



Scholars Research Library

Der Pharma Chemica, 2012, 4(4):1506-1511
(<http://derpharmachemica.com/archive.html>)



ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis, Characterization and Antimicrobial Activity of Metal Chelates of 2-[(8-hydroxyquinolinyl)-5-aminomethyl]-3-(4-Bromophenyl)-3(H)-quinazolin-4-one

R. T. Vashi*, S. B. Patel and H. K. Kadiya**

*Department of Chemistry, Navyug Science College, Rander Road, Surat-395009, India.

**C. U. Science College, Ashram Road, Ahmedabad-380014, Gujarat-India.

ABSTRACT

Synthesis and characterization of 2-[(8-hydroxyquinolinyl)-5-aminomethyl]-3-(4-bromophenyl)-3(H)-quinazolin-4-one ligand called HABQ was studied. To prepare this ligand anthranilic acid was converted into 2-chloromethyl-3-(4-bromophenyl)-3(H)-quinazolin-4-one. This compound was finally condensed with 5-amino-8-hydroxyquinoline. The transition metal complexes of Cu^{2+} , Ni^{2+} , Zn^{2+} , Mn^{2+} and Co^{2+} of this ligand HABQ were prepared and characterized by reflectance, NMR as well as IR spectroscopy, elemental analysis and magnetic measurements. The stoichiometry of the complexes has been found to be 1: 2 (Metal : ligand). The data suggested an octahedral geometry around Co^{2+} , Ni^{2+} and Mn^{2+} complexes, a distorted octahedral geometry around Cu^{2+} and a tetrahedral geometry around Zn^{2+} have been proposed. These complexes have been tested for their antifungal activities.

Keywords: Ligand, 8-hydroxyquinoline, IR and NMR spectral studies, magnetic moment, antifungal study.

INTRODUCTION

8-hydroxyquinolinyl or 8-quinolol is well known as an analytical reagent [1-2]. Its various derivatives [3] are also useful in pharmaceuticals. Several azo dyes based on 8-quinolinol are also reported for dyeing of textiles as well as their chelating properties [4]. One of the derivatives, viz 5-amino-8-hydroxyquinoline can be synthesized easily and studied extensively for a number of derivatives [5].

The chemistry of heterocyclic compounds continuously to be an explore field in the organic chemistry. Infectious diseases caused by micro and micro organisms; viz. bacteria, fungi, viruses and parasites are still a major threat to human health, despite tremendous inventions in drug chemistry. The emergence of wide spread drug resistance, particularly multi-drug resistance [6] against gram-positive bacteria is a major concern.

The heterocyclic nitrogen compounds especially quinazolinone derivatives play a vital role in many biological processes and as synthetic drugs [7]. A Quinazolin-4-one derivative possesses biological activities such as antifungal [8-9]. The formation of 8-hydroxyquinoline and quinazolin-4-one molecules into one molecule has not received any attention in spite of well-defined applications of both the molecules. Hence the initial work in this direction has been carried out [10]. Thus in the extension of this work [10] present communication comprises the synthesis, characterization and chelating properties of novel quinazolin-4-one-8-hydroxyquinoline derivatives.

on water bath at 70°C for about 2 h. The solid mass was filtered, washed with 1:1 mixture of water-ethanol and finally with acetone and then dried. The percentage yield of complexes was in the range of 60-82 %. All the complexes were powdered well and dried at 70°C over a period of 24 h.

Measurements: The elemental analysis of metal chelates were determined by TF-Flash-1101 EA (ITALY). The metal contents of metal chelates were determined volumetrically by Vogel's methods [11]. ¹H NMR spectra of ligand was recorded on Bruker NMR spectrophotometer using TMS as an internal standard in CDCl₃/DMSO-d₆ [12]. The molar conductance of the complexes in DMF (10⁻³M) 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 cm⁻¹ with a Nicolet-760 spectrophotometer. Reflectance spectra of complexes were recorded on a Beckman-DK-2A spectrophotometer using MgO as reference. Magnetic susceptibility was measured by Gouy's method [13] at room temperature (300 K) using Hg [Co(CNS)₄] as calibrant [14], and the effective magnetic moment from relation [12], $\mu_{\text{eff}} = 2.84\sqrt{X_m \times T}$, where T is the absolute temperature. Diamagnetic corrections were made by using Pascal's constants.

