

Journal of Applicable Chemistry 2013, 2 (2):150-163

(International Peer Reviewed Journal)



Synthesis, Characterization and Antimicrobial Activities of New N₄-donor Ligands and their Co(II), Ni(II), Cu(II) and Zn(II) Complexes

Sunkari Jyothi, Kundha Shashank, Gundapaneni Raghava Rao, Anjali Reddy, Pola Someshwar and Sreedasyam Jagannatha Swamy*

*Department of Chemistry, Kakatiya University, Warangal 5-6009, A. P., India

Email: sj_swamy@yahoo.com Received on 28th February and finalized on 07th March 2013.

ABSTRACT

Two new N_4 -donors, N,N'-(ethane-1,2-diyl)bis(2-prop-1-eneaminobenzamide) [EBEAB] and N,N'-(propane-1,3-diyl)bis(2-prop-1-eneaminobenzamide) [PBEAB] have been prepared and characterized. Their complexes with Co(II), Ni(II), Cu(II) and Zn(II) are obtained by reaction with metal salts in methanol. The physicochemical and spectral studies reveal that the complexes have the formula, [MLX₂].n H_2O , where M = Co, Ni, Cu, L = EBEAB or PBEAB, X = Cl and n = 1; and M = Zn, $X = CH_3COO^{-}$ and n = 0. The antibacterial activity of the ligands and the metal complexes against four gram-negative and two gram-positive bacterial strains have been evaluated using disc diffusion method. The complexes are found to be more active than the ligands and among the metal complexes, the Cu(II) complexes exhibited better activity and comparable with the activity of the standard, amoxicillin.

Keywords: N₄-ligands, Metal complexes, Antibacterial activity, Spectral studies of metal complexes.

INTRODUCTION

The steady advancement of conflict in microorganisms against existing drugs necessitates an enduring exploration for novel compounds that have antimicrobial *i.e.*, antibacterial or anti-viral properties. Viruses have rapidly advanced resistance against current drugs [1]. There is a need to develop new classes of antibiotic drugs, especially those that show broad-spectrum properties. Wide range of organic compounds containing nitrogen or oxygen or both as donor atoms known to exhibit biological/pharmacological activities and can act as good ligands for metal chelation. Activities of such organic compounds varies greatly on chelation to different metals and present a promising area of research in designing novel therapeutic methodologies to deal with this problem of ever increasing "microbial resistance". Many metal ions are known to play a significant role in different biological processes [2, 3]. For example, Zn(II) and Cu(II) ions are the second- and third most abundant transition metals present in humans. They are found either at the bioactive sites or as structural constituents of enzymes or coenzyme in biochemical processes [4]. Most of the studies are aimed to understand the role of metal cations in metalloenzymes in terms of structure–function relationships. The compounds containing amide and amine groups are very useful in coordination of metals through nitrogen atoms and help in developing novel metal-organic frameworks [5] and other biologically important molecules [6-9]. Presently research is focused on developing new N₄-

donar ligands and their transition metal complexes with potential applications [10-13]. Their biological activities are considered to be due to their ability to form chelates with metal ions. Biological activities of the metal complexes generally differ from those of the ligand and the metal ion, and such reports are well documented especially for biologically active metal ions like Cu(II), Zn(II) and Fe(III) [14-17]. Our interest has been to design and develop new ligands and their complexes with biological and catalytic properties [10-13]. In this paper, we present the preparation of two new ligands and their complexes with Co(II), Ni(II), Cu(II) and Zn(II) ions, their structural characterization and antibacterial activity.

MATERIALS AND METHODS

All chemicals used were the products of Aldrich or Merk. The reagents and solvents were used as obtained from the supplier or recrystallized/redistilled as necessary. Thin-layer chromatography (TLC) was performed for checking the purity of the compounds. Infrared (IR: KBr/CsI disc) spectra were recorded with a PerkinElmer BX series-Fourier transform infrared spectrophotometer. ¹H and ¹³C{¹H} NMR spectra were obtained on a Bruker AV500 MHz spectrometer with chemical shifts referenced to Si(Me)₄. Mass spectra were recorded using the HR FAB and HR -EI techniques on JMS-700 double focusing mass spectrometer (JEOL, Tokyo, Japan) with a resolution of 8000(3000) (5% valley definition) at Mass Spectrometry facility, IICT Hyderabad. Thermogravimetric analysis (TGA) was carried out using Mettler–Toledo, TGA 822e series instrument at a heating rate of 10°C per min. CHN analyses were carried out using Elemental Analyzer Flash EA 1112. Conductance of the metal complexes was measured on Digisun digital conductivity meter model DI-909. Magnetic susceptibility measurements of the metal complexes in the solid state were performed on the Gouy's balance at room temperature. Melting points were recorded on a Cintex apparatus. The electronic spectra were recorded using Shimadzu UV–Vis spectrophotometer model 2401 PC. ESR spectra of Cu(II) complexes were recorded at liquid nitrogen and room temperatures on JEOL-JES-PE-3X ESR spectrometer using DPPH as the g-marker.

