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Some new Cu(II) complexes containing an ON donor Schiff base: Synthesis, characterization and antibacterial activity

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Crystal structure
2-Hydroxy-4-methoxy-benzaldehyde

ABSTRACT

Six new copper(II) complexes, $CuLCl{\cdot}H_2O$ (**1**), $CuL(NO_3){\cdot}2H_2O$ (**2**), $[Cu(L)_2]$ (**3**), $CuL(SCN){\cdot}2H_2O$ (**4**), $CuL(ClO_4){\cdot}2H_2O$ (**5**) and $(CuL)_2(SO_4){\cdot}4H_2O$ (**6**), where HL = 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one, have been synthesized. The characterization of the newly formed compounds was done by ^1H NMR, UV–Vis, IR, ESR spectroscopy, elemental analysis and molar electric conductivity. The crystal structure of 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one has been determined by X-ray diffraction studies, as well as the crystal structure of one of its copper(II) complexes, $[Cu(L)_2]$ (**3**). The copper atom is coordinated to two nitrogen and two oxygen atoms of the Schiff base ligand. The in vitro antibacterial activity against *Klebsiella pneumoniae ATCC 100131*, *Staphylococcus aureus var. Oxford 6538*, *Pseudomonas aeruginosa ATCC 9027* and *Escherichia coli ATCC 10536* strains was studied and compared with that of free ligand. The anti-microbial activity was dependent on the microbial species tested and the metal salt anion used.

1. Introduction

Pyrazolones constitute a group of organic compounds that have been extensively studied due to their properties and applications. On the other hand, pyrazolone-based Schiff base chemistry is less extensive. Some groups have reported the synthesis and characterization of pyrazolone-based Schiff base ligands and their Cu(II) complexes [1–4]. The Schiff base of 4-aminoantipyrine and its complexes have a variety of applications in biological, clinical, analytical and pharmacological areas [5–7]. Studies of a new kind of chemotherapeutic Schiff base are now attracting the attention of biochemists [8,9].

In a previous paper [10] we presented the synthesis of Cu(II) complexes derived from the new Schiff base ligands obtained by condensation of 4-amino-antipyrine with 2-hydroxybenzaldehyde, terephthalic aldehyde, 4-hydroxy-5-methoxy-isophthalaldehyde, 4,5-dihydroxy-isophthalaldehyde and 3-formyl-6-methyl-chromone. This paper is a continuation of our previous research and it presents the synthesis and characterization of new complexes of Cu(II) with a new Schiff base (Fig. 1) obtained by the condensation of 4-aminoantipyrine with 2-hydroxy-4-methoxy-benzaldehyde. The complexes and ligand were also tested for their in vitro antibacterial activity against *K. pneumoniae*, *S. aureus*, *P. aeruginosa* and *E. coli* strains using the paper disc diffusion method and the serial dilutions in liquid broth method [11,12].

2. Experimental

2.1. Materials

2-Hydroxy-4-methoxy-benzaldehyde (Aldrich) and 1-phenyl-2,3-dimethyl-4-amino-3-pyrazolin-5-one (Merck) were used as received. The metal salts $CuCl_2{\cdot}2H_2O$, $Cu(NO_3)_2{\cdot}3H_2O$, $CuSO_4{\cdot}5H_2O$, $Cu_2(OAc)_4{\cdot}(H_2O)_2$, $Cu(ClO_4)_2{\cdot}6H_2O$ and KSCN (Merck) were used as supplied. Solvents used for the reactions were purified and dried by conventional methods [13]. *Caution*! Perchlorate complexes of metals with organic ligands are potentially explosive and should be handled with care.

2.2. Synthesis of the Schiff base 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one (HL)

A solution of 1-phenyl-2,3-dimethyl-4-amino-3-pyrazolin-5-one (0.203 g, 1 mmol) in ethanol (10 mL) was added to a solution

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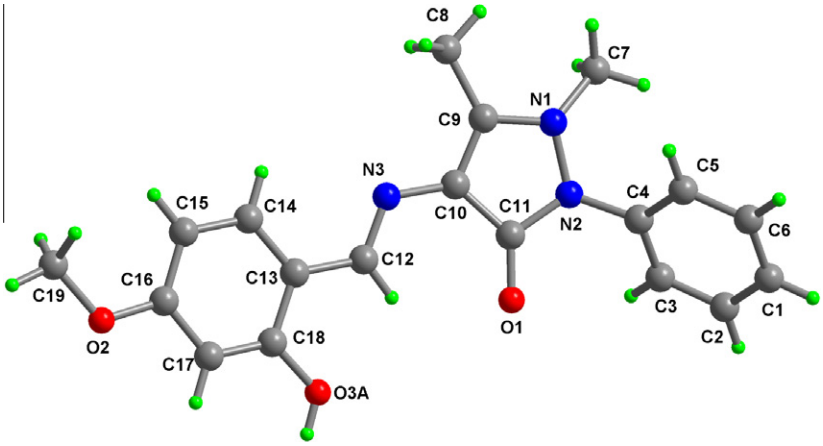


Fig. 1. Perspective view of the HL molecule, along with atom numbering scheme.

of 2-hydroxy-4-methoxy-benzaldehyde (0.152 g, 1 mmol) in ethanol (20 mL). The reaction mixture was stirred for 2 h at room temperature, then heated to reflux for 2 h and kept at 4 °C for three days. The characteristic yellow precipitate obtained was filtered and recrystallized by dissolving in methanol. Fine yellow crystals obtained upon slow evaporation at room temperature were characterized, including single crystal X-ray diffraction.

Yield 76%; M.p.: 192–193 °C; M.wt.: 337; *Anal.* Calc. for $C_{19}H_{19}N_3O_3$: C, 67.65; H, 5.63; N, 12.46. Found: C, 68.17; H, 5.22; N, 12.08%. The IR spectrum of the obtained ligand confirms the occurrence of an absorption band at 1629 cm^{-1} (st, intense), specific for the azomethinic group [14]. ^1H NMR ($CDCl_3$, δ, ppm, *J*, Hz): 2.35 (s, 3H, CH_3-8); 3.15 (s, 3H, N–CH_3-7); 3.76 (s, 3H, OCH_3); 6.42 (d, 8.5, 1H, H-17); 6.50 (d, 8.5, 1H, H-18); 7.32 (s 1H, H-15); 7.42–7.50 (m, 5H, 1, 2, 3, 5, 6); 9.57 (s, 1H, H-12, CH=N); ^{13}C NMR (DMSO-d_6, δ, ppm): 9.90 (C-8); 35.33 (C-7); 55.49 (OCH_3); 132.83 (CH-15); 134.39 (C-4); 149.68 (C-10); 157.97 (C-16); 159.43 (C-12); 162.58 (C-14).

