



Original article

Synthesis, spectral characterization, *in-vitro* microbiological evaluation and cytotoxic activities of novel macrocyclic bis hydrazonePrakash Gouda Avaji^a, C.H. Vinod Kumar^b, Sangamesh A. Patil^c, K.N. Shivananda^d, C. Nagaraju^{b,*}^a Department of Organic Chemistry, Indian Institute of Science, Bangalore 560012, Karnataka, India^b Department of Chemistry, S.V. University, Tirupathi 517502, Andhra Pradesh, India^c Department of Chemistry, Karnatak University, Dharwad 580003, Karnataka, India^d Department of Chemistry, Bangalore University, Bangalore 560001, Karnataka, India

ARTICLE INFO

Article history:

Received 17 August 2008

Received in revised form

26 February 2009

Accepted 12 March 2009

Available online 5 April 2009

Keywords:

Synthesis

Characterization

Biological

Toxicity

Hydrazone

ABSTRACT

A macrocyclic hydrazone Schiff base was synthesized by reacting 1,4-dicarbonyl phenyl dihydrazide with 2,6-diformyl-4-methyl phenol and a series of metal complexes with this new Schiff base were synthesized by reaction with Co(II), Ni(II) and Cu(II) metal salts. The Schiff base and its complexes have been characterized by elemental analyses, IR, ¹H NMR, UV–vis, FAB mass, ESR spectra, fluorescence, thermal, magnetic and molar conductance data. The analytical data reveal that the Co(II), Ni(II) and Cu(II) complexes possess 2:1 metal–ligand ratios. All the complexes are non-electrolytes in DMF and DMSO due to their low molar conductance values. Infrared spectral data suggest that the hydrazone Schiff base behaves as a hexadentate ligand with NON NON donor sequence towards the metal ions. The ESR spectral data shows that the metal–ligand bond has considerable covalent character. The electrochemical behavior of the copper(II) complex was investigated by cyclic voltammetry. The Schiff base and its complexes have also been screened for their antibacterial (*Escherichia coli*, *Staphylococcus aureus*, *Shigella dysenteriae*, *Micrococcus*, *Bacillus subtilis*, *Bacillus cereus* and *Pseudomonas aeruginosa*) and antifungal activities (*Aspergillus niger*, *Penicillium* and *Candida albicans*) by MIC method. The brine shrimp bioassay was also carried out to study their *in-vitro* cytotoxic properties.

© 2009 Elsevier Masson SAS. All rights reserved.

1. Introduction

Hydrazones are a special group of compounds in the Schiff base family. They are characterized by the presence of $>C=N-N=C<$. The presence of two inter-linked nitrogen atoms was separated from imines, oximes, etc. Hydrazone Schiff bases of acyl, aroyl and heteroacroyl compounds have an additional donor sites like C=O. The additional donor sites make them more flexible and versatile. This versatility has made hydrazones good polydentate chelating agents that can form a variety of complexes with various transition and inner transition metals and have attracted the attention of many researchers.

Various hydrazones are obtained depending on the experimental conditions; which have application as biologically active compounds [1] and as analytical reagents [2]. As biologically active compounds, hydrazones find applications in the treatment of diseases such as anti-tumor [3], tuberculosis [4], leprosy and

mental disorder [1]. Tuberculostatic activity is attributed to the formation of stable chelates with transition metals present in the cell. Thus many vital enzymatic reactions catalyzed by these transition metals cannot take place in the presence of hydrazones [5–7]. Hydrazones also act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators.

Hydrazones are used as plasticizers and stabilizers for polymers, polymerization initiators, antioxidants, etc., they act as intermediates in preparative chemistry. In analytical chemistry, hydrazones find application in detection, determination and isolation of compounds containing the carbonyl group. More recently, they have been extensively used in detection and determination of several metals. They also find applications as indicators and spot test reagents [2].

Recently, a number of attempts have been made to obtain Mn(III), Fe(III) and Co(III) complexes with bis hydrazone formed by condensation of isatin monohydrazone with 2-hydroxy-1-naphthaldehyde, which have been well characterized by elemental analyses and spectral data [7]. Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and UO₂(VI) complexes have been synthesized by the condensation of

