# Simple Synthesis of L- and D-Vinylglycine (2-Aminobut-3-enoic Acid) and Related Amino Acids

**Keith O. Hallinan, David H. G. Crout* and William Errington**
*Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK*

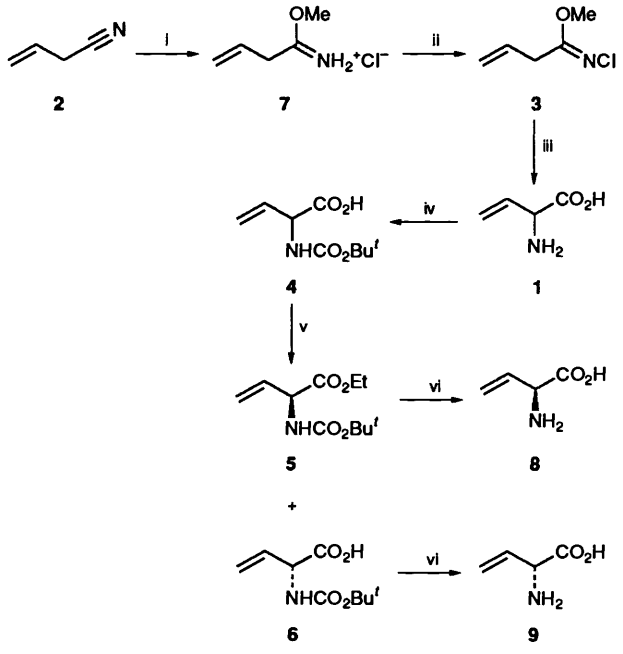
A three-step synthesis of vinylglycine **1** has been developed using a readily available starting material (but-3-enenitrile **2**), based on the Neber rearrangement of the corresponding *N*-chloroimidate, and using cheap, convenient reagents. Also described is a convenient optical resolution of the *N*-*tert*-butoxycarbonyl derivative by papain-catalysed enantioselective esterification in a two-phase system. From the optically active amino acid, related amino acids obtained *via* epoxidation, dihydroxylation and cyclopropanation have been prepared. The related β,γ-unsaturated amino acids (*E*)-2-aminopent-3-enoic acid **20** and (*E*)-2-amino-3-methylpent-3-enoic acid **22** have been synthesised using the same approach.

Vinylglycine **1**, a non-protein amino acid, has been isolated from fungi[1] and has been shown to inhibit a number of enzymes.[2] It has been shown to be an irreversible inhibitor of aspartate aminotransferase,[3] serine glyoxylate aminotransferase,[4] alanine racemase,[5] heart α-ketoglutarate dehydrogenase,[6] cystathionine γ-synthase[7] and other pyridoxal-dependent enzymes.[2] Vinylglycine acts as a suicide (mechanism-based) inhibitor of the kynurenine synthase of the yeast *Hansenula schneggii*. This enzyme also catalysed its deamination and γ-addition reactions.[8] Tryptophan synthase of *Escherichia coli* was found to catalyse the β-addition to vinylglycine of thiols and selenols.[9] Vinylglycine and vinylglycine β-lactam derivatives displayed antibacterial properties against *Bacillus subtilis* and *E. coli*.[10] It has also been shown to be a specific inhibitor of photorespiration in rice[11] and to be useful in plant growth regulation as a photosynthesis stimulator.[12]

Owing to its biological activity, vinylglycine has been the subject of many synthetic studies since it was first prepared in 1974.[13] Recently, enantiomerically pure vinylglycine has been prepared by decarboxylative elimination of a glutamic acid derivative in five steps, to give vinylglycine in 45% overall yield,[14,15] from D-mannitol in seven steps and in 8% overall yield,[16] by Schöllkopf's method from cyclo(L-valylglycine) in three steps and in 25% overall yield,[17] and by decarboxylative rearrangement of protected glutamic acid esters of *N*-hydroxy-2-selenopyridines in three steps and in 45% overall yield.[18] A protected form of vinylglycine has been prepared from L-methionine by thermolysis of the corresponding sulfoxide in three steps and in 20% overall yield.[19] Three other syntheses based on methionine have been reported.[20-22]

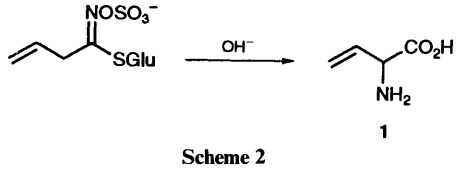
Racemic vinylglycine has been prepared by a Strecker reaction from acrolein in four steps and in 7% overall yield,[23] by oxidative rearrangement of allylic selenides in the presence of amine nucleophiles in four steps and in 18% overall yield,[24,25] and from (*Z*)-but-2-ene-1,4-diol in four steps and in 26% overall yield.[26] Protected vinylglycine has also been prepared from electrophilic glycine equivalents and Grignard reagents.[27-29] Deuterium labelled racemic vinylglycine has been prepared from an alkyl sulfone in three steps and in 49% overall yield.[30] Syntheses based on homoserine[12] and serine[32] have been reported.

We were interested in providing a route to the enantiomers of vinylglycine from achiral starting materials, efficient and inexpensive enough to make it readily available as a building block for other chiral compounds. The approach selected was based on the Neber rearrangement, which has been successfully applied to the synthesis of other β,γ-unsaturated amino acids.[33]




**Scheme 1** *Reagents:* i, MeOH–HCl; ii NaOCl; iii, $OH^-$–$H_2O$; iv, $(Bu^tOCO)_2O$–$OH^-$; v, papain, EtOH; vi, $H^+$–$H_2O$

The approach envisaged is shown in Scheme 1, and follows closely the route used to prepare (*E*)-2-amino-3-methylbut-3-enoic acid.[33] The last step in this synthesis employed methoxide to induce the Neber rearrangement. However, it had been reported that sinigrin (allyl glucosinolate, Scheme 2) underwent Neber rearrangement simply on treatment with aqueous alkali (Scheme 2).[13] Accordingly, a further simplification of the route



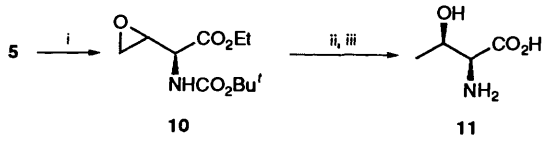

**Scheme 2**

shown in Scheme 1 was envisaged in which the Neber rearrangement (**3**→**1**) would be induced by aqueous alkali in the same way. In the event, the synthesis proceeded as expected, using the reagents given in Scheme 1, and starting from the cheap, readily available precursor, but-3-enenitrile **2**. The first

two steps proceed in 100 and 95% yield, respectively. The Neber rearrangement step gave vinylglycine in 53% yield, giving an overall yield of 50%. For the isolation of vinylglycine in the last step, a cation exchange resin was used, but this gave rise to unaccountable losses of material. These losses were a function of the reaction mixture applied to the column, as they did not occur if pure vinylglycine was isolated from an aqueous solution by the same procedure. However, this problem could be circumvented by preparing the *N-tert*-butoxycarbonyl (Boc) derivative *in situ* after alkali treatment of the *N*-chloroimidate **3**, leading to the isolation of the Boc derivative **4** of vinylglycine in 67% yield. This procedure was particularly convenient in delivering vinylglycine protected in a form suitable for the enzymatic resolution.

