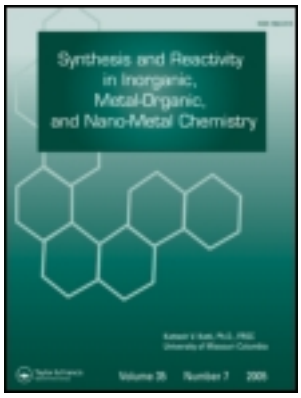

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Synthesis, Structural Characterization, and Antibacterial Activity of a Cu(II) Complex, $[Cu(CH_3COO)(HL1)H_2O]\cdot H_2O$

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A new copper(II) complex $[Cu(CH_3COO)(HL)H_2O]\cdot H_2O$, (where HL stands for 4-Nitro-2-[N-(2-{dimethylamino}ethyl-N′-methyl)aminomethyl]phenol), was synthesized and characterized by XRD, EPR, UV-Vis, and IR techniques. It crystallized in monoclinic system and $P2_1/c$ space group. The Cu(II) ion is coordinated by a tridendate HL ligand, an acetate anion, and a water molecule in a distorted square-pyramidal geometry. It is paramagnetic and has a potential antibacterial activity.

Keywords anti-bacterial, copper(II) complex, EPR, IR, UV-VIS, XRD

INTRODUCTION

Among the trace transition metals, copper is found in numerous proteins and enzymes. The presence of Cu(II) ion in enzymes and proteins ligated with O,N-coordinating ligands as mimetic systems has a great interest.[1] The structure and magnetic properties of these metalloproteins are well studied.[2,3] The metal carboxylate complexes are the models of metalloproteins.[4,5] The ligands containing carboxylate group have a greater biological relevance.[6] The carboxylate group that bridges between two metal ions forms a wide variety of polynuclear complexes.[7–10] Analysis of Cu(II) compounds with EPR spectroscopy technique is immense interest because of its high sensitivity and accessibility to measure the samples in different physical states (i.e., solids and liquids [crystal, polycrystalline, and frozen solution]). The EPR spectra of the Cu(II) complex gives hyperfine lines (^{65}Cu $I = 3/2$) through which one can determine the g-tensor parameters ($g_\parallel$ and $g_\perp$). Keeping all these in mind, we have successfully synthesized a new mononuclear copper(II) complex from polydentate ligand derived from Mannich base reaction. It was characterized by using single crystal XRD, EPR, UV-Vis, and IR. Also, we herein report the antibacterial activity of this complex.

EXPERIMENTAL

Chemicals and General Methods

All the chemicals for the synthesis of ligand as well as copper complex were purchased from Sigma-Aldrich (Bangalore, India) and were used without further purification. UV-Vis spectra was measured on a Shimadzu UV-2450 PC spectrophotometer (Tokyo, Japan) at room temperature. Infrared (IR) spectra were recorded on a Nicolet iS10 instrument using KBr pellets (Thermo Scientific, India). The single-crystal X-ray structure was performed on an Oxford Diffraction Xcalibur Diffractometer (Virginia) equipped with graphite monochromatic Mo-Ka radiation ($\lambda = 0.71073$Å) at 296 K. The antibacterial activity of the Cu(II) complex was assessed by well diffusion method. Electron paramagnetic resonance (EPR) spectra were recorded with a JEOL TES100 EPR spectrometer (Tokyo, Japan). Low temperature measurements were recorded at the liquid N_2 temperature (77 K) using ES-UCD3X insertion type Dewar.

Synthesis

Synthesis of 4-Nitro-2-[N-(2-{dimethylamino}ethyl-N′-methyl)aminomethyl]phenol (abbreviated as HL1)

4-Nitrophenol (5.29 g, 0.038 mol) in ethanol (150 mL) was mixed with N,N,N′-trimethylethylenediamine (3.882 g, 0.038 mol) under stirring and cooled in ice. Formaldehyde (9 mL, 35%, 0.114 mol) was added dropwise with constant stirring. The mixture was stirred at room temperature (28°C) for 24 h and then refluxed for 8 h. The solvent was removed under *vacuo* and the resulting oily product was neutralized with

