ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis and Spectroscopic Studies of Bivalent Transition Metal Complexes with Benzimidazole Derivative

Suman Malik[1], Supriya Das[1*], and Bharti Jain[2]

[1]Department of Chemistry, Sadhu Vaswani College, Bairagarh, Bhopal 462 001 India
[2]Department of Chemistry, Sarojni Naidu Government Girls College, Bhopal 462 003 India

ABSTRACT

In the paper we have reported synthesis of hetero chelates of the type $ML_2.2H_2O$ and ML_2 of Lansoprazole drug 2 [[[methyl – 4 (2,2,2 trifluroethoxy) 2 – pyridinyl] methyl] sulfonyl] – 1H – benzimidazole] with metal salts nickel(II) chloride ,cobalt(II) chloride and Mercury(II) chloride in 1:2 ratio . The ligand behaves as bidentate O, N donor and forms coordinate bonds through C=N and S=O groups. IR, NMR, Magnetic susceptibility, UV-Visible spectral studies suggests that Ni (II) and Co (II) complexes are paramagnetic and possess octahedral geometry whereas Hg(II) complex is diamagnetic and exhibit tetrahedral geometry. Ligand and their metal complexes have been screened for their antibacterial and antifungal activities against bacteria Pseudomonas, Staphylococcus aureus and fungi Aspergillus Niger and A.flavous.

Keywords: Spectroscopic, benzimidazole, complexes, transition

**Corresponding author*

INTRODUCTION

The literature reveals that a large number of drugs have been used to synthesize the complex with many metals with a view to enhance their therapeutic action [1,2]. Some important examples of inorganic based drugs are metallocene anti-tumor complexes [3], gold anti-arthritic compounds [4], lithium antidepressants [5]. In all these cases, work is largely focused on elucidating the mechanism of action of these complexes. Lansoprazole (LAN) is a very common PPI [6,7]. PPIs have demonstrated gastric acid suppression superior to that of histamine H2 receptor blockers. Investigations are going on the formation of metal complexes with benzimidazole ring containing ligands because benzimidazole and its derivatives play an important role in analysis and in several biological reactions [8]. Considering the importance of drugs and their complexes it has been desired to synthesize and study the metal complexes of Lansoprazole with metals. The present paper describes the synthesis and characterization of Ni (II), Co (II) and Hg(II) complexes with Lansoprazole.

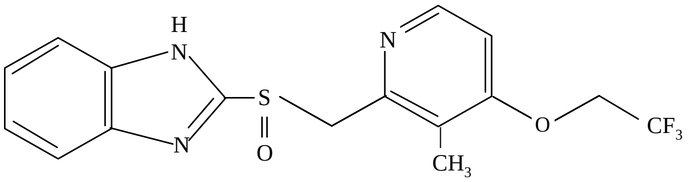

Figure 1: Structure of LANSAPROZOLE

EXPERIMENTAL

Materials and Methods

All chemicals used were of Analytical Grade. Pure sample of Lansoprazole having molecular formula, $C_{16}H_{14}F_3N_3O_2S$, and molecular weight 369.363 gm/mol was obtained from Cipla Pharmaceutical Limited Mumbai. Metal salts were of Merck Chemicals. Melting point of Lansoprazole is 166^0 C and the solvent used were acetone and distilled water. Metal-ligand ratio was calculated using Systronics digital conductivity meter. IR spectra were obtained from CDRI Lucknow. Magnetic susceptibility measurements were received from CAT Indore (Instrument used-Vibrating Sample Magnetometer). Nitrogen was determined by the Dumas method and sulphur was estimated by the Messenger's method. The elemental microanalyses of C, H, and N for ligand were carried out with Thomas and Coleman Analyzer Carlo Erba 7106.

Ligand – metal ratio

To confirm the Ligand-metal ratio, conductometric titration using mono-variation method was carried out at 21 ^{0}C. 0.01 M solution of Lansoprazole drug was prepared in 60:40 mixture of acetone and water. 20 ml of ligand was diluted to 200 ml with the same solvent. The ligand was titrated against 0.02 M metal solutions of metal salts $NiCl_{2.}$ $4H_2O$, $CoCl_2$.6H2O and $HgCl_2$ prepared in same solvent using mono-variation method and conductance was recorded after each addition of metal salt. From the equivalence point in the graph, it has been concluded that the complex formation takes place in the ratio of 2:1

(L: M). Further, stability constants and free energy changes were also calculated using Job's method [9] of continuous variation modified by Turner and Anderson [10].

