100. Nitroacetyl Group as a Peptide Synthon: Synthesis of Dipeptides with an α,α-Bisallylglycine Residue at the N-Terminus[1])

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(21.V.91)

N-Nitroacetyl derivatives of L-proline, L-valine, and L-phenylalanine esters were prepared in two steps under mild conditions (*Scheme 2*). Regiospecific mono- and bis-allylation of these nitroacetyl derivatives were accomplished in presence of a Pd(0) catalyst. The bis-allyl derivatives **7–9** were obtained in 40–75% yield. The tertiary NO_2 group in these compounds could be transformed into an acetylamino group by $Zn/AcOH/Ac_2O$. The final products **11–13** are dipeptides in which the N-terminal glycine residue bears two α-allyl substituents.

Introduction. – The synthesis of oligopeptides of predetermined conformation, capable of exhibiting specific chemical and biological properties, has become a major area of interest for both organic and biochemists [1]. These synthetic targets very often incorporate non-proteinogenic amino acids, especially α-alkyl-α-amino acids (α,α-disubstituted glycine residues). This has assumed special importance after the isolation of the antibiotic alamethicin and the elucidation of its role in membrane transport. The reason is that this molecule contains α-aminoisobutyric acid (Aib) as one of the constituents [2], a residue known to promote helical folding, leading to α and 3_{10} helices [3].

In the last few years, several excellent methods have been developed for the stereospecific synthesis of α-alkyl-α-amino acids possessing a quaternary C-atom (which may even be chiral) [4]. However, the incorporation of such a residue in a peptide chain poses some difficulty because of low yields in the peptide coupling reaction due to steric hindrance [5]. Ingenious new reactions have, therefore, been devised to synthesise quaternary-C(α)-containing peptides without recourse to a 'peptide coupling'. Prominent among these are *Heimgartner*'s method which involves the use of a substituted azirine [6] and *Yamada*'s use of the *Ugi* reaction [7]. A radically different approach involves regiospecific and stereospecific enolate alkylation of preformed peptides [8].

We now describe a totally new concept for the synthesis of dipeptides incorporating an α,α-disubstituted glycine residue at the N-terminus. Our method involves three main steps: *i*) Nitroacetylation of an amino-acid derivative to form the *N*-(nitroacetyl)amino-acid ester (or amide), *ii*) regiospecific bis-allylation of the methylene group of the nitroacetyl moiety, and *iii*) generation of the free terminal NH_2 from the NO_2 group and its conversion to an *N*-acetyl derivative. *Scheme 1* summarizes our approach to this problem.

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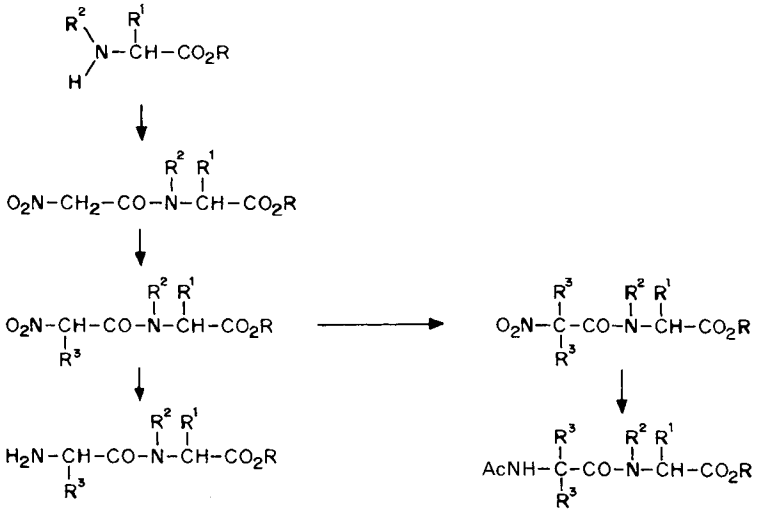
[1]) NCL Communication No. 5185.

Scheme 1



Critical to the success of this synthesis was the ability to nitroacetylate amino-acid derivatives efficiently under mild conditions. The method we had described earlier [9] proved quite general and gave us access to the required nitroacetyl derivatives in good yields.

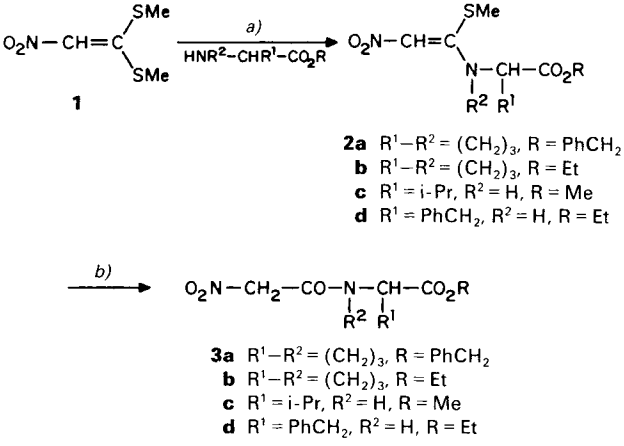
For the second step in the postulated synthetic sequence, we chose the Pd(0)-catalysed allylation rather than enolate alkylation, since we suspected that the latter might result exclusively or to a large extent in the nitronate ester rather than in the *C*-alkylated product. As reported recently [10], we have succeeded in the Pd(0)-catalysed diastereoselective mono-allylation of the *N*-(nitroacetyl)proline esters. We have also established the feasibility of converting the NO_2 group of the mono-allylated derivatives to an amino group, thereby achieving the synthesis of a dipeptide. In the process, we have established the absolute configuration of the newly created chiral centre in both diastereoisomers.

We now report the second allylation of the *N*-(nitroacetyl)amino-acid esters which already contain one α-allyl moiety. Thereby, we generate a quaternary C-atom in the nitroacetyl unit. In order to avoid getting diastereoisomer mixtures, we confined ourselves to the synthesis of derivatives bearing two identical allyl groups. Finally, we also succeeded in converting the tertiary NO_2 group of these compounds (*Scheme 1*) to the corresponding acylamino derivative, thereby achieving the objective of generating a dipeptide incorporating an α,α-disubstituted glycine residue.

Results and Discussion. – Esters of L-proline, L-valine, and L-phenylalanine were reacted with 1,1-bis(methylthio)-2-nitroethylene (**1**) as reported earlier [9] and the resultant (nitroenamino)esters **2a–d** subjected to $HgCl_2$-mediated hydrolysis to generate the *N*-nitroacetyl derivatives **3a–d** of L-proline, L-valine, and L-phenylalanine, respectively (*Scheme 2*).

Treatment of nitroacetyl derivatives **3** with an allyl acetate in presence of a base (DBU) and catalytic amount of Pd(0) catalyst prepared *in situ* by the addition of

Scheme 2



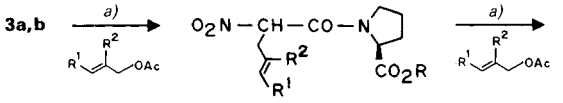
a) L-Amino-acid ester, cat. TsOH, MeCN, 30–80°. *b*) $HgCl_2$, $MeCN/H_2O$ 3:1, r.t.

$Pd(dba)_2$ (3 mol-%) and PPh_3 (12 mol-%) at 25–30° for 8–10 h gave the mono-allyl derivatives **4a–e**, **5a**, **b**, and **6a**, **b** in yields of 40–80% (*Scheme 3*), the diastereoisomeric excess (*de*) being 10–45%, as reported earlier [10]. Subsequent allylation under essentially the same conditions gave the α,α-disubstituted products **7a–e**, **8a**, **b**, and **9a**, **b** in 40–75% yield. The products were fully characterised by ^{1}H- and ^{13}C-NMR spectroscopy. The signals in the ^{13}C-NMR spectra were assigned to the individual C-atoms by their chemical-shift values and by the appropriate use of a DEPT experiment. The quaternary C-atom in all these compounds gave a characteristic signal at *ca.* 96 ppm. Interestingly, for the L-proline derivatives **7a–e**, only one set of peaks was observed in both ^{1}H- and ^{13}C-NMR spectra, indicating the absence of *cis*/*trans* rotamers [9–11], whereas the unsubstituted and monosubstituted precursors **3a**, **b** and **4a–e**, respectively, showed two sets. In analogy with the earlier studies [11] [12] of *N*-acylprolines bearing a quaternary C-atom, the *trans*-amide configuration was assigned to **7a–e**.

