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Synthesis of Some New Quinoline-Acryloyl Amino Acid Derivatives

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ABSTRACT. The synthesis of a number of β-(2-quinolyl)-acryloylamino acid methyl esters (II-IX), β-(2-quinolyl)-α, β-dibromoacryloylamino acid methyl esters (XXVI-XXX) and β-[2-(4-hydroxy-6-nitro)-quinolyl]-acryloylamino acid methyl esters (XXXII-XXXV) have been carried out by the condensation of the correpsonding acids (I or XXV or XXXI) with amino acid methyl ester hydrochlorides in THF-Et_3N medium using DCC procedure. Hydrazinolysis of the methyl esters (II-IX and XXXII-XXXV) in methanol or ethanol gave the corresponding hydrazides (X-XVII and XXXVI-XXXIX), respectively. The azides from (XI-XVII) on coupling with L-Tyr-Ome gave the desired dipeptides (XVIII-XXIV). β-(2-quinolyl)-acryloyl-L-Leu-OMe (V) and β-(2-quinolyl)-α,β-dibromoacryloyl-Gly-OMe (XXVI) were found to be active against a number of microorganisms.

Many substituted quinoline derivatives exhibit antimalarial, fungistatic, bacteriostatic and antihistaminic activities (Albert 1968, Iones 1977, Manske 1953, Rahway 1976). Recently, several acryloylamino acid derivatives containing heterocyclic residues were reported and found to be biologically active (El-Naggar *et al.* 1976, 1980, 1981, 1983). These observations attracted the authors to synthesize several quinoline-acryloylamino acid derivatives (II-XXXVI) which may enhance the activity of these compounds or verify their biological action. In the synthesized derivatives L-valine, L-leucine, L-phenylalanine and L-tyrosine were selected for combination with three substituted quinolylacryloyl residues. The criteria of selection was based upon their importance of exhibiting a high level of antimicrobial activity in many polypeptide antibiotics such as gramicidin S, tyrocidines, polymyxins and bacitracin (Schroder and Lubke 1966).

Discussion and Results

When β-(2-quinolyl)-acrylic acid (I) (Albert and Bachamn 1935, El-Gazzar 1981) was reacted with amino acid methyl ester hydrochlorides in the presence of THF-Et_3N medium using the DCC method, β-(quinolyl)-acryloylamino acid methyl esters (*cf.* Table 1 and Scheme 1) were obtained in high yields. Products II-IX were purified by repeated recrystallizations and TLC-pure materials obtained.

In the preparation of Ser-, Tyr- and Trep- derivatives (VII-IX), the coupling reactions did not require the prior protection of the side chain groups and no side reactions were observed.

Complete acid hydrolysis of II for 24 hr using 6*N* HCl at 105°C and subsequent chromatography yielded glycine (ninhydrin test).

Scheme 1. General scheme for synthesis of the dipeptide methyl esters (XVIII-XXIV).

β-(2-Quinolyl)-acrylic acid + Amino acid methyl ester hydrochlorides
(I)
DCCD/Et_3N
THF
↓
β-(2-Quinolyl)-acryloylamino acid methyl esters (II-IX)
↓ N_2H_4/MeOH
β-(2-Quinolyl)-acryloylamino acid hydrazides (X-XVII)
↓ $NaNO_2$/HCl-ACOH
β-(2-Quinolyl)-acryloylamino acid azides
↓ L-Tyr-OMe. HCl/Et_3N-EtOAc
β-(2-Quinolyl)-acryloyldipeptide methyl esters (XVIII-XXIV)

The structures assigned to II-IX were supported by their elemental analyses, IR, UV and amino acid analysis.

An attempt to synthesize compounds II-IX starting from β-(2-quinolyl)-acryloyl acid chloride and amino acid methyl ester hydrochlorides in THF or dioxane-

Et_3N medium under different reaction conditions gave chromatographically nonhomogeneous products containing some undesirable cyclic products. Moreover, compounds IV-VI and VIII-IX were isolated *via* the acid chloride method in a very low yield (10-15%), and high degree of racemization (50-60%) was reported. Therefore, the dicyclohexylcarbodiimide was preferred for preparation of compounds II-IX.

