* (*Z*)-**15e**. *N*-BOC-β-Alanine **9d** and (*Z*)-4-[(1,1-dimethylethyl)dimethylsilyloxy]-pent-2-en-1-ol (4.5 mmol) gave the *ester* (*Z*)-**15e** (1.46 g, 84%) as a colourless oil; ν_{max}/cm^{-1} 3380 and 1720; $\delta_H(90)$ 0.00 (6 H, s, Me_2Si), 0.84 (9 H, s, Bu^{t}Si), 1.36 (9 H, s, Bu^{t}O), 2.15–2.39 (2 H, m, $CH_2C{=}$), 2.46 [2 H, t, *J* 7, $CH_2C(O)$], 3.34 (2 H, app. q, *J* 7, NCH_2), 3.48 (2 H, d, *J* 7, CH_2OSi), 4.61 [2 H, d, *J* 7, $CH_2OC(O)$], 4.89–5.15 (1 H, br, NH) and 5.51–5.74 (2 H, m, CH=CH) (Found: C, 58.9; H, 9.8; N, 3.5%).

But-1-*en*-3-*yl* 3-(tert-*butoxycarbonylamino*)*propanoate* **18**. *N*-BOC-β-Alanine **9d** and but-1-en-3-ol (10 mmol) gave the *ester* **18** (2.26 g, 93%) as a colourless oil; ν_{max}/cm^{-1} 3375, 1717, 1698, 1520 and 1175; $\delta_H(90)$ 1.30 (3 H, d, *J* CH_3CH), 1.45 (9 H, s, Bu^t), 2.52 [2 H, t, *J* 7, $CH_2C(O)$], 3.38 (2 H, app. q, *J* 7, NCH_2), 5.04–5.52 (3 H, m, $=CH_2$ and OCH) and 5.83 (1 H, ddd, *J* 17, 10 and 7, =CH); *m/z* 187 [M^+–$(CH_3)_2C{=}CH_2$, 20%], 133 (19), 132 (14), 116 (43), 98 (11), 88 (30), 70 (11), 59 (18), 57 (100) and 55 (45) [Found: C, 59.2; H, 8.6; N, 5.6; M^+–$(CH_3)_2C{=}CH_2$, 187.0855. $C_{12}H_{21}NO_4$ requires C, 59.3; H, 8.7; N, 5.8%; $C_8H_{13}NO_4$ requires *M*, 187.0844].

(E)-*But*-2-*enyl* 3-*pyrrolidinopropanoate* **11e**.—Propenoyl chloride (11.2 cm^3) was added dropwise during 25 min to a stirred, ice-cold solution of (*E*)-but-2-en-1-ol **10** (10.0 g) and triethylamine (20 cm^3) in dry ether (200 cm^3). The resulting mixture was stirred without cooling overnight and then filtered. The combined filtrate and ether washings were washed successively with water (50 cm^3), 2 mol dm^{-3} hydrochloric acid (2 × 60 cm^3), water (50 cm^3) and brine (50 cm^3) then dried and evaporated to leave crude (*E*)-but-2-enyl propenoate (13.43 g, 77%); $\delta_H(90)$ 1.73 (3 H, d, *J* 6, MeCH=), 4.58 (2 H, br d, *J* 6, CH_2O), 5.60–5.99 (3 H, m), 6.20 (1 H, d, *J* 10, =CH) and 6.41 (1 H, d, *J* 17, =CH). The crude ester (13.43 g) was stirred in dry ether (150 cm^3) while pyrrolidine (10.7 cm^3) was added dropwise and the resulting solution stirred at ambient temperature for 72 h. It was then concentrated and distilled. The fraction b.p. 132 °C at 11 mmHg, (21.1 g) was collected to afford the ester **11e**, as a colourless oil, ν_{max}/cm^{-1} 1734; $\delta_H(90)$ 1.66–1.87 (7 H, m, Me and CH_2CH_2), 2.43–2.66 (6 H, m, 3 × CH_2N), 2.73–2.91 (2 H, m, CH_2CO), 4.55 (2 H, br d, *J* 6, CH_2O) and 5.43–6.06 (2 H, m, 2 × =CH).

(Z)-*But*-2-*enyl* 3-(tert-*butoxycarbonylamino*)*propanoate* (*Z*)-**15a**.—A solution of the foregoing acetylenic ester (1.5 g) in ethyl acetate (40 cm^3) containing 5% Pd-$BaSO_4$ (Fluka; 35 mg) was stirred under hydrogen (1 atm) in the dark until 1 equiv. had been absorbed (~ 3.5 h). The solution was then filtered through a mixture of Celite and silica gel and the solid washed with further ethyl acetate. Evaporation of the combined filtrates gave the (*Z*)-*alkenyl ester* (*Z*)-**15a** (1.43 g, 94%) as a colourless oil; ν_{max}/cm^{-1} 3390, 1712br, 1515 and 1171; $\delta_H(90)$ 1.47 (9 H, s, Bu^t), 1.72 (3 H, d, *J* 6, $CH_3C{=}$), 2.56 (2 H, t, *J* 7.5, $CH_2C{=}O$), 3.43 (2 H, app. q, *J* 7.5, NCH_2), 4.70 (br d, *J* 6, $OCH_2C{=}$), 4.95–5.27 (1 H, br, NH) and 5.41–6.00 (2 H, m, 2 × =CH); *m/z* 187 [M^+ – $(CH_3)_2C{=}CH_2$], 16%), 133 (12), 132 (13), 116 (58), 98 (29), 88 (35), 71 (25), 70 (27), 59 (40), 57 (100) and 55 (69) [Found: C, 59.1; H, 8.9; N, 5.6; M^+–$(CH_3)_2C{=}CH_2$, 187.0863. $C_{12}H_{21}NO_4$ requires C, 59.3; H, 8.7; N, 5.8% $C_8H_{13}NO_4$ requires *M*, 187.0844.

