

Transition Metal Complexes of Biologically Important Chelating Agent

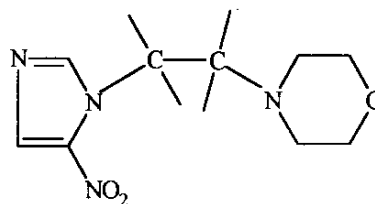
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(Received 18th November, 1995, revised 5th June, 1996)

Summary: The coordination chemistry of 1-(N- β -ethyl-morpholine)-5-nitroimidazole, a chemotherapeutic agent, is carried out and is reported. This ligand can be compared with that of DME and DMP in its structure. In this paper the synthesis and characterization of 1-(N- β -ethyl-morpholine)-5-nitroimidazole(EMNI) compounds of the type $M(ENMI)X_2$ where $M = Co(II), Ni(II), Cu(II), Zn(II), Cd(II)$ and $Hg(II)$, while $X=Cl, Br, I$, and NO_3 and based on the usual physical methods *i.e.* spectroscopic, magnetic and conductance measurements. Thermal studies (thermogravimetric analysis) are carried out to explain the mode of decomposition, results are reported and discussed.

Introduction

The coordination chemistry of compounds containing the grouping $-(N(CH_2)_n-N)-$ having acyclic and cyclic structures have been studied [1-9]. These chelating agents confer several geometries which covers the range from octahedral to tetrahedral and square-planar [10-13]. The ligands dimorpholinoethane (DME) and dimorpholinopropane (DMP), which can be viewed as N,N -substituted ethylenediamine and propylenediamine respectively act as a stereospecific chelating agents. It has been observed that certain metal compounds cause destruction or diminution of virus which causes cancer while others are found for antitumor activity [14,15]. As a result considerable interest has been developed to design metal complexes which could minimize the interaction of metal ion with DNA [16-18]. Realizing the importance of metal chelates in the biological activity, we have thought it, of interest to synthesize and study the coordination chemistry of ligands which have biologically active sites linked to the grouping $-(N(CH_2)_n-N)-$ by replacing morpholine moiety of DME by imidazole or its derivative. Imidazole has been proved to be of prime importance in biological systems [19-21]. The coordination chemistry of imidazole and its derivatives has been drastically studied [19-33]. The compound chosen for metal chelation is 1-(N- β -ethylmorpholine)-5-nitroimidazole (EMNI), as it has $-(N(CH_2)_n-N)-$ linkage and imidazole unit in its structure.



1-(N- β -ethyl-morpholine)-5-nitroimidazole

The EMNI, synthesized by Giraldi, *et al.* [34] has a wide applications in pharmacological industry. It is chemotherapeutic agent with a high activity against trichomonas vaginalis and other protozoa [35,36]. In the present paper we report $Co(II), Cu(II), Zn(II), Cd(II)$ and $Hg(II)$ complexes with that of EMNI, and their molecular properties are compared with DME. The structural assignments have been justified by magnetic, conductance, analytical and U.V visible and I.R. data.

Results and Discussion

Characterization of the ligand and complexes

The ligand EMNI has been characterized by its melting point, elemental analysis, mass spectra, NMR and IR spectra. The complexes are characterized by their elemental analysis, conductance measurements, magnetic susceptibility, IR and Uv-visible spectra. In

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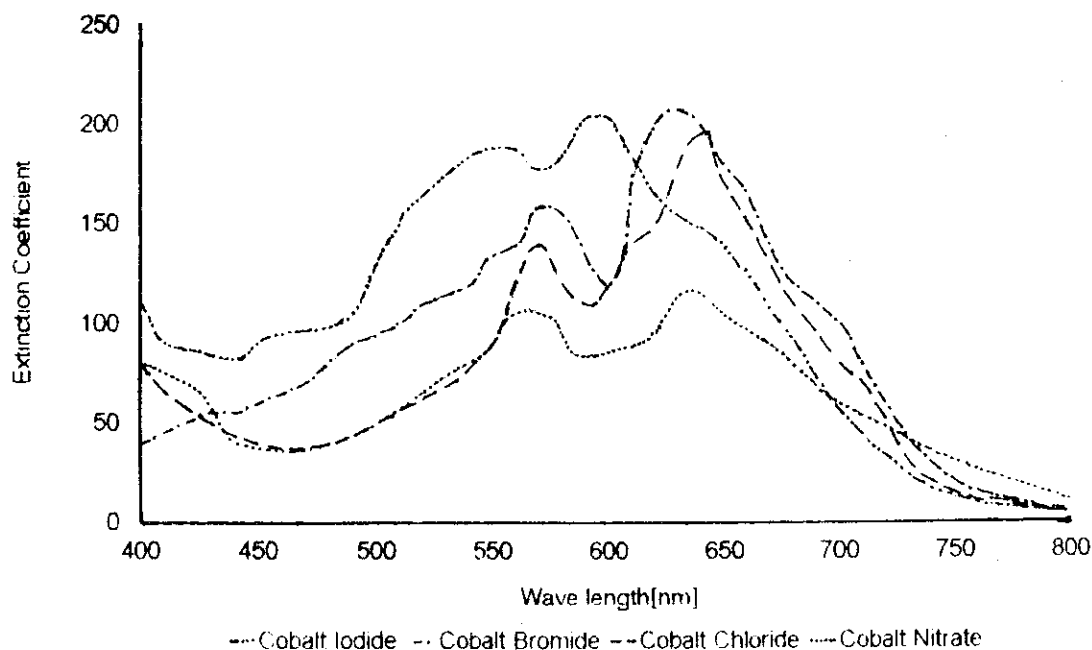


