Qatar Univ. Sci. Bull. (1983), 3: 79 - 89

SYNTHESIS AND BIOLOGICAL ACTIVITY OF SOME NEW 4-(AMINOACYL) AMINOPYRIDINES AND 2-(AMINOACYL) AMINOPYRIMIDINE DERIVATIVES

A. M. El-NAGGAR, F. S. M. AHMED, A. M. ABD EL-SALAM, M. S. A. LATIF AND H. M. ABD EL-BARY

Chemistry Department, Faculty of Science, Al-Azhar University, Nasr-City, Cairo, Egypt.

Key Words: 4 - (Aminoacyl) aminopyridines and 2 - (Aminoacyl) aminopyrimidine Derivatives.

ABSTRACT

The synthesis of 4-(N-Tos and N-Pht-aminoacyl) aminopyridines (III - XIV) and 2-(N-Pht-aminoacyl)-aminopyrimidines (XV-XXIV) has been achieved employing the acid chloride and carbodiimide methods. Hydrazinolysis of 4-(N-Pht-Gly or -B-Ala-) aminopyridines or 2-(N-Pht-L-Phe- or -B-Ala-) aminopyrimidines in ethanol afforded the desired 4-(Gly- or B-Ala) aminopyridines (XXV - XXVI) and 2-(L-Phe- or B-Ala) aminopyrimidines (XXVII - XXVIII) respectively. 4-(N-Pht- or N-Tos-dipeptidyl) aminopyridines (XXIX - XXXVI) are synthesized via the DCC method and 2-(N-Tos-L-Val-L-Leu) aminopyrimidine (XXXVII) via the azide method. The amino acid derivatives (XV, XVI, XXI, XXII, XXV, XXVI, XXVIII) and the dipeptide (XXXVII) are found to be active against a number of microorganisms.

INTRODUCTION

The interesting pharmacological properties of 2- aminopyrimidine and 4- aminopyridine derivatives (Abramovitch, 1974 and Brown, 1970) suggested the possibility of potential activity of simple 2-(aminoacyl) aminopyrimidine and 4-(aminoacyl) aminopyridine derivatives. It seem therefore desirable to synthesize some 4-(aminoacyl) aminopyridine and 2-(aminoacyl)-aminopyrimidine derivatives which may be of verified or intensified pharmaceutical effects. In continuation of our previous work (El-Naggar and Zaher 1977, El-Naggar and Ismail 1977 and El-Naggar *et al* 1981) the synthesis and microbiological studies of some 4-(N-Tos- or N-Pht-aminoacyl or aminoacyl or N-Pht- or N-Tos-dipeptidyl) amino pyridines and 2-(N-Tos- or N-Pht-aminoacyl or aminopyrimidines or N-Tos-L-Tos-L-Val-L-Leu) aminopyridines are reported in this paper.

EXPERIMENTAL

Melting points reported are uncorrected. TLC was carried out using silica gel-G and developed with benzene-ethyl acetate (1:1) mixture. Visualization of spots was done by spraying with iodine-potassium iodide (20%) solution. Benzidine, ninhydrin, silver nitrate and hydroxamate reactions were used as visualizing reagents (PC-spot reactions). E- electrophoretic mobility : 1000 V, 2 hr., 2N acetic acid. Optical rotation $[\alpha]_D^{20}$ were measured in DMF. IR spectra (KBr, ν_{max} in cm^{-1}) were recorded on a Unicam SP 1200 spectrophotometer, UV spectra

(ethanol,λ_{max} nm (log ϵ) on Unicam SP 8000 spectrophotometer. The NMR spectra in DMSO-D_6 were run in Varian T-60 A spectrophotometer using TMS as the internal standard (chemical shift in δ -ppm).

General procedure for synthesis of
4-(N-Pht- or N-Tos-aminoacyl)- aminopyridines (III-XIV)-

N-Phthaloyl- or N-tosylamino acid chloride (0.005 mole) was dissolved in dioxane (20 ml) and added dropwise during 30 min. to a cooled solution (−5°) of 4- aminopyridine (1, 0.47 g, 0.005 mole) in dioxane (25 ml) containing tri-ethylamine (4 ml). The reaction mixture was stirred for 2 hr at 0° and 3-4 hr at room temperature. At the end of the reaction, solid obtained was filtered, washed with water and recrystallized from methanol, ethanol, water or their mixture. The products (III-XIV) were chromatographically homogeneous (ninhydrin negative spot).

