

RESEARCH ARTICLE

CHEMISTRY

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF A SCHIFF BASE DERIVED FROM ISATIN AND 2-AMINO, 4-METHYL PHENOL AND ITS TRANSITION METAL COMPLEXES

SURAJ B. ADE^{1*}, D.G. KOLHATKAR² AND M.N. DESHPANDE²

^{1*}Department of Chemistry, Shri Shivaji College, Parbhani-431401, India

²P.G. Department of Chemistry, NES, Science College, Nanded-431605, India



*Corresponding author



SURAJ B. ADE

Department of Chemistry, Shri Shivaji College, Parbhani-431401, India

ABSTRACT

Biological active tridentate Schiff base ligand derived from 2-amino, 4-methyl phenol with isatin and their Ti(IV), Zr(IV), Cd(II) and Hg(II) metal complexes have been synthesized and characterized on the basis of IR, Elemental analysis, Electronic spectral data, Molar conductance and ¹H NMR. The Schiff base and its metal complexes have been tested for their antimicrobial activity using disc diffusion methods and the results were interpreted.

KEYWORDS

Schiff base, Metal complexes, Spectral parameter studies and Antimicrobial activity.

INTRODUCTION

Isatin (indole-2, 3 dione) and its derivatives have shown a wide scale of biological activities such as antibacterial¹, antifungal^{2, 3}, anticonvulsant⁴, anti-HIV⁵, anticancer and enzyme inhibitors⁶. Isatin is a unique molecule possessing both amide and keto carbonyl groups. The C-3 carbonyl group of isatin is strongly electrophilic and it readily undergoes condensation and addition reactions. These organic compounds can act as ligands, having functional groups with nitrogen and oxygen as donor atoms^{7, 8}. Schiff bases derived from isatin have shown different antimicrobial activity due to different nature of the carbonyl and amino components as well as its substituent⁹. Metal complexes of the Schiff bases formed by condensation of the active ketonic and aldehyde compounds with aromatic amines have been reported^{10, 11}. Our purpose is to synthesize metal complexes of 3-(2-Hydroxy-5-methyl-phenylimino)-1, 3-dihydro-indol-2-one with Ti(IV), Zr(IV), Cd(II) and Hg(II) metal ions.

MATERIALS AND METHODS

All the chemicals and solvents used were of A.R. grade. Elemental analysis was done on Egar-300 analyzer. IR spectra were recorded on Perkin Elmer Spectrum 100. UV spectra were recorded on UV-Vis spectrophotometer 119 in the 200-1000 nm ranges in DMF solution (10^{-3}).

Molar conductance of the metal chelates were determined in DMF on conductivity meter Equip-tronics model No-EQ665. Melting points were recorded by open capillary method and are uncorrected. ¹H-NMR spectra of chelating agent and its metal chelates were recorded on Bruker 300 MHz spectrometer in DMSO-d₆.

In our studies we have conducted some microbial activity to see whether chelating agent (Schiff base) and metal chelates have any action microbial activities. Bacteria species like Escherichia coli, Bacillus subtilis, Aspergillus flavus and Aspergillus niger were used and screened by disc diffusion methods.

Synthesis of 3-(2-Hydroxy-5-methyl-phenylimino)-1, 3-dihydro-indol-2-one (AMPI)

The Schiff base (AMPI) was prepared by condensing of 2-amino, 4-methyl phenol and isatin (0.01M) were dissolved in ethanol to obtain 1:1 ratio in presence of glacial acetic acid for 2 to 3 hours on water bath. The reaction mixture was pouring in ice, where yellow precipitate was obtained. Then yellow precipitate filtered, washed with distilled water and warm ethanol apparent to dryness. Schiff base dried in vacuum dessicator and recrystallized from ethanol. The purity of ligand was checked by TLC. Further the structure of Schiff base was confirmed by subjecting them to IR, ¹H-NMR and Elemental analysis.

Synthesis of Ti (IV), Zr(IV), Cd(II) and Hg(II) Metal complexes

60ml of 0.01M alcoholic solution of metal chloride were mixed with 60ml of 0.01M hot alcoholic solution of (AMPI) in round bottom flask with constant stirring. The P^H of reaction mixture was adjusted about 6.9 to 7.3 by adding alcoholic ammonia drop wise. The resulting mixture was refluxed for 5 to 6 hours on water bath and cooled. The black colour precipitate appears and it is filtered through whatmann filter paper, washed with alcohol for two to three times. Obtained product is dried in vacuum dessicator and stored in sample glass bottle.

