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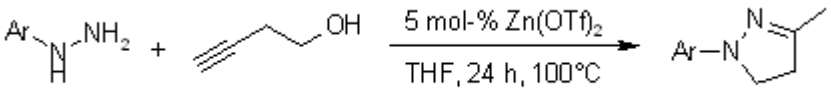
Synthesis of some Pyrazolines and their derivatives-A review

Suchita Nimbalkar[1] Shital P. Bhoyar [2]
[1] *Department of Applied Chemistry, St. Vincent Pallotti College of Engineering & Technology, Nagpur*
[2] *Department of Applied Chemistry, Shri Datta Meghe Polytechnic, Nagpur, India*

ABSTRACT

Pyrazoline derivatives is quite stable and has inspired chemists, to utilize pyrazoline fragment in bioactive moieties, to synthesize new pyrazoline derivatives. A series of substituted pyrazoline derivatives have been synthesized by the various reactions .The past studies of pyrazoline derivative revealed that they are useful in pharmaceutical and agrochemical research. Pyrazoline derivatives display various biological activities such as antitumor, antitubercular, antimicrobial, antibacterial, anti-inflammatory and antioxidant etc. Pyrazoline derivatives, being used as potential medicinal agents



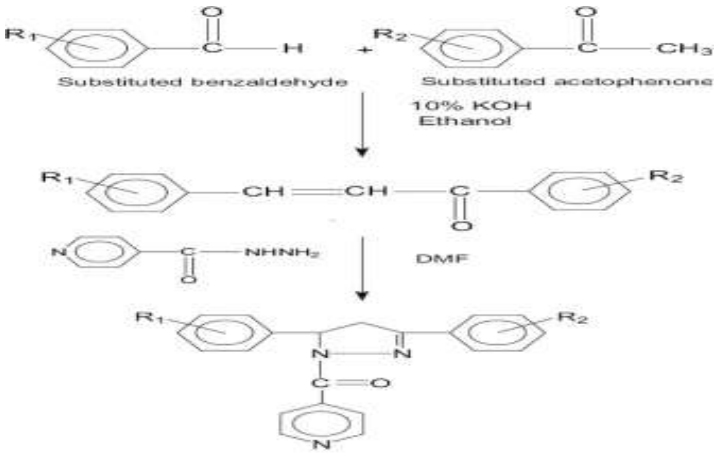
INTRODUCTION

Pyrazolines are well known and important nitrogen containing five membered heterocyclic compounds and various methods have been worked out for their synthesis. Numerous pyrazoline derivatives have been found to possess considerable biological activities, which stimulated the research activity in this field. They have found to possess anti-fungal [1], anti-bacterial [2], anti-inflammatory [3],anti-oxidant[4], ,anti-convulsant [5], anti-depressant [6], antiviral [7], anti-cancer [8], anti-microbial[9] , anti-tumor [10], antidiabetic [11] , anti-malarial, anesthetic, anti-analgesic[12],anti-tuberculosis[13], blue photo luminescence and electro luminescence, food and chemical toxicology, herbicidal, hypoglycaemic, hypertensive. Moreover, many selectively chloro-substituted organic compounds show peculiar pharmacological and agrochemical properties.

Based on the above biological activities exhibited by the pyrazoline compounds, we report here, the synthesis and biological evaluation of some new pyrazoline derivatives. The study of biological evaluation of pyrazoline derivatives has been an interesting field of medicinal chemistry. The synthesis of pyrazoline derivatives and investigation of their chemical and biological behaviour has gained more important in recent decades for biological and pharmaceutical reasons.

