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SYNTHESIS OF SOME 4-AROYLAMINOPHENYL PYRAZOLE DERIVATIVES AND STUDIES OF THEIR ANTIMICROBIAL ACTIVITIES

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ABSTRACT

One pot synthesis of 4-nitrophenyl hydrazine, aldehyde and ethyl aceto acetate produces 4-nitrophenylpyrazole , which on further reduced with iron powder in presence of acetic acid to give 4-Aroylaminophenyl pyrazole. And when it reacts with substituted benzoyl chlorides produces derivatives. Its structures have been assigned on the basis of spectral studies. Most of the compounds shows significant activities against Gram positive and Gram negative strains.

Keywords 4-nitrophenyl hydrazine, EAA, Pyrazole

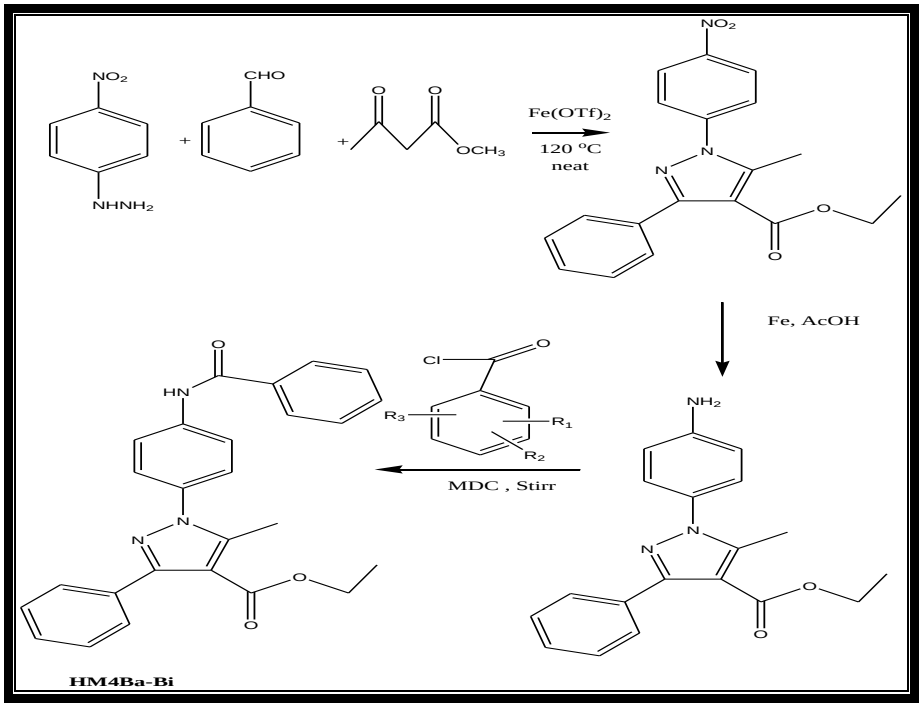
Introduction

Many amide derivatives of pyrazole also shows importance in medical treatment. Patients suffering from inflammatory disorders including rheumatoid arthritis (RA) require therapeutic agents that not only to demonstrate anti-inflammatory properties but also to protect against cartilage degradation[1].

Last decade of 20th century and early part of 21st century is contradictory to the remarkable success of medical sciences for the treatment of infectious diseases. This is mainly due to emergence of resistant strains of organisms which resulted in ineffectiveness of many antibiotics in the clinical treatment and also lackluster approach of giant pharmaceutical company towards new antimicrobial drug research [2-4]. Most of the available antibacterial agents have now become least effective or ineffective against methicillin

resistant Staphylococcus aureus, vancomycin resistant Staphylococcus aureus, resistant strains of Escherichia coli and new bacteria which express genes encoded for carbepenamase etc.[5]. Apart from this, not a single antibiotic with different chemical structure and mechanism of action has reached to clinical stage. Thus infectious diseases are still known to be the cause of mortality among the third world countries including India and the need of potent and safe clinical agents to contain infectious disease still persists[6]. Pyrazole and its derivatives occupy an important position in medicinal and pesticide chemistry due to a wide range of bioactivities such as antimicrobial[7], anticancer[8], anti-inflammatory[9], antidepressant, anticonvulsant, anti-hyperglycemic, antipyretic, antibacterial, antifungal, antiviral[10] and selective enzyme inhibitory activities [11]. Substituted pyrazole and its analogs have been used as precursors for synthesis of various biologically active molecules[12].

Reaction Scheme



Experimental

Preparation of Amine derivative

Iron powder (0.01 mole) was added portion wise to a mixture of compound no.4 and acetic acid (10 mL). The reaction mixture was refluxed for 5 hr. cooled than the solid formed was filtered and crystallized from ethanol. Yield = 55-60%.

Preparation of acid chlorides

Benzoic acid (15mmol) was suspended in neat thionylchloride (5mL) and refluxed for 5-6 hour. After 5-6 hour, obtained product was washed with hexane, and dissolved in dichloromethane to use for further reaction.

