Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(2):7-12
(http://www.derpharmachemica.com/archive.html)

Zn (II) and Cd(II) Complexes of 3-(2-(2-hydroxybenzylidene)hydrazinyl) quinoxalin-2(1H)-one: Synthesis, Characterization and DNA Binding Studies

Sukanya P[1], Venkata Ramana Reddy CH[2]*

[1]*Department of Chemistry, Vasavi College of Engineering, Hyderabad, India*
[2]*Department of Chemistry, Jawaharlal Nehru Technological University, Hyderabad 500085, India*

ABSTRACT

Zn (II) and Cd(II) complexes of the tridentate Schiff base ligand 3-(2-(2-hydroxybenzylidene)hydrazinyl) quinoxalin-2(^{1}H)-one(L) have been synthesized and characterized by ^{1}H-NMR,IR, UV-Visible, Mass spectroscopy and CHN analysis data. The ligand (L) formed 1:2 complexes, ML_2 with M=Zn(II) and Cd(II) and behaved as O,N,O-tridentate ligand. The complexes were found to be fairly stable. The interaction of the complexes with Calf Thymus DNA was investigated by UV spectroscopic studies and the intrinsic binding constant, K_b values are calculated. The base binding constants of the DNA with Zn(II) and Cd(II) complexes were found to be 7.18×10^5 and 8.18×10^9 M^{-1} respectively.

Keywords: Tridentate ligand, Schiff base, Octahedral geometry, Calf thymus DNA

INTRODUCTION

Quinoxalins belongs to an important class of Nitrogen containing heterocyclic compounds known as Diazonaphthalenes. They process biological activities such as antiviral, antibacterial, anti-inflammatory, antiprotozoal, antidepressant, anticarcinogenic, antifungal, anthelmintic, DNA binding abilities etc. [1-6]. Quinoxaline derivatives are also used in electroluminescent devices, dyes, chemosensors, catalysts, waste water treatment, and in corrosion inhibition [7-13]. In view of the chemical and biological importance of the quinoxaline based metal complexes, we have synthesized Zn (II) and Cd(II) metal ion (M) complexes of the tridentate Schiff base ligand (L) 3-(2-(2-hydroxybenzylidene)hydrazinyl) quinoxalin-2(^{1}H)-one(HSHQO) and investigated their interaction with Calf Thymus(CT) DNA by absorption spectroscopic studies.

MATERIALS AND METHODS

The chemicals used were of reagent grade. Oxalic acid, o-phenylene diamine, zinc perchlorate, cadmium chloride, salicylic acid and solvents were purchased from Merck/Aldrich and were used as received. CT-DNA was purchased from Sigma. IR spectra were recorded on JASCO FTIR-5300 spectrometer in KBr pellets from 400 to 4000 cm^{-1}. ^{1}H NMR spectrum was recorded on Bruker 500 MHz spectrometer using DMSO d_6 solvent. Electronic spectra were recorded on Shimadzu UV-3600 spectrometer. LCMS was recorded using Shimadzu mass spectrometer. Elemental analysis was carried out on FLASH Ea 1112 SERIES CHNS analyzer.

Synthesis of ligand (HSHQO)(L)

The ligand (HSHQO) was prepared by a reported three step procedure involving the synthesis of quinoxaline 2,3-dione and 3-hydrazino quinoxaline-2-one [14-16]. 1.76 g of 3-hydrazino quinoxaline-2-one was dissolved in hot methanol and 1.2 ml of salicylaldehyde was added to it. The mixture was refluxed for about 1 hr, the yellow product separated out was filtered hot, washed with methanol and n-hexane. The product was recrystallised from methanol. (MP 296ºC Yeild 78.57%) ^{1}H NMR spectrum of the ligand was recorded in DMSO-d_6: δ 12.44(^{1}H, quinoxaline ring NH), δ 11.8 (^{1}H, OH), δ 11.68 (^{1}H, free NH), δ 8.71(^{1}H, =C-H), δ 7.48-6.92 (8H, Ar-H) (Figures 1 and 2).

