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SYNTHESIS AND BIOLOGICAL ACTIVITY OF CERTAIN IMIDAZO[4,5-b]PYRIDINES

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ABSTRACT

The synthesis of certain imidazo[4,5-b]pyridine derivatives namely; 3-(p-(un)substitutedphenacyl) imidazo[4,5-b]pyridin-2-ones, their ketoximes and 1,3-bis(p-(un)substitutedphenacyl)imidazo[4,5-b]pyridin-2-ones, were under-taken. In addition the synthesis of a series of 2-methylaminoimidazo[4,5-b]pyridines and their corresponding ketoximes are discussed. Some of the synthesized imidazo[4,5-b]-pyridin-2-ones derivatives showed reasonable analgesic activity in comparison to Aspirin and Indomethacin. Compounds of 2-methylaminoimidazo [4,5-b] pyridines and their corresponding ketoximes have been tested for their anthelmintic activity against Ascaris Vitulorum of cattle in comparison to Mebendazole.

INTRODUCTION

Imidazo [4,5-b] pyridines are known to possess a wide range of pharmacological activities [1-8]. Incorporation of various pharmacophoric moieties into the structure of this heterocyclic system was effective in inducing pharmacological properties comparable to or different from those of the corresponding benzimidazoles.

Looking for novel potent analgesic and antiinflammatory compounds which are neither acidic nor steroidal; certain 2-acylaminoimidazo[4,5-b]-pyridines [9] and imidazo [4,5-b]pyridin-2-ones and thiones[10-11] have been synthesized and found to possess pronounced analgesic and antiinflammatory activities. A group of imidazo[4,5-b]-pyridine with different substituents on the 2- and 3-position has been prepared and showed a promising anthelmintic activity [12-13]. Imidazo [4,5-b]pyridines carrying carbamates and alkyl carbamates at the 2-position exhibited good anthelmintic activity [14,15].

With this rationale and literature precedent, the synthesis and test for analgesic activity of certain 3-(p-(un)substitutedphenacyl) imidazo[4,5-b]pyridin-2-ones (1a-L) their ketoximes (2a-L) as well as 1,3-bis(p-(un)substitutedphenacyl) imidazo [4,5-b]pyridin-2-ones (3a-L) was carried out. Compounds having a methylamino function at position 2 of imidazo [4,5-b] pyridine (4a-L), and corresponding oximes (5a-L) were prepared and tested for anthelmintic activity.

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EXPERIMENTAL

Melting points were determined in open glass capillaries and are uncorrected. Elemental analyses were performed at the unit of microanalysis, Cairo University, and Faculty of Science Assiut University, Egypt. Infrared spectra were recorded, for KBr discs, on a Pye Unicam SP 1000 Infrared Spectrophotometer. Mass spectra were carried out on a Perkin Elmer Mass Spectrometer using direct chemical ionization technique (utilizing methane gas) at Merck Sharp and Dhome research center, Philadelphia, USA. NMR spectra were recorded on a EM360-90 MHz Varian NMR spectrometer with DMSO-d_6 as solvent and TMS as internal standard.

Ethyl 3-pyridyl carbamate, ethyl 3-(2-nitropyridyl) carbamate,3-amino -2-nitropyridine, 2-amino-5-bromo-pyridine, 3-amino-5-bromo-3-nitro-pyridine and 5-bromo-2,3-diamino-pyridine were prepared according to reported procedures[16,17].

Imidazo[4,5-b]pyridin-2-ones:

A mixture of 2,3-diaminopyridine (1.1 g, 0.01 mole) and urea (0.6 g, 0.01 mole) was fused on an oil bath at 180°C for one hour. The cooled dark brown solid was dissolved in sodium hydroxide solution (2.5 N, 20 ml), decolourized with charcoal, filtered and the filtrate was acidified with HCl. The precipitate was filtered and crystallized from glacial acetic acid. Yield 0.8 g (58.8 %); m.p. > 300°C as reported[18]. The same procedure was applied to the synthesis of 6-bromoimidazo [4,5-b]pyridin-2-one using 5-bromo-2,3-diaminopyridine as starting material. Yield 1.0 g (62 %); m.p. > 300°C as reported[19].