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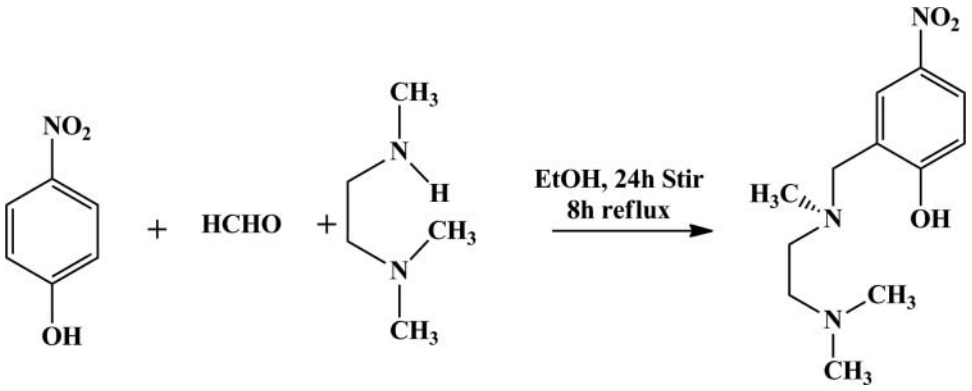

FIG. 1. The synthetic route of ligand.

saturated sodium carbonate and extracted with chloroform (4 × 50 mL), the organic layers were combined and dried over anhydrous magnesium sulfate followed by filtration afforded a yellow semisolid product. This was purified by column chromatography on silica gel ($CHCl_3$/MeOH). A yellow solid was obtained (Yield: 87%). The synthetic route is shown in Figure 1.

Synthesis of [Cu(HL1)(CH_3COO)(H_2O)] H_2O

The methanolic solution of copper(II) acetate (10 mL, 0.1 mmol) was added dropwise to a methanolic solution of HL1 (50 mL, 0.1 mmol) with constant stirring and was refluxed for 4 h. The final clear dark green solution was allowed to stand at room temperature for several days. Green Plate shaped crystals suitable for single-crystal X-ray diffraction analysis. The yield was (68.3%) based on ligand.

X-Ray Crystallography

A suitable single crystal of title compound was selected and mounted on a Xcalibur, Eos diffractometer (Europe, UK). Using Olex2,[11] the structure was solved with the ShelXS[12] structure solution program by Direct Methods. Refinements were performed using the ShelXL[13] refinement package using least-squares minimization. All of the non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms bonded to carbon atoms were placed in calculated positions with a C–H bond distance of 0.93 Å. Table 1 lists crystallographic details.

Antibacterial Activity by Well Diffusion Method

The antibacterial activity was carried out by well diffusion method as described by Tagg and McGiven.[14] *Bacillus subtilis*, which is a gram-positive bacterium, and *Pseudomonas fluorescens*, which is a gram-negative bacterium, were used in this study. Overnight grown bacterial culture was mixed with molten nutrient agar at 55°C and poured into the petriplates under sterile conditions. After solidification, wells were made in the plate using sterile cork borer. In each plate, three wells of 8 mm diameter were made. These wells were filled with the test compounds at a concentration if 900 μg/30 μL methanol. The antibacterial activity of the monomeric Cu(II) complex was compared with that of standard antibiotic streptomycin at a concentration 900 μg/30 μL methanol/well. Methanol was used as

TABLE 1
Crystal data and structure refinement

Empirical formula	$C_{14}H_{25}N_3O_7Cu$
Formula weight	410.92
Temperature/K	296
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	20.3222(11)
b/Å	7.7896(3)
c/Å	11.9849(5)
α/°	90.00
β/°	106.111(5)
γ/°	90.00
Volume/Å^3	1822.73(15)
Z	4
ρ_{calc}mg/mm^3	1.497
m/mm^{-1}	1.238
F(000)	860.0
Crystal size/mm^3	0.4 × 0.2 × 0.08
2Θ range for data collection	5.64 to 49.98°
Index ranges	$-20 \le h \le 24$, $-9 \le k \le 9$, $-13 \le l \le 14$
Reflections collected	8711
Independent reflections	3205[R(int) = 0.0518]
Data/restraints/parameters	3205/0/234
Goodness-of-fit on F^2	1.011
Final R indexes [$I \ge 2\sigma$ (I)]	$R_1 = 0.0485$, $wR_2 = 0.0917$
Final R indexes [all data]	$R_1 = 0.0817$, $wR_2 = 0.1045$
Largest diff. peak/hole / e Å^{-3}	0.36/−0.32

solvent control. The plates were incubated at 37°C for 24 h. The inhibition was measured in millimeter using antibiotic zone scale (HiMedia, Mumbai)

RESULTS AND DISCUSSION

Spectroscopic Characterization

Ligand: IR: 1454 (Aromatic); 1370 (N-CH$_2$); 2920–2800 cm (C—H aliphatic); 3400–3500 (OH). 1317, (N-CH$_3$).

