SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF Mn(II), Fe(II), Ni(II), Co(II) AND Zn(II) COMPLEXES OF SCHIFF BASE DERIVED FROM 2,2-DIMETHYLPROPANE 1, 3-DIAMINE AND 5-CHLORO ISATIN

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ABSTRACT

A new Schiff base Ligand (L) (where L = 3Z,3'Z)-3,3'-(((2,2-dimethylpropane-1,3-diyl)bis(azanylylidene))bis(5-chloroindolin-2-one) has been synthesized by condensation of 5-Chloroisatin and 2, 2-dimethyl propane-1, 3-diamine respectively in the molar ratio of 2:1. The synthesized ligand(L) was used to synthesis metal complexes of transition metals ( Mn(II), Fe(II), Co(II), Ni(II), and Zn(II)). The ligand and its metal complexes have been characterized by elemental analysis, FT-IR, UV-Visible, ESI-Mass spectrometry and ¹H-NMR and ¹³C- NMR spectra. On the basis of Spectral data it is revealed that the ligand is N, N, O, O tetradentate and coordinated to the metal ion to both azomethine N atoms and O atoms of lactum group. All the metal complexes show octahedral geometry except Ni(II) and Zn(II) they possess square planar geometry. The ligand and its metal complexes were tested for antibacterial activities. Metal Complexes showed better antibacterial activities as compare to Ligand.

Keywords: Schiff Base, Metal(II) Complexes, 2,2-Dimethylpropane-1,3-diamine, 5-Chloroisatin, Octahedral Geometry, Antimicrobial activity.

INTRODUCTION

Schiff base ligands usually contain O and N donor atoms have played important role in coordination chemistry and recently considerable attention has been paid to the chemistry of the metal complexes of Schiff base containing nitrogen and other donors. This may be attributed to their stability, biological activity and potential applications in many fields such as oxidation, catalysis, electrochemistry. Tetradentate Schiff base is one of the most extensively studied ligands in the coordination chemistry. They can coordinate with large number of transition metals. One type of Schiff base ligand is N, N, O, O-tetradentate donor set which possesses many advantages such as facile approach, relative tolerance, readily adjusted ancillary ligands and tuneable steric and electronic coordination environments on the metal centre. Isatin (1H-Indoline-2, 3-dione) is an endogenous compound isolated in 1841 by Erdman and Laurent as a product from oxidation of indigo by nitric acid & chromic acid and reported to possess a wide range of activities involving the central nervous system. Isatin and its Schiff base derivatives and Mannich bases have been reported to possess a variety of biological and pharmacological activities such as antimicrobial, antidepressant, cytotoxicity, analgesic, anticonvulsant, insecticides, DNA Binding, anticancer, tuberculostatic, and anti-inflammatory, antibacterial, antifungal, antiviral, anti-HIV, and antihelmintic activities. These complexes not only play an important role in the development of coordination chemistry related to catalysis and enzymatic reactions, magnetism and molecular architectures, but also exhibit interesting biological activities. Most of the compounds show versatile biological properties such as antioxidant, especially antibacterial activities.
Although much attention has been paid towards the study of Schiff bases and Mannich bases derived from isatins, no investigations have been reported in the literature to describe the Schiff bases derived from 2, 2-Dimethylpropane-1,3-diamine and 5-chloroisatin. Therefore, as a part of our ongoing study on Schiff base derived from 2, 2-Dimethylpropane-1,3-diamine, we report herein the synthesis, characterization, and antibacterial activity of novel Schiff base formed by condensation of 5-Chloroisatin and 2, 2-Dimethylpropane-1,3-diamine (Scheme-1) and its metal complexes of Mn(II), Fe(II), Co(II), Ni(II) and Zn(II) (Scheme-2).