Methyl 3-*methyl*-2-(*phthalimidomethyl*)*pent*-4-*enoate* **14b**.—LDA (9.3 mmol) was generated using the general procedure (see below) in THF (45 cm^3). Following the addition of HMPA (9 cm^3), the mixture was cooled to −110 °C and treated with a solution of *tert*-butyldimethylchlorosilane (1.51 g, 10 mmol) in THF (3 cm^3) during 3 min, followed by a solution of the ester **11b** (0.85 g, 3.11 mmol) in THF (5 cm^3) during 10 min. After being stirred at −100 °C for 2 h, the mixture was slowly warmed to ambient temperature and then refluxed for 9 h. Following the usual work-up and esterification procedure, SG chromatography (15% ethyl acetate in petroleum) gave the *ester* **14b**, a colourless oil (0.11 g, 12%), as a mixture of two diastereoisomers (2:1) which showed ν_{max}/cm^{-1} 1770, 1715, 1600 and 1480; δ_H 1.08 (1 H, d, *J* 7, 3-Me), 1.15 (2 H, d, *J* 7, 3-Me), 2.43–3.08 (2 H, m, 2- and 3-H), 3.65 (3 H, s, OMe), 3.81–4.12 (2 H, m, CH_2N), 4.95–5.28 (2 H, m, $=CH_2$) and 5.62–6.07 (1 H, m, =CH); *m/z* 255 (M^+–MeOH, 27%), 227 (9), 200 (11), 173 (9), 160 (100), 148 (9), 127 (22), 104 (10), 80 (16), 76 (10) and 51 (9) (Found: M^+–MeOH, 255.0890. $C_{15}H_{13}NO_3$ requires *M*, 255.0895). (*E*)-Crotyl alcohol was also isolated.

Methyl (2SR,3SR)-2-(*Methoxycarbonylaminomethyl*)-3-*methylpent*-4-*enoate* **14c**.—By the general procedure (see below), rearrangement of the *N*-methoxycarbonyl (*E*)-but-2-enyl ester **11c** (0.74 g, 3.68 mmol) led largely to the (2SR,3SR)-*ester* **14c**, as a colourless oil (0.56 g, 71%), ν_{max}/cm^{-1} 3360, 1728, 1530, 1260 and 920; $\delta_H(400)$ [major (2*SR*,3*SR*) isomer] 1.06 (3 H, d, *J* 6.8, 3-Me), 2.53 (1 H, ddd, *J* 7.4, 6.9 and 6.7, CHCO), 2.62–2.69 (1 H, m, MeC*H*CH=), 3.26–3.37 (1 H, m, NCH_A), 3.42–3.49 (1 H, m, NCH_B), 3.65 (3 H, s, OMe), 3.69 (3 H, s, OMe), 4.79–4.92 (1 H, br, NH), 5.03–5.09 (2 H, m, $=CH_2$) and 5.77 (1 H, ddd, *J* 17.0, 10.3 and 7.8, =CH); δ_C(major) 17.18 (3-Me), 38.28 (CH), 40.17 (CH_2), 50.60 (CH), 51.60 (Me), 52.07 (Me), 115.07 ($=CH_2$), 140.30 (=CH), 157.11 C(O)N) and 174.36 (CO_2); *m/z* (both isomers) 215 (M^+, 2%), 184 (16), 156 (22), 140 (11), 128 (52), 113 (25), 101 (17), 96 (17), 88 (100), 81 (17), 80 (23), 76 (14), 60 (15), 67 (17), 59 (28) and 55 (30) (Found: M^+, 215.1154. $C_{10}H_{17}NO_4$ requires *M*, 215.1158).

The minor (2*RS*,3*SR*) isomer was quantified by integration of resonances at δ_H 1.05 (d, *J* 6.8, 3-Me) and 5.62–5.70 (m, =CH); the minor isomer also showed δ_C 18.19 (3-Me), 38.70 (CH), 40.80 (CH_2), 50.97 (CH), 51.71 (Me) (other Me obscured), 115.50 ($=CH_2$), 140.35 (=CH), 157.11 [C(O)N] and 174.63 (CO_2). The ratio was 84:16.

Methyl 3-Methyl-2-(pyrrolidino-1-ylmethyl)pent-4-enoate **14e**.—By the general procedure (see below), LDA (6.14 mmol) in THF (15 cm^3) was prepared at −78 °C and treated at this temperature with trimethylsilyl chloride (0.8 cm^3, 6.3 mmol). After 3 min, a solution of the pyrrolidinylpropanoate **11e** (0.96 g, 4.87 mmol) in THF (2.5 cm^3) was added to the mixture during 5 min. After 1 h, the mixture was warmed to ambient temperature during 0.5 h and then refluxed for 6 h. The cooled suspension was concentrated and the residue subjected to SG chromatography [acetone followed by 10% methanol in acetone] to give the desired acid (0.6 g) which was treated with diazomethane in the usual way to give the *esters* **14e**, a colourless oil (0.64 g, 63%), as a mixture of diastereoisomers (62:38); ν_{max}/cm^{-1} 1738, 1640, 1255, 1150 and 915; *m/z* 211 (M^+, 2%), 170 (4), 85 (15), 84 (100) and 55 (6) (Found: M^+, 211.1591. $C_{12}H_{21}NO_2$ requires *M*, 211.1572); δ_H(major isomer) 0.99 (d, *J* 6.7, 3-Me), 1.67–1.79 (4 H, m, CH_2CH_2), 2.35–2.60 (6 H, m, 3 × CH_2N), 2.77–2.91 (1 H, m, C*H*CO_2Me) (common to both isomers), 3.70 (s, OMe), 4.96–5.07 (2 H, m, $=CH_2$) (common to both isomers) and 5.65 (ddd, *J* 17.1, 10.2 and 8.3, =CH); δ_H(minor isomer) 1.05 (d, *J* 6.9, 3-Me), 3.66 (s, OMe) and 5.72 (partly obscured) (ddd, *J* 17.2, 10.2 and 8.1, =CH). The isomer ratio was determined by careful integration of the two methyl ester resonances at δ_H 3.70 and 3.68 (OMe). In another experiment, rearrangement using 1.1 equiv. of LDA–THF −78 °C, TBDMSCl and 12 equiv. of HMPA, followed by a 6 h period under reflux gave *ca.* 78% conversion according to ^1H NMR analysis of the crude silyl ester, but very little reaction (~10%) was observed under similar conditions but using 1.1 equiv. of LDA in THF at −78 °C and TBDMSCl, followed by a 3 h period under reflux (both 1 mmol scale).