General pocedure for synthesis of
2-(N-Pht- or N-Tos-aminoacyl)- aminopyrimidines (XV-XXIV)-

N-Phthaloyl- or N-Tosylamino acid (0.01 mole) and 2- aminopyrimidine (II, 0.01 mole) were dissolved in dioxane (50 ml). The mixture was cooled to 0-5°, dicyclohexylcarbodiimide (2.4 g) added and the mixture stirred for 1-2 hr at 0° and left 24 hr at room temperature. The dicyclohexylurea was filtered off and 4 drops of gl. acetic acid added and the solution refiltered and the filtrate evaporated in vacuo. The residual solid was recrystallized from methanol, ethanol, water or their mixtures. The materials were chromatographically homogeneous when developed with iodine solution or benzidine (ninhydrin and hydroxamate negative spots).

4-(Gly- or β -Ala) aminopyridines (XXV - XXVI) and 2-(L-Phe- or B-Ala) aminopyrimidines (XXVII - XXVIII)-

Each of 4-(N-Pht-Gly- or β -Ala) aminopyridine (III-IV) or 2-(N-Pht-β-Ala or -L-Phe) aminopyrimidine (XVII or XIX) (0.003 mole) was dissolved in dioxane (25 ml) then treated with 0.5 M hydrazine hydrate in ethanol (13 ml.). The reaction mixture was refluxed for 6 hr. The residue obtained after evaporation of the solvent was treated with 2N HCl (50 ml) for 10 min at 50°C. The reaction mixture was cooled and the insoluble phthalyl-hydrazide filtered off. The filtered was treated with Et_3N (5 ml) for 30 min at 20°C, then Et_3N.HCl filtered off and the solvent evaporated in vacuum and the residual material was recrystallized from ethanol. The products (XXV-XXVIII) were chromatographically homogeneous when developed with iodine solution, benzidine and gave a positive ninhydrin reaction.

General procedure for synthesis of
4-(N-Tos- or N-Pht- dipeptidyl)- aminopyridines (XXIX - XXXVI)-

4-(Gly- or β -Ala) aminopyridine (XXV - XXVI) (0.003 mole) was dissolved in tetrahydrofuran (50 ml) containing triethylamine (2.5 ml) and the mixture stirred for 30 min., and N-tosyl- or N-phthaloylamino acid (0.003 mole) added. The reaction mixture was cooled to 0-5°, dicyclohexylcarbodiimide (0.9 g) added and the reaction mixture worked up as described for (XV - XXIV). The dipeptides (XXIX-XXXVI) were recrystallized from ethanol - water to be

homogeneous (PC detection with benzidine) and showed negative ninhydrin and silver nitrate reactions.

2 - (N-Tos-L-Val-L-Leu) aminopyrimidine (XXXVIII)-

N-Tos-L-Val-L-Leu-N_2H_3 (El-Naggar and Latif 1981) (0.0024 mole) was dissolved in a mixture of acetic acid (4 ml) conc. HCl. (2 ml) and water (25 ml). The mixture was cooled to −5° and sodium nitrite (0.54 g) in water (6 ml) added to it. The dipeptide azide was extracted with ethyl acetate (85 ml), washed successively with HCl (0.5 N), H_2O, sodium bicarbonate (3 %), water and dried (Na_2SO_4). Compound (XXXVII) was prepared by the addition of the dipeptide azide to a cooled (−5°) solution of 2-aminopyrimidine (0.0024 mole) in ethyl acetate (40 ml) and keeping the reaction mixture for 24 hr at 0° and for another 24 hr at room temperature. It was washed successfully with HCl (0.2 N), water, sodium bicarbonate (3 %), water and dried (Na_2SO_4). The solvent wa removed and the residual materials recrystallized from methanol. The dipeptide (XXXVII) was found to be homogenous (PC single spot with benzidine) and gave negative ninhydrin test.