Synthesis of complexes

For the synthesis of complexes, Lansoprazole was dissolved in 100 ml of acetone–water (60:40) mixture and added slowly to the metal salt solutions. The mixtures were refluxed and the solutions were kept for few days. A pink crystalline complex of cobalt, green crystalline complex of nickel and white granular complex of mercury was separated. Complexes were washed with 60:40 mixtures of acetone & water, filtered, dried, weighed and melting points were recorded. Carbon, hydrogen, nitrogen, metal and water were estimated micro analytically at CDRI, Lucknow

RESULTS AND DISCUSSION

The synthesized complexes are stable solids. They are soluble in DMF and DMSO and insoluble in all other organic solvents. Analytical data and conductometric studies suggest 2:1 [L: M] ratio. Measured conductance values of these complexes are too low to account for their electrolytic behavior. The magnetic studies indicate the Co(II) and Ni(II) complexes to be paramagnetic with magnetic moment of 4.87 B.M and 3.06 B.M respectively while Hg(II) complex to be diamagnetic.

.

Table 1 : Analytical data of Complexes

S. No.	Composition of Complex (m-wt.)	Color	Yield %	m.p .	Elemental Analyses (%) : Found (Cal)			
					C	H	N	M
1	$C_{16}H_{14}F_3N_3O_2S$ (369.36)	White		166 ^{0}C	52.71	3.05	11.05	—
2	$(C_{16}H_{14}F_3N_3O_2S)_2Co.2H_2O$ (833. 686)	Pink	65	180 ^{0}C	46.10 (46.20)	3.38 (3.51)	10.08 (10.47)	7.06 (7.12)
3	$(C_{16}H_{14}F_3N_3O_2S)_2Ni.2H_2O$ (833.44)	Green	72	195 ^{0}C	46.11 (46.16)	3.38 (3.25)	10.08 (10.42)	7.04 (7.25)
4	$(C_{16}H_{14}F_3N_3O_2S)_2Hg$ (939.31)	White	68	205 ^{0}C	40.91 (40.50)	3.00 (3.44)	8.94 (8.80)	21.35 (27.7)

Table 2: Stability Constant, Free Energy Change, Molar Conductance and Magnetic- Moment Data of Complexes

S.No.	Composition of Complex (m-wt.)	Stability constant logK (L/mole)	Free Energy change -ΔF (Kcal/mole)	Molar conductance ($ohm^{-1}cm^2mol^{-1}$)	Magnetic Moment (B.M.)
1	$(C_{16}H_{14}F_3N_3O_2S)_2Co.2H_2O$	11.4208	16.039	11.08	4.87
2	$(C_{16}H_{14}F_3N_3O_2S)_2Ni.2H_2O$	12.0888	17.038	12.1	3.06
3	$(C_{16}H_{14}F_3N_3O_2S)_2Hg$	10.5231	15.5905	10.9	_

Infrared Spectra

The IR spectra [11-14] of ligand and complexes have been recorded and the probable assignments are given in the Table 3.The IR spectra of the complexes indicate that the ligand behaves as a bidentate and co-ordinate to the metal via C=N and sulphonic acid group. In the ligand, band appearing at 3456 cm^{-1} due to NH stretching remains unaffected in the complex. The band due to ν C= N in the ligand at 1590 cm^{-1} is shifted to lower wave number at 1590-1576 cm^{-1} in the complexes there by confirming the coordination through the azomethine nitrogen atom. The shifting of S=O stretching vibration to the lower wave number side as compared to the free ligand is indicative of participation of sulphonic acid group in coordination . In both Ni(II) and Co(II) complexes, bands appearing at region 3654-3640 cm^{-1} are due to coordinated water molecules. The appearance of bands in the far IR region at 429-409 cm^{-1} in the complex may be assignable to M-N frequency. Additional bands in the complex in the region 615-608cm^{-1} compared with IR spectra of free ligand have tentatively been assigned to M-O frequency and new band appearing at 1380-1390 cm^{-1} in the complexes might be due to chelate ring formation in the complexes.

Table 3: IR Absorption data of the complexes

Ligand and complex	ν(NH)cm^{-1}	ν (C = N) cm^{-1}	ν(S = O)cm^{-1}	ν(M-N)cm^{-1}	ν(M-O)cm^{-1}	ν(H_2O)cm^{-1}
$C_{16}H_{14}N_3O_3S$	3456	1590	1028	-	-	-
$(C_{16}H_{14}N_3O_3S)_2Co.2H_2O$	3453	1574	1014	426	613	3650
$(C_{16}H_{14}N_3O_3S)_2$ Ni.2H_2O	3454	1585	1012	414	610	3644
$(C_{16}H_{14}N_3O_3S)_2$ Hg	3452	1580	1020	410	615	-

