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Novel synthesis, characterization and antimicrobial activity of some new 3, 5-diarylpyrazolines

M.P. BHISE[1], V.M. RAUT[1], R.P. PAWAR[1], G.P. GULWADE[1], N.A. JUNGHARE[2] and G.H. MURHEKAR[1]

[1]Department of Chemistry, Govt. Vidarbha Institute of Science & Humanities, Amravati (India)
[2]MCT's Rajiv Gandhi Institute of Technology, Andheri (W) Mumbai (India).

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ABSTRACT

3-Aroyl flavanones were allowed to react with hydrazine hydrate in dioxane containing little piperidine to give corresponding 3-(2-hydroxyphenyl)-4-aroyl-5-arylpyrazolines. Their structural assignment are based on elemental analysis, spectral data (IR, UV & NMR) and chemical properties. All these compounds were tested in vitro for their antibacterial activity by disk-diffusion method against gram positive and gram negative bacterias. In some of the compounds the results are found to be encouraging.

Key word: 3-(2-Hydroxyphenyl)-4-aroyl-5-arylpyrazoline, Antimicrobial activity.

INTRODUCTION

Pyrazoles containing heterocylic compounds plays an important role in medicinal chemistry. Since a very long time the usefulness and great therapeutic value of pyrazole nucleus has been recognized and the wide range of biological activities[1, 2] of their nucleus evaluated.

Pyrazolines are dihydro derivatives of pyrazoles

Pyrazoline ring has fairly accessible properties and hence attracted much attention in the fast developing area of synthetic chemistry. Besides traditional interest in the synthesis of drugs and dyes, pyrazoline derivaties also reported to have anaesthetic properties[3, 4] and strong antibacterial activities[5, 12]

Keeping these facts in view, the titled compounds (Table II) have been synthesized and were screened for their antibacterial activity against some gram positive and gram negative bacterias like Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus albus, Salmonella typhymurium, Vibrio cholerae and Shigella dysentery.

EXPERIMENTAL

Action of Hydrazine hydrochloride on 3-benzoyl-6-methylflavanone mixture of 3-benzoyl-6-methylflavanone (Ia-j) (0.01 mol) and hydrazine hydrochloride (0.02 mol) was refluxed in dioxine containing piperidine for 4-5 hours. The cooled reaction mixture was diluted with water and acidified with 1:1 HCl when a semisolid was isolated. The product was triturated with and crystallized from ethanol to get the products (IIa-j) Table-I. These compounds gave dark green colouration with ethanolic $FeCl_3$ and were soluble in NaOH indicating thereby the presence of free phenolic -OH group.

Reaction

Spectral Analysis

Their IR spectra showed bands at 1585 (C = N stretching of pyrazoline). 1650 – 1630 (C = O stretching of Coph group), 3020 – 2900 (N – H stretching) and 3500 (O-H stretching).

Their UV spectrum showed λmax at 270 and 375 nm, which indicates carbonyl function, and PMR spectra recorded in $CDCl_3$ showed δ2.34 (3H, s, Ar-CH_3), 3.75 (3H, s, Ar-OCH_3), 5.1 (1H, d, H_B), 5.9 (1H, d, H_A), 6.8, 6.98, 7.26-7.8 (H, H, 1OH, d, d, m, Ar-H).

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

The Infra red spectra were scanned on Nicolt Magma I.R. 550'spectrophotometer, in KBr pellets, The UV-visible spectra were recorded in methanol on Perkin-Elmer 202'-spectrophotometer. The PMR spectra were drawn on Bruker AC-300 F NMR spectrometer in $CDCl_3$ using TMS a reference.

