2-Benzoyl-2-ethoxycarbonylvinyl-1 and 2-Benzoylamino-2-methoxycarbonylvinyl-1 as *N*-Protecting Groups in Peptide Synthesis. Their Application in the Synthesis of Dehydropeptide Derivatives Containing *N*-Terminal 3-Heteroarylamino-2,3-dehydroalanine

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Dedicated to Emeritus Professor Hans Suschitzky, University of Salford, on the occasion of his 80th birthday

Ethyl 2-benzoyl-3-dimethylaminopropenoate (**6**) and methyl 2-benzoylamino-3-dimethylaminopropenoate (**46**) were used as reagents for the protection of the amino group with 2-benzoyl-2-ethoxycarbonylvinyl-1 and 2-benzoylamino-2-methoxycarbonylvinyl groups in the peptide synthesis. Reactions of ethyl 2-benzoyl-3-dimethylaminopropenoate (**6**) with α-amino acids gave *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-α-amino acids **13-19**. These were coupled with various amino acid esters to form *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-protected dipeptide esters **20-31**. The removal of 2-benzoyl-2-ethoxycarbonylvinyl-1 group, which was achieved by hydrazine monohydrochloride or hydroxylamine hydrochloride, afforded hydrochlorides of dipeptide esters **32-41** in high yields. Similarly, the substitution of the dimethylamino group in methyl 2-benzoylamino-3-dimethylaminopropenoate (**46**) by glycine gave *N*-(2-benzoylamino-2-methoxycarbonylvinyl-1)glycine (**47**), which was coupled with glycine ethyl ester to give *N*-[*N*-(2-benzoylamino-2-methoxycarbonylvinyl-1)glycyl]glycine ethyl ester (**48**). Treatment of **48** with 2-amino-4,6-dimethylpyrimidine afforded *N*-[glycyl]glycine ethyl ester hydrochloride (**34**) in high yield. Amino acid esters and dipeptide esters were employed in the preparation of tri- **58-70**, tetra- **71-82**, and pentapeptide esters **83-85** containing *N*-terminal 3-heteroarylamino-2,3-dehydroalanine. 2-Chloro-4,6-dimethoxy-1,3,5-triazine was employed as a coupling reagent for the preparation of peptides **58-85**.

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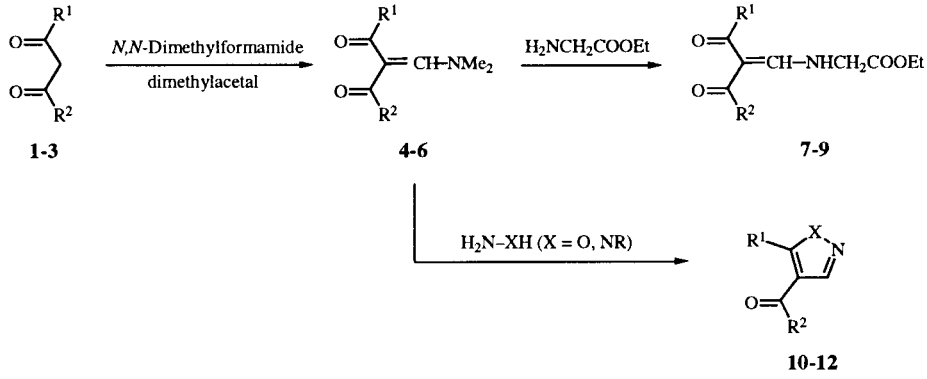
In this paper we describe the application of substituted 3-dimethylaminopropenoates as reagents for the protection of the amino group in the peptide synthesis. 3-Dimethylaminopropenoates, generally synthesised from the corresponding 2-substituted acetates and *N,N*-dimethylformamide dimethylacetal, are versatile reagents for the synthesis of various heterocyclic systems and β-heteroaryl- and β-heteroarylamino-α-amino acid derivatives. Reactions with nucleophiles always proceed by substitution of dimethylamino group as the first step and then, when possible, further cyclisation takes place [1-4]. In this manner enamines, such as 3-dimethylaminomethylenepentane-2,4-dione **4**, ethyl 2-acetyl-3-dimethylaminopropenoate **5**, and ethyl 2-benzoyl-3-dimethylaminopropenoate **6** (prepared from *N,N*-dimethylformamide dimethylacetal and 1,3-dicarbonyl

Scheme 1



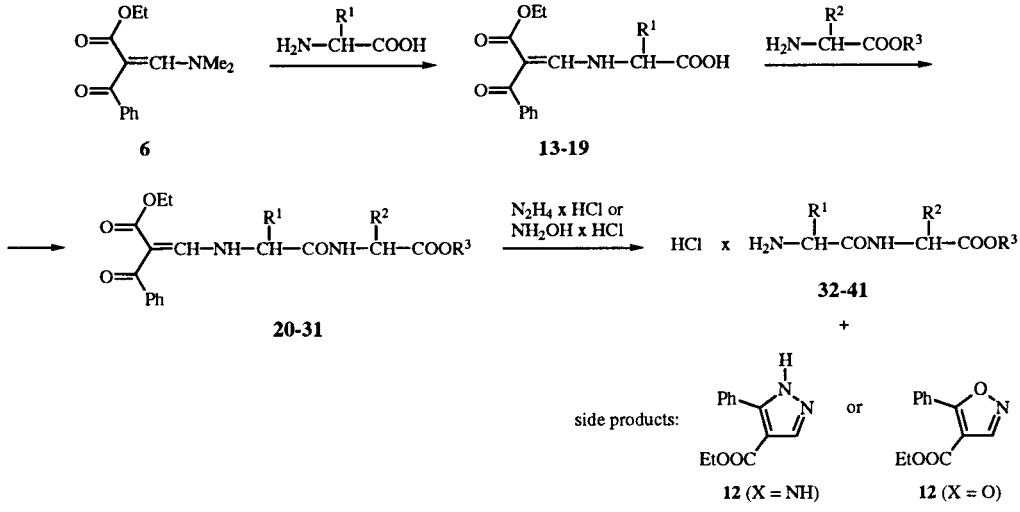
1-3 **4-6** **7-9** **10-12**

Compound	R^1	R^2	X
1, **4**, **7** and **10**	Me	Me	O, NR
2, **5**, **8**, and **11**	Me	OEt	O, NR
3, **6**, **9**, and **12**	Ph	OEt	O, NR

compounds pentane-2,4-dione **1**, ethyl acetoacetate **2**, and ethyl benzoylacetate **3**) [3-7], react with hydrazines or hydroxylamine giving azoles **10, 11,** and **12** [6,7], while with glycine ethyl ester only the formation of substitution products **7, 8,** and **9** has been observed (Scheme 1).

On the basis of this information, we decided to use these types of compounds as *N*-protective reagents in the peptide synthesis. For these studies, we selected ethyl 2-benzoyl-3-dimethylaminopropenoate **6**, since it can be easily prepared in pure form [3-5]. Substitution of dimethylamino group with various amino acids proceeded smoothly in glacial acetic acid at 80° giving *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)amino acids **13-19** as products. In this manner the following *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)amino acids **13-19**, *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)alanine (**13**), *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycine (**14**), L-*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)leucine (**15**), *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)methionine (**16**), *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)norleucine (**17**), L-*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-3-phenylalanine (**18**), and *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)valine (**19**), were prepared. Coupling of these *N*-protected amino acids with an amino acid esters into a *N*-protected dipeptide esters proceeded by using *N*,*N*-dicyclohexylcarbodiimide in dichloromethane. The following *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-protected peptide esters were prepared: *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)alanyl]glycine ethyl ester (**20**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-alanine ethyl ester (**21**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-glutamic acid diethyl ester (**22**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycine ethyl ester (**23**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-leucine methyl ester (**24**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-3-phenylalanine methyl ester (**25**), *N*-[*N*-(2-ben-

Scheme 2



Compounds **13-41**	-NHCH(R¹)CO-	-NHCH(R²)CO-	R³
13	alanyl		
14	glycyl		
15	L-leucyl		
16	methionyl		
17	norleucyl		
18	L-3-phenylalanyl		
19	valyl		
20	alanyl	glycyl	Et
21, 32	glycyl	L-alanyl	Et
22, 33	glycyl	L-glutamyl	Et
23, 34	glycyl	glycyl	Et
24, 35	glycyl	L-leucyl	Me
25, 36	glycyl	L-3-phenylalanyl	Me
26, 37	glycyl	L-tyrosyl	Me
27, 38	L-leucyl	L-3-phenylalanyl	Me
28, 39	methionyl	glycyl	Et
29	norleucyl	glycyl	Et
30, 40	L-3-phenylalanyl	L-leucyl	Me
31, 41	valyl	glycyl	Et

zoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-tyrosine methyl ester (**26**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-L-leucyl]-L-3-phenylalanine methyl ester (**27**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)methionyl]glycine ethyl ester (**28**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)norleucyl]glycine ethyl ester (**29**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-L-3-phenylalanyl]-L-leucine methyl ester (**30**), and *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)valyl]glycine ethyl ester (**31**). The removal of 2-benzoyl-2-ethoxycarbonylvinyl-1 group was achieved by hydrazine monohydrochloride or hydroxylamine hydrochloride in boiling methanol or ethanol. The products were hydrochlorides of dipeptide esters **32-41** and the corresponding azoles **12** (X = O, NH; not isolated). *N*-[Glycyl]glycine ethyl ester hydrochloride (**34**) and *N*-[L-leucyl]-L-3-phenylalanine methyl ester hydrochloride (**38**) were isolated in crystalline form (Scheme 2).

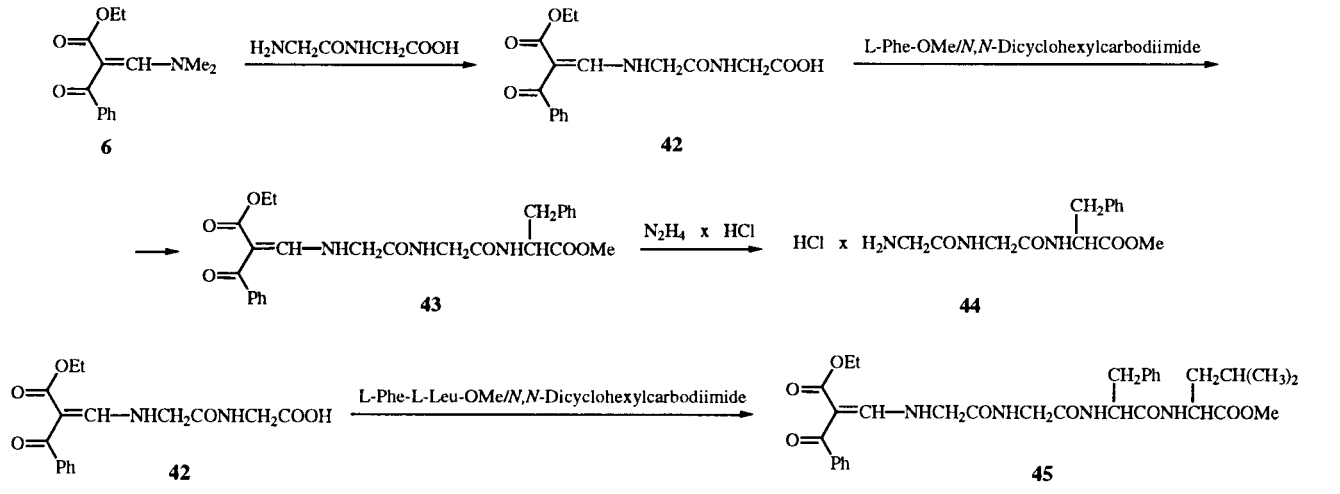
Similarly *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-glycyl]glycine (**42**) was prepared from **6** and *N*-[glycyl]-glycine in glacial acetic acid [8]. Coupling of *N*-protected dipeptide **42** with L-3-phenylalanine methyl ester gave *N*-[*N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-glycyl]-L-3-phenylalanine methyl ester (**43**), which gave, upon treatment with hydrazine monohydrochloride in methanol, *N*-[*N*-[glycyl]glycyl]-L-3-phenylalanine methyl ester hydrochloride (**44**). When *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycine (**42**) was coupled with *N*-[L-3-phenylalanyl]-L-leucine methyl ester, a *N*-protected tetrapeptide ester **45** was formed (Scheme 3).

We also tried to use methyl 2-benzoylamino-3-dimethylaminopropenoate (**46**) [1] as the *N*-protective reagent, however, the substitution of dimethylamino group took place only with glycine to give *N*-(2-benzoylamino-2-methoxycarbonylvinyl-1)glycine (**47**). Coupling of **47** with glycine ethyl ester by *N*,*N*-dicyclohexylcarbodiimide in *N*,*N*-dimethylformamide gave *N*-[*N*-(2-benzoylamino-2-methoxycarbonylvinyl-1)glycyl]glycine ethyl ester (**48**). The removal of 2-benzoylamino-2-methoxycarbonylvinyl-1 group was achieved by substitution of *N*-[glycyl]-glycine ethyl ester substituent by 2-amino-4,6-dimethylpyrimidine hydrochloride in boiling ethanol. The products were *N*-[glycyl]glycine ethyl ester hydrochloride (**34**) and methyl 2-benzoylamino-3-(4,6-dimethyl-2-pyrimidinyl)propenoate (**49**) [9] (Scheme 4).