Hydrazinolysis of the methyl esters II-IX in methanol gave the corresponding hydrazides X-XVIII as crystalline solids, which gave the positive benzidine and silver nitrate reactions. The structures of all hydrazides were well supported by their characteristic IR and UV spectra.

Synthesis of β-(2-quinolyl)-acryloyldipeptide methyl esters XVIII-XXIX were achieved starting from β-(2-quinolyl)-acryloyl amino acid hydrazides X-XVII which were first converted into the corresponding azides. The azides on coupling with amino acid methyl esters gave the dipeptides (*cf.* Table 1 and Scheme 1, XVIII-XXIV), which were isolated and purified by repeated recrystallizations. All the products XVIII-XXIV were obtained in crystalline form in 50-69% yield and all were chromatographically homogeneous. Complete hydrolysis of XIX with 6*N* HCl at 105° for 24 hr and subsequent chromatography gave positive results for both valine and tyrosine.

The dipeptide methyl esters XVIII-XXIV gave dark blue 1:1 complexes with Cu (II), λ_{max} 610-650 nm.

For the preparation of β-(2-quinolyl)-α,β-dibromoacryloylamino acid methyl esters XXVI-XXX and β-[2-(4-hydroxy-6-nitro)-quinolyl] acryloylamino acid methyl esters XXXII-XXXV, β-(2-quinolyl)-α,β-dibromoacrylic acid (XXV) or β-[2-(4-hydroxy-6-nitro)-quinolyl] acrylic acid (XXXI) (Albert and Bachamn 1935, El-Gazzar 1981) was reacted with amino acid methyl ester hydrochlorides in THF-Et_3N medium using DCC procedure (*cf.* Schemes 2 and 3 and Table 1). Coupling reactions *via* the carbodiimide method did not require the prior protection of the 4-hydroxyl group of the quinoline moiety and no side reactions were observed. All the products XXVI-XXXV were obtained in crystalline form in 40-65% yield and all were chromatographically homogeneous.

Scheme 2. General scheme for synthesis of compounds (XXVI-XXX).

β-(2-Quinolyl)-α,β-dibromoacrylic acid (XXV) + THF + Amino acid methyl ester hydrochlorides + DCCD + Et_3N

↓

β-(2-Quinolyl)-α,β-dibromoacryloylamino acid methyl esters (XXVI-XXX).

Scheme 3. General scheme for synthesis of compounds (XXXVI-XXXIX).

β-[2-(Hydroxy-6-nitro)-quinolyl]acrylic acid (XXXI) + Amino acid methyl ester hydrochlorides + DCCD + Et_3N + THF ⟶

β-[2-(4-Hydroxy-6-nitro)-quinolyl]acryloylamine acid methyl esters (XXXII-XXXV) $\xrightarrow{N_2H_4/EtOH \text{ or } MeOH}$

β-[2-(4-Hydroxy-6-nitro)-quinolyl]acryloylamino acid hydrazides (XXXVI-XXXIX).

The structures of XXVI-XXXV were assigned on the basis of elemental analysis, IR and UV spectra. Complete hydrolysis of XXVIII or XXXIII with 8*N* H_2SO_4 at 105° for 24 hr and subsequent chromatography gave positive spot of valine (ninhydrin test).

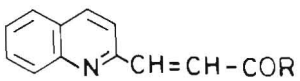
The hydrazides XXXVI-XXXIX were prepared by treatment of the corresponding methyl esters with hydrazine hydrate in methanol. The products were purified by repeated recrystallizations.

Compounds II-XXXIX were prepared and characterized for the first time (*cf.* Table 1 and Schemes 1-3). The methods used for studying the copper (II) complexes were the same as described previously (El-Naggar *et al.* 1966, El-Naggar and Poddubnaya 1967).