Complex: The peak observed at 1445 cm^{-1} is the characteristic for the stretching vibrations of the aromatic skeleton. The peak at 1339 cm^{-1} is assigned to the N-CH$_3$ stretching frequency and the one at the region 2938–2816 cm^{-1} C—H to aliphatic stretching frequency. The O-H stretching frequency is occurred at 1290 cm^{-1}. The Cu-OH$_2$ stretching frequency is occurred at 3480 cm^{-1}. Cu-N stretching frequency is occurred at 451 cm^{-1}, which confirmed the participation of the nitrogen atom in the complex formation. The binding of acetate to metal complex give a characteristic IR absorption at 1599 cm^{-1}, which is attributable to the antisymmetric ν_{as}(COO) stretching frequency. Electronic spectrum of the complex contains four bands in the region 683, 376, 289, and 235 nm. The calculated absorbance values are 14641, 26595, 34602, and 42553 cm^{-1}. The absorption bands at 289 and 235 nm are attributed to intraligand charge transfer transition and 376 nm is assigned to phenoxo to copper LMCT.[15] A broad band around 683 nm indicates d-d transition.

Description of the Crystal Structure

The structure was solved, achieving a final R value of 4.85%; an ORTEP view is given in Figure 2. Selected bond distances and angles are shown in Table 2. The Cu(II) ion is pentacoordinated with a square pyramidal geometry. The base of the pyramid is formed by the tridentate HL1 and monodentate acetate anions. Although the distances Cu(1)-N(1), Cu(1)- N(2), Cu(1)-O(3), and Cu-O(5) span only 0.127 Å (Table 2), distortion from the ideal square plane is evidenced by the smaller bond angles of N(1)-Cu(1)-N(2) {86.18°}, O(3)-Cu(1)-O(5) {88.09°}, and N(1)-Cu(1)-O(5) {89.61°} as compared to larger bond angles of N(2)-Cu(1)-O(3) {92.73°}. The aqua molecule is in the apical position (distance of Cu(1)-O(4) = 2.31 Å). Similar to the great majority of real square-pyramidal structure,[16] in the present system also the XRD crystal structure reveals that the Cu(II) ion is slightly displaced out of the basal plane toward the apical ligand.

TABLE 2
Selected bond lengths (Å) and bond angles (°) of the complex

Atom	Atom	Length/Å	Atom	Atom	Atom	Angle/°
Cu1	O3	1.926 (3)	O3	Cu1	O5	88.10 (11)
Cu1	O5	1.967 (3)	O3	Cu1	N2	92.72 (12)
Cu1	N1	2.054 (3)	O3	Cu1	O4	99.82 (11)
Cu1	N2	2.040 (3)	O5	Cu1	N1	89.62 (12)
Cu1	O4	2.310 (3)	O5	Cu1	O4	95.69 (10)
			N1	Cu1	O4	91.21 (11)
			N2	Cu1	N1	86.17 (13)
			O3	Cu1	N1	168.90 (12)
			O5	Cu1	N2	162.25 (11)
			N2	Cu1	O4	101.63 (11)

Symmetry code: (i) −x, 1/2 + y, 1/2−z.