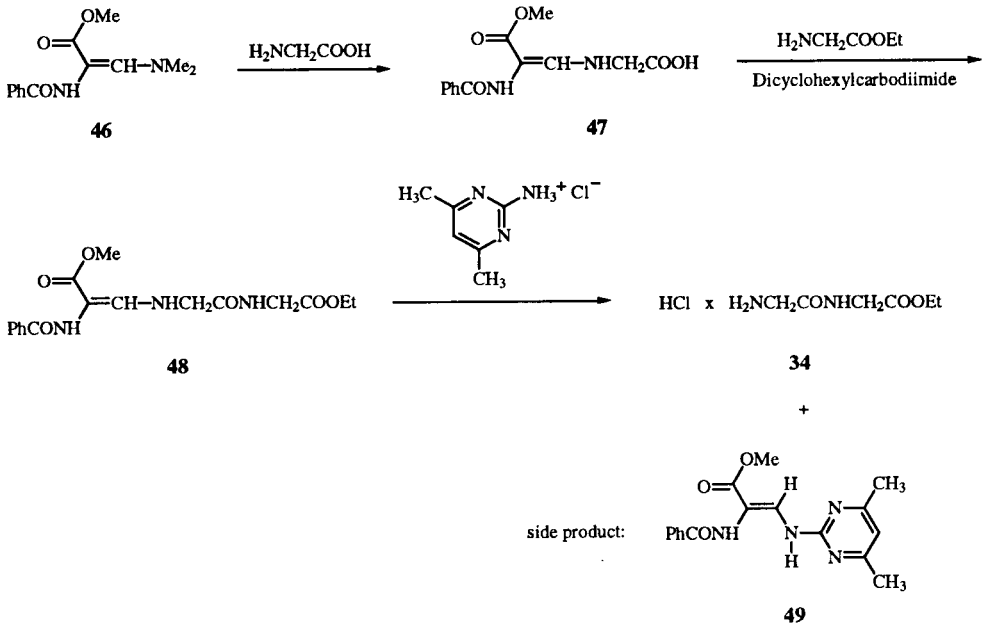
Amino acid esters and peptide esters were also employed in the preparation of peptides containing the *N*-terminal 3-heteroarylamino-2,3-dehydroalanine moiety. Dehydropeptides **51-56** and dehydrotripeptides **57** with a free carboxy group, prepared from 4-heteroarylaminomethylen-5(4*H*)-oxazolones **50** and amino acids as described previously [8], were used for the preparation of the dehydropeptide chain with various amino acid esters and peptide esters. The following 4-heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolones: 3-nitropyridinyl-2- **50a**, 3,5-dibromopyridinyl-2- **50b**, 5-methylisoxazolyl-3- **50c**, 6-chloropyridazinyl-3- **50d**, 4,6-dimethylpyrimidinyl-2- **50e**, 4-chloro-6-methylpyrimidinyl-2- **50f**, 5-ethoxycarbonyl-2-methylthiopyrimidinyl-4- **50g**, and 3-methoxycarbonylpyrazinyl-2- **50h**, were employed for the preparation of *N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-β-alanine **51**, *N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycine **52**, *N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]methionine **53**, *N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]norleucine **54**, *N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-3-phenylalanine **55**, and *N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]proline **56** (Scheme 5).

2-Chloro-4,6-dimethoxy-1,3,5-triazine, readily available from cianuric chloride [10], has been reported as the coupling reagent in the chemistry of peptides [11,12]. The coupling proceeds by formation of a 2-acyloxy-4,6-

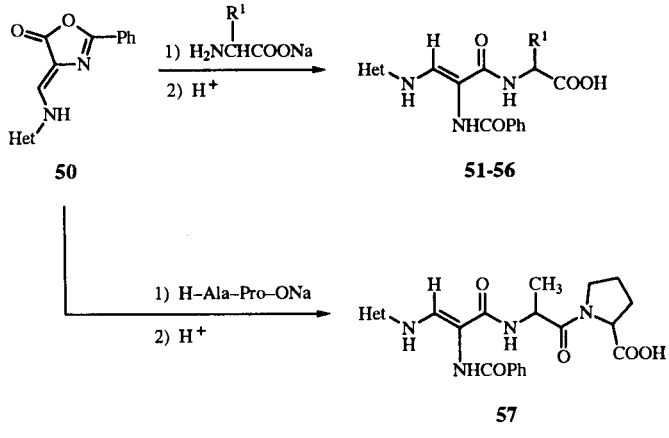
Scheme 3



Scheme 4



Scheme 5



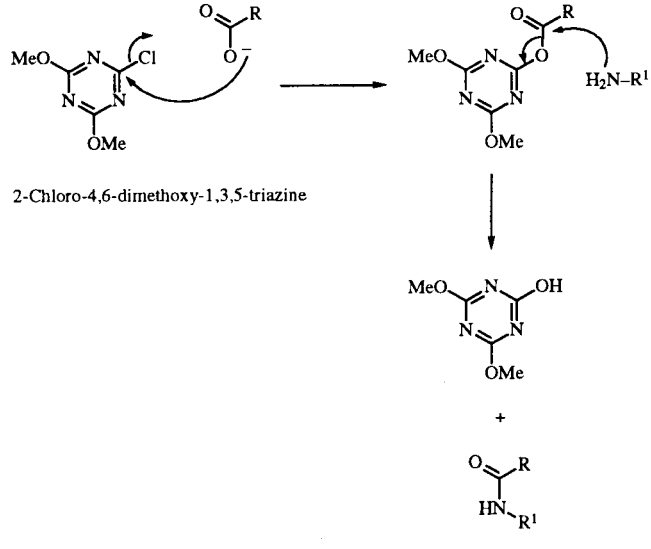
Compounds **50-57**	Heterocyclic moiety
a	3-nitropyridinyl-2
b	3,5-dibromopyridinyl-2
c	5-methylisoxazolyl-3
d	6-chloropyridazinyl-3
e	4,6-dimethylpyrimidinyl-2
f	4-chloro-6-methylpyrimidinyl-2
g	5-ethoxycarbonyl-2-methylthiopyrimidinyl-4
h	3-methoxycarbonylpyrazinyl-2

Compounds **51-56**	-NH-CH(R^1)COOH
51	β-alanine
52	glycine
53	methionine
54	norleucine
55	3-phenylalanine
56	proline

dimethoxy-1,3,5-triazine [13] in the first step followed by the nucleophilic attack of the amino component when an amide bond is formed (Scheme 6).

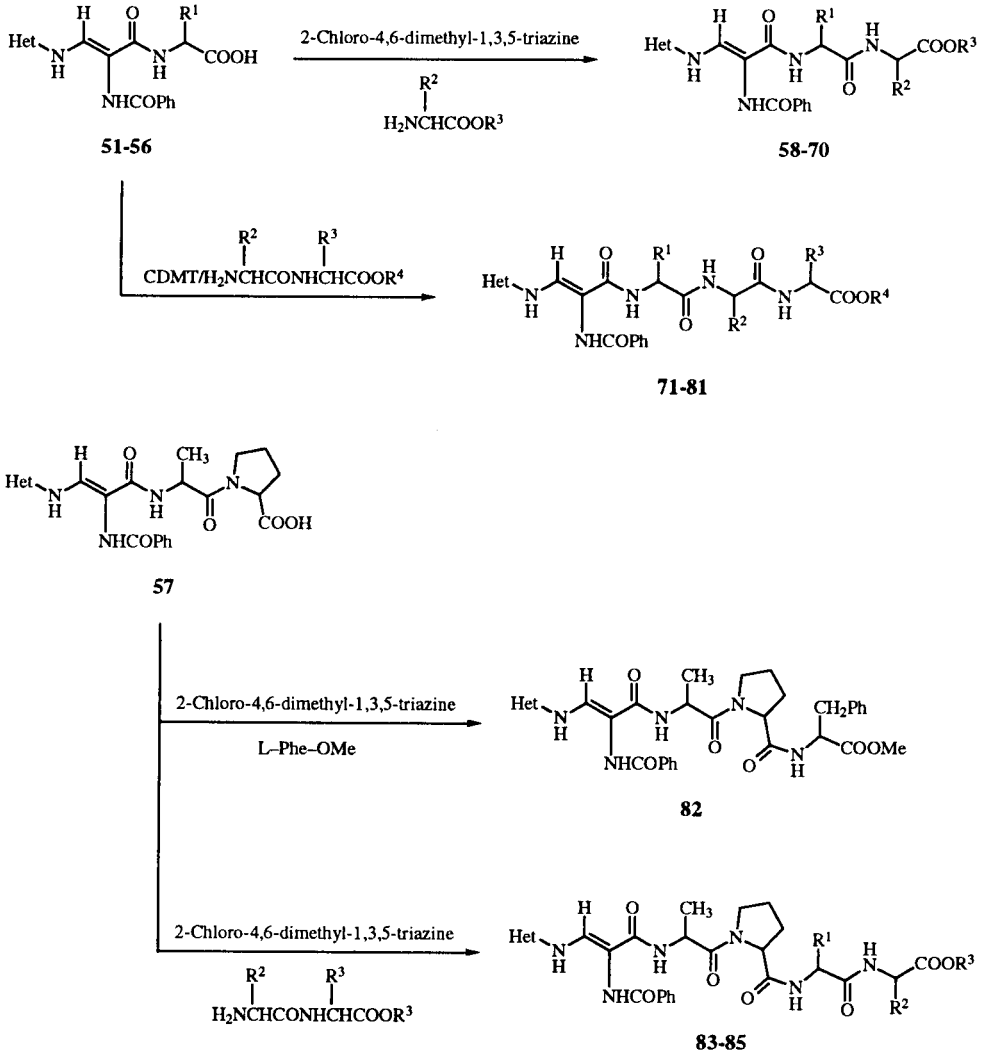
Various α-amino acid esters, piperidine-3-carboxylic acid ethyl ester, piperidine-4-carboxylic acid ethyl ester and dipeptide esters **32-41** were employed as amino-components. In this manner the following *N*-protected tripeptide esters **58-70**, tetrapeptide esters **71-82** and pentapeptide esters **83-85** were prepared using 2-chloro-4,6-dimethoxy-1,3,5-triazine as the coupling reagent: *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-β-alanyl]glycine ethyl ester (**58**), *N*-[*N*-[*N*-

Scheme 6



benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-β-alanyl]-L-3-phenylalanine methyl ester (**59**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]-3-piperidinecarboxylic acid ethyl ester (**60**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]-4-piperidinecarboxylic acid ethyl ester (**61**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]-L-glutamic acid diethyl ester (**62**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]glycine ethyl ester (**63**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]-L-3-phenylalanine methyl ester (**64**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]-L-tyrosine methyl ester (**65**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-norleucyl]-L-3-phenylalanine methyl ester (**66**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-3-phenylalanyl]-glycine ethyl ester (**67**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-3-phenylalanyl]-L-3-phenylalanine methyl ester (**68**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]prolyl]-glycine ethyl ester (**69**), *N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]prolyl]-L-3-phenylalanine methyl ester (**70**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]glycyl]-L-alanine ethyl ester (**71**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]glycyl]-L-glutamic acid diethyl ester (**72**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]glycyl]glycine ethyl ester (**73**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]glycyl]-L-3-phenylalanine methyl ester (**74**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]glycyl]-L-tyrosine methyl ester (**75**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]glycyl]methionyl]glycine ethyl ester (**76**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]methionyl]valyl]glycine ethyl ester (**77**),

Scheme 7



Scheme 7 (Continued)

Compounds **49-84**	Heterocyclic moiety
a	3-nitropyridinyl-2
b	3,5-dibromopyridinyl-2
c	5-methylisoxazolyl-3
d	6-chloropyridazinyl-3
e	4,6-dimethylpyrimidinyl-2
f	4-chloro-6-methylpyrimidinyl-2
g	5-ethoxycarbonyl-2-methylthiopyrimidinyl-4
h	3-methoxycarbonylpyrazinyl-2

Compounds **58-70**	-HNCH(R^1)CO-	-HNCH(R^2)CO-	R^3
58	β-alanyl	glycyl	Et
59	β-alanyl	L-3-phenylalanyl	Et
60	glycyl	3-carbonylpiperidinyl-1	Et
61	glycyl	4-carbonylpiperidinyl-1	Et
62	glycyl	L-glutamyl	Et
63	glycyl	glycyl	Et
64	glycyl	L-3-phenylalanyl	Me
65	glycyl	L-tyrosyl	Me
66	norleucyl	L-3-phenylalanyl	Me
67	L-3-phenylalanyl	glycyl	Et
68	L-3-phenylalanyl	L-3-phenylalanyl	Me
69	prolyl	glycyl	Et
70	prolyl	L-3-phenylalanyl	Me

Compounds **71-81**	-HNCH(R^1)CO-	-HNCH(R^2)CO-	-HNCH(R^3)CO-	R^4
71	glycyl	glycyl	L-alanyl	Et
72	glycyl	glycyl	L-glutamyl	Et
73	glycyl	glycyl	glycyl	Et
74	glycyl	glycyl	L-3-phenylalanyl	Me
75	glycyl	glycyl	L-tyrosyl	Me
76	glycyl	methionyl	glycyl	Et
77	methionyl	valyl	glycyl	Et
78	L-3-phenylalanyl	glycyl	glycyl	Et
79	L-3-phenylalanyl	glycyl	L-leucyl	Me
80	L-3-phenylalanyl	glycyl	L-3-phenylalanyl	Me
81	L-3-phenylalanyl	glycyl	L-tyrosyl	Me

Compounds **83-85**	-HNCH(R^1)CO-	-HNCH(R^2)CO-	R^3
83	glycyl	glycyl	Et
84	glycyl	L-3-phenylalanyl	Me
85	valyl	glycyl	Et

N-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]glycine ethyl ester (**78**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-leucine methyl ester (**79**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-3-phenylalanine methyl ester (**80**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-tyrosine methyl ester (**81**), *N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]alanyl]prolyl]-L-3-phenylalanine methyl ester (**82**), *N*-[*N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]alanyl]prolyl]glycyl]glycine ethyl ester (**83**), *N*-[*N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]alanyl]prolyl]glycyl]-L-3-phenylalanine methyl ester (**84**), and *N*-[*N*-[*N*-[*N*-[*N*-benzoyl-3-heteroarylamino-2,3-dehydroalanyl]alanyl]prolyl]valyl]glycine ethyl ester **85** (Scheme 7).