**EXPERIMENTAL**

The chemicals, 5-Chloroisatin and 2, 2-Dimethylpropane-1,3-diamine of analytical grades were purchased from Sigma Aldrich. Solvents such as ethanol, glacial acetic acid, methanol, diethyl ether and hydrated metal acetate/chloride salts were purchased from Qualigen. Chemicals and solvents were used as received without further purification. Melting points were determined by using open capillary method and were uncorrected. The infrared (IR) spectra were recorded on a Perkin Elmer system 2000 FTIR spectrometer by KBr Disc methods (4000-400 cm⁻¹). The ES-Mass Spectra were recorded on a Agilent Q-TOF LC-MS mass Spectrometer. ¹H NMR and ¹³C NMR spectra were recorded on Bruker 400 or 300 MHz spectrometer at 25°C using tetramethylsilane as an internal standard and DMSO-d₆ as solvent.

**Synthesis of Schiff Base (L)**

To ethanolic solution of 2, 2-Dimethyl Propane-1, 3-diamine (10 mmol, 1.02g) in 20ml, ethanolic solution of 5-Chloroisatin (20 mmol, 3.620gm) was added. The two hot solutions were mixed in a 250 ml round bottom flask in the presence of few drops of glacial acetic acid as a catalyst. The resulting mixture was refluxed for 8 h at 80-90°C. The reaction was monitored with TLC and then after cooling at room temperature, poured into ice-cold water. The precipitate was filtered off, washed with water, cold ethanol, dry diethyl ether respectively and air dried at room temperature with yield 66% (Scheme-1).

**Synthesis of Complexes (Scheme-2)**

(a) **Synthesis of [MnL(H₂O)₂]₂AcO**

To ethanolic solution of Mn(OAc)₂·4H₂O (0.025 mmol, 0.061g) in 10 ml, ethanolic solution of Schiff base (L) (0.025 mmol, 0.107g) in 10 ml was added. The two solutions were mixed in a 50 ml round bottomed flask and the mixture was refluxed for 12-15 h. The reaction mixture was concentrated to a small volume by evaporation method, cooled and after cooling at room temperature, the precipitate was filtered off, washed with ethanol, and dried under vacuum over anhydrous CaCl₂.

(b) **Synthesis of [FeL(H₂O)₂]₂Cl**

To an ethanolic solution of FeCl₂·2H₂O (0.025 mmol, 0.0418g) in 10 ml, an ethanolic solution of Schiff base (L) (0.025 mmol, 0.107g) was added and then the mixture was refluxed for 15 h. The reaction mixture was evaporated to a small volume, on cooling solid metal complex was obtained. The metal complex was then washed with ethanol and dried under vacuum over anhydrous CaCl₂.

(c) **Synthesis of [CoL(H₂O)₂]₂AcO**

The ethanolic solution of Co(OAc)₂·4H₂O (0.024mmol, 0.062g) in 10 ml was added to ethanolic solution of Schiff base (L) (0.025 mmol, 0.107g) in 10 ml and the mixture was refluxed for 10 h. The reaction mixture was evaporated to a small volume, on cooling solid metal complex was obtained. The metal complex was then washed with ethanol and dried under vacuum over anhydrous CaCl₂.

(d) **Synthesis of complex [NiL]₂Cl**

The ethanolic solution of NiCl₂·6H₂O (0.025mmol, 0.059g) in 10 ml was added to ethanolic solution of Schiff base (L) (0.025mmol, 0.107g) in 10ml. The reaction mixture was refluxed in 50ml round bottom flask for 12 h. The reaction mixture was evaporated to a small volume, on cooling solid metal complex thus obtained was washed with ethanol and dried under vacuum over anhydrous CaCl₂.
(e) **Synthesis of complex[ZnL]2AcO**

To ethanolic solution of Zn(OAc)$_2$·2H$_2$O (0.025mmol, 0.046g) in 10 ml, ethanolic solution of Schiff base (L) (0.025mmol, 0.107 g) was added. The reaction mixture was refluxed in 50ml round bottom flask for 16 h. The reaction mixture was evaporated to a small volume, on cooling solid metal complex obtained was washed with ethanol and dried under vacuum over anhydrous CaCl$_2$.

