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SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF SOME BENZIMIDAZOLYL PYRAZOLES

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ABSTRACT

The reaction of benzimidazolyl chalcone (1) with bromine in Chloroform gave corresponding dibromo chalcones (2) which underwent condensation with hydrazine hydrate to afford the title compounds 3- benzimidazolyl -5-aryl-2-pyrazole (3). Newly prepared pyrazoles were screened for their antimicrobial activity in vitro, some of has exhibited promising activity.

Key Words: Benzimidazolyl Chalcones, Dibromides, Pyrazole, antimicrobial.

INTRODUCTION

Among Various nitrogen containing heterocycles the benzimidazoles constitute an important group of compounds having medicinal value. A wide variety of benzimidazole derivatives have been described for their chemotherapeutic importance [1-6]. Literature reveals that pyrazoles, pyrazolones and alkyl pyrazoles have also exhibited wide range of pharmacological applications[7]. We report herein the synthesis of some novel pyrazole derivatives containing benzimidazole moiety, for evaluation of their antimicrobial activities.

Benzimidazolyl chalcones[8] (1) were brominated using bromine in chloroform at room temperature to get corresponding benzimidazolyl chalcone dibromides (2). When these dibromides were treated with hydrazine hydrate under refluxing condition, desired pyrazoles (3) were obtained in 60-70%yield. However when reaction was carried out under MWI condition a mixture of two products was obtained as indicated by TLC. The reaction mixture when dissolved in alcohol, some residue remained insoluble which was filtered off. The Soluble part after concentration under vacuum was left at room temperature. The Solid separated was identified to be the pyrazole (3) on the basis of Co-TLC, m.m.p. and superimposable IR Spectra with the product obtained by conventional heating method. The Identification of insoluble part is in progress.

EXPERIMENTAL

All the melting points reported are uncorrected and taken in the open capillaries. The purity of compounds and progress of reaction was checked by TLC using silica gel G absorbent and benzene -ethyl acetate as eluent .IR Spectra were recorded on Perkin-Elmer 1600 Spectrometer using KBr (ν cm^{-1}). PMR spectra were taken on Brucker-DRX-600 Spectrometer using TMS as internal standard. Mass spectra (FAB) were obtained on Jeol-5X-DA-600 Mass spectrometer using m –nitrobenzyl alcohol as matrix. The Matrix peaks were obtained at m/z 136, 137, 154, 209 and 307 respectively. MWI was carried out in domestic microwave oven (Samsung 1630 N, 600 Watts)

Synthesis of Benzimidazolyl chalcone dibromides (2):

Chalcone (0.01 Mole) was dissolved in $CHCl_3$ (30 ml). To it a solution of bromine (0.012 Mole) in $CHCl_3$ (20 ml) was added with continuous stirring during a period of 30 minutes. After complete addition the mixture was further stirred for 30 minutes. It was then poured over crushed ice and separated solid was filtered off. After drying it was crystallized from alcohol as cream colored crystals of (2).

Synthesis of Benzimidazolyl Pyrazoles:

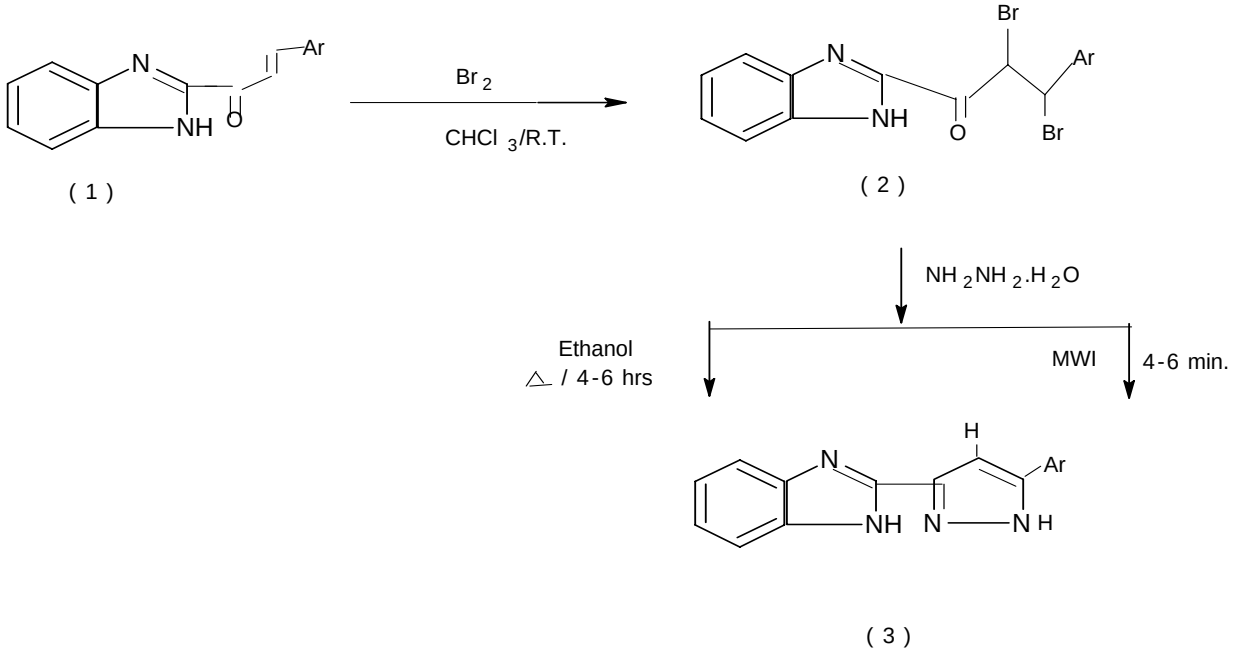
Conventional Method: Compound (2) (0.01 Mole) and hydrazine hydrate (0.01 Mole) in ethanol (30ml) were refluxed on water bath for 4-6 hours. After Complete reaction, the mixture was cooled to room temperature. Separated Solid was filtered off, dried and crystallized from benzene –ethanol as colorless crystals of (3).

