PART III

SYNTHESIS OF 3, 5-DIARYL-4-BENZOYL-1-PYRIDOYL PYRAZOLES
## PART III

**SYNTHESIS OF 3, 5-DIARYL-4-BENZOYL-1-PYRIDOYL PYRAZOLES.**

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PART III
SYNTHESIS OF 3,5-DIARYL-4-BENZOYL-1-PYRIDOYL PYRAZOLEs

CHAPTER I
ORIGIN OF THE PROBLEM

Borkhade\(^1\) reported the formation of pyrazoles from 2-hydroxydibenzoyl methanes or chalconedibromides and phenyl hydrazine in pyridine medium. Thakar\(^2\) synthesised 4-aroyl -3-aryl-5-(o-hydroxyphenyl) pyrazoles from 2-aroyl - chromones with hydrazine in methanol. Synthesis of 3,5-diarylparyrazoles have been reported\(^3\) by the condensation of 1,3-diketones or flavones with hydrazine hydrates in alcohol as a solvent. Chincholkar\(^4\) reported the synthesis of 4-aroyl -3, 5-diarylparyrazoles from 3-aroyl flavones. Joshi\(^5\) prepared 3-methyl -4- aroyl-5- (2-hydroxy phenyl) pyrazoles from 3-aroyl-2 methyl chromones. Kakade\(^6\) reported the isomeric pyrazoles from 1,3-dibenzoyl methanes and isomeric pyrazoles from 1, 3-dibenzoyl methanes and Ph NH NH\(_2\) in DMSO solvent.

From the survey of the literature, it was cleared that 3,5-diarylparyrazoles are not synthesised from 3-aroyl flavones using pyridine medium. It was therefore thought of interest to attempt to synthesise 3,5-diarylparyrazoles using pyridine medium.

Tayde\textsuperscript{7,8} et al have synthesised 3,5-diaryl-1-pyridoyl pyrazoles and 3,5-diaryl-1-phenyl pyrazoles.

Parmar\textsuperscript{9} have reported 3,5-disubstituted pyrazoles. Mogha A. Abdallan\textsuperscript{10} et al have prepared 5-amino-4-(2-benzothiazolyl) pyrazoles.

**PROBLEM**

The work presented in this part of the thesis deals with the synthesis of 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles from 3-aryloyl flavones and isoniazide in pyridine medium. The structures and identity of the compounds synthesised have been confirmed by spectral (UV, IR, NMR) and elemental analysis. The probable mechanism has also been discussed.

**SCHEME**

```
  R
R2   OH              R2
R3

acetylation

R
R2
OCOCH3
R3

(la-c)

F, M

R
R2
OH
R3
COCH3

(2a-c)

B, V, T

R
R2
OH
R3
COCH2CO-C3H5

(4a-c)

CHO

R
R2

(5a-j)

\[\text{SeO}_2\]

(7a-j)

\[\text{Isoniazide}\]

(8a-j)
```
CHAPTER II

SUMMARY OF THE WORK

Starting materials:

2-Hydroxy acetophenones (2a-e), 2-benzoyloxy acetophenones (3a-e), 1,3-propanediones (4a-e) and 3-aryl flavanones (5a-e) were prepared by the procedures as described in chapter II of part II of this thesis.

3-Aroyl flavones (7a-j):

3-Aroyl flavones (7a-j) were prepared by refluxing 3-aryloxy flavanones (5a-j) with SeO₂ in dioxane solvent. Thus 3-benzoyl-6-methyl flavone (7a), m.p. 132°C; 4'-methoxy-3-benzoyl-6-methyl flavone (7b), m.p. 156°C; 3-benzoyl-6-methyl-8-bromo flavone (7c), m.p. 180°C; 4'-methoxy-3-benzoyl-6-methyl-8-bromo flavone (7d), m.p. 195°C; 3-benzoyl-8-methyl flavone (7e), m.p. 152°C; 4'-methoxy-3-benzoyl-8-methyl flavone (7f), m.p. 176°C; 3-benzoyl-7-methyl flavone (7g), m.p. 148°C; 4'-methoxy-3-benzoyl-7-methyl flavone (7h), m.p. 162°C; 3-benzoyl flavone (7i), m.p. 145°C and 4'-methoxy-3-benzoyl flavone (7j), m.p. 185°C were prepared. The structure of (7d) was confirmed on the basis of (IR, UV, PMR) spectra.