![Scheme-1: Route of Synthesis of Ligand](image)

**RESULTS AND DISCUSSION**

We have developed a simple and highly reliable route for synthesis for Novel Schiff base Ligand and its complexes. This strategy can be successfully applied to prepare wide range of complexes of 5-Chloro isatine which can be widely used as potent compounds possess a wide spectrum of medicinal properties and have been studied for antibacterial activity and anti fungal activities. The newly synthesized ligand and its metal complexes are stable at room temperature in solid state. The ligand is soluble in common...
Spectral Characterization of Ligand and Metal Complexes

The IR spectra of ligand shows a sharp band at 1722 cm\(^{-1}\) and 1617 cm\(^{-1}\) which show the presence of \(\nu (C=O)\) and \(\nu (C=N)\) vibrations respectively. In the IR spectra of metal complexes, \(\nu (C=O)\) and \(\nu (C=N)\) are shifted by 10-20 cm\(^{-1}\) which shows the coordination of (C=O) and (C=N). A new band appeared in the range 460-485 cm\(^{-1}\) and 550-590 cm\(^{-1}\) may be assigned \(\nu (M-N)\) and \(\nu (M-O)\) vibrations respectively.

In the UV-Vis spectra of Mn(II) complexes show two bands in the regions 22500 - 22650 and 18500 - 18850 cm\(^{-1}\) which may be assigned to \(\Delta A_{1g} \rightarrow \Delta T_{2g}\) and \(\Delta A_{1g} \rightarrow \Delta T_{1g}\). The electronic spectra of the cobalt (II) complex exhibited bands between 18400 - 21500 cm\(^{-1}\) which are characteristic of nickel(II) square planar geometry. Since zinc(II) ion has d\(^{10}\) configuration the absorption at 26910 cm\(^{-1}\) could be assigned to a charge transfer transition.

\(^1\)H and \(^{13}\)C NMR Spectra

\(^1\)H NMR and \(^{13}\)C NMR of ligand in DMSO-d\(_6\) solution show that they are NMR active. The \(^1\)H-NMR spectrum of free ligand shows a singlet at 0.98 ppm due to CH\(_2\) proton, 3.45 ppm due to CH\(_3\) proton, and 7.30 due to Ar-CH respectively. \(^{13}\)C-NMR spectrum of free ligand show at 161.4 ppm in the range due to imine carbon, 118.23 ppm due aromatic carbons, 153.88 ppm due to C=O. Thus, \(^1\)H and \(^{13}\)CNMR spectral data support proposed structure of ligand and metal complexes and as well coordination behavior of ligand. The molar conductance (\(A_{\text{ml}}\)) values of all complexes were measured in DMSO and show electrolyte nature of complexes.

\((3Z,3'Z)-3,3'-(2,2-dimethylpropane-1,3-diyli)bis(azanylyidene))bis(5-chloroindolin-2-one)

Color: Light purple, Yield: 66%, mp.: 264-268°C decomposition. Analysis for C\(_{32}\)H\(_{38}\)Cl\(_2\)MnN\(_2\)O\(_6\): C, 58.75; H, 4.23; Cl, 16.52; N, 13.05; O, 7.45 found C, 58.80; H, 4.19; Cl, 16.55; N, 13.07; O, 7.39; IR (KBr) \(\nu\) cm\(^{-1}\): 3248 (N-H str.), 1722.4 (C=O str.), 1617 (C=N str.); \(^1\)H NMR (DMSO-d\(_6\), 6 ppm): 0.98 (d, 2H,-CH\(_3\)), 3.45 (d, 2H, -CH\(_2\)), 7.26-7.89 (m, 6H, Ar-CH), 7.98 (d, 2H, NH); Mass spectra (m/z): 429.29.