For the resolution of *N-tert*-butoxycarbonylvinylglycine, a biotransformation was used. Papain has been found to be useful for the kinetic resolution of amino acid derivatives, particularly when used in the synthetic direction.[34-37] The problem of an unfavourable equilibrium constant when the esterification is conducted in a purely aqueous medium can be circumvented by carrying out the esterification in a two-phase system. Provided that the product of esterification is preferentially partitioned into the organic phase, relative to the substrate, a significant increase in the equilibrium constant favouring ester synthesis can be achieved. The new effective equilibrium constant is a function of the partition coefficients of substrate and product between water and the organic solvent, and of the volumes of the two phases. For resolution of the Boc-derivative **4** the organic phase was dichloromethane and the esterifying alcohol was ethanol. A single incubation gave the ethyl ester **5** of the L-derivative in 80% yield. To obtain the D-isomer in optically pure form, a second incubation was carried out to remove remaining L-isomer. When this was done, the unesterified D-Boc derivative **6** was obtained in 90% yield. Hydrolysis of the ethyl ester **5** and the D-Boc derivative **6** gave L-vinylglycine **8** and D-vinylglycine **9**, respectively, both in 95% yield.

As the foregoing synthesis provided ready access to vinylglycine in either racemic or homochiral form, some further reactions of derivatives of this compound were studied. Thus, epoxidation of the derivative **5** (Scheme 3) gave a



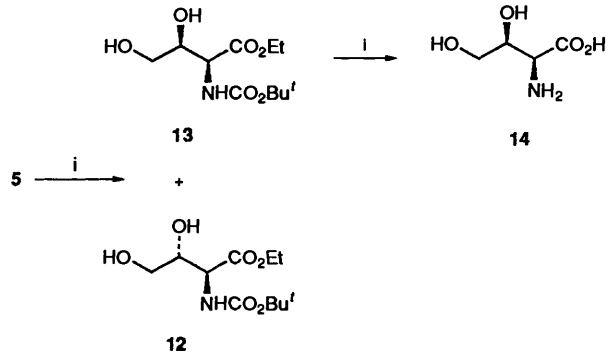

**10** **11**

**Scheme 3** *Reagents:* i, *m*-chloroperbenzoic acid; ii, Raney Ni; iii, HCl

diastereoisomeric mixture of 60% diastereoisomeric excess (de) in chloroform and 71% de in carbon tetrachloride. Reduction ($H_2$/Raney nickel) of the epoxide **10** proceeded regioselectively (Scheme 3). The product mixture was hydrolysed to the free amino acid mixture in which L-threonine **11** was identified as the major component, confirming that the major product of the epoxidation had the 2*S*,3*S*-configuration. A similar result had been obtained on epoxidation of the *N*-benzyloxycarbonyl derivative of vinylglycine methyl ester, which similarly gave predominantly the (2*SR*,3*SR*)-diastereoisomer.[38-40]

Hydroxythreonine **14** is an amino acid of considerable interest. It has been found as a constituent of actinomycin Z1 produced by *Streptomyces fradiae*.[41] It is produced by an unidentified *Streptomyces* species,[42] and also by the plant pathogen *Pseudomonas andropogonis*.[43] However, its importance has been highlighted by recent evidence implicating it as a precursor of pyridoxol (vitamin $B_6$).[44] It was originally synthesised from DL-glyceraldehyde,[45] from D-glyceraldehyde,[46] and from L-erythronic and L-threonic acids.[47] A revisiting of the glyceraldehyde route has resulted in a diastereoselective synthesis from the cyclohexylidene derivative of *R*-glyceraldehyde by a rather lengthy sequence (ten steps from the derivative).[48] L-Hydroxythreonine has been prepared recently by hydrolysis of the corresponding 4-chloro compound, itself prepared by ring opening of a derivative of the corresponding epoxide.[49]

The simple synthesis of vinylglycine described here opened the way to a rather direct synthesis. Thus, hydroxylation of derivative **5** with osmium tetraoxide gave a mixture of hydroxylated derivatives of 33% de (Scheme 4). The product




**13** **14** **12**

**Scheme 4** *Reagents:* i, $OsO_4$, *N*-methylmorpholine *N*-oxide; ii, HCl

isomers were readily separated by chromatography. X-Ray structure determination of the crystalline minor isomer showed it to have the relative (and hence absolute) configuration 2*S*,3*R* (Fig. 1 and **12**, Scheme 4). The major isomer **13** (the 2*S*,3*S* isomer) was hydrolysed to give the pyridoxol precursor L-hydroxythreonine **14**.

Molecular modelling of the substrate **5** for these oxidative reactions revealed a minimum energy extended conformation [Fig. 2(*a*)]. The unsaturated side chain adopts a conformation in which the plane of the olefinic system lies nearly perpendicular to the extended backbone chain and in which the Boc system hinders access to the double bond. A conformation of similar energy was found in which the carbonyl groups were *anti*-parallel rather than *syn*-parallel and in which one face of the double bond was also masked by the Boc group [Fig. 2(*b*)]. However, in both of these conformations, a further conformation of nearly identical energy was found in which the unsaturated side chain had undergone a 180° rotation. Thus, although attack of the double bond by electrophilic reagents is probably highly directional, taking place from the side of the

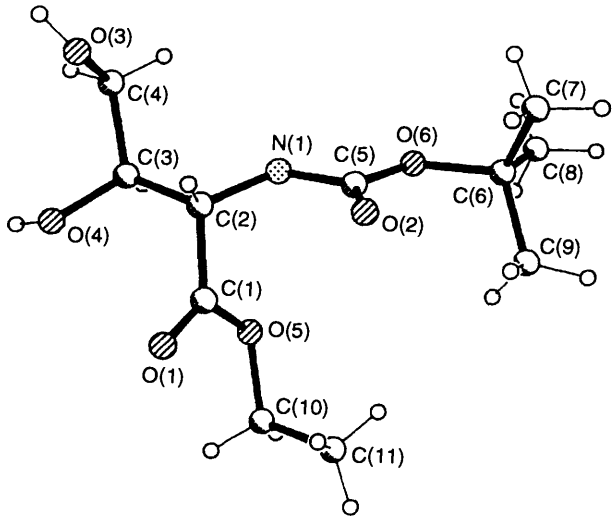



**Fig. 1** X-Ray crystal structure of (2*S*,3*R*)-ethyl 2-*tert*-butoxycarbonylamino-3,4-dihydroxybutanoate **12**

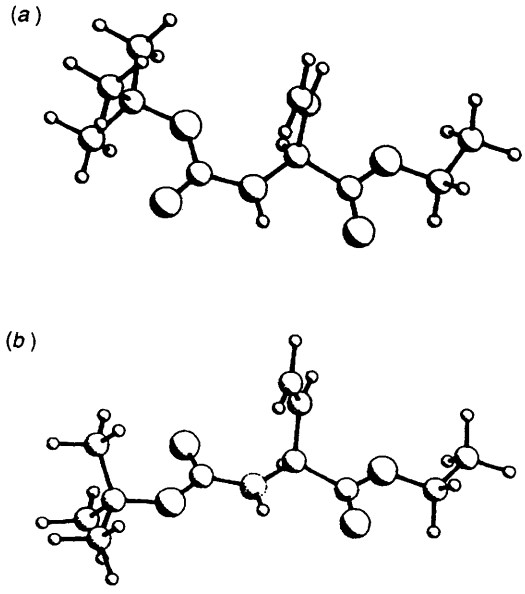
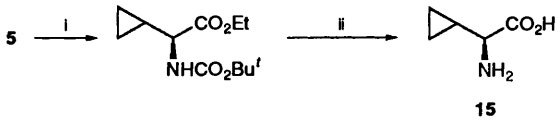



**Fig. 2** Energy minimised conformations of ethyl *N*-(*tert*-butoxycarbonyl)vinylglycinate **5**; (*a*) *syn*-parallel, (*b*) *anti*-parallel orientation of the carbonyl groups

ethoxycarbonyl group, the existence of conformers of nearly equal energy in which either the *re*- or *si*-face of the alkene is presented to the reagent, accounts for the modest diastereoisomeric excesses observed in the oxidative transformations.