2.3. General procedure for the preparation of the metal complexes (**1**–**6**)

Complexes **1**–**3**, **5** and **6** were prepared by the direct reaction between the ligand and the corresponding metal salts. Complex **4** was obtained by refluxing a mixture of $CuCl_2{\cdot}2H_2O$ and 1-phenyl-2,3-dimethyl-4-(N-2-hydroxy-4-methoxy-benzaldehyde)-3-pyrazolin-5-one with addition of KSCN [15].

2.3.1. Synthesis of the complex $CuLCl{\cdot}H_2O$ (**1**)

An ethanol solution of $CuCl_2{\cdot}2H_2O$ (2 mmol, 15 mL aqueous/ethanol 1:2 v/v) was added dropwise to a stirred ethanol solution of the Schiff base ligand HL (2 mmol, 15 mL). The resulting solution was stirring for 3 h at room temperature. The green–brown colored solid was filtered, washed with hot water, then ethanol followed by ether and dried in *vacuo*. Yield: 77%; M.p. >220 °C; M.wt.: 453; *Anal.* Calc. for $C_{19}H_{20}CuN_3O_4Cl$: C, 50.33; H, 4.41; N, 9.27; Cu, 14.01. Found: C, 50.72; H, 4.27; N, 8.98; Cu, 13.92%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1636; υ(C=N) 1607; υ(Ar–OH) 1120; υ(Ar–O–$C_{aliphatic}$) 1240, 1025, υ(OH^-) 3450. The complex is soluble in DMF and DMSO, and is partially soluble in chloroform and methanol.

2.3.2. $CuL(NO_3){\cdot}2H_2O$ (**2**)

Dark-green solid. Yield: 89%; M.p. 220 °C; M.wt.: 497.5; *Anal.* Calc. for $C_{19}H_{22}CuN_4O_8$: C, 45.83; H, 4.42; N, 11.25; Cu, 12.76. Found: C, 46.14; H, 4.16; N, 11.02; Cu, 12.59%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1636; υ(C=N) 1602; υ(Ar–OH) 1117; υ(Ar–O–$C_{aliphatic}$) 1242, 1022; υ(OH^-) 3434; υ_5(NO_3^-) 1494; υ_1(NO_3^-) 1297; υ_2(NO_3^-) 925. The complex is soluble in DMF and DMSO, and is partially soluble in methanol.

2.3.3. $[CuL_2]$ (**3**)

Brown solid, X-ray quality single crystals were obtained. Yield: 83%; M.p. >220 °C; M.wt.: 735.5; *Anal.* Calc. for $C_{38}H_{36}CuN_6O_6$: C, 61.99; H, 4.89; N, 11.42; Cu, 8.63. Found: C, 62.28; H, 4.33; N, 11.16; Cu, 8.48%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1648; υ(C=N) 1609; υ(Ar–OH) 1121; υ(Ar–O–$C_{aliphatic}$) 1243, 1024. The complex is soluble in chloroform, DMF and DMSO, and is partially soluble in methanol.

2.3.4. $CuL(SCN){\cdot}2H_2O$ (**4**)

Green solid. Yield: 78%; M.p. >220 °C; M.wt.: 493.5; *Anal.* Calc. for $C_{20}H_{22}CuN_4O_5S$: C, 48.63; H, 4.45; N, 11.34; Cu, 12.86. Found: C, 49.08; H, 4,22; N, 11.07; Cu, 12.60%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1632; υ(C=N) 1610; υ(Ar–OH) 1120; υ(Ar–O–$C_{aliphatic}$) 1241, 1029; υ(OH^-) 3437. The complex is soluble in DMF, DMSO and chloroform, and is partially soluble in methanol.

2.3.5. $CuL(ClO_4){\cdot}2H_2O$ (**5**)

Green solid. Yield: 72%; M.p. >220 °C; M.wt.: 535; *Anal.* Calc. for $C_{19}H_{22}CuN_3O_9Cl$: C, 42.61; H, 4.11; N, 7.85; Cu, 11.86. Found: C, 43.14; H, 3.88; N, 7.55; Cu, 11.47%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1637; υ(C=N) 1605; υ(Ar–OH) 1120; υ(Ar–O–$C_{aliphatic}$) 1240, 1027; υ(OH^-) 3440. The complex is soluble in DMF, DMSO and chloroform, and is partially soluble in methanol.

2.3.6. $(CuL)_2(SO_4){\cdot}4H_2O$ (**6**)

Dark-green solid. Yield: 83%; M.p. >220 °C; M.wt.: 967; *Anal.* Calc. for $C_{38}H_{44}Cu_2N_6O_{14}S$: C, 47.15; H, 4.55; N, 8.68; Cu, 13.13. Found: C, 47.63; H, 4.31; N, 8.36; Cu, 12.76%. Main IR peaks (KBr, cm^{-1}): υ(C=O) 1636; υ(C=N) 1606; υ(Ar–OH) 1119; υ(Ar–O–$C_{aliphatic}$) 1243, 1024; υ(OH) 3436, υ_3(SO_4^{-2}) 1113; υ_4(SO_4^{-2}) 616. The complex is soluble in chloroform, DMF and DMSO, and is partially soluble in ethanol and methanol.