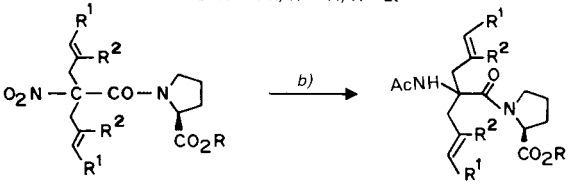
Among the many methods known for the conversion of a NO_2 group to a NH_2 group, the most widely used one is catalytic hydrogenation using noble metals like Pd/C or PtO_2. Earlier, we were successful in converting ethyl *N*-(nitroacetyl)-L-prolinate (**3b**) to the corresponding cyclic dipeptide by catalytic hydrogenation (20% Pd/C (*w*/*w*), EtOH, 50 psi) in a *Parr* apparatus [13]. However, the tertiary NO_2 group in **7a** and **7b** was resistant to reduction under these conditions, the products being the nitroacylamino acids **10a**, **b** obtained by hydrogenolysis of the benzyl ester and hydrogenation of the side-chain double bonds (*Scheme 4*; IR: NO_2 at 1550*s* and 1390*m* cm^{-1}; ^{13}C-NMR: quaternary C-atom adjacent to the NO_2 group at *ca.* 96 ppm).

Very recently, *Vettiger* and *Seebach* have reported the reductive acetylation of aliphatic nitro compounds to the corresponding acetylamino derivatives using Zn/$AcOH/Ac_2O$ [14]. This procedure turned out to be successful with our substrates as well. *E.g.*, stirring a suspension of **7a** in $AcOH/Ac_2O$ with Zn dust at 40–60° for 6–12 h gave the *N*-acetyldipeptide benzyl ester **11a** in 75% yield (^{13}C-NMR: quaternary C-atom at 67.72

Scheme 3

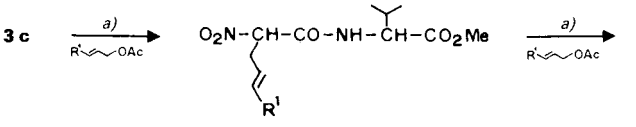


4a $R^1 = R^2 = H$, $R = PhCH_2$
b $R^1 = Ph$, $R^2 = H$, $R = PhCH_2$
c $R^1 = H$, $R^2 = Me$, $R = PhCH_2$
d $R^1 = R^2 = H$, $R = Et$
e $R^1 = Ph$, $R^2 = H$, $R = Et$

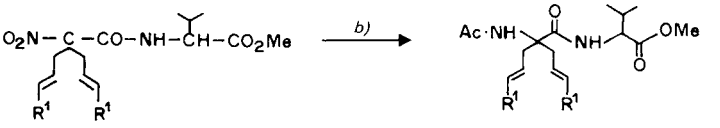


7a $R^1 = R^2 = H$, $R = PhCH_2$
b $R^1 = Ph$, $R^2 = H$, $R = PhCH_2$
c $R^1 = H$, $R^2 = Me$, $R = PhCH_2$
d $R^1 = R^2 = H$, $R = Et$
e $R^1 = Ph$, $R^2 = H$, $R = Et$

11a $R^1 = R^2 = H$, $R = PhCH_2$
b $R^1 = Ph$, $R^2 = H$, $R = PhCH_2$
c $R^1 = H$, $R^2 = Me$, $R = PhCH_2$
d $R^1 = R^2 = H$, $R = Et$
e $R^1 = Ph$, $R^2 = H$, $R = Et$

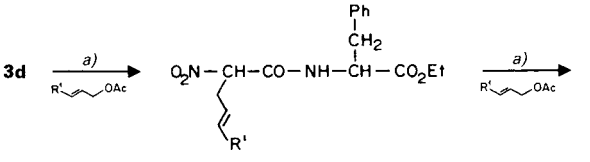


5a $R^1 = H$
b $R^1 = Ph$

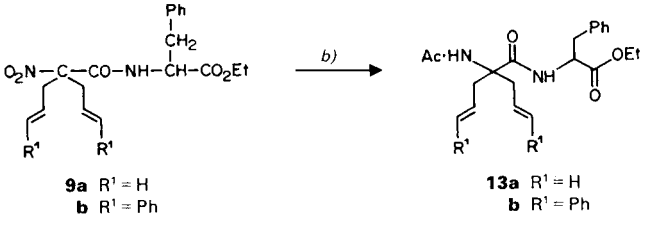


8a $R^1 = H$
b $R^1 = Ph$

12a $R^1 = H$
b $R^1 = Ph$



6a $R^1 = H$
b $R^1 = Ph$

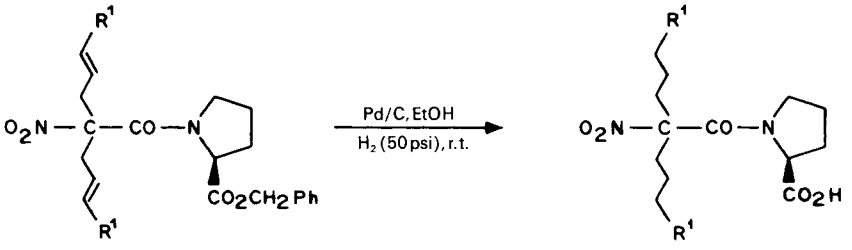


9a $R^1 = H$
b $R^1 = Ph$

13a $R^1 = H$
b $R^1 = Ph$

a) DBU, $Pd(dba)_2$ (3 mol-%), PPh_3 (12 mol-%). *b*) Zn, $AcOH/Ac_2O$, 40–60°.

Scheme 4



7a R^1 = H
b R^1 = Ph

10a R^1 = H
b R^1 = Ph

ppm). All nitro compounds **7–9** were similarly converted to the *N*-acetyldipeptide derivatives **11–13**, respectively.

We thank the *CSIR* and *UGC* for the award of research fellowships to *S.G.M.* and *P.C.*, respectively.

Experimental Part

1. *General.* M.p.: uncorrected; in open capillary; *Campbell-Electronic-Thermonik* instrument. Optical rotations: *Jasco-181* digital polarimeter, Na light (5893 Å) source. IR spectra (cm^{-1}): *Perkin-Elmer-Infracord* spectrometer, NaCl optics. ^{1}H- and ^{13}C-NMR spectra: *Bruker-WH-90* (*Spectrospin*), *Bruker-MSL-300*, or *Varian-FT-80A* instrument; tetramethylsilane as internal standard, δ values in ppm. MS: *Finnigan-MAT-1020B* spectrometer. Abbreviations: $Pd(dba)_2$ = bis(dibenzylidene)palladium(0), DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

2. N-*Nitroacetyl Derivatives* **3** *of Amino-Acid Esters: General Procedure.* A soln. of amino-acid ester (10 mmol) in MeCN (10 ml) was added slowly to a suspension of 1,1-bis(methylthio)-2-nitroethene (**1**; 10 mmol) in MeCN (15 ml) containing TsOH (catalytic amount) at 30–80°. The mixture was stirred at the same temp. for 10–24 h. The MeCN was evaporated and the residue treated with EtOH at ice temp. to precipitate unreacted **1**. The solid was filtered and the filtrate evaporated to give a gum. The gum was washed twice with petroleum ether (50 ml) and the residue purified by column chromatography (silica gel, 60–120 mesh; benzene/AcOEt) to give (nitroenamino)ester **2** which was used as such for further reaction. A soln. of **2** (10 mmol) in $MeCN/H_2O$ 3:1 (10 ml) was added slowly to a soln. of $HgCl_2$ (10 mmol) in the same solvent (15 ml), and the mixture was stirred at 30° for 3–18 h. The mixture was then filtered through a *Celite* pad to remove the Hg-salt, and the filtrate was taken up in $CHCl_3$ (50 ml). The org. extract was washed with H_2O, dried (Na_2SO_4), and evaporated: the *N*-nitroacetyl derivative **3** was further purified by column chromatography.

