



## Synthesis and Spectroscopic Studies of Some Metal Complexes Derived from Benzofuran Schiff Base

## KEYWORDS

Benzofuran, Schiff base, Metal complexes, Spectral studies, DNA cleavage

## Madappa B. Halli

Department of P. G. Studies and Research in Chemistry,  
Gulbarga University, Gulbarga, Karnataka (India)  
585106.

## Sadu Suryakant S

Department of P. G. Studies and Research in Chemistry,  
Gulbarga University, Gulbarga, Karnataka (India)  
585106.

## Naghma Shaishta

Department of P. G. Studies and Research in Chemistry,  
Gulbarga University, Gulbarga, Karnataka (India)  
585106.

## Mallikarjun Kinni

Department of P. G. Studies and Research in Chemistry,  
Gulbarga University, Gulbarga, Karnataka (India)  
585106.

**ABSTRACT** New Schiff base transition metal complexes have been synthesized via the condensation of 3-amino-5-bromobenzofuran-2-carboxamide and Salicylaldehyde. Tentative structures for the synthesized complexes have been elucidated on the basis of analytical, elemental, UV-VIS, IR, <sup>1</sup>HNMR, ESR and Mass spectral studies. All the complexes are soluble in DMF and DMSO. The measured molar conductance values suggest that the complexes are non-electrolytic in nature. We propose the octahedral geometry for Co(II), Ni(II) and Cu(II) complexes, based on electronic spectral data, magnetic data and ligand field parameters. The Cd(II), Zn(II) & Hg(II) complexes show the tetrahedral geometry. The Schiff base and their metal complexes were screened for their anti-bacterial, anti-fungal and DNA cleavage activities.

## Introduction:

Benzofuran compounds are distributed widely in the nature and most of them occur in plant kingdom<sup>1,2</sup> these compounds are extremely important and useful in many areas of agriculture<sup>3</sup>, Pharmaceutical chemistry<sup>4</sup>, Industrial chemistry<sup>5</sup>, Biology<sup>6</sup> etc., Number of studies have shown that on complexation with metal ions, benzofuran derivatives show enhanced biological and catalytic activity<sup>7-11</sup>. It is also reported that halide substitution on the aromatic ring greatly increased the antibacterial activity<sup>12</sup>. Antimicrobial property of the compound either kills the microbe or prevents their multiplication by blocking active sites<sup>13</sup>.

Salicylaldehyde is an important precursor to a variety of chelating agents, some of which have commercial importance<sup>14</sup>. Schiff bases of salicylaldehyde are well known as the polydentate ligands, coordinating as a deprotonated or neutral forms<sup>15</sup>. These Schiff bases resulting from the condensation of salicylaldehyde with primary amines represents an important class of chelating ligands studied widely.

In view of the extensive use of Schiff bases derived from salicylaldehyde and its metal complexes in the area of coordination chemistry, we thought it is worthwhile to prepare the benzofuran Schiff base and its metal complexes derived from salicylaldehyde.

The current article describes synthesis of Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes with Schiff base derived from condensation of 3-amino-5-bromobenzofuran-2-carboxamide and salicylaldehyde (Figure 1). All the synthesized compounds characterized by spectroscopic (IR, UV-VIS, ESR, and Mass spectra) and physical data. Further Schiff base complexes subjected to antibacterial, antifungal activity and DNA cleavage studies.

## Experimental:

All the chemicals used are of AR grade with a highest purity available. Benzofuran-2-carboxamide synthesized according to the literature procedure<sup>16</sup>. The metal and the chloride content were determined according to the Vogel's procedure<sup>17</sup>.

### Synthesis of Schiff base 3-(2-hydroxybenzylideneamino)-5-bromobenzofuran-2-carboxamide [L].

A mixture of 3-amino-5-bromobenzofuran-2-carboxamide and salicylaldehyde (1:1) in ethanol (30 mL) are refluxed on water bath for about 8h in presence of few drops of glacial acetic acid with occasional shaking. The product that separated out as crystalline solids on cooling was collected and recrystallized from ethanol. C<sub>16</sub>H<sub>11</sub>BrN<sub>2</sub>O<sub>3</sub> [L]: Molecular Weight = 359.17, mp = 210°C, Yield= 65%.

