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RESEARCH ARTICLE

Synthesis, Characterization and Antimicrobial Activity of Substituted Pyrazolines

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Abstract: Some novel series of substituted pyrazoline were synthesized from chalcones. Various substituted pyrazoline prepared by cyclization of chalcones with substituted phenylhydrazine in ethanolic solution. The synthesized compounds were characterized by their physical properties of IR, ^{1}H & ^{13}C NMR and elemental analysis studies. The antimicrobial activity of all the compounds (CP01-CP04) showed significant activity against all the bacteria and fungus.

Keywords: Chalcones, Pyrazoline, Phenylhydrazine, Antimicrobial activity

Introduction

Pyrazoles are five member ring heterocyclic compounds, have some structural features with two nitrogen atoms in adjacent position and are also called as azoles[1]. The best described property of almost every group of pyrazoles is in the treatment of inflammation and inflammation associated discord, such as arthritis[2]. Pyrazole derivatives are the subject many research studies due to their widespread potential biological activities such as antimicrobial[3], antiviral[4], antitumor[5,6], antihistaminic[7], antidepressant[8], insecticides and fungicides[9].

Several pyrazole derivatives have been found to possess significant activities such as 5 α-red-ukase inhibitor[10], anttiproliferative[11], antiphrastic[12], herbicides[13], a good number of pyrazoles have also been reported to have interesting biological activities like anti-inflammatory[14] and antiprotozoal[15-16] which render them valuable active ingredients of medicine and plant protecting agents. Further current literature indicates 1,2 pyrazole derivatives to possess various biological activities[17].

These compounds are useful in the field of medicine and are used as a starting material for the synthesis of new drugs[18-27]. In view of these data we have undertaken the synthesis, characterization and antimicrobial evaluation of substituted pyrazolines. All the synthesized compounds were characterized on the basis of their physical properties, IR, ^{1}H & ^{13}C NMR spectral data and elemental analysis. The physical data of titled compounds are summarized in Table 1.

Table 1. Physical and analytical data of the synthesized compounds

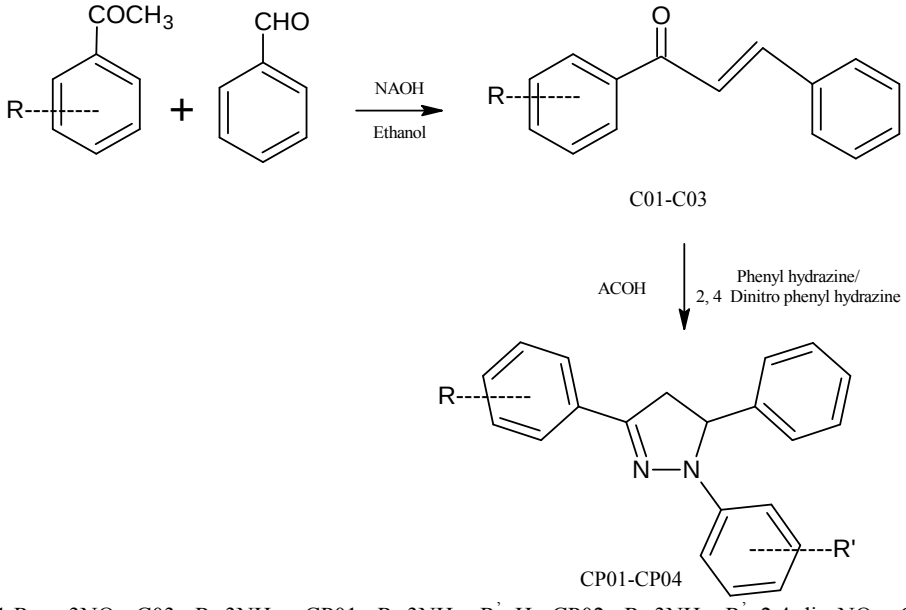
Compd.	R	R'	Compound Name	Molecular formula	M. Wt	M.P ^{O}C	% Yield	Elemental Analysis % (Calculated) Found		
								C	H	N
CO1	3-NO_2	-	1-(3-nitrophenyl)-3-phenylprop-2-en-1-one	$C_{15}H_{11}NO_2$	253.25	204	56	(71.07) 71.05	(4.34) 4.32	(5.52) 5.50
CO3	3-NH_2	-	1-(3-amniophenyl)-3-phenyl prop-2-en-1-one	$C_{15}H_{13}NO$	223.15	198	62	(80.66) 80.85	(5.82) 5.85	(6.27) 6.25
CPO1	3-NH_2	H	3-(1,5 diphenyl-4,5-drohydro-1,4 pyrazol-3-yl)aniline	$C_{15}H_{19}N_3$	313.39	223	60	(80.41) 80.40	(6.06) 6.05	(13.40) 13.42
CPO2	3-NH_2	2,4-di-NO_2	3 [1(2,4 dinitro phenyl)-5-phenyl-4,5 dihydro)-1- pyrazol-3-yl)aniline	$C_{21}H_{17}N_5O_4$	403.39	217	64	(62.47) 62.45	(4.21) 4.20	(17.35) 17.32
CPO3	3-NO_2	H	3 (3- nitro phenyl)-1,5-diphenyl-4,5 dihydro-1-pyrazole	$C_{21}H_{17}N_3O_2$	343.37	203	59	(73.39) 73.40	(4.95) 4.98	(12.23) 12.25
CPO4	3-NO_2	2,4-di-NO_2	[1(2,4 dinitro phenyl)-3-(3- dinitro phenyl) -5-phenyl-4,5-dihydro)-1-pyrazole	$C_{21}H_{15}N_5O_6$	433.75	214	62	(58.09) 58.10	(3.45) 3.40	(16.13) 16.10

