PART V

ANTIBACTERIAL ACTIVITIES OF 3, 5-DIARYL-4-
BENZOYL-1-PYRIDOYL-$\Delta^2$-PYRAZOLINES AND 3, 5-
DIARYL-4- BENZOYL-1-PYRIDOYL PYRAZOLES
PART V

ANTIBACTERIAL ACTIVITIES OF 3, 5-DIARYL -4-
BENZOYL -1-PYRIDOYL -Δ²-PYRAZOLINES AND 3, 5-
DIARYL -4-BENZOYL -1-PYRIDOYL PYRAZOLES

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<th>Title</th>
<th>Page</th>
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PART-V

ANTIBACTERIAL ACTIVITIES OF 3,5-DIARYL-4-
BENZOYL-1-PYRIDOYL-\(\alpha^2\)-PYRAZOLINES AND 3,5-
DIARYL-4-BENZOYL-1-PYRIDOYL PYRAZOLES.

CHAPTER - 1

ORIGIN OF THE PROBLEM

From the survey of literature it was found that much work has been done over many
of the heterocyclic compounds for their antibacterial activities on gram positive and gram
negative bacteria.

Many synthetic flavones are known to possess various physiological activities\(^{10}\) Thakar
and Gill\(^{10}\), Hogale\(^{11}\) synthesised some flavones and tested them for antibacterial activities. In
many flavanoids, a large group of plant products are known to possess bactericidal and anti-
inflammatory and analgesic activities.\(^{12}\)

1. Mertzer, C.,
2. Griffith, J., Krewson, C.F. and
Maghashi, J.,

3. Koike, H.,
Folia Pharmacol. Japan, 1931, 12, 89.

4. Fukuda, T.,

5. Willman, J.J.,

6. Dimaggio, G.,
Chem. Abs., 1954, 48, 8888.

7. Highby, J.,

8. Nakamura, H., Octa, J and Fukuchi, G.,

9. Murti, V.V.S., Rao, N.V.S. and
Sheshadri, T.R.,

10. Thakar, K. A. and Gill, C. H.,

11. Hogale, M. B., Pawar, B. N. and
Nikam, B. P.,

12. Leshghbol, A., Leshghnol, C.,
Lesieur, D., Cazin, J.C., Lazin and
Randon, C.,
Chim. Ther. (T.), (1972), 356, Chem, abstr.,
78 (1973), 52753c.
A persual of the literature\textsuperscript{13-17} on pyrazolines have revealed that these compounds are not only use in textile and cinematographic films but they have also shown widely differing bacteriological activities. Substituted pyrazolines have been reported as antibacterial and antimicrobial agents.\textsuperscript{18,19} In pyrazolines N-heterocyclic nucleus incorporated with carbonyl group show significant biological activities. Similarly, pyrazoles are also found to possess uretic\textsuperscript{20} antihelminthetic\textsuperscript{21} activities in addition to fungicidal activity.\textsuperscript{22,23} Some substituted pyrazoles are also found to be antibacterial agents.\textsuperscript{24} Literature survey showed that 3,5-diaryl-4-benzyol-1-pyridoyl-\Delta^2-pyrazoline and 3,5-diaryl-4-benzyol-1-pyridoyl pyrazoles (prepared in part III and IV) have not yet been studied for anti bacterial activities. Hence it was though of interest to synthesise these compounds and study their anti-bacterial activities using gram positive and gram negative bacterias disc diffusion method.

\begin{itemize}
\end{itemize}
PROBLEM

The work presented in this chapter deals with the study of anti-bacterial activities of newly synthesised heterocyclic compounds against selected pathogenic organisms Escherichia Coli, Pseudomonas aeruginosa, Staphylococcus aureus, Citrobacter freundii, Proteus mirabilis, Bacillus megatherium and Salmonella typhi.

The following compounds were tested -

1. 3, 5-Diaryl-4-benzoyl-1-pyridoyl-Δ2-pyrazolines (6a-j)
2. 3, 5-Diaryl-4-benzoyl-1-pyridoyl pyrazoles (8a-j)
CHAPTER II

SUMMARY OF THE WORK

In the present work, following compounds were synthesised and were tested against seven bacteria for the study of their antibacterial activity.

3,5-Diaryl-4-benzoyl-1-pyridoyl-Δ²-pyrazolines (6a-i):

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Name of the compounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>(6a) 3- (2-Hydroxy -5-methyl phenyl) -4- benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>2.</td>
<td>(6b) 3 - (2-Hydroxy -5-methyl phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>3.</td>
<td>(6c) 3- (2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>4.</td>
<td>(6d) 3- (2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>5.</td>
<td>(6e) 3- (2-Hydroxy -3-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>6.</td>
<td>(6f) 3- (2-Hydroxy -3-methyl phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>7.</td>
<td>(6g) 3- (2-Hydroxy -4-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>8.</td>
<td>(6h) 3- (2-Hydroxy -4-methyl phenyl) - 4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>9.</td>
<td>(6i) 3- (2-Hydroxy phenyl) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
<tr>
<td>10.</td>
<td>(6j) 3- (2-Hydroxy phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline</td>
</tr>
</tbody>
</table>
3. 5-Diaryl -4-benzoyl -1-pyridoyl pyrazoles (8a-j):

11. (8a) 3-(2-Hydroxy -5-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole.
12. (8b) 3-(2-Hydroxy -5-methyl phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl - pyrazole.
13. (8c) 3-(2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole.
14. (8d) 3-(2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl -2-pyrazole.
15. (8e) 3-(2-Hydroxy -3-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole.
16. (8f) 3-(2-Hydroxy -3-methyl phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl pyrazole.
17. (8g) 3-(2-Hydroxy -4-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole.
18. (8h) 3-(2-Hydroxy -4-methyl phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl pyrazole.
19. (8i) 3-(2-Hydroxy phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole.
20. (8j) 3-(2-Hydroxy phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl pyrazole.

All the above compounds were synthesised and experimental details have been given in the part II and III of this thesis.

Structures of all the above compounds (at Sr.No.1-20) were confirmed on the basis of chemical properties, elemental analysis and spectral data (IR, UV and PMR). (Part V &III)

These compounds were tested against following seven pathogenic bacteria for their antibacterial activities using disc -diffusion method.