(p(un)Substitutedphenacyl) imidazo[4,5-b]pyridin -2-ones (1a-L):

To a mixture of dimethylformamide (20 ml), and sodium hydride (0.04 g, 0.01 mole), a mixture (1:1) of imidazo[4,5-b]pyridin-2-one (0.01 mole) and the appropriate phenacyl bromide (0.01 mole) was added over a period of 30 minutes while stirring at room temperature.

The reaction mixture was acidified with dilute hydrochloric acid and the precipitate formed was filtered, washed with water and recrystallized from the appropriate solvent (Table 1). 6-Bromo-3-(p-(un) substitutedphenacyl) imidazo [4,5-b] pyridin-2-ones-(1g-L) were prepared according to the same procedure using 5-bromoimidazo[4,5-b]pyridin-2-one as starting material.

Ketoxime of 3-(p-(un)Substitutedphenacyl) imidazo[4,5-b] pyridin-2-ones(2a-L):

A mixture of appropriate 3-(p-(un)substitutedphenacyl)imidazo [4,5-b] pyridin-2-one (0.01 mole), hydroxylamine hydrochloride (0.03 mole), pyridine (10 ml), and methanol (30 ml) was refluxed for 2 hours. The solvents were evaporated under reduced pressure, the residue was washed with water and then crystallized from 50 % V/V aqueous ethanol (Table 11).

1,3-bis(p-(un)Substitutedphenacyl Imidazo[4,5-b] pyridin-2-ones(3a-L):

Were prepared as mentioned for mono phenacyl derivatives but using 2 molar equivalents of the phenacyl bromide derivatives.

N-(2-Aminopyrid-3-yl)-N-methylthiourides:

Mixture of 2,3-diaminopyridine(1.09 g, 0.01 mole), or 5-bromo-2,3-diaminopyridine (1.80 g, 0.01 mole), and methyl isothiocyanate (0.73g, 0.01 mole) in benzene (40 ml) was refluxed for 5 hours. The solvent was removed under reduced pressure and the separated product was crystallized from ethanol.

Yield 1.86 g (97%) m.p. 167-168°C and 2.41 g(92%) m.p. 212-214°C respectively.

2-Methylaminoimidazo[4,5-b] pyridines:

Method A): N-(2-aminopyrid-3-yl)N-methylthiourea (18.2 g, 0.1 mole), or N-(2-amino-5-bromopyrid-3-yl)-N-methylthiourea(0.1 mole), was added to a stirred suspension of excess yellow mercuric oxide (60 g) in ethanol (300 ml) over 10 minutes. The mercuric compounds were filtered and washed with hot ethanol; the filtrates were combined and evaporated. The solid product was dissolved in water (50 ml), acidified with HCl, and filtered off to remove the insoluble material. The filtrate was made alkaline with NH_4OH to pH 8-9 and the precipitated solid was filtered and crystallized from aqueous ethanol. Yield of 9.5 g (63 %); m.p. 196-198°C and of 16 g (70 %) m.p. 204-207°C.

Method B): A solution of N-(2-aminopyrid-3-yl)-N-methylthiourea (0.1 mole) or N-(2-amino-5-bromopyrid-3-yl)-N-methylthiourea (0.1 mole) and dicyclohexylcarbodimide (0.15 mole) in benzene (100 ml) was refluxed for five hours. The mixture was cooled and shaken with HCl 10% (3X50 ml). The aqueous part was made alkaline with NH_4OH and extracted with chloroform. The extract was dried and evaporated to dryness. The solid product was crystallized from aqueous ethanol; m.p. 196-198°C and 204-207°C.

2-Methylamino-3-(p(un)substitutedphenacyl)imidazo[4,5-b]-pyridines(4_a-L) :

2-Methylaminoimidazo[4,5-b] pyridine (0.01 mole) or 6-bromo-2-methylamino [4,5-b] pyridine (0.01 mole) and sodium methylate (0.01 mole) were dissolved in ethanol (50 ml). Appropriate phenacyl bromide (0.01 mole) in ethanol (20 ml) was added and the reaction mixture was refluxed for 2 hours. Most of the solvent was distilled off and the residue was poured onto ice-cooled water.

The precipitate was filtered out, washed with water, and crystallized from the appropriate solvent (Table IV).