Cyclopropylglycine **15** (Scheme 5) has interesting biological

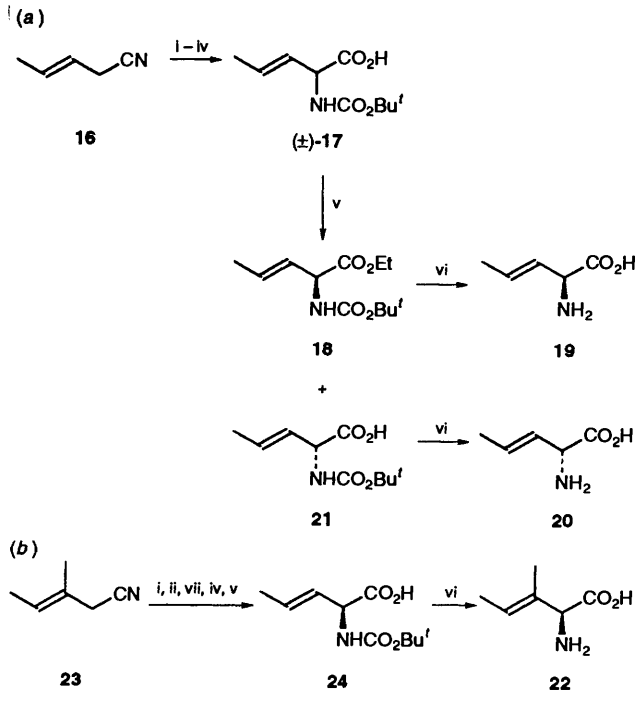



**Scheme 5** *Reagents:* i, $CH_2N_2$–$Pd(OAc)_2$; ii, HCl

properties. Thus, it is an inhibitory analogue of valine, substituting for this amino acid in valyl tRNA-catalysed reactions.[50,51] It has been prepared in racemic form by the Strecker reaction[52] and from benzyl 2-chloro-2-cyclopropylideneacetate.[53] Cyclopropylglycine has been resolved using acylase I,[54] but no other preparation of optically active material has been described. The ready availability of the enantiomers of vinylglycine provided a ready route to L-cyclopropylglycine **15** *via* $Pd^{II}$-catalysed cyclopropanation of the derivative **5** (Scheme 5).

The synthesis of analogues of vinylglycine was also studied. Although imidate hydrochloride formation and *N*-chlorination of (*E*)-pent-3-enenitrile **16** [Scheme 6(*a*)] proceeded efficiently, the Neber rearrangement using aqueous alkali proceeded in only poor yield (14%). However, direct conversion to the Boc derivative **17** of (*E*)-2-aminopent-3-enoic acid gave an improved yield (29%) [Scheme 6(*a*)] as in the preparation of the corresponding derivative of vinylglycine. The corresponding (*S*)-ethyl ester **18**, efficiently obtained using papain, was hydrolysed to (2*S*)-2-aminopent-3-enoic acid **19**. Previously, 2-aminopent-3-enoic acid had been prepared in optically active form by the Schöllkopf procedure only as a mixture of *E*,*Z*-isomers.[55] It has been obtained in racemic form as a mixture of *E*,*Z*-isomers[23] and as the pure (*E*)- and (*Z*)-isomers in racemic form.[56] The D-isomer **20** was obtained by hydrolysis of the Boc derivative **21** obtained from the papain-catalysed resolution.

Better yields of the (*E*)-dehydroisoleucine analogue **22** were obtained [Scheme 6(*b*)]. The required nitrile **23** was readily




**Scheme 6** *Reagents:* i, MeOH–HCl; ii, NaOCl; iii, NaOH; iv, $(Bu^tOCO)_2O$; v, papain, EtOH; vi, HCl; vii, NaOMe

obtained from tiglic acid [(*E*)-2-methylbut-2-enoic acid]. Use of aqueous alkali in the Neber rearrangement gave poor yields, but, with sodium methoxide as base, a 58% yield was obtained. Direct conversion into the Boc derivative proceeded in 50% yield. The corresponding ethyl ester was not resolved as efficiently using papain as the previous two examples, so that only the L-isomer **22** could be obtained readily in a state of high optical purity. This compound, which is produced by the fern *Coniogramme intermedia*,[57] has not previously been synthesised in optically active form.

The work described here demonstrates that for certain amino acids, the Neber rearrangement opens the way to short and convenient syntheses. The rearrangement is encouraged by the increased carbon acidity of the allylic proton in the unsaturated *N*-chloroimidate precursors, which makes the method particularly appropriate for the synthesis of β,γ-unsaturated amino acids. Further, the suitability of derivatives of the products for resolution by papain-catalysed esterification offers a viable and convenient route to a number of the products in optically active form.

## Experimental

$^1H$ NMR specta were determined at 220 MHz using a Perkin-Elmer R34 spectrometer, at 250 MHz using a Bruker AC 250 spectrometer, or at 400 MHz using a Bruker WH400 spectrometer. All coupling constants are quoted in Hz. $^{13}C$ NMR spectra were determined at 100.62 MHz using a Bruker WH400 spectrometer. Mass spectra were determined using a Kratos MS 80 mass spectrometer. IR spectra were determined on a Perkin-Elmer 580-B spectrometer. Optical rotations were determined using an AA-100 polarimeter (Optical Activity Ltd.) and are given in units of $10^{-1}$ deg $cm^2$ $g^{-1}$. Papain was obtained from the Sigma Chemical Company Ltd. Light petroleum used had b.p. 40–60 °C. Molecular modelling was carried out using PCMODEL and NMR simulation using the program PCPMR (both from Serena Software, Bloomington, Indiana, USA).

*Methyl But-3-enimidate Hydrochloride* **7**.—Into a stirred solution of allyl cyanide (but-3-enenitrile) **2** (10 g, 15.2 mmol) in anhydrous methanol (10 $cm^3$) under nitrogen at 0 °C was passed anhydrous HCl gas for 1 h. The flask was stoppered and its contents were stirred for 12 h at 2 °C. The reaction mixture was diluted with anhydrous diethyl ether (250 $cm^3$), the resulting precipitate was filtered off and washed with diethyl ether (50 $cm^3$) to give the imidate hydrochloride **7** as a colourless hygroscopic solid (19.28 g, 95%); $\nu_{max}$(Nujol)/$cm^{-1}$ 1669 (C=N); $\delta_H$(250 MHz; $D_2O$) 3.40 (2 H, d, *J* 6.8, $CH_2$), 4.08 (3 H, s, OMe), 5.31 [1 H, d, *J* 16.4, CH=C*H* (*trans*)], 5.33 [1 H, d, *J* 10.8, CH=CH*H* (*cis*)] and 5.90 (1 H, ddt, *J* 10.8, 16.4, 6.8, $CH_2CH$=); *m*/*z* (relative abundance) (CI, $NH_3$) 100 ($M^+$, 100%), 86 (47) and 68 (2).

