

The Coordination ability of N,N'-Ethylene Bis(2-amino 1-butanol) Dihydrochloride Towards Transition and Representative Metals

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Summary: N,N'-Ethylene Bis (2-amino 1-butanol) Dihydrochloride (EBAB) reacts with divalent first row transition and representative metals to give complexes of the stoichiometry, MLX_2 when $L = EBAB$, $M = Cu(II)$, $Ni(II)$, $Co(II)$, $Cd(II)$ and $Hg(II)$ $X = Cl$, Br , NO_3 . These complexes have been characterized by elemental analysis, conductivity measurements, room temperature magnetic moment studies, electronic and IR spectra. The ligand in these complexes behaves as bidentate like substituted ethylenediamine coordinating through nitrogen atoms. The solid state IR study and other data support distorted tetrahedral geometry of the type MN_2X_2 .

Introduction

It has been observed that metal ions have considerable effect on the antimicrobial activity of antibiotics [1-11]. Similarly metal complexes are known for their antitumour activity [12-13]. Therefore, interest has been shown by number of workers to study the interaction of metal ions with certain antibiotics [14-15]. Our present work is of the same nature and concerns with the coordinating

ability of N,N'-Ethylene Bis(2-amino 1-butanol) Dihydrochloride (EBAB) [1], an oral chemotherapeutic agent marketed under the name of Ethambutol or Myambutol [16] which is specially effective against actively growing micro-organisms of genus *Mycobacterium* including *M. Tuberculosis*. The effect of this drug on the blood level of trace elements during treatment of tuberculosis has been

studied [17]. The estimation of EBAB in urine was carried out through ascending paper chromatography [18-19] to control medication dosage and its formation constants with Cu(II) and Zn(II) were measured potentiometrically. Estimation of EBAB in biological fluids using Cu(II) reveals that such active pharmaceutical product can act as a chelating agent [18].

As in certain cases the metal complexes of the ligand showing biological activity are more active than the free ligand [20-22]. Moreover, the use of metal chelates of EBAB could prove a better route of administration instead of the free antibiotics which could reduce the risk of side effect caused by this drug due to decrease in the blood level of trace elements like iron, zinc and copper.

In spite of considerable importance of this molecule no work has been done on the synthesis of metal complexes of this ligand in solid state. Therefore, present work was undertaken with specific view to synthesize, isolate, and characterize solid complexes of transition and representative metals from *N,N'*-Ethylene Bis(2-amino 1-butanol) Dihydrochloride and study the biological activity of its metal complexes.

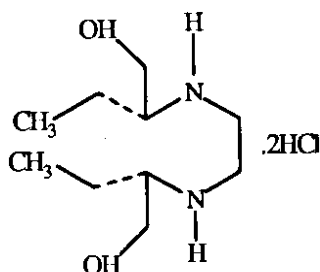


Fig. 1

Results and Discussion

Several complexes of *N,N'*-Ethylene Bis(2-amino 1-butanol) Dihydrochloride with the first row transition and representative metals have been synthesized and studied. Their characterization and assignment of their geometry was based on the elemental analysis, conductance measurements, magnetic susceptibilities and spectral measurements. The ligand EBAB behaves as a bidentate ligand and bears resemblance to 1,2-dimorpholino-

ethane (DME) and 1,3-dimorpholinopropane (DMP) [23-24] in terms of chromophoric environment. Analytical data shown in Table-1 indicates that only one EBAB molecule like DME and DMP is found to coordinate with metal ion and form complexes of the general formula $[M(EBAB)X_2]$, $M=Cu(II), Ni(II), Co(II), Zn(II), Cd(II)$ and $Hg(II)$ $X=Cl^-, Br^-, NO_3^-$. Table-1 contains a summary of the analytical data and Table-2 conductance and absorption spectral results.

The complexes are soluble in DMSO and pyridine with the exception of $[Ni(EBAB)Cl_2]$ which is insoluble. In acetonitrile all complexes are soluble with the exception of $[Cd(EBAB)(NO_3)_2]$ and $Hg(EBAB)Cl_2$. Representative metal complexes are soluble in water and ethanol whereas transition metal complexes decompose in these solvents. $[Co(EBAB)Cl_2]$ is soluble in 1-propanol, while the remaining complexes are either insoluble or slightly soluble.

