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Palladium-Catalyzed Heck Couplings of L-Vinylglycine Derivatives With Vinyl and Aryl Halides and Triflates.

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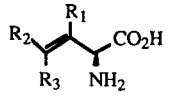
Key Words: Palladium-catalyzed coupling; vinylglycine; aryl halide; vinyl triflate; aryl triflate.

Abstract: The coupling of aryl and vinyl halides and triflates with L-vinylglycine derivatives under the influence of a palladium catalyst is described. The coupling is regioselective and stereoselective with the absolute configuration of the α-amino acid centre being retained.

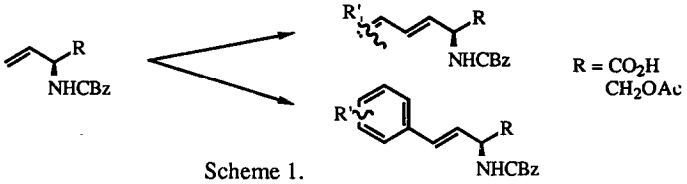
The synthesis of non-proteinogenic α-amino acids has attracted much attention recently from organic chemists.[1] The potential biological activity of these compounds as enzyme inhibitors, pharmaceuticals, antibiotics and protease resistors has stimulated much of this activity.[2,3] In addition to this biological potential modified α-amino acids are useful as chiral synthons and chiral auxiliaries for asymmetric synthesis.[4]

The family of α-amino acids possessing unsaturation in the side chain such as β,γ-olefinic α-amino acids display significant activity as suicide substrates for pyridoxal phosphate dependent enzymes such as alanine racemase, glutamate-aspartate transaminase and β-cystathionase.[3] L-Vinylglycine **1** (R_1,R_2, R_3 = H) is the simplest member of this family and considerable effort has been directed towards its synthesis in optically pure form. Among these the oxidative degradation of suitably modified, optically pure, amino acids (eg. L-methionine, L-glutamic acid and L-homoserine) have proved to be the most efficient.[5] Several routes to the structurally more diverse vinylglycines **1** (R_1 and/or R_2 and/or $R_3 \neq$ H) have had to deal with the sensitivity and lability of the olefinic function which can lead to isomerisation and racemisation.[6] Methods which have been reported to give good geometric control of the side chain double bond are the Wittig reaction of serine derived phosphoranes and phosphonates with aldehydes and ketones (exclusive *trans* product),[6a] the amidoalkylation of alkenylsilanes with glycine cation intermediates (*cis* or *trans* depending on the geometry of the alkenylsilane),[6b] the Grignard attack on α-chloroglycinates (*trans* Grignard gave *trans* product),[6c] and the oxidative rearrangement of γ-phenyl seleno-α,β-unsaturated ester (*trans* only).[6d] Methods which have furnished vinylglycines **1** with high optical purities have included the alkylation-elimination sequence of *bis*-lactim ethers,[7a] alkynylation-reduction of an electrophilic chiral glycine template,[7b] alkylation-elimination of an L-aspartic acid derivative,[7c] alkylation-elimination-desulphonylation of a L-serine derived sulphone[7d] and Wittig reaction of L-serine derived synthons.[7e,f]



1

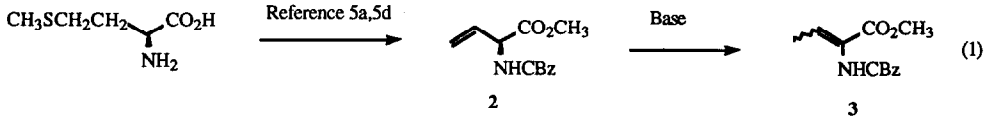
As part of our efforts directed towards conceptually simple approaches to the elaboration of α-amino acids[8] we have examined the palladium-catalyzed Heck couplings between vinylglycine derivatives and a variety of sp^2 derived halides and triflates (trifluoromethanesulphonates) as outlined in Scheme 1. We required a reaction which would be compatible with the α chiral centre of the amino acids and which would deliver the unsaturated product with a high degree of regio and stereocontrol. Our search of the literature showed only one example of the Heck coupling of a vinylglycine derivative and this was during the reported synthesis of wybutosine when *N*-methoxycarbonyl-L-vinylglycine was reacted with an iodonucleoside under the influence of a palladium catalyst.[9] We therefore examined the scope and versatility of this rection by preparing L-vinylglycine derivatives and subjecting them to palladium-catalyzed Heck couplings.[10]



Scheme 1.

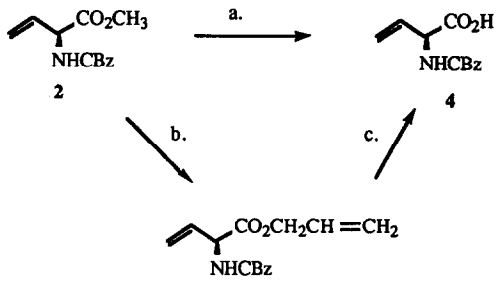
RESULTS AND DISCUSSION

Methyl *N*-benzyloxycarbonyl-L-vinylglycine **2** was most conveniently prepared from 98% optically pure L-methionine following the procedure of Rapoport (Equation 1).[5a,d,e] This method, which involved a thermal elimination of sulphenic acid from an intermediate sulphoxide, could be conveniently performed on a multigram scale with negligible isomerisation or racemisation of the product **2**.



(1)

The methyl ester **2** was not suitable as a substrate for palladium-catalyzed Heck couplings as the base required for the Heck process rapidly converts **2** into the dehydro-analogue **3**.[5a] Reasoning that the corresponding carboxylic acid **4** would be protected from this undesired isomerization under basic conditions a method was sought for the selective conversion of **2** into **4**. Careful acid hydrolysis of **2**, according to a literature procedure,[11] gave **4** in moderate yields. A milder and potentially more general method was found for this deesterification which should be compatible with a wide variety of *N*-protecting groups. Thus **2** was reacted with allyl alcohol in the presence of the *trans*-esterification catalyst $Ti(OPr^i)_4$ to effect the replacement of the methyl group of the ester with an allyl group in high yield.[12] Subsequent removal of the allyl group by palladium-catalyzed hydrogenolysis with tri-*n*-butylstannane gave the desired product **4** in excellent yield (Scheme 2).[13] The optical rotations of **4** prepared by the two different routes were similar. Complete hydrolysis of **4** with 6N HCl gave the corresponding vinylglycine hydrochloride salt which exhibited an optical rotation in agreement with that reported in the literature.[5]



Scheme 2.

a. CH_3CO_2H, 1N HCl, reflux, 68%. b. allyl alcohol, $Ti(OPr^i)_4$, reflux, 83%. c. $PdCl_2(PPh_3)_2$, Bu_3SnH, dioxane, reflux, 93%.

Initial Heck coupling methodology studies were carried out on cyclohex-1-en-1-yl triflate and *N*-benzyloxy carbonyl-L-vinylglycine **4** (Equation 2). Performing the coupling under the mild phase transfer conditions described by Jeffrey (catalytic palladium acetate, potassium carbonate, tetra-*n*-butyl ammonium chloride in dimethylformamide)[14] resulted in instantaneous decomposition of the catalyst to palladium black. Presumably the presence of the carboxylic acid group is deleterious to the active palladium catalyst. The addition of two equivalents (relative to palladium) of tri-*o*-tolylphosphine to the reaction mixture proved efficacious. Gradual heating of the mixture with simultaneous monitoring of the solution by thin layer chromatography showed that the reaction began at *ca.* 50° and after one hour no starting materials were observed and a black precipitate of palladium had formed. Acidification of the mixture and extractive workup followed by chromatography on silica gel gave the expected product **5** in good yield (entry 1, Table 1). A number of minor side products were also formed during the reaction but these were not isolated and characterized. The major product **5** resulted from carbon-carbon bond formation only at the least hindered terminus of the double bond of L-vinylglycine **4** and spectroscopic data indicated only formation of the *trans*-substituted alkene. Thus the Heck coupling had delivered the modified α-amino acid with good regiocontrol and stereocontrol. The general procedure for the coupling (described in Table 1 as Condition A) was thus *N*-CBz-L-vinyl glycine **4** (1.1-2.0eq), vinyl or aryltriflate (1.0eq), palladium acetate (0.1eq), tri-*o*-tolyl phosphine (0.2eq), potassium carbonate (5.0eq) and tetra-*n*-butyl ammonium chloride (1.0eq) in dimethylformamide. Extending this methodology to more complex vinyl triflates showed that the steroidal triflates (shown in entries 2-5 in Table 1) gave the expected products (**6-9**) under Condition A. The ^1H n.m.r. spectra of some of the coupled products displayed a second set of resonances, slightly offset from the main signals, which is assumed to belong to a minor conformation of the main product. These signals are not due to side products since during decoupling experiments irradiation of the signal from the α-protons of the major conformers caused the disappearance of the corresponding resonances of the assumed minor conformers. Conformers could arise from either s-*trans* or s-*cis* arrangements of the diene unit or from either an *E* or *Z* arrangement of the urethane functional group.

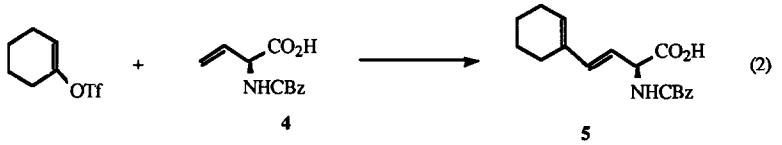
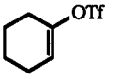
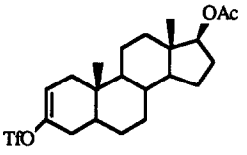
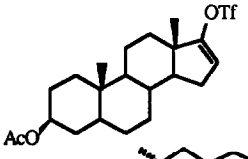
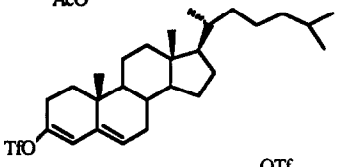
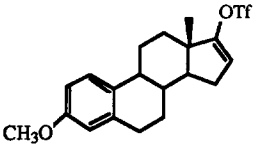
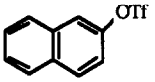
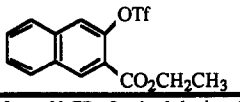


Table 1. Coupling of Vinylglycine L-4 with Vinyl and Aryl triflates.