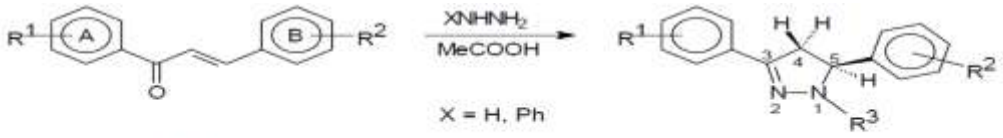
LITERATURE REVIEW

Some pyrazoles and their novel derivatives were synthesized by cyclization of substituted chalcone in presence of hydrazine hydrate [14]. Antifungal & antibacterial activities were also performed as in-vitro antimicrobial screening against fungal strains & bacterial strain respectively.



R_1 = N $(CH_3)_2$, OCH_3, CH_3
R_2 = OH, NO_2

2-pyrazolines [15] has been synthesized by the reaction of α,β-unsaturated ketones and hydrazines can be used for biological and pharmaceutical trials without the risk of undesirable decomposition.



1-12 13-27

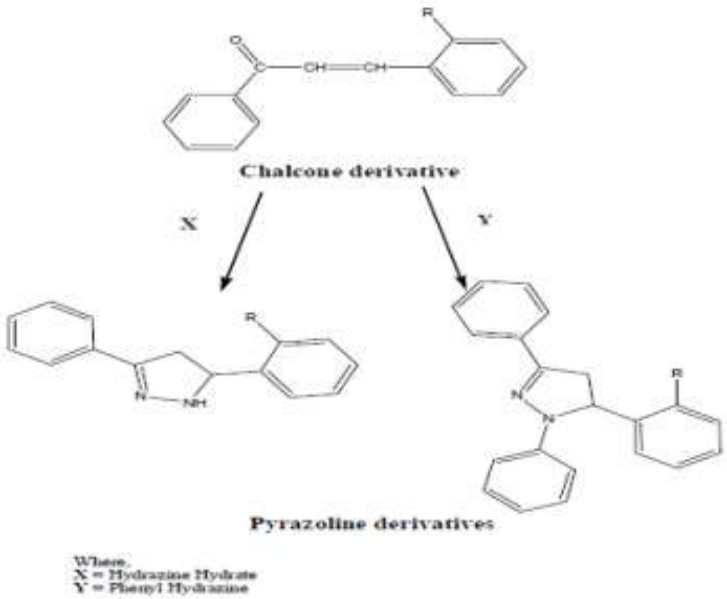
1, **13**: R^1 = 2-OH, R^2 = 4-iPr, R^3 = Ac
2, **14**: R^1 = 2-OH, R^2 = 4-Cl, R^3 = Ac
3, **15**: R^1 = 2-OH, R^2 = 2,4-Cl_2, R^3 = Ac
4, **16**: R^1 = 2-OH, R^2 = 2,3-$(MeO)_2$, R^3 = Ac
5, **17**: R^1 = 2-OH, R^2 = 3,4,5-$(MeO)_3$, R^3 = Ac
4, **18**: R^1 = 2-OH, R^2 = 2,3-$(MeO)_2$, R^3 = Ph
6, **19**: R^1 = 2-OH, R^2 = 2-Cl, R^3 = Ph
7, **20**: R^1 = 2-OH, R^2 = 3-Cl, R^3 = Ph

8, **21**: R^1 = 3-OH, R^2 = 4-MeO, R^3 = Ac
9, **22**: R^1 = 3-OH, R^2 = 2,6-Cl_2, R^3 = Ac
9, **23**: R^1 = 3-OH, R^2 = 2,6-Cl_2, R^3 = Ph
10, **24**: R^1 = 4-OH, R^2 = 2,4-Cl_2, R^3 = Ac
11, **25**: R^1 = 4-OH, R^2 = 2,6-Cl_2, R^3 = Ac
12, **26**: R^1 = 4-OH, R^2 = 3,4-Cl_2, R^3 = Ac
10, **27**: R^1 = 4-OH, R^2 = 2,4-Cl_2, R^3 = Ph

