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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL INVESTIGATIONS ON METAL COMPLEXES OF 2-[5-ACETYL-2, 4-DIHYDROXYBENZYL]-1H-ISOINDOLE-1, 3 (2H) – DIONE

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ABSTRACT

The more significant biologically active Cu (II), Ni (II), Co (II) and Mn (II) complexes were synthesized by using N-hydroxymethyl phthalimide and 2,4-dihydroxyacetophenone as ligand. Synthesized complexes were characterized by elemental analysis, conductance, magnetic susceptibility, IR and reflectance spectral studies. Coordination of the ligand atom to the metal ion was deduced by IR and reflectance spectral data. Structures of the complexes were also confirmed by magnetic studies. All the complexes have been screened for antibacterial and antifungal activities.

Key words: Hydroxylmethyl phthalimide, Antibacterial, Antifungal, 2, 4-Dihydroxyacetophenone

INTRODUCTION

Survey of literature revealed the importance of N-aryl hydroxymethyl phthalimide derivatives as biologically, pharmacologically and industrially important molecules. The complexes obtained from the ligands having acetyl, benzyl, hydroxy and ketone functional groups have been investigated exhaustively.

Receiving impetus from the above observations and in continuation of our research programmed on complexes of HMP derivatives, in this paper, We report the synthesis of ligand 2-[5-acetyl-2,4-dihydroxy benzyl]-1H-isoindole-1,3 (2H)- dione and its complexes with Cu (II), Ni (II), Mn (II) and Co (II) and also biological activities of these complexes. Hydroxymethyl phthalimide, a potential donor ligand with four coordination sites, is having the structure –

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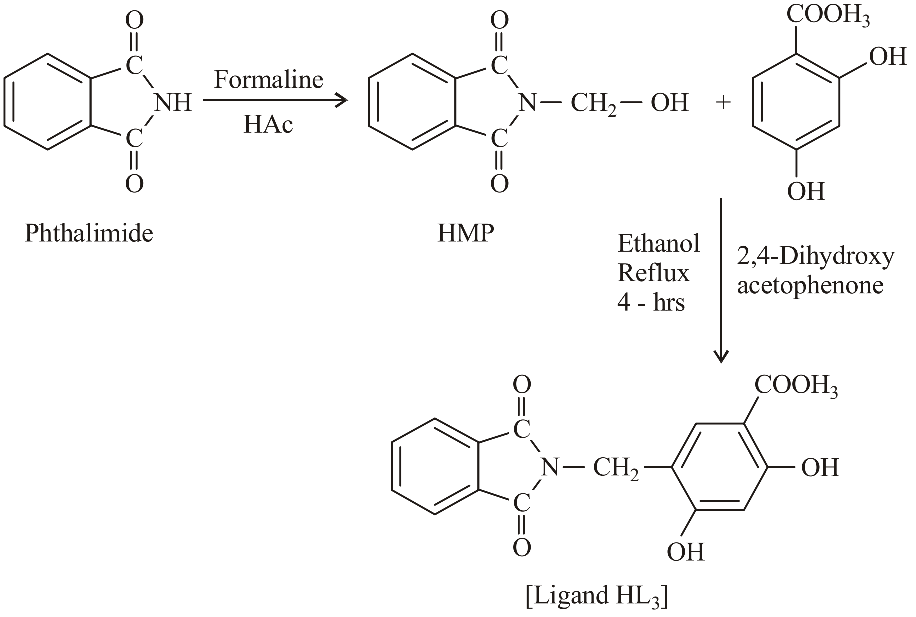

EXPERIMENTAL

Phthalimide and the salts used for synthesis of novel phthalimide derivatives were obtained from the market. The metal salts and other chemicals used were of laboratory grade. Solvent were dried and distilled before used. The following metal salts were used to prepare complexes: copper acetate, cobalt acetate, nickel acetate and manganese acetate for the preparation of ligand 2- [5-acetyl-2,4-dihydroxy benzyl]-1H-isoindole-1,3 (2H)- dione.