1. **Pseudomonas aeruginosa:**

These are gram negative bacillus. They are widely distributed in soil and water. P. aeruginosa produces a water soluble blue pigment, pyocyanin and a water soluble fluores-
cent pigment, pyoverdin. The organisms are also frequently opportunistic pathogen and can often be isolated from wounds, burns and urinary tract infections.

2. **Staphylococcus aureus**
   Staphylococcus are gram positive, nonmotile cocci arranged in groups. They are parasites occurring in the skin and mucous membranes of humans and animals.

3. **Citrobacter freundii**
   These are gram positive bacillus. These are found in respiratory tract, intestine and urinary tract. It is opportunistic pathogens and some times produces pneumonia urinary tract infections and suppurative infections.

4. **Escherichia Coli**
   These are gram negative bacillus. E.Coli occurs in the lower portion of the intestine of humans and animals, where it is part of the normal flora. Some strains can cause gastroenteritis, other can cause urinary tract infections.

5. **Proteus mirabilis**
   The gram negative rods P.mirabilis accounts for the majority of proteus infections in man. It is fairly uniform in its sensitivity to antibiotics and usually susceptible to penicillin, ampicillin and cephalosporin.

6. **Bacillus megatherium**
   Bacillus megatherium are gram positive bacillus arranged in groups. It may on occasion act as an opportunistic pathogen, causitive eye infection and septicaemia. They are generally motile but with peritrichous flagella. Optimum temperature 35°C - 37°C good growth occurs on ordinary media.

7. **Salmonella typhi**
   These are gram negative bacillus. They are pathogenic for humans, causing typhoid, gastroenteritis and septicemia, many strains also infect a variety of animals. Over 2000 different types of Salmonellae occur.
CHAPTER III

EXPERIMENTAL & DISCUSSION OF THE RESULTS

The compounds (Sr.No. 1 - 20) have been characterised on the basis of chemical properties, elemental analysis and spectral data (UV, IR, PMR). The melting points were recorded on 'Tempo' melting point apparatus and are uncorrected. The procedure for the preparation of 3, 5-diaryl-4-benzoyl-1-pyridoyl-$\Delta^2$-pyrazolines (6a-j) (at Sr.No. 1-10) has been described in chapter II of part III of this thesis and the procedure for the preparation of 3, 5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (8a-j) (at Sr.No. 11-20) has been given in chapter II of part IV of this thesis.

Material and Methods:

The compounds enlisted above were tested against pathogenic bacteria for their antibacterial activities using disk diffusion test method. The organisms tested were Pseudomonas aeruginosa, Staphylococcus aureus, Citrobacter freundii, Escherichia coli, Proteus mirabilis, Bacillus megatherium and Salmonella typhi.

Preparation Of Wet Discs For Antibiotic Sensitivity tests.

Method: Discs (6.25 mm) in diameter from No.1 Whatman filter paper were punched and batches of 100 in screw-capped bottles were dispersed and sterilised by dry heat at 140°C for 60 minutes. The solution of the compounds in DMF solvent was prepared so that 1ml contains 100 times the amount of the compound required in the disc. 1 ml solution of the compounds was added to each bottle of 100 discs and as the whole of this volume is absorbed it was assumed that each disc contains approximately 0.01ml. Discs in wet conditions were stored.
**Culture medium:**

The medium used throughout the experiment was HI-media (Indian Make) nutrient agar and having following composition.

**Composition of nutrient agar:**

- Peptone : 5.0 g/litre.
- Sodium chloride : 5.0 g/litre.
- Beef extract : 1.5 g/litre.
- Yeast extract : 1.5 g/litre.
- Agar : 15 g/litre.
- pH (Approx.) : 7.4 ± 0.2

The media was prepared by suspending 28 g ingredients in 1000 ml distilled water. It was boiled to dissolve the medium completely and was sterilised by Autoclave at 15 lbs/inch² pressure at 121°C temperature for 15 minutes. After sterilization it was cooled down to about 50°C and poured into sterile petriplates and allowed to solidify.

<table>
<thead>
<tr>
<th>Medium used</th>
<th>Nutrient agar medium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Plate 8.5 cm in diameter</td>
</tr>
<tr>
<td>Depth of agar</td>
<td>14 mm</td>
</tr>
<tr>
<td>Distance between 2 discs</td>
<td>2 cm away from each other.</td>
</tr>
<tr>
<td>Diameter of the antibiotic disc</td>
<td>6.25 mm in diameter.</td>
</tr>
<tr>
<td>Not more than five disks were used</td>
<td></td>
</tr>
</tbody>
</table>

**Test procedure:**

The culture material was inoculated in a nutrient broth and it was kept at 37°C for 24 hours incubation. The culture plate nutrient agar was dried until its surface was free from visible moisture. The inoculating material was then flooded on the surface of nutrient agar uniformly in presence of taking with all aseptic precautions and supernatant was discarded.
The plate was dried again for up to 30 minutes without further delay and the compound discs were applied to at adequate spacing (2 cm or more apart) to the surface of the plate with sterile fine-pointed forceps and gently pressed to ensure full contact with the medium and moistening of the disc. Control was run using plane DMF solvent for aseptic conditions. The plates were incubated at 37°C for 18-24 hrs. After incubation degree of sensitivity to drugs is determined by measuring the visible clear areas of growth of free zones (zones of inhibition) produced by diffusion of antibiotics into the media from the discs.

Width of the zone of inhibition depends on:

1. Size of inoculum
2. Nature of culture medium
3. Presence of inhibitors
4. Concentration of agar in the medium
5. Thickness of the medium in the plate.
6. Condition and time of incubation.
7. Composition of antibiotic disk.

Zones of inhibition are measured (including 6 mm of disk diameter) and reported. The results are cited in Table No. 1 and 2.