3, 5-Diaryl -4-benzoyl -1-pyridoyl pyrazoles (8a-i):

3, 5-Diaryl -4-benzoyl -1-pyridoyl pyrazoles (8a-i) were synthesised on refluxing of 3-aryloxy flavones (7a-j) and isoniazide in pyridine solvent for 8 to 10 hours. Thus 3- (2-hydroxy -5-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole (8a
m.p. 252°C; 3-((2-hydroxy-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl-2-pyrazole (8b), m.p. 232°C; 3-((2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8c), m.p. 215°C; 3-((2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl-2-pyrazole (8d), m.p. 245°C; 3-((2-hydroxy-3-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8e), m.p. 270°C; 3-((2-hydroxy-3-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (8f), m.p. 231°C; 3-((2-hydroxy-4-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8g), m.p. 240°C; 3-((2-hydroxy-4-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (8h), m.p. 234°C; 3-((2-hydroxy phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8i), m.p. 215°C and 3-((2-hydroxy phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (8j), m.p. 210°C were prepared.

The structure of (8a) was confirmed on the basis of elemental analysis, chemical properties and spectral analysis (IR, UV, PMR). The probable mechanism for the formation of pyrazoles have been discussed.
CHAPTER III

EXPERIMENTAL AND DISCUSSION OF THE RESULTS.

Borkhade et al.\(^1\) reported the formation of pyrazoles from o-hydroxydibenzoyle methanes or chalconedibromides and phenylhydrazine in pyridine. 3,5-Diphenyl pyrazoles have been reported\(^1\) by condensation of 1,3-diketones or flavones with hydrazine hydrate in alcohol solvent. 4-Aroyl\(^2\) and acyl\(^11\) substituted pyrazoles have also been synthesised. Chinholkar and Jamode\(^4\) further reported the synthesis of 4-aryl-3,5-diaryl pyrazoles from 3-aryl flavones. Joshi \(^5\) prepared 3-methyl -4-aryl -5- (2-hydroxyphenyl) pyrazoles from 3-aryl -2-methyl chromones. Nair\(^12\), further reported the synthesis of 3-methyl -4-(2'-furanyl)-5-(2" hydroxy phenyl) pyrazoles from 3-(2'- furanyl) -2-methyl -chromones and hydrazine hydrate in ethanol. Kakade\(^6\) reported the formation of 3,5-diaryl-1-phenyl pyrazoles from 2-hydroxy-dibenzoyle methanes and phenylhydrazine in DMSO solvent.

Tayde\(^7\) et. al have synthesised 3,5-diaryl-1-pyridoyl pyrazoles and 3,5-diaryl-1- phenyl pyrazoles.

Parmar\(^8\) have reported 3,5-disubstituted pyrazoles. Mogha A. Abdallah\(^10\) et. al have prepared 5-amino-4-(2-benzothiazolyl) pyrazoles.

This part deals with the synthesis of 3, 5-diaryl-4-benzoyle-1- pyridoyl pyrazoles (3a-j) from 3-aryl flavones (7a-j) on treatment with isoniazide in pyridine medium.

The compounds synthesised here were characterised on the basis of chemical properties, elemental and spectral analysis. The melting points are uncorrected. The IR spectra were recorded in "Perkin-Elmer-577" spectrophotometer in KBr pellets and UV-VIS spectra was recorded in "Perkin-Elmer-202" spectrophotometer. The proton magnetic resonance spectra (PMR) was recorded on (Bruker) AC 300 F NMR spectrophotometer.

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The elemental and spectral analysis were carried out at RSIC Punjab University, Chandigarh. The purity of the pyrazoles, was tested by TLC on microscopic slides with silica gel -G layers. The chemicals used were of laboratory reagent grade.

**Preparation of starting materials:**

2-Hydroxy acetophenones (2a-e), 2-benzoxyloxy acetophenones (3a-e), 1,3-propanediones (4a-e) and 3-aryl flavanones (5a-e) were prepared by the procedures as described in chapter II of part II of this thesis.