MWI Method: An intimate mixture of compound (2) (0.01 Moles) and hydrazine hydrate (0.01 Mole) was subjected to MWI at 300 Watt Power for 3-5 minutes. After completion of reaction, the residue was cooled to room temperature. It was dissolved in Ethanol. The insolubles were filtered off and filtrate was concentrated in vacuum. On keeping at room temperature the separated solid was filtered, dried and crystallized to afford analytical sample of (3).

RESULTS AND DISCUSSION

The reaction of Benzimidazolyl chalcones(1) with bromine afforded chalcone dibromides which on reaction with hydrazine hydrate underwent cyclisation followed by dehydrobromination to afford pyrazoles (3) by both conventional and MWI Method The Identify of newly prepared pyrazoles was established on the basis of their elemental analysis and spectral data. The IR Spectra of compounds (3) exhibited absorption band at 3010-2990cm^{-1} (-C-H Stret.) , 3320-3250 cm^{-1}(broad band , combined NH Stret of benzimidazole and pyrazole rings), 1450-1430cm^{-1}(C=N) , 1410 -1350cm^{-1}(C=C and N-N Combined vibrations). The PMR Spectra of these compound gave signal at δ 1.83 (C_4-H of pyrazoline) δ 8.86 and 8.41 (NH of benzimidazole and pyrazoline) and a multiplet at 7.63-8.10 for aromatic protons.
The mass Spectra of these compounds gave molecular ion peaks corresponding to their molecular masses.

Antimicrobial activity: Newly prepared compounds were screened for their anti fungal against Candida albicons and Aspergillus niger and anti bacterial against E.Coli, P.aeruginusa, B.Subtilis, K.Pneumoniae in vitro at a concentration 250mg/ml. Standard drugs used were fluncazole and ciproflaxange respectively. The Screening results have been tabulated in table 2.



(1) (2) (3)

Scheme-1

Table-1: Physical Data of Compounds (3)

Compound	Ar	Molecular Formula	m.p.	% Yield		Reaction Time	
		Mol. Weight	°C	Conv	MWI	Conv (Hrs)	MWI (Min)
2a	Phenyl	$C_{16}H_{12}N_2OBr_2$(408)	148	62	85	5.00	3.50
2b	4-OMe Phenyl	$C_{17}H_{14}N_2O_2Br_2$(438)	166	64	87	5.00	3.50
2c	3-4di OMe Phenyl	$C_{18}H_{16}N_2O_3Br_2$(468)	228	67	88	5.00	4.50
2d	3-4-5 tri OMe Phenyl	$C_{19}H_{18}N_2O_4Br_2$(498)	102	61	85	4.50	4.00
2e	4-Cl-Phenyl	$C_{16}H_{11}N_2ClOBr_2$(442.5)	130	64	88	5.00	4.50
2f	2-Furfuryl	$C_{14}H_{10}N_2O_2Br_2$(398)	110	60	82	5.50	5.00
3a	Phenyl	$C_{16}H_{12}N_4$(260)	166	67	88	6.00	5.00
3b	4-OMe Phenyl	$C_{17}H_{14}N_4O$(290)	141	66	86	6.50	4.50
3c	3-4di OMe Phenyl	$C_{18}H_{16}N_4O_2$(320)	156	66	86	5.00	4.00
3d	3-4-5 tri OMe Phenyl	$C_{19}H_{18}N_4O_3$(350)	117	68	88	5.50	4.00
3e	4-Cl-Phenyl	$C_{16}H_{11}N_4Cl$(294.5)	96	62	84	6.00	4.50
3f	2-Furfuryl	$C_{14}H_{10}N_4O$ (250)	122	60	82	6.50	5.50

Table-2: Biological screening results of compounds (3)

Zone Of Inhibition (mm)						
	Anti Bacterial				Anti Fungal	
COMPOUND	E. COLI	K.PNEUMONIAE	B.SUBTILIS	P. AERUGINUSA	Candida albicans	Aspergillus fumigatus
3(a)	17	9	16	15	19	15
3(b)	12	8	14	12	12	10
3 (c)	13	10	16	12	18	13
3(D)	14	9	15	10	-	-
3(E)	15	10	17	15	17	12
3(F)	13	8	16	17	16	10
STANDARD CIPROFLAXANGE	20	24	21	23	-	-
STANDARD FLUCANZOLE	-	-	-	-	18	16

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