Methyl N-*[1-(Methylthio)-2-nitroethenyl]*-L-*valinate* (**2c**). Yield 60%. IR (neat): 3150*m*, 1750*s*, 1550*s*, 1380*m*, 1150*s*. ^{1}H-NMR ($CDCl_3$): 0.9–1.15 (2*d*, 2 CH_3–C(3)); 2.1–2.5 (*m*, H–C(3)); 2.25 (*s*, MeS); 3.8 (*s*, MeO); 4.15–4.4 (*m*, H–C(2)); 6.6 (*s*, C=$CHNO_2$); 10.6–11 (br. *d*, NH). Anal. calc. for $C_9H_{16}N_2O_4S$ (248.3): C 43.53, H 6.49, N 11.28, S 12.91; found: C 43.82, H 6.65, N 11.20, S 13.0.

Ethyl N-*[1-(Methylthio)-2-nitroethenyl]*-L-*phenylalaninate* (**2d**). Yield 50%. IR (neat): 3180*w*, 1750*s*, 1575*s*, 1490*w*, 1430*m*, 1360*m*, 1240*s*, 1210*m*. ^{1}H-NMR ($CDCl_3$): 1.15–1.33 (*t*, CH_3CH_2O); 2.4 (*s*, MeS); 3.1–3.28 (*m*, $PhCH_2$(3)); 4.0–5.0 (*m*, CH_3CH_2O, H–C(2)); 6.2 (*s*, C=$CHNO_2$); 7.0–7.62 (*m*, $PhCH_2$(3)); 10.6–10.84 (br. *d*, NH). Anal. calc. for $C_{14}H_{18}N_2O_4$ (310.37): C 54.17, H 5.84, N 9.02, S 10.33; found: C 54.0, H 5.91, N 9.28, S 10.13.

Methyl N-*(Nitroacetyl)*-L-*valinate* (**3c**). Yield 90%. $[\alpha]_D = -19.8$ ($c = 2$, EtOH). IR (neat): 3340*s*, 1750*s*, 1690*s*, 1580*s*, 1450*s*, 1380*m*, 1220*m*. ^{1}H-NMR ($CDCl_3$): 0.9–1.0 (*m*, 2 CH_3–C(3)); 2.0–2.44 (*m*, H–C(3)); 3.73 (*s*, MeO); 4.48–4.64 (*m*, H–C(2)); 5.11 (*s*, CH_2NO_2); 7.1–7.28 (br. *d*, NH). ^{13}C-NMR ($CDCl_3$): 17.28, 18.35 (2 CH_3–C(3)); 30.77 (C(3)); 51.98 (C(2)); 57.62 (MeO); 77.49 (CH_2NO_2); 160.96 (CO); 171.53 (CO). MS: 218 (M^+), 159, 130, 113, 98, 88, 70. Anal. calc. for $C_8H_{14}N_2O_5$ (218.22): C 44.03, H 6.46, N 12.83; found: C 44.32, H 6.67, N 12.57.

Ethyl N-*(Nitroacetyl)*-L-*phenylalaninate* (**3d**). Yield 90%. M.p. 82–84°. $[\alpha]_D = +21.25$ ($c = 2$, EtOH). IR (nujol): 3320*s*, 1740*s*, 1660*s*, 1570*s*, 1470*s*, 1390*s*, 1240*m*, 1220*m*, 720*w*. ^{1}H-NMR ($CDCl_3$): 1.26 (*t*, CH_3CH_2O); 3.08–3.1 (*d*, $PhCH_2$(3)); 4.06–4.28 (*q*, CH_3CH_2O); 4.66–5.0 (*m*, H–C(2)); 5.0 (*s*, CH_2NO_2). ^{13}C-NMR ($CDCl_3$):

13.71 (CH_3CH_2O); 37.37 (PhCH_2(3)); 53.64 (C(2)); 61.66 (CH_3CH_2O); 77.32 (CH_2NO_2); 126.98, 128.31, 128.56, 128.78, 129.03, 135.17; 160.08 (CO); 170.69 (CO). MS: 280 (M^+), 266, 235, 207, 176, 161, 148, 131, 91, 77. Anal. calc. for $C_{13}H_{16}N_2O_5$ (280.28): C 55.71, H 5.75, N 9.99; found: C 55.44, H 5.81, N 9.75.

3. *Allylation of Nitroacetyl Derivatives: General Procedure.* To a soln. of the *N*-nitroacetyl derivative (1 mmol) in degassed MeCN (15 ml), DBU (1 mmol) was added and stirred under Ar for 5 min. $Pd(dba)_2$(3 mol-%) and PPh_3 (12 mol-%) were added to the mixture and stirred for another 5 min. Finally, the soln. of an allyl acetate (1 mmol) in MeCN (5 ml) was added and the mixture stirred for 8–10 h. After cooling to −15 to −20°, the mixture was made acidic by the addition of 5% aq. HCl soln. and extracted with benzene, the org. extract washed well with H_2O and brine, dried (Na_2SO_4), and evaporated, and the orange gum further purified by column chromatography (silica gel, 60–120 mesh, petroleum ether/AcOEt) to give the pure nitro(substituted allyl)acetyl derivative.

Methyl N-*[2-Nitro-2-(prop-2-en-1-yl)acetyl]*-L-*valinate* (= *Methyl* N-*(2-Nitropent-4-enoyl)*-L-*valinate*, **5a**). Yield 60%. IR (neat): 3340*m*, 1755*s*, 1680*s*, 1580*s*, 1380*m*. ^{1}H-NMR ($CDCl_3$): 0.9–1.0 (*m*, 2 CH_3–C(3)); 2.0–2.48 (*m*, H–C(3)); 2.9–3.15 (*m*, CH_2=CHCH_2); 3.8 (*s*, MeO); 4.53–4.7 (*m*, H–C(2)); 5.1–6.0 (*m*, CH_2=CHCH_2, $CHNO_2$); 7.0 (br. *s*, NH). Anal. calc. for $C_{11}H_{18}N_2O_5$ (258.27): C 51.15, H 7.02, N 10.84; found: C 51.0, H 7.31, N 11.0.

Methyl N-*[2-Nitro-2-(3-phenylprop-2-en-1-yl)acetyl]*-L-*valinate* (= *Methyl* N-*(2-Nitro-5-phenylpent-4-enoyl)*-L-*valinate*; **5b**). Yield 45%. IR (neat): 3345*m*, 1760*s*, 1680*s*, 1580*s*, 1380*m*. ^{1}H-NMR ($CDCl_3$): 0.8–1.06 (*m*, 2 CH_3–C(3)); 1.9–2.48 (*m*, H–C(3)); 3.0–3.31 (*t*, PhCH=CHCH_2); 3.71–3.8 (2*s*, MeO); 4.42–4.73 (*m*, H–C(2)); 5.1–5.4 (*m*, $CHNO_2$); 5.94–6.71 (*m*, PhCH=CHCH_2); 7–7.1 (*m*, Ph, NH). Anal. calc. for $C_{17}H_{22}N_2O_5$ (334.37): C 61.06, H 6.63, N 8.37; found: C 61.0, H 6.51, N 8.43.