Fig. 1: Absorption spectra of EMNI with cobalt salts.

addition to characterization of complexes the thermal measurements are also studied.

The principal bands in infra red spectra of the ligand and its complexes is given in Table-3. The free ligand EMNI has both morpholine and nitroimidazole moieties in its structure. The spectra exhibits strong absorption bands in the region $1060 - 920 \text{ cm}^{-1}$ which are due to C-O-C stretching vibration [37,38]. There are also strong absorption bands in the region $1130-1105 \text{ cm}^{-1}$ which are assigned to C-N stretching vibration of the morpholine [39]. In addition to these bands a strong band also appears at 1140 cm^{-1} which is assigned to C-N stretching frequency of nitroimidazole moiety. This band also appears in nitroimidazole compound with a shoulder at 1150 cm^{-1} . In all these complexes the C-N stretching vibrations have been reduced to either two or three bands as compared to EMNI, where four bands are observed. This clearly indicates the coordination of tertiary nitrogen of imidazole and morpholine moieties with the metal ion. In the free ligand the band in the region $1060-910 \text{ cm}^{-1}$ assigned to C-O-C stretching vibration either shift to higher or lower frequency which may be due to weak interactions of metal atoms with oxygen of the

ligand, due to solid state effect. The far IR spectra of the complexes shows multiple bands in the region of $470-490 \text{ cm}^{-1}$ and $260-300 \text{ cm}^{-1}$. The former bands are due to $\nu(\text{M-X})$ vibrations and later bands are assigned to $\nu(\text{M-N})$ stretching vibration. All the bands observed are weak and broad (Table-4).

Cobalt(II) complexes

The elemental analysis and conductance data shows that the complexes of cobalt has the formula $[\text{Co}(\text{EMNI})\text{X}_2]$, X stands for Cl, Br, I, and NO_3 . The magnetic moments ranges from 4.02 B.M to 4.56 B.M indicating the three unpaired electrons. These complexes exhibit a broad band between $600-700 \text{ nm}$ (Fig. 1). Within this band one is able to distinguish two maximum at 570 and 640 nm . The first band could be assigned to components of ${}^4\text{A}_2(\text{F}) \rightarrow {}^4\text{T}_1(\text{F})$ transition in tetrahedral symmetry and the second set of bands to the components of ${}^4\text{A}_2(\text{F}) \rightarrow {}^4\text{T}_1(\text{P})$ transition [40].

Copper(II) complexes

The solution spectra of $[\text{Cu}(\text{EMNI})\text{I}_2]$ and $[\text{Cu}(\text{EMNI})(\text{NO}_3)_2]$ are almost similar (Fig. 2). The spectral data is presented in Table-5. The broad