Entry	Triflate	Conditions[a]	Product	% Isolated Yield
1		A	5	77
2		A	6	50
3		A	7	34
4		A	8	69
5		A	9	54
6		A	10[b]	57
7		A	11	8

a. Conditions A refer to *N*-CBz-L-vinylglycine 4 (1-2eq), triflate (1eq), $Pd(OAc)_2$ (0.1eq), P(*o*-Tol)$_3$ (0.2eq), Bu_4NCl (1.0eq) and K_2CO_3 (5.0eq) in DMF.

b. Mixture of dehydro isomers also isolated in 21% yield.

Attempts to extend this coupling process to other vinyltriflates met with little success. Thus the vinyltriflates shown in Figure 1 gave none of the expected coupled products under reaction Conditions A. The vinyltriflates were consumed during the reaction but the vinylglycine **4** remained. Attempts to perform the couplings under standard Heck conditions[10] (eg. $PdCl_2(PPh_3)_2$, triethylamine, dimethylformamide at 100°) also gave none of the desired products.

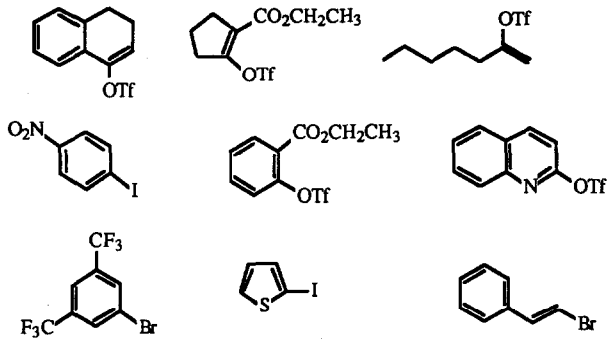


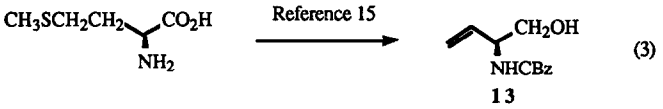
Figure 1.
Vinyl and aryl triflates and halides which gave none of the expected products when coupled with *N*-CBz-L-vinylglycine **4**.

Aryl triflates were then reacted with **4** under the standard Conditions A in order to prepare α-amino acids containing aryl side chains. 2-Naphthyl triflate coupled with **4** to give **10** in moderate yield as shown by entry 6 in Table 1. In addition to the expected product **10** a complex mixture of isomeric materials (up to 21%) was also isolated from this reaction. The functionalized analogue 2-ethoxycarbonyl-3-naphthyl triflate coupled with **4** to give only a very low yield of the expected product **11** (entry 7). No other identifiable products were isolated from this reaction. Attempts to couple other arylhalides or triflates (as shown in Figure 1) with **4** also met with little success .

In order to show that the base-assisted coupling did not give partial racemisation of the α centre of the amino acid products compound **5** was analysed by high field ^1H n.m.r. in the presence of the chiral shift reagent *tris*[3-(heptafluoromethylhydroxymethylene)-(-)-camphorato]europium(III), $Eu(hfc)_3$. Addition of $Eu(hfc)_3$ to **5** in $CDCl_3$ caused a dramatic coalescence of all of the proton signals. In order in circumvent this problem the methyl ester of **5** was prepared by the addition of diazomethane to a dichloromethane solution of **5**. The derivitisation proceeded without any isomerization of the double bonds. An authentic sample of the racemate of methyl ester of **5** was required for comparative purposes and this was prepared from *N*-CBz-D,L-vinylglycine **4** (prepared by an analogous route as for L-**4** utilizing D,L-methionine) and cyclohex-1-en-1-yl triflate under Condition A, followed by derivitisation with diazomethane. Addition of $Eu(hfc)_3$ to a $CDCl_3$ solution of the methyl ester of D,L-**5** caused a doubling of the methyl singlet, whereas addition of $Eu(hfc)_3$ to a $CDCl_3$ solution of the methyl ester of L-**5** gave no such doubling of the methyl singlet in the high field ^1H n.m.r.

An alternative to the use of the free carboxylic acid in the Heck coupling procedure is to reduce the carboxylate to the corresponding primary alcohol thus giving rise to compound L-**13** . The primary alcohol group would not be able to assist the isomerization of the double bond as could the carboxylate

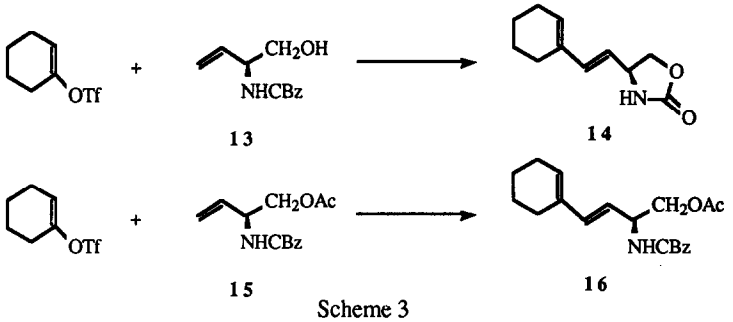
group. Compound L-**13** was prepared uneventfully from L-methionine according to a literature procedure (Equation 3).[15]



(3)

13

Coupling of cyclohex-1-en-1-yl triflate with L-**13** under Conditions A gave only a low yield of the cyclic urethane **14** (Scheme 3). Conversion of **13** into the corresponding acetate **15** with acetic anhydride and base also gave a material which was not sensitive to base induced isomerization when compared to the analogous carboxylic ester **2**. Coupling of L-**15** with cyclohex-1-en-1-yl triflate in the presence of palladium acetate and potassium acetate in dimethylformamide (therefore in the absence of tri-*o*-tolyl phoshine or tetra-*n*-butylammonium chloride and designated as Condition C in Table 2) gave a moderate yield of the desired product **16** (entry 1, Table 2). All of the vinyl and aryl triflates which had undergone successful coupling with compound L-**4** could also be coupled with L-**15** under Conditions C (Table 2). The yield of the coupled products could be improved dramatically by the addition of tetra-*n*-butyl ammonium chloride to the above mixture (designated as Condition B in Table 2). Although not all of the vinyl triflates/halides shown in Figure 1 were coupled with L-**15**, the attempted coupling with *trans*-β-bromostyrene and α-tetralenyl triflate gave none of the expected product.



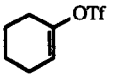
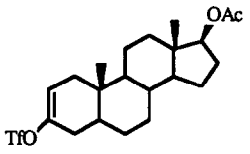
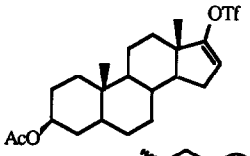
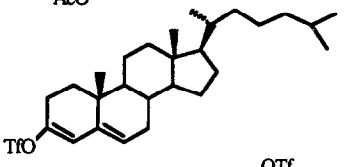
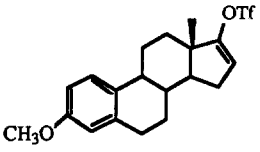
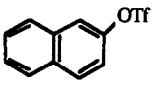
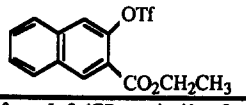
13 **14**

15 **16**

Scheme 3

Attempted coupling of L-**15** with 2-naphthyl triflate under Conditions B or C gave none of the expected product **22**. However, utilisation of the more traditional Heck reaction conditions ($PdCl_2(PPh_3)_2$, triethylamine in dimethylformamide)[10] for the coupling of L-**15** with 2-naphthyl triflate gave **22** in good yield (entry 7, Table 2). Using a similar procedure (designated as Condition D), coupling between L-**15** and 2-ethoxycarbonyl-3-naphthyl triflate gave a modest yield of **23** (although this yield is four times higher than the corresponding yield from the coupling of this triflate with the carboxylate L-**4**). This procedure could also be used to successfully couple iodobenzene with L-**15**, a reaction that was not possible for *N*-CBz-L-vinylglycine **4**. Unfortunately the coupling of the remaining aryl triflates/halides shown in Figure 1 were not successful.

Table 2. Coupling of Vinylglycine **15** with Vinyltriflates and Aryl Triflates/Iodides.

Entry	Halide or Triflate	Conditions	Product	% Isolated Yield
1		B[a] C[b]	**16**	77 43
2		B C	**17**	82 31
3		B	**18**	68
4		B C	**19**	54 25
5		B C	**20**	83 42
6		D[c]	**21**	86
7		D	**22**	84
8		D	**23**	32

a. Conditions B refer to L-2-(CBz-amino)but-3-enyl acetate **15** (1.0eq), triflate (1.2-1.5eq), $Pd(OAc)_2$ (0.1eq), Bu_4NCl (1.0eq) and K_2CO_3 (5.0eq) in DMF.

b. Conditions C refer to L-2-(CBz-amino)but-3-enyl acetate **15** (1.0-2.0eq), triflate (1.0eq), $Pd(OAc)_2$ (0.1eq) and KOAc (5.0eq) in DMF.

c. Conditions D refer to L-2-(CBz-amino)but-3-enyl acetate **15** (1.0eq), triflate/iodide (2.0-2.5eq), $PdCl_2(PPh_3)$ (0.1eq) and Et_3N (5.0eq) in DMF.