Ethyl N-*[2-Nitro-2-(prop-2-en-1-yl)acetyl]*-L-*phenylalaninate* (= *Ethyl* N-*(2-Nitropent-4-enoyl)*-L-*phenylalaninate*; **6a**). Yield 62%. IR ($CHCl_3$): 3300*m*, 1750*s*, 1680*s*, 1380*m*. ^{1}H-NMR ($CDCl_3$): 1.26 (*t*, CH_3CH$_2$O); 2.77–3.0 (*m*, CH_2=CHCH_2); 3.1–3.2 (*d*, PhCH_2(3)); 4.1–4.33 (*q*, CH_3CH_2O); 4.66–6.0 (br. *m*, $CHNO_2$, H–C(2), CH_2=CHCH_2): 6.8–7.55 (*m*, Ph, NH). ^{13}C-NMR ($CDCl_3$): 13.88 (CH_3CH$_2$O); 34.63, 35.1 (CH_2=CHCH_2); 37.41, 37.45 (PhCH_2(3)); 53.47 (C(2)); 61.75 (CH_3CH_2O); 88.46, 88.59 ($CHNO_2$); 120.16, 120.29 (CH_2=CHCH_2); 127.19, 128.50, 129.03, 129.11, 129.96, 130.08, 134.97, 135.06; 161.87 (CO); 162.17 (CO); 170.42 (CO). Anal. calc. for $C_{16}H_{20}N_2O_5$ (320.34): C 59.99, H 6.29, N 8.74; found: C 59.72, H 6.42, N 8.92.

Ethyl N-*[2-Nitro-2-(3-phenylprop-2-en-1-yl)acetyl]*-L-*phenylalaninate* (= *Ethyl* N-*(2-Nitro-5-phenylpent-4-enoyl)*-L-*phenylalaninate*; **6b**). Yield 55%. IR ($CHCl_3$): 3320*m*, 1750*s*, 1680*s*, 1560*s*, 1380*m*. ^{1}H-NMR ($CDCl_3$): 1.2 (*t*, CH_3CH$_2$O); 2.8–3.35 (*m*, PhCH_2(3), PhCH=CHCH_2); 4.0–4.35 (*m*, CH_3CH_2O); 4.65–5.15 (*m*, H–C(2), $CHNO_2$); 5.8–6.6 (*m*, PhCH=CHCH_2); 6.7–7.5 (*m*, 2 Ph, NH). ^{13}C-NMR ($CDCl_3$): 13.69 (CH_3CH$_2$O); 33.7, 34.0 (PhCH=CHCH_2); 37.28 (PhCH_2(3)); 53.51 (C(2)); 61.60 (CH_3CH_2O); 88.12 ($CHNO_2$); 121.0, 121.12 (PhCH=CHCH_2); 126.09, 126.94, 127.32, 128.27, 128.90, 129.00, 134.84, 135.00, 136.05; 162.23, 162.45, 170.54. Anal. calc. for $C_{22}H_{24}N_2O_5$ (396.44): C 66.54, H 6.10, N 7.06; found: C 66.37, H 6.29, N 7.28.

Allylation of Benzyl N-*[2-Nitro-2-(prop-2-en-1-yl)acetyl]*-L-*prolinate* (**4a**) *to Benzyl* N-*[2-Nitro-2,2-bis(prop-2-en-1-yl)acetyl]*-L-*prolinate* (= *Benzyl* N-*[2-Nitro-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*prolinate*; **7a**). Yield 75%. $[\alpha]_D$ = −100.5 (*c* = 2, $CHCl_3$). IR (neat): 3100*w*, 1750*s*, 1650*s*, 1550*s*, 1420*s*, 1370*w*, 1190*s*. ^{1}H-NMR ($CDCl_3$): 1.5–2.5 (*m*, CH_2(3), CH_2(4)); 2.7–3.6 (*m*, CH_2(5), 2 CH_2=CHCH_2); 4.4–4.7 (*m*, H–C(2)); 4.7–5.3 (*m*, PhCH_2, 2CH_2=CHCH_2); 5.3–5.9 (*m*, 2 CH_2=CHCH_2); 7.1–7.4 (*m*, *Ph*CH_2). ^{13}C-NMR ($CDCl_3$): 24.94 (C(4)); 27.45 (C(3)); 37.03, 39.02 (CH_2=CHCH_2); 46.33 (C(5)); 60.41 (C(2)); 66.29 (PhCH_2); 94.35 (CNO_2); 120.66 (CH_2=CHCH_2); 127.60, 127.75, 128.03, 129.24, 129.43 (CH_2=CHCH_2); 135.17; 163.21 (CO); 170.86 (CO). Anal. calc. for $C_{20}H_{24}N_2O_5$ (372.41): C 64.50, H 6.49, N 7.52; found: C 64.23, H 6.65, N 7.15.

Cinnamylation of Benzyl N-*[2-Nitro-2-(3-phenylprop-2-en-1-yl)acetyl]*-L-*prolinate* (**4b**) *to Benzyl* N-*[2-Nitro-2,2-bis(3-phenylprop-2-en-1-yl)acetyl]*-L-*prolinate* (= *Benzyl* N-*[2-Nitro-5-phenyl-2-(3-phenylprop-2-en-1-yl)-pent-4-enoyl]*-L-*prolinate*; **7b**). Yield 70%. $[\alpha]_D$ = +10.29 (*c* = 2, $CHCl_3$). IR (nujol): 3020*w*, 1760*s*, 1660*s*, 1560*s*, 1430*m*, 1380*m*, 1230*s*, 1190*s*, 770*s*. ^{1}H-NMR ($CDCl_3$): 1.55–2.1 (*m*, CH_2(3), CH_2(4)); 2.75–3.6 (*m*, CH_2(5), 2 PhCH=CHCH_2); 4.4–4.67 (*m*, H–C(2)); 5.05 (*s*, PhCH_2); 5.65–6.62 (*m*, 2 PhCH=CHCH_2); 6.9–7.52 (*m*, 3 Ph). ^{13}C-NMR ($CDCl_3$): 25.30 (C(4)); 27.76 (C(3)); 37.17, 39.55 (PhCH=CHCH_2); 46.82 (C(5)); 60.74 (C(2)); 66.73 (PhCH_2); 95.19 (CNO_2); 120.84, 120.95 (PhCH=CHCH_2); 126.23, 126.35, 127.52, 127.63, 128.09, 128.37, 135.44, 135.72, 136.40, 136.52; 163.74 (CO); 171.36 (CO). Anal. calc. for $C_{32}H_{32}N_2O_5$ (524.61): C 73.26, H 6.15, N 5.34; found: C 73.42, H 5.98, N 5.51.

Methallylation of Benzyl N-*[2-Nitro-2-(2-methylprop-2-en-1-yl)acetyl]*-L-*prolinate* (**4c**) *to Benzyl* N-*[2-Nitro-2,2-bis(2-methylprop-2-en-1-yl)acetyl]*-L-*prolinate* (= *Benzyl* N-*[4-Methyl-2-(2-methylprop-2-en-1-yl)-2-nitro-pent-4-enoyl]*-L-*prolinate*; **7c**). Yield 30%. $[\alpha]_D$ = −40.1 (*c* = 1.6, $CHCl_3$). IR (neat): 3100*w*, 1760*s*, 1660*s*, 1560*s*, 1420*m*, 1380*m*, 1185*s*. ^{1}H-NMR ($CDCl_3$): 1.55 (*s*, 2 CH_2=C(CH_3)CH_2); 1.6–2.2 (*m*, CH_2(3), CH_2(4)); 3.0 (*s*, 2 CH_2=C(CH_3)CH_2); 3.22 (*t*, CH_2(5)); 4.45 (*t*, H–C(2)); 4.55 (*s*, PhCH_2); 4.8, 4.9 (2*s*, 2 H), each 2

CH_2=C(CH_3)CH_2; 7.3 (*s*, Ph). ^{13}C-NMR ($CDCl_3$): 23.16 (CH_2=C(CH_3)CH_2); 25.29 (C(4)); 27.68 (C(3)); 41.40, 42.75 (CH_2=C(CH_3)CH_2); 46.85 (C(5)); 61.00 (C(2)); 66.35 (PhCH_2); 95.00 (CNO_2); 117.09, 117.23 (CH_2=C(CH_3)CH_2); 127.75, 127.84, 128.13, 135.34, 138.14, 138.36 (CH_2=C(CH_3)CH_2, Ph); 164.14 (CO); 170.93 (CO). Anal. calc. for $C_{22}H_{28}N_2O_5$ (400.50): C 65.98, H 7.05, N 6.99; found: C 65.65, H 6.80, N 7.3.

