Synthesis and Antibacterial Activity Screening of Pyrazole-Pyridine Derivatives

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ABSTRACT

Fused heterocyclic compounds, 6-(5-(4-alkyl phenyl)furan-2-yl)-3-methyl-1-phenyl-1H- pyrazolo[3,4-b] pyridine-5-carbonitrile 3(a-e) were synthesized by the reaction of 3-Methyl-1-phenyl- 1H-pyrazol -5-amine(1) with 5-(4-alkylphenyl)furan- 2-carbaldehyde (2a-e) in presence of Acetoacetonitrile. The structures of all the compounds series (3a-e) were characterized by elemental and spectral studies. The compounds were also screened for antibacterial activity.

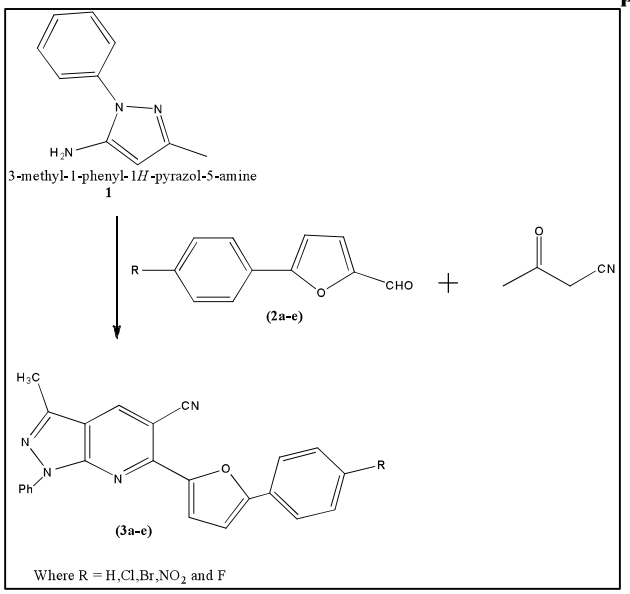
Keywords: *3*-Methyl-1-phenyl- 1H-pyrazol -5-amine, 5-(4-alkylphenyl)furan-2-carbaldehyde, antibacterial activity and spectral studies.

I INTRODUCTION

Heterocyclic compounds shows number of pharmaceutical activity as well antibacterial activity. [1] Among the all the heterocyclic compounds, the Nitrogen containing are important and applied in chemistry and biology. They have vital role in the all the bio-chemical reaction (i.e. metabolism) [2, 4]. Pyrazole moiety containing heterocyclic compounds shows various biological activities such as anti-inflammatory, antimicrobial, analgesic, antifungal, antitumor and anxiolytic activities [5-9]. Pyrazolo[3,4-b]pyridine Skeleton have proven to be interesting classes of heterocycles due to diverse biological properties including antitubercular, antibacterial and antioxidant activities [10-14]. Recently, many authors [15-17] synthesized pyrazolo[3,4-b]pyridine by novel methods. Hence, pyrazole-pyridine containing compounds into one molecule have good medicinal property. Thus it was thought to synthesize this type of fuse molecules. The present communication deals with the synthetic approach shown in scheme-1.

II EXPERIMENTAL

scheme-1



All the chemicals were used laboratory grade. The methods in [16] and [17] were followed for the synthesis of 3-Methyl-1-phenyl- 1H-pyrazol -5-amine(1) and 5-(4-alkylphenyl)furan-2-carbaldehyde 2(a-e), respectively.

^{1}HNMR spectra were recorded on a Bruker (400 MHz) spectrometer. Deuterated DMSO was used as a solvent. The FTIR spectra produced substances were scanned in KBr disc by using on a NICOLET-400D spectrophotometer. LC-MS spectra of two samples of series were recorded by LC-MSD-Trap-SL-01046 instrument. All the compounds were checked for their purity by TLC. The characterization data of all these compounds are given in Table.1.

The antibacterial activities of the series of compounds (3a-e) were studied against gram +Ve and –Ve bacteria shown in Table-2. The activity was measured at a conc., 50µg/ml by agar-cup plate method [18]. The percentage inhibition of growth of bacteria by the compounds is shown in Table-2.

