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# Synthesis and Antimicrobial Activity of 5[(1, 3 dioxo-1, 3 dihydro-2H- isoindol-2-yl) methyl] - 2-hyroxy benzoic acid and their Metal Complexes.

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*The N- hydroxyl methyl phthalimide (HMP) is one of the organic products which has tendency to react phenolic derivative. While there are number of ligands are employed for the formation of phthalimide derivatives. Hence the present work has been undertaking with following objectives.*

*The transition metal complexes (i.e. $Cu^{+2}$,$Co^{+2}$,$Ni^{+2}$,$Zn^{+2}$, $Mn^{+2}$) of ligand 5[(1,3 dioxo-1,3 dihydro-2H-isoindol 2-yl)methyl]-2-hydroxy benzoicacid have been determined.*

*All the metal complexes were monitored for their antimicrobial activity. The plant pathogens were employed for this purpose. The results give these conclusions. All the complexes are toxic more or less to fungi. The substitution of phenyl rings does not have more effect on the fungicidal activity of chelates but in each series, the Cu-chelates have much toxicity. This is expected because the cupper salts are mostly used as fungicides.*

*Most of the compounds inhibit the growth of above organisms which cause decease in many plants.*

***Key Words: HMP, Metal complexes, Antimicrobial activity, Fungicidalactivity***

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The N-hydroxy methyl phthalimide (HMP) is one of the organic product which has tendency to react phenolic derivative While there are number of ligands are not employed for the formation of phthalimide derivatives . Hence the present work has been undertaking with following objectives.

**Objectives of the Present Work:**

Hitherto the various ligands have not been reacted with N-hydroxymethyl phthalimide. Hence the proposed work be the formation of phthalimide-ligand derivatives and to study their complexation properties. In view of the above objectives the research work was carried out on the complexation studies of novel phthalimide-ligand molecules. The ligand was prepared by condensation of N-hydroxymethyl phthalimide and salicylic acid.Formation of phthalimide-ligand derivaties and to study their complexation properties. The ligand designated as $HL_1$ were characterized by elemental analysis.

**Synthesis of Hydroxymethyl Phthalimide (HMP):** To a well stirred solution of 0.5 (mole) phthalimide and 0.5 (mole) formalin [40 ml], 50 ml glacial acetic acid (HAC) and 100 ml distilled water was mixed. The reaction mixture was kept about 4 hours at room temperature. After completion of the reaction the precipitates were filtered off, washed with acetone and air-dried. M.P. = $180^{O}$ C. The yield as 88 %. [1-2]

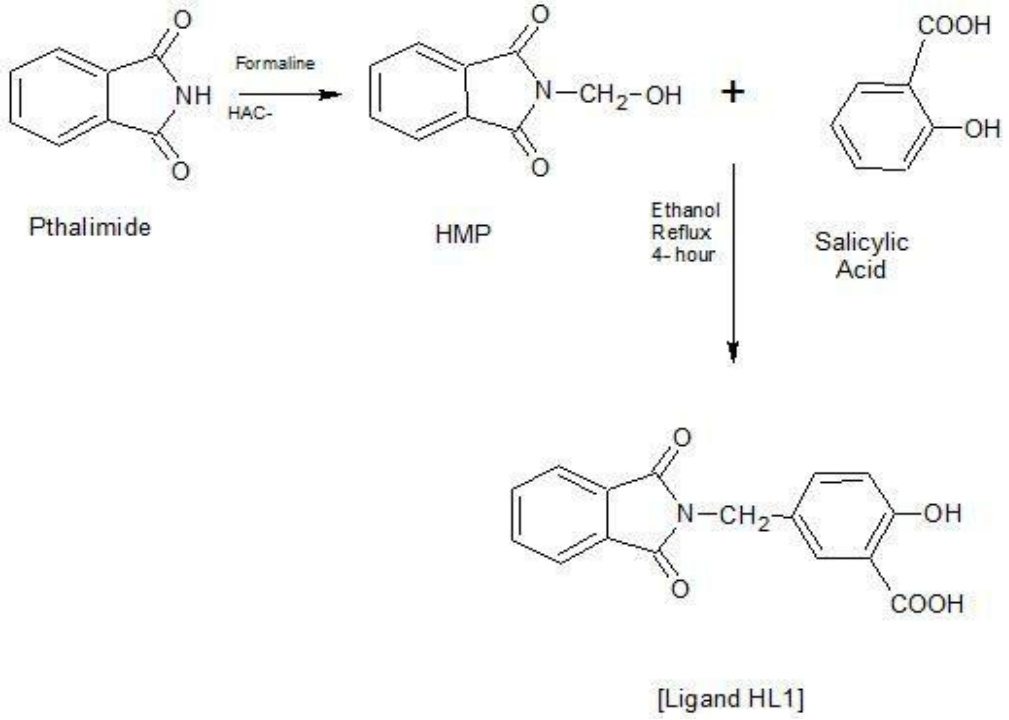
**Synthesis of 5[(1, 3 dioxo-1, 3 dihydro-2H- isoindol-2-yl) methyl] - 2-hyroxy benzoic Acid (Formation of ligand $HL_1$)**