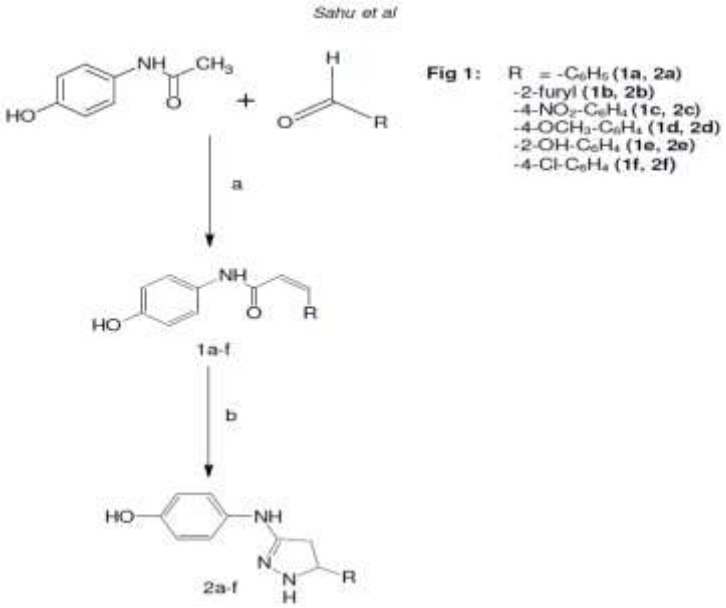
Series of 3,5-diphenylpyrazoline and N-phenyl-3,5-diphenylpyrazoline derivatives [16] are synthesized. These compound P1 and P2 shows significant antibacterialactivity against *S. aureus*, P1 and P4 against *E. coli* and P5 against *S. epidermidis.* Also P3 compound shows adequate activity against *E. coli* and *S.epidermidis.*

Compound	MIC (mg/ml)	% Inhibition		
		S.aureus	*E.coli*	*S.epidermidis*
P_1	2	59	54	50
P_2	2	62	-	45
P_3	2	-	48	52
P_4	2	51	56	52
P_5	2	51	48	56

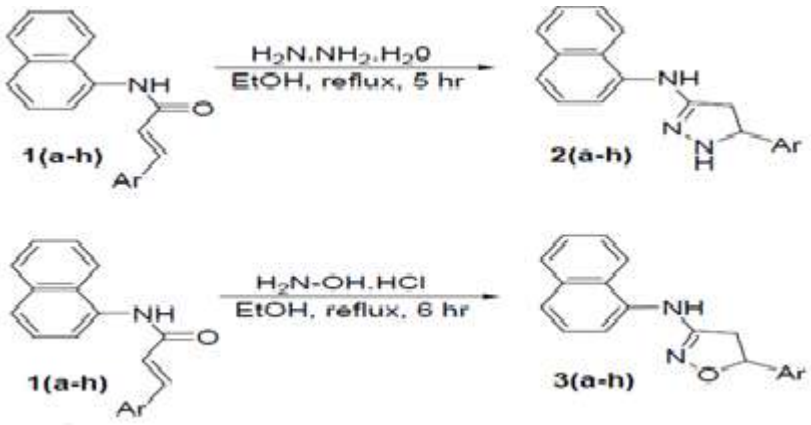
(-) Indicates bacteria are resistant to the compounds at concentration 2mg/ml, MIC - minimum inhibitory concentration, i.e., lowest concentration to completely inhibit bacterial growth.



Novel 4-(5-substituted aryl-4, 5-dihydropyrazole-3-yl-amino) pyrazolines [17] have been synthesized by treating substituted aryl-N-chalconyl amino phenols with hydrazine hydrate. The synthesized compounds were investigated for analgesic, antinflammatory & antimicrobial activities.



New series of 2-pyrazoline and isoxazoline derivatives 2(a-h), 3(a-h) [18] are synthesized by the treatment of 1-(napthyl amino)-3-aryl-2-propene-1-ones 1(a-h) with hydrazine hydrate and hydroxyl amino hydrochloride respectively. Further these compounds were evaluated for their antibacterial activity. Some of the compounds showed good activity against gram positive and gram negative bacterial strains.