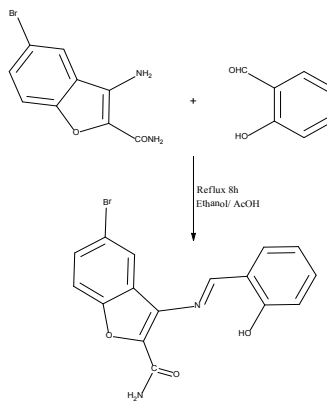


Figure-1. Synthesis of ligand [L]

### General procedure for preparation of metal complexes of Co (II), Ni (II), Cu (II), Zn (II), Cd (II) and Hg (II) with the Schiff base (L).

Metal chloride (0.01 mol) was mixed with Schiff base (0.01 mol) in an ethanolic medium 30 mL and reaction mixture was refluxed for about 3h on water bath, then aqueous solution of sodium acetate added to the mixture to adjust the pH between 5 to 6 and further refluxed for about an hour. The complexes separated were filtered off and washed with distilled water, then with alcohol, and finally dried in vacuum over fused calcium chloride.

**Physical measurements:**

All physical measurements, biological activity and DNA cleavage studies have been carried out as per the procedure given in the reference<sup>18</sup>.

**Results and Discussion:**

The physical appearance and analytical results show that  $\text{Cu}_2\text{Cl}_2$ ,  $\text{CoL}_2$ ,  $\text{NiL}_2$  and  $\text{MLCl}$  (Where  $M = \text{Zn/Cd/Hg}$ ). The low molar conductance values ( $13.10$  to  $17.80 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ ) indicate the non-electrolytic nature of the complexes. All the complexes are light colored, stable and non-hygroscopic in nature having high melting points ( $>300 \text{ }^\circ\text{C}$ ).

**IR Studies:**

The IR spectrum of the ligand compared with those of IR spectra of the metal complexes. The broad band observed in the complexes at  $3444 - 3381 \text{ cm}^{-1}$  are attributed to  $\nu(\text{OH})$  frequency of phenolic group. The bonding through phenolic oxygen after deprotonation is observed by disappearance of the  $\nu(\text{OH})$  frequency in all the complexes. The band observed at  $3360 \text{ cm}^{-1}$  in free ligand is assigned to  $\nu(\text{N-H})$  vibration of the primary amide group and this band is unchanged or slightly shifted to higher frequency in the spectra of the complexes indicating that the  $\text{NH}_2$  group is not involved in coordination<sup>19</sup>. The strong band observed at  $1665 \text{ cm}^{-1}$  is assigned to  $\nu(\text{C=O})$  stretch of amide group undergo negative shift by  $20 - 30 \text{ cm}^{-1}$  in the complexes indicating the involvement of carbonyl group in coordination. The Schiff base shows strong to medium intensity band at  $1581 \text{ cm}^{-1}$  due to  $\nu(\text{C=N})$  stretching vibrations, this band undergoes negative shifts in the spectra of the complexes showing involvement of the azomethine group in the coordination with the metal ions<sup>20</sup>. The band at  $1192 \text{ cm}^{-1}$  is assigned to  $\nu(\text{C-O-C})$  stretch of the furan ring in free ligand<sup>21</sup>. This band is unchanged on complexation indicating non-involvement of the furan ring oxygen in the bonding. In the far IR spectra of the complexes, the bands in the region  $536 - 520 \text{ cm}^{-1}$  and  $457 - 420 \text{ cm}^{-1}$  assigned to M-O and M-N stretching vibrations respectively in all the complexes<sup>20</sup>. All the above value indicates that the ligand acts as the bidentate, with azomethine nitrogen and carbonyl oxygen atom as a donor sites.

**Mass spectral studies:**

The LC-MS mass spectra of the Schiff base (L) has showed a molecular ion peak at  $m/z$  360, which is one mass unit more than that of the molecular weight of the Schiff base suggesting the proposed structure.

