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Antibacterial Activity of Macrocyclic Complexes of Cu(II), Ni(II) and VO(II) Derived from *o*-Aminobenzaldehyde

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Abstract: Novel Cu(II), Ni(II) and VO(II) complexes are synthesized with N^1,N^4-bis(2-aminobenzylidene)benzene-1,4-diamine (L). Complexes were characterized by elemental analysis, molar conductance, IR, UV and EPR. Spectral studies reveals a square planner geomentry for Cu(II), Ni(II) complexes and square pyramidal for VO(II) complex. The ligand and its complexes were also evaluated against the growth of gram positive bacteria and gram negative bacteria.

Keywords: Macrocyclic, Electrolytic, Cu(II), Ni(II), VO(II), *o*-Aminobenzaldehyde

Introduction

Metal complexes containing synthetic macrocyclic ligands have attracted a great deal of attention because they can be used as models for more intricate biological macrocyclic systems like metalloporphyrins (hemoglobin, myoglobin, cytochromes, chlorophylls), corrins (vitamin B12) and antibiotics (valinomycin, nonactin). So it attracted the attention of both inorganic and bioinorganic chemists[1]. These discoveries have created supramolecular chemistry and its enormous diversity. The formation of macrocyclic complexes mainly depends on size of the internal cavity and rigidity of the macrocycle formed[2]. Schiff bases having donor atoms such as N_2O_2 and N_4 around the metal ion have received more attention, mainly because of their extensive applications as catalysts for carbonylation, hydrogenation hydroformylation, epoxidation, nucleicacid modification, electrochemical reduction, alkanehydroxylation, Diels–Alder transformations, carboxylic acid decarboxylation, amines oxidation and medicinal studies as models for mimicking the superoxide dismutase[3–8]. The chemistry of macrocyclic complexes is also important due to its use as dyes, pigments and NMR shift reagents[9].

Metal condensation reaction with the ligand often provides selective routes towards product that are not obtainable in absence of metal ions. A rational control of the nuclearity of transition metal complexes is important to design systems with the desired properties,

as some of these applications require the presence of more than one metal center in the particular complex. Indeed, binuclear complexes may have very different reactivity than mononuclear counterparts, thereby enabling transformations inaccessible to single metal ions[10]. For instance, nucleic acid hydrolysis is postulated to be facilitated by the cooperative action of two metal ions[11]. Furthermore, bi or oligo nuclear complexes containing transition metals may be formed by bridging ligands that can mediate magnetic interactions between paramagnetic metal ions[12].

Experimental

Materials

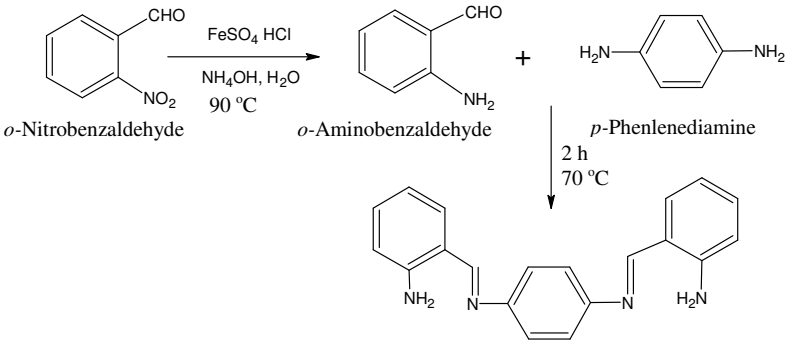
o-Phthalaldehyde and *p*-phenylenediamine were purchased from Aldrich. Ethanol, methanol, DMSO and DMF were used as solvents. The solvents metals and reagents with analytical grade were obtained commercially and used without further purification.

