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Synthesis and Biological Activity of Some New 4-(Aminoacyl)-Aminopyridines and 2-(Aminoacyl) Aminopyrimidine Derivatives

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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-β-Ala-) aminopyridines or 2-(N-Pht-L-Phe-or-β-Ala-) aminopyrimidines in ethanol afforded the desired 4-(Gly-or-β-Ala) aminopyridines (XXV-XXVI) and 2-(L-Phe-or-β-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 (XXXVIII) *via* the azide method. The 2-(aminoacyl) aminopyrimidine derivatives (XV, XVI, XXI, XXII, XXVIII and XXXVII) and the 4-(aminoacyl)-aminopyridine derivatives (XXV, XXVI) are found to possess various antimicrobial and antifungal properties (as compared to I & II) towards different microorganisms with MIC values ranging from 5 to 250 μg/ml.

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 seems 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 *et al.* 1977 and

* Abbreviations for all the amino acids are those proposed by IUPAC-IUB Commission on Biochemical Nomenclature, J. Biol. Chem., **247**, 977 (1972); o-Aba-ortho-aminobenzoic acid residue; Pht- = phthaloyl residue; Tos= p-tosyl residue; DCC= dicyclohexylcarbodiimide; Et_3N= triethylamine and MIC = minimal inhibitory concentration.

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 aminoacyl or N-Tos-L-Val-L-Leu) aminopyrimidines 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). The electrophoretic mobilities (E) were measured using vertical high voltage paper electro-phoresis: Whatman No. 1 paper, 1000 V, 2 hr, 2*N* acetic acid. Optical rotations $[\alpha]_D^{20^\circ}$ were measured in DMF. IR spectra (KBr, λ_{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 on 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 (I, 0.47 g, 0.005 mole) in dioxane (25 ml) containing triethylamine (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 mixtures. The products (III-XIV) were chromatographically homogeneous (ninhydrin negative spot).

General procedure 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 β-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 2*N* HCl (50 ml) for 10 min. at 50°C. The reaction mixture was cooled and the insoluble phthalyl-hydrazide filtered off. The filtrate 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, found to be homogeneous (PC detection with benzidine) and showed negative ninhydrin and silver nitrate reactions.

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

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 mixure for 24 hr at 0° and for another 24 hr at room temperature. It was washed successively with HCl (0.2*N*), water, sodium bicarbonate (3%), water and dried (Na_2SO_4). The solvent was removed and the residual material recrystallized from methanol. The dipeptide (XXXVII) was found to be homogeneous (PC single spot with benzidine) and gave negative ninhydrin test

Results 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 dioxane-triethylamine 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 (>C=O), 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 chromphore. NMR spectra of compounds (III-XIV) exhibit four pyridyl protons 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 chlorides with 2-aminopyrimidines in benzene-Et_3N medium gave the products (XV-XXIV) with the same melting points, R_f and $[\alpha]_D^{20}$ 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 characteristic absorption of the IR spectrum at: 3340, 3140, 3040, (N, NH, CONH), 2940, 2860, 1750, 1390, (pyrimidine nucleus), 1650, 1560, 1260 (amide I, II and III), 1730 (>C=O). The UV absorption showed maxima at 292 (2.90), 242 (3.85) and 252 (3.90) characteristic of the pyrimidine chromophore. The NMR spectra of compounds (XV-XXIV) exhibit three pyrimidyl protons in the rage 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 hydrate 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, $E_{(\text{for all the remaining})}$=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 β-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 (>C=O), 1660, 1580, 1360 (amide I, II and III), 3060, 2960, 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 NMR 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 as 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 Screening Results:

The antimicrobial activity of the compounds which were synthesized (III-XXXVII) were tested using the following methods:

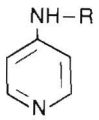
(a) The hole plate method - The procedure described by Carlson (1948) was employed using the nutrient agar medium (g %), 0.5 peptone; 0.15 beef extract; 0.15 yeast extract; 0.1 glucose; 0.5 sodium chloride; 1.5 agar and 100 ml tap water; pH 7 and incubation period 24 hr at 70°C.