RESULTS AND DISCUSSION

All the metal chelates were coloured and stable in air, insoluble in common organic solvents but soluble in DMF, DMSO. All the results of elemental analysis are given in Table No.1. For the estimation of chloride by Volhard's method¹², metal ion percentage is determined by standard method¹³.

Presence of lattice water molecules present in the metal complexes was recorded by keeping the known weight of the complex in

previously weighed crucible in oven at 110°C for one hour. The difference in weight gives the amount of lattice water in the complex.

The compounds give satisfactory elemental analysis. Values are in close agreement with the values calculated for expected molecular formulae assigned to these complexes, suggesting 1:1 ratio for Ti(IV), Zr(IV), Cd(II) and Hg(II) complexes. The molar conductance of all these complexes in DMF reveals their electrolytic nature^{14, 15} expect Hg(II) complex.

Table No.1
Analytical data and physical properties of ligand (AMPI) and its metal chelates.

Ligand / Metal Complexes Empirical Formula	Mol. Wt. Colour/ (D.P.°C)	M:L Ratio/ Yield (%)	Molar Cond. ($\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$)	Elemental analysis % Cal (Obs)				
				C	H	N	M	Cl
AMPI $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2$	252.28 Yellow (196)	- 70	-	71.35 (71.42)	4.75 (4.63)	11.95 (11.09)	-	-
[Ti(AMPI)Cl ₂ .H ₂ O] Cl.2H ₂ O $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_5\text{Cl}_3\text{Ti}$	459.40 Black (>300)	1:1 64	50.94	39.18 (39.02)	3.70 (3.81)	6.09 (5.82)	10.42 (9.83)	23.18 (23.07)
[Zr(AMPI)Cl ₂ .H ₂ O] Cl.H ₂ O $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_4\text{Cl}_3\text{Zr}$	484.72 Grey brown (>300)	1:1 59	65.35	37.13 (37.01)	3.09 (3.34)	5.77 (5.58)	18.81 (19.34)	21.97 (21.85)
[Cd(AMPI)H ₂ O]Cl $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_3\text{ClCd}$	416.90 Brown grey (>300)	1:1 66	80.10	43.17 (42.80)	3.11 (3.05)	6.71 (6.89)	26.96 (26.58)	8.51 (8.57)
[Hg(AMPI)Cl]2H ₂ O $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_4\text{ClHg}$	523.90 Grey (>300)	1:1 65	11.52	34.41 (34.08)	2.86 (2.75)	5.35 (5.11)	38.34 (38.05)	6.78 (6.71)

Electronic Spectra

Electronic spectra of the metal complexes show the transition is shifted towards higher or lower frequencies which confirm the coordination of the ligand to the metal ions. Also, electronic spectra of all complexes display absorption bands at 29498 cm^{-1} , 30030 cm^{-1} , 30487 cm^{-1} and

30864 cm^{-1} assigned ligand to metal transfer band^{16, 17}.

Infrared Spectra

The IR spectra of the free ligand AMPI exhibits a band in the region 3250 cm^{-1} , a medium intensity band has disappeared in the complexes and indicating its involvement in the

band formation process¹⁸. This has been further indicated by appearance of phenolic ν (C-O) at 1295cm^{-1} in ligand. This band is shifted towards lower frequency in the spectra of complexes indicates, that phenoxide oxygen has coordinated to the metal ion¹⁹.

Besides, stretching frequency vibration of ν (NH) at 3170cm^{-1} in free ligand remains largely unaffected in the metal chelates providing evidence for its non-coordination. Further the band at 1728cm^{-1} , ν (C=O) ketonic carbonyl and a band at 1628cm^{-1} due to ν (C=N) azomethine

group shifted towards lower values in metal chelates indicating that carbonyl oxygen and azomethine group of isatin residue is the coordinating sites^{20, 21}.