Preparation of 4-aroylaminophenyl pyrezole derivatives

Amino compound (14 mmol) was dissolved in dichloromethane (10 mL) containing 15mmol Triethylamine. To this corresponding aromatic acid chloride solution was added drop wise and reaction was stirred at room temperature for 1 hour. On completion of reaction, added sat. $NaHCO_3$ solution and organic layer was washed with brine, separated and dried over Na_2SO_4. Organic layer was evaporated to dryness to give crude product which was recrystallized using chloroform and hexane, to afford desired product, 85-90% yield.

The physical constants are given in table no.1.

Code	Substitution R_1	MF/MW	M.P. ^oC	Yield %	% Composition Calcd. / Found		
					C	H	N
HM4Ba	3-OMe	$C_{27}H_{25}N_3O_4$ 455.51	251-253	97	71.19 71.10	5.53 5.51	9.22 9.20
HM4Bb	4-F	$C_{26}H_{22}FN_3O_3$ 443.48	276-278	97	70.42 70.41	5.00 4.96	9.48 9.46
HM4Bc	3-OH	$C_{26}H_{23}N_3O_4$ 441.48	300-302	94	70.73 70.69	5.25 5.19	9.52 9.51
HM4Bd	4-OMe	$C_{27}H_{25}N_3O_4$ 455.51	295-297	95	71.19 71.11	5.53 5.49	9.22 9.20
HM4Be	3-Cl	$C_{26}H_{22}ClN_3O_3$ 459.93	278-280	91	67.90 67.81	4.82 4.80	9.14 9.08
HM4Bf	3,4,5-triOMe	$C_{29}H_{29}N_3O_6$ 515.57	315-317	91	67.56 67.52	5.67 5.56	8.15 8.11
HM4Bg	2-OH	$C_{26}H_{23}N_3O_4$ 441.48	288-290	86	70.73 70.71	5.25 5.21	9.52 9.51
HM4Bh	4-NO_2	$C_{26}H_{22}N_4O_5$ 470.48	265-267	89	66.37 66.31	4.71 4.68	11.91 11.88
HM4Bi	2-NO_2	$C_{26}H_{22}N_4O_5$ 470.48	240-242	86	66.37 66.30	4.71 4.65	11.91 11.88
HM4Bj	H	$C_{26}H_{23}N_3O_3$ 425.49	255-257	95	73.39 73.28	5.45 5.39	9.88 9.85
HM4Bk	2-F	$C_{26}H_{22}FN_3O_3$ 443.48	222-224	88	70.42 70.38	5.00 4.99	9.48 9.45
HM4Bl	4-Br	$C_{26}H_{22}BrN_3O_3$ 504.39	215-217	92	61.91 61.88	4.40 4.36	8.33 8.29

