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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW 4- PHENYL-2-(*o*-,*m*- & *p*-CARBOXYPHENYL) 5.6 BENZO-1:3-ISOINDOLINDIONE AMINO ACID AND PEPTIDE DERIVATIVES

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The synthesis of 4-phenyl-2(o-or m-or *p*-carboxyphenyl) 5:6-benzo-1:3-isoindolindione (*I-III*) and their corresponding acid chlorides (IV-VI)is described.4-phenyl-2(*o*- or *m*- or *p*-benzoyl chloride) 5:6-benzo-1:3- isoindolindione (IV-VI) was reacted with amino acid methyl ester hydrochloride to give the corresponding esters (XIX-XXX). Acid hydrolysis of the esters (XIX-XXX) gave the corresponding free carboxylic acid derivatives (VII-XVII). The acid azides (XXXI-XXXIII) were prepared by the reaction of the corresponding acid chlorides (IV-VI) with sodium azide. The carbonate derivatives (XXXIV-XXXIX) were prepared through curtius rearrangement with appropriate alcohol. Some tripeptide derivatives (XL-XLII) were synthesized via dicyclohexylcarbodiimide method. Most of the synthesized compounds were found to be active against a number of microorganisms.

Key Words: Synthesis; Antimicrobial Activity; 4-Phenyl-2-(*o*-, *m*-& *p*-Carboxyphenyl) 5:6 Benzo-1 : 3-Isoindolindione; Amino Acid; Peptide

Introduction

Many aromatic amines and their derivatives are known to have cancer-producing activity in mammals[1]. However, several halogenated and nitro; -phthaloyl, -naphthaloylaromatic amino acid and peptide derivatives were reported and found to possess different biological activities[2-5]. Also synthesis of some novel 4-phenyl-2-(p-carboxyphenyl) 5:6-benzo-1:3- isoindolindione derivatives, 1-phenyl-2,3-naphthaloyl-L-aspartoylamino acid and peptide derivatives and 4-phenyl-2-(L-glutamoylamino acid), 5:6-benzo-1:3-isoindolindione derivatives and their biological activity were reported[6-8]. These observations attracted the authors to synthesize a new class of 4-phenyl-2-(o-, m-, p-carboxyphenyl) 5:6 benzo-1:3-isoindolindione, amino acid, ester, azide carbamate and tripeptide derivatives (I-XLII) which is expected to have antimicrobial activity.

Discussion

(4-Phenyl-2-(*o*-or *m*- or *p*-carboxyphenyl) 5:6-benzo-1:3-isoindolindione (I-III) were readily prepared by condensation of 4-phenyl-5:6-benzophthalic anhydride[9-10] with *o*-or *m*- or *p*-aminobenzoic acid in glacial acetic acid for 6-8 hours. The time required for completion of the reaction was monitored by TLC. The products (I-III)were easily isolated purified and obtained in 65-95% yield (cf. Table I).

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The corresponding acid chloride (IV-VI) were obtained by subsequent treatment of (I-III) with thionyl chloride in benzene. Compounds (IV-VI) were used as starting material in the synthesis of various 4-phenyl-5:6-benzophthalamino acid derivatives.

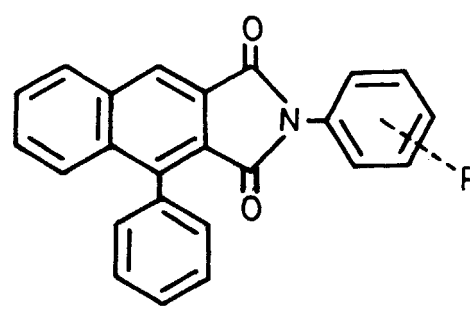
Condensation of the acid chlorides (IV-VI)with the appropriate amino acid or Gly-Gly methyl ester hydro-chloride in dioxane-triethylamine for 4 hours afforded 4- phenyl-2-(*o*- or *m*- or *p*-carboxyphenylamino acid, Gly-Gly methyl esters) 5:6 benzo- 1:3-isoindolindione (XIX-XXX) which were easily isolated as chromatographically homogeneous solid materials in 72-92% (cf.Table I).

Synthesis of 4-phenyl-2-(*o*- or *m*- or *p*-carboxyphenylamino acid, Gly-Gly) 5:6-benzo 1:3-isoindolindione derivatives (VII-XVII) were achieved through acid hydrolysis (2N HCL and 4-5 hours). The free carboxylic acid derivatives (VII-XVIII)were easily isolated as chromatographically homogeneous solid materials in 69-95% yields) (cf.Table I).