Enolate Claisen Rearrangement: General Procedure.—Rearrangement of (E)-*But-2-enyl* 3-(tert-*Butoxycarbonylamino*)-*propanoate* (*E*)-**15a** [=**11d**] *to* (2SR,3SR)-*Methyl* 2-(tert-*butoxycarbonylaminomethyl*)-3-*methylpent*-4-*enoate* **16a**.—To a stirred solution of lithium diisopropylamide (LDA) [prepared from diisopropylamine (1.44 cm^3, 10.3 mmol) and butyllithium 1.6 mol dm^{-3} solution in hexanes; 6.4 cm^3, 10.2 mmol)] in tetrahydrofuran (THF) (8 cm^3), maintained at −78 °C, was added dropwise *via* a syringe, a solution of the ester (*E*)-**15a** [=**11d**] (1.0 g, 4.11 mmol) in THF (3 cm^3) during 5 min. The resulting pale yellow solution was stirred at this temperature for 20 min. and then treated dropwise with trimethylsilyl chloride (1.3 cm^3, 10.2 mmol). After a further 20 min at −78 °C, the mixture was warmed to ambient temperature during 0.5 h to give a colourless suspension which was stirred and heated at reflux for 2 h. It was then cooled to ambient temperature during 1 h before acidification to pH 2 using ice-cold 2 mol dm^{-3} hydrochloric acid. The mixture was further diluted with water (20 cm^3) and the product then extracted into chloroform (3 × 20 cm^3). The combined extracts were washed with water (20 cm^3) and brine (20 cm^3), dried and evaporated. The resulting yellow oil was separated by SG chromatography [chloroform followed by chloroform–20% methanol] to give the amino acids [*cf.* **18**] (see below) as a colourless solid (0.88 g, 88%). Conversion into the corresponding methyl ester using diazomethane in the usual manner followed by filtration of the resulting ethereal solution through silica gave the *ester* **16a** as a colourless oil (0.918 g, 87% overall); ν_{max}/cm^{-1} 3380, 1718br, 1508 and 1170; δ_H(400) [major (2*SR*,3*SR*) isomer] 1.04 (3 H, d, *J* 6.8, 3-Me), 1.43 (9 H, s, Bu^t), 2.53 (1 H, ddd, *J* 7.6, 6.7 and 6.7, CHCO), 2.60–2.68 (1 H, m, MeC*H*CH=), 3.18–3.27 (1 H, m, NCH_A), 3.38–3.47 (1 H, m, NCH_B), 3.69 (3 H, s, OMe), 4.80–4.91 (1 H, br, NH), 5.02 (1 H, ddd, *J* 10.3, 1.6 and 0.9, CH=CH_cCH_t), 5.04 (1 H, ddd, *J* 17.1, 1.4 and 0.9, CH=CH_cCH_t) and 5.75 (1 H, ddd, *J* 17.1, 10.3 and 7.7, =CH); δ_C 17.11 (Me), 28.38 (Bu^t), 38.31, 39.71, 50.72, 51.55, 79.36 (C), 114.96 (CH_2), 140.43 (CH), 155.83 [C(O)N] and 174.42 (CO_2); *m/z* 201 (M^+–Me_2C=CH_2, 12%), 184 (7), 170 (10), 157 (8), 128 (13), 113 (10), 97 (7), 81 (6), 71 (6) and 57 (100) (Found: M^+–Me_2C=CH_2, 201.1001. $C_9H_{15}NO_4$ requires *M*, 201.1009).

The minor (2*RS*,3*SR*) diastereoisomer **17a** was quantified by integration of resonances at δ_H 3.71 (OMe) and 5.63–5.74 (=CH).

Alternatively, the crude acidic product was treated directly with diazomethane and the ester finally purified by SG chromatography using the eluents specified below.

In another experiment, the intermediate acid was crystallised from ether–light petroleum (1:5) to give a pure sample of the major (2SR,3SR)-*acid* **18** as colourless plates, m.p. 103–104 °C; ν_{max}/cm^{-1} ($CHCl_3$) 3460, 3050 and 1707; δ_H 1.09 (3 H, d, *J* 7, 3-Me), 1.47 (9 H, s, Bu^t), 2.39–2.74 (2 H, m), 3.15–3.46 (2 H, m), 4.93–5.18 (2 H, m, $=CH_2$), 5.59–6.02 (1 H, m, =CH), 6.30–6.62 (1 H, br, NH) and 9.35–9.64 (1 H, br, CO_2H) (Found: C, 59.4; H, 8.8; N, 5.7. $C_{12}H_{21}NO_4$ requires C, 59.2; H, 8.7; N, 5.8%). The mixture of acids could also be separated by careful chromatography using silica gel eluted by ethyl acetate–petroleum (1:1); the major acid showed R_f ~0.5 in this solvent system.

(2RS,3SR)-*Methyl* 2(tert-*Butoxycarbonylaminomethyl*)-3-*methylpent*-4-*enoate* **17a**.—By the general procedure, rearrangement of the (*Z*)-but-2-enyl ester (*Z*)-**15a** (0.90 g, 3.7 mmol) followed by esterification and SG chromatography (12% ethyl acetate in petroleum) gave the 2RS,3SR-*aminoester* **17a** as a colourless oil (0.69 g, 73%); ν_{max}/cm^{-1} 3380, 1715, 1505 and 1170; δ_H(400) [major (2*RS*,3*SR*) isomer] 1.04 (3 H, d, *J* 6.5, 3-Me), 1.42 (9 H, s Bu^t), 2.46–2.57 (2 H, m, 2- and 3-H), 3.13–3.21 (1 H, m, NCH_A), 3.42–3.48 (1 H, m, NCH_B), 3.71 (3 H, s, OMe), 4.76–4.88 (1 H, br, NH), 5.02 (1 H, ddd, *J* 10.1, 0.9 and 0.5, CH_cH_t=CH), 5.05 (1 H, ddd, *J* 16.1, 0.7 and 0.7, CH_cH_t=CH) and 5.63–5.74 (1 H, m, =CH); *m/z* 201 (M^+–Me_2C=CH_2, 24%), 184 (15), 170 (21), 157 (17), 152 (11), 146 (6), 142 (15), 128 (29), 113 (30), 102 (12), 101 (13), 97 (15), 81 (25), 80 (11), 74 (10), 71 (19), 70 (13), 69 (15), 67 (16), 59 (25), 58 (16) and 57 (100) (Found: M^+–Me_2C=CH_2, 201.0992). The minor (2*SR*,3*SR*)-isomer **16a** was quantified by integration of resonances at δ_H 3.69 (OMe), 2.60 (MeC*H*CH=) and 5.75 (=CH).

