REACTIONS OF HETEROCYCLIC N-OXIDES. THE SYNTHESIS OF α-HETEROARYL-α-AMINO ACID DERIVATIVES AND DIPEPTIDES

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Abstract - Heteroaryl substituted oxazolinylidene derivatives (3) and (4) were converted by opening of the oxazolinone ring under hydrolytic conditions, followed by decarboxylation into acylaminomethyl derivatives (5) and (6), with hydrazine hydrate into the corresponding hydrazides (7), with liquid ammonia under pressure into amides (8), and with amino acids into dipeptides (9-11).

Heterocyclic N-oxides[1-3] have been the subject of intensive investigations[1-3] in the last decades, since they undergo both the electrophilic[2] and nucleophilic substitution[2] more easily than the parent systems. They are often useful intermediates in the synthesis of functionalized heterocyclic systems, which can not be easily prepared by other methods.[3] Of great interest is alkylation with carbon nucleophiles used for the preparation of a variety of functionalized compounds.[3]
Oxazolinones,[4] thiazolinones[5] and rhodanine[6] have been used as carbon nucleophiles to give intermediates, which have been hydrolyzed under

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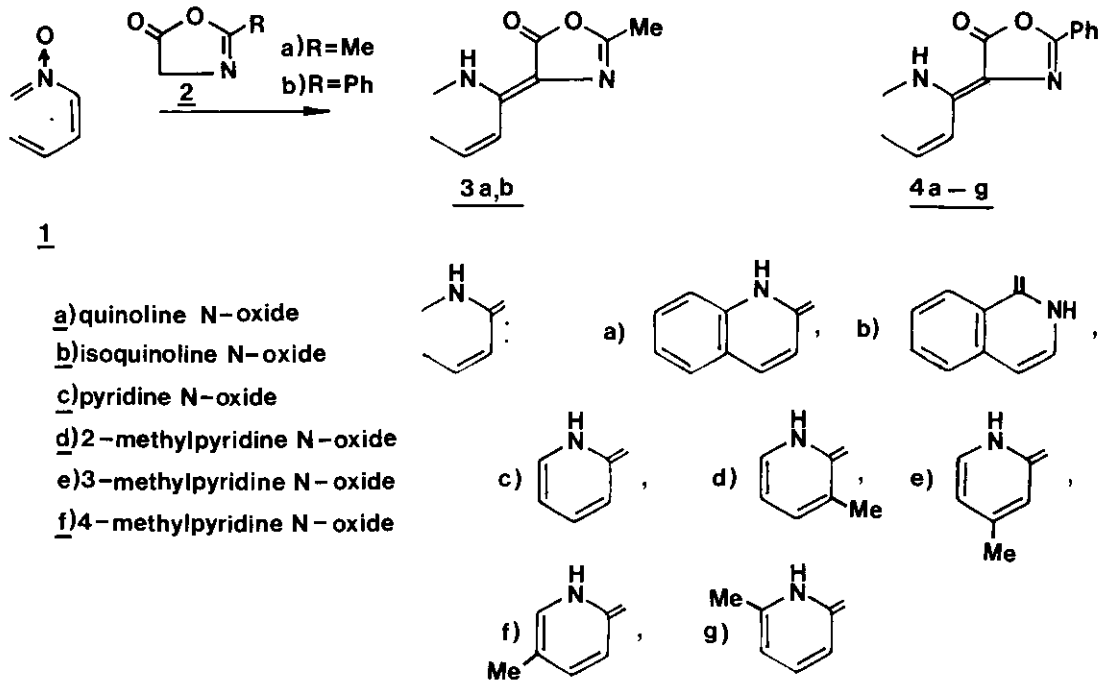
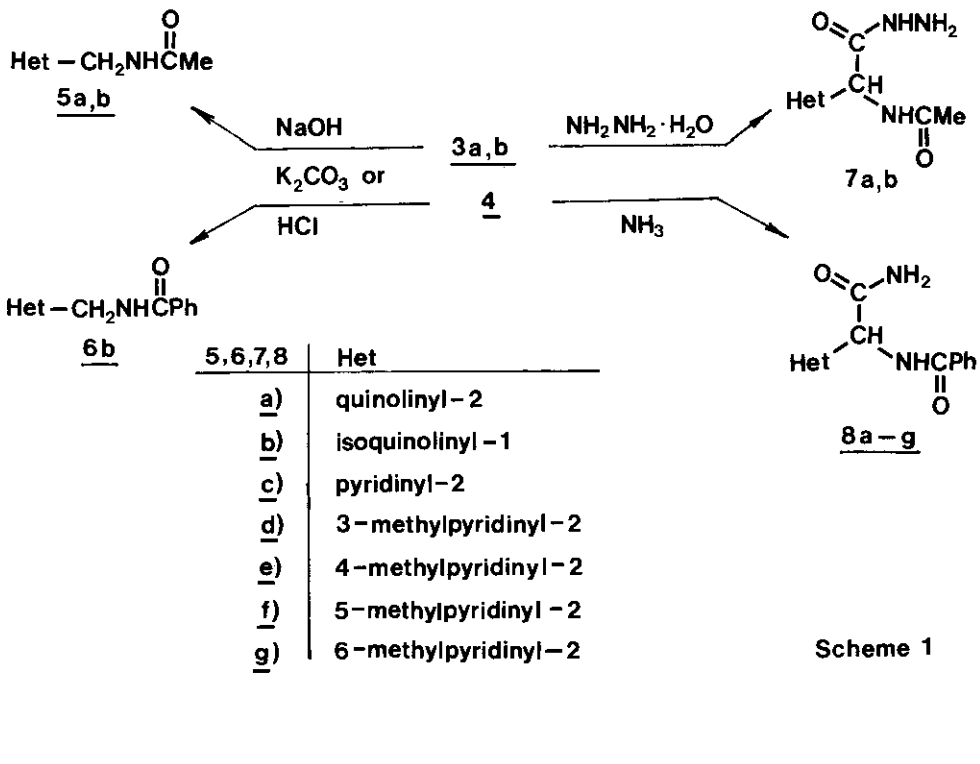
Dedicated to Dr. Masatomo Hamana, Professor Emeritus of Kyushu University, on the occasion of his 75th birthday.

