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Synthesis and study of antimicrobial activity of some new 3-(-Hydroxy-5-methylphenyl)-4-benzoyl-5-phenylpyrazole

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ABSTRACT

3-Aroyl-6-methyl flavones (Ia-f) were allowed to react with hydrozine hydrochloride in DMSO containing piperidine to give the corresponding 3-2-hydroxyphenyl-5-methyphenyl)-4-aroyl 5-arylpyrazoles (IIa-f) Their structural assignments are based on elemental analysis, spectral data (ir, uv and nmr) and chemical properties. All these compounds were tested *in vitro* for their antimicrobial (antibacterial and antifungal) activity by disk diffusion against gram positive, gram negative bacteria and fungi. In some of the compounds the results are found to be encouraging.

Key words: 3-(-Hydroxy-5-methylphenyl)-4-aroyl-5-arylpyrazole.

INTRODUCTION

Literature on pyrazoles revealed that these compounds are found to possess antiduretic, antihelmintic fungicidal activity[1]. Substituted pyrazoles have been reported as antimicrobial agent[2], hypolipidermic agents, antidibetic and excellent antifogant[3], as well as strong antiparasitic[4,5] and herbicides[5].

The formation of substituted pyrazoles from 1,3, dicarbonyl compounds and substituted hydrazines[6,7] Wadokar and Doifode[8] reported the formation of 1-(2,4-dinitrophenyl)-3-phenyl -5-(2-hydroxy-4-methoxyphenyl) pyrazole by the interaction of 2-hydroxy-4'-methoxy dibenzoylmethane and DNPH acetic acid containing a little concentrated H_2SO_4 several 3, 5-diarylpyrazole have been reported from 2,4,6-triphenylpyrylium salt and hydrazine[9]. Asahi Chem Industry[10] Jpn. Prepared chloropyrazoles by esterification with ROH, It shows biological activity against *E. coli, S. juncoides*, Sagattari etc. Giri[11] & Co-workders have reported the synthesis and antifungal activity of 1-substituted-3(2-hydroxy phenyl)-5-(4-nitrophenyl) pyrazoles.

Keeping these facts in view, the title compounds have been synthesised and were screened for their antibacterial activity against gram positive and gram negative bacteria.

In the present study 3-aroylflavones (Ia-f) and hydrazine hydrochloride were refluxed in DMSO containing few drops of piperidine to give the corresponding 3-(2-hydroxy-5-methylphenyl)-4-benzoyl-5-phenylpyrazole (IIIa-f). (Table 1). These compounds (IIa-f) were tested in vitro for antimicrobial activity against some gram positive and gram negative bacteria, as well as antifungal activity against some common pathogenic fungi.

EXPERIMENTAL

Action of Hydrazine hydrochloride on 3-benzoyl-6-methyl flavone (I)

Mixture of 3-benzoyl-6-flavone (Ia-f) (0.01mol) and hydrazine hydrochloride (0.02mol) was refluxed in dimethyl - sulphoxide (20ml) containing piperidine (0.5ml) for 4-5 hours. The cooled reaction mixture was diluted with water and acidified by 1:1 HCl (15ml) when a semisolid was isolated. The product was triturated with and crystalised from ethanol to get the products (IIa-f).

Properties of Com IIa:

1. TLC. Solvent (CCl_4) height 2-4cm, solute height 1.9cm, Rf value = 0.79.
2. The compound (IIa) did not gave any colouration with ethanolic $FeCl_3$ but it was found to be soluble in dilute NaOH, indicating the presence of phenolic-OH group.
3. It did not respond to Knorr's test for pyrazolines, but yellow colouration was obtained when paper soaked inthe solution of this compound in benzene was exposed to bromine vapours.
4. It gave yellow colouration with conc. H_2SO_4.
5. From analytical result the molecular formula of compound is $C_{23}H_{18}N_2O_2$.
6. Their IR spectra showed absorption bands at 1624-1548 (C=N stretching of pyrazoles), 1670 (C=0 stretching of COph group), 2848 (C-H stretching (aliphatic) 2930 C-H stretching (aromatic), 3460 cm^{-1} (O-H stretching). Their UV spectrum showed lmax at 280 and 390 nm which indicate carbonyl function and PMR spectrum recorded in $CDCl_3$ showed d2.48 (3H, S, Ar-CH_3) & 7.38 - 8.04 (14H, m, Ar-H).

