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# Synthesis of Pyrazoline Derivatives from Chalcones and their Antibacterial Activity

**Shaik Khadar Yazdan*, K. Renuka Sowjanya, K. Sai Avinash and M. Ratna Kumari**

*Department of Pharmaceutical Chemistry, Victoria College of Pharmacy, Nallapadu, Guntur - 522005, **INDIA**

Email: sk_yazdani@yahoo.com

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## ABSTRACT

*Pyrazoline derivatives shown antibacterial, antiviral and anti-inflammatory activities. Claisen-Schmidt Condensation method was adopted to get chalcones. Acetophenone on condensation with aldehyde gives chalcone. Chalcones were subjected for reaction with hydrazine hydrate to give pyrazoline derivative of chalcone. These compounds were tested for their antibacterial activity.*

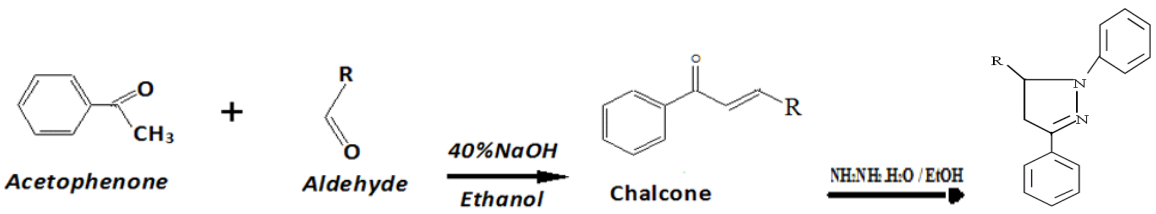
**Keywords:** Pyrazoline derivatives, Chalcone, Claisen-Schmidt condensation, Antibacterial activity.

## INTRODUCTION

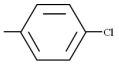
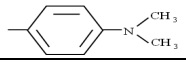
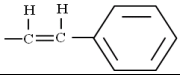
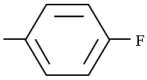
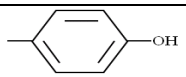
Pyrazoline is a five membered heterocyclic compound. Pyrazolines occupy unique position for their antibacterial[1], antiviral[2], antipyretic, analgesic, insecticidal[3], fungicidal[4], muscle relaxant properties. One of the important application of pyrazoline is as a fluorescent brightening agents. Chalcone on reaction with hydrazine hydrate in presence of ethanol and acetic acid gives pyrazoline derivatives [5]. Chalcones are one of the major classes of natural products, which are widely distributed in various plant species[6-8]. Chalcones can also be prepared from Claisen-Schmidt synthetic method. In this method, acetophenone is condensed with aldehyde in presence of ethanolic sodium hydroxide solution and gives chalcone[9,10]. The chalcones displayed a broad spectrum of pharmacological activities, which includes antimalarial, anticancer, antiprotozoal, antioxidant, anti-inflammatory activities[11].

## MATERIALS AND METHODS

**Scheme for Synthesis**




Substituted Pyrazoline Derivative of Chalcone

| COMPOUNDS | R |
|---|---|
| $A_i$, $B_i$ |  |
| $A_{ii}$, $B_{ii}$ |  |
| $A_{iii}$, $B_{iii}$ |  |
| $A_{iv}$, $B_{iv}$ |  |
| $A_v$, $B_v$ |  |
| $A_{vi}$, $B_{vi}$ |  |

Ai, Aii, Aiii, Aiv, Av, Avi ⟶ Chalcones

Bi, Bii, Biii, Biv, Bv, Bvi ⟶ Pyrazoline Derivatives

**Synthesis of a Chalcone:** Equimolar concentration of acetophenone (0.01mol) and substituted benzaldehyde (0.01mol) was dissolved in 20 ml of methanol. To it, a little amount of freshly prepared 40% sodium hydroxide solution was added (which acts as catalyst). The reaction mixture was kept undisturbed for 24 h. The mixture was then acidified with 1:1 hydrochloric acid and water. Then it was filtered through vacuum, washed with water, dried and recrystallized using methanol.

**Synthesis of Pyrazoline Derivatives:** A mixture of chalcone (0.01mol) and hydrazine hydrate (0.02 mol) were dissolved in ethanol (50ml) and acetic acid (7.0ml) mixture and then refluxed for 4 h. The reaction mixture was concentrated, cooled and poured into ice cold water. The precipitate obtained was filtered, washed, dried and recrystallized by using ethyl alcohol. The completion of the reaction was monitored by TLC.