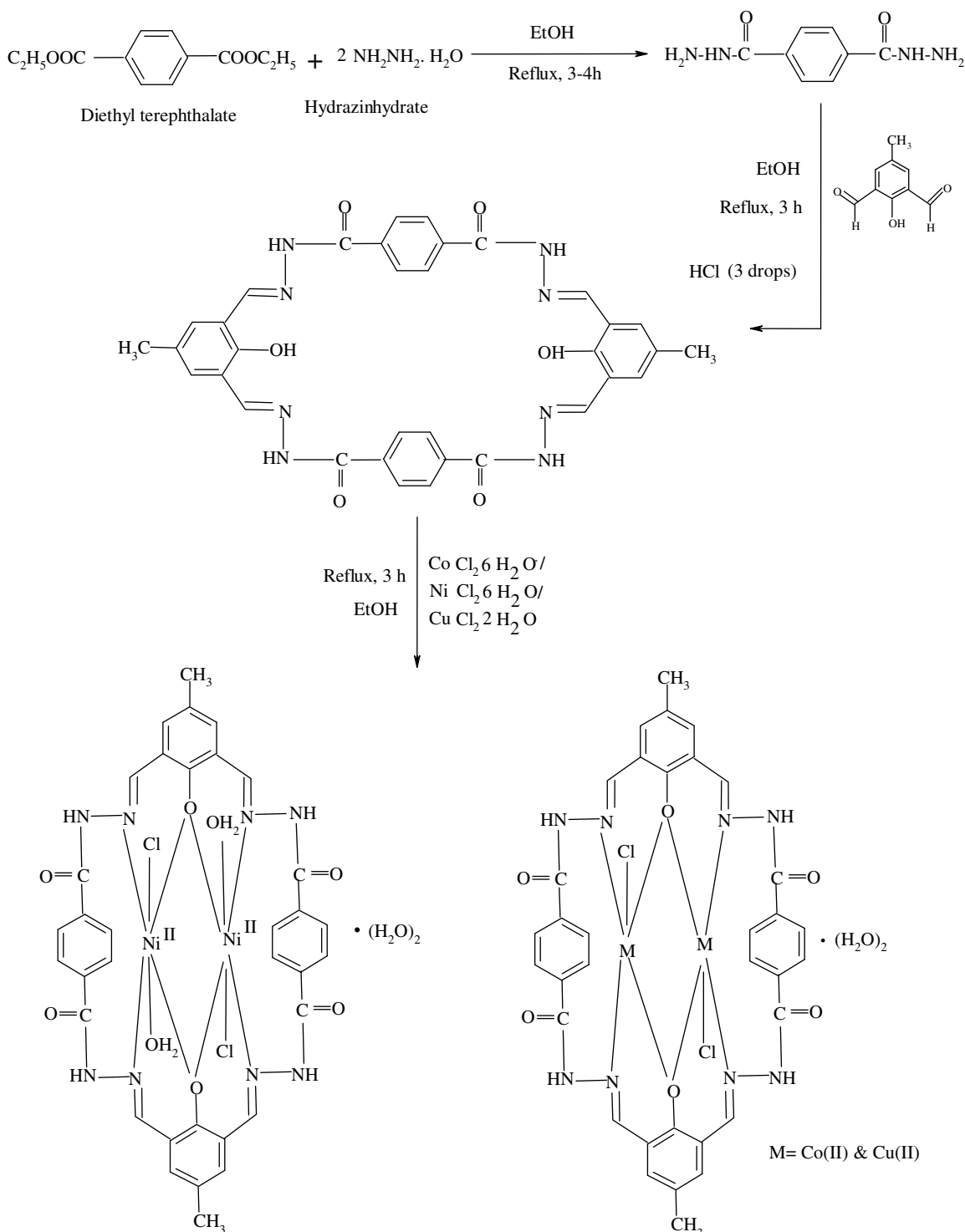
* Corresponding author. Fax: +91 877 2249611.

E-mail address: cnraju.962@rediffmail.com (C. Nagaraju).

2-amino-4-hydrazino-6-methyl pyrimidine with *o*-hydroxyacetophenone [8] and Mn(II) complexes have been synthesized from the bis-Schiff bases of 2,6-diacetylpyridine and anthraniloyl hydrazide/benzoyl hydrazide/salicyloyl hydrazide [9]. All these compounds have been characterized by elemental analyses, magnetic, thermal, IR, ^1H NMR, UV–vis, FAB mass, ESR and X-ray spectral data.

A survey of the literature reveals that no work has been carried out on the synthesis of metal complexes with macrocyclic

hydrazone Schiff base derived from 1,4-dicarbonyl phenyl dihydrazide with 2,6-diformyl-4-methyl phenol. This Schiff base has donor sites with the NON NON sequence and varied coordination abilities. This nature of the Schiff base (Scheme 1) has attracted our attention and aroused our interest in elucidating the structure of Co(II), Ni(II) and Cu(II) complexes. These are evaluated for their antibacterial and antifungal properties against various pathogenic bacterial strains using the minimum inhibitory concentration method.



Scheme 1.

2. Chemistry

2.1. Methods

2.1.1. Synthesis of diethyl terephthalate

Terephthalic acid (1.6 g) in super dry ethanol (60 mL) containing 2–3 drops of concentrated H_2SO_4 (AR) was refluxed till it dissolves. Then, the reaction mixture was poured onto ice cold water, immediately a solid started separating from the clear solution. To this a solution of sodium bicarbonate was added till the effervescence seized. The ester thus obtained was filtered and washed with water for several times (mp 44°C).

2.1.2. Synthesis of dihydrazide of terephthalic acid

A mixture of diethyl ester of terephthalic acid (2.22 g) and hydrazine hydrate (98% 2 cc) in ethanol was refluxed for 4–5 h. The reaction mixture was allowed to cool to room temperature then, the cooled solution was poured onto ice cold water. The dihydrazide of terephthalic acid thus obtained was filtered and recrystallized from ethanol.

2.1.3. Preparation of 2,6-diformyl-4-methyl phenol

2,6-Diformyl-4-methylphenol was prepared by reported method [10–12].

2.1.4. Synthesis of macrocyclic terephthalic acid hydrazone Schiff base

2,6-Diformyl-4-methylphenol (2 mmol) in ethanol (20 mL) was added to an ethanolic solution of 1,4-dicarbonyl phenyl dihydrazide (2 mmol, 30 mL) containing a few drops of concentrated HCl. The reaction mixture was refluxed for 3 h. The mixture was cooled to room temperature and the solvent removed under reduced pressure until a solid product was formed that was washed with cold ethanol and dried under vacuum. Yield 70–75%.

2.1.5. Synthesis of Co(II), Ni(II) and Cu(II) complexes

A mixture of ligand (0.01 mol) and metal chloride (0.02 mol) was refluxed for an hour in alcohol. To the reaction mixture sodium acetate (0.02 mol) in water was added and the reflection was continued for another 2 h. The complex was precipitated by adding distilled water. The complex separated was filtered, washed with water, then with hot alcohol and finally dried in vacuum desiccator over P_2O_5 (yield 60–70%).

3. Pharmacology

3.1. In-vitro antibacterial and antifungal assays

The biological activities of the newly synthesized Schiff base and its metal complexes have been studied for their antibacterial and antifungal activities by disc diffusion method [13,14]. The antibacterial activities were done by using the following organisms (*Escherichia coli*, *Staphylococcus aureus*, *Shigella dysentery*, *Micrococcus* species, *Bacillus subtilis*, *Bacillus cereus* and *Pseudomonas aeruginosa*). These bacterial strains were chosen as they are the known pathogens of human body and *Aspergillus niger*, *Penicillium* and *Candida albicans* were used for antifungal activities at 10, 25, 50 and $100\ \mu\text{g mL}^{-1}$ concentrations in solvent DMF. The bacteria were subcultured in agar medium. The Petri dishes were incubated for 24 h at 37°C . Standard antibacterial drug (Gentamycin) was also screened under similar conditions for comparison. The fungi were subcultured in potato dextrose agar medium. Standard antifungal drug (Fluconazole) was used for comparison. The Petri dishes were incubated for 48 h at 37°C (Figs. 1 and 2).