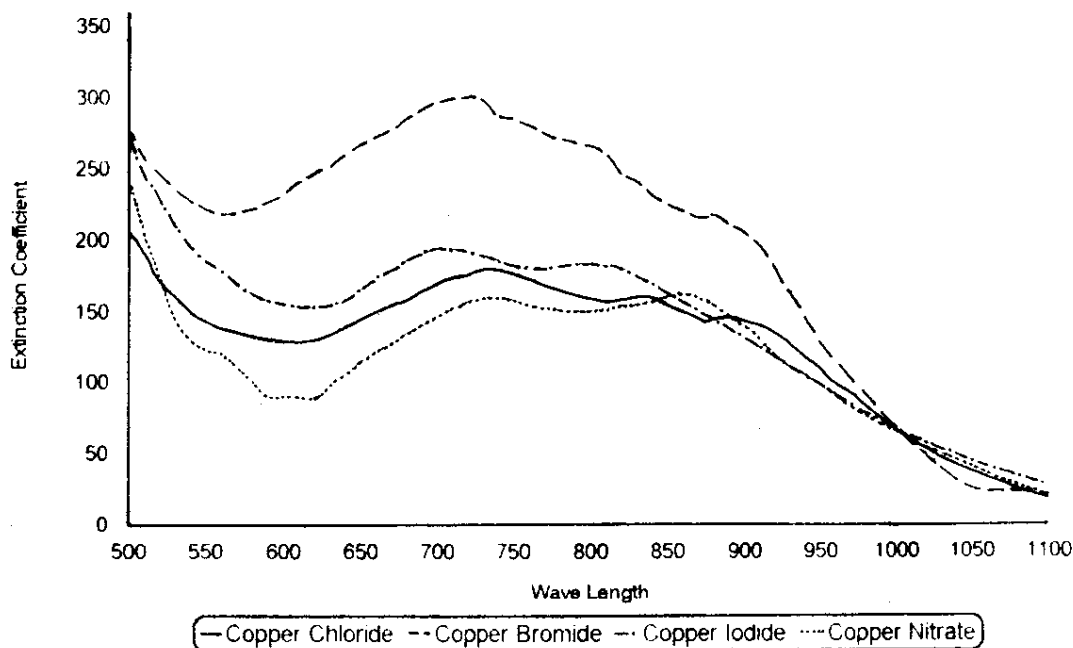


Fig. 2: Absorption spectra of EMIN with copper salts.

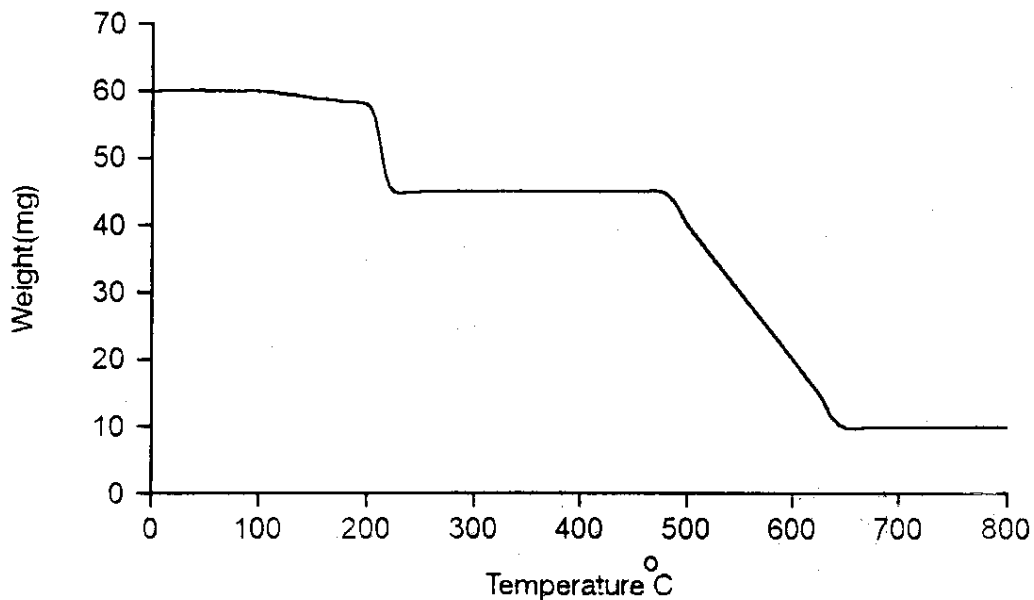


Fig. 3: Representative thermogram of zinc bromide complex of EMNI

absorption band is observed from 600-1000 nm. Two maxima at 705 and 795 nm are observed for nitro complex. In C_{2v} symmetry four transition would be expected [41]. It seems that in the spectra of copper complexes two peaks are buried in the

absorption peak like that of $[Cu(DME)X_2]$ complexes [42]. Similar spectra were observed for the other copper complexes having CuN_2Cl_2 chromophore environment [43,44], suggesting tetrahedral geometry for copper complexes. The

