The Transformations of 4-Heteroarylaminomethylene-5(4*H*)-oxazolones into Dehydropeptide Derivatives.

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2-Phenyl-4-heteroarylaminomethylene-5(4*H*)-oxazolones **3**, which were prepared from the corresponding *N,N*-dimethyl-*N'*-heteroarylformamidines **1** and hippuric acid **2** in acetic anhydride, react with amino acids giving dehydropeptide derivatives **4**, **5**, and **6** as products. Dehydration of *N*-protected peptides **7-10**, containing glycine at the C-terminal, followed by the reaction with formamidines **1** gave 2-substituted-4-heteroarylaminomethylene-5(4*H*)-oxazolones **11-14**.

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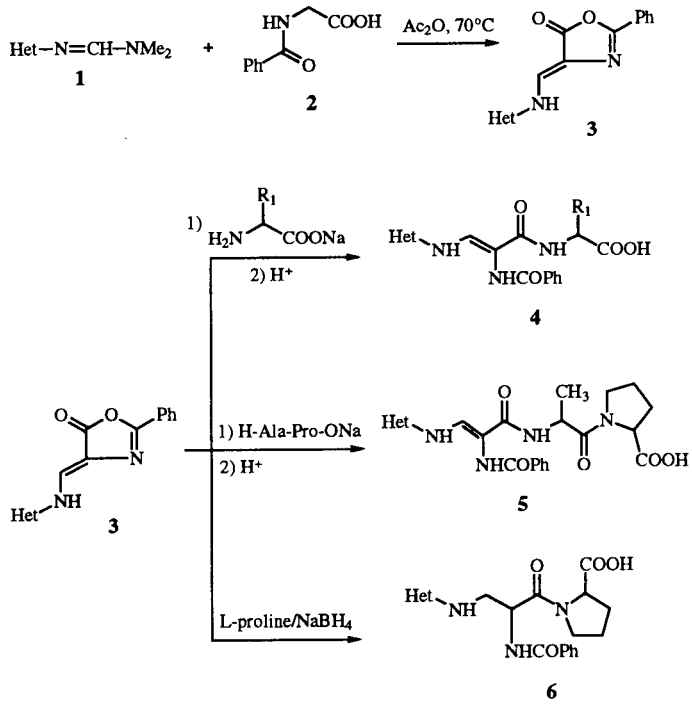
In our previous communications we have reported the synthesis of β-heteroaryl- and β-heteroarylamino-α-amino acid derivatives and their α,β-dehydro analogues [1-5]. The synthetic pathway proceeds *via* 4-heteroarylaminomethylene-5(4*H*)-oxazolones, which are prepared by reacting *N,N*-dimethyl-*N'*-heteroarylformamidines with *N*-acylglycines in the presence of a dehydrating agent. Oxazolone ring can be cleaved by various nucleophiles giving the corresponding β-heteroaryl- and β-heteroarylamino-α,β-dehydro-α-amino acid derivatives. When ring opening was performed under reductive conditions, also the saturation of a C=C double bond took place.

In this paper we wish to report some reactions of 4-heteroarylaminomethylene-5(4*H*)-oxazolones with amino acids and peptides. The following *N,N*-dimethyl-*N'*-heteroarylformamidines, prepared from the corresponding heteroarylamines and *N,N*-dimethylformamide dimethyl acetal (DMFDMA) [6], 2-methoxycarbonyl-3-pyridyl **1a**, 3-nitro-2-pyridyl **1b**, 5-nitro-2-pyridyl **1c**, 3,5-dibromo-2-pyridyl **1d**, 3-isoxazolyl **1e**, 5-methyl-3-isoxazolyl **1f**, 6-chloro-3-pyridazinyl **1g**, 2-pyrimidinyl **1h**, 4-methyl-2-pyrimidinyl **1i**, 4,6-dimethyl-2-pyrimidinyl **1j**, 4-chloro-6-methyl-2-pyrimidinyl **1k**, 5-ethoxycarbonyl-2-methylthio-4-pyrimidinyl **1l**, 3-methoxycarbonyl-2-pyrazinyl **1m**, and 4-(2,1,3-benzothiadiazolyl) **1n**, were employed for the preparation of 4-heteroarylaminomethylene-5(4*H*)-oxazolones (**3**).

When sodium salt of an amino acid reacted with 2-phenyl-4-heteroarylaminomethylene-5(4*H*)-oxazolone **3**, the ring opening and the formation of a dehydrodipeptide **4** took place. Analogously the reaction of **3** with *N*-alanyl-proline gave a dehydrotripeptide **5**. Ring opening with proline was performed in the presence of sodium borohydride and the saturation of a C=C double bond took place giving a dipeptide **6**. The attempts to prepare peptides **6** with amino acids other than proline were unsuccessful (Scheme 1).

Since peptides were derived from *N*-benzoylglycine, the β-heteroarylamino substituted amino acid fragment was located at the *N*-terminal of the peptide chain. In order to prepare some peptides containing β-heteroarylaminosubstituted amino acid fragment at the C-terminal

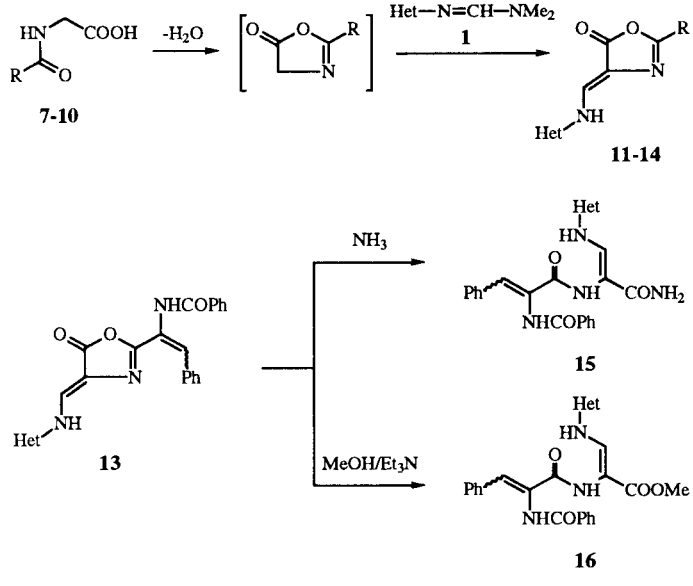
Scheme 1



Compounds **1, 3-6, 11-16**	Heterocyclic moiety
a	2-methoxycarbonyl-3-pyridyl
b	3-nitro-2-pryidyl
c	5-nitro-2-pyridyl
d	3,5-dibromo-2-pyridyl
e	3-izoxazolyl
f	5-methyl-3-izoxazolyl
g	6-chloro-3-pyridazinyl
h	2-pyrimidinyl
i	4-methyl-2-pyrimidinyl
j	4,6-dimethyl-2-pyrimidinyl
k	4-chloro-6-methyl-2-pyrimidinyl
l	5-ethoxycarbonyl-2-methylthio-4-pyrimidinyl
m	3-methoxycarbonyl-2-pyrazinyl
n	4-(2,1,3-benzothiadiazolyl

of the peptide chain we decided to carry out the dehydration of some peptides having glycine at the C-terminal. The following peptides were chosen for this purpose: *N*-[*N*-benzoylglycyl]glycine **7** [7], *N*-[*N*-benzyloxycarbonylglycyl]glycine **8** [8], *N*-[*N*-(1-benzoylamino-2-phenyl-1-vinyl)glycyl]glycine **9** [9], and *N*-[*N*-(2-benzoyl-2-ethoxycarbonyl-1-vinyl)glycyl]glycine **10**. In all cases the dehydration followed by the reaction with *N,N*-dimethyl-*N'*-heteroarylformamidine gave the corresponding 2-substituted-4-heteroarylaminomethylene-5(4*H*)-oxazolones **11-14**. Ring opening of **13** with methanol or ammonia afforded bis(dehydro)dipeptides **15** and **16** (Scheme 2).