Synthesis of 6-(5-(4-alkyl phenyl)furan-2-yl)-3-methyl -1-phenyl-1H-pyrazolo[3,4-b] pyridine-5-carbonitrile 3(a-e)

A mixture of 3-Methyl-1-phenyl- 1H-pyrazol -5-amine(1) (2 mmol), Acetoacetonitrile (2 mmol) and 5-(4-alkyl phenyl) furan-2-carbaldehyde 2(a-e) (2 mmol) in acetic acid (25 ml) and in the presence of TEA (1.5 ml) was refluxed for 6-7 hours. The resultant viscous mass was added slowly in ice cold water (50 ml). The solid mass was resulted which was collected by filtration, washed with water and recrystallized from Ethyl alcohol give pure 3(a-e). The details are presented in Table-1.

Table-1
Characterization of the Produced Compounds (3a-e)

Comp. No.	M. F. (Mol. Wt)	M.P. @ °C	Analysis of C, H, N in %age		
			C	H	N
			Calculated (Found)	Calculated (Found)	Calculated (Found)
3a	$C_{24}H_{16}N_4O$ (376)	162-163	76.58 (76.5)	4.28 (4.2)	14.88 (14.8)
3b	$C_{24}H_{15}N_4OCl$ (410.5)	168-169	7016 (70.1)	3.68 (3.6)	13.64 (13.6)
3c	$C_{24}H_{15}N_4OBr$ (454)	174-175	63.31 (63.3)	3.32 (3.3)	12.3 (12.3)
3d	$C_{24}H_{15}N_5O_3$ (421)	166-167	68.40 (68.3)	3.59 (3.5)	16.62 (16.6)
3e	$C_{24}H_{15}N_4OF$ (394)	179-180	73.09 (73.0)	3.83 (3.8)	14.21 (14.2)

@Uncorrected LC-MS data for 3b:412, 3e: 397

III RESULTS AND DISCUSSIONS

Here we accomplished synthesis of pyrazolo[3,4-b]pyridine derivatives **3(a-e)** in which the multi component reactions of Acetoacetonitrile, 5-aminopyrazole **(1)** and 5-(4-alkyl phenyl) furan -2-carbaldehyde 2(a-e) were carried out in acetic acid (as shown in scheme).

The molecular structures of series **(3a-e)** were assigned by C, H, N contents and IR spectral features. The IR spectral bands at 3032 cm^{-1} (aromatic C-H), 2215 cm^{-1} (C≡N), 1585, 1375(NO_2), 2960, 1370 cm^{-1} (-CH_3), 690(C-Br), 1080 (-Cl), 1180-1200 cm^{-1}(C-O bond). NMR signals: at δ *ppm*: 8.51(m, 1H, of pyridine ring), 2.08(s, 3H, from methyl group), 7.12(d, 2H of furan ring), **(3a):**8.25-7.42 (m,10H, of two phenyl rings); **(3b)-(3d)**:8.25-7.40 (m,9H,of two phenyl rings); **(3e)**: 8.32-7.42 (m, 9H, of two phenyl rings). The C, H, N content of all synthesized heterocycles are illustrated in Table-1.

Table-2
Antibacterial Activity of Compounds (3a-e)

Comp. No.	Zone of Inhibition(mm)			
	Gram +ve		Gram -ve	
	Bacillus subtilis	Staphylococcus aureus	Kllebsiella promioe	E.coli
3a	59	42	67	64
3b	65	46	71	69
3c	62	44	69	67
3d	64	45	72	66
3e	60	41	68	63
Tetracycline	79	55	87	72

All the elemental and spectral features suggest that the values are agreed with the molecular structure presented in Scheme-1 are matching with the proposed molecular structural frame scanned in Scheme-1.The LC-MS of selected compounds shows the peak of M^+ ion which is consistent of their molecular weight. All these facts confirm the structures 3(a-e).

The examination of antibacterial activity data reveals that all compounds toxic against microbes and the compounds **3b** and **3e** found more active against the gram-positive and gram-negative bacteria. The results show that the compounds are good toxic for microbes.

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