**Synthesis of 3-Aroyl Flavones (7a-j):**

Chalcones and flavanones are reported to give corresponding flavones by $\text{SeO}_2$ dehydration. Baker and Venkataraman rearranged o-arylxyloxy acetophenones with bases like $\text{K}_2\text{CO}_3$, $\text{Na}_2\text{CO}_3$, $\text{NaNH}_2$, pyridine etc. to obtain o-hydroxydibenzoyl methanes which on cyclisation give flavones. Thakar et al. synthesised 2-(2'-furyl) -3-hydroxy chromone by cyclodehydration of 1,3-propanediones with acetic acid and HCl. 3-Aroyl flavones were synthesised by oxidation of arylidene derivatives of 2-hydroxy-dibenzoylmethanes with $\text{SeO}_2$ in amyl alcohol.

3-Aroyl flavones has also been prepared from 3-aryl flavanones by subjecting them to $\text{SeO}_2$ oxidation in dioxane. Jerzmahoska et al. obtained simple C-3-derivatives of flavones from the arylidene derivatives and resublimed $\text{SeO}_2$ in dioxane. Thakar and Ingle prepared 3-aryl-2-aryl-chromones by oxidative cyclisation of 2-aryl-3-arylacylophenones using $\text{SeO}_2$ in isoamyl alcohol. Flavonones were prepared by Voigtländer et al. by heating corresponding flavanones with $\text{I}_2$ in pyridine.

---

13. Baker, W.,
14. Malal, H. S. and Venkataraman, K.,
15. Thakar, K. A. and Maley, P. R.,
16. Baker, W. and Glockling, F.,
17. Thakar, K. A., and Ingle, V. N.,
18. Voigtlander, H. W. and Hachtner Hartmut.
In this part 3-aryl flavones had been synthesised from 3-aryl flavanones by carrying out oxidation by SeO₂ in dioxane solvent. By using dioxane the yield was increased as compared to amyl alcohol or DMSO.

**General procedure for the preparation of 3-aryl flavones (7a-j):**

**Experiment No. 1-10:**

3-Aryl flavanones (5a-j) (0.01mol) and SeO₂ (0.001 mol) were refluxed in dioxane for about 18 hours. The reaction mixture was poured in cold water through a funnel fitted with glass wool. The solid separated was filtered, washed with sodium thiosulphate (5%) and then with water. It was crystallized from ethanol-acetic acid mixture to get white crystalline solid. Yield 80-95%.

![Chemical Structure](attachment:image.png)

(5a-j) \[\rightarrow\] \[(7a-j)\]

**Properties and constitution of the compounds (7a-j):**

1. The compounds (7a-j) are white crystalline solids (7a) m.p. - 132°C (132°C), (7b) m.p. -156°C (157°C), (7c) m.p. - 180°C (180°C), (7d) m.p. - 195°C (195°C), (7e) m.p. - 152°C (154°C), (7f) m.p. - 176°C (177°C), (7g) m.p. - 148°C (148°C), (7h) m.p. - 162°C (162°C), (7i) m.p. - 145°C (146°C) and (7j) m.p. - 185°C (186°C).

2. The alcoholic solution of these compounds did not give any colouration with FeCl₃ indicating the absence of phenolic -OH group. However, they gave yellow colouration with conc H₂SO₄.

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3. These compounds formed red colour with Mg/HCl.
4. With bromine water and KMnO₄ solution, these compounds showed unsaturation test.
5. From the analytical results, the molecular formulae for these compounds were found is follows.

