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# Synthesis and Antimicrobial Evaluation of Some New Pyrazoline Derivatives

KEYWORDS: Chalcones, Hydrazine hydrate, Acetyl Pyrazolines, Antimicrobial activities.

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**ABSTRACT** *A new series of acetyl pyrazoline derivatives (2a-j) have been synthesized by conventional method in excellent yields and in less reaction time using ethanol via cyclization reaction of chalcones (1a-j), hydrazine hydrate and few drops of glacial acetic acid. These newly synthesized compounds were screened for their antimicrobial activities which reflects moderate to good activity against different strains of bacteria and fungi employed. All the synthesized compounds were confirmed by IR, $^1$HNMR and Mass spectral data.*

## INRODUCTION

Pyrazolines are novel class of heterocyclic compounds possessing wide variety of biological and physiological activities [1]. Pyrazoline derivatives are found to show good Antimicrobial [2-4], Anti-inflammaory[5-6], Anticancer [7], Antitubercular [8], Analgesic [9], Antiviral [10], Antiangiogenic [11], Antioxidant [12], COX-2 inhibitor [13], Antimalarial [14] Antidepressant and Anticonvulsant [15] activiies. Pyrazolines are well known and important nitrogen conaining five membered heterocyclic compounds. Several pyrazoline derivatives have been found to possess considerable biological activities [16-18]. Keeping in view the importance of these biological activities, it was considered of interest to synthesize some new acetyl derivatives of pyrazolines

In the present work substituted chalcones were cyclized in the presence of hydrazine hydrate and few drops of glacial acetic acid to give acetyl pyrazoline derivatives

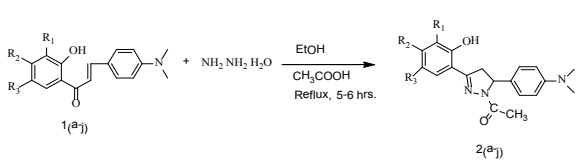
## MATERIALS AND METHODS

### Experimental

All the melting points were determined in open capillary method and are uncorrected. IR spectra were recorded in KBr spectrometer. $^1$HNMR spectra on a Avance 300 MHz spectrometer with DMSO as a solvent and TMS internal standard chemical shift, the chemical shift values are expressed in part per million (ppm) downfield from the internal standard and signals are quoted as s (singlet), d (doublet), t (triplet) and m (multiplet). Purity of the compounds is 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 Acetyl pyrazolines:

A mixture of chalcone (0.001mol), hydrazine hydrate (0.002mol) and few drop of glacial acetic acid in 15 ml ethanol was refluxed for 5-6 hrs. After completion of reaction (monitored by TLC) the reaction mixture was distilled off to remove the excess solvent and then it was poured into crushed ice. The solid obtained was washed with cold water, dried and recrystllised from ethanol. The yields and melting points of the compounds are tabulated below.(**Table-1**)




**Scheme-I**

**Table-1: Physical data of synthesized Acetyl pyrazoline derivatives (2a-j)**

| Sr. No. | Entry | $R_1$ | $R_2$ | $R_3$ | Molecular Formula | Yield (%) | M.P.$^0$C |
|---|---|---|---|---|---|---|---|
| 1 | 2a | Cl | H | Cl | $C_{19}H_{19}O_2Cl_2N_3$ | 90 | 198 |
| 2 | 2b | I | H | Cl | $C_{19}H_{19}O_2ClIN_3$ | 80 | 187 |
| 3 | 2c | Br | H | Cl | $C_{19}H_{19}O_2BrClN_3$ | 92 | 196 |
| 4 | 2d | Br | H | Br | $C_{19}H_{19}O_2Br_2N_3$ | 91 | 192 |
| 5 | 2e | H | H | Br | $C_{19}H_{20}O_2BrN_3$ | 85 | 90 |
| 6 | 2f | H | H | Cl | $C_{19}H_{20}O_2ClN_3$ | 88 | 177 |
| 7 | 2g | Br | $CH_3$ | Cl | $C_{20}H_{21}O_2BrClN_3$ | 86 | 182 |
| 8 | 2h | I | $CH_3$ | Cl | $C_{20}H_{21}O_2IClN_3$ | 90 | 152 |
| 9 | 2i | Cl | H | $CH_3$ | $C_{20}H_{21}O_2BrN_3$ | 92 | 164 |
| 10 | 2j | Cl | H | Br | $C_{19}H_{19}O_2BrIN_3$ | 85 | 147 |

## RESULTS AND DISCUSSION

A series of some novel Acetyl pyrazoline derivatives were synthesized by refluxing chalcone derivatives, hydrazine hydrate and few drops of glacial acetic acid. The uses of different chalcones for the synthesis of acetyl pyrazoline have been investigated. The presence of bromo, chloro, iodo, hydroxy and methyl groups at different position of benzene ring of the chalcones, the use of hydrazine hydrate and glacial acetic acid resulted in synthesis of new acetyl pyrazoline derivatives with significantly high yield.