2.4. Physical measurements

C, H and N analyses were performed with a Carlo-Erba LA-118 microdosimeter whereas an AAS-1 N Carl-Zeiss-Jena spectrometer was used for the determination of Cu(II). Physico-chemical analyses were performed after drying the complexes at 105 °C. Infrared spectra (4000–400 cm^{-1}) were recorded on a BioRad FTS 135

spectrophotometer, using KBr pellets. The ^{1}H NMR spectra were recorded on a Bruker 400 DRX spectrometer in $CDCl_3$ solution, using TMS as the internal standard. Diffuse reflectance spectra were recorded on a Jasco V-670 spectrophotometer, in diffuse reflectance, using MgO dilution matrices. Electron paramagnetic resonance (EPR) measurements were performed on polycrystalline powders and DMSO solutions, at room temperature and 77 K, with a MiniScope MS200, Magnettech Ltd., X-band spectrometer (9.3–9.6 GHz), connected to a PC equipped with a 100 kHz field modulation unit. The magnetic susceptibility measurements were carried at room temperature in the polycrystalline state on a Faraday magnetic balance (homemade). The complexes were studied by thermogravimetry (TG) in static air atmosphere, with a sample heating rate of 10 °C/min. using a DuPont 2000 ATG thermo balance. The molar conductances of the complexes in dimethylformamide solutions (10^{-3} M), at room temperature, were measured using a Consort type C-533 conductivity instrument.

2.5. X-ray crystallography

A summary of the crystallographic data and details of the data collection of **HL** and **3** are given in Table 1. Selected bond lengths and bond angles are given in Table 2. A crystal of suitable size was selected from the mother liquor and immersed in paratone oil, then mounted on the tip of a glass fiber and cemented using epoxy resin. XRD data were collected on a STOE IPDS II image plate detector using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å), at room temperature. Data collection: Stoe x-area. Cell refinement: Stoe x-area [16a]. The structures were solved by direct methods and refined with anisotropic displacement parameters based on F^2, using SHELXS 97 [16b] and SHELXL 97 [16c] programs. Packing and H-bonding diagrams are generated by the DIAMOND program. Non-hydrogen atoms were refined anisotropically until convergence was reached. The hydrogen atoms were stereochemically fixed in their ideal positions with fixed isotropic *U* values.

2.6. Antibacterial activity

The free ligand and metal complexes were screened for their *in vitro* antibacterial activity against *K. pneumoniae*, *S. aureus*, *P. aeruginosa* and *E. coli* strains using the paper disc diffusion method [17a] (for the qualitative determination) and the serial dilutions in liquid broth method [17b] (for determination of MIC). Streptomycin was used as internal standard.

Suspensions of microorganisms in sterile peptone water were adjusted to 0.5 McFarland. Muller–Hinton petri dishes of 90 mm were inoculated using these suspensions. Paper disks (6 mm in diameter) containing 10 μL of the substance to be tested (at a concentration of 2048 μg/mL in DMSO) were placed in a circular pattern in each inoculated plate. Incubation of the plates was done at 37 °C for 24 h. The reading of the results was done by measuring the diameters of the inhibition zones generated by the tested substances, using a ruler. Determination of MIC (μg/mL) was done using the serial dilutions in liquid broth method. The materials used were 96-well plates, suspensions of microorganism (0.5 McFarland), Muller–Hinton broth (Merck) and solutions of the substances to be tested (2048 μg/mL in DMSO). The following concentrations of the substances to be tested were obtained in the 96-well plates: 1024; 512; 256; 128; 64; 32; 16; 8; 4; 2 μg/mL. After incubation at 37 °C for 24 h, the MIC for each tested substance was determined by macroscopic observation of microbial growth. It corresponds to the well with the lowest concentration of the tested substance where microbial growth was clearly inhibited.

Table 1
Crystallographic data, details of data collection and structure refinement parameters for compound **HL** and **3**.

Compound	HL	3
Chemical formula	$C_{19}H_{19}N_3O_3$	$C_{38}H_{36}CuN_6O_6$
M (g mol^{-1})	337.37	736.27
Temperature, (K)	293	293
Wavelength, (Å)	0.71073	0.71073
Crystal system	monoclinic	triclinic
Space group	$C2/c$	$P\bar{1}$
a (Å)	30.760(5)	10.755(3)
b (Å)	6.9320(8)	13.083(3)
c (Å)	17.077(3)	14.461(3)
α (°)	90	105.997(18)
β (°)	110.387(13)	102.276(18)
γ (°)	90	110.404(18)
V (Å^3)	3413.2(9)	1722.4(7)
Z	8	2
D_{calc} (g cm^{-3})	1.313	1.420
μ (mm^{-1})	0.091	0.691
F(0 0 0)	1424	766
Goodness-of-fit on F^2	0.948	0.947
Final R_1, wR_2 [$I > 2\sigma(I)$]	0.0675, 0.1401	0.0780, 0.1556
R_1, wR_2 (all data)	0.1476, 0.1670	0.1429, 0.1766
Largest difference in peak and hole (e Å^{-3})	−0.220, 0.272	−0.933, 0.529

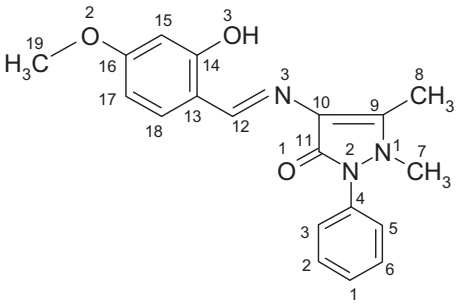
Table 2
Selected bond lengths (Å) and bond angles (°) of HL and compound **3**.