Physical measurement

The elemental analysis was performed using Carlo-Eraba 1106 instrument. Molar conductance of the complexes in DMF solution was measured with ELICO CM 185 Conductivity Bridge. The Infrared spectra were recorded on the Perkin Elmer FT-IR-8300 model spectrometer using KBr disc. Electronic absorption spectra in the UV-Visible range were recorded on Perkin Elmer Lambda-25 between 200-800 nm by using DMSO as the solvent. ESR spectra of the complexes were recorderd as powder samples at room temperature on an E4-EPR spectrometer using DPPH as the g-marks. Magnetic susceptibility data were collected on powdered sample of the compounds at the room temperature with PAR155 vibrating sample magnetometer.

Synthesis of Schiff base ligand

The starting material *o*-aminobenzaldehyde was prepared according to the literature procedure[13]. An ethanolic solution of freshly prepared *o*-aminobenzaldehyde was mixed slowly with stirring ethanolic solution of *p*-phenylenediamine. The mixture was refluxed at ≈ 70°C for 2 h. On cooling yellow colored precipitate was separated out, filtered, washed with ethanol, diethylether and dried in vaccum[14]. The binucleating Schiff base ligand is shown in Figure 1. Yield 71%. Elemental analysis: $C_{20}H_{18}N_4$, calculated C, 76.43, H, 5.73, N, 17.83%, Found C, 75.96, H, 5.54, N,17.89% ν(C=N), 1622 cm^{-1}, ν(NH_2), 3442 cm^{-1}, UV-vis (λ_{max}) DMSO: π-π*-228 nm, 280 nm, n-π*-390 nm.



N^1,N^4-bis(2-aminobenzylidene)benzene-1,4-diamine

Figure 1. Synthesis of the ligand (L)

Synthesis of Cu(II) complex

The Cu(II) complex was prepared by methanolic solution of $Cu(ClO_4)_2.6H_2O$ salt. This was slowly added with stirred hot methanolic solution of binucleating Schiff base ligand. After half an hour phthalaldehyde was added drop wise to the same solution. The strring was continued for 1 h, after it undergoes reflux for 10-12 h at ≈70 °C. A dark blue colored precipitate formed was filtered, washed several times with methanol, diethylether and dried in vaccum[15]. Yield 64%. Elemental analysis: $C_{56}H_{40}N_8Cu_2Cl_4O_{16}$ Calcd; C, 49.88, H, 2.96, N, 8.31, Cu, 9.43%. Found: C, 50.18, H, 309, N, 8.38, Cu, 9.29% Λm, 265 ($\Omega^{-1}cm^2m^{-1}$), ν(C=N), 1609 cm^{-1}, ν(M-N), 510 cm^{-1}, ν(ClO_4) 1110 cm^{-1} and 620 cm^{-1} , UV-vis (λ_{max}) DMSO: d↔d, 580 nm.

Synthesis of Ni(II) complex

The same procedure was adopted for $Ni(ClO_4)_2.6H_2O$ complex. It undergone reflux until dark green color precipitate was formed. Yield 66%. Elemental analysis: $C_{56}H_{40}N_8Ni_2Cl_4O_{16}$, Calcd: C, 50.24, H, 2.99, N,8.37, Ni, 8.77%, Found: C, 50.43, H, 2.89, N, 8.25, Ni, 8.80% Λm 223 ($\Omega^{-1}cm^2m^{-1}$), IR (KBr pellet) ν(C=N),1617 cm^{-1}, ν(M-N), 538 cm^{-1}, ν(ClO_4) 1086, $cm^{-1}$and 626 cm^{-1}, UV-vis (λ_{max}) DMSO: d↔d, 520 nm.

Synthesis of vanadyl complex

The same procedure was adopted for $VOSO_4.4H_2O$ complex. It gave steel blue color precipitate. Yield 62%, $C_{56}H_{40}N_8V_2S_2O_{10}$, Calcd: C, 58.44, H, 3.47, N, 9.74,V2, 8.86%, Found: C,57.98, H, 3.29, N, 9.30, V2, 9.92% Λm, 139 ($\Omega^{-1}cm^2m^{-1}$), ν(C=N), 1599 cm^{-1}, ν(M-N), 515 cm^{-1}, ν(SO_4) 1084 cm^{-1}, ν(V=O) 943 cm^{-1} , UV-vis (λ_{max}) DMSO: d↔d, 531 nm.

