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Synthesis of substituted pyrazole derivatives and evaluation of their antimicrobial activity

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ABSTRACT

Cyclization of substituted phenyl hydrazine with EAA was done to get pyrazolone derivatives. It were further reacted with various substituted benzoyl chlorides to get substituted pyrazole moiety. The structure of the synthesized compounds has been assigned on the bases of spectral studies. The compounds were evaluated for microbial screening against Gram positive & Gram negative bacteria and fungal strain. Most of the compounds show significant activity against all the spices of bacteria and fungi.

Key words: Phenyl hydrazine, Pyrazole, Pyrazolone, Benzoyl chloride, Antimicrobial activity.

INTRODUCTION

Pyrazoles are present in many natural (in seeds of watermelon) and synthetic compounds. They are also known as azoles[1]. It is reveled from the literature survey that it possesses versatile biological activities like anti microbial[2], anti-histaminic[3], anti depressant[4], insecticides[5], anti-inflammatory[6] and fungicides. Further current literature indicates substituted pyrazole derivatives posses various biological activities.

Looking to this multifold properties exhibited by pyrazole we are reporting here the synthesis and antimicrobial activity of some pyrazole derivatives. In the present study, this strategy is used for the synthesis of these compounds in the hope that they may possesses potent biological activities.

MATERIALS AND METHODS

All the melting points are uncorrected. TLC method was used to check reaction progress.

Preparation of 5-Methyl-2-(3-nitro)-1,2-dihydropyrazol-3-one
0.01 mole of substituted 3-Nitro phenyl hydrazine dissolved in 15mL of ethanol, 0.01mole EAA dissolved in 15mL of ethanol was added and the mixture was refluxed for 3-8 h. Ethanol was recovered by distillation. The residue was dissolved in chloroform, washed & dried to get pyrazolone derivative.

General procedure for compounds (A-K)
Pyrazolone (2 mmol) was dissolved in 25mL dioxane and calcium hydroxide (4 mmol) was added. To this stirred mixture freshly prepared different acid chloride was added dropwise within 10 mins. The reaction was refluxed for 3-5 h. Reaction was monitored by TLC. On completion of reaction solvent was evaporated and residue was crystalized in MDC.

The physical data are recorded in (Table-1)

Antimicrobial activity

Compounds A-K were screened for their antibacterial and antifungal activity using cup-plate agar diffusion method[7,8] at a concentration of 40 mg, using Gram positive bacterial strains such as *B. cocous and B.subtillus* and Gram negative bacterium strain such as *Proteus vulgaris* and *Escherichia coli*. The antifungal testing was carried out against *Aspergillus niger*. Known antibiotics like Amoxycillin, Benzoylpenicillin, Ciprofloxacin, Erythromycin, and antifungal activity was compared with Greseofulvin. The zone of inhibition measured in mm.By visualizing the antimicrobial data, it could be observed that most of the compounds exhibited significant activity (Table-2).

Table-1

Sr. No.	R	M.F.	M.P. ^{O}C	Yield (%)	% of Nitrogen	
					Calc.	Found
A	4-F	$C_{17}H_{12}FN_3O_4$	196	76	12.15	12.14
B	3,4-dimethoxy	$C_{19}H_{17}N_3O_6$	206	79	10.85	10.82
C	-H	$C_{17}H_{13}N_3O_4$	192	65	13	12.96
D	4-OCH_3	$C_{18}H_{15}N_3O_5$	198	68	11.89	11.85
E	2-OH	$C_{17}H_{13}N_3O_5$	214	71	12.38	12.40
F	2-Cl	$C_{17}H_{12}ClN_3O_4$	198	58	11.75	11.78
G	3-OH	$C_{17}H_{13}N_3O_5$	216	70	12.38	12.35
H	3-Cl	$C_{17}H_{12}ClN_3O_4$	196	61	11.75	11.72
I	2-Br	$C_{17}H_{12}BrN_3O_4$	196	72	10.45	10.44
J	3-OCH_3	$C_{18}H_{15}N_3O_5$	202	70	11.89	11.85
K	3-OCF_3	$C_{17}H_{12}F_3N_3O_5$	200	55	10.32	10.30