Since in most cases the racemic mixtures of amino acids were used in these experiments (unless otherwise stated), no further attempts were undertaken in order to determine the configurations at chiral centres of peptides. Nevertheless, 2-benzoyl-2-ethoxycarbonylvinyl-1 group and 2-benzoylamino-2-methoxycarbonylvinyl-1 group were introduced and removed under relatively mild conditions.

Table 1

Experimental Data

Compound	Yield %	mp °C	Molecular Formula Analyses
N-(2,2-Diacetylvinyl-1)glycine ethyl ester (**7**)	57	120-121 (from ethanol/water)	$C_{10}H_{15}NO_4$ Calcd. C, 56.31; H, 7.09; N, 6.57 Found C, 56.04; H, 7.23; N, 6.79
N-(2-Acetyl-2-ethoxycarbonylvinyl-1)glycine ethyl ester (**8**)	49	60-70 (from ethanol/water)	$C_{11}H_{17}NO_5$ Calcd. C, 54.30; H, 7.05; N, 5.76 Found C, 54.47; H, 7.18; N, 5.70
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycine ethyl ester (**9**)	81	115-117 (from ethanol/water)	$C_{16}H_{19}NO_5$ Calcd. C, 62.92; H, 6.28; N, 4.59 Found C, 62.98; H, 6.35; N, 4.44
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)alanine (**13**)	50	119-121 (from ethanol/water)	$C_{15}H_{17}NO_5$ Calcd. C, 61.83; H, 5.89; N, 4.81 Found C, 61.69; H, 6.01; N, 4.98
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycine (**14**)	79	178-179 (from ethanol/water)	$C_{14}H_{15}NO_5$ Calcd. C, 60.63; H, 5.46; N, 5.05 Found C, 60.35; H, 5.78; N, 4.96
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)methionine (**16**)	61	116-117 (washed with diethyl ether)	$C_{17}H_{21}NO_5S$ Calcd. C, 58.10; H, 6.03; N, 3.99 Found C, 58.18; H, 6.38; N, 4.12
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)valine (**19**)	85	116-120 (washed with diethyl ether)	$C_{17}H_{21}NO_5$ Calcd. C, 63.92; H, 6.63; N, 4.39 Found C, 63.71; H, 6.98; N, 4.34
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)alanyl]glycine ethyl ester (**20**)	39	119-121 (from ethyl acetate/ diisopropyl ether)	$C_{19}H_{24}N_2O_6$ Calcd. C, 60.61; H, 6.43; N, 7.45 Found C, 60.52; H, 6.79; N, 7.70
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-alanine ethyl ester (**21**)	77	129-131 (from methanol/water)	$C_{19}H_{24}N_2O_6$ Calcd. C, 60.61; H, 6.43; N, 7.45 Found C, 60.65; H, 6.67; N, 7.65
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycine ethyl ester (**23**)	89	111-112 (from ethanol/water)	$C_{18}H_{22}N_2O_6$ Calcd. C, 59.64; H, 6.12; N, 7.73 Found C, 59.73; H, 6.39; N, 7.78
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-3-phenylalanine methyl ester (**25**)	85	103-105 (from methanol/water)	$C_{24}H_{26}N_2O_6$ Calcd. C, 65.73; H, 5.98; N, 6.39 Found C, 65.99; H, 6.28; N, 6.69
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)-L-leucyl]-L-3-phenylalanine methyl ester (**27**)	80	100- 102 (from ethyl acetate/ *n*-heptane/diisopropyl ether)	$C_{28}H_{34}N_2O_6$ Calcd. C, 67.98; H, 6.93; N, 5.67 Found C, 68.36; H, 7.08; N, 5.66
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)methionyl]glycine ethyl ester (**28**)	73	81-83 (from ethyl acetate/ diisopropyl ether)	$C_{21}H_{28}N_2O_6S$ Calcd. C, 57.78; H, 6.47; N, 6.42 Found C, 57.77; H, 6.80; N, 6.79
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)norleucyl]glycine ethyl ester (**29**)	56	84-86 (from methanol/water)	$C_{22}H_{30}N_2O_6$ Calcd. C, 63.13; H, 7.23; N, 6.70 Found C, 63.35; H, 7.47; N, 7.04
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)valyl]glycine ethyl ester (**31**)	35	105-108 (from ethyl acetate/ diisopropyl ether)	$C_{21}H_{28}N_2O_6$ Calcd. C, 62.35; H, 6.98; N, 6.93 Found C, 62.08; H, 7.30; N, 7.06
N-[*N*-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycyl]-L-3-phenylalanine methyl ester (**43**)	97	130-134 (from methanol/water)	$C_{26}H_{29}N_3O_7$ Calcd. C, 63.00; H, 5.90; N, 8.48 Found C, 62.98; H, 6.28; N, 8.43
N-[*N*-[*N*-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl] glycyl]-L-3-phenylalanyl]-L-leucine methyl ester (**45**)	52	158-162 (from *n*-butyl acetate)	$C_{32}H_{40}N_4O_8$ Calcd. C, 63.13; H, 6.63; N, 9.21 Found C, 63.48; H, 6.85; N, 9.47
N-(2-Benzoylamino-2-methoxycarbonylvinyl-1)glycine (**47**)	65	205-208 (from ethanol/DMF)	$C_{13}H_{14}N_2O_5$ Calcd. C, 56.10; H, 5.07; N, 10.07 Found C, 56.03; H, 5.17; N, 10.16
N-[*N*-(2-Benzoylamino-2-methoxycarbonylvinyl-1)glycyl]-glycine ethyl ester (**48**)	64	215-218 (from methanol)	$C_{17}H_{21}N_3O_6$ Calcd. C, 56.18; H, 5.83; N, 11.57 Found C, 56.46; H, 5.96; N, 11.54
N-[*N*-[*N*-Benzoyl-3-(3-nitropyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]glycine ethyl ester (**58a**)	20	86-92 (washed with petroleum ether)	$C_{22}H_{24}N_6O_7$ Calcd. C, 54.53; H, 5.00; N, 17.35 Found C, 54.22; H, 5.19; N, 17.19
N-[*N*-[*N*-Benzoyl-3-(3,5-dibromopyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]glycine ethyl ester (**58b**)	18	216-218 (washed with petroleum ether)	$C_{22}H_{23}Br_2N_5O_5$ Calcd. C, 44.37; H, 3.90; N, 11.77 Found C, 44.49; H, 3.81; N, 11.36

Table 1 (Continued)

Compound	Yield %	mp °C	Molecular Formula Analyses
N-[*N*-[*N*-Benzoyl-3-(3-nitropyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]-L-3-phenylalanine methyl ester (**59a**)	21	94-96 (washed with petroleum ether)	$C_{28}H_{28}N_6O_7$ Calcd. C, 59.98; H, 5.04; N, 15.00 Found C, 60.18; H, 4.91; N, 14.66
N-[*N*-[*N*-Benzoyl-3-(3,5-dibromopyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]-L-3-phenylalanine methyl ester (**59b**)	13	95-97 (washed with petroleum ether)	$C_{28}H_{27}Br_2N_5O_5$ Calcd. C, 49.94; H, 4.04; N, 10.40 Found C, 49.81; H, 3.99; N, 10.20
N-[*N*-[*N*-Benzoyl-3-(6-chloropyridazinyl-3)amino-2,3-dehydroalanyl]-β-alanyl]-L-3-phenylalanine methyl ester (**59d**)	14	105-109 (washed with petroleum ether)	$C_{27}H_{27}ClN_6O_5$ Calcd. C, 58.89; H, 4.95; N, 15.27 Found C, 58.70; H, 4.98; N, 14.96
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-3-piperidinecarboxylic acid ethyl ester (**60f**)	27	108-111 (from ethyl acetate/petroleum ether)	$C_{25}H_{29}ClN_6O_5$ Calcd. C, 56.80; H, 5.53; N, 15.91 Found C, 56.65; H, 5.61; N, 15.79
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-4-piperidinecarboxylic acid ethyl ester (**61f**)	51	108-110 (washed with petroleum ether)	$C_{25}H_{29}ClN_6O_5$ Calcd. C, 56.80; H, 5.53; N, 15.91 Found C, 56.49; H, 5.48; N, 15.50
N-[*N*-[*N*-benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-L-glutamic acid diethyl ester (**62f**)	32	92-94 (washed with petroleum ether)	$C_{26}H_{31}ClN_6O_7$ Calcd. C, 54.34; H, 5.44; N, 14.63 Found C, 54.02; H, 5.47; N, 14.82
N-[*N*-[*N*-Benzoyl-3-(3-nitropyridinyl-2)amino-2,3-dehydroalanyl]glycyl]glycine ethyl ester (**63a**)	38	113-117 (from ethyl acetate/petroleum ether)	$C_{21}H_{22}N_6O_7$ Calcd. C, 53.60; H, 4.72; N, 17.87 Found C, 53.33; H, 4.69; N, 17.55
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]glycine ethyl ester (**63f**)	16	111-114 (washed with petroleum ether)	$C_{21}H_{23}ClN_6O_5$ Calcd. C, 53.15; H, 4.89; N, 17.72 Found C, 53.20; H, 4.96; N, 17.70
N-[*N*-[*N*-Benzoyl-3-(5-methylisoxazolyl-3)amino-2,3-dehydroalanyl]glycyl]-L-3-phenylalanine methyl ester (**64c**)	18	115-120 (washed with petroleum ether)	$C_{26}H_{27}N_5O_6$ Calcd. C, 61.76; H, 5.39; N, 13.86 Found C, 61.45; H, 5.51; N, 13.50
N-[*N*-[*N*-Benzoyl-3-(3-methoxycarbonylpyrazinyl-2)amino-2,3-dehydroalanyl]glycyl]-L-3-phenylalanine methyl ester (**64h**)	21	102-105 (washed with petroleum ether)	$C_{28}H_{28}N_6O_7$ Calcd. C, 59.98; H, 5.04; N, 15.00 Found C, 69.71; H, 5.13; N, 14.69
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-L-tyrosine methyl ester (**65f**)	30	134-136 (washed with petroleum ether)	$C_{27}H_{27}ClN_6O_6$ Calcd. C, 57.23; H, 4.81; N, 14.84 Found C, 56.86; H, 4.95; N, 14.67
N-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]norleucyl]-L-3-phenylalanine methyl ester (**66e**)	41	92-96 (from ethyl acetate/petroleum ether)	$C_{32}H_{38}N_6O_5$ Calcd. C, 65.50; H, 6.53; N, 14.33 Found C, 65.26; H, 6.88; N, 14.08
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]norleucyl]-L-3-phenylalanine methyl ester (**66f**)	20	96-99 (washed with petroleum ether)	$C_{31}H_{35}ClN_6O_5$ Calcd. C, 61.36; H, 5.82; N, 13.86 Found C, 61.33; H, 5.94; N, 13.71
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]norleucyl]-L-3-phenylalanine methyl ester (**66g**)	10	130-134 (washed with petroleum ether)	$C_{34}H_{40}N_6O_7S$ Calcd. C, 60.33; H, 5.96; N, 12.42 Found C, 59.93; H, 5.92; N, 12.39
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-3-phenylalanyl]-glycine ethyl ester (**67g**)	13	128-131 (washedwith petroleum ether)	$C_{31}H_{34}N_6O_7S$ Calcd. C, 58.65; H, 5.40; N, 13.25 Found C, 58.93; H, 5.48; N, 12.99
N-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]-3-phenylalanyl]-L-3-phenylalanine methyl ester (**68e**)	27	180-184 (washed with petroleum ether)	$C_{35}H_{36}N_6O_5$ Calcd. C, 67.71; H, 5.85; N, 13.55 Found C, 67.58; H, 5.87; N, 13.56
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]-3-phenylalanyl]-L-3-phenylalanine methyl ester (**68f**)	51	150-154 (washed with petroleum ether)	$C_{34}H_{33}ClN_6O_5$ Calcd. C, 63.73; H, 5.19; N, 13.12 Found C, 63.78; H, 5.24; N, 13.24
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-3-phenylalanyl]-L-3-phenylalanine methyl ester (**68g**)	20	187-192 (washed with petroleum ether)	$C_{37}H_{38}N_6O_7S$ Calcd. C, 62.51; H, 5.39; N, 11.83 Found C, 62.84; H, 5.42; N, 12.04
N-[*N*-[*N*-Benzoyl-3-(3,5-dibromopyridinyl-2)amino-2,3-dehydroalanyl]prolyl]glycine ethyl ester (**69b**)	11	99-102 (washed with petroleum ether)	$C_{24}H_{25}Br_2N_5O_5$ Calcd. C, 46.38; H, 4.06; N, 11.27 Found C, 46.16; H, 3.95; N, 10.97
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]prolyl]glycine ethyl ester (**69g**)	7	106-110 (from ethyl acetate/petroleum ether)	$C_{27}H_{32}N_6O_7S$ Calcd. C, 55.46; H, 5.52; N, 14.38 Found C, 55.38; H, 5.53; N, 14.12
N-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]prolyl]-L-3-phenylalanine methyl ester (**70e**)	8	135-139 (washed with petroleum ether)	$C_{31}H_{34}N_6O_5$ Calcd. C, 65.23; H, 6.01; N, 14.73 Found C, 65.24; H, 5.99; N, 14.62