Ethyl N-*[2-Nitro-2,2-bis(prop-2-en-1-yl)acetyl]*-L-*prolinate* (= *Ethyl* N-*[2-Nitro-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*prolinate;* **7d**). Yield, 65%. $[\alpha]_D = -98.7$ (*c* = 1.7, $CHCl_3$). IR (neat): 1760*s*, 1670*s*, 1560*s*, 1430*s*, 1380*m*, 1200*s*, 1050*m*, 940*m*. ^{1}H-NMR ($CDCl_3$): 1.24 (*t*, CH_3CH_2O); 1.84–2.33 (*m*, CH_2(3), CH_2(4)); 2.9–3.05 (*m*, 2 CH_2=CHCH_2); 3.15–3.64 (*m*, CH_2(5)); 4.2 (*q*, CH_3CH_2O); 4.25–4.57 (*m*, H–C(2)); 5.05–6.0 (*m*, 2 CH_2=CHCH_2). ^{13}C-NMR ($CDCl_3$): 13.90 (CH_3CH_2O); 25.23 (C(4)); 27.84 (C(3)); 37.33, 39.35 (CH_2=CHCH_2); 46.62 (C(5)); 60.72 (CH_3CH_2O); 61.01 (C(2)); 94.72 (CNO_2); 121.0 (CH_2=$CHCH_2$); 129.48, 129.67 (CH_2=$CHCH_2$); 163.55 (CO); 171.39 (CO). MS: 310 (M^+), 264 ([M – NO_2]$^+$), 237, 219, 206, 190, 166, 142, 121, 93, 79, 70. Anal. calc. for $C_{15}H_{22}N_2O_5$ (310.35): C 58.05, H 7.14, N 9.02; found: C 58.16, H 7.09, N 8.95.

Ethyl N-*[2-Nitro-2,2-bis(3-phenylprop-2-en-1-yl)acetyl]*-L-*prolinate* (= *Ethyl* N-*[2-Nitro-5-phenyl-2-(3-phenylprop-3-en-1-yl)pent-4-enoyl]*-L-*prolinate;* **7e**). Yield 50%. $[\alpha]_D = +20.15$ (*c* = 2, $CHCl_3$). IR ($CHCl_3$): 1750*s*, 1660*s*, 1555*s*, 1430*m*, 1380*w*, 1230*m*, 1200*m*. ^{1}H-NMR ($CDCl_3$): 1.27 (*t*, CH_3CH_2O); 1.83–2.28 (*m*, CH_2(3), CH_2(4)); 3–3.8 (*m*, CH_2(5), 2 PhCH=CHCH_2); 4–4.22 (*q*, CH_3CH_2O); 4.55–4.71 (*m*, H–C(2)); 6–6.71 (*m*, 2 PhC*H*=C*H*CH_2); 7.37 (*m*, 2 Ph). ^{13}C-NMR ($CDCl_3$): 13.39 (CH_3CH_2O); 25.22 (C(4)); 27.76 (C(3)); 37.12, 39.45 (PhCH=CHCH_2); 46.75 (C(5)); 60.75 (CH_3CH_2O); 60.97 (C(2)); 95.16 (CNO_2); 120.90, 126.18, 127.57, 128.06, 135.64, 136.39 (*Ph*CH=*C*HCH_2); 163.60 (CO); 171.40 (CO). MS: 462 (M^+), 416 ([M – NO_2]$^+$), 273, 255, 245, 211, 167, 141, 128, 117, 91, 70. Anal. calc. for $C_{27}H_{30}N_2O_5$ (462.54): C 70.11, H 6.53, N 6.05; found: C 70.29, H 6.85, N 6.26.

Methyl N-*[2-Nitro-2,2-bis(prop-2-en-1-yl)acetyl]*-L-*valinate* (= *Methyl* N-*[2-Nitro-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*valinate;* **8a**). Yield 60%. $[\alpha]_D = -48.3$ (*c* = 1, EtOH). IR (neat): 3380*m*, 1750*s*, 1690*s*, 1560*s*, 1450*w*, 1380*w*, 1300*s*. ^{1}H-NMR ($CDCl_3$): 0.8–0.93 (2*d*, 2 CH_3–C(3)); 1.93–2.4 (*m*, H–C(3)); 2.9–3.0 (*d*, 2 CH_2=CHCH_2); 3.73 (*s*, MeO); 4.4–4.57 (*m*, H–C(2)); 5.0–5.9 (*m*, 2 CH_2=CHCH_2); 6.9–7.0 (*d*, NH). ^{13}C-NMR ($CDCl_3$): 17.4, 18.58 (2 CH_3–C(3)); 30.80 (C(3)); 38.56, 38.87 (CH_2=CHCH_2); 51.94 (C(2)); 57.52 (MeO); 95.95 (CNO_2); 121.06, 121.0 (CH_2=$CHCH_2$); 129.32, 129.51 (CH_2=$CHCH_2$); 164.96 (CO); 171.23 (CO). MS: 298 (M^+), 281, 268, 252 ([M – NO_2]$^+$), 239, 193, 152, 130, 121, 98, 93,79, 72, 59, 55. Anal. calc. for $C_{14}H_{22}N_2O_5$ (298.36): C 56.36, H 7.43, N 9.39; found: C 56.35, H 7.70, N 9.25.

Methyl N-*[2-Nitro-2,2-bis(3-phenylprop-2-en-1-yl)acetyl]*-L-*valinate* (= *Methyl* N-*[2-Nitro-5-phenyl-2-(3-phenylprop-2-en-1-yl)pent-4-enoyl]*-L-*valinate;* **8b**). Yield 45%. $[\alpha]_D = -8$ (*c* = 2, EtOH). IR (neat): 3360*m*, 1750*s*, 1690*s*, 1560*s*, 1440*w*, 1380*m*, 1220*s*, 980*m*. ^{1}H-NMR ($CDCl_3$): 0.82–0.96 (2*d*, 2 CH_3–C(3)); 2.08–2.53 (*m*, H–C(3)); 3.15–3.24 (*d*, 2 PhCH=CHCH_2); 3.51 (*s*, MeO); 4.48–4.66 (*m*, H–C(2)); 5.8–6.77 (*m*, 2 PhC*H*=C*H*CH_2); 7.0–7.55 (*m*, 2 Ph, NH). ^{13}C-NMR ($CDCl_3$): 17.49, 18.65 (2 CH_3–C(3)); 30.89 (C(3)); 38.94, 39.21 (PhCH=CHCH_2); 51.96 (C(2)); 57.71 (MeO); 96.78 (CNO_2); 120.39, 120.60 (=C–); 126.20, 126.25, 127.70, 128.09, 128.34 (arom. C); 136.06, 136.26 (=C–); 165.14 (CO); 171.19 (CO). MS: 450 (M^+), 404 ([M – NO_2]$^+$), 273, 245, 167, 117, 105, 91, 77, 55. Anal. calc. for $C_{26}H_{30}N_2O_5$ (450.53): C 69.31, H 6.71, N 6.21; found: C 69.50, H 6.95, N 6.0.