3.1.1. Minimum inhibitory concentration (MIC)

Compounds showing promising antibacterial/antifungal activity were selected for minimum inhibitory concentration studies. The minimum inhibitory concentration was determined by assaying at 100, 50 and $25\ \mu\text{g mL}^{-1}$ concentrations along with standards at the same concentrations.

3.1.2. Pharmacology results

The microbial results of Schiff base and its Co(II), Ni(II) and Cu(II) complexes are systematized in Table 1. The biological activity of the Schiff base exhibited a considerable enhancement on coordination with the metal ions against all fungal strains. However, the metal complexes showed good antifungal activity against *A. niger*, *Penicillium* and *C. albicans*. It was evident from the data that this activity significantly increased on coordination. This enhancement in the activity may be rationalized on the basis that their structures mainly possess an additional C=N bond. It has been suggested that the Schiff base with nitrogen and oxygen donor systems inhibit enzyme activity, since the enzymes which require these groups of their activity appear to be especially more susceptible to deactivation by metal ions on coordination. Moreover, coordination

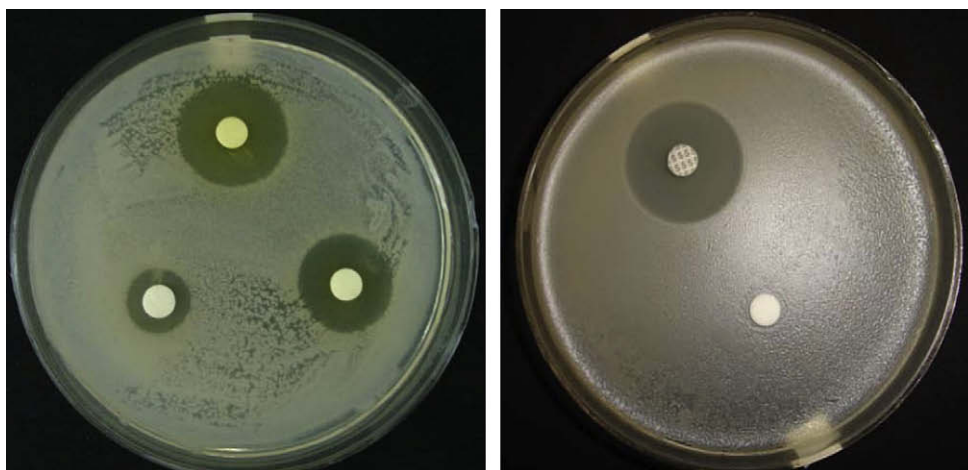


Fig. 1. Photograph (*Bacillus subtilis*) showing antibacterial screening of Schiff base and Gentamycin.



Fig. 2. Photograph (*A. niger*) showing antifungal screening of Schiff base and Fluconazole.

reduces the polarity [15,16] of the metal ion mainly because of the partial sharing of its positive charge with the donor groups [17,18] within the chelate ring system formed during coordination. This process, in turn, increases the lipophilic nature of the central metal atom, which favors its permeation more efficiently through the lipid layer of the microorganism [19–21] thus destroying them more aggressively.

Some important factors such as the nature of the metal ion, nature of the ligand, coordinating sites, geometry of the complex, concentration, hydrophilicity, lipophilicity and presence of co-ligands have considerable influence on antibacterial activity. Certainly, steric and pharmacokinetic factors also play a decisive role in deciding the potency of an antimicrobial agent. Apart from this, the mode of action of these compounds may also invoke hydrogen bond through the $>C=N-N=CH-$ group with the active centers and thus interfere with normal cell process. The presence of lipophilic and polar substituents is expected to enhance antibacterial activity. Heterocyclic ligands with multifunctionality have a greater chance of interaction either with nucleoside bases (even after complexation with metal ion) or with biologically essential metal ions present in the biosystem and can be promising candidates as bactericides since they always tend to interact especially

with some enzymatic functional groups, in order to achieve higher coordination numbers [22]. Thus antibacterial property of metal complexes cannot be ascribed to chelation alone, but it is an intricate blend of several contributions.

3.1.3. In-vitro cytotoxicity

The synthesized Schiff base and its Co(II), Ni(II) and Cu(II) complexes were screened for their cytotoxicity (brine shrimp bioassay) by using the protocol of Meyer et al. [17]. Brine shrimp (*Artemia salina* leach) eggs were hatched in a shallow rectangular plastic dish (22×32 cm) filled with artificial seawater, which was prepared with a commercial salt mixture and double distilled water. An unequal partition was made in the plastic dish with the help of a perforated device. Approximately 50 mg of eggs were sprinkled into the large compartment, which was darkened while the minor compartment was open to ordinary light. After two days nauplii were collected by a pipette from the lighted side.

A sample of the test compound was prepared by dissolving 20 mg of each compound in 2 mL of DMF. From this stock solution 100, 50 and $10 \mu\text{g mL}^{-1}$ were transferred to nine vials (three for each dilutions were used for each test sample and LD_{50} is the

Table 1

Bacteriological results of Schiff base and its Co(II), Ni(II) and Cu(II) complexes at $10 \mu\text{g mL}^{-1}$ concentration.