**Table 1**: Antibacterial activities of 3, 5-diaryl-4-benzoyl-1-pyridoyl-Δ2-pyrazolies (6a-j).

**Table 2**: Antibacterial activities of 3, 5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (8a-j).

**N.B.**

++++: Strongly active, range > 12 mm
++++: Moderately active, range 8-12 mm
++ : Weakly active, range < 8 mm
-- : Inactive.
### TABLE-1
Antibacterial Activities of 3, 5-diaryl -4-benzoyl -1-pyridoyl -Δ²-pyrazolines (6a-j)

<table>
<thead>
<tr>
<th>Organisms</th>
<th>6a</th>
<th>6b</th>
<th>6c</th>
<th>6d</th>
<th>6e</th>
<th>6f</th>
<th>6g</th>
<th>6h</th>
<th>6i</th>
<th>6j</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.aeruginosa</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>S.aureus</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>C.frundii</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>E.coli</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>+++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>P.mirabilis</td>
<td>++</td>
<td>--</td>
<td>++</td>
<td>+++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>++</td>
</tr>
<tr>
<td>B.megatherium</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>S.typhi</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>+++</td>
<td>--</td>
</tr>
</tbody>
</table>

### TABLE-2
Antibacterial Activities of 3, 5-diaryl -4-benzoyl -1-pyridoyl pyrazoles (8a-j)

<table>
<thead>
<tr>
<th>Organism</th>
<th>8a</th>
<th>8b</th>
<th>8c</th>
<th>8d</th>
<th>8e</th>
<th>8f</th>
<th>8g</th>
<th>8h</th>
<th>8i</th>
<th>8j</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.aeruginosa</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>S.aureus</td>
<td>--</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>C.frundii</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>E.coli</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>P.mirabilis</td>
<td>+++</td>
<td>--</td>
<td>+++</td>
<td>+++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>B.megatherium</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>++</td>
</tr>
<tr>
<td>S.typhi</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>+++</td>
<td>--</td>
</tr>
</tbody>
</table>
Discussion of the Results:

All the seven organisms studied were human pathogens. From the result of screening it is cleared that the following compounds are effective against the said organisms.

I) 3, 5-Diaryl-4-benzoyl-1-pyridoyl-Δ2-pyrazolines.

From the Table 1, the compound 6a showed moderate activities against S. aureus and C. frunidii, weak activities against P.mirabilis, B.megatherium and S. typhi and was inactive towards Paeruginosa and E.Coli.

The compound 6b was weakly active towards S.aureus, C. frunidii and S typhi and was inactive towards P.aeruginosa, E.Coli, P.mirabilis and B.megatherium.

The compound 6c was moderately active against B.megatherium and S.typhi while it showed weak activities against S.aureus, C.frunidii, E.Coli and P.mirabilis and was inactive towards Paeruginosa.

The compound 6d showed moderate activities towards E.Coli, P.mirabilis, B.megatherium and S.typhi while was weakly active towards S.aureus and C.frunidii.

The compounds 6e was weakly active against E.Coli, P.mirabilis and B.megatherium and was inactive towards Paeruginosa, S.aureus, C.frunidii and S.typhi.

The compound 6f was inactive against all organisms.

The compound 6g was only moderately active against C.frunidii.

The compound 6h was moderately active against C.frunidii and weakly active against S.typhi and was inactive against rest of the organisms.

The compound 6i was moderately active against C.frunidii, E.Coli, B.megatherium and S.typhi while weakly active against A.aureus and inactive against Paeruginosa and P.mirabilis.

The compound 6j was moderately active against C.frunidii and weakly active against S.aureus, E.coli and P.mirabilis and inactive towards Paeruginosa, B.megatherium and S.typhi.
II) 3, 5-Diaryl-4-benzoyl-1-pyridoyl pyrazoles.

From the Table 2, the compound 8a showed strong activities against P. mirabilis and B. megatherium, moderate activities against C. frundii, E. coli and S. typhi, weak activities against P. aeruginosa and inactive against S. aureus.

The compound 8b was strongly active against B. megatherium, moderately active towards E. coli and S. typhi, weakly active against S. aureus and C. frundii and inactive against P. aeruginosa and P. mirabilis.

The compound 8c was strongly active towards S. typhi and B. megatherium, moderately active against E. coli and P. mirabilis, weakly active towards S. aureus and C. frundii and inactive towards P. aeruginosa.

The compound 8d showed activities against all the organisms. It was moderately active against E. coli, P. mirabilis, B. megatherium and S. typhi and was weakly active against P. aeruginosa, S. aureus and C. frundii.

The compound 8e was moderately active against C. frundii, E. coli, B. megatherium and S. typhi and was inactive against rest of the organisms.

The compound 8f was moderately active against C. frundii and E. coli and was inactive against rest of the organisms.

The compound 8g was moderately active against E. coli and B. megatherium and inactive against rest of the organisms.

The compound 8h was totally inactive towards all organisms.

The compound 8i was weakly active against C. frundii only.

The compound 8j was moderately active to S. typhi, weakly active towards C. frundii, P. mirabilis and B. megatherium and inactive towards P. aeruginosa, S. aureus and E. coli.

In view of the structure activity relationship the appreciable enhancement of the antibacterial activity was observed. It has been also found that the antibacterial activities of the test compounds increases with increase in structure complexity.

Thus, from the results of screening, it was observed that most of the heterocyclic
compounds were found more or less effective against the organisms. The bromo-containing pyrazolines and pyrazoles were found more effective against all the organisms. Hence, these compounds can easily be used for the treatment of diseases caused by test pathogens only when they do not have any toxic and other side effects.

Pyrazolines 6a, 6c, 6d and 6j and pyrazoles 8a, 8b, 8c and 8d could be examined further for obtaining more convincing results which shall be encouraging therefore, to incorporate therapeutic values of these compounds in future.
LIST OF NEW COMPOUNDS

3, 5-Diaryl -4-benzoyl -1-pyridoyl -Δ²-pyrazolines, (6a -j).

1. 3- (2-Hydroxy -5-methyl phenyl ) -4- benzoyl -5-phenyl -1-pyridoyl-Δ²-pyrazoline, (6a).

2. 3 -(2-Hydroxy -5-methyl phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline, (6b).

3. 3- (2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline, (6c).

4. 3- (2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline, (6d).

5. 3-(2-Hydroxy -3-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline, (6e).

6. 3-(2-Hydroxy -3-methyl phenyl) -4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline, (6f).

7. 3- (2-Hydroxy -4-methyl phenyl ) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline, (6g).

8. 3-(2-Hydroxy -4-methyl phenyl) - 4-benzoyl -5-(4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline, (6h).

9. 3- (2-Hydroxy phenyl) -4-benzoyl -5-phenyl -1-pyridoyl -Δ²-pyrazoline,(6i).