Table-1: Elemental analysis of EMNI and its complexes

Compound	Colour	D.pt	C%	N%	H%	Cation%	Anion%
EMNI	Yellow	110	47.60 (47.78)	24.72 (23.94)	6.05 (6.18)	--	--
Co(EMNI)Cl ₂	Blue	213	30.01 (30.36)	16.04 (15.37)	3.79 (3.68)	16.25 (16.55)	19.67 (19.91)
Co(EMNI)Br ₂	D.Blue	196	24.30 (24.29)	12.91 (12.59)	2.91 (2.94)	12.06 (13.03)	35.17 (35.91)
Co(EMNI)I ₂	Blue	182	21.00 (20.05)	10.37 (10.39)	2.42 (2.43)	11.02 (10.93)	46.00 (47.09)
Co(EMNI)(NO ₃) ₂	Blue	180	27.30 (26.24)	13.26 (13.69)	3.53 (3.20)	14.40 (14.04)	--
Cu(EMNI)Cl ₂	Green	173	30.00 (29.93)	16.89 (15.55)	4.77 (3.90)	15.31 (16.10)	17.53 (17.89)
Cu(EMNI)Br ₂	D.Red	159	25.84 (24.04)	13.64 (13.46)	3.49 (3.14)	13.90 (14.14)	35.95 (33.60)
Cu(EMNI)I ₂	D.Green	174	19.93 (19.89)	10.56 (10.31)	2.49 (2.41)	10.87 (11.69)	46.83 (46.90)
Cu(EMNI)(NO ₃) ₂	Brown	169	26.31 (26.12)	13.67 (13.54)	3.29 (3.17)	15.15 (15.53)	--
Zn(EMNI)Cl ₂	white	238	28.39 (29.82)	15.75 (15.45)	3.85 (3.61)	17.71 (18.03)	19.63 (19.56)
Zn(EMNI)Br ₂	white	237	24.21 (23.94)	11.76 (12.41)	3.36 (2.90)	14.46 (14.53)	36.79 (35.40)
Zn(EMNI)I ₂	white	228	20.32 (19.82)	10.39 (10.27)	2.47 (2.40)	12.37 (11.98)	46.61 (46.53)
Cd(EMNI)Cl ₂	dirty white	139	26.29 (26.39)	13.58 (13.68)	3.00 (3.20)	27.44 (27.44)	17.21 (17.31)
Cd(EMNI)Br ₂	dirty white	130	21.57 (21.69)	11.31 (11.24)	2.90 (2.63)	21.78 (22.55)	32.13 (32.06)
Cd(EMNI)I ₂	white white	143	19.75 (19.93)	10.42 (10.23)	2.27 (2.21)	18.62 (18.97)	42.51 (42.84)
Cd(EMNI)(NO ₃) ₂	dirty white	140	23.12 (23.36)	12.18 (12.11)	2.69 (2.83)	24.43 (24.29)	--
Hg(EMNI)Cl ₂	White	129	23.04 (22.12)	11.84 (11.26)	3.15 (2.84)	40.00 (40.29)	31.91 (31.26)
Hg(EMNI)Br ₂	white	127	18.68 (18.42)	9.41 (9.55)	2.66 (2.40)	33.81 (34.19)	26.89 (27.25)
Hg(EMNI)I ₂	white	136	15.33 (15.88)	7.81 (8.23)	1.76 (1.93)	29.68 (29.47)	37.42 (37.29)
Hg(EMNI)(NO ₃) ₂	white	132	19.36 (19.62)	9.79 (2.38)	2.47 (10.17)	35.07 (36.42)	--

Theoretical percentages are given in paranthesis.

complexes of Cadmium(II), Zinc(II) and Mercury(II) are tetrahedral due to their usual tendencies.

Thermogravimetric analysis

The thermogravimetric analysis (TGA) of the EMNI complexes of Co(II), Cu(II), Zn(II), Cd(II) and Hg(II) have been carried out. The thermal behaviour of all the complexes except that of Hg(II) is similar. In the complexes loss of weight take place in two different steps at different temperatures (pointing towards different stabilities). In first step the ethylenemorpholine (EM) moiety of the ligand (EMNI) detaches in the range 170-260°C and the rest of the portion of the

ligand and anion vaporizes in the range 260-500°C leaving metal oxides behind. The representative thermogram and thermogravimetric data are reported in Figure: 3 and Table-6. The Hg(II) complexes either decomposes or sublimates.

Experimental

Materials

Metal salts of, Cobalt(II), Copper(II), Zinc(II), Cadmium(II) and Mercury(II) were obtained from standard source suppliers. They were of analytical grade and used without further purification. The nonaqueous solvents (properly dried) used in synthetic work were distilled twice.