2-Methylamino-3-(p(un)substitutedphenacyl Ketoxime)imidazo [4,5-b]pyridines-(5_a-L)

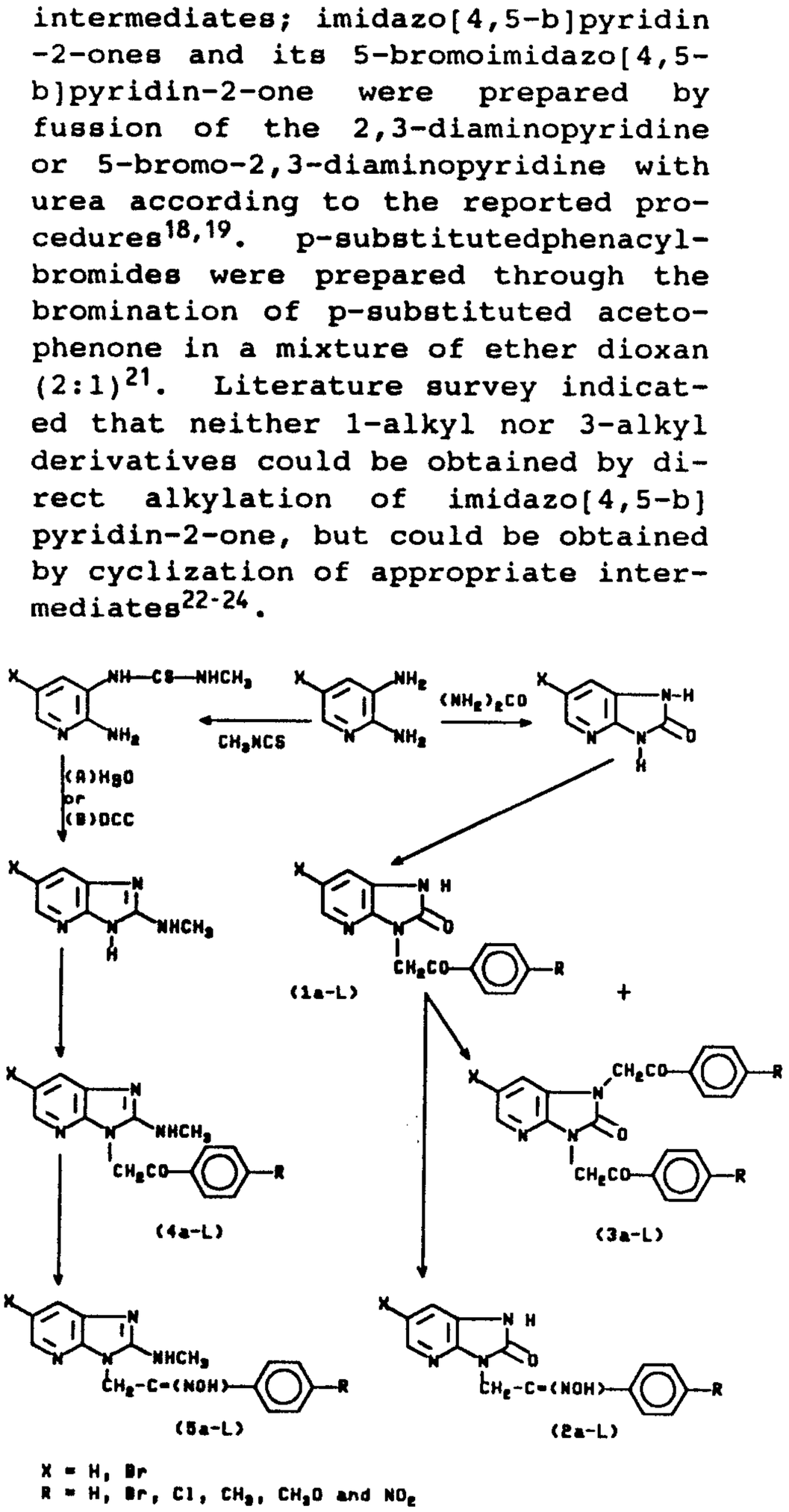
To 2-methylamino-3-(p(un)substitutedphenacyl) imidazo[4,5-b]pyridine (0.01 mole), or 6-bromo-2-methylamino-3-(p(un)substitutedphenacyl)imidazo[4,5-b]pyridine(0.01 mole), hydroxylamine HCl (0.03 mole), and methanol (40 ml) were added and the mixture refluxed for two hours. The solvents were removed under reduced pressure, residue washed with water and crystallized from 50% V/V aqueous ethanol.