1-(1-Hydroxy-naphthalen-2-yl)-3-phenyl-propenone [19] were prepared by carrying out the reactions of 2-hydroxy-1-aceto naphthone with 4-chloro benzaldehyde, 4-nitro benzaldehyde, benzaldehyde and ethanol using aqueous sodium hydroxide and (PEG-400) as a catalyst. The synthesized compounds were screened for antioxidant activity by DPPH method.

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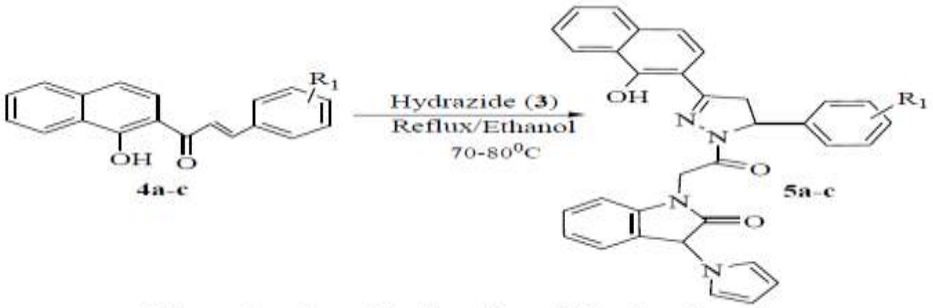
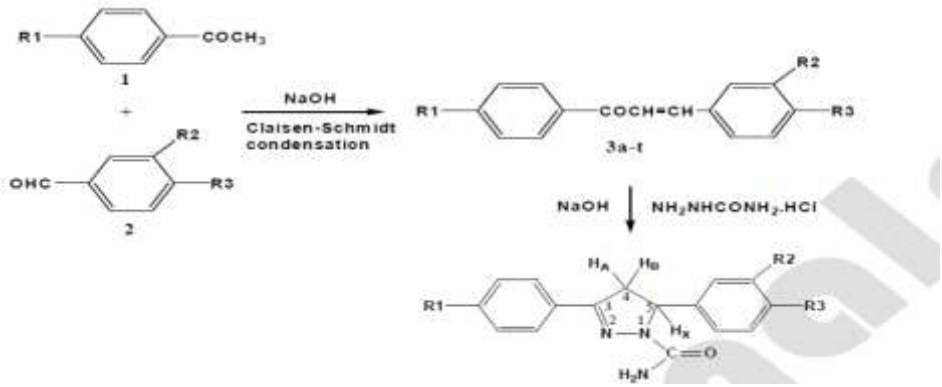
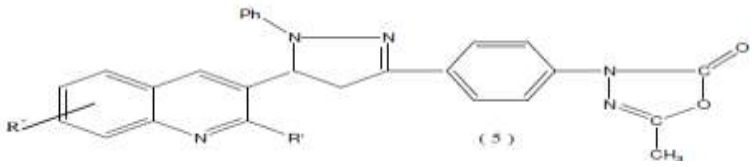


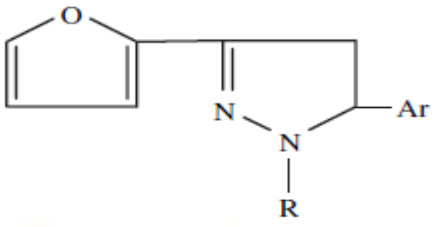
Substituted 3,5-diphenyl-2-pyrazoline-1-carboxamide derivatives [20] were synthesized from appropriate substituted 1,3-diphenylprop-2-en-1-one (chalcone) on reaction with semicarbazide hydrochloride. Compounds were evaluated for anticonvulsant activity by the maximal electroshock seizure (MES) method.



