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# SYNTHESIS AND BIOLOGICAL EVALUATION OF NEW 1-H-3 (4'-HYDROXYPHENYL)- 5-ARYL- 2-PYRAZOLINE DERIVATIVES

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## ABSTRACT

Organic reactions in aqueous media have attracted increasing interest recently because of environmental issues and the understanding of biochemical processes. In the present investigation eight new pyrazoline derivatives were synthesized by condensing different hydroxyl chalcones with hydrazine hydrate in dilute ethanolic potassium hydroxide or sodium hydroxide solution at room temperature according to Claisen-Schmidt condensation reaction. All these compounds were characterized by IR and NMR spectral data. These synthesized compounds were screened for pharmacological activity such as antimicrobial and anthelmintic activity.

**Keywords:** *Pyrazole; Pyrazoline; Cyclization of pyrazoline; Antimicrobial activity.*

## INTRODUCTION

Pyrazoles were synthesized by the reaction of á, â-unsaturated aldehydes with hydrazine and subsequent dehydrogenation[1,2,3]. Pyrazoline derivatives were reported for their Anticonvulsant, Antihypertensive, Antidepressant activities, Analgesic, Anti-inflammatory, Antipyretic, Antibacterial activities[4, 5, 6]. Among various pyrazoline derivatives, 2-pyrazolines seem to be the most important hetrocycle[7, 8]. A classical synthesis of these compounds involves the base-catalyzed aldol condensation reaction of aromatic ketones and aldehydes to give á,â-unsaturated ketones (chalcones), which undergo a subsequent cyclization reaction with hydrazines affording 2-pyrazolines[9,10]. Newly synthesized 3,5-diphenyl-2-pyrazolines exhibit efficient antimicrobial activity against a variety of test organisms[11].

## EXPERIMENTAL

All the chemicals used were obtained from E-Merck Ltd. Mumbai, and S.D. Fine Chem. Ltd. Mumbai. New pyrazoline derivatives were synthesized and characterized by physical methods as reported in Table1.

***Table 1.*** *physical data of Pyrazoline derivatives(**1-8**)*

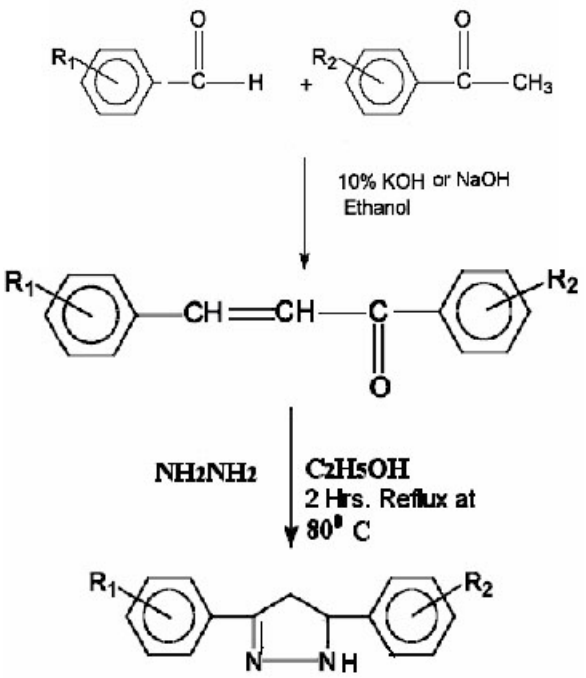
| Comp. No. | Mol. Formula | Mol. Wt. | Reaction Time | Melting Point | Percentage Yield | Rf Value |
|---|---|---|---|---|---|---|
| 1 | $C_{15}H_{14}N_2$ | 221 | 3hr | 54-58°C | 71.79% | 1.10 |
| 2 | $C_{15}H_{13}N_2O$ | 237 | 3hr | 152155°C | 81.56% | 1.00 |
| 3 | $C_{15}H_{13}N_2OBr$ | 315 | 3.20hrs | 55-57°C | 57.05% | 0.90 |
| 4 | $C_{15}H_{13}N_2OCl$ | 271 | 3hrs | 210-215°C | 96.00% | 0.80 |
| 5 | $C_{16}H_{16}N_2O$ | 251 | 3.15hrs | 194-196°C | 87.61% | 1.20 |
| 6 | $C_{16}H_{16}N_2O$ | 280 | 3hrs | 134-139°C | 72.11% | 0.90 |
| 7 | $C_{16}H_{16}N_2O$ | 287 | 3hrs | 184-187°C | 78.25% | 0.85 |
| 8 | $C_{16}H_{16}N_2O_2$ | 283 | 2.30hrs | 214-217°C | 46.92% | 0.83 |