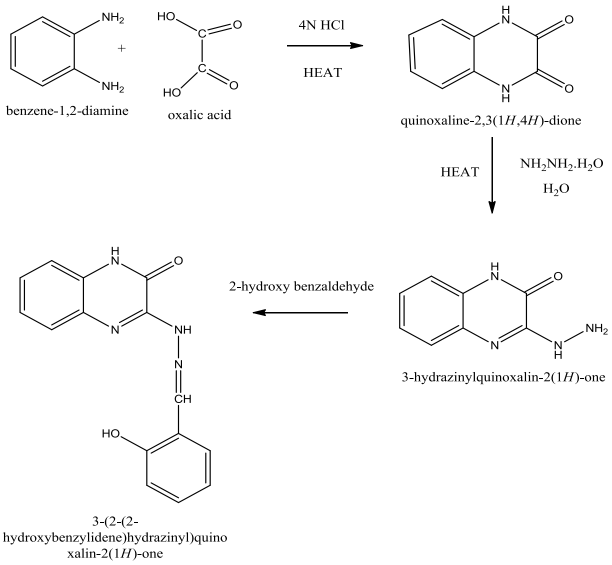

Figure 1: Scheme of ligand synthesis

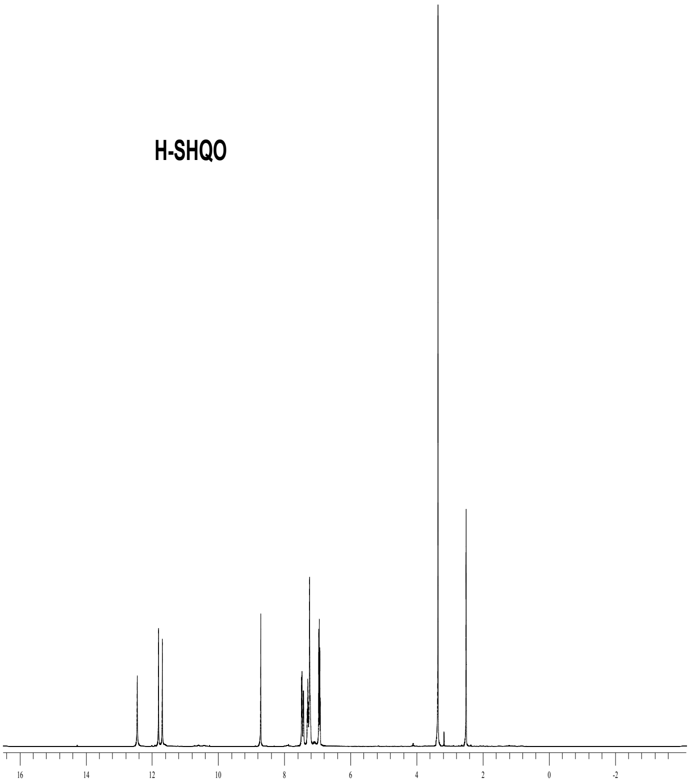

Figure 2: ^{1}H NMR spectrum of the ligand

Synthesis of Zn(II) complex

Zn(II) perchlorate hydrate (0.1 mole 0.372 g) in methanol was ultrasonicated for 15 min. To the resulting solution, a methanolic suspension of (0.2 moles 0.56 g) ligand was added in small increments for about 20 min. A clear solution was obtained after each addition as the ligand dissolved completely in the presence of Zn(II) ion. The pH of the resulting mixture was adjusted to 7 using 1% methanolic ammonia solution and the solution was refluxed on a water bath for 2 hrs. The bright orange colored product separated was filtered hot and washed successively with hot methanol and finally with petroleum ether and dried over anhydrous calcium chloride. Elemental data: Found C=57.63%, H=3.61% and N=17.81%. Cal C=57.74%, H=3.55% and N=17.95%.

Synthesis of Cd(II) complex

$CdCl_2.H_2O$ (0.1 mole 0.201 g) in water was heated and a hot methanolic suspension (0.2 moles 0.56 g) of ligand was added in small increments. The pH of the resulting mixture was adjusted to 7 using 1% methanolic ammonia solution and the solution was refluxed on a water bath for 2 hrs. The bright yellow colored product separated was filtered hot and washed successively with hot methanol and finally with petroleum ether and dried over anhydrous calcium chloride. Elemental data: Found C=53.48%, H=3.16% and N=16.36%. Cal C=53.70%, H=3.30% and N=16.70%.