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

Antimicrobial activity

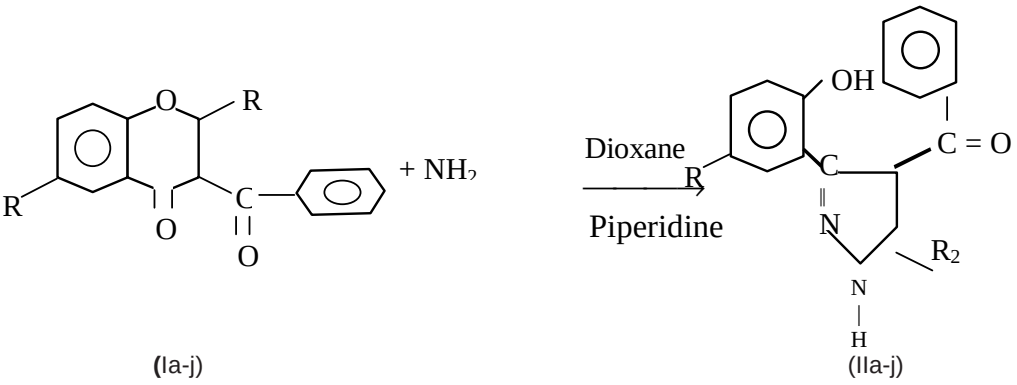
The compound (IIa – j) are 3-(2-hydroxyphenyl)-4-benzoyl-5-phenylpyrazolines. All these compounds stated in Table-III were tested in vitro for their antibacterial activity by disk-diffusion method[13, 14] in Dimethyl formamide (DMF) solvent at a concentration of 100 mg/ml using gram positive bacteria, *Staphylococcus aureus, Staphylococcus* albus and gram negative bacteria[15] like *Escheria coli, Klebsiellla pneumoniae, Pseudomonas aeruginosa, Salmonella typhi, Vibrio cholerae* and *Shigelle dysentery.*

RESULTS AND DISCUSSION

Most of the compounds showed significant antibacterial activity as stated in (Table 3). However, the compounds IIa, IIb and IIc showed moderate activity against *E.Coli, Klebsiella pneumoniae, Staph.* aureus, weak activity against *Salmonella typhi Vibrio chlorae,* Shingella dysentery and found inactive against *Pseudomonas aeroginosa* and *Staph albus*. The compound IId showed moderate activity against all organisms. The compound IIe showed strong inhibition zone against *E.coli,*

Table 1

S. No.	Compound Code	R_1	R_2
1.	Ia , IIa	$-CH_3$	$-C_6H_5$
2.	Ib , IIb	$-CH_3$	$-4'-CH_3O-C_6H_4$
3.	Ic , IIc	$-CH_3$	$-3', 4'O-CH_2-O-C_6H_3$
4.	Id , IId	$-CH_3$	$-2'-OH-C_6H_4$
5.	Ie , IIe	$-CH_3$	-2' –Furyl
6.	If , IIf	-H	$-C_6H_5$
7.	Ig , IIg	-H	$4'-CH_3O-C_6H_4$
8.	Ih , IIh	-H	$-3', 4'O-CH_2-O-C_6H_3$
9.	Ii , IIj	-H	$2'-OH-C_6H_4$
10.	Ij , IIj	-H	2'-Furyl



(Ia-j) (IIa-j)

Scheme 1

Table 2: Characterization data of synthesize compounds

Compound code	Compound II	Yield	M.P. (°C)	Mol. Formula	%found (Calc)		
					C	H	H
IIa	3-(2-hydroxy-5-methylphenyl)-4-benzoyl-5-phenylpyrazoline	60%	145-146	$C_{23}H_{20}N_2O_2$	77.15 (77.52)	5.32 (5.60)	7.72 (7.87)
IIb	3-(2-hydroxy-5-methylphenyl)-4-benzoyl-5-(4'methoxypnenyl) pyrazolines	85%	170-171	$C_{24}H_{22}N_2O_3$	74.41 (74.61)	5.37 (5.60)	7.01 (7.25)
IIc	3-(2-hydroxy-5-methylphenyl)-4-benzoyl-5-(3',4'-methylenedioxy phenyl) pyrazoline	70%	149	$C_{24}H_{20}O_4N_2$	71.92 (72.00)	4.89 (5.00)	6.89 (7.00)
IId	3-(2-hydroxy phenyl) -4 - benzoyl - 5-(2'-hydroxyphenyl) pyrazoline	60%	161	$C_{23}H_{20}O_3N_2$	71.03 (74.19)	5.27 (5.37)	7.38 (7.53)
IIe	3-(2-hydroxy-5-methylphenyl) -4 - benzoyl –5-(2'-furyl) pyrazoline	65%	160	$C_{21}H_{18}O_3N_2$	72.73 (72.83)	5.02 (5.20)	7.99 (8.09)
IIf	3-(2-hydroxyphenyl) -4- benzoyl - 5 – phenylpyrazoline	61%	151	$C_{22}H_{18}O_2N_2$	76.98 (77.19)	5.17 (5.26)	8.02 (8.19)
IIg	3-(2-hydroxyphenyl)-4-benzoyl – 5-(4'-methoxyphenyl) pyrazoline	85%	138	$C_{23}H_{20}O_3N_2$	74.05 (74.19)	5.29 (5.38)	7.41 (7.53)
IIh	3-(2-hydroxyphenyl)-4-benzoyl – 5-(3',4'-methylenedioxyphenyl) pyrazoline	65%	119	$C_{23}H_{18}O_4N_2$	71.39 (71.50)	4.61 (4.66)	7.00 (7.25)
IIi	3-(2-hydroxyphenyl)-4-benzoyl – 5-(2'-hydroxyphenyl) pyrazoline	60%	160	$C_{22}H_{18}O_3N_2$	73.64 (73.74)	4.92 (5.03)	7.63 (7.82)
IIj	3-(2-hydroxyphenyl)-4-benzoyl – 5-(2'-furyl) pyrazoline	65%	160	$C_{20}H_{16}O_3N_2$	72.21 (72.28)	4.76 (4.82)	8.30 (8.43)