Empirical formula	Activity against bacteria (mm)							Activity against fungi (mm)		
	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>B. cereus</i>	<i>S. aureus</i>	<i>S. dysentery</i>	<i>Micrococcus</i>	<i>B. subtilis</i>	<i>A. niger</i>	<i>Penicillium</i>	<i>C. albicans</i>
$\text{C}_{34}\text{H}_{28}\text{N}_8\text{O}_6$	16	14	16	10	16	14	20	22	20	16
$[\text{Co}(\text{C}_{34}\text{H}_{26}\text{N}_8\text{O}_6)\text{Cl}_2] \cdot 2\text{H}_2\text{O}$	10	16	16	12	14	12	12	20	18	18
$[\text{Ni}(\text{C}_{34}\text{H}_{26}\text{N}_8\text{O}_6)\text{Cl}_2 \cdot 2\text{H}_2\text{O}] \cdot 2\text{H}_2\text{O}$	14	12	14	10	16	16	16	20	18	18
$[\text{Cu}(\text{C}_{34}\text{H}_{26}\text{N}_8\text{O}_6)\text{Cl}_2] \cdot 2\text{H}_2\text{O}$	12	14	10	12	16	10	14	18	20	20
Gentamycin	20	20	20	20	20	20	20	–	–	–
Fluconazole	–	–	–	–	–	–	–	24	24	24
DMF	12	12	12	12	12	12	12	12	12	12

Key for interpretation: less than 12 mm – inactive; 12–14 mm – weakly active; 14–16 mm – moderately active; above 16 mm – highly active.

mean of three values) and one vial was kept as control having 2 mL of DMF only. The solvent was allowed to evaporate overnight. After two days, when shrimp larvae were ready, 1 mL of seawater and 10 shrimps were added to each vial (30 shrimps/dilution) and the volume was adjusted with seawater to 5 mL per vial. After 24 h the number of survivors was counted. Data were analyzed by a Finney computer program to determine the LD₅₀ values [23]. In the case of cytotoxic activity it was observed that the Schiff base and its Co(II), Ni(II) and Cu(II) complexes displayed weak cytotoxic activity against *A. salina*, therefore they can be considered non-cytotoxic.

4. Results and discussion

All the Co(II), Ni(II) and Cu(II) complexes are colored non-hygroscopic solids, stable in air. They are sparingly soluble in common organic solvents, but soluble in DMF and DMSO. The elemental analyses show that the Co(II), Ni(II) and Cu(II) complexes have stoichiometry of the type [M₂LX₂]·2H₂O (M = Co(II), Cu(II) and X = Cl) and [Ni₂LX₂(H₂O)₂]·2H₂O. The molar conductance values are too low to account for any dissociation of non-electrolytes in DMF.

4.1. IR spectra

The important infrared frequencies of Schiff base and its Co(II), Ni(II) and Cu(II) complexes. It is well established that the Schiff base having *O*-hydroxy group either on aldehyde or on aniline residue can form intramolecular hydrogen bond [24,25]. This has direct impact on the $\nu(\text{OH})$ vibration, and shifts to the lower frequency with broadening. The extent of shift depends on the strength of hydrogen bonding.

The broad band at 3439 cm⁻¹, a strong band at 1626 and 1687 cm⁻¹ in the IR spectrum of the Schiff base are assigned to H-bonded -OH stretching, $\nu(\text{C}=\text{N})$ of azomethine and carbonyl $\nu(\text{C}=\text{O})$ vibrations, respectively. An intense band at 3100 cm⁻¹ is due to the -NH- vibrations of the hydrazine group, a broad medium intense band was observed at 2921 cm⁻¹ due to methyl groups and the band at 1068 cm⁻¹ is assigned to hydrazinic $\nu(\text{N}-\text{N})$ of the free ligand.

For the Co(II), Ni(II) and Cu(II) complexes, we observed the following changes; the high intense band due to phenolic -OH appeared in the region at 3439 cm⁻¹ in the Schiff base was disappeared in the complexes. These observations support the formation of M-O bonds via deprotonation. So the H-bonded -OH groups have been replaced by the metal ion. The presence of broad stretching vibrations in the 3598–3570 cm⁻¹ region can be attributed to coordinated or lattice water molecules in all these complexes.

The medium intense band at 1601 cm⁻¹ due to $\nu(\text{C}=\text{N})$ indicates that the C=N of the ligand coordinates to the metal through nitrogen. A broad band at 3565 cm⁻¹ in addition to a medium to high intense band at 850 cm⁻¹ is attributed to the symmetric and antisymmetric -OH stretching modes of coordinated water [26]. The unaltered position of the $\nu(\text{C}=\text{O})$ (carbonyl) confirms non-involvement in coordination. The $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ bands have been assigned in the region 540–550 cm⁻¹ and 425–450 cm⁻¹, respectively [27,28].

4.2. ¹H NMR spectra

The Schiff base exhibits signals at 13.42 ppm due to NH protons [29]. These protons are D₂O exchangeable and confirm the assignment. It also exhibits resonance due to phenolic -OH protons around 10.20 ppm [30]. The other characteristic resonance due to azomethine proton in the Schiff base appears at 8.20 ppm. Signals

in the region 6.80–7.75 ppm due to aromatic protons. A signal in the region 2.50–2.82 ppm is assigned to methyl protons [30]. All these observations support the infrared conclusions.

4.3. Electronic spectral studies

The electronic spectra of Co(II) complex exhibit absorption bands in the region 11 015, 17 212 and 20 032 cm⁻¹ which can be assigned to the transitions ${}^4\text{A}_2 + {}^4\text{E} \rightarrow {}^4\text{B}_1$, ${}^4\text{A}_2 + {}^4\text{E} \rightarrow {}^4\text{E}(\text{P})$ and ${}^4\text{A}_2 + {}^4\text{E} \rightarrow {}^4\text{A}_2(\text{P})$ respectively which are characteristic of square pyramidal geometry [31]. The Ni(II) complex shows three bands around 10 882, 16 752 and 26 342 cm⁻¹ which are assigned to ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})(\nu_1)$, ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})(\nu_2)$ and ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})(\nu_3)$ transition respectively, indicating octahedral geometry [31]. The ligand field parameters are listed in Table 2. The Cu(II) complex exhibited a high intensity band at 27 523 cm⁻¹ in the UV region. Appearance of this band is due to $\pi \rightarrow \pi^*$ transition associated with the azomethine linkage and L → M charge transfer transition. The electronic spectrum of Cu(II) complex shown three bands at 10 952, 14 798 and 23 228 cm⁻¹, these bands have been assigned to the transition ${}^2\text{B}_1 \rightarrow {}^2\text{A}_1(\nu_1)$, ${}^2\text{B}_1 \rightarrow {}^2\text{B}_2(\nu_2)$ and ${}^2\text{B}_1 \rightarrow {}^2\text{E}(\nu_3)$ respectively. These transitions are characteristic of square pyramidal geometry [32].