EXPERIMENTAL

General: Infrared spectra were obtained using a Hitachi 270-30 infrared spectrophotometer, as a neat film, chloroform solution or nujol mull as indicated. ^{1}H n.m.r. spectra and ^{13}C n.m.r. spectra were recorded using a Bruker ACP 300 Fourier Transform n.m.r. spectrometer. All n.m.r. samples were prepared as deuterochloroform solutions,chemical shifts given relative to tetramethylsilane and $CDCl_3$, respectively. Optical rotations were obtained using a Perkin Elmer 141 Polarimeter. Electron impact mass spectra and accurate mass measurements were obtained using a AEI-GEC MS3074 mass spectrometer. Where the electron impact technique was unsuccessful in giving a molecular ion, mass spectra were obtained using the FAB technique using a VG ZAB 2HF mass spectrometer. All solvents were distilled prior to use. The analytical t.l.c plates used were Merck Alufolien Kieselgel 60 PF_{254} and were visualized by UV light (254 nm) and by staining with an acidic solution of ammonium molybdate followed by development with heat. Flash chromatography was carried out on Merck Silica gel 60 (230-400 mesh). Melting points were recorded using a Kofler hot stage melting point apparatus with a Reichert microscope and are uncorrected. Microanalyses were performed by Chemical and Microanalytical Services, Melbourne, Australia.
The following compounds were prepared by literature procedures: methyl *N*-benzyloxycarbonyl-L-vinyl glycine **2**,[5a,d,e] cyclohex-1-en-1-yl triflate,[16c] 2-quinolyl triflate,[17] ethyl 2-(trifluoromethanesulphonyl) oxycyclopent-1-encarboxylate,[18] 2-(trifluoromethanesulphonyl)oxyhept-1-ene,[16a] ethyl 2-(trifluoromethane sulphonyl)oxybenzenoate,[16] 2-naphthyl triflate.[16a]

Allyl *N*-benzyloxycarbonyl-L-vinylglycinate.
To a stirred solution of methyl *N*-benzyloxycarbonyl-L-vinylglycinate **2**[5] (0.20g, 0.80mmol) in allyl alcohol (10mL) under a nitrogen atmosphere was added titanium tetraisopropoxide (1.06mL, 0.36mmol) *via* syringe. The solution was heated at 65-70° for 30h. A further charge of titanium tetraisopropoxide (5.00mL, 1.68mmol) was added to the warm solution and heating continued for another 24h. The solution was acidified with 1N hydrochloric acid solution and extracted with dichloromethane. The extracts were washed with saturated brine and the solvents evaporated to an orange oil. Chromatography on silica gel gave the title compound as a clear oil (0.184g, 83%). B.p. *ca.* 150°/ 0.045mm (Kugelrohr).
^{1}H nmr δ 4.65 (*d*, 2H, *J* 5.5Hz), 4.96 (*br*, 1H, α-proton), 5.13 (*s*, 2H, $PhCH_2$), 5.20-5.41 (*m*, 4H, CH_2=CH), 5.50 (*br*, 1H, NH), 5.90 (*m*, 2H, CH_2=CH). ^{13}C nmr δ 56.19 (α-carbon), 66.21 (CO_2CH_2), 67.12 ($PhCH_2$), 117.78 (CH_2=CH), 118.88 (CH_2=CH), 128.08, 128.50, 131.30 (CH_2=CH), 132.34 (CH_2=CH), 136.15, 155.49 (urethane C=O), 173.67 (ester C=O). IR (neat): 3352(*br, m*), 1724(*br, s*), 1646*w*, 1516*s*, 1458*m*, 1334*m*, 1272*w*, 1240*w*, 1190*w*, 1048*m*, 1028*w*, 990*m*, 936*m*, 776*w*, 740*m*, 700*m*. MS (EI): 276 ([M+H]$^+$ 11%), 275 (M$^+$ 7%), 232 (6), 214 (3), 190 (51), 146 (20), 91 (100), 41 (58). HRMS calc. for $C_{15}H_{17}NO_4$: 275.1158, found: 275.1171. $[\alpha]_D$= -8.9° (*c* 0.56, $CHCl_3$).

***N*-benzyloxycarbonyl-L-vinylglycine (4) - Method 1 (palladium hydrogenolysis).**
A solution of allyl *N*-benzyloxycarbonyl-L-vinylglycinate (0.108g, 0.39mmol) and $PdCl_2(PPh_3)_2$ (0.028g, 0.039mmol) was brought to reflux in dioxane. Tri-*n*-butyltin hydride (0.114g, 0.39mmol) was added dropwise *via* syringe to the boiling solution. After 10min the black solution was cooled, the dioxane removed *in vacuo*, and the residue chromatographed on silica gel (ethyl acetate:light petroleum:acetic acid - 10:10:1) to yield *N*-CBz-L-vinylglycine **4** (0.086g, 93%) which was recrystallised from ethyl acetate/light petroleum to give white flakes. M.p. 126-128° (lit. 130-131°)[11]. ^{1}H nmr δ 4.87 (*br*, 1H, α-proton), 5.11 (*s*, 2H, $PhCH_2$), 5.23 (*dd*, 1H, *J* 1.1, 10.2Hz, CH_2=CH), 5.36 (*dd*, 1H, *J* 1.0, 17.2Hz, CH_2=CH), 5.90 (*br d*, 1H, NH), 5.95 (*ddd*, 1H, *J* 5.4, 10.3, 17.3Hz, CH_2=CH), 7.34 (*br s*, 5H), 7.77 (*br*, 1H, CO_2H). ^{13}C nmr δ 55.92 (α-carbon), 66.57 ($PhCH_2$), 116.81 (CH_2=CH), 127.73, 128.13, 132.60 (CH_2=CH), 132.98, 136.04, 155.50 (urethane C=O), 171.87 (CO_2H). IR (nujol mull): 3404*m*, 3200-2400(*br, m*) , 1746*m*, 1730*m*, 1668*s*, 1538*m*, 1418*w*, 1342*w*, 1254*m*, 1204*m*, 1180*w*, 1090*m*, 992*m*, 938*m*, 776*w*, 730*m*, 696*w*. MS (EI): 236 ([M+H]$^+$, 32%), 235 (M$^+$, 23), 217 ([M-H_2O]$^+$, 10), 190 ([M-CO_2H]$^+$, 100), 174 (36), 146 (65), 108 (71), 91 (88). HRMS calc. for $C_{12}H_{13}NO_4$: 235.0845, found: 235.0835). $[\alpha]_D$= +13.3° (*c* 1.48, $CHCl_3$) (measured prior to recrystallisation). Calc. for $C_{12}H_{13}NO_4$: C 61.27%, H 5.57, N 5.95. Found: C 61.18, H 5.37, N 5.80.

***N*-benzyloxycarbonyl-L-vinylglycine (4) - Method 2 (acid hydrolysis).[11]**
A solution of methyl *N*-CBz-L-vinylglycinate **2** (5.0g, 20.1mmol) in 1N hydrochloric acid (40mL) and acetic acid (40mL) was heated at reflux for 90min. Most of the solvent was evaporated and the residue extracted with ethyl acetate (4x25mL). The extracts were dried and the solvent evaporated. The yellow

solid thus obtained was recrystallised from ethyl acetate/light petroleum to yield two crops of the title compound as white plates (3.2g, 68%). M.p. 128-130° (lit.[11] 130-131°). $[\alpha]_D$= +13.6° (*c* 1.70, $CHCl_3$) No $[\alpha]_D$ was reported in the literature. Other spectral data as for product of *Method 1* above. Complete hydrolysis[5] of **4** in 6N HCl gave vinylglycine hydrochloride with an $[\alpha]_D$= +80.4° (*c* 0.54, H_2O). Literature values[5] varied in the range $[\alpha]_D$= +78.2-83.5°.

The following procedure is representative for the synthesis of the steroidal vinyl triflates. These triflates have been reported in the literature although no experimental or spectroscopic data have appeared.[19]

Cholesta-3,5-dien-3-yl trifluoromethanesulphonate.
Triflic anhydride (1.31mL, 2.2g, 7.8mmol) was added *via* syringe to a solution of (+)-4-cholestenone (2.0g, 5.2mmol) and 2,6-di-*t*- butyl-4-methylpyridine (1.7g, 8.3mmol) in dichloromethane (20mL). The solution was stirred for 6h at room temperature, by which time t.l.c. analysis indicated some enone remained so further charges of triflic anhydride (0.43mL, 0.73g, 2.6mmol) and base (0.57g, 2.8mmol) were added and the mixture stirred for a further 15h. The solvent was evaporated and pentane was added to the residue. Filtration of the pyridinium salt, evaporation of the pentane from the filtrate and chromatography of the residue on silica gel gave an off white solid. Recrystallisation from methanol/ethyl acetate/water gave the title compound as a white solid (1.3g, 46%). M.p. 124-126°. ^{1}H nmr δ 0.68 (*s*, 3H), 0.84 (*d*, 6H, *J* 6.8Hz), 0.89 (*d*, 3H, *J* 6.4Hz), 0.93 (*s*, 3H), 0.50-2.70 (*m*, 41H), 5.55 (*m*, 1H), 5.96 (*s*, 1H). ^{13}C nmr δ 11.93, 18.60, 18.67, 21.15, 22.54, 22.80, 23.93, 24.14, 25.54, 27.99, 28.18, 31.57, 31.93, 33.73, 35.74, 36.12, 39.47, 39.57, 47.67, 56.05, 56.65, 120.53, 125.41, 126.37, 146.90. IR (nujol mull): 1660*w*, 1636*w*, 1420*s*, 1310*w*, 1246*s*, 1204*s*, 1146*s*, 1054*s*, 1004*m*, 920*s*, 902*s*, 870*w*, 832*w*, 788*w*, 740*w*, 660*w*, 608*m*. MS (EI): 516 (M^+, 16%)), 384 (19), 383 ([M-CF_3SO_2]$^+$, 21), 229 (15), 43 (100). HRMS calc. for $C_{28}H_{43}F_3O_3S$: 516.2885, found: 516.2875. $[\alpha]_D$= -70.1° (*c* 0.75, $CHCl_3$).

