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Synthesis and antimicrobial studies of some novel pyrazolines

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ABSTRACT
The Chalcones Condensed with hydrazine hydrate in ethanol to get the corresponding novel pyrazolines (I-X). The compounds were synthesized and characterized by TLC, melting points, IR, ^{1}H-NMR and mass spectra. The synthesized compounds have been screened for their antimicrobial activity against different micro-organisms. All the compounds show moderate to good activity against different micro-organisms.

Keywords: Chalcones, Hydrazine hydrate, Pyrazolines, Antimicrobial Activity.

INTRODUCTION

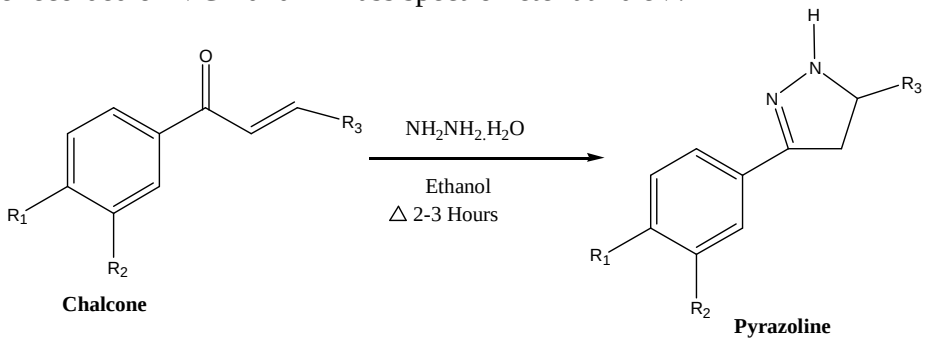
Pyrazolines are well known biologically important nitrogen containing heterocycles. Nitrogen containing heterocyclic compounds [1] like pyrazolines have received considerable attention in recent years. Pyrazolines exhibit a plethora of bioactivities viz, COX-2 inhibitior[2], antiandrogenic[3], antibacterial[4], antifungal[5], antitumor[6], antidepressant[7], insecticidal[8], antidiabetic[9], photochemical[10],herbicidal[11] molluscicidal[12], antinociceptive[13] and antiamoebic activity[14]. Pyrazolines are also used in the treatment of Parkinson's, Alzehimer's disease and Cerebral edema[15]. Besides Being Biologicallly active they are also used as useful synthons in organic synthesis[16-18]. Hence synthesis of Pyrazolines are largely on account of their biological activity. Herein we report the synthesis of some novel pyrazolines by using the chalcones and hydrazine hydrate.

MATERIALS AND METHODS

Experimental

Melting points were determined in open capillary tubes and are uncorrected. Purity of the compounds was checked by TLC on silica gel G. UV light or iodine vapour accomplished

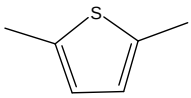
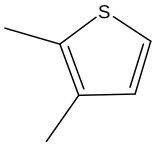
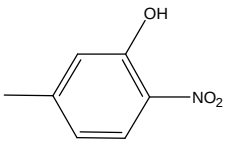
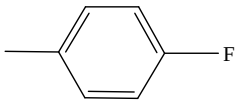
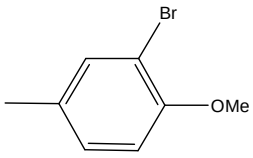
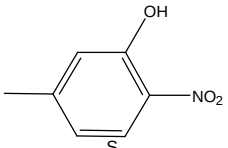
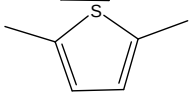
visualization. The IR Spectra were recorded on FTIR perkin-Elmer 1420 spectrometer and PMR spectra ($CDCl_3$) on a varian-300 MHZ spectrometer using TMS as internal standard. Mass spectra were recorded on VG 7070 H Mass spectrometer at 70 eV.

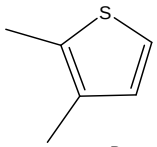
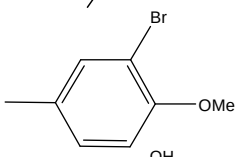
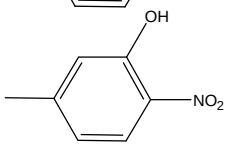


Chalcone **Pyrazoline**

(I-X)

Scheme I

Entry	R_1	R_2	R_3
I	H	Br	
II	H	Br	
III	H	Br	
IV	H	Br	
V	H	Br	
VI	OMe	H	
VII	Br	H	

VIII	Br	H	
IX	Br	H	
X	Br	H	

General Procedure for synthesis of Pyrazolines:

A solution of chalcones (0.01 mole) in ethanol (20ml) and hydrazine hydrate (99%, 0.01 mole) was refluxed for 2 to 3 hr. After completion of the reaction some solvent distilled out under reduced pressure. The reaction mixture was cooled, the solid separated was collected and recrystallized from ethanol.

