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SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NEW PYRAZOLINES

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ABSTRACT:

Title compounds 2-pyrazoline have been prepared by reaction of 2'-hydroxy-3', 5' di iodo-4'-ethoxy substituted phenyl chalcone react with 2,4-di nitro phenyl hydrazine hydrate to gives 1-2,4-di nitro-3-(2'-hydroxy-3' ,5' di iodo-4'-ethoxy phen-1' yl)-5-substituted phenyl-2-pyrazoline **(1a-g).**

The structural assignment of the compounds was based on elements analysis and IR, ^{1}H NMR and Mass spectral data. All the synthesized compounds have been screened for their antimicrobial activity to gram-positive and gram-negative bacterial strains and antifungal activity. The antimicrobial activities of the synthesized compounds have been compared with standard drugs like Amoxycillin, Ciprofloxecine and Griseofulvin. The purity of synthesized compounds have been checked by TLC.

KEY WORDS: *Chalcone, Pyrazoline, Antimicrobial.*

INTRODUCTION:

A number of biological activity are associated with pyrazoline[1-3], pyrazoline heterocycles having two nitrogens at 1, 2 position, respectively. The pyrazoline function is quite stable and inspired chemists to utilize this stable fragment on bioactive moieties to synthesize new compounds possessing biological activities.

Numerous reports have appeared in literature ascribbing antimicrobial[4-5], analagesic[6], antipyretic[7], insectidal[8], diuretic[9], and cardiovascular[10] properties of heterocyclic ring such a pyrazoline[11-13]. Nitrogen containing heterocyclic compounds[14] like pyrazolines have received considerable attention in recent years due to their biological activity like anti-inflammatory[15], anticonvulsant[16] and antidiabetic[17]. Pyrazolines and their derivatives are also reported to possess antiprotcolytic[18] and antiviral[19] activities. Many substituted pyrazolines are known to possess acaricidal[20] activities and are in the treatment of cerebral edema[21]. 1-pheny-2-pyrazolines are found to be useful as antioxidants[22].

Owing to the widespread application of pyrazoline and their derivatives and potential of iodine atom, it was thought worthwhile to prepare some iodinated pyrazoline and their derivatives.

In the present investigation 2'-hydroxy-3', 5' di iodo-4'-ethoxy substituted phenyl chalcone have been prepared by the Claisen-Schmidt condensation of 2'-hydroxy-3', 5' di iodo-4'-ethoxy acetophenone and various substituted aromatic aldehyde by known literature method.

The desired 1-2,4-di nitro-3-(2'-hydroxy-3' ,5' di iodo-4'-ethoxy phen-1' yl)-5-substituted phenyl-2-pyrazoline **(1a-g)** were prepared by condensation of 2'-hydroxy-3', 5' di iodo-4'-ethoxy substituted phenyl chalcone with hydrazine hydrate in ethanol as solvent **(scheme-I)**. Their structures were established by elemental and spectral study.

Antimicrobial Activity

The antibacterial activity of the synthesised compounds was screened by cup borer method[23]. The test contained 50 µg compound. The activity was shown against gram-positive bacteria *S.aureus* and *B.subtilis* and gram-negative bacteria *E.coli* and *S.typhi.* Similarly the antifungal activity of the compounds was also screened by cup borer method[23] and the test contained 100 µg compound. The activity was shown against fungus *A.niger*. The antimicrobial activities of the synthesized compounds have been compared with standard drugs like Amoxycillin, Ciprofloxecine and Griseofulvin. DMF was used as a solvent. The antimicrobial activities are summarized in the Table 1.

MATERIALS AND METHODS:

Experimental

Melting points were taken in open capillaries and are uncorrected. The IR spectra were recorded on a Shimadzu FTIR 8400 spectrophotometer, PMR spectra were recorded on a BRUKER (300 MHz) spectrometer using TMS as internal standard and Mass spectra were recorded on a Jeol SX-102 (FAB) Mass spectrophotometer. The purity of synthesized compounds have been checked by TLC.

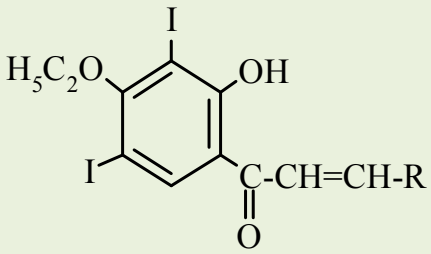
General procedure for the preparation of 1-2,4-di nitro-3-(2'-hydroxy-3' ,5' di iodo-4'-ethoxy phen-1' yl)-5-substituted phenyl-2-pyrazoline: [1 a-h]

2'-hydroxy-3', 5' di iodo-4'-ethoxy substituted phenyl chalcone (0.01 mole) and 2,4-di nitro phenyl hydrazine hydrate (0.015 mole) in ethanol (50 ml) were refluxed gently on water bath at 60-70°C for 4-5 hours. The resulting mixture was then concentrated and allowed to cool. The resulting solid obtained was filtered, washed with ethanol, dried and crystallized from ethanol as greenish yellow needles.

Similarly, all other compounds **[1a-g]** were synthesized. Their physical constants and antimicrobial activity are recorded in Table **1**.

Spectroscopic data of synthesized compounds : **IR (KBr) cm^{-1} 1c** : 3350 (Ar-OH), 1580 (C=N), 3370, 2890 (C-H), 517 (C-I), 2975 (C-H asym), 2850 (C-H sym), 1210 (C-O-C).**^{1}H NMR (δ ppm) 1b** : 1.48-1.54 (t, 3H,C$\underline{H}_3$-CH_2), 4.10-4.20 (q, 2H, C$\underline{H}_2$-CH_3), 3.03-3.10 (dd, 1H,C$\underline{H}_{2A}$), 3.47-3.56 (dd,1H, C$\underline{H}_{2B}$), 5.26-5.33 (dd,1H, C$\underline{H}$x), 2.40 (s, 3H, Ar-CH_3) 6.12 (s, 1H,OH), 7.10- 7.60 (m,5H,Ar-H). **Mass m/e 1c :** M+1 760.