10. 3 -(2-Hydroxy phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl -Δ²-pyrazoline, (6j).
3, 5-Diaryl -4-benzoyl -1-pyridoyl pyrazoles (8a-j)

11. 3- (2-Hydroxy -5-methyl phenyl ) -4- benzoyl -5-phenyl -1-pyridoyl pyrazole, (8a).
12. 3 - (2-Hydroxy -5-methyl phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl pyrazole, (8b).
13. 3- (2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole, (8c).
14. 3- (2-Hydroxy -3-bromo -5-methyl phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl pyrazole, (8d).
15. 3- (2-Hydroxy -3-methyl phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole, (8e).
16. 3- (2-Hydroxy -3-methyl phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl pyrazole, (8f).
17. 3- (2-Hydroxy -4-methyl phenyl ) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole, (8g).
18. 3- (2-Hydroxy -4-methyl phenyl) - 4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl pyrazole, (8h).
19. 3- (2-Hydroxy phenyl) -4-benzoyl -5-phenyl -1-pyridoyl pyrazole, (8i).
20. 3- (2-Hydroxy phenyl) -4-benzoyl -5- (4-methoxy phenyl) -1-pyridoyl pyrazole, (8j).
LIST OF RESEARCH PAPERS PUBLISHED

Asian Journal of Chemistry -

1. Synthesis of 3, 5-Diaryl-4-Benzoyl-1-Pyridoyl-Δ²-Pyrazolines

2. Synthesis and Characterization of 3, 5-Diaryl-4-Benzoyl-1-Pyridoyl Pyrazoles

3. Studies in Co(II), Cu(II) and Ni(II) Complexes with Substituted Pyrazoline and Pyrazole
   0.1 Ionic Strength pH-metrically.
   Vol. 11, No. 2 (1999), 420-423.

4. Antimicrobial activities of 3, 5-Diaryl-4-Benzoyl-1-Pyridoyl-Δ²-Pyrazolines
   Vol. 11, No. 3 (1999), 1064-1066.

5. Antimicrobial activities of 3, 5-Diaryl-4-Benzoyl-1-Pyridoyl Pyrazoles
   Vol. 11, No. 3 (1999), 1077-1079.
Synthesis of 3,5-Diaryl-4-Benzoyl-1-Pyridoyl-Δ²-Pyrazolines

M. V. KADU*, and V.S. JAMODE
Post-Graduate Department of Chemistry
Amravati University, Amravati-444 602, India

Some new 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ²-pyrazolines (3) have been synthesised by the action of isoniazid on 3-aryl flavanones (2) in pyridine medium. Structures of these compounds have been established by spectral analysis (NMR, IR and UV) and elemental analysis.

The literature survey reveals the importance of chalcones and flavanones as a valuable starting materials for the synthesis of heterocycles like pyrazolines, pyrazoles and isoxazolines etc. Formation of pyrazolines has been reported\(^{1\text{-}3}\) by the action of hydrazines or phenyl hydrazines on chalcones and flavanones in different solvents like DMSO or ethanol, etc.

Pyrazolines were formally regarded only as an intermediate in the synthesis of pyrazoles, but these have recently come to notice for their use as effective bleaching agents, as luminescents, fluorescent\(^{4\text{-}8}\) and as oxidised forms in the development of cine films\(^{9}\) apart from drugs. Pyrazoline derivatives have been found to be effective insecticides\(^{10}\), pharmaceuticals and fungicidal agents.\(^{11}\) Thus from the survey of literature it is cleared that 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ²-pyrazolines are not yet synthesised. It was, therefore, thought of interest to synthesise 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ²-pyrazolines (3) from 3-aryl flavanones (2).

The present work deals with the synthesis of 3,5-diaryl-1-benzoyl-1-pyridoyl-
Δ²-pyrazoline (3) from 3-aryloyl flavonoes (2) and isoniazide in pyridine medium. Structures of these compounds have been established by elemental analysis and spectral analysis.

Melting points are uncorrected. IR spectra in KBr were recorded on PE-983/PE-781 IR spectrophotometer, NMR in DMSO on Varian EM 390-cw NMR spectrophotometer and UV on Varian Cary 2390 UV spectrophotometer.

(1) Preparation of 1,3-diaryl-1,3-propanedione (1a–1j)

2-Benzoyloxy acetophenone (0.05) was dissolved in dry pyridine (40 mL) (dried over KOH). The solution was warmed up to 60°C and pulverised KOH (0.1 M) was added slowly with constant stirring. After 4 h, the reaction mixture was acidified by adding ice-cold HCl (1:1). The brownish yellow product obtained was filtered, washed with sodium bicarbonate solution (2%) and sufficient water. The product obtained was crystallised from ethanol-acetic acid mixture.

(2) Preparation of 3-aryloyl flavonones (2a–2j)

1,3-Diaryl-1,3 propanediones (1) (0.01 M) and aromatic aldehyde (benzaldehyde and anisaldehyde) (0.01 M) were refluxed for about 1 h in ethanol (25 mL) containing a few drops of piperidine. The reaction mixture was cooled and the product separated was crystallised from ethanol-acetic acid mixture.

Spectral interpretation of 2d

IR (ν<sub>max</sub>) : 1625 cm<sup>-1</sup> ν(C=O); 1600 cm<sup>-1</sup> ν(C=O) (two C=O groups);
552 cm<sup>-1</sup> ν(C=Br); 1235 ν(C—O—C).

NMR : δ 2.32 (S, 3H, Ar—CH<sub>3</sub>); 3.73 (S, 3H, O—CH<sub>3</sub>); 5.04 (d, 1H);
5.91 (d, 1H); 6.3–7.8 (m, 10H, Ar–H).

UV (λ<sub>max</sub>) : 340 nm.

(3) Preparation of 3,5-diaryl-4-benzoyl-1-pyridoyl-Δ²-pyrazolines (3a–3j)

3-Aroyl flavonones (2a–j) (0.1 M) were refluxed with isoniazide (0.2 M) for 8–10 h in pyridine solvent. The reaction was decomposed by acidified water, filtered and washed with sufficient water. It was crystallised from ethanol-acetic acid mixture to obtain a white crystalline solid. Yield 60–80%.

Spectral interpretation of 3d

IR (ν<sub>max</sub>) : 3400 cm<sup>-1</sup> ν(C—OH); 550 cm<sup>-1</sup> ν(C—Br); 1550 cm<sup>-1</sup> ν(C=O);
1200 cm<sup>-1</sup> ν(C—N); 1150 cm<sup>-1</sup> ν(C—O).

NMR : δ 2.4 (S, 3H, —CH<sub>3</sub>); 3.6 (d, 1H, —CH); 6.8 (d, 1H, —CH); 8 to
8.5 (m, 17H, Ar—H); 11.8 (S, 1H, —OH).