drastic conditions into α-aminomethyl and α-mercaptomethyl derivatives of various heterocyclic systems. On the other hand, the products obtained from heterocyclic N-oxides and oxazolinones could be, under mild conditions, transformed into derivatives of α-heteroaryl substituted α-amino acids and dipeptides.[7]

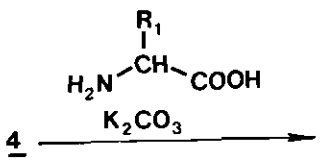
In this connection, we report now some further transformations of oxazolinylidene derivatives of heteroaromatic systems, prepared from the corresponding N-oxides and 2-substituted oxazolin-5-one derivatives. Quinoline N-oxide (1a), isoquinoline N-oxide (1b), pyridine N-oxide (1c) and its 2-methyl- (1d), 3-methyl- (1e), and 4-methyl- (1f) derivatives were treated with 2-methyl-2-oxazolin-5-one (2a) or 2-phenyl-2-oxazolin-5-one (2b) in acetic anhydride to give 3a,b and 4a-g, respectively. The intermediates (3a,b) were hydrolyzed under mild conditions in the presence of sodium hydroxide, potassium carbonate or aqueous hydrochloric acid into acetylaminomethyl derivatives (5a,b), while the compound (4a) gave the corresponding benzoylaminomethyl compound (6b), as the product of the hydrolysis of oxazolinone ring followed by decarboxylation. The oxazolinylidene derivatives (3a,b) were transformed with hydrazine hydrate into the corresponding hydrazides (7a,b), and with ammonia under pressure and elevated temperatures the corresponding amides (8a-g) were obtained. In our previous report,[7] dipeptide derivatives with the terminal ester group has been prepared from the corresponding hydrazide by conversion into the azide followed by treatment with ethyl glycinate. Now we report a direct conversion of oxazolinylidene derivatives (4a,c,e) with free amino acids by heating in ethanol in the presence of potassium carbonate into the dipeptides (9) with quinolinyl-2,(10) with pyridinyl-2,and (11) with 4-methylpyridinyl-2 substituent at α-position in the first amino acid component of the dipeptides. Racemization of the amino acid components was observed under these conditions. The structure of the new compounds were determined

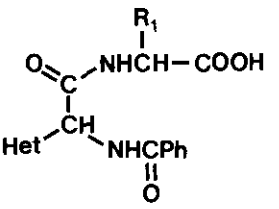




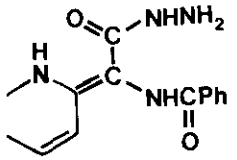
5,6,7,8	Het
a)	quinolinyl-2
b)	isoquinolinyl-1
c)	pyridinyl-2
d)	3-methylpyridinyl-2
e)	4-methylpyridinyl-2
f)	5-methylpyridinyl-2
g)	6-methylpyridinyl-2

Scheme 1





	R1
a	H
b	Me
c	CH_2Ph
d	CH_2CHMe_2
e	$(CH_2)_3Me$
f	CH_2OH
g	$(CH_2)_3SMe$
h	$CHMe_2$



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	Het
9	quinolinyl-2
10	pyridinyl-2
11	4-methylpyridinyl-2

Scheme 2

on the basis of their elemental analyses and ^{1}H nmr spectra. The acylaminomethyl derivatives (5a,b) and (6a) exhibit besides the signals for heteroaromatic and methyl or phenyl protons a doublet at δ = 4.53-5.27 ppm with a coupling constant J_{CH_2NH} = 4.1-5.9 Hz due to the coupling with the adjacent NH group, confirming thus that decarboxylation of the free carboxy group took place by ring opening of the oxazolinylidene part of the molecule. While hydrazides with a benzoylamino group exist in the tautomeric form (12), the corresponding hydrazides with an acetylamino group exist in form (7a,b), since the α-CH group appears in the ^{1}H nmr spectrum as a doublet at δ = 5.70-6.46 ppm with the coupling constant J_{CHNH} = 8.0-9.0 Hz, due to the coupling with the adjacent NH group of the acetylamino group. Similarly, the amides (8a-g) show doublets for the α-CH group in the range of δ = 5.70-6.55 ppm with a coupling constant J_{CHNH}= 5.6-8.3 Hz due to the coupling with the NH group of the adjacent benzoyl-

amino group. In dipeptide derivatives (9-11) multiplets for α-CH were observed due to overlapping of signals corresponding to various diastereoisomers, indicating that racemization of amino acid components occurred during the reaction.