<table>
<thead>
<tr>
<th>3-Aroyl flavones</th>
<th>Molecular formula</th>
<th>Analysis %</th>
<th>Found</th>
<th>Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>C₂₁H₁₈O₃</td>
<td>C</td>
<td>81.09</td>
<td>81.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.00</td>
<td>4.70</td>
</tr>
<tr>
<td>7b</td>
<td>C₂₄H₂₆O₄</td>
<td>C</td>
<td>77.75</td>
<td>77.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.78</td>
<td>4.86</td>
</tr>
<tr>
<td>7c</td>
<td>C₂₁H₁₅O₄Br</td>
<td>C</td>
<td>65.79</td>
<td>65.87</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>3.49</td>
<td>3.57</td>
</tr>
<tr>
<td>7d</td>
<td>C₂₅H₂₆O₄Br</td>
<td>C</td>
<td>64.09</td>
<td>64.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>3.69</td>
<td>3.79</td>
</tr>
<tr>
<td>7e</td>
<td>C₂₂H₂₄O₃</td>
<td>C</td>
<td>81.09</td>
<td>81.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.00</td>
<td>4.70</td>
</tr>
<tr>
<td>7f</td>
<td>C₂₅H₂₄O₄</td>
<td>C</td>
<td>77.75</td>
<td>77.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.78</td>
<td>4.86</td>
</tr>
<tr>
<td>7g</td>
<td>C₂₁H₁₅O₃</td>
<td>C</td>
<td>81.09</td>
<td>81.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.00</td>
<td>4.70</td>
</tr>
<tr>
<td>7h</td>
<td>C₂₁H₁₅O₄</td>
<td>C</td>
<td>77.75</td>
<td>77.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.78</td>
<td>4.86</td>
</tr>
<tr>
<td>7i</td>
<td>C₂₂H₂₄O₃</td>
<td>C</td>
<td>80.89</td>
<td>80.98</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.21</td>
<td>4.29</td>
</tr>
<tr>
<td>7j</td>
<td>C₂₃H₂₄O₄</td>
<td>C</td>
<td>77.46</td>
<td>77.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H</td>
<td>4.41</td>
<td>4.49</td>
</tr>
</tbody>
</table>
6. TLC:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solvent height (CCl₄) cm</th>
<th>Solute height cm</th>
<th>Rf</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>1.8</td>
<td>1.3</td>
<td>0.72</td>
</tr>
<tr>
<td>7b</td>
<td>2.0</td>
<td>1.9</td>
<td>0.95</td>
</tr>
<tr>
<td>7c</td>
<td>2.2</td>
<td>1.4</td>
<td>0.63</td>
</tr>
<tr>
<td>7d</td>
<td>1.7</td>
<td>1.2</td>
<td>0.70</td>
</tr>
<tr>
<td>7e</td>
<td>1.8</td>
<td>1.1</td>
<td>0.61</td>
</tr>
<tr>
<td>7f</td>
<td>2.4</td>
<td>2.1</td>
<td>0.87</td>
</tr>
<tr>
<td>7g</td>
<td>2.4</td>
<td>2.0</td>
<td>0.83</td>
</tr>
<tr>
<td>7h</td>
<td>2.5</td>
<td>2.0</td>
<td>0.8</td>
</tr>
<tr>
<td>7i</td>
<td>2.4</td>
<td>2.1</td>
<td>0.87</td>
</tr>
<tr>
<td>7j</td>
<td>2.3</td>
<td>1.9</td>
<td>0.82</td>
</tr>
</tbody>
</table>

7. Spectral Data:

IR, UV and PMR spectras of the compound (7d) were recorded and showed the following results, (IR: spectrum No.10, UV spectrum No. 11 and PMR spectrum No.12)

The IR spectrum of the compound (7d) (spectrum No. 10) was recorded in Nujol and showed the following absorption bands

<table>
<thead>
<tr>
<th>Frequency cm⁻¹</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1650</td>
<td>m</td>
<td>C = O  Stretching</td>
</tr>
<tr>
<td>1590 - 1585</td>
<td>s</td>
<td>C = C  Stretching</td>
</tr>
<tr>
<td>1245</td>
<td>s</td>
<td>C - O - C  Stretching</td>
</tr>
</tbody>
</table>
The UV-visible spectrum of the compound (7d) (spectrum No. 11) was recorded in DMSO. λ max 322 nm, corresponding to \( n \rightarrow \pi^* \) transition.

The proton NMR spectrum of the compound (7d) (spectrum No. 12) was recorded in CDCl₃. The observed chemical shifts can be correlated as:

<table>
<thead>
<tr>
<th>Chemical shift δ ppm</th>
<th>Nature of peak</th>
<th>No. of protons</th>
<th>Type of protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.50</td>
<td>s</td>
<td>3H</td>
<td>Ar - CH₃</td>
</tr>
<tr>
<td>3.80</td>
<td>s</td>
<td>3H</td>
<td>Ar - O - CH₃</td>
</tr>
<tr>
<td>6.7 - 8.3</td>
<td>m</td>
<td>11H</td>
<td>Ar - H</td>
</tr>
</tbody>
</table>

From the properties, analytical results, and spectral analysis, the compound (7d) was assigned the following structure:

(7d)

Thus, the following flavones (7a-j) were synthesised:

(7a)

3 - Benzoyl -6- methyl flavone

(7b)

4' - Methoxy -3- benzoyl -6- methyl flavone
3 - Benzoyl -6- methyl -8- bromo flavone.