HL		3	
C10 N3	1.402(4)	C29 N1	1.426(8)
C12 N3	1.284(4)	C31 N1	1.307(7)
C11 O1	1.233(3)	C11 O3	1.226(8)
C16 O2	1.373(4)	C3 O1	1.353(8)
C19 O2	1.432(5)	C1 O1	1.442(8)
C8 C9	1.484(4)	C7 O2	1.309(7)
C9 N1	1.354(4)	C33 O4	1.297(7)
C9 C10	1.371(4)		
C11 N2	1.396(4)	Cu1 O4	1.901(4)
C10 C11	1.440(4)	Cu1 O2	1.912(5)
C16 C17	1.390(5)	Cu1 N2	1.966(4)
C17 C18	1.363(4)	Cu1 N1	1.972(5)
N1 N2	1.407(3)		
C4 N2	1.428(4)		
C5 C6	1.384(5)		
C7 N1	1.467(4)		
N3 C10 C11	128.8(2)	O4 Cu1 O2	92.75(19)
C12 N3 C10	120.7(3)	O4 Cu1 N2	144.3(2)
O1 C11 C10	131.5(3)	O2 Cu1 N2	95.99(19)
N2 C11 C10	104.8(2)	O4 Cu1 N1	95.64(18)
N3 C12 C13	121.5(3)	O2 Cu1 N1	137.1(2)
C9 N1 N2	106.9(2)	N2 Cu1 N1	101.06(19)
C9 N1 C7	125.5(3)		
N2 N1 C7	118.2(2)		
C11 N2 N1	109.4(2)		
C11 N2 C4	122.4(2)		
N1 N2 C4	120.5(2)		
O1 C11 N2	123.6(3)		
C16 O2 C19	117.5(3)		

3. Results and discussion

The present Schiff base HL (Scheme 1) was prepared under the method described elsewhere [10], by refluxing in ethanol (30 mL) an equimolar mixture of 4-aminoantipyrine with 2-hydroxy-4-methoxy-benzaldehyde. The structure of formed Schiff bases was established by IR, ^{1}H NMR and ^{13}C NMR spectroscopies and by X-ray crystallography.

All compounds were prepared by direct reaction between ligand and the corresponding metal salts, while compound **4** was prepared by using a mixture of $CuCl_2{\cdot}2H_2O$ and HL with addition



Scheme 1. Schiff base ligand HL (numbering similar to Fig. 1).

of KSCN. The obtained complexes are microcrystalline solids which are stable in air and have melting points above 220 °C. They are insoluble in organic solvents such as acetone, but soluble in methanol, DMF and DMSO. The molar conductivity values (8–12 ohm^{-1} cm^2 mol^{-1}) of the complexes **1**–**5** in 10^{-3} M solution DMF show that they are non-electrolytes and **6** (79 ohm^{-1} cm^2 mol^{-1}) is electrolyte [18]. The elemental analyses data of the Schiff base and complexes (reported in Section 2) are in agrement with structure of the ligand and with structures of the complexes (Scheme 2), respectively.

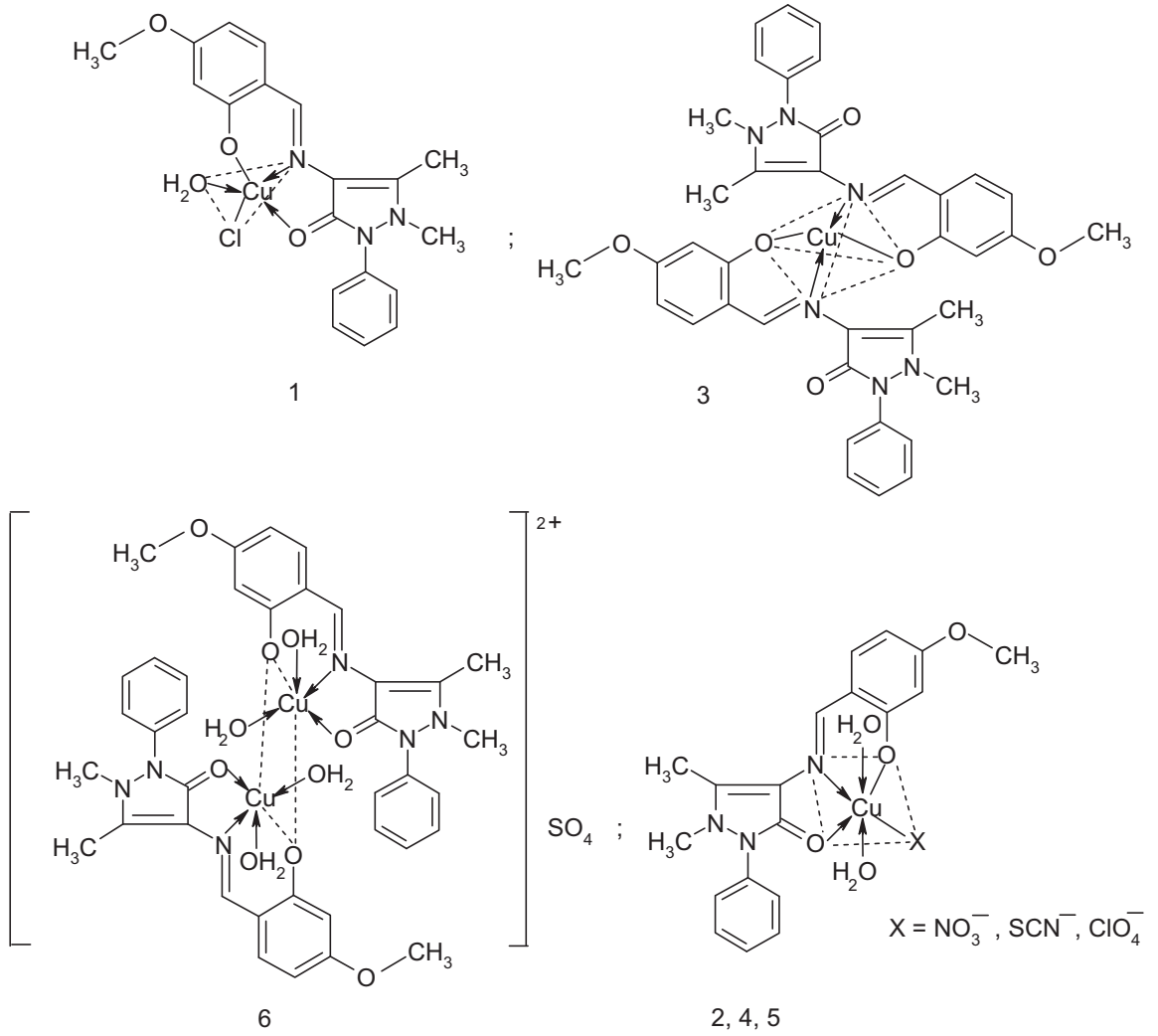
3.1. Structural characterization of HL and [Cu(L)$_2$] (**3**)

The structure of the Schiff base ligand HL is shown in Fig. 1. This ligand crystallizes in the monoclinic system, space group *C*2/*c*.