RESULTS AND DISCUSSION

The most common synthetic approach to pyrazoline synthesis involves cyclization of propenones with hydrazines in the presence of acetic acid as cyclizing agent.[19]. Herein we reported the synthesis of novel pyrazolines by condensing chalcones with hydrazine hydrate in ethanol. The newly synthesized compounds evaluated for antimicrobial activity. Structures of newly synthesized compounds were confirmed by spectral analysis.

Compound VI

5-[5-(4-Methoxy-phenyl)-3,4-dihydro-2H-pyrazol-3-yl]-2-nitro-phenol:

IR(KBr):1150cm^{-1}(OCH_3), 1622cm^{-1}(C=N), 3400 cm^{-1}(N-H), 1518 cm^{-1} (N-O) , 1220cm^{-1}(C-N); ^{1}HNMR($CDCl_3$): δ 2.9(dd, 1H, H_a), δ 3.4(dd, 1H, H_b), δ 3.8(s, 3H ,CH_3), δ 4.8(dd, 1H ,H_x), δ 5.9(s, 1H ,NH), δ 6.8-8.2 (m, 7H ,Ar-H), δ 10.5(s, 1H ,OH). MS: MI=(m=313, m+1=314).

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

Entry	Molecular formula	Yield (%)	Melting point (°C)
I	$C_{14}H_{13}BrN_2S$	78	130
II	$C_{14}H_{13}BrN_2S$	85	125
III	$C_{15}H_{12}BrN_3O_3$	88	135
IV	$C_{15}H_{12}BrN_2F$	87	220
V	$C_{16}H_{14}Br_2N_2O$	88	113
VI	$C_{16}H_{15}N_3O_4$	78	145
VII	$C_{14}H_{13}BrN_2S$	86	160
VIII	$C_{14}H_{13}BrN_2S$	79	144
IX	$C_{16}H_{14}Br_2N_2O$	83	86
X	$C_{15}H_{12}BrN_3O_3$	90	146

Compound VIII

3-(4-Bromo-phenyl)-5-(3-methyl-thiophen-2-yl)-4,5-dihydro-1H-pyrazoline:

IR(KBr): 1620 cm^{-1}(C=N),3447 cm^{-1}(N-H),1190cm^{-1}(C-N); ^{1}HNMR($CDCl_3$): 2.15(s,3H,CH_3), δ 2.85(dd,1H, H_a), δ 3.3(dd,1H, H_b), δ 5.1(dd, 1H ,H_x), δ 6.0(s,1H ,NH), δ 6.7-7.7 (m, 6H ,Ar-H); MS: MI= (m=321, m+2=323).

Antimicrobial activity

Antimicrobial screening of synthesized pyrozolines compounds (I-X) was conducted by using cup plate method [20-21] at a concentration of 100µg/ml. The compound were evaluated for antibacterial activity against Bacillus subtilis gr +ve, Pseudomonas aeruginosa gr –ve , Staphylococcus aureus gr +ve, Escherichia coli gr –ve and antifungal activity against Aspergillus niger, Aspergillus Flavus, Curvularia, Alternaria. DMSO was used as solvent control . The results of antimicrobial data are summarized in table 2. All compounds show the moderate to good activity against bacteria and fungi.

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

	Bacteria (Zone of Inhibition in mm)				Fungi (Zone of Inhibition in mm)			
Products	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**
I	19	21	08	17	---	---	26	17
II	23	21	18	18	11	10	21	20
III	24	17	27	20	14	---	17	10
IV	11	---	12	---	12	15	11	---
V	16	34	14	24	---	---	21	14
VI	14	16	15	17	---	---	16	---
VII	16	19	15	19	17	10	19	13
VIII	13	17	10	11	11	---	09	---
IX	13	14	09	15	---	---	14	15
X	18	24	16	12	18	13	19	15

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

CONCLUSION

In summary, we have synthesized some novel pyrazolines. The newly synthesized pyrazolines are characterized by spectral data and further evaluated for antimicrobial activity. All compounds show moderate to good activity.

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