Ethyl N-*[2-Nitro-2,2-bis(prop-2-en-1-yl)acteyl]*-L-*phenylalaninate* (= *Ethyl* N-*[2-Nitro-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*phenylalaninate;* **9a**). Yield 63%. $[\alpha]_D = +23.36$ (*c* = 1.25, $CHCl_3$). IR ($CHCl_3$): 3400*m*, 1750*s*, 1690*s*, 1560*s*, 1480*m*, 1230*m*. ^{1}H-NMR ($CDCl_3$): 1.26 (*t*, CH_3CH_2O); 2.8–3.0 (*d*, 2 CH_2=CHCH_2); 3.06–3.26 (*m*, PhCH_2(3)); 4.1–4.3 (*q*, CH_3CH_2O); 4.75–5.9 (*m*, 2 CH_2 = CHCH_2, H–C(2)); 6.84–6.9 (*d*, NH); 7.1–7.46 (*m*, *Ph*CH_2(3)). ^{13}C-NMR ($CDCl_3$): 13.83 (CH_3CH_2O); 37.48, 38.84 (CH_2=CHCH_2); 39.05 (C(3)); 53.56 (C(2)); 61.55 (CH_3CH_2O); 95.83 (CNO_2); 121.10, 121.09 (CH_2=$CHCH_2$); 127.08, 128.34, 128.46, 128.60, 129.06, 129.48, 135.27 (CH_2=$CHCH_2$, *Ph*CH_2); 164.68 (CO); 170.47 (CO). MS: 360 (M^+), 314 ([M – NO_2]$^+$), 287, 241, 176, 148, 131, 120, 91, 79. Anal. calc. for $C_{19}H_{24}N_2O_5$ (360.4): C 63.32, H 6.71, N 7.77; found: C 63.04, H 6.66, N 7.84.

Ethyl N-*[2-Nitro-2,2-bis(3-phenylprop-2-en-1-yl)acetyl]*-L-*phenylalaninate* (= *Ethyl* N-*[2-Nitro-5-phenyl-2-(3-phenylprop-2-en-1-yl)pent-4-enoyl]*-L-*phenylalaninate;* **9b**). Yield 44%. $[\alpha]_D = +35.54$ (*c* = 1, $CHCl_3$). IR ($CHCl_3$): 3400*m*, 1750*s*, 1690*s*, 1560*s*, 1540*s*, 1460*w*, 1390*w*, 1360*w*, 1230*s*. ^{1}H-NMR ($CDCl_3$): 1.2 (*t*, CH_3CH_2O); 3.0–3.5 (*m*, H–C(3), 2 PhCH=CHCH_2); 4.0–4.26 (*q*, CH_3CH_2O); 4.77–5.0 (*m*, H–C(2)); 5.91–6.6 (*m*, 2 PhC*H*=C*H*CH_2); 6.93–7.42 (*m*, 3 Ph, NH). ^{13}C-NMR ($CDCl_3$): 13.83 (CH_3CH_2O); 37.53 (PhCH_2(3)); 38.64, 38.89 (PhCH=CHCH_2); 53.68 (C(2)); 61.56 (CH_3CH_2O); 96.44 (CNO_2); 120.47, 120.64, 126.29, 127.11, 127.74, 128.38, 129, 135.19, 136.03, 136.07, 136.31 (*Ph*CH=*C*H, *Ph*CH_2); 164.78 (CO); 170.40 (CO). MS: 512 (M^+), 466 ([M – NO_2]$^+$), 273, 255, 245, 167, 155, 141, 128, 117, 91, 77, 65. Anal. calc. for $C_{31}H_{32}N_2O_5$ (512.6): C 72.63, H 6.29, N 5.46; found: C 72.51, H 6.46, N 5.27.

4. *Hydrogenation of* **7a, b** *to* **10a, b**: *General Procedure.* The *N*-[2-nitro-2,2-bis(substituted allyl)acetyl]amino derivative **7a** or **7b** (100 mg) in EtOH (25 ml) was hydrogenated in a *Parr* apparatus at 50 psi of H_2 in presence of

20% Pd/C (*w/w*) for 14 h. The catalyst was filtered off and the filtrate evaporated to give a semisolid which was purified by column chromatography (silica gel, $CHCl_3$).

N-*(2-Nitro-2,2-dipropylacetyl)*-L-*proline* (= N-*(2-Nitro-2-propylpentanoyl)*-L-*proline;* **10a**). From **7a**. Yield 95%. M.p. 135–140°. $[\alpha]_D = -60.66$ (*c* = 1, EtOH). IR (nujol): 3100*m*, 1760*m*, 1745*m*, 1610*s*, 1550*s*, 1460*s*, 1380*w*, 1350*w*, 1220*m*, 1195*m*. ^{1}H-NMR ($CDCl_3$): 0.8–1.0 (*q*, 2 CH_3); 1.1–1.5 (*m*, 2 CH_2); 1.9–2.5 (*m*, CH_2(3), CH_2(4), 2 CH_2); 3.2–3.5 (*m*, 1 H, CH_2(5)); 3.4–3.5 (*m*, 1 H, CH_2(5)); 4.6–4.7 (*m*, H–C(2)); 7.9 (br. *s*, COOH). ^{13}C-NMR ($CDCl_3$): 13.62, 13.96, 16.35, 16.44; 25.29 (C(4)); 27.64 (C(3)); 34.60, 36.99, 46.67 (C(5)); 60.67 (C(2)); 96.18 (CNO_2); 165.11 (CO); 176.44 (CO). Anal. calc. for $C_{13}H_{22}N_2O_5$ (286.32): C 54.33, H 7.74, N 9.78; found: C 54.10, H 7.74, N 9.65.

N-*[2-Nitro-2,2-bis(3-phenylpropyl)acetyl]*-L-*proline* (= N-*[2-Nitro-5-phenyl-2-(3-phenylpropyl)pentanoyl]*-L-*proline;* **10b**). From **7b**. Yield 95%. M.p. 156–160°. $[\alpha]_D = -13.83$ (*c* = 1, EtOH). IR (nujol): 3160*m*, 1760*s*, 1620*s*, 1550*s*, 1460*s*, 1390*m*, 1180*s*. ^{1}H-NMR ($CDCl_3$): 1.3–3.3 (*m*, 18 H); 4.45–4.55 (*m*, CHN); 7.1–7.4 (*m*, 2 Ph). Anal. calc. for $C_{25}H_{30}N_2O_5$ (438.52): C 68.47, H 6.89, N 6.39; found: C 68.73, H 7.26, N 6.4.

5. *Reductive Acylation of* **7–9** *to* **11–13** *by Zn/AcOH/*Ac_2O*: General Procedure.* The *N*-[2-nitro-2,2-bis(substituted allyl)acetyl]amino-ester **7**, **8**, or **9** (250 mg) was stirred with Zn dust (400 mg) in AcOH (4 ml) and Ac_2O (5 ml) at 40–60° for 6–12 h. The inorg. solid was filtered off and the filtrate poured on ice. An oil separated out which was then extracted with benzene. The org. extract was washed well with H_2O, dried (Na_2SO_4), and evaporated to give a gum which was further purified by column chromatography (silica gel, 60–120 mesh; $CHCl_3$): pure **11–13**.

Benzyl N-*[*N-*Acetyl-2,2-bis(prop-2-en-1-yl)glycyl]*-L-*prolinate* (= *Benzyl* N-*[2-(Acetylamino)-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*prolinate;* **11a**). From **7a**. Yield 75%. $[\alpha]_D = -49.7$ (*c* = 1, EtOH). IR (neat): 3220*w*, 1750*s*, 1640*s*, 1400*m*, 1250*s*, 1180*s*, 1020*m*, 940*m*. ^{1}H-NMR ($CDCl_3$): 1.7–2.1 (*m*, CH_2(3), CH_2(4), Ac); 2.25–2.6 (*m*, 2 CH_2=CHCH_2); 3.8–4.1 (*m*, CH_2(5)); 4.45–4.55 (*m*, H–C(2)); 4.9–5.2 (*m*, PhCH_2, 2 CH_2=$CH$$CH_2$); 5.55–5.8 (*m*, 2 CH_2=$CH$$CH_2$); 7.2–7.4 (*m*, Ph, NH). ^{13}C-NMR ($CDCl_3$): 18.81 (CH_3CO); 25.70 (C(4)); 25.72 (C(3)); 36.38, 36.52 (CH_2=CHCH_2); 48.15 (C(5)); 60.96 (C(2)); 66.39 (PhCH_2); 67.63 (CNH); 119.53, 119.67 (CH_2=$CH$$CH_2$); 127.87, 127.93 ($CH_2$=$CH$$CH_2$); 128.28, 131.63, 135.70; 169.34 (CO); 169.75 (CO); 171.99 (CO). Anal. calc. for $C_{22}H_{28}N_2O_4 \cdot H_2O$ (384.57): C 65.64, H 7.01, N 6.96; found: C 65.85, H 7.36, N 6.82.