**Magnetic Properties:**

The cobalt complex exhibit magnetic moment value of 4.86 B.M. suggesting octahedral geometry. The Ni(II) complex show magnetic moment value of 2.89 B.M. slightly higher than spin only value (2.83 B.M), indicating an octahedral environment. The observed magnetic moment values for the Cu(II) complex are 1.87 suggesting a distorted octahedral geometry<sup>21</sup>.

**Electronic spectral studies:**

The electronic spectra of the Co(II), Ni(II) and Cu(II) complexes were recorded for freshly prepared solution in DMF ( $10^{-3} \text{ M}$ ) at room temperature. The electronic spectra of the Co(II) complex show the band at  $15,748 \text{ cm}^{-1}$  and  $21,052 \text{ cm}^{-1}$ . These two bands are assigned to  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{1g}(\text{v}_2)$  and  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{v}_3)$  transitions respectively in an octahedral environment. The Ni(II) complex exhibit two bands at  $15,460$  and  $26,460 \text{ cm}^{-1}$  assignable to  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})(\text{v}_2)$  and  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})(\text{v}_3)$  transitions respectively in an octahedral environment. The band  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})(\text{v}_1)$  is missing due to limited range of the instrument. However, it is calculated using band fitting procedure.

The copper complex exhibit broad asymmetric band in the region  $12,820 - 17,094 \text{ cm}^{-1}$ . The broadness of the band indicates the three transitions  ${}^2\text{B}_{1g}(\text{F}) \rightarrow {}^2\text{A}_{1g}(\text{v}_1)$ ,  ${}^2\text{B}_{1g}(\text{F}) \rightarrow {}^2\text{B}_{2g}(\text{v}_2)$  and  ${}^2\text{B}_{1g}(\text{F}) \rightarrow {}^2\text{E}_g(\text{v}_3)$  which are similar in energy and

gives rise to only one broad asymmetric band in the region  $12,820 - 17,094 \text{ cm}^{-1}$ . The broadness of the band may be due to *Jahn-Teller distortion*. All the above data suggest the distorted octahedral geometry around Cu(II).

The octahedral geometry for Co(II) complex is supported by the values of ligand field parameters such as Racah inter-electronic repulsion parameter ( $B = 950 \text{ cm}^{-1}$ ), ligand field splitting energy ( $10\text{Dq} = 823 \text{ cm}^{-1}$ ), covalency factor ( $\beta = 0.978$ ) and ligand field stabilization energy ( $\text{LFSE} = 14.11 \text{ K.cal/mole}$ )<sup>22</sup>, ratio  $\nu_2/\nu_1 = 1.337$ . The 'B' values for the complex are lower than free ion value, which is an indication of orbital overlap and delocalization of d-orbitals. The  $\beta$  values obtained are less than unity suggesting a considerable amount of covalent character for the metal-ligand bonds. The ligand field parameters for Ni(II) such as ( $10\text{Dq} = 941 \text{ cm}^{-1}$ ), ( $B = 912 \text{ cm}^{-1}$ ), covalency factor ( $\beta = 0.877$ ) and ligand field stabilization energy ( $\text{LFSE} = 32.263 \text{ K.cal/mole}$ ), ratio  $\nu_2/\nu_1 = 1.642$ . The  $\beta$  values for Ni(II) complex is less than Co(II) complex, indicating more covalency of M-L.

**<sup>1</sup>HNMR spectral studies:**

<sup>1</sup>HNMR spectra of the ligand shows signal at  $\delta 12.83$  (s, -OH),  $\delta 12.34$  (s, -CONH<sub>2</sub>) and  $\delta 8.29$  (s, HC=N). This supports the formation of the Schiff base.

**ESR Spectra of Cu(II) complex:**

The ESR spectra of the Cu(II) complex at room temperature displayed a poorly resolved broad asymmetric signal with Hamiltonian parameter  $g_{\parallel} = 2.2977$  and  $g_{\perp} = 2.1828$ . These values are in agreement with values for distorted octahedral structure with no hyperfine splitting in the parallel features. The exchange interaction parameter G in the complex is less than 4, indicating that, the absence of copper-copper exchange coupling interaction between copper (II) centres in the solid state<sup>23</sup>.