Table 1 (Continued)

Compound	Yield %	mp °C	Molecular Formula Analyses
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]glycyl]glycyl]-L-alanine ethyl ester (**71f**)	26	124-126 (washed with petroleum ether)	$C_{24}H_{28}ClN_7O_6$ Calcd. C, 52.83; H, 5.18; N, 17.98 Found C, 52.98; H, 5.21; N, 17.86
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]glycyl]glycyl]-L-glutamic acid diethyl ester (**72f**)	39	97-101 (washed with petroleum ether)	$C_{28}H_{34}ClN_7O_8$ Calcd. C, 53.23; H, 5.43; N, 15.53 Found C, 53.24; H, 5.47; N, 15.57
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]glycyl]glycyl]glycine ethyl ester (**73f**)	26	120-123 (washed with petroleum ether)	$C_{23}H_{26}ClN_7O_6$ Calcd. C, 51.96; H, 4.93; N, 18.45 Found C, 51.63; H, 4.98; N, 18.08
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]glycyl]glycyl]-L-3-phenylalanine methyl ester (**74f**)	41	115-119 (washed with petroleum ether)	$C_{29}H_{30}ClN_7O_6$ Calcd. C, 57.31; H, 4.98; N, 16.14 Found C, 56.99; H, 4.98; N, 16.09
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]glycyl]glycyl]-L-tyrosine methyl ester (**75f**)	15	134-137 (washed with petroleum ether)	$C_{29}H_{30}ClN_7O_7$ Calcd. C, 55.84; H, 4.85; N, 15.73 Found C, 55.53; H, 5.07; N, 15.81
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]glycyl]methionyl]glycine ethyl ester (**76f**)	34	112-116 (washed with petroleum ether)	$C_{26}H_{32}ClN_7O_6S$ Calcd. C, 51.55; H, 5.33; N, 16.20 Found C, 51.75; H, 5.36; N, 16.53
N-[*N*-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]methionyl]valyl]glycine ethyl ester (**77e**)	15	91-95 (washed with petroleum ether)	$C_{30}H_{41}N_7O_6S$ Calcd. C, 57.39; H, 6.59; N, 15.63 Found C, 57.36; H, 6.64; N, 15.81
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]glycine ethyl ester (**78f**)	40	105-110 (washed with petroleum ether)	$C_{30}H_{32}ClN_7O_6$ Calcd. C, 57.95; H, 5.19; N, 15.78 Found C, 57.95; H, 5.29; N, 15.48
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]glycine ethyl ester (**78g**)	28	101-105 (washed with petroleum ether)	$C_{33}H_{37}N_7O_8S$ Calcd. C, 57.29; H, 5.39; N, 14.18 Found C, 57.56; H, 5.32; N, 13.97
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-leucine methyl ester (**79f**)	43	114-118 (washed with petroleum ether)	$C_{33}H_{38}ClN_7O_6$ Calcd. C, 59.71; H, 5.77; N, 14.78 Found C, 59.41; H, 5.85; N, 14.81
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-leucine methyl ester (**79g**)	21	117-121 (washed with petroleum ether)	$C_{36}H_{43}N_7O_8S$ Calcd. C, 58.91; H, 5.91; N, 13.37 Found C, 58.78; H, 6.02; N, 13.25
N-[*N*-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-3-phenylalanine methyl ester (**80e**)	34	95-98 (from ethyl acetate/petroleum ether)	$C_{37}H_{39}N_7O_6$ Calcd. C, 65.55; H, 5.80; N, 14.47 Found C, 65.21; H, 5.74; N, 14.53
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-3-phenylalanine methyl ester (**80g**)	19	116-119 (washedwith petroleum ether)	$C_{39}H_{41}N_7O_8S$ Calcd. C, 61.00; H, 5.39; N, 12.78 Found C, 60.92; H, 5.27; N, 12.89
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-tyrosine methyl ester (**81f**)	26	132-136 (washed with petroleum ether)	$C_{36}H_{36}ClN_7O_7$ Calcd. C, 60.57; H, 5.09; N, 13.74 Found C, 60.32; H, 5.14; N, 14.07
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio-pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-tyrosine methyl ester (**81g**)	31	107-112 (washed with petroleum ether)	$C_{39}H_{41}N_7O_9S$ Calcd. C, 59.75; H, 5.28; N, 12.51 Found C, 59.78; H, 5.44; N, 12.32
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]alanyl]prolyl]-L-3-phenylalanine methyl ester (**82f**)	26	198-201 (washed with petroleum ether)	$C_{33}H_{36}ClN_7O_6$ Calcd. C, 59.89; H, 5.49; N, 14.82 Found C, 60.09; H, 5.72; N, 14.77
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]alanyl]prolyl]-L-3-phenylalanine methyl ester (**82g**)	25	94-96 (washed with petroleum ether)	$C_{36}H_{41}N_7O_8S$ Calcd. C, 59.08; H, 5.65; N, 13.40 Found C, 58.72; H, 5.53; N, 13.29
N-[*N*-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]alanyl]prolyl]glycyl]glycine ethyl ester (**83f**)	16	123-126 (washed with petroleum ether)	$C_{29}H_{35}ClN_8O_7$ Calcd. C, 54.19; H, 5.49; N, 17.44 Found C, 53.80; H, 5.78; N, 17.00
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]alanyl]prolyl]glycyl]-L-3-phenylalaninemethylester (**84f**)	34	121-124 (washed with petroleum ether)	$C_{35}H_{39}ClN_8O_7$ Calcd. C, 58.47; H, 5.47; N, 15.60 Found C, 58.69; H, 5.45; N, 15.30
N-[*N*-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]alanyl]prolyl]valyl]glycine ethyl ester (**85f**)	16	122-125 (washed with petroleum ether)	$C_{32}H_{41}ClN_8O_7$ Calcd. C, 56.12; H, 6.04; N, 16.37 Found C, 56.28; H, 6.08; N, 16.29

Table 2

^{1}H NMR Data

Compound	^{1}H NMR	δ (TMS)
N-(2,2-Diacetylvinyl-1)glycine ethyl ester (**7**)	$CDCl_3$	1.31 (3H, t, CH_3CH_2), 2.27 (3H, s, CH_3CO), 2.49 (3H, s, CH_3CO), 4.10 (2H, d, CH_2NH), 4.27 (2H, q, CH_2CH_3), 7.71 (1H, d, *CH*NH), 11.06 (1H, br m, N*H*CH), $J_{CH_3CH_2}$ = 7.1 Hz, J_{CHNH} = 12.9 Hz
N-(2-Acetyl-2-ethoxycarbonylvinyl-1)glycine ethyl ester (**8**)	$CDCl_3$	1.30 (6H, t, CH_3CH_2), 2.49 (3H, s, CH_3CO), 4.09 (2H, d, CH_2NH), 4.20 (2H, q, CH_2CH_3), 4.26 (2H, q, CH_2CH_3), 7.93 (1H, d, *CH*NH), 11.07 (1H, br m, NH), $J_{CH_3CH_2}$ = 7 1 Hz, J_{CH_2NH} = 6.1 Hz, J_{CHNH} = 13.4 Hz
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycine ethyl ester (**9**)	$CDCl_3$	0.916 and 0.943 (3H, 2t, CH_3CH_2), 1.311 (3H, t, CH_3CH_2), 3.938 and 4.017 (2H, 2q, CH_2CH_3), 4.114 and 4.137 (2H, 2d, CH_2NH), 4.268 (2H, q, CH_2CH_3), 7.27-7.63 (5H, m, Ph), 7.733 and 7.980 (1H, 2d, *CH*NH), 9.25 and 10.57 (1H, 2br m, NH), $J_{CH_3CH_2}$ = 7.1 Hz, J_{CH_2NH} = 6.1 Hz, J_{CHNH} = 13.8 Hz
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)alanine (**13**)	DMSO	0.81 and 0.89 (3H, 2t, CH_3CH_2), 1.46 and 1.48 (3H, 2d, CH_3CH), 3.88 and 3.90 (2H, 2q, CH_2CH_3), 4.38-4.59 (1H, m, *CH*COOH), 7.30-7.45 (5H, m, Ph), 7.91 and8.13 (1H, 2d, *CH*NH), 9.17-9.42 and 10.44-10.51 (1H, 2m, N*H*CH), COOH exchanged, $J_{CH_3CH_2}$ = 7.0 Hz, J_{CH_3CH} = 7 1 Hz, J_{CHNH} = 14.3 Hz
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycine (**14**)	DMSO	0.817 and 0.888 (3H, 2t, CH_3), 3.88 and 3.91 (2H, 2q, CH_2CH_3), 4.20-4.30 (2H, m, CH_2NH), 7.38-7.51 (5H, m, Ph), 7.84 and 8.06 (1H, 2d, *CH*NH), 9.14 and 10.20 (1H, 2br d, N*H*CH), COOH exchanged, $J_{CH_3CH_2}$ = 7 1 Hz, J_{CHNH} = 14.5 Hz.
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)methionine (**16**)	$CDCl_3$	0.89 (3H, t, CH_3CH_2), 2.00-2.73 (4H, m, CH_2CH_2), 3.99 (2H, q, CH_2CH_3), 4.30 (1H, m, *CH*COOH), 7.40 (5H, m, Ph), 8.08 (1H, 2d, *CH*NH), 9.34 and 10.35 (1H, 2m, N*H*CH), COOH exchanged, $J_{CH_3CH_2}$ = 7.0 Hz, J_{CHNH} = 14.0 Hz
N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)valine (**19**)	$CDCl_3$	0.90 and 0.92 (3H, 2t, CH_3CH_2), 1.01 and 1.04 (6H, 2d, $(CH_3)_2CH$), 2.33 (1H, m, $CH(CH_3)_2$), 3.99 and 4.02 (2H, 2q, CH_2CH_3), 3.86-4.13 (1H, m, *CH*COOH), 7.27-7.65 (5H, m, Ph), 7.85 and 8.01 (1H, 2d, *CH*NH), 9.32 and 10.62 (1H, 2m, N*H*CH), COOH exchanged, $J_{CH_3CH_2}$ = 7 0 Hz, J_{CH_3CH} = 6 7 Hz, J_{CHNH} = 14.2 Hz
N-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)alanyl]glycine ethyl ester (**20**)	$CDCl_3$	0.86-1.02 (3H, m, CH_3CH_2), 1.27 (3H, t, CH_3CH_2), 1.55 and 1.59 (3H, 2d, CH_3CH), 3.86-4.32 (7H, m, $3CH_2$ and $CHCH_3$), 6.93 (1H, br, N*H*CH_2), 7.27-7.61 (5H, m, Ph), 7.84 and 8.05 (1H, 2d, *CH*NH), 9.30 and 10.64 (1H, 2br m, N*H*CH), $J_{CH_3CH_2}$ = 7.0 Hz, J_{CH_3CH} = 7.0 Hz, J_{CHNH} = 13.9 Hz
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-alanine ethyl ester (**21**)	$CDCl_3$	0.94 (3H, t, CH_3CH_2), 1.28 (3H, t, CH_3CH_2), 1.42 (3H, d, CH_3CH), 4.00 (2H, q, CH_2CH_3), 4.11 (2H, d, CH_2NH), 4.20 (2H, q, CH_2CH_3), 4.60 (1H, t, $CHCH_3$), 6.79 (1H, br d, N*H*CHCOOEt), 7.27-7.69 (5H, m, Ph), 8.00 (1H, d, *CH*NH), 9.24 and 10.61 (1H, 2m, N*H*CH), $J_{CH_3CH_2}$ = 7 2 Hz, J_{CH_3CH} = 7.1 Hz, J_{CHNH} = 13.2 Hz
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycine ethyl ester (**23**)	$CDCl_3$	0.94 (3H, t, CH_3CH_2), 1.27 (3H, t, CH_3CH_2), 3.87-4.32 (8H, m, $4CH_2$), 6.87 (1H, br t, N*H*CH_2COOEt), 7.33 (1H, d, *CH*NH), 7.39 (5H, s, Ph), 7.99 (1H, br d, N*H*CH), $J_{CH_3CH_2}$ = 7 1 Hz, J_{CHNH} = 12 8 Hz.
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-3-phenylalanine methyl ester (**25**)	$CDCl_3$	0.95 (3H, t, CH_3CH_2), 3.12 (2H, d, CH_2Ph), 3.73 (3H, s, OMe), 3.99 (4H, m, $2CH_2$), 4.89 (1H, dt, *CH*COOMe), 6.50 (1H, br d, N*H*CHCOOMe), 7.09-7.41 (10H, m, Ph), 7.93 (1H, d, *CH*NH), N*H*CH exchanged, J_{CHNH} = 12.9 Hz
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)-L-leucyl]-L-3-phenylalanine methyl ester (**27**)	$CDCl_3$	0.87-1.03 (9H, m, CH_3CH_2 and $(CH_3)_2CH$), 1.70 (3H, m, $CH_2CH(CH_3)_2$), 3.11 (2H, br d, CH_2Ph), 3.73 (3H, s, OMe), 3.87-4.11 (3H, m, CH_2O and $CHCH_2CH(CH_3)_2$), 4 88 (1H, dt, $CHCH_2Ph$), 6.48 (1H, br m, N*H*$CHCH_2Ph$), 7.00-7.53 (10H, m, Ph), 7.97 (1H, d, *CH*NH), 9.17 and 10.49 (1H, 2br m, N*H*CH), J_{CHNH} = 13.4 Hz
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)methionyl]glycine ethyl ester (**28**)	$CDCl_3$	0.82-1.03 (3H, m, CH_3CH_2), 1.28 (3H, t, CH_3CH_2), 2.11 (3H, s, SCH_3), 2.11-2.32 (2H, m, CH_2CH), 2.55-2.62 (2H, m, SCH_2), 3.87-4.32 (7H, m, $2CH_2O$, CH_2NH and $CHCH_2$), 6.84-7.03 (1H, br m, N*H*CH_2), 7.27-7.63 (5H, m, Ph), 7.86 and 8.05 (1H, 2d, *CH*NH), 9.32 and 10.62 (1H, 2br m, N*H*CH) ,$J_{CH_3CH_2}$ = 7.0 Hz, J_{CHNH} = 13.7 Hz.