4.4. Magnetic studies

The magnetic moments of the Co(II), Ni(II) and Cu(II) complexes obtained at room temperature are listed in Table 3. The Co(II) and Ni(II) complexes shown magnetic moment values around 4.28 and 3.34 BM respectively which are lower than the respective spin values only and indicates weak antiferromagnetic coupling interaction between the metal ions which further confirm the dinuclear nature of the complexes. The Cu(II) complex showed a magnetic moment around 1.45 BM which is considerably lower than the spin only value for Cu(II) complexes. The low value of the magnetic moment is attributed to the antiferromagnetic coupling interaction between two metal ions. This fact suggests the dinuclear nature of the Cu(II) complexes [33].

4.5. FAB mass spectrum

The FAB mass spectrum of the Schiff base has been depicted in Fig. 3. The spectrum showed a molecular ion peak at m/z 645 which is equivalent to its molecular weight [L + H]⁺.

The FAB mass spectrum of Cu(II) complex is depicted in Fig. 4. The spectrum showed a molecular ion peak M⁺ at m/z 876, which is equivalent to its molecular weight of the Cu(II) complex. The molecular ion peak fragmentation with the loss of two water molecules, gave a peak A₁ at m/z 840 due to the fragment ion [Cu₂(C₃₄H₂₆N₈O₆)Cl₂]⁺. Further, the fragments leading to the formation of the species [Cu₂L]⁺ which undergo demetallation to form the species [L + H]⁺ gave fragment ion at m/z 644. All these fragmentation patterns are well observed in the FAB mass spectrum. These entire fragmentation patterns are well observed in the FAB mass spectrum (Fig. 4). It clearly indicates dinuclear nature of the complex and two Cu(II) ions are held in the macrocyclic compartment of the Schiff base. The metal ions are bonded to two phenoxo bridges, which endogenously coordinated to the metal ions and the other coordinating sites in the ligand are the azomethine nitrogen atoms. Both phenoxide and azomethine groups surround the two metal ions, which are in close proximity within the ligand molecule to form a square base. A chloride ion coordinates to each metal ion from opposite sides to give square pyramidal configuration to the metal ions. The FAB mass spectrum confirms the dinuclear nature of the metal complex.

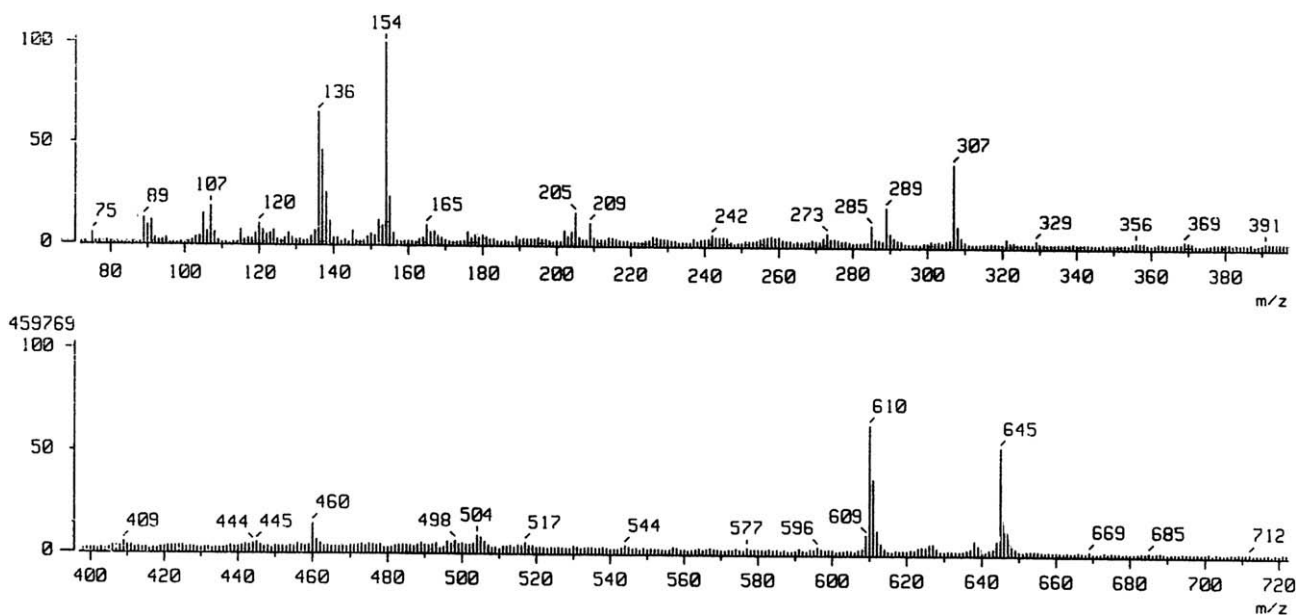


Fig. 3. FAB mass spectrum of Schiff base.

4.6. Thermal studies

TG and DTG studies were carried out for Co(II), Ni(II) and Cu(II) complexes. These complexes decompose gradually with the formation of respective metal oxide above 500 °C. The nature of proposed chemical change with the temperature range and the percentage of metal oxide obtained are given in Table 4. The thermal decomposition of respective Co(II) and Cu(II) complexes takes place in three steps as indicated by DTG peaks around 110–120, 200–210 and 240–250 °C corresponding to the mass loss of two coordinated water molecules, two aldehyde moieties and two bis hydrazine moieties respectively, Fig. 5. Whereas, one representative Ni(II) complex decomposes in four steps as indicated by DTG peaks around 200–210, 230–235, 280–290 and 410–450 °C corresponding to the mass loss of two coordinated/adhered water

molecules, two aldehyde moieties and two bis hydrazine moieties respectively.