The OH bond is found to be disordered over two positions with a site occupational factor (s.o.f.) refined to 0.7 (O3) and 0.3 (O3A). The distance between the atoms C(12)–N(3) is 1.284(4) Å, suggesting the formation of an azomethine bond. Also, the bite angle [C(10)–N(3)–C(12) = 120.7(3)°] is proof of the sp^2 hybridization at the C(12) and N(3) atoms.

A perspective view of the molecule and its association through hydrogen bonds is represented in Fig. 2. In the crystal structure two types of hydrogen bonds coexist. Intramolecular interactions (70% molecules), Fig. 2a, are established between the O(3) and azomethine nitrogen atoms [O3A–N3 = 2.62 Å]. Intermolecular interactions, dimers present only in a small quantity (<30%), are established between the ligand molecules through O(1), the exocyclic ketonic oxygen of the antipyrine ring, and O(3A) of the 2-hydroxy-4-methoxy-benzaldehyde ring [O1···O3A = 2.87 Å], Fig. 2b.

The packing of the molecules in the crystal, Fig. 3, is influenced by van der Waals' interactions and π–π contacts (3.34–3.83 Å), established between the phenyl ring from one molecule and the antipyrine ring from another molecule. The 2-hydroxy-4-methoxy-benzaldehyde ring is almost in the same plane with central five-membered ring of the antipyrine moiety.



Scheme 2. Proposed structures of the metal complexes.

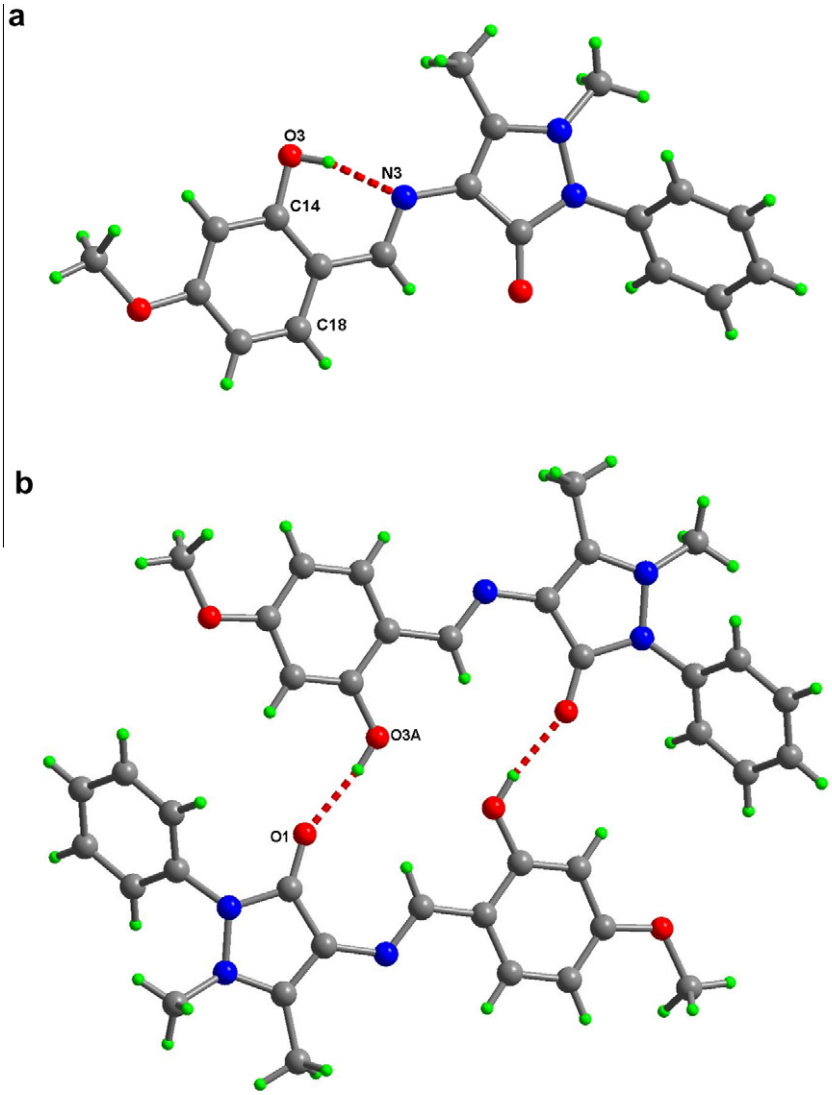


Fig. 2. Hydrogen bonding interactions: (a) intramolecular (b) intermolecular in **HL**.

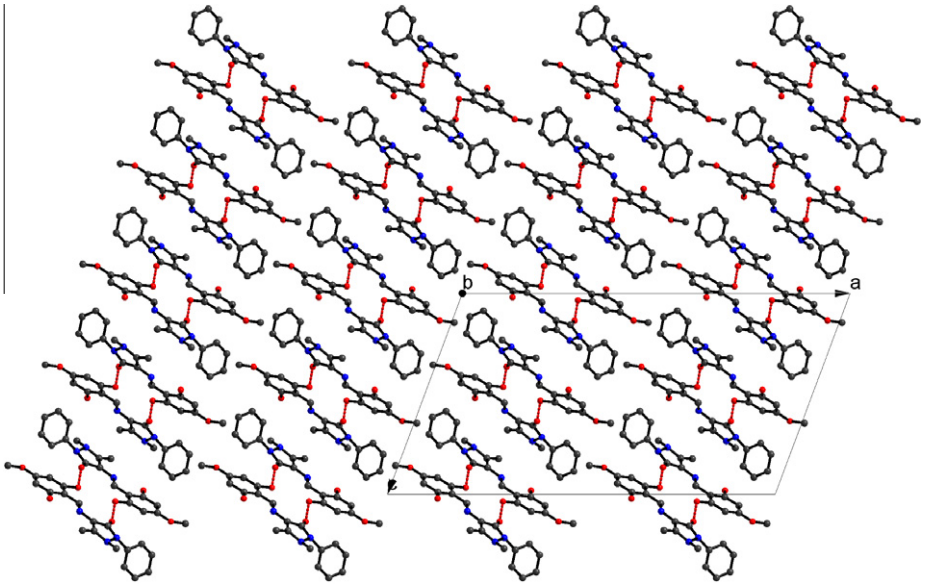


Fig. 3. Packing diagrams in the crystal **HL**.

