Synthesis Characterization and Biological Investigations on Metal Complexes of 2-[(8-Hydroxy-1-quinolin-5-yl) methyl]-1*H*-isoindole-1, 3 (2*H*) dione

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Received 3 January 2009; Accepted 5 March 2009

Abstract: The more significant biologically active Cu(II), Ni(II), Co(II) and Mn(II) complex were synthesized by using *N*-hydroxymethyl phthalimide and 8-hydroxy quinoline as ligand. Synthesized complexes were characterized by elemental analysis, conductance, magnetic susceptibility measurements, IR and reflectance spectral studies. Coordination of the ligand atom to the metal ion was deduced by IR and reflecting spectral data. Structures of the complexes were confirmed by magnetic studies. All the complexes have been screened for antibacterial and antifungal.

Keywords: Hydroxy methyl phthalimide, Antibacterial, Antifungal, Isoindole.

Introduction

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

Receiving impetus from the above observation and in continuation of our research programmed on complexes of HMP derivatives. In this paper, we report the synthesis of 2-[(8-hydroxy-1-quinolin-5-yl) methyl]-1*H*-isoindole-1, 3 (2*H*)-dione and its complexes with Cu(II), Ni(II), Mn(II) and Zn(II) and also biological activities of these complexes. Hydroxy methyl phthalimide a potential donor ligand with four coordination sites is having structure (Scheme 1).

Scheme 1

Experimental

Phthalimide and the ligands used for synthesis of novel phthalimide derivatives were obtained from local 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 [Cu(COO)₂], cobalt acetate [Co(COO)₂], nickel acetate, manganese acetate [Mn(COO)₂] for the preparation of ligand 2-[(8-hydroxy-1-quinolin-5-yl) methyl]-1*H*-isoindole-1,3 (2*H*)-dione.

To a solution of (0.04 mole) 8-hydroxy quinoline in ethanol and solution of (0.04 mole) hydroxy methyl phthalimide (HMP) in 50 mL ethanol, 5 drops of con. HCl was added. The two resultant 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 75% and melting point was 142 °C (Uncorrected). The ligands HL₂ described above have been taken. The Cu²⁺, Mn²⁺, Co²⁺ and Ni²⁺ metal ion complexes of HL₂ were prepared. The procedure is given below.

To the solution of metal acetate (0.01 M) in water (25 mL) and solution of ligand HL₂ (0.02 M) in formic acid: 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 h. The solid complexes was 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 °C. Yield was about 65 to 75%. The details of the elemental analysis, molar conductance of the complexes are given in Table 1. Ligand HL₂ 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 measured by elemental analyzer Thermo Finiggan 1101 Flash EA.

The molar conductance of the complexes was measured using Elico CM-28. Magnetic susceptibility measurements were made on a Gouy balance at room temperature using conductivity water and mercury tetrathiocyanatocobaltate(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 spectrophotometer. The IR spectra of metal complexes were recorded in KBr in the range of 4000-400 cm⁻¹ Unicam FTIR (research spectrophotometer series) and in the range of 4000-200 cm⁻¹ were recorded on Perkin Elmer -577IR 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 h old cultures of two bacteria, namely *Staphylococcus aureus* and *E. coli* and 48 h old culture of two fungi, namely *Nigrospora sp.* and *Rhizopus nigricum*.

Table 1. Physical and analytical data of ligand and their metal complexes.

Metal Complex	Yield %	M.Wt g/mole	Elemental analysis						Metal %		Condu- ctivity, Mohs. cm ²
			C %		H %		N %				
			Calc.	Found	Calc.	Found	Calc.	Found	Calcu.	Found	
(HMT) C ₁₈ H ₁₂ N ₂ O ₃	75	304	71.05	67.1	3.94	3.8	9.21	9.1	-	-	-
(HL ₂) ₂ Cu ²⁺ ·2H ₂ O	73	703.5	61.4	61.0	3.69	3.6	7.95	7.9	9.03	9.0	7.7
(HL ₂) ₂ Co ²⁺ ·2H ₂ O	71	698.9	61.8	61.2	3.71	3.7	8.01	8.0	8.43	8.4	9.3
(HL ₂) ₂ Ni ²⁺ ·2H ₂ O	70	698.6	61.82	61.4	3.71	3.7	8.01	8.0	8.40	8.2	8.0
(HL ₂) ₂ Mn ²⁺ ·2H ₂ O	70	694.9	62.16	62.0	3.74	3.7	8.05	8.0	7.9	7.7	10.7

Table 2. Experimental data of magnetic moment for metal chelates of HL₂

Metal Chelates	$\chi_g \times 10^{-6}$ cgs	$\chi_m \times 10^{-6}$ cgs	Magnetic moment	$\mu_{\text{off}} = \sqrt{n(n+2)}$ BM	μ_{off} , BM
			μ_{off} , BM	Obs.	Expected
(HL ₂) ₂ Mn ²⁺	19.46	13529	5.73	5.91	5.2-6.0
(HL ₂) ₂ Co ²⁺	12.52	8757	4.61	3.87	4.4-5.2
(HL ₂) ₂ Ni ²⁺	5.55	3883	3.07	2.82	2.9-3.4
(HL ₂) ₂ Cu ²⁺	2.22	1566	1.95	1.73	1.7-2.2