Reaction of the acid chloride derivatives (IV-VI) with sodium azide in acetone afforded 4-phenyl-5:6-benzophthalimido-*o*- or *m*- or *p*-benzoic acid azides (XXXI-XXXIII) in 66-79% yields (cf.Table I).

Acid azide (XXXI-XXXIII) undergo Curtius rearrangement[6] to give isocyanate derivatives by heating which were reacted with methanol or ethanol to give the corresponding carbamate derivatives (XXXIV-XXXIX) in 79-89% yield (cf.Table I).

For the preparation of 4-phenyl-2-(*o*- or *m*- or *p*-carboxyphenyltripeptide methyl ester) 5:6-benzo- 1:3-isoindolindione derivatives (XL-XLII), the appropriate 4-phenyl-2-(*o*- or *m*- or *p*-carboxyphenyl-L-leucine 5:6-benzo-1:3-isoindolindione) (X-XII) were reacted with glycylglycine methyl ester hydrochloride in dioxane-THF Et_3N medium using DCC procedure. The tripeptide derivatives (XL-XLII) were obtained as TLC pure materials in 35-45% yield.



Compounds (I-XLII)

Table I

Physical data of various 4-phenyl-2-(o- or m- or p-carboxyphenyl -) 5: 6-benzo- 1 : 3-isoindolindione amino acid and peptide derivatives (I-XLII)