**General Synthetic procedure: (Fig 1)**

**Step1- Synthesis of 4-hydroxy chalcone**

0.01mole of ethanolic solution of p-hydroxy acetophenone and 0.01mole of aldehyde were mixed together and stirred. 10 ml of 40% NaOH solution was

***Fig 1.*** *General synthetic scheme of 1-H-3(4'-Hydroxyphenyl)-5-aryl-2-Pyrazoline derivatives:*




Where, $R_1$ = $NO_2$, Cl, $Br_2$, $OCH_3$, $CH_3$, $N(CH_3)_2$, Ph, Naphthyl
$R_2$ = OH

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added to it. The mixture was kept overnight at room temperature. The content was then poured over crushed ice and acidified with dilute HCl. The solid obtained was filtered, dried and recrystallized with ethanol.

**Step 2- Synthesis 1-*H*-3(4'-hydroxyphenyl)-5-aryl 2-pyrazolines**

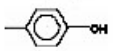
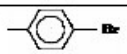
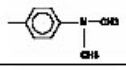
A mixture of 4-hydroxy chalcone (0.01 mole) & 99% hydrazine hydrate (0.015 mole) in 10 ml ethanol were refluxed on a water bath at 70-80 $^0$C for 2 hours. The mixture was concentrated & allowed to cool. The resulting solid was filtered, dried & recrystallized from ethanol.

**Biological Evaluation**

**Antimicrobial activity**

The synthesized compounds of the series were screened for their antimicrobial activity against the growth of two bacteria by disc diffusion method. The bacteria used are *Escherichia coli,* and *Staphylococcus aureus*. A 4% and 2% solutions were prepared in ethylene glycol/dimethylformamide. The activities of the compounds were compared with standard antibacterial (Ampicillin) substance under the same condition. The results are reported in Table 2.

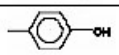
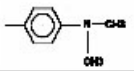
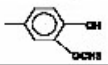
***Table 2.*** *antimicrobial activity of Pyrazoline derivatives(**1-8**)*

| Compound No. | Substituents | E. coli 4% | E. coli 2% | S. aureus 4% | S. aureus 2% |
|---|---|---|---|---|---|
| 1 |  | 11 | 10 | 13 | 10 |
| 2 |  | 17 | 15 | 12 | 15 |
| 3 |  | 13 | 12 | 14 | 13 |
| 4 |  | 14 | 12 | 15 | 10 |
| 5 |  | 15 | 10 | 15 | 12 |
| 6 |  | 18 | 16 | 17 | 16 |
| 7 |  | 14 | 11 | 15 | 12 |
| 8 |  | 16 | 15 | 13 | 10 |
| 9 | Ampicillin | 22 | 18 | 24 | 20 |

**Anthelmintic activity**

For determination of anthelmintic activity earthworms were selected. A 4% solution of compounds was prepared in DMF. Two earthworms were placed in the Petri dish containing test solution of synthesized compounds and movements of earthworms were observed. The earthworms got stimulated and death supervened. The time taken for complete paralysis and death is reported in Table 3. The activity was compared with standard anthelmintic solution under the same condition [6, 11].

***Table 3.*** *Anthelmintic activity of Pyrazoline derivatives(**1-8**)*

| Compound No. | Substituents | Anthelmintic activity | |
|---|---|---|---|
| | | Lethal time [minute] | Paralytic time [minute] |
| 1 |  | 15 | 21 |
| 2 |  | 13 | 20 |
| 3 |  | 17 | 23 |
| 4 |  | 16 | 22 |
| 5 |  | 18 | 24 |
| 6 |  | 20 | 26 |
| 7 |  | 18 | 25 |
| 8 |  | 14 | 21 |
| 9 | Standard (Piperazine Phosphate) | 11 | 20 |

**RESULTS AND DISCUSSION**

The purity and structure of synthesized compounds were confirmed by thin layer chromatography, melting point/boiling point, $^1$H NMR & IR spectroscopy. $^1$H NMR was recorded on 'Jeol My 60 FTNMR' spectrometer in $CCl_4$ / $CDCl_3$ using TMS as an internal standard. IR spectra were recorded by using FTIR (KBr, cm$^{-1}$) spectrophotometer. Melting points were determined in open capillary tube method and are uncorrected.

