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Synthesis and biological evaluation of some novel pyrazolines

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Abstract

A new series of Chalcones **(2a-j)** were prepared by reacting Furfuraldehyde with substituted acetophenones in alcohol medium in presence of strong base. The resulted chalcones undergoes cyclization with hydrazine hydrate to yield 2- Pyrazolines **(3a-j).** The structures of the final synthesized compounds were confirmed from IR, MASS, & ^{1}H-NMR spectral data. Some of the synthesized compounds showed very good antifungal activity, when compared to the antibacterial activity.

Key words: Pyrazolines, Chalcones, Antibacterial activity, Antifungal activity.

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1.0 Introduction

Nitrogen containing heterocyclic compounds like Pyrazolines has received considerable attention due to their varied biological activities and occupies a unique place in the field of medicinal chemistry. The literature survey reveals that Pyrazolines have been found to possess many biological activities like anticancer, anticonvulsant, herbicidal, antimicrobial, antidepressant [1,2] etc. The chemistry of chalcones has been recognized as a significant field of study. Chalcones show impressive physiological properties and some of them possess wide range of activities such as antibacterial, antiviral, antitubercular [3-7] etc. Prompted by the varied biological and pharmacological activities of Chalcones and Pyrazolines, it was contemplated to synthesize Pyrazolines starting from Furfuraldehyde. The Claisen-Schmidt reaction of furfuraldehyde with various substituted acetophenones in strong alkaline medium gave substituted Chalcones **(2a-j)** in good yields. The resulted chalcones undergoes cyclization with hydrazine hydrate in alcohol to yield the Pyrazolines **(3a-j).** The reaction sequence leading to the formation of title compounds is outlined in **Scheme-1.**

2.0 Materials and methods

Melting points were determined using open capillary tube method and are uncorrected. Thin layer chromatography [silica gel G (E.Merck) plates] was used to monitor the reactions and purity of the newly synthesized compounds. IR spectra were recorded using KBr disk on a Shimadzu Perkin-Elmer 8201 FT-IR. The PMR spectra were recorded on Bruker Avance II 400 NMR Spectrometer. Chemical shift values are reported as values in ppm relative to TMS (δ=0) as internal standard. The FAB mass spectra were recorded on JEOL SX-102/DA-6000 Mass spectrometer operating at 70ev.

Synthesis of 3-(furan-2-yl)-1-phenylprop-2-en-1-ones (2a-j)

A mixture of furfuraldehyde (0.01 mol) and substituted acetophenones (0.01 mol) in ethanol (20 ml) was stirred together for 24 hr, in presence of 40% NaOH (8ml). The mixture was poured into crushed ice and acidified with HCl. The product which is obtained is filtered, washed with water and re-crystallized from aqueous alcohol. The physical data of the compounds **(2a-j)** is given in Table-1.

2b: IR (KBr): 3120, 2915, (C-H), 1667 (C=O), 1581 (CH=CH), 1077(C-O-C). **^{1}H NMR:** 7.5-7.7 (m, Ar-H, 4H), 7.9-8.14 (m, furan, 3H), 6.8 (d, =CH, 1H), 6.5(d, =CH, 1H), 10.8 (s, OH, 1H). **MS:** m/z 214(M^+), & 215 (M+1).

Synthesis of 3-(furan-2-yl)-5-phenyl-4, 5-dihydro-1H pyrazoles (3a-j)

A mixture of substituted chalcones (0.01 mol) in 20 ml of alcohol and hydrazine hydrate (0.01 mol), in presence of catalytic amount of piperdine, was refluxed for 8-12- hrs. The reaction mixture is allowed to cool and poured into crushed ice and the product which is separated was filtered and re-crystallized from ethanol. The physical data of compounds **(3a-j)** is given in Table-2.

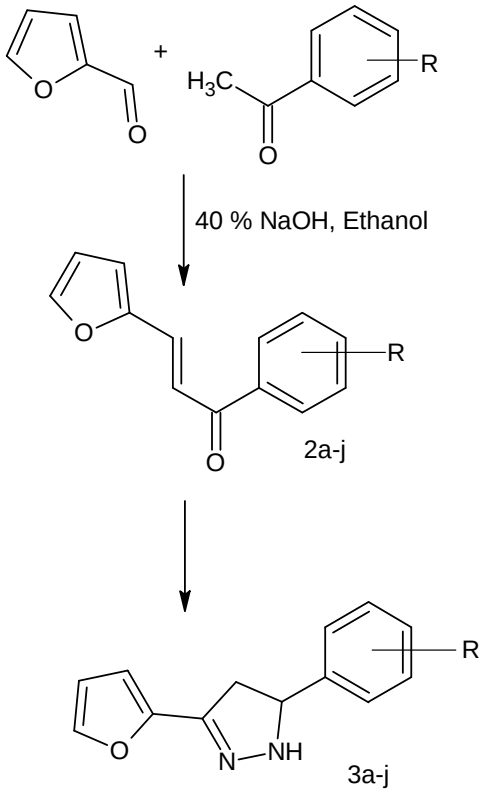
3e: IR (KBr): 3381 (NH), 2922(CH_2), 1677(C=N), 1588(N=N), 1489(C=C), 1281(C-O-C). **^{1}H NMR:** 7.24-7.28 (m, furan, 3H), 7.03-7.16 (m, Ar-H, NH), 2.17(s, CH_3, 3H), 3.86-4.3 (dd, H_a, H_b 2H), 4.7 (dd, H_X 1H). **MS:** m/z 228 (M+2).