The characteristic bands in the infrared spectra ($4000-600\text{ cm}^{-1}$) of EBAB and its metal complexes in nujol mull are given in Tables 3 and 4. The bands at 3400 cm^{-1} and 3120 cm^{-1} exhibited by free ligand are tentatively assigned to O-H and N-H stretching vibrations respectively [24-26]. In Cu(II), Co(II) and Ni(II) complexes, the band at 3400 cm^{-1} remained unchanged in position while in some Cd(II) and Hg(II) complexes the band was shifted slightly to higher frequency in relation to the free ligand. The band due to $\nu(N-H)$ was shifted considerably to lower frequency in all the complexes and in most cases was split into two or three bands. An intense absorption at 1570 cm^{-1} in the uncoordinated ligand assigned to $\nu(N-H)$ bending vibrations was split into two bands and shifted to lower frequency in $[Cu(EBAB)Cl_2]$. In $[Cu(EBAB)Br_2]$, the band position remained unchanged but was comparatively reduced in intensity while in $[Cu(EBAB)(NO_3)_2]$ this band was not observed. In Co(II), Ni(II), Cd(II) and Hg(II) complexes this band was shifted to lower energy by 30 cm^{-1} . A set of strong intensity bands, at 1175 cm^{-1} and 1140 cm^{-1} with shoulder at 1125 cm^{-1} , in the free ligand, is assigned to C-N stretching vibrations. These bands were reduced in number and broadened in $[Cu(EBAB)Cl_2]$, while shifting to lower frequency with change in intensity in $[Cu(EBAB)Br_2]$ and $[Cu(EBAB)(NO_3)_2]$. Identical

Table-1: Analytical data and magnetic moments of EBAB complexes

| Compound | Colour | Dec. Point °C | %C Found (Calc.) | % H Found (Calc.) | %N Found (Calc.) | μ_{eff} (BM) |
|--|---------------|---------------|------------------|-------------------|------------------|-------------------------|
| (C ₁₀ H ₂₂ N ₂ O ₂).2HCl | Colorless | 198.5 | 43.02 (43.32) | 8.55 (8.73) | 9.95 (10.10) | — |
| [Cu(C ₁₀ H ₂₂ N ₂ O ₂)Cl ₂] | Yellow | 153.0 | 35.30 (35.46) | 7.20 (7.14) | 8.31 (8.27) | 2.06 |
| [Cu(C ₁₀ H ₂₂ N ₂ O ₂)Br ₂] | Reddish Brown | 164.0 | 28.20 (28.09) | 5.50 (5.66) | 6.45 (6.55) | 1.67 |
| [Cu(C ₁₀ H ₂₂ N ₂ O ₂)(NO ₃) ₂] | Green | 150.0 | 31.03 (30.65) | 6.20 (6.17) | 13.96 (14.30) | 2.02 |
| [Co(C ₁₀ H ₂₂ N ₂ O ₂)Cl ₂] | Blue | 184.0 | 35.99 (35.95) | 7.13 (7.24) | 8.25 (8.38) | 4.27 |
| [Ni(C ₁₀ H ₂₂ N ₂ O ₂)Cl ₂] | Light green | 178.0 | 36.14 (35.97) | 7.32 (7.24) | 8.45 (8.39) | 3.12 |
| [Cd(C ₁₀ H ₂₂ N ₂ O ₂)Cl ₂] | Colorless | 189.0 | 31.20 (30.99) | 6.19 (6.24) | 7.30 (7.23) | — |
| [Cd(C ₁₀ H ₂₂ N ₂ O ₂)Br ₂] | Colorless | 167.0 | 25.0 (25.21) | 5.11 (5.08) | 5.64 (5.88) | — |
| [Cd(C ₁₀ H ₂₂ N ₂ O ₂)(NO ₃) ₂] | Colorless | 209.0 | 27.13 (27.25) | 5.35 (5.49) | 12.50 (12.71) | — |
| [Hg(C ₁₀ H ₂₂ N ₂ O ₂)Cl ₂] | Colorless | 190.0 | 25.20 (25.24) | 5.13 (5.09) | 5.92 (5.89) | — |