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. ^{1}H Nmr spectra were obtained on a JEOL JNM 90 Q FT or VARIAN spectrometer with TMS as internal standard, and elemental analyses for C, H, and N on a PERKIN-ELMER CHN Analyzer 2400. The oxazolinylidene derivatives (4a-g) were prepared according to the procedure described in the literature.[7]

2(1H)-2-Methyl-5-oxooxazolinylidenequinoline (3a). - To a solution of quinoline N-oxide (1a) (290 mg, 0.002 mol) in acetic anhydride (2 ml) N-acetylglycine (234 mg, 0.002 mol) was added and the mixture was stirred (2 h) at room temperature. The precipitate was than collected by filtration to give 3a (220 mg, 50%), mp 162-167°C (from ethanol/water), nmr ($CDCl_3$) δ: 2.31 (3H, s, Me), 7.27-7.60 (7H, m, H_3 , H_4, H_5, H_6, H_7, H_8, NH). Anal. Calcd for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.46; N, 12.38. Found: C, 69.15; H, 4.58; N, 12.26.

In the same manner the following compound was prepared:

1(2H)-2-Methyl-5-oxooxazolinylideneisoquinoline (3b). - This compounds was prepared from 1b and acetylglycine in 49 % yield, mp 228-231°C (from ethanol/water), nmr ($CDCl_3$) δ 2.39 (3H, s, Me), 6.75 (1H, d, J = 5.8 Hz, H_3), 7.26-7.40 (m) and 7.57-7.78 (5H, H_5, H_6, H_7, H_8, NH), 9.73 (1H, d, J = 5.8 Hz, H_4). Anal. Calcd for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.46; N, 12.38. Found: C, 69.22; H, 4.49; N, 12.41.

2-Acetylaminomethylquinoline (5a). - Method A: A mixture of 3a (266 mg, 0.001 mol) and potassium carbonate (138 mg, 0.001 mol) in ethanol (10 ml) and water (2 ml) was heated under reflux (5h). The solvent was evaporated in vacuo, water (2 ml) was added and the solution was neutralized with 10 % hydrochloric acid. The precipitate formed after standing at room temperature (2 weeks) was coolected by filtration to give 5a (90 mg, 45 %), mp 125-127°C (from ethanol/water), nmr (DMSO-d_6) δ: 2.60 (3H, s, Me), 7.64 (1H, d, J = 8.4 Hz, H_3), 7.90 (1H, br s, NHCO), 8.00-8.30 (4H, m, H_5, H_6, H_7, H_8), 8.76 (1H, d, J = 8.4 Hz, H_4). Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.82; H, 6.24; N, 13.76.

Method B: To a suspension of 3a (226 mg, 0.001 mol) in water (5 ml) 36 % hydrochloric acid (0.1 ml) was added and the mixture was heated under reflux (10 min). The solution was, after cooling, neutralized with 20 % sodium hydroxide and the precipitate was collected by filtration to give 5a (102 mg, 51 %).

In the same manner the following compounds were prepared:

1-Acetylaminomethylisoquinoline (5b). - This compound was prepared from 3b, method A, in 95 % yield, mp 133-135°C (from ethanol/water) lit.,[8] mp 130-131°C, nmr ($CDCl_3$) δ : 2.20 (3H, s, Me), 7.06 (1H, d, J = 6.6 Hz, H_3), 7.69-7.87 (3H, m, H_5, H_6, H_7), 7.82 (1H, d, H_4), 8.30-8.40 (1H, m, H_8). Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.16; H, 5.96; N, 13.66.

1-Benzoylaminomethylisoquinoline (6b). - This compound was prepared from 2b, method A, in 80 % yield, mp 121-123°C (from ethanol/water), nmr ($CDCl_3$) δ: 5.27 (2H, d, J = 4.2 Hz, CH_2NH), 7.67 (1H, d, J = 5.7 Hz, H_3), 7.45-8.17 (9H, m, H_5, H_6, H_7, H_8, Ph), 8.20-8.49 (1H, t, J = 4.2 Hz, CH_2NH), 8.46 (1H, d, J = 5.7 Hz, H_4). Anal. Calcd for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68. Found: C, 78.04; H, 5.37; N, 10.64.

2-Acetylamino-2-(2-quinolyl)acetic hydrazide (7a). - A mixture of 3a (425 mg, 0.0019 mol) and 80 % hydrazine hydrate (1.4 ml, 0.028 mol) in methanol (5 ml) was heated under reflux (1 h). The solvent was evaporated in vacuo, water (10 ml) was added to the residue. The precipitate, formed during the standing in refrigerator (2 h), was collected by filtration to give 8 (270 mg, 55 %), mp 208-211°C (from ethanol), nmr (DMSO-d_6) δ : 1.98 (3H, s, Me), 4.31 (2H, br s, NH_2), 5.70 (1H, d, J = 8.0 Hz, CHNH), 7.63 (1H, d, J = 8.7 Hz, H_3), 7.67-8.03 (4H, m, H_5, H_6, H_7, H_8) (1H, d, J = 8.7 Hz, H_4), 8.66 (1H, d, J = 8.0 Hz, 6 HNH), 9.60 (1H, br s, NH). Anal. Calcd for $C_{13}H_{14}N_4O_2$: C, 60.45; H, 5.46; N, 21.69. Found: C, 60.35; H, 5.80; N, 21.30.