**Antibacterial and antifungal activities:**

The antibacterial and antifungal activity of the Schiff base and its metal complexes were screened against the bacteria *Escherichia coli* (*E.coli*) (gram negative), *Staphylococcus aureus* (*S. aureus*) (gram positive) and *Aspergillus niger* (*A. niger*) and *Aspergillus fumigatus* (*A. fumigatus*) fungi species by minimum inhibitory concentration (MIC) method. The MIC values of the tested compounds are shown in Figure 2 and 3. The comparative study of the values obtained by MIC method of Schiff base and its metal complexes showed that the complexes have higher growth inhibiting property than the Schiff base. This property of the complex can be explained on the basis of the Overtone's concept<sup>24</sup> and the Tweedy's chelation theory<sup>25</sup>. The metal complexes also affect the respiration process by blocking the protein synthesis which retards the growth of the organism. The mode of action of the compound may involve the formation of a hydrogen bond through, the azomethine group with the active centre of the cell resulting in interference with the normal cell process. In general, metal complexes are more active than corresponding ligand because metal complexes may serve as the vehicle for activation of ligand as the principle cytotoxic species<sup>26</sup>.

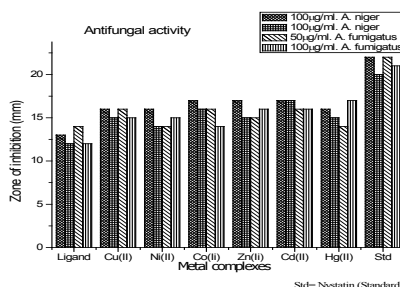


Figure – 2

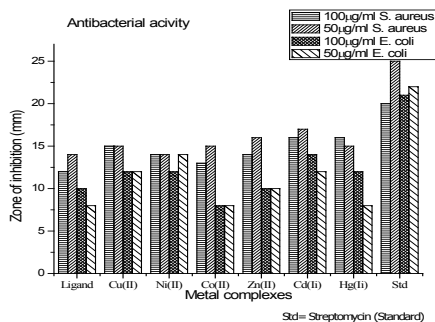
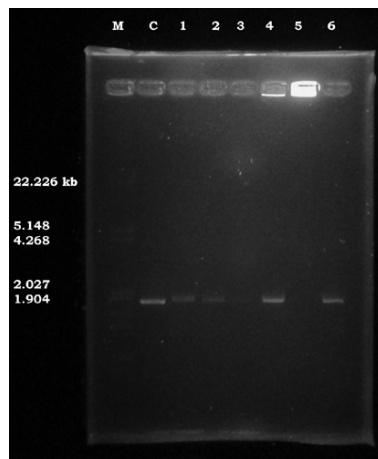


Figure - 3

**Electrophoretic analysis:**

The Schiff base metal complexes subjected to DNA cleavage analysis by agarose gel Electrophoretic method and represented in the Figure-4. The gel after the electrophoresis clearly revealed that the intensity of all the treated DNA samples has diminished because of the cleavage of the DNA. The complete cleavage of DNA was observed by Ni(II) and Zn(II) complexes (lane 3 and 5 respectively) and partial cleavage of DNA was observed by complexes Hg(II) (lane 1) and Cu (II) (lane 2) complexes. The differences observed in the bands of the complexes (lane 1-6) compared to that of the control DNA. This shows that the control DNA alone does not show any apparent cleavage whereas complexes shown. The results indicated the important role of metal ions in these isolated DNA cleavage reactions. As the compound was observed to cleave the DNA, it can be concluded that the compounds inhibits the growth of the pathogenic organism by cleaving the genome<sup>27</sup>.

**Figure 4: The cleavage analysis**

Note: In the photograph M- Standard DNA molecular weight marker ( $\lambda$  DNA EcoR1)

Hind-III double digest, Bangalore Genei, Bangalore (India))

C- Control DNA (untreated pUC 18)

1-Hg(II), 2-Cu(II), 3-Ni (II), 4-Co(II), 5-Zn(II), 6-Cd(II) complex

**Acknowledgement:**

Authors are thankful to the Professor and Chairman, Department of Chemistry, Gulbarga University, Gulbarga, for encouragement and facilities.