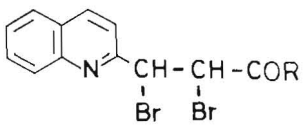
Biological Screening Results

The antimicrobial activities of the compounds I-XXXIX were tested using the hole plate method and filter paper disc method (Carlson 1948, Vincent and Vincent 1944, Epstein 1944, Irving 1946), and the results compared with the activity of the parent compounds (I, XXV and XXXI). Out of 36 synthesized and tested compounds, only β-(2-quinolyl)-L-Leu-OMe (V) showed a maximum activity at (MIC 0.5-10 μg/ml) against *Bacillus subtilis* (ICC-strain), *Bacillus mycoids* (USSR) and *Bacillus cereus* (NRRL-B-569) and inactive against *Escherichia coli* (NRRL-B-210) and *Penicillium chrysogenum* (250 μg/ml). In addition, β-(2-quinolyl)-α,β-dibromoacryloyl-Gly-OMe (XXVI) showed marked antibacterial activity as compared to XXV against *Bacillus subtilis*, *Bacillus cereus*, *Bacillus mycoids* and *Escherichia coli* with MIC values ranging from 1-10 μg/ml, and inactive against *Penicillium chrysogenum* (MIC 250-500 μg/ml). None of the β-[2-(4-hydroxy-6-nitro)-quinolyl]acryloylamino acid derivatives showed any significant activity (MIC 250-500 μg/ml) against all microorganisms tested as compared to the parent compound (XXXI). The remaining compounds were inactive at test concentrations (250 μg/ml).

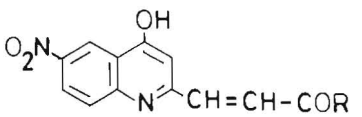
The present investigation indicated that introduction of amino acids and dipeptides to the quinolylacryloyl nucleus led in many cases to a remarkable increase in their antimicrobial activity. However, substitution in the 4- and 6-positions of the quinoline nucleus with hydroxy and nitro groups and the hydrazinolysis of the methyl esters resulted in biologically inactive compounds. Other pharmacological studies are now in progress.



(Compounds II-XXIV)



(Compounds XXVI-XXX)



(Compounds XXXII-XXXIX)

Experimental Procedures

Melting points were recorded in Kofler block and are uncorrected. IR spectra (KBr, ν_{max} in cm^{-1}) were recorded on a Unican SP 1200 spectrophotometer, and UV spectra (ethanol, λ_{max} in nm) on a Unicam SP 800 spectrophotometer. TLC (R_f values) was carried out on SiO_2/G (BDH), using benzene-ethyl acetate (1:1) as solvent system and an iodine-potassium iodide (20%) or chlorosulphonic acid-acetic acid (1:3) mixture as detection reagent. Benzidine, ninhydrin, silver nitrate and hydroxamate reactions were used for detection of amino acid derivatives on Whatman No. 1 paper chromatograms (spot reactions). The electrophoretic mobilities (E) were measured on Whatman No. 1 paper, with 1000 V, 2 hr, in pyridine-acetate buffer (pH 5.6). Optical rotations $[\alpha]_D^{20}$ were taken in a Zeiss polarimeter (c = 3), 1 dm tube in the solvents: (A) = ethanol and (B) = acetone (*cf.* Table 1).

β-(2-Quinolyl)-acrylic Acid (I)

This was prepared according to the procedure described in the literature (Albert and Bachamn 1935, El-Gazzar 1981).

Table 1. Physical data of various substituted Quinoline-acryloyl amino acid derivatives (II-XXXIX).

