

Transition Metal Complexation Studies on Heterocyclic Ligands

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Two new ligands, HL₁ and HL₂ were synthesized from anthranilic acid and 5-bromo anthranilic acid, respectively. For this, quinazolin-4-one 8-hydroxyquinoline (QH) merged molecules were used. The complexes of first transition metals like Cu(II), Ni(II), Co(II), Mn(II) and Zn(II) with HL₁ and HL₂ have been prepared and characterized by physico-chemical methods such as elemental analysis, conductometric studies, magnetic susceptibility, infrared, NMR and electronic spectral data. The stoichiometry of the complexes has been found to be 1:2 (metal:ligand). An octahedral geometry around Co(II), Ni(II) and Mn(II), distorted octahedral geometry around Cu(II) and tetrahedral geometry around Zn(II) have been proposed. These complexes also been tested for their antifungal activities.

Key Words: 8-Hydroxy quinoline ligands, Complexes, IR, Electronic and NMR spectral studies, Antifungal activity.

INTRODUCTION

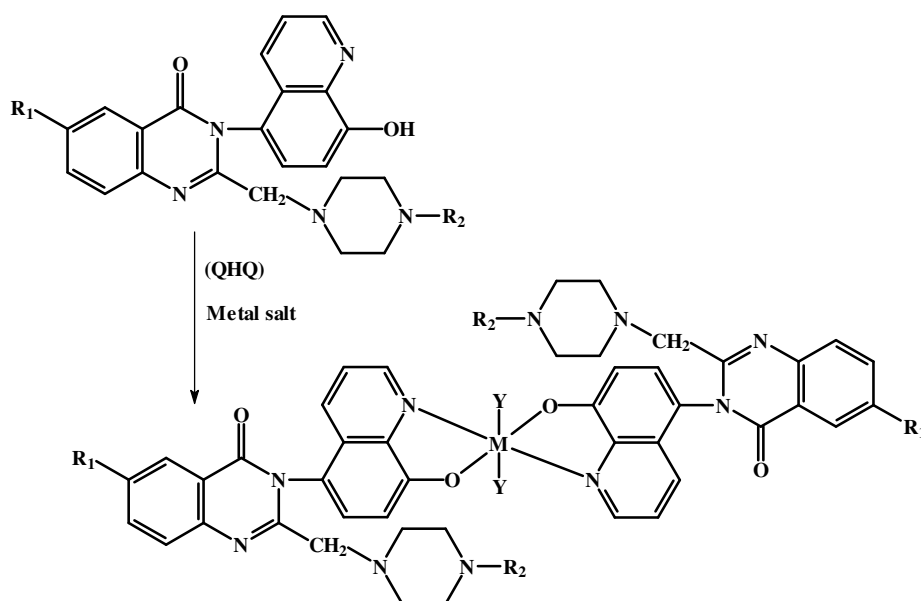
The heterocyclic nitrogen compounds especially quinazolinone derivatives play a vital role in many biological processes and as synthetic drugs¹⁻⁴. Quinazolin-4-one is also well known for many pharmaceutical products⁵⁻⁸. Ligand, 8-hydroxyquinoline is not only act as a complexing agent but also applied for drug synthesis^{9,10}. The 8-hydroxyquinoline and quinazolin-4-one molecules merged into one molecule has not received any attention in spite of well-defined applications of both the molecules. Hence it was thought to explore the study of quinazolin-4-one 8-hydroxyquinoline merged molecules as ligands HL₁ and HL₂ with their complexes with Cu(II), Ni(II), Co(II), Mn(II) and Zn(II) metal ion. Antimicrobial activities of both the ligands and complexes have also been studied. General structure of formation of complexes is shown as Fig. 1.

EXPERIMENTAL

All the chemicals used were of pure grade (Merck and B.D.H). Double distilled water was used throughout the experiment. The melting points of all complexes were determined by open capillary method and were uncorrected.