Table-2: Magnetic and conductance data for EMNI complexes

Compound	Temp. K°	Λ (mho mol ⁻¹ cm ²)	$10^6 \times \chi_m^{cor}$ (cgsu)	μ_{eff} (B.M)
Co(EMNI)Cl ₂	298	2.7	8662	4.56
Co(EMNI)Br ₂	298	3.1	8379	4.49
Co(EMNI)I ₂	298	3.7	6756	4.02
Co(EMNI)(NO ₃) ₂	298	3.8	7368	4.19
Cu(EMNI)Cl ₂	298	0.1	1560	1.92
Cu(EMNI)Br ₂	298	5.8	1803	2.06
Cu(EMNI)I ₂	298	0.6	1428	1.85
Cu(EMNI)(NO ₃) ₂	298	3.1	1664	2.00
Zn(EMNI)Cl ₂	298	0.9	168	dia-magnetic
Zn(EMNI)Br ₂	298	0.86	190	do
Zn(EMNI)I ₂	298	1.4	212	do
Cd(EMNI)Cl ₂	298	1.4	233	do
Cd(EMNI)Br ₂	298	1.2	353	do
Cd(EMNI)I ₂	298	0.76	429	do
Cd(EMNI)(NO ₃) ₂	298	2.8	169	do
Hg(EMNI)Cl ₂	298	2.2	276	do
Hg(EMNI)Br ₂	298	2.8	401	do
Hg(EMNI)I ₂	298	1.2	226	do
Hg(EMNI)(NO ₃) ₂	298	3.9	168	do

$$\mu_{eff} = 2.84 \sqrt{\chi_m T}$$

A required amount of partially dehydrated salt was dissolved in a minimum amount of methanol/ethanol mixture. For the preparation of all complexes 1:2 metal/ligand ratio was employed. The ligand (in methanol/ethanol mixture) was slowly added to the metal ion solution and was stirred for 3-4 hours. The complexes were either precipitated on standing or evaporating in vacuum at 50°C. The product obtained were filtered through sintered glass crucible, washed several times with dry acetone and dried under vacuum and were recrystallized from suitable solvents.

Analytical data (Table-1)

Cations were determined by using XRF-500 link system England, and C, H, and N elemental analysis were performed through the Courtesy of

Table-3: IR bands for EMNI and its complexes.

Compound	ν_{C-N} cm ⁻¹	ν_{C-O-C} cm ⁻¹	ν_{C-N} cm ⁻¹	ν_{C-NO_2} cm ⁻¹
EMNI	1140s, 1125s, 1115w, 1105s	1060 m	1520, 1440vs	1375vs
Co(EMNI)Cl ₂	1135s, 1116b, 1112s	1060m	1515s, 1460s	1375vs
Co(EMNI)Br ₂	1140s, 1122s, 1112w	1065m, 1068s	1520s, 1462s	1375vs
Co(EMNI)I ₂	1138s, 1125w, 1112w	1070m, 1075s	1520s, 1462s	1375vs
Co(EMNI)(NO ₃) ₂	1152s, 1125w, 1110w	1055m, 1060s	1520s, 1464s	1375vs
Cu(EMNI)Cl ₂	1150s, 1110b	1068m	1480s, 1468s	1375vs
Cu(EMNI)Br ₂	1138s, 1110b	1065m	1528, 1465s	1372vs
Cu(EMNI)I ₂	1155s, 1110w	1070m	1518s, 1468s	1377vs
Cu(EMNI)(NO ₃) ₂	1150s, 1110w	1065m	1515s, 1468s	1376vs
Zn(EMNI)Cl ₂	1145s, 1130w	1055m, 1060b	1520s, 1462s	1375vs
Zn(EMNI)Br ₂	1142s, 1130b	1055m, 1070b	1520s, 1460s	1375vs
Zn(EMNI)I ₂	1130s, 1125b	1050m, 1065m	1520s, 1460s	1376vs
Cd(EMNI)Cl ₂	1120s, 1110s	1060m, 1050m	1540s, 1460s	1375vs
Cd(EMNI)Br ₂	1120s, 1110w	1070m	1530s, 1460s	1375vs
Cd(EMNI)I ₂	1120s, 1110s	1070m	1522, 1460s	1375vs
Cd(EMNI)(NO ₃) ₂	1125s, 1110w	1060m	1525s, 1460s	1375vs
Hg(EMNI)Cl ₂	1140s, 1125w, 1115s	1070m	1510, 1460s	1375vs
Hg(EMNI)Br ₂	1120, 1115w	1060m	1540s, 1465s	1375vs
Hg(EMNI)I ₂	1135s, 1120s, 1115w	1062m, 1065m	1520s, 1462s	1375vs
Hg(EMNI)(NO ₃) ₂	1130s, 1122m, 1110w	1060m, 1068m	1520s, 1465s	1375vs

s sharp; vs very sharp; b broad; m medium; w weak

Ligand

The ligand 1-(N-β-ethyl-morpholine)-5-nitroimidazole(EMNI) was first prepared in 1970 [34] and is available in the market in the form of a yellow colored tablets, manufactured by Punjab drug house, Lahore (Pak.) under the licence of Carlo Erba and used after necessary extraction and purification.