RESULTS AND DISCUSSION

A-Chemistry

The designed imidazo[4,5-b]pyridin-2-one, and 2-methylaminoimidazo [4,5-b] pyridine derivatives were prepared in this investigation, according to Scheme 1. The starting 2,3-diaminopyridine was synthesized from nicotinic acid through Curtius reaction[20] and 3-bromo-2,3-diaminopyridine was synthesized from 2-aminopyridine by bromination using

Br2/HOAc. 2-Amino-3,5-dibromopyridine was formed as by-product and could be separated by extraction with ether leaving the less soluble 2-amino-5-bromopyridine which was nitrated and reduced to afford 5-bromo-2,3-diaminopyridine. The intermediates; imidazo[4,5-b]pyridin-2-ones and its 5-bromoimidazo[4,5-b]pyridin-2-one were prepared by fussion of the 2,3-diaminopyridine or 5-bromo-2,3-diaminopyridine with urea according to the reported procedures[18,19]. p-substitutedphenacylbromides were prepared through the bromination of p-substituted acetophenone in a mixture of ether dioxan (2:1)[21]. Literature survey indicated that neither 1-alkyl nor 3-alkyl derivatives could be obtained by direct alkylation of imidazo[4,5-b]pyridin-2-one, but could be obtained by cyclization of appropriate intermediates[22-24].



Following a modified Patcher and Kloetzel method[25] for the preparation of alkylated imidazo[4,5-b]pyridin-2-ones, the required 1-alkyl and 1,3-bis-alkyl imidazo[4,5-b]pyridin-2-ones were conveniently prepared. Alkylation was carried out by interaction of the appropriate phenacyl bromide with the sodium salt of the specific imidazo[4,5-b]pyridin-2-one, in DMF at room temperature. Mono or dialkylated derivatives could be obtained preferentially by changing the proportions of the reactants and their mode of addition. The mono derivative was obtained, for the first time by portionwise addition of (1:1) mixture of imidazo[4,5-b]pyridin-2-ones, and phenacyl bromide to a solution of sodium hydride in DMF while stirring at room temperature for half an hour.

Conversion of the 3-(p(un)substitutedphenacyl)-imidazo[4,5-b]pyridin-2-one derivatives to their corresponding ketoximes was carried out to investigate the role of both the ketone and ketoxime on the biological activity, if any. Ketoximes were prepared by heating the phenacyl derivatives with either free hydroxylamine in methanol at pH 5,8-6.0[26] or with hydroxylamine HCl in the presence of pyridine and methanol[27].

The cyclodesulfurization of thioureas using mercuric oxide[28] or D.C.C[29-32] into 2-methylaminoimidazo[4,5-b]pyridines was achieved in high yields. Trials made to cyclize the thioureas using alkyl halides[33,34] as methyl iodide were unsuccessful. The products isolated were 1-alkyl-2-alkylaminoimidazo[4,5-b]pyridines.

The reaction of 2-methylaminoimidazo[4,5-b]pyridine and/or 6-bromo derivative with the appropriate p-(un)substitutedphenacyl bromide in ethanol in the presence of sodium ethoxide gave 2-methylamino-3-(p(un)substitutedphenacyl)imidazo [4,5-b]pyridine and its 6-bromo derivatives were obtained.

Being typical carbonyl compounds the 2-methylamino-3-(p(un)substitutedphenacyl)imidazo[4,5-b]pyridines readily reacted with hydroxylamine HCl in the presence of pyridine at pH 5.8-6.0 in methanol and afforded the corresponding ketoximes in high yields.

The structures of the prepared compounds were confirmed by Microanalyses ^{1}H-NMR and Mass Spectroscopy. (Table I,II,III,IV,V and VI).

B-Analgesic Activity[35] :

The newly synthesized compounds were evaluated for analgesic activity in comparison to Aspirin and Indomethacin using phenylquinone squirming test in mice. Phenylquinone (1% W/V aqueous solution) was used as pain inducing agent (PIA). The tested compounds as well as the standard drug were suspended in 1% Tween 20 solution in normal saline.