Synthesis of ligands HL₁ and HL₂: For the preparation of ligand HL₁, a mixture of 2-chloromethyl-3-(8-hydroxyquinolin-5-yl)-3(H) quinazolin-4-one (0.01 mol) and 1-ethyl-piperazine (0.01 mol) and for the preparation of ligand HL₂ a mixture of 6-bromo-2-chloromethyl-3-(8-hydroxyquinolin-5-yl)-3(H) quinazolin-4-one (0.01 mol)

and 1-ethyl-piperazine (0.01 mol) were taken in dry pyridine (20 mL) and was refluxed for 12 h. Pyridine was distilled off as much as possible and the residue was poured into a little crushed ice with stirring. The products were separated out, filtered, washed with water and finally with ethanol. The air-dried products were quantitative. m.p. > 230 °C.



where Mt: Cu²⁺, Ni²⁺, Co²⁺, Mn²⁺, Zn²⁺ *etc.*, R₁: H, Br; R₂: ethyl; Y: H₂O or acetate
Fig. 1. QHQ-metal chelates

Synthesis of chelates: A dried sample of ligand, either HL₁ or HL₂ (0.01 M) was stirred in 85 % (v/v) formic acid and then it was diluted by water until complete dissolution. The resultant solution was designated as reagent solution. This solution was used for preparation of chelates with particular ligand with transition metal ions. The formic acid solution of ligand was added drop wise to a solution of cupric nitrate hexahydrate, nickel nitrate hexahydrate, cobalt nitrate hexahydrate, manganese chloride hexahydrate, zinc nitrate hexahydrate (0.005 mol) in 100 mL of water with rapid stirring. The resultant pH 4.5 (for Cu²⁺ ion), pH 6.0 (for Ni²⁺ and Co²⁺) and pH 5.6 (for Mn²⁺ and Zn²⁺) was maintained by adding of sodium acetate. A dark coloured solid precipitated out. It was allowed to settle and digested on water bath at 70 °C for *ca.* 2 h. The solid mass was filtered, washed with 1:1 mixture of water-ethanol and finally with acetone then dried. The percentage yield of chelates was in the range of 59-80 %. All the chelates were powdered well and dried at 70 °C over a period of 24 h.

The C, H and N contents of metal chelates were determined on elemental analyzer Thermofinigan 1101 Flash EA. The metal contents were estimated using standard methods¹¹. The halogen content was determined by Carius method¹². The molar conductance of the complexes in DMF (10^{-3} M) solutions were measured at room temperature using Systronics model 305 direct reading conductivity bridge. The infrared spectra (KBr) were recorded in the range $4000-600\text{ cm}^{-1}$ with a Nicolet-760 spectrophotometer. Electronic spectra of chelates were recorded on a Beckman-DK-2A spectrophotometer using MgO as reference. Magnetic susceptibility ' χ_m ' was measured by Gouy's method¹³ at room temperature (300 K) using Hg [Co(CNS)₄] as calibrant¹⁴ and the effective magnetic moment from relation¹⁵, $\mu_{\text{eff}} = 2.84\sqrt{\chi_m \times T}$, where T is the absolute temperature. Diamagnetic corrections were made by using Pascal's constants.

The ligands and their metal chelates were screen at 1000 ppm concentration *in vitro* for their antifungal activity against five fungi viz. *Botrydepladia* thiobromine, *Nigrospora sp.*, *Rhizopus nigricans*, *Aspergillus fumigatus* and *Candida albicans*. The antifungal activity of the compounds was measured by plate method. Five days old cultures were suspended in potato dextrose agar (PDA) medium and autoclaved at $1200\text{ }^\circ\text{C}$ for 15 minutes at 15 atmospheric pressure. The percentage inhibition of fungi was calculated after 5 days using the formula given below:

$$\text{Percentage of inhibition} = 100 (X-Y)/X$$

where X= area of colony in control plate (without sample) and Y = area of colony in test plate.

RESULTS AND DISCUSSION

The complexes are microcrystalline coloured powders having melting points higher than the ligands. They are stable in air at room temperature. All compounds gave satisfactory elemental analysis, suggesting 1:2 (metal: ligand) stoichiometry. Elemental and molar conductance data are shown in Table-1. The result indicates that they are less polar in DMF. Very low molar conductance values in the range of 6.09 to $21.80\text{ ohm}^{-1}\text{ cm}^2\text{ mol}^{-1}$ in Mn(II), Ni(II), Cu(II) and Zn(II) chelates indicates that they are non-electrolytic¹⁶ and monomeric in nature (ML_2 type chelates). The low Λ_m values may be attributed to the large cations¹⁷. The electrical conductivity of these chelates were found in the decreasing order: Co > Ni > Zn > Mn > Cu.