Table-2: Molar conductance and absorption spectral data of EBAB complexes

| Complex | Solvent | Molar Conductance dm cm ⁻¹ mole ⁻¹ | Absorption Max (cm ⁻¹) | Max L-mol ⁻¹ cm ⁻¹ |
|--|--------------|--|------------------------------------|---|
| [Cu(EBAB)Cl ₂] | Acetone | 5.18 | 20408 16667 11905 | (93.00) (82.00) (70.00) |
| [Cu(EBAB)Br ₂] | Acetone | 5.96 | 21645 21276 14285 | (245.70) (233.70) (122.00) |
| [Cu(EBAB)(NO ₃) ₂] | Acetonitrile | 6.57 | 21142 16949 14598 13699 | (73.45) (120.30) (130.00) (105.00) |
| [Co(EBAB)Cl ₂] | Acetonitrile | 2.89 | 16949 14598 | (94.67) (104.00) |
| [Ni(EBAB)Cl ₂] | - | - | - | - |
| [Cd(EBAB)Cl ₂] | Ethanol | 1.26 | - | - |
| [Cd(EBAB)Br ₂] | Ethanol | 7.00 | - | - |
| [Cd(EBAB)(NO ₃) ₂] | Ethanol | 6.30 | - | - |
| [Hg(EBAB)Cl ₂] | Ethanol | 7.00 | - | - |

splittings and shifts in these bands were observed for Co(II) and Ni(II) chloride complexes. The $\nu(\text{C-N})$ bands splitting pattern for Cd(II) complexes and [Hg(EBAB)Cl₂] were identical, with major band undergoing red shift by 15 cm⁻¹ in comparison to the free ligand.

Infrared spectra of metal complexes clearly indicate that C-N stretching frequencies are shifted to lower frequencies with changes in sharpness and intensities. This is caused by the withdrawal of electron density from the C-N bond where nitrogen

atoms become coordinated to the metal ion. Thus N,N'-Ethylene Bis(2-amino 1-butanol) Dihydrochloride behaves as bidentate ligand like substituted ethylenediamine coordinating through nitrogen atoms only.

The solution spectra of [Co(EBAB)Cl₂] in acetonitrile is shown in Fig. 2 and data is presented in Table-2. The complex exhibits a broad adsorption band between 14,000 - 17,000 cm⁻¹ within this band one is able to distinguish clearly two maxima at 14,598 cm⁻¹ and 16,494 cm⁻¹. This band could be

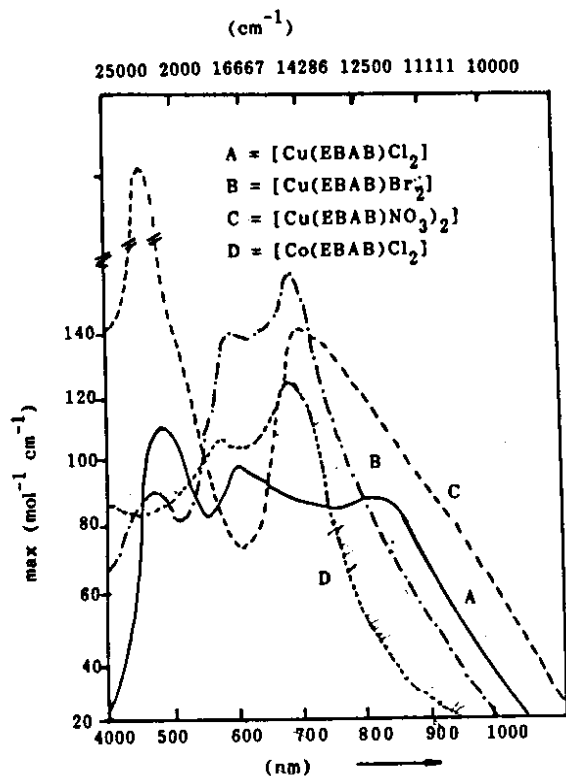


Fig. 2: Electronic spectra (missing in original copy)

assigned to the transition ${}^4A_2(F) \rightarrow {}^4T_1(P)$, 4V_3 in T_d symmetry [27]. The low energy transition ${}^4A_2(F) \rightarrow {}^4T_2(F)$ V_2 was not observed. The complex is non-electrolyte in 1-propanol and has μ_{eff} 4.27 BM at room temperature. The data indicate tetrahedral stereochemistry of the complex.

