

## Synthesis, Characterization and Antimicrobial Activity of Substituted Phenyl-5-(8-hydroxy quinolinol-5-yl) Pyrazolines

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Various chalcone derivatives (3a-e) were prepared by the well known Claisen-Schmidt condensation reaction of 8-hydroxy-5-quinoline carboxaldehyde (1) and different substituted acetophenones (2a-e). The chalcones (3a-e) were then reacted with hydrazine in aqueous alkali and yielded 3-substituted phenyl 5-(8-hydroxy quinolinol-5-yl) pyrazolines (4a-e). All the pyrazoline derivatives were characterized by elemental analysis, spectral studies and antimicrobial activities. One of the pyrazolines (4b) was then treated with transition metal salts and afforded metal chelates of 4b. All the metal chelates were characterized by metal : ligand (M : L) ratio, magnetic moment, reflectance spectra and antimicrobial activities.

**Key Words:** Synthesis, Antimicrobial activity, Substituted phenyl-5-(8-hydroxy quinolinol-5-yl) pyrazolines.

### INTRODUCTION

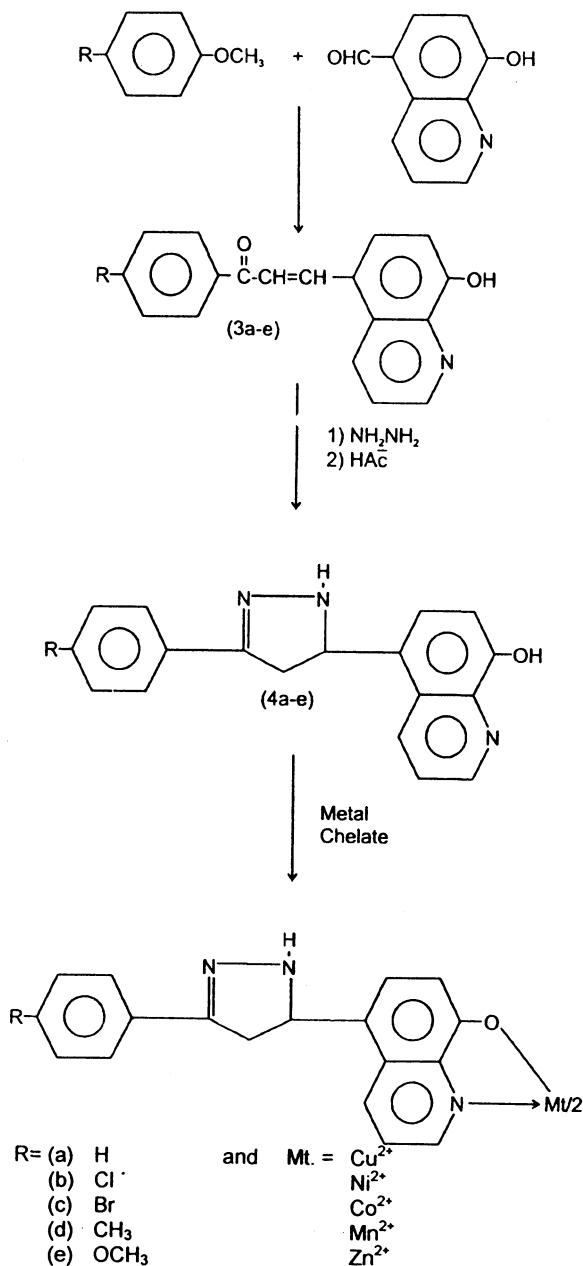
Perusal of the literature reveals that the pyrazoline derivatives are found to be active pharmacological agents<sup>1-6</sup>. Most of these pyrazoline rings contain phenyl rings. Hitherto no report has been found in literature about the pyrazoline derivative containing well known chelating agent say 8-hydroxy quinoline (*i.e.*, oxine). If this compound is introduced into such a pyrazoline derivative, it may change the biological activity up to some extent. With this view, this work containing chalcone based pyrazoline derivatives has been undertaken. The present communication deals with the synthesis, characterization and antimicrobial activities of (8-hydroxy quinolinol-5-yl) pyrazoline. The chelating properties of one of the derivatives is also summarized.