UV (λ<sub>max</sub>) : 280 nm

Physical data of series (3a–3j) were recorded in Table 1.
TABLE-I
PHYSICAL CHARACTERISATION DATA OF SYNTHESISED COMPOUNDS
3.5-Diaryl-4-benzoyl-1-pyridoyl-Δ²-pyrazolines (3a–3j)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>Molecular formula</th>
<th>N% found (calcd.)</th>
</tr>
</thead>
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<tr>
<td>3a</td>
<td>H</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>67</td>
<td>250</td>
<td>C₂₀H₂₃O₄N₃</td>
<td>8.5 (9.1)</td>
</tr>
<tr>
<td>3b</td>
<td>H</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>OCH₃</td>
<td>70</td>
<td>215</td>
<td>C₂₀H₂₅O₄N₃</td>
<td>7.8 (8.5)</td>
</tr>
<tr>
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<td>Br</td>
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<td>H</td>
<td>65</td>
<td>237</td>
<td>C₂₅H₂₂O₅N₃Br</td>
<td>7.2 (7.7)</td>
</tr>
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<td>Br</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>OCH₃</td>
<td>72</td>
<td>227</td>
<td>C₂₅H₂₄O₄N₃Br</td>
<td>8.3 (7.3)</td>
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<td>H</td>
<td>H</td>
<td>H</td>
<td>66</td>
<td>256</td>
<td>C₂₉H₂₃O₃N₃</td>
<td>9.7 (9.1)</td>
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<td>3f</td>
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<td>H</td>
<td>H</td>
<td>OCH₃</td>
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<td>225</td>
<td>C₂₅H₂₅O₅N₃</td>
<td>8.1 (8.5)</td>
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<td>3g</td>
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<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>70</td>
<td>236</td>
<td>C₂₅H₂₃O₃N₃</td>
<td>8.7 (9.1)</td>
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<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>OCH₃</td>
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<td>214</td>
<td>C₂₅H₂₄O₄N₃</td>
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<td>H</td>
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<td>215</td>
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<td>8.9 (9.3)</td>
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<td>3j</td>
<td>H</td>
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<td>H</td>
<td>H</td>
<td>OCH₃</td>
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<td>210</td>
<td>C₂₉H₂₃O₄N₃</td>
<td>7.5 (8.8)</td>
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REFERENCES


(Received: 1 September 1997; Accepted: 14 November 1997) AJC-1396
Synthesis and Characterization of 3,5-Diaryl-4-Benzoyl-1-Pyridoyl Pyrazoles

M.V. KADU* and V.S. JAMODE
Post-Graduate Department of Chemistry
Amravati University, Amravati-444 602, India.

Some new 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles have been synthesised by the action of isoniazid on 3-aryl flavones in pyridine medium. Structures of these compounds have been established by spectral analysis (NMR, IR and UV) and elemental analysis.

INTRODUCTION

The literature survey reveals the importance of chalcones and flavanones as a valuable starting materials for the synthesis of heterocycles like pyrazolines, pyrazoles isoxazolines etc. Formation of pyrazoles has been reported\(^1\) by the action of hydrazines or phenyl hydrazines on flavones and chalcones in different solvents like methanol, DMSO, acetic acid, etc. Pyrazole is a class of compounds which are widely useful in drugs and dyes\(^4\). These compounds also show physiological activities.\(^5\) Trifluoromethyl-1-aryl derivatives of pyrazoles are used as analgesics, antipyretic and antiinflammatory agents.\(^6\) 1-phenyl derivatives are effective antidiabetics.\(^7\) Acyl amino and chloro pyrazoles have been found to be effective herbicides.\(^8\) Phenyl pyrazoles act as insecticides\(^9\) and alkyl pyrazoles are also used as hypolipidemic agents.\(^10\)

The literature survey clearly indicates that 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles are not yet synthesised. It was, therefore, thought of interest to synthesise 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (4) from 3-aryl flavones (3). Thus present work deals with the synthesis of some new 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (4) from 3-aryl flavones (3) (Scheme-1) and isoniazid in pyridine medium. Structures of these compounds have been established by elemental analysis and spectral analysis.

EXPERIMENTAL

Melting points are uncorrected. IR spectra in KBr were recorded on PE-983/PE-781 IR spectrophotometer. NMR in DMSO on Varian EM 390-cw NMR spectrophotometer and UV on Varian Cary 239 OUV spectrophotometer.

(1) Preparation of 1,3-diaryl-1,3-propanedione (1a–1j)—2-Benzoyloxy acetophenone (0.05 M) was dissolved in dry pyridine (40 mL) (dried over KOH). The solution was warmed up to 60°C and pulverised KOH (0.1 M) was added slowly with constant stirring. After about 4 h, the reaction mixture was acidified
by adding ice-cold HCl (1:1). The brownish yellow product obtained was filtered, washed with sodium bicarbonate solution (2%) and sufficient water. The product obtained was crystallised from ethanol-acetic acid mixture.

(2) Preparation of 3-aryloxylanones (2a–2j): 1,3-Diaryl-1,3-propanediones (1) (0.01 M) and aromatic aldehyde (benzaldehyde and anisaldehyde) (0.01 M) were refluxed for about 1 h in ethanol (25 mL) containing a few drops of piperidine. The reaction mixture was cooled and the product separated was crystallised from ethanol-acetic acid mixture. The structures of these compounds are confirmed by spectral analysis.19

(3) Preparation of 3-aryloxylanones (3a–3j)—3-Aroyl flavanones (2a–j) (0.01 M) and SeO₂ (0.001 M) were refluxed in dioxane for about 18 h. 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 water. It was recrystallized from ethanol-acetic acid mixture. Yield 80 to 95%.

Spectral interpretation of 3a:

IR (v_max) 1650 cm⁻¹ ν(C=O); 1615 cm⁻¹ ν(C=O); 1590–1585 cm⁻¹ ν(C=C); 1245 cm⁻¹ ν(C−O−C).

¹H NMR: δ 2.30 (S, 3H, Ar−CH₃); 3.80 (S, 3H, Ar−O−CH₃); 6.7–8.3 (m, 11H, Ar−H).

UV (λ_max) 322 nm.

