

# Study on the Synthesis, Characterization and Antimicrobial studies of the Transition Metal Complexes of the Novel Mannich Base Derived from Pyridazine Derivative

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**Abstract-** In this study, we report the synthesis of a novel Mannich base derived from maleichydrazide and its transition metal complexes. We tried this with maleichydrazide compound as a precursor and treated with formaldehyde and dicyclohexylamine. The so formed base was complexed with transition metals. The Mannich base ligand as well as the metal complexes were characterized by various physical methods. The structure of the synthesized compounds are confirmed by UV, IR, and <sup>1</sup>H NMR spectroscopic techniques. The antibacterial activity of the ligands and the complexes were examined using different bacteria.

**Index Terms-** Mannich base, Pyridazine, Maleichydrazide, transition metal complex, and antibacterial study

## I. INTRODUCTION

Transition metal complexes particularly derived from Mannich bases contribute much to the field of organometallic chemistry. Mannich bases are also known to play a vital role in the development of synthetic pharmaceutical chemistry. The literature studies revealed that Mannich bases are very reactive and can be easily converted to other compounds, for example, reduced to form physiologically active amino alcohols<sup>1</sup>. Mannich bases are known to possess potent activities like anti-inflammatory<sup>2, 3</sup>, anticancer<sup>4,5</sup>, antifilarial<sup>6</sup>, antibacterial<sup>7,8</sup>, antifungal<sup>9, 10</sup>, anticonvulsant<sup>11</sup>, anthelmintic<sup>12</sup>, antitubercular<sup>13,14</sup>, analgesic<sup>15</sup>, anti-HIV<sup>16</sup>, antimalarial<sup>17</sup>, antipsychotic<sup>18</sup>, antiviral<sup>19</sup> activities and so forth.. Along with biological activities Mannich bases are also known for their uses in detergent additives<sup>20</sup> resins, polymers, surface active agents<sup>21</sup>, and so on. Prodrugs of Mannich bases of various active compounds have been prepared to overcome the limitations<sup>22</sup>. Mannich bases (optically pure chiral) of 2-naphthol are employed for catalysis (ligand accelerated and metal mediated) of the enantioselective carbon-carbon bond formation. Mannich bases and their derivatives are intermediates for the synthesis of bioactive molecules<sup>23,24</sup>. Mannich reaction is widely used for the construction of nitrogen containing compounds<sup>26</sup>. Mannich

bases have gained importance due to their application in antibacterial activity<sup>27</sup> and other applications are in agrochemicals such as plant growth regulators.

In the present work, we report the synthesis, characterization, antibacterial studies of a new Mannich base Dicyclohexylamino methyl maleichydrazide (DCAMMH) from maleichydrazide and its transition metal complexes.