Preparation of Ligands

1. Synthesis of N,N'-(ethane-1,2-diyl)bis(2-prop-1-eneaminobenzamide)EBEAB(2a) and N,N'-(propane-1,3-diyl)bis(2-prop-1-eneaminobenzamide)PBEAB (2b)



Scheme-1

10 mmol of N,N'-(ethane-1,3-diyl)bis-(2-aminobenzamide) (1a) [12] or N,N-propane-bis-(2-aminobenzamide) (1b) [12] was dissolved in 20 ml of DMF and 0.02 mol (2.76 g) of anhydrous potassium carbonate was added to the solution and the solution was stirred continuously for about 15 min. The solution was cooled to 0° C and 20 mmol. (2.40g) of allyl bromide (3-bromoprop-1-ene) was added very slowly. The reaction mixture was refluxed for about 6 h under N₂, while monitoring with by TLC and then the mixture was poured into ice-cold water, followed by extraction of the product into ethyl acetate. The product was further purified by column chromatography using 60-120 mesh silica with ethyl acetate: hexane as eluent. The spectral data of the compounds are presented below and the ¹H-NMR and mass spectra of the ligands 2a and 2b are presented in the figures 1 - 4.

Fig 1: 1H-NMR spectrum of EBEAB

Fig 2: 1H-NMR spectrum of PBEAB

Fig 1: 1H-NMR spectrum of EBEAB

Fig 2: 1H-NMR spectrum of PBEAB

N,N'-(ethane-1,2-diyl)bis(2-*prop-1-eneaminobenzamide*) 2*a*: Yield 92%. ¹H-NMR (300 MHz, CDCl₃), δ (ppm): 7.40-7.50(-CO-N<u>H</u>-, 2H), 6.50-7.30(aromatic, 8H), 5.85-6.00(-C<u>H</u>=CH₂, 2H), 5.10-5.35(-CH=C<u>H₂</u>, 4H), 3.80(-C<u>H</u>₂-CH=CH₂, 4H), 3.50(-CO-NH-C<u>H</u>₂-, 4H), 1.80(-CH₂-CH₂-, 2H); ¹³C-NMR (100 MHz, CDCl₃) δ 169.3(>C=O), 115.02-150.02 (aromatic carbons), 134.07 (-<u>C</u>H=CH₂), 115.38 (-CH=<u>C</u>H₂), 46.02 (-NH-<u>C</u>H₂-CH=CH₂), 37.07 (-CO-NH-<u>C</u>H₂-), 29.81 (-CH₂-<u>C</u>H₂-CH₂-). HRMS (FAB+), found: 393.00(M +1)⁻⁺.

N,N'-(propane-1,3-diyl)bis(2-*prop-1-eneaminobenzamide*) 2*b*: Yield 70%, (2.64g); ¹H-NMR (300 MHz, CDCl3), δ (ppm): 6.52-7.70 (aromatic, 8H), 5.65-6.0 (-C<u>H</u>=CH₂, 2H), 5.12-5.15 (-CH=C<u>H₂</u>, 4H), 3.62-3.85 (-C<u>H₂</u>-CH=CH₂, 4H), 3.42-3.60 (-CH₂-CH₂-, 4H); ¹³C-NMR (100 MHz, CDCl₃) δ 168.50(>C=O), 114.91-149.02 (aromatic carbons), 134.04(-CH=CH₂), 115.35 (-CH=CH₂), 40.05 (-CH₂-CH=CH₂), 32.38 (-CO-NH-CH₂). HRMS (FAB+), found: 379.89 (M+1)^{□+}.





Fig 3: Mass spectrum of EBEAB

Fig 4: Mass spectrum of PBEAB

Preparation of Metal complexes: To methanolic solution (20 ml) of respective ligand (2.00 mmol), a solution of metal salt [chloride of Co(II), Ni(II), Cu(II) or acetate of Zn(II)] (2.00 mmol) was added with constant stirring. The mixture was refluxed for 4 h. On cooling, solid complex was precipitated out. It was filtered, washed with cold MeOH and dried under vacuum over anhydrous CaCl₂⁻

RESULTS AND DISCUSSION

Elemental Analyses: The physicochemical and analytical data of all the metal(II) complexes with new ligands **EBEAB** and **PBEAB** are given in table 1. The experimental data coincide well with contents of elements C, H, N, Cl and metal calculated for the formulae $MLCl_2.H_2O$ for Co(II), Ni(II) and Cu(II) and $[M(L)(OAc)_2]$ for Zn(II) complexes respectively, where L= EBEAB/ PBEAB ligands. These formulae support well the data acquired from thermal and other spectral studies of all complexes.

Conductivity Studies: The conductance values of all complexes were determined in DMF at 10^{-3} *M* concentration. The results are presented in Table 1. The calculated molar conductance values are found to be between 8.99 and 10.36 ohm⁻¹ cm² mol⁻¹ that confirm that all the complexes are non-electrolytes [18].