Table 2 (Continued)

Compound	^{1}H NMR	δ (TMS)
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)norleucyl]glycine ethyl ester (**29**)	$CDCl_3$	0.82-1.02 (6H, m, $2CH_3CH_2$), 1.28 (3H, t, CH_3CH_2), 1.28-1.35 (4H, m, $CH_2CH_2CH_3$), 1.90 (3H, m, CH_2CH), 3.86-4.33 (6H, m, $2CH_2O$ and CH_2NH), 6.69 (1H, br m, $NHCH_2$), 7.27-7.52 (5H, m, Ph), 7.79 and 8.02 (1H, 2d, CHNH), 9.23 and 10.56 (1H, 2br m, NHCH), $J_{CH_3CH_2}$ = 7.0 Hz, J_{CHNH} = 13.8 Hz
N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)valyl]glycine ethyl ester (**31**)	$CDCl_3$	0.86-1.02 (3H, m, CH_3CH_2), 1.02 (6H, d, $(CH_3)_2CH$), 1.27 (3H, t, CH_3CH_2), 2.37 (1H, m, $CH(CH_3)_2$), 3.69-4.32 (7H, m, $3CH_2$ and $CHCH(CH_3)_2$), 6.81-7.01 (1H, br, $NHCH_2$), 7.27-7.62 (5H, m, Ph), 7.81 and 8.04 (1H, 2d, CHNH), 9.42 and 10.80 (1H, 2br m, NHCH), $J_{CH_3CH_2}$ = 7.0 Hz, J_{CH_3CH} = 6 7 Hz, J_{CHNH} = 13.7 Hz
N-[*N*-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycyl]-L-3-phenylalanine methyl ester (**43**)	$CDCl_3$	0.82 and 0.88 (3H, 2t, CH_3CH_2), 2.99 (2H, br d, CH_2Ph), 3.67 (3H, s, OMe), 3.80-4.10 (6H, m, $2CH_2NH$ and CH_2O), 4.50-4.95 (1H, br m, $CHCH_2Ph$), 7.00-7.40 (7H, m, 5H-Ph and 2NHCO), 7.40 (5H, s, Ph), 7.80 and 7.98 (1H, 2d, CHNH, 9.20 and 10.50 (1H, 2br m, NHCH), $J_{CH_3CH_2}$ = 7 Hz, J_{CH_2CH} = 6 Hz, J_{CHNH} = 14 Hz
N-(2-Benzoylamino-2-methoxycarbonylvinyl-1)glycine (**47**)	DMSO	3.55 (3H, s, OMe), 3.90 (2H, d, CH_2), 6.46-6.74 (1H, br m, $NHCH_2$), 7.34-7.50 (4H, m, 3H-Ph and CHNH), 7.92-8.00 (2H, m, Ph), 8.91 (1H, s, NHCOPh), COOH exchanged, J_{CH_2CH} = 5.7 Hz
N-[*N*-(2-Benzoylamino-2-methoxycarbonylvinyl-1)glycyl] glycine ethyl ester (**48**)	DMSO	1.19 (3H, t, CH_3CH_2), 3.57 (3H, s, OMe), 3.85-3.92 (4H, m, $2CH_2NH$), 4.10 (2H, q, CH_2O), 6.89 (1H, br m, $NHCH_2$), 7.33-7.87 (4H, m, 3H-Ph and CHNH), 7.91-8.02 (2H, m, Ph), 8.45 (1H, t, NHCH), 9.04 (1H, s, NHCOPh), J_{CH3CH2} = 7 1 Hz, J_{CH2NH} 5.7 Hz
N-[*N*-[*N*-Benzoyl-3-(3-nitropyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]glycine ethyl ester (**58a**)	DMSO	1.17 (3H, t, CH_3CH_2), 2.40-2.50 (2H, m, CH_2), 3.26-3.53 (2H, m, CH_2), 3.80 (2H, d, CH_2NH), 4.06 (2H, q, CH_2CH_3), 7.13 (1H, dd, $H_{5'}$), 7.52-7.60 (3H, m, 3H-Ph), 7.94-8.67 (7H, m, 2H-Ph, $H_{4'}$, $H_{6'}$, CH=C and 2NH), 9.60 (1H, s, NHCOPh), 9.90 (1H, d, NHCH=C), $J_{H4'H5'}$ = 8.3 Hz, $J_{H5'H6'}$ = 4.63 Hz, J_{CH3CH2} = 7.08 Hz, J_{CH_2NH} = 6.11 Hz, J_{NH-CH} = 10.99 Hz
N-[*N*-[*N*-Benzoyl-3-(3,5-dibromopyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]glycine ethyl ester (**58b**)	DMSO	1.17 (3H, t, CH_3CH_2), 2.39-2.50 (2H, m, CH_2), 3.11-3.45 (2H, m, CH_2), 3.80 (2H, d, CH_2NH), 4.05 (2H, q, CH_2CH_3), 7.40-7.58 (3H, m, 3H-Ph), 7.71 (1H, d, CH=C), 7.93-8.78 (6H, m, 2H-Ph, $H_{4'}$, $H_{6'}$ and 2NH), 9.44 and 9.66 (1H, 2s, NHCOPh), 11.61 (1H, d, NHCH=C), $J_{CH_3CH_2}$ = 7.03 Hz, J_{CH_2NH} = 5.86 Hz, J_{NH-CH} = 10.55 Hz
N-[*N*-[*N*-Benzoyl-3-(3-nitropyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]-L-3-phenylalaninemethylester (**59a**)	DMSO	2.35-2.50 (2H, m, CH_2), 2.94-3.07 (2H, m, CH_2Ph), 3.26-3.47 (2H, m, CH_2), 3.57 (3H, s, OMe), 4.32-4.60 (1H, m, $CHCH_2$), 7.04-7.23 (6H, m, 5H-Ph and $H_{5'}$), 7.42-7.60 (3H, m, 3H-Ph), 8.00-8.70 (7H, m, 2H-Ph, $H_{4'}$, $H_{6'}$, CH=C and 2NH), 9.70 (1H, br s, NHCOPh), 9.83 (1H, d, NHCH=C)
N-[*N*-[*N*-Benzoyl-3-(3,5-dibromopyridinyl-2)amino-2,3-dehydroalanyl]-β-alanyl]-L-3-phenylalaninemethylester (**59b**)	DMSO	2.36-2.50 (2H, m, CH_2), 2.60-2.98 (2H, m, CH_2Ph), 3.04-3.49 (2H, m, CH_2), 3.56 (3H, s, OMe), 4.33-4.62 (1H, m, $CHCH_2$), 7.23 (5H, br s, Ph), 7.56-8.54 (10H, m, 5H-PhCO, $H_{4'}$, $H_{6'}$, CH=C and 2NH, 9.54 (2H, m, NHCH=C)
N-[*N*-[*N*-Benzoyl-3-(6-chloropyridazinyl-3)amino-2,3-dehydroalanyl]-β-alanyl]-L-3-phenylalanine methyl ester (**59d**)	DMSO	2.18-2.39 (2H, m, CH_2), 2.86-3.01 (2H, m, CH_2Ph), 3.17-3.47 (2H, m, CH_2), 3.57 (3H, s, OMe), 7.24 (5H, br s, Ph), 7.30-8.37 (10H, m, 5H-Ph, $H_{4'}$, $H_{5'}$, CH=C and 2NH), 9.33 (1H, s, NHCOPh)
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-3-piperidinecarboxylic acid ethyl ester (**60f**)	DMSO	1.18 (3H, t, CH_3CH_2), 1.43-2.18 (4H, m, $2CH_2$), 2.38 (3H, s, 6'-CH_3), 2.54-3.33 (2H, m, CH_2), 3.58-4.37 (7H, m, $3CH_2$ and $CHCOOEt$), 7.01 (1H, s, $H_{5'}$), 7.41-7.57 (4H, m, 3H-Ph and NH), 7.98-8.22 (3H, m, 2H-Ph and CH=C), 9.35 (1H, s, NHCOPh), 10.13 (1H, d, NHCH=C), $J_{CH_3CH_2}$ = 7 Hz, J_{NH-CH} = 11 Hz
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-4-piperidinecarboxylic acid ethyl ester (**61f**)	DMSO	1.18 (3H, t, CH_3CH_2), 1.62-3.30 (8H, m, $4CH_2$), 2.38 (3H, s, 6'-CH_3), 3.43-3.81 (3H, m, CH_2 and $CHCOOEt$), 4.07 (2H, q, CH_2CH_3), 7.01 (1H, s, $H_{5'}$), 7.43-7.56 (4H, m, 3H-Ph and NH), 7.98-8.20 (3H, m, 2H-Ph and CH=C), 9.32 (1H, s, NHCOPh), 10.05 (1H, d, NHCH=C), $J_{CH_3CH_2}$ = 7 08 Hz, J_{NH-CH} = 11.96 Hz

Table 2 (Continued)