4’-Methoxy -3- benzoyl -6- methyl -8- bromo flavone

3 - Benzoyl -8- methyl flavone.

4’- Methoxy -3-benzoyl -8- methyl flavone.

3 - Benzoyl -7- methyl flavone.
4'-Methoxy-3-benzoyl-7-methyl flavone.

3-Benzoyl flavone

4'-Methoxy-3-benzoyl flavone

Synthesis of 3,5-Diaryl-4-benzoyl-1-pyridoyl pyrazoles:

Flavones\textsuperscript{19} are reported to react with hydrazine or phenylhydrazine to give pyrazoles. 3-\text{o}-hydroxy phenyl-5-alkyl or aryl pyrazoles\textsuperscript{20} are synthesised by the action of hydrazine or substituted hydrazine on chromone, thiochromone or flavone. Pyridine\textsuperscript{1} has been used for the synthesis of 3-\text{o}-hydroxy phenyl-1,5-diphenyl pyrazoles from flavones and phenyl hydrazine hydrochloride. Synthesis of 4-aryl-3,5-diaryl pyrazoles has been reported from 3-aryl flavones and phenylhydrazine using pyridine\textsuperscript{2}, methanol\textsuperscript{2-17}, ethanol\textsuperscript{11} solvents.

\begin{enumerate}
\item Baker, W., Harborne, J. D., and Ollis, W. D., J. Chem Soc. (1952), 1303.
\end{enumerate}
In this part 3, 5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (8a-j) are synthesised by the action of isoniazide on 3-aryloyl flavones (7a-j).

**Preparation of 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (8a-j):**

**General procedure for the preparation of 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (8a-j):**

3-Aroyl flavones (7a-j) (0.01 mol) was refluxed with isoniazide (0.02 mol) for about 8-10 hours in pyridine solvent. The reaction mixture was cooled, decomposed by acidified water, filtered and washed with sufficient water. It was recrystallised from ethanol - acetic acid mixture to obtain a white crystalline solid. Yield 60 - 80%.

**Experiment No. 11:**

**Action of isoniazide on 3-benzoyl-6-methyl flavone (7a):**

**Preparation of 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8a):**

3-Benzoyl -6-methyl flavone (7a) (0.01 mol) (3.409g) was refluxed with isoniazide (0.02 mol) (2.74g) for about 8 hours in pyridine (25ml) medium. The reaction mixture was cooled, decomposed by acidified water, filtered and washed with sufficient water. It was recrystallised from ethanol - acetic acid mixture to obtain a white crystalline solid (8a) m.p. 252°C, yield - 70%.

[Diagram of reaction]
Properties and constitution of the compound (8a):

1. It did not give any colouration with ethanolic ferric chloride solution. The presence of phenolic-OH group has been found by its solubility in dilute NaOH.

2. It does not give Knorr's test for pyrazolines but yellow colouration was obtained when paper soaked in the solution of this compound in benzene was exposed to bromine vapours.

3. It gave yellow colouration with conc. H₂SO₄.

4. TLC: Solvent (CCl₄) height : 1.6 cm
   Solute height : 1.4 cm
   Rf value : 0.87.

5. From the analytical data of the compound (8a) the molecular formula was found to be C₂₀H₂₀O₄N₅.

   Elemental analysis -

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>75.72</td>
<td>4.50</td>
<td>8.9</td>
</tr>
<tr>
<td>Calculated</td>
<td>75.81</td>
<td>4.57</td>
<td>9.1</td>
</tr>
</tbody>
</table>

6. On the basis of chemical properties and analytical results, the compound (8a) was assigned the structure as 3-(2-hydroxy-5-methyl phenyl) -4-benzyol -5-phenyl -1-pyridoyl pyrazole.
Experiment No. 12:
Action of isoniazide on 4'-methoxy-3'-benzoyl-6-methyl flavone (7b):
Preparation of 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (8b).

4'-Methoxy-3'-benzoyl-6-methyl flavone (7b) (0.01 mol) (3.70 g) was refluxed with isoniazide (0.02 mol) (2.74 g) for about 10 hours in pyridine (25 ml) medium, and was processed as in experiment No. 11 to get (8b) m.p. 232°C yield - 71%.