Scheme 2



Compound	R
7, 11	benzoylaminomethyl
8, 12	benzyloxycarbonylaminoethyl
9, 13	1-benzoylamino-2-phenyl-1-vinyl
10, 14	2-benzoyl-2-ethoxycarbonyl-1-vinyl

Since in most cases the racemic mixtures of amino acids were used in these experiments, no further attempts were undertaken in order to determine the configurations at chiral centers in the peptides.

Table 1

Experimental Data

Compound	Yield %	mp °C	Molecular formula Analyses
3a	31	337-339 (from ethanol)	$C_{18}H_{15}N_3O_4$ Calcd. C, 64.09; H, 4.48; N, 12.46 Found C, 64.09; H, 4.38; N, 12.09
3b	81	198-199 (washed with ethanol)	$C_{15}H_{10}N_4O_4$ Calcd. C, 58.07; H, 3.25; N, 18.06 Found C, 58.06; H, 3.31; N, 18.25
3c	85	263-265 (from DMF/ ethanol)	$C_{15}H_{10}N_4O_4$ Calcd. C, 58.07; H, 3.25; N, 18.06 Found C, 57.72; H, 3.33; N, 18.42
3d	73	186-188 (washed with ethanol)	$C_{15}H_9Br_2N_3O_2$ Calcd. C, 42.59; H, 2.14; N, 9.93 Found C, 42.86; H, 2.11; N, 10.02
3e	21	151-153 (from ethanol)	$C_{13}H_9N_3O_3$ Calcd. C, 61.18; H, 3.55; N, 16.46 Found C, 61.25; H, 3.77; N, 16.06
3f	35	223-225 (from ethanol/ DMF)	$C_{14}H_{11}N_3O_3$ Calcd. C, 62.45; H, 4.12; N, 15.61 Found C, 62.13; H, 4.11; N, 15.54
3m	75	203-205 (washed with ethanol)	$C_{16}H_{12}N_4O_4$ Calcd. C, 59.26; H, 3.73; N, 17.28 Found C, 58.91; H, 3.66; N, 17.16
3n	39	206-207 (from ethanol)	$C_{16}H_{10}N_4O_2S$ Calcd. C, 59.62; H, 3.13; N, 17.38 Found C, 59.64; H, 3.31; N, 17.51
4b-Ala-OH	30	191-193 (from acetonitrile/ DMF/water)	$C_{18}H_{17}N_5O_6$ Calcd. C, 54.14; H, 4.29; N, 17.54 Found C, 53.90; H, 4.27; N, 17.50
4b-Asp-OH	40	151-153 (from aceto- nitrile/water)	$C_{19}H_{17}N_5O_8$ Calcd. C, 51.47; H, 3.86; N, 15.80 Found C, 51.73; H, 3.83; N, 15.91
4b-Gla-OH	56	126-130 (from aceto- nitrile/water)	$C_{20}H_{19}N_5O_8$ Calcd. C, 52.52; H, 4.19; N, 15.31 Found C, 52.54; H, 4.40; N, 15.21
4b-Gly-OH	43	208-212 (from acetonitrile)	$C_{17}H_{15}N_5O_6$ Calcd. C, 52.99; H, 3.92; N, 18.17 Found C, 53.23; H, 3.62; N, 18.23
4b-Leu-OH	37	114-116 (from aceto- nitrile/water)	$C_{21}H_{23}N_5O_6$ Calcd. C, 57.14; H, 5.25; N, 15.86 Found C, 57.39; H, 5.44; N, 15.82
4b-Met-OH	79	165-166 (from aceto- nitrile/water)	$C_{20}H_{21}N_5O_6S$ Calcd. C, 52.28; H, 4.61; N, 15.24 Found C, 51.94; H, 4.83; N, 15.33
4b-Phe-OH	51	202-204 (from aceto- nitrile/water)	$C_{24}H_{21}N_5O_6$ Calcd. C, 60.63; H, 4.45; N, 14.73 Found C, 60.94; H, 4.51; N, 14.52
4b-Pro-OH	59	185-186 (from aceto- nitrile/water)	$C_{20}H_{19}N_5O_6$ Calcd. C, 56.47; H, 4.50; N, 16.46 Found C, 56.38; H, 4.52; N, 16.40
4b-Ser-OH	33	158-162 (from aceto- nitrile/water)	$C_{18}H_{17}N_5O_7$ Calcd. C, 52.05; H, 4.13; N, 16.86 Found C, 52.25; H, 4.22; N, 16.50
4c-Gly-OH	39	229-232 (from ethanol/ DMF/water)	$C_{17}H_{15}N_5O_6$ Calcd. C, 52.99; H, 3.92; N, 18.17 Found C, 52.93; H, 4.05; N, 18.07
4c-Pro-OH	17	237-238 (from ethanol/ DMF/water)	$C_{20}H_{19}N_5O_6$ Calcd. C, 56.47; H, 4.50; N, 16.46 Found C, 56.22; H, 4.45; N, 16.35
4d-Ala-OH	9	125-127 (from acetonitrile/ DMF/water)	$C_{18}H_{16}Br_2N_4O_4$ Calcd. C, 42.21; H, 3.15; N, 10.94 Found C, 41.85; H, 2.99; N, 10.59
4d-Phe-OH	18	102-105 (from aceto- nitrile/water)	$C_{24}H_{20}Br_2N_4O_4$ Calcd. C, 49.00; H, 3.43; N, 9.52 Found C, 48.59; H, 3.40; N, 9.20
4d-Pro-OH	61	91-93 (from aceto- nitrile/water)	$C_{20}H_{18}Br_2N_4O_4$ Calcd. C, 44.63; H, 3.37; N, 10.41 Found C, 44.30; H, 3.14; N, 10.28

Table 1 (continued)