Experimental

The melting points were carried out in open capillary tube and were uncorrected. Thin layer chromatography was performed using silica gel coated on a glass plate and spots were visualized by exposure to iodine vapor. IR spectra of compounds were scanned on Shimadzu IR spectrophotometer using KBr disc and expressed in cm^{-1}. ^{1}H & ^{13}C NMR spectra were recorded in DMSO-D_6 on BRUKER (400MHz) spectrometer using TMS as an internal standard (chemical shifts in δ, ppm) (Table 2). The elemental analysis for C, H, and N were in an agreement with the calculated values. The synthesis of the target compounds was accomplished according to the reaction sequence illustrated in Scheme 1.

Table 2. Spectral data of the compounds

Compd.	IR(KBr) ν_{max} in cm^{-1}	^{1}H NMR(DMSO-d_6), δ, ppm	^{13}C NMR-DMSO-d_6), δ, ppm
C01	3086 (aromatic C-H str), 2624 (aliphatic C-H str), 1658 (C=O), 1604 (aromatic C=C), 1442 (aliphatic C=C str), 1342 (NO_2 str).	4.587(s, 1H, aliphatic C-H), 4.331 (s, 1H, aliphatic C-H), 7.482-8.828 (m, 9H, Ar-H).	187(C=O), 121-148(Ar-H, & HC=CH).
C03	3464 (NH str), 3055 (aromatic C-H str), 2924 (aliphatic C-H str), 1658 (C=O str), 1589 (aromatic C=C str), 1489 (aliphatic C=C str).	2.72 (s, 2H, NH_2) 4.17 (s, 1H, aliphatic C-H), 4.25 (s, 1H, aliphatic C-H), 6.89-7.94 (m, 9H, Ar-H).	196 (C=O), 117-150(Ar-H, & HC=CH).
CP01	3309(NH str), 3032 (aromatic C-H str), 2924 (aliphatic C-H str), 1666 (C=N str), 1597 (aromatic C=C), 1489 (aliphatic C-C str).	2.063 (s, 2H, Ar-NH), pyrazoline ring, 3.011-3.070 (dd, 1H, H_A), 3.814-3.888 (dd, 1H, H_M), 5.161 (dd, 1H, H_X), 6.702-8.047 (m, 9H, Ar-H);	168 (C=N), 111-147 (Ar-C), pyrazoline ring, 63 (CH_2), 23 (CH)
CP02	3456 (NH str), 3086 (aromatic C-H str), 2924 (aliphatic C-H str), 1666 (C=N str), 1604 (aromatic C=C), 1419 (aliphatic C-C str), and 1327 (NO_2 str).	2.075 (s, 2H, Ar-NH), pyrazoline ring, 3.22 (dd, 1H, H_A), 4.010(dd, 1H, H_M), 5.582(dd, 1H, H_X), 7.116-8.868 (m, 9H, Ar-H)	169 (C=N), 116-149 (Ar-C), pyrazoline ring, 63 (CH_2), 23 (CH)
CP03	3032 (aromatic C-H str), 2924 (aliphatic C-H str), 1674 (C=N str), 1597 (aromatic C=C str), 1496 (aliphatic C-C str), and 1350 (NO_2 str)	pyrazoline ring, 3.169-3.227 (dd, 1H, H_A), 3.938-4.013(dd, 1H, H_M), 5.555-5.600 (dd, 1H, H_X), 6.743--8.476 (m, 14H, Ar-H)	163 (C=N), 105-148 (Ar-C), pyrazoline ring, 63 (CH_2), 22 (CH).
P04	3032 (aromatic C-H str), 2924 (aliphatic C-H str), 1674 (C=N str), 1597 (aromatic C=C str), 1496 (aliphatic C-C str), and 1350 (NO_2 str)	pyrazoline ring, 3.169-3.227 (dd, 1H, H_A), 3.938-4.013 (dd 1H, H_M), 5.555-5.600 (dd, 1H H_X), 6.743--8.476 (m, 14H, Ar-H);	163 (C=N), 105-148 (Ar-C), pyrazoline ring, 63 (CH_2), 22 (CH).