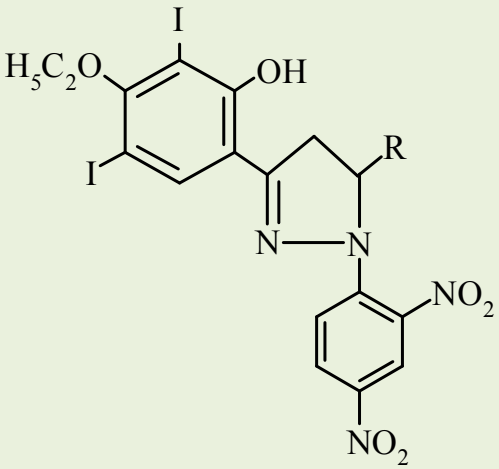
REACTION SCHEME



2'-hydroxy-3',5'- di iodo-4'-ethoxy substituted phenyl chalcone

2,4-di nitro phenyl hydrazine hydrate

Ethanol



1-2,4-di nitro-3- (2'-hydroxy-3',5'-di iodo-4'-ethoxy-phen-1' yl)-5- substituted phenyl - 2 - pyrazolines. **[1a-g]**

R = 2-chloro, 4-methyl, 3,4-di methoxy, 2-hydroxy,4-N,N di methyl, 3,4,5-tri methoxy,4-nitro, 3,4-di chloro

Table-1: Physical constants of synthesized compounds.

Compd No.	R	Molecular Formula	M.W.	M.P. °C	Rf	% of Yield	% of Halogen	
							Calc.	Found
1a	2-Cl-C_6H_4	$C_{23}H_{17}O_6N_4ClI_2$	734.5	200	0.71	58 %	39.41	39.45
1b	4-CH_3-C_6H_4	$C_{24}H_{20}O_6N_4I_2$	714	180	0.65	55 %	35.57	35.50
1c	3,4-di OCH_3-C_6H_3	$C_{25}H_{22}O_8N_4I_2$	760	130	0.71	61 %	33.42	33.48
1d	2-OH-C_6H_4	$C_{23}H_{18}O_7N_4I_2$	716	160	0.66	60 %	35.47	35.46
1e	4-N-N-di CH_3-C_6H_4	$C_{25}H_{23}O_6N_5I_2$	743	150	0.69	64 %	34.18	34.14
1f	3,4,5-tri OCH_3-C_6H_2	$C_{26}H_{24}O_9N_4I_2$	790	180	0.66	57 %	32.15	32.18
1g	4-NO_2-C_6H_4	$C_{23}H_{17}O_8N_5I_2$	745	190	0.72	58 %	34.09	34.10

- TLC Solvent system : - Ethyl acetate : Benzene (1.5 : 8.5)

Table-2: Antimicrobial activity of synthesised compounds.

Compd No.	Antibacterial activity (zone of inhibition in mm)				Antifungal activity (mm)
	S.aureus	*B.subtilis*	*E.coli*	*S.typhi*	*A.niger*
2a	12	NA	12	NA	13
2b	13	NA	12	NA	12
2c	15	15	14	13	12
2d	18	12	14	11	15
2e	14	15	13	12	16
2f	18	12	18	13	12
2g	19	15	14	09	11
Standard drugs					
Amoxicillin	22	23	24	24	
Ciprofloxacin	26	25	24	25	
Griseofulvin					26

RESULT AND DISCUSSION:

IR spectra of pyrazolines observed -CH_2 ring stretching between 2900-2800 cm^{-1}. There is also -CH deformation at 698-690 cm^{-1}. Spectra also showed absorption band around 1600-1500 cm^{-1}, which is a characteristics of -C=N some time it could not observed due to >C=C< skeletal in plane vibration of aromatic ring showed with one or more shoulder. IR spectrum of pyrazoline exhibits an intense sharp band around 1220-1020 cm^{-1} due to C-N stretch vibration.

The absence of -NH band provided additional proof for substituted derivatives of pyrazolines. Nitro derivatives of Pyrazoline showed characteristics stretch band of -N=O at 1550-1500 cm^{-1}.

In NMR Spectrum of pyrazoline and its derivative resonance due to two protons attached to C-4 and one attached to C-5 of pyrazoline ring showed up in form of three doublets, exhibiting a typical splitting pattern of ABX system of protons.

The first doublet of doublet observed at 2.50-3.20 δppm was assigned, to H_A, signal due to H_B also appear as doublet of doublet at around at 3.45-3.80 δppm. Signal due to third proton of pyrazoline also showed up as a doublet of doublet observed at 4.95-5.75 δppm. attributed H_X.

A singlet at the region 8.1-10.1δ ppm. for -N-H Proton was observed. The absence of -N-H peak at 8.1 - 10.1 δ ppm. provided additional provement of substituted derivatives of pyrazolines. The observed values of carbon, hydrogen, nitrogen and halogen analysis are in agreement with the calculated values.

Perusal of Table-2 revels that most of these compounds were found active against all bacteria viz gram-positive *S.aureus, B.subtilis* gram-negative *E.coli, S.typhi.*

All the tested compounds were found poor to moderately active (11-16 mm zone of inhibition) against fungi *A.niger*. The presence of pyrazoline nucleus in the molecule may be the causes of bioactivity of such compounds.

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