4.7. ESR studies

The X-band ESR spectrum of Cu(II) complex was recorded at room temperature using DPPH as a reference standard. The g_{\parallel} and g_{\perp} values have been found to be 2.25 and 2.09 respectively. In general, dinuclear Cu(II) complexes give broad ESR peaks and the broadening is assigned to a dipolar interaction [34]. The observed ESR spectrum is characteristic of square pyramidal geometry. The g_{av} value was calculated to be 2.14. The existence of $g_{\parallel} > g_{\perp}$ suggests that $d_{x^2-y^2}$ orbital is in the ground state and d^9 configuration is $(eg)^4(a_{1g})^2(b_{2g})^2(b_{1g})^1$. The 'g' values are related to the axial symmetry and $g_{\parallel} > g_{\perp}$ suggests square pyramidal geometry of

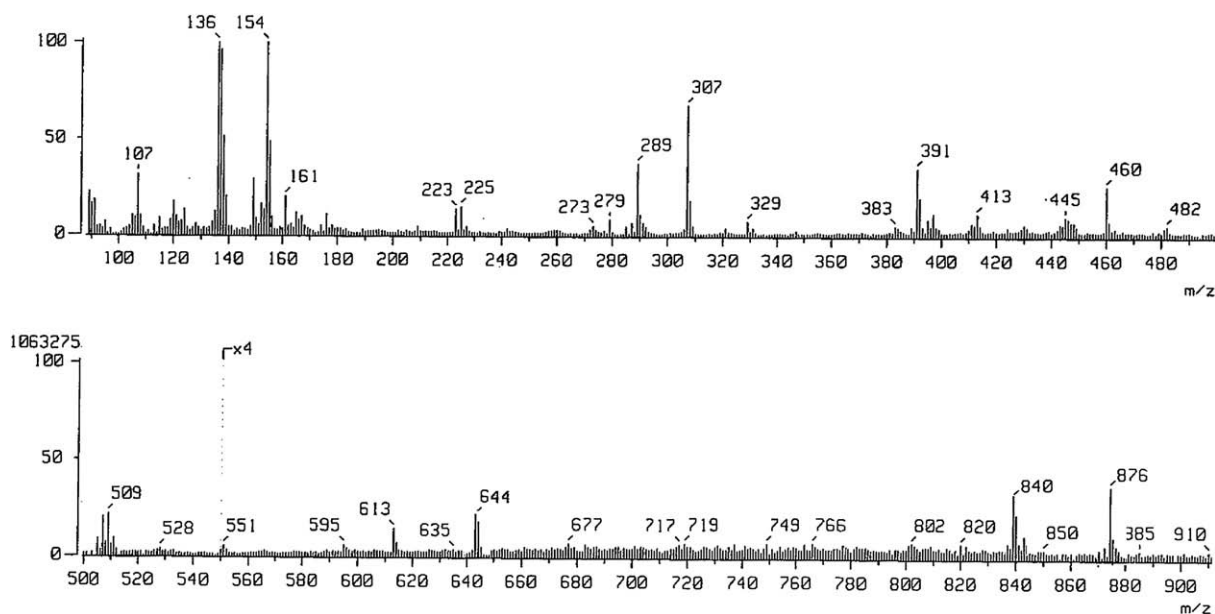


Fig. 4. FAB mass spectrum of Cu(II) complex.