The ligand and its metal complexes were screened at 1000 ppm concentration in vitro for their antifungal activity against five fungi viz. *Erysiphe pisi*, *Nigrospora* sp., *Trichoderma* sp., *Aspergillus niger*, *Curvularia lunata*. 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 120°C for 15 minutes and 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)

Y = area of colony in test plate.

RESULTS AND DISCUSSION

The synthesis of Ligand HABQ was performed by method reported for 2-Chloromethyl-3-(4-Bromophenyl)-3(H)-Quinazoline-4-one. The resultant HABQ ligand was an amorphous dark brown powder. The C, H and N contents of HABQ (Table-1) are consistent with the structure predicted (Scheme 1).

The non-aqueous conductometric titration of ligand gave the proton of -CH₂ and -OH group in ligand. The complexes are microcrystalline colored powders having melting points higher than the ligand. They are stable in air at room temperature. All compounds gave satisfactory elemental analysis, suggesting 1:2 (metal: ligand) stoichiometry. Elemental data are shown in Table-1.

The result indicates that they are less polar in DMF. Very low molar conductance (Λ_M) values in the range of 8.33 to 23.11 ohm⁻¹cm² mol⁻¹ in Mn²⁺, Ni²⁺, Cu²⁺ and Zn²⁺ complexes indicates that they are non-electrolytic and monomeric in nature (ML₂ type complexes). The low Λ_M values may be attributed to the large cations [10]. The electrical conductivity of these complexes found in the order: Co > Zn > Cu > Ni > Mn.

NMR spectra: The ¹H NMR spectra of ligand HL₅ gave the multiplet between 6.88-7.8 δ ppm for aromatic protons, signal at 5.74-5.98 δ ppm for phenolic -OH group, 3.35-3.77 δ ppm due to CH₂ bridge and 11.1-11.35 δ ppm due to -NH group.

IR spectra: IR spectrum of ligand HL₅ show a broad band extended from 3300 to 2600 cm⁻¹ which might be responsible to phenolic -OH group bonded to N atom of 8-hydroxyquinoline moieties [15]. The inflexions at 2925, 2855 and 1470 cm⁻¹ are due to aromatic -CH₂- and methylene group of bridge [16-19]. The strong band at 1720 cm⁻¹ is attributed to -C=O of quinazoline 4-one moiety. Several bands appeared between 1500 and 1600 cm⁻¹ region may arise from aromatic breathing. Band at 3400 cm⁻¹ for -NH group. The IR band at 1580 cm⁻¹ (C=N of 8-quinolinol system) of HL₅ ligand shifted to higher frequency side ~1600 cm⁻¹ in the spectra of the metal complexes indicating involvement of nitrogen in the complexes formation [15-20]. Most of the IR spectral features of complexes resembles to those of the corresponding ligand. The broad band due to free OH group observed in the spectra of ligand became due to participation of the OH group in formation of complex or co-ordination bond formation.

The metal and C, H, N contents of metal chelates of HABQ (Table 1) are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal chelates is 1:2.

Table – 1 Analysis of HABQ ligand and its Metal Chelates.

Molecular Formula	M.W. (g/mol)	Yield (%)	Elemental Analysis (%)				
			Found (Calcd.)				
			C	H	N	Br	M
C ₂₄ H ₁₇ N ₄ O ₂ Br	473.00	64	60.70 (60.88)	3.50 (3.59)	11.70 (11.83)	16.81 (16.89)	-
C ₄₈ H ₃₂ N ₈ O ₄ Br ₂ Cu ⁺² .2H ₂ O	1042.54	82	55.10 (55.25)	3.10 (3.45)	10.60 (10.74)	15.20 (15.33)	5.80 (6.09)
C ₄₈ H ₃₂ N ₈ O ₄ Br ₂ Ni ⁺² .2H ₂ O	1038.69	76	55.40 (55.51)	3.40 (3.47)	10.70 (10.79)	15.30 (15.40)	5.40 (5.66)
C ₄₈ H ₃₂ N ₈ O ₄ Br ₂ Mn ⁺² .2H ₂ O	1033.93	62	55.60 (55.71)	3.30 (3.48)	10.50 (10.83)	15.40 (15.46)	5.30 (5.31)
C ₄₈ H ₃₄ N ₈ O ₄ Br ₂ Co ⁺² .2H ₂ O	1037.93	60	55.40 (55.50)	3.40 (3.47)	10.40 (10.79)	15.30 (15.40)	6.50 (6.58)
C ₄₈ H ₃₂ N ₈ O ₄ Br ₂ Zn ⁺² .2H ₂ O	1044.39	65	55.00 (55.15)	3.30 (3.45)	10.70 (10.72)	15.20 (15.30)	6.20 (6.26)