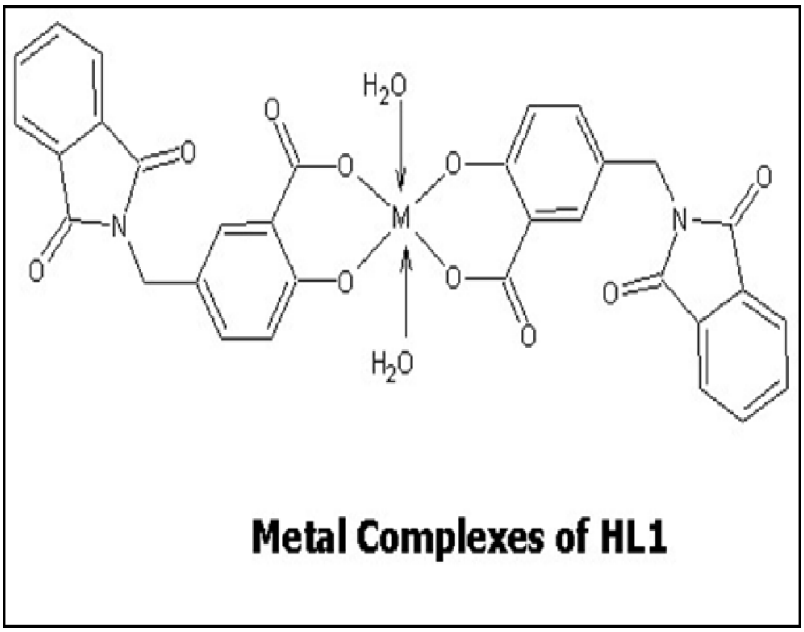
A solution of 0.04 mole salicylic acid in ethanol and solution of 0.04 mole hydroxymethyl phthalimide (HMP) was taken in 50 mL ethanol and 5 drops of con. HCl were added. The two solutions were mixed with vigorous stirring at room temperature. The resultant mixture was refluxed for about 4 hours and cooled. The precipitates were separated, dried and crystallized with acetone. The yield was about 60% and M.P. = $140^{0}$ C .[3-4]

**Synthesis of 5[(1, 3 dioxo-1, 3 dihydro-2H- isoindol-2-yl) methyl] - 2-hyroxy benzoic Acid and their Metal Complexes:**

The $Cu^{2+}$, $Mn^{2+}$, $Zn^{2+}$, $Co^{2+}$ and $Ni^{2+}$ metal ions complexes of $HL_1$ were prepared in a similar manner. The resultant pH was exacted of all the metal complexes. To solution of metal acetate (0.01M) in water (100 mL), a sodium salt of ligand $HL_1$ (0.02M) was added gradually with vigorous stirring at room temperature. The

solid complexes obtain. It was allowed to settle then it was digested on water bath at 65°c for about two hrs. The precipitates were filtered and washed several times with ethanol - water (1 : 1 ratio). and finally with acetone, dried complexes. Yield was about 70 to 80%. [5-7]




**Antimicrological Activity of HMPL and their MetalComplexes:**

Infection is a major category of human disease andskilled management of antimicrobial drugs is of the first importance. The term chemotherapy is used for the drug treatment of parasitic infections in which the parasites(*viruses, bacteria, protozoa, fungi, and worms*) are destroyed or removed without injuring the host. All theligands and their chelates used for their antimicrobial study. All other chemicals used were of laboratory grade. To test the fungicidal activity of the entire sample various plant pathogenic organisms were employed.

**Antifungal Activity:**

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were Penicillium expansum, Botrydepladia thiobromine, Nigrospora Sp., As Pergillus fumigatus, and Rhizopus nigricum. The antifungal activity of all the compounds was measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium such a PDA medium contained potato 200 gm.,dextrose 20 gm, agar 20 gm, and water 1 liter. Five days old cultures were employed. The compounds to be tested were suspended (1000 ppm) in a PDA mediumand autoclaved at 120º C for 15 min and at 15 atm pressure. These media were poured into sterile Petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below.[8-9]

Percentage of inhibition = 100(X-Y)/X

Where X = Area of colony in control plate.
Y = Area of colony in test plate.