A series of 2-pyrazolines has been synthesized [21] by reaction with quinoline and acetyl sydnone derivatives as the starting materials. The antimicrobial studies of the synthesized compounds have shown promising activities towards the fungal strains viz., *A niger* and *A. sereus* and moderate activities of towards the bacterial strains *viz., E.coli* and *B.subtilis.*

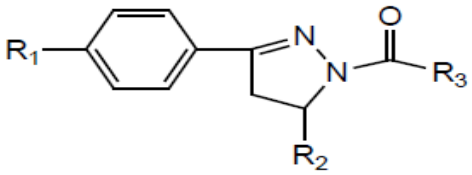


Twelve 1-phenyl-, 1-thiocarbamoyl- and 1-N-substituted thiocarbamoyl-3-(2-furyl)-5-phenyl/(2-furyl)-2-pyrazoline derivatives [22] were showing antidepressant activities, investigated by Porsolt's behavioural despair (forced swimming) test on albino mice.

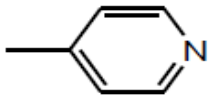
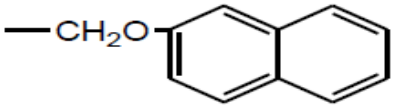


Compounds	Ar	R	Yield (%)	m.p. (°C)	Crystallization solvents
1	Phenyl	Phenyl	64	125–126	Ethanol
2	2-Furyl	Phenyl	78	92–93	Ethanol–water
3	Phenyl	$CSNH_2$	63	176–177	Ethanol
4	2-Furyl	$CSNH_2$	57	162–163	Ethanol
5	Phenyl	$CSNHCH_3$	58	133–134	Ethanol–water
6	Phenyl	$CSNHC_2H_5$	61	99–100	Ethanol–water
7	Phenyl	$CSNHC_3H_5$	47	116–117	Ethanol–water
8	Phenyl	$CSNHC_6H_5$	77	126–127	Ethanol
9	2-Furyl	$CSNHCH_3$	36	164–165	Ethanol–water
10	2-Furyl	$CSNHC_2H_5$	47	135–136	Methanol
11	2-Furyl	$CSNHC_3H_5$	49	113	Methanol
12	2-Furyl	$CSNHC_6H_5$	68	149–150	Ethanol

When varieties of acetophenones were condensed with varieties of substituted benzimidazole derivatives to get verious chalcone derivatives [23] which undergo condensation followed by cyclisation with isoniazid and 1-(2-napthyloxy acetate) hydrazine two get the final 2-pyrazoline derivatives. The synthesized compounds were found to have good antimicrobial activity in the range of 20-70 µg/ml.



R_1 = -Cl , -OH ; R_2 = 4-$NO_2C_6H_5$- , 2-furyl , 2-thienyl

R_3 =  , 

CONCLUSION

. Present research work involved synthesization, characterization and evaluation of novel pyrazoline derivative such as 1-substituted 3,5-diaryl-2-pyrazolines to afford in high yields. 3,5diphenylpyrazoline, N phenyl 3,5diphenylpyrazoline derivatives, 1,5-disubstituted pyrazoline derivatives, 2-pyrazoline and isoxazoline derivatives containing napthyl amino moiety. Chalcone derivatives, quinoline base pyrazoline derivative, 3-(2-furyl)-pyrazoline derivatives are also synthesized by simple methods are discussed above. To explore these pyrazoles are also fuctions as antitumor, antitubercular, antimicrobial, antibacterial, anti-inflammatory and antioxidant etc. Hence, it is concluded that there is ample scope for further study in developing these as good lead compounds for the treatment of bacterial strain as well as fungal strain. Most of the pyrazolines *are playing a vital role against some* microorganisms like *E. coli, S. epidermidis, S. aurious, S. shigella , A. niger , Pseudomonas aeruginosa, Streptococcus pyogenes, Klebsiella pneumoniae, Proteusmirabillis, Shigella dysentry* and *Salmonella typhii etc.*

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