The conductance values remain unchanged even after 48 hours indicating that, there is no perceptible ionization and also that there are strong interactions between the metal ions, the ligand **EBEAB** or **PBEAB** and the chloride/acetate ions. As a result, these complexes may be formulated as [MLX₂]. nH₂O, where M = Co(II)/Ni(II)/Cu(II) and X = Cl⁻, n = 1; and Zn(II), X = CH₃COO⁻, n = 0

Thermogravimetric Analysis: The thermal decomposition and stabilities of all the complexes with **EBEAB** and **PBEAB** were studied to access their relative thermal stability and decomposition process. The TGA data of all the complexes were acquired under N₂ atmosphere between 50 and 1000°C at a heating rate of 5°C min⁻¹and given in Table-2. Thermal study reveals that the Co(II), Ni(II) and Cu(II) complexes of **EBEAB** and **PBEAB** decompose in three stages. The Co(II), Ni(II) and Cu(II) complexes (Figures-5 to 8) lose a weight of around 3.4% (calc. 3.50%) in the range 65–185°C. The observed weight loss in the first step corresponds to the loss of one lattice held water molecule [19, 20]. In the second and third steps two coordinated chloride ions and ligand moiety were decomposed in the temperature range 280–900°C, with a mass loss for Co(II) 63.73% (calcd. 64.92%) and in the case of Ni(II) and Cu(II) with a loss of weight 84.12% (calcd. 85.39%) and 83.98% (calcd. 84.56%) respectively. The percentage of Co₃O₄, NiO and CuO residue left and the data supports the elemetal analysis [21]. Similarly, Co(II), Ni(II) and Cu(II) complexes of both the ligands two stage decomposition is observed. Two coordinated acetate ions as well as ligand part were lost in the temperature range 320–900°C in the Zn(II) complexes of **EBEAB** and **PBEAB** and **PBEAB**. The residue left in the crucible accounts for ZnO [22, 23].

Compound	D.T.	%C	%H	%N	% Cl	%M	μ_{eff}	Λ° ∗
m/z(calc),	°C						B.M.	
Yield%								
[Co((EBEAB))Cl ₂]. H ₂ O	314	50.25	5.29	10.59	14.43	11.24	4.56	10.08
526.14 (525.09); 78		(50.20)	(5.26)	(10.64)	(13.47)	(11.20)		
[Ni((EBEAB))Cl ₂]. H ₂ O	356	50.31	5.37	10.60	13.51	11.15	3.11	8.99
548.30 (524.09); 74		(50.23)	(5.36)	(10.55)	(13.48)	(11.16)		
[Cu((EBEAB))Cl ₂]. H ₂	348	43.89	4.75	11.96	15.26	13.71	1.89	9.89
O 530.05 (529.08); 81		(43.93)	(4.77)	(12.05)	(15.25)	(13.67)		
Zn((EBEAB))(OAc) ₂]	319	55.89	5.71	9.96	-	11.70	-	9.95
561.33 (560.14); 58		(55.57)	(5.74)	(9.97)		(11.64)		
[Co(PBEAB)Cl ₂].H ₂ O	333	51.22	5.57	10.33	13.17	10.92	4.48	10.21
540.92 (539.89); 69		(51.12)	(5.60)	(10.37)	(13.12)	(10.91)		
[Ni(PBEAB)Cl ₂].H ₂ O	362	51.19	5.58	10.39	13.21	10.88	3.03	9.67
540.28 (539.30); 75		(51.15)	(5.60)	(10.37)	(13.13)	(10.91)		
[Cu(PBEAB)Cl ₂].H ₂ O	347	50.75	5.52	10.31	12.99	11.70	1.91	10.36
567.54 (543.10); 74		(50.69)	(5.55)	(10.28)	(13.01)	(11.66)		
[Zn(PBEAB)(OAc) ₂]	333	56.39	5.97	9.69	-	11.41	-	10.06
599.30 (574.10); 65		(56.30)	(5.95)	(9.73)		(11.35)		

 Table – 1: Analytical and Physicochemical data of M(II) complexes





Fig 5: Thermogram of [Co(EBEAB)Cl₂].H₂O





Fig 7: Thermogram of [Co(PBEAB)Cl₂].H₂O

Fig 8: Thermogram of [Zn(PBEAB)(OAc)₂]

Mass spectral studies: The mass spectra of all complexes (Figures 9 to 12) show the high mass peak assignable to as $[(MLX_2)].nH_2O]^{+}$ (n = 0 or 1). Another peak that verifies the coordination of the ligand to the metal ion is that of ML^{+} fragment. One of the daughter ions appeared in the mass spectra of the complexes corresponds to that of the respective ligand. Thus the mass spectral data supports the analytical and thermal data and confirm the formulae of the complexes as $[M(L)X_2].H_2O$, where (L = **EBEAB/PBEAB**, M = Co(II), Ni(II) and Cu(II)) [12]. Similarly, Zn(II) complexes of **EBEAB** and **PBEAB** show the molecular ion $[M(L) (OAc)_2]^{-+}(L =$ **EBEAB**or**PBEAB**) and the fragment ion peaks of the ligands [24].