*Methyl* N-*Chlorobut-3-enimidate* **3**.—The imidate hydrochloride **7** (3.0 g) was added directly to aqueous sodium hypochlorite (12–14%, 100 $cm^3$) at 0 °C. The mixture was stirred for 1 h and then extracted with light petroleum 3 × 30 $cm^3$). (**CAUTION:** on one occasion, in the hands of inexperienced operators, an explosion occurred after the mixture had been stirred for approximately 1 h. On investigation, it was concluded that this was attributable to the ingress of water during the preparation of the imidate hydrochloride, some of which had undergone hydrolysis to ammonium chloride. The explosion was attributed to the formation of nitrogen trichloride on treatment of the impure imidate hydrochloride by sodium hypochlorite. The reaction has been repeated by experienced operators many times without incident.) The extracts were dried ($MgSO_4$) and then concentrated under reduced pressure to give the *N*-chloroimidate **3** as a colourless oil (mixture of *Z*- and *E*-isomers) (2.95 g, 100%); $\delta_H$(250 MHz; $CDCl_3$) [major isomer (80% of product mixture)] 3.37 (2 H, ddd, *J* 6.7, 1.5, 1.4, $CH_2$), 3.80 (3 H, s $OCH_3$), 5.186 [1 H, ddt, *J* 9.4, 1.4, 1.4, HC=C*H*H (*cis*)] and 5.201 [1 H, ddt, *J* 16.9, 1.4, 1.5, HC=CH*H* (*trans*)], 5.86 (ddt, *J* 16.9, 9.4, 6.7, *H*C=$CH_2$). (*N.b.* This spectrum contained many overlapping resonances. The coupling constants quoted were derived by inspection and the spectrum was then simulated using the program PCPMR. The simulated and observed spectra were in good agreement.) $\delta_C$(100 MHz; $CDCl_3$) (major isomer) 36.30 ($CH_2$), 54.77 ($OCH_3$), 118.97 ($CH_2C$=), 129.29 ($CH_2$=) and 173.99 (C=N); *m*/*z* (relative abundance) (EI) 136 [$(M + H)^+$, $^{37}Cl$, 2.3%], 134 [$(M + H)^+$, $^{35}Cl$ (6.9)], 98 (21), 94 (4), 92 (11), 82 (2), 68 (14), 58 (48) and 41 (100).

DL-*Vinylglycine* **1**.—A solution of *N*-chloroimidate **3** (0.88 g, 6.6 mmol) in sodium hydroxide solution (0.79 g, 19.8 mmol, 50 $cm^3$) was stirred for 10 h at room temperature. The solution was applied to a column of Dowex 50W-X8 cation exchange resin ($H^+$ form, 10 g). The column was washed with deionised water and eluted with 2% aqueous pyridine until the ninhydrin test was negative. The eluate was evaporated under reduced pressure to give DL-vinylglycine **1** (0.35 g, 53%), m.p. 215–218 °C (decomp.) [lit.,[58] 218–220 °C (decomp.); lit., [24,25] 218–220 °C (decomp.)] [Found: $(M + H)^+$ 102.0555. $C_4H_8NO_2$ requires 102.0555]; $\delta_H$(400 MHz; $D_2O$) 4.21 (1 H, d, *J* 7.5, $CHCO_2^-$), 5.42 [1 H, d, *J* 10.6, CH=C*H*H (*cis*)], 5.42 [1 H, d, *J* 16.3, CH=CH*H* (*trans*)] and 5.91 (1 H, ddd, *J* 7.5, 10.6, 16.3, C*H*=$CH_2$); $\delta_C$(100 MHz; $D_2O$) 57.84 ($CHNH_3^+$), 122.14 ($CH_2$=), 130.95 (*C*H=$CH_2$) and 173.65 ($CO_2^-$); *m*/*z* (relative abundance) (CI, $NH_3$) 102 [$(M + H)^+$, 100%] and 56 (45).

N-DL-(tert-*Butoxycarbonyl*)*vinylglycine* **4**.—A solution of freshly prepared *N*-chloroimidate **3** (1.1 g, 8.3 mmol) in a solution of sodium hydroxide (1.079 g, 27 mmol) in water (50 $cm^3$) was stirred at room temperature for 10 h. Dioxane (50 $cm^3$) was added, the mixture was cooled to 0 °C, di-*tert*-butyl dicarbonate (2.14 g, 10 mmol) was added and the mixture was stirred for 8 h with the cooling source removed so that the temperature gradually increased to room temperature. The dioxane was removed under reduced pressure and the remaining solution was extracted with ethyl acetate (10 $cm^3$). To the aqueous phase was added ethyl acetate (15 $cm^3$). The aqueous phase was brought to pH 2 (1 mol $dm^{-3}$ $KHSO_4$), a further quantity of ethyl acetate (15 $cm^3$) was added and the two phases were shaken together. The organic phase was washed with saturated aqueous sodium chloride (15 $cm^3$), dried ($MgSO_4$) and then concentrated under reduced pressure to give the derivative **4** as a colourless oil (1.11 g, 67%) [Found $(M + H)^+$ 202.1067. $C_9H_{16}NO_4$ requires 202.1079]; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1720; $\delta_H$(250 MHz; $CDCl_3$, mixture of atropisomers) 1.42 (9 H, s, $Me_3C$), 4.66 and 4.86 (together 1 br s, C*H*$CO_2H$), 5.25 [1 H, d, *J* 10.4, CH=C*H*H (*cis*)], 5.35 [1 H, d, *J* 17.2, CH=CH*H* (*trans*)], 5.91 (1 H, m, C*H*=$CH_2$) and 8.9 (2 H, br s, $CO_2H$, NH); $\delta_C$(100 MHz; $CDCl_3$) 28.1 ($CMe_3$), 55.62 and 57.01 ($Me_3C$), 80.31 and 81.64 (*C*H$CO_2H$), 117.49 ($CH_2$=), 132.21 and 132.63 (CH=), 155.20 and 156.73 (CONH) and 173.59 and 174.57 ($CO_2H$); *m*/*z* (relative abundance) (CI, $NH_3$) 219 [$(M + NH_4)^+$, 10%], 202 (10), 163 (100), 156 (9), 146 (35), 102 (25) and 56 (80).

*Resolution of* N-(tert-*Butoxycarbonyl*)*vinylglycine* **4**.—A mixture of papain (Sigma, type II, 0.3 g), L-cysteine (45 mg), EDTA tetrasodium salt (1 mol $dm^{-3}$; 75 $cm^3$) in citrate–phosphate buffer (1 mol $dm^{-3}$; 15 $cm^3$, pH 4.2) was stirred for 10 min. The racemic DL-*N*-(*tert*-butoxycarbonyl)vinylglycine **4** (0.5 g, 2.5 mmol) dissolved in a mixture of dichloromethane (3 $cm^3$) and ethanol (2 $cm^3$) was added. The mixture was stirred for 2 days at 37 °C. The mixture was filtered (Celite) and washed with ethyl acetate (10 $cm^3$) and water (10 $cm^3$). The organic phase was separated off, ethyl acetate (10 $cm^3$) was added to it and the aqueous phase was carefully acidified to pH 1 (Congo red) with $KHSO_4$ (1 mol $dm^{-3}$). The mixture was shaken, and the combined organic layer and washings were extracted with aqueous sodium hydrogen carbonate (5%, 2 × 5 $cm^3$), washed with water (10 $cm^3$) and saturated aqueous sodium chloride (10 $cm^3$), dried ($MgSO_4$) and then concentrated under reduced pressure. The residue was purified by flash chromatography with light petroleum–ethyl acetate (9:1, v/v) as eluent to give ethyl L-*N*-(*tert*-butoxycarbonyl)vinylglycinate **5** as an oil (0.2 g, 80%) [Found: $(M + H)^+$ 230.1394. $C_{11}H_{20}NO_4$ requires 230.1392]; $\nu_{max}$(CHCl)/$cm^{-1}$ 3440 (NH), 1738 and 1711 (CO); $\delta_H$(400 MHz; $CDCl_3$) 1.27 (3 H, t, *J* 7.1, *Me*$CH_2$), 1.43 (9 H, s, $Me_3C$), 4.20 (2 H, q, *J* 7.1, Me*C*$H_2$), 4.83 (1 H, m, C*H*$CO_2$Et), 5.19 (1 H, br s, NH), 5.24 [1 H, dd, *J* 10.3, 1.7, =C*H*H (*cis*)], 5.33 [1 H, dd, *J* 17.1, 1.7, =CH*H* (*trans*)] and 5.89 (1 H, m, C*H*=$CH_2$); $\delta_C$(100 MHz; $CDCl_3$) 13.96 ($CH_3CH_2$), 28.15 ($CH_3C$), 55.68 ($Me_3C$), 61.56 ($CH_2O$), 79.90 (*C*CO), 117.07 ($CH_2$=), 132.68 (C=), 155.00 (CON) and 170.60 ($CO_2$); *m*/*z* (relative abundance) (CI, $NH_3$) 247 (9%), 230 (29), 191 (100), 174 (48), 163 (2), 156 (6), 130 (96) and 56 (50).