Complex[MnL(H\(_2\)O)\(_2\)]\(_2\)AcO

Color: Brown, Yield: 65.5% Analysis for C\(_{33}\)H\(_{36}\)Cl\(_2\)MnN\(_2\)O\(_6\): C, 25.03; H, 2.20; Ac, 45.12; Cl, 7.05; Mn, 5.46; N, 5.57; O, 9.52 found C, 25.01; H, 2.18; Ac, 45.16; Cl, 7.06; Mn, 5.44; N, 5.60; O, 9.45; IR (KBr) cm\(^{-1}\): 1710 (C=O str.), 1609 (C=N str.), 490 (M-N str.), 601 (M-O str.); Mass spectra(m/z): 553.03.

Complex [FeL(H\(_2\)O)\(_2\)]\(_2\)Cl

Color: Brown, Yield: 75.5 %, Analysis for C\(_{33}\)H\(_{36}\)Cl\(_2\)FeN\(_2\)O\(_4\) : C, 42.60; H, 3.75; Cl, 23.95; Fe, 9.43; N, 9.46; O, 10.81 found C, 42.55; H, 3.78; Cl, 23.98; Fe, 9.42; N, 9.42 ; O, 10.85; IR (KBr) cm\(^{-1}\) : 3241 (N-H str.), 1712 (C=O str.), 1612 (C=N str.) 480(M-N str.), 593 (M-O str.); Mass spectra(m/z): 589.97.

Complex[CoL(H\(_2\)O)\(_2\)]\(_2\)AcO

Color: Brown, Yield: 63.9%, Analysis for C\(_{33}\)H\(_{36}\)Ac\(_2\)CoN\(_2\)O\(_6\) : C, 24.97; H, 2.19; Cl, 7.02; N, 5.55; O, 9.50; Ac, 44.94; Co, 5.83; found C, 24.90; H, 2.22; Cl, 7.01; N, 5.60; O, 9.50; Ac, 44.89; Co, 5.88 IR
(KBr) \( \nu \text{cm}^{-1} \): 3245 (N-H str.), 1708 (C=O str.), 1610 (C=N str.), 553 (M-N str.), 654 (M-O str.); Mass spectra (m/z): 557.02.

**Complex** [NiL]2Cl

Color: Brown, Yield: 39.6 %, Analysis for C\(_{21}\)H\(_{18}\)Cl\(_2\)N\(_4\)NiO\(_2\); C, 51.69; H, 3.72; Cl, 14.53; N, 11.48; Ni, 12.03; O, 6.56 found C, 51.70; H, 3.74; Cl, 14.50; N, 11.51; Ni, 12.07 O, 7.46; IR (KBr) \( \nu \text{cm}^{-1} \): 3242 (N-H str.), 1714 (C=O str.), 1612 (C=N str.), 450 (M-N str.), 580 (M-O str.); Mass spectra (m/z): 490.01.

**Complex** [ZnL].2AcO

Color: Brown, Yield: 38.4%, Analysis for C\(_{21}\)H\(_{18}\)Ac\(_2\)Cl\(_2\)ZnN\(_4\)O\(_4\); C, 25.72; H, 1.85; C, 46.29; Cl, 7.23; Zn, 6.67; N, 5.71; O, 6.53 found C, 25.75; H, 1.88; C, 46.25; Cl, 7.25; Zn, 6.70; N, 5.73; O, 6.54 IR (KBr) \( \nu \text{cm}^{-1} \): 3240 (N-H str.), 1712 (C=O str.), 1610 (C=N str.), 483 (M-N str.), 540 (M-O str.); Mass spectra (m/z): 527.99.

**Antimicrobial Activities**

The antimicrobial activities of ligands and its complexes were tested in vitro against *S. epidermidis*, *E. Coli*, *A. flavus*, *A. niger* and *C. lunata* by reported method. On comparing the antimicrobial activities of Schiff base (L) and its metal (Mn, Fe, Co, Ni and Zn) complexes, we found that the complexes exhibit more activity than that of the ligand. The increase in the activity of the complexes compared to that of the ligand could be explained on the basis of Overtone’s concept and Tweedy’s chelation theory. It has also been found that the ligand showed no activity against *E. coli*.