(b) The filter paper disc method - The procedure described by Vincent and Vincent (1944) and Epstein (1944) was employed using small discs of filter paper and 5 mg of the sample was dissolved in 10 ml acetone and serial dilution were made using acetone for dilution, incubation period for bacteria 24 hr at 30° and for fungi 5 days at 24°. In the case of antifungal agents the method of Irving (1946) was employed using 5 ml of the spore suspension and 40 ml of Czapek - Sucrose - agar (g.%) (2 sucrose; 0.2 $NaNO_3$; 0.1 KH_2PO_4; 0.05 KCl; 0.05 $MgSO_4$ $7H_2$; 2.0 agar and 100 ml tap water) at 45°. The results were compared with the activity of the parent 4-aminopyridine (I) and 2-aminopyrimidine (II). The data of the activity (A) and minimal inhibitory concentration (MIC) values are summarized in Table (2).

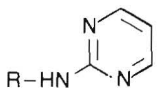
Table 1. Physical Data of Various 4-(N-Tos- or N-Pht-aminoacyl, aminoacyl, N-Tos- or N-Pht-dipeptidyl) aminopyridine and 2-(N-Tos- or N-Pht-aminoacyl, aminoacyl, N-Tos-dipeptidyl) aminopyrimidine Derivatives (III-XXXVII)

Compd. (Type)	R	Yield (%)	m.p. (°C)	R_f (TLC)	$[\alpha]_D^{20}$ (deg.)
III-(A)	Pht-Gly-	49	236-238	0.76	—
IV-(A)	Pht-β-Ala-	58	191-193	0.88	—
V-(A)	Pht-L-Ala-	52	186-188	0.79	−16.8 (c, 3.5)
VI-(A)	Pht-DL-Ala-	45	166-168	0.74	—
VII-(A)	Pht-L-Val-	63	219-221	0.90	−22 (c, 4.5)
VIII-(A)	Pht-DL-Phe-	65	223-225	0.65	—
IX-(A)	Pht-*O*-Aba-*	58	250-252	0.70	—
X-(A)	Tos-Gly-	72	256-258	0.55	—
XI-(A)	Tos-β-Ala-	63	88-90	0.62	—
XII-(A)	Tos-L-Ala-	64	178-180	0.65	−10 (c, 0.6)
XIII-(A)	Tos-L-Val-	75	142-144	0.60	14.5 (c, 0.6)
XIV-(A)	Tos-*O*-Aba-	51	79-81	0.90	—
XV-(B)	Pht-Gly-	45	173-175	0.82	—
XVI-(B)	Pht-L-Ala-	60	205-207	0.66	+20 (c, 5.4)
XVII-(B)	Pht-β-Ala-	41	180-182	0.70	—
XVIII-(B)	Pht-L-Leu-	53	210-212	0.79	−15.5 (c, 5)
XIX-(B)	Pht-L-Phe-	43	150-152	0.55	+11 (c, 4.7)
XX-(B)	Tos-Gly-	58	160-162	0.93	—
XXI-(B)	Tos-L-Ala-	48	170-172	0.65	+18.9 (c, 5)
XXII-(B)	Tos-β-Ala	50	198-200	0.85	—
XXIII-(B)	Tos-DL-Val-	58	175-177	0.54	—
XXIV-(B)	Tos-L-Phe-	65	191-193	0.70	+15.5 (c, 6)
XXV-(A)	Gly-	67	202-204	0.50	—
XXVI-(A)	β-Ala-	61	90-92	0.54	—
XXVII-(B)	β-Ala-	90	175-177	0.43	—
XXVIII-(B)	L-Phe-	82	168-170	0.74	−12.5 (c, 5.6)
XXIX-(A)	Pht-Gly-Gly-	52	161-163	0.75	—
XXX-(A)	Pht-Gly-β-Ala-	43	165-167	0.97	—
XXXI-(A)	Pht-*O*-Aba-Gly-	49	202-204	0.83	—
XXXII-(A)	Pht-*O*-Aba-β-Ala-	53	222-224	0.60	—
XXXIII-(A)	Tos-β-Ala-Gly-	73	114-116	0.77	—
XXXIV-(A)	Tos-L-Leu-Gly-	61	116-118	0.65	−20.5 (c, 0.6)
XXXV-(A)	Tos-β-Ala-β-Ala-	72	120-122	0.80	—
XXXVI-(A)	Tos-DL-Ala-β-Ala-	78	128-130	0.87	—
XXXVII-(B)	Tos-L-Val-L-Leu-	48	180-182	0.82	−20.5 (c, 5.5)

* *O*-Aba = ortho-Aminobenzoic acid residue.