### EXPERIMENTAL

All the chemicals pertaining to this research work have been obtained from Alza Chemicals, Nadiad.

**Synthesis of Chalcones:** To a well mechanical stirred and cooled suspension of 8-hydroxy-5-quinoline carboxaldehyde (0.01 mol) and substituted acetophenone (2a-e) (0.01 mole) in THF (50 mL) was added 50% aq. KOH (10 mL) during 0.5 h. The resulting mixture was kept aside with stirring for 5 h at room

temperature. It was then poured in cold water and acidified with dil. HCl. The greenish yellow solid was filtered off, washed with THF and then with H<sub>2</sub>O and air dried. The details about all chalcones are given in Table-1 (Scheme-1).



Scheme-1

TABLE-1  
CHARACTERIZATION OF CHALCONES (3a-e)

| Sample No. | m.f.  | Yield (%) | Elemental analysis (%) |       |        |       |        |       |
|------------|---|-----------|------------------------|-------|--------|-------|--------|-------|
|            |   |           | C                      |       | H      |       | N      |       |
|            |   |           | Calcd.                 | Found | Calcd. | Found | Calcd. | Found |
| 3a         | C <sub>18</sub> H <sub>13</sub> NO <sub>2</sub>   | 71        | 78.50                  | 78.10 | 4.72   | 4.65  | 5.09   | 5.01  |
| 3b         | C <sub>18</sub> H <sub>12</sub> ClNO <sub>2</sub> | 75        | 69.70                  | 69.90 | 3.87   | 3.78  | 4.52   | 4.48  |
| 3c         | C <sub>18</sub> H <sub>12</sub> BrNO <sub>2</sub> | 78        | 61.03                  | 61.00 | 3.39   | 3.35  | 3.95   | 3.89  |
| 3d         | C <sub>19</sub> H <sub>15</sub> NO <sub>2</sub>   | 76        | 78.80                  | 78.20 | 5.19   | 5.10  | 4.84   | 4.80  |
| 3e         | C <sub>19</sub> H <sub>15</sub> NO <sub>3</sub>   | 73        | 74.75                  | 73.90 | 4.91   | 4.86  | 4.59   | 4.52  |

**Synthesis of 3-substituted phenyl-5-(8-hydroxy quinolinol-5-yl)pyrazolines (4a-e):** A solution of chalcone derivative (3a-e) and hydrazine at stoichiometric ratio and acetic acid with pyridine was refluxed for 12 h. The resultant mixture was added into cold water and the precipitates were obtained by neutralization of mixture by dilute HCl. The product was then filtered off, washed by water and air-dried. The details about all the (4a-e) derivatives are shown in Table-2 (Scheme-1).

TABLE-2  
CHARACTERIZATION OF PYRAZOLINES (3a-e)

| Sample No. | m.f.  | Yield (%) | Elemental analysis (%) |       |        |       |        |       |
|------------|---|-----------|------------------------|-------|--------|-------|--------|-------|
|            |   |           | C                      |       | H      |       | N      |       |
|            |   |           | Calcd.                 | Found | Calcd. | Found | Calcd. | Found |
| 4a         | C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> O              | 69        | 74.74                  | 74.41 | 5.19   | 5.10  | 14.50  | 14.30 |
| 4b         | C <sub>18</sub> H <sub>15</sub> ClN <sub>3</sub> O            | 73        | 66.76                  | 66.63 | 4.32   | 4.27  | 12.98  | 12.91 |
| 4c         | C <sub>18</sub> H <sub>14</sub> BrN <sub>3</sub> O            | 77        | 58.71                  | 58.12 | 3.80   | 3.69  | 11.41  | 11.35 |
| 4d         | C <sub>19</sub> H <sub>17</sub> N <sub>3</sub> O              | 72        | 75.20                  | 75.15 | 5.61   | 5.56  | 13.86  | 13.76 |
| 4e         | C <sub>19</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> | 77        | 71.40                  | 70.98 | 5.32   | 5.25  | 13.16  | 13.09 |

**Synthesis of metal chelates of 4b:** To a solution of 4b (0.02 mol) in formic acid, water-metal acetate solution (0.01 mol) in water was added dropwise under stirring at room temperature. The mixture was then added by solid sodium acetate till the completion of precipitation of metal chelate. It was then filtered, washed by water and air dried. The detailed analysis of metal chelates of 4b are summarized in Table-3 (Scheme-1).