Compd. No.	–R	Yield* %	m.p. °C	R_f	$[\alpha]_D^{20}$**
	Compounds of the type (A)				
II	-Gly-OMe	55	171-173	0.62	–
III	-β-Ala-OMe	52	128-130	0.46	–
IV	-L-Val-OMe	60	114-116	0.36	+33.5 (A)
V	-L-Leu-OMe	56	164-166	0.52	+46.5 (A)
VI	-L-Phe-OMe	55	169-171	0.58	+48.5 (A)
VII	-DL-Ser-OMe	58	117-119	0.40	–
VIII	-L-Tyr-OMe	57	183-185	0.44	+50.6 (A)
IX	-L-Tyr-OMe	50	146-148	0.65	+45.7 (A)
X	-Gly-N_2H_3	60	92-94	0.65	–
XI	-β-Ala-N_2H_3	60	111-113	0.53	–
XII	-L-Val-N_2H_3	55	122-124	0.41	+48.5 (B)
XIII	-L-Leu-N_2H_3	65	120-122	0.58	+56.6 (B)
XIV	-DL-Ser-N_2H_3	62	108-110	0.45	–
XV	-L-Phe-N_2H_3	60	114-116	0.62	+95 (B)
XVI	-L-Tyr-N_2H_3	56	118-120	0.47	+90.5 (B)
XVII	-L-Try-N_2H_3	55	104-106	0.67	+93 (B)
XVIII	-β-Ala-L-Tyr-OMe	69	100-102	0.41	+25 (A)
XIX	-L-Val-L-Tyr-OMe	50	107-109	0.32	+47 (A)
XX	-L-Leu-L-Tyr-OMe	53	159-161	0.45	+45.5 (A)
XXI	-DL-Ser-L-Tyr-OMe	55	103-105	0.37	+32.5 (A)
XXII	-L-Phe-L-Tyr-OMe	52	156-158	0.53	+48 (A)
XXIII	-L-Tyr-L-Tyr-OMe	50	111-113	0.38	+54.5 (A)
XXIV	-L-Try-L-Tyr-OMe	56	149-151	0.59	+46.5 (A)
	Compounds of the type (B)				
XXVI	-Gly-OMe	40	181-183	0.70	–
XXVII	-β-Ala-OMe	50	217-219	0.78	–
XXVIII	-L-Val-OMe	42	211-213	0.75	+31.6 (A)
XXIX	-L-Phe-OMe	48	186-188	0.73	+37.5 (A)
XXX	-L-Tyr-OMe	46	190-192	0.69	+42.5 (A)
	Compounds of the type (C)				
XXXII	-β-Ala-OMe	65	188-190	0.67	–
XXXIII	-L-Val-OMe	64	196-198	0.58	+57 (A)
XXXIV	-L-Leu-OMe	60	209-211	0.62	+60.5 (A)
XXXV	-L-Tyr-OMe	62	193-195	0.63	+55 (A)
XXXVI	-β-Ala-N_2H_3	50	207-209	0.68	–
XXXVII	-L-Val-N_2H_3	55	111-113	0.61	+56.5 (B)
XXXVIII	-L-Leu-N_2H_3	54	200-202	0.64	+50 (B)
XXXIX	-L-Tyr-N_2H_3	58	191-193	0.65	+40.5 (B)

* Crystallization solvent for compounds II, X-XVII and XXXII-XXXVI = ethanol; and for compounds III-IX, XVIII-XXX and XXXVII-XXXIX = ethanol-water (1:1) mixture.