The IR spectra of all the chelates are identical. Most of bands appeared in the spectra of corresponding ligand are observed at their metal complexes. The important IR Spectral data are shown in Table 2.

Table - 2 Spectral features and magnetic moment of HABQ metal Chelates

Metal chelates	Magnetic moment μ_{eff} (B.M.)	Electronic spectral data, cm ⁻¹	Transition
HABQ-Cu ⁺²	1.92	24000 15895	Charge Transfer ${}^2B_{1g} \rightarrow {}^2A_{1g}$
HABQ-Ni ⁺²	2.88	22480 15625	${}^3A_{2g} \rightarrow {}^3T_{1g}(\text{P})(\nu_2)$ ${}^3A_{2g} \rightarrow {}^3T_{1g}(\text{F})(\nu_1)$
HABQ-Co ⁺²	4.23	24170 17600 8000	${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{1g}(\text{P})(\nu_3)$ ${}^4T_{1g}(\text{F}) \rightarrow {}^4A_{2g}(\text{F})(\nu_2)$ ${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{1g}(\text{F})(\nu_1)$
HABQ-Mn ⁺²	5.17	24350 18520 16987	${}^6A_{1g} \rightarrow {}^4T_{1g}({}^4\text{P})(\nu_3)$ ${}^6A_{1g} \rightarrow {}^4T_{2g}({}^4\text{G})(\nu_2)$ ${}^6A_{1g} \rightarrow {}^4T_{1g}({}^4\text{G})(\nu_1)$
HABQ-Zn ⁺²	Diamag.	24000 15895	-----

Magnetic moment and electronic spectra

The room temperature μ_{eff} value for the Co⁺² complex is 4.23 B.M. (Table-2) suggest high spin octahedral geometry, which is further supported by the electronic spectral data. The electronic spectrum of the Co⁺² complex shows three bands at 8000, 17600 and 24170 cm⁻¹, assignable to ${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{1g}(\text{F})(\nu_1)$, ${}^4T_{1g}(\text{F}) \rightarrow {}^4A_{2g}(\text{F})(\nu_2)$ and ${}^4T_{1g}(\text{F}) \rightarrow {}^4T_{1g}(\text{P})(\nu_3)$ transitions, respectively for an octahedral geometry [11]. The value of transition ratio ν_2 / ν_1 is 2.20 providing further evidences for octahedral geometry for the Co⁺² complex.

In the Ni⁺² complex, μ_{eff} values at room temperature is 2.88 B.M. as expected for six coordinated spin free Ni⁺² species [16]. The reflectance spectra of the Ni⁺² complex, exhibit two strong bands at 15625 cm⁻¹ and 22480 cm⁻¹, assignable to ${}^3A_{2g}(\text{F}) \rightarrow {}^3T_{1g}(\text{F})(\nu_1)$ and ${}^3A_{2g}(\text{F}) \rightarrow {}^3T_{1g}(\text{P})(\nu_2)$ respectively. The spectral bands are well within the range observed for hexacoordinate octahedral complexes reported earlier [17-18].