Antibacterial studies

The antibacterial activity of the macrocyclic binuclear Cu(II), Ni(II) and VO(II) complexes were checked by the disc diffusion technique[16]. This was done on gram negative bacterial like *Klebsiella pneumoniae*, *Escherichia coli* and gram positive bacterial like *Staphylococcus aureus* at 37°C. The disc of Whatman no. 4 filter paper having the diameter 8.00 mm were soaked in the solution of compounds in DMSO (1.0 mg cm^{-1}). After drying it was placed on nutrient agar plates. The inhibition areas were observed after 36 hours. DMSO was used as a control and *Stremptomycin* as a standard.

Results and Discussion

A novel macrocyclic binuclear Cu(II), Ni(II) and VO(II) Schiff base complexes have been synthesized by template condensation of binucleating schiff base ligand with metal salt and *o*-phthalaldehyde. All the complexes were crystalline in nature, dark colored solid, stable at room temperature and soluble in DMF or DMSO. The ligand can be confirmed by ^{1}H NMR. All the complexes gave satisfactory elemental analysis results with the proposed structure of the complexes. The formation and their geometry were further confirmed by IR, UV Vis, magnetic, EPR spectral studies. The ligand and complexes were also screened for antibacterial activity against bacteria species.

^{1}H NMR spectra of Schiff base ligand

The formation of Schiff base ligand was observed by peak ratios in the ^{1}H NMR spectra. ^{1}H-NMR spectra of the ligand was taken using DMSO d6 solvent (Figure 2). The aromatic region was a set of multiplets in the range of 6–7.5 ppm, while the azomethine proton was observed in the range 8.25 ppm.

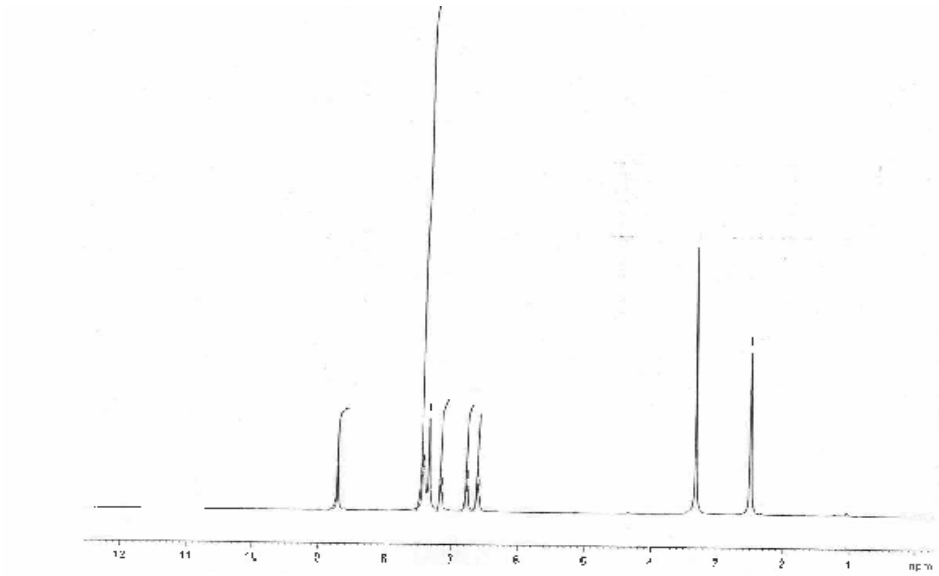


Figure 2. ^{1}H NMR Spectra of ligand in DMSO-d_6

Magnetic and electronic studies

The electronic spectra of the Schiff base ligand and its complexes were recorded in DMSO solution. The absorption spectrum of free ligand consist of an intense bands centered at 265 nm and 370 nm attributed to π–π* and n– π* transition within the Schiff base ligand. These transitions are also found in spectra of the complexes, but they shifted, confirming the coordination of ligand to metal ions[17]. Further, the d-d transition showed a strong band at 580 nm for Cu(II) complex, this is due to $^{2}B_1g \rightarrow {}^{2}A_1g$. This transition shows the square plannar geometry around the metal[18]. In room temperature magnetic moment values for Cu(II) is 1.65 B.M. In general, the low magnetic moment values of binuclear copper complex are attributed to the antiferromagnetic interaction between two central Cu(II) metal ions[19].