Four groups, each of ten Albino mice (18-22 g), were used. Each group of animals was subcutaneousely injected with the compounds in a dose of 5,10,20, or 50 mg/kg body weight. Thirty minutes later, each mouse was injected with 0.2 ml of an aqueous solution of phenylquinone. The total number of writhes exhibited by each animal during 30 min was recorded and the results compared with the control group treated on the same way using 0.5 ml of 1% Tween 20 solution in saline. Aspirin and Indomethacin were using for the comparison.

$$\%\text{Inhibition} = \frac{\text{No of writhes in treated group}}{\text{No of writhes in control group}} \times 100 - 100$$

Table I,II,& III shows the % inhibition effect of the tested compounds which revealed reasonable analgesic activity in comparison to Aspirin and Indomethacin. Correlation of the observed activity with electronic "δ" and lipophilic "π" parameters, use g% Inhibition = $a+b\delta+C\pi^2$ indicated a deviation from Hammet "δ" constant in all dose levels, while the regression showed inverted parabolic relations of activity to "π" especially in the low dose levels. Trials made to improve the curve fitting, by including the "δ" as another descriptor of activity together with "π" in multiple regression analysis, showed better fitting with good correlation coefficient and confidence levels. Accordingly, it was concluded that the tested compounds have moderate activity. The bis-substituted derivatives are the most active, followed by the monosubstituted, then the oximes of the mono derivatives.

The activity is negative "δ" dependent and the presence of electron withdrawing group decreased the activity while the activity is positive "π" dependent.

C-Anthelmintic Activity[36] :

All synthesized 2-methylamino-3-(p(un)substitutedphenacyl)imidazo[4,5-b]pyridines and their corresponding ketoximes were tested for anti-parasitic activity against Ascaris Vitulorum of cattle in comparison to Mebendazole.

The tested compounds and the reference drug were dissolved in dimethylformamide in 10 mg/ml. Tyrode solution was used as a medium for experiment to keep the worm alive. The time required for relaxation was recorded and a control experiment, using plain dimethylformamide, was used.

From the time required for relaxation of the worms (Table IV & V) we could conclude that the onset of action of ketoximes is longer than that of their precursors and accordingly the activity of the ketonic compounds is more than that of their

corresponding ketoximes. It was observed that the presence of a lipophilic group substitutents (p-Cl, p-Br) on the phenyl moiety in both the ketonic compounds or ketoximes, improves the antiparasitic activity.

Table I : 3-[p-(un) Substituted Phenacyl] imidazo [4,5-b] Pyridin-2-ones (1a-l)

Comp. No.	R	X	Yield %	m.p. °C	Molecular formula	Microanalyses Calc./Found(%) C	H	N	Analgesic activity Inhibition %
1a	H	H	69	245-6c	$C_{14}H_{11}N_3O_2$	66.40 66.35	4.34 4.72	16.60 17.04	8,14,32,47
b	Br	H	87	276-7c	$C_{14}H_{10}BrN_3O_2$	50.60 50.30	3.01 3.40	12.65 12.50	16,37,49,59
c	Cl	H	73	233-5d	$C_{14}H_{10}ClN_3O_2$	58.34 58.56	3.47 3.76	14.48 14.48	17,28,37,51
d	CH_3	H	66	265-6b	$C_{15}H_{13}N_3O_2$	67.41 67.80	4.86 4.90	15.73 15.60	PIA,PIA,PIA,I
e	OCH_3	H	61	213-5a	$C_{15}H_{13}N_3O_3$	63.60 63.90	4.59 4.70	14.84 14.90	PIA, I, I, I
f	NO_2	H	58	246-8a	$C_{14}H_{10}N_4O_4$	56.37 56.63	3.35 3.52	18.79 18.66	8 ,21, 36,47
g	H	Br	70	253-5c	$C_{14}H_{10}BrN_3O_2$	50.60 50.50	3.01 2.90	12.65 12.30	
h	Br	Br	93	276-8c	$C_{14}H_9Br_2N_3O_2$	40.87 41.10	2.18 2.30	10.21 10.00	
i	Cl	Br	81	265-6a	$C_{14}H_9BrClN_3O_2$	45.84 45.40	2.46 2.60	11.59 11.50	
j	CH_3	Br	67	246-8b	$C_{15}H_{12}BrN_3O_2$	52.02 52.40	3.46 3.60	12.13 11.70	
k	OCH_3	Br	65	243-4a	$C_{15}H_{12}BrN_3O_3$	49.72 50.10	3.31 3.40	11.60 11.10	
l	NO_2	Br	67	254-7d	$C_{14}H_9BrN_4O_4$	44.56 44.86	2.38 2.73	14.85 15.20	
Acetyl salicylic acid									35,42,51,65
Indomethacin									32,57,78,95

Crystallization Solvents : A = absolute ethanol, b = 50% v/v aqueous ethanol
c = aqueous DMF. and d = isopropanol.