(2SR,3SR)- *and* (2RS,3SR)-*Methyl* 2-(tert-*butoxycarbonylaminomethyl*)-3-*phenylpent*-4-*enoate* **16b** *and* **17b**.—(*a*) By the general procedure, except that the trimethylsilyl chloride was added to the LDA solution followed immediately by the (*E*)-3-phenylprop-2-enyl ester (*E*)-**15b** (3 mmol) and finally SG chromatography (15% ethyl acetate in petroleum) gave a 56:44 mixture of the (2*SR*,3*SR*)-**16b** and (2*RS*,3*SR*)-**17b** *diastereoisomers* as a pale yellow oil (31%); ν_{max}/cm^{-1} 3370, 1715br, 1610 and 1495 (Found: C, 67.5; H, 7.8; N, 4.4. $C_{18}H_{25}NO_4$ requires C, 67.7; H, 7.9; N, 4.4%). The major (2*SR*,3*SR*)-isomer **16b** showed δ_H(400) 1.38 (9 H, s, Bu^t), 2.98–3.17 (3 H, m), 3.43–3.60 (2 H, m, CH_2N), 3.68 (3 H, s, OMe), 4.82 (1 H, br, NH), 5.13 (1 H, dd, *J* 10.3 and 1.0, CH_cH_t=CH), 5.18 (1 H, dd, *J* 16.9 and 0.9, CH_cH_t=CH) and 5.92–6.05 (1 H, m, =CH); δ_C 28.37 (Bu^t), 40.96 (CH_2N), 50.82 (2 × CH), 51.81 (OMe), 79.41 (Bu^{t}C), 115.95 ($=CH_2$), 127.16, 127.82, 128.98, 138.89 (all =CH), 140.31 (C), 155.60 [C(O)N] and 174.28 (CO_2). The minor (2*SR*,3*SR*) isomer **17b** showed δ_H(400) 1.42 (9 H, s, Bu^t), 2.98–3.17 (3 H, m), 3.26 (1 H, ddd, *J* 13.8, 9.3 and 5.9, CHCO), 3.40 (3 H, s, OMe), 3.43–3.60 (2 H, m, CH_2N), 4.65 (1 H, br, NH), 5.03 (1 H, br d, *J* 10.2, CH_cH_t=CH) and 5.08 (1 H, br d, *J* 17.0, CH_cH_t=CH); δ_C 28.73 (Bu^t), 41.05 (CH_2N), 50.95 (2 × CH), 51.67 (OMe), 79.41 Bu^t*C*), 117.19 ($=CH_2$), 126.92, 127.67, 128.62, 138.13 (all =CH), 140.31 (C), 155.60 [C(O)N] and 174.28 (CO_2).

The material balance was mostly made up of the corresponding cinnamyl alcohol (with *E*- or *Z*-geometry preserved) and *N*-BOC-β-alanine **9d**, isolated as its methyl ester, after esterification and chromatography of the acidic reaction

products. Variable amounts of apparently *C*-silylated material were also detected by NMR and mass spectra.

(*b*) Using the same LDA–TMSCl pre-mix method, rearrangement of the corresponding *Z*-isomer (*Z*)-**15b** (2 mmol) gave the same two diastereoisomers (**16b** and **17b**) in a ratio of 77:23 respectively (40%), which exhibited spectral data identical with those of the foregoing (except ratios).

(2SR,3SR)- and (2RS,3SR)-*Methyl* 2-(tert-*Butoxycarbonylaminomethyl*)-3-(1-*methylethyl*)*pent*-4-*enoate* **16c** *and* **17c**.—(*a*) By the general procedure, rearrangement of the (*E*)-4-methylpent-2-enyl ester (*E*)-**15c** (4.5 mmol) followed by SG chromatography of the intermediate acidic products (20% ethyl acetate in petroleum followed by 10% methanol in chloroform) and finally esterification (CH_2N_2) gave the *esters* **16c** and **17c** (80:20) as a colourless oil (1.08 g, 84%); ν_{max}/cm^{-1} 3390, 1715br, 1505 and 1170; *m*/*z* 229 ($M^+-Me_2C{=}CH_2$, 5%), 212 (5), 198 (5), 170 (7), 156 (8), 147 (7), 142 (10), 125 (6), 114 (6), 113 (34), 103 (7), 83 (7), 82 (9), 81 (7), 70 (5), 67 (7), 59 (7), 58 (7) and 57 (100) (Found: $M^+-Me_2C{=}CH_2$, 229.1333. $C_{11}H_{19}NO_4$ requires *M*, 229.1314). The major (2*SR*,3*SR*) isomer **16c** showed δ_H(400) 0.84 (3 H, d, *J* 6.8, MeCH), 0.93 (3 H, d, *J* 6.7, MeCH), 1.43 (9 H, s, Bu^t), 1.69–1.80 (1 H, m), 1.93–2.01 (1 H, m), 2.86 (1 H, ddd, *J* 8.7, 7.3 and 4.7, CHCO), 3.22–3.39 (2 H, m, CH_2N), 3.66 (3 H, s, OMe), 4.79–4.90 (1 H, br, NH), 4.97 (1 H, dd, *J* 17.0 and 1.9, $CH_cH_t{=}CH$), 5.07 (1 H, dd, *J* 10.2 and 2.0, $CH_cH_t{=}CH$) and 5.60 (1 H, ddd, *J* 17.0, 10.2 and 10.1, =CH); δ_C 18.52 (Me), 21.31 (Me), 28.37 (Bu^t), 40.93 (CH_2), 47.24 (CH), 51.44 (CH), 51.45 (OMe), 79.37 (Me_3C), 117.76 (=CH_2), 136.33 (=CH), 155.86 [C(O)N] and 174.64 (CO_2). The minor (2*RS*,3*RS*) diastereoisomer **17c** showed resonances at δ_H 0.85 (3 H, d, *J* 6.7, MeCH), 1.59–1.68 (1 H, m), 2.12–2.22 (1 H, m), 2.79 (1 H, ddd, *J* 9.5, 8.9 and 3.1, CHCO), 3.10 (1 H, ddd, *J* 14.9, 9.5 and 5.0, NCH_A), 3.47 (1 H, ddd, *J* 14.9, 7.1 and 3.1, NCH_B), 3.70 (3 H, s, OMe) and 5.13 (1 H, dd, *J* 10.2 and 2.0, $CH_cH_t{=}CH$), (the remainder were obscured by those of the major isomer) and δ_C 18.15 (Me), 21.23 (Me), 28.15 (Bu^t), 39.97 (CH_2), 48.14 (CH), 51.33 (CH), 51.75 (OMe), 79.37 (Me_3C), 118.65 (=CH_2), 135.77 (=CH), 155.83 [C(O)N] and 175.21 (CO_2).