RESULT AND DISCUSSION

For the preparation of 4-(N-Pht- or N-Tos-aminoacyl)- aminopyridine derivatives (III-XIV), N-phthaloyl- or N-tosylamino acid chloride was reacted with 4- aminopyridine (I) in dioxanetriethylamine medium using acid chloride procedure. All the products (III-XIV) were obtained in crystalline form in 40 - 75% yield and all gave chromatographically homogeneous spots. Structures of the synthesized pyridine derivatives (III-XIV) are supported by their IR, UV and NMR spectral data. Their IR spectra generally showed a characteristic bands at: 3340, 3140 (NH, N, CONH), 1660, 1560, 1360 (amide I, II and III), 1690 ($\geq$C = 0), 3070, 2960, 2780, 1780 and 1440 (pyridine nucleus), thereby confirming their structures. Their UV spectra showed λ_{max} (log ϵ): 262 (2.55), 256 (2.70) characteristic of the pyridyl chromophore. NMR spectra of compounds (III-XIV) exhibit four pyridyl protones in the range δ 7.00 to 7.60 and other protons assignable to aromatic and amino acid residues.

Coupling of N-phthaloyl- or N-tosylamino acids with 2- aminopyrimidine (II) in dioxane or THF - Et_3N medium using DCC procedure gave the desired 2-(N-Pht- or N-Tos-aminoacyl)-aminopyrimidines (XV-XXIV). Alternatively coupling of N-phthaloyl- or N-tosylamino acid clorides with 2- aminopyrimidines in benzene-Et_3N medium gave the products (XV-XXIV) with the same melting points, R_f and $[\alpha]^{20}_D$ and as those obtained by the DCC procedure. The compounds obtained by the acid chloride method needed several recrystallizations (yield 15-35 %). In general, the DCC method gave pure products with higher yield and hence was preferred. Each of the aminoacyl- aminopyrimidine derivatives (XV-XXIV) has the charateristic absorption of the IR spectrum at: 3340, 3140, 3040 (N, NH, CONH), 2940, 2860, 1570, 1390 (pyrimidine nucleus), 1650, 1560, 1260 (amide I, II and III), 1730 ($\geq$C = O) The UV absorption showed maxima at 292 (2.90), 242 (3.85) and 252 (3.90) charateristic of the pyrimidine chromophere.

The NMR spectra of compounds (XV-XXIV) exhibit three pyrimidyl protons in the range of δ 7.15 to 7.85 and other protons assignable to aromatic and amino acid residues.

Treatment of 4-(N-Pht-aminoacyl) aminopyridines or 2-(N-Pht-aminoacyl) aminopyrimidines with 1 molar solution of hydrazine in ethanol under mild reflux afforded compounds (XXV-XXVIII). The time required for completion of the reaction was monitored by TLC. Chromatographic and electrophoretic studies on compounds (XXV-XXVIII) revealed their homogeneity (positive ninhydrin reaction, E_{XXV} = 15 cm, E_{XXVI} = 19 cm, E_{XXVII} = 16 cm, E_{XXVIII} = 12 cm, E (for all the remaining compounds) = zero), and their structures were convincingly supported by the IR, UV and NMR spectral data.

4-(N-Tos- or N-Pht-dipeptidyl) aminopyridines (XXIX-XXXVI) were successively prepared by coupling of N-Tos- or N-Pht-amino acid with 4-(Gly- or -Ala) aminopyridine (XXV-XXVI) in THF containing Et_3N and using the DCC method. Most of the dipeptides were easily isolated, purified and recrystallized from the proper solvent. The IR spectra of compounds (XXIX-XXXVI) showed characteristic bands: 3370, 3330, 3040 (NH, N, CONH), 1730 ($\geq$C = 0), 1660, 1580, 1360 (amide I, II and III), 3060, 2960, 2880, 1460 (pyridine moiety) and other bands due to dipeptide and pyridine moieties, thereby supporting their structures. Elemental analysis of (XXIX - XXXVI), UV and PMR spectra were consistent with their structures (Table 1).

Synthesis of 2-(N-Tos-L-Val-L-Leu) aminopyrimidine (XXXVII) was achieved starting from the hydrazide Tos-L-Val-L-Leu-N_2H_3, which was converted into the corresponding azide. The azide on coupling with 2-aminopyrimidine (II) furnished the dipeptide (XXXVII), which was isolated and purified in the usual manner (El-Naggar *et al* 1977, 1981). The structure of (XXXVII) was confirmed on the basis of its elemental analysis, chromatographic studies, IR, UV and NMR spectral data.

Biological screeing results

The biological activities of the synthesized compounds were tested using the hole plate method and filter paper disc method, (Carlson- 1948; Eastern, 1944; Irving, 1946 and Vincent *et al* 1944), ad the results compared with the activity of the starting amino compounds (I and II).