Properties and constitution of the compound (8b):

Properties of the compound (8b) were found similar to those of compound (8a):

1. TLC: Solvent (CCl₄) height : 2.4 cm,
   Solute height : 1.9 cm
   Rf value : 0.79

2. From the analytical data the molecular formula of the compound (8b) was found to be
   \( C_{30}H_{26}O_5N_2 \).
   Elemental analysis -

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.55</td>
<td>4.62</td>
<td>8.4</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.61</td>
<td>4.70</td>
<td>8.5</td>
</tr>
</tbody>
</table>

3. On the basis of chemical properties and analytical results, the compound (8b) was assigned the structure as 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole.
Experiment No. 13:

Action of isoniazide on 3-benzoyl-6-methyl-8-bromo flavone (7c):

Formation of 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridovl pyrazole (8c):

3-Benzoyl-6-methyl-8-bromo flavone (7c) (0.01 mol) (4.19 g) was refluxed with isoniazide (0.02 mol) (2.74 g) for about 10 hours in pyridine (25 ml) medium, and was processed as in experiment No. 11 to get (8c), mp. 215°C. yield - 65%.

Properties and constitution of the compound (8c):

Properties of the compound (8c) were found similar to those of compound (8a).

1. TLC: Solvent (CCl₄) height : 2.6 cm.
   Solute height : 1.7 cm.
   Rf value : 0.65

2. From the analytical data the molecular formula for the compound (8c) was found to be C₂₅H₂₀O₃N₃Br.

Elemental analysis:

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>64.59</td>
<td>3.67</td>
<td>7.5</td>
</tr>
<tr>
<td>Calculated</td>
<td>64.68</td>
<td>3.71</td>
<td>7.8</td>
</tr>
</tbody>
</table>
3. On the basis of chemical properties and analytical results, the compound (8c) was assigned the structure as 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole.

Experiment No. 14:

Action of isoniazide on 4'-methoxy-3-benzoyl-6-methyl-3-bromo flavone (7d):

Formation of 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (8d).

4'-Methoxy-3-benzoyl-6-methyl-8-bromo flavone (7d) (0.01 mol) (4.49 g) was refluxed with isoniazide (0.02 mol) (2.74 g) for about 10 hours in pyridine (25 ml) medium and was processed as in experiment No. 11 to get (8d), m.p. 245°C. Yield - 77%.

Properties and constitution of the compound (8d):

Properties of the compound (8d) were found similar to those of compound (8a).

1. TLC: Solvent (CCl₄) height: 2.5 cm.
   Solute height: 1.7 cm.
   Rf value: 0.68.
2. From the analytical data the molecular formula for the compound (8d) was found to be $C_{36}H_{22}O_{4}N_{4}Br$.

Elemental analysis:

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>63.29</td>
<td>3.79</td>
<td>7.1</td>
</tr>
<tr>
<td>Calculated</td>
<td>63.38</td>
<td>3.87</td>
<td>7.3</td>
</tr>
</tbody>
</table>

3. On the basis of chemical properties and analytical results, the compound (8d) was assigned the structure as 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole.

![Chemical structure of 8d](image)

**Experiment No. 15:**

**Action of isoniazide on 3-benzoyl-8-methyl flavone (7e):**

**Formation of 3-(2-hydroxy-3-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8e).**

3-Benzoyl-8-methyl flavone (7e) (0.01 mol) (3.40 g) was refluxed with isoniazide (0.02 mol) (2.74 g) for about 10 hours in pyridine (25 ml) medium and was processed as in experiment No. 11 to get (8e), m.p. 270°C. Yield -67%.

![Chemical structures (7e) and (8e)](image)
Properties and constitution of the compound (8e):

Properties of the compound (8e) were found similar to those of compound (8a):

1. TLC: Solvent (CCl₄) height : 2.5 cm.
   Solute height : 1.7 cm,
   Rf value : 0.68

2. From the analytical data the molecular formula for the compound (8e) was found to be C₂₁H₂₁O₃N₅.

Elemental analysis:

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>75.72</td>
<td>4.50</td>
<td>8.9</td>
</tr>
<tr>
<td>Calculated</td>
<td>75.81</td>
<td>4.57</td>
<td>9.1</td>
</tr>
</tbody>
</table>

3. On the basis of chemical properties and analytical results, the compound (8e) was assigned the structure as 3-(2-hydroxy-3-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole.