Compound	^{1}H NMR	δ (TMS)
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-L-glutamic acid diethyl ester (**62f**)	DMSO	1.16 (3H, t, CH_3CH_2), 1.17 (3H, t, CH_3CH_2), 2.04 (2H, m, CH_2CH), 2.38 (3H, *s*, 6'-CH_3), 3.76 (2H, d, CH_2NH), 3.95-4.20 (3H, m, CH_2COOEt and $CHCOOEt$), 4.04 (2H, q, CH_2CH_3), 4.08 (2H, q, CH_2CH_3), 7.01 (1H, *s*, $H_{5'}$), 7.48-7.57 (3H, m, 3H-Ph), 7.95-8.08 (5H, m, 2H-Ph, CH=C and 2NH), 9.45 (1H, *s*, NHCOPh), 10.07 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7.08 Hz, J_{CH_2NH} = 5.61 Hz, J_{NH-CH} = 11.71 Hz
N-[*N*-[*N*-Benzoyl-3-(3-nitropyridinyl-2)amino-2,3-dehydroalanyl]glycyl]glycine ethyl ester (**63a**)	DMSO	1.19 (3H, t, CH_3CH_2), 3.84-3.91 (4H, m, $2CH_2$), 4.10 (2H, q, CH_2CH_3), 7.16 (1H, dd, $H_{5'}$), 7.61-7.63 (3H, m, 3H-Ph), 8.02-8.70 (7H, m, 2H-Ph, $H_{4'}$, $H_{6'}$, CH=C and 2NH), 9.84 (1H, *s*, NHCOPh), 9.97 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7 08 Hz, $J_{H4'H5'}$ = 8.2 Hz, $J_{H5'H6'}$ = 4.5 Hz, J_{NH-CH} = 10.5 Hz
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]glycine ethyl ester (**63f**)	DMSO	1.19 (3H, t, CH_3CH_2), 2.38 (3H, *s*, 6'-CH_3), 3.75-3.89 (4H, m, $2CH_2$), 4.09 (2H, q, CH_2CH_3), 7.00 (1H, *s*, $H_{5'}$), 7.51-7.56 (4H, m, 3H-Ph and NH), 7.88-8.13 (4H, m, 2H-Ph, CH=C and NH), 9.35 (1H, *s*, NHCOPh), 9.95 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7 08 Hz, J_{NH-CH} = 11.72 Hz
N-[*N*-[*N*-Benzoyl-3-(5-methylisoxazolyl-3)amino-2,3-dehydroalanyl]glycyl]-L-3-phenylalanine methyl ester (**64c**)	DMSO	2.31 (3H, *s*, 5'-CH_3), 3.00 (2H, d, CH_2Ph), 3.57 (3H, *s*, OMe), 3.73 (2H, d, CH_2NH), 4.36-4.62 (1H, m, $CHCH_2$), 5.99 and 6.00 (1H, 2s, $H_{4'}$), 7.22 (5H, br *s*, Ph), 7.48-8.09 (8H, m, 5H-Ph, CH=C and 2NH, 8.88 (1H, d, N*H*CH=C), 9.27 (1H, *s*, NHCOPh), J_{CH_2CH} = 7 6 Hz, J_{CH_2NH} = 6.1 Hz, J_{NH-CH} = 11.5 Hz
N-[*N*-[*N*-Benzoyl-3-(3-methoxycarbonylpyrazinyl-2)amino-2,3-dehydroalanyl]glycyl]-L-3-phenylalanine methyl ester (**64h**)	DMSO	2.98-3.06 (2H, m, CH_2Ph), 3.58 (3H, *s*, OMe), 3.81 (3H, *s*, OMe), 3.92-4.60 (3H, m, CH_2 and CH), 7.23 (5H, br *s*, Ph), 7.36-7.60 (3H, m, 3H-Ph), 7.96-8.57 (7H, m, 2H-Ph, $H_{5'}$, $H_{6'}$, CH=C and 2NH), 9.80 (1H, *s*, NHCOPh), 10.08 (1H, d, N*H*CH=C), J_{NH-CH} = 10.5 Hz
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]glycyl]-L-tyrosine methyl ester (**65f**)	DMSO	2.38 (3H, *s*, 6'-CH_3), 2.90 (2H, d, CH_2CH), 3.55 (3H, *s*, OMe), 3.75 (2H, d, CH_2NH), 4.27-4.49 (1H, m, $CHCH_2$), 6.58-6.68 (2H, m, Ar), 6.90-7.01 (2H, m, Ar), 7.01 (1H, *s*, $H_{5'}$), 7.56-8.32 (8H, m, Ph, CH=C and 2NH, 9.44 (1H, *s*, NHCOPh), 10.05 (1H, d, N*H*CH=C), ArOH exchanged, J_{CH2-CH} = 6.8 Hz, J_{CH_2NH} = 5.8 Hz, J_{NH-CH} = 11 Hz
N-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]norleucyl]-L-3-phenylalanine methyl ester (**66e**)	DMSO	0.8-2.2 (9H, m, *n*-Bu), 2.3 (6H, *s*, 4', 6'-CH_3), 2.9-3.2 (2H, m, CH_2Ph), 3.5 (3H, *s*, OMe), 4.4 (2H, m, 2CHCO), 6.7 (1H, *s*, $H_{5'}$), 7.2 (5H, br *s*, Ph) 7.6-8.3 (8H, m, PhCO, CH=C and 2NH), 9.3 (1H, *s*, NHCOPh), 9.5 (1H, d, N*H*CH=C)
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]norleucyl]-L-3-phenylalanine methyl ester (**66f**)	DMSO	0.8-2.2 (9H, m, *n*-Bu), 2.4 (3H, *s*, 6'-CH_3), 3.0-3.1 (2H, m, CH_2Ph), 3.6 (3H, *s*, OMe), 4.4-4.5 (2H, m, 2CHCO), 7.0 (1H, *s*, $H_{5'}$), 7.2-8.1 (13H, m, 2Ph, CH=C and 2NH), 9.4 (1H, *s*, NHCOPh), 10.0 (1H, d, NHCH=C)
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]norleucyl]-L-3-phenylalanine methyl ester (**66g**)	DMSO	0.5-1.9 (9H, m, *n*-Bu), 1.2 (3H, t, CH_3CH_2), 2.6 (3H, *s*, SMe), 3.1 (2H, d, CH_2Ph), 3.6 (3H, *s*, OMe), 3.9-4.3 (4H, m, CH_2CH_3 and 2CHCO), 7.2 (5H, *s*, Ph), 7.5-8.2 (8H, m, PhCO, CH=C and 2NH), 8.8 (1H, *s*, $H_{6'}$), 10.0 (1H, *s*, NHCOPh), 10.2 (1H, d, N*H*CH=C)
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-3-phenylalanyl] glycine ethyl ester (**67g**)	DMSO	1.1-2.0 (6H, m, $2CH_3CH_2$), 2.6 (3H, *s*, SMe), 2.9-3.2 (2H, m, CH_2Ph), 3.9-4.3 (7H, m, $2CH_2CH_3$, CH_2NH and CHCO), 7.2-8.1 (13H, m, 2Ph, CH=C and 2NH), 8.8 (1H, *s*, $H_{6'}$), 9.7 (1H, *s*, NHCOPh), 10.0 (1H, d, N*H*CH=C)
N-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]-3-phenylalanyl]-L-3-phenylalanine methyl ester (**68e**)	DMSO	2.3 (6H, *s*, 4', 6'-CH_3), 2.5-3.1 (4H, m, $2CH_2Ph$), 3.6 (3H, *s*, OMe), 4.4-4.6 (2H, m, 2CHCO), 6.7 (1H, *s*, $H_{5'}$), 7.1-8.4 (18H, m, 3Ph, CH=C and 2NH), 9.3 (1H, br *s*, NHCOPh), 10.6 (1H, d, NHCH=C)
N-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)amino-2,3-dehydroalanyl]-3-phenylalanyl]-3-phenylalanine methyl ester (**68f**)	DMSO	2.4 (3H, *s*, 6'-CH_3), 3.1 (4H, m, $2CH_2Ph$), 3.6 (3H, *s*, OMe), 4.4-4.6 (2H, m, 2CHCO), 7.0-8.1 (19H, 3Ph, $H_{5'}$, CH=C and 2NH), 9.4 (1H, *s*, NHCOPh), 10.0 (1H, d, N*H*CH=C)
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio-pyrimidinyl-4)amino-2,3-dehydroalanyl]-3-phenylalanyl]-L-3-phenylalanine methyl ester (**68g**)	DMSO	1.2 (3H, t, CH_3CH_2), 2.6 (3H, *s*, SMe), 3.0 (4H, d, $2CH_2Ph$), 3.1 (3H, *s*, OMe), 4.2 (2H, q, CH_2CH_3), 4.5 (2H, m, 2CHCO), 7.1-8.6 (18H, m, 3Ph, CH=C and 2NH), 8.8 (1H, *s*, $H_{6'}$), 9.7 (1H, *s*, NHCOPh), 10.4 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7 08 Hz, J_{NH-CH} = 11.33 Hz

Table 2 (Continued)

Compound	^{1}H NMR	δ (TMS)
N-[*N*-[*N*-Benzoyl-3-(3,5-dibromopyridinyl-2)amino-2,3-dehydroalanyl]prolyl]glycine ethyl ester (**69b**)	DMSO	1.17-1.37 (3H, m, CH_3), 2.33-2.41 (4H, m, $2CH_2$), 2.90-4.60 (7H, m, $3CH_2$ and CH), 7.54-8.61 (11H, 5H-Ph, $H_{4'}$, $H_{6'}$, CH=C and 3NH)
N-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio-pyrimidinyl-4)amino-2,3-dehydroalanyl]prolyl]glycine ethyl ester (**69g**)	DMSO	1.2-1.9 (12H, m, $2CH_3CH_2$ and $3CH_2$), 2.5 (3H, *s*, SMe), 3.9-4.3 (7H, m, $2CH_2CH_3$, CH_2NH and CHCO), 7.5-9.9 (10H, m, Ph, CH=C, $H_{6'}$ and 3NH)
N-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]prolyl]-L-3-phenylalanine methyl ester (**70e**)	DMSO	1.2-1.9 (6H, m, $3CH_2$), 2.3 (6H, *s*, 4',6'-CH_3), 3.1 (2H, m, CH_2Ph), 3.6 (3H, *s*, OMe), 4.4-4.6 (2H, m, 2CHCO), 6.7 (1H, *s*, $H_{5'}$), 7.1-8.0 (12H, m, 2Ph, NH and CH=C), 9.7 (2H, m, 2NH)
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]glycyl]glycyl]-L-alanine ethyl ester (**71f**)	DMSO	1.17 (3H, t, CH_3CH_2), 1.29 (3H, d, CH_3CH), 2.38 (3H, *s*, 6'-CH_3), 3.76 (4H, d, $2CH_2NH$), 3.93-4.32 (1H, m, CHCO), 4.07 (2H, q, CH_2CH_3), 7.02 (1H, *s*, $H_{5'}$), 7.57-8.16 (9H, m, Ph, CH=C and 3NH), 9.38 (1H, *s*, NHCOPh), 10.05 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7.08 Hz, J_{CH_3-CH} = 7.81 Hz, J_{CH_2-NH} = 5.62 Hz, J_{NH-CH} = 11.5 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]glycyl]glycyl]-L-glutamic acid diethyl ester (**72f**)	DMSO	1.15 (3H, t, CH_3CH_2), 1.17 (3H, t, CH_3CH_2), 1.82-2.10 (2H, m, CH_2CH), 2.37 (3H, *s*, 6'-CH_3), 3.54-4.11 (11H, d, $5CH_2$ and CHCO), 7.02 (1H, *s*, $H_{5'}$), 7.56-8.08 (9H, m, Ph, CH=C and 3NH), 9.36 (1H, *s*, NHCOPh), 10.03 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7 08 Hz, J_{NH-CH} = 11.7 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]glycyl]glycyl]glycine ethyl ester (**73f**)	DMSO	1.18 (3H, t, CH_3CH_2), 2.38 (3H, *s*, 6'-CH_3), 3.79 (6H, d, $3CH_2NH$), 4.08 (2H, q, CH_2CH_3), 7.02 (1H, *s*, $H_{5'}$), 7.48-7.58 (3H, m, 3H-Ph), 8.02-8.20 (6H, m, 2H-Ph, CH=C and 3NH), 9.39 (1H, *s*, NHCOPh), 10.08 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7 08 Hz, J_{CH_2-NH} = 6.84 Hz, J_{NH-CH} = 11.72 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]glycyl]glycyl]-L-3-phenylalanine methyl ester (**74f**)	DMSO	2.35 (3H, *s*, 6'-CH_3), 2.92-3.02 (2H, m, CH_2Ph), 3.56 (3H, *s*, OMe), 3.70-3.80 (4H, d, $2CH_2NH$), 4.49-4.57 (1H, m, CHCO), 7.01 (1H, *s*, $H_{5'}$), 7.22 (5H, br *s*, Ph), 7.56-8.32 (9H, m, Ph, CH=C and 3NH), 9.38 (1H, *s*, NHCOPh), 10.04 (1H, d, N*H*CH=C), J_{NH-CH} = 11 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]glycyl]glycyl]-L-tyrosine methyl ester (**75f**)	DMSO	2.35 (3H, *s*, 6'-CH_3), 2.80-2.92 (2H, m, CH_2Ar), 3.55 (3H, *s*, OMe), 3.70-3.81 (4H, d, $2CH_2NH$), 4.26-4.51 (1H, m, CHCO), 6.56-6.69 (2H, m, Ar), 6.91-7.01 (2H, m, Ar), 7.01 (1H, *s*, $H_{5'}$), 7.49-8 20 (9H, m, Ph, CH=C and 3NH), 9.22 (1H, *s*, OH), 9.36 (1H, *s*, NHCOPh), 10.04 (1H, d, N*H*CH=C), J_{NH-CH} = 11 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]glycyl]methionyl]glycine ethyl ester (**76f**)	DMSO	1.18 (3H, t, CH_3CH_2), 1.84-2.08 (2H, m, CH_2CH), 2.03 (3H, *s*, SMe), 2.38 (3H, *s*, 6'-CH_3), 2.81-2.99 (2H, m, CH_2S), 3.79-4.46 (7H, d, $3CH_2$ and CHCO), 7.02 (1H, *s*, $H_{5'}$), 7.56-8.21 (9H, m, Ph, CH=C and 3NH), 9.29 (1H, br *s*, NHCOPh), 9.83-10.05 (1H, m, N*H*CH=C), $J_{CH_3CH_2}$ = 7 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]methionyl]valyl]glycine ethyl ester (**77e**)	DMSO	0.92 (6H, d, $(CH_3)_2CH$), 1.17 (3H, t, CH_3CH_2), 1.50-2.14 (3H, m, CH_2CH and $CH(CH_3)_2$), 2.00 (3H, *s*, SMe), 2.32 (6H, *s*, 4', 6'-CH_3), 3.58-4.59 (8H, m, $3CH_2$ and 2CHCO), 6.77 (1H, *s*, $H_{5'}$), 7.47-8.46 (9H, m, Ph, CH=C and 3NH), 9.34 (2H, m, 2NH), JCH_3-CH_2 = 7.1 Hz, J_{CH_3-CH} = 6.7 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]glycine ethyl ester (**78f**)	DMSO	1.18 (3H, t, CH_3CH_2), 2.37 (3H, *s*, 6'-CH_3), 2.94-3.10 (2H, m, CH_2Ph), 3.50-3.80 (4H, m, $2CH_2$), 4.08 (2H, q, CH_2CH_3), 4.49-4.63 (1H, m, CHCO), 7.01 (1H, *s*, $H_{5'}$), 7.18 (5H, br *s*, Ph), 7.50-8.05 (9H, m, Ph, CH=C and 3NH), 9.36 (1H, *s*, NHCOPh), 10.04 (1H, d, N*H*CH=C), $J_{CH_3CH_2}$ = 7 08 Hz, J_{NH-CH} = 11 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]glycine ethyl ester (**78g**)	DMSO	1.12-1.39 (6H, m, $2CH_3CH_2$), 2.59 (3H, *s*, SMe), 2.95-3.17 (2H, m, CH_2Ph), 3.78-4.74 (9H, m, $4CH_2$ and CHCO), 7.22-8.35 (14H, m, 2Ph, CH=C and 3NH), 8.77 (1H, *s*, $H_{6'}$), 9.74-10.19 (2H, m, 2NH)
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-leucine methyl ester (**79f**)	DMSO	0.86-1.65 (9H, m, *sec*-Bu), 2.37 (3H, *s*, 6'-CH_3), 2.93-3.05 (2H, m, CH_2Ph), 3.59 and 3.61 (3H, 2s, OMe), 3.72-3.83 (2H, m, CH_2NH), 4.20-4.64 (2H, m, 2CHCO), 7.02 (1H, *s*, $H_{5'}$), 7.16-8.36 (14H, m, 2Ph, CH=C and 3NH), 9.34 (1H, *s*, NHCOPh), 10.04 (1H, m, N*H*CH=C), J_{NH-CH} = 11 Hz

