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Research Article

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Synthesis, spectral studies and antibacterial screening of some novel derivatives of pyrazoline based on chalcones

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ABSTRACT

Pyrazolines are one of the heterocyclic compounds with very important biological activites. In this view, it was proposed to synthesize some novel pyrazolines from chalcones. Here the synthesis of pyrazolines using piperazine chalcones and phenyl hydrazine under basic condition in presence of ethanol. The structures of synthesized were assigned on the basis of elemental analysis, IR and ^{1}H NMR spectroscopy data. These compounds were screened for their anti-bacterial activity.

Keywords: Pyrazolines, Antibacterial activity, chalcones, Phenyl hydrazine.

INTRODUCTION

Heterocyclic compounds are the well known class of compounds for its biological applications [1-5] out of which pyrazolines occupy unique position due to dominate applications. Pyrazolines are heterocyclic compounds which posses wide range of biological activities such as anti bacterial [6,7], anti depressant [8,9], anti tubercular [10,11], anti amoebic [12], anti inflammatory [13], herbicidal and insecticidal [14,15], cardiovascular [16] activity etc. One of the important applications of pyrazoline is the use of pyrazolines as a fluorescent brightening agent [17]. They can absorb light of 300-400 nm and emit blue fluorescence. Pyrazolines are also acting as hole transporting material in OELD (organic electroluminescent device) because of formation of p-л conjugated system due to one of the nitrogen atom.

In the present communication, we report the reaction of different chalcone derivatives with phenyl hydrazine hydrochloride to form pyrozalines. The structures of various synthesized compounds were assigned on the basis of elemental analysis, IR and ^{1}H NMR spectral data. These compounds were also screened for anti bacterial activities.

EXPERIMENTAL SECTION

All the melting points were determined in open capillary method and are uncorrected. IR spectra were recorded on Perkin-Elmer 237 spectrometer. 1HNMR spectra on a Bruker Avance DPX400 MHz spectrometer with $CDCl_3$ as a solvent and TMS internal standard. The chemical shift values are expressed in part per million (ppm) downfield from the internal standard and signals are quoted as s (singlet), d (doublet), t (triplet) and m (multiplate). Purity of the compounds is checked by TLC plates (Merck) using benzene and ethyl acetate .

General procedure for synthesis of pyrazolines
Preparation of various chalcones (1a-j)
To a well stirred solution of Benzaldehyde (1.06 gm, 0.01 mole) and acetophenone(1.2 gm, 0.01 mole) in ethanole (25 ml), 40% KOH added till the solution become basic. The reaction mixture was stirred for 24 hrs. The contents were poured into ice, acidified, filtered and crystallized from ethanol.

Similarly, other substituted Chalcones have been prepared

Synthesis of pyrazoline derivatives from chalcones (2a-j)
A mixture of Chalcones (2.08 gm, 0.01 mole) in 25 ml of absolute alcohol, add hydrazine hydrate (0.5 gm, 0.01 mole) was refluxed in water bath at temp. 80-90 ºC for 8 hrs. The reaction mixture was poured in to ice. The product was isolated and crystallized from ethanol

Synthesis of 2-[4-(3-chlorophenyl) piparazine-1-yl-methyl]-3,5-substituted phenyl-pyrazoline (3a-j).
A mixture of 3,5-di phenyl -2H- Pyrazoline (0.01 mole) and formaldehyde (40%, 1.5 ml) in ethanol (20 ml) was stirred at room temp. With a solution of 1-(3-chlorophenyl) piparazine (0.01 mole) in ethanol (10 ml) for 30 min. The solid product that separated out on standing for a 1 hrs was collected by filtration, washed with ethanol & dried. It was recrystallized from ethanol to yield the compound (3a-j). Which were obtained in 65-85% yield. Synthetic scheme in Figure-1 and The physical data are decribed in Table-1

Spectral data of pyrazoline derivatives
IR spectra of 3,5-substituted phenyl pyrazolines (2a-j)
pyrazoline is a heterocyclic compound. The bands due to $-CH_2$ bridge are at nearer to 3100 cm^{-1}. The corresponding N-H in plane and out of plane bending vibrations occurs at 1630 and 699 cm^{-1} respectively. The other band due to aromatic segments at 3 and 5-position are appeared at their respective position. The other unknown bands are due to substitution in aromatic segments.

NMR spectra of 3,5-substituted phenyl pyrazolines (2a-j)
The NMR spectra of all the compounds show the following common features, while individual ligand having additional signals is due to substitution on aromatic segment.