Donor-acceptor distances indicate hydrogen bonds among coordinated and non-coordinated water molecules {O(4)-O(7), 2.810 Å} and also between the oxygen atoms of lattice water and HL[1] ligand {O(7)-O(3), 2.930 Å and O(7)-O(2), 2.885 Å}. Lattice water molecules are bridging the three moeties leading to the formation of two-dimensional network (Figure 3). When the crystal packing is viewed along b direction (Figure 4), it appears that there are π-π interactions; however, the centroid-centroid distance measurement (6.425 Å) reveals that the π-π interac-

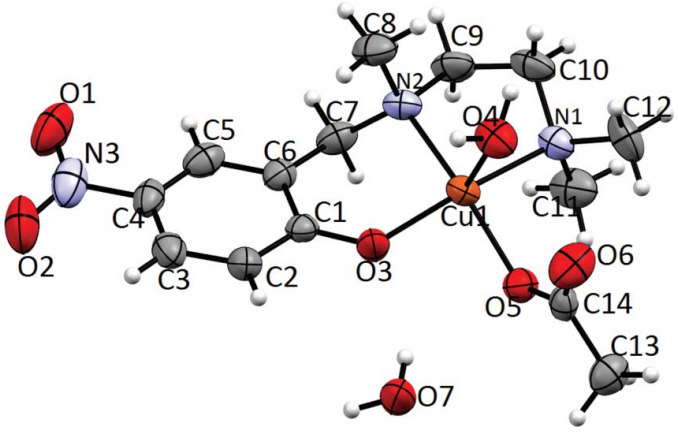

FIG. 2. ORTEP structure of the title compound viewed along c direction with atom numbering scheme (50% displacement ellipsoids) (color figure available online).

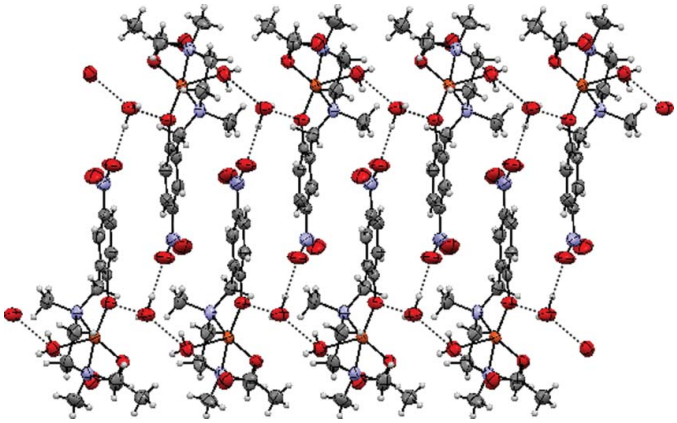

FIG. 3. The 2D network of the title compound bridged by water molecule through hydrogen bonding (color figure available online).

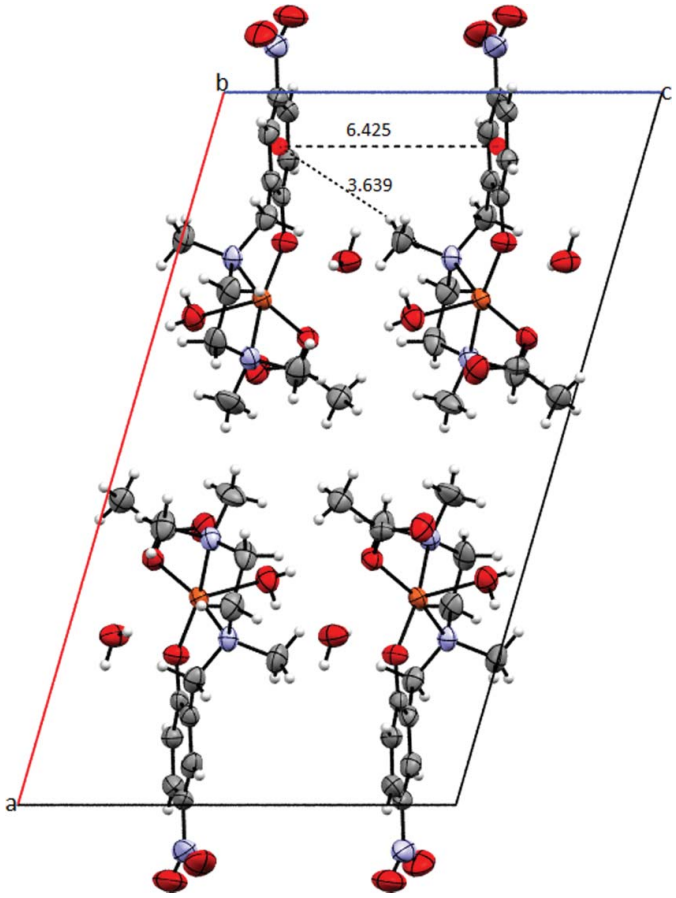

FIG. 4. Crystal packing viewed along *b* direction with centroid-centroid and C—H···π distances (Å) (color figure available online).

tions are very unlikely. The presence of C—H···π interaction is evident from the distance measurement (3.639 Å).