(*b*) Rearrangement of the corresponding *Z*-isomer (*Z*)-**15c** (1.2 mmol) using the general procedure gave a similar ratio (81:19) of diastereoisomers (**16c** and **17c**) in 81% yield, which exhibited spectral data identical with the foregoing.

(2SR,3SR)- *and* (2RS,3SR)-*Methyl* 2-(tert-*butoxycarbonylaminomethyl*)-3-[(1,1-*dimethylethyl*)*dimethylsilyloxymethyl*]*pent*-4-*enoate* **16d** *and* **17d**.—(*a*) The (*E*)-4-silyloxybut-2-enyl ester (*E*)-**15d** (2.3 mmol) was rearranged using the general procedure; SG chromatography (10% ethyl acetate in petroleum) gave the (2SR,3SR)-*ester* **16d** as a colourless oil (0.685 g, 77%); ν_{max}/cm^{-1} 3380 and 1720br; δ_H(400) 0.03 (3 H, s, MeSi), 0.04 (3 H, s, MeSi), 0.88 (9 H, s, Bu^{t}Si), 1.43 (9 H, s, Bu^{t}O), 2.52–2.67 (1 H, m), 2.79 (1 H, ddd, *J* 8.4, 8.2 and 4.1, CHCO), 3.24 (1 H, ddd, *J* 14.1, 8.4 and 6.1, NCH_A), 3.37–3.48 (1 H, m, NCH_B), 3.61–3.75 (2 H, m, CH_2O), 3.69 (3 H, s, OMe), 4.70–5.10 (1 H, br, NH), 4.95–5.11 (2 H, m, =CH_2) and 5.68 (1 H, ddd, *J* 16.9, 10.5 and 9.4, =CH); δ_C −5.43 (2 × MeSi), 18.38 (Me_3CSi), 25.95 (Bu^t), 28.46 (Bu^t), 40.05 (CH_2), 46.40 (CH), 46.73 and 46.91 (CH), 51.59 and 51.81 (OMe), 64.03 and 64.63 (CH_2O), 79.34 (Me_3CO), 117.68 and 118.10 (=CH_2), 136.39 (=CH), 155.77 [C(O)N] and 174.77 (CO_2) [Found: M^+ + H (FAB), 388.2516. $C_{19}H_{38}NO_5Si$ requires *M*, 388.2519]. The minor (2*SR*,3*SR*) diastereoisomer **17d** was identified in the foregoing using the data given immediately below and quantified by integration of the methyl ester resonances at δ_H 3.66 and 3.69.

(*b*) Rearrangement of the (*Z*)-silyloxybut-2-enyl ester (*Z*)-**15d** (0.89 mmol) using the general procedure and SG chromatography (10% ethyl acetate in petroleum) gave the (2RS,3SR)-*ester* **17d** as a colourless oil (0.234 g, 68%); ν_{max}/cm^{-1} 3375 and 1720br; δ_H(250) 0.04 (6 H, s, 2 × MeSi), 0.86 (9 H, s, Bu^t), 1.41 (9 H, s, Bu^t), 2.39–2.51 (1 H, m), 2.61–2.70 (1 H, m), 3.12–3.63 (4 H, m), 3.66 (3 H, s, OMe), 4.82–4.92 (1 H, m, NH), 4.97–5.11 (2 H, m, =CH_2) and 5.58 (1 H, ddd, *J* 16.9, 10.1 and 9.8, =CH); δ_C −5.29 (2 × MeSi), 18.03 and 18.29, (Me_3CSi), 25.73 and 25.99 (Bu^t), 28.45 (Bu^t), 35.01 and 35.16 (CH_2), 41.05 and 41.28 (CH), 49.92 (CH, br), 51.46 (OMe), br), 60.57 (CH_2O), 79.46 (Me_3CO, sl. br), 117.14 and 117.65 (=CH_2), 138.25 (=CH, sl. br), 155.84 [C(O)N, sl. br] and 174.06 (CO_2) [Found: M^+ + H (FAB), 388.2511]. Integration of the methyl ester region showed the presence of −6% of the (2*SR*,3*SR*) isomer **16d**.

(2SR,3SR) *and* (2RS,3SR)-*Methyl* 2-(tert-*Butoxycarbonylaminomethyl*)-3-*hydroxyethylpent*-4-*enoate* **16e** *and* **17e**.—(*a*) By the general procedure, rearrangement of the (E)-5-silyloxypent-2-enyl ester (*E*)-**15e** (2.5 mmol) gave a crude product containing the desired silyloxy ester **16e**. This (*ca.* 1 g) was dissolved in dry THF (10 cm^3) and the stirred solution cooled to 0 °C before the dropwise addition of tetrabutylammonium fluoride (TBAF) 1 mol dm^{-3} solution in THF (3 mmol, 3 cm^3). The resulting solution was stirred at 0 °C until TLC indicated completion of desilylation (0.75 h) when it was evaporated. The residue was partitioned between ethyl acetate (70 cm^3) and water (20 cm^3). The aqueous layer was further extracted with ethyl acetate (25 cm^3) and the combined extracts were dried and evaporated. Purification of the residue by SG chromatography [40% EtOAc in petroleum] gave the (2SR,3SR)-*hydroxy ester* **19** (0.53 g, 74%) as a colourless oil, ν_{max}/cm^{-1} 3450br and 1710br; δ_H(400) 1.43 (9 H, s, Bu^t), 1.55–1.80 (2 H, m), 1.95 (1 H, br s, OH), 2.32–2.80 (2 H, m), 3.34 (2 H, app. t, *J* 7, CH_2N), 3.57–3.75 (2 H, m), 3.71 (3 H, s, OMe), 4.85–4.96 (1 H, br, NH), 4.98–5.22 (2 H, m, =CH_2) and 5.65 (1 H, ddd, *J* 17, 10 and 9.5, =CH); δ_C 28.42 (Bu^t), 34.83 (CH_2), 39.68 (CH_2), 41.48 (CH), 50.05 (CH), 51.85 (OMe), 60.59 (CH_2), 79.62 (Me_3C), 117.82 (=CH_2), 138.21 (=CH), 156.07 [C(O)N] and 174.15 (CO_2) (Found: C, 58.9; H, 8.7; N, 5.1. $C_{14}H_{25}NO_5$ requires C, 58.5; H, 8.8; N, 4.9%).