The signal at 5.7 ppm is responsible for $-CH_2$ bridge of pyrazoline, signal at 11.1 is responsible for N-H proton of pyrazoline, multiple signals between 6.15-7.8 ppm are responsible for aromatic proton. While signal at 2.5 and 3.7-3.9 are due to $-CH_3$ and $-OCH_3$ respectively.

CMR spectra of 3,5-substituted phenyl pyrazolines (2a-j)
Besides the PMR spectroscopy, the CMR spectroscopy is now more précised method to determine the structure or organic molecules. Considerably greater sensitivity is required for ^{13}C than for ^{1}H due to low natural abundance of ^{13}C and the lower magnetic moment compared to that of the proton. However, greater resolution is possible with ^{13}C.

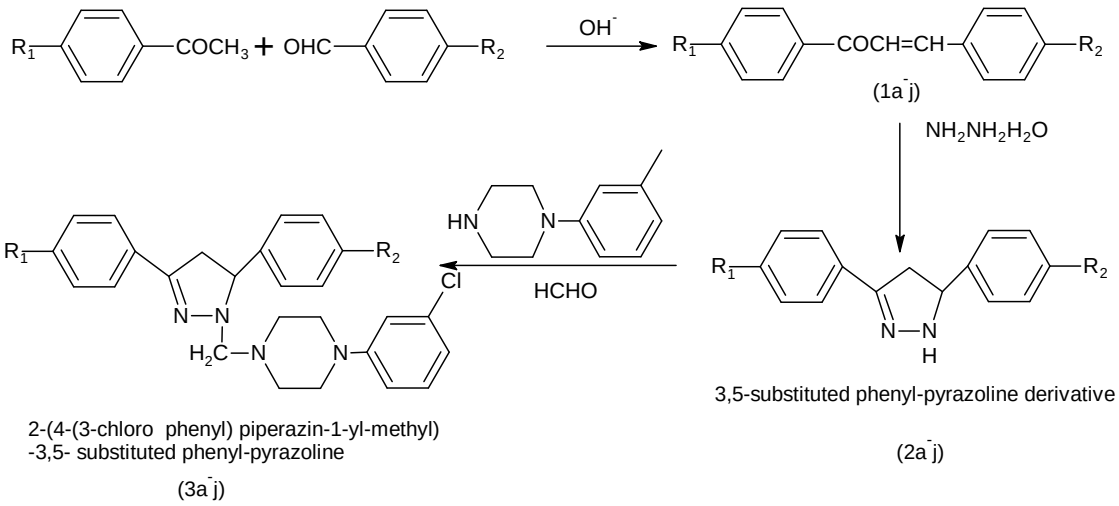
The CMR spectra of all the compounds show the following common features, while individual ligand having additional signals is due to substitution on aromatic segment.

The signals at 135-148 ppm are responsible for $-CH_2$ bridge of pyrazoline, multiple signals between 114-130 ppm are responsible for aromatic segments. While signal at 21 and 56 are due to $-CH_3$ and $-OCH_3$ respectively.

Also LC-MS data of 2j compounds shows molecular ion peak at 303.8 which is consistence with theoretical molecular weight i.e 301.5 g/mole.

Spectral data of 1-(3-chlorophenyl) piparazine-pyrazolines (3a-j)
IR: 3030,1500,1600 (Aromatic C-H stretching), 2850, 2920,1450 (-CH_2- of piperazine ring) **, NMR:** 7.1-8.84 (multiplet, aromatic), 3.47 (CH_2 linkage), 3.44-3.52(CH_2 of piperazine+CH_2 bridge), **^{13}CMR:** 136-145 (pyrazoline), 114-130 (benzene), 48 (piperazine)

Figure 1: Synthesis of piperazine- phenyl pyrazolines



Where,

R_1= -H, -Cl

R_2= -H, -CH_3, -OCH_3, -Cl, -NO_2

Table 1: Physical Constant of piperazine - pyrazoline derivatives (3a-j)