(Compound Type A)



(Compound Type B)

Molecular formula	Elemental analysis, %					
	Calc.			Found		
	C	H	N	C	H	N
$C_{15}H_{11}N_3O_3$	64.05	3.90	14.90	64.15	3.93	14.89
$C_{16}H_{13}N_3O_3$	65.08	4.42	14.23	64.99	4.70	14.30
$C_{16}H_{13}N_3O_3$	65.08	4.42	14.23	65.09	4.45	14.24
$C_{16}H_{13}N_3O_3$	65.08	4.42	14.23	65.18	4.80	14.26
$C_{18}H_{17}N_3O_3$	66.87	5.26	13.00	66.95	5.37	13.10
$C_{22}H_{17}N_3O_3$	71.10	4.58	11.32	71.20	4.58	11.35
$C_{20}H_{13}N_3O_3$	69.97	3.79	12.24	70.07	3.90	12.50
$C_{14}H_{15}N_3O_3S$	55.08	4.91	13.77	54.99	4.95	13.90
$C_{15}H_{17}N_3O_3S$	56.42	5.32	13.16	56.46	5.60	13.20
$C_{15}H_{17}N_3O_3S$	56.42	5.32	13.16	56.70	5.39	13.18
$C_{17}H_{21}N_3O_3S$	58.78	6.05	12.10	58.80	6.23	12.17
$C_{19}H_{17}N_3O_3S$	62.12	4.63	11.44	62.21	4.69	11.48
$C_{14}H_{10}N_4O_3$	59.57	3.54	19.85	59.60	3.94	19.96
$C_{15}H_{12}N_4O_3$	60.81	4.05	18.91	60.86	4.11	18.90
$C_{15}H_{12}N_4O_3$	60.81	4.05	18.91	60.85	4.21	18.96
$C_{18}H_{19}N_4O_3$	63.71	5.60	16.51	63.82	5.63	16.54
$C_{21}H_{16}N_4O_3$	67.74	4.30	15.00	67.80	4.38	15.20
$C_{13}H_{14}N_4O_3S$	50.98	4.57	18.30	50.97	4.58	18.29
$C_{14}H_{16}N_4O_3S$	52.50	5.00	17.50	52.54	4.98	17.50
$C_{14}H_{16}N_4O_3S$	52.50	5.00	17.50	52.53	5.11	17.45
$C_{16}H_{20}N_4O_3S$	55.17	5.74	16.09	55.31	5.72	16.20
$C_{20}H_{20}N_4O_3S$	60.60	5.05	14.14	60.58	5.10	14.22
$C_7H_{10}N_3OCl$	44.80	5.33	22.40	45.01	5.41	22.53
$C_8H_{12}N_3OCl$	47.60	5.93	20.84	47.69	6.01	20.98
$C_7H_{10}N_4O$	50.60	6.02	33.73	50.70	6.29	33.80
$C_{13}H_{15}N_4O$	64.19	6.17	23.04	64.31	6.23	23.21
$C_{17}H_{14}N_4O_4$	60.36	4.14	16.57	60.34	4.21	16.63
$C_{18}H_{16}N_4O_4$	61.36	4.55	15.90	61.40	4.62	16.03
$C_{22}H_{16}N_4O_4$	66.00	4.00	14.00	66.09	4.30	14.12
$C_{23}H_{18}N_4O_4$	66.76	4.35	13.53	66.86	4.42	13.61
$C_{17}H_{20}N_4O_4S$	54.26	5.32	14.89	54.31	5.34	14.95
$C_{20}H_{20}N_4O_4S$	57.42	6.22	13.59	57.50	6.40	13.60
$C_{18}H_{22}N_4O_4S$	55.38	5.64	14.36	55.42	5.71	14.41
$C_{18}H_{22}N_4O_4S$	55.38	5.64	14.36	55.45	5.72	14.45
$C_{22}H_{31}N_5O_4S$	57.26	6.27	15.18	57.35	6.47	15.44