The (2*RS*,3*SR*) isomer **20** was detected using the data given immediately below and quantified (8%) by integration of the methyl ester resonances at δ_H 3.68 and 3.71.

(*b*) Rearrangement of the (*Z*)-5-silyloxypent-2-enyl ester (*Z*)-**15e** (2 mmol), followed by desilylation as described above gave largely the (2RS,3SR)-*hydroxy ester* **20** (0.37 g, 65%) as a colourless oil; ν_{max}/cm^{-1} 3450 and 1710br; δ_H(400) 1.43 (9 H, s, Bu^t), 1.56 (1 H, dddd, *J* 13.9, 8.8, 5.8 and 5.5, $CH_ACH_BCH_2$-OH), 1.79–1.89 (1 H, m, $CH_ACH_BCH_2OH$), 2.09 (1 H, br s, OH), 2.48–2.57 (1 H, m), 2.70 (1 H, ddd, *J* 7.5, 6.3 and 5.5), 3.30–3.41 (2 H, m, CH_2N), 3.58 (1 H, ddd, *J* 10.7, 7.9 and 5.8, CH_ACH_BOH), ~3.69 (1 H, m, partly obscured, CH_ACH_BOH), 3.68 (3 H, s, OMe), 4.93–5.01 (1 H, br, NH), 5.06–5.12 (2 H, m, =CH_2) and 5.63 (1 H, ddd, *J* 17.7, 9.5 and 9.2, =CH); δ_C 28.42 (Bu^t), 34.95 (CH_2), 40.31 (CH_2), 41.18 (CH), 49.60 (CH), 51.62 (OMe), 60.38 (CH_2O), 79.62 (Me_3C), 117.45 (=CH_2), 138.21 (=CH), 156.11 [C(O)N] and 174.15 (CO_2) (Found: C, 58.6; H, 8.6; N, 4.7%).

Integration of the methyl ester resonances showed the presence of 15% of the (2*SR*,3*SR*) diastereoisomer **19**.

(E)-*Methyl* 2-(tert-*Butoxycarbonylaminomethyl*)*hex*-4-*enoate* **22**.—By the general method, rearrangement of the but-3-en-2-yl ester **21** (1.23 mmol) and purification by SG chromatography [20% ethyl acetate in petroleum] gave the (*E*)-hex-4-enoate **22** (0.20 g, 64%) as a colourless oil; ν_{max}/cm^{-1} 3380, 1712br, 1510, 1440, 1170 and 970; δ_H(90) 1.46 (9 H, s, Bu^t), 1.66 (3 H, d, *J* 7, Me), 2.18–3.46 (5 H, m), 3.75 (3 H, s, OMe), 4.81–5.07 (1 H, br, NH) and 5.39–5.59 (2 H, m, 2 × =CH); δ_C 17.90

(6-Me), 28.39 (3 × Me), 32.94, 41.25, 45.69, 51.74 (OMe), 79.35 (Me_3CO), 126.86 (=CH), 128.18 (=CH), 155.85 [C(O)N] and 174.97 (CO_2); *m/z* 201 (M^+–$Me_2C{=}CH_2$, 19%), 184 (12), 170 (14), 157 (22), 141 (14), 140 (11), 127 (13), 81 (20), 80 (22), 70 (10), 59 (11) and 57 (100) (Found: M^+–$Me_2C{=}CH_2$, 201.1030. $C_9H_{15}NO_4$ requires *M*, 201.1009).

The sample was a single geometric isomer according to the ^{13}C NMR data.

cis-3-tert-*Butoxycarbonylaminomethyl*-4-*vinyltetrahydrofuran*-2-*one* **24**.—A solution of the crude acid **23a** (0.21 g, ~0.56 mmol), obtained from rearrangement of the (*E*)-4-silyloxybut-2-enyl ester (*E*)-**15d** by the general procedure, in dry THF (5 cm^3) was cooled to 0 °C and treated dropwise with TBAF (1 mol dm^{-3} solution in THF; 1 cm^3, 1 mmol). The cooling bath was removed and the resulting solution stirred for 0.5 h; the bulk of the solvent was then evaporated. The residue was partitioned between ice-cold 0.2 mol dm^{-3} hydrochloric acid (3 cm^3) and ethyl acetate (10 cm^3). The separated aqueous layer was further extracted with ethyl acetate (2 × 10 cm^3) and the combined organic solutions were dried and evaporated, finally using high vacuum. The residue, consisting mainly of the hydroxy acid **23b**, was stirred in dry, ice-cooled dichloromethane (5 cm^3) and the resulting solution treated sequentially with triethylamine (0.6 cm^3) and 2-chloro-1-methylpyridinium iodide (0.57 g, 2.2 mmol). The mixture was stirred for 16 h without cooling and then diluted with dichloromethane (50 cm^3) and washed with water (2 × 10 cm^3) and brine (10 cm^3); it was then dried and evaporated. SG chromatography of the residue (15% ethyl acetate in petroleum) then separated the cis-*lactone* **24** (0.093 g, 69%) as a colourless oil, ν_{max}/cm^{-1} 3375, 1745 and 1710; δ_H(400) 1.44 (9 H, s, Bu^t), 2.90 (1 H, ddd, *J* 8.6, 8.3 and 5.8, 3-H), 3.12–3.22 (1 H, m, NCH_A), 3.24 (1 H, dddd, *J* 9.1, 5.8, 5.8 and 2.3, 4-H), 3.43–3.52 (1 H, m, NCH_B), 4.18 (1 H, dd, *J* 9.3 and 2.3, 5-H_A), 4.37 (1 H, dd, *J* 9.3 and 5.8, 5-H_B), 5.19–5.28 (2 H, m, $=CH_2$) and 5.77 (1 H, ddd, *J* 17.0, 9.9 and 9.1, =CH); δ_C 28.37 [$C(CH_3)_3$], 37.60 (CH_2NH), 42.96, 43.38 (3- and 4-CH), 71.41 (CH_2O), 79.68 [$C(CH_3)_3$], 119.07 ($=CH_2$), 133.04 (=CH), 155.79 [C(O)N] and 177.78 (CO_2) [Found: M^+ + H (FAB), 242.1386. $C_{12}H_{20}NO_4$ requires *M*, 242.1392].