17β-acetyloxyandrost-2-en-3-yl trifluoromethanesulphonate.
Reaction of 17β-acetyloxyandrosterone with triflic anhydride and 2,6-di-*t*-butyl-4-methylpyridine gave the title compound after triflic acid catalysed isomerisation[19a] as a white solid (*ca.* 5:1 Δ^2:Δ^3 isomers). ^{1}H nmr δ 0.75 (*s*, 6H), 1.98 (*s*, 3H), 0.65-2.40 (*m*, 20H), 4.54 (*t*, 1H, *J* 8.2Hz), 5.33 (*s*, Δ^3-isomer, vinylic H, 16%), 5.60 (*br d*, Δ^2-isomer, vinylic H, 84%). ^{13}C nmr δ Major isomer 11.52, 11.96, 20.65, 21.06, 23.42, 27.42, 27.99, 30.90, 31.97, 35.15, 36.74, 38.34, 42.10, 42.45, 50.51, 53.22, 82.63, 116.35 & 120.61 (central peaks of *q*, CF_3, J_{CF}321Hz), 116.98 (C-OTf), 147.54 (CH=COTf), 171.08. IR (nujol mull): 1734*s*, 1700*w*, 1464*s*, 1408*s*, 1246*s*, 1198*s*, 1154*w*, 1140*s*, 1036*s*, 1006*w*, 900*m*, 892*m*, 866*s*, 622*m*. MS (EI): 464 (M^+, 9%) 449 ([M-Me]$^+$, 1), 404 ([M-AcOH]$^+$, 59), 389 ([M-AcOH-Me]$^+$, 50), 331 ([M-CF_3SO_2]$^+$, 68), 271 (77), 262 ([M-C_4H_6OTf]$^+$, 68), 202 ([C_4H_5OTf]$^+$, 86), 201 (100). HRMS calc. for $C_{22}H_{31}F_3O_5S$: 464.1844, found: 464.1838. $[\alpha]_D$= +31.2° (*c* 0.60, $CHCl_3$).

3-*O*-Methylestr-16-en-17-yl trifluoromethanesulphonate.
Reaction of 3-*O*-methylestrone with triflic anhydride and 2,6-di-*t*-butyl-4-methylpyridine gave the title compound as a thick oil (69%). ^{1}H nmr δ 1.00 (*s*, 3H), 1.2-2.5 (*m*, 11H), 2.87 (*m*, 2H), 3.78 (*s*, 3H), 5.61 (*m*, 1H, CH=COTf), 6.64 (*d*, 1H, *J* 2.6Hz), 6.72 (*dd*, 1H, *J* 2.8, 8.5Hz), 7.21 (*d*, 1H, *J* 8.7Hz). ^{13}C nmr δ 15.31, 25.79, 26.72, 28.35, 29.43, 32.69, 36.66, 44.16, 45.05, 53.50, 55.18, 111.47, 113.88, 114.46 (CH=COTf), 116.46 & 120.69 (central peaks of *q*, CF_3, J_{CF} 319Hz), 125.95, 132.10, 137.65, 157.56, 159.28 (C-OTf). IR (neat): 2924*s*, 2850*s*, 1628*m*, 1612*m*, 1576*w*, 1504*s*, 1466*m*, 1424*s*, 1378*m*, 1310*m*, 1284*m*, 1244*s*, 1212*s*, 1144*s*, 1072*m*, 1056*s*, 1036*m*, 966*w*, 918*s*, 860*s*, 822*m*, 766*w*, 720*w*, 606*m*. MS (EI): 416 (M^+, 100%), 283 ([M-CF_3SO_2]$^+$, 23), 199 (15), 173 (21), 160 (35). HRMS calc. for $C_{20}H_{23}F_3O_4S$: 416.1269, found: 416.1282. $[\alpha]_D$= +65.3° (c 0.59, $CHCl_3$).

3β-acetyloxyepiandrost-16-en-17-yl trifluoromethanesulphonate.
Reaction of 3β-acetyloxyepiandrosterone with triflic anhydride and 2,6-di-*t*-butyl-4-methylpyridine gave the title compound as a white solid (33%). ^{1}H nmr δ 0.65-0.81 (*m*, 1H), 0.81 (*s*, 3H), 0.91 (*s*, 3H), 0.85-1.10 (*m*, 2H), 1.10-1.70 (*m*, 14H), 1.70-1.80 (*m*, 1H), 1.80-2.00 (*m*, 1H), 1.97 (*s*, 3H), 2.10-

2.20 (*m*, 1H), 4.64 (*tt*, 1H, *J* 5.0, 11.3Hz), 5.51 (*dd*, 1H, *J* 1.7, 3.2Hz). ^{13}C nmr δ 12.07, 15.23, 20.41, 21.39, 27.30, 28.15, 28.45, 30.66, 32.57, 33.36, 33.86, 35.63, 36.38, 44.75, 54.06, 54.50, 73.41, 114.41 (CH=COTf), 120.62, 159.22 (CH=COTf), 170.64. IR (nujol mull): 1738*s*, 1630*w*, 1462*s*, 1244*s*, 1214*s*, 1144*s*, 1074*m*, 1050*m*, 1026*m*, 930*m*, 914*m*, 870*m*, 850*m*, 820*m*. MS (EI): 464 (M^+, 1%), 449 ([M-Me]$^+$, 10, HRMS calc. for $C_{21}H_{28}F_3O_5S$: 449.1610, found: 449.1643), 403 (49), 388 (100), 349 (16), 334 (16), 313 (27), 253 (27), 239 (27). $[\alpha]_D$= +10.5° (*c* 0.61, $CHCl_3$).

3,4-Dihydronaphth-1-yl trifluoromethanesulphonate (α-tetralenyl triflate).

Reaction of α-tetralone with triflic anhydride and 2,6-di-*t*- butyl-4-methylpyridine using the above procedure gave the title compound as a fragrant, clear oil (26%). B.p. (Kugelrohr): 90°/0.04mm. ^{1}H nmr δ 2.48 (*br*, 2H), 2.86 (*t*, 2H, *J* 7.7Hz), 6.03 (*br s*, 1H, CH=C), 7.00-7.50 (*m*, 4H). ^{13}C nmr δ 22.17, 26.70, 116.47 & 120.70 (central peaks of *q*, CF_3, J_{CF} 319Hz), 117.78, 121.09, 126.82, 127.69, 129.10, 136.15. IR (neat): 3068*w*, 3024*w*, 2936*m*, 2836*w*, 1652*m*, 1604*w*, 1488*m*, 1456*w*, 1422*s*, 1362*m*, 1338*m*, 1248*m*, 1216*s*, 1142*s*, 1058*m*, 1014*s*, 902*s*, 848*m*, 826*m*, 808*m*, 762*s*, 738*m*, 702*m*, 622*m*, 600*m*. MS (EI): 278 (M^+, 78%), 145 ([M-CF_3SO_2]$^+$, 100), 129 (22), 128 (18), 127 (13), 117 (22), 115 (21).

2-(Ethoxycarbonyl)naphth-3-yl trifluoromethanesulphonate.

The title compound was prepared (46%) according to the general procedure I of reference 16a. M.p. 111-114° (light petroleum). ^{1}H nmr δ 1.44 (*t*, 3H, *J* 7.3Hz), 4.48 (*q*, 2H, *J* 7.2Hz), 7.61 (*m*, 2H), 7.70 (*s*, 1H), 7.84 (*d*, 1H, *J* 8.1Hz), 7.94 (*d*, 1H, *J* 7.9Hz), 8.60 (*s*, 1H). ^{13}C nmr δ 14.08, 62.12, 116.70 & 120.95 (central peaks of *q*, CF_3, J_{CF} 320Hz), 120.87, 127.40, 127.66, 127.98, 129.03, 129.63, 131.35, 134.65, 134.83, 163.94. IR (nujol mull): 1720*s*, 1630*w*, 1600*w*, 1510*w*, 1484*w*, 1422*s*, 1368*m*, 1292*s*, 1248*s*, 1202*s*, 1146*s*, 1052*s*, 1014*s*, 924*s*, 894*m*, 880*m*, 828*m*, 776*m*, 760*m*, 720*m*, 656*m*, 624*w*. MS (EI): 348 (M^+, 46%, HRMS calc. for $C_{14}H_{11}F_3O_5S$: 348.0279, found: 348.0290), 303 ([M-OEt]$^+$, 17), 215 ([M-CF_3SO_2]$^+$, 37), 170 (46), 143 (100), 115 (49), 114 (49).

The following procedure is representative of all the coupling reactions of *N*-CBz-L-vinylglycine **4**:

L-2-[(benzyloxycarbonyl)amino]-4-cyclohex-1-en-1-ylbut-3-enoic acid (5)

A mixture of tetra-*n* -butylammonium chloride (0.076g, 0.27mmol), palladium(II) acetate (0.005g, 0.022mmol), tri-*o* -tolylphosphine (0.013g, 0.043mmol), cyclohex-1-en-1-yl triflate (0.052g, 0.23 mmol), potassium carbonate (0.155g, 1.1mmol) and *N*-CBz-L-vinylglycine **4** (0.057g, 0.24mmol) was heated at 50° for 6h in DMF (3mL). T.l.c. showed no olefin remained and a new intensely u.v.-active spot had appeared. Dilute hydrochloric acid (50mL) was added to the cooled solution which was then extracted with ether (5x50mL). The combined ether extracts were dried and the solvent evaporated. The residue was flash chromatographed on silica gel, gradient eluting with 30-50% ethyl acetate/light petroleum then 0.5-2% acetic acid in 50% ethyl acetate/light petroleum, to yield the title compound as a thick oil (0.059g, 77%). ^{1}H nmr δ *Major conformer* 1.50-1.75 (*m*, 4H), 2.00-2.20 (*m*, 4H), 4.95 (*br t*, 1H, α-proton), 5.12 (*s*, 2H), 5.52 (*m*, 2H, CH=C & NH), 5.81 (*br s*, 1H), 6.32 (*d*, 1H, *J* 15.4Hz), 7.32 (*m*, 5H). *Minor conformer* 4.80 (*br*, 1H), 5.74 (*br s*, 1H), 6.27 (*d*, 1H, obscured by major conformer). ^{13}C nmr δ 22.22, 22.28, 24.29, 25.84, 55.71, 67.20, 118.64, 128.12, 128.46, 131.87, 134.44, 136.06, 137.16, 155.68, 174.62. IR ($CHCl_3$ solution): 3450*w*, 2936*m*, 3040*w*, 2870*w*, 1722(*br*, *s*), 1580*w*, 1504*m*, 1456*m*, 1425*w*, 1340*m*, 1218*m*, 1190*w*, 1140*w*. MS (EI) 315 (M^+ - not detected), 269 ([M-HCO_2H]$^+$, 0.5%, HRMS calc. for $C_{17}H_{19}NO_2$: 269.1416, found: 269.1409), 179 (4), 151 (10), 108 (98), 107 (92), 91 (100). MS (FAB): 316 ([M+H]$^+$). $[\alpha]_D$= +38.5° (*c* 0.59, $CHCl_3$).

