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Research Article

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Synthesis, characterization and biocedal activities of pyrazole compounds derived from chalcone

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ABSTRACT

The 1- (3-Methyl-1-Phenyl-5-thioxo-4,5-dihydro-1H-Pyrazole-4-yl)-Ethanone condensation with various substituted aldehydes was yielding various Chalcone. Further this Chalcone conversed into pyrazole by condensation with various synthesized Chalcone with isoniazide. In the present research article a new series of pyrazole derivatives have been synthesized. The structure of newly synthesized compounds is characterized on the basis of IR, ^{1} H NMR, Mass spectroscopes and elemental analysis. The newly synthesized compounds were studied for biocedal activity.

Key words: Synthesis, Chalcone, isoniazide, pyrazole, spectral studies and biocedal activity

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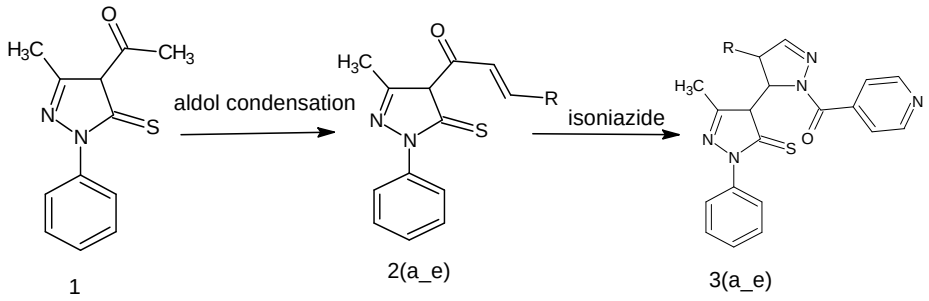
INTRODUCTION

The discovery and development of antimicrobial agent are among the most significant and successful achievements of modern science and technology for the control of plants and human pathogenic microbes. Pyrazoline are well known important nitrogen containing five member heterocyclic compounds. They process a broad spectrum of biological activities viz antibacterial, antifungal, antitumor, antidepressant, anticonvulsant, insecticidal and antiiocieptive. pyrazoline is used extensively as useful synthon in organic synthesis. The chemistry of Chalcone has generated intensive scientific interest due to their biological and industrial application. Chalcone are exhibiting various biological activities, such as antioxidant, anti-inflammatory, anti malarial, anticancer and antitileshamanial. In addition, Chalcone are very important compounds as a Michael acceptor in organic synthesis. In continuation of our earlier research work, the facile synthesis of pyrazole derivatives from Chalcone and isoniazide in the presence of pyridine is described in scheme 1.The synthesized compounds were evaluated for its antifungal and antibacterial activity.



where (a) Ph (b) 2 - $CH_3C_6H_4$ (c) 2 - OHC_6H_4 (d) 4 - OHC_6H_4
(e) 4 - $OCH_3C_6H_4$ (f) 4 - $CH_3C_6H_4$ (g) 4 - ClC_6H_4 (h) 4 - BrC_6H_4

EXPERIMENTAL SECTION

The 4-acetyl-5-methyl-2-(4-methylphenyl)-2, 4-dihydro-3H-pyrazole-3-one was prepared by reported method. the IR spectra were recorded by a Perkin-Elmer 237 spectrometer and H^1 NMR spectra were recorded in DMSO with TMS as internal standard on broker AM 400 instrument (at 400 MHz). Mass spectra were recorded on M S route JMS 600-H. Melting points were determined in open capillary tubes and were uncorrected. All the synthesized compounds were purified by recrystaline method. The reaction was following up and the purity of compounds was checked on pre-coated TLC plates.

Synthesis of 3- methyl-1-p-tolyl-4-(3-arylacryloyl)-1H-pyrazol-5-(4H)-one 2(a-h);
A mixture of substituted aromatic aldehyade (0.001mol) and 4-acetyl-3-methyl-1-(p-tolyl)-pyrazol-5(4H)-one (0.001mol) in 95% ethanol (20ml) were mix in round bottom flask,10 ml of 60% aqueous sodium hydroxide solution added drop wise. Resulting mixture was stirred for 2hrs at 5-10 ^{0}C, poured into crushed ice and acidified with dilute HCL. The precipitate obtain was filtered and washed twice with cold water. The resulting solid was allowed to air dry and recrystalized from ethanol. The yields, melting points and other characterization data of these compounds are given in Table 1.