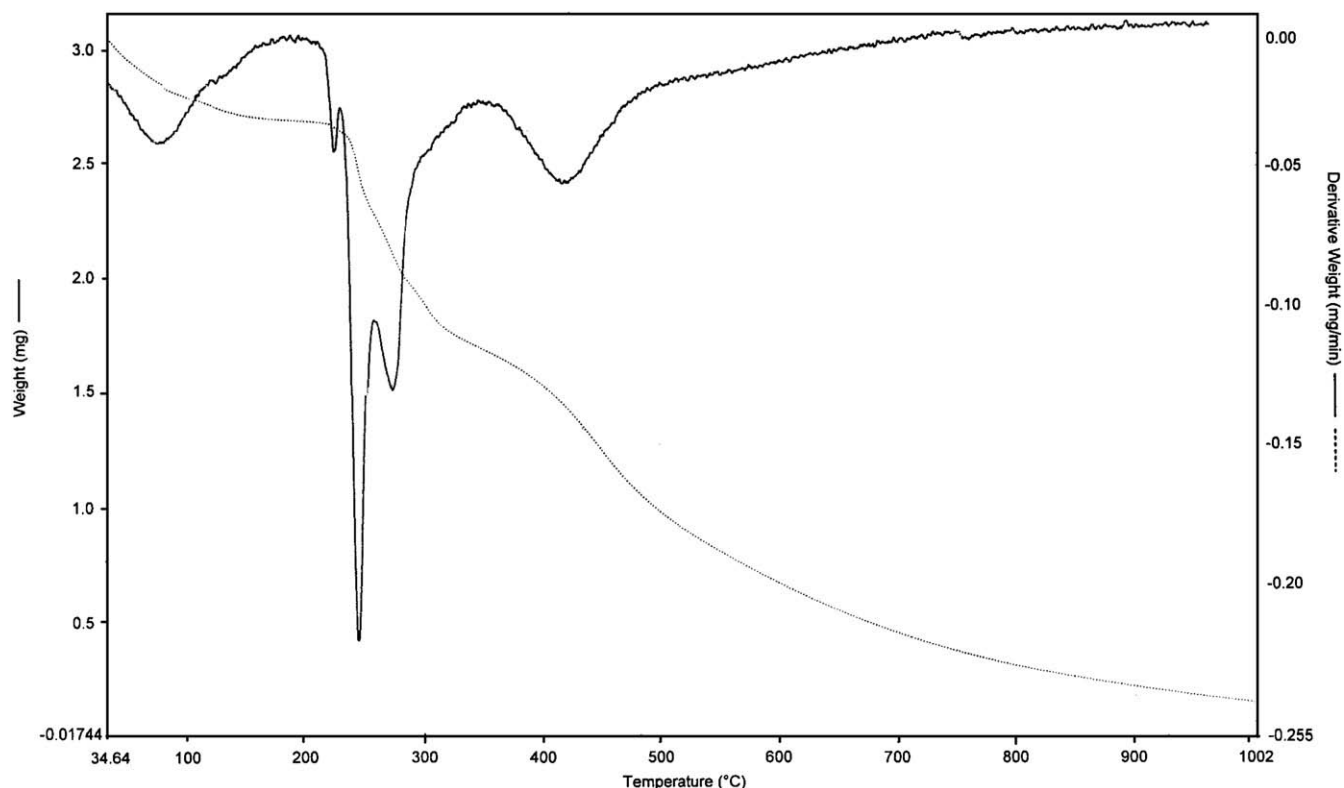


Fig. 5. TG/DTG spectrum of Ni(II) complex.

Cu(II) complex. The axial symmetry parameter $G = 2.542$ which has less than 4.0 indicates considerable exchange interaction between metal ions in the solid complex [35] which further supports the dinuclear nature of the Cu(II) complex.

4.8. Cyclic voltammetry

The electrochemical behavior of Cu(II) complex was examined by employing glassy carbon as working electrode, Ag/AgCl as reference electrode and platinum wire as auxiliary electrode (Fig. 6). The working media consisted of DMF and $n\text{-Bu}_4\text{N}^+\text{ClO}_4^-$ as supporting electrolyte. The cyclic voltammogram of Cu(II) complex in

10^{-3} M solution was recorded at room temperature in the potential range -3.0 V to $+2.4$ V with a scan rate 100 mV s^{-1} . The complex shows a redox process corresponding to the Cu(II) \rightarrow Cu(I) couple at $E_{\text{pa}} = +1.40$ V and associated cathodic peak at $E_{\text{pc}} = -0.60$ V. This couple is found to be quasi-reversible as the peak separation between the anodic and cathodic potential is very high. But the ratio between the anodic and cathodic currents suggests that the process is simple one-electron transfer, quasi-reversible process [36,37]. On comparing the cyclic voltammograms, we observed that the variation in oxidation and reduction potential may be due to distortion in the geometry of the complex which arises due to different anions coordinated to the metal ion [38].

4.9. Fluorescence studies

The emission spectrum of Schiff base was investigated in various solvents viz., DMF, DMSO, MeCN and THF.

The Schiff base characterized by emission band around 470 nm in above solvents (DMF, DMSO, THF, and MeCN) is due to phenoxide anion in the Schiff base. On addition of aqueous alkali (2% NaOH) to all the above solutions, we observed that, the intensity of 422 nm band was reduced. The changes in this spectrum of Schiff base in all the solutions clearly indicate that, proton transferred (H-bonded ion pair) species exist in equilibrium. In the case of DMF solution as the addition of aqueous alkali (2% NaOH) the λ_{max} of Schiff base undergoes red shift in DMF may be due to the hydrogen bond formation.

5. Conclusion

The newly synthesized compound acts as hexadentate Schiff base. The metals are coordinated to azomethine nitrogen and phenolic oxygen atoms. The analytical, spectral, magnetic, and

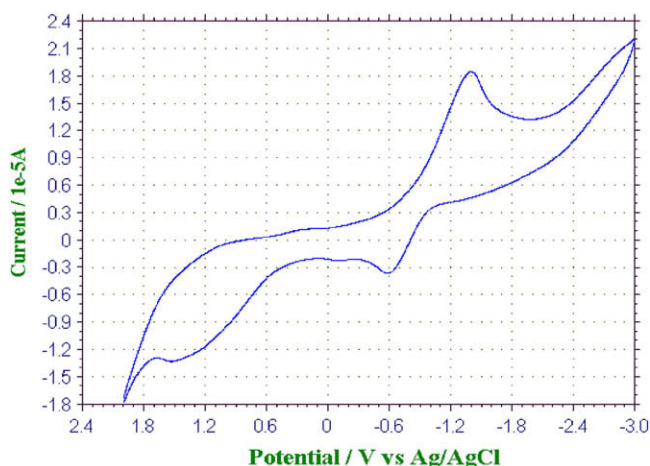


Fig. 6. CV spectrum of Cu(II) complex.

thermal studies confirm the bonding of Schiff base to metal ions. Electrochemical study of Cu(II) complex can provide the degree of the reversibility of one-electron transfer reaction and they have a quasi-reversible character. Schiff base was found potentially active towards microbial strains. All these observations put together lead us to propose the following structure (Scheme 1) in which the Ni(II) complex shows octahedral geometry and Co(II) and Cu(II) complexes exhibit square pyramidal geometry.

6. Experimental protocol

6.1. Chemistry

All chemicals and solvents used were of AR grade. All metal(II) salts were used as their chlorides. Further remaining pure reagents were purchased from Ranbaxy Chemicals. The metal contents were determined gravimetrically by the known method. The results of elemental analyses, molar conductance and magnetic data are listed in Table 3.

The IR spectra of the Schiff base and its Co(II), Ni(II) and Cu(II) complexes were recorded on a HITACHI-270 IR spectrophotometer in the 4000–350 cm^{-1} region in KBr discs. The electronic spectra of the complexes were recorded in DMF on a VARIAN CARY 50-BIO UV spectrophotometer in the 200–1100 nm region. The ^1H NMR spectra of Schiff base and complexes were recorded in $\text{DMSO}-d_6$ on a BRUKER-300 MHz spectrometer at room temperature using TMS (Me_4Si) as an internal reference. FAB mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer/data system using argon/xenon (6 kV, 10 A) as the FAB gas. The accelerating voltage was 10 kV and the spectra were recorded at room temperature; *m*-nitrobenzyl alcohol was used as the matrix. The mass spectrometer was operated in the positive ion mode. Thermogravimetric data were measured from room temperature to 1000 $^\circ\text{C}$ at a heating rate of 10 $^\circ\text{C min}^{-1}$. The data were obtained by using a Perkin–Elmer Diamond TG/DTG instrument. Molar conductivity measurements were recorded on an Elico-CM-82 T conductivity bridge with a cell having cell constant 0.51; magnetic moments were determined on a Faraday balance.