Infrared spectra: IR spectrum of ligands HL₁ and HL₂ show a broad band extended from 3450 to 2600 cm^{-1} which might be responsible to phenolic group bonded to N atom of 8-hydroxyquinoline moiety^{18,19}. The inflexions at 3030 , 2930 and 2850 cm^{-1} are due to aromatic CH and methylene group of bridge and piperazine ring²⁰⁻²³. The strong band at 1700 cm^{-1} is attributed to C=O of quinazoline 4-one moiety. Several bands appeared in $1600-1500\text{ cm}^{-1}$ region may arised from aromatic breathing. The IR band at *ca.* 1580 cm^{-1} (C=N of 8-quinolinol system) of HL₁ and HL₂ ligands shifted to higher frequency side *ca.* 1600 in the spectra of the metal

TABLE-1
ANALYTICAL AND PHYSICAL DATA OF
LIGANDS AND THEIR METAL COMPLEXES

Ligand/ Compl. (m.f.)	m.w. (g/mol) (Yield, %)	Elemental analysis (%): Found (calcd.)					μ_{eff} (B.M.)	Λ_M (ohm^{-1} $\text{cm}^2 \text{mol}^{-1}$)
		C	H	N	Br	M		
HL ₁ (C ₂₄ H ₂₅ N ₅ O ₂)	413 (75)	69.20 (69.39)	5.90 (6.02)	16.70 (16.86)	-	-	-	-
HL ₂ (C ₂₄ H ₂₄ N ₅ O ₂ Br)	494 (79)	58.20 (58.29)	4.80 (4.85)	15.90 (14.50)	16.50 (16.60)	-	-	-
Cu ²⁺ (HL ₁) (C ₄₈ H ₅₂ N ₁₀ O ₆ Cu ²⁺)	928 (72)	62.00 (62.03)	5.50 (5.60)	15.00 (15.07)	-	6.80 (6.84)	1.89	8.29
Cu ²⁺ (HL ₂) (C ₄₈ H ₅₂ N ₁₀ O ₆ Cu ²⁺ Br ₂)	1086 (79)	53.10 (53.15)	4.60 (4.61)	12.90 (12.92)	14.50 (14.58)	5.80 (5.86)	1.97	7.69
Ni ²⁺ (HL ₁) (C ₄₈ H ₅₂ N ₁₀ O ₆ Ni ²⁺)	923 (74)	62.30 (62.42)	5.50 (5.63)	15.10 (15.17)	-	6.20 (6.36)	3.05	9.20
Ni ²⁺ (HL ₂) (C ₄₈ H ₅₂ N ₁₀ O ₆ Ni ²⁺ Br ₂)	1081 (72)	53.20 (53.29)	4.50 (4.62)	12.90 (12.95)	14.60 (14.62)	5.40 (5.43)	3.12	9.10
Co ²⁺ (HL ₁) (C ₄₈ H ₅₂ N ₁₀ O ₆ Co ²⁺)	923 (80)	62.30 (62.41)	5.60 (5.63)	15.10 (15.16)	-	6.30 (6.38)	4.83	21.80
Co ²⁺ (HL ₂) (C ₄₈ H ₅₂ N ₁₀ O ₆ Co ²⁺ Br ₂)	1081 (59)	53.20 (53.25)	4.50 (4.62)	12.80 (12.95)	14.50 (14.61)	5.40 (5.44)	5.02	20.12
Zn ²⁺ (HL ₁) (C ₄₈ H ₅₂ N ₁₀ O ₆ Zn ²⁺)	929 (70)	61.90 (61.97)	5.50 (5.59)	15.00 (15.06)	-	7.00 (7.03)	-	9.81
Zn ²⁺ (HL ₂) (C ₄₈ H ₅₂ N ₁₀ O ₆ Mn ²⁺ Br ₂)	1087 (76)	52.90 (52.97)	4.50 (4.59)	13.20 (13.21)	14.75 (14.53)	6.00 (6.01)	-	9.10
Mn ²⁺ (HL ₁) (C ₄₈ H ₅₂ N ₁₀ O ₆ Mn ²⁺)	919 (69)	62.50 (62.68)	5.60 (5.65)	15.20 (15.23)	-	5.80 (5.91)	5.10	6.09
Mn ²⁺ (HL ₂) (C ₄₈ H ₅₂ N ₁₀ O ₆ Mn ²⁺ Br ₂)	1077 (69)	53.40 (53.48)	4.60 (4.64)	12.90 (13.00)	14.60 (14.67)	5.00 (5.04)	5.89	9.68