Compound	Yield %	mp °C	Molecular formula Analyses
4f-Gly-OH	60	186-190 (from ethanol/ water)	$C_{16}H_{16}N_4O_5$ Calcd. C, 55.81; H, 4.68; N, 16.27 Found C, 55.93; H, 4.76; N, 15.94
4g-β-Ala-OH	31	217-218	$C_{17}H_{16}ClN_5O_4$ Calcd. C, 52.38; H, 4.14; N, 17.97 Found C, 52.26; H, 4.18; N, 18.16
4g-Pro-OH	26	211-213 (from acetonitrile)	$C_{19}H_{18}ClN_5O_4$ Calcd. C, 54.88; H, 4.36; N, 16.84 Found C, 54.86; H, 4.44; N, 16.82
4j-Gly-OH	44	240-247 dec (from ethanol/ water)	$C_{18}H_{19}N_5O_4$ Calcd. C, 58.53; H, 5.18; N, 18.96 Found C, 58.60; H, 5.29; N, 18.90
4j-Nle-OH	59	165-175 (from ethanol/ water)	$C_{22}H_{27}N_5O_4$ Calcd. C, 62.10; H, 6.40; N, 16,46 Found C, 62.11; H, 6.56; N, 16.53
4j-Phe-OH	31	203-210 (from ethanol/ water)	$C_{25}H_{25}N_5O_4$ Calcd. C, 65.35; H, 5.48; N, 15.24 Found C, 65.74; H, 5.67; H, 15.23
4j-Pro-OH	72	115-130 (from ethanol/ water)	$C_{21}H_{23}N_5O_4 + H_2O$ Calcd. C, 59.00; H, 5.90; N, 16.38 Found C, 59.21; H, 6.04; N, 16.43
4j-Trp-OH	36	247-250 (from ethanol/ water)	$C_{27}H_{26}N_6O_4$ Calcd. C, 65.05; H, 5.26; N, 16.86 Found C, 65.28; H, 5.44; N, 16.75
4k-Nle-OH	32	150-155 (from ethanol/ water)	$C_{21}H_{24}ClN_5O_4$ Calcd. C, 56.57; H, 5.43; N, 15.71 Found C, 56.59; H, 5.49; N, 15.74
4k-Phe-OH	44	159-163 (from ethanol/ water)	$C_{24}H_{22}ClN_5O_4$ Calcd. C, 60.06; H, 4.62; N, 14.59 Found C, 60.06; H, 4.59; N, 14.41
4l-Gly-OH	71	244-248 (washed with water)	$C_{20}H_{21}N_5O_6S$ Calcd. C, 52.28; H, 4.61; N, 15.24 Found C, 52.51; H, 4.62; N, 15.15
4l-Nle-OH	72	87-90 (washed with water)	$C_{24}H_{29}N_5O_6S$ Calcd. C, 55.91; H, 5.67; N, 13.58 Found C, 56.24; H, 5.65; N, 13.28
4l-Phe-OH	81	91-93 (washed with water)	$C_{27}H_{27}N_5O_6S$ Calcd. C, 59.01; H, 4.95; N, 12.74 Found C, 58.89; H, 5.08; N, 12.97
4l-Pro-OH	84	130-134 (from ethanol/ water)	$C_{23}H_{25}N_5O_6S$ Calcd. C, 55.30; H, 5.04; N, 14.02 Found C, 55.42; H, 5.12; N, 13.95
4m-Gly-OH	73	206-208 (washed with ether)	$C_{18}H_{17}N_5O_6 \times H_2O$ Calcd. C, 51.80; H, 4.59; N, 16.78 Found C, 51.48; H, 4.53; N, 16.41
5b	40	127-132 (from ethanol/ water)	$C_{23}H_{24}N_6O_7$ Calcd. C, 55.64; H, 4.87; N, 16.93 Found C, 55.61; H, 4.62; N, 16.98
5k	36	175-180 (from methanol/water)	$C_{23}H_{25}ClN_6O_5 \times H_2O$ Calcd. C, 53.23; H, 5.24; N, 16.19 Found C, 53.22; H, 5.17; N, 16.17
5l	39	103-105 (washed with water and ether)	$C_{26}H_{30}N_6O_7S$ Calcd. C, 54.73; H, 5.30; N, 14.73 Found C, 54.43; H, 5.10; N, 14.53
6g	57	170-174 (from methanol/water)	$C_{19}H_{20}ClN_5O_4$ Calcd. C, 54.61; H, 4.82; N, 16.76 Found C, 54.28; H, 4.82; N, 16.71
6k	42	120-140 (washed with water)	$C_{20}H_{22}ClN_5O_4$ Calcd. C, 55.62; H, 5.13; N, 16.21 Found C, 55.42; H, 5.14; N, 16.16
10	84	181-183 (from water)	$C_{16}H_{18}N_2O_6$ Calcd. C, 57.48; H, 5.43; N, 8.38 Found C, 57.68; H, 5.64; N, 7.94

Table 1 (continued)

Compound	Yield %	mp °C	Molecular formula Analyses
11h	31	211-214 (washedwith methanol)	$C_{16}H_{13}N_5O_3$ Calcd. C, 59.44 H, 4.05; N, 21.66 Found C, 59.76; H, 4.31; N, 21.38
12h	42	193-195 (from toluene/ 1-propanol)	$C_{17}H_{15}N_5O_4$ Calcd. C, 57.79; H, 4.28; N, 19.82 Found C, 58.08; H, 4.39; N, 19.81
12i	23	165-167 (from toluene)	$C_{18}H_{17}N_5O_4$ Calcd C, 58.85; H, 4.66; N, 19.06 Found C, 59.16; H, 4.79; N, 18.72
13i	33	222-224 dec (washed with toluene)	$C_{24}H_{19}N_5O_3$ Calcd. C, 67.76; H, 4.50; N, 16.46 Found C, 67.62; H, 4.67; N, 16.47
13j	48	245-248 (washed with toluene)	$C_{25}H_{21}N_5O_3$ Calcd. C, 68.33; H, 4.82; N, 15.94 Found C, 68.58; H, 5.05; N, 15.82
13k	51	250-253 (washed with methanol)	$C_{24}H_{18}ClN_5O_3$ Calcd. C, 62.68; H, 3.94; N, 15.23 Found C, 63.05; H, 4.05; N, 15.26
14h	26	146-148 (from ethanol)	$C_{21}H_{19}N_5O_5$ Calcd. C, 59.85; H, 4.54; N, 16.62 Found C, 60.10; H, 4.64; N, 16.99
14i	15	159-161 (from methanol)	$C_{22}H_{21}N_5O_5$ Calcd. C, 60.69; H, 4.86; N, 16.08 Found C, 60.66; H, 4.97; N, 15.91
14j	26	170-173 (from ethanol)	$C_{23}H_{23}N_5O_5$ Calcd. C, 61.46; H, 5.16; N, 15.58 Found C, 61.18; H, 5.45; N, 15.64
15j	90	242-245 (from meth-anol/water)	$C_{25}H_{24}N_6O_3$ Calcd. C, 65.78; H, 5.30; N, 18.41 Found C, 65.58; H, 5.64; N, 18.74
16i	72	136-140 (from meth-anol/water)	$C_{25}H_{23}N_5O_4$ Calcd. C, 65.64; H, 5.07; N, 15.31 Found C, 65.42; H, 5.10; N, 15.16