S. No.	Complex	Thermal Process	Temperature	rature Pyrolysis product, 9	
			Range, ⁰ C	Found	Calc.
1	[CoL ₁ Cl ₂].H ₂ O	$\begin{bmatrix} CoL_1Cl_2 \end{bmatrix} H_2O \rightarrow \begin{bmatrix} CoL_1Cl_2 \end{bmatrix}$ $\begin{bmatrix} CoL_1Cl_2 \end{bmatrix} \rightarrow \begin{bmatrix} CoCl_2 \end{bmatrix} \rightarrow \begin{bmatrix} Co_3O_4 \end{bmatrix}$	63.5-182.2 325.3-899.1	3.397 63.73	3.50 64.92
2	[NiL ₁ Cl ₂].H ₂ O	$ [NiL_1Cl_2].H_2O \rightarrow [NiL_1Cl_2] [NiL_1Cl_2] \rightarrow [NiCl_2] \rightarrow [[NiO] $	72.8-183.6 283.5-862.8	3.421 84.119	3.435 85.392
3	[CuL ₁ Cl ₂].H ₂ O	$ [CuL_1Cl_2].H_2O \rightarrow [CuL_1Cl_2] [CuL_1Cl_2] \rightarrow [CuCl_2] \rightarrow [CuO] $	50.8-177.5 367.5-830.1	3.321 83.975	3.403 84.559
4	[ZnL ₁ (OAc) ₂]	$[ZnL_1(OAc)_2] \rightarrow [ZnO]$	338.5-864.8	83.922	85.733
5	[CoL ₂ Cl ₂].H ₂ O	$CoL_2Cl_2].H_2O \rightarrow [CoL_2Cl_2]$ $[CoL_2Cl_2] \rightarrow [CoCl_2] \rightarrow [Co_3O_4]$	56.0-186.9 278.4-885.2	3.24 65.04	3.33 65.96
6	[NiL ₂ Cl ₂].H ₂ O	$\begin{bmatrix} NiL_2Cl_2 \end{bmatrix} H_2O \rightarrow \begin{bmatrix} NiL_2Cl_2 \end{bmatrix}$ $\begin{bmatrix} NiL_2Cl_2 \end{bmatrix} \rightarrow \begin{bmatrix} NiCl_2 \end{bmatrix} \rightarrow \begin{bmatrix} NiCl_2 \end{bmatrix} \rightarrow \begin{bmatrix} NiCl_2 \end{bmatrix}$	67.2-139.5 220.0-719.1	3.410 84.554	3.338 85.818
7	[CuL ₂ Cl ₂].H ₂ O	$ [CuL_2Cl_2].H_2O \rightarrow [CuL_2Cl_2] [CuL_2Cl_2] \rightarrow [CuCl_2] \rightarrow [CuO] $	83.0-165.4 269.7-752.6	3.299 83.699	3.315 84.971
8	$[ZnL_2(OAc)_2]$	$[ZnL_2(OAc)_2] \rightarrow [ZnO]$	320.6-909.3	85.510	86.086

Fable –2: Thermal	data of M	(II) complexes

 $(L_1 = EBEAB, L_2 = PBEAB)$





Fig 10: Mass spectrum of [Cu(EBEAB)Cl₂].H₂O



Fig 11: Mass spectrum of [Co(PBEAB)Cl₂].H₂O Fig 12: Mass spectrum of [Zn(PBEAB)(OAc)₂]

Infrared Spectra: The IR spectral absorptions of the complexes along with assignments are presented in Table (3) and representative spectra are shown in figures 13 to 15. The bonding modes of the ligands were elucidated by comparing IR spectra of ligands EBEAB/PBEAB and their complexes. The strong bands appeared in the region 2862–2968 cm⁻¹ in the IR spectra of ligands are assigned to symmetric and asymmetric v(C-H) stretching modes of the allylic group. The strong bands observed at 3396.6 and 3479.5 cm⁻¹ in the spectra of ligands are attributed to the stretching vibrations of the amide (N-H) and secondary amine (Ar-NH-Allyl), groups respectively [25]. In all the complexes, the shift of v(C=O) to higher frequencies reveals the non-coordination of carbonyl oxygen and low frequency shift in the amide and amine N-H frequencies by 20 cm⁻¹ indicate coordination of these nitrogen atoms to the metal ions [26-27]. Two new vibronic modes in the far-IR spectra of Co(II), Ni(II) and Cu(II) complexes, one around 434 cm^{-1} and the other around 264cm⁻¹ are observed. These may be assigned to v(M-N) [27] and v(M-Cl) [28] respectively. While the Zn(II) complexes exhibit two new bands assignable to v(Zn-O) around 518 cm⁻¹ [29] and v(Zn-N) around 430 cm⁻¹ [29]. These absorptions in the infrared spectra of complexes indicate that the metal ions are coordinated to EBEAB/PBEAB through two amide and two secondary amine nitrogen atoms. Further, the presence of two chloride or two acetate ions in the coordination sphere confirms that the ligands are neutral and supports the low conductance values of the complexes. The absorptions resultant of asymmetric and symmetric stretching of the acetate groups in Zn(II) complexes were observed at 1608 and 1392 cm⁻¹ respectively and additionally these bands also indicate the monodentate binding of the acetate ions [29]. The data confirm that M(II) ions in all the complexes investigated are coordinated to four nitrogen atoms (two amide and two amine groups) and two chloride or acetate ions. The water molecule is present outside the coordination sphere in the case of Co(II). Ni(II) and Cu(II) complexes.