** Optical rotations $[\alpha]_D^{20}$ were measured (c = 3) in the solvents: (A) = ethanol and (B) = acetone.

Molecular formula	Elemental analysis, %					
	Calculated			Found		
	C	H	N	C	H	N
$C_{15}H_{14}N_2O_3$	66.67	5.18	10.37	66.69	5.35	10.51
$C_{16}H_{16}N_2O_3$	67.61	5.63	9.86	67.87	5.84	9.89
$C_{18}H_{20}N_2O_3$	69.23	6.41	8.97	69.54	6.67	9.00
$C_{19}H_{22}N_2O_3$	69.94	6.74	8.59	70.11	6.90	8.64
$C_{22}H_{20}N_2O_3$	73.33	5.56	7.78	73.41	5.71	7.91
$C_{16}H_{16}N_2O_4$	64.00	5.34	9.33	64.21	5.41	9.61
$C_{22}H_{20}N_2O_4$	70.21	5.32	7.45	70.34	5.61	7.39
$C_{24}H_{21}N_3O_3$	72.18	5.26	10.52	72.19	5.31	10.54
$C_{14}H_{14}N_4O_2$	62.22	5.18	20.74	62.31	5.22	20.75
$C_{15}H_{16}N_4O_2$	63.38	5.63	19.72	63.66	5.73	19.67
$C_{17}H_{20}N_4O_2$	65.38	6.41	17.95	65.40	6.69	18.11
$C_{18}H_{22}N_4O_2$	66.26	6.75	17.18	66.30	6.71	16.99
$C_{15}H_{16}N_4O_3$	60.00	5.34	18.67	60.21	5.49	18.72
$C_{21}H_{20}N_4O_2$	70.00	5.56	15.56	70.09	5.59	15.71
$C_{21}H_{20}N_4O_3$	67.02	5.32	14.89	67.12	5.37	14.93
$C_{23}H_{21}N_5O_2$	69.17	5.26	17.54	69.20	5.47	17.58
$C_{25}H_{25}N_3O_5$	67.11	5.59	9.39	67.13	5.83	9.52
$C_{27}H_{29}N_3O_5$	68.21	6.11	8.84	68.24	6.36	8.95
$C_{28}H_{31}N_3O_5$	68.71	6.34	8.59	68.84	6.50	8.64
$C_{25}H_{25}N_3O_6$	64.79	5.40	9.07	65.01	5.42	9.32
$C_{31}H_{29}N_3O_5$	71.13	5.54	8.03	71.09	5.62	8.11
$C_{31}H_{29}N_3O_6$	69.02	5.38	7.79	69.05	5.41	7.76
$C_{33}H_{30}N_4O_5$	70.46	5.34	9.94	70.41	5.35	9.98
$C_{15}H_{14}N_2O_3Br_2$	42.06	3.27	6.54	42.09	3.31	6.55
$C_{16}H_{16}N_2O_3Br_2$	43.44	3.62	6.33	43.67	3.71	6.42
$C_{18}H_{20}N_2O_3Br_2$	45.96	4.26	5.96	45.99	4.28	5.89
$C_{22}H_{20}N_2O_3Br_2$	50.97	3.86	5.41	50.99	4.01	5.50
$C_{22}H_{20}N_2O_4Br_2$	49.44	3.75	5.24	49.60	3.83	5.22
$C_{16}H_{15}N_3O_6$	55.65	4.35	12.17	55.81	4.59	12.20
$C_{18}H_{19}N_3O_6$	57.91	5.09	11.26	57.89	5.34	11.30
$C_{19}H_{21}N_3O_6$	58.91	5.43	10.85	59.01	5.44	10.93
$C_{22}H_{19}N_3O_7$	60.41	4.35	9.61	60.44	4.29	9.88
$C_{15}H_{15}N_5O_5$	52.17	4.35	20.29	52.20	4.59	20.21
$C_{17}H_{19}N_5O_5$	54.69	5.09	18.77	54.71	5.35	18.80
$C_{18}H_{21}N_5O_5$	55.81	5.43	18.09	55.93	5.48	17.99
$C_{21}H_{19}N_5O_6$	57.67	4.35	16.02	57.92	4.39	16.11

General Procedure for Synthesis of β-(2-Quinolyl)acryloylamino Acid Methyl Esters (II-IX)

To a solution of amino acid methyl ester hydrochloride (0.003 mole) in THF (20 ml) was added triethylamine (1 ml). The solution was stirred for 30 min at 20° and cooled to 0°. The precipitated triethylamine hydrochloride was filtered off and washed with THF (5 ml).

A solution of β-(2-quinolyl)-acrylic acid (I, 0.0025 mole) in THF (20 ml) and dicyclohexyl carbodiimide (0.0025 mole) was added to the filtrate at 0°C. The reaction was then allowed to proceed: (i) for 2 hr at 0° with stirring; (ii) for 12 hr at 0°; (iii) for 24 hr at room temperature and (iv) for 2 hr at 10°. The dicyclohexylurea was removed by filtration and the solvent evaporated to dryness under reduced pressure. The residual material was recrystallized from ethanol or ethanol-water (1:1) mixture. The products II-IX were soluble in DMSO, ethanol, methanol, DMF, dioxane and nitromethane and insoluble in water, ether and petroleum ether. The materials were shown to be homogeneous by paper chromatography when developed with iodine solution, benzidine or chlorosulphonic acid-acetic acid (1:3) mixture. Ninhydrin tests were negative. Electrophoretic mobilities (E) for compounds II-IX = zero.

The IR spectrum of β-(2-quinolyl)-acryloyl-Gly-OMe (II) showed characteristic bands at: 3140, 3080 (NH and N); 1660, 1550, 1340, (amide I, II and III); 1760, 1420, 1340 ($COOCH_3$); 2880, 2800, 2720, 1720, 1420, 1320 ($-CH_2-$ and $-CH=CH-$) and other characteristic bands due to quinolyl and amino acid moieties. The UV spectrum of II showed (log ε): 225 (4.42), 270 (3.16) and 315 (3.49) characteristic of the quinoline moiety.

