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SYNTHESIS AND ANTIMICROBIAL SCREENING OF SOME NEW PYRAZOLINE DERIVATIVES

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ABSTRACT

A new series of pyrazoline derivatives (2a-j) have been synthesized in excellent yields from hydroxychalcones (1a-j). These newly synthesized compounds were screened for their antimicrobial activities which showed moderate to good activity against the different strains of bacteria and fungi tested. All the synthesized compounds were confirmed by IR, ^{1}HNMR and Mass spectral data.

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

INTRODUCTION

A large number of Pyrazoline derivatives are well documented in the literature for Anti-microbial [1-3], Anti-inflammatory [4], Anti-cancer [5], Anti-tubercular [6], Anti-viral [7], Anti-oxidant [8], Cyclo-oxygenase (COX-2) [9], Anti-malarial [10], Anti-depressant and Anti-convulsant activities [11]. Considering these medicinal activities, we herein report some new pyrazoline derivatives from substituted chalcones which were cyclized using hydrazine hydrate and these newly synthesized compounds were screened for their antibacterial and antifungal activities.

MATERIALS AND METHODS

Experimental

All the melting points were determined in open capillary and are uncorrected. IR spectra of the compounds were scanned on Perkin-Elmer FTIR spectrometer. ^{1}H NMR spectra were recorded on a Gemini 200 MHz instrument using TMS as an internal standard (Chemical shifts are given in □ ppm). The mass spectra (MS) were recorded on VG 7070H mass spectrometer using ionisation energy of 70eV. Purity of the compounds was checked by TLC plates using benzene and ethyl acetate as an eluent in the ratio of (7:3 v/v).

General procedure for synthesis of Pyrazolines

A mixture of chalcone and hydrazine hydrate in methanol was heated under reflux for 4-5 hr. It was cooled and poured onto crushed ice. The solid thus separated was filtered, washed with water, dried and recrystallised from ethanol. The purity of synthesised 3,5-di(subst.)aryl-2-pyrazolines was checked by TLC. Their structures were assigned by spectral studies (IR, ^{1}H NMR and MS). The M.Ps, yields and elemental analyses are shown in Table-**1**.

Characteristic Tests for Pyrazolines

1. A paper soaked in solution of pyrazoline in benzene was exposed to bromine vapours turned bluish and thus gave positive Knorr's test [12] for pyrazolines.

Pyrazolines didn't give positive Wilson Test[13] and red colouration with conc. H_2SO_4 showing absence of α,β-unsaturated carbonyl group.

RESULTS AND DISCUSSION

A series of some novel pyrazoline derivatives were synthesized by refluxing hydroxy chalcones with hydrazine hydrate in methanol. The structures of the synthesized compounds (2a-j) were confirmed on the basis of spectral analysis. The IR spectra of pyrozolines showed the absorption in the region of 1590-1650cm^{-1} due to -

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C=N- of pyrazoline. The absorption band at 3300-3380cm^{-1} is due to -NH stretching. 1400-1470 cm^{-1} due to CH_2 of pyrazoline, while the absorption band at 1200-1280cm^{-1} is due to –N-N=C- stretching in aromatic tert. amine of pyrazoline ring and 3000-3100cm^{-1} is due to OH stretching. Whenever single OH is at ortho position, the band is not appeared may be due to hydrogen bonding. Beside these bands, the bands in the region 1310-1330cm^{-1} due to –OCH_3 str, 680-800cm^{-1} due to C-Cl str and 600-700cm^{-1} due to C-Br appear whenever present in the respective compound. ^{1}H NMR Spectra of some representative compounds were recorded which show the characteristic peaks at - δ 3.1-3.6 (dd, 2H, CH_2 i. e. H_A and H_B of pyrazoline ring); δ 4.8-5.6 (t, 1H, CH i. e. H_X of pyrazoline ring); δ 6.8-7.8 (m, Ar-H); δ 5.8-8.0(s, 1H,-NH) and δ 11.0-13.0 (s, 1H, OH) while the peaks at δ 2.15-2.6 (s, 3H, Ar-CH_3); δ 3.86-3.9 (s, 6H or 9H, OCH_3) are observed. Mass spectrum of the representative compound also support the formation of pyrazoline.

All the synthesized compounds screened for antibacterial activity were also studied for antifungal activity against the selected strains. The compounds 2a, 2c, 2h and 2j showed moderate activity, while 2b, 2e, 2f and 2i showed significant activity in comparison with standard drugs (Penicilin and Greseofulvin). The presence of pyrazoline moiety, the substituent's particularly bromo, chloro, iodo, hydroxy and methyl groups in the ring may be responsible for antimicrobial activity of this class of compounds.

Spectroscopic data of synthesized compounds:

Compound 2a

^{1}H NMR ($CDCl_3$): δ2.68(s, 3H, CH_3), 3.15(dd, 1H, H_A), 3.48(dd, 1H, H_B), 3.8(s, 9H, 3×OCH_3) 4.82(t, 1H, Hx), 6.18(s, 1H, NH), 7.2- 7.96(m, 3H, Ar-H), 13.04(s, 1H, Ar-OH).

Compound 2e

^{1}H NMR ($CDCl_3$)δ3.1(dd, 1H, H_A), 3.5(dd, 1H, H_B), 3.85(s, 3H, OCH_3),3.89(s, 3H, OCH_3), 3.93(s, 3H, OCH_3), 4.92(t, 1H, Hx), 6.58(s, 1H, NH), 6.6-7.51(m,3H,ArH), 6.79(s, 1H, Ar- OH),7.25(s,1H,ArOH).