Table-2

Sr. No.	R	Antimicrobial activity Zone of inhibition (mm)				Antifungal activity Zone of inhibition (mm)
		B. cocous	*B.subtillus*	*P.vulgaris*	*E. coli*	*A. niger*
A	4-F	15	17	17	18	19
B	3,4-dimethoxy	14	18	17	19	18
C	-H	16	16	17	18	15
D	4-OCH_3	17	16	18	18	14
E	2-OH	17	16	19	17	12
F	2-Cl	19	18	15	17	18
G	3-OH	16	20	18	17	16
H	3-Cl	17	22	14	16	14
I	2-Br	19	19	16	19	14
J	3-OCH_3	18	17	16	18	14
K	3-OCF_3	16	15	18	17	15
	Amoxycillin	21	26	20	24	-
	Benzoylpenicillin	22	22	25	22	-
	Ciprofloxacin	19	21	23	22	-
	Erythromycin	21	16	18	21	-
	Greseofulvin	-	-	-	-	26

RESULTS

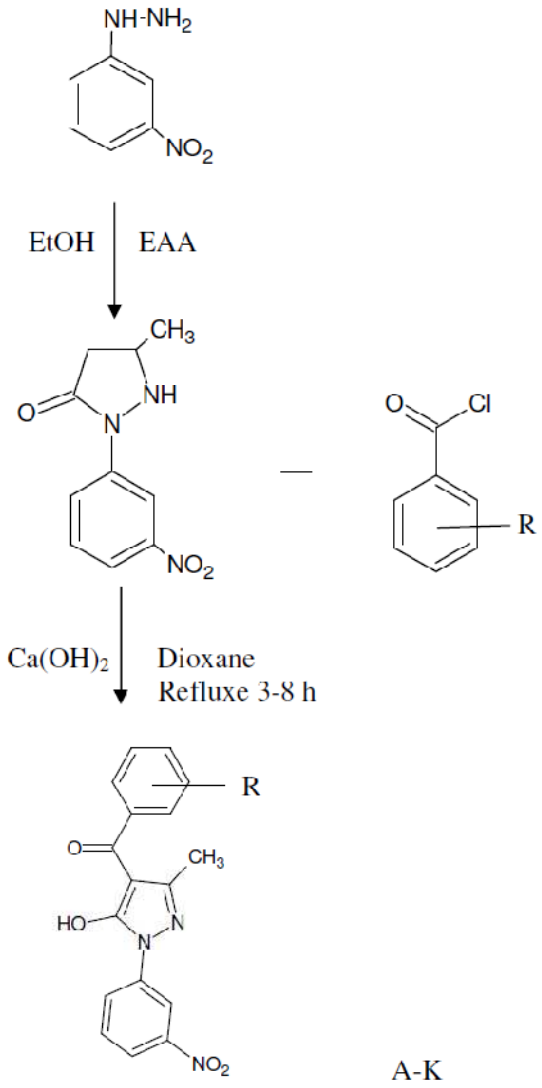
a) *(4-fluorophenyl)(5-hydroxy-3-methyl-1-(3-nitrophenyl)-1H-pyrazol-4-yl)methanone*

Yield: 76%. Mp. 196°C, m/z 341.5, ^{1}H NMR ($CDCl_3$- 400MHz): δ ppm 2.3 (1H, s, CH_3), δ 6.3 (1H, s, OH), δ 7.19-7.23 (2H, t, J=8.5, Ar-CH), δ 7.60-7.64 (1H, t, J=8.1, Ar-CH), δ 8.05 (1H, dd, J=0.8, 8.0, Ar-CH), δ 8.13-8.20 (3H, m, 3 x Ar-CH), δ 8.59-8.60 (1H, d, Ar-CH).

b) *(3,4-dimethoxyphenyl)(5-hydroxy-3-methyl-1-(3-nitrophenyl)-1H-pyrazol-4-yl)methanone*

Yield: 79%. Mp. 206°C m/z 383.3, ^{1}H NMR ($CDCl_3$ - 400MHz): δ ppm 2.37 (1H, s, CH_3), δ 3.93 (1H, s, CH_3), δ 3.97 (1H, s, CH_3), δ 6.32 (1H, s, OH), δ 6.95-6.97 (1H, d, J=7.6, Ar-CH), δ 7.57-7.61 (2H, m, Ar-CH), δ 7.81-7.83 (1H, d, J=6.7, Ar-CH), δ 8.06-8.14 (2H, m, Ar-CH), δ 8.62 (1H, s, Ar-CH).

Reaction Scheme



DISCUSSION

Spectral analysis supports the synthesis of compounds A-K. Some of synthesized compounds have shown significant antimicrobial activity and remaining compounds are moderately active against all experimental strains of bacteria and fungi. It is there for important to anticipate that appropriate molecular manipulation of these compounds, may result in the compounds with potent antimicrobial action.

CONCLUSION

All the synthesized compounds are either potent or moderately active towards Gram positive and Gram negative bacteria as well as it show antifungal activity. Certain structural alteration did not increase antimicrobial activity and working ahead in that direction may give quite promising results.

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