Appendix. Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.ejmech.2009.03.032.

References

- [1] J.P. Corhnelissen, J.H. Van Diemen, L.R. Groeneveld, J.G. Haasnoot, A.L. Spek, J. Reedisk, *Inorg. Chem.* 31 (1992) 198.
- [2] S.N. Dubey, B. Kaushik, *Indian J. Chem.* 24A (1985) 950.
- [3] D.R. Richardson, P.V. Bernhardt, *J. Biol. Inorg. Chem.* 4 (1999) 266–273.
- [4] L. Ramamohan, R.K. Shikkaragol, S.D. Angadi, V.H. Kulkarni, *Asian J. Pure Appl. Chem.* 1 (2) (1995) 86.
- [5] M.S. Yadawe, S.A. Patil, *Transition Met. Chem.* 22 (1997) 220.
- [6] G. Darnell, D.R. Richardson, *Blood* 94 (2) (1999) 781.
- [7] B. Murukan, K. Mohanan, *J. Enzyme Inhib. Med. Chem.* 22 (1) (2007) 65–70.
- [8] S.M.E. Khalil, H.S. Seleem, B.A. El-Shetary, M. Shebl, *J. Coord. Chem.* 55 (8) (2002) 883–899.
- [9] S. Naskar, D. Mishra, S. Kumar Chattopadhyay, M. Corbella, A.J. Blake, *Dalton Trans.* (2005) 2428–2435.
- [10] D.A. Denton, N. Suschitzky, *J. Chem. Soc.* (1963) 4741.
- [11] R.R. Gange, C.L. Spiro, T.J. Smith, C.A. Hamann, W.R. Thies, A.K. Shiemke, *J. Am. Chem. Soc.* 103 (1981) 4073.
- [12] F. Ullmann, K. Brittner, *Chem. Ber.* 42 (1909) 2539.
- [13] E.O. Offiong, S. Martelli, *Il Farmaco* 49 (1994) 513.
- [14] J.G. Collee, J.P. Duguid, A.G. Farser, B.D. Marmion (Eds.), *Practical Medical Microbiology*, Churchill Livingstone, New York, 1989.
- [15] C.J. Balhausen, *An Introduction to Ligand Field*, McGraw Hill, New York, 1962.
- [16] A.B.P. Lever, *Inorganic Electronic Spectroscopy*, Elsevier, Amsterdam, 1984, p. 23.
- [17] B.N. Meyer, N.R. Ferrigni, J.E. Putnam, L.B. Jacobsen, D.E. Nichols, J.L. McLauhglin, *Planta Med.* 45 (1982) 31.
- [18] Z.H. Chohan, A. Scozzafava, C.T. Supran, *J. Enzyme Inhib. Med. Chem.* 17 (2003) 261.
- [19] Z.H. Chohan, H. Pervez, M.K. Khan, A. Rauf, C.T. Supuran, *J. Enzyme Inhib. Med. Chem.* 19 (2004) 85.
- [20] Z.H. Chohan, K.M. Khan, C.T. Supuran, *Appl. Organomet. Chem.* 18 (2004) 305.
- [21] Z.H. Chohan, *Synth. React. Inorg. Met.-Org. Chem.* 34 (2004) 833.
- [22] W. Levingson, P. Mikeleus, J. Jackson, W. Kaska, in: G.N. Schranzer (Ed.), *Inorganic and Nutritional Aspects of Cancer*, Plenum Press, New York, 1978.
- [23] A.W. Bauer, W.M. Kirby, J.C. Sherris, M. Turck, *Am. J. Clin. Pathol.* 45 (1966) 493.
- [24] H.H. Freedman, *J. Am. Chem. Soc.* 83 (1956) 2900.
- [25] A.W. Baker, A.T. Shulgin, *J. Am. Chem. Soc.* 83 (1959) 1523.
- [26] K. Nakamoto, *Infrared Spectra of Inorganic and Coordination Compounds*, Wiley-Interscience, New York, 1970.
- [27] B.B. Mohapatra, S.K. Saraf, *J. Indian Chem. Soc.* 80 (2003) 696.
- [28] C.K. Choudhary, R.K. Choudray, L.K. Mishra, *J. Indian Chem. Soc.* 80 (2003) 693.
- [29] M.S. Gunthkal, T.R. Goudar, S.A. Patil, *Oriental J. Chem.* 16 (2000) 151–154.
- [30] Sayaji Rao, *Asian J. Chem.* 17 (2005) 2663–2668.
- [31] D.N. Satyanarayana, *Electronic Absorption Spectroscopy and Related Techniques*, University Press, Hyderabad, 2001.
- [32] N. Sengottuvelan, J. Mohanmani, M. Kondaswamy, *Polyhedron* 21 (2002).
- [33] R. Kannappan, R. Mahalakshmy, T.M. Rajchdiran, R. Venkateshan, P. Sambashiva Rao, *Proc. Indian Acad. Sci. (Chem. Sci.)* (2003) 115.
- [34] M.C. Jain, A.K. Shrivastava, P.C. Jain, *Inorg. Chim. Acta* 23 (1977) 199.
- [35] A. Jaggi, S. Chandra, K.K. Sharma, *Polyhedron* 4 (1958) 163.
- [36] Z. Shirin, R.M. Mukherjee, *Polyhedron* 11 (1992) 2625.
- [37] A. Shyamala, A.R. Chakravarty, *Polyhedron* 12 (1993) 1545.
- [38] S. Chandra, L.K. Gupta, Sangeetika, *Synth. React. Inorg. Met.-Org. Chem.* 34 (2004) 1591.