Table 2

^{1}H NMR Data

Compound	Solvent	δ (TMS)
3a	$CDCl_3$	1.53 (3H, t, C*H*$_3$CH$_2$), 4.60 (2H, q, CH$_2$CH$_3$), 7.46-7.85 (6H, m, 3H-Ph, H$_{4'}$, H$_{5'}$, C*H*NH, , 8.46 (1H, dd, H$_{6'}$) 11.35 (1H, d, NH), $J_{CH_3\text{-}CH_2}$ = 7.1 Hz, $J_{CH\text{-}NH}$ = 11.7 Hz, $J_{H5'H6'}$ = 4.1 Hz, $J_{H4'H6'}$ = 1.5 Hz
3b	$CDCl_3$	7.1-7.6 (5H, m, Ph), 8.0-8.2 (2H, m, H5' and 6'), 8.65 (1H, dd, H4'), 8.66 (1H, d, C*H*NH, 8.9 (1H, d, NH), $J_{H5'H6'}$ = 7.6 Hz, $J_{CH\text{-}NH}$ = 11.7 Hz
3c	DMSO	7.45 (1H, d, H$_{3'}$), 7.59-7.65 (3H, m, Ph), 7.97-8.08 (2H, m, Ph), 8.33 (1H, s, C*H*NH, 8.55 (1H, d, H$_{4'}$), 9.18 (1H, d, H$_{6'}$), 11.64 = (1H, br s, NH), $J_{H3'H4'}$ = 9.3 Hz, $J_{H4'H6'}$ = 2.4 Hz
3d	DMSO	2.9 (1H, br s, NH), 7.1-8.0 (5H, m, Ph), 8.2-8.8 (3H, m, C*H*NH, H$_{4'}$ and H$_{6'}$)
3e	DMSO	6.63 (1H, d, H$_{4'}$), 7.52-7.68 (3H, m, Ph), 7.70 (1H, d, C*H*NH), 7.95-8.05 (2H, m, Ph), 8.82 (1H, d, H$_{5'}$), 10.98 (1H, d, NH), $J_{H4'H5'}$ = 1.7 Hz, $J_{CH\text{-}NH}$ = 11.7 Hz
3f	DMSO	2.39 (3H, s, CH$_3$), 6.28 (1H, s, H$_{4'}$), 7.55-7.69 (4H, m, 3H-Ph and C*H*NH), 7.93-8.04 (2H, m, Ph), 11.01 (1H, br s, NH).

Table 2 (continued)