chelates indicating involvement of nitrogen in the chelate formation^{18,24,25}. Most of the bands appeared in the spectra of corresponding ligand are observed at their metal chelates. Only a new band at 1095 cm^{-1} had appeared in the spectra of metal chelates. This may be assigned to $\nu(\text{C-O})$ of C-O-M bond formation. All the complexes show additional bands at 840-830 cm^{-1} indicating the presence of coordinated water²⁶.

Magnetic moment and electronic spectra: At room temperature the magnetic moment ' μ_{eff} ' values for the Co(II) complexes lies in the range 4.83-5.02 BM (Table-1) suggest high spin octahedral geometry, which is further supported by the electronic spectral data. The electronic spectra of the Co(II) complexes display three absorption bands in the range 8745-8965, 19658-19856 and 23656-24859 cm^{-1} , assigned to the transitions ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$ (ν_1), ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}(\text{F})$ (ν_2) and ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{1g}(\text{P})$ (ν_3), respectively²⁷. The values of transition ratio ν_2/ν_1 is 2.24 providing further evidences for octahedral geometry for the Co(II) complexes.

In the Ni(II) complexes, μ_{eff} values at room temperature are observed in the range 3.05-3.12 BM as expected for six coordinated spin free Ni(II) species. The reflectance spectra of the Ni(II) complexes, exhibit two strong bands at 13589-15485 cm^{-1} and 23458-24875 cm^{-1} , assignable to ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$, respectively. The ν_2/ν_1 ratio for the chelate is 1.60 occurs in the usual range (1.6-1.82 BM) for octahedral Ni(II) chelates²⁸. The spectral bands are well within the range observed for hexacoordinate octahedral complexes reported earlier^{29,30}. The Cu(II) complexes exhibit normal magnetic moments (1.89-1.97 BM) indicating the distorted octahedral geometry, which is in agreement with data reported by several research workers^{31,32}. These complexes show broad asymmetric bands in the region 15485-15715 cm^{-1} and at 23687 cm^{-1} assignable to ${}^2B_{1g} \rightarrow {}^2A_{1g}$ and charge transfer transition, respectively^{33,34}. These results reveal the distorted octahedral geometry for these complexes. The former band may be due to ${}^2E_g \rightarrow {}^2T_{2g}$ accounted due to Jahn Teller effect suggesting thereby a distorted octahedral geometry for these complexes³⁵. The values of transition ratio ν_2/ν_1 is 1.52.

Zn(II) complexes are diamagnetic as expected for d^{10} systems and may have tetrahedral geometry^{36,37}. There is no evidence for the characteristic bands of coordinated water in IR spectra.

The electronic spectra of the Mn(II) exhibited three spin allowed bands in the region 15896-15985 cm^{-1} , 17895-17965 cm^{-1} and 23458-24889 cm^{-1} assigned to the transitions ${}^6A_{1g} \rightarrow {}^4T_{1g} ({}^4G)$, ${}^6A_{1g} \rightarrow {}^4T_{2g} ({}^4G)$ and ${}^6A_{1g} \rightarrow {}^4E_g, {}^4T_{1g} ({}^4P)$, respectively, indicating octahedral geometry^{38,39}. The observed magnetic moment (5.10-5.89 BM) of the complexes indicates high spin octahedral environment⁴⁰.

Antifungal activity: The complexes show inhibition of fungal in the following order: Co(II) < Zn(II) < Mn(II) < Ni(II) < Cu(II). The substitutions of phenyl rings by chlorine have much more effect on the fungicidal activity. The results suggest that the variation in structure on coordination affects the growth of micro organisms and may result in to inhibitory or reduction in toxicology of metal ions towards some organisms⁴¹.

Conclusion

The ligands act as a hexadentate ligand in all complexes. Bonding either among N(4) depending upon the nature of the metal ions. Octahedral structures for Ni(II), Co(II) and Mn(II) complexes, tetrahedral polymeric structure for Zn(II) and distorted octahedral for Cu(II) complex have been tentatively proposed. Present work will contribute in the field of new antifungal for some plant pathogenic organisms.

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