The solution spectra of $[\text{Cu}(\text{EBAB})\text{Cl}_2]$, $[\text{Cu}(\text{EBAB})\text{Br}_2]$ and $[\text{Cu}(\text{EBAB})(\text{NO}_3)_2]$ is shown in Fig. 2 and data in Table-2.

The $[\text{Cu}(\text{EBAB})\text{Cl}_2]$ solution spectrum in acetonitrile exhibits a broad absorption band from 11,000 - 21,000 cm^{-1} with maxima at 11,905 cm^{-1} , 16,667 cm^{-1} and 20,408 cm^{-1} . The complex is non-electrolyte with magnetic moment 2.06 B.M. at room temperature. Similar spectra are obtained for $[\text{Cu}(\text{EBAB})\text{Br}_2]$ and $[\text{Cu}(\text{EBAB})(\text{NO}_3)_2]$ complexes with some changes in position as well as in extinction coefficients. The complexes are non-electrolyte in acetone and acetonitrile respectively having magnetic moments 1.67 B.M. for bromide complex and 2.02 B.M. for nitrate complex.

The electronic spectra are consistent with C_{2v} symmetry [28]. The fourth peak expected in C_{2v} symmetry seems to be buried in the broad

Table-3: Principal infrared (cm^{-1}) in EBAB complexes

| | EBAB | $[\text{Cu}(\text{L})\text{Cl}_2]$ | $(\text{Cu}(\text{L})\text{Br}_2)$ | $[\text{Cu}(\text{L})(\text{NO}_3)_2]$ | $[\text{Co}(\text{L})\text{Cl}_2]$ | $[\text{Ni}(\text{L})\text{Cl}_2]$ |
|----|--------|------------------------------------|------------------------------------|--|------------------------------------|------------------------------------|
| | 3430sh | - | - | - | - | - |
| | 3400sh | 3400w | 3400w | 3400w | 3410w | 3400w |
| | 3370sh | - | - | - | - | 3380w |
| | 3330vs | 3290vs | 3320vs | 3240m | 3300vs | 3360sh |
| | - | - | 3280sh | 3220m | - | - |
| | - | - | - | - | - | 3320s |
| a) | 3120w | 3040w | 3100w | 3100w | - | 3140w |
| | - | - | 3060w | - | 3060w | 3095w |
| | - | - | 3050w | 3050w | - | 3050w |
| | 1570vs | 1550vs | - | - | 1545s | 1570ws |
| | - | - | - | - | - | 1560sg |
| b) | - | 1515w | 1570s | - | 1525w | 1535w |
| | 1175vs | 1150bw | 1170m | 1150m | 1155w | 1170s |
| c) | 1140vs | 1125m | 1140s | 1120s | 1125m | 1140vs |
| | 1125sh | - | 1120sh | 1115w | - | 1125w |
| | 1085vs | 1070s | 1080s | 1095m | 1070s | 1080s |
| | 1060vs | 1050vs | 1060s | 1070s | 1050s | 1060s |
| | 1035vs | 1020vs | 1030vs | 1045sh | 1020vs | 1030vs |
| | - | - | - | 1030s | - | - |
| | 970vs | 990sh | 875s | 970s | 990sh | 975s |
| | - | 955s | 965s | 935d | 955vs | 965s |
| | 905s | 905m | 900m | - | 910m | 900m |

(a) (N-H) stretch; (b) $\nu(\text{N-H})$ bending; (c) (C-N) stretch

L; EBAB s=strong, vs=very strong, b=broad, m=medium, w=weak, sh=shoulder, d=doublet