Appearance of a new bands at 3390cm^{-1} in Ti(IV)²², 3355cm^{-1} in Zr(IV)²³ and 3350cm^{-1} in Cd(II) complexes²⁴ suggested presence of coordinated water molecules. The new bands in spectra of Ti(IV), Zr(IV), Cd(II) and Hg(II) metal complexes at $491\text{-}635\text{ cm}^{-1}$ due to ν (M-N)²⁵⁻²⁸. Also, Metal-oxygen bonding ν (M-O) at $580\text{-}732\text{cm}^{-1}$ ²⁹⁻³².

Table No.2

Infrared spectral data of ligand (AMPI) and its Ti(IV), Zr(IV), Cd(II) and Hg(II) metal complexes.

Compounds	$\nu(\text{H}_2\text{O})$	$\nu(\text{OH})$	$\nu(\text{NH})$	$\nu(\text{C-O})$	$\nu(\text{C=O})$	$\nu(\text{C=N})$	$\nu(\text{M-N})$	$\nu(\text{M-O})$
AMPI	-	3250	3170	1295	1728	1628	-	-
[Ti(AMPI)Cl ₂ .H ₂ O] Cl ₂ .H ₂ O	3390	-	3175	1246	1713	1618	491	670
[Zr(AMPI)Cl ₂ .H ₂ O] Cl.H ₂ O	3355	-	3172	1244	1712	1620	495	666
[Cd(AMPI)H ₂ O] Cl	3350	-	3177	1240	1702	1614	515	580
[Hg(AMPI)Cl] ₂ H ₂ O	-	-	3178	1230	1705	1615	635	732

¹H-NMR Spectra

¹H-NMR spectra AMPI exhibit signals at δ 2.20 (s) for methyl group attached to aromatic ring, δ 6.58-7.35 (m, 7H) due to Ar-H and strong signals is observed at δ 9.09 ppm and δ 10.90 ppm due to isatin moiety NH and Ar-OH respectively.

On complexation, all these signals have changed in four metal complexes. A peak due to Ar-H at δ 6.58-7.35 (m, 7H) is also shifted towards lower region. A corresponding peak of NH group has been shifted to up field region at δ 8.0 ppm, it indicates that ketonic oxygen and

azomethine nitrogen group involving in coordination with metal ions. The disappearance of peak at δ 10.9 ppm due to Ar-OH may be attributed to deprotonation of phenolic OH group which on involving in bonding³³. Except Hg (II) complex, a new additional signal at δ 2.0 ppm is observed due to corresponding protons of coordinated water molecule in Ti (IV), Zr(IV) and Cd(II) complexes³⁴.

Thus, on the basis of ¹H-NMR ligand AMPI binds to the metal ions through phenoxide oxygen, tertiary nitrogen and ketonic oxygen as well as involvement of water molecule.

Proposed structures for the metal complexes:

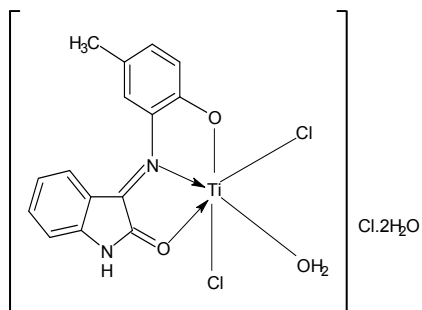


Figure 1

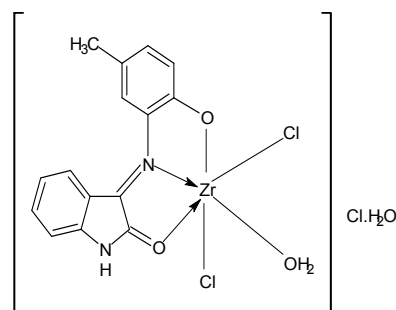


Figure 2

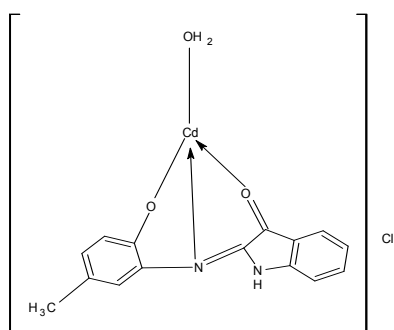


Figure 3

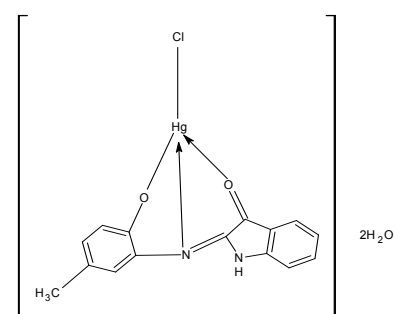


Figure 4

ANTIMICROBIAL ACTIVITY

The ligand (AMPI) and their [Ti (IV) AMPI], [Zr(IV) AMPI], [Cd(II) AMPI] and [Hg(II) AMPI] complexes antimicrobial tests were