The structures of the synthesized compounds **(2a-j)** were confirmed on the basis of spectral analysis. The IR spectrum of **(2a-j)** exhibited a band due to 1608 cm$^{-1}$ (C=O acetyl pyrazoline ring), 1582 cm$^{-1}$ (C=N), 3333 cm$^{-1}$ (Ar-OH), also 750-700 cm$^{-1}$ due to C-Cl stretching. Further, in their $^1$HNMR (DMSO) spectra, the appearance of a signal at δ3.2-3.3 (dd, 1H, $H_A$ pyrazoline) δ 3.5-3.8 (dd, 1H, $H_B$ pyrazoline), δ 5.3-5.5 (t, 1H, $H_X$ pyrazoline) and δ 2.25-2.3 (s, 3H, CO-$CH_3$ acetyl group), the absence of the single peak at δ 7.2-7.4 (s, 1H, N-H) of pyrazoline, confirms the presence of the acetyl pyrazoline ring.

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 acetyl pyrazoline moiety, the

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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**

1-Acetyl-(3-(5-chloro-3-iodo-2-hydroxy-phenyl)-5-(4'-(dimethylamino-phenyl)-4, 5-dihydro-1H-pyrazole (2b)

IR (KBr): 1604 cm-I (C=O), 3333 $cm^{-1}$ (Ar-OH), 1582$cm^{-1}$ (C=N), 1246 $cm^{-1}$ (C-N);

$^1$HNMR (DMSO): δ 2.25 (s, 3H, CO-$CH_3$) δ 2.85 (s, 6H, $(CH_3)_2$), δ 3.25 (dd, 1H, $H_A$), δ 3.85 (dd, 1H, $H_B$), δ 5.40 (t, 1H, $H_X$), δ 6.61-8.1 (m, 6H, Ar-H), δ 11.01 (s, 1H, OH),

M.S. (m/z): m+1 = 483

1- Acetyl-(3-(5-chloro-3-bromo-2-hydroxy-phenyl)-5-(4'-(dimethylamino-phenyl)-4, 5-dihydro-1H-pyrazole (2c)

IR (KBr): 1612 $cm^{-1}$ (C=O), 3198 $cm^{-1}$ (Ar-OH), 1523 $cm^{-1}$ (C=N), 1234 $cm^{-1}$ (C-N);

$^1$H NMR (DMSO): δ 2.25 (s, 6H, CO-$CH_3$), δ 2.86 (s, 6H, $(CH_3)_2$) δ 3.30 (dd, 1H, $H_A$), δ 3.87 (dd, 1H, $H_B$), δ5.40 (t, 1H, $H_X$), δ 6.61-7.9 (m, 6H, Ar-H), δ 11.0 (s, 1H, OH),

M.S. (m/z): m+1 = 437

1-Acetyl-(3-(3, 5-Dibromo-2-hydroxy-phenyl)-5-(4'-(dimethylamino-phenyl)-4, 5-dihydro-1H-pyrazole (2d)

IR (KBr): 1609 $cm^{-1}$ (C=O), 3224 $cm^{-1}$ (Ar-OH) 1527 $cm^{-1}$ (C=N) 1230 $cm^{-1}$ (C-N);

$^1$H NMR (DMSO): δ 2.15 (s, 3H, CO-$CH_3$), δ 2.84 (s, 6H, $(CH_3)_2$), δ 3.25 (dd, 1H, $H_A$), δ 3.83 (dd, 1H, $H_B$), δ 5.45 (t, 1H, $H_X$), δ 6.60-7.9 (m, 6H, Ar-H), δ 11.1 (s, 1H, OH),

M.S. (m/z): m+1=440, m+2 = 481

## CONCLUSION

In summary all the synthesized acetyl pyrazolines (**2a-j**) are new derivatives with electron releasing groups and compounds having pharmacophores such as chloro, bromo, iodo, hydroxyl and methyl groups exhibited best antimicrobial activity. The data reported in this article may be helpful in guiding the medicinal chemist to explore the new entities with more potent activities.

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