The sodium hydrogen carbonate solution was extracted with ethyl acetate (15 $cm^3$). A further portion of ethyl acetate (15 $cm^3$) was added to it and the aqueous phase was carefully acidified to pH 2 with aqueous potassium hydrogen sulfate (1 mol $dm^{-3}$). The organic layer was washed with saturated aqueous sodium chloride (10 $cm^3$), dried ($MgSO_4$) and then concentrated under reduced pressure to give D-*N*-(*tert*-butoxycarbonyl)vinylglycine **6**. This was subjected to a repetition of the enzymatic resolution, as above, to give D-*N*-(*tert*-butoxycarbonyl)vinylglycine **6** (0.24 g, 90%). This was boiled under reflux in HCl (6 mol $dm^{-3}$; 5 $cm^3$) for 1 h. The solution was evaporated under reduced pressure at 30 °C. The residue was dissolved in the minimum amount of water and applied to a column of Dowex 50W-X8 ion exchange resin ($H^+$ form). The

column was washed with water and eluted with 4% aqueous pyridine. The ninhydrin-positive fractions were combined and freeze-dried to give D-vinylglycine **9** (95%); $[\alpha]_D^{23}$ −96.3 (*c* 0.25 in $H_2O$); $[\alpha]_D^{23}$ −92 (*c* 0.16 in 1 mol $dm^{-3}$ HCl). The spectroscopic data ($^1H$ NMR) were identical with those of the L-isomer. Ethyl L-*N*-(*tert*-butoxycarbonyl)vinylglycine was hydrolysed as above to give L-vinylglycine **8** (95%); $[\alpha]_D^{26}$ +94.7 (*c* 0.46 in $H_2O$) {lit.,[22] $[\alpha]_D$ +88.6 (*c* 0.59 in $H_2O$)}; $[\alpha]_D^{25}$ +86 (*c* 0.41 in 1 mol $dm^{-3}$ HCl) {lit.,[14] (hydrochloride) $[\alpha]_D^{25}$ +77.5 (*c* 0.5 in $H_2O$)}; {lit.,[19] (hydrochloride) $[\alpha]_D$ +78.5 (*c* 1.9 in $H_2O$), +96 (*c* 1 in 2 mol $dm^{-3}$ HCl)}.

*Ethyl* (S)-2-tert-*Butoxycarbonylamino*-3,4-*epoxybutanoate* **10**.—*m*-Chloroperbenzoic acid (0.23 g) was added to a solution of ethyl (*S*)-2-*tert*-butoxycarbonylaminobut-3-enoate **5** (0.19 g) in $CCl_4$ (5 $cm^3$) at 0 °C under $N_2$. The mixture was stirred for 2 h and then evaporated under reduced pressure. The residue was purified by flash chromatography (EtOAc–light petroleum, 1:10) to give the epoxide **10** as an oil (0.123 g, 60%) as a mixture of diastereoisomers (71% de). Data were recorded for the major diastereoisomer [Found: $(M + H)^+$ 246.1341. $C_{11}H_{19}NO_5$ requires 246.1341]; $\nu_{max}$(Nujol)/$cm^{-1}$ 3430, 1770 and 1705; $\delta_H$(250 MHz; $CDCl_3$) 1.28 (3 H, t, *J* 7.1, $CH_3CH_2O$), 1.42 (9 H, s, $Me_3$), 2.64 [1 H, dd, *J* 4.5, 2.5, CH*H* (epoxide)], 2.75 [1 H, dd, *J* 4.5, 4.3, C*H*H (epoxide)], 3.42 [1 H, m, O-CH(epoxide)], 4.23 (2 H, q, *J* 7.1, $MeCH_2$), 4.60 (1 H, dd, *J* 8.5, 1.7, CHCO) and 5.0 (1 H, br d, *J* 8.5, NH); $\delta_C$(100 MHz; $CDCl_3$) 14.0 ($CH_3CH_2$), 28.2 ($Me_3$), 43.7 (CH=), 51.5 [*C*(CHNH)=], 52.7 ($CH_2Me$), 61.8 (CHNH), 80.1 ($Me_3C$), 155.4 (CONH) and 169.8 ($CO_2Et$); *m*/*z* (CI, $NH_3$) 246 [$(M + H)^+$, 18%], 190 (99), 172 (22), 146 (9), 128 (4), 116 (14) and 72 (80).

*Ethyl* (2S,3R)-3-*Hydroxy*-2-tert-*butoxycarbonylaminobutanoate*.—A solution of ethyl (*S*)-2-*tert*-butoxycarbonylamino-3,4-epoxybutanoate **10** (0.11 g), Raney nickel and ethanol (50 $cm^3$) was shaken at 100 °C and 10 atm pressure for 1 h and allowed to cool overnight. The mixture was filtered (Celite) and the Celite was washed with ethanol (10 $cm^3$). The filtrate plus washings were evaporated under reduced pressure and the residue was purified by flash chromatography (ethyl acetate–light petroleum, 3:1) to give ethyl (2*S*,3*R*)-3-hydroxy-2-*tert*-butoxycarbonylaminobutanoate (60%, 70% de). Data were recorded for the major diastereoisomer; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 3439 and 1713; $\delta_H$(220 MHz; $CDCl_3$) 1.29 [6 H, m, $CH_3CH(OH)$, $CH_3CH_2O$], 1.47 (9 H, s, $Me_3$), 3.86 [1 H, q, *J* 8, C*H*(OH)], 4.23 (2 H, q, *J* 7.1, $MeCH_2$), 4.34 [1 H, m, C*H*(NH)] and 5.46 (1 H, m, NH).

L-*Threonine* **11**.—The ethyl (2*S*,3*R*)-3-hydroxy-2-*tert*-butoxycarbonylaminobutanoate prepared as above was hydrolysed as before to give a mixture of L-threonine and L-*allo*-threonine in which L-threonine was identified as the major component by paper chromatography against authentic compounds using the solvent system butanol–butan-2-one–conc. ammonia–water, 15:9:4:2 with ninhydrin as the visualisation reagent.