Methyl L-2-[(benzyloxycarbonyl)amino]-4-cyclohex-1-en-1-ylbut-3-enoate.

Diazomethane (2.0mL) was added dropwise to a stirred solution of **5** (0.038g, 0.12mmol) in dichloromethane (10mL). T.l.c. analysis of the mixture after 10min showed that no carboxylic acid remained. Evaporation of the solvent gave a thick oil (0.033g 83%). ^{1}H nmr δ 1.50-1.66 (*m*, 4H), 2.00-2.14 (*m*, 4H), 3.72 (*s*,3H, CO_2CH_3), 4.88(*m*, 1H, α-proton), 5.08(*s*, 2H, $PhCH_2$), 5.40-5.50 (*m*,2H, NH and CH=CH), 5.77 (*br s*, 1H, CH=C), 6.26 (*d*, 1H, *J* 15.6Hz, CH=CH) 7.32 (*m*, 5H). ^{13}C nmr δ 22.19, 22.25, 24.27, 25.83, 52.62, 55.79, 66.99, 118.92, 128.10, 128.46, 131.87,

134.39, 135.86, 136.98. MS (EI) 329 (M^+ 2%),305 ([M-C_2H_4]$^+$),270 ([M-CO_2CH_3]$^+$, 19%, HRMS calc. for $C_{17}H_{20}NO_2$: 270.1494, found: 270.1489), 226 (30), 194 (48), 178 (78), 107 (70), 91 (100).

L-2-[(benzyloxycarbonyl)amino]-4-(17β-acetyloxyandrost-2-en-3-yl)but-3-enoic acid (6)

Reaction of *N*-CBz-L-vinylglycine **4** (0.34mmol) with 17β-acetyloxyandrost-2-en-3-yl trifluoromethane sulphonate (0.31mmol) for 3h at 70° gave the title compound as a thick oil (50%). ^{1}H nmr δ 0.72 (*s*, 3H), 0.78 (*s*, 3H), 0.80-1.80 (*m*, 17H), 2.04 (*s*, 3H), 1.80-2.20 (*m*, 3H), 4.58 (*t*, 1H, *J* 8.2Hz), 4.96 (*br t*, 1H, α-proton - minor conformer at δ 4.81), 5.12 (*br s*, 2H), 5.40-5.60 (*m*, 2H), 5.70 (*br s*, 1H), 6.30 (*d*, 1H, *J* 15.5Hz), 7.35 (*m*, 5H). ^{13}C nmr δ 11.89, 12.02, 20.48, 21.20, 23.49, 27.47, 28.57, 29.37, 31.24, 34.90, 35.31, 36.84, 40.51, 41.16, 42.48, 50.61, 53.72, 67.24, 82.94, 128.14, 128.52, 130.74, 132.53, 136.62, 155.50, 171.48. IR (KBr disc): 3336(*m*, *br*), 2924*s*, 1734(*s*, *br*), 1512*m*, 1456*w*, 1378*w*, 1342*w*, 1248*s*, 1044*s*, 968*m*, 776*w*, 740*w*, 698*m*. MS (EI): 549 (M^+ - not present), 532 ([M-OH]$^+$, 0.1%), 503 ([M-HCO_2H]$^+$, 0.1), 446 (0.2), 441 (0.2), 370 (4), 328 (3), 256 (3), 202 (4), 179 (6), 151 (18), 108 (67), 107 (57), 91 (81), 88 (100). MS (FAB): 550 ([M+H]$^+$). $[\alpha]_D$= +86.9° (*c* 0.57, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]-4-(3β-acetyloxyepiandrost-16-en-17-yl)but-3-enoic acid (7)

Reaction of *N*-CBz-L-vinylglycine **4** (0.17mmol) with 3β-acetyloxyepiandrost-16-en-17-yl-trifluoro methanesulphonate (0.21mmol) for 1h at 80-85° gave the title compound as a foam (34%). ^{1}H nmr δ 0.60-0.75 (*br*, 1H), 0.81 (*s*, 6H), 0.82-1.98 (*m*, 17H), 1.99 (*s*, 3H), 2.00-2.15 (*m*, 2H), 4.65 (*m*, 1H, AcO-CH), 4.75 & 4.90 (2x*br*, total 1H, α-protons of two different conformers, *ca.* 1:1), 5.03 (*d*, *J* 13.0Hz, diastereotopic benzylic proton of conformer #1), 5.08 (*s*, diastereotopic benzylic proton of conformer #2), 5.09 (*s*, diastereotopic benzylic proton of conformer #2), 5.15 (*d*, *J* 13.0Hz, diastereotopic benzylic proton of conformer #1), 5.47 (*br d*, NH of one conformer), 5.63 & 5.70 (2x*br s*, steroidal C16 vinylic protons of two conformers), 5.70-5.85 (*m*, C3 vinylic proton and NH of other conformer), 6.22 & 6.25 (2x*d*, C4 vinylic protons, *J* 15.5 & 15.6Hz respectively), 7.23-7.35 (*m*, 5H). ^{13}C nmr δ 12.12, 15.97, 21.02, 21.44, 27.35, 28.40, 31.28, 31.68, 33.76, 33.91, 35.17, 35.58, 36.44, 44.72, 46.21, 54.52, 57.03, 66.97, 67.16, 73.75, 121.05, 127.76, 128.11, 128.50, 129.05, 131.64, 170.98. IR ($CDCl_3$ solution): 3444*w*, 3032*w*, 2932*s*, 2852*m*, 1722*s*, 1504*m*, 1454*w*, 1418*w*, 1370*w*, 1346*w*, 1256*s*, 1154*w*, 1132*w*, 1062*m*, 1028*m*, 964*m*. MS (EI): 549 (M^+, <0.5%), 505 ([M-CO_2]$^+$, 1, HRMS calc. for $C_{32}H_{43}NO_4$: 505.3192, found: 505.3213), 449 (10), 446 (10), 404 (48), 489 (94), 305 (52), 105 (100). $[\alpha]_D$= +73.3° (*c* 0.18, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]-4-(cholesta-3,5-dien-3-yl)but-3-enoic acid (8)

Reaction of *N*-CBz-L-vinylglycine **4** (0.64mmol) with cholesta-3,5-dien-3-yl trifluoromethanesulphonate (0.43mmol) for 2h at 60° gave the title compound as a thick oil (69%). ^{1}H nmr δ 0.67 (*s*, 3H), 0.83 (*d*, 3H, *J* 6.6Hz), 0.84 (*d*, 3H, *J* 6.4Hz), 0.85 (*s*, 3H), 0.89 (*d*, 3H, *J* 6.5Hz), 0.90-2.30 (*m*, 26H), 4.87 (*br*, 1H, α-proton - minor conformer present at 4.81 [*ca.* 25%]), 4.99 (*d*, 1H, *J* 12.1Hz, diastereotopic benzylic proton), 5.08 (*d*, 1H, *J* 12.0Hz, diastereotopic benzylic proton), 5.45 (*br s*, 1H), 5.59 (*dd*, 1H, *J* 15.3, 6.0Hz), 5.76 (*br*, 1H, NH), 5.87 (*br s*, 1H), 6.27 (*d*, 1H, *J* 15.3Hz), 7.26 (*m*, 5H), 8.70 (*br*, 1H, CO_2H). ^{13}C nmr δ 11.94, 18.71, 19.08, 20.79, 21.10, 21.87, 22.54, 22.81, 23.87, 24.14, 27.97, 28.23, 31.67, 32.07, 33.39, 35.08, 35.80, 36.16, 39.47, 39.75, 42.42, 48.08, 56.18, 56.85, 67.07, 120.41, 126.07, 128.07, 128.45, 131.62, 132.11, 135.92, 136.13, 142.00. IR ($CDCl_3$ solution): 3440*w*, 2940*s*, 2864*s*, 3600-2250(*br*, *m*), 1712 (*br*, *s*), 1628*w*, 1504*m*, 1468*w*, 1428*w*, 1382*w*, 1336*w*, 1250(*br*, *m*), 1058*m*, 964*m*. MS (EI): 601 (M^+ - not present), 557 ([M-CO_2]$^+$, 4%, HRMS calc. for $C_{38}H_{55}NO_2$: 557.4233, found: 557.4249), 511 (1), 493 (2), 466 (2), 450 (2), 449 (2), 350 (3), 335 (7), 108 (100), 91 (88), 79 (92), 44 (96). $[\alpha]_D$= -36.0° (*c* 0.30, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]-4-(3-*O*-methylestr-16-en-17-yl)but-3-enoic acid (9)

Reaction of *N*-CBz-L-vinylglycine **4** (0.64mmol) with 3-*O*-methylestr-16-en-17-yl trifluoromethane sulphonate (0.425mmol) for 4h at 75° gave the title compound as a thick oil (54%). ^{1}H nmr δ 0.88 (*s*, 3H), 1.20-2.5 (*m*, 11H), 2.87 (*m*, 2H), 3.78 (*s*, 3H), 4.98 (*m*, 1H, α-proton, minor conformer at 4.83), 5.13 (*m*, 2H, diastereotopic benzylic protons), 5.48 (*br d*, 1H, NH), 5.70-5.95 (*m*, 2H), 6.33 (*d*, 1H, *J*