TABLE-3  
CHARACTERIZATION OF METAL CHELATES OF 4b

| Metal chelates      | Elemental analysis (%) |       |        |       |        |       | M      |       | $\mu_{\text{eff}}$ (BM) |
|---------------------|------------------------|-------|--------|-------|--------|-------|--------|-------|-------------------------|
|                     | C                      |       | H      |       | N      |       |        |       |                         |
|                     | Calcd.                 | Found | Calcd. | Found | Calcd. | Found | Calcd. | Found |                         |
| 4b-Cu <sup>2+</sup> | 55.80                  | 55.50 | 3.61   | 3.56  | 10.80  | 10.41 | 16.40  | 16.10 | 1.95                    |
| 4b-Ni <sup>2+</sup> | 56.50                  | 56.10 | 3.66   | 3.62  | 10.90  | 10.81 | 15.31  | 15.25 | 3.12                    |
| 4b-Co <sup>2+</sup> | 56.40                  | 55.99 | 3.66   | 3.61  | 10.90  | 10.89 | 15.42  | 15.36 | 4.68                    |
| 4b-Mn <sup>2+</sup> | 57.08                  | 57.00 | 3.69   | 3.67  | 11.09  | 11.01 | 14.50  | 14.42 | 5.25                    |
| 4b-Zn <sup>2+</sup> | 55.55                  | 55.19 | 3.61   | 3.58  | 10.80  | 10.79 | 16.79  | 16.71 | Diamag                  |

Elemental analyses of all the compounds were performed on C, H, N elemental analyzer. IR spectra were recorded in KBr pellets on Perkin-Elmer spectrophotometer and <sup>1</sup>H NMR. Spectra were scanned in CDCl<sub>3</sub> or DMSO. Metal contents of all the metal chelates were estimated by known method<sup>7</sup>. Magnetic susceptibility measurements of all the metal chelates were carried out at room temperature by the Gouy method. Mercury tetrathiocyanato cobalt(II) [Hg[Co(NCS)<sub>4</sub>]] was used as a calibrant. The diffuse reflectance spectra of all the chelates were recorded on a Shimadzu spectrophotometer with a solid reflectance attachment. MgO was employed as the reference compound. The antifungal activity of all the compounds and chelates was carried out by the method reported earlier<sup>8</sup>. The plant pathogens listed in Table-4 have been selected for the study.

TABLE-4  
ANTIFUNGAL ACTIVITIES OF METAL CHELATES

| Samples             | Zone of Inhibition at 100 ppm (%) |                                    |                       |                   |                           |
|---------------------|-----------------------------------|------------------------------------|-----------------------|-------------------|---------------------------|
|                     | <i>Pencillium expansum</i>        | <i>Boltrydepladia thioibromide</i> | <i>Nigrospora</i> sp. | <i>Trieno</i> sp. | <i>Raizopus nigricans</i> |
| 4a                  | 78                                | 89                                 | 75                    | 83                | 90                        |
| 4b                  | 98                                | 96                                 | 94                    | 100               | 93                        |
| 4c                  | 96                                | 100                                | 96                    | 99                | 94                        |
| 4d                  | 87                                | 91                                 | 72                    | 93                | 96                        |
| 4e                  | 74                                | 98                                 | 90                    | 84                | 94                        |
| 4b-Cu <sup>2+</sup> | 100                               | 99                                 | 100                   | 98                | 98                        |
| 4b-Ni <sup>2+</sup> | 96                                | 92                                 | 96                    | 99                | 100                       |
| 4b-Co <sup>2+</sup> | 97                                | 100                                | 97                    | 97                | 99                        |
| 4b-Mn <sup>2+</sup> | 99                                | 97                                 | 99                    | 98                | 95                        |
| 4b-Zn <sup>2+</sup> | 98                                | 98                                 | 97                    | 100               | 97                        |

## RESULTS AND DISCUSSION

All the pyrazoline derivatives are in the form of amorphous yellow to dark brown powder. They did not melt up to 250°C. The C, H and N contents of chalcones (**3a-e**) and the pyrazolines (**4a-e**) are shown in Tables 1 and 2 respectively. The results indicate that the values are consistent with the predicted ones as shown in Scheme-1.