2-(N-Pht-Gly) aminopyrimidine (XV) and the corresponding derivatives of N-Pht-L-Ala (XVI and N-Tos-L-Ala (XXI) were found to be active against *Bacillus subtilis* and inactive against *Bacillus mycoids, Bacillus cereus, Esch. coli, Salmonella typhosa* and *Penicillum chrysogenum.* 2-(N-Tos-L-Val-L-Leu) aminopyrimidine (XXXVII) was found to be active against *Bacillus subtilis* and *Bacillus mycoids* only. 2-(N-Tos-β-Ala) aminopyrimidine (XXII) inhibited the growth of *Bacillus subtilis* and *Bacillus cereus,* while did not inhibit the growth of *Esch. coli, Bacillus mycoids, Salmonella typhosa* and *Penicillum chrysogenum.* 2.-(L-Phe) aminopyrimidine (XXVIII) possesses high antimicrobial activity against *Bacillus subtilis* and *Esch. coli.* All the protected 4-(N-Pht- or N-Tos-aminoacyl or -dipeptidyl) aminopyridine (III-XIV and XXIX-XXXVI) were found to be biologically inactive towards all the tested microorganisms. On the other hand, 4-(Gly-or β -Ala) aminopyridines (XXV - XXVI) were found to possess high biological activities against *Bacillus subtilis, Bacillus mycoids, Bacillus cereus, Salmonella typhosa, Esch. coli.* and *Penicillum chrysogenum.*

Table 1

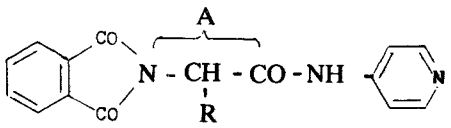
Physical data of various 4-(N-Tos or N-Pht-aminoacyl, aminoacyl, N-Tos- or N-Pht-dipeptidyl) aminopyridine and 2-(N-Tos- or N-Pht-aminoacyl, aminoacyl, N-Tos-dipeptidyl) aminopyrimidine Derivatives (III-XXXVII)