Experiment No. 16:

Action of isoniazide on 4'-methoxy-3-benzoyl-8-methyl flavone (7f):

Formation of 3-(2-hydroxy-3-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (8f).

4'-Methoxy-3-benzoyl-8-methyl flavone (7f) (0.01 mol) (3.70g) was refluxed with isoniazide (0.02) (2.74g) for about 10 hours in pyridine (25 ml) medium, and was processed in experiment No. 11 to get (8f), m.p. 231°C. Yield-72%.
**Properties and constitution of the compound (8f):**

1. Properties of the compound (8f) were found similar to those of compound (8a).
   - TLC: Solvent (CCl₄) height = 2.4 cm.
   - Solute height = 1.4 cm.
   - Rf value = 0.58

2. From the analytical data, the molecular formula for the compound (8f) was found to be C₃₀H₂₃O₄N₃.

   **Elemental analysis:**

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.55</td>
<td>4.62</td>
<td>8.1</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.61</td>
<td>4.70</td>
<td>8.5</td>
</tr>
</tbody>
</table>

3. On the basis of chemical properties and analytical results, the compound (8f) was assigned the structure as 3-(2-hydroxy-3-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole.

**Experiment No. 17:**

**Action of isoniazide on 3-benzoyl-7-methyl flavone (7g):**

**Formation of 3-(2-hydroxy-4-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8g).**
3-benzoyl-7-methyl flavone (7g) (0.01) (3.40g) was refluxed with isoniazide (0.02mol) (2.74g) for about 10 hours in pyridine (25 ml) medium, and was processed as in experiment No. 11 to get (8g) m.p. 240°C. Yield -70%.

Properties and constitution of the compound (8g):

1. Properties of the compound (8g) were found similar to those of compound (8a).
   TLC: Solvent (CCl₄) height : 2.7 cm.
   Solute height : 1.9 cm.
   Rf value : 0.70

2. From the analytical data the molecular formula for the compound (8g) was found to be C₇₅H₃₂O₃N₃.
   Elemental analysis -

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>75.72</td>
<td>4.50</td>
<td>9.8</td>
</tr>
<tr>
<td>Calculated</td>
<td>75.81</td>
<td>4.57</td>
<td>9.1</td>
</tr>
</tbody>
</table>

3. On the basis of chemical properties and analytical results, the compound (8g) was assigned the structure as 3-(2-hydroxy-4-hydroxy methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole.
Experiment No. 18:
Action of isoniazide on 4'-methoxy-3-benzoyl-7-methyl flavone (7h):
Formation of 3-(2-hydroxy-4-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-
pyridoyl pyrazole (8h).

4'-Methoxy-3-benzoyl-7-methyl flavone (7h) (0.01 mol) (3.70g) was refluxed with
isoniazide (0.02mol) (2.74g) for about 10 hours in pyridine (25 ml) medium, and was
processed as in experiment No.11 to get (8h). m.p. 234°C. Yield 70%.

Properties and constitution of the compound (8h):

1. Properties of the compound (8h) were found similar to those of compound (8a):
   
   TLC: Solvent (CCl₄) height : 2.8 cm
   Solute height : 1.9 cm
   Rf value : 0.67

2. From the analytical data the molecular formula for the compound (8h) was found to
   be C₃₅H₂₃O₄N₃

   Elemental analysis:

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.55</td>
<td>4.62</td>
<td>8.3</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.61</td>
<td>4.70</td>
<td>8.5</td>
</tr>
</tbody>
</table>

3. On the basis of chemical properties and analytical results, the compound (8h) was
   assigned the structure as 3-(2-hydroxy-4-methyl phenyl)-4-benzoyl-5-(4-methoxy
   phenyl)-1-pyridoyl pyrazole.
Experiment No. 19:
Action of isoniazide on 3-benzoyl flavone (7i):
Formation of 3-(2-hydroxy phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole (8i).

3-Benzoyl flavone (7i) (0.01 mol) (3.26g) was refluxed with isoniazide (0.02mol) (2.74g) for about 10 hours in pyridine (25 ml) medium, and was processed as in experiment No. 11 to get (8i). m.p. 215°C. Yield 70%.