Electronic Spectra and Magnetic Susceptibility Data

The spectra of Co(II) complex of Lansoprazole shows three bands at 8600 cm-^{1} ,18000 cm-^{1} and 22000cm-^{1} respectively corresponding to the transitions $^4T_{2g}(F) \leftarrow {}^4T_{1g}(F)$ (ν_1), $^4A_{2g}$ (F)$\leftarrow {}^4T_{1g}(F)$ (ν_2), $^4T_{1g}(P) \leftarrow {}^4T_{1g}(F)$ (ν_3) indicating octahedral[15]geometry of the complex. The proposed geometry is further confirmed by high μ_{eff} value in the range [16,17] 4.89-5.24 B.M. The electronic spectra of Ni(II) complex displays and three absorption bands at 8333 cm-^{1} ,13700 cm-^{1} and 24640 cm-^{1} which may be assigned to$^3T_{2g}(F) \leftarrow {}^3A_{2g}$ (F) (ν_1), $^3T_{1g}(F) \leftarrow {}^3A_{2g}$ (F) (ν_2) and $^3T_{1g}(P) \leftarrow {}^3A_{2g}(F)$($\nu_3$) transitions indicating octahedral [15] geometry of the complex. The geometry of Ni (II) complex is further confirmed [16,17] by the high μ_{eff} value in the range 3.09-3.20 B.M. As expected Hg(II) complex is diamagnetic. The complex is suggested to be tetra-coordinated probably having tetrahedral geometry based on analytical, I.R. and conductance data.

NMR Spectra

The ^{1}H NMR spectra of the ligand have the expected characteristic signals. The CH_3 proton shows singlet at δ 2.2 and O- CH_2CH_3 proton at δ 3.5 .The doublet peak observed at δ 4.36 and 4.66 ppm is attributed to CH_2 protons. In addition a multiplet peak at δ 6.9-8.3 may be due to aromatic protons and peak at δ13.2 may be due to NH proton of benzimidazole ring. Signals observed in the complexes at region of δ 8.18-8.23 due to the azomethine proton are either remained unaffected or shifted slightly downfield with reference to those of the parent ligand and the position of signal due to NH proton remains unaffected in the complexes .The aromatic protons show downfield shifts in the complexes. These observations support the assigned structure to the complex.

Scanning Electron Micrographs [S.E.M.]

S.E.M. of metal complexes indicates the presence of well defined crystals free from any shadow of the metal ion on their external surface. The representative micrographs of a) Ligand; b) $[CoL_2(H_2O)_2]$;c) $[NiL_2(H_2O)_2]$ are shown in Fig.3

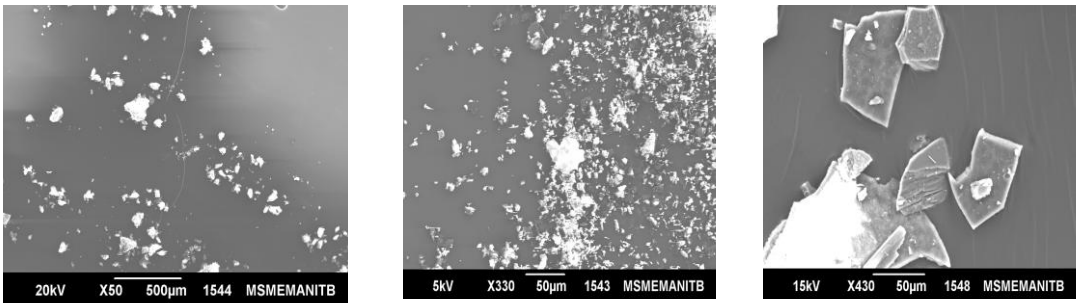

Figure 2: Scanning electron micrograph of Ligand and its Complexes

Antimicrobial Activity

The antimicrobial activity of the ligand and the complexes were determined by the disc diffusion technique [18]· The compounds were screened in vitro against *Pseudomonas, Staphylococcus aureus* and two strains of fungi, *Aspergillus Niger* and *A.Flavous*. A 1mg/ml solution in DMF was used. The standard used was gentamycin sulphate. The bacterium was maintained on nutrient agar and the agar media were incubated for different microorganism culture tests. After 24h of incubation at 37^0C for bacteria and 72h of incubation at 25^0C for fungi , the diameter of zone of inhibition (mm) thus formed around each disc containing the test compound were measured accurately .The Co(II) , Ni(II) complexes show moderate activity against bacteria *Pseudomonas* and *Staphylococcus aureus* and fungi *Aspergillus niger* and *A. flavous* compared to the ligand and the Zn(II) complex shows significant activity against bacteria Pseudomonas and Staphylococcus aureus and fungi Aspergillus niger and A. flavous as compared to ligand.