Compd (Type)	R	Yield (%)	m.p. (°C)	R_f (TLC)	$[\alpha]_D^{20}$ (deg.)	Mol. Formula	Elemental analysis, %					
							Calc.			Found		
							C	H	N	C	H	N
III-(A)	Pht-Gly-	49	236-238	0.76	———	$C_{15}H_{11}N_3O_3$	64.05	3.90	14.90	64.15	3.93	14.89
IV-(A)	Pht-β- Ala-	58	191-193	0.88	———	$C_{16}H_{13}N_3O_3$	65.08	4.42	14.23	64.99	4.70	14.30
V-(A)	Pht-L-Ala-	52	186-188	0.79	-16.8 (c 3.5)	$C_{16}H_{13}N_3O_3$	65.08	4.42	14.23	65.09	4.45	14.24
VI-(A)	Pht-DL-Ala	45	166-168	0.74	———	$C_{16}H_{13}N_3O_3$	65.08	4.42	14.23	65.18	4.80	14.26
VII-(A)	Pht-L-Val	63	219-221	0.90	-22 (c 4.5)	$C_{18}H_{17}N_3O_3$	66.87	5.26	13.00	66.95	5.37	13.10
VIII-(A)	Pht-DL-Phe	65	223-225	0.65	———	$C_{22}H_{17}N_3O_3$	71.10	4.58	11.32	71.20	4.58	11.35
IX-(A)	Pht-o-Aba-*	58	250-252	0.70	———	$C_{20}H_{13}N_3O_3$	69.97	3.97	12.24	70.07	3.90	12.50
X-(A)	Tos-Gly-	72	256-258	0.55	———	$C_{14}H_{15}N_3O_3S$	55.08	4.91	13.77	54.99	4.95	13.90
XI-(A)	Tos- β -Ala-	63	88-90	0.62	———	$C_{15}H_{17}N_3O_3S$	56.42	5.32	13.16	56.46	5.60	13.20
XII-(A)	Tos-L-Ala	64	178-180	0.65	-10 (c 0.6)	$C_{15}H_{17}N_3O_3S$	56.42	5.32	13.16	56.70	5.39	13.18
XIII-(A)	Tos-L-Val	75	142-144	0.60	-14.5 (c 0.6)	$C_{17}H_{21}N_3O_3S$	58.78	6.05	12.10	58.80	6.23	12.17
XIV-(A)	Tos-o-Aba	51	79-81	0.90	———	$C_{19}H_{17}N_3O_5S$	62.12	4.63	11.44	62.21	4.69	11.48
XV-(B)	Pht-Gly-	45	173-175	0.82	———	$C_{14}H_{10}N_4O_3$	59.57	3.54	19.85	59.60	3.94	19.96
XVI-(B)	Pht-L-Ala-	60	205-207	0.66	+20 (c 5.4)	$C_{15}H_{12}N_4O_3$	60.81	4.05	18.91	60.86	4.11	18.90
XVII-(B)	Pht-β-Ala	41	180-182	0.70	———	$C_{15}H_{12}N_4O_3$	60.81	4.05	18.91	60.85	4.21	18.96
XVIII-(B)	Pht-L-Leu	53	210-212	0.79	- 15.5 (c 5)	$C_{18}H_{19}N_4O_3$	63.71	5.60	16.51	63.82	5.63	16.54
XIX-(B)	Pht-L-Phe	43	150-152	0.55	+ 11 (c 4.7)	$C_{21}H_{16}N_4O_3$	67.74	4.30	15.00	67.80	4.38	15.20
XX-(B)	Tos-Gly-	58	160-162	0.93	———	$C_{13}H_{14}N_4O_3S$	50.98	4.57	18.30	50.97	4.58	18.29
XXI-(B)	Tos-L-Ala	48	170-172	0.65	+ 18.9 (c 5)	$C_{14}H_{16}N_4O_3S$	52.50	5.00	17.50	52.54	4.98	17.50
XXII-(B)	Tos-β-Ala-	50	198-200	0.85	———	$C_{14}H_{16}N_4O_3S$	52.50	5.00	17.50	52.33	5.11	17.45
XXIII-(B)	Tos-DL-Val-	58	175-177	0.54	———	$C_{16}H_{20}N_4O_3S$	55.17	5.74	16.09	55.31	5.72	16.20
XXIV-(B)	Tos-L-Phe-	65	191-193	0.70	+ 15.5 (c 6)	$C_{20}H_{20}N_4O_3S$	60.60	5.05	14.14	60.58	5.10	14.22
XXV-(A)	Gly-	67	202-204	0.50	———	$C_7H_{10}N_3OCl$	44.80	5.33	22.40	45.01	5.41	22.53
XXVI-(A)	β-Ala-	61	90-92	0.54	———	$C_8H_{12}N_3OCl$	47.60	5.95	20.84	47.69	6.01	20.98
XXVII-(B)	β-Ala-	90	175-177	0.43	———	$C_7H_{10}N_4O_4$	50.60	6.02	33.73	50.70	6.29	33.80
XXVIII-(B)	L-Phe-	82	168-170	0.74	- 12.5 (c 5.6)	$C_{13}H_{15}N_4O$	64.19	6.17	23.04	64.31	6.23	23.21
XXIX-(A)	Pht-Gly-Gly-	52	161-163	0.75	———	$C_{17}H_{14}N_4O_4$	60.36	4.14	16.57	60.34	4.21	16.63
XXX-(A)	Pht-Gly-β-Ala	43	165-167	0.97	———	$C_{18}H_{16}N_4O_4$	61.36	4.55	15.90	61.40	4.62	16.03
XXXI-(A)	Pht-o-Aba-Gly	49	202-204	0.83	———	$C_{22}H_{16}N_4O_4$	66.00	4.00	14.00	66.09	4.30	14.12
XXXII-(A)	Pht-o-Aba- -Ala	53	222-224	0.60	———	$C_{23}H_{18}N_4O_4$	66.76	4.35	13.53	66.86	4.42	13.61
XXXIII-(A)	Tos-β-Ala-Gly	73	114-116	0.77	———	$C_{17}H_{20}N_4O_4S$	54.26	5.32	14.89	54.31	5.34	14.95
XXXIV-(A)	Tos-L-Leu-Gly	61	116-118	0.65	- 20.5 (c 0.6)	$C_{20}H_{20}N_4O_4S$	57.42	6.22	13.59	57.50	6.40	13.60
XXXV-(A)	Tos-β-Ala-β-Ala-	72	120-122	0.80	———	$C_{18}H_{22}N_4O_4S$	55.38	5.64	14.36	55.42	5.71	14.41
XXXVI-(A)	Tos-DL-Ala-β-Ala-	78	128-130	0.87	———	$C_{18}H_{22}N_4O_4S$	55.38	5.64	14.36	55.45	5.72	14.45
XXXVII-(B)	Tos-L-Val-L-Leu-	48	180-182	0.82	- 20.5 (c 5.5)	$C_{22}H_{31}N_5O_4S$	57.26	6.27	15.18	57.35	6.47	15.44