Preparation of complexes

The complexes were prepared by a general procedure as outlined below:

H.E.J. Research Institute of Chemistry, University of Karachi on Carlo Erba Mod 1106, where as anions were determined by usual methods [45].

Magnetic susceptibility measurements (Table-2)

The magnetic moments of the solid complexes at room temperature were determined by the Gouy method. A double ended Gouy tube was calibrated using Hg[Co(SCN)₄] as standard. Pascal's constants were used to the correct molar susceptibilities of crystalline complexes for the diamagnetism of the ligand and the anions involved [46].

Table-4: Absorption frequencies in far IR region.

Complex	V(M-X) cm^{-1}	V(M-N) cm^{-1}
Co(EMNI)Cl ₂	480-465	290-280
Co(EMNI)Br ₂	480-475	285
Co(EMNI)I ₂	485-470	290,270
Co(EMNI)(NO ₃) ₂	485-460	285,260
Cu(EMNI)Cl ₂	475-460	290
Cu(EMNI)Br ₂	475	285-275
Cu(EMNI)I ₂	480-475	275-260
Cu(EMNI)(NO ₃) ₂	485-470	270
Zn(EMNI)Cl ₂	480-470	-
Zn(EMNI)Br ₂	485-470	280
Zn(EMNI)I ₂	480-465	270
Cd(EMNI)Cl ₂	480-465	290-280
Cd(EMNI)Br ₂	480-475	285
Cd(EMNI)I ₂	485-470	280
Cd(EMNI)(NO ₃) ₂	480-475	28,270
Hg(EMNI)Cl ₂	475-465	315,280
Hg(EMNI)Br ₂	480	300,275
Hg(EMNI)I ₂	485	295,280
Hg(EMNI)(NO ₃) ₂	480	290,280

Table-5: UV visible spectra of EMNI complexes..

Complex	λ_{max}	$V[\text{cm}^{-1}]$	$\epsilon_{\text{max}} [\text{M}^{-1} \text{cm}^{-1}]$
Co(EMNI)Cl ₂	570	17543	140
	640	15625	195
Co(EMNI)Br ₂	575	17391	160
	630	15873	208
Co(EMNI)I ₂	550	18181	195
	590	16949	205
Co(EMNI)(NO ₃) ₂	565	17699	108
	635	15748	117
Cu(EMNI)Cl ₂	730	13699	100
	840	11905	160
	890	11236	145
Cu(EMNI)Br ₂	720	13889	300
	800	12500	260
Cu(EMNI)I ₂	890	11236	200
	705	14184	205
Cu(EMNI)(NO ₃) ₂	795	12378	197
	730	13698	163
	860	11627	165

Electrolytic conductance measurements (Table-2)

The electrolytic conductance of the complexes were determined by conductivity bridge made by mullard, Inc. England. The conductivity cell was properly calibrated. The observed conductivity was always corrected for the specific conductance of the pure solvent used [47].

Infra-red spectra (Table-3 and 4)

The Infra-red absorption spectra of the solid complexes were obtained with I.R. Spectrometer Model SP-3-100 PYE Unicam A.M. in the range of 4000-400 cm^{-1} . The IR spectra were examined as KBr and CsI discs in the region 400-200 cm^{-1} (FT IR-Shimadzu).