(Scheme-1)

Physical data of the series (3a–3j) were recorded in Table-1
TABLE-1
PHYSICAL CHARACTERISATION DATA OF SYNTHESISED COMPOUNDS
3-Aroyl Flavones (3a–3j)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>Molecular formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>85</td>
<td>132</td>
<td>C₂₃H₁₆O₅</td>
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<tr>
<td>3b</td>
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<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>OCH₃</td>
<td>85</td>
<td>156</td>
<td>C₂₄H₁₈O₄</td>
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<td>180</td>
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</tr>
<tr>
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<td>195</td>
<td>C₂₄H₁₇O₄Br</td>
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<td>H</td>
<td>H</td>
<td>H</td>
<td>92</td>
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</tr>
<tr>
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<td>H</td>
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<td>C₂₄H₁₈O₃</td>
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<td>H</td>
<td>H</td>
<td>H</td>
<td>70</td>
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<td>C₂₃H₁₆O₃</td>
</tr>
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<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>OCH₃</td>
<td>72</td>
<td>162</td>
<td>C₂₄H₁₈O₄</td>
</tr>
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<td>3i</td>
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<td>H</td>
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<td>C₂₃H₁₆O₃</td>
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<td>80</td>
<td>185</td>
<td>C₂₃H₁₆O₄</td>
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</table>

(4) Preparation of 3,5-diaryl-4-benzoyl-1-pyridyl pyrazoles (4a–4j):
3-Aroyl flavones (3a–j) (0.01 M) were refluxed with isoniazide (0.2 M) for 8–10 h in pyridine solvent. The reaction mixture was 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%.

Spectral interpretation of 4a:
IR (νₘₐₓ) 1625 cm⁻¹ ν(C=O); 3350 cm⁻¹ ν(OH); 1620 cm⁻¹ ν(C=–N); 1500 cm⁻¹ ν(C=C); 1390 cm⁻¹ ν(C=N); 1035 cm⁻¹ ν(C–O) (phenol).
NMR: δ 1.9 (S, 3H, –CH₃); 7.2–7.6 (m, 17H, Ar–H); 12 (S, 1H, =OH).
UV (λₘₐₓ) 256 nm.
Physical data of series (4a–4j) were recorded in Table-2.

TABLE-2
PHYSICAL CHARACTERISATION DATA OF SYNTHESISED COMPOUNDS
3,5-Diaryl-4-Benzoyl-1-Pyridyl Pyrazoles (4a–4j)

<table>
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<tr>
<th>Compound</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
<th>Yield (%)</th>
<th>m.p. (°C)</th>
<th>Molecular formula</th>
<th>N % found (calc)</th>
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<tbody>
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<td>H</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
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<td>252</td>
<td>C₂₅H₂₁O₃N₃</td>
<td>8.9 (9 )</td>
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<td>4b</td>
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<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>OCH₃</td>
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<td>232</td>
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<td>8.4 (8.5)</td>
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<td>H</td>
<td>H</td>
<td>65</td>
<td>215</td>
<td>C₂₅H₂₀O₃N₃Br</td>
<td>7.5 (7.8)</td>
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<td>H</td>
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<td>234</td>
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<td>H</td>
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<td>9.2 (9.4)</td>
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<td>C₂₅H₂₁O₄N₃</td>
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REFERENCES


(Received: 4 November 1997; Accepted: 29 December 1997) AJC-1424
Studies in Co(II), Cu(II) and Ni(II) Complexes with Substituted Pyrazoline and Pyrazole at 0.1 Ionic Strength pH-metrically

M.V. KADU*, V.S. JAMODE and M.L. NARWADE†

Department of Chemistry
Amravati University
Amravati-444 602, India

The interaction of Co(II), Cu(II) and Ni(II) with 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl-Δ2-pyrazoline and 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole have been investigated by Bjerrum method as adopted by Calvin and Wilson. The stability constants of 1:1 and 1:2 complexes of Co(II), Cu(II) and Ni(II) have been studied at constant temperature (27 ± 0.1°C) and 0.1 M ionic strength (NaOH) in 70% DMF-water mixture. It is observed that formation of 1:1 and 1:2 complexes is occurring simultaneously.

INTRODUCTION

Metal chelates of 3-(o-hydroxyphenyl)-5-phenyl isoxazole with Be(II), Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and UO2(II) have been investigated by Vithalrao et al.1 The spectral properties of 3-(o-hydroxy phenyl)-5-phenyl isoxazole were reported by Murthy et al.2 Metal ligand stability constants of lanthanides with some substituted pyrazolines and diketones are studied by Sawalakhe and Narwade.3 Manadkare et al.4 have studied the metal-ligand stability constant of Cu(II) with some substituted coumarins pH-metrically in 70% dioxane-water mixture. Sondawale et al.5 have determined metal-ligand stability constants and adiabatic compressibility of Cu(II)-peptide complexes recently. Gudadhe et al.6 have performed the study of stability constants of Th(IV) complexes with some substituted pyrazolines.

In view of the analytical applications of pyrazolines and pyrazoles, it is of interest to study the physico-chemical properties such as stability constants of Co(II), Cu(II) and Ni(II) complexes with 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl-Δ2-pyrazoline and 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole. In the present investigation 70% DMF-water mixture is used as a solvent for preparation of solution.

†Department of Chemistry, Vidarbha Mahavidyalaya, Amravati-444 604, India.
EXPERIMENTAL

All chemicals such as sodium hydroxide, nitric acid, potassium nitrate and metal salts of AnalR grade were used in the present investigation.

3-(2-Hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl-Δ3-pyrazoline (ligand-1) and 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole (ligand-2) were prepared by following literature method. Both ligands were crystallized and their purity was checked by TLC before use. The solutions of purified ligands were prepared in DMF and standardised by potentiometric techniques.

ELICO pH-meter model LI-10 (accuracy ± 0.05 unit) with a glass electrode and saturated calomel electrode was used for the measurement of pH. It was calibrated by buffer of pH 4.0, 7.0 and 9.2 at 27°C before proceeding for titrations.

The experimental procedure involved pH-metric titrations of (i) free acid (0.01 M) (ii) free acid (0.01 M) and ligand (20 × 10⁻⁴ M) and (iii) free acid (0.01 M) + ligand (20 × 10⁻⁴ M) + metal ion (4 × 10⁻⁴ M) against standard NaOH solution. The ionic strength of all the solutions was maintained constant (0.1 M) by adding an appropriate quantity of 1 M potassium nitrate.