*Ethyl* 2-tert-*Butoxycarbonylamino*-3,4-*dihydroxybutanoate* (**12** + **13**).—A solution of ethyl (*S*)-2-*tert*-butoxycarbonylaminobut-3-enoate **5** (0.1 g), 4-methylmorpholine *N*-oxide (0.1 g) and osmium tetraoxide (0.1 mol per mol of unsaturated ester) in *tert*-butyl alcohol–water (8:1) (5 $cm^3$) was stirred for 24 h at room temperature. Sodium sulfite (0.9 g) was added to it and the mixture was partitioned between ethyl acetate (10 $cm^3$) and water (10 $cm^3$). The organic phase was washed with water (10 $cm^3$) and saturated brine (10 $cm^3$), dried ($MgSO_4$) and then evaporated under reduced pressure. The residue was subjected to flash chromatography [ethyl acetate–light petroleum (2:1)] to give a minor component of low $R_f$ (0.23) (19 mg, 17%) and a major component of higher $R_f$ (45 mg, 40 mg). The low $R_f$ component crystallised (solvent) (m.p. 77–78 °C) and was shown by X-ray crystallography to have the relative (and hence absolute) configuration 2*S*,3*R* (**12**). The major component **13** was accordingly assigned the 2*S*,3*S*-configuration. For the 2*S*,3*R* isomer: $\nu_{max}$(CHCl)/$cm^{-1}$ 1792 and 1713; $\delta_H$(400 MHz; $CDCl_3$) 1.29 (3 H, t, *J* 7.2, $CH_3CH_2$), 1.43 (9 H, s, $Me_3$), 3.67 (1 H, dd, *J* 11.9, 4.4, CH*H*OH), 3.70 (1 H, dd, *J* 11.9, 4.2, C*H*HOH), 3.86 (1 H, m, C*H*OH), 4.23 (2 H, q, *J* 7.2, $MeCH_2O$), 4.34 (1 H, t, *J* 7.02, C*H*NH) and 5.46 (1 H, br d, *J* 7.7 NH); $\delta_C$(100 MHz; $CDCl_3$) 14.0 ($CH_3CH_2$), 28.1 [($CH_3$)$_3$], 55.7 ($MeCH_2$), 61.9 ($CH_2OH$), 62.7 [CH(NH)], 73.0 [CH(OH)], 80.8 ($Me_3C$), 156.3 (NHCO) and 170.7 ($CO_2Et$); *m*/*z* (CI, $NH_3$) 264 [$(M + H)^+$, 11%], 235 (3), 225 (41), 208 (38), 188 (6), 179 (35), 164 (51), 144 (9), 118 (4) and 90 (3).

*X-Ray Structural Analysis of Ethyl* (2S,3R)-2-tert-*Butoxycarbonylamino*-3,4-*dihydroxybutanoate* **12**.—Crystal data: orthorhombic space group $P2_12_12_1$; $a$ = 5.431(6), $b$ = 9.952(12), $c$ = 24.44(4) Å; $D_x$ = 1.32 Mg $m^{-3}$; $Z$ = 4; crystal size 0.12 × 0.12 × 0.25 mm.

*Data Collection*.—Siemens P3R3 diffractometer; monochromatized Mo-Kα radiation; 1398 independent reflections were measured; $\omega$–$2\theta$ scan.

*Structure Solution and Refinement*.—The structure was solved using direct methods with SHELEXTL. Refinement was on F by least squares; this involved 814 reflections [$I/\sigma(I) \geqslant 2.0$] refining 187 parameters. A weighting scheme of the form $w = 1/[\sigma^2(F) + gF^2]$ with $g$ = 0.0086 was used and shown to be satisfactory. The final $R$ = 0.056 and $S$ = 1.3. Tables of positional and thermal parameters and bond lengths and angles have been deposited with the Cambridge Crystallographic Data Base.*

*Ethyl* (2S,3S)-2-tert-*Butoxycarbonylamino*-3,4-*dihydroxybutanoate* **13**.—The major component ethyl (2*S*,3*S*)-2-*tert*-butoxycarbonylamino-3,4-dihydroxybutanoate ($R_f$ 0.26 [EtOAc–light petroleum (2:1)] was obtained as an oil; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1738 and 1697; $\delta_H$(400 MHz; $CDCl_3$) 1.27 (3 H, t, *J* 7.1, $CH_3CH_2$), 1.27 (9 H, $Me_3$), 3.46 (1 H, dd, *J* 11.3, 7.7, HOCH*H*), 3.59 (1 H, dd, *J* 11.5, 6.3, HOC*H*H), 4.2 (3 H, m, dq, J 7.2, C*H*OH, $MeCH_2$), 4.44 (1 H, dd, 8.2, 1.5, C*H*NH) and 5.56 (1 H, br d, *J* 8.2, NH); $\delta_C$(100 MHz; $CDCl_3$) 14.0 ($CH_3CH_2$), 28.1 ($Me_3$), 55.0 ($MeCH_2$), 61.9 ($HOCH_2$), 62.7 (CHNH), 72.0 [CH(OH)], 80.7 ($Me_3C$), 156.8 (CONH) and 170.8 ($CO_2Et$); *m*/*z* (CI, $NH_3$) 264 [$(M + H)^+$, 9%], 235 (6), 225 (29), 208 (25), 190 (2), 179 (36), 164 (43), 147 (4), 118 (2) and 90 (3). The free amino acid was obtained by hydrolysis as before as a very hygroscopic solid $[\alpha]_D^{23}$ − 9 (*c* 0.25 in $H_2O$) {lit.,[59] $[\alpha]_D$ −13.5 (*c* 2.0 in $H_2O$)}; $\delta_H$(400 MHz, $D_2O$) 3.67 (2 H, m, $CH_2OH$), 3.70 (1 H, d, *J* 3.9, C*H*$NH_3^+$, 4.1 [1 H, m, C*H*(OH)].

*Ethyl* (2S)-2-tert-*Butoxycarbonylamino*-2-*cyclopropylethanoate*.—An excess of ethereal diazomethane was added slowly to a solution of ethyl (*S*)-2-*tert*-butoxycarbonylaminobut-3-enoate **5** (0.23 g) in diethyl ether (10 $cm^3$). Palladium(II) acetate (5 mg) was added with an immediate evolution of gas. The excess of diazomethane was removed using a stream of nitrogen, the organic phase was filtered, washed with water (10 $cm^3$), saturated brine (10 $cm^3$), dried ($MgSO_4$) and then evaporated under reduced pressure. The residue was purified by flash chromatography [EtOAc–light petroleum (1:10)] and distillation (Kugelrohr) to give ethyl (2*S*)-2-*tert*-butoxycar-

* For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1994, Issue 1.

bonylamino-2-cyclopropylethanoate as an oil (0.1 g, 80%) shown by NMR to be a mixture of atropisomers, b.p. 220 °C/0.6 mmHg; $\delta_H$(400 MHz; $CDCl_3$) 0.31–0.58 [4 H, m, $(CH_2)_2CH$], 1.02 [1 H, m, $CH(CH_2)_2$], 1.27 (3 H, t, *J* 7.1, $CH_3CH_2$), 1.41 (9 H, s, $Me_3$), 3.45 (1 H, br s, CHNH), 3.75 (1 H, t, *J* 7.8, CHNH), 4.2 (2 H, m, $MeCH_2$), 4.8 (1 H, br s, NH) and 5.05 (1 H, d, *J* 6.8, NH); $\delta_C$(100 MHz; $CDCl_3$) 2.62 [$(CH_2)_2CH$], 13.7 [$CH(CH_2)_2$], 14.1 ($CH_3CH_2$), 28.2 ($Me_3$), 56.5 ($MeCH_2$), 61.0 (CHNH), 79.7 ($Me_3C$), 151.6 (CONH) and 172.1 ($CO_2Et$); *m/z* (CI, $NH_3$) 244 [$(M + H)^+$, 4%], 205 (10), 188 (25), 170 (4), 144 (23), 109 (1), 84 (3) and 70 (15).