DNA binding studies

Electronic absorption titrations were performed in KH_2PO_4 and K_2HPO_4 buffer using 10^{-4} molar solution of metal complexes in DMSO solution. The concentration of CT-DNA was determined from the absorption intensity at 260 nm and ε value (6600 $M^{-1}cm^{-1}$). The titrations were carried out by keeping the concentration of metal complex constant and varying the DNA concentration. The solution after each addition of DNA was incubated for 10 min before the absorption spectra were recorded. The intrinsic binding constant (K_b) was determined using the following equation.

$$[DNA]/(\varepsilon_a-\varepsilon_f)=[DNA]/(\varepsilon_b-\varepsilon_f)+1/K_b(\varepsilon_b-\varepsilon_f)$$

Where [DNA] is the concentration of DNA in base pairs, $\varepsilon_{a,}\varepsilon_b$ and ε_f are apparent extinction coefficient, extinction coefficient for free metal complex and extinction coefficient for the metal complex in fully bound form respectively [13]. The K_b values were determined from the ratio of the slope to the intercept in the plots of $[DNA]/(\varepsilon_b-\varepsilon_f)$ *vs.* [DNA].

RESULTS AND DISCUSSION

The complexes were colored, Non hygroscopic and stable in air. They are insoluble in common organic solvents but soluble in DMF and DMSO.

IR spectra

IR spectrum of the ligand and its Zn(II) and Cd(II) complexes were compared (Figures 3-5). The medium intensity band at 3029 cm^{-1} in H-SHQO is due to the–OH group (intramolecularly hydrogen bonded). Absence of this band in the complex suggests the cleavage of intramolecular hydrogen bond, subsequent deprotonation and coordination through phenolic oxygen. The intense band