In the same manner the following compound was prepared:

2-Acetylamino-2-(1-isoquinolinyl)acetic acid hydrazide (7b). - This compound was prepared from 3b and hydrazine in 74 % yield, mp 212-214°C (from ethanol), nmr (DMSO-d_6) δ: 1.94 (3H, s, Me), 4.35 (2H, br s, NH_2), 6.46 (1H, d, J = 9.0 Hz, CHNH), 7.60-8.24 (4H, m, H_3, H_5, H_6, H_7), 8.30-8.85 (2H, m, H_4, H_8), 8.80 (1H, d, J = 9.0 Hz, CHNH), 9.50 (1H, br s, NH). Anal. Calcd for $C_{13}H_{14}N_4O_2$: C, 60.45; H, 5.46; N, 21.69. Found: C, 60.17; H, 5.65; N, 21.59.

2-Benzoylamino-2-(2-quinolinyl)acetamide (8a). - A mixture of 4a (576 mg, 0.002 mol) and liquid ammonia (20 ml) was heated (100°C) in an autoclave (2 days). Ammonia was, after cooling, evaporated at room temperature to give 8a (500 mg, 82 %), mp 190-192°C (from ethanol), nmr ($CDCl_3$) δ: 6.55 (1H, d, J = 8.3 CHNH), 7.49 (1H, d, J = 7.3 Hz, H_3), 7.45-8.05 (7H, m, H_5, H_6, H_7, H_8, Ph), 7.81 (2H, s, NH_2), 7.92 (1H, d, J = 7.3 Hz, H_4), 8.39-8.60 (2H, m, Ph), 9.02 (1H, d, J = 8.3 Hz, CHNH). Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.76; H, 5.03; N, 13,83.

In the same manner the following compounds were prepared:

2-Benzoylamino-2-(1-isoquinolinyl)acetamide (8b). - This compound was prepared from 4b and liquid ammonia (80°C, 8 h) in 86 % yield, mp 227-229°C (from ethanol/water), nmr ($CDCl_3$) δ : 5.90 (1H, d, J = 6.0 Hz, CHNH), 6.55 (1H, d, J = 6.2 Hz, H_3), 7.10-8.20 (9H, m, H_5, H_6, H_7, H_8, Ph), 7.70 (2H, s, NH_2), 8.51 (1H, d, J = 6.2 Hz, H_4), 8.98 (1H, d, J = 6.0 Hz, CHNH). Anal. Calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.72; H, 4.98; N, 13.65.

2-Benzoylamino-2-(2-pyridinyl)acetamide (8c). - This compound was prepared from 4c and 25 % ammonia (reflux, 2 h) in 61 % yield, mp 185-187 °C (from ethanol/water), nmr (DMSO-d_6) δ : 5.70 (1H, d, J = 7.8 Hz, CHNH), 7.34 (1H, dd, J = 7.3 Hz, J = 1.2 Hz, H_3), 7.35 (1H, dd, J = 4.9 Hz, J = 1.2 Hz, H_5), 7.47-7.56 (3H, m, Ph), 7.65 (2H, s, NH_2), 7.88-8.00 (2H, m, Ph), 7.80 (1H, dd, J = 7.3 Hz, J = 1.7 Hz, H_4), 8.57 (1H, dd, J = 4.9 Hz, H_6). Anal. Calcd for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.60; H, 5.30; N, 16.24.

2-Benzoylamino-2-(3-methyl-2-pyridinyl)acetamide (8d). - This compound was prepared from 4d and 25 % aqueous ammonia (25 %) (reflux, 1 h) in 32 % yield, mp 175-177°C (from ethanol/water), nmr ($CDCl_3$) δ 2.44 (3H, s, Me), 5.93 (1H, d, J = 6.3 Hz, CHNH), 7.20 (1H, dd, J = 7.3 Hz, J = 4.4 Hz, H_5), 7.26 (2H, s, NH_2), 7.46-7.60 (4H, m, H_4, 3H, Ph), 7.86-8.00 (2H, m, Ph), 8.17 (1H, d, J = 4.4 Hz, H_6), 8.47 (1H, d, J = 6.3 Hz, CHNH). Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.63; H, 5.72; N, 15.48.

2-Benzoylamino-2-(4-methyl-2-pyridinyl)acetamide (8e). - This compound was prepared from 4e and 25 % aqueous ammonia (reflux, 4 h) in 52 % yield, mp 148-150°C (from ethanol/water), nmr($CDCl_3$) δ : 2.33 (3H, s, Me), 5.77 (1H, d, J = 5.6 Hz, CHNH), 6.06 (1H, s, H_3), 7.09 (1H, d, J = 5.3 Hz, H_5), 7.31 (2H, s, NH_2), 7.30-7.58 (3H, m, Ph), 7.89-8.00 (2H, m, Ph), 8.25 (1H,

d, J = 5.3 Hz, H_6), 8.42 (1H, d, J = 5.6 Hz, CHNH). Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.76; H, 5.72; N, 15.82.