Sr. No.	R_1	R_2	Molecular Formula	Molecular Weight gm/mole	M.P. ^{0}C	Yield %	C, H, N & Cl (Calc. and Found)			
							C	H	N	Cl
3a	-H	-H	$C_{26}H_{26}N_4Cl$	429.5	235-237	85	72.6 72.2	6.0 5.8	13.0 13.0	8.3 8.2
3b	-H	-CH_3	$C_{27}H_{28}N_4Cl$	443.5	258-260	83	73.0 72.8	6.3 6.2	12.6 12.5	8.0 8.0
3c	-H	-OCH_3	$C_{27}H_{28}N_4Ocl$	459.5	216-218	82	70.5 70.4	6.1 6.0	12.2 12.0	7.7 7.5
3d	-H	-Cl	$C_{26}H_{25}N_4Cl_2$	464	224-226	77	67.2 67.0	5.4 5.4	12.1 12.0	15.3 15.1
3e	-H	-NO_2	$C_{26}H_{25}N_5O_2Cl$	474.5	236-237	62	65.8 65.6	5.3 5.0	14.7 14.5	7.5 7.3
3f	-Cl	-H	$C_{26}H_{25}N_4Cl_2$	464	225-226	64	67.2 67.0	5.4 5.2	12.1 11.8	15.3 15.0
3g	-Cl	-CH_3	$C_{27}H_{27}N_4Cl_2$	478	217-219	57	67.8 67.4	5.6 5.3	11.7 11.4	14.9 14.6
3h	-Cl	-OCH_3	$C_{27}H_{27}N_4Ocl$	494	218-220	54	65.6 65.2	5.5 5.3	11.3 11.0	14.4 14.2
3i	-Cl	-Cl	$C_{26}H_{24}N_4Cl_3$	498.5	228-230	58	62.6 62.4	4.8 4.8	11.2 10.8	21.4 21.1
3j	-Cl	-NO_2	$C_{26}H_{24}N_5O_2Cl_2$	509	231-233	55	61.3 61.2	4.7 4,5	13.8 13.5	13.9 13.7

RESULTS AND DISCUSSION

Antibactarial activity of 1-(3-chlorophenyl) piparazine-pyrazolines (3a-j)

The study has been conducted according to the method adopted by Cruickshank et al. Nutrient agar broth was melted in a water bath and cooked to 45^{O}C with gentle shaking to bring about uniform cooling. It was inoculated with 0.5-0.6 ml of 24 hour old culture especially and mixed well by gentle shaking before pouring on the sterilized Petri dish (25 ml each). The poured material was allowed to set (1.5 hour) and there after the “cups” were made by punching into the agar surface with a sterile cork borer and sooping out the punched part of agar. Into this “cups” 0.1

ml of test solution (prepared by dissolving 10gm of sample in 10ml DMF) was added by sterile micropipette. The bacterial data are shown given in Table-4.
Ampicillin, Tetracycline, Gentamycine and Chloramphenicol were used as standard drugs and a solvent control was also run to know the activity of solvent. Activity of standards and inhibition due to DMF are given in Table-3. The results shown by compounds and standards are corrected for DMF.

Table:3 Antimicrobial activity of Standards and Solvent (DMF)

No.	Name of compound	Zone of inhibition (in mm)			
		Gram positive		Gram negative	
		B.Subtillis	*S.Aureus*	*E.Coli*	*Ps.Aeruginosa*
1	DMF	6	6	6	6
2	Ampicillin	18	15	20	20
3	Tetracycline	21	20	16	24
4	Gentamycin	20	17	18	22
5	Chloramphenicol	18	25	18	23

Table-4 Antimicrobial activity of 2-[4-(3-chlorophenyl) piparazine-1-yl-methyl]-3,5-substituted phenyl pyrazoline. (3 a-j)

Compound	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	B.Subtillis	*S.Aureus*	*E.Coli*	*Ps.Aeruginosa*
3a	12	14	13	11
3b	11	15	11	12
3c	12	12	11	11
3d	10	10	09	10
3e	12	11	08	14
3f	17	16	11	18
3g	18	20	12	16
3h	12	11	12	13
3i	15	14	16	17
3j	16	11	13	14

CONCLUSION

The novel pyrazolines were synthesized by condensation of various chalcones with alcohol and hydrazine hydrate in ethanol. After that the compounds were purified by crystallization. The structures of the synthesized compounds were established on the basis of spectral data. Newly synthesized compounds of pyrazolines (3a to 3j) have been tested for their anti bacterial activity against gram positive bacteria *B. subtillis*, *S. aureus*, and gram negative bacteria *P. aeruginosa* and *E.coil* by the help of borer in agar medium and filled with 0.04ml (40µg) solution of sample in DMF. The compounds 3b, 3f, 3g and 3j were shown significant activities and compound 3a, 3c, 3d, 3e, 3h and 3i have shown moderate activity.

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