The spectra of Ni(II) complex in the visible region at about 520 nm and 480 nm is assigned to $^{1}A_1g \rightarrow {}^{1}A_2g$, $^{1}A_1g \rightarrow {}^{1}B_1g$, transitions, suggesting an approximate square planar geometry of the ligand around the metal ions[20]. The magnetic moment data of VO(II) complex was 1.75 B.M., which confirms the binuclear structure of the complex. The intense charge transfer band at 531 nm in VO(II) complex assigned to $^{2}B_2 \rightarrow {}^{2}E$ transition. This is due to electron delocalization over whole molecule on complexation. Based on these data, a square pyramidal geometry has been assigned to the complex VO(II)[21,22]

EPR spectral studies

The X-band EPR spectrum of the Cu(II) and VO(IV) complexes were recorded at room temperature. Cu(II) complex consists of an axial symmetrical signal with g_{II}= 2.12 and $g_{\perp}$= 2.05. The unpaired electron lies in the (dx2–y2) orbital giving ^{2}B1g as the ground state with the $g_{II} > g\perp > g$e (2.0023 free spin value)[23]. The observed g_{II} value for square planner geometry Cu(II) complex is less than 2.3, which is in agreement with the covalent character of metal ligand bond[24]. G value less than 4 indicates a considerable metal - metal interaction in a complex[25]. Vanadyl complexes show peaks with g_{II}= 2.08 and $g_{\perp}$ = 2.01 which indicates that the unpaired electron is present in the dxy orbital with square pyramidal geometry around the VO(II) chelates[26].

Antibacterial activity

The Schiff base ligand and their macrocyclic binuclear Schiff base complexes were tested *in vitro* to assess their growth inhibitory activity against Gram negative bacterial like Klebsiella pneumoniae, *Escherichia coli* and gram positive bacterial like *Staphylococcus aureus* are given in Table 1. The antibacterial activity of complexes arises due presence of several azomethine groups which coordinate with metal ions. Cu(II) has more activity than ligand and other complexes. Difference in the effectiveness was depends on the impermeability of microbial cells or on the difference in ribosome of microbial cells[27]. The increase in antibacterial activity of metal chelates with increase in concentration is due to the effect of metal ion on normal cell processes. Such increases in activity of metal chelates can be explained on the basis of chelation theory[28]. On chelating, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charge of metal ion with donor groups. Further, it increases the delocalization of π-electrons, enhances liphophilicity and penetration of the complexes which blocks metal binding sites on enzymes of microorganism. These complexes also disturb the respiration process of cell and thus block the synthesis of proteins, which restricts further growth of organism[29,30].

Table 1. Antibacterial activity of the ligand and complexes

Compound	Bacterial inhibition, %		
	S.aureus	*K. pneumoniae*	*E.coli*
$C_{20}H_{18}N_4$	+++	+++	+++
$C_{56}H_{40}N_8Cu_2Cl_4O_{16}$	++	++	++
$C_{56}H_{40}N_8Ni_2Cl_4O_{16}$	+++	++	+++
$C_{56}H_{40}N_8V_2S_2O_{10}$	+++	+++	++

**50% growth by ++, less than 50% growth by +++*

Conclusion

A novel macrocyclic binuclear schiff base ligand and complexes have been synthesized by using freshly prepared *o*-aminobenzaldehyde with *p*-phenylenediamine, and *o*-phthalaldehyde with respective metal salts. The metal-ligand ratio of 1:1 has been arrived at by estimating the elemental contents. The presence of counter ions has been confirmed from the IR and high molar conductance values. ^{1}H NMR confirms the complete condensation of the ligand. ESR shows a covalent bonding nature of the complexes and also the geometry of the complexes. The antibacterial activity for Cu(II) complexes was more pronounced because of the chelation theory.

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