**Table 1.** Characterization Data of Synthesized Compounds

| S. No. | Substituent | M P (°C) | YIELD (%) | $R_f$ | Molecular Formula | Nature |
|---|---|---|---|---|---|---|
| **Ai** | $-C_6H_5O$ | 164 | 99.5 | 0.26 | $C_{15}H_{12}O_2$ | Yellowish green colour |
| **Bi** | $-C_6H_5O$ | 144 | 88 | 0.28 | $C_{15}H_{14}ON_2$ | Brown colour semisolid |
| **Aii** | $-C_6H_4Cl$ | 117 | 99 | 0.2 | $C_{15}H_{11}0Cl$ | White coloured powder |
| **Bii** | $-C_6H_4Cl$ | 186 | 49 | 0.33 | $C_{15}H_{13}N_2Cl$ | Dark brown / orange |
| **Aiii** | $-C_8H_{10}N$ | 140 | 70 | 0.13 | $C_{17}H_{17}0N$ | Yellowish orange colour |
| **Biii** | $-C_8H_{10}N$ | 210 | 62 | 0.12 | $C_{17}H_{19}N_3$ | Black colour powder |
| **Aiv** | $-C_8H_7$ | 136 | 67 | 0.86 | $C_{17}H_{14}O$ | Yellowish orange colour |
| **Biv** | $-C_8H_7$ | 155 | 42 | 0.85 | $C_{17}H_{16}N_2$ | Orange red colour |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Av** | $-C_6H_4$ F | 106 | 63.7 | 0.31 | $C_{15}H_{11}OF$ | Yellowish green crystals |
| **Bv** | $-C_6H_4F$ | 92 | 58 | 0.80 | $C_{15}H_{13}N_2F$ | Yellowish red colour |
| **Avi** | $-C_6H_5O$ | 244 | 51 | 0.25 | $C_{15}H_{12}O_2$ | Pale biscuit colour |
| **Bvi** | $-C_6H_5O$ | 170 | 22 | 0.70 | $C_{15}H_{14}N_2O$ | Orange red colour |

**Table 2.** Spectral Data of the Compounds

| Compound | IR ($Cm^{-1}$, KBr) | $^1H$ NMR ($CDCl_3$, ppm) | $M^+$ Ion (m/z) |
|---|---|---|---|
| Ai | 3563.21(O-H), 1638.86(C=C), 1221.13(C-O), 3086.82(C-H), 1557.92(C=C) | 6.393(1H,S,$2^1$ Ar-OH), 6.89-6.98(4H,M,$3^1$,$4^1$,$5^1$,$6^1$,Ar-H), 7.42-7.60(5H,m,2,3,4,5,6, Ar-H), 5.69-5.72(1H,d,Ar-CH=CH-C=O), 7.94-7.96(1H,d,Ar,-CH=CH-C=O) | 223.1 |
| Bi | 1171.94(C-O), 1121.95(C-N), 1584.67(C=C) | 3.56-3.63(2H,dd,$^1$H s at $4^{th}$ position), 5.14-5.20(1H,dd,$^1$H at $5^{th}$ position), 6.83-6.98(4H,m,Ar-H), 7.25-7.43(5H,m,Ar-H), 7.64-7.56(5H,m,Ar-OH) | 341.2 |
| Aiii | 1680.98(C=O),1219.37(C-N), 2891.75(C-H),1650.31(C=C), 1517.79(C=C) | --- | --- |
| Av | 1726.30(C=O),1654.14(C=C), 3058.28(C-H),1590.82(C=C), | --- | --- |

## APPLICATIONS

**Antibacterial Activity:** All the synthesized pyrazoline derivatives and chalcones were screened for their in-vitro antibacterial activity at conc. of 90 µg $mL^{-1}$ in chloroform against gram-positive *Bacillus subtilis* and gram-negative *Pseudomonas aeruginosa* bacteria by the paper disc diffusion method. The zone of inhibition was measured in mm after 24 h. of incubation at 37°C. Standard drug Ampicillin was used as reference and the solvent chloroform was used.

**Table 3.** Antibacterial Activity

| Compounds | Zone of inhibition in mm for 90µg $mL^{-1}$ concentration | |
|---|---|---|
| | ***Bacillus subtilis*** | ***Pseudomonas aeruginosa*** |
| Ai | 4mm | 3.5mm |
| Bi | 1.5mm | 1.2mm |
| Aii | 2.5mm | 2.3mm |
| Bii | Nil | Nil |
| Aiii | 2.2mm | 1.8mm |
| Biii | Nil | Nil |
| Aiv | 2.0mm | 2.0mm |
| Biv | Nil | Nil |
| Av | 4.2mm | 3.9mm |
| Bv | Nil | Nil |

| | | |
|---|---|---|
| Avi | 1.8mm | 2.2mm |
| Bvi | Nil | Nil |
| Standard (Ampicillin) | 19mm | 17mm |
| Control (Chloroform) | 0 mm | 0 mm |

## RESULTS AND DISCUSSION

The yield of the compounds $\mathbf{A_i}$, $\mathbf{A_{ii}}$, $\mathbf{A_{iii}}$, $\mathbf{A_{iv}}$, $\mathbf{A_v}$ and $\mathbf{A_{vi}}$ is high when compared with the yield of the Pyrazoline derivatives $\mathbf{B_i}$, $\mathbf{B_{ii}}$, $\mathbf{B_{iii}}$, $\mathbf{B_{iv}}$, $\mathbf{B_v}$ and $\mathbf{B_{vi}}$. All the chalcones were easily recrystallized than the Pyrazoline derivatives of these chalcones. On the basis of results obtained from the antibacterial activity, the following generalization could be made.

**Activity against Gram Positive Organism (*Bacillus subtilis*):** The compounds $\mathbf{A_i}$ and $\mathbf{A_v}$ showed weak antibacterial activity at a concentration of 90 µg $mL^{-1}$. The other compounds did not show the activity against *Bacillus subtilis*.

**Activity against Gram Negative Organism (*Pseudomonas aeruginosa*):** The compounds $\mathbf{A_i}$ and $\mathbf{A_v}$ showed weak antibacterial activity at a concentration of 90 µg $mL^{-1}$. The other compounds did not show the activity against *Pseudomonas aeruginosa.*

## CONCLUSIONS

Some of the compounds, which were synthesized, showed weak antibacterial activity at 90 µg $mL^{-1}$ concentration. These compounds may show more antibacterial activity at high concentrations. Change of functional groups on the pyrazole moiety of these derivatives may give better antibacterial activity.

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