Table-6: Thermogravimetric data

Complex	Initial weight (mg)	Weight Loss (mg) 140-250°C (Ethylenemor-pholine)	Weight loss (mg) 260-620°C (Nitroimidzole)	Residue (mg)
Co(EMNI)Cl ₂	95	27.1 (27.3)	43.4 (43.7)	11.1 (11.4)
Co(EMNI)Br ₂	82	20.8 (21.0)	49.9 (50.1)	13.7 (13.8)
Co(EMNI)I ₂	96	20.0 (20.3)	64.9 (65.0)	13.0 (13.4)
Co(EMNI)(NO ₃) ₂	91	49.0 (49.4)	24.8 (24.9)	16.7 (16.7)
Cu(EMNI)Cl ₂	60	17.0 (18.0)	30.5 (30.7)	13.0 (13.2)
Cu(EMNI)Br ₂	71.5	18.5 (18.1)	44.5 (43.0)	8.5 (10.4)
Cu(EMNI)I ₂	51	10.7 (10.8)	33.8 (34.3)	7.6 (7.5)
Cu(EMNI)(NO ₃) ₂	70	37.6 (37.6)	18.9 (19.0)	13.3 (13.5)
Zn(EMNI)Cl ₂	51	15.8 (16.1)	25.5 (25.7)	11.7 (11.5)
Zn(EMNI)Br ₂	58	14.9 (14.7)	34.0 (34.9)	10.9 (10.5)
Zn(EMNI)I ₂	62	12.6 (13.0)	41.1 (41.6)	9.0 (9.2)
Cd(EMNI)Cl ₂	61	16.0 (16.9)	27.5 (27.4)	17.0 (16.6)
Cd(EMNI)Br ₂	60	13.5 (13.7)	33.0 (32.9)	13.5 (13.4)
Cd(EMNI)I ₂	66	12.8 (12.8)	40.5 (40.8)	14.0 (14.3)
Cd(EMNI)(NO ₃) ₂	56	26.8 (26.9)	13.4 (13.6)	15.7 (15.5)
Hg(EMNI)Cl ₂	70	Sublimed	--	--
Hg(EMNI)Br ₂	60	Sublimed	--	--
Hg(EMNI)I ₂	45	Sublimed	--	--
Hg(EMNI)(NO ₃) ₂	47	Sublimed	--	--

Calculated values are given in parenthesis

UV-Visible spectra (Table-5)

Visible and ultraviolet spectra of the complexes in different solvents were obtained with JASCO UNIDEC-1 recording spectrophotometer using set of matched 1 cm quartz cells. The absorption spectra were always recorded using freshly prepared solutions.

Nuclear Magnetic Resonance Spectrum

The ¹H-NMR and ¹³C-NMR data for the ligand were obtained by NMR spectrophotometer Model JNM-PMX at 300 MHz. All of the spectra for proton and ¹³C were measured relative to tetramethylsilane (TMS) as an external standard in CDCl₃.

Mass spectra of EMNI

The mass spectra of the ligand was obtained with VG-Micromass 12 spectrometer.

Thermogravimetric analysis (Table-6)

Thermal characterization of EMNI complexes have been studied by means of different thermal and thermogravimetric analyses. Thermogravimetric analysis were performed on Recording Stanton (England) thermogravimetric balance. Analytically pure anhydrous complexes were used and triplicate measurements were made for each complex.