3g: IR (KBr): 3366 (NH), 2922(CH_2), 1597(C=N), 1516(N=N), 1177(C-O-C), 1533 & 1340 (NO_2). **^{1}H NMR: 7.7-7.**9 (m, furan, 3H), 7.2-7.58(m, Ar-H, NH), 3.38-3.56 (dd, H_a, H_b 2H), 4.32 (dd, H_X 1H). **MS:** m/z 257 (M^+).

3h: IR (KBr): 3343 (NH), 1594(C=N) (C=C), 1518(N=N), 1176(C-O-C). **^{1}H NMR:** 6.68-6.80 (m, furan, 3H), 7.38 (s, NH_2, 2H), 7.5-7.8 (m, Ar-H, NH), 3.16-3.54 (dd, H_a, H_b 2H), 4.68 (dd, H_X 1H). **MS:** m/z 227 (M^+).

Antimicrobial activity

The newly synthesized compounds were screened for their antibacterial activity using Cup-plate agar diffusion method by measuring the zone of inhibition in mm at the conc of 100µg/ml against *E.coli, S.aureus, P.aeruginosa, and B.Subtilis*. Gentamycin was used as standard drug. The antifungal activity of the compounds was evaluated against *C.albicans* at the conc of 100µg/ml using Gresiofulvin as standard drug. DMF was used as solvent control. The antimicrobial activity data is reported in Table-3.



3.0 Results and Discussion

In the present work, a new series of pyrazolines were synthesized and their subsequent biological evaluation. The title compounds were synthesized from the key intermediate furfuraldehyde chalcones. The later compounds were prepared by reacting furfuraldehyde with substituted ketones in alcohol medium, in presence of strong base, NaOH.

Comp	Ar-$COCH_3$	MP (^OC)	Yield (%)
2a	2-OH	158	55
2b	4-OH	102	57
2c	4-Cl	113	52
2d	4-OCH_3	136	60
2e	4-CH_3	123	62
2f	3-NO_2	141	62
2g	4-NO_2	156	64
2h	4-NH_2	110	66
2i	4-F	137	59
2j	4-Br	166	60

Table-1: Physical data of Compounds (2a-j)

Comp	Ar-$COCH_3$	MP (^OC)	Yield (%)
3a	2-OH	188	62
3b	4-OH	202	63
3c	4-Cl	178	55
3d	4-OCH_3	212	58
3e	4-CH_3	194	52
3f	3-NO_2	165	49
3g	4-NO_2	154	58
3h	4-NH_2	196	60
3i	4-F	171	52
3j	4-Br	214	59

Table-2: Physical data of Compounds (3a-j)

The resulted chalcones **(2a-j)** undergoes selective cyclization in presence of hydrazine hydrate, in alcohol medium yields the title compounds **(3a-j)**. All the newly synthesized compounds were evaluated for their *In-Vitro* antibacterial and antifungal activity.

Compound	*S.aureus*	*B.subtilis*	*E.coli*	*P.aeruginosa*	*C.albicans*
3a	08	11	12	13	14
3b	11	09	11	12	15
3c	10	08	10	13	14
3d	11	12	14	12	14
3e	09	13	09	14	15
3f	08	12	09	13	15
3g	10	07	08	09	13
3h	13	12	12	10	14
3i	09	10	08	07	16
3j	12	12	11	10	15
Gentamycin	21	22	20	22	-
Gresiofulvin	-	-	-	-	20

Table-3: Antimicrobial and Antifungal activities of Compounds (3a-j)

[Values in Diameter of zone of inhibition (mm)]

In the antibacterial activity, among the compounds tested **3a, 3b, 3d, 3h, 3j** showed high activity against all the organisms and other compounds **3c, 3f** exhibited moderate activity. The remaining compounds showed weak activity against all the organisms. In the antifungal activity, compounds **3b, 3e, 3f, 3i, 3j** exhibited high activity and remaining compounds showed moderate antifungal activity against the fungi organism.

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