trans-3-tert-*Butoxycarbonylaminomethyl*-4-*vinyltetrahydrofuran*-2-*one* **26**.—A solution of the crude acid **25a** (0.34 g, ~0.9 mmol), obtained from rearrangement of the (*Z*)-4-silyloxybut-2-enyl ester (*Z*)-**15d** by the general procedure, in dry THF (10 cm^3) was cooled to 0 °C and treated dropwise with TBAF (1 mol dm^{-3} solution in THF; 1.5 cm^3, 1.5 mmol). After 2 h, the reaction mixture was worked up as described above; SG chromatography of the crude product (15% ethyl acetate in petroleum) separated the trans-*lactone* **26** (0.184 g, 85%) as a colourless oil; ν_{max}/cm^{-1} 3380, 1750 and 1710; δ_H(400) 1.44 (9 H, s, Bu^t), 2.52 (1 H, ddd, *J* 11.5, 5.8 and 4.9, 3-H), 2.99 (1 H, dddd, *J* 11.5, 10.5, 8.2 and 7.8, 4-H), 3.37 (1 H, ddd, *J* 14.2, 6.2 and 5.8, NCH_A), 3.52 (1 H, ddd, *J* 14.2, 6.6 and 4.9, NCH_B), 3.94 (1 H, dd, *J* 10.5 and 9.0, 5-H_A), 4.41 (1 H, dd, *J* 9.0 and 8.2, 5-H_B), 5.26 (1 H, ddd, *J* 10.1, 0.9 and ~0.9, CH=CH_cCH_t), 5.33 (1 H, br d, *J* 17.1, CH=CH_cCH_t) and 5.74 (1 H, ddd, *J* 17.1, 10.1 and 7.8, $CH{=}CH_cCH_t$); δ_C 28.34 [$C(CH_3)_3$], 37.88 (CH_2NH), 43.62, 46.13 (3- and 4-CH), 70.35 (CH_2O), 79.65 [$C(CH_3)_3$], 119.69 ($=CH_2$), 133.88 (=CH), 155.97 [C(O)N] and 177.49 (CO_2) [Found: C, 60.0; H, 8.0; N, 5.7%; M^+ + H (FAB), 242.1387. $C_{12}H_{19}NO_4$ requires C, 59.7; H, 7.9; N, 5.8%].

Similar treatment of the (2*RS*,3SR)-ester **17d** (0.10 g, 0.26 mmol), derived from acid **25a**, with TBAF (1 mol dm^{-3} solution in THF; 0.4 cm^3, 0.4 mmol) for 2 h also led, after chromatography, to the *trans*-lactone **26** (0.051 g, 82%) which exhibited spectral data identical with the foregoing.

Similarly, treatment of the (2*SR*,3*SR*)-ester **16d** (0.11 g, 0.29 mmol), derived from the (E)-4-silyloxybut-2-enyl ester (*E*)-**15d**, with TBAF (1 mol dm^{-3} solution in THF; 0.4 cm^3) at ambient temperature for 20 h also gave the *trans*-lactone **26** (0.050 g, 72%) as the only isolable product after chromatography.

(3RS,4SR) *and* (3SR,4SR)-3-(tert-*Butoxycarbonylaminomethyl*)-4-*vinyl*-3,4,5,6-*tetrahydropyran*-2-*one* **28** *and* **29**.—The intermediate crude silyloxy acids **27a** (0.58 g, ~1.5 mmol), obtained from rearrangement of the (Z)-5-silyloxypent-2-enyl ester (*Z*)-**15e**, were desilylated and the resulting hydroxy acids **27b** lactonized using 2-chloro-1-methylpyridinium iodide, as described above for the preparation of the *cis*-lactone **24**, to give, after careful SG chromatography (15% ethyl acetate in petroleum), the (3RS,4SR)-(trans)-*lactone* **28** (0.248 g, 65%) as a colourless oil; ν_{max}/cm^{-1} 3370 and 1720br; δ_H 1.43 (9 H, s, Bu^t), 1.83 (1 H, ddd, *J* 14.5, 6.8, 6.8 and 4.1, 5-H_A), 2.11 (1 H, dddd, *J* 14.5, 7.6, 6.5 and 4.4, 5-H_B), 2.43–2.49 (2 H, m, 3-and 4-H), 3.29 (1 H, br ddd, *J* ~ 14.4, 5.5 and 5.5, NCH_A), 3.62 (1 H, br ddd, *J* ~ 14.4, 7.4 and 2.4, NCH_B), 4.32 (1 H, ddd, *J* 11.3, 6.8 and 4.5, 6-H_A), 4.39 (1 H, ddd, *J* 11.3, 7.6 and 4.1, 6-H_B), 5.23 (1 H, br d, *J* 9.9, CH=CH_cCH_t), 5.24 (1 H, br d, *J* 17.4, CH=CH_cCH_t) and 5.83 (1 H, ddd, *J* 17.4, 9.9 and 7.9, =CH); δ_C 28.39 (Bu^t), 29.06 (5-CH_2), 38.01 (CH), 39.13 (CH_2N), 45.73 (CH), 66.94 (6-CH_2), 79.34 (Me_3C), 117.17 ($=CH_2$), 138.54 (=CH), 155.99 [C(O)N] and 173.85 (CO_2) [Found: C, 61.0; H, 8.1; N, 5.4. $C_{13}H_{21}NO_4$ requires C, 61.2; H, 8.3; N, 5.5%] and the (3SR,4SR)-(cis)-*lactone* **29** (0.034 g, 9%), ν_{max}/cm^{-1} 3380 and 1720br; δ_H(400) 1.43 (9 H, s, Bu^t), 1.76 (1 H, dddd, *J* 14.6, 10.0, 5.2 and 4.0, 5-H_{ax}), 2.22 (1 H, dddd, 14.6, 8.5, 4.4 and 4.2, 5-H_{eq}), 2.81 (1 H, ddd, *J* 9.5, 6.5 and 4.0, 3-H), 2.98 (1 H, dddd, *J* 9.8, 8.5, 6.5 and 5.2, 4-H), 3.15 (1 H, ddd, *J* 13.8, 9.5 and 4.0, CH_ACH_BN), 3.32 (1 H, ddd, *J* 13.8, 8.8 and 4.0, CH_ACH_BN), 4.28 (1 H, ddd, *J* 10.4, 10.0 and 4.4, 6-H_{ax}), 4.36 (1 H, ddd, *J* 10.4, 4.2 and 4.0, 6-H_{eq}), 5.11 (1 H, br d, *J* ~ 10.0, CH=CH_cCH_t), 5.12 (1 H, br d, *J* ~ 16.8, CH=CH_cCH_t), 5.16–5.26 (1 H, m, NH) and 5.54 (1 H, ddd, *J* 16.8, 10.0 and 9.8, =CH); δ_C 28.40 (Bu^t), 28.89 (5-CH_2), 38.32 (CH), 39.57 (CH_2N), 43.14 (CH), 65.95 (6-CH_2), 79.46 (Me_3C), 117.66 ($=CH_2$), 137.01 (=CH), 156.01 [C(O)N] and 174.22 (CO_2) [Found: M^+ + H (FAB), 256.1545. $C_{13}H_{22}NO_4$ requires *M*, 256.1549].