**Spectral data**

**1. 1-H-3(4'-hydroxyphenyl) -5-aryl -2-pyrazolines**

$^1$HNMR ä: 6.89 to 7.66 (9H, m, Ar), 5.00 (1H, s, NH), 5.14 (1H, OH). IR (cm$^{-1}$ KBr): 3030 (C-H), 1452 (C=C), 3314 (Ar-OH), 1600 (C=N), 1288 (C-N), 1520 (N-H)

**2. 1-H-3 (4'-hydroxyphenyl) -5-(4'- hydroxyphenyl) -2-pyrazolines**

$^1$HNMR ä: 6.54 to 7.92 (8H, m, Ar), 5.10 (1H, s, NH), 5.12 (1H, OH). IR (cm$^{-1}$ KBr): 3028 (C-H), 1453 (C=C), 3311 (Ar-OH), 1602 (C=N), 1284 (C-N), 1522 (N-H)

**3. 1-H-3 (4'-hydroxyphenyl) -5-(4'- bromophenyl) -2-pyrazolines**

$^1$HNMR ä: 6.86 to 7.66 (8H, m, Ar), 5.07 (1H, s, NH), 5.11 (1H, OH). IR (cm$^{-1}$ KBr): 3032 (C-H), 1450 (C=C), 3311 (Ar-OH), 1602 (C=N), 1289 (C-N), 1518 (N-H), 740 (C-Br)

**4. 1-H-3 (4'-hydroxyphenyl) -5-(2'- chlorophenyl) -2-pyrazolines**

$^1$HNMR ä: 6.83 to 7.96 (8H, m, Ar), 5.01 (1H, s, NH), 5.09 (1H, OH). IR (cm$^{-1}$ KBr): 3030 (C-H), 1448 (C=C), 3318 (Ar-OH), 1608 (C=N), 1288 (C-N), 1508 (N-H), 780 (C-Cl)

**5. 1-H-3 (4'-hydroxyphenyl) -5-(2'-methylphenyl) -2-pyrazolines**

$^1$HNMR ä: 6.86 to 7.66 (8H, m, Ar), 5.07 (1H, s, NH), 5.11 (1H, OH), 2.15 (3H, s $CH_3$). IR ($cm^{-1}$ KBr): 3032 (C-H), 1450 (C=C), 3311 (Ar-OH), 1602 (C=N), 1289 (C-N), 1514 (N-H)

**6. 1-H-3 (4'-hydroxyphenyl) -5-(4' -N-dimethylamino -phenyl) -2-pyrazolines**

$^1$HNMR ä: 6.90 to 7.89 (8H, m, Ar), 5.10 (1H, s, NH), 5.11 (1H, OH), 2.65 (6H, s $CH_3$). IR ($cm^{-1}$ KBr): 3033 (C-H), 1452 (C=C), 3316 (Ar-OH), 1606 (C=N), 1280 (C-N), 1515 (N-H)

**7. 1-H-3 (4'-hydroxyphenyl) -5-(4'- napthyl)-2-pyrazolines**

$^1$HNMR ä: 6.80to 7.64 (8H, m, Ar), 8.00 (1H, s, NH), 5.10 (1H, OH), 6.80 to 7.64 (10H, m, Ar). IR ($cm^{-1}$ KBr): 3032 (C-H), 1456 (C=C), 3301 (Ar-OH), 1600 (C=N), 1283 (C-N), 1510 (N-H)

**8. 1-H-3(4'-hydroxyphenyl)-5-(4'-hydroxy,3'-methoxyphenyl)-2-pyrazolines**

$^1$HNMR ä: 6.90 to 7.89 (8H, m, Ar), 5.10 (1H, s, NH), 5.11 (1H, OH), 3.65 (6H, s, $OCH_3$). IR ($cm^{-1}$ KBr): 2933 (C-H), 1442 (C=C), 3310 (Ar-OH), 1603 (C=N), 1288 (C-N), 1515 (N-H)

## CONCLUSION

Newer Pyrazoline derivatives were synthesized successfully by a simple and convenient method in a short period of time. All synthesized pyrazoline derivatives are having better antimicrobial activity. Amongst these, compound 6 is having maximum antimicrobial activity.

## ACKNOWLEDGMENT

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