Tabel II: Ketoxime of 3-[p-(un)substituted Phenacy] Imidazo [4,5-b]pyridin-2-ones (2a-l).

Comp. No.	R	X	Yield %	m.p. °C	Molecular formula	Microanalyses Calc./Found C	H	N	Analgesic activity Inhibition
2a	H	H	77	219-21	$C_{14}N_{12}N_4O_2$	62.68 62.20	4.47 4.60	20.89 21.10	3,9,17,24
b	Br	H	93	235-6	$C_{14}H_{11}BrN_4O_2$	48.41 48.90	3.17 3.60	16.14 16.40	10,18,32,43
c	Cl	H	84	246-9	$C_{14}H_{11}ClN_4O_2$	55.53 55.20	3.63 3.00	18.51 18.70	9,18,23,31
d	CH_3	H	81	211-5	$C_{15}H_{14}N_4O_2$	63.82 64.05	4.96 4.88	19.85 19.93	2, 6,13,21
e	OCH_3	H	79	205-8	$C_{15}H_{14}N_4O_3$	60.40 60.80	4.69 4.20	18.79 19.20	PIA,PIA,PIA,PIA(2 Died)
f	NO_2	H	75	214-8	$C_{14}H_{11}N_5O_4$	53.67 53.69	3.51 3.38	22.36 21.98	5,14,20,27
g	H	Br	89	215-7	$C_{14}H_{11}BrN_4O_2$	48.41 48.90	3.17 3.60	16.13 16.60	
h	Br	Br	90	231-3	$C_{14}H_{10}Br_2N_4O_2$	39.44 39.00	2.35 2.40	13.15 13.20	
i	Cl	Br	85	217-9	$C_{14}H_{10}BrClN_4O_2$	44.03 44.20	2.62 2.30	14.67 14.30	
j	CH_3	Br	83	206-10	$C_{15}H_{13}BrN_4O_3$	49.86 50.10	3.60 3.50	15.51 15.30	
k	OCH_3	Br	80	213-6	$C_{15}H_{13}BrN_4O_3$	47.74 48.10	3.44 3.60	14.85 15.20	
l	NO_2	Br	76	216-9	$C_{14}H_{10}BrN_4O_5$	42.63 43.28	2.55 2.68	14.25 14.30	
Acetyl salicylic acid									35,42,51,65
Indomethacine									32,57,78,95

T = Toxic to the mice PIA = Pain inducing agent.

All Compound were crystallized from 50% v/v aqueous ethanol.

Table III: 1,3-Bis[p-(un)substituted Phenacyl]imidazo[4,5-b]pyridin-2-ones(3a-l).

Comp No.	R	X	Yield %	m.p °C	Molecular Formula	Microanalyses Calc./Found(%) C	H	N	Analgesic activity Inhibition %
3a	H	H	93	276-8a	$C_{22}H_{17}N_3O_3$	71.16	4.58	11.32	13,29,53,69
						71.40	4.90	11.60	
b	Br	H	97	297-9c	$C_{22}H_{15}Br_2N_3O_3$	49.91	2.84	7.94	23,49,62,89.1
						50.30	3.20	8.00	
c	Cl	H	89	283-5c	$C_{22}H_{15}Cl_2N_3O_3$	60.00	3.41	9.55	19.3,33,47.7,61
						59.60	3.40	9.40	
d	CH_3	H	76	235-6b	$C_{24}H_{21}N_3O_3$	72.18	5.26	10.53	T,T,
						71.50	5.50	10.80	
e	OCH_3	H	79	248-50b	$C_{24}H_{21}N_3O_5$	66.82	4.87	9.75	PIA,PIA,T.
						66.50	4.70	9.90	
f	NO_2	H	80	268-70c	$C_{22}H_{15}N_5O_7$	57.27	3.25	15.18	12,27,37.5,53.9
						57.60	3.50	15.00	
g	H	Br	91	248-9c	$C_{22}H_{16}BrN_3O_3$	58.67	3.56	9.33	
						59.20	4.10	9.00	
h	Br	Br	96	293-4c	$C_{22}H_{14}Br_3N_3O_3$	43.42	2.30	6.90	
						43.40	2.40	7.00	
i	Cl	Br	87	278-80c	$C_{22}H_{14}BrCl_2N_3O_3$	50.87	2.70	8.09	
						51.20	3.10	8.00	
j	CH_3	Br	76	259-61b	$C_{24}H_{20}BrN_3O_3$	60.25	4.18	8.79	
						60.20	4.80	8.80	
k	OCH_3	Br	78	278-9c	$C_{24}H_{20}BrN_3O_5$	55.47	3.92	8.24	
						55.70	4.20	8.00	
l	NO_2	Br	87	254-6c	$C_{22}H_{14}BrN_5O_7$	48.89	2.59	12.96	
						49.30	2.70	12.50	
Acetyl salicylic acid									35,42,51,65
Indomethacine									32,57,78,95