Benzyl N-*[*N-*Acetyl-2,2-bis(3-phenylprop-2-en-1-yl)glycyl]*-L-*prolinate* (= *Benzyl* N-*[2-(Acetylamino)-5-phenyl-2-(3-phenylprop-2-en-1-yl)pent-4-enoyl]*-L-*prolinate;* **11b**). From **7b**. Yield 70%. $[\alpha]_D = -4.0$ (*c* = 1, EtOH). IR ($CHCl_3$): 3220*w*, 1755*s*, 1645*s*, 1410*m*, 1230*s*, 1180*m*, 780*s*. ^{1}H-NMR ($CDCl_3$): 1.7–2.15 (*m*, CH_2(3), CH_2(4), Ac); 2.5–2.75 (*m*, 2 PhCH=CHCH_2); 3.85–4.15 (*m*, CH_2(5)); 4.45–4.55 (*m*, H–C(2)); 4.9–5.3 (*m*, PhCH_2); 5.95–6.25 (*m*, 2 PhCH=$CH$$CH_2$); 6.25–6.45 (*m*, 2 Ph$CH$=CH$CH_2$); 6.9–7.3 (*m*, 3 Ph); 7.5 (br. *s*, NH). ^{13}C-NMR ($CDCl_3$): 13.97 (CH_3CO); 25.83 (C(4)); 27.74 (C(3)); 36.77 (PhCH=CHCH_2); 48.40 (C(5)); 61.14 (C(2)); 66.50 (PhCH_2); 66.67 (CNH); 123.39, 123.68 (PhCH=$CH$$CH_2$); 126.11, 126.20, 127.31, 127.92, 128.01, 128.37, 134.38, 134.47, 135.80, 136.94; 169.65 (CO); 169.90 (CO); 172.17 (CO). Anal. calc. for $C_{34}H_{36}N_2O_4 \cdot H_2O$ (536.66): C 73.62, H 6.54, N 5.05; found: C 73.30, H 6.43, N 5.12.

Benzyl N-*[*N-*Acetyl-2,2-bis(2-methylprop-2-en-1-yl)glycyl]*-L-*prolinate* (= *Benzyl* N-*[2-(Acetylamino)-4-methyl-2-(2-methylprop-2-en-1-yl)pent-4-enoyl]*-L-*prolinate;* **11c**). From **7c**. Yield 30%. $[\alpha]_D = -83.8$ (*c* = 1, EtOH). IR (neat): 3220*w*, 1750*s*, 1635*s*, 1450*m*, 1230*s*, 1180*m*, 770*s*. ^{1}H-NMR ($CDCl_3$): 1.7–2.2 (*m*, 2 CH_2=C(CH_3)CH_2, CH_2(3), CH_2(4)); 2.3–2.7 (*m*, 2 CH_2=C(CH_3)CH_2); 3.8–3.95 (*m*, 1 H, CH_2(5)); 4.0–4.15 (*m*, 1 H, CH_2(5)); 4.45–4.55 (*m*, H–C(2)); 4.75 (*s*, 2 H, 2 CH_2=C(CH_3)CH_2); 4.85 (*s*, 2 H, 2 CH_2=C(CH_3)CH_2); 5.05–5.3 (*m*, PhCH_2); 7.2–7.4 (*m*, Ph). ^{13}C-NMR ($CDCl_3$): 18.75 (CH_3); 24.14 (CH_3); 25.67 (C(4)); 27.70 (C(3)); 41.85, 48.15; 61.17 (C(2)); 66.18 (PhCH_2); 68.47 (CNH); 115.15, 128.16, 127.78, 135.65, 140.55, 170.01, 171.82. Anal. calc. for $C_{24}H_{32}N_2O_4$ (412.52): C 69.88, H 7.82, N 6.79; found: C 69.32, H 8.21, N 6.60.

Ethyl N-*[*N-*Acetyl-2,2-bis(prop-2-en-1-yl)glycyl]*-L-*prolinate* (= *Ethyl* N-*[2-(Acetylamino)-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*prolinate;* **11d**). Yield 68%. $[\alpha]_D = -43.41$ (*c* = 1.5, $CHCl_3$). IR (neat): 3300*m*, 1750*s*, 1650*s*, 1540*w*, 1450*s*, 1380*w*, 1250*s*, 1200*m*, 1050*m*. ^{1}H-NMR ($CDCl_3$): 1.22 (*t*, CH_3CH_2O); 1.73–2.26 (*m*, CH_2(3), CH_2(4)); 2.05 (*s*, Ac); 2.42–2.66 (*m*, 2 CH_2=CHCH_2); 3.75–4.2 (*m*, CH_2(5), CH_3CH_2O); 4.22–4.66 (br. *m*, H–C(2)); 5–5.15 (*m*, 2 CH_2=$CH$$CH_2$); 5.42–6 (*m*, 2 CH_2=$CH$$CH_2$); 7.33 (*s*, NH). ^{13}C-NMR ($CDCl_3$): 13.96 (CH_3CH_2O); 18.92 (CH_3CO); 25.73 (C(4)); 27.79 (C(3)); 36.38, 36.52 (CH_2=CHCH_2); 48.16 (C(5)); 60.68 (CH_3CH_2O); 61.0 (C(2)); 67.65 (C); 119.53, 119.75 (CH_2=$CH$$CH_2$); 131.7, 131.98 ($CH_2$=$CH$$CH_2$); 169.38 (CO); 169.67 (CO). MS: 293, 279, 264, 237, 223, 205, 181, 168, 142, 108, 70. Anal. calc. for $C_{17}H_{26}N_2O_4 \cdot H_2O$ (322.4): C 59.98, H 7.69, N 8.22; found: C 60.2, H 7.95, N 8.34.

Ethyl N-*[*N-*Acetyl-2,2-bis(3-phenylprop-2-en-1-yl)glycyl]*-L-*prolinate* (= *Ethyl* N-*[2-(Acetylamino)-5-phenyl-2-(3-phenylprop-3-en-1-yl)pent-4-enoyl]*-L-*prolinate;* **11e**). Yield 60%. $[\alpha]_D = -5.30$ (*c* = 2.5, $CHCl_3$). IR (neat): 3260*w*, 1750*s*, 1650*s*, 1420*m*, 1250*s*, 1200*s*, 780*s*. ^{1}H-NMR ($CDCl_3$): 1.24 (*t*, CH_3CH_2O); 1.78–2.44 (*m*, CH_2(3), CH_2(4)); 2.05 (*s*, Ac); 2.62–2.75 (*m*, 2 PhCH=CHCH_2); 4–4.2 (*m*, CH_2(5), CH_3CH_2O); 6–6.48 (*m*, 2

PhC*H*=C*H*CH$_2$); 7.2–7.4 (*m*, 2 Ph); 7.55 (*s*, NH). ^{13}C-NMR ($CDCl_3$): 14.05 (*C*H$_3$CH$_2$O); 19.06 (*C*H$_3$CO); 25.84 (C(4)); 27.82 (C(3)); 36.79 (PhCH=CH*C*H$_2$); 48.4 (C(5)); 60.8 (CH$_3$*C*H$_2$O); 61.18 (C(2)); 68.67 (C); 123.48, 123.74, 126.17, 127.30, 128.40, 134.34, 134.50, 137.60; 169.80 (CO); 172.40 (CO). MS: 431, 415, 313, 268, 262, 239, 170, 142, 117, 114, 91, 70. Anal. calc. for $C_{29}H_{34}N_2O_4 \cdot H_2O$ (474.59): C 70.71, H 6.95, N 5.68; found: C 70.43, H 6.93, N 5.72.