The molecular structure of compound **3** is depicted in Fig. 4, and representative bond length and bond angle values are collected in Table 2. This compound crystallizes in the triclinic system, space group $P\bar{1}$.

The copper atom is coordinated to two nitrogen and two oxygen atoms of the Schiff base ligand. The dihedral angle θ between the two M(NO) planes is 53.74°. For a planar (local D_{2h}) geometry θ would be 0°, and for pseudo-tetrahedral (local D_{2d}) geometry θ would be 90°; the metal ion is therefore in a geometry that is much closer to pseudo-tetrahedral than planar. The bite angles O(1A)–Cu(1)–O(1) (92.75(19)°), N(3)–Cu(1)–O(1) (95.99(19)°), N(3A)–Cu(1)–O(1A) (95.64(18)°), N(3A)–Cu(1)–O(1) (137.1°), N(3)–Cu(1)–O(1A) (144.3°) and N(3)–Cu(1)–N(3A) (101.06°) also support the distortion from the tetrahedral geometry.

The C(7)–O(1) and C(33)–O(1A) bond lengths in the coordinated ligand are between the values for a double (1.23 Å) and single (1.43 Å) bond, which indicates significant delocalization of the π electrons of the 2-hydroxy-4-methoxy-benzaldehyde ring towards the oxygen atoms O(1) and O(1A), respectively [19].

The four independent Cu–N and Cu–O distances are in the range 1.901(4)–1.972(5) Å. The molecules are packed along the *c*-axis. The interactions between the phenyl ring of one molecule and the pyrazol moiety of another one reinforce crystal structure cohesion in the molecular packing in the crystal lattice.

3.2. Infrared spectra

The ligand and complexes have been characterized in detail by recording their IR spectra. The proposed assignments are based on previous results [10] and pertinent bibliography [24]. The ν(C=N) band of the ligand at 1629 cm^{-1} is found to be shifted to lower energies (1610–1602 cm^{-1}) in the spectra of the complexes, indicating coordination *via* the azomethine nitrogen. This is confirmed by bands in the range 467–463 cm^{-1}, which have been assigned to the ν(Cu–N) band [4,14a,20]. The ν(C=O) band of the ligand at 1646 cm^{-1}, for the exocyclic carbonyl group, is shifted by 10–14 cm^{-1} to lower energies in the spectra of the complexes **1**, **2**, **4–6**. This indicates that the exocyclic carbonyl oxygen is bonded to the metallic ions [4,14,20]. In the IR spectrum for complex **3**, ν(C=O) remains un-modified, indicating that the exocyclic ketonic oxygen of the antipyrine ring is not involved in the coordination [20].

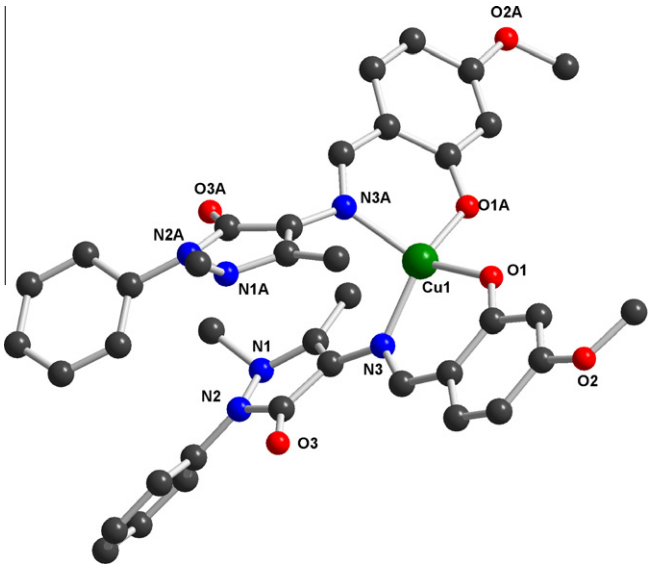


Fig. 4. Perspective view of complex **3** along with the atom numbering scheme.

In the IR spectrum of HL, a broad medium intensity band occurs in the 3500–3390 cm^{-1} range, along with a narrow band of medium intensity (1135 cm^{-1}), ascribed to the ν(OH) vibration of the hydroxymethyl group and H_2O. In the IR spectra of complexes **1**, **2**, **4–6**, a considerable peak observed in the 3450–3434 cm^{-1} range supports the presence of $\nu(H_2O)$ in the complexes [21].

The phenolic ν(C–O) stretching vibration in the free Schiff base is observed at 1135 cm^{-1} [17a], which is shifted by 14–18 cm^{-1} towards lower wavenumbers in the complexes, thus indicating coordination of the phenolic oxygen to the Cu^{2+} ion [22].

The nitrato complex **2** has two bands at 1494 and 1297 cm^{-1} corresponding to ν_5 and ν_1, with a separation of 197 cm^{-1}, and a medium band at 925 cm^{-1} assigned to ν_2 of the nitrato group. The separation ν_5–ν_1 can be used as a near criterion to distinguish between the degree of covalence of the nitrate coordination. These values indicating the presence of a terminal monodentate nitrato group [14a,14b,23].

The thiocyanato complex **4** exhibits a strong and sharp band at 2096 cm^{-1}, a weak band at 745 cm^{-1} and another weak band at 484 cm^{-1} which can be attributed to ν(CN), ν(CS) and δ(NCS), respectively. These values are typical for N-bonded thiocyanato complexes [23a,23b].

The perchlorate complex **5** shows a single band at 1087 cm^{-1} and a strong band at 628 cm^{-1}, indicating the presence of ionic perchlorate. The band at 1087 cm^{-1} is assignable to $\nu_3(ClO_4)$ and the band at 628 cm^{-1} is assignable to $\nu_4(ClO_4)$. The splitting of these bands shows the presence of a coordinated perchlorate group [14,24].The sulfato complex **6** has bands at 1113 and 616 cm^{-1}, assignable to ν_3 and ν_4, indicating the presence of a non-coordinated sulfato group [14,25].