The Cu⁺² complex exhibit normal magnetic moment 1.92 B.M. corresponding to one unpaired electron indicating the distorted octahedral geometry, which is in agreement with data reported by other research worker [19]. Electronic spectra of these complex show broad asymmetric bands in the region 15895 cm⁻¹ and at 24000 cm⁻¹ assignable ${}^2B_{1g} \rightarrow {}^2A_{1g}$ and charge transfer transition respectively [20]. These results reveal the distorted octahedral geometry for this complex. The former band may be due to ${}^2E_g \rightarrow {}^2T_{2g}$ accounted due to John Teller effect suggesting thereby a distorted octahedral geometry for this chelate.

Zn^{+2} complex is diamagnetic in nature and its electronic spectra do not furnish any characteristic d-d transitions except charge transfer (C.T.) bands as expected for d^{10} systems and may have tetrahedral geometry [21]. There is no evidence for the characteristic bands of coordinated water in IR spectra. IR spectra of Zn^{+2} complex is shown in Fig.1.

The electronic spectra of the Mn^{2+} complex exhibited three spin allowed bands in the region 16987 cm^{-1} , 18520 cm^{-1} and 24350 cm^{-1} assigned to the transitions ${}^6A_{1g} \rightarrow {}^4T_{1g} ({}^4G)(\nu_1)$, ${}^6A_{1g} \rightarrow {}^4T_{2g} ({}^4G)(\nu_2)$ and ${}^6A_{1g} \rightarrow {}^4E_g, {}^4T_{1g} ({}^4P_g)(\nu_3)$ respectively, indicating octahedral geometry [22]. The observed magnetic moment of the Mn^{2+} complex is 5.17 B.M. corresponding to five unpaired electrons indicates high spin octahedral environment [23].

Antifungal activity: The examination of antifungal activity of HABQ ligand and its chelates reveals that the ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand (Table-3). Among all the chelates the Cu^{+2} chelate was found to be more toxic against fungi. The antifungal activity of the metal chelates was found to be in the order: $Cu(II) > Co(II) > Ni(II) > Mn(II) > Zn$. Hence such type of chelates may find as agricultural and garden fungicides.

Table-3 Antifungal activity of HABQ ligand and its metal chelates.

Sample	Zone of inhibition at 1000 ppm (%)				
	E	N	T	AN	C
HABQ	88	85	80	72	63
HABQ- Cu^{+2}	77	75	73	74	77
HABQ- Mn^{+2}	74	67	56	58	59
HABQ- Zn^{+2}	72	79	74	74	68
HABQ- Co^{+2}	61	67	68	66	88
HABQ- Ni^{+2}	60	65	67	75	72

E = Erysiphepisi, N = Nigrospora sp., T = Trichoderma sp., AN = Aspergillus niger, C = Curvularialumata.

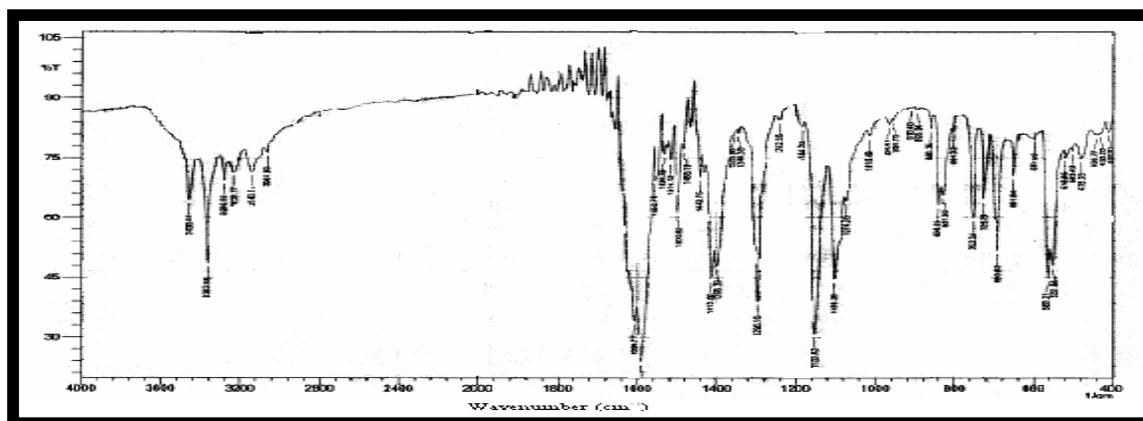


Fig. 1. IR Spectrum of $[HL_5] Zn^{2+}$ complex..