**Table-1:** Antimicrobial Effects of the Ligands and their Metal Complexes

| S.No. | Compound                  | Inhibition Zone (mm) |
|-------|--------------------------|----------------------|
|       |                          | E.Coli | S.epidermidis | A.flavus | A.niger | C.lunata |
| 1     | Schiff base(L)           | ---    | 6            | 9        | 11      | 10       |
| 2     | [MnL(H\(_2\)O)\(_2\)].2AcO | 11     | 16           | 15       | 14      | 18       |
| 3     | [FeL(H\(_2\)O)\(_2\)].2Cl | 15     | 15           | 14       | 16      | 15       |
| 4     | [CoL(H\(_2\)O)\(_2\)].2AcO | 16     | 14           | 17       | 16      | 17       |
| 5     | [NiL].2Cl                | 14     | 16           | 18       | 14      | 19       |
| 6     | [ZnL].2AcO               | 12     | 12           | 15       | 15      | 16       |

**CONCLUSION**

On the basis of above mentioned studies we have proposed the octahedral geometry for all metal complexes except Ni(II) and Zn(II) complexes they show square planar geometry and the antimicrobial results showed that these metal complexes were more potent than that of ligand. The newly synthesized Schiff base (L) and its metal complexes were screened for their microbial activity against different pathogenic microbes for their antibacterial and antifungal activities using well defined methods. The compounds were screened for their antibacterial activity against *E. coli*, *S. aureus*, *P. vulgaris* and for antifungal activity against *C. albicans* and *A. niger* in potato dextrose agar medium.

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**REFERENCES**

1. M. Wang, H. Zhu, K. Jin, D. Dai and L. Sun, *Journal of Catalysis*. 220, 2 (2003), DOI:10.1016/s0021-9517(03)00306-3.
2. F. Marchetti, C. Pettinari, R. Pettinari, A. Cingolani, D. leonesiand and A. Lorenzotti *Polyhedron*. 18, 23(1999), DOI:1001016/s0277-5387(99)00230-2.
3. D. Mandal and B. Mandal, *Rasayan Journal of Chemistry* **12**(2), 754(2019), DOI:10.31788/RJC.2019.1225230

4. V. Glover, J.M. Halket, P.J. Watkins, A.Clove, B.L. Goddwin and M.J. Sandler, *Neurochemistry*. **51**,65(1988), DOI:10.111/j.1471-4159.1988.tb01089.x.

5. S.K. Bhattacharya, V. Glover, I. McIntyre, G. Oxenkrug and M. Sandler, *Neuroscience Letter*, **92**(2), 218(1988), DOI:10.1016/0304-3940(88)90064-x

6. S.K. Bhattacharya, S.K. Mitra, S.B. Acharya, *Journal of Psychopharmacol* **5**,202(1991), DOI:10.1177/026988119100500304.

7. M.S. Gil-Turner, M.E. Hay and W. Fenical, *Science*. **246**, 116(1989), DOI:10.1126/Science.2781297.

8. M. Sahihovic, M. Pazalja, I.M. Dizdarevic, A. J. Mujkic, J. Suljagic, S.S. Halilovic and A. Sapcanin, *Rasayan Journal of Chemistry*, **11**(3), 1074(2018), DOI:10.31788/RJC.2018.1133077

9. G. Puthilibai and S. Vasudhevan, *Rasayan Journal of Chemistry*, **12**(2), 855(2019)

10. A. Jarrahpour, D. Khalili, E.D. Clercq, C. Salmi and J.M. Brunel, *Molecules*. **12**,1720(2007), DOI:10.3390/12081720.

11. J.F.M. Silva, S. J. Garden, and A. C. Pinto, *Journal of Brazilian Chemical Society*. **12**,273(2001), DOI:10.1590/s0103-50532001000020.