## II. MATERIALS AND METHODS

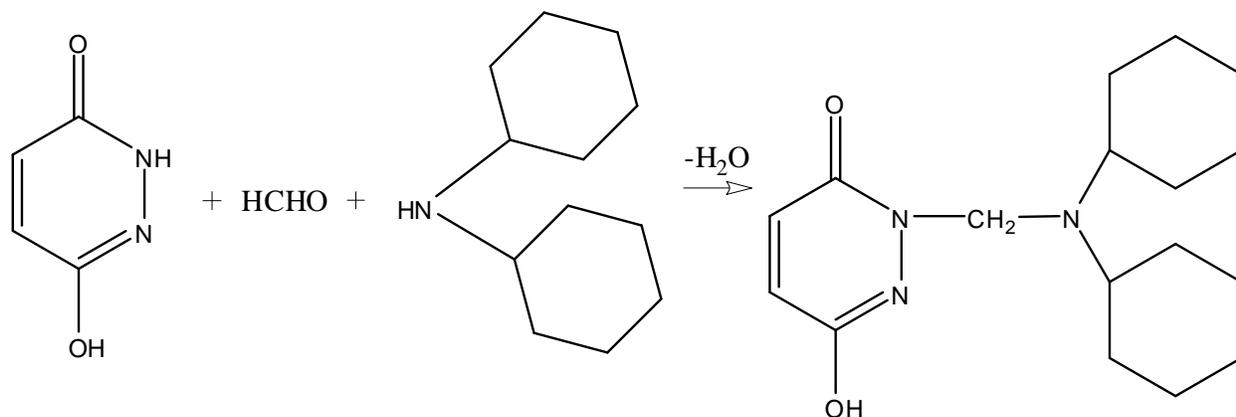
### 2.1. General

Reagents such as maleichydrazide, formaldehyde, dicyclohexylamine were of Sigma-Aldrich products and were used as such. The solvents were dried before use by the conventional methods and moisture was removed from the glass apparatus using CaCl<sub>2</sub> drying tube. The melting point of all the synthesized compounds was determined in open capillaries and is uncorrected. The UV-Vis spectra were recorded in DMSO solvent on Shimadzu UV mini-1240 spectrophotometer, IR spectra were recorded on Agilent FT-IR spectrophotometer using KBr pellets and <sup>1</sup>H NMR spectra were recorded with Bruker AMX400 NMR spectrophotometer using DMSO solvent.

### 2.2 Experimental

#### 2.2.1 Synthesis of the Mannich Base Ligand

0.05 mol of dicyclohexylamine and 0.05 mol of Formaldehyde are dissolved in 50mL of ethanol and taken in a 100mL RB flask. Then 0.05 mol of the maleichydrazide dissolved in 20 mL ethanol added in small aliquots to the reaction mixture kept in icebath and the stirring was continued for about 6hrs. Then the contents of the mixture were refluxed for 3-5 hours and kept in refrigerator for overnight. The next day, the solvent was recovered from the mixture by distillation. Progress of the reaction was monitored using TLC. Once the Mannich base separates out as colorless precipitate, it is filtered and washed with hot water, recrystallised in alcohol and dried in air-oven at 60°C.

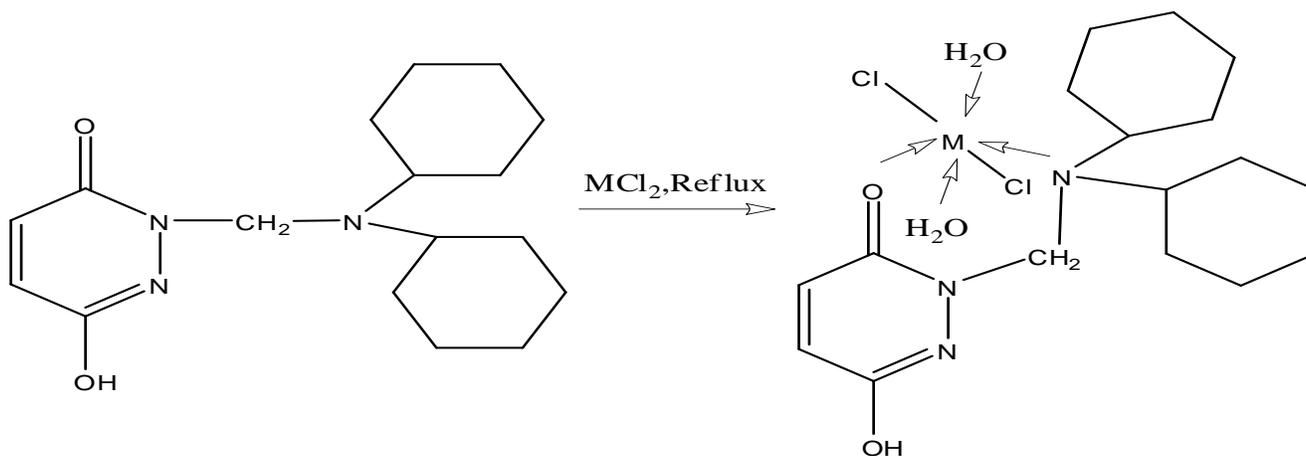


**Scheme 1. Synthesis of the Mannich base ligand**

### 2.2.2 Synthesis of the metal complexes

Hot ethanolic solution of the ligand ( 1 equivalent ) was slowly mixed with hot ethanolic solution of metal chloride ( 1 equivalent) under reflux condition with constant stirring.The

mixture was refluxed for 1-2 hours and after that it was cooled and kept in refrigerator for few hours. The colored solid complexes were separated out in each case,it was filtered washed with alcohol and finally dried in air oven.