2-Benzoylamino-2-(5-methyl-2-pyridinyl)acetamide (8f). - This compound was prepared from 4f and 25 % aqueous ammonia (reflux, 1 h) in 15 % yield, mp 196-198°C (from ethanol/water), nmr (DMSO-d_6) δ 2.36 (3H, s, Me), 5.75 (1H, d, J = 7.8 Hz, CHNH), 7.39 (1H, d, J = 7.8 Hz, H_3), 7.44 (1H, d, J = 7.8 Hz, H_4), 7.34-7.60 (3H, m, Ph), 7.65 (1H, s, H_6), 7.86-8.00 (2H, m, Ph), 8.95 (2H, br s, NH_2), 10.82 (1H, d, J = 7.8 Hz, CHNH). Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.64; H, 5.65; N, 15.30.

2-Benzoylamino-2-(6-methyl-2-pyridinyl)acetamide (8g). - This compound was prepared from 4g and 25 % aqueous ammonia (reflux, 5 h) in 64 % yield, mp 183-185°C (from water), nmr (DMSO-d_6) δ : 3.35 (3H, s, Me), 5.63 (1H, d, J = 7.6 Hz, CHNH), 7.21 (1H, d, J = 7.6 Hz, H_5), 7.39 (1H, d, J = 7.8 Hz, H_3), 7.43-7.72 (4H, m, H_4, (3H)Ph), 7.72 (2H, s, NH_2), 7.80-8.00 (2H, m, Ph), 8.68 (1H, d, J = 7.6 Hz, CHNH). Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.79; H, 5.82; N, 15.72.

The Synthesis of Dipeptides (9-11). General Procedure. - To a boiling solution of the amino acid (0.002 mol) and potassium carbonate (150 mg, 0.0011 mol) in a mixture of ethanol and water (1:1, 10 ml) 4 (0.002 mol) was added and the mixture was heated under reflux (3-12 h). The solvent was evaporated in vacuo, water (3 ml) was added to the residue and the solution was neutralized with 10 % hydrochloric acid. The precipitate was collected by filtration and recrystallized from a mixture of ethanol and water.

In this manner the following compounds were prepared:

N-[2-Benzoylamino-2-(2-quinolyl)ethanoyl]glycine (9a). - This compound was prepared from 4a and glycine (reflux, 10 h) in 64 % yield, mp 165-170°C,

nmr (DMSO-d_6) δ : 3.85 (2H, d, J = 5.7 Hz, $C\underline{H}_2NH$), 6.02 (1H, d, J = 7.5 Hz, $C\underline{H}NH$), 7.45-8.13 (9H, m, H_5, H_6, H_7, H_8, Ph), 7.83 (1H, d, J = 8.8 Hz, H_3), 8.41 (1H, d, J = 8.8 Hz, H_4), 7.76 (1H, t, J = 5.7 Hz, $CH_2N\underline{H}$), 9.06 (1H, d, J = 7.5 Hz, CHN$\underline{H}$); Anal. Calcd for $C_{20}H_{17}N_3O_4$: C, 66.11; H, 4.72; N, 11.56. Found: C, 66.36; H, 4.82; N, 11.39.

N-[2-Benzoylamino-2-(2-quinolyl)ethanoyl]-D,L-alanine (9b). - This compound was prepared and L-alanine (reflux 3h) in 65 % yield, mp 225-230°C (decomp.), nmr (DMSO-d_6) δ : 1.30 (3H, d, J = 5.8 Hz, $\underline{Me}CH$), 4.32 (1H, dq, J = 5.8 Hz, J = 8.2 Hz, $C\underline{H}COOH$), 6.52 (1H, d, J = 8.2 Hz, $C\underline{H}NH$), 7.40-8.40 (10H, m, H_3, H_5, H_6, H_7, H_8, Ph), 8.65-8.85 (1H, d, J = 8.2 Hz, $N\underline{H}CHCOOH$), 8.90 (1H, d, J = 5.2 Hz, H_4), 9.18 (1H, d, J = 8.2 Hz, CHN$\underline{H}$); Anal. Calcd for $C_{21}H_{19}N_3O_4$: C, 66.83; H, 5.07; N, 11.13. Found: C, 66.69; H, 5.03; N, 10.88.

N-[2-Benzoylamino-2-(quinolyl)ethanoyl]-D,L-phenylalanine (9c). - This compound was prepared from 4a and L-phenylalanine (reflux, 12 h) in 21 % yield, mp 148-153°C, nmr (DMSO-d_6) δ : 3.10-3.20 (2H, m, $C\underline{H}_2Ph$), 4.40-4.50 (1H, m, $C\underline{H}CH_2Ph$), 6.02 (1H, d, J = 8.2 Hz, $C\underline{H}NH$), 7.13 (5H, br s, Ph), 7.00-7.25 (m) and 7.43-8.02 (m) (11H, H_3, H_4, H_5, H_6, H_7, H_8, PhCO), 8.11-8.33 (1H, m, $N\underline{H}CHCOOH$), 8.72 (1H, d, J = 7.7 Hz, H_4), 9.00 (1H, d, J = 8.2 Hz, CHN$\underline{H}$). Anal. Calcd for $C_{27}H_{23}N_3O_4$: C, 71.51; H, 5.11; N, 9.27. Found: C, 71.38; H, 5.16; N, 9.29.

