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Research Article

A PRECIOUS ADDITION OF SOME NOVEL PYRAZOLINES TO THE LIBRARY OF BIOACTIVE COMPOUNDS

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ABSTRACT

In present investigation, we reported here the synthesis of pyrazolines from pyrrolidine chalcones and hydrazine hydrate in basic condition using methanol as a solvent for the reaction. These synthesized compounds were established on the basis of IR, ^{1}H NMR, Mass spectroscopic data which were further screened for their antimicrobial studies using different strains of bacteria and fungi. The synthesized compounds showed moderate to good activity.

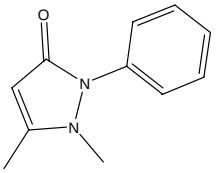
Keywords: Chalcones, Hydrazine hydrate, Pyrazolines, Antimicrobial activity

INTRODUCTION

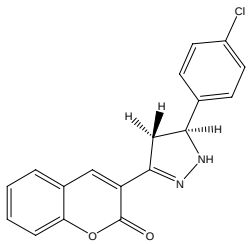
Heterocyclic compounds are the well known class of compounds for its biological application[1-4]. One of these heterocyclic compounds i.e. pyrazoline has attracted much of attention from the researchers due to possession of broad spectrum of biological applications. Pyrazolines are known to possess antmicrobial[5-7], antiinflammatory[8], antimycobacterial[9-10], antihistaminic[11], acetyl cholinesterase inhibitor[12], antiamoebic[13], antitumor[14], antidepressant[15], insecticidal[12] and anticoagulant[16] activities.

Amoebiasis is reported to be second leading cause of death all over the world[13] the credit of important chronic communicable diseases in the world goes to tuberculosis (TB) as reported by WHO[9] On studying various diseases we can withdraw the conclusion that every disease has its own place in spreading hazards in this world & need considerable attention of the chemist. Pyrazoline has evolved as a potent molecule for such issues as we mentioned above.

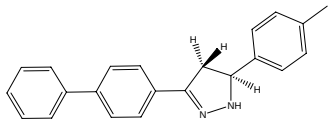
Literature survey shows that pyrazolines are having clinical applications such as NSAIDS (non-steroidal anti-inflammatory drugs). To this support it provides us the use of antipyrine (**a**) and other derivatives of pyrazolines (**b**) and (**c**) as the potent anti-inflammatory agent[17].



(a)Antipyrine



(b)



(c)

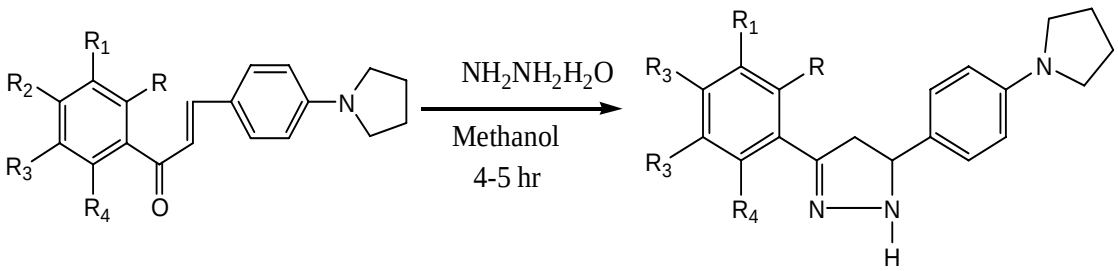
MATERIALS AND METHODS

Experimental

All the melting points were determined in open capillary method and are uncorrected. IR spectra were recorded as a KBr pellets on Perkin-Elmer FT IR 240-c 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 (7:3 v/v).

General Procedure for synthesis of pyrazolines:

To a mixture of pyrrolidine chalcone (2 mmol) and hydrazine hydrate (2 mmol) in methanol (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 methanol. The physical data of the synthesized compounds is mentioned in **table1**.



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	F	OCH_3	H	H
VI	OCH_3	H	H	OCH_3	H
VII	H	H	OH	H	H
VIII	OH	H	H	H	H
IX	OH	H	OH	H	H
X	OH	Cl	H	H	H
XI	OH	H	H	Cl	H
XII	OH	I	H	Cl	H
XIII	OH	H	H	CH_3	H
XIV	OH	H	CH_3	Cl	H
XV	OH	Cl	H	Cl	H
XVI	OH	H	CH_3	H	H

RESULTS AND DISCUSSION

A series of novel pyrazolines were synthesized by refluxing pyrrolidine chalcones and hydrazine hydrate in presence of alkali. The reaction is completed within few hours as monitored by TLC providing good to excellent yield. All the synthesized compounds which are tested for antimicrobial activity exhibited moderate to good activity.