				_		
Complex	v(O=C- <u>N-CH₂</u>)	v(Ar- NH- allyl)	v(C=O) amide-I	v(M-Cl)	v(M-N)	v(M-O)
[Co(EBEAB)Cl ₂].H ₂ O	3402	3364	1636, 1560	258	409	-
[Ni(EBEAB)Cl ₂].H ₂ O	3436	3392	1654, 1617	270	428	-
[Cu(EBEAB)Cl ₂].H ₂ O	3448	3382	1654, 1618	264	440	-
[Zn(EBEAB)(OAc) ₂]	3350	3423	1636, 1526		434	518
[Co(PBEAB)Cl ₂].H ₂ O	3441	3412	1641, 1609	263	416	-
[Ni(PBEAB)Cl ₂].H ₂ O	3447	3408	1637, 1612	276	422	-
[Cu(PBEAB)Cl ₂].H ₂ O	3446	3342	1637, 1620	259	432	-
[Zn(PBEAB)(OAc) ₂]	3393	3402	1647, 1596		438	521

Table – 3: Infrared spectral data (cm⁻¹) of M(II) complexes





 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 30
 <





Fig 15: IR spectrum of [Ni(PBEAB)Cl₂].H₂O

Magnetic moment: The magnetic moment values of the Co(II), Ni(II) and Cu(II) complexes obtained at room temperature are presented in table 1. The magnetic moment values of Co(II) complexes of **EBEAB** and **PBEAB** are 4.56 and 4.48 B.M respectively indicating the presence of three unpaired electrons [30]. These high spin values of Co(II) complexes confirm that they have octahedral geometry. The magnetic moment values of the Ni(II) complexes studied are found to be 3.11 and 3.03 B.M. respectively [31-33]. These values are in tune with high spin configuration and accounts for octahedral environment around the Ni(II) ion in the complexes. The room temperature magnetic moment values of [Cu(EBEAB)Cl₂].H₂O and [Cu(PBEAB)Cl₂].H₂O are 1.89 and 1.91 B.M. respectively, which are typical for mononuclear of Cu(II)

compounds with a S = 1/2. These high values over 1.73 B.M. (spin only value) indicate that both the complexes exhibit paramagnetic coupling of spins at this temperature. Thus the Cu(II) complexes are assumed to be tetragonally distorted with orbitally non-degenerate B ground state due to John-Teller distortions [33]

Electronic spectral properties: The optical spectra of Co(II), Ni(II) and Cu(II) complexes were recorded in DMF and typical spectra are shown in figures 16 to 19. The spectral absorptions are given in table 4.

Co(II) Complexes- In general, the electronic spectra of Co(II) complexes exhibit two to three absorptions. The electronic spectra of Co(II) octahedral complexes are fairly complex and often pose problems in correct assignment due to the admixture of spin forbidden transitions to doublet states ²G and ²H, spin-orbit coupling and vibrations of low symmetry components.³⁸ The electronic spectra of the Co(II) complexes recorded in DMF solution exhibit three absorptions: which may be assigned to the transitions ⁴T_{1g}(F) \rightarrow ⁴T_{1g}(P) (v_1), ⁴T_{1g} \rightarrow ⁴A_{2g} (F) (v_2) and ⁴T_{1g}(F) \rightarrow ⁴T_{2g}(F), (v_3), supporting the octahedral environment around Co(II) ion [30].

Complex	Absorptio	n maxima
	cm^{-1}	nm
[Co((EBEAB))Cl ₂].H ₂ O	14803, 16393, 16957	675.5, 610.0, 589.7
[Ni((EBEAB))Cl ₂].H ₂ O	14471, 16129, 17182	691.0, 620.0, 582.0
[Cu((EBEAB))Cl ₂].H ₂ O	14285	700.8
[Co(PBEAB)Cl ₂].H ₂ O	14261, 16716, 17267	701.2, 679.5, 601.4
[Ni(PBEAB)Cl2].H2O	14836, 16460, 17525	674.0, 607.5, 570.6
[Cu(PBEAB)Cl ₂].H ₂ O	14534	688.0

 Table – 4 : Electronic spectral absorptions of M(II) complexes



Fig 16: Electronic spectrum of [Co(EBEAB)Cl₂].H₂O Fig 17: Electronic spectrum of [Ni(EBEAB)Cl₂].H₂O





Fig 19: Electronic spectrum of [Ni(PBEAB)Cl₂].H₂O

The absorption spectra of the Ni(II) complexes of the ligands **EBEAB** and **PBEAB**, exhibit three absorption bands at 14471, 14261, 16129 and 16716, 17182,17267 cm⁻¹ respectively. The observed bands may be assigned to the three spin allowed transitions ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{2g}(F)$ (v₁), ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{1g}(F)$ (v₂) and ${}^{3}A_{2g}(F) \rightarrow {}^{3}T_{1g}(P)$ (v₃), respectively [27]. In the case of Cu(II) complexes of D_{4h} or $C_{4\nu}$ symmetry, the eg and t_{2g} levels of the ${}^{2}D$ free ion term will split into B_{1g}, A_{1g} and B_{2g}, Eg levels respectively. [Cu(EBEAB)Cl₂] and [Cu(PBEAB)Cl₂] display one broad band centered at 14285 and 14534 cm⁻¹ respectively. The absorption may be assigned to ${}^{2}E_{g} \rightarrow {}^{2}T_{2g}$ transition [33].