N-[2-Benzoylamino-2-(quinolyl)ethanoyl]-D,L-leucine (9d). - This compound was prepared from 4a and L-leucine (reflux, 10 h), in 22 % yield, mp 115-120°C, nmr (DMSO-d_6) δ : 0.80-0.94 (6H, m, $CH\underline{Me}_2$), 1.61-1.73 (2H, m, $C\underline{H}_2CH$), 4.20-4.30 (1H, m, $C\underline{H}COOH$), 6.58 (1H, d, J = 7.6 Hz, $C\underline{H}NH$), 7.57 (1H, d, J = 4.9 Hz, H_3), 7.49-8.42 (9H, m, H_5, H_6, H_7, H_8, PhCO), 8.76-8.80 (1H, m, $N\underline{H}CHCOOH$), 8.94 (1H, d, J = 4.9 Hz, H_4), 9.19 (1H, d, J = 7.6 Hz, CHN$\underline{H}$). Anal. Calcd for $C_{24}H_{25}N_3O_4 \cdot H_2O$: C, 66.04; H, 6.00; N, 9.63; Found: C, 66.12; H, 5.67; N, 9.76.

N-[2-Benzoylamino-2-(2-quinolylethanoyl]-D,L-norleucine (9e).- This compound was prepared from 4a and D,L-norleucine (reflux, 9 h) in 13 % yield, mp 175-180°C, nmr (DMSO-d_6) δ : 0.60-1.20 (3H, m, MeCH$_2$), 1.35-1.75 (6H, m, CH$_2$CH$_2$CH$_2$), 4.10-4.40 (1H, m, CHCOOH), 6.10 (1H, d, J = 7.5 Hz, CHNH), 6.55 (1H, d, J = 8.0 Hz, H_3), 7.40-8.15 (9H, m, H_5, H_6, H_7, H_8, Ph), 8.20 (1H, m, NHCHCOOH), 8.46 (1H, d, J = 8.0 Hz, H_4), 8.90 (1H, d, J = 7.5 Hz, CHNH). Anal. Calcd for $C_{24}H_{25}N_3O_4$: C, 68.72; H, 6.01; N, 10.02. Found: C, 69.04; H, 5.94; N, 10.13.

N-[2-Benzoylamino-2-(2(1H)-quinolynidene)ethanoyl]-D,L-serin (9f). - This compound was prepared from 4a and D,L-serine (reflux, 9h) in 2 % yield, mp 108-110°C nmr (DMSO-d_6) δ: 3.34 (2H, br s, CH$_2$OH), 4.96 (1H, dt, J = 11.2 Hz, J = 5.6 Hz, CHCOOH), 7.47-8.02 (10H, m, H_3, H_5, H_6, H_7, H_8, Ph), 8.43 (1H, d, J = 8.0 Hz, H_4), 9.13-9.38 (1H, m, NHCHCOOH). Anal. Calcd for $C_{21}H_{19}N_3O_5$: C, 64.12; H, 4.87; N, 10.68. Found: C, 63.85; H, 5.18; N, 10.52.

N-[2-Benzoylamino-2-(2-pyridyl)ethanoyl]glycine (10a). - This compound was prepared from 4c and glycine (reflux, 5 h) in 42 % yield, mp 195-198°C, nmr (DMSO-d_6) δ : 3.82 (2H, d, J = 5.6 Hz, CH$_2$NH), 5.85 (1H, d, J = 7.8 Hz, CHNH), 7.32 (1H, d, J = 7.1 Hz, H_3), 7.36 (1H, dd, J = 6.8 Hz, J = 4.6 Hz, H_5), 7.42-7.59 (3H, m, Ph), 7.79 (1H, dd, J = 7.1 Hz, J = 2.0 Hz, H_4), 7.89-8.01 (2H, m, Ph), 8.55-8.65 (1H, dd, J = 4.6 Hz, J = 2.0 Hz, H_6), 8.61 (1H, t, CH$_2$NH), 8.44 (1H, d, J = 7.8 Hz, CHNH). Anal. Calcd for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.83; N, 13.44. Found: C, 61.51; H, 4.90; N,13,44..

N-[2-Benzoylamino-2-(2-pyridyl)ethanoyl]-D,L-alanine (10b). - This compound was prepared from 4c and L-alanine (reflux, 5 h) in 80 % yield, mp: 100-103°C, nmr (DMSO-d_6) δ : 1.34 (3H, d, J = 7.0 Hz, MeCH), 4.20-4.29 (1H, m, CHCOOH), 5.84 (1H, d, J = 8.1 Hz, CHNH), 7.32 (1H, dd, J = 2.7 Hz, J = 1.4 Hz, H_3), 7.35 (1H, dd, J = 5.6 Hz, J = 5.1 Hz, H_5), 7.47-7.59 (3H, m, Ph), 7.79 (1H, dd, J = 7.2 Hz, J = 1.8 Hz, H_4), 7.89-8.00 (2H, m, Ph),

8.53-8.70 (2H, m, H_6, NHCHCOOH), 9.07 (1H, d, J = 8.1 Hz, CHNH). Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.38; H, 5.23; N, 12.84. Found: C, 61.98; H, 5.34; N, 12.69.