References

1. D.W. Meek and S.A. Ehrhardt, *Inorg. Chem.*, **4**, 584 (1965).
2. H. Irving and J.M.M. Griffiths, *J. Chem. Soc.*, 213 (1954).
3. D.L. Leussing, *Inorg. Chem.*, **2**, 77 (1963).
4. S.F. Povkovic and D.W. Meek, *ibid.*, **4**, 20 (1965).
5. D.W. Meek, *ibid.*, **4**, 250 (1965).
6. R. Nasanen, M. Koshinen, R. Salonen and A. Niiski, *Suomen Keistilehli, B.*, **38**, 81 (1965).
7. G.A. Carlson, J.P. Mc Reaynolds, and F.H. Verhoek, *J. Am. Chem. Soc.*, **67**, 1334 (1945).
8. F. Basolo and R.K. Murmann, *ibid.*, **74**, 5243 (1952) and **76**, 211 (1954).
9. W. Kenneth Musker and M. Sakhawat Hussain, *Inorg. Chem.*, **8**, 529 (1969).
10. W.A. Baker Jr. and P.M. Brown, *J. Am. Chem. Soc.*, **88**, 1314 (1966).
11. L.A. Mitscher, A.C. Bonacci, B. Slater-Eng., A.K. Hacker and T.D. Sokolosko, *Antimicro, Agents Chemother.*, 111 (1969).
12. R.P. Gupta, B.N. Yadav, O.P. Tiwari and A.K. Srivastava, *Inorg. Chim. Acta.*, **32**, 195 (1979).
13. C.F. Bell, Oxford Chemistry Series, "Metal Chelation Principle and Application" p. 124 Clarendon Press, Oxford (1977).
14. Oncol, *J. Chem. Harabol.*, **7** (1977) and references therein.
15. T.A. Connors and J.J. Roberts, Ed., "Platinum Coordination in Cancer Chemotherapy" Springer Verlag New York (1974).
16. G. Pneumaticakis, N. Hadjiliadis and T. Theophanides, *Inorg. Chim. Acta*, **22**, L1-L2 (1977)
17. D.J. Hodgson, *Inorg. Chem.*, **23**, 211 (1977).
18. A.S. Mildvan "The Enzyme" 3rd Ed. (Editor, P.D. Boy) Academic Press, New York, Vol. II, Page 445 (1970).
19. J. Steinhardt and S. Beychok, The Proteins, 2nd Ed. (Editor, H. Neurath) Academic Press, New York, Vol. II, 261-276 (1964).
20. B.I. Valee and W.E.C. Wacker in the Proteins, 2nd Ed. (Editor, H. Neurath) Academic Press, New York, 1970, Vol. V, pp. 69-71, 77, 82-90, 100, 114, 146, 149.
21. R.W. Mc. Gilvery "Biochemistry", a functional Approach, W.B. Saunders Co., Philadelphia, Pa. p. 14 (1970).
22. R.E. Dickerson and I. Geis, "The Structure and Action of Proteins" Harper and Row, New York, p. 44-51 (1969).
23. A.S. Mildvan, "Bio-Inorganic Chemistry", (Editor F.S. Gould), American Chemical Society Washington, D.C. p. 409 (1981).
24. T.L. Blundell, G.G. Drelson, D.C. Hodgkin and M. Vigayan, "Recent advan. Horm. Res.," **27**, 19 (1971).
25. W.J. Eilbeck, F. Holmes and A.E. Underhill, *J. Chem. Soc.*, (A), 757 (1967).
26. W.J. Eilbeck, F. Holmes, C.E. Taylor and A.E. Underhill, *J. Chem. Soc.*, (A), 128 (1968).
27. H. Montgomery and E.C. Lingafelter, *J. Phys. Chem.*, **60**, 831 (1960).
28. M. Goodgame and L.I.B. Haines, *J. Chem. Soc.*, (A), 174 (1966).
29. M.J.M. Cambell, D.W. Card. M. Goldstein and R. Grzeskowiak, *J. Chem. Soc. Dalton*, 1968 (1972).
30. B. Chiswell, F. Lions and B. Morviz, *Inorg. Chem.*, **3**, 110 (1964).
31. R.J. Dossier and A.E. Underhill, *J. Chem. Soc.*, (A) 88 (1970).
32. A.K. Bannerjee and S.P. Gosh, *J. Indian Chem. Soc.*, **38**, 237 (1961).
33. S.M. Ali, N. Ahmad and M.S. Hussain, *Pak. J. Sci. Res.*, **18**, 29 (1966).
34. P.N. Giraldi, *A. Zeinith Forsch.*, **20**, 52 (1970).
35. Romano, *J. Planar Chroatoogr.*, 233 (1994).
36. J.C. Dora, *J. Pharm. Belg.*, 45 (1990).
37. M.D. Joesten, J.G. Clause and K.P. Lanhart, *J. Inorg. Nucl. Chem.*, **29**, 1421 (1967).
38. A.D. Cross, "Introduction to Practical Infrared

- Spectroscopy", p. 86-70, Page Bros., Norschich Ltd., (1960).
39. M.S. Hussain, T. Ali and S.M. Ali, *Pak. Jr. Sci. and Ind. Research.*, **19**, 50 (1976).
 40. B.N. Figgis and J. Lewis, "Modern Coordination Chemistry", p. 290, Interscience Publication Co., New York, N.Y. (1960).
 41. G. Basee, R. Belford and R. Dickerson, *Inorg. Chem.*, **I**, 438 (1962).
 42. E. Boschmann, L.M. Weinstock and M. Germack, *Inorg. Chem.*, **13**, 1297 (1974) and references therein.
 43. S.N. Choi, R.D. Bereman and J.R. Wasson, *J. Inorg. Nucl. Chem.*, **37**, 2087 (1975).
 44. E. Boschmann, I.M. Weinstock and M. Germack, *Inorg. Chem.*, **13**, 1297 (1974) and references therein.
 45. A.I. Vogel, "Qualitative Inorganic Analysis", English Language Book Society, 650-795 (1975).
 46. B.N. Figgis and J. Lewis, "Modern Coordination Chemistry", p. 412, Interscience Publication Co., New York, N.Y. (1960).
 47. D.P. Shoemaker and C.W. Garland, "Experiments in Physical Chemistry", p. 196, McGraw-Hill Book Co. Inc. New York, N.Y. (1962).