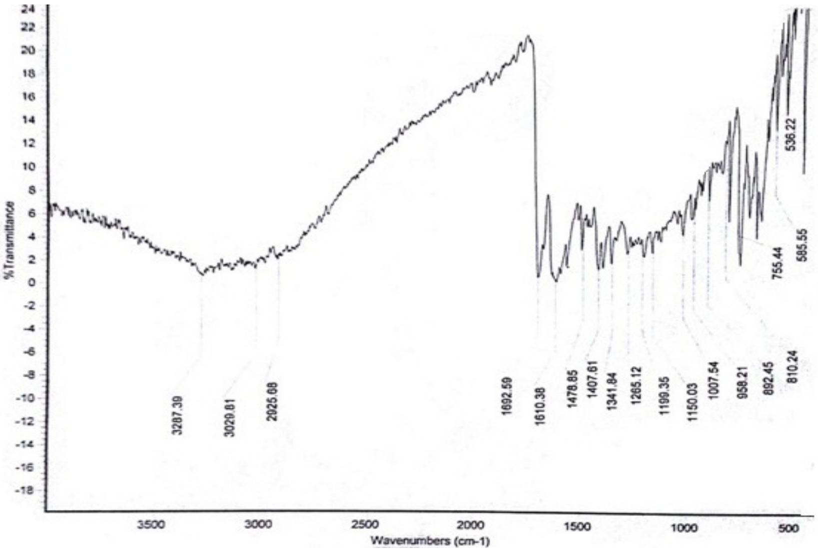

Figure 3: IR spectrum of HSHQO

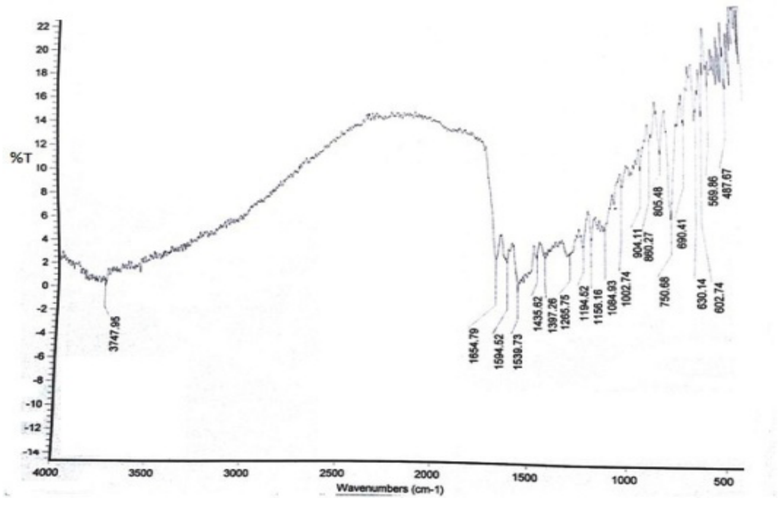

Figure 4: IR spectrum of Zn(II) complex

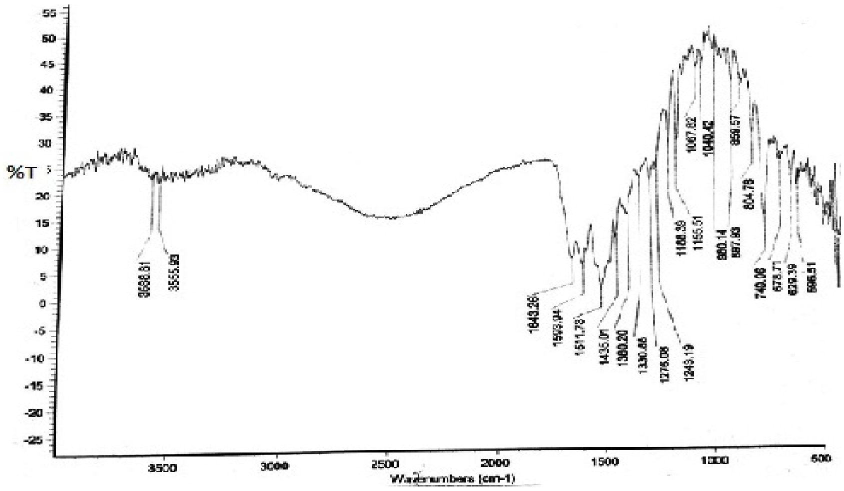

Figure 5: IR Spectrum of Cd(II) Complex

observed at 1692 cm^{-1} has been assigned to the lactum carbonyl stretching frequency. The negative shift of this band to 1654 cm^{-1} in Zn(II) complex and to 1643 in Cd(II) complex supports coordination through lactum carbonyl oxygen. The shift of the band due to υ $C=N_{(free)}$ observed at 1610 cm^{-1} in the ligand to 1594 cm^{-1} in both the complexes suggests the participation of free azomethine nitrogen in coordination. The deprotonation and subsequent participation of phenolic oxygen in coordination is indicated by the shift of υ C-O from 1341 cm^{-1} to 1397 cm^{-1} in Zn(II) complex and to 1380 in Cd(II) complex.

Electronic spectra

Electronic absorption spectra of the ligand and its complexes were recorded in DMSO in the range of 200-1200 nm at room temperature. The ligand exhibits strong peaks at 264 and 276 nm corresponding to π-π^* transitions. Zn(II) complex exhibits a peak at 430 nm due to intraligand charge transfer and the peaks at 452 and 484 nm are due to ligand metal charge transfer [17-19]. In Cd(II) complex intraligand charge transfer peak is noticed at 446 nm.

Mass spectra

The LCMS of Zn(II) complex showed a well-defined molecular ion peak at m/z 624 corresponding to the formula weight $C_{30}H_{22}N_8O_4Zn$ and for Cd(II) complex and the ESI mass spectrum of Cd(II) complex showed molecular ion peak at 671.5094 corresponding to the formula weight $C_{30}H_{22}N_8O_4Cd$ (Figures 6 and 7). The CHN analysis and mass spectral data suggests that the molecular composition of the complexes is ZnL_2 and CdL_2 respectively. Based on the spectral and analytical data the structure proposed for the complexes is given in Figure 8.

DNA binding studies

Electronic absorption titrations were carried out by keeping the concentration of metal complex constant and varying the CT-DNA concentration. The solution after each addition of DNA was incubated for 10 min before the absorption spectra were recorded. On increasing the concentration of CT-DNA, significant hypochromism is noticed for both the complexes, indicating that the complexes interact with DNA through intercalation mode. The base binding constants of the complexes with DNA were found to be 7.18×10^5 and 8.18×10^9 M^{-1} respectively for Zn(II) and Cd(II) complexes. The Kb values suggest that both the complexes exhibit significant binding abilities and the Cd(II) complex has much higher binding ability in comparison with Zn(II) complex (Figure 9).