3.3. Electronic spectra

The significant electronic absorption bands in the spectra of the ligand and all the complexes are presented in Table 3. The energy values of the d–d transitions suggest a tetragonal geometry for complexes **2**, **4–6**, a tetrahedral distorted geometry for complex **3** and a trigonal bipyramidal geometry for complex **1** [26]. The charge transfer band for the complexes appeared at 26 300–25 000 cm^{-1} with a shoulder at 23 250–22 250 cm^{-1}[21].

The values of μ_{eff} (1.76–2.06 BM) for complexes **1–5** suggest the presence of an unpaired electron. Also, it indicates the existence of monomeric species of copper(II). Complex **6** shows a very low magnetic moment of 1.44 BM per copper center, measured at room

Table 3
Electronic spectra (cm^{-1}) and magnetic moment (BM) of the complexes **1–6**.

Metal complex molecular formula	Transitions d–d (cm^{-1})			μ_{eff} MB	Geometry
$[Cu(L)(H_2O)Cl]$ (**1**)	$^2A_{1g} \rightarrow {}^2B_{1g}$ 11 900		$^2A_{1g} \rightarrow {}^2B_{2g}$ 17 240	2.06	Trigonal bipyramidal
$[Cu(L)(NO_3)(H_2O)_2]$ (**2**)	$^2B_{1g} \rightarrow {}^2A_{1g}$ -	$^2B_{1g} \rightarrow {}^2E_g$ 18 310	$^2B_{1g} \rightarrow {}^2B_{2g}$ 13 550	1.89	Tetragonal
$[Cu(L)_2]$ (**3**)	$^2B_2 \rightarrow {}^2E$-		$^2B_2 \rightarrow {}^2B_1(^2A_1)$ 14710	1.97	Tetrahedral (distortion)
$[CuL(SCN)(H_2O)_2]$ (**4**)	$^2B_{1g} \rightarrow {}^2A_{1g}$ -	$^2B_{1g} \rightarrow {}^2E_g$ 17 880	$^2B_{1g} \rightarrow {}^2B_{2g}$ 13 250	1.76	Tetragonal
$[CuL(ClO_4)(H_2O)_2]$ (**5**)	$^2B_{1g} \rightarrow {}^2A_{1g}$ -	$^2B_{1g} \rightarrow {}^2E_g$ 18 310	$^2B_{1g} \rightarrow {}^2B_{2g}$ 13 620	1.78	Tetragonal
$[Cu_2(L)_2(H_2O)_4]SO_4$ (**6**)	$^2B_{1g} \rightarrow {}^2A_{1g}$ -	$^2B_{1g} \rightarrow {}^2E_g$ 18 510	$^2B_{1g} \rightarrow {}^2B_{2g}$ 13 790	1.44	Tetragonal

temperature. The subnormal magnetic moment indicates that the copper centers are antiferromagnetically coupled [27].

3.4. EPR spectra

The EPR spectra of polycrystalline samples at 298 K, and DMSO solutions at 298 and 77 K were recorded in the X-band using 100-kHz modulation and g factors were quoted relative to the standard marker TCNE ($g = 2.00277$). EPR spectral assignments of the copper(II) complexes and orbital reduction parameters are in Table 4. The EPR spectra of the complexes recorded in the polycrystalline state provide information about the coordination environment around copper(II). The EPR spectra of complexes **1–6** in the polycrystalline state at 298 K shows different types of geometrical species. The spectrum of complex **1** (Fig. 5) shows three g values: $g_3 = 2.236$, $g_2 = 2.127$, $g_1 = 2.055$, which indicate a trigonal bipyramidal geometry [28]. In trigonal bipyramidal complexes the unpaired electron lies in the d_z^2 orbital, giving $^2A_{1g}$ as the ground state. The g and $A_{//}$ tensor values ($g_{//} = 2.405$, $g_\perp = 2.052$, $A_{//} = 117$ G) suggests that complex **3** has a distorted tetrahedral geometry, which is in good agreement with the X-ray determined structure.

The spectra of the complexes **2** and **4–6** show axial symmetry with well-defined $g_{//}$ and $g_\perp$ values. In these Cu(II) complexes, tensor values of $g_{//} > g_\perp$ are consistent with a $d_x^2 - y^2$ ground state [29]. For complex **6**, a half field signal at $g = 4.187$ was observed, indicating a dimeric species [10d,24].

The geometric parameter G, which is a measure of the exchange interaction between copper centers in a polycrystalline compound, is calculated using the equation $G = (g_{//} - 2)/(g_\perp - 2)$ for axial spectra, and for rhombic spectra, $G = (g_3 - 2)/(g_\perp - 2)$ and $g_\perp = (g_1 + g_2)/2$. G values less than 4.0 are consistent with a $d_x^2 - y^2$ ground state having a small exchange coupling (complexes **2**, **4–6**). If G is higher than 4.0, the exchange interaction is negligible (complex **3**) [30].

The EPR spectra of complex **1** in DMSO solution at 77 K, shows a typical distorted tetrahedral geometry, with values: $g_{//} = 2.413$ and $g_\perp = 2.080$ and hyperfine splitting into four lines. The EPR spectra of complexes **2–6** in DMSO solution at 77 K are axial. These show four well defined hyperfine lines in the parallel region corresponding to the electron spin-nuclear spin interaction. The EPR spectra of complexes **1**, **3** and **6** in DMSO solution at 77 K are given in Fig. 6.

The $g_{//}$ values are nearly the same for all the complexes, indicating that the bonding is dominated by the 4-amino-antipyrine moiety. In all the complexes, $g_{//} > g_\perp$. The fact that $g_{//}$ values are less than 2.3 is an indication of significant covalent character to the M–L bond [29a,29c].