Compound	Solvent	δ (TMS)
3m	DMSO	4.0 (3H, s, OMe), 7.6-8.0 (5H, m, Ph), 8.4 (1H, d, C*H*NH), 8.5 (1H, d, NH), 8.45 (1H, d, $H_{5'}$), 8.6 (1H, d, $H_{6'}$), J_{CH-NH} = 12 Hz, $J_{H5'H6'}$ = 2.2 Hz
3n	$CDCl_3$	7.21-7.36 (9H, m, Ar), 7.56 (1H, dd, $H_{5'}$), 7.75 (1H, dd, $H_{6'}$), 8.28 (1H, dd, H_7), 8.46 (1H, s, C*H*NH), $J_{H5'H6'}$ = 5.1 Hz, $J_{H5'H7'}$ = 1.2 Hz, $J_{H6'H7'}$ = 8.5 Hz
4b-Ala-OH	DMSO	1.35 (3H, d, CH_3), 4.37 (1H, m, C*H*CH_3), 7.15 (1H, dd, $H_{5'}$), 7.53-7.61 (3H, m, Ph), 8.01-8.12 (3H, m, 2H-Ph and N*H*C*H*CH_3), 8.47 (1H, d, C*H*NH), 8.57 (1H, dd, $H_{4'}$), 8.68 (1H, dd, $H_{6'}$), 9.68 (1H, s, N*H*COPh), 9.88 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H4'H6'}$ = 1.7 Hz, $J_{H5'H6'}$ = 4.6 Hz, J_{CH3-CH} = 7.3 Hz, J_{NH-CH} = 10.75 Hz
4b-Asp-OH	DMSO	2.72-2.79 (2H, m, CH_2), 4.59-4.81 (1H, m, C*H*COOH), 7.15 (1H, dd, $H_{5'}$), 7.55-7.61 (3H, m, Ph), 7.99-8.12 (3H, m, 2H-Ph and N*H*CHCOOH), 8.49 (1H, d, C*H*NH, 8.51 (1H, dd, $H_{4'}$), 8.65 (1H, dd, $H_{6'}$), 9.68 (1H, s, N*H*COPh), 9.94 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H5'H6'}$ = 4.6 Hz, $J_{H4'H6'}$ = 1.7 Hz, J_{NH-CH} = 11.0 Hz
4b-Gla-OH	DMSO	1.93-2.14 (2H, m, CH_2), 2.27-2.43 (2H, m, CH_2), 4.28-4.52 (1H, m, C*H*COOH), 7.15 (1H, dd, $H_{5'}$), 7.56-7.62 (3H, m, Ph), 8.02-8.23 (3H, m, 2H-Ph and N*H*CHCOOH), 8.48 (1H, d, C*H*NH, 8.58 (1H, dd, $H_{4'}$), 8.68 (1H, dd, $H_{6'}$), 9.72 (1H, s, N*H*COPh), 9.96 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H5'H6'}$ = 4.6 Hz, $J_{H4'H6'}$ = 1.7 Hz, J_{NH-CH} = 11.0 Hz
4b-Gly-OH	DMSO	3.84 (2H, d, CH_2), 7.15 (1H, dd, $H_{5'}$), 7.48-7.61 (3H, m, Ph), 8.02-8.13 (3H, m, 2H-Ph and N*H*CH_2), 8.39 (1H, d, C*H*NH), 8.57 (1H, dd, $H_{4'}$), 8.67 (1H, dd, $H_{6'}$), 9.75 (1H, s, N*H*COPh), 9.93 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H4'H6'}$ = 1.7 Hz, $J_{H5'H6'}$ = 4.6 Hz, J_{CH2-NH} = 5.9 Hz, J_{NH-CH} = 11.1 Hz
4b-Leu-OH	DMSO	0.85-0.97 (6H, m, $2CH_3$), 1.53-1.82 (5H, m, CH_2CH_2CH$(CH_3)_2$), 4.26-4.54 (1H, m, C*H*COOH), 7.15 (1H, dd, $H_{5'}$), 7.56-7.61 (3H, m, Ph), 8.01-8.42 (3H, m, 2H-Ph and N*H*CHCOOH), 8.57 (1H, d, C*H*NH), 8.58 (1H, dd, $H_{4'}$), 8.68 (1H, dd, $H_{6'}$), 9.67 (1H, s, N*H*COPh), 10.02 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H4'H6'}$ = 1.7 Hz, $J_{H5'H6'}$ = 4.6 Hz, J_{NH-CH} = 10.75 Hz
4b-Met-OH	DMSO	1.98-2.13 (2H, d, CH_2CH), 2.04 (3H, s, SMe), 2.55 (2H, m, CH_2S), 4.40 (1H, m, C*H*CH_2), 7.15 (1H, dd, $H_{5'}$), 7.54-7.62 (3H, m, Ph), 8.01-8.10 (3H, m, 2H-Ph and N*H*CHCOOH), 8.47 (1H, d, C*H*NH), 8.56 (1H, dd, $H_{4'}$), 8.68 (1H, dd, $H_{6'}$), 9.75 (1H, s, N*H*COPh), 9.96 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H5'H6'}$ = 4.6 Hz, $J_{H4'H6'}$ = 1.7 Hz, J_{NH-CH} = 11.5 Hz
4b-Phe-OH	DMSO	3.08 (2H, d, CH_2CH), 4.52-4.59 (1H, m, C*H*CH_2), 7.15 (1H, dd, $H_{5'}$), 7.54-7.62 (3H, m, Ph), 7.82-8.08 (3H, m, 2H-Ph and N*H*CHCH_3), 8.46 (1H, d, C*H*NH), 8.61-8.70 (2H, m, $H_{4'}$ and $H_{6'}$), 9.65 (1H, s, N*H*COPh), 10.02 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.2 Hz, $J_{H5'H6'}$ = 4.5 Hz, J_{CH2-CH} = 7.1 Hz, J_{NH-CH} = 11.48 Hz
4b-Pro-OH	DMSO	1.80-2.19 (4H, m, $2CH_2$), 3.22-3.76 (2H, m, CH_2), 4.30-4.49 (1H, m, CH-Pro), 7.17 (1H, dd, $H_{5'}$), 7.60-8.74 (9H, m, Ph, $H_{4'}$, $H_{6'}$, N*HCH*), 9.90-10.88 (1H, m, NH), $J_{H4'H5'}$ = 8.2 Hz, $J_{H5'H6'}$ = 4.5 Hz
4b-Ser-OH	DMSO	3.76 (2H, d, CH_2), 4.26-4.52 (1H, m, C*H*COOH), 7.14 (1H, dd, $H_{5'}$), 7.56-7.63 (3H, m, Ph), 7.86 (1H, d, NHCHCOOH), 8.02-8.29 (2H, m, Ph), 8.51 (1H, d, C*H*NH), 8.54-8.70 (2H, m, $H_{4'}$ and $H_{6'}$), 9.83 (1H, s, N*H*COPh), 9.95 (1H, d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H5'H6'}$ = 4.6 Hz, J_{CH2-CH} = 4.4 Hz, J_{NH-CH} = 11.5 Hz
4c-Gly-OH	DMSO	3.90 (2H, d, CH_2), 7.12 (1H, d, $H_{3'}$), 7.50-7.58 (3H, m, 3H-Ph), 7.66-8.12 (3H, m, 2H-Ph and N*H*CHCOOH), 8.37 (1H, d, C*H*NH), 8.39 (1H, dd, $H_{4'}$), 9.10 (1H, d, $H_{6'}$), 9.42 (1H, s, N*H*COPh), 10.64 (1H, d, N*H*CH), $J_{H3'H4'}$ = 9.28 Hz, $J_{H4'H6'}$ = 2.44 Hz, J_{CH2-NH} = 6.34 Hz, J_{NH-CH} = 10.99 Hz
4c-Pro-OH	DMSO	1.88-2.25 (4H, m, $2CH_2$), 3.30-3.59 (2H, m, CH_2), 4.33-4.41 (1H, m, CHCOOH), 7.05 (1H, d, H3'), 7.52-7.99 (6H, m, 5H-Ph and CHNH), 8.35 (1H, dd, H4'), 9.07 (1H, d, H6'), 9.64 (1H, s, NHCOPh), 9.82 (1H, d, N*H*CH), $J_{H3'H4'}$ = 9.28 Hz, $J_{H4'H6'}$ = 2.44 Hz, J_{NH-CH} = 10.99 Hz
4d-Ala-OH	DMSO	1.30 (3H, d, CH_3), 4.32 (1H, m, C*H*COOH), 7.60-8.50 (approx. 10H, m, Ph, C*H*, N*H*, $H_{4'}$, $H_{6'}$)
4d-Phe-OH	DMSO	3.15 (2H, d, CH_2), 4.01-4.57 (1H, m, C*H*COOH), 7.18-8.50 (14H, m, 10H-Ph, N*HCH*, $H_{4'}$ and $H_{6'}$)
4d-Pro-OH	DMSO	1.77-2.38 (4H, m, $2CH_2$), 3.59-3.94 (2H, m, CH_2), 4.24-4.37 (1H, m, C*H*COOH), 7.35-8.56 (8H, m, 5H-Ph, C*H*NH, $H_{4'}$ and $H_{6'}$)
4f-Gly-OH	DMSO	2.31 (3H, s, 5'-Me), 3.76 (2H, d, CH_2), 5.97 (1H, s, $H_{4'}$), 7.16-8.11 (7H, m, 5H-Ph, N*H*CH_2 and C*H*NH), 9.02 (1H, d, N*H*CH), 9.25 (1H, br s, N*H*COPh), J_{CH2-NH} = 5.37 Hz, J_{NH-CH} = 11 Hz
4g-β-Ala-OH	DMSO	2.34-2.52 (2H, m, CH_2), 3.06-3.81 (2H, m, CH_2), 7.36 (1H, d, $H_{4'}$), 7.65 (1H, d, $H_{5'}$), 7.57-7.67 (4H, m, 3H-Ph and N*H*CH_2), 8.00-8.10 (2H, m, 2H-Ph), 8.32 (1H, d, C*H*NH), 9.25 (1H, d, N*H*CH), 9.32 (1H, s, N*H*COPh), $J_{H4'H5'}$ = 9.52 Hz, J_{NH-CH} = 11.96 Hz
4g-Pro-OH	DMSO	1.89-2.07 (4H, m, $2CH_2$), 3.52-3.69 (2H, m, CH_2), 4.27-4.43 (1H, m, C*H*COOH), 7.33 (1H, d, H4'), 7.50-7.56 (3H, m, 3H-Ph), 7.64 (1H, d, H5'), 7.83 (1H, d, C*H*NH), 8.00-8.10 (2H, m, 2H-Ph), 9.33 (1H, d, N*H*CH), 9.62 (1H, s, NHCOPh), $J_{H4'H5'}$ = 9.52 Hz, JNH-CH = 11.96 Hz
4j-Gly-OH	DMSO	2.32 (6H, s, 4',6'-CH_3), 3.78 (2H, d, CH_2), 6.74 (1H, s, $H_{5'}$), 7.48-7.56 (3H, m, Ph), 7.72 (1H, t, N*H*CH_2), 7.94-8.08 (2H, m, Ph), 8.24 (1H, d, C*H*NH-Het), 9.23 (1H, s, N*H*COPh), 9.30 (1H, d, CHN*H*-Het), J_{NH-CH_2} = 5.7 Hz, J_{CH-NH} = 11.8 Hz

Table 2 (continued)