General Procedure for Synthesis of β-(2-Quinolyl)acryloylamino Acid Hydrazides (X-XVII)

A solution of β-(2-quinolyl)acryloylamino acid methyl ester (II-IX, 0.001 mole) in methanol (35 ml) and hydrazine hydrate (85%, 0.005 mole) in methanol (20 ml) was first kept for 24 hr at 0°, and then for another 24 hr at room temperature. The crystalline product which was separated from the mixture was collected, washed with cold methanol and recrystallized from ethanol. The hydrazides X-XVII were found to be homogeneous (TLC and PC using iodine solution, benzidine or chlorosulphonic acid-acetic acid (1:3) mixture as the spray reagent), and showed negative ninhydrin and hydroxamate reactions.

The IR spectra of the hydrazides X-XVII exhibited bands at: 3430, 3140, 3070 (NH_2, NH, N and CONH); 1650, 1450, 1360 (amide I, II and III); 1670, 1420 ($-CH=CH-$) and other characteristic bands due to quinolylacryloyl- and amino acid residues. UV spectra of X-XVII showed (log ε): 228 (4.50), 270 (3.18) and 315 (3.46) characteristic of the quinoline moiety.

General Procedure for Synthesis of β-(2-Quinolyl)-acryloyldipeptide Methyl Esters (XVIII-XXIV)

The amino acid hydrazide (X-XVII, 0.005 mole) was dissolved in a mixture of acetic acid (8 ml), 5 *N* HCl (2 ml) and water (20 ml) and cooled to −5°. Sodium nitrite (0.56 g) in water (4 ml) was added and the mixture stirred for 10 min at 0° to −5°. The azide was precipitated as a syrup and then was extracted with cold ethyl acetate (50 ml) and the extract washed successively with water, sodium bicarbonate (3%), water and briefly dried (Na_2SO_4). Compounds XVIII-XXIV were prepared by the addition of ethyl acetate solution of the azide to a cooled (−5°) solution of the free amino acid methyl ester (prepared from 0.006 mole of the amino acid methyl ester hydrochloride and 0.9 ml triethylamine) and keeping the reaction mixture for 6 hr at room temperature. It was washed successively with HCl (0.5 *N*), water, sodium hydrogen carbonate (3%) and water and dried (Na_2SO_4). The solvent was removed and the residual material recrystallized from ethanol-water (1:1) mixture. All the dipeptides XVIII-XXIV were found to be homogeneous (TLC gave single spot with benzidine or iodine solution) and gave positive hydroxamate reaction. Electrophoretic mobilities (E) for all dipeptides XVIII-XXIV = zero.

IR spectra of compounds XVIII-XXIV showed bands at 3140, 3120, 3080 (NH, CONH, N); 1670, 1560, 1260 (amide I, II and III), 2880, 2800, 2720 (–CH=CH–); 1760, 1720 ($\gtrless$C=O); 1760, 1720, 1430, 1320 ($COOCH_3$) and other characteristic bands due to quinolyl, acryloyl and dipeptide residues. UV spectra of compounds XVIII-XXIV showed (log ε): 225 (4.49), 276 (3.38) and 315 (3.89) (quinoline moiety).

β-(2-Quinolyl)-α,β-dibromoacrylic Acid (XXV); and β-[2-(4-Hydroxy-6-nitro)quinolyl] Acrylic Acid (XXXI)

The titled compounds were prepared according to the procedure described earlier (Albert and Bachamn 1935, El-Gazzar 1981).