*) o - Aba = Ortho-Aminobenzoic acid residue

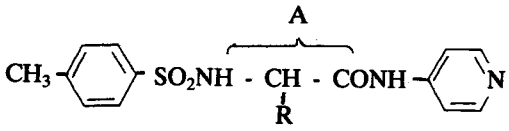
The present investigation reveals that introduction of N-Pht- or N-Tos-aminoacyl, aminoacyl, or N-Tos-dipeptidyl moieties in combination with 2- aminopyrimidine residue induces high and specific biological properties in 2-(N-Pht- or N-Tos-aminoacyl, aminoacyl or N-Tos-dipeptidyl) aminopyrimidines. However, in 4- aminopyridine derivatives blocking of the N-terminal amino group of the aminoacyl moiety with N-phthaloyl- or N-tosyl group results in biologically inactive compounds. In general, the unprotected 2-(aminoacyl) aminopyrimidine and 4-(aminoacyl) aminopyridine derivatives possess the highest antibacterial properties. Other pharmacological studies are in progress.

CHEMICAL STRUCTURES OF COMPOUNDS (III-XXXVII):



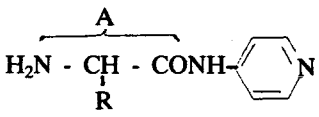
Compounds III - IX and XXIX - XXXII

III, A = Gly
IV, A = β-Ala
V, A = L-Ala
VI, A = DL-Ala
VII, A = L - Val
VIII, A = DL-Phe
IX, A = O-Aba
XXIX, A = Gly - Gly
XXX, A = Gly - β - Ala
XXXI, A = O - Aba - Gly
XXXII, A = O - Aba - β - Ala



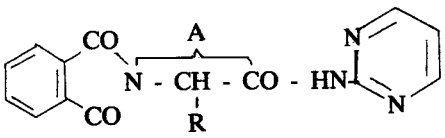
Compounds X - XIV and XXXIII - XXXVI

X, A = Gly
XI, A = β - Ala
XII, A = L - Ala
XIII, A = L - Val
XIV, A = O - Aba
XXXIII, A = β - Ala - Gly
XXXIV, A = L - Leu - Gly
XXXV, A = β - Ala - β - Ala
XXXVI, A = DL - Ala - β - Ala



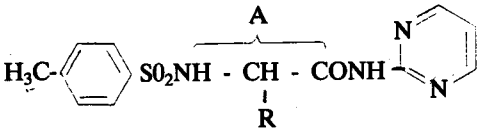
(XXV - XXVI)

XXV, A = Gly
XXVI, A = β - Ala



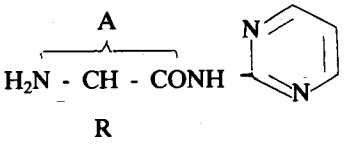
(XV - XIX)

XV, A = Gly
XVI, A = L - Ala
XVII A = β - Ala
XVIII, A = L - Leu
XIX, A = L- Phe



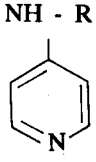
(XX - XXIV)

XX, A = Gly
XXI, A = L - Ala
XXII, A = β - Ala
XXIII, A = DL - Val
XXIV, A = L - Phe
XXXVII, A = L - Val - L - Leu

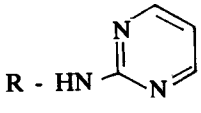


(XXVII - XXVIII)

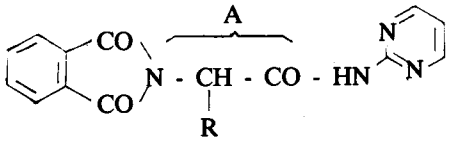
XXVII, A = β - Ala
XXVIII, A = L - Phe



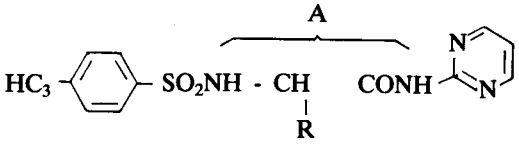
(Compounds Type A)



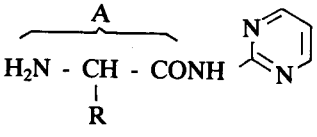
(Compounds Type B)