Results and discussion

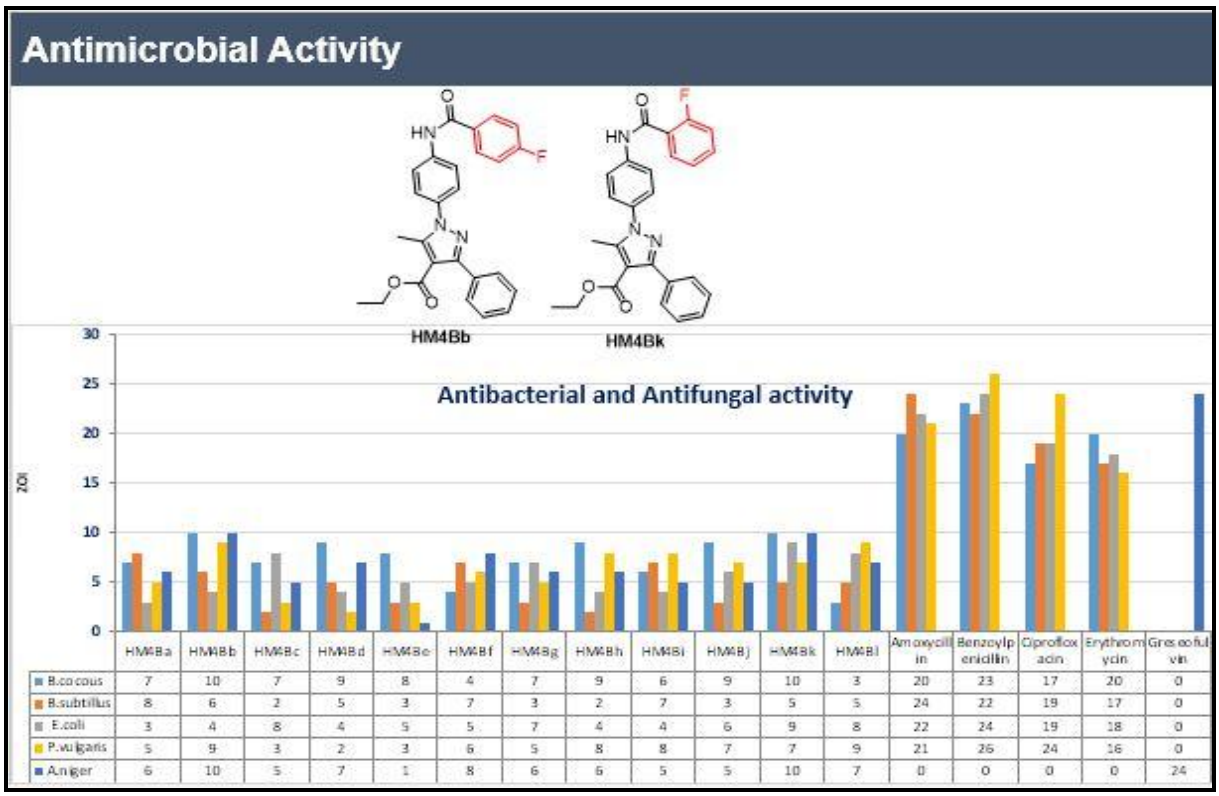
Antibacterial activity

The purified products were screened for their antibacterial activity. The nutrient agar broth prepared by the usual method, was inoculated aseptically with 0.5 ml of 24 hrs. Old subcultures of *B. subtilis*, *B.cocous*, *E. coli* and *P. vulgaris* in separate conical flasks at 40-50

^{0}C and mixed well by gently shaking. About 25 ml content of the flasks were poured and evenly spreaded in a petridish (13 cm in diameter) and allowed to set for two hrs. The cups (10 mm in diameter) were formed by the help of borer in agar medium and filled with 0.04 ml (40 µg) solution of sample in DMF. The plates were incubated at 37 ^{O}C for 24 hrs. And the inhibition of the bacterial growth were measured in millimeter and recorded as shown in Table No. 2.

Antifungal activity

A. niger was employed for testing antifungal activity using cup-plate method. The culture was maintained on Sabouraud's agar slants. Sterilised Sabouraud's agar medium was inoculated with 72 hrs. Old 0.5 ml suspension of fungal spores in a separate flask. About 25 ml of the inoculated medium was evenly spreaded in a petridish and allowed to set for two hrs. The cups (10 mm 34 in diameter) were punched. The plates were incubated at 30°C for 48 hrs. After the completion of incubation period, the zone of inhibition of growth in the form of diameter in mm was measured. Along the test solution in each petridish one cup was filled up with solvent which acts as control. The zones of inhibition are recorded in Table No. 2.



	HM4Ba	HM4Bb	HM4Bc	HM4Bd	HM4Be	HM4Bf	HM4Bg	HM4Bh	HM4Bi	HM4Bj	HM4Bk	HM4Bl	Amoxycillin	Benzoylpenicillin	Ciprofloxacin	Erythromycin	Griseofulvin
B.cocous	7	10	7	9	8	4	7	9	6	9	10	3	20	23	17	20	0
B.subtillus	8	6	2	5	3	7	3	2	7	3	5	5	24	22	19	17	0
E.coli	3	4	8	4	5	5	7	4	4	6	9	8	22	24	19	18	0
P.vulgaris	5	9	3	2	3	6	5	8	8	7	7	9	21	26	24	16	0
A.niger	6	10	5	7	1	8	6	6	5	5	10	7	0	0	0	0	24

Conclusion

The compounds having fluoro substitution on ortho and para position of amide are potent

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REFERENCES

1. Almekinders L.C., Gilbert J.A.; Am J Sports Med; 1986,14: 303-308.
2. Murad S., Pinnel S.R., Alexandria ;. Sci Exch; 1998, 7: 33-36.
3. Wood J.D., Gorecki D.K., Dimmock J.R., Hawes E.M. ; *Can J Physiol Pharmacol*; **1993**; 53: 47-55.
4. van Hal S.J., Barbagiannakos T., Jones M., Wehrhahn M.C., Mercer J., et al.; *J Antimicr Chemother 66 Suppl 10*;**2011**: 2284-2287.
5. Pattan S.R., Dighe N.S., Nirmal S.A., Merekar A.N., Laware R.B., et al.; *Asian J Res Chem*;**2009**, 2: 196-201.
6. Vipin M., Vashishtha; *Ind Pediat*; **2010**;47: 505-506.
7. Moged A.B., Evelin B.M. ; *Eur J Pharm Sci 20 Suppl 2*;**2003**: 173-179.
8. Quiroga J., Rodrigo A., Manuel N., Sanchez A., Justo C.; *Bioorg Med Chem*; **2010**; 18: 4965–4974.
9. Shin-Ru S., Tzu-Yun C., Gadarla R., Sung-Nain T., Hsiun C., et al. *J of Biomed Sci 17 Suppl*;**2010;** 13: 1-9.
10. Livermore D.M. ;*Clin Microbiol Infect 10 Suppl*;**2004**; 4: 1-9.
11. Dumas J., Hatoum H., Sibley R.N., Smith R.A., Scott W.J., et al. *Bioorg Med Chem Lett*;**2002**; 12: 1559-1562.
12. Priyadarsini P., Ujwalaa B., Rao B., Rao M.V. ; *Der Pharm Lett 4 Suppl*;**2012**; 4: 1123-1128.