Table 2 (Continued)

Compound	^{1}H NMR	δ (TMS)
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-leucine methyl ester (**79g**)	DMSO	0.78-1.76 (12H, m, CH_3CH_2 and *sec*-Bu), 2.59 (3H, *s*, SMe), 2.94-3.12 (2H, m, CH_2Ph), 3.61 (3H, *s*, OMe), 3.68-4.65 (6H, m, $2CH_2$ and 2CHCO), 7.21-8.32 (14H, m, 2Ph, CH=C and 3NH), 8.77 (1H, s, H6'), 9.74-10.03 (2H, m, 2NH)
N-[*N*-[*N*-[*N*-Benzoyl-3-(4,6-dimethylpyrimidinyl-2)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-3-phenylalanine methyl ester (**80e**)	DMSO	2.31 (6H, *s*, 4',6'-CH_3), 2.73-3.03 (4H, m, $2CH_2Ph$), 3.57 (3H, m, OMe), 3.74-3.82 (2H, m, CH_2NH), 4.03-4.52 (2H, m, 2CHCO), 6.73 (1H, m, $H_{5'}$), 7.16-7.23 (10H, m, 2Ph), 7.56-8.42 (9H, m, Ph, CH=C and 3NH), 9.29 (1H, *s*, NHCOPh), 9.43 (1H, d, NHCH=C), J_{NH-CH} = 11.5 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-3-phenylalanine methyl ester (**80g**)	DMSO	1.13-1.33 (3H, m, CH_3CH_2), 2.58 (3H, *s*, SMe), 2.81-3.08 (4H, m, $2CH_2Ph$), 3.58 (3H, *s*, OMe), 3.73-4.56 (6H, m, $2CH_2$ and 2CHCO), 7.09-8.38 (19H, 3Ph, CH=C and 3NH), 8.61-8.83 (1H, m, H6), 2NH exchanged
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-tyrosine methyl ester (**81f**)	DMSO	2.36 (3H, *s*, 6'-CH_3), 2.86-3.07 (4H, m, $2CH_2Ar$), 3.60 (3H, *s*, OMe), 3.72-4.61 (4H, m, CH_2NH and 2CHCO), 6.59-6.76 (2H, m, Ar), 6.94-7.05 (3H, m, 2H-Ar and $H_{5'}$), 7.16-8.28 (14H, m, 2Ph, CH=C and 3NH), 9.24-9.36 (2H, m, OH and NHCOPh), 10.02 (1H, m, NHCH=C), 1NH exchanged
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]-L-3-phenylalanyl]glycyl]-L-tyrosine methyl ester (**81g**)	DMSO	1.04-1.33 (3H, m, CH_3CH_2), 2.62 (3H, *s*, SMe), 2.73-3.08 (4H, m, $2CH_2CH$), 3.58 (3H, *s*, OMe), 3.77-4.51 (6H, m, $2CH_2$ and 2CHCO), 6.47-8.41 (18H, 4H-Ar, 2Ph, CH=C and 3NH), 8.61-9.76 (3H, m, OH, NH and $H_{6'}$)
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2) amino-2,3-dehydroalanyl]alanyl]prolyl]-L-3-phenylalanine methyl ester (**82f**)	DMSO	1.19 (3H, d, CH_3CH), 1.74-1.97 (4H, m, $2CH_2$), 2.37 (3H, *s*, 6'-CH_3), 2.86-2.99 (2H, m, CH_2Ph), 3.42-3.73 (2H, m, CH_2), 3.54 (3H, *s*, OMe), 4.24-4.67 (3H, m, 3CHCO), 7.01 (1H, *s*, $H_{5'}$), 7.21 (5H, br *s*, Ph), 7.24-8.18 (8H, m, Ph, CH=C and 2NH), 9.27 (1H, *s*, NHCOPh), 9.94 (1H, d, NHCH=C), J_{CH_3-CH} = 6.8 Hz, J_{NH-CH} = 11.5 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(5-ethoxycarbonyl-2-methylthio pyrimidinyl-4)amino-2,3-dehydroalanyl]alanyl]prolyl]-L-3-phenylalanine methyl ester (**82g**)	DMSO	1.13-1.38 (6H, m, $2CH_3$), 1.73-2.08 (4H, m, $2CH_2$), 2.58 (3H, *s*, SMe), 2.88-3.00 (2H, m, CH_2Ph), 3.56 (3H, *s*, OMe), 3.65-4.74 (7H, m, $2CH_2$ and 3CHCO), 7.22 (5H, br s, Ph), 7.60-8.29 (8H, m, Ph, CH=C and 2NH), 8.77 (1H, s, $H_{6'}$), 9.73 (1H, *s*, NHCOPh), 10.14 (1H, d, NHCH=C), J_{NH-CH} = 11 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]alanyl]prolyl]glycyl]glycine ethyl ester (**83f**)	DMSO	1.10-1.26 (6H, m, $2CH_3$), 1.75-2.16 (4H, m, $2CH_2$), 2.38 (3H, *s*, 6'-CH_3), 3.61-4.27 (8H, m, $3CH_2$ and 2CHCO), 4.07 (2H, q, CH_2CH_3), 7.01 and 7.07 (1H, 2*s*, $H_{5'}$), 7.55-8.04 (9H, m, Ph, CH=C and 3NH), 9.26 and 9.50 (1H, 2*s*, NHCOPh), 10.08 and 12.31 (1H, 2d, NHCH=C), $J_{CH_3CH_2}$ = 7.03 Hz, J_{NH-CH} = 10 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]alanyl]prolyl]glycyl]-L-3-phenylalanine methyl ester (**84f**)	DMSO	1.15-1.26 (3H, m, CH_3CH), 1.75-2.13 (4H, m, $2CH_2$), 2.37 (3H, *s*, 6'-CH_3), 2.89-2.98 (2H, m, CH_2Ph), 3.35-4.49 (7H, m, $2CH_2$ and 3CHCO), 3.56 (3H, *s*, OMe), 7.01 (1H, *s*, $H_{5'}$), 7.22 (5H, br *s*, Ph), 7.49-8.37 (9H, m, Ph, CH=C and 3NH), 9.25 (1H, *s*, NHCOPh), 10.00 (1H, d, NHCH=C), J_{NH-CH} = 11 Hz
N-[*N*-[*N*-[*N*-Benzoyl-3-(4-chloro-6-methylpyrimidinyl-2)-amino-2,3-dehydroalanyl]alanyl]prolyl]valyl]glycine ethyl ester (**85f**)	DMSO	0.82-2.17 (17H, m, $2CH_3CH_2$, $2CH_2$ and $CH(CH_3)_2$), 2.37 (3H, *s*, 6'-CH_3), 3.34-4.82 (9H, m, $3CH_2$ and 3CHCO), 7.02 (1H, *s*, $H_{5'}$), 7.55-8.33 (9H, m, Ph, CH=C and 3NH), 9.27 (1H, *s*, NHCOPh), 10.06 (1H, m, NHCH=C)

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were obtained on a Varian EM360L and JEOL JNM 90Q FT spectrometers with TMS as internal standard. The microanalyses for C, H, and N were determined on a Perkin-Elmer Analyser 240 C.

Ethyl 2-Benzoyl-3-dimethylaminopropenoate (**6**) [5].

This compound was prepared by slightly modified procedure described in the literature [5]. A mixture of ethyl benzoylacetate **3** (1.920 g, 0.01 mole), toluene (10 ml) and *N*,*N*-dimethylformamide dimethylacetal (1.5 ml) was refluxed for two hours, cooled and volatile components evaporated *in vacuo*. The residue was triturated with a mixture of diethyl ether and *n*-hexane, precipitate collected by filtration and recrystallized from *n*-heptane to give **6** in 79% yield, mp 63-64°, lit [5] mp 63-65°.

N-(2,2-Diacetylvinyl-1)glycine Ethyl Ester (**7**).

A mixture of 2,4-pentanedione **1** (1.00 g, 0.01 mole), toluene (10 ml) and *N,N*-dimethylformamide dimethylacetal (1.5 ml) was refluxed for two hours, cooled and volatile components evaporated *in vacuo*. Glacial acetic acid (5 ml) and glycine ethyl ester hydrochloride (1.40 g, 0.01 mole) were added to the residue and the whole mixture was heated at 100° for one hour, cooled, solvent evaporated *in vacuo* and the residue crystallised from a mixture of ethanol and water. The precipitate was collected by filtration to give **7**. The experimental and analytical data for compound **7** are given in Tables 1 and 2.

N-(2-Acetyl-2-ethoxycarbonylvinyl-1)glycine Ethyl Ester (**8**).

A mixture of ethyl acetoacetate **2** (1.30 g, 0.01 mole), toluene (10 ml) and *N,N*-dimethylformamide dimethylacetal (1.5 ml) was refluxed for two hours, cooled and volatile components evaporated *in vacuo*. Glacial acetic acid (5 ml) and glycine ethyl ester hydrochloride (1.40 g, 0.01 mole) were added to the residue and the whole mixture was heated at 100° for one hour, cooled, solvent evaporated *in vacuo* and the residue crystallised from a mixture of ethanol and water. The precipitate was collected by filtration to give **8**. The experimental and analytical data for compound **8** are given in Tables 1 and 2.

N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycine Ethyl Ester (**9**).

A mixture of crude ethyl 2-benzoyl-3-dimethylaminopropenoate **6** (2.470 g, 0.01 mole), ethanol (20 ml) and glycine ethyl ester hydrochloride (1.40 g, 0.01 mole) was refluxed for two hours, cooled, solvent evaporated *in vacuo* and the residue crystallised from a mixture of ethanol and water. The precipitate was collected by filtration to give **9**. The experimental and analytical data for compound **9** are given in Tables 1 and 2.