Spectroscopic data of synthesized compounds:

3-Phenyl-5-(4-pyrrolidin-1-yl-phenyl)-4,5-dihydro-1H-pyrazole (I)

IR(KBr): 1610cm^{-1}(C=N), 3336 cm^{-1}(N-H); **^{1}HNMR:** δ 1.9 (t,4H,CH_2), δ 2.8(dd, 1H, H_a), δ 3.2 (t,4H,CH_2), δ 3.35(dd, 1H, H_b), δ 4.70 (dd, 1H ,H_x), δ 6.5 (s, 1H ,NH), δ 7.0-7.8 (m,9H,Ar-H); **M.S. (m/z):** m+1= 292.2

3-(4-Bromo-phenyl)-5-(4-pyrrolidin-1-yl-phenyl)-4,5-dihydro-1H-pyrazole (III)

IR(KBr): 1612cm^{-1}(C=N), 3330 cm^{-1}(N-H); **^{1}HNMR:** δ 1.9 (t,4H,CH_2), δ 2.7(dd, 1H, H_a), δ 3.2 (t,4H,CH_2), δ 3.3(dd, 1H, H_b), δ 4.65 (dd, 1H ,H_x), δ 6.4 (s, 1H ,NH), δ 7.2-7.9 (m,8H,Ar-H); **M.S. (m/z):** m+1= 370

3-(4-Methoxy-phenyl)-5-(4-pyrrolidin-1-yl-phenyl)-4,5-dihydro-1H-pyrazole (IV)

IR(KBr): 1618cm^{-1}(C=N), 3332cm^{-1}(N-H); **^{1}HNMR:** δ 1.9 (t,4H,CH_2), δ 2.65(dd, 1H, H_a), δ 3.2 (t,4H,CH_2), δ 3.3(dd, 1H, H_b), δ 3.8 (s,3H,OCH_3), δ 4.65 (dd, 1H ,H_x), δ 6.45 (s, 1H ,NH), δ 7.1-7.9 (m,8H,Ar-H); **M.S. (m/z):** m+1= 322.1

Table 1: Physical data of synthesized compounds (I-XVI)

Entry	Molecular formula	Yield (%)	Melting point (°C)
I	$C_{19}H_{21}NO$	85	158
II	$C_{19}H_{20}BrNO$	89	216
III	$C_{19}H_{20}BrNO$	84	180
IV	$C_{20}H_{23}NO_2$	88	142
V	$C_{20}H_{22}FNO_2$	87	143
VI	$C_{21}H_{25}NO_3$	88	110
VII	$C_{19}H_{21}NO_2$	85	> 300
VIII	$C_{19}H_{21}NO_2$	92	150
IX	$C_{19}H_{21}NO_3$	89	>300
X	$C_{19}H_{20}ClNO_2$	88	161
XI	$C_{19}H_{20}ClNO_2$	78	148
XII	$C_{19}H_{19}ClINO_2$	92	175
XIII	$C_{20}H_{23}NO_2$	89	210
XIV	$C_{20}H_{22}ClNO_2$	83	205
XV	$C_{19}H_{19}Cl_2NO_2$	82	182
XVI	$C_{20}H_{23}NO_2$	87	280

Biological Screening

For establishment of antimicrobial activity of the synthesized compounds we utilized the reported cup plate method[18-19]. The experiment is performed at a concentration of 100µg/ml. we checked the activity of these molecules against different strains of bacteria and fungi as mentioned in table2. DMSO was used as solvent control. The obtained data of activity of all these tested compounds is shown in **table 2**.

CONCLUSION

In conclusion, we put forth here some novel pyrazolines using pyrrolidine chalcones and hydrazine hydrate possessing good to moderate antimicrobial activity. In this letter we have tested this library of compounds for the antimicrobial activity however such type of compounds which bears chloro, bromo, and iodo substituent possess variety of biological and pharmacological activities and hence will be explored in our future work.

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

Products	Bacteria (Zone of Inhibition in mm)				Fungi (Zone of Inhibition in mm)			
	A	B	C	D	E	F	G	H
I	14	11	24	12	---	---	---	---
II	17	12	12	11	---	---	---	---
III	13	18	23	10	---	---	---	---
IV	12	12	12	---	---	---	---	---
V	26	16	13	---	---	---	---	---
VI	13	14	25	11	---	---	---	---
VII	12	13	15	---	27	---	---	---
VIII	20	11	11	13	25	---	---	---
IX	13	16	20	13	25	---	---	---
X	25	13	25	27	---	---	---	---
XI	18	19	12	18	---	---	---	---
XII	25	26	14	22	33	---	---	---
XIII	17	12	25	19	24	---	---	---
XIX	19	13	13	20	28	---	---	---
XV	20	14	13	15	28	---	---	---
XVI	11	12	18	17	22	---	---	---

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*.

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