A Synthesis reaction mixture of 3- methyl-1-p-tolyl-4-(3-arylacryloyl)-1H-pyrazol-5-(4H)-one 2(a-h) (0.01mol) and isoniazide (0.01mol) in pyridine (10ml) was refluxed in oil bath on magnetic stirrer for 2.5 hrs. The completion of reaction was observed by TLC using cyclohexane/ethyl acetate. The reaction mixture was cooled to room temperature and poured into ice-cold water, then neutralized by dilute HCL. The obtained solid was filtered, washed with water and recrystlized from r-spirit. The yields, melting points and other characterization data of these compounds are shown in following table l

Table 1 Analytical data and Elemental analysis of compound 2 (a-h)

Compd	Molecular formula	M.P ^{0}C	Yield	Elemental analysis							
				% C		% H		% N		% S	
				Calcd.	found	Calcd.	found	Calcd.	Found	Calcd.	Found
3a	$C_{20}H_{18}N_2OS$	142-143	82	71.84	71.85	5.42	5.40	8.37	8.39	9.57	9.56
3b	$C_{21}H_{18}N_2OS$	156-158	78	72.40	72.41	5.79	5.80	8.03	8.00	9.18	9.17
3c	$C_{20}H_{18}N_2OS$	135-138	80	68.57	68.59	5.17	5.16	7.99	8.02	9.13	9.12
3d	$C_{20}H_{18}N_2OS$	237-239	74	68.57	68.55	5.17	5.19	7.99	7.97	9.13	9.16
3e	$C_{21}H_{20}N_2OS$	194-196	77	72.40	72.41	5.79	5.82	8.03	8.06	9.18	9.15
3f	$C_{21}H_{20}N_2OS$	152-453	79	72.40	72.39	5.79	5.81	8.03	7.99	9.18	9.20
3g	$C_{20}H_{17}N_2OSCl$	198-199	75	65.10	65.12	4.63	4.62	7.60	7.62	8.65	8.66
3h	$C_{20}H_{17}N_2OSBr$	201-203	73	58.18	58.20	4.14	4.15	6.80	6.82	7.75	7.76

Table 2 Analytical data and Element analysis of compound 3 (a-h)

Compd	Molecular formula	M.P ^{0}C	Yield	Elemental analysis							
				% C		% H		% N		% S	
				Calcd.	found	Calcd.	found	Calcd.	Found	Calcd.	Found
3a	$C_{26}H_{23}N_5OS$	162-164	76	68.86	68.85	5.11	5.10	6.17	6.19	7.05	6.99
3b	$C_{27}H_{25}N_5OS$	155-156	79	69.29	69.30	5.38	5.36	14.96	14.95	6.83	6.81
3c	$C_{26}H_{23}N_5O_2S$	167-169	70	66.52	66.50	4.93	4.94	14.91	14.90	6.81	6.79
3d	$C_{26}H_{23}N_5O_2S$	154-156	75	66.52	66.51	4.93	4.95	14.91	14.89	6.81	6.82
3e	$C_{27}H_{25}N_5O_2S$	149-152	70	67.10	67.11	5.21	5.19	14.50	14.51	6.62	6.61
3f	$C_{27}H_{25}N_5OS$	146-147	71	69.29	69.28	5.38	5.39	14.96	14.98	6.83	6.82
3g	$C_{26}H_{22}N_5OSCl$	152-153	74	63.86	63.85	4.53	4.54	14.31	14.29	6.54	6.55
3h	$C_{26}H_{22}N_5OSBr$	147-149	73	58.70	58.72	4.16	4.15	13.16	13.17	6.01	6.02

BIOLOGICAL SCREENING

Antibacterial activities

The antibacterial activities of all the compounds were studied against gram-positive bacteria (staphylococcus aurous and bacillus subtilis) and gram negative bacteria (E-coli and Klebsiella promioe) at a concentration of 50 ug /ml by agar cup plate method. A methanol system was used to control in this method. Similar conditions using tetracycline as control was used standard for comparison. The area of inhibition of zone measured in mm. Compounds 3g and 3e were found more toxic for microbes. Other compounds found to be less or moderate active shown in Table 3

Antifungal activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organism used was Aspergillums Niger, botrydepladia thiobromine, Nigrospora sp. and Rhizopus nigricum .The antifungal activities of all compounds 3(a-h) were measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200g, dextrose 20g, agar 20g and water

1c.Five day's old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120 ^{0}C for 15 min .at 15atm. Pressure. These media were poured into sterile Petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below;

Percentage of inhibition = 100(x-y)/x
Where, x = area of colony in control plate
Y= Area of colony in test plate

The fungal activity displayed by various compounds 3 (a-h) in shown in Table 4.