The titrations were carried out in 100 mL pyrex glass beaker kept in a water bath maintained at constant temperature (27 ± 0.1°C). Nitrogen gas was slowly bubbled through the solution to remove the oxygen and carbon dioxide. The pH-meter readings were taken only after the gas bubbling was completely stopped. In aqueous-organic mixture pH values were corrected by use of Van-Uitert and Hass equation.
RESULTS AND DISCUSSION

Proton-ligand formation constants: The deviation of acid-ligand curves from acid curves started around pH = 5.70 for both ligands and increased continuously up to pH 12.0. It shows that dissociation of —OH group occurs which is present in the ligand part of the complex structure. The values of $\tilde{n}_A$ were calculated by Irving-Rossotti’s expression. The pKa values for both systems were calculated by half integral and pointwise calculations which are presented in Table-1.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>System</th>
<th>Constant pK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Half integral</td>
</tr>
<tr>
<td>1.</td>
<td>3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl-$\Delta^2$-pyrazoline</td>
<td>7.80</td>
</tr>
<tr>
<td>2.</td>
<td>3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole</td>
<td>7.40</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S. No.</th>
<th>System</th>
<th>Constants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>log $K_1$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Half integral</td>
</tr>
<tr>
<td>1.</td>
<td>Co(II) 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl-$\Delta^2$-pyrazoline</td>
<td>9.045</td>
</tr>
<tr>
<td>2.</td>
<td>Cu(II) 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl-$\Delta^2$-pyrazoline</td>
<td>8.045</td>
</tr>
<tr>
<td>3.</td>
<td>Ni(II) 3-(2-hydroxy-5-methyl phenyl)-4-benzoyl-5-phenyl-1-pyridoyl-$\Delta^2$-pyrazoline</td>
<td>8.015</td>
</tr>
<tr>
<td>4.</td>
<td>Co(II) 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole</td>
<td>6.448</td>
</tr>
<tr>
<td>5.</td>
<td>Cu(II) 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole</td>
<td>6.978</td>
</tr>
<tr>
<td>6.</td>
<td>Ni(II) 3-(2-hydroxy-3-bromo-5-methyl phenyl)-4-benzoyl-5-(4-methoxy phenyl)-1-pyridoyl pyrazole</td>
<td>6.558</td>
</tr>
</tbody>
</table>

Metal-ligand stability constants: The values of $\tilde{n}$ were evaluated from Irving-Rossotti’s expression which were used to calculate the metal-ligand stability constants. The metal-ligand stability constants for all the systems were calculated by half integral and pointwise calculation methods. These values are presented in Table-2. It could be seen from Table-2 that there is no differences
as such between the log K values for both the complexes. It showed that there must be simultaneously complex formations and not stepwise formation. The order of stability of metal-ligand complexes is Co(II) > Cu(II) > Ni(II) for pyrazoline ligand and Co(II) < Cu(II) < Ni(II) for pyrazole ligand. The lesser values of log K in case of pyrazole may be due to the presence of bromine atom as an electron withdrawing group.

REFERENCES


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NOTE

Antibacterial Activities of 3,5-Diaryl-4-Benzoyl-1-Pyridoyl–
$\Delta^2$-Pyrazolines

M.V. KADU*, V.S. JAMODE and D.H. TAMBEKART†
Post Graduate Department of Chemistry
Amravati University, Amravati-444 602, India

3,5-Diaryl-4-benzoyl-1-pyridol-$\Delta^2$-pyrazolines have been synthesised
from 3-aryyl flavanones and isoniazide in pyridine medium. Structures of
these compounds have been characterised by spectral analysis. These com-
ounds were tested for their antibacterial activities against pathogenic
bacteria and are found to have remarkable activity.

From the survey of literature pyrazolines have been found to be effective
insecticides$^{1-3}$, antinflammatory$^4$, bacterial$^5-8$, pharmaceutical$^9$, fungicidal$^{5,10,11}$
and herbicidal agents$^{12}$.

The present work deals with the study of antibacterial activities of 3,5-diaryl-
4-benzoyl-1-pyridol-$\Delta^2$-pyrazolines (3a–j). These compounds were tested against
P. aeruginosa, S. aureus, C. freundii, E. coli, P. mirabilis, B. megatherium and
S. typhi. Some of them were found to be highly active against microbes.

Melting points were uncorrected. The structures of these compounds were
established on the basis of their elemental analysis and spectral data. Preparation
and characterization of 3,5-diaryl-4-benzol-1-pyridoyl-$\Delta^2$-pyrazolines (3a–j) are
already reported$^{13}$ (Physical data of pyrazolines (3a–j) is recorded in Table-1.)

<table>
<thead>
<tr>
<th>Compounds</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>R₅</th>
<th>m.p. (°C)</th>
<th>m.f.</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>250</td>
<td>C₂₉H₂₃O₃N₃</td>
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<tr>
<td>3b</td>
<td>H</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>OCH₃</td>
<td>215</td>
<td>C₂₉H₂₃O₄N₃</td>
</tr>
<tr>
<td>3c</td>
<td>Br</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>237</td>
<td>C₂₉H₂₂O₃N₃B</td>
</tr>
<tr>
<td>3d</td>
<td>Br</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>OCH₃</td>
<td>227</td>
<td>C₂₉H₂₃O₄N₃Bt</td>
</tr>
<tr>
<td>3e</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>256</td>
<td>C₂₉H₂₂O₃N₃</td>
</tr>
<tr>
<td>3f</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>OCH₃</td>
<td>225</td>
<td>C₂₉H₂₃O₄N₃</td>
</tr>
<tr>
<td>3g</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>236</td>
<td>C₂₉H₂₃O₃N₃</td>
</tr>
<tr>
<td>3h</td>
<td>H</td>
<td>CH₃</td>
<td>H</td>
<td>H</td>
<td>OCH₃</td>
<td>214</td>
<td>C₂₉H₂₃O₄N₃</td>
</tr>
<tr>
<td>3i</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>215</td>
<td>C₂₉H₂₃O₃N₃</td>
</tr>
<tr>
<td>3j</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>OCH₃</td>
<td>210</td>
<td>C₂₉H₂₃O₄N₃</td>
</tr>
</tbody>
</table>

* Post Graduate Department of Microbiology, Amravati University, Amravati-444 602, India
† Post Graduate Department of Chemistry, Amravati University, Amravati-444 602, India
Antibacterial activity

The titled compounds were screened for their antibacterial activities using bacteria *Pseudomonas aeruginosa, Staphylococcus aureus, Citrobacter freundii, Escherichia coli, Proteus mirabilis, Bacillus megatherium* and *Salmonella typhi* by paper disc method at a concentration of 50 µg/2 mL using DMF as a solvent. After 24 h of inhibition at 37°C the zones of inhibition are measured in mm and are recorded in Table-2.