EPR Studies : Representative spectra of [Cu(EBEAB)Cl₂] and [Cu(PBEAB)Cl₂] are shown in Figures 20 and 21. The EPR spectra for the polycrystalline sample and in DMF solution have similar features. This hyperfine interaction observed is attributable to interaction with the four nitrogen nuclei bonded to the copper ion. The g_{\parallel} and g_{\perp} values were computed from the spectra. The 'g' values and spin Hamiltonian parameters are summarized in Table 5. Kivelson and Neiman have reported the g_{\parallel} value <2.3 for covalent character of the metal-ligand bond and >2.3 for ionic character. The g_{\parallel} values are formed to be less than 2.3 and hence the M-L bond can be assumed to be covalent. The trend $g_{\parallel} > g_{\perp} > g_e$ ($g_e = 2.0023$) observed for these complexes shows that the unpaired electron is localized in d_{x-y}^2 orbital of the Cu(II) ions and the spectral features are characteristics of axial symmetry. The powder ESR spectra of both the complexes did not exhibit the forbidden half field signals typical for binuclear triplet-state species. The solid state spectrum of $[Cu(EBEAB)Cl_2]$ exhibits a single, nearly an isotropic and exchange-narrowed signal (Δ Hpp = 66 G) at g_{av} = 2.13 (g_{II} = 2.25 and g = 2.065) and G = 3.85. The ESR spectral line shape in Figure 23 is same as that for common mononuclear Cu(II) complexes in magnetically undiluted crystals. The observed line narrowing is probably due to the exchange interaction between crystallographically equivalent Cu(II) centers and the observed g-values reflect the local copper(II) ion environment [31]. In addition there is exchange coupling interaction involving two copper centers explained by Hathaway expression G = $(g_{\parallel}-2)/(g_{\perp}-2)$. The value, G < 4, suggests the presence of an exchange coupling between two adjacent Cu(II) centers in solid state [32-34].

Table – 5: ESR parameters of Cu(II) complexes

Complex	g∥	g_{\perp}	g _{ave}	G	$\mu_{calc.}$	$\mu_{expt.}$
[Cu(EBEAB)Cl ₂].H ₂ O	2.25	2.065	2.13	3.85	1.84	1.89
[Cu(PBEAB)Cl ₂].H ₂ O	2.29	2.080	2.15	3.62	1.86	1.91





Fig 21: ESR spectrum of [Cu(PBEAB)Cl₂].H₂O

NMR Spectra: The ¹H and ¹³C-NMR spectra of diamagnetic Zn(II) complexes were recorded in d_6 -DMSO. The spectra exhibit well resolved signals and comparison with those of the ligands, give an idea of the coordination of the ligands to the metal ion. The resonance signals of those protons which are at a few bonds away from the coordinating atoms show a considerable shift.

¹*H-NMR Studies:* The ¹*H* NMR representative spectrum of a Zn(II) complex is shown in figure 22. The amine $(-N\underline{H})$ proton resonance signal observed at 4.05 ppm in the spectrum of ligand EBEAB is shifted to down field side by 0.20 - 0.25 ppm confirming that the nitrogen atoms are coordinated to Zn(II) metal ion

[25]. The aromatic, spacer group, (ethylene/ propylene) and the allyl proton resonance signals show a very small shifts towards downfield side. The spectra of Zn(II) complexes exhibit one new signal observed at 2.23 ppm, that is attributable to the methyl protons of the coordinated acetate ion [25]. The amide ($-C=O-N\underline{H}$) protons resonance signal observed at 7.70 ppm in the spectrum of ligand is found to have shifted to down field side by 0.30 ppm [25]. The allylic($-CH=CH_2$) group protons resonance signals observed at 6.00 and 3.42 ppm in the spectrum of the ligand have not exhibited any considerable shift, while the methylene protons' ($-HN-CH_2-CH=CH_2$) signal shifted from 3.85 to 3.80 ppm indicating the coordination of secondary amine nitrogen atom.

¹³*C*-*NMR* Studies: The carbon atoms attached to the amide $(H_2\underline{C}-NH-\underline{C}=O)$ group show signals around 32.38 and 168.50 ppm in the spectrum of ligands and they are found to have shifted to downfield side by 1.5 and 2.5 ppm, indicating that amide $H_2\underline{C}-N-\underline{C}=O$ nitrogen atoms are coordinated [11] to Zn(II) metal ion. The aromatic and aliphatic carbon atoms ($-H_2C-CH_2$ - and $-NH-CH_2$) resonance signals have exhibited very small shifts towards downfield side in the ¹³C-NMR spectra of complexes as compared to those in the spectra of the ligand. The spectra of Zn(II) complexes exhibit two new signals one at 180.93 ppm, and another at 22.9 ppm (figures 23 and 24) which are characteristic of the coordinated acetate ion. The amide ($-\underline{C}=O-NH$) and $NH-\underline{C}H_2$) carbons of Zn(II)-PBEAB complex, exhibit a down field shift by 2.05 and 1.25 ppm respectively from 169.1 and 37.07 ppm as observed in the spectrum of ligand. The allylic ($-CH_2$ - $CH=CH_2$) group resonance signals.



Observed at 46.02, 134.07 and 115.38 ppm in the spectrum of the ligand are found to be shifted to down field side by 0.65 and 0.35 ppm. Two new signals are observed at 22.15 and 183.93 ppm which may be assigned to the methyl and carboxylic C atoms of the coordinated acetate ion.



Fig 23: 13C-NMR spectrum of [Zn(EBEAB)(OAc)₂]



Fig 24: 13C-NMR spectrum of [Zn(PBEAB)(OAc)₂]

Based on the data obtained from physicochemical and spectral studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes, the tentative structures proposed are presented below.