Compound	Solvent	δ (TMS)
4j-Nle-OH	DMSO	0.83 (3H, t, CH_3CH_2), 1.13-1.29 (4H, m, $CH_2CH_2CH_3$), 1.52-1.81 (2H, m, $CH_2CHCOOH$), 2.32 (6H, s, 4',6'-CH_3), 4.07-4.35 (1H, m, *CH*COOH), 6.74 (1H, s, $H_{5'}$), 7.35-7.56 (4H, m, 3H-Ph and N*H*CHCOOH), 7.94-8.07 (2H, m, Ph), 8.21 (1H, d, *CH*NH-Het), 9.23 (1H, s, N*H*COPh), 9.32 (1H, d, CHN*H*-Het), J_{CH-NH} = 12.4 Hz
4j-Phe-OH	DMSO	2.32 (6H, s, 4',6'-CH_3), 3.03 (2H, d, CH_2Ph), 4.42-4.62 (1H, m, *CH*CH_2Ph), 6.74 (1H, s, $H_{5'}$), 7.15 (5H, s, *Ph*CH_2), 7.29 (1H, t, N*H*CHCOOH), 7.51-7.56 (3H, m, PhCO), 7.84-8.07 (2H, m, PhCO), 8.24 (1H, d, *CH*NH), 9.21 (1H, s N*H*COPh), 9.40 (1H, d, N*H*CH), J_{CH_2-CH} = 6.4 Hz, $J_{COCH-NH}$ = 7.1 Hz J_{CH-NH} = 11.8 Hz
4j-Pro-OH	DMSO	1.87 (4H, m, $2CH_2$), 2.31 (6H, s, 4',6'-CH_3), 3.54 (2H, m, CH_2), 4.32 (1H, m, CHCO), 6.71 (1H, s, $H_{5'}$), 7.47-7.74 (3H, m, 3H-Ph), 7.93-8.04 (2H, m, 2H-Ph), 7.67 (1H, d, CH=C), 9.37 (1H, d, N*H*CH=C), 9.48 (1H, s, N*H*COPh), J_{CH-NH} = 11.4 Hz
4j-Trp-OH	DMSO	2.31 (6H, s, 4',6'-CH_3), 3.13-3.22 (2H, m, CH_2), 4.57-4.65 (1H, m, *CH*COOH), 6.73, (1H, s, $H_{5'}$) 6.89-7.56 (8H, m, Ar), 7.97-8.05 (2H, m, Ph), 8.27 (1H, d, *CH*NH-Het), 9.23 (1H, s, N*H*COPh), 9.37 (1H, d, CHN*H*-Het), 10.82 (1H, s, NH-indole), J_{CH-NH} = 11.8 Hz
4k-Nle-OH	DMSO	0.83 (3H, t, CH_3CH_2), 1.248 (4H, m, $CH_2CH_2CH_3$), 1.70 (2H, m, $CH_2CHCOOH$), 2.38 (3H, s, 6' -CH_3), 4.27 (1H, dt, *CH*COOH), 7.01 (1H, s, $H_{5'}$), 7.45-7.55 (4H, m, 3H-Ph and N*H*CHCOOH), 8.01-8.09 (2H, m, Ph), 8.07 (1H, d, *CH*NH-Het), 9.26 (1H, s, N*H*COPh), 9.97 (1H, d, CHN*H*-Het), J_{CH_2-CH} = 5.7 Hz, $J_{COCH-NH}$ = 7.1 Hz, J_{CH-NH} = 11.8 Hz
4k-Phe-OH	DMSO	2.38 (3H, s, 6'-CH_3), 3.02 (2H, d, CH_2), 4.50 (1H, dt, *CH*COOH), 7.02 (1H, s, $H_{5'}$), 7.15 (5H, s, *Ph*CH_2), 7.40 (1H, d, N*H*CHCOOH), 7.49-7.67 (3H, m, PhCO), 7.98-8.06 (2H, m, PhCO), 8.06 (1H, d, CHNH-Het), 9.26 (1H, s, N*H*COPh), 10.03 (1H, d, CHN*H*-Het), J_{CH_2-CH} = 5.7 Hz, $J_{COCH-NH}$ = 7.1 Hz, J_{CH-NH} = 12.0 Hz
4l-Gly-OH	DMSO	1.1-1.4 (3H, m, CH_3CH_2), 2.6 (3H, s, SMe), 3.8 (2H, d, CH_2NH), 4.2-4.6 (2H, m, CH_2CH_3), 7.5-8.8 (8H, m, 5H-Ph, N*H*CH_2, *CH*NH and $H_{6'}$), 9.7 (1H, br s, N*H*COPh), 10.2 (1H, d, N*H*CH)
4l-Nle-OH	$CDCl_3$	0.8-2.6 (15H, $3CH_3$ and $3CH_2$), 4.2-4.6 (3H, m, CH_2CH_3 and *CH*COOH), 7.2-8.8 (9H, m, 5H-Ph, 2NH, *CH*NH and $H_{6'}$), 10.1 (1H, d, N*H*CH)
4l-Phe-OH	DMSO	1.1-1.4 (3H, m, CH_3CH_2), 2.6 (3H, s, SMe), 3.4 (2H, d, CH_2Ph), 4.2-4.7 (3H, m, CH_2CH_3 and *CH*COOH), 7.2-8.8 (13H, m, 10H-Ph, NHCHCOOH, *CH*NH and $H_{6'}$), 9.6 (1H, s, N*H*COPh), 10.1 (1H, d, N*H*CH)
4l-Pro-OH	DMSO	1.2 (3H, t, CH_3CH_2), 1.4-2.2 (4H, m, $2CH_2$), 2.6 (3H, s, SMe), 3.1-3.6 (2H, m, CH_2), 4.1-4.4 (3H, m, CH_2CH_3 and *CH*COOH), 7.6-8.1 (7H, m, 5H-Ph, N*H*COPh and *CH*NH), 8.8 (1H, s, $H_{6'}$), 10.1 (1H, m, N*H*CH)

Table 2 (continued)