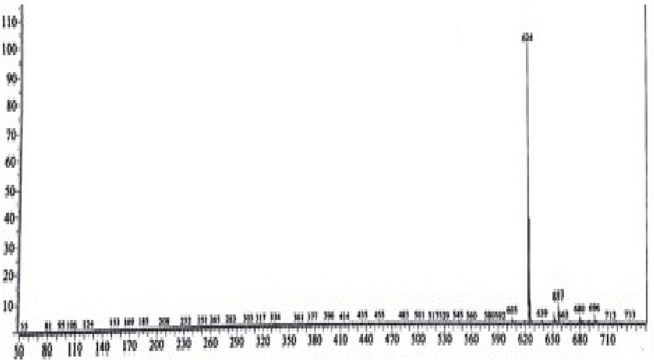

Figure 6: Mass spectrum of Zn(II) complex

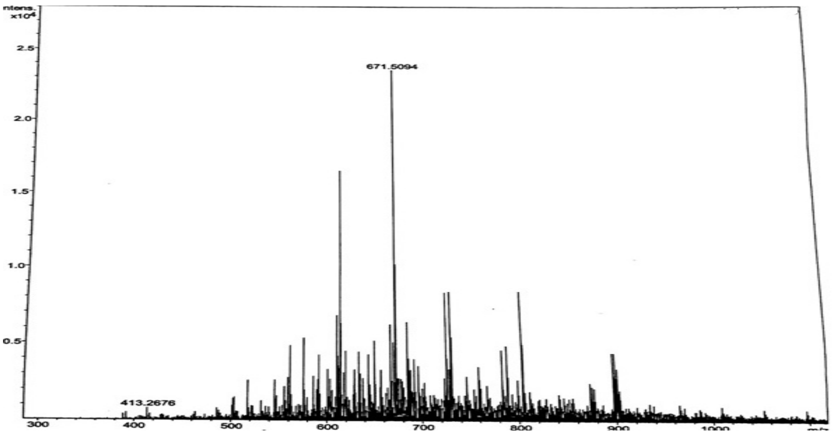

Figure 7: Mass spectrum of Cd(II) complex

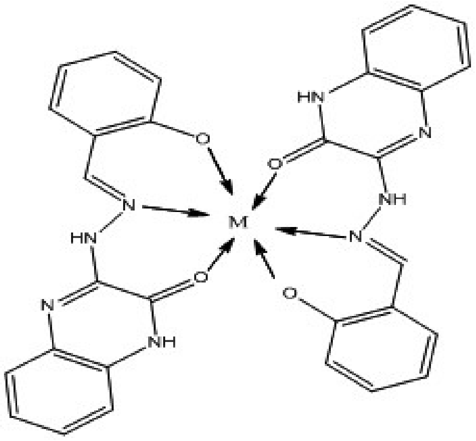

Figure 8: Proposed structure of complexes M=Zn(II) or Cd(II)

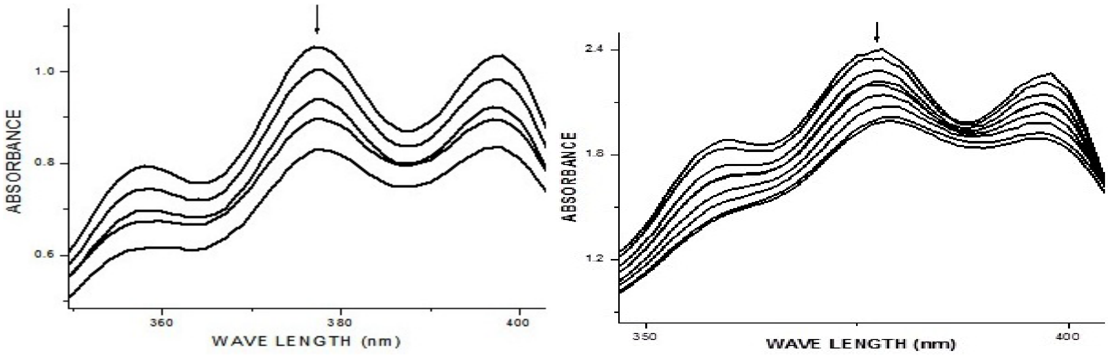

Figure 9: The absorption spectra of Zn (II) and Cd(II) complexes in the presence and absence of CT DNA