Results and Discussion

The data of electrical conductivity of all the complexes in acetone indicates that they are less polarising in DMF. The magnetic moment of CO, Ni, and Cu(II) complexes were calculated from the corrected magnetic susceptibilities (*cf.* Table 2). 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 octahedral structure. The Mn(II) complex exhibited magnetic moment of the order of 5.9 B.M. showed highly paramagnetic property

The electronic spectrum of Co(II) complexes exhibited three bands around, 23809, 19607 and 8196 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 (Table 3). The electronic spectrum of Ni(II) complex also showed three bands. In electronic spectra of Cu^{+2} metal chelate of each of the ligands may be assigned to ${}^2B_{1g} \rightarrow {}^2A_{1g}$ and charge transfer transition respectively. These results reveal the distorted octahedral geometry for these chelates.

Table 3. Reflectance spectral data of metal complexes of ligand HL₂.

Metal complex	Absorption, cm^{-1}	Transitional	
(HL ₂) ₂ —Mn ²⁺	23785	${}^6A_{1g}$	$\rightarrow {}^4A_{1g}(4EG)$
	18412	${}^6A_{1g}$	$\rightarrow {}^4T_{2g}(4G)$
	16724	${}^6A_{1g}$	$\rightarrow {}^4T_{1g}(4G)$
(HL ₂) ₂ —Co ²⁺	23809	${}^4T_{1g}(F)$	$\rightarrow {}^4T_{2g}(F)$
	19607	${}^4T_{1g}(F)$	$\rightarrow {}^4A_{2g}$
	08196	${}^4T_{1g}(F)$	$\rightarrow {}^4T_{2g}(P)$
(HL ₂) ₂ —Ni ²⁺	22106	${}^3A_{2g}$	$\rightarrow {}^3T_{1g}(P)$
	15472	${}^3A_{2g}$	$\rightarrow {}^3T_{1g}(F)$
(HL ₂) ₂ —Cu ²⁺	24165	Charge	$\rightarrow$ Transfer
	14970	${}^2B_{1g}$	$\rightarrow {}^2A_{1g}$

The reflectance spectra of the metal chelates in the visible region were recorded against MgO on Beckman-DK-2A spectrophotometer (Figure 1). The assignment of significant bands present in the reflectance spectra of each of the metal chelates are furnished in Table 3.

Figure 1. Reflectance spectra of HL₂ metal complexes (1) HL₂ Cu (2) HL₂ Ni (3) HL₂ Co (4) HL₂ Mn (The band value in nm is converted into cm^{-1} and discussed in text).

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 1730 cm^{-1} on complex formation. A new band at 1095 cm^{-1} had appeared in the spectra of metal chelates.

Table 4. Infrared frequencies of HL₂ and their metal complexes.

Ligand	Frequency cm ⁻¹			
	Aromatic	Metal ligand	Imides group	C=O ketone
HL ₂	1598 C=C str.	3370 str.	1682 str.	
	1497 C-H bends.	1357 bend.	1578 str.	1716 str.
	3028 C-H str.		1388 str.	
HL ₂ -M				-CH ₂ group, Bridge
	1598 C=C str.		1578 str.	2922 str. (Asym.)
	1497 C-H bends.	580-450	1388 str.	2849 str. (Sym.)
	3028 C-H str.		1388 str.	1454 bend.

This may be assigned to Vc-o of C-O-Metal bond formation. The important bands are observed at their respective positions. The bands at 1680 cm⁻¹ is due to imides group. The bands at 3030,1600 and 820 cm⁻¹ are mainly from 1,4 disubstituted aromatic ring .the bands 2850, 2920 and 1450 cm⁻¹ is assigned to -CH₂ bridge system.

Metal Complexes of HL₂

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

Table 5. Antibacterial and antifungal activity of ligand HL₂ and their metal complexes.

Sample	Zone of inhibition, in mm		Zone of inhibition at 1000 ppm, %	
	Gram + ve	Gram - ve		
	<i>Staphylococcus aureus</i>	<i>Ps. aeruginosa</i>	<i>Penicillium expansum</i>	<i>Nigrospora sp.</i>
HL ₂	17	19	64	65
HL ₂ -Cu ⁺²	20	11	82	87
HL ₂ Mn ⁺²	16	14	75	71
HL ₂ -Co ⁺²	18	17	75	64
HL ₂ -Ni ⁺²	09	16	72	61

The ligands of 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 fungi against *Penicillium expansum* and *Nigrospora sp.*

Acknowledgment

The author is thankful to Exe. Principal Dr. M.V. HATHI, R.R Mehta science college palanpur for providing laboratory facilities and to the director, CICART providing elemental, spectral and antimicrobial activity data.

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