Compound	Solvent	δ (TMS)
4m-Gly-OH	DMSO	3.80 (3H, s, OMe), 3.80-3.96 (2H, m, CH_2), 7.59-7.61 (3H, m, 3H-Ph), 8.12-8.20 (3H, m, 2H-Ph and N*H*CHCOOH), 8.28 (1H, d, $H_{5'}$), 8.41 (1H, d, *CH*NH), 8.58 (1H, d, $H_{6'}$), 9.68 (1H, s, N*H*COPh), 9.97 (1H, d, N*H*CH), $J_{H5'H6'}$ = 2.20 Hz, J_{NH-CH} = 11.72 Hz
5b	DMSO	1.19-1.27 (5H, m, CH_3CH and CH_2), 1.33-1.35 (2H, m, CH_2), 3.57 (2H, m, CH_2), 4.11-4.31 (2H, m, 2CHCO), 7.21 (1H, dd, $H_{5'}$), 7.56-7.62 (m, 3H-Ph and NH), 7.89-8.05 (2H, m, 2H-Ph), 8.39 (1H, d, *CH*NH), 8.54-8.72 (2H, m, $H_{4'}$ and $H_{6'}$), 9.61 and 9.79 (1H, 2s, N*H*COPh),10.18 and 11.98 (1H, 2d, N*H*CH), $J_{H4'H5'}$ = 8.3 Hz, $J_{H5'H6'}$ = 4.64 Hz, J_{NH-CH} = 11.11 Hz
5k	DMSO	1.19-1.30 (3H, m, CH_3CH), 1.84-2.01 (4H, m, $2CH_2$), 2.37 (3H, s, 6'-CH_3), 3.27-3.70 (2H, m, CH_2), 4.18-4.67 (2H, m, 2CH), 7.01 and 7.07 (1H, 2s, $H_{5'}$), 7.50-7.57 (4H, m, 3H-Ph and NH), 7.97-8.05 (2H, m, 2H-Ph), 8.18 (1H, d, CH=C), 9.33 and 9.57 (1H, 2s, N*H*COPh), 9.99 (1H, d, N*H*CH=C), J_{CH-NH} = 11.7 Hz
5l	DMSO	1.23-1.44 (4H, m, $2CH_3$), 1.95-2.17 (2H, m, CH_2), 2.59 (3H, s, SMe), 3.35-4.66 (8H, m, $3CH_2$ and 2*CH*CO), 7.57-8.82 (8H, m, 5H-Ph, *CH*NH, N*H*$CHCH_3$ and $H_{6'}$), 9.74 (1H, br s, N*H*COPh)
6g	$CDCl_3$	2.03 (4H, m, $CH_2CH_2CHCOOH$), 2.24 and 2.33 (3H, 2s, 6'-CH_3), 3.84 (4H, m, CH_2N and CH_2NH-Het), 4.50 (1H, m, *CH*COOH), 5.31 (1H, m, *CH*NHCOPh), 6.37 and 6.44 (1H, 2s, $H_{5'}$), 7.27-7.43 (3H, m, Ph), 7.73-8.00 (2H, m, Ph)
6k	DMSO	1.98 (4H, m, $CH_2CH_2CHCOOH$), 3.40-3.88 (4H, m, CH_2N and CH_2NH-Het), 4.26-4.38 (1H, m, *CH*COOH), 5.00-5.18 (1H, m, *CH*NHCOPh), 6.99 (1H, d, $H_{5'}$), 7.21-7.56 (4H, m, 3H-Ph and $H_{4'}$), 7.83-7.96 (2H, m, Ph), 8.75 (1H, d, N*H*COPh) J_{NH-CH} = 8.1 Hz
10	DMSO	0.78 and 0.87 (3H, 2t, CH_3CH_2), 3.60-3.90 (4H, m, $2CH_2NH$), 4.00-4.18 (2H, m, CH_2O), 7.28-7.39 (5H, m, Ph), 7.83-8.05 (1H, br m, *CH*NH), 8.36 (1H, br t, N*H*CH_2COOH), 9.00 and 10.20 (1H, 2br m, N*H*CH), $J_{CH_3CH_2}$ = 7 Hz
11h	DMSO	4.42 (2H, d, CH_2NH), 7.15 (1H, t, $H_{5'}$), 7.44-7.58 (3H, m, Ph), 7.83-8.00 (2H, m, Ph), 8.22 (1H, d, *CH*NH), 8.65 (2H, d, $H_{4'}$ and $H_{6'}$), 9.08 (1H, t, N*H*CH_2), 11.30 (1H, d, N*H*CH), J_{CH_2-NH} = 5.5 Hz, J_{CH-NH} = 12.9 Hz, $J_{H4'H5'}$ = $J_{H5'H6'}$ = 5.0 Hz
12h	DMSO	4.18 (2H, d, CH_2NH), 5.09 (2H, s, CH_2Ph), 7.18 (1H, t, $H_{5'}$), 7.40 (5H, s, Ph), 7.95 (1H, d, *CH*NH), 8.12-8.28 (1H, m, N*H*CH_2), 8.68 (2H, d, $H_{4'}$ and $H_{6'}$), 11.28 (1H, br d, N*H*CH), $J_{H4'H5'}$ = $J_{H5'H6'}$ = 5 Hz, J_{CH_2-NH} = 6 Hz, J_{CH-NH} = 7 Hz
12i	DMSO	2.45 (3H, s, 4'-CH_3), 4.18 (2H, d, CH_2NH), 5.10 (2H, s, CH_2Ph), 7.08 (1H, t, $H_{5'}$), 7.40 (5H, s, Ph), 7.91 (1H, m, N*H*CH_2), 8.25 (1H, s, *CH*NH), 8.51 (1H, d, $H_{6'}$), 11.00 (1H, br s, N*H*CH), $J_{H5'H6'}$ = 5 Hz, J_{CH-NH} = 6 Hz
13i	DMSO	2.42 (3H, s, 4'-CH_3), 7.04 (1H, d, $H_{5'}$), 7.30-7.70 (9H, m, 8H-Ph and *CH*Ph), 7.98-8.12

Table 2 (continued)

Compound	Solvent	δ (TMS)
		(2H, m, Ph), 8.28 (1H, d, C*H*NH), 8.49 (1H, d, $H_{6'}$), 10.10 (1H, s, N*H*COPh), 11.23 (1H, d, N*H*CH), $J_{H5'H6'}$ = 5 Hz, J_{CH-NH} = 12 Hz
13j	$CDCl_3$	2.30 and 2.35 (6H, 2s, 4',6'-CH_3), 6.63 and 6.70 (1H, 2s, $H_{5'}$), 7.25-7.65 (9H, m, 8H-Ph and C*H*Ph), 7.85-8.02 (2H, m, Ph), 8.10-8.70 (2H, m, C*H*NH and N*H*COPh), 9.15 and 9.47, (1H, 2br d, N*H*CH), J_{CH-NH} = 13 Hz
13k	DMSO	2.78 (3H, s, 6'-CH_3), 7.24 (1H, s, $H_{5'}$), 7.33-7.76 (9H, m, 8H-Ph and C*H*Ph), 8.00-8.23 (3H, m, 2H-Ph and C*H*NH), 10.16 (1H, s, N*H*COPh), 11.50 (1H, br d, N*H*CH)
14h	$CDCl_3$	0.88 (3H, t, CH_3CH_2), 3.95 (2H, q, OCH_2CH_3), 4.43 (2H, d, CH_2NH), 7.01 and 7.09 (1H, 2t, $H_{5'}$), 7.46 (5H, s, Ph), 7.98 and 8.12 (1H, 2d, C*H*NHCH$_2$), 8.46 (1H, broad d, C*H*NH-Het), 8.54-8.70 (2H, m, $H_{4'}$ and $H_{6'}$), 9.57 (1H, broad d, N*H*-Het), 10.70 (1H, br d, N*H*CH$_2$), $J_{CH_3-CH_2}$ = 7 Hz
14i	$CDCl_3$	0.90 (3H, t, CH_3CH_2), 2.45 (3H, s, 4'-CH_3), 3.93 (2H, broad q, OCH_2CH_3), 4.30 (2H, d, CH_2NH), 6.84 (1H, broad d, $H_{5'}$), 7.47 (5H, s, Ph), 7.88-8.57 (2H, m, C*H*NHCH$_2$ and C*H*NH-Het), 8.46 (1H, broad d, C*H*NH-Het), 8.35 (1H, d, $H_{6'}$), 9.28 (1H, broad d, N*H*-Het), 10.70 (1H, br d, N*H*CH$_2$), $J_{CH_3-CH_2}$ = 7 Hz, J_{CH_2-NH} = 6 Hz, J_{CH-NH} = 12 Hz
14j	$CDCl_3$	0.90 (3H, t, CH_3CH_2), 3.37 and 3.43 (6H, 2s, 4',6'-CH_3), 3.81-4.20 (2H, m, OCH_2CH_3), 4.37-4.53 (2H, m, CH_2NH), 6.75 and 6.80 (1H, 2s, $H_{5'}$), 7.45 (5H, s, Ph), 7.90-9.70 (3H, br m, C*H*NH and N*H*CH$_2$), $J_{CH_3-CH_2}$ = 7 Hz
15j	DMSO	2.38 (6H, s, 4',6'-CH_3), 6.79 (1H, s, $H_{5'}$), 6.98 (2H, s, NH_2), 7.37-7.77 (9H, m, 8H-Ph and C*H*Ph), 8.10-8.26 (2H, m, Ph), 8.26 (1H, d, C*H*NH, 9.27 (1H, s, N*H*COPh), 10.45 (1H, s, NH), J_{CH-NH} = 12 Hz
16i	$CDCl_3$	2.41 (3H, s, 4'-CH_3), 3.81 (3H, s, OMe), 6.65 (1H, d, $H_{5'}$), 7.22-7.52 (9H, m, 8H-Ph and C*H*Ph), 7.86-8.02 (2H, m, Ph), 8.25 (1H, d, $H_{6'}$), 8.40 (1H, d, C*H*NH), 9.27 (1H, d, CHN*H*), $J_{H5'H6'}$ = 5 Hz, J_{CH-NH} = 12 Hz

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^{1}H nmr spectra were obtained on a JEOL 90Q FT and Varian E-60 spectrometer with TMS as internal standard. Elemental analyses for C, H, and N were obtained on a Perkin-Elmer CHN Analyzer 240 C. Except for L-proline and L-alanyl-L-proline, racemic amino acids were used for the transformations.