A solution of 0.04 mole 2,4-dihydroxyacetophenone 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^{o} C (uncorrected).

The metal ion complexes of ligand HL_3 with Cu^{2+}, Mn^{2+}, Co^{2+} and Ni^{2+} were prepared. The procedure is –

To solution of metal acetate (0.01M) in water (25 mL), a solution of ligand HL_3 (0.02M) in ethanol : water mixture (50 : 50 v/v) (100 mL) was added gradually with vigorous stirring at room temperature. The resultant mixture was refluxed for about 4 hrs. The solid complexes were separated by concentrating the resultant solution and adding ethanol : water mixture (70 : 30 ratio). The precipitates were filtered and washed several times with ethanol : water (70 : 30 ratio). The precipitates were dried at about 60^{o}C. Yield was about 75 to 80%.

The details of the elemental analysis, molar conductance of the complexes are given in Table 1.

Ligand HL_3 and its synthesized complexes were insoluble in water, slightly soluble in methanol, ether, chloroform, benzene and other organic solvents. They were soluble in DMF and acetonitrile. All the samples were analysed by elemental analyzer Thermo Finiggan 1101 Flash EA. Melting points were determined in open capillary and are uncorrected.

Table 1: Physical and analytical data of ligand HL_3 and their metal complexes

Metal complex	Yield (%)	Mol. wt. (g/mole)	Elemental analysis						Metal %		Condu-ctivity Mohs. cm^2
			C %		H %		N %				
			Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	
$(HL_3)_2$ $Cu^{2+}2H_2O$	80	719.54	56.70	56.6	3.05	3.0	3.89	3.8	8.83	8.8	7.6
$(HL_3)_2$ $Co^{2+}2H_2O$	78	714.94	57.06	57.0	3.07	3.0	3.91	3.9	8.25	8.2	9.4
$(HL_3)_2$ $Ni^{2+}2H_2O$	78	714.69	57.08	57.0	3.07	3.0	3.91	3.8	8.24	8.2	8.4
$(HL_3)_2$ $Mn^{2+}2H_2O$	77	710.93	57.38	57.3	3.09	3.0	3.93	3.9	7.72	7.7	11.0

The molar conductance of the complexes was measured using Elico CM-28. Magnetic suscepetibility measurements were made on a Gouy balance at room temperature using conductivity water and mercury tetrathiocynatocobaltate (II) $[HgCo(CNS)_4]$ as calibrant. The reflectance spectra of the metal chelates in the visible region were recorded against MgO on Beckman-DK-2A spectrophotmter. The IR spectra of metal complexes were recorded in KBr in the range of 4000-400 cm^{-1} Unicom FTIR (research spectrophotometer series) and in the range of 4000-200 cm^{-1} were recorded on Perkin Elmer–577 IR spectrophotometer. The antimicrobial activities of the synthesized metal complexes were carried out by the cup–plate method. *In vitro* antimicrobial activity was carried out against 24 hrs old cultures of two bacteria, namely *Staphylococcus aureus* and *E.Coli* and 48 hrs old culture of two fungi, namely *Nigrospora Sp.* and *Rhizopus nigricum*.

RESULTS AND DISCUSSION

The data of electrical conductivity of all the complexes in acetone indicate that they are less polarising in DMF. The magnetic moment of Co, Ni and Cu complexes were calculated from the corrected magnetic susceptibilities. The magnetic moment value of 2.82 B.M. was observed for complex of Ni (II), which is well within the range of 2.9-3.4 B.M. expected for octahedral complexes. The Cu (II) complex exhibited magnetic moment of the order of 1.95 B.M., which agrees well with the spin only value, suggesting an octahedral structure. The Mn (II) complex exhibited magnetic moment of the order of 5.9 B.M., which show highly paramagnetic nature.