CONCLUSION

Zn (II) and Cd(II) complexes of the ligand, HSHQO have been synthesised and characterized on the basis of various spectro-analytical data. HSHQO act as tridentate ligand with phenolic oxygen, imino nitrogen and ketonic oxygen as the donor centers. Both the metal ions formed 1:2 complexes (ML_2) with the ligand. DNA binding studies revealed that the complexes exhibit significant ability to bind with CT-DNA through intercalation mode.

ACKNOWLEDGEMENTS

The authors are thankful to JNTUH, Hyderabad and Vasavi College of Engineering, Hyderabad for providing necessary facilities to carry out this work.

REFERENCES

[1] N. Padmaja, M. Ravinder, P. Shilpa, J. Srihari *J. Pharm. Chem*., **2011**, 5, 31-34.

[2] R. Mogili, M. Ravinder, K. Mamatha, N. Padmaja, N. Srihari, *J. Pharm. Chem*., 1, **2007**, 35-39.

[3] A. Rogier, A. Smits, D. Herman D. Lim, A. Hanzer, O.P. Zuiderveld, E. Guaita, M. Adami, G. Coruzzi, R. Leurs, I.J.P. de Esch, *J. Med. Chem*., **2008**, 51, 2457-2467.

[4] R. Mugdha, Suryawanshi, M. Vithal, Kulkarni, K.R. Mahadik, S.H. Bhosale, *Arch. Appl. Sci. Res.*, **2011**, 3, 380-391.

[5] R. Sarges, H.R. Howard, R.G. Browne, L.A. Lebel, P.A. Seymour, B. Kenneth, *J. Med. Chem*., **1990**, 33, 2240-2254.

[6] P. Krishnamoorthy, P. Sathyadevi, A.H. Cowley, R.R. Butorac, N. Dharmaraj, *Eur. J. Med. Chem*., **2011**, 46, 3376-3387.

[7] K.R. Justin Thomas, M. Velusamy, J.T. Lin, C.H. Chuen, Y.T. Tao, *Chem. Mater*., **2005**, 17, 1861.

[8] A. Venkateswararao, P. Tyagi, K.R. Justin Thomas, P.W. Chen, K.C. Ho, *Tetrahedron.,* **2014**, 70, 6318-6327.

[9] X. Fang, G. Zhao, Y. Xiao, J. Xu, W. Yang, *Tetrahedron. Lett*., **2013**, 54, 806-810.

[10] A. Zarrouk, A. Dafali, B. Hammouti, H. Zarrok, S. Boukhris, M. Zertoubi, *Int. J. Electrochem. Sci*., **2010**, 5, 46-55.

[11] S. Adewuyi, Gangli, S. Zhang, W. Wang, P. Hao, W.H. Sun, N. Tang, Jianjun, *J. Organomet. Chem*., **2007,** 692**,** 3532-3541.

[12] M. Sebatian, V. Arun, P.P. Robinson, A. Anna Varghese, R. Abraham, E. Suresh, K.K. Mohammed Yusuff, *Polyhedron*., **2010**, 29, 3014-3020.

[13] S. Pushpa Latha, *Int. Conf. Sci. Technol. Manag.*, 1391-1400.

[14] M. Alexandra Phillips, *J. Chem. Soc*., **1928**, 2393-239**.**

[15] G.W.H. Cheeseman, M. Rafiq *J. Chem. Soc*., **1971**, 453.

[16] P.V.A. Lakshmi, D.S. Rani, V. Jayatyagaraju, *Asian. J. Chem.*, **1995**, 7, 296-306.

[17] J. Dhanaraj Chellian, J. Johnson, *Spectrochim. Acta.*, Part A, **2014**, 127, 396-404.

[18] C. Justin Dhanaraj, J. Johnson, *Spectrochim. Acta.*, Part A, **2014**, 118, 624-631.

[19] A. Guha, J. Adhikary, T. Kumar Mandal, D. Das, *Indian. J. Chem*., Sect A, 2011, 50, 1463-1468.