Compound No.	R	M.P °C	Cryst. solvent	Yield %	$R_f(\alpha)_D^{20}$ (TLC)	C=5 aceton	Molecular Formula	Elemental analyses Calc. C	H	N	Found C	H	H
I	*o*-COOH	248-250	a	85	0.89	—	$C_{25}H_{15}NO_4$	76.34	3.82	3.56	76.30	3.80	3.40
II	*m*-COOH	257-259	a	80	0.90	—	$C_{25}H_{15}NO_4$	76.34	3.82	3.56	75.90	4.00	3.50
III	*p*-COOH	293-295	a	95	0.90	—	$C_{25}H_{15}NO_4$	76.34	3.82	3.56	76.00	3.90	3.52
IV	*o*-COCl	158-160	b	79	0.95	—	$C_{25}H_{14}NO_3Cl$	72.90	3.40	3.40	72.80	3.50	3.45
V	*m*-COCl	148-150	b	75	0.89	—	$C_{25}H_{14}NO_3Cl$	72.90	3.40	3.40	72.99	3.45	3.50
VI	*p*-COCl	229-231	b	70	0.71	—	$C_{25}H_{14}NO_3Cl$	72.90	3.40	3.40	73.00	3.50	3.50
VII	*o*-CO-DL-Ala	119-121	c	95	0.79	—	$C_{28}H_{20}N_2O_5$	72.41	4.31	6.03	72.40	4.30	6.00
VIII	*m*-CO-DL-Ala	185-187	c	90	0.92	—	$C_{28}S_{20}N_2O_5$	72.41	4.31	6.03	72.30	4.20	6.10
IX	*p*-CO-DL-Ala	139-141	c	89	0.90	—	$C_{28}H_{20}N_2O_5$	72.41	4.31	6.03	72.50	4.50	6.00
X	*o*-CO-L-Leu	122-124	d	80	0.93	+110	$C_{31}H_{28}N_2O_5$	73.52	5.14	5.53	73.50	5.00	5.50
XI	*m*-CO-L-Leu	145-147	d	77	0.89	+75	$C_{31}H_{28}N_2O_5$	73.52	5.14	5.53	73.40	5.10	5.40
XII	*p*-CO-L-Leu	115-117	d	75	0.81	+90	$C_{31}H_{28}N_2O_5$	73.52	5.14	5.53	73.60	5.20	5.60
XIII	*o*-CO-L-phe	108-110	c	89	0.89	+92	$C_{34}H_{24}N_2O_5$	75.55	4.44	5.18	75.50	4.40	5.10
XIV	*m*-CO-L-phe	103-105	d	92	0.75	+15	$C_{34}H_{24}N_2O_5$	75.55	4.44	5.18	75.60	4.60	5.00
XV	*p*-CO-L-phe	130-132	c	93	0.73	+70	$C_{34}H_{24}N_2O_5$	75.55	4.44	5.18	75.40	4.50	5.20
XVI	*o*-CO-Gly-Gly	162-164	d	95	0.92	—	$C_{29}H_{23}N_3O_6$	68.64	4.14	8.28	68.60	4.10	8.20
XVII	*m*-CO-Gly-Gly	180-182	d	81	0.91	—	$C_{29}H_{23}N_3O_6$	68.64	4.14	8.28	68.50	4.00	8.30
XVIII	*p*-CO-Gly-Gly	248-250	d	80	0.90	—	$C_{29}H_{23}N_3O_6$	68.64	4.14	8.28	68.70	4.20	8.40
XIX	*o*-CO-DL-Ala-OMe	143-145	c	80	0.82	—	$C_{29}H_{26}N_2O_5$	72.80	4.60	5.86	72.70	4.60	5.80
XX	*m*-CO-DL-Ala-OMe	192-194	c	90	0.80	—	$C_{29}H_{26}N_2O_5$	72.80	4.60	5.86	72.90	4.50	5.90
XXI	*p*-CO-DL-Ala-OMe	127-129	d	92	0.79	—	$C_{29}H_{26}N_2O_5$	72.80	4.60	5.86	73.00	4.70	6.00
XXII	*o*-CO-L-Leu-OMe	85-87	d	82	0.90	+70	$C_{32}H_{30}N_2O_5$	73.85	5.38	5.38	73.80	5.30	5.50
XXIII	*m*-CO-L-Leu-OMe	198-200	d	89	0.91	+55	$C_{32}H_{30}N_2O_5$	73.85	5.38	5.38	73.70	5.40	5.30
XXIV	*p*-CO-L-Leu-OMe	105-107	d	87	0.82	+15	$C_{32}H_{30}N_2O_5$	73.85	5.38	5.38	73.90	5.50	5.40
XXV	*o*-CO-L-Phe-OMe	94-96	c	82	0.80	+120	$C_{35}H_{28}N_2O_5$	75.81	4.69	5.05	75.80	4.70	5.00
XXVI	*m*-CO-L-Phe-OMe	139-141	c	81	0.77	+18	$C_{35}H_{28}N_2O_5$	75.81	4.69	5.05	75.70	4.60	5.10
XXVII	*p*-CO-L-Phe-OMe	182-184	c	79	0.69	+45	$C_{35}H_{28}N_2O_5$	75.81	4.69	5.05	75.90	4.80	5.20
XXVIII	*o*-CO-Gly-Gly-OMe	81-83	d	75	0.81	—	$C_{30}H_{25}N_3O_6$	69.10	4.41	8.06	69.10	4.40	8.00
XXIX	*m*-CO-Gly-Gly-OMe	180-182	d	72	0.82	—	$C_{30}H_{25}N_3O_6$	69.10	4.41	8.06	69.20	4.50	8.10
XXX	*p*-CO-Gly-Gly-OMe	260-262	c	91	0.84	—	$C_{30}H_{25}N_3O_6$	69.10	4.41	8.06	69.00	4.30	8.20
XXXI	*o*-CO-N_3	229-231	—	75	0.60	—	$C_{25}H_{11}N_4O_3$	71.77	3.35	13.40	71.70	3.30	13.40
XXXII	*m*-CO-N_3	138-140	—	66	0.59	—	$C_{25}H_{11}N_4O_3$	71.77	3.35	13.40	71.80	3.40	13.20
XXXIII	*p*-Co-N_3	142-144	—	79	0.65	—	$C_{25}H_{11}N_4O_3$	71.77	3.35	13.40	71.60	3.20	13.30
XXXIV	*o*-$NHCOOCH_3$	173-175	c	82	0.75	—	$C_{26}H_{18}N_2O_7$	73.93	4.27	6.64	73.90	4.20	6.60
XXXV	*m*-$NHCOOCH_3$	135-137	c	83	0.72	—	$C_{26}H_{18}N_2O_7$	73.93	4.27	6.64	74.00	4.30	6.70
XXXVI	*p*-NH_2OOCH_3	150-152	c	89	0.80	—	$C_{26}H_{18}N_2O_7$	73.93	4.27	6.64	74.10	4.40	6.50
XXXVII	*o*-$NHCOOC_2H_5$	120-122	d	87	0.92	—	$C_{27}H_{20}N_2O_7$	74.31	4.59	6.42	74.30	4.60	6.40
XXXVIII	m-$NHCOOC_2H_5$	240-242	d	79	0.89	—	$C_{27}H_{20}N_2O_7$	74.31	4.59	6.42	74.20	4.50	6.50
XXXIX	*p*-$NHCOOC_2H_5$	211-213	c	80	0.82	—	$C_{27}H_{20}N_2O_7$	74.31	4.59	6.42	74.10	4.70	6.30
XL	*o*-CO-L-Leu-Gly-Gly -OMe	150-152	c	45	0.89	+72	$C_{36}H_{31}N_4O_7$	68.41	5.36	8.83	68.10	5.30	8.80
XLI	*m*-CO-L-Leu-Gly-Gly -OMe	201-203	d	39	0.87	+25	$C_{36}H_{31}N_4O_7$	68.41	5.36	8.83	68.00	5.40	8.90
XLII	*p*-CO-L-Leu-Gly-Gly -OMe	176-178	c	35	0.90	+60	$C_{36}H_{31}N_4O_7$	68.41	5.36	8.83	68.20	5.50	8.70