**Scheme 2. Synthesis of metal complexes**

**Table 1 : Physical data of the ligand and the complexes**

| Compound      | Yield (%) | Colour     | Mp (°C) |
|---------------|-----------|------------|---------|
| DCAMMH Ligand | 78        | Colorless  | 253     |
| DCAMMH -Co    | 75        | Pale pink  | 255     |
| DCAMMH -Ni    | 72        | Pale green | 232     |
| DCAMMH -Cu    | 68        | Pale green | 246     |

### 2.2.3 Antibacterial activity

For the antibacterial study, nutrient agar was used as the medium.All the compounds were screened for antibacterial activity against certain pathogenic bacteria by disc diffusion method at concentration of 10µg / ml in DMSO using gram

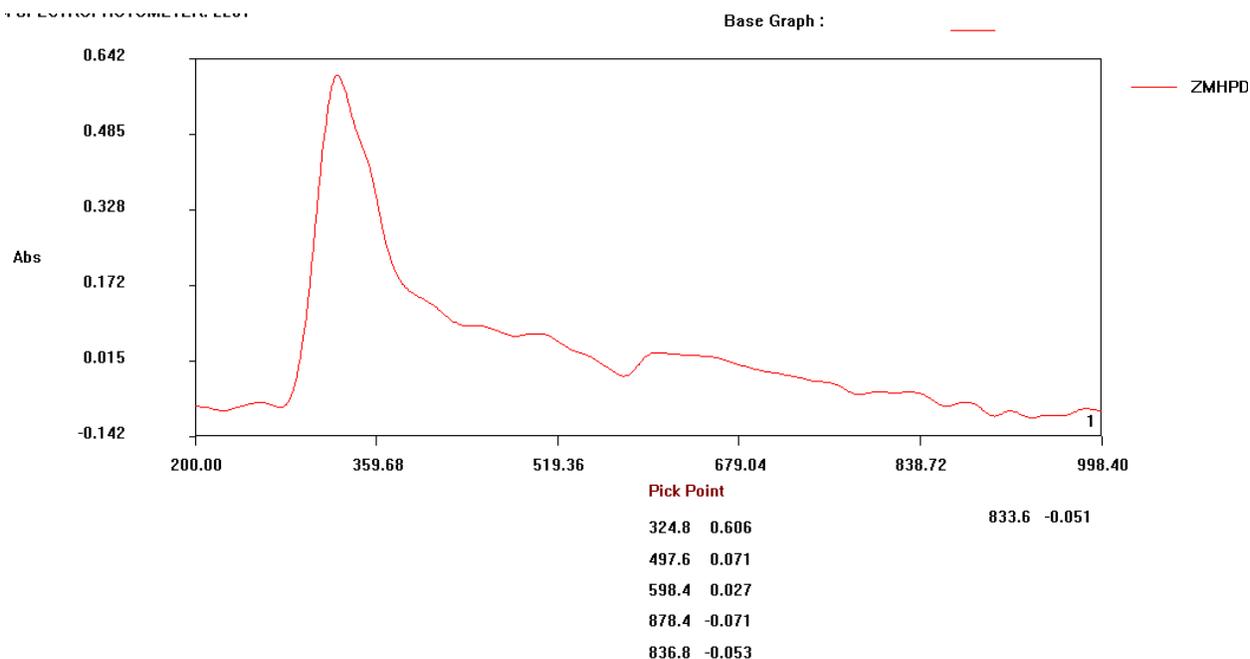
positive *Bascillus subtilis*, *Staphylococcus aureus*,and gram negative *Proteus vulgaris*, *Klesiella pneumoniae* The zone of inhibition was measured in mm and the activity was compared with Gentamycin in 1 µg / disc.The results are tabulated in Table.2.