Proposed structures of [Ni(EBEAB)Cl₂] and [Cu(PBEAB)Cl₂]

Biological activity

Antibacterial studies of the ligands EBEAB, PBEAB and their complexes of Co(II), Ni(II), Cu(II) and Zn(II): Antibacterial activities of the new ligands **EBEAB**, **PBEAB** and their M(II) complexes (M = Co, Ni, Cu and Zn) were determined against four gram-negative (Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi and Shigella flexneri) and two gram-positive (Bacillus subtilis and Staphylococcus *aureus*) bacterial strains. The anti-bacterial activity of the compounds is compared with that of the standard drug amoxicillin (Table 6). Both the ligands exhibited low activity against the tested strains. The metal complexes of the ligands were found to be more active against the bacterial strains compared to the free ligands. The activity of the Cu(II) complexes against all the bacterial strains is very encouraging as compared to the activity of other metal complexes. These results confirm our earlier results and also the reports of other workers [2, 36, 37] that biologically inactive compounds become active and less active compounds become more active upon coordination/complexation. Such induction or enhancement in activity of the metal complexes can be explained on the basis of Overtone's concept and Tweedy's chelation theory [38]. According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid soluble materials and the lipid solubility is considered to be a significant factor that controls antimicrobial activity. On chelation, the polarity of the metal ion alters favorably due to the overlap of the ligand orbitals and partial sharing of the positive charge of the metal ion by the donor groups. Further, it also increases the delocalization of π -electrons over the whole chelate ring and enhances the lipophilicity of the complex. This improved lipophilicity in turn increases the diffusion of the complexes into lipid membranes and blocks metal binding sites on the enzymes of the microorganisms [38]. The metal in the complex may also be a medium for activation of the ligand as the cytotoxic agent. Further coordination may lead to a noteworthy reduction of anti-bacterial resistance. In addition to this, other factors such as solubility, conductivity and dipole moment contribute to the improvement of the bactericidal activity of the metal complexes as compared to the uncomplexed ligands.

Inhibition zone (mm)							
	Gram-negat	ive		Gram-positive			
Compounds	А	В	С	D	Е	F	
EBEAB	2.25	2.14	1.86	0	0.85	0.64	
Co(EBEAB)Cl ₂	23.16	18.36	13	19	23	22	
Ni(EBEAB)Cl ₂	18.8	16.62	17.11	16.5	21.23	18	
Cu(EBEAB)Cl ₂	28.3	23.59	18	14	29.12	26	
Zn(EBEAB)Cl ₂	26.13	21.97	20.65	23.2	27.90	23	

Fable-6 : Antibacterial activit	v data of the	prepared ligands	and their M(II) complexes
	, and a and	or open our ingenies		/ • • • • • • • • • • • • • •

A: Escherichia coli; B: Pseudomonas aeruginosa; C: Salmonella typhi; D: Shigella flexneri; E: Bacillus subtilis; F: Staphylococcus aureus.

0: Absence of measurable inhibitory action; >9: weak; 9–16: moderate; >16: significant. No activity observed against negative control.

APPLICATIONS

The antibacterial activity of the two prepared N_4 ligands and their metal complexes of Co(II), Ni(II), Cu(II) against four gram-negative and two gram-positive bacterial strains have been evaluated using disc diffusion method. The complexes are found to be more active than the ligands and among the metal complexes, the Cu(II) complexes exhibited better activity and comparable with the activity of the standard, amoxicillin.

CONCLUSIONS

The two new N₄ ligands obtained by reaction between two diamine-diamides organic moieties and 3bromoprop-1-ene form complexes on reaction with metal salts. The analytical and spectral investigations reveal that the complexes have the molecular formula of $[MLX_2]$. n H₂O [where M = Co(II), Ni(II) or Cu(II), X = CI; n = 1 or M = Zn(II), X = CH₃COO⁻ and n = 0]. The antibacterial studies on two gramnegative (*Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi*) and two gram positive (*Shigella flexneri, Bacillus subtilis, Staphylococcus aureus*) confirm that the metal complexes are more active than the free ligands and the Cu(II) complexes exhibit very encouraging activity which is comparable to that of the standard, amoxicillin. Further investigations on exploiting the antibacterial activities of the Cu(II) complexes are in progress.

ACKNOWLEDGEMENTS

The authors thank the UGC-SERO, Hyderabad for financial assistance in the form of MRP to SJ (F.MRP-3589/11/MRP/UGC-SERO).

REFERENCES

- [1] G. Koev and W. Kati. *Expert Opin. Invest. Drugs*, **2008**, 17, 303–319.
- [2] L.J. Ming, Med. Res. Rev. 2003, 23, 697–762.
- [3] A.Y. Louie, *Med Chem Rev.***1999**, 99, 2711–2734.
- [4] S.E. Castillo-Blum and N. Barba-Behrens. *Coord. Chem. Rev.***2000**, 196, 3–30.