* Crystallization solvent

a = acetic-water *b* = benzene-petroleum ether *c* = Ethanol

(-) = washed with cold water *d* = Ethanol-water

Complete acid hydrolysis (XLII) (6N-HCl 24 hours 105° C) followed by subsequent paper chromatography gave ninhydrin positive spots of L-leucine and glycine.

Compounds (I-XLII) gave IR, UV and NMR spectra consistent with their assigned structures.

Biological Screening Results

The antimicrobial activities of compounds (I-XLII) were tested using the hole plate and filter paper disc methods [11-14]. The microorganisms included gram positive: *Staphylococcus aureus* (ATCC-6538-P). *Bacillus cereus* (NRRL-B-569): gram negative *Serratia marcesens* (IMRU-70), *Proteus merabilies* (NTC-289) and Fungi, *Aspergillus niger* (PP-29).

Qualitative screening were done for all compounds while quantitative determination were performed for the biologically active compounds only.

Studies on the biological properties of compounds (I-II) have revealed that the synthesized products (I-III), exhibited pronounced antimicrobial activities against all the tested microorganisms (MIC 25-125 μg/ml) (cf.Table I).

The conversion of carboxylic group into acid chloride led to slight decrease of the antimicrobial activities of the acid chloride derivatives (IV-VI) towards most of the tested microorganisms (cf.Table II).

Reaction of (IV-VI) with some of amino acid or Gly-Gly methyl ester hydrochloride led to marked decrease of the antimicrobial activities of the compounds (XIX-XXX) against most of the tested microorganisms (cf.Table II).

Synthesis of 4-phenyl-2-(*o*- or *m*- or *p*-carboxyphenyl-amino acid, Gly-Gly) 5:6-benzo-1:3 isoindolindione derivatives (VII-XVIII) by acid hydrolysis of the ester derivatives (XIX-XXX) led to high increase of the antimicrobial activities of the compounds (XIX-XXX) against most of the tested microorganisms (MIC 25-50 Mg/m) (cf.Table II).

Substitution of the carboxyl group by carbamate group, compounds (XXXIV-XXXIX) or convertion acid chloride into acid azide derivatives (XXXI-XXXIII) led to marked decrease in the biological properties (cf. Table II). Elongation of the peptide chain led also to marked decrease or completely abolished in the biological properties.

The present investigation has revealed that the introduction of 4-phenyl-2-(*o*- or *m*- or *p*-carboxyphenyl) 5:6-benzo- 1:3 isoindolindione moiety, in combination with amino acids showed high biological activities. Moreover, esterification of the carbonyl group led to slight decrease in the biological activities. On the other hand elongation of the peptide chain or conversion of carboxylic group into acid chloride, acid azide or carbamate derivatives afforded compounds with marked decrease on the activity.

Table II

Biological activities of the synthesized compounds (I-XLII) (MIC μg/ml)