General Procedure for Synthesis of β-(2-Quinolyl)-α,β-dibromoacryloylamino Acid Methyl Esters (XXVI-XXX) and β-[2-(4-Hydroxy-6-nitro) quinolyl] Acryloylamino Acid Methyl Esters (XXXII-XXXV)

β-(2-Quinolyl)-α,β-dibromoacrylic acid (XXV, 0.001 mole) or β-[2-(4-hydroxy-6-nitro) quinolyl]-acrylic acid (XXXI, 0.001 mole) and amino acid methyl ester hydrochloride (0.0012 mole) were dissolved in THF (40 ml) or in a mixture of THF (30 ml) and DMF (10 ml), containing triethylamine (0.0013 mole). The mixture was cooled to 0°, dicyclohexylcarbodiimide (0.0011 mole) added and the reaction mixture stirred for 3-4 hr at 0° and left for 24 hr at 0°, and for another 24 hr at 20°. The precipitated dicyclohexylurea was filtered off, acetic acid (0.5 ml) added, the reaction mixture filtered again and the solvent removed *in vacuo*. The residual

material was recrystallized from ethanol or ethanol-water (1:1) mixture. The products XXVI-XXX and XXXII-XXXV were TLC-pure when developed with iodine, benzidine, chlorosulphonic acid-acetic acid (1:3) mixture or hydroxamate reaction, gave negative ninhydrin test. Electrophoretic mobilities (E) for compounds XXVI-XXX and XXXII-XXXV = zero.

The IR spectra of compounds XXVI-XXX showed bands at: 3340, 3160, 3080 (NH, CONH, N); 1650, 1550, 1360 (amide I, II and III); 1760, 1420, 1360 ($COOCH_3$); 2880, 2760, 1740, 1670 (–CH=CH–, CH_3, CH_2); 780, 690, 650, 620 (Br), and other bands characteristic of quinolyl and amino acid residues. UV spectra of compounds XXVI-XXX showed (log ε): 226 (4.33), 275 (3.98), and 316 (3.88) (quinoline moiety).

The IR spectra of compounds XXXII-XXXV showed bands at: 3440 (OH); 3360, 3120, 3080 (NH, CONH, N); 1650, 1560, 1320 (amide I, II and III); 1760, 1720 ($\geq$C=O); 1760, 1720, 1410, 1360 ($COOCH_3$); 1740, 1540, 1400 and 1260 (NO_2) and other characteristic bands due to quinolyl and amino acid residues. The UV spectra of compounds XXXII-XXXV showed (log ε); 229 (3.86), 282 (4.11) and 318 (3.98) characteristic of the quinoline moiety.

General Procedure for Synthesis of β-[2-(4-Hydroxy-6-nitro)-quinolyl]acryloyl-amino Acid Hydrazides (XXXVI-XXXIX)

Each of the methyl ester derivatives (XXXII-XXXV 0.01 mole) was dissolved in abs. ethanol (35 ml) and hydrazine hydrate (85%, 2.5 ml, 0.05 mole) added. The reaction mixture was stirred for 3-4 hr and left for 24 hr at 0° and for another 24 hr at room temperature. The crystalline products (XXXVI-XXXIX) were filtered, washed with cold ethanol, water and recrystallized. The products were chromatographically homogeneous (detection with benzidine or chlorosulphonic acid-acetic acid (1:3) mixture) and gave positive silver nitrate reaction.

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تحضير بعض مشتقات كينولين - أكريلويل الأحماض الأمينية

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يتضمن البحث تخليق مجموعة من المشتقات الجديدة لمركبات بيتا (٢ - كينولين) أكريلويل - حمض أميني ميثيل إستر و بيتا - (٢ - كينولين) - ألفا وبيتا - ثنائي برومو أكريلويل حمض أميني ميثيل إستر وبيتا - [٢ - (٤ - هيدروكسي - ٦ - نيترو) كينولين] أكريلويل حمض أميني ميثيل إستر وذلك بتكثيف الأحماض المناظرة لهذه المركبات مع الإستر الميثيلي للأحماض الأمينية في وجود تتراهيدروفيوران وثلاثي إيثيل أمين باستخدام طريقة الكاربودايميد.

وبمعالجة الإسترات الميثيلية لبعض هذه المركبات بهيدرازين الهيدرات في وجود الميثانول أو الإيثانول نتجت الهيدرازيدات المناظرة. وبتحويل المركبات الأخيرة إلى الآزيد المقابل ومفاعلته مع الإستر الميثيلي للتيروزين تم تخليق الببتيدات الثنائية باستخدام طريقة الآزيد.

وبدراسة النشاط البيولوجي للمركبات التى تم تحضيرها اتضح أن بعض المركبات لها نشاط بيولوجي مميز تجاه مختلف الكائنات الدقيقة.