**REFERENCE**

1. Nguyen, Tien Dat., Phan, Van Kiem., Xing, Fu Cai., Quanghai, Shen., Ki Hwan, Bae, Young, Ho Kim. *Gymnastone*. *Arch. Pharm. Res.* 2004, 27, 1106-1108. | 2. Mastubara, H., Botyk Kogaku. 1954, 19, 15. | 3. B.C. Echezona., J.E. Asiegubu.,Izuagba., A. A. African Crop Science Journal 2010,18, 97-105. | 4. Shinichiro, Ono., Tomohiro., Yoshida., Kazuhiro., Maeda., Keigo., Kosaka., Yoshihisa., Inoue., Teruaki, Imada., Chikara, Fukaya., Norifumi, Nakamura. *Chem. Pharm. Bull.* 1999, 47(12)1694-1712. | 5. Kumar, S., Dhar, D. N., Saxena, P. N. J. *Scientific and Industrial Research*, 2009, 68,181-187. | 6. Arifa, Banu K., Aruna, Devraj. *J. Pharm. Sci. Innovation* 2013, 22-25. | 7. Ketan, M. Patel., K. N. Patel., N. H. Patel., M. N. Patel., M. N. Patel. *Synth. React. Inorg. Met.-Org. Chem.* 2000, 1965-1973. | 8. K. Shivakumar., Shashidhar, P., Vithal Reddy., M. B. Halli. *J. Coord. Chem.* 2008, 61, 2274-2287. | 9. Anant, Prakash., Devjani, Adhikari. *Inter. J. Chem. Tech. Research.* 2011, 3(4)1891-1896. | 10. Shalin, Kuar., Durga, Nath Dhar., P. N. Saxena. *J. Sci.Ind. Research* 2009, 68,181-187. | 11. Hai-Fu,Guo.,Yong, Pan., De-Yun, Ma., Kuan, Lu., Liang, Qin. *Trans. Met Chem.*2012, 37, 661-669. | 12. Shi, L., Ge, H. M., Tan, S. H., Li, H. Q., Song, Y. C., Zhu, H. L., Tan, R. X. *Eur. J. Med. Chem.*2007,42, 558-564. | 13. Mishra, A.P. J. *Indian Chem. Soc.*1999, 46, 3537. | 14. Brian, E. Love., Edward, G. Jones. *J. Org. Chem.*1999, 64, 3755-3756. | 15. Boyd, D.B. J. *Med. Chem.* 1983, 26, 1010. | 16. Kavas, Y., Nakayama, M., Tamatskuri, Bull. Chem. Soc. Japan 1962, 35, 149. | 17. Vogel, A. I. "A Text Book of Quantitative Inorganic Analysis", 3rd ed., Longman ELBS, London, 1968. | 18. M.B. Halli, R.B. Sumathi and Mallikarjun Kinni. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy.* 2012, 99. | 19. R C Maurya., J Chourasia and P Sharma. *Ind. J. Chem.* 2007, 46A. | 20. K. Ramakrishna Reddy., K. Madhusudhan Reddy and K. N. Mahendra. *Indian J. Chem.* 45A, 377-381. 2006. | 21. Earnshaw, A. *Introduction to Magnetochemistry*, Academic Press Inc. Limited, London, 1968. | 22. Hathway, B. J. *Struct. Bonding* 1973, 14, 60. | 23. Raman, N., Sakthivel, A., Rajasekaran, K. J. *Coord. Chem.* 2009, 62, 1661. | 24. Belaid, S., Landreau, A., Djebbar, S., Benali-Baitich, O., Bouet, G., Bouchara, J. P. J. *Inorg. Biochem.* 2008, 102, | 25. Petering, D. H. In *Metal Ions in Biological Systems*, Sigel, H., Ed., Marcel Dekker, New York, 1973. | 26. Kulkarni, A., Patil, S. A., Badami, P. S. *Eur. J. Med. Chem.* 2009, 44, 2904-2912. |