Similarly, by starting with the initial silyloxy acids (*cf.* **16e** and **19**) derived from the (E)-5-silyloxypent-2-enoate (*E*)-**15e**, largely the *cis*-valerolactone **29** was obtained (^1H and ^{13}C NMR characterisation only).

(3SR,4SR)-*Methyl* 4-*Vinylpiperidine*-3-*carboxylate* **30**.—The (2*SR*,3*SR*)-hydroxy ester **19** (0.215 g, 0.75 mmol), derived from rearrangement of the (*E*)-5-silyloxy-pent-2-enyl ester (*E*)-**15e**, was dissolved in dry dichloromethane (5 cm^3) containing diisopropylethylamine (0.17 cm^3) and the resulting solution was stirred in an ice-bath during the dropwise addition of a solution of methanesulfonyl chloride (0.10 g, 0.88 mmol) in dichloromethane (2 cm^3). The resulting solution was stirred without cooling for 6 h and then diluted with dichloromethane (20 cm^3). The resulting mixture was washed with water (10 cm^3), ice-cold 1 mol dm^{-3} hydrochloric acid (10 cm^3), water (5 cm^3) and brine (5 cm^3) and then dried and evaporated to leave a crude mesylate (0.25 g, 91%); δ_H(90) 1.44 (9 H, s, Bu^t), 1.55–2.10 (2 H, m), 2.44–2.82 (2 H, m), 3.02 (3 H, s, $MeSO_2$), 3.29–3.49 (2 H, m, CH_2N), 3.74 (3 H, s, OMe), 4.16–4.39 (2 H, m, CH_2OMs), 4.80–5.01 (1 H, br, NH), 5.09–5.38 (2 H, m, $=CH_2$) and 5.52–5.76 (1 H, m, =CH).

The crude mesylate (0.25 g) was treated with a solution of trifluoroacetic acid (1 cm^3) in dichloromethane (4 cm^3) and the resulting solution stirred at ambient temperature for 0.75 h. It was then evaporated and the residue was first dried *in vacuo* and then suspended in dichloromethane (6 cm^3) containing triethylamine (0.2 cm^3). After being stirred at ambient temperature

overnight the mixture was evaporated to dryness. SG chromatography of the residue (5% methanol in chloroform containing 1% triethylamine) then separated the (3SR,4SR)-(trans)-*piperidine* **30** (0.080 g, 63%) as a colourless oil, ν_{max}/cm^{-1} 3400 and 1730; δ_H(400) 1.72 (1 H, dddd, *J* 12.0, 11.2, 10.9 and ~2.0, 5-H_{ax}), 1.89 (1 H, dddd, *J* 12.0, 3.1, ~2.0 and ~2.0, 5-H_{aq}), 2.47 (1 H, dddd, *J* 11.2, 10.3, 7.8 and 3.1, 4-H_{ax}), 2.71 (1 H, ddd, *J* 10.3, 10.3 and 2.1, 3-H_{ax}), 2.89 (1 H, ddd, *J* 11.5, 10.9 and ~2.0, 6-H_{ax}), 2.98 (1 H, dd, *J* 11.7 and 10.3, 2-H_{ax}), 3.36 (1 H, ddd, *J* 11.5, ~2.0 and ~2.0, 6-H_{eq}), 3.44 (1 H, dd, *J* 11.7 and 2.1, 2-H_{eq}), 3.67 (3 H, s, OMe), 4.72–4.95 (1 H, br, NH), 5.07 (1 H, br d, *J* 10.3, CH=C$H_c$$H_t$), 5.09 (1 H, br d, *J* 17.1, CH=C$H_c$$CH_t$) and 5.69 (1 H, ddd, *J* 17.1, 10.3 and 7.8, =CH); δ_C 28.34 (5-CH_2), 41.62 (CH), 43.70 (CH_2N), 45.32 (CH_2N), 45.61 (CH), 51.98 (OMe), 116.57 (=CH_2), 138.26 (=CH) and 171.95 (CO_2) [Found: $M^+ + H$ (FAB), 169.1107. $C_9H_{15}NO_2$ requires *M*, 169.1103]. The material was essentially a single isomer according to the ^{13}C NMR spectrum.

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