CONCLUSION

- The ligand molecule acts as a hexadentate ligand in all the studied cases of Chelates. Bonding either among N (4) depending upon the nature of the metal ions.
- Octahedral structures for Ni^{2+} , Co^{2+} and Mn^{2+} Chelates, tetrahedral polymeric structure for Zn^{2+} and distorted octahedral for Cu^{2+} Chelates have been tentatively proposed.
- Present work will contribute in the field of new antifungal for some plant pathogenic organisms.

Acknowledgement

The authors are thankful to Department of Chemistry, Navyug Science College, Surat for providing laboratory facility.

REFERENCES

- [1] M. M. Raikhshtat, S. B. Savvin and L. A. Gribov, *Zh Anal Khim.*, **1979**, 34, 1886.
- [2] L. A. Gribov, S. B. Savvin and M. M. Raikhshtat, *Zh Anal Khim.*, **1980**, 35, 1469.
- [3] K. A. Oster and M. J. Golden, *J Am Pharm Assoc Sci Ed.*, **1947**, 37, 283.
- [4] J. P. Philips, *Chem Review*, **1984**, 56, 271.
- [5] J. H. Barkhate and R. I. Teib, *J Org Chem.*, **1968**, 26, 4078.
- [6] I. N. Okeke, R. Laxmanarayan, Z. A. Bhutta, A. G. Duse, P. Jenkins, T.F.O' Brien, A. Pablos-Mendez and K. P. Klugman, *Lancet Infect Dis.*, **2005**, 5, 481.
- [7] Pratibha Desai, Jiten Naik, C.M. Desai and Dinesh Patel, *Asian J. Chem.*, **1998**, 10(4), 993-994.
- [8] N. B. Patel and J. N. Patel, *J. Indian Chem. Soc.*, **2009**, 86, 1231- 1236.
- [9] R. T. Vashi and S. B. Patel, *E-J. Chem.*, **2009**, 6(S₁), S445-S451.
- [10] R. T. Vashi and C. D. Shelat, *Asian J. Chem.*, **2010**, 22(3), 1745-1750.
- [11] A. I. Vogel, *A Text book of Quantitative Inorganic Analysis* 3 rd. ed., ELBS, London, **1978**.
- [12] R. T. Vashi, C. D. Shelat and P. S. Desai, *J. Environ. Res. and Devel.* **2008**, 2(4), 652-658.
- [13] J. Lewis and R. G. Wilkins, "*Modern Coordination Chemistry.*" Interscience, New York, **1964**.
- [14] B. N. Figgis and J. Lewis, *The Magneto Chemistry of Complexes in Modern Coordination Chemistry*, Interscience, New York, **1960**.
- [15] A. B. P. Lever, *Inorganic Electronic Spectroscopy* ", Elsevier, New York **1968**.
- [16] F. A. Cotton and G. Wilkinson *Advanced Inorganic Chemistry*, 5th Ed., Wiley, New York, **1988**.
- [17] D. P. Singh, N. Shishodia, B. P. Yadav and V. B. Rana, *J. Indian Chem. Soc.*, **2004**, 81, 287-290.
- [18] A. S. Bull, R. B. Martin and R. J. P. William, in "*Electronic Aspects of Biochemistry*", ed. B. Pullmann, Academic, New York **1964**.
- [19] Chandra Sulekh and Gautam Archana, *J. Indian Chem. Soc.*, **2008**, 85, 980-984.
- [20] G. L. Chaudhary, S. R. Prasad and A. Rahman, *J. Indian Chem. Soc.*, **1997**, 74, 683-685.
- [21] M. Yildiz, B. Dulger, S.Y. Koyuncu and B. M. Yanpici, *J. Indian Chem. Soc.*, **2004**, 81, 7 -12.
- [22] A. S. Aswar and N.S. Bhave, Structural, *J. Indian Chem. Soc.*, **1997**, 74, 75-78.
- [23] M. M. Patel and H. R. Patel, *J. Indian Chem. Soc.*, **1996**, 73, 313-317.