C01:R = $3NO_2$ C03: R=$3NH_2$,; CP01: R=$3NH_2$, R'=H; CP02: R=$3NH_2$, R'=2,4-di- NO_2; CP03: R=$3NO_2$, R'=H; CP04: R=$3NO_2$, R'=2,4-di- NO_2

Scheme 1

General procedure

Synthesis of 1-(3-nitrophenyl)-3-phenylprop-2-en-1-one (C01)[28]

A mixture of 3-nitro acetophenone (0.01 mol) and benzaldehyde (0.01 mol) was dissolved in ethanolic NaOH (20 mL) and stirred about 2-3 hours with a mechanical stirrer and kept in refrigerator for 24 hours. The content was poured into crushed ice and acidified with HCl. The solid separated was filtered and recrystalization from ethanol.

Synthesis of 1-(3-amniophenyl)-3-phenyl prop-2-en-1-one (C03)

A mixture of 3-amnio acetophenone (I) (0.05 mol) and benzaldehyde (0.05 mol) was dissolved in ethanolic NaOH (20 mL) and stirred about 2-3 hours with a mechanical stirrer and kept in refrigerator for 24 hours. The content was poured into crushed ice and acidified with HCl. The solid separated was filtered and recrystalisation from ethanol.

Synthesis of substituted pyrazolines[29] *(CP01-CP04)*

A mixture of chalcones (0.001 mole) and appropriate phenylhydrazine and substituted phenyl hydrazine (0.001 mole) in glacial acid (25 mL) was heated under refluxed for 4 hours, then the mixture was poured in to ice water (100 mL. The precipitate obtained was filtered washed with water and recrystallized from absolute ethanol.

Antimicrobial activity

In vitro antibacterial activity was determined by Kirby-Bauer disc diffusion method against bacteria such as *Staphylococcus aureus* and *Bacillus* (Gram +ve), *Salmonella typhi* and *Pseudomonas aeruginosa* (Gram -ve) using *Ampicilin* as standard a standard drug. The standard and test compounds were prepared in DMSO at different concentrations. The zone of inhibition was compared with standard drug after 24 h incubation at 35-37 ^{0}C.

Similarly antifungal activity was performed against Candida. The standard and test compounds were prepared in DMSO at different concentrations. The zone of inhibition was compared with standard drug after 48 h at 25 ^{0}C. The results of antibacterial and antifungal activity are presented in Table 3.

Results and Discussion

Synthesis of substituted pyrazolines was obtained through above Scheme 1. The required chalcones (C01, C03) was synthesized according to the procedure reported in the literature. Chalcones with phenylhydrazine gave good yield of pyrazolines (CP01-CP04). The spectral analysis of all the compounds was done by IR, ^{1}H and ^{13}C NMR and the spectral data were consistent with the assigned structures.

In vitro antibacterial activity of selected compounds was carried out by Kirby-Bauer disc diffusion method against bacteria such as *Staphylococcus aureus, Bacillus, Salmonella typhi, Pseudomonas aeruginosa.* The compounds CP01-CP04 showed significant activity against all the bacteria. Antifungal activity was performed on *candida.* The compounds CP01, CP03, CP04 showed moderate activity against the fungus. The compound CP02 was more active among screened compounds.

Table 3. Antimicrobial activity of the synthesized compounds Zone of inhibition (mm) of synthesized compounds

Sample code	Anti-bacterial activity																Anti-fugal activity			
	Gram positive								Gram negative											
	Staphylococcus.spp				*Bacillus.spp*				*Salmonella.spp*				*Pseudomonas.spp*				*Candida*			
	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std	100 mcg	50 mcg	25 mcg	Std
CP01	7	5	4	11	7	3	-	11	3	2	-	9	6	4	3	9	8	-	-	14
CP02	6	5	2	5	8	6	5	6	5	3	-	5	8	7	5	10	9	6	4	12
CP03	8	6	4	9	9	6	5	9	9	8	5	10	9	8	6	8	8	5	3	21
CP04	9	7	6	12	13	9	5	10	6	5	3	10	9	8	5	10	7	5	4	15

Conclusion

In conclusion, the reaction profile explained in the present work is very efficient to synthesized substituted pyrazolines. The prepared compounds showed potent antimicrobial activities and these are promising compounds for further pharmacological studies.

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