(S)-2-*Amino*-2-*cyclopropylethanoic Acid* [(S)-*Cyclopropylglycine*] **15**.—Ethyl (2*S*)-2-*tert*-butoxycarbonylamino-2-cyclopropylethanoate (97 mg) was boiled under reflux in HCl (6 mol $dm^{-3}$; 5 $cm^3$) for 1 h. The product was isolated using an ion exchange resin as above, to give (*S*)-2-amino-2-cyclopropylethanoic acid (cyclopropylglycine) **15** (30 mg, 66%), m.p. 189 °C (decomp.); $[\alpha]_D^{20}$ +58.7 (*c* 0.23 in $CHCl_3$); $\delta_H$(400 MHz; $D_2O$) 0.33–0.60 (1 H, m, CH-cyclopropyl), 0.72–0.61 (3 H, m, CH-cyclopropyl), 1.01–1.10 [1 H, m, $CH(CH_2)_2$] and 3.02 (1 H, d, *J* 9.8, CHNH); $\delta_C$(100 MHz; $D_2O$) 3.92 [$(CH_2CH_2)CH$], 4.64 [$(CH_2CH_2)CH$], 12.7 [$CH(CH_2)_2$], 60.3 (CHNH) and 174.8 (CO); *m/z* (EI, FAB) 116 [$(M + H)^+$, 14%], 93 (100), 75 (35) and 58 (32).

(E)-2-*Aminopent*-3-*enoic Acid*.—Methyl *N*-chloropent-3-enimidate was prepared (87%) from pent-3-enenitrile **16** as for methyl *N*-chlorobut-3-enimidate above. This was converted (97%) into the corresponding *N*-chloropent-3-enimidate which was converted into 2-aminopent-3-enoic acid (as **20**, 14%) as for vinylglycine, above, m.p. 178 °C (decomp.) (Found $M^+$ 116.0712. $C_5H_{10}NO_2$ requires 116.0711); $\delta_H$(250 MHz; $D_2O$) 1.6 (3 H, dd, *J* 6.5, 1.7, Me), 4.1 (1 H, d, *J* 8.5, $CH_2$), 5.35 (1 H, ddq, *J* 8.5, 1.7, 15.3, MeC*H*=) and 5.9 (1 H, ddq, *J* 6.5, 15.3, 0.8); $\delta_C$(63 MHz; $CDCl_3$) 18.0 (Me), 57.6 [$CH(NH)_2$], 123.4 (Me*C*H=), 135.9 [=*C*HC($NH_2$)] and 174.5 (CO); *m/z* (EI) 116 $(M + H)^+$ (11), 70 (2) and 35 (11).

(E)-2-tert-*Butoxycarbonylaminopent*-3-*enoic Acid* **17**.—This was prepared as for vinylglycine, above, from (*E*)-*N*-chloropent-3-enimidate (0.6 g) to give (*E*)-2-*tert*-butoxycarbonylaminopent-3-enoic acid (0.35 g, 29%). The NMR spectra revealed the presence of a mixture of atropisomers [Found *m/z* 216.1236. $C_{10}H_{18}NO_4$ $(M + H)^+$ requires 216.1236]; $\delta_H$(250 MHz; $CDCl_3$) 1.39 (9 H, s, $Me_3$), 1.67 (3 H, d, *J* 6.7, *Me*CH=), 4.54–4.75 (1 H, m, CH), 5.30–5.45 (1 H, dd, *J* 15, 5, C*H*=CHMe), 5.51 (1 H, m, NH) and 5.8 (1 H, dqd, *J* 15.3, 6.3, 1.1, MeC*H*); $\delta_C$(100 MHz; $CDCl_3$) 17.6 (Me), 28.1 ($Me_3$), 55.1 [$CH(NH_2)$], 56.6 [$CH(NH_2)$], 80.1 ($CMe_3$), 81.5 ($CMe_3$), 125.0 (Me*C*H), 129.7 [=*C*HC($NH_2$)], 130.0 [=*C*HC($NH_2$)], 155.1 (COBoc), 156.6 (COBoc), 175.2 ($CO_2H$) and 177.5 ($CO_2H$).

*Ethyl* (S)-(E)-2-tert-*Butoxycarbonylaminopent*-3-*enoate* **18**.—The esterification and papain-catalysed resolution of (*E*)-2-*tert*-butoxycarbonylpent-3-enoic acid (0.3 g) was carried out as for vinylglycine, above, to give (*R*)-(*E*)-2-*tert*-butoxycarbonylaminopent-3-enoic acid (0.084 g, 28%, 56% of theoretical), and ethyl (*S*)-2-*tert*-butoxycarbonylaminopent-3-enoate **18** (0.13 g, 38%, 76% of theoretical). The NMR spectra revealed the presence of a mixture of atropisomers [Found *m/z* 244.1550; $C_{12}H_{22}NO_4$ $(M + H)^+$ requires 244.1549]; $\nu_{max}$($CHCl_3$)/$cm^{-1}$ 1760, 1708 and 1493; $\delta_H$(250 MHz; $CDCl_3$) 1.23 (3 H, t, *J* 7.2, *Me*$CH_2O$), 1.41 (9 H, s, $Me_3$), 1.65 (3 H, d, *J* 5.1, *Me*CH=), 4.17 (2 H, q, *J* 7.0, *Me*$CH_2$), 4.67 (1 H, m, C*H*$NH_2$), 5.1 (1 H, br s, NH), 5.35 (1 H, dd, *J* 15.5, 4.8, C*H*=CHMe) and 5.71 (1 H, dqd, *J* 15.4, 6.6, 1.4, MeC*H*=); $\delta_C$(63 MHz; $CDCl_3$) 14.0 ($CH_3CH_2O$), 17.6 ($CH_3CH$=), 28.2 ($Me_3$), 27.85 ($Me_3$), 55.7 ($MeCH_2O$), 61.4 [$CH(NH_2)$], 79.9 ($Me_3C$), 125.5 (MeCH=) and 129.2 (*C*H=CHMe); *m/z* (CI,$NH_3$) 244 [$(M + H)^+$, 0.8%], 205 (31), 188 (87), 170 (48), 144 (88), 127 (20), 114 (29), 99 (6) and 70 (26). The free amino acids were obtained by hydrolysis as before. For (*S*)-2-aminopent-3-enoic acid **19** $[\alpha]_D^{25.6}$ +111.9 (*c* 0.2 in $H_2O$). For (*R*)-2-aminopent-3-enoic acid **20** $[\alpha]_D^{29.5}$ −114.2 (*c* 0.2 in $H_2O$) [Found (*S*-enantiomer) *m/z* 116.0712. $C_5H_{10}NO_2$ $(M + H)^+$ requires 116.0711]. Other data were identical with those of the racemic compound, above.