N-[2-Benzoylamino-2-(2-pyridyl)ethanoyl]-D,L-phenylalanine (10c). - This compound was prepared from 4c and L-phenylalanine (reflux, 4 h) in 72 % yield, mp 95-98°C, nmr (DMSO-d_6) δ : 2.54-3.02 (2H, m, CH_2Ph), 4.28-4.60 (1H, m, CHCOOH), 5.84 (1H, d, J = 8.0 Hz, CHNH), 7.02-7.19 (5H, m, Ph), 7.31 (1H, d, J = 7.1 Hz, H_3), 7.37 (1H, dd, J = 6.2 Hz, J = 4.9 Hz, H_5), 7.49-7.57 (3H, m, PhCO), 7.73 (1H, dd, J = 7.1 Hz, J = 1.7 Hz, H_4), 7.88-7.98 (2H, m, PhCO), 8.50-8.60 (1H, m, NHCHCOOH). Anal. Calcd for $C_{23}H_{21}N_3O_4$: C, 68.47; H, 5.25; N, 10.42. Found: C, 68.41; H, 5.37; N, 10.24.

N-[2-Benzoylamino-2-(2-pyridyl)ethanoyl]-D,L-leucine (10d). - This compound was prepared from 4c and L-leucine (reflux, 4 h) in 54 % yield, mp 92-95°C, nmr ($CDCl_3$) δ : 0.70-1.05 (6H, m, $CHMe_2$), 1.40-1.90 (2H, m, CH_2CH), 4.40-4.90 (1H, m, NHCHCOOH), 6.16 (1H, d, J = 8.0 Hz, CHNH), 7.20-7.80 (6H, m, H_3,, H_4, H_5, Ph), 7.80-8.20 (3H, m, H_6, Ph), 8.60 (1H, d, J = 8.0 Hz, NHCHCOOH), 8.85 (1H, d, J = 8.0 Hz, CHNH). Anal. Calcd for $C_{20}H_{23}N_3O_4$: C, 65.03; H, 6.28; N, 11.37. Found: C, 64.90; H, 6.39; N, 11.37.

N-[2-Benzoylamino-2-(2-pyridyl)ethanoyl]-D,L-norleucine (10e). - This compound was prepared from 4c and D,L-norleucine (reflux, 6 h) in 54 % yield, mp 82-85°C, nmr (DMSO-d_6) δ : 0.78 (3H, t, J = 7.2 Hz, $MeCH_2$), 0.9-1.4 (4H, m, CH_2CH_2Me), 1.40-1.80 (2H, m, $CH_2CHCOOH$), 4.00-4.40 (1H, m, CHCOOH), 5.79 (1H, d, J = 8.0 Hz, CHNH), 7.15-7.72 (6H, H_3, H_4, H_5, Ph), 7.78-8.02 (2H, m, Ph), 8.38-8.68 (2H, m, H_6, NHCHCOOH). Anal. Calcd for $C_{20}H_{23}N_3O_4$: C, 65.03; H, 6.28; N, 11.37. Found: C, 64.91; H, 6.27; N, 11.32.

N-[2-Benzoyl-2-(2-pyridylethanoyl]-D,L-serine (10f). - This compound was prepared from 4c and D,L-serine (reflux, 4 h) in 77 % yield, mp 107-110°C, nmr (DMSO-d_6) δ : 3.6-3.9 (2H, m, CH_2OH), 4.00-4.40 (1H, m, NHCHCOOH), 6.02

(1H, d, J = 8.0 Hz, CHNH), 7.3-7.9 (6H, m, H_3, H_4, H_5, Ph), 7.90-8.20 (2H, m, Ph), 8.52-8.80 (2H, m, H_6, NHCHCOOH), 8.98 (1H, d, J = 8.0 Hz, CHNH). Anal. Calcd for $C_{17}H_{17}N_3O_5$: C, 59.47; H, 4.99; N, 12.23. Found: C, 59.51; H, 4.90; N, 11.98.

N-[2-Benzoylamino-2-(2-pyridyl)ethanoyl]-D,L-methionine (10g). - This compound was prepared from 4c and D,L-methionine (reflux, 4 h) in 34 % yield, mp 132-134°C, nmr (DMSO-d_6) δ : 1.93 (3H, s, Me), 2.21-2.48 (4H, m, CH_2CH_2CH), 4.37 (1H, t, J = 6.5 Hz, CH_2CH), 5.89 (1H, d, J = 8.1 Hz, CHNH), 7.26 (1H, dd, J = 7.3 Hz, J = 7.3 Hz, H_3), 7.35 (1H, dd, J = 5.9 Hz, J = 6.4 Hz, H_5), 7.47-7.56 (3H, m, Ph), 7.80 (1H, dd, J = 7.3 Hz, J = 6.9 Hz, H_4), 7.89-7.92 (2H, m, Ph), 8.54-8.59 (2H, m, H_6, NHCHCOOH), 8.69 (1H, d, J = 8.1 Hz, CHNH). Anal. Calcd for $C_{19}H_{21}N_3O_4S$: C, 58.90: H, 5.46; N, 10.85. Found: C, 58.77; H, 5.49; N, 10.74.