Table 2: Experimental data of magnetic moment for metal chelates of HL_3

Metal chelates	$\chi_g \times 10^{-6}$ (cgs)	$\chi_m \times 10^{-6}$ (cgs)	Magnetic moment μ_{eff} (BM)	$\mu_{eff} = \sqrt{n(n+2)}$ BM obs	μ_{eff} (BM) Expected
$(HL_3)_2Mn^{2+}$	15.10	10739	5.11	5.91	5.2-6.0
$(HL_3)_2Co^{2+}$	12.88	9215	4.63	3.87	4.4-5.2
$(HL_3)_2Ni^{2+}$	5.27	3770	3.00	2.82	2.9-3.4
$(HL_3)_2Cu^{2+}$	1.93	1394	1.79	1.73	1.7-2.2

The electronic spectrum of Co (II) complexes exhibited three bands around, 24875,19230 and 8932 cm^{-1}, which are assigned to (V_1) $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, (V_2) $^4T_{1g}(F) \rightarrow {}^4A_{2g}$ and (V_3) $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$, respectively in an octahedral environment field. The electronic spectrum of Ni (II) complex also showed three bands. In electronic spectra of Cu^{2+} metal chelate, the band may be assigned to $^2B_{1g} \rightarrow {}^2A_{1g}$ and charge transfer transition, respectively. These results reveal the distorted octahedral geometry for these chelates.

The reflectance spectra of the metal chelates in the visible region were recorded against MgO on Beckman-DK-2A spectrophotometer. The assignment of significant bands present in the reflectance spectra of each of the metal chelates are given in Table 3.

Table 3: Reflectance spectral data of metal complexes of ligand HL_3

Metal complex	Absorption (cm^{-1})	Transional		
$(HL_3)_2$—Mn^{2+}	23882	$^6A_{1g}$	→	$^4A_{1g}$ (4EG)
	18340	$^6A_{1g}$	→	$^4T_{2g}$ (4G)
	16855	$^6A_{1g}$	→	$^4T_{1g}$ (4G)
$(HL_3)_2$—Co^{2+}	24875	$^4T_{1g}$ (F)	→	$^4T_{2g}$ (F)
	19230	$^4T_{1g}$ (F)	→	$^4A_{2g}$
	8932	$^4T_{1g}$ (F)	→	$^4T_{2g}$ (P)
$(HL_3)_2$—Ni^{2+}	22425	$^3A_{2g}$	→	$^3T_{1g}$ (P)
	15368	$^3A_{2g}$	→	$^3T_{1g}$ (F)
$(HL_3)_2$—Cu^{2+}	23990	Charge transfer		
	15765	$^2B_{1g}$	→	$^2A_{1g}$

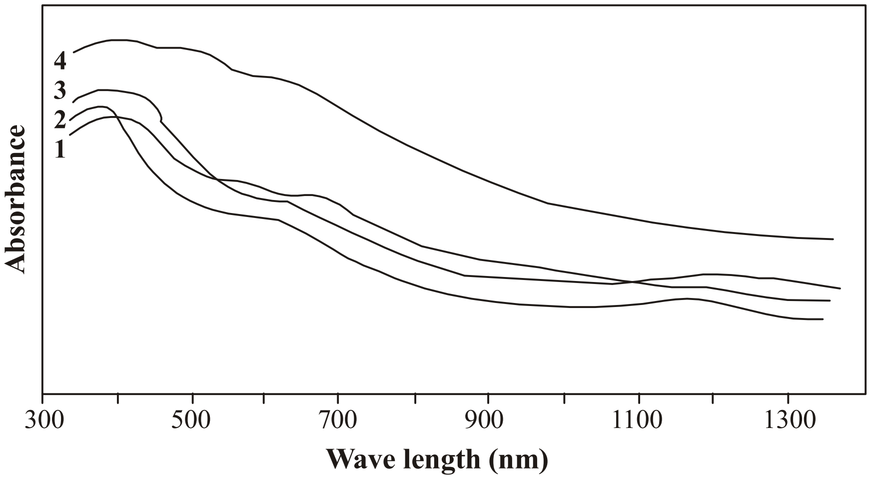

Fig. 1: Reflectance spectra of HL_3 metal complexes (1) HL_3 -Cu (2) HL_3 -Ni (3) HL_3 -Co and (4) HL_3 -Mn

The band value in nm was converted into cm^{-1} and discussed. The only observable difference in the IR spectra of metal chelates and corresponding ligands has been the disappearance of the C=O stretching vibration in ligands at 1717 cm^{-1} on complex formation. A new band at 1095 cm^{-1} has appeared in the spectra of metal chelates.