Methyl N-*[*N*-Acetyl-2,2-bis(prop-2-en-1-yl)glycyl]*-L-*valinate* (= *Methyl* N-*[2-(Acetylamino)-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*valinate;* **12a**). $[\alpha]_D = +11.8$ (*c* = 3.2, EtOH). Yield 64%. IR (neat): 3370*m*, 3250*m*, 2985*m*, 1760*s*, 1680*s*, 1520*s*, 1450*m*, 1215*s*. ^{1}H-NMR ($CDCl_3$): 0.86–1.0 (2*d*, 2 CH$_3$–C(3)); 2.07 (*s*, Ac); 2.0–2.35 (*m*, H–C(3)); 2.42–2.64 (*d*, 2 CH$_2$=CHC*H*$_2$); 3.77 (*s*, MeO); 4.44–4.6 (*m*, H–C(2)); 5.0–5.24 (*m*, 2 *C*H$_2$=CHCH$_2$); 5.6–6.1 (*m*, 2 CH$_2$=C*H*CH$_2$); 7.31, 7.37 (2*s*, 2 NH). ^{13}C-NMR ($CDCl_3$): 17.58, 18.8 (2 *C*H$_3$–C(3)); 18.91 (*C*H$_3$CO); 30.71 (C(3)); 37.48 (CH$_2$=CH*C*H$_2$); 51.80 (C(2)); 56.99 (MeO); 67.05 (C); 119.48, 119.60 (*C*H$_2$=CHCH$_2$); 131.48, 131.60 (CH$_2$=*C*HCH$_2$); 169.55 (CO); 171.57 (CO); 171.85 (CO). MS: 295 ([*M* – 15]$^+$), 285, 267, 252, 168, 130, 108, 98, 81, 68, 55. Anal. calc. for $C_{16}H_{26}N_2O_4 \cdot H_2O$ (310.42): C 58.52, H 7.98, N 8.53; found: C 58.34, H 8.21, N 8.30.

Methyl N-*[*N*-Acetyl-2,2-bis(3-phenylprop-2-en-1-yl)glycyl]*-L-*valinate* (= *Methyl* N-*[2-(Acetylamino)-5-phenyl-2-(3-phenylprop-2-en-1-yl)pent-4-enoyl]*-L-*valinate;* **12b**). $[\alpha]_D = -3.3$ (*c* = 2, EtOH). Yield 55%. IR (neat): 3380*m*, 3240*m*, 1750*s*, 1680*s*, 1525*s*, 1450*m*, 1380*w*, 1240*s*. ^{1}H-NMR ($CDCl_3$): 0.86–0.93 (2*d*, 2 CH$_3$–C(3)); 2.08 (*s*, Ac); 2.0–2.22 (*m*, H–C(3)); 2.66–2.73 (*d*, 2 PhCH=CHC*H*$_2$); 3.64 (*s*, MeO); 4.44–4.64 (*m*, H–C(2)); 6.0–6.68 (*m*, 2 PhC*H*=C*H*CH$_2$); 7.0–7.6 (*m*, 2 Ph, 2 NH). ^{13}C-NMR ($CDCl_3$): 17.58, 18.84 (*C*H$_3$–C(3), *C*H$_3$CO); 30.84 (C(3)); 37.42, 37.60 (PhCH=CH*C*H$_2$); 51.74 (C(2)); 57.11 (MeO); 68.03 (C); 123.13, 126.12, 127.30, 128.34, 134.36, 136.81; 169.74 (CO); 171.76 (CO). MS: 447 ([*M* – 15]$^+$), 419, 403, 361, 215, 158, 130, 117, 91, 55. Anal. calc. for $C_{28}H_{34}N_2O_4 \cdot H_2O$ (462.64): C 69.97, H 7.13, N 5.82; found: C 69.58, H 7.10, N 5.64.

Ethyl N-*[*N*-Acetyl-2,2-bis(prop-2-en-1-yl)glycyl]*-L-*phenylalaninate* (= *Ethyl* N-*[2-(Acetylamino)-2-(prop-2-en-1-yl)pent-4-enoyl]*-L-*phenylalaninate;* **13a**). Yield 62%. $[\alpha]_D = +29.37$ (*c* = 1.5, $CHCl_3$). IR ($CHCl_3$): 3400*m*, 3250*w*, 1750*s*, 1680*s*, 1525*s*, 1230*s*, 1040*w*. ^{1}H-NMR ($CDCl_3$): 1.26 (*t*, *C*H$_3$CH$_2$O); 2.0 (*s*, Ac); 2.31–2.53 (*t*, 2 CH$_2$=CHC*H*$_2$); 3.06–3.22 (*m*, PhC*H*$_2$(2)); 4.1–4.35 (*q*, CH$_3$*C*H$_2$O); 4.75–6.1 (*m*, H–C(2), 2 *C*H$_2$=C*H*CH$_2$); 7.06–7.5 (*m*, Ph, NH). ^{13}C-NMR ($CDCl_3$): 13.92 (*C*H$_3$CH$_2$O); 18.76 (*C*H$_3$CO); 37.39, 37.48 (CH$_2$=CH*C*H$_2$); 37.77 (C(3)); 52.98 (C(2)); 61.16 (CH$_3$*C*H$_2$O); 66.81 (C); 119.25, 119.50 (*C*H$_2$=CHCH$_2$); 126.79, 128.32, 129.02, 130.08 (arom. C); 129.02 (CH$_2$=*C*HCH$_2$); 169.55 (CO); 171.13 (CO); 171.35 (CO). MS: 329 ([*M* – Ac]$^+$), 288, 273, 220, 168, 120, 108, 91, 81, 77, 68. Anal. calc. for $C_{21}H_{28}N_2O_4 \cdot H_2O$ (372.46): C 64.59, H 7.22, N 7.17; found: C 64.63, H 7.29, N 7.03.

Ethyl N-*[*N*-Acetyl-2,2-bis(3-phenylprop-2-en-1-yl)glycyl]*-L-*phenylalaninate* (= *Ethyl* N-*[2-(Acetylamino)-5-phenyl-2-(3-phenylprop-2-en-1-yl)pent-4-enoyl]*-L-*phenylalaninate;* **13b**). Yield 51%. $[\alpha]_D = +21.67$ (*c* = 1.85, $CHCl_3$). IR ($CHCl_3$): 3450*m*, 3250*w*, 1750*s*, 1685*s*, 1530*m*, 1460*w*, 1380*w*, 1240*s*. ^{1}H-NMR ($CDCl_3$): 1.2 (*t*, *C*H$_3$CH$_2$O); 2.0 (*s*, Ac); 2.62 (*t*, 2 PhCH=CHC*H*$_2$); 3.08–3.2 (*m*, PhC*H*$_2$(3)); 4.0–4.26 (*q*, CH$_3$*C*H$_2$O); 4.77–5.04 (*m*, H–C(2)); 5.99–6.68 (*m*, 2 PhC*H*=C*H*CH$_2$); 7.24–7.55 (*m*, 3 Ph, 2 NH). ^{13}C-NMR ($CDCl_3$): 13.85 (*C*H$_3$CH$_2$); 18.80 (*C*H$_3$CO); 37.12, 37.40 (PhCH=CH*C*H$_2$); 37.79 (PhC*H*$_2$(3)); 53.01 (C(2)); 61.13 (CH$_3$*C*H$_2$O); 67.66 (C); 123.06, 126.08, 126.75, 127.22, 127.28, 128.29, 128.94, 134.16, 134.25, 135.96, 136.74, 136.80; 169.68 (CO); 171.02 (CO); 171.39 (CO). MS: 481 ([*M* – Ac]$^+$), 364, 220, 192, 117, 91, 77. Anal. calc. for $C_{33}H_{36}N_2O_4 \cdot H_2O$ (524.65): C 73.04, H 6.68, N 5.16; found: C 73.27, H 6.93, N 5.4.

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