12. A. P. Mishra, R. Jain and S. Gupta, *Mycobiology*. **40**,20(2012), DOI:10.5941/MYCO.2012.40.1.020.

13. Z. H. Chohan and M. F. Jaffery, *Metal Based Drugs*. **7**, 265(2000), DOI:10.1159/000007182.

14. J. R. Anacona and G. D. Silva, *Journal of Chilean Chemical Society*. **50**, 447(2005), DOI:10.4067/s0717.9707200500001.

15. S. N. Pandeya, D. Sriram, G. Nath and E. De Clercq, *Chemotherapy*. **45**,192(1999), DOI:10.1159/000007182.

16. S. N. Pandeya, P. Yogeswari, D. Sriram, G. Nath, E. De Clercq, C. Pannecouque and M. Witvrouw, *Chemotherapy*. **35**,249(2000), DOI:10.1016/S0223-5234(00)00125-2.

17. S. I. AL-Resayes, M. Shakir, A. Abbasi, K. M. Y. Amin and A. Lateef, *Spectrochimica acta part A: Molecular and biomolecular spectroscopy*, **93**, 86(2012), DOI:10.1067/j.saa.2012.02.099.

18. S. N. Pandeya, P. Yogeswari, D. Sriram, G. Nath, E. De Clercq, C. Pannecouque and M. Witvrouw, *European Journal of Medicinal Chemistry*. **35**, 86(2000), DOI:10.1016/S0223-5234(00)00125-2.

19. V. A. Neacsu, C. Maxim, A. M. Madalan, M. Hillebrand, C. Gonzalez-Arellano, S. Soriano, E. Rentschler and M. Andruh, *Polyhedron*, **150**,77(2018), DOI:10.1016/j.poly.2018.05.007.

20. J. Mayans, M. Font-Bardia and A. Escuer, *Dalton Transactions*, **47**, 8392(2018), DOI:10.1039/C8DT01684D.

21. (a) M. T. Kaczmarek, M. Zabiszak, M. Nowak and R. Jastrzab, *Coordination Chemistry Reviews*, **370**, 42(2018), DOI:10.1016/j.ccr.2018.05.012. (b) N. A. Illan-Cabeza, S. B. Jimenez-Pulido, F. Hueso-Urena, M. J. Ramirez-Exposito, P. Sanchez-Sanchez, J. M. Martinez-Martos and M. N. Moreno-Carretero, *Journal of Inorganic Biochemistry*, **185**, 52(2018), DOI:10.1016/j.jinorgbio.2018.04.022. (c) J. Valentova, S. Varenyi, P. Herich, P. Baran, A. Bilkova, J. Kozisek and L. Habala, *Inorganica Chimica. Acta*, **480**,16(2018), DOI:10.1016/j.ica.2018.04.058.
27. R. M. Ramadan, A. K. Abu Al-Nasr and O. A. M. Ali, *Journal of Molecular Structure*, **1161**, 100 (2018), [DOI:10.1016/j.molstruc.2018.01.071]

28. H. Keypour, M. Mahmoudabadi, A. Shooshtari, L. Hosseinzadeh, F. Mohsenzadeh and R. W. Gable, *Polyhedron*, **127**, 345 (2017), [DOI:10.1016/j.poly.2017.02.008].

29. A. Ahlawat, P. Khatkar, V. Singh and S. Asija, *Research on Chemical Intermediates*, **44**, 4415 (2018), [DOI:10.1007/s11164-018-3395-z].

30. W. J. Geary, *Coordination Chemistry Reviews*, **7**, 81 (1971), [DOI:10.1016/S0010-8545(00)80009-0]

31. J. Parekh, P. Inamdhar, R. Nair, S. Baluja and S. Chandra, *Journal of Serbian Chemical Society* **70**, 1155, (2005), [DOI:10.2298/JSC0510155P].

32. J.S. Sultan, S.M Lateaf and D.K. Rashid, *Open Journal of Inorganic Chemistry*, **5**, 102, (2015), [DOI:10.4236/ojic.2015.54011].

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