2-[2-Benzoylamino-2-(2-pyridyl)ethanoyl]-D,L-valine (10h). - This compound was prepared from 4c and D,L-valine (reflux, 4 h) in 54 % yield, mp 182-185°C, nmr(DMSO-d_6) δ : 0.75-0.96 (5H, m, $CHMe_2$), 2.10-2.30 (1H, m, $CHMe_2$), 4.16 (1H, d, J = 8.1 Hz, NHCHCOOH), 5.98 (1H, d, J = 8.1 Hz, CHNH), 7.32 (1H, d, J = 7.3 Hz, H_3), 7.35 (1H, dd, J = 6.9 Hz, J = 5.1 Hz, H_5), 7.48-7.60 (3H, m, Ph), 7.81 (1H, dd, J = 7.3 Hz, J = 6.9 Hz, H_4), 7.85-7.98 (2H, m, Ph), 8.43-8.61 (2H, m, H_6, NHCHCOOH), 8.74 (1H, d, J = 8.1 Hz, CHNH). Anal. Calcd for $C_{19}H_{21}N_3O_4$: C, 64.21; H, 5.96; N, 11.82. Found: 64.31; H, 6.09; N, 11.65.

N-[2-Benzoylamino-2-(4-methyl-2-pyridyl)ethanoyl]glycine (11a). - This compound was prepared from 4e and glycine (reflux, 6 h) in 62 % yield, mp 110-113°C, nmr (DMSO-d_6) δ : 2.33 (3H, s, Me), 3.90 (2H, d, J = 5.6 Hz, $NHCH_2COOH$), 5.77(1H, d, J = 8.0 Hz, CHNH), 7.21 (1H, d, J = 5.0 H_5), 7.40 (1H, s, H_3), 7.35-7.68 (3H, m, Ph), 7.80-8.12 (2H, m, Ph), 8.46 (1H, d, J = 5.0 Hz, H_6), 8.65 (1H, t, J = 5.6 Hz, $NHCH_2COOH$), 8.44 (1H, d, J =

8.0 Hz, CHNH). Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.37; H, 5.24; N, 12.84. Found: C, 62.09; H, 5.46; N, 12.67.

N-[2-Benzoylamino-2-(4-methyl-2-pyridyl)ethanoyl]-L-alanine (11b). - This compound was prepared from 4e and L-alanine (reflux, 4 h) in 44 % yield, mp 95-100°C, nmr (DMSO-d_6) δ : 1.33 (3H, d, J = 6.6 Hz, MeCH), 2.32 (3H, s, Me), 4.23 (1H, q, J = 6.6 Hz, MeCH), 5.80 (1H, d, J = 8.3 Hz, CHNH), 7.19 (1H, d, J = 4.9 Hz, H_5), 7.47-7.56 (4H, m, H_3, (3H)Ph), 7.88-8.00 (2H, m, Ph), 8.42 (1H, d, J = 4.9 Hz, H_6), 8.52-8.70 (1H, m, NHCHCOOH), 8.81 (1H, d, J = 8.3 Hz, CHNH). Anal. Calcd for $C_{18}H_{19}N_3O_4$: C, 63.33; H, 5.61; N, 12.31. Found: C, 63.24; H, 5.84; N, 12.11.

N-[2-Benzoylamino-2-(4-methyl-2-pyridyl)ethanoyl]-D,L-phenylalanine (11c). This compound was prepared from 4e and L-phenylalanine (reflux, 6 h) in 19 % yield, mp 110-115°C, nmr (DMSO-d_6) δ : 2.30 (3H, s, Me), 2.60-3.10 (2H, m, CH_2Ph), 4.30-4.70 (1H, m, CHCOOH), 5.79 (1H, d, J = 8.1 Hz, CHNH), 7.08-7.19 (5H, m, CH_2Ph), 7.35 (1H, s, H_3), 7.47 (1H, d, J = 4.6 Hz, H_5), 7.54-7.57 (3H, m, PhCO), 7.87-7.97 (2H, m, PhCO), 8.40 (1H, d, J = 4.6 Hz, H_6), 8.46-8.84 (1H, m, NHCHCOOH), 8.65 (1H, d, J = 8.1 Hz, CHNH). Anal. Calcd for $C_{24}H_{23}N_3O_4$: C, 69.05; H, 5.55; N, 10.07. Found: C, 68.87; H, 5.57; N, 9.83.

N-[2-Benzoylamino-2-(4-methyl-2-pyridyl)ethanoyl]-L-leucine (11d). - This compound was prepared from 4e and L-leucine (reflux, 4 h), in 12 % yield, mp 168-170°C, nmr (DMSO-d_6) δ : 0.86-0.93 (6H, m, $CHMe_2$), 1.39-1.81 (3H, m, CH_2CH_2), 2.32 (3H, s, Me), 2.12-4.44 (1H, m, CHCOOH), 5.79 (1H, d, J = 8.1 Hz, CHNH), 7.19 (1H, d, J = 4.9 Hz, H_5), 7.47 (1H, s, H_3), 7.47-7.56 (3H, m, Ph), 7.87-8.00 (2H, m, Ph), 8.41 (1H, d, J = 4.9 Hz, H_6), 8.79 (1H, d, J = 8.1 Hz, CHNH), 8.44-8.50 (1H, m, NHCHCOOH). Anal. Calcd for $C_{21}H_{25}N_3O_4$: C, 65.78; H, 6.57; N, 10.96. Found: C, 65.81; H, 6.75; N, 10.87.

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