**Table 2: Antibacterial activity**

| Sl. No. | Bacteria                     | Standard Antibiotic Disc (Gentamycin) | Zone of inhibition mm in diameter (10 µg/disc) |           |           |           |
|---------|------------------------------|---------------------------------------|--|-----------|-----------|-----------|
|         |                              |                                       | DCAMMH-L                                       | DCAMMH-Co | DCAMMH-Ni | DCAMMH-Cu |
| 1       | <i>Staphylococcus aureas</i> | 22                                    | 12   | 14        | 14        | 18        |
| 2       | <i>Bascilla subtilis</i>     | 16                                    | 15   | 18        | 16        | 20        |
| 3       | <i>Proteus vulgaris</i>      | 28                                    | 10   | 17        | 13        | 17        |
| 4       | <i>Klesiella pneumoniae</i>  | 16                                    | 09   | 15        | 12        | 19        |

III. RESULTS AND DISCUSSION

3.1 UV-Visible spectra

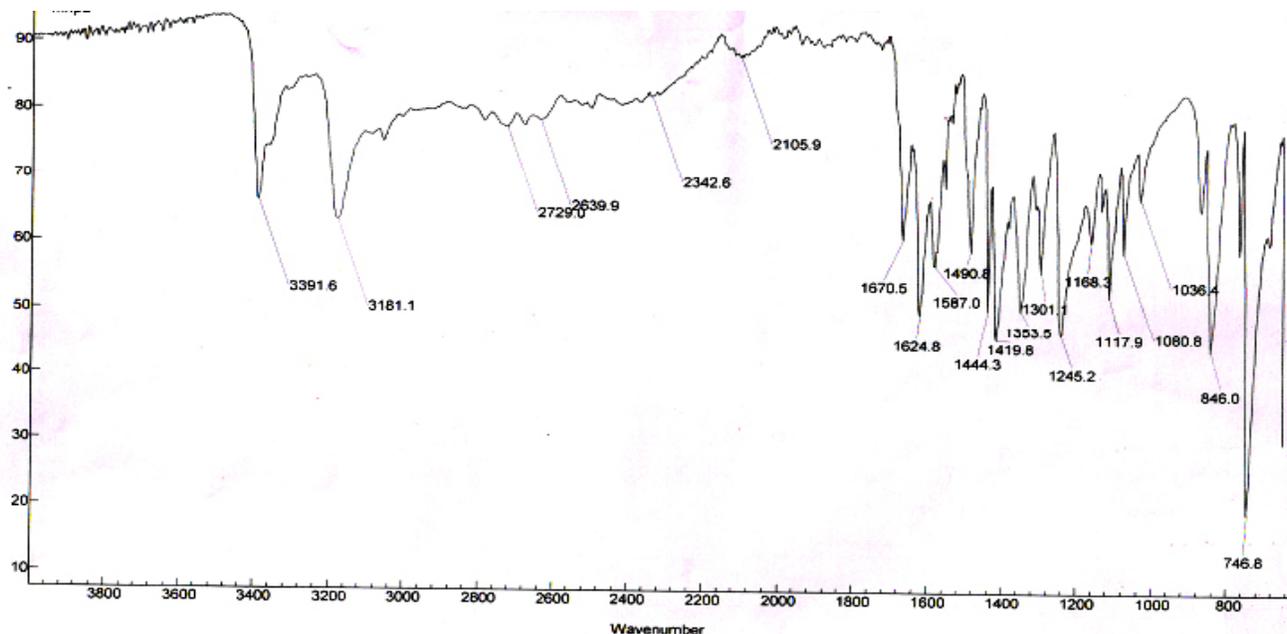


**Fig.1 UV-Visible spectra of the complex**

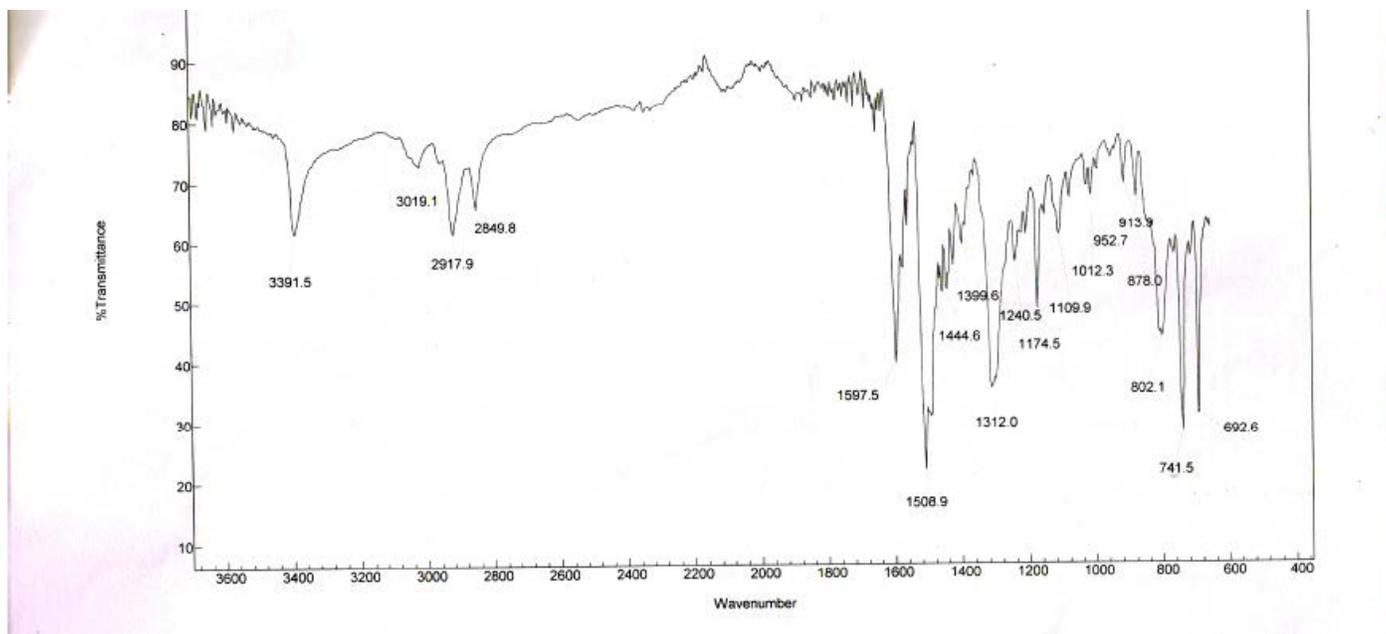
The UV-Visible spectra of the complexes(Fig.1) were recorded in the range of 200-950 nm. The UV spectrum The Cu (II) complex under present study exhibit a broad band in the region 11560- 15640cm-1 , 18450 cm-1 and 22700 cm-1 due to transition between  $^2 B_{1g} \rightarrow ^2 A_{1g}$ ,  $^2 B_{1g} \rightarrow ^2 B_{2g}$  and  $^2 B_{1g} \rightarrow ^2 E_g$  which indicated the distorted octahedral geometry. The Ni (II) complex showed broad signals in the region 12542 cm-1 and

28325 cm-1 which is assigned to  $^3 A_{2g} \rightarrow ^3 T_{1g}$  and  $^3 A_{2g} \rightarrow ^3 T_{1g}$  (P) transitions respectively is indicative of its octahedral geometry. The position of bands observed for Co (II) complex at 26564 cm-1 and 15268 cm-1 corresponding to the transitions  $^4 T_{1g} \rightarrow ^4 T_{1g}$  (P) and  $^4 T_{1g} \rightarrow ^4 A_{2g}$  shows it is also having the octahedral geometry.