<table>
<thead>
<tr>
<th>Organism</th>
<th>3a</th>
<th>3b</th>
<th>3c</th>
<th>3d</th>
<th>3e</th>
<th>3f</th>
<th>3g</th>
<th>3h</th>
<th>3i</th>
<th>3j</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. aeruginosa</em></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td><em>S. aureus</em></td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td><em>C. freundii</em></td>
<td>8</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>8</td>
<td>10</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>-</td>
<td>-</td>
<td>7</td>
<td>11</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>P. mirabilis</em></td>
<td>6</td>
<td>-</td>
<td>7</td>
<td>11</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>B. megatherium</em></td>
<td>7</td>
<td>-</td>
<td>8</td>
<td>8</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td><em>S. typhi</em></td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7</td>
<td>9</td>
</tr>
</tbody>
</table>

Strongly active range: > 12 mm; Moderately active range: 8–12 mm; Weakly active range: < 8 mm; Inactive.

In case of antibacterial activities from Table-2 it has been observed that all compounds (3a–j) were inactive against *P. aeruginosa*.

The compound 3a showed moderate activities against *S. aureus* and *C. freundii* and weak activity against *P. mirabilis, B. megatherium* and *S. typhi*.

The compound 3b showed weak activities towards *S. aureus, C. freundii* and *S. typhi*.

The compound 3c showed moderate activities against *B. megatherium* and *S. typhi* and was weakly active against *S. aureus, C. freundii, E. coli* and *P. mirabilis*.

The compound 3d showed moderate activities towards *E. coli, P. mirabilis, B. megatherium* and *S. typhi* and was weakly active against *S. aureus* and *C. freundii*.

The compound 3e showed weak activities against *E. coli, P. mirabilis* and *B. megatherium*.

The compound 3f was inactive against all the organisms.

The compound 3g was moderately active only against *C. freundii*.

The compound 3h was moderately active against *C. freundii* and weakly active against *S. typhi*.

The compound 3i showed moderate activities against *C. freundii, E. coli, B. megatherium* and *S. typhi*, while weak activity against *A. aureus*.

The compound 3j was moderately active against *C. freundii* and showed weak activities against *S. aureus, E. coli* and *P. mirabilis*.

Bromo substituted pyrazolines (3c) and (3d) are more active towards each
micro organism as compared to other pyrazolines. This may be due to the presence of bromine atom in the structure of pyrazolines.

ACKNOWLEDGEMENT

The authors are thankful to Miss S.N. Bhure and Miss N.M. Pathak, Microbiology Department, Amravati University, Amravati for providing facilities for testing the compounds against pathogenic bacteria and for their kind cooperation.

REFERENCES


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NOTE

Antibacterial Studies of 3,5-Diaryl-4-Benzoyl-1-Pyridoyl Pyrazoles

M. V. KADU* and V.S. JAMODE
Post-Graduate Department of Chemistry
Amravati University
Amravati-444 602, India

3,5-Diaryl-4-benzoyl-1-pyridoyl pyrazoles (4a–j) had been synthesized from 3-aryl flavones and isoniazide in pyridine medium. Structures of these compounds have been confirmed by spectral analysis. These compounds were tested for their antibacterial activities against pathogenic bacteria and are found to have moderate activity.

The survey of literature reveals that 3,5-diaryl pyrazoles possess diverse biological activities. It has been reported that pyrazoles possess pharmacological, anticancer, fungicidal, herbicidal, and anti-bacterial activities. They are also found to be antidiabetic, pesticides, anti-inflammatory, and hypolipidemic agents.

Pyrazoles have also been found to possess antiparasitic and effective insecticides.

The present work deals with the study of antibacterial activities 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles. These compounds were tested against P. aeruginosa, S. aureus, C. freundii, E. coli, P. mirabilis, B. megatherium, and S. typhi. Some of them were found to be highly active against these organisms.

Melting points were uncorrected. The structures of these compounds were established on the basis of their elemental analysis and spectral data. Preparation and characterization of 3,5-diaryl-4-benzoyl-1-pyridoyl pyrazoles (4a–j) are already reported. (Physical data of pyrazoles (4a–j) is recorded in Table-1.)

Antibacterial activity

The titled compounds were tested against pathogenic bacteria for their antibacterial activity by paper disc method. The organisms tested were Pseudomonas aeruginosa, Staphylococcus aureus, Citrobacter freundii, Escherichia coli, Proteus mirabilis, Bacillus megatherium and Salmonella typhi. The solution of these compounds were prepared in DMF as a solvent at a concentration of 50 μg/2 mL. The culture medium used was nutrient agar medium. After 24 h of incubation at 37°C, the zones of inhibition were measured in mm and are recorded in Table-2.

In case of antibacterial activity from Table-2 it has been observed that the compound 4a showed strong activities against P. mirabilis and B. megatherium, moderate activities against C. freundii, E. coli and S. typhi and was weakly active against P. aeruginosa.
The compound 4b was strongly active against *B. megatherium*, moderately active against *E. coli* and *S. typhi* and showed weak activities against *S. aureus* and *C. freundii*.

The compound 4c showed strong activities against *S. typhi* and *B. megatherium*, moderate activity towards *E. coli* and *P. mirabilis* and weak activity against *S. aureus* and *C. freundii*.

The compound 4d showed activities against all the organisms. It was moderately active against *E. coli*, *P. mirabilis*, *B. megatherium* and *S. typhi* and was weakly active against *P. aeruginosa*, *S. aureus* and *C. freundii*.

The compound 4e was moderately active against *C. freundii*, *E. coli*, *B. megatherium* and *S. typhi*.

The compound 4f showed moderate activities against *C. freundii* and *E. coli* only.

The compound 4g showed moderate activities towards *E. coli* and *B. megatherium*.
The compound 4h showed no activities against all the organisms.
The compound 4i was weakly active only against *C. fruindii*.
The compound 4j was moderately active to *S. typhi* and showed weak activities
towards *C. fruindii*, *P. mirabilis* and *B. megatherium*.
Bromo-substituted pyrazole (4c) and (4d) are more active towards each microorganism as compared to other pyrazoles. This may be due to the presence of bromine atom in the structure of pyrazoles.

REFERENCES