S.No	Compound	R_1	R_2
1.	Ia-IIa	CH_3	-C_6H_5
2.	Ib-IIb	CH_3	-4'-$CH_3OC_2H_4$
3.	Ic-IIc	CH_3	-2'-furyl
4.	Id-IId	H	-C_6H_5
5.	Ie-IIe	H	-4'-$CH_3OC_2H_4$
6.	If-IIf	H	-2'-furyl

M.Ps. reported are uncorrected and wee recorded 'Tempo' melting point apparatus. The purity of the compounds synthesised was tested by TLC on miroscopic slides with silica gel G-layers.

The Infra red spectra were scanned on Nicolt Magma I.R. 550' spectrophotometer in KBr pellets. This UV-visible spectra were recorded in methanol on Perkin-Elmer 202' spectrophotometer. The PMR spectra were drawn on Burker AC-300 F

Table 1: Formation and physical data 3-(2-Hydroxy-5 methylphenyl)-4-aroyl-5-aryl pyrazole(II)

Compound (I)	Compound (II)	Yield (%)	m.p. (°C)	% found (Calc.) C	H	N
3-benzoyl-6-methylflavone (Ia)	3-(2-hydroxy-5-methylphenyl) 4-benzoyl-5-phenylpyrazole (IIa)	62	223-24	77.15 (77.96)	4.95 (5.08)	7.27 (7.90)
3-benzoyl-4'-methoxy-6-methylflavone (Ib)	3-(2-hydroxy-5-methylphenyl) 4-benzoyl-5-methoxypnehyl pyrazole (IIb)	85	186	74.14 (75.61)	5.02 (5.20)	7.01 (7.29)
3-benzoyl-2-(2'-furyl)-6-methylchromone(Ic)	3-(2-hydroxy-5-methylphenyl) 4-benzoyl-5-(2'-furyl pyrazole (IIc)	65	196	72.77 (73.83)	4.36 (4.65)	7.99 (8.13)
3-benzoylflavone (Id)	3-(2-hydroxy phenyl)-4-benzoyl -5-phenylpyrazole (IId)	67	151	76.96 (77.64)	4.56 (4.70)	8.02 (8.23)
3-benzoyl-4'-methoxy flavone (Ie)	3-(2-hydroxy phenyl)-4-benzoyl 5-anisylpyrazole (IIe)	66	138	74.05 (74.59)	4.51 (4.86)	7.41 (7.56)
3-benzoyl-2-(2'-furyl) chromone(If)	3-(2-hydroxy phenyl)-4-benzoyl -5-(2'-furyl)-pyrazole (IIf)	65	199	72.21 (72.72)	4.05 (4.24)	8.30 (8.48)

Reacent : 3-Aroyl flavones (Ia-f) and Hydrazine hydrochloride (0.02mol)

Table 2: Actibacterial activity data of compound

S. No.	Name of Compound	Zone of Inhibition								
		E coli	*Kl. nuemoniae*	*Pseu Aeruginsoa*	*Staph. Aureus*	*Staph. albus*	*Salm. typhi*	*Vibrio Cholerae*	*Shigella Dysentery*	*Proteus Mirbaiis*
1.	3-(2-Hydroxy)-5-methylphenyl -4-benzoyl-5-phenylpyrazole	11	10	-	12	-	8	9	9	10
2.	3-(2-Hydroxy-5-methylphenyl) -4-benzoyl-5(4' methoxyphenyl) pyrazole	12	10	-	12	-	10	9	8	10
3.	3-(2-Hydroxy-5-methylphenyl) -4-benzoyl-(2'-furyl pyrazole	13	12	10	14	10	11	11	10	12
4.	3-(2-Hydroxyphenyl) -4-benzoyl -5-phenylpyrazole	11	10	-	11	-	9	8	9	10
5.	3-(2-Hydroxyphenyl)-4-benzoyl-5 -(4-methoxyphenyl)pyrazole	12	11	12	13	-	11	11	12	12
6.	3-(2-Hydroxyphenyl)-4- benzoyl-5-(2'-furyl)-pyrazole	14	12	12	14	10	12	12	13	13