Table-4: Principal infrared bands (cm^{-1}) in EBAB complexes

| EBAB | [Cu(L)Cl ₂] | (Cu(L)Br ₂) | [Cu(L)(NO ₃) ₂] | [Hg(L)Cl ₂] |
|-----------|-------------------------|-------------------------|---|-------------------------|
| 3430sh | 3480w | 3480w | 3480w | 3480w |
| - | 3450m | 3440w | 3450w | 3450w |
| - | 3420w | 3410w | 3410w | 3420w |
| 3370sh | 3380m | 3380m | 3380m | 3380m |
| 3330vs | - | - | - | - |
| a) 3120w | 3100m | 3100w | 3100w | 3100w |
| - | 3050w | 3050w | 3045w | 3045w |
| b) 1570vs | 1540vs | 1545vs | 1545w | 1540s |
| 1175vs | 1160s | 1160dw | 1170d | 1160m |
| c) 1140vs | 1130s | 1125w | 1120m | 1130d |
| 1125sh | 1120sh | - | - | - |
| 1085vs | 1080w | 1085sh | 1060sh | 1085sh |
| 1060vs | 1060s | 1065m | 1050s | 1070m |
| 1035vs | 1045s | 1045m | 1040w | 1050m |
| - | 1025vs | 1025s | 1020d | 1040s |
| 970vs | 960s | 960m | 965m | 960m |
| - | 920vs | 940w | 950w | - |
| 905s | - | 920s | 930w | 915s |

a) (N-H) stretch; (b) (N-H) bending; (c) (C-N) stretch

s=strong, vs=very strong, b=broad, m=medium, w=weak, sh=shoulder, d=doublet

absorption envelope. Similar spectra were observed for other Cu(II) complexes having CuN_2X_2 chromophore [27,29].

Experimental

Materials

Metal salts used were of reagent grade and used without further purification. The partial dehydration of the salt was done by drying the hydrated salts in vacuum oven for several hours at 80-100°C. All solvents were distilled at least once before using.

The ligand N,N'-Ethylene Bis(2-amino 1-butanol) Dihydrochloride (EBAB) supplied by cynamid (Pakistan)Limited Karachi-1 in high grade purity was used without further purification.

Preparation of solid complexes

All the complexes were prepared using similar general procedure. Approximately 10 m moles of partially dehydrated salt was dissolved in minimum amount of anhydrous solvent. Methanol was used as solvent for the preparation of CoCl_2 , CuBr_2 and NiCl_2 complexes and ethanol for the synthesis of CuCl_2 and $\text{Cu(NO}_3)_2$ complexes while 1-propanol was used for rest of the metal complexes. The ligand EBAB, an excess over 1:2 metal to ligand ratio was also dissolved in minimum amount of the same solvent and slowly

added to the hot metal salt solution with constant stirring. The mixture was stirred and kept at 50°C for half an hour, then cooled for about 20 minutes. The metal complexes precipitated either immediately or on cooling, while all transition metal complexes were obtained in crystalline form only by addition of 30 ml of dry ether to the cooled solution. The complexes were further washed three times with ether and dried at 40°C in vacuum oven.

Instrumentation

Infrared spectra were taken in the range of 4000-600 cm^{-1} on PYE UNICAM infrared spectrophotometer as nujol mulls on NaCl plates or KBr disc.

Ultra violet and visible absorption spectra of the complexes in the range 200-900 nm using different solvents were obtained on Jasco DEC-1 spectrophotometer with 1 cm matched quartz-cells.

Molar conductance of the solution of metal complexes were carried out with a conductivity meter type OK 102/1-Radel-Kiss, Electrochemical Instruments, Hungary. All measurements were done at room temperature on freshly prepared solutions.

Magnetic susceptibilities were measured by Gouy method at room temperature using

Hg[Co(SCN)₄] as standard. The magnetic moments were calculated by the procedure [30].

The elemental analysis were carried out at the Department of Chemistry, University of Exeter, England and Analytical Laboratory, University of Bonn, West Germany.

Conclusion

The stoichiometry of the complexes indicates that one EBAB molecule is found to coordinate with metal ion. Therefore, it is evident that the ligand, under the existing conditions, prefer to form only mono complexes. The conductance measurements studies carried out in various solvents shows that all the complexes are non-electrolyte in nature further reveal the fact that anions are coordinated in the complex. The ligand is having four donor sites two oxygens and two nitrogens but the solid state IR spectra clearly favours the formation of nitrogen coordination site and thus support the bidentate behaviour of the ligand to form tetrahedral complexes of the type [MLX₂]. The magnetic moment studies and the solution electronic spectra further substantiate the tetrahedral coordination geometry around the central metal ion.

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