IR: δMax

3352, 3100, 1591, 1422, 1328, 1232, 1120,647cm^{-1}.

Compound 2f:418(M^+,14), 405(04), 342(02), 305(31), 292(09), 290(06), 277(14), 256(01), 211(02), 181(02), 149(05), 137(02), 124(06), 109(12), 97(04), 84(100), 70(18), 57(60), 43(38).

Antimicrobial Activity

For antimicrobial activity of the synthesized compounds, Cup Plate method[14] was employed. The experiment was performed at a concentration of 100µg/ml; we checked the activity of these molecules against different strains of bacteria and fungi as mentioned in Table 2. DMSO was used as solvent control. The observed data of activity of all these tested compounds is shown in Table 2.

Table 1. Physical data of synthesized Pyrazoline derivatives (2a-j)

Sr.No.	Entry	R	R_1	R_2	R_3	Ar	Molecular Formula	Yield (%)	M.P.^{0}C
1.	2a	OH	I	CH_3	Cl	Ar_3	$C_{19}H_{20}O_4N_2ICl$	82	230
2.	2b	OH	I	CH_3	Cl	Ar_4	$C_{14}H_{12}ON_2IClS$	87	158
3.	2c	OH	Br	OH	Br	Ar_1	$C_{17}H_{17}O_2N_3Br_2$	78	235
4.	2d	OH	Br	OH	Br	Ar_2	$C_{17}H_{16}O_4N_2Br_2$	72	178
5.	2e	OH	Br	OH	Br	Ar_3	$C_{18}H_{18}O_5N_2Br_2$	80	218
6.	2f	OH	Br	OH	Br	Ar_4	$C_{13}H_{10}O_2N_2Br_2$	83	204
7.	2g	H	I	OH	I	Ar_1	$C_{17}H_{17}ON_3I_2$	92	160
8.	2h	H	I	OH	I	Ar_2	$C_{17}H_{16}O_3N_2I_2$	86	110
9.	2i	H	I	OH	I	Ar_3	$C_{18}H_{18}O_4N_2I_2$	79	118
10.	2j	H	I	OH	I	Ar_4	$C_{13}H_{10}ON_2I_2S$	88	135

All synthesised compounds were recrystallised from ethyl alcohol.

(Where Ar_1-*p*-dimethylaminophenyl; Ar_2-3,4-dimethoxyphenyl; Ar_3-3,4,5-trimethoxyphenyl; Ar_4-2-thienyl)

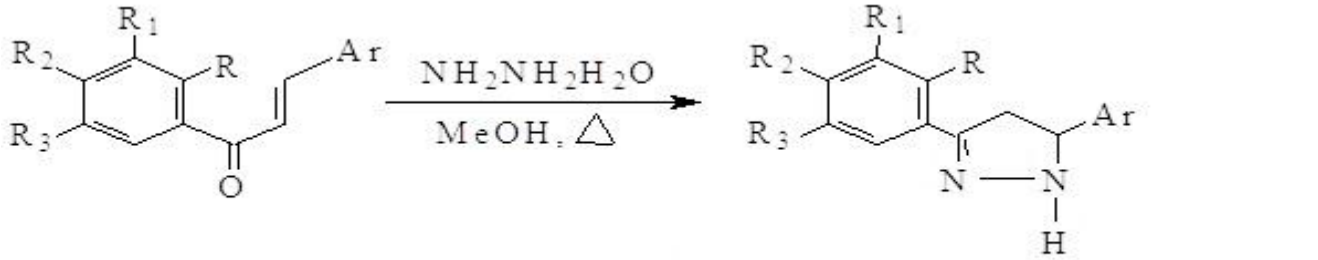
Table 2. Antimicrobial activityof synthesized pyrazoline derivatives (2a-j)

	Bacteria (Zone of inhibition in mm)				Fungi (Zone of inhibition in mm)			
Entry	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**
2a	10	08	20	16	-ve	-ve	-ve	RG
2b	14	06	20	21	-ve	-ve	-ve	-ve
2c	12	11	22	18	RG	-ve	-ve	RG
2d	--	14	18	20	-ve	RG	-ve	-ve
2e	10	17	23	16	RG	RG	-ve	RG
2f	11	14	20	20	RG	RG	-ve	RG

2g	08	10	18	17	-ve	-ve	-ve	RG
2h	10	--	21	22	RG	-ve	-ve	RG
2i	10	14	18	17	-ve	-ve	-ve	-ve
2j	13	--	19	20	-ve	-ve	-ve	-ve
Penicillin	12	20	34	22	X	X	X	X
Griseofulvin	X	X	X	X	-ve	-ve	-ve	-ve

(Zone of Inhibition in mm)
A= *Escherichia coli*, B=*Salmonella typhi*, C= *Staphylococcus aureus*, D=*Bacillus subtilis*, E=*Aspergillusniger* F=*Penicillium chrysogenum*, G=*Fusarium moneliforme*, H= *Aspergillus flavus*, -- = No Antibacterial activity, RG= Reduced Growth (Moderate Activity), -ve = Growth (Antifungal Activity Observed) X = Not applicable.

Scheme-I



CONCLUSION

It can be concluded that, all the newly synthesized pyrazolines (2a-j) with electron releasing groups and those having pharmacophores such as chloro, bromo, iodo, hydroxyl and methyl groups exhibited best antimicrobial activity against the tested pathogens. Hence this data reported may be helpful in exploring the new entities with more potent activities.

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