Table 2. Antimicrobial activity (A)* and minimal inhibitory concentration (MIC in μg/ml) of the biologically active compounds**

Compd. No.	Comparison with	*B. subtilis* ICC-strain		*B. mycoids* (USSR)		*B. cereus* (NRRL-B-569)		*E. coli* (NRRL-B-210)		*Salm. Typhosa* (NRRL-B-573)		*Pen. chryso-genum*	
		MIC	A	MIC	A	MIC	A	MIC	A	MIC	A	MIC	A
XV	II	50	++	–	–	–	–	–	–	–	–	–	–
XVI	II	50	++	–	–	–	–	–	–	–	–	–	–
XXI	II	50	++	–	–	–	–	–	–	–	–	–	–
XXII	II	25	+++	–	–	–	–	–	–	–	–	–	–
XXV	I	15	+++	250	+	25	+++	125	++	25	+++	10	+++
XXVI	I	15	+++	250	+	25	+++	125	++	25	+++	10	+++
XXVIII	II	5	+++	–	–	–	–	10	+++	–	–	–	–
XXVII	II	25	+++	15	+++	–	–	–	–	–	–	–	–
I	–	250	+	500	+	250	+	–	–	–	–	125	++
II	–	125	++	250	+	125	++	250	+	–	–	–	–

* Antimicrobial activity (A) +++ = highly active;
++ = moderately active; + = slightly active;
– = inactive and MIC = minimal inhibitory concentration in μg/mg.

** Compounds (III - XIV; XVII - XX; XXIII - XXIV; XXVII; XXIX - XXXVI) were biologically inactive (MIC 500 μg/ml) towards all the microorganisms given in Table 2.

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-(Tos-β-Ala) aminopyrimidine (XXII) inhibited the growth of *Bacillus subtilis* and *Bacillus cereus,* while did not inhibit the growth of *E. coli, Bacillus mycoids, Salmonella typhosa* and *Penicillum chrysogenum.* 2-(L-Phe) aminopyrimidine (XXVIII) possess high antimicrobial activity against *Bacillus subtilis* and *E. coli.* All the protected 4-(N-Pht- or N-Tos-aminoacyl or -dipeptidyl) aminopyridines (III-XIV and XXIX-XXXVI) were found to be biologically inactive towards all the test 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, E. coli.* and *Penicillum chrysogenum.*

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.

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تحضير والنشاط البيولوجي لبعض المشتقات الجديدة لمركبات ٤ ـ أمينو آسيل أمينو بيريدين و ٢ ـ أمينو آسيل أمينو بيريدين

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تضمن البحث تخليق مجموعة جديدة من مركبات ٤ ـ (ن ـ توزيل أو ن ـ فثاليل ـ أمينو آسيل) أمينو بيريدين و ٢ ـ (ن ـ توزيل أو ن ـ فثاليل ـ أمينو آسيل) أمينو بيريدين وذلك باستخدام طريقة الكلوريد الحامضي والكاربوداميد. وبمعالجة مركبات ٤ ـ (ن ـ فثاليل جلاسيل أو الانيل) أمينو بيريدين ومشتقات ٢ ـ (ن ـ فثاليل فينيل الأنيل أو بيتا الأنيل) أمينو بيريدين في الأيثانول نتجت المشتقات الطليقة المحتوية على مجموعات الأمين الغير محمية.

وشمل البحث على تخليق مجموعة من مركبات ٤ ـ (ن ـ فثاليل أو ن ـ توزيل ـ ببتيد ثنائي) أمينو بيريدين وذلك باستخدام طريقة الكاريوداميد ومركب ٢ ـ (ن ـ توزيل فثاليل ـ ليوسيل) أمينو بيريدين باستخدام طريقة الآزيد.

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