The EPR spectrum of the title complex recorded at room temperature in polycrystalline form is shown in Figure 5. The

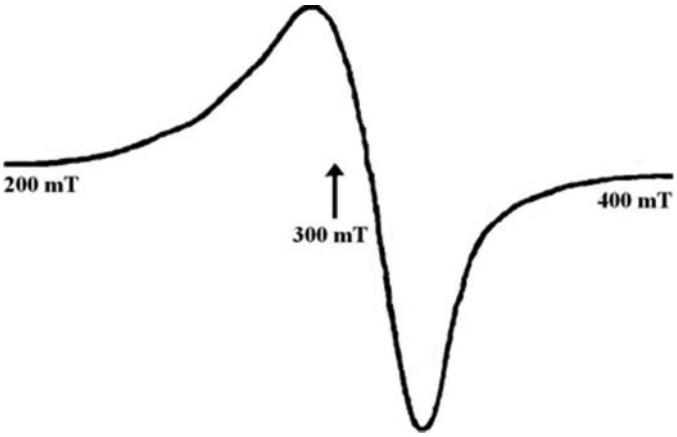

FIG. 5. Powder EPR spectrum of complex at $\nu = 9.20481$ GHz.

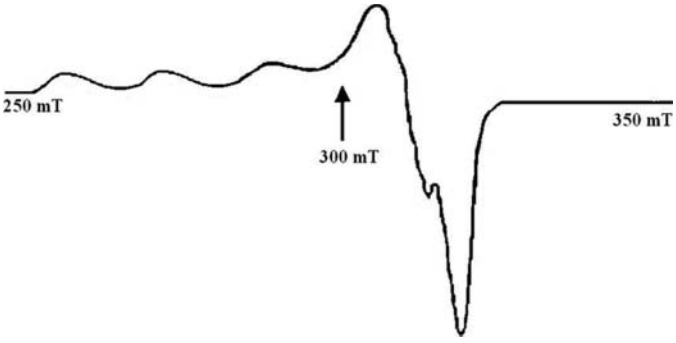

FIG. 6. EPR spectrum of complex in methanol at liquid N_2 temperature $\nu = 9.03128$ GHz.

signal exhibits a characteristic line shape for powder sample containing a paramagnetic ion without any hyperfine splitting. Due to dipolar-dipolar interaction, the spectrum shows only one broad line $g_{iso} = 2.12$. The frozen solution spectrum of complex shown in Figure 6 gives the signature spectrum for an axially symmetric complex with a $d_x{}^2{}_{-y}{}^2$ ground state ($g_\parallel > g_\perp > 2.0$). The hyperfine lines are not resolved at perpendicular component. It is possible to infer that the trend for the location of magnetic electron (in $d_x{}^2{}_{-y}{}^2$orbital) continues due to $g_\parallel > g_\perp > 2$. An analysis of the frozen state spectrum gives $g_\parallel = 2.28$, $g_\perp = 2.05$, and $A_\parallel = 15.76$ mT. On the whole, these observations suggest a distorted square-pyramidal geometry.

Antibacterial Activity

In *Pseudomonas fluorescens* plate the acetate monomer showed a zone of inhibition 23 mm as compared with streptomycin 23 mm. Interestingly, the antibacterial activity of title Cu(II) complex was more pronounced against *Bacillus subtilis* plate with a zone of inhibition of 30 mm as compared with that of 23 mm against streptomycin.[17–19] Methanol alone did not show any inhibition.

CONCLUSION

We have successfully synthesized a new mononuclear copper(II) complex having a slight distorted square-pyramidal structure as observed by XRD data. As revealed by EPR studies, it is paramagnetic in nature. Although the antibacterial activity of this complex against *Pseudomonas fluorescens* was only equivalent to that of standard streptomycin, it was found to be more pronounced against *Bacillus subtilis*.

SUPPLEMENTARY MATERIALS

Crystallographic information of the complex has been deposited with the Cambridge Crystallographic Data Centre, CCDC no. 867608. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data–request/cif.

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