### 3.2 IR Spectra



**Fig.2 IR Spectra of the ligand**



**Fig.3 IR Spectra of the complex**

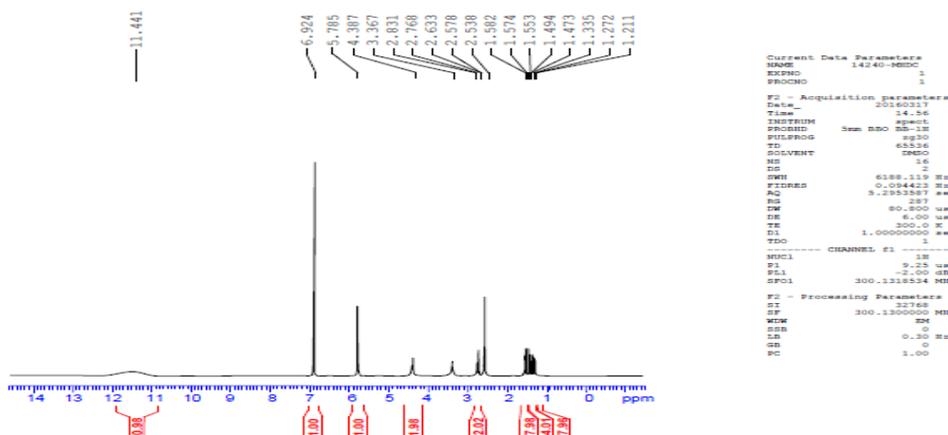
The IR spectra of the ligand and the complex are shown in Fig.2 and Fig.3 respectively and the results are given in the Table.3. The important observation is the presence of an intense band at  $\sim 1670 \text{ cm}^{-1}$  which is due to  $\nu\text{C=O}$  carbonyl group. The most notable change in the IR spectra is the disappearance of the  $-\text{NH}$  stretching vibration and appearance of an intense band at  $1245 \text{ cm}^{-1}$  due to  $\nu\text{C-N-C}$  stretching which is formed due to the aminomethylation. A band at  $3391 \text{ cm}^{-1}$  is due to  $-\text{OH}$  stretching in the pyridazine ring. The absence of band at  $3300 \text{ cm}^{-1}$  due to

amino  $-\text{NH}$  disappears implying its condensation after deprotonation. These results confirms the formation of the Mannich base. In all the complexes, band due to  $\nu\text{C=O}$  and  $\nu\text{C-N}$  shifted towards lower frequency clearly indicating the nitrogen and carbonyl oxygen are involved in coordination with metal ions. Further, the appearance of new bands around  $810 \text{ cm}^{-1}$  corresponding to  $\text{M-O}$  bond and a signal at  $692 \text{ cm}^{-1}$  corresponding to  $\text{M-Cl}$  bond confirms the formation of the metal complex.

**Table 3 : IR Spectral data of the ligand and the complexes**

| Compound   | Vibrational frequency of various functional groups (in cm <sup>-1</sup> ) |      |      |      |      |
|------------|---|------|------|------|------|
|            | -OH   | -C=O | CNC  | M-N  | M-Cl |
| DCAMMH     | 3391  | 1670 | 1245 | ---- | ---- |
| DCAMMH -Co | 3391  | 1597 | 1240 | 741  | 692  |
| DCAMMH -Ni | 3391  | 1597 | 1240 | 741  | 691  |
| DCAMMH Cu  | 3391  | 1597 | 1240 | 743  | 692  |

### 3.3 <sup>1</sup>H NMR Spectra



**Fig.4 <sup>1</sup>H NMR spectra of the Mannich base**

The <sup>1</sup>H NMR spectra of the Mannich base is given in Fig.4. The ligand under study exhibit multiple signals between 1.2 -1.5 ppm corresponding to the hydrogens of the cyclohexane ring. The appearance of peak at 4.3 ppm indicates the methylene hydrogens attached to the nitrogen. Further, the signals at 5.7 and 6.9 ppm corresponds to the ethylenic hydrogens of the pyridazine ring. A peak at 11.4ppm indicates the -OH of the pyridazine ring in the enol form. The formation of the ligand is ascertained by the disappearance of a signal at ~6.5 ppm corresponding to the -NH proton of secondary amine as it was eliminated in the Mannich reaction.

### 3.4 Antibacterial activity

The ligand and the complexes are subjected to their in vitro antibacterial activity by disc diffusion method. The activities were observed at concentration of 10µg / ml in DMSO using gram positive *Bacillus subtilis*, *Staphylococcus aureus*, and gram negative *Proteus vulgaris*, *Klesiella pneumoniae*. The zone of inhibition was measured in mm and the activity was compared with Gentamycin in 1 µg / disc. The results are tabulated in Table.2. From the results it may be observed that the complexes are possessing better activity against both types of bacterias than the free ligand. Among them, copper complex has more active than all other complexes.

## IV. CONCLUSION

It may be concluded that a new Mannich base have been synthesised through Mannich reaction between maleic hydrazide, formaldehyde and dicyclohexylamine. Three transition metal complexes have also been prepared using this as ligand. All the compounds are characterized by physical and spectral studies. The ligand behaves as a bidentate chelating agent and the spectroscopic data is in good agreement of our proposed octahedral structure. The antimicrobial property of the complexes were studied and found that the metal complexes possess better antibacterial property than that of the free ligand.

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