Table 3 Antibacterial activity of compounds 3(a-h)

Compounds	Gram + Ve		Gram – Ve	
	Bacillus subtilis	*Staphylococcus aureus*	*Klebsiella promioe*	*E. Coli*
3a	53	58	51	57
3b	55	60	56	60
3c	54	63	58	62
3d	57	64	57	61
3e	61	67	66	65
3f	54	58	59	57
3g	64	66	69	68
3h	56	61	56	60

Table 4 Antifungal activities of compounds 3 (a-h)

Zone of Inhibition at 1000 ppm (%)				
Compounds	***Aspergillus Niger***	***Rhizopus Nigricum***	***Nigrospora sp.***	***Botrydepladia Thiobromine***
3a	53	58	55	56
3b	57	59	58	57
3c	60	61	61	62
3d	59	62	63	61
3e	63	67	64	65
3f	56	60	59	60
3g	66	69	67	62
3h	59	60	62	60

RESULTS AND DISCUSSION

It was observed that 4-acetyl-3-methyl-1-(p-tolyl)-pyrazol-5(4H)-one(1), on condensation with aromatic aldehydes,yields 3-methyl-1-p-tolyl-4-(3-arylacryloyl)-1H-pyrazol-5(4H)-one 2(a-h). The structures of 2(a-h) were confirmed by elemental analysis and IR spectra showing an absorption band at 1620-1640 (C=N), 3030-3080 cm-1(C-H of Ar.), 1720-1750cm-1(-CO), 1665-1650cm-1(α,β-unsaturated ketones), 1600-1548 cm-1(conjugated C=C), 2950, 1370cm-1 (-CH_3), 3345-3325(OH), 2815-2850cm^{-1}(-OCH_3), 1075 (ArC-Cl), 1060(Ar C-Br). ^{1}HNMR: 7.23–7.67(9H, m, Ar-H), 6.94, 7.64(2H, d, CH=CH), 3.4 (1H, s, CH), 1.96(3H, s, CH_3), 2b; 2.38 (3H, s, CH_3), 2c, 4.22(1H, s, OH), 2d; 4.18(1H, s, OH), 2e: 3.68(3H, s, CH_3). 2f; 2.35 (3H, s, CH_3). The C, H, N analysis data of all compounds are presented in Table -1. The structures assigned to 1-isonicotinoyl-3'-methyl-5-aryl-1'-p-tolyl-4,5-dihydro-1H, 1'H-3,4'-bipyrazol-5'(4'H)-one3(a-h) were supported by the elemental analysis and IR spectra showing an absorption bands at 1620-1656(C=N), 3030-3080 cm^{-1} (C-H, of Ar.), 1720-1750 cm^{-1} (-CO), 1275 (C-O), 2950, 1370 cm^{-1} (-CH_3), 3345-3325(OH), 2815-2850 cm^{-1} (-OCH_3), 1075(ArC-Cl), 1060(ArC-Br). ^{1}H NMR: 6.82–8.92(13H, m, Ar-H), 2.42 (1H, s, CH of pyrazolone ring), S-H Str. showed at 2400 cm^{-1} 3.16-2.92(2H, d, CH_2), 5.23(1H, t, CH), 2.56, 1.96 (6H, s, CH_3), 3b; 2.38(3H, s, CH_3), 3c, 4.22 (1H, s, -OH), 3d; 4.18(1H, s, -OH), 3e: 3.68 (3H, s, CH_3), 3f; 2.35 (3H, s, CH_3), 3.4(1H, s, SH).

The C, H, N and S analysis data of all compounds are presented in Table-2.The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme-1. The IR data also direct for assignment of the predicted structure. The final structure of all compounds is confirmed by LC-MS. LC-MS data of all compounds are presented in Tables-1 and 2. Compounds3g and 3e were shows good antimicrobial activity.

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