performed by the standard disc diffusion method³⁵. The antibacterial and antifungal activity in vitro against *Escherichia coli*, *Bacillus subtilis*, *Aspergillus flavus* and *Aspergillus niger*.

Table No.3
Result of antibacterial study of transition metal complexes

Sr. No.	Compounds	<i>Escherichia coli</i>	<i>Bacillus subtilis</i>
1	AMPI	12 mm	11 mm
2	[Ti(IV) AMPI]	-ve	6 mm
3	[Zr(IV) AMPI]	-ve	-ve
4	[Cd(II) AMPI]	12 mm	11 mm
5	[Hg(II) AMPI]	5 mm	16 mm
6	Streptomycin	24 mm	30 mm
7	Control (DMSO)	10 mm	14 mm

-ve –No antibacterial activity, zone of inhibition -----mm.

Table No.4
Result of antifungal study of transition metal complexes

Sr. No.	Compounds	<i>Aspergillus flavus</i>	<i>Aspergillus niger</i>
1	AMPI	13 mm	15 mm
2	[Ti(IV) AMPI]	-ve	-ve

3	[Zr(IV) AMPI]	-ve	-ve
4	[Cd(II) AMPI]	15 mm	30 mm
5	[Hg(II) AMPI]	13 mm	20 mm
6	Fluconazole	15 mm	10 mm
7	Control (DMSO)	-ve	-ve

-ve –No antifungal activity, zone of inhibition -----mm.

[Ti (IV) 3-(2-Hydroxy-5-methyl-phenylimino)-1, 3-dihydro-indol-2-one (AMPI)] and [Zr(IV) 3-(2-Hydroxy-5-methyl-phenylimino)-1, 3-dihydro-indol-2-one (AMPI)] metal complexes have negative zone of inhibition efficiency while only [Ti(IV) AMPI] show less inhibition efficiency i.e, 6 mm.

Further [Cd(II) AMPI] metal complex have 12 mm and 11 mm zone of inhibition towards *Escherichia coli* and *Bacillus subtilis*. [Hg (II) AMPI] metal complex produce 5 mm and 16 mm zone of inhibition towards *Escherichia coli* and *Bacillus subtilis* respectively. Observed result of antifungal activity regarding organic ligand and their metal complexes i.e, 3-(2-Hydroxy-5-methyl-phenylimino)-1, 3-dihydro-indol-2-one (AMPI) produces inhibition zone for *Aspergillus flavus* and *Aspergillus niger* 13 mm and 15 mm respectively.

The [Ti (IV) AMPI] and [Zr(IV) AMPI] metal chelates have negative zone of inhibition towards fungal growth. [Cd(II) AMPI] and [Hg(II) AMPI] metal chelates produces the zone of

inhibition towards both the fungal species were given in (Table No.4).

CONCLUSION

From the results of the analysis carried out on the metal complexes, it is therefore proposed that [Ti (AMPI) Cl₂.H₂O] Cl.2H₂O and [Zr(AMPI)Cl₂.H₂O]Cl.H₂O complexes indicates octahedral geometry. Also, [Cd(AMPI)H₂O]Cl and [Hg(AMPI)Cl]2H₂O metal chelates exhibits tetrahedral geometry. The ligand (AMPI) behaves as uninegative tridentate in nature.