**Antifungal Activity of Ligands $HL_1$ and its MetalChelates:**

| Sample | Zone of inhibition at 1000 ppm (%) | | | | |
|---|---|---|---|---|---|
| | Penicillium Expansum | Botrydepladia Thiobromine | NigrosporaSp. | As Pergillus Fumigatus | Rhizopus nigricums |
| $HL_1$ | 75 | 76 | 84 | 72 | 60 |
| $HL_1$-$Cu^{+2}$ | 90 | 94 | 85 | 88 | 87 |
| $HL_1$-$Mn^{+2}$ | 82 | 89 | 83 | 72 | 73 |
| $HL_1$-$Zn^{+2}$ | 88 | 90 | 81 | 86 | 70 |
| $HL_1$-$Co^{+2}$ | 87 | 87 | 77 | 82 | 68 |
| $HL_1$-$Ni^{+2}$ | 84 | 86 | 84 | 71 | 69 |

**Bacteria:**

The Danish physician Christian Gram in 1884, discovered a strain known as Gram strain, whichcan divide all bacteria into two classes "*Gram positive*"and "*Gram negative.*" The *Gram positive bacteria* resist discoloration with acetone, alcohol and remainstrained (methyl violet) as dark blue color, which *Gramnegative bacteria* are decolorized.

Bacteria can be classified according to their morphological characteristics as lower and higher bacteria. The lower bacteria have generally unicellular structures, never in the form of mycelium or sheathed filaments, e.g. cocci, bacilli, etc. the higher bacteria arefilamentous organisms, few being sheathed having certain cells specialized for producing diseases in animalor human, are known as "*Pathogens.*" Various methodshave used from time to time by several worker to evaluate the antimicrobial activity. The evaluation canbe done by the Agar diffusion methods.

Agar diffusion method is again of three types Agar cup method, Agar ditch method and Paper disc method. In present work Agar cup method is used.

The culture medium preparation
Nutrient agar medium was used. Chemical composition of the medium was,

| | |
|---|---|
| Peptone | 1.0 gm |
| NaCl | 0.5 gm |
| Meat extracts | 0.3 gm |
| Distilled water | 100 ml |
| pH | 7.0 |
| Agar | 2.0 gm |

The ingredient were weighed and dissolved in distilled water, pH was adjusted to 7.6 and then agar powder was added to it. The medium was dispensed in 25 ml quantity in different test tubes. The test tubes were plugged by cotton-wool and sterilized at 121.5º C and 15 pound per square inch (psi) pressure for 15 minutes.[10-11]

**Antibacterial Activity of Ligands $HL_1$ and its Metal Chelates:**

| Sample | Zone of inhibition (in mm) | | | |
|---|---|---|---|---|
| | Gram + ve | | Gram - ve | |
| | BacillusSubtillis | StaphylococcusAureus | Ps. Aeruginosa | E.Coli |
| $HL_1$-$Cu^{+2}$ | 12 | 20 | 14 | 18 |
| $HL_1$-$Mn^{+2}$ | 09 | 16 | 08 | 09 |
| $HL_1$-$Zn^{+2}$ | 12 | 14 | 14 | 13 |
| $HL_1$-$Co^{+2}$ | 10 | 18 | 10 | 12 |
| $HL_1$-$Ni^{+2}$ | 17 | 09 | 13 | 18 |

**Results and Discussion:**

The legends $HL_1$were characterize with Elemental analysis, IR Spectral studies and Functional group determination. All the IR spectra are giving the important features of almost all aspects. All the metal chelate was examine with IR-Spectral analysis, Magnetic susceptibility, and Reflectance spectral study.

The complexes are toxic more or less fungi. The substitution of phenyl rings do not have more effect on the fungicidal activity of chelates but -COOH more effect on the bactericidal activity of complex. In eachseries the Cu-chelates have much toxicity. This is expected because the copper salts are mostly used as fungicides. Most of the compounds inhibit the growthof the above organisms which cause decease in manyplants. Ligands $HL_1$ are more toxic because of the presence of -COOH group. Dye prepared from salicylicacid is more toxic than all other Ligand because it is antifungal and antibacterial. Out of all metal chelates, $Cu^{+2}$ metal chelates is more toxic than others and the order for is

$Cu^{+2} > Zn^{+2} > Co^{+2} > Ni^{+2} > Mn^{+2}$

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