Properties and constitution of the compound (8i):

1. Properties of the compound (8i) were found similar to those of compound (8a).

   TLC: Solvent (CCl₄) height : 2.6 cm
   Solute height : 1.7 cm
   Rf value : 0.65

2. From the analytical data the molecular formula for the compound (8i) was found to be C₂₅H₁₉O₃N₃.

   Elemental analysis:
   
<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>75.44</td>
<td>4.20</td>
<td>9.2</td>
</tr>
<tr>
<td>Calculated</td>
<td>75.50</td>
<td>4.26</td>
<td>9.4</td>
</tr>
</tbody>
</table>

3. On the basis of chemical properties and analytical results, the compound (8i) was assigned the structure as 3-(2-hydroxy phenyl)-4-benzoyl-5-phenyl-1-pyridoyl pyrazole.
Experiment No. 20:

Action of isoniazide on 4'-methoxy-3-benzoyl flavone (7j):

Formation of 3-(2-hydroxy phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (8j).

4'-Methoxy-3-benzoyl flavone (7j) (0.01 mol) (3.56g) was refluxed with isoniazide (0.02 mol) (2.74g) for about 10 hours in pyridine (25 ml) medium, and was processed as in experiment No. 11 to get (8j). m.p. Yield 70%.

Properties and constitution of the compound (8j):

1. Properties of the compound (8j) were found similar to those of compound (8a).
   - TLC: Solvent (CCl₄) height 2.8 cm.
   - Solute height 1.7 cm
   - Rf value 0.60.

2. From the analytical data the molecular formula for the compound (8j) was found to be C₂₉H₂₁O₄N₅.

   Elemental analysis -

<table>
<thead>
<tr>
<th>Analysis</th>
<th>%C</th>
<th>%H</th>
<th>%N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>73.20</td>
<td>4.39</td>
<td>8.5</td>
</tr>
<tr>
<td>Calculated</td>
<td>73.26</td>
<td>4.42</td>
<td>8.8</td>
</tr>
</tbody>
</table>
3. On the basis of chemical properties and analytical results, the compound (8j) was assigned the structure as 3-(2-hydroxy phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole.

![Chemical structure](image)

(8j)

**Spectral analysis of the compound (8a):**

a) The IR spectra of the compound (8a) (spectrum No.13) showed the following absorption bands:

<table>
<thead>
<tr>
<th>Frequency cm(^{-1})</th>
<th>Intensity</th>
<th>Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1625</td>
<td>m</td>
<td>C = O stretching</td>
</tr>
<tr>
<td>3350</td>
<td>s</td>
<td>O - H stretching</td>
</tr>
<tr>
<td>1620</td>
<td>s</td>
<td>C = N stretching</td>
</tr>
<tr>
<td>1500</td>
<td>s</td>
<td>C = C stretching</td>
</tr>
<tr>
<td>1390</td>
<td>s</td>
<td>C - N stretching</td>
</tr>
<tr>
<td>1035</td>
<td>s</td>
<td>C - O (Phenolic)</td>
</tr>
</tbody>
</table>

b) The UV - VIS spectra of the compound (8a) (spectrum No.14) recorded in DMSO showed \(\lambda\) max at 256 nm for \(n \rightarrow \pi^*\) transition.

---

c. PMR spectrum of the compound (8a) (spectrum No. 15) recorded in DMSO showed following absorption peaks:

<table>
<thead>
<tr>
<th>Chemical Shift in δ</th>
<th>Nature of peak</th>
<th>No. protons</th>
<th>Type of protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.9</td>
<td>s</td>
<td>3H</td>
<td>- CH₃</td>
</tr>
<tr>
<td>7.2 - 7.6</td>
<td>m</td>
<td>17H</td>
<td>Ar - H</td>
</tr>
<tr>
<td>12</td>
<td>s</td>
<td>1H</td>
<td>- OH</td>
</tr>
</tbody>
</table>

**Probable Mechanism:**

As it has been explained (in the mechanism of pyrazoline, part II, chapter III) that electron donating group such as -OCH₃ at 4'-position of the side phenyl ring in flavone causes an increase in the yield. This may be attributed to the increase in electron density on oxygen of carbonyl group, due to electron flow from -OCH₃ group. This increased electron density accelerates the process of 1,2-addition of isoniazide which results in the formation of an intermediate adduct. This then loses the molecule of water, and undergoes cyclisation to give pyrazole.