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An introduction of some novel pyrazolines to synthetic chemistry and antimicrobial studies

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ABSTRACT

As a persuasion to our duties being a chemist we reported here the synthesis of pyrazolines using piperazine chalcones and phenyl hydrazine under basic condition in presence of ethanol. The reaction is carried out in refluxing conditions. The newly synthesized compounds were tested for antimicrobial activities.

Keywords: Chalcones, Phenyl hydrazine, Pyrazolines, Antimicrobial activity.

INTRODUCTION

Heterocyclic compounds are well known for their wide range of biological applications [1-5] out of which pyrazolines occupy unique position due to dominant applications. Pyrazolines are known to possess antimicrobial [6-7], antitubercular [8], antiviral [9], anti HIV [10], molluscicidal [11] and cerebroprotective [12] properties etc.

One of the important applications of pyrazoline is the use of pyrazolines as a fluorescent brightening agent [13]. 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-π conjugated system due to one of the nitrogen atom.

Pyrazolines have variety of methods for its synthesis but one of the popular methods is of Fischer and Knoevenagel i.e. the reaction of α,β-unsaturated ketones with phenyl hydrazine in acetic acid

under refluxing condition. However depending on the reactivity of molecules and need of the chemist they have synthesized the pyrazolines under different solvent media & acidic or basic conditions [14-16].

Such a glamour history prompted us to synthesize pyrazolines as an urgent need which can possess biological and medicinal importance. Therefore we have synthesized here some novel pyrazolines from piperazine chalcones and phenyl hydrazine in basic condition.

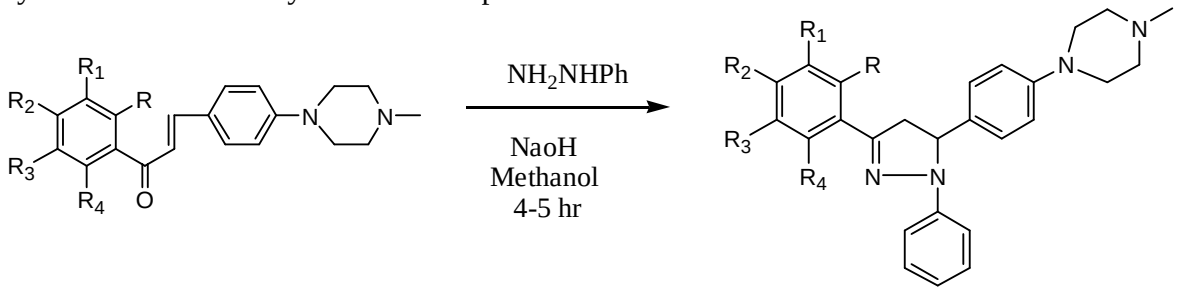
EXPERIMENTAL SECTION

All the melting points were determined in open capillary method and are uncorrected. IR spectra were recorded on Perkin-Elmer 237 spectrometer. ^{1}HNMR 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 as an eluent in the ratio of (9:1 v/v).

General Procedure for synthesis of pyrazolines:

To a mixture of chalcone (2 mmol) and phenyl hydrazine (2 mmol) in ethanol (15 ml) was added sodium hydroxide (2.5 mmol). The reaction mixture was then refluxed for 4-5 hrs. After completion of reaction (monitored by TLC) the reaction mixture was distilled to remove the excess solvent then it is poured into crushed ice. The solid obtained washed with water and recrystalised from ethanol.

Physical data of all the synthesized compounds is mentioned in **table-1**.



Scheme I : Synthesis of Phenyl Pyrazolines

(I-X)

Entry	R	R_1	R_2	R_3	R_4
I	H	H	H	H	H
II	H	Br	H	H	H
III	H	H	Br	H	H
IV	H	H	OCH_3	H	H
V	H	H	OH	H	H
VI	OH	H	H	H	H
VII	OH	Cl	H	H	H
VIII	OH	H	H	Cl	H
IX	OH	I	H	Cl	H
X	OH	H	H	CH_3	H

RESULTS AND DISCUSSION

A series of novel pyrazolines were synthesized by refluxing piperazine chalcones and phenyl hydrazine in presence of alkali. The reaction is completed within few hours as monitored by TLC providing good to excellent yield.

All the newly synthesized pyrazolines were screened for antimicrobial studies and exhibited moderate to good activity.