16.1Hz), 6.63 (*d*, 1H, *J* 2.5Hz), 6.71 (*dd*, 1H, *J* 2.6, 16.1Hz), 7.18 (*d*, 1H, *J* 8.5Hz), 7.33 (*m*, 5H). ^{13}C nmr δ 16.03, 26.52, 27.63, 29.67, 31.11, 35.27, 37.08, 44.14, 46.46, 55.18, 56.29, 56.38, 111.37, 113.78, 126.02, 128.16, 128.16, 128.53, 131.69, 132.52, 133.61, 137.90, 151.21, 157.36. IR (Nujol mull): 3320(*m*,*br*), 1712(s,*br*), 1610*w*, 1502*m*, 1344*w*, 1254*m*, 1048*m*, 968*w*, 774*w*, 722*w*, 698*w*. MS (EI): 501 (M^+ - not present), 457 ([M-CO_2]$^+$, 10%, HRMS calc. for $C_{30}H_{35}NO_3$: 457.2617, found: 457.2630), 393 (10), 366 (10), 322 (24), 108 (100), 91 (97). MS (FAB): 502 ([M+H]$^+$). $[\alpha]_D$= +64.4° (*c* 0.86, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]-4-(2-naphthyl)but-3-enoic acid (10)
Reaction of *N*-CBz-L-vinylglycine **4** (0.43mmol) with 2-naphthyl triflate (0.21mmol) for 4h at 40-60° gave the title compound as an amorphous white solid (57%). ^{1}H nmr δ 5.02 (*br*, 1H, α-proton), 5.08 (*s*, 2H), 5.99 (*br d*, 1H, NH), 6.35 (*dd*, 1H, *J* 5.5, 15.8Hz), 6.76 (*d*, 1H, *J* 15.9Hz), 7.21-7.80 (*m*,12H). ^{13}C nmr δ 55.31, 65.76, 122.73, 124.18, 125.22, 125.53, 125.80, 126.77, 127.13, 127.35, 127.61, 131.29, 132.14, 132.58, 132.85, 171.34. IR (Nujol mull): 3600-2400(*m*, *br*), 3296*m*, 1728*s*, 1680*s*, 1532*m*, 1334*w*, 1252*m*, 1062*m*, 1014*w*, 966*m*, 820*m*, 734*m*, 696*w*, 652*w*. MS (EI): 361 (M^+ - not present), 253 ([M- $PhCH_2OH$]$^+$, 9%), 209 (16), 180 (26), 141 (30), 108 (60), 69 (100). MS (FAB): 362 ([M+H]$^+$). $[\alpha]_D$= +35.8° (*c* 0.11, MeOH).

L-2-[(benzyloxycarbonyl)amino]-4-(2-ethoxycarbonyl-3-naphthyl)but-3-enoic acid (11)
Reaction of *N*-CBz-L-vinylglycine **4** (0.64mmol) with 2-(ethoxycarbonyl)naphth-3-yl trifluoromethane sulphonate (0.43mmol) for 4h at 60° gave the title compound as a thick oil (8%). ^{1}H nmr δ 1.29 (*t*, 3H, *J* 7.1Hz), 4.28 (*q*, 2H, *J* 6.9Hz), 4.95-5.25 (*m*, 3H, α & benzylic methylene protons), 5.81 (*br d*, 1H, NH), 6.10 (*m*, 1H), 7.10-7.30 (*m*, 6H), 7.30-7.50 (*m*,3H), 7.60-7.80 (*m*, 2H), 8.32 (*s*, 1H). ^{13}C nmr δ 14.21, 55.97, 61.36, 67.19, 125.11, 126.69, 127.06, 127.70, 128.10, 128.45, 128.66, 131.79, 131.88, 132.89, 134.05, 134.72, 136.04, 155.92, 167.33, 174.52. IR ($CHCl_3$ solution): 3550-2400(*m*, *br*), 3432*m*, 2980 (*m*, *br*), 1716(*s*, *br*), 1630*w*, 1502*s*, 1458*m*, 1398*w*, 1334*w*, 1282(*s*, *br*), 1174*m*, 1134*m*, 1062(*s*, *br*), 962*w*, 912*w*. MS (EI): 433 (M^+ - not present), 386 (1%), 368 (5), 326 (5), 317 (6), 305 (20), 197 (16), 181 (18), 149 (32), 108 (52), 91 (100). MS (FAB): 434 ([M+H]$^+$). $[\alpha]_D$= +7.5° (*c* 0.19, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]but-3-enyl acetate (15)
To a solution of L-2-[(benzyloxycarbonyl)amino]-4-(methylsulphinyl)butan-1-ol[15] (6.95g, 24.4 mmol), acetic anhydride (3.45mL, 36.5mmol) and triethylamine (5.09mL, 36.5mmol) in chloroform (125mL) was added 4-dimethylaminopyridine (0.60g, 4.28mmol.) The solution was stirred for 60min then washed with 1N hydrochloric acid, dried and the chloroform evaporated to yield a thick oil (8.63g) . A portion (0.600g) was dissolved on *o*-dichlorobenzene (10mL) and heated at 170° for 24h. The solvent was removed *in vacuo*, and the residue chromatographed on silica gel to yield the title compound (0.411g, 92%). Recrystallisation from dichloromethane/light petroleum gave fine white needles. M.p. 54-56°. ^{1}H nmr δ 1.95 (*s*, 3H), 4.06 (*m*, 2H, CH_2OAc), 4.43 (*br*, 1H, α-proton), 4.94-5.07 (*br*, 1H, NH), 5.04 (*s*, 2H, $PhCH_2$), 5.15 (*d*, 1H, *J* 10.6Hz, CH_2=CH), 5.20 (*d*, 1H, *J* 17.6Hz, CH_2=CH), 5.71 (*ddd*, 1H, *J* 5.4, 10.6, 17.5Hz, CH_2=CH), 7.29 (*br s*, 5H). ^{13}C nmr δ 20.68 (CH_3CO_2), 52.20 (α-carbon), 65.53 (CH_2OAc), 66.89 ($PhCH_2$), 116.87 (CH_2=CH), 128.12, 128.16, 128.49, 134.35 (CH_2=CH), 136.20, 155.69 (urethane C=O), 170.86 (acetate C=O). IR (nujol mull): 3332*s*, 1730*s*, 1696*s*, 1540*s*, 1348*w*, 1302*w*, 1276*w*, 1250*m*, 1110*w*, 1088*w*, 1044*w*, 964*w*, 928*w*, 740*w*, 698*w*. MS (EI): 264 ([M+H]$^+$, 4%), 263 (M^+, 6, HRMS calc. for $C_{14}H_{17}NO_4$: 263.1158, found: 263.1144), 203 ([M-AcOH]$^+$, 24), 190 ([M-CH_2OAc]$^+$, 99), 146 (99), 91 (100), 43 (100). Calc. for $C_{14}H_{17}NO_4$: C 63.86, H 6.51, N 5.32. Found: C 63.97, H 6.55, N 5.34. $[\alpha]_D$= -43.2° (*c* 0.94, $CHCl_3$).

A portion of **15** (0.100g, 0.38mmol) was stirred in methanol (10mL) containing potassium hydroxide (0.001g, 0.018mmol) at room temperature. After 8h, some acetate remained (t.l.c.) so further potassium hydroxide (0.003g, 0.054mmol) was added and the solution stirred for a further 3 days. The methanol was evaporated, the residue taken up into dichloromethane and washed with water. The organic phase was dried and the solvent evaporated. Flash chromatography on silica gel gave the alcohol **13** (0.069g, 82%) which had an $[\alpha]_D$= -29.6° (*c* 0.69, $CHCl_3$) [lit.[15] value of -32.1° (*c* 3.1,$CHCl_3$)].

The following procedure is representative of all the coupling reactions of L-2-(CBz-amino)but-3-enyl acetate **15** with vinyl triflates (Table 2, Conditions B):

L-2-[(benzyloxycarbonyl)amino]-4-(cyclohex-1-en-1-yl)but-3-enyl acetate (16)
A mixture of tetra-*n*-butylammonium chloride (0.106g, 0.38mmol), palladium(II) acetate (0.0085g, 0.038mmol), cyclohex-1-en-1-yl triflate (0.131g, 0.57mmol), potassium carbonate (0.262g, 1.9 mmol) and L-2-(CBz-amino)but-3-enyl acetate **15** (0.100g, 0.38mmol) was heated in DMF (3mL) at 65° for 60min in a nitrogen atmosphere. T.l.c. showed that some diene had formed, but much of the olefin remained, so the reaction mixture was heated to 75° and stirred at that temperature for 3 more hours. The mixture was cooled, water added (50mL) and extracted with diethyl ether (5x50mL). The combined extracts were dried and the solvent evaporated. The residue was subjected to flash chromatography on silica gel, gradient eluting with 20-30% ethyl acetate/light petroleum to yield the title compound as a thick oil (0.101g, 77%). ^{1}H nmr δ 1.45-1.65 (*m*, 4H), 1.94 (*s*, 3H), 1.90-2.10 (*m*, 4H), 4.04 (*d*, 2H, *J* 5.0Hz), 4.45 (*br*, 1H, α-proton), 5.03 (*s*, 2H), 4.90-5.15 (*br*, 1H, **NH**), 5.32 (*dd*, 1H, *J* 15.8, 6.2Hz), 5.68 (*br s*, 1H), 6.14 (*d*, 1H, *J* 15.8Hz), 7.28 (*m*, 5H). ^{13}C nmr δ 20.70, 22.28, 24.28, 25.74, 51.94, 65.97, 66.75, 120.98, 128.05, 128.42, 130.79, 134.54, 135.77, 136.28, 155.62, 170.88. IR (neat): 3332*m*, 3028*w*, 2928*m*, 2832*w*, 1726(*br, s*), 1650*w*, 1532(*br, s*), 1234(*br, s*), 1050(*br, s*), 970*m*, 740*m*, 698*m*. MS (EI): 343 (M^+, 0.2%, HRMS calc. for $C_{20}H_{25}NO_4$: 343.1784, found: 343.1799), 283 ($[M\text{-}AcOH]^+$, 2), 270 ($[M\text{-}CH_2OAc]^+$, 8), 226 (8), 192 (12), 148 (5), 107 (10), 91 (100). $[\alpha]_D$= -7.5° (*c* 0.56, $CHCl_3$).
Coupling of L-2-(CBz-amino)but-3-en-1-ol **13** with cyclohex-1-en-1-yl triflate under identical conditions gave a low yield of cyclic urethane **14**. ^{1}H n.m.r. δ 1.59-1.68 (*m*, 4H), 2.10-2.14 (*m*, 4H), 4.05 (*dd*, 1H, *J* 6.8, 8.2Hz), 4.42 (*m*,1H), 4.53 (*t*,1H, *J* 8.3Hz), 5.44 (*dd*, 1H, *J* 7.9, 15.5Hz, C3 **CH**=CH), 5.82 (*br s*, 1H, **CH**=C), 6.20 (*d*,1H, *J* 15.6Hz, C4 CH=**CH**).