Table 3: Antibacterial activity Data of 3-(2-Hydroxyphenyl)-4-benzoyl-5-phenyl pyrazolines (2a-j)

Compounds code	Substituents		Antibacterial activity zone of inhibition (mm)							
	R_1	R_2	*E. coli*	*Kl. pneumoniae*	*Pseu aeruginosa*	*Staph. aureus*	*Staph. albus*	*Salm. typhi*	*Vibrio cholerae*	*Shigella dysentery*
2a	$-CH_3$	$-C_6H_5$	12	10	-	12	-	9	9	8
2b	$-CH_3$	$-4'-CH_3O-C_6H_4$	11	10	-	12	-	10	8	9
2c	$-CH_3$	$-3', 4'-O-CH_2-O-C_6H_3$	13	10	-	12	-	9	9	8
2d	$-CH_3$	$-2'-OH-C_6H_4$	12	11	10	12	10	12	12	11
2e	$-CH_3$	-2' –Furyl	15	13	10	14	10	11	11	12
2f	-H	$-C_6H_5$	11	10	-	10	-	9	8	9
2g	-H	$4'-CH_3O-C_6H_4$	12	10	-	12	-	12	11	12
2h	-H	$3',4'-O-CH_2-O-C_6H_3$	13	10	-	12	-	11	10	10
2i	-H	$2'-OH-C_6H_4$	14	12	12	13	10	13	12	13
2j	-H	2'-Furyl	15	13	12	14	10	12	11	12

Klebsiella pneumoniae, Staph. aureus and moderate activity against rest of the organisms. The compound IIf showed moderate activity against *E.Coli, Staph. aureus, Klebsiella pneumoniae* and weakly active against Salmonella typhi, *Vibrio cholerae*, Shigella dysentery and found inactive against *Pseudomonas aeroginosa* and *Staph. albus.* The compound IIg, IIh showed moderate activity gainst *E.Coli, Staph aureus, Salmonella typhi, Vibrio, cholorae*, Shigella dysentery, *Klebsiella pneumoniae* and found inactive against Pseudomonas aeruginosa and staph. albus. The compound IIi showed strong inhibition zone against E.coli, Staph. aureus, Salmonella typhi, Shigella dysentery and moderate activity against *Klebsiella pneumoniae, Vibrio Chiolerae, Pseudomonas aeruginosa* and *Staph. albus*. The compound IIj showed strong inhibition against *E.coli, Staph aureus, Klebsiella pneumoniae* and moderate activity against *Salmonella typh*i, Shigella dysentery, Vibrio cholerae, Pseudomonas aeruginosa and Staph. albus.

From the above results, it is observed that most of these 4-aroylsubstituted pyrazolines were found more or less effective against *E. coli, Klebsiella pneumoniae, Salmonella typhi, Shigella dysentery,* Vibrio cholerae, Staph. aureus, while these compounds showed lesser activity or found inactive against *Pseudomonas aeruginosa* and *Staph. albus.*

It has been interesting to note that the antibacterial activity invariably increased with the presence of furyl groups. So these compounds can easily be used for the treatment of diseases caused by test pathogens, only when they does not have toxic and others side effects.

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