(E)-3-*Methylpent*-3-*enenitrile* **23**.—(*E*)-1-Bromo-2-methylbut-2-ene (5.3 g) {prepared from tiglic acid [(*E*)-2-methylbut-2-enoic acid] *via* the corresponding alcohol[60]} was added to a solution of sodium cyanide (2.1 g) in dimethyl sulfoxide (30 $cm^3$) at 50 °C. The solution was stirred and allowed to cool to room temperature. The mixture was diluted with water (250 $cm^3$) and extracted with light petroleum (4 × 25 $cm^3$). The organic extracts were washed with water (30 $cm^3$) and saturated brine (30 $cm^3$), dried ($MgSO_4$) and then evaporated under reduced pressure. The residue was distilled under reduced pressure to give (*E*)-3-methylpent-3-enenitrile **23** (2.5 g, 73%), b.p. 54 °C/18 mmHg [lit.,[61] b.p. 90–91 °C (80–84 mmHg)]; $\delta_H$(220 MHz; $CDCl_3$) 1.64 (3 H, d, *J* 7, $CH_3CH$=), 1.73 (3 H, s, $CH_3$), 3.04 (2 H, s, $CH_2$) and 5.6 (1 H, q, *J* 7, CH=).[62]

*Methyl* (E)-3-*Methylpent*-3-*enimidate Hydrochloride*.—(*E*)-3-Methylpent-3-enenitrile (1.63 g) was converted into methyl (*E*)-3-methylpent-3-enimidate hydrochloride (2.75 g, 100%) as for vinylglycine, above; $\nu_{max}$(Nujol)/$cm^{-1}$ 1656, 1465 and 1448; $\delta_H$(220 MHz; $CDCl_3$) 1.68 (3 H, d, *J* 2.8, $CH_3CH$=), 1.70 (3 H, s, $CH_3C$=), 3.33 (2 H, s, $CH_2$), 4.21 (3 H, s, $OCH_3$) and 5.15 (1 H, q, *J* 2.8, $CH_3C$=).

*Methyl* (E)-N-*Chloro*-3-*methylpent*-3-*enimidate*.—The *N*-chloroimidate was prepared (100%) from the corresponding imidate hydrochloride as for vinylglycine, above. (From the NMR spectra, the compound exists as an *E*,*Z* mixture.) $\nu_{max}$(Nujol)/$cm^{-1}$ 1608 and 1445; $\delta_H$(400 MHz; $CDCl_3$) 1.58 (3 H, d, *J* 6.7, MeCH=), 1.60 (3 H, apparent s, Me), 3.22 (2 H, s, $CH_2$), 3.74, 3.76 (3 H, s, OMe) and 5.28 (1 H, qq, *J* 6.7, 1.3, CH=); $\delta_C$(100 MHz; $CDCl_3$) 13.3 ($CH_3CH$=), 15.7 ($CH_3C$=), 40.4 (OMe), 41.1 (OMe), 54.4 ($CH_2$), 56.8 ($CH_2$), 122.9 (CH=), 128.1 (C=), 128.5 (C=) and 174.0 (C=N); *m/z* (CI, $NH_3$) 178 [$(M + NH_3)^+$, 1.3%], 162 [$(M + H)^+$, 57], 146 (1), 126 (12), 111 (0.8) and 85 (0.8).

(±)-(E)-2-*Amino*-3-*methylpent*-3-*enoic Acid* (*as* **22**).—(±)-(*E*)-2-Amino-3-methylpent-3-enoic acid (as **22**) was prepared from (*E*)-*N*-chloro-3-methylpent-3-enimidate (0.46 g) using sodium methoxide, as below (0.22 g, 58%); $\delta_H$(400 MHz; $D_2O$) 1.56 (3 H, dq, *J* 1.2, 1.0, $CH_3C$=), 1.60 (3 H, dq, *J* 1.0, 6.7, $CH_3CH$=), 4.11 (1 H, s, CH) and 5.71 (1 H, qq, *J* 6.7, 1.2, CH=); $\delta_C$(100 MHz; $D_2O$) 11.8 ($CH_3CH$=), 13.7 [$CH_3C(CHNH_2)$=], 62.9 [$CH(NH_2)$], 128.8 (C=), 130.7 (CH=) and 174.1 (CO); *m/z* (EI, FAB) 259 [(2 M + H)$^+$, 11%], 222 (11), 185 (7), 130 [$(M + H)^+$, 100], 113 (14) and 93 (10).

(E)-3-*Methyl*-2-tert-*butoxycarbonylaminopent*-3-*enoic Acid* (*as* **24**).—A solution of methyl (*E*)-*N*-chloro-3-methylpent-3-enimidate (0.79 g) in light petroleum (3 $cm^3$) was added to a solution prepared from sodium (0.34 g) in methanol (6 $cm^3$). The mixture was stirred at room temperature for 24 h, diluted with water (20 $cm^3$) and dioxane (20 $cm^3$) and treated with di-*tert*-butyl carbonate (1.27 g). The product was isolated as before to give (*E*)-3-methyl-2-*tert*-butoxycarbonylaminopent-3-enoic acid (as **24**) (0.75 g, 50%). The NMR spectra indicated the presence of a mixture of atropisomers; $\delta_H$(250 MHz;

$CDCl_3$) 1.42 (9 H, s, $Me_3$), 1.63 (3 H, d, *J* 6.0, $CH_3C$=), 1.64 (3 H, s, $CH_3C$=), 4.51 [C*H*($NH_2$)], 4.70 [C*H*($NH_2$)], 5.26 (br, NH) and 5.63 (1 H, m, CH=); $\delta_C$(63 MHz; $CDCl_3$) 28.3 ($Me_3$), 60.31 [CH($NH_2$)], 61.69 [CH($NH_2$)], 80.2 ($Me_3C$), 125.1 [*C*(CHNH)=], 125.2 [*C*(CHNH)=], 130.6 (CH=), 155.4 (NHCO), 174.0 (*C*CO) and 175.2 (*C*CO); *m*/*z* (CI, $NH_3$) 230 [$(M + H)^+$, 6%], 191 (48), 174 (51), 146 (5), 130 (17), 112 (8), 84 (44) and 79 (6).

*Ethyl* (S)-(E)-3-*Methyl*-2-tert-*butoxycarbonylaminopent*-3-*enoate*.—Ethyl (*S*)-(*E*)-3-methyl-2-*tert*-butoxycarbonylaminopent-3-enoate was prepared from (*RS*)-(*E*)-3-methyl-2-*tert*-butoxycarbonylaminopent-3-enoate acid by papain-catalysed esterification as for the corresponding derivative of vinylglycine, above, as an oil, in 26% yield (52% of theoretical). The free amino acid was obtained by hydrolysis as before to give (*S*)-(*E*)-2-amino-3-methylpent-3-enoic acid **22** $[\alpha]_D^{21}$ +65.4 (*c* 0.26 in $H_2O$). NMR data were identical with those of the racemic compound, above. For the ethyl ester: $\nu_{max}(CHCl_3)/cm^{-1}$ 2928, 1712 and 1496; $\delta_H$(400 MHz; $CDCl_3$) 1.42 (9 H, s, $Me_3$), 1.60 (3 H, s, $CH_3C$=), 1.62 (3 H, d, *J* 6.0, $CH_3CH$=), 4.17 (1 H, q, *J* 7.1, $MeCH_2$), 4.18 (1 H, q, *J* 7.1, $MeCH_2$), 4.65 [1 H, d, *J* 7.3 C*H*($NH_2$)], 5.27 (1 H, br s, NH) and 5.57 (1 H, q, *J* 5.9, CH=); $\delta_C$(100 MHz; $CDCl_3$) 12.7 [$CH_3C$(CNH)=], 13.4 ($CH_3CH$=), 14.0 ($CH_3CH_2$), 29.6 ($Me_3$), 60.4 ($MeCH_2$), 61.3 [CH(NH)], 79.7 ($Me_3C$), 124.3 (CH=), 131.0 [*C*(CHNH)=], 154.8 (NHCO) and 171.3 [CH($NH_2$)*C*O]; *m*/*z* (CI, $NH_3$) 258 [$(M + H)^+$, 12%], 219 (31), 202 (53), 158 (85), 157 (4), 110 (1) and 84 (40).

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