L-2-[(benzyloxycarbonyl)amino]-4-(17β-acetyloxyandrost-2-en-3-yl)but-3-enyl acetate (17)
Reaction of L-2-(CBz-amino)but-3-enyl acetate **15** (0.29mmol) with 17β-acetyloxyandrost-2-en-3-yl trifluoromethanesulphonate (0.43mmol) for 3h at 75° gave the title compound as a thick oil (82%). ^{1}H nmr δ 0.72 (*s*, 3H), 0.79 (*s*, 3H), 0.80-2.20 (*m*, 20H), 2.03 (*s*, 3H), 2.04 (*s*, 3H), 4.12 (*br d*, 2H, *J* 4.7Hz), 4.55 (*br*, 1H, α-proton), 4.58 (*t*, 1H, *J* 8.0Hz), 5.05-5.15 (*br*, 1H, **NH**), 5.11 (*s*, 2H), 5.40 (*dd*, 1H, *J* 15.9, 6.1Hz), 5.65 (*br*, 1H), 6.20 (*d*, 1H, *J* 15.7Hz), 7.35 (*m*, 5H). ^{13}C nmr δ 11.83, 11.97, 20.42, 20.76, 21.14, 23.44, 27.42, 28.55, 29.37, 31.19, 34.86, 35.25, 36.78, 40.40, 41.13, 42.41, 50.55, 53.68, 65.98, 66.77, 82.79, 121.27, 128.08, 128.45, 129.48, 133.33, 135.00, 135.20, 136.31, 155.65, 170.92, 171.21. IR ($CHCl_3$ solution): 3448*w*, 2916*m*, 2848*w*, 1726*s*, 1650*w*, 1504*m*, 1456*m*, 1378*m*, 1258*s*, 1042*m*, 970*w*. MS (EI): 577 (M^+), 517 ($[M\text{-}AcOH]^+$, HRMS calc. for $C_{33}H_{43}NO_4$: 517.3192, found: 517.3210), 504 ($[M\text{-}CH_2OAc]^+$), 460. $[\alpha]_D$= +45.8° (*c* 1.37, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]-4-(3β-acetyloxyepiandrost-16-en-17-yl)but-3-enyl acetate (18)
Reaction of L-2-(CBz-amino)but-3-enyl acetate **15** (0.17mmol) with 3β-acetyloxyepiandrost-16-en-17-yl trifluoromethanesulphonate (0.25mmol) for 4h at 75-80° gave the title compound as a foam (68%). ^{1}H nmr δ 0.70 (*m*, 1H), 0.79 (*s*, 1H), 0.81 (*s*, 1H), 0.85-1.00 (*m*, 2H), 1.10-1.96 (*m*, 15H), 1.98 (*s*, 6H), 2.06 (*m*, 1H), 4.09 (*m*, 2H), 4.48 (*br*, 1H, α-proton), 4.65 (*tt*, 1H, *J* 5.0, 11.2Hz), 4.99 (*br d*, 1H, **NH**), 5.08 (*s*, 2H), 5.63 (*dd*, 1H, *J* 6.1, 16.1Hz), 5.65 (*br d*, 1H), 6.12 (*d*, 1H, *J* 16.2Hz), 7.29 (*m*, 5H). ^{13}C nmr δ 12.12, 15.96, 20.74, 21.05, 21.44, 27.36, 28.40, 31.21, 31.68, 33.77, 33.93, 35.20, 35.54, 36.45, 44.73, 46.22, 52.25, 54.52, 57.04, 65.86, 66.85, 73.60, 123.73, 127.73, 128.13, 128.49, 130.42, 136.28, 151.60, 155.65, 170.69, 170.90. IR ($CDCl_3$ solution): 3444*w*, 3032*w*, 2932*s*, 2848*m*, 1726(*s, br*), 1648*w*, 1506*s*, 1454*m*, 1374*m*, 1340*w*, 1252(*s, br*), 1154*w*, 1132*w*, 1046*m*, 1026*m*, 966*w*. MS (EI): 577 (M^+, 1%, HRMS calc. for $C_{35}H_{47}NO_6$: 577.3403, found: 577.3351), 576 ($[M\text{-}H]^+$, 1), 561 ($[M\text{-}CH_4]^+$, 0.6%), 515 (17), 503 (6), 459 (9), 457 (11), 441 (13), 426 (15), 425 (19), 408 (17), 107 (91), 89 (96), 31 (100). $[\alpha]_D$= +4.4° (*c* 0.29, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]-4-(cholesta-3,5-dien-3-yl)but-3-enyl acetate (19)
Reaction of L-2-(CBz-amino)but-3-enyl acetate **15** (0.27mmol) with cholesta-3,5-dien-3-yl trifluoromethanesulphonate (0.40mmol) for 3h at 75° gave the title compound as a thick oil (54%). ^{1}H nmr δ 0.63 (*s*, 3H), 0.79 (*d*, 3H, *J* 6.5Hz), 0.80 (*d*, 3H, *J* 6.7Hz), 0.84 (*s*, 3H), 0.85-2.20 (*m*, 29H), 1.96 (*s*, 3H), 4.07 (*br d*, 2H, *J* 4.9Hz), 4.50 (*br*, 1H, α-proton), 4.95-5.04 (*br*, 1H, NH), 5.41 (*dd*, 1H, *J* 6.2Hz, partially obscured), 5.44 (*br*, 1H), 5.86 (*s*, 1H), 6.18 (*d*, 1H, *J* 15.8Hz), 7.29 (*m*, 5H). ^{13}C nmr δ 11.97, 18.66, 19.06, 20.77, 21.04, 21.94, 22.52, 22.78, 23.77, 24.12, 27.96, 28.18, 29.65, 31.67, 32.05, 33.42, 35.14, 35.74, 36.11, 39.44, 39.68, 42.39, 48.13, 56.06, 56.81, 65.97, 66.87, 122.41, 125.88, 128.13, 128.49, 131.51, 131.72, 135.02, 136.28, 142.01, 155.70, 170.98. IR ($CHCl_3$ solution): 3448*m*, 2948*s*, 2864*m*, 1724*s*, 1630*m*, 1504*s*, 1468*m*, 1384*m*, 1368*w*, 1240*s*, 1050(*s* ,*br*), 966*m*. MS (EI): 629 (M^+ - not present), 569 ([M-AcOH]$^+$, 2%, HRMS calc. for $C_{39}H_{55}NO_2$: 569.4233, found: 569.4218), 478 (2), 434 (3), 322 (3), 180 (9), 112 (21), 91 (47), 57 (100). $[\alpha]_D$= +1.0° (*c* 0.80, $CHCl_3$).

L-2-[(benzyloxycarbonyl)amino]-4-(3-*O*-methylestr-16-en-17-yl)but-3-enyl acetate (20)
Reaction of L-2-(CBz-amino)but-3-enyl acetate **15** (0.32mmol) with 3-O-methylestr-16-en-17-yl trifluoromethanesulphonate (0.48mmol) for 4h at 70-80° gave the title compound as a thick oil (83%). ^{1}H nmr δ 0.87 (*s*, 3H), 1.30-2.40 (*m*, 11H), 2.03 (*s*, 3H), 2.86 (*m*, 2H), 3.77 (*s*, 3H), 4.15 (*m*, 2H), 4.54 (*br*, 1H, α-proton), 5.08 (*br*, 1H, NH), 5.13 (*s*, 2H), 5.73 (*dd*, 1H, *J* 6.2, 16.0Hz, partially obscured), 5.74 (*br*, 1H), 6.21 (*d*,1H, *J* 16.2Hz), 6.63 (*d*, 1H, *J* 2.6Hz), 6.71 (*dd*, 1H, *J* 2.7, 8.5Hz), 7.19 (*d*, 1H, *J* 8.6Hz), 7.35 (*m*, 5H). ^{13}C nmr δ 15.94, 20.72, 26.49, 27.58, 29.61, 30.98, 35.24, 37.04, 44.09, 46.38, 52.25, 55.09, 56.33, 65.83, 66.82, 111.32, 113.71, 116.84, 123.89, 125.95, 127.65, 128.10, 128.46, 130.28, 132.66, 136.27, 137.84, 151.68, 155.65, 157.32, 170.87. IR ($CHCl_3$ solution): 3448*m*, 3000*w*, 2932*m*, 2856*w*, 1728*s*, 1610*m*, 1502*s*, 1458*m*, 1376*m*, 1238*s*, 1038*s*, 968*m*. MS (EI): 529 (M^+, 6%, HRMS calc. for $C_{33}H_{39}NO_5$: 529.2828, found: 529.2813), 514 ([M-Me]$^+$, 4), 469 ([M-AcOH]$^+$, 52%), 456 ([M-CH_2OAc]$^+$, 15), 421 (26), 378 (50), 361 (44), 227 (100), 147 (74), 91 (70), 79 (69). $[\alpha]_D$= +55.3° (*c* 1.03, $CHCl_3$).

The following procedure is representative of all the coupling reactions of L-2-(CBz-amino)but-3-enyl acetate **15** with aryl triflates and iodides (Table 2, Conditions D):

L-2-[(benzyloxycarbonyl)amino]-4-phenylbut-3-enyl acetate (21)
A mixture of *bis*-triphenylphosphinepalladium(II) chloride (0.0133g, 0.019mmol), iodobenzene (0.50mL, 0.091g, 0.45mmol), triethylamine (0.133mL, 0.096g, 0.95mmol) and L-2-(CBz-amino)but-3-enyl acetate **15** (0.050g, 0.19mmol) was heated at 100° for 6h in DMF (3mL) under a nitrogen atmosphere. 1N Hydrochloric acid (50mL) was added to the cooled mixture which was then extracted with diethyl ether (5x50mL). The combined extracts were dried and the solvent evaporated. The residue was flash chromatographed on silica gel, gradient eluting with 20-30% ethyl acetate/light petroleum, to yield the title compound as an amorphous white solid (0.0553g, 86%). An analytical sample was obtained after recrystallisation from dichloromethane/light petroleum. M.p. 96-98° (needles). ^{1}H nmr δ 2.03 (*s*, 3H), 4.18 (*br d*, 2H), 4.68 (*br*, 1H), 5.13(*s*, 2H), 5.10-5.20 (*br*, 1H), 6.10 (*dd*, 1H, *J* 6.1, 16.0Hz), 6.59 (*d*, 1H, *J* 16.0Hz), 7.22-7.36 (*m*, 10h). ^{13}C nmr δ 20.74, 52.03, 65.81, 66.96, 125.49, 126.46, 127.92, 128.18, 128.50, 128.54, 132.14, 136.06, 136.19, 155.67, 170.91. IR (nujol mull): 3304*m*, 1728*s*, 1688*s*, 1546*s*, 1278*s*, 1260*s*, 1066*m*, 1042*m*, 970*m*, 756*m*, 730*w*, 698*m*. MS (EI): 339 (M^+ - not present), 279 ([M-AcOH]$^+$, 3%, HRMS calc. for $C_{18}H_{17}NO_2$: 279.1259, found: 279.1264), 266 ([M-CH_2OAc]$^+$, 52), 222 (58), 188 (99), 171 (51), 160 (48), 91 (100). $[\alpha]_D$=+20.2° (*c* 0.24, $CHCl_3$). Calc. for $C_{20}H_{21}NO_4$: C 70.78%, H 6.24, N 4.13. Found: C 70.78, H 6.48, N 4.20.