Table 4 : Antibacterial activity- zone of inhibition {in mm}

S. No.	Compound	*P. Aeroginosa*	*S. Aureus*	*A. niger*	*A. flavous*
1.	Lansoprazole	13.1	11.2	14.22	12.11
2.	Zn L_2	15.7	13.3	16.80	16.00
3.	Ni L_2 $2H_2O$	12.11	12.11	14.82	12.11
4.	Co L_2 $2H_2O$	14.37	10.53	15.34	13.30

CONCLUSION

The ligand molecule acts as a bidentate ligand. The spectroscopic results show the involvement of C=N and S=O groups in coordination to the central metal ion. Spectral studies suggests that Ni (II) and Co (II) complexes possess octahedral geometry and Zn(II) complex posses tetrahedral geometry. It is observed that the formed complexes are better anti-bacterial agents in comparison to ligand. In view of the foregoing discussions, the high melting points and insolubility in common organic solvents, we have assigned following probable structure of the complexes of Lansoprazole.

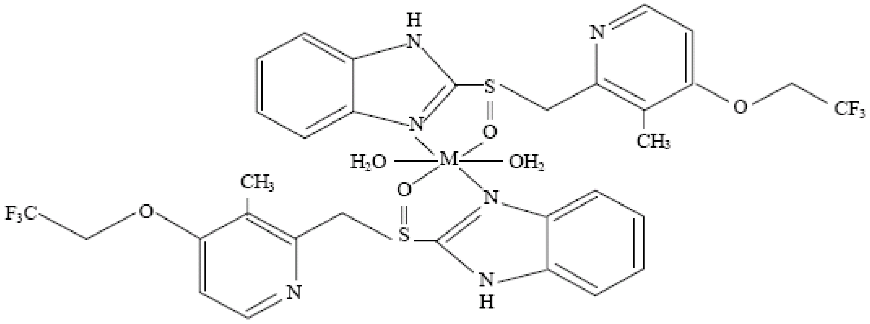

Figure 3: Structure of Lansoprazole complex with, Co(II), Ni(II) metals

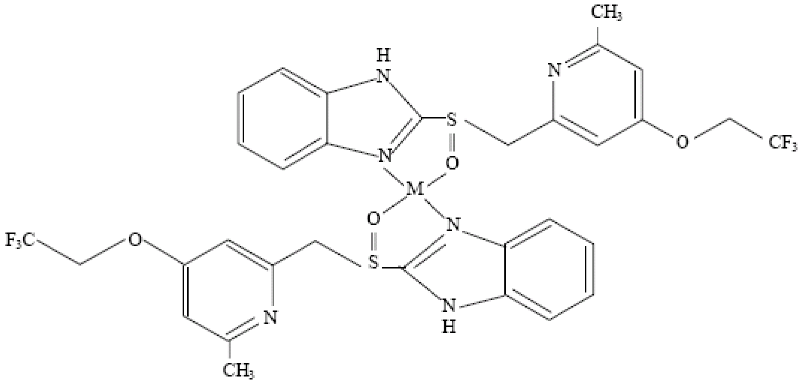

Figure 4: Structure of Lansoprazole complex with Zn(II) metal

ACKNOWLEDGEMENT

The authors are thankful to Principal, Sadhu Vaswani College Bairagarh for providing necessary facilities for research work, DST for granting FIST program to the college and UGC for sanctioning UGC Research award to Dr. Suman Malik , one of the co-author

REFERENCES

.
[1] Reedijk J. Pure Appl Chem 1987;59:181
[2] Lochrer PJ and Einhorn LH . Ann Inten Med 1984;100:704
[3] Toney J. H. Brock CP and MarksT. J Am Chem Soc 1986; 108:7265
[4] Forestier J. J Lab Clin Med 1935;20:827-40
[5] Bansal A and Singh RV. Synth React Inorg Metal-Org Chem 2001; 31:381
[6] Sexena RK and Srivastava SK. J Indian Chem Soc 1987; 64:446
[7] Preston PN. Chem Rev 1974; 74: 279
[8] Sluka J, Navakand J and Budesinsk Z. Coll. Czech, Chem. Com 1976;41:3628
[9] Job P. Ann Chem 1928; 10: 113
[10] Turner SE and Anderson RC. J Am Chem Soc 1949; 71 : 912

[11] Nakamotto K. Infrared Spectra of Inorganic and Co-Ordination Compounds, John Wiley, New York, 1976

[12] Vogel I. Quantitative Inorganic Analysis ,Longman Green and Co. ,London 1954 pp 455

[13] Bellamy LJ. Chemical application of spectroscopy, Int. Sci. Pub., New York 1956

[14] Rao CNR. Chem. Application of IR Spectroscopy, Academic press ,New York, 1963 pp260-262

[15] Krishna CH , Maha Patra CM and Dash K A. J Inorg Nucl Chem 1977;39:1253

[16] Carlin RL and Van Dryneveledt AJ. Magnetic Properties of Transition Metal Compounds, Springer- Verlag , New York 1997

[17] Figgis BN. Introduction to Ligand Fields, Wiley Eastern Ltd., New Delhi, 1976 pp 279

[18] Collins CH and Lyne, Microbiological Methods,4th Ed. Butter-worth, London, 1976 pp 235-240