Compound No.	*Staphylococcus aureus*	*Bacillus cereus*	*Serratia marcesens*	*Proteus merabilies*	*Aspergillus niger*
	MIC	MIC	MIC	MIC	MIC
I	75	50	75	75	125
II	50	50	50	50	—
III	25	25	25	25	25
IV	125	50	125	125	125
V	50	50	125	50	125
VI	125	100	75	—	250
VII	50	25	25	25	25
VIII	25	50	25	50	50
IX	50	25	50	50	—
X	75	50	25	25	50
XI	25	50	25	25	25
XII	25	25	50	25	50
XIII	25	25	50	25	25
XIV	50	25	25	25	—
XV	50	25	25	25	—
XVI	25	25	25	50	25
XVII	25	25	25	50	25
XVIII	50	25	25	50	50
XIX	125	125	125	125	25
XX	125	250	125	250	—
XXI	125	25	125	250	100
XXII	250	500	500	—	—
XXIII	250	125	125	—	—
XXIV	—	125	—	250	—
XXV	—	—	125	250	—
XXVI	—	—	500	500	—
XXVII	250	100	250	—	—
XXVIII	125	250	125	125	—
XXIX	—	125	—	125	—
XXX	125	—	—	—	500
XXXI	—	—	250	—	—
XXXII	—	500	—	50	—
XXXIII	250	500	250	—	—
XXXIV	250	—	—	—	—
XXXV	500	—	250	—	—
XXXVI	500	500	500	250	—
XXXVII	250	500	—	—	—
XXXVIII	250	500	500	250	—
XXXIX	—	500	—	—	—
XL	500	—	500	500	—
XLI	250	25	500	500	—
XLII	—	500	—	—	—

Experimental

Thin layer chromatography (R_f) for analytical purposes was taken on silica gel G-1 plastic sheets and developed with (*n*-butanol : acetic acid : water) (4:1:1) using iodine, ninhydrin and benzidine solutions as spraying agents. Melting points were uncorrected. Optical rotations $[\alpha]_D^{20}$ were measured for all compounds in acetone at λ_{max} 589nm on Bellingham Stanely polarimeter using 5 cm tube at 20°C. The infrared spectra υ_{max}; cm^{-1} were taken in KBr discs (pellets using Shimadzu IR-408 instrument. The NMR spectra (Chemical shifts (δ) in ppm, in DMSO-d_6] were measured using Varian EM-360L, 60-MHz spectrometer and TMS as internal standard.

Preparation of 4-phenyl-2-(o-, m-, p-carboxyphenyl) 5:6- benzo-1:3-isoindolindione (I-III)

4-Phenyl-5:6-benzophthalic anhydride and *o*- or *m*- or *p*-aminobenzoic acid in 100ml acetic acid were refluxed for 8 hours. The solvent was evaporated *in vacuo* and the products (I-III) were recrytallized from acetic acid-water (cf. Table I). NMR spectrum of (III, in DMSO-d_6) showed signals at 7.8-8.1 (*m*, 14H, Ar-H] and 10.6 [s, 1H, COOH concelled with D_2O].

Preparation of the Acid Chlorides (IV-VI)

A solution of (I or II or III, 0.01 mol), thionyl chloride (30 ml) in benzene was refluxed for 2 hours. Excess benzene-thionyl chloride was distilled off under vacuum to give (IV-VI) (cf. Table I).

General Procedure for Synthesis of 4-Phenyl-2- (*o*- or *m*- or *p*-Carboxyphenylamino acid, Gly-Gly Methyl Esters) 5:6-Benzo 1:3-Isoindolindione (XIX-XXX)

To a suspension of amino acid methyl ester hydro-chloride (0.0043 mole) in dioxane (30ml) was added triethylamine (2ml). The mixture was stirred at 20°C for 15min and cooled to 0°C. To the mixture at 0°C was added acid chlorides (IV or V or VI) (0.0042 mole) and the reaction mixture was stirred for 1 hr. at 5°C and 3-4 hours at room temperature and then kept overnight at room temperature. The precipitated triethylamine hydrochloride and unreacted materials were filtered off and the filtrate was evaporated *in vacuo*. The residual solid was recrystallized from the proper solvent. Compounds (XIX-XXX) were chromatographically homogeneous when detected with benzidine and all compounds gave a negative ninhydrin test.

IR spectra of compounds (XIX-XXX) showed characteristic bands at : 1745, 1727, 1400 and 1100cm^{-1} (CO and $COOCH_3$) AND 3340, 3140 (-CONH). The

NMR spectrum of the compound (XIX) showed bands at 3.9 (*s*, 3H, OCH_3), 6.6(*s*, 1H, NH), 7.8-8.3 (m, 14H, Ar-H).