L-2-[(benzyloxycarbonyl)amino]-4-(2-naphthyl)but-3-enyl acetate (22)
Reaction of L-2-(CBz-amino)but-3-enyl acetate **15** (0.19mmol) with 2-naphthyl triflate (0.38mmol) for 7h at 100° gave the title compound as a white solid (84%). ^{1}H nmr δ 2.01 (*s*, 3H), 4.08-4.22 (*m*, 2H), 4.70 (*br*, 1H), 5.12 (*s*, 2H), 5.25 (*br d*, 1H, *J* 6.6Hz), 6.18 (*dd*, 1H, *J* 6.0, 15.9Hz), 6.71 (*d*, 1H, *J* 15.9Hz), 7.20-7.52 (*m*, 9h), 7.64-7.77 (*m*, 3H). ^{13}C nmr δ 20.72, 52.08, 65.77, 66.93, 123.29, 125.80, 125.98, 126.27, 126.43, 126.67, 127.57, 127.92, 128.15, 128.47, 132.09, 132.19, 132.99, 133.35, 133.47, 136.18, 155.71, 170.90. IR ($CHCl_3$ solution): 3448*m*, 3028(*m*, *br*), 1726*s*, 1504*s*, 1458*m*, 1240(*s*, *br*),

1052(*m, br*), 968*m*. MS (EI): 389 (M^+, 3%, HRMS calc. for $C_{24}H_{23}NO_4$: 389.1627, found: 389.1606), 329 ([M-AcOH]$^+$, 33), 316 ([M-CH2OAc]$^+$, 29), 272 (38), 255 (26), 238 (79), 91 (100). $[\alpha]_D$=+28.3° (*c* 0.22, $CHCl_3$)

L-2-[(benzyloxycarbonyl)amino]-4-(2-ethoxycarbonyl-3-naphthyl)but-3-enyl acetate (23) Reaction of L-2-(CBz-amino)but-3-enyl acetate **15** (0.19mmol) with 2-(ethoxycarbonyl)naphth-3-yl trifluoromethanesulphonate (0.38mmol) for 7h at 100° gave the title compound as a thick oil (32%). ^{1}H nmr δ 1.38 (*t*, 3H, *J* 7.2Hz),2.02 (*s*, 3H), 4.23 (*m*, 2H), 4.71 (*br*, 1H), 5.11 (*s*, 2H), 5.22 (*br d*, 1H), 6.02 (*dd*, 1H, *J* 5.6, 15.7Hz), 7.06 (*m*, 8H), 7.75-7.85 (*m*, 3H), 8.42 (*s*, 1H). ^{13}C nmr δ14.32, 20.79, 51.99, 61.16, 65.72, 66.94, 126.63, 126.80, 126.96, 127.55, 127.64, 128.14, 128.39, 128.50, 128.69, 131.78, 134.58, 134.76, 136.28, 155.74 (urethane carbonyl), 167.13 (ethyl ester carbonyl), 171.01 (acetate carbonyl). IR ($CHCl_3$ solution): 3444*m*, 2988(*m, br*), 1722(*s, br*), 1628*w*, 1504*s*, 1458*m*, 1384*w*, 1368*m*, 1334*w*, 1272(*s, br*), 1134*m*, 1060(*s, br*), 966*m*, 914*w*. MS (EI): 461 (M^+, 0.5%, HRMS calc. for $C_{27}H_{27}NO_6$: 461.1838, found: 461.1811), 401 ([M-AcOH]$^+$, 4, HRMS calc. for $C_{25}H_{23}NO_4$: 401.1627, found: 401.1631), 388 ([M-CH_2OAc]$^+$, 4), 344 (6), 220 (27), 155 (24), 91 (100). $[\alpha]_D$=+9.9° (*c* 0.24, $CHCl_3$).

REFERENCES.

1. a) *α-Amino Acid Synthesis*, Tetrahedron Symposium in Print Number 33, O'Donnell, M.J., Ed: Ed: London, **1988**, *44*, 17.
   b) *Amino Acids, Peptides and Proteins*, Specialist Periodical Reports, The Royal Society of Chemistry: London, **1969-1987**, Vol. 1-18.
   c) Williams, R.M. *Synthesis of Optically Active α–Amino Acids*, Baldwin, J.E., Ed., Organic Chemistry Series, Pergamon Press: Oxford, **1989**.
2. a) Barrett, G.C. *Chemistry and Biochemistry of the Amino Acids*, Chapman & Hall: London, **1985**.
   b) Greenstein, J.P.; Winitz, M. *Chemistry of the Amino Acids*, Robert E. Krieger: FL, **1984**, Vol. 1-3.
3. Walsh, C. *Tetrahedron* **1982**, *38*, 871.
4. Coppala, G.M.; Schuster, H.F. *Asymmetric Synthesis: Construction of Chiral Molecules Using Amino Acids* , Wiley Interscience: New York, **1987**.
5. a) Azfali-Ardakani, A.; Rapoport, H *J. Org. Chem.* **1980**, *45*, 4817.
   b) Hanessian, S.; Sahoo, S.P. *Tetrahedron Lett.* **1984**, *25*, 1425.
   c) Pelliciari, R.; Natalini, B.; Marinozzi, M. *Synth. Commun.* **1988**, *18*, 1715.
   d) Meffre, P.; Vo-Quang, L.; Vo-Quang, Y.; Le Goffic, F. *Synth. Commun.* **1989**, *19*, 3457.
   e) Shaw, K.J.; Luly, J.R.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 4515.
   f) Wade, P.A.; Singh, S.M.; Pillay, M.K. *Tetrahedron* **1984**, *40*, 601.
6. a) Bicknell, A.J.; Burton, G.; Elder, J.S. *Tetrahedron Lett.* **1988**, *27*, 3361.
   b) Angst, C. *Pure Appl. Chem.* **1987**, *59*, 373.
   c) Castelhano, A.L.; Horne, S.; Taylor, G.J.; Billedeau, R.; Krantz, A. *Tetrahedron* **1988**, *44*, 5451.
   d) Shea, R.G.; Fitzner, J.N.; Fankhayser, J.E.; Spaltenstein, A.; Carpino, P.A.; Peevey, R.M.; Pratt, D.V.; Tenge, B.J.; Hopkins, P.B. *J. Org. Chem.* **1986**, *51*, 5243
7. a) Schöllkopf, U.; Nozulak, J.; Groth, U. *Tetrahedron* **1984**, *40*, 1409.
   b) Williams, R.M.; Zhai, W. *Tetrahedron* **1988**, *44*, 5425.
   c) Baldwin, J.E.; Moloney, M.G.; North, M. *Tetrahedron* **1989**, *45*, 6319.
   d) Sasaki, N.A.; Hashimoto, C.; Pauley, R. *Tetrahedron Lett.* **1989**, *30*, 1943.
   e) Sibi, M.P.; Renhowe, P.A. *Tetrahedron Lett.* **1990**, *31*, 7407.
   f) Beaulieu, P.L.; Duceppe, J.-S.; Johnson, C. *J. Org. Chem.* **1991**, *56*, 4196.
8. a) Crisp, G.T.; Bubner, T.P. *Synth. Commun.* **1990**, *20*, 1665.
   b) Crisp, G.T.; Robertson, T.A. *Tetrahedron* **1992**, Accepted.
9. Itaya, T.; Shimomichi, M.; Osaza, M. *Tetrahedron Lett.* **1988**, *29*, 4129.
10. a) Heck, R.F. *Org. React. (N.Y.)* **1982**, *27*, 345.
    b) Heck, R.F. *Pure Appl. Chem.* **1981**, *53*, 2323.
11. Miller, M.J.; Rajendra, G. *J. Org. Chem.* **1987**, *52*, 4471
12. a) Weidmann, B.; Seebach, D. *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 31.
    b) Rehinkle,H.; Steglich,W. *Synthesis* **1982**, 826.
13. Tsuji, J. *Tetrahedron* **1986**, *42*, 4361.

14. a) Jeffrey, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287.
b) Jeffrey, T. *Tetrahedron Lett.* **1985**, *26*, 2667.
15. Ohfune, Y.; Kurokawa, N. *Tetrahedron Lett.* **1984**, *25*, 1071.
16 a) Stang, P.J.; Hanack, M.; Subramanian, L.R. *Synthesis* **1982**, 85.
b) Stang, P.J.; Treptow, W. *Synthesis* **1980**, 283.
c) Collins, C.J.; Martinez, A.G.; Alvarez, R.M.; Aguirre, J.A. *Chem. Ber.* **1984**, *117*, 2815.
17. Echavarren, A.M.; Stille, J.K. *J. Am. Chem. Soc.* **1987**, *109*, 5478.
18. Saulinier, M.G.; Kadow, J.F.; Tun, M.M.; Langley, D.R.; Vyas, D.M. *J. Am. Chem. Soc.* **1989**, *111*, 8320.
19. a) Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1984**, *25*, 2271.
b) Cacchi, S.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1985**, *26*,1109.
c) Arcadi, A.; Cacchi, S.; Marinelli, F.; Morera, E.; Ortar, G. *Tetrahedron* **1990**, *46*, 7151.