Table 3: Antifungal activity data of compounds

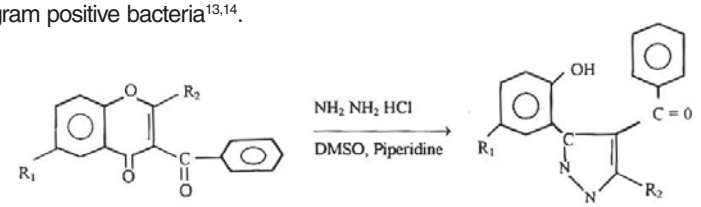
S. No.	Name of Compound	Zone of Inhibition								
		Cry neo	*Cand. albi.*	*Tri menta*	*Micro gypseam*	*Mucor* Spp.	*Rhizopus* Spp.	*Asp. niger*	*Asp. flavus*	*Asp. funmigatus*
1.	3-(2-Hydroxy)-5-methylphenyl -4-benzoyl-5-phenylpyrazole	11	9	12	10	10	9	8	7	8
2.	3-(2-Hydroxy-5-methylphenyl) -4-benzoyl-5(4' methoxyphenyl) pyrazole	12	11	13	12	11	11	10	10	11
3.	3-(2-Hydroxy-5-methylphenyl) -4-benzoyl-(2'-furyl pyrazole	14	12	14	14	12	12	12	11	12
4.	3-(2-Hydroxyphenyl) -4-benzoyl -5-phenylpyrazole	10	8	10	10	9	10	9	8	9
5.	3-(2-Hydroxyphenyl)-4-benzoyl-5 -(4-methoxyphenyl)pyrazole	12	11	13	12	12	13	12	11	11
6.	3-(2-Hydroxyphenyl)-4- benzoyl-5-(2'-furyl)-pyrazole	14	12	14	14	13	13	12	12	11

NMR spectrometer in $CDCl_3$ using TMS as a reference.

From the chemical properties, analytical results and spectral analysis, the compound (IIa) was assigned the structure as 3-(2-hydroxy 5-methylphenyl)-4-benzoyl-5-phenylpyrazole.

Antimiocrobial activity

The compounds (IIa-f) are 3,5 diaryl-4-aroypyrazoles. All these compound were tested in vitro for antimicrobial activity by disk-diffusion method[12] in dimethyl formamide (DMF) solvent at a concentration of 100 µg/ml using gram positive bacteria[13,14].



(I) (II)

Scheme 1

However, the antibacterial activity wash highest against *Staphylococus aureus. E. coli, Proteus mirabilis* in comparision to salm typhy, K1. Pneumoniate V. Cholerae & shigella dysentery, while in pseu aerugimosa & staph albus showed lesser activity or found in active.

On the basis of average percentage inhibition of all the compounds were found to display moderate to good level of toxicity against all fungi.

Staphylococcus aureus, staph, albus and gram negative bacteria *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, salmonella typhi, vibrio cholerae* and shigella dysentary, Proteus mirabilis, as well as antifungal activity against some common pathogenic fungi such as *Candida albicans, Cryptococcus neofromans, Aspergillus fumigatus, Aspegillus niger, Aspergillus flavus, Mucor* spp and *Rhizopus* spp.

Most of the compounds showed significant antibacterial & antifungal activity as stated in table 2&3 respectively.

They were, howeve more toxic against Crypto. neoformans, Candida albicans, trichophyton mentagrophytes, Microsporum gypseum, Mucor spp. & Rhizpus spp. than against *Aspergillus niger, Aspergillus flavus* & *Aspergillus fumigatus*.

It has been interesting to note that the antibacterial and antifungal activity invariably increased with the presence of methoxy & furyl groups.

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