1-[4-(2,5-Diphenyl-3,4-dihydro-2H-pyrazol-3-yl)-phenyl]-4-methyl-piperazine (I):
IR(KBr): 1596cm^{-1}(C=N), 2937 cm^{-1}(CH_3), 1504 cm^{-1}(N-C_6H_5); **^{1}HNMR($CDCl_3$):** δ 2.2(s, 3H, CH_3), δ 2.4 (t, 4H, CH_2), δ 3.0 (t, 4H, CH_2), δ 3.1(dd, 1H, H_a), δ 3.8(dd, 1H, H_b), δ 5.3 (dd, 1H, H_x), δ δ 6.8-7.9 (m, 14H, Ar-H), **M.S. (m/z):** m+1= 397.

1-{4-[5-(4-Bromo-phenyl)-2-phenyl-3,4-dihydro-2H-pyrazol-3-yl]-phenyl}-4-methyl-piperazine (III):
IR(KBr): 1603cm^{-1}(C=N), 2937 cm^{-1}(CH_3), 1510 cm^{-1}(N-C_6H_5); **^{1}HNMR($CDCl_3$):** δ 2.2 (s, 3H, CH_3), δ 2.4 (t, 4H, CH_2), δ 3.0 (t, 4H, CH_2), δ 3.15(dd, 1H, H_a), δ 3.9(dd, 1H, H_b), δ 5.4 (dd, 1H, H_x), δ 6.9-8.1 (m, 13H, Ar-H), **M.S. (m/z):** m+1= 475.

1-{4-[5-(4-Methoxy-phenyl)-2-phenyl-3,4-dihydro-2H-pyrazol-3-yl]-phenyl}-4-methyl-piperazine (IV):
IR(KBr): 1593cm^{-1}(C=N), 2937cm^{-1}(CH_3), 1515cm^{-1}(N-C_6H_5); **^{1}HNMR($CDCl_3$):** δ 2.2 (s, 3H, CH_3), δ 2.4 (t, 4H, CH_2), δ 3.0 (t, 4H, CH_2), δ 3.1(dd, 1H, H_a), δ 3.8 (s, 3H, OCH_3), δ 4.0(dd, 1H, H_b), δ 5.35 (dd, 1H, H_x), δ 6.9-8.1 (m, 13H, Ar-H), **M.S. (m/z):** m+1= 427.

Table1. Physical data of synthesized compounds (I-X)

Entry	Molecular formula	Yield (%)	Melting point (°C)
I	$C_{26}H_{28}N_4$	83	235
II	$C_{26}H_{27}BrN_4$	89	270
III	$C_{26}H_{27}BrN_4$	87	242
IV	$C_{27}H_{30}N_4O$	82	205
V	$C_{26}H_{28}N_4O$	81	>300
VI	$C_{26}H_{28}N_4O$	88	>300
VII	$C_{26}H_{27}ClN_4O$	92	>300
VIII	$C_{26}H_{27}ClN_4O$	81	>300
IX	$C_{26}H_{26}ClIN_4O$	87	208
X	$C_{27}H_{20}N_4O$	89	>300

Antimicrobial activity

Antimicrobial screening was done by using cup plate method [17-18] at a concentration of 100µg/ml. All compounds were checked for their in vitro antimicrobial activity against different strains of bacterias and mentioned fungi as described in table 2. DMSO was used as solvent control. The obtained data of activity of all these tested compounds is as shown in **table 2**.

Table 2: Antimicrobial activity of synthesized compounds (I-X)

Products	Bacteria (Zone of Inhibition in mm)				Fungi (Zone of Inhibition in mm)			
	A	B	C	D	E	F	G	H
I	13	20	16	21	---	---	---	
II	14	15	19	11	---	---	---	---
III	12	17	20	18	---	---	---	---
IV	11	22	13	14	---	---	---	---
V	14	13	16	12	12	---	---	---
VI	11	18	13	14	17	---	---	---
VII	15	16	18	19	13	---	---	---
VIII	12	18	12	20	12	---	---	---
IX	11	11	13	11	22	---	---	---
X	15	17	16	12	17	---	---	---

A= Bacillus subtilis gr +ve, B= Pseudomonas aeruginosa gr –ve,C= Staphylococcus aureusgr +ve,D= Escherichia coli gr –ve, E= Aspergillus niger, F= Aspergillus Flavus, G= Curvularia H=Alternaria.

CONCLUSION

In conclusion, we have reported some novel pyrazolines using piperazine chalcones and phenyl hydrazine possessing moderate to good antimicrobial activity. These newly synthesized molecules were screened only for their antimicrobial activity however such type of molecules have the greater probability of exhibiting broad spectrum of biological and medicinal utilities because of presence of piperazine ring, cholro, bromo, Iodo type of attachments. In our future studies we will explore these ideas.

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