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REFERENCES

1. Cerhiaro G., Ferreira A.M.D., J. Brazilian Chem. Soc., 17(8), 1473, (2006).
2. Sharma V.K., Srivastava S., Srivastava A., Polish J. Chem., 80, 387, (2006).
3. Sharma V.K., Srivastava A., Srivastava S., J. Serbian Chem., 71(8-9),917,(2006).
4. Pandeya S.N., Raju A.S., Stables J.P., J. Pharmacy Pharma. Sci., 5(3), 266, (2002).
5. Bal T.R., Anand B., Yogeewari P., Sriram D., Bioinorg. Med. Chem. Lett., 15(20), 4451, (2005).
6. Pandeya S.N., Smitha S., Jyoti M., Sridhar S.K., Acta Pharma, 55, 27, (2005).
7. Hassaan A.M., Soliman E.M. and El-Shabasy M., Inorg. Met. Org. Chem., 19, 773, (1989).
8. Hassaan A.M. and Soliman E.M., Int. J. Chem., 2, 119, (1991).
9. Rai A., Sengupta S.K. and Pandey O.P., Indian J. Chem., 39A, 1198, (2000).
10. Fachinetti G., Floriani C. and Zanazzi P., Inorg. Chem., 18, 3469, (1979).



11. Hobday M.D. and Smith T.D., *J. Chem. Soc. Dalton Trans.*, 20, 2287, (1972).
12. Gh. C., Analiza M.C., *Chimica, Cantitativa Anorganica (Inorganic quantitative chemical analysis) Editura, Academiei, R.S.R. Bucuresti*, 364, (1969).
13. Vogel A.I., *A Text Book Quantitative Inorganic Analysis*, 3rd Edn, ELBS and Langman's Green and Co. Ltd., London, (1962).
14. Derebe M.G., Raju V.J.T. and Retta N., *Bull.Chem.Soc.Ethiop*, 16(1), 53, (2002).
15. Varghese S., Nair M.M.K., *R.J.P.B.C.S.*, 1(2), 347, (2010).
16. Seetharamppa J., *Turk. J. Chem.*, 23, 429, (1999).
17. Pandey R.N. and Nag A.K., *Rasayan J. Chem.*, 2(4), 990, (2009).
18. Canpolat E., *Polish J. Chem.*, 79, 619, (2005).
19. Kriza A., Parnau C., Popa N., *J. Analele Uni. Bucuresti Chimie*, XI(I), 191, (2002).
20. Turan N. and Sekerci M., *J. Chem. Soc. Pak.*, 31(4), (2009).
21. De R.L., Mandal M., Roy L., Mukherjee J., Bhawal R. and Maiti K., *I.J. Chem.*, 47A, 1480, (2008).
22. Chen S., Guo S., Ji M., Hu R. and Shi Q., *Chem. Pap.*, 56(3), 162,(2002).
23. Aliyu H.N. and Mohammed A.S., *Bayero J. Pure and App. Sci.*, 2(1), 132, (2009).
24. Joshi K., Aravindakshan K.K., *J. Chem. Tech. and Biotech.*, 57(1), (2007).
25. Rathore K., Singh R.K. and Singh H.B., *E-Journal of Chem.*, 7(S1), S566, (2010).
26. Agnihotri S. and Arora K., *E-Journal of Chem.*, 7(3), 1045, (2010).
27. Malik S., Ghosh S. and Jain B., *Arch. Appl. Sci. Res.*, 2(2), 304, (2010).
28. Mittal P., Joshi S., Panwar V., Uma V., *I.J. Chem. Res.*, 1(2) 225,(2009).
29. Poonia K., Swami M., Chaudhary A. and Singh R.V., *I.J. Chem.*, 47A, 996,(2008).
30. Ahmed A.A., BenGuzzi S.A. and Agoob A.O., *Rasayan J. Chem.*, 2(2), 271, (2009).
31. Mishra A.P. and Jain R.K., *J. Chem. Pharm. Res.*, 2(6), 51, (2010).
32. Agwara M.O., Yufanyl M.D., Foba-Tendo J.N., Atamba M.A. and Ndinteh D.T., *J. Chem. Pharm. Res.*, 3(3), 196, (2011).
33. Liviu Mitu et al. *J. Serb. Chem. Soc.*, 75(8), 1075, (2010).
34. Pingalkar S.R. and Deshpande M.N., *Orient. J. Chem.*, 23(1), 265, (2007).
35. Drew W.L., Barry A.L., Toole R.O., Sherris J.C., *Appl. Environ. Microbiol.*, 24, 240, (1972).