General Procedure for Synthesis of 4-Phenyl-2- (*o*- or *m*- or *p*-carboxyphenylamino Acid, Gly-Gly) 5:6-benzo 1:3-isoindolindione derivatives (VII-XVIII)

To ethanolic solution of 4-phenyl-2- (*o*- or *m*- or *p*-carboxyphenylamino acid, Gly-Gly methyl esters) 5:6-benzo 1:3-isoindolindione (XIX-XXX) (0.003 mole) was added 10ml 2N HCl and the reaction mixture was stirred for 4-5 hours at room temperature. The precipitated solid material was filtered and recrystallized from ethanol or ethanol water. The isolated products (VII-XVIII) were chromatographically homogeneous when developed with benzidine or iodine solution.

IR spectra of compounds (VII-XVIII) showed the presence of bands at: 1735, 1700cm^{-1} (C=O); 3240, 1700, 1235cm^{-1} (COOH) and the other bands due to naphthaloyl and amino acid moieties. The UV spectra of (VII-XVIII) showed bands σ_{max} (log ε) at : 206nm (4.06) and 250nm (4.33) characteristic for 4-phenyl-2-(*o*- or *m*- or *p*-carboxy-phenyl) 5:6 benzo-1:3-isoindolindiones residue. NMR spectrum of (VII) showed signals at δ, 8.1 (*s*, 1H-CONH), 7.8-8.1 (*m*, 14H, Ar-H), 10.6 (*s*, 1H, COOH) and no peaks for ($COOCH_3$) which confirm the structure (VII). The other derivatives (VIII-XVIII) showed similar bands in support of their assigned structures.

Synthesis of the Acid Azides (XXXI-XXXIII)

To a solution of (IV or V or VI) (0.01 mol in acetone (50ml), sodium azide (0.015 mol) in least amount of water was added dropwise while stirring was continued for 0.5 hour. The reaction mixture was poured into ice-cold water and the product filtered and washed with cold water (XXXI-XXXIII) (Table I). IR spectra showed bands at 2200-2250 cm^{-1} (N_3).

Synthesis of the Carbomate Derivatives (XXXIV-XXXIX)

A solution of (XXXI-XXXIII) (0.01 mol) in the appropriate alcohol (20ml) was refluxed for 4 hours. The solvent was evaporated and the obtained product was recrystallized from the proper solvent. IR spectra showed bands at 3320-3350 cm^{-1} (NH) and 2950 cm^{-1}(CH aliphatic). NMR spectrum of (XXXVII) showed signals at δ 11.13 (CH_3), 3.9-4.2 (CH_2 ester) and 7.9-8.2 aromatic protons which confirm the structure (XXXVII). The other carbamate derivatives (XXXIV-XXXIX) showed similar bands in support of their assigned structure.

General Procedure for synthesis of 4-Phenyl-2-(*o*- or *m*- or *p*-carboxyphenyltripeptide Methyl Esters) 5:6-benzo 1:3-isoindolindione (XL-XLII)

4-Phenyl-2-(*o*- or *m*- or *p*-carboxyphenyl-L-leucine) 5:6-benzo 1:3-isoindalindione (0.003 mole) and Gly-Gy methyl ester hydrochloride (0.0033 mole) were dissolved in THF (40ml) containing triethylamine (0.0033 mole). The mixture was shaken for 30 minutes at 20°C cooled to 0°C and dicyclohexylcarbodiimide (DCC, 0.003 mole) was added. The mixture was stirred for 5 hours at 0°C and then left at room temperature for 24 hours. The dicyclohexylurea (DCU) was filtered off and glacial acetic acid (1ml) was added. After 24 hours the reaction mixture was filtered and the solvent evaporated *in vacuo*. The solid residue was purified by several recrystallizations from the proper solvent. The product materials (XL-XLII) were chromatographically homogeneous when developed with iodine or benzidine while gave negative ninhydrin reaction. The tripeptide derivatives (XL-XLII) were soluble in ethyl acetate, dioxane, acetone, DMF, THF, methanol & ethanol while in soluble in diethyl ether and water.

The IR spectra of the tripeptide methyl esters (XL-XLII) showed bands at: 3416, 3333cm^{-1} (NH), 1625, 1570, 1365cm^{-1} (amide I, II and III) 1710, 1254, 916 (C=0) and 1771 cm^{-1} (C=0 of $COOCH_3$). Compounds (XL-XLII) showed UV peaks at: λ_{max} 206nm (log ε 4.06) and 250nm (log ε 4.33) and NMR signals at: *d* 8.0 (s, 1H NH), 3.76 (*s*, 3H, OCH_3), 7.9-8.3 (14H, Ar-H) and other signals in support of the proposed structures.

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