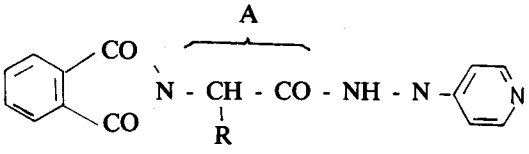
(XV - XIX)



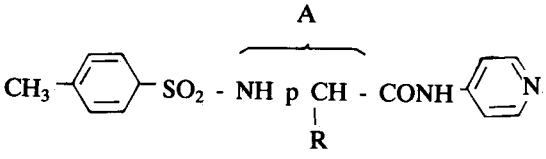
(XX - XXIV)



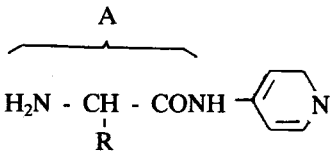
(XXVII - XXVIII)



Compounds III - IX and XXI - XXXII



Compounds X - XIV and XXXIII - XXXVI



(XXV - XXVI)

REFERENCES

Abramovitch, R.A. 1974. "The chemistry of heterocyclic compounds", vol. 14, "Pyridine and its derivatives", Interscience, John Wiley, New York, 41-52.

Brown, D.J. 1970. "The chemistry of heterocyclic compounds," vol. 16, "The Pyrimidines", John Wiley, New York, 230-242.

Carlson, H.J. 1948. Determination of the antimicrobial activity of different compounds using the hole plate method, J. Bacteriol., 55; 607-612.

El-Naggar, A.M. and **Zaher, M.R. 1977.** Synthesis of some peptides containing hippuric acid, urea, thiourea and 2-aminopyridine, Indian J. Chem., 15B; 863-865.

El-Naggar, A.M., Ismail, I.M. and **Gommaa, A.M. 1977.** Synthesis of some 2-(N-tosyl or N-phthalylaminoacyl) aminopyridines and some aminothiazole derivatives, Indian. J. Chem., 15B; 850-853.

El-Naggar, A.M., Ahmed, F.S.M. and **Badie, M.F. 1981.** Synthesis of some 2-(N-protected of free aminoacyl) aminophenazines and aminophenazone derivatives, J. Heterocyclic Chem., 18; 91-95.

Epstein, J.A. 1944. Applications and modification of the filter paper disc method, Lab. Clin. Med., 29; 319-325.

Irving, G.W. 1946. Filamentous mold fungi as test organism, J. Bacteriol., 52; 10-18.

Vincent, J.C. and **Vincent, H.W. 1944.** A new method for the determination of antimicrobial properties. The filter paper disc method, Pract. Exptl. Biol., 55; 162-167.

التحضير والنشاط البيولوجى لبعض المشتقات الجديدة لمركبات ٤ ـ أمينو اسيل أمينو بيريدين و٢ ـ أمينو اسيل امينو بيريدين

أحمد محمد النجار فايق سعيد محمد أحمد

عبد المنعم عبد السلام محسن سعيد حسن عبد البارى

تضمن البحث تخليق مجموعة جديدة من مركبات ٤ ـ (ن ـ توزيل أو ن ـ فثاليل ـ امينو اسيل) امينو بيريدين و٢ ـ (ن ـ توزيل أو ن ـ فثاليل ـ امينو اسيل) امينو بيريدين وذلك باستخدام طريقة الكلوريد الحامضى والكاريودايميد . ومعالجة مركبات ٤ ـ (ن ـ فثاليل جلاسيل أو الانيل) امينو بيريدين ومشتقات ٢ ـ (ن ـ فثاليل فينيل الانيل او بيتا الانيل) امينو بيريدين في الايثانول نتجت المشتقات الطليقة المحتوية على مجموعات الامين الغير محمية .

وشمل البحث على تخليق مجموعة من مركبات ٤ ـ (ن ـ فثاليل او ن ـ توزيل ـ بيتيد ثنائى) امينو بيريدين وذلك باستخدام طريقة الكاريودايميد ومركب ٢ ـ (ن ـ توزيل فثاليل ـ ليوسيل) امينو بيريدين باستخدام طريقة الازيد .

وبدراسة النشاط البيولوجى للمركبات التي تم تخليقها اتضح ان عدد ثمانية مركبات ذات نشاط بيولوجي عال تجاه مختلف الكائنات الدقيقة .