Crystallized Solvents : a=ethanol B=50% v/v aqueous ethanol. C=50% v/v aqueous DME.

Table IV: 2-Methylamino-3-[p(un)substituted Phenacyl]imidazo[4,5-b]Pyridines (4a-l).

Comp No.	R	X	Yield %	m.p. °C	Molecular Formula	Microanalyses: Calc./Found C	H	N	Anthelmintic Activity Onset of action minutes
4a	H	H	90	234-6a	$C_{15}H_{14}N_4O$	67.67 67.90	5.26 5.80	21.05 21.30	32
b	Br	H	95	256-7c	$C_{15}H_{13}BrN_4O$	52.17 52.60	3.77 4.00	16.23 16.60	24
c	Cl	H	93	239-41b	$C_{15}H_{13}ClN_4O$	59.90 59.40	4.33 4.50	18.64 18.90	30
d	CH_3	H	83	243-5a	$C_{16}H_{16}N_4O$	68.57 68.90	5.71 5.40	20.00 19.90	46
e	OCH_3	H	79	215-7d	$C_{16}H_{16}N_4O_2$	64.86 64.30	5.40 5.80	18.91 18.90	59
f	NO_2	H	86	237-9c	$C_{15}H_{13}N_5O_3$	57.88 58.00	4.18 4.30	22.51 22.70	42
g	H	Br	91	248-50c	$C_{15}H_{13}BrN_4O$	52.17 51.70	3.77 4.40	16.23 15.90	41
h	Br	Br	96	293-4c	$C_{15}H_{12}Br_2N_4O$	42.45 42.10	2.83 3.20	13.21 13.60	28
i	Cl	Br	93	285-7b	$C_{15}H_{12}BrClN_4O$	47.43 47.40	3.16 3.40	14.67 14.60	46
j	CH_3	Br	89	246-8a	$C_{16}H_{15}BrN_4O$	53.48 53.30	4.18 4.70	15.60 15.80	58
k	OCH_3	Br	85	256-7b	$C_{16}H_{15}BrN_4O_2$	51.20 50.90	4.00 4.40	14.93 15.20	87
l	NO2	Br	90	239-41c	$C_{15}H_{12}BrN_5O_3$	46.15 46.60	3.08 3.70	17.94 18.00	75
Mebenazole									7

Crystallized Solvents : a=absolute ethanol b=50% aqueous ethanol c=50% v/v aqueous DMF
d=50% aqueous isopropanol.

Table V: Ketoxime of 2-Methylamino-3-[p(un)substituted Phenacyl]imidazo[4,5-b]pyridines(5a-l).

Comp. No.	R	X	Yield %	m.p. °C	Molecular Formula	Microanalyses Calc./Found C	H	N	Anthelmintic activity Onset of action minutes
5a	H	H	89	199-200	$C_{15}H_{15}N_5O$	64.06 63.80	5.34 5.40	24.91 25.20	54
b	Br	H	94	210-13	$C_{15}H_{14}BrN_5O$	50.00 50.30	3.89 4.10	19.44 19.60	46
c	Cl	H	90	219-21	$C_{15}H_{14}ClN_5O$	57.05 57.40	4.44 4.80	22.19 22.06	58
d	CH_3	H	85	186-9	$C_{16}H_{17}N_5O$	65.08 65.00	5.76 5.90	23.73 24.20	87
e	OCH_3	H	85	201-5	$C_{16}H_{17}N_5O_2$	61.74 61.60	5.47 5.30	22.51 22.80	96
f	NO_2	H	87	215-9	$C_{15}H_{14}N_6O_3$	55.21 55.60	4.29 4.70	25.77 25.90	89
g	H	Br	90	224-6	$C_{15}H_{14}BrN_5O$	50.00 50.30	3.89 4.30	19.44 19.50	76
h	Br	Br	93	246-9	$C_{15}H_{13}Br_2N_5O$	41.00 40.80	2.96 3.30	15.95 15.60	65
i	Cl	Br	91	224-6	$C_{15}H_{13}BrClN_5O$	45.62 45.40	3.30 3.80	17.74 18.00	89
j	CH_3	Br	86	185-7	$C_{16}H_{16}BrN_5O$	51.34 51.70	4.25 4.40	18.71 19.20	121
k	OCH_3	Br	83	201-4	$C_{16}H_{13}BrN_6O_2$	47.88 48.00	3.24 3.20	20.44 20.80	103
l	NO_2	Br	85	214-6	$C_{15}H_{13}BrN_6O_3$	44.44 44.40	3.46 3.30	20.76 21.20	96
Mebendazole									7