Table 4: Infrared frequencies of HL_3 and their metal complexes

Frequency (cm^{-1})					
Ligand	**Aromatic**	**Metal ligand**	**Imides group**	**C=O ketone**	**$-CH_2$ group (Bridge)**
HL_3	1598 C=C str.	3370 str.	1681 str.	1717 str.	2920 str. (Asym.)
	1498 C-H bend.		1580 str.		2850 str. (Sym.)
	3028 C-H str.		1389 str.	1685 str. $-CH_3$	1453 bend.
HL_3-M	1598 C=C str.	580-450	1681str.	1717 str.	2920 str. (Asym.)
	1498 C-H bend.		1580 str.		2850 str. (Sym.)
	3028 C-H str.		1389str.		1453 bend.

This may be assigned to νc-o of C-O-metal bond formation. The important bands are observed at their respective positions. The bands at 1681 cm^{-1} is due to imides group. The bands at 3030,1600 and 820 cm^{-1} are mainly from 1,4-disubstituted aromatic ring where as the bands at 2920, 2850 and 1453 cm^{-1} are assigned to $-CH_2$ bridge system.

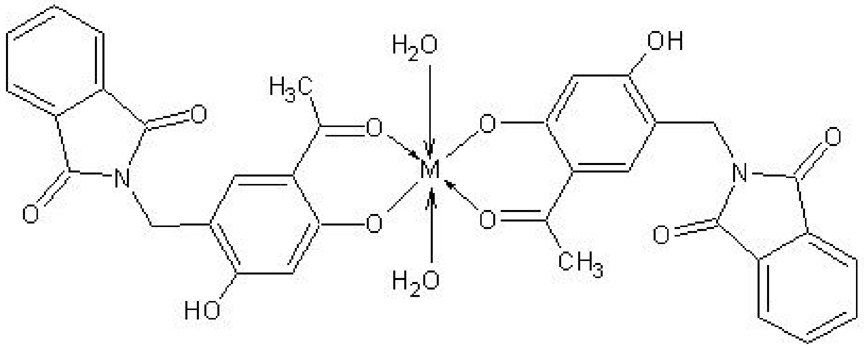

Fig. 2: Metal complexes of HL_3

M = Cu (II), Ni (II), Co (II) and Mn (II)

Table 5: Antibacterial and antifungal activity of ligand HL_3 and their metal complexes

Sample	Zone of inhibition (in mm)		Zone of inhibition at 1000 ppm (%)	
	Gram + ve	Gram - ve		
	Staphylococcus Aureus	***Ps. Aeruginosa***	***Penicillium Expansum***	***Nigrospora Sp.***
HL_3	19	18	79	80
HL_3-Cu^{+2}	18	10	80	89
HL_3Mn^{+2}	14	12	83	81
HL_3-Co^{+2}	09	12	78	66
HL_3-Ni^{+2}	19	11	71	69

The ligand, all the complexes synthesized in the present investigation and the respective metal salts were evaluated for antimicrobial activity.

Ligand and all the metal complexes were screened for their antibacterial activity against two bacterial strains viz. *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Table 5). These compounds were also evaluated for their antifungal activity against two fungi viz, *Penicillium Expansum* and *Nigrospora Sp*.

CONCLUSION

The structures of all the complexes have been assigned based on various spectral and physical parameters. All the complexes possess octahedral geometry. Two water molecules are also involved in complexation. All the complexes exhibited considerable antibacterial activity against *staphylococcus aureus* and *pseudomonas aeruginosa* and anti- fungal activity against *Penicillium Expansum* and *Nigrospora Sp*.

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