N-(2-Benzoyl-2-ethoxycarbonylvinyl-1)amino Acids **13-19**. General Procedure.

A mixture of ethyl 2-benzoyl-3-dimethylaminopropenoate **6** (1.235 g, 0.005 mole), glacial acetic acid (5 ml) and amino acid (0.0055 mole) was stirred at 80° for two hours, cooled and solvent evaporated *in vacuo*. Water (25 ml) was added to the residue, tritruated and left at room temperature until the oily residue crystallised (about 2-12 hours). The precipitate was collected by filtration to give a *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)amino acid. The experimental and analytical data for compounds **13**, **14**, **16**, and **19** are given in Tables 1 and 2.

When the crystallisation of *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)amino acid failed, the residue, obtained after evaporation of acetic acid, was redissolved in chloroform (25 ml), washed first with dilute hydrochloric acid (20 ml, 1%), then twice with water (20 ml), dried over anhydrous sodium sulphate, filtered and the solvent was evaporated *in vacuo*. Dry toluene (25 ml) was added, stirred and the solvent reevaporated *in vacuo*. The crude oily L-*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)leucine (**15**), *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)norleucine (**17**), and L-*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-3-phenylalanine (**18**) were employed for further transformations.

Coupling of *N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)amino Acids with Amino Acid Esters. Preparation of Peptides **20-31**. General Procedure.

A mixture of *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)amino acid **13-19** (0.005 mole), dichloromethane (20 ml) and amino acid ester hydrochloride (0.005 mole) was stirred at 0° for five minutes, then 4-methylmorpholine (0.55 ml) and after five minutes *N,N*-dicyclohexylcarbodiimide (1.030 g, 0.005 mole) was added. The mixture was stirred at 0° for one hour. *N,N'*-Dicyclohexylurea, which precipitated, was filtered off, washed with 10 ml of dichloromethane and the filtrate was washed first with dilute hydrochloric acid (20 ml, 1%), then with aqueous sodium bicarbonate (20 ml, 5%) and finally with water (20 ml), dried over anhydrous sodium sulphate, filtered and the solvent evaporated *in vacuo*. The residue was dissolved in 5 ml of ethyl acetate, *n*-hexane (10-20 ml) was added and left, with occasional trituration, at room temperature until the oily precipitate crystallised (several hours in most cases). The crystalline precipitate was collected by filtration to give *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-protected dipeptide esters **20-31**. The experimental and analytical data for *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)dipeptides **20**, **21**, **23**, **25**, **27**, **28**, **29**, and **31** are given in Tables 1 and 2.

The following *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)dipeptides: *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-glutamic acid diethyl ester (**22**), *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-leucine methyl ester (**24**), and *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-L-tyrosine methyl ester (**26**), and *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-L-3-phenylalanyl]-L-leucine methyl ester (**30**) were not isolated in a pure form. They were used without purification for the preparation of the corresponding dipeptide esters **32-41** hydrochlorides.

The Removal of the 2-Benzoyl-2-ethoxycarbonylvinyl-1 Group. Preparation of Hydrochlorides of Peptide Esters **32-41**. General Procedure.

A mixture of *N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)peptide ester **20-31** (0.002 mole), methanol (10 ml) and hydrazine monohydrochloride (0.002 mole) was refluxed for five hours, cooled and the solvent evaporated *in vacuo* at 30°. The residue was triturated with ethyl acetate (5 ml) and the precipitate collected by filtration to give a hydrochloride of a peptide ester **32-41**.

The same results were obtained, when hydroxylamine hydrochloride was employed instead of hydrazine monohydrochloride, or when methanol was used instead of ethanol as the solvent. The following peptide esters were prepared in this manner:

N-[Glycyl]glycine Ethyl Ester Hydrochloride (**34**) [14].

This compound was prepared from *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycine ethyl ester (**23**) and hydrazine monohydrochloride in ethanol in 83% yield, mp 182-185° (washed with dichloromethane), lit [14] mp 182°.

N-[L-Leucyl]-L-3-phenylalanine Methyl Ester Hydrochloride (**38**) [15].

This compound was prepared from *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-L-leucyl]-L-3-phenylalanine methyl ester (**27**) and hydrazine monohydrochloride in methanol in 78% yield, mp 185-188° (washed with ethyl acetate/*n*-heptane), lit [15] mp 186-187°.

Hydrochlorides of the following dipeptide esters: *N*-[glycyl]-L-alanine ethyl ester (**32**), *N*-[glycyl]-L-glutamic acid diethyl ester (**33**), *N*-[glycyl]-L-leucine methyl ester (**35**), *N*-[glycyl]-L-3-phenylalanine methyl ester (**36**), *N*-[glycyl]-L-tyrosine methyl ester (**37**), *N*-[methionyl]glycine ethyl ester (**39**), *N*-[L-3-phenylalanyl]-L-leucine methyl ester (**40**), and *N*-[valyl]-glycine ethyl ester (**41**) were not isolated in pure form. They

were used without purification in the preparation of tetrapeptides **71-81** and pentapeptides **83-85**.

N-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycine (**42**) [8].

This compound was prepared according to the procedure described in the literature [8].

N-[*N*-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycyl]-L-3-phenylalanine Methyl Ester (**43**).

This compound was prepared from **42** and L-3-phenylalanine methyl ester according to the procedure described above for the preparation of dipeptides **20-31**. The experimental and analytical data for compound **43** are given in Tables 1 and 2.

N-[*N*-[Glycyl]glycyl]-L-3-phenylalanine Methyl Ester Hydrochloride (**44**) [16].

This compound was prepared from **43** and hydrazine monohydrochloride in methanol according to the procedure described above for the preparation of dipeptide hydrochlorides **32-41** in 93% yield, mp 181-183° (from methanol/ethyl acetate), lit [16] mp 182-183°.

N-[*N*-[*N*-[*N*-(2-Benzoyl-2-ethoxycarbonylvinyl-1)glycyl]-glycyl]-L-3-phenylalanyl]-L-leucine Methyl Ester (**45**).

A mixture of crude L-*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)-3-phenylalanine **18** (prepared from 0.01 mole of **6** and 0.011 mole of L-3-phenylalanine as described above for the preparation of *N*-protected amino acids **13-19**), dichloromethane (40 ml) and L-leucine methyl ester hydrochloride (1.815 g, 0.01 mole) was stirred at 0° for five minutes, then 4-methylmorpholine (1.10 ml) and after five minutes *N,N*-dicyclohexylcarbodiimide (2.060 g, 0.01 mole) was added and the mixture was stirred at 0° for one hour. *N,N'*-Dicyclohexylurea, which precipitated, was filtered off, washed with 10 ml of dichloromethane and the filtrate was washed first with dilute hydrochloric acid (40 ml, 1%), then with aqueous sodium bicarbonate (40 ml, 5%) and finally with water (40 ml), dried over anhydrous sodium sulphate, filtered and the solvent was evaporated *in vacuo*. The residue was dissolved in methanol (50 ml), hydrazine monohydrochloride (685 mg, 0.01 mole) was added and the mixture was refluxed for five hours, cooled and the solvent evaporated *in vacuo*. The residue was dissolved in 30 ml of chloroform and the product extracted three times with 10 ml of water. Aqueous phases were collected, washed with chloroform (10 ml) and water evaporated *in vacuo* at 50°. In order to remove residual water, the following procedure was employed three times: The residue was dissolved in dichloromethane (10 ml), toluene (20 ml) was added and the solvent evaporated *in vacuo* at 40-50°. The yield of crude *N*-[L-3-phenylalanyl]-L-leucine methyl ester **40** hydrochloride was 2.871 g (87%, oil).

A mixture of crude *N*-[L-3-phenylalanyl]-L-leucine methyl ester hydrochloride **40** (2.871 g, 0.00874 mole), dichloromethane (40 ml) and *N*-[*N*-(2-benzoyl-2-ethoxycarbonylvinyl-1)glycyl]glycine **42** (2.921 g, 0.00874 mole) was stirred at 0° for five minutes, then 4-methylmorpholine (0.96 ml, 0.00874 mole) and after five minutes *N,N*-dicyclohexylcarbodiimide (1.800 g, 0.00874 mole) was added and the mixture was stirred at 0° for one hour and then at room temperature for another two hours. *N,N'*-Dicyclohexylurea, which precipitated, was filtered off, washed with 20 ml of dichloromethane and the filtrate washed first with dilute hydrochloric acid (30 ml, 1%), then with aqueous sodium bicarbonate (30 ml, 5%) and finally with water (30 ml), dried over anhydrous sodium sulphate, filtered and the solvent was evaporated *in vacuo*. Diethyl ether (20 ml) was added to the residue and left, with occasional tritruation, at room temperature until the oily precipitate crystallised (several hours). The crystalline precipitate was filtered off and crystallised from appropriate solvent to give **45**. The experimental and analytical data for compound **45** are summarized in Table 1. The ^{1}H nmr data are not given because a large number of similar protons disabled our ability to distinguish among them.

N-(2-Benzoylamino-2-methoxycarbonylvinyl-1)glycine (**47**).

A mixture of methyl 2-benzoylamino-3-dimethylaminopropenoate **46** (2.480 g, 0.01 mole), glycine (0.750 g, 0.01 mole) and aqueous methanol (50%, 20 ml) was stirred at 20° for 5 minutes, then hydrochloric acid (36%, 1 ml) was added and the mixture was stirred at 20° for another 2 hours. The precipitate was collected by filtration to give **47**. The experimental and analytical data for compound **47** are given in Tables 1 and 2.

N-[*N*-(2-Benzoylamino-2-methoxycarbonylvinyl-1)glycyl]-glycine Ethyl Ester (**48**).

A mixture of *N*-(2-benzoylamino-2-methoxycarbonylvinyl-1)-glycine **47** (0.556 g, 0.002 mole), anhydrous *N,N*-dimethylformamide (10 ml) and glycine ethyl ester hydrochloride (0.280 g, 0.002 mole) was stirred at 0° for five minutes, then 4-methylmorpholine (0.22 ml) and after five minutes *N,N*-dicyclohexylcarbodiimide (0.412 g, 0.002 mole) was added. The mixture was stirred at 0° for 3 hours. *N,N'*-Dicyclohexylurea, which precipitated, was filtered off and washed with 5 ml of chloroform. The filtrate was evaporated *in vacuo* and the solid residue recrystallized from aqueous ethanol to give **48**. The experimental and analytical data for compound **48** are given in Tables 1 and 2.

The Removal of the 2-Benzoylamino-2-methoxycarbonylvinyl-1 Group. Preparation of *N*-[Glycyl]glycine Ethyl Ester Hydrochloride (**34**).

A mixture of *N*-[*N*-(2-benzoylamino-2-methoxycarbonylvinyl-1)glycyl]glycine ethyl ester **48** (0.726 g, 0.002 mole), anhydrous ethanol (10 ml), 2-amino-4,6-dimethylpyrimidine (0.246 g, 0.002 mole) and hydrochloric acid (36%, 0.2 ml) was refluxed for five hours, cooled and the solvent was evaporated *in vacuo*. The residue was triturated with dichloromethane (15 ml) and the precipitate collected by filtration to give **34** in 79% yield, mp 182-184° (washed with dichloromethane), lit [14] mp 182°.

4-Heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolones **50**, Dehydrodipeptides **51-56** and Dehydrotripeptides **57** [8].

4-Heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolones **50**, dehydrodipeptides **51-56** and dehydrotripeptides **57** were prepared according to the procedure described in the literature [8].

Coupling of Dehydropeptides **51-56** with Dipeptide Esters **32-41** and Amino Acid Esters by 2-Chloro-4,6-dimethoxy-1,3,5-triazine [10]. Preparation of Dehydropeptides **58-85** [11,12]. General Procedure.

Couplings by 2-chloro-4,6-dimethoxy-1,3,5-triazine [10] were performed by a slightly modified procedure described in the literature [11,12]. While stirring at 0° *N*-methylmorpholine (0.11 ml) was added to the mixture of carboxy component **51-57** (0.001 mole), anhydrous *N,N*-dimethylformamide (5 ml) and 2-chloro-4,6-dimethoxy-1,3,5-triazine [10] (0.001 mole) and stirring was

continued for another three hours. Ice cold solution of a hydrochloride of amino-component (0.001 mole) and *N*-methylmorpholine (0.11 ml) in 5 ml of anhydrous *N,N*-dimethylformamide was poured into initial reaction mixture and the whole mixture was stirred at 0° for another three hours. Then solvent was evaporated *in vacuo*, residue redissolved in 15 ml of ethyl acetate and washed first with water (5 ml) then with 10% hydrochloric acid (5 ml), saturated aqueous sodium bicarbonate (5 ml) and finally with water (5 ml). Organic phase was dried over anhydrous sodium sulphate, filtered and solvent evaporated *in vacuo*. The residue was tritruated with petroleum ether and the precipitate collected by filtration to give dehydropeptides **58-85**. The experimental and analytical data for dehydropeptides **58-85** are given in Tables 1 and 2.

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