The spectra of all the chalcones (**3a-e**) are identical in all aspects. The noticeable band at 1610 cm<sup>-1</sup> is due to chalcone moiety —CH=CH—CO—. This is also confirmed by obtaining blue colorization when (**3a-e**) is treated with concentrated H<sub>2</sub>SO<sub>4</sub>. Other bands at 1427, 1484, 1507 and 1600 cm<sup>-1</sup> are characteristic of 8-hydroxy quinoline moiety<sup>9</sup>. Similarly IR spectra of pyrazoline derivatives are also identical in all aspects, but the new bands at 3400, 3200 cm<sup>-1</sup> are merely due on —NH group attached at 4-position.

The metal chelates with different metal ions Zn, Cu, Ni, Co and Mn are varying in colour from light green to brown, on the basis of the proposed structure as shown in Scheme-1, which upon chelation is assumed to be coordinated with one central metal atom. This has been confirmed from the results of elemental analysis of metal chelates and their parent ligand. The data of elemental analysis in Table-1 are found in agreement with the calculated values. IR spectra of all the metal chelates of **4b** are not shown here. But the comparison of the IR spectrum of parent ligand of **4b** with those of metal chelate have revealed certain changes.

One of the significant changes to be expected is the presence of more broadened bands in the region of 3500–3300 cm<sup>-1</sup> of metal chelate as the oxygen of the O—H ligand has formed coordination with both the metal ions.

Magnetic moments ( $\mu_{\text{eff}}$ ) of the metal chelates are given in Table-3. Examination of these data reveals all metal chelates other than that of Zn<sup>2+</sup> are diamagnetic. The diffuse electronic spectrum of **4b-Cu**<sup>2+</sup> shows two broad bands at 15873 and 22988 cm<sup>-1</sup> due to <sup>2</sup>E<sub>g</sub> → <sup>2</sup>T<sub>g</sub> transition and charge transfer respectively, suggesting a distorted octahedral structure for **4b-Cu**<sup>2+</sup> which is further confirmed by high values of  $\mu_{\text{eff}}$ . The **4b-Ni**<sup>2+</sup> and **4b-Co**<sup>2+</sup> gave two absorption bands respectively at 15625, 22471 and 16528 cm<sup>-1</sup> corresponding to <sup>4</sup>T<sub>1g</sub> → <sup>2</sup>T<sub>1g</sub> and <sup>4</sup>T<sub>1g</sub> → <sup>4</sup>T<sub>1g</sub>(P) transitions<sup>9</sup>. Thus the absorption band and the values of  $\mu_{\text{eff}}$  indicates on octahedral configuration for **4b-Ni**<sup>2+</sup> and **4b-Co**<sup>2+</sup>. The spectra of **4b-Mn**<sup>2+</sup> show bands at 14665, 19750 and 25575 cm<sup>-1</sup>, assigned to the transition <sup>6</sup>A<sub>1g</sub> → <sup>4</sup>T<sub>1g</sub>(4G), <sup>6</sup>A<sub>1g</sub> → <sup>4</sup>T<sub>1g</sub>(4G) and <sup>6</sup>A<sub>1g</sub>(F) → <sup>4</sup>T<sub>1g</sub> respectively suggests an octahedral structure for the **4b-Mn**<sup>2+</sup>. As the spectrum of **4b-Zn**<sup>2+</sup> is not well resolved, it is not interpreted, but its  $\mu_{\text{eff}}$  value reveals it is diamagnetic as expected.

The antifungal activity of all the (**4a-e**) compounds and metal chelates of **4b** shows (Table-4) that all the compounds are toxic against all fungi. The halogen derivatives are more toxic and particularly Cu<sup>2+</sup> chelate is more toxic. The results show that the produced samples can display as garden fertilizers.

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