- [5] D. Farrusseng, L. Hong Wee, L. Alaerts, J. A. Martens and D. De Vos. "*Metal-organic frameworks as catalysts for organic reactions*," **2011**, 191-212.
- [6] D. Pucci, A. Bellusci, S. Bernardini, R. Bloise, A. Crispini, G. Federici, P. Liguori, M.F. Lucas, N. Russo and A. Valentini. *Dalton Trans.* 2008, 5897–5904.
- [7] C.M. Topham and J.C. Smithy, *Biophys. J.* 2007, 92, 769-786.
- [8] S.K. Lee, K.H. Choi, S.J. Lee, S.W. Suh, B.M. Kim and B.J. Lee. *Bioorg. Med. Chem. Lett.*, 2010, 20, 4317–4319.
- [9] D. Kang, J. Seo, S.Y. Lee, J.Y. Lee, K.S. Choi and S.S. Lee. Inorg. Chem. Commun., Vol. 10, no. 12, pp.1425–1428, 2007.
- [10] S.J. Swamy, B. Veerapratap, D. Nagaraju, K. Suresh and P. Someshwar. *Tetrahedron*, 2003, 59, 10093–10096.
- [11] S.J. Swamy, S. Jyothi, P. Someshwar, K. Shasahak and G.R. Rao. J. Appl. Chem., **2012**, 1, 218-231.
- [12] S.J. Swamy and S. Pola, *Spectrochim. Acta A*, 2008, 70, 929 -933.
- [13] S.J.Swamy, B.Veerapratap, P. Someshwar, K.Suresh and D.Nagaraju. J. Chem. Res. 2005, 313-315.
- [14] D. Kovala-Dimertzi, A. Domopoulou, M.A. Demertzis, A. Papa-georgiou and D.X. West. *Polyhedron*, **1997**, 16, 3625–3633.
- [15] A. Castineiras, E. Bermejo, D.X. West, L.J. Ackerman, J. Valdes-Martinez and S. Hernadez-Orgega. *Polyhedron*, **1999**, 18, 1463–1469.
- [16] U. Abram, K. Ortner, R. Gust and K. Sommer. J. Chem. Soc., Dalton Trans. 2000, 735–744.
- [17] D. P. Singh, V. Malik, K. Kumar, C. Sharma and K. R. Aneja. *Spectrochimica Acta A.* **2010**, 76, 45-49.
- [18] W.J. Geary, *Coord. Chem. Rev.* **1971**, 7, 81-122.
- (a) A. H. Kianfara, L. Keramata, M. Dostania, M. Shamsipurb, M. Roushanib and F. Nikpour. *Spectrochim. Acta A.* 2010, 77, 424-429. (b) A. Anthonysamy and S. Balasubramanian. *Inorg. Chem. Commun.*, 2005, 8, 908-911. (c) B.S. Garg and D.N. Kumar. *Spectrochim. Acta A.* 2003, 59, 229-234.
- [20] H. Temel and S. Ilhan. *Spectrochim. Acta A.* **2008**, 69, 896-903.
- [21] A.L. El-Ansary, A.A. Soliman, O.E. Sherif, J.A. Ezzat. Synth. React. Inorg. Met. Org. Chem. 2002, 32, 1301-1318.
- [22] T. Hatakeyama and Z. Liu. Handbook of Thermal Analysis Wiley, Chichester, UK, 1998.
- [23] A. S. Al-Shihri, Spectrochim. Acta A. 2004, 60, 1189-1192.
- [24] C.R.K. Rao and P.S. Zacharias. *Polyhedron* **1977**, 16, 1201-1209.
- [25] M. Shakir, S.P. Varkey and P.S. Hameed. *Polyhedron* **1993**, 12, 2775-2780.
- [26] N. Nawar and N.M. Hosny. Trans. Met. Chem. 2000, 25, 1-8.
- [27] E. E. Chufan, J. C. Pedregosa, S. Ferrer and J. Borras. *Vibrational Spectroscopy*. **1999**, 20, 35-45.
- [28] B. Bersuker, Coord. Chem. Rev. 1975, 14, 357-412.
- [29] A.J. Atkins, D. Black, R.L. Finn, A. Marin-Becerra, A.J. Blake, L. Ruiz-Ramirez, W.S. Li and M. Schroder. *Dalton Trans.* **2003**, 1730-1737.
- [30] S. Chandra and L. K. Gupta. *Spectrochim. Acta A.* **2004**, 60, 1563-1571.
- [31] (a) L. Sacconi, *Coord. Chem. Rev.* 1966, 1, 126-132. (b) T. M. A. Ismail, A. A. Saleh and M. A. El Ghamry. *Spectrochim. Acta A.* 2012, 86, 276-288.

- [32] A. L. El-Ansary, H. M. Abdel-Fattah and N. S. Abdel-Kader. *Spectrochim. Acta A.* 2011, 79, 522-528.
- S. Chattopadhyay, M.S. Ray, S. Chaudhuri, G. Mukhopadhyay, G. Bocelli, A. Cantoni and A. Ghosh. *Inorg. Chem. Acta*, 2006, 359, 1367-1375. (b) M.S. Ray, S. Chaudhuri, L. Right, G. Bocelli, G. Mukhopadhyay and A. Ghosh. *Polyhedron*, 2003, 22, 671-624.
- [34] (a) B.J. Hathaway and D.E. Billing. *Coord. Chem. Rev.* **1970**, *5*, 143-207.
- [35] I.B. Afanaseva, E.A. Ostrakhovitch, E.V. Mikhalchik, G.A. Ibragimova and L.G. Korkina. **2001**, 61, 677–684.
- [36] S. J. Swamy, et.al." manuscript communicated to J. Chem. Sci.
- [37] N. Raman, V. Muthuraj, S. Ravichandran and A. Kulandaisamy. *Proc. Indian Acad. Sci.* 2003, 115, 161–167.
- [38] B. G. Tweedy, *Phytopathology* **1964**, 55, 910-914.