The following compounds were prepared according to the procedures described in the literature: *N*-[*N*-benzoylglycyl]-glycine (**7**) [7], *N*-[*N*-benzyloxycarbonylglycyl]glycine (**8**) [8].

4-Heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolones (**3**). General Procedure.

These compounds were prepared by a modified procedure described previously [5]. A mixture of heteroarylamine (0.01 mole), toluene (10 ml) and DMFDMA (1.5 ml) was heated under reflux for 2 hours, cooled and solvent evaporated *in vacuo*. Acetic anhydride (10 ml) and hippuric acid (2 g) were added to the residue and the mixture was stirred at 70° for 3 hours, cooled and the product collected by filtration. The experimental and analytical data for unpublished 4-heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolones **3** are summarized in Tables 1 and 2. The experimental and analytical data for other 4-heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolones have been previously reported in the literature [5].

N-[*N*-Benzoyl-2,3-dehydro-3-heteroarylaminoalanyl]peptides (**4**). General Procedure.

A mixture of 4-heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolone **3** (0.001 mole), amino acid (0.00115 mole), sodium carbonate (0.00055 mole), acetonitrile (5 ml) and water (2 ml) was heated under reflux for 2 hours. The reaction mixture was cooled, acetonitrile evaporated *in vacuo* and water (10 ml) was added. The solution was, while stirring, carefully acidified with diluted hydrochloric acid to *p*H = 1, the precipitate collected by filtration and washed with water. The experimental and analytical data for compounds **4** are given in Tables 1 and 2.

N-[*N*-[*N*-Benzoyl-2,3-dehydro-3-heteroarylaminoalanyl]-alanyl]prolines (**5**). General Procedure.

A mixture of 4-heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolone **3** (0.001 mole), L-alanyl-L-proline (0.00115 mole), sodium carbonate (0.00055 mole), acetonitrile (5 ml) and water (2 ml) was heated under reflux for 2 hours. The reaction mixture was then cooled, acetonitrile evaporated *in vacuo* and water (10 ml) was added. While stirring, the solution was carefully acidified with diluted hydrochloric acid to *p*H 1, the precipitate collected by filtration and washed with water. The experimental and analytical data for compounds **5** are given in Tables 1 and 2.

N-[*N*-Benzoyl-3-heteroarylaminoalanyl]prolines (**6**). General Procedure.

A mixture of 4-heteroarylaminomethylene-2-phenyl-5(4*H*)-oxazolone 3 (0 001 mole), L-proline (140 mg) and anhydrous ethanol (3 ml) was stirred at room temperature (20°) for 5 minutes, sodium borohydride (70 mg) was added and the mixture was stirred at this temperature for 12 hours. Water (20 ml) was added and the mixture was left at room temperature for several days. The precipitate was collected by filtration. The experimental and analytical data for compounds **6** are given in Tables 1 and 2.

N-[*N*-(1-Benzoylamino-2-phenyl-1-vinyl)glycyl]glycine (**9**).

This compound was prepared by a slightly modified procedure described in the literature [9]. A mixture of glycine (4 g), sodium carbonate (2.65 g) and 50% aqueous ethanol (200 ml) was heated under reflux for 10 minutes, then 4-benzylidene-2-phenyl-5(4*H*)-oxazolone (12.45 g) was added and the mixture was heated under reflux for another 3 hours. Then the solution was cooled, solvent evaporated *in vacuo*, water (100 ml) was added and the solution was acidified with 5*N* hydrochloric acid to *p*H = 3. The precipitate was collected by filtration and recrystallized from the mixture of ethanol and water to give **9** in 57% yield, mp 200-202°, lit [9] mp 208-209°.

N-[*N*-(2-Benzoyl-2-ethoxycarbonyl-1-vinyl)glycyl]glycine (**10**).

A mixture of *N*-[glycyl]glycine (0.01 mole), glacial acetic acid (10 ml) and ethyl 2-benzoyl-3-dimethylaminopropenoate

[10] (0.01 mole) was stirred at 80° for 2 hours. The solvent was then evaporated *in vacuo,* water (50 ml) was added and the precipitate collected by filtration to give **10**. The experimental and analytical data are given in Tables 1 and 2.

Oxazolones **11**, **12**, **13** and **14**. General Procedure.

A mixture of a dipeptide **7**, **8**, **9** or **10** (0.001 mole), dichloromethane (4 ml) and acetic anhydride (0.12 ml) was stirred at 20° for five minutes, then ethyl chloroformate (0.08 ml), *N*-methymorpholine (0.11 ml) and after 30 minutes also *N,N*-dimethyl-*N'*-heteroarylformamidine (**1**) were added. The mixture was stirred at room temperature for another 12 hours, when methanol (20 ml) was added and the solvent was left to evaporate at room temperature. Methanol (5 ml) was added to the residue and the precipitate collected by filtration. The experimental and analytical data for compounds **11**, **12**, **13**, and **14** are given in Tables 1 and 2.

N-[*N*-Benzoyl-2,3-dehydro-3-phenylalanyl]-2,3-dehydro-3-(4,6-dimethyl-2-pyrimidinylamino)alaninamide (**15**).

A mixture of 4-(4,6-dimethyl-2-pyrimidinylamino)-2-(1-benzoylamino-2-phenyl-1-vinyl)-5(4*H*)-oxazolone **13** (0.00055 mole, ethanol (4 ml) and 25% aqueous ammonia (2 ml) was heated under reflux for 2 hours, cooled and ethanol evaporated *in vacuo.* Methanol (2 ml) was added and the mixture was left overnight at room temperature. The precipitate was collected by filtration. The experimental and analytical data are given in Tables 1 and 2.

N-[*N*-Benzoyl-2,3-dehydro-3-phenylalanyl]-2,3-dehydro-3-(4-methyl-2-pyrimidinylamino)alanine Methyl Ester (**16**).

A mixture of 4-(4-methyl-2-pyrimidinylamino)-2-(1-benzoylamino-2-phenyl-1-vinyl)-5(4*H*)-oxazolone (**13**) (0.0005 mole, methanol (3 ml) and triethylamine (0.1 ml) was heated under reflux for one hour, cooled and the solvent evaporated *in vacuo.* Methanol (3 ml) was added and the precipitate collected by filtration. The experimental and analytical data are given in Tables 1 and 2.

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