All Compounds were crystallized from 50% v/v aqueous ethanol.

Table VI: Characterization Spectra of Imidazo[4,5-b]pyridines.

Comp. No.	^{1}H-NMR (DMSO-d_6) TMS (ppm)	m/e
Ib		Base peak at m/e 214 and [M+H]+at m/e 410 [$C_{14}H_9BrN_3O_2$+H+].
Ig	(DMSO-d_6),5.5(2H,S),7.5-7.7(3Hump), 7.8(1H,d),8.0-8.1(3H,m),11.8(1H,S, DISAPPEARED ON ADDITION OF D_2O).	
Ih	(DMSO-d_6),5.5(2H,S),7.6-8.1(6H,m), and 11.8(1H,S).	
2c	(DMSO-d_6),5.2(2H,S),7.1-7.9(7H,m), 11.8(1H.S)&12.2(1H,S)in addition of D_2O both NH and OH disappeared.	
3c	(DMSO-D_6),5.5(2H,S),5.62(2H,S),7.16 (1H,m),7.5(1H,d),7.7(1H,d),7.9(4H,m), 8.1(4H,m).	Base peak at m/e 440 $[M+H]^+$ $[C_{22}H_{15}Cl_2N_3O_3+H]$
3g		Molecular ion at m/e 450$[M+H]^+$ $[C_{22}H_{16}BrN_3O_3+H]$. Base peak at, m/e 332$[M+H-C_6H_5COCH_2]^+$
3h	(DMSO-d_6),5.45(S,2H),5.65(2H,S),7.5 (4H,m),7.7-7.9,(2H,m)and 8.2(4H,m).	Base peak at 412[M+H-$BrC_6H_4COCH_2$+ H]$^+$;Molecular ion peak at m/e 605 $[C_{22}H_{14}Br_3N_3O_3+H]$.
4a	(DMSO-d_6),2.85(3H,d),5.9(2H,S),6.6 6.8(2H,m),7.3-7.7(5H,m),8.8-8.15 (2H,m)addition of D_2O(Signal NH-dis-appeared.	
4b	(DMSO-d_6),2.8(3H,d),5.9(2H,S),6.5-6.8(2H,m),7.15-7.4(2H,d),7.7-8.1 (4H,m),addition of D_2O disappear of NH signal	Base peak at m/e 345$[M+H]^+$ $[C_{15}H_{13}BrN_4O+H]^+$
5a	(DMSO-d_6),2.8(3H,d),5.75(2H,S),7.0 7.7(7H,m)7.7-7.9(1H,d),8.6(1H, Hump).	Base peak at m/e 282$[M+H]^+$ $[C_{15}H_{15}N_5O+H]^+$

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تخليق بعض مشتقات أيميدازو (٤.٥ - ب) البيريدين ذات الفاعلية البيولوجية المتوقعة

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يتعلق البحث بتخليق بعض مركبات أيميدازو (٤.٥ - ب) بيريدين مثل مشتقات ٣.١ ثنائى (فيناسيل) أيميدازو (٤.٥ - ب) بيريدين - ٢ - أون ، ٣ -(فيناسيل) أيميدازو (٤.٥ - ب) بيريدين - ٢ - أون وكذلك ٢ - ميثيل أمينو - ٣ - (فيناسيل) أيميدازو (٤.٥ - ب) بيريدين هذا بالاضافة الى تحضير مشتقات الاوكزيم.

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