The EPR parameters $g_{//}$, $g_\perp$, $A_{//}$ (Cu) and the energies of the d–d transition were used to evaluate the bonding parameters α^2, β^2 and δ^2, which may be regarded as measures of the covalency of the in-plane σ bonds, in-plane π bonds and out-of-plane π bonds [30a,31]. The orbital reduction factors $K_{//} = \alpha^2\beta^2$ and $K_\perp = \alpha^2\delta^2$ were calculated using expressions reported elsewhere [32]. Hathaway has pointed out that for pure σ bonding, $K_{//} \approx K_\perp \approx 0.77$ and for in-plane π-bonding, $K_{//} < K_\perp$, while for out-of-plane π-bonding, $K_{//} > K_\perp$ [33].

Table 4
EPR spectral parameters of the copper(II) complexes **1–6**.

	1	2	3	4	5	6
Polycrystalline(298 K)						
$g_{//}$	2.236(g_3)	2.220	2.405	2.256	2.240	2.363
$g_\perp$	2.055(g_1) 2.127(g_2)	2.068	2.052	2.065	2.062	2.162
DMSO (77 K)						
$g_{//}$	2.413	2.292	2.290	2.287	2.289	2.285
$g_\perp$	2.08	2.078	2.070	2.062	2.072	2.07
$A_{//}$	125	152	160	148	154	166
α^2	0.830	0.784	0.801	0.760	0.782	0.812
β^2	0.990	0.980	0.887	0.991	0.979	0.943
δ^2	0.873	0.998	0.963	0.904	0.963	0.918
$K_{//}$	0.822	0.768	0.710	0.753	0.766	0.766
$K_\perp$	0.525	0.783	0.771	0.687	0.753	0.746

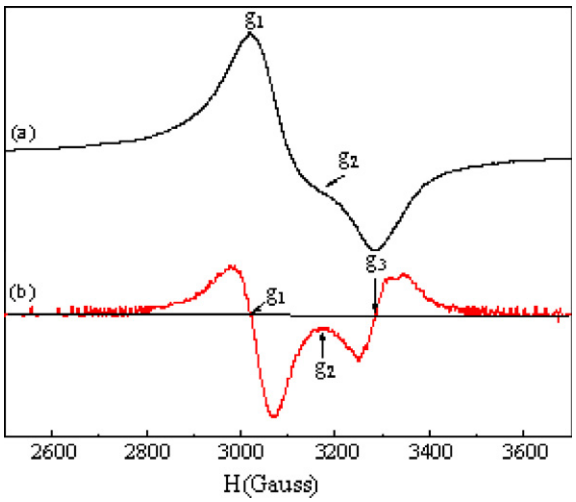


Fig. 5. (a) EPR spectrum of **1** in the polycrystalline state at 77 K; (b) second derivative spectrum at 77 K.

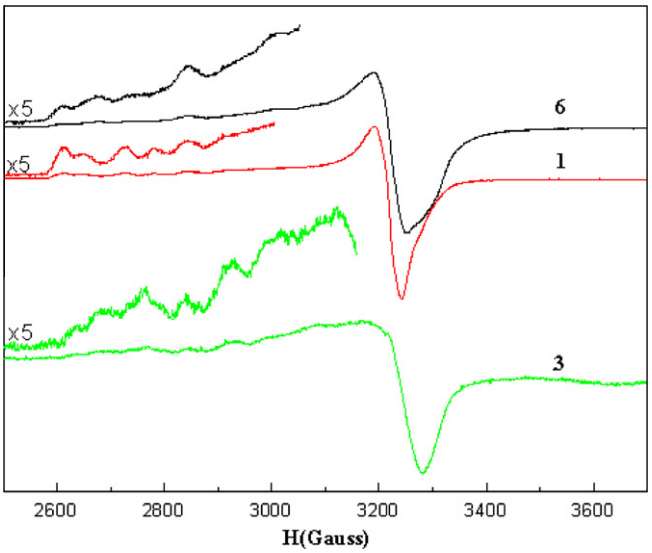


Fig. 6. EPR spectra of **1**, **3** and **6** in DMSO solution at 77 K.

The empirical factor $f = g_{//}/A_{//}$ cm^{-1} is an index of tetragonal distortion. Values of this factor may vary from 105 to 135 for small to extreme distortions in square planar complexes and it depends on the nature of the coordinated atoms [34]. The f values of complexes **2–6** are found to be in the range 137–154, indicating significant distortion from planarity.

3.5. Anti-microbial activity

The free ligand and its metal complexes were screened for their antibacterial activity. The results (Table 5) indicate that the ligand does not have any significant activity, whereas its complexes showed more activity against the some microorganisms under identical experimental conditions.

Table 5
Antibacterial activities of ligand HL and its Cu(II) complexes **1**–**6** as MIC values (μg/mL).

Compound	Gram-positive bacteria[a]		Gram-negative bacteria[b]	
	Kp	***Sa. Oxf***	***Pa***	***Ec***
HL	128	256	256	512
$[Cu(L)Cl(H_2O)]$ (**1**)	16	8	128	16
$[Cu(L)(NO_3)(H_2O)_2]$ (**2**)	128	128	256	256
$[Cu(L)_2]$ (**3**)	8	4	16	64
$[CuL(SCN)(H_2O)_2]$ (**4**)	64	64	256	512
$[CuL(ClO_4)(H_2O)_2]$ (**5**)	256	128	256	512
$[Cu_2(L)_2(H_2O)_4]SO_4$ (**6**)	8	16	128	16
$CuCl_2{\cdot}2H_2O$	512	512	512	1024
$Cu(NO_3)_2{\cdot}3H_2O$	1024	512	1024	1024
$Cu(OAc)_2{\cdot}H_2O$	512	1024	1024	512
$Cu(ClO_4)_2{\cdot}6H_2O$	512	1024	1024	1024
$CuSO_4{\cdot}5H_2O$	512	512	1024	512
Streptomicina	8	4	16	8

[a] Kp (*Klebsiella pneumoniae* ATCC 31488); Sa (*Staphylococus aureus* var. Oxford ATCC 6538).
[b] Pa (*Pseudomonas aeruginosa* ATCC 9027); Ec (*Escherichia coli* ATCC 10536).

The synthesized Schiff base has an inhibitory effect (MIC values in range 128–512 μg/mL) on the growth of the tested strains. All the complexes show greater bactericidal activities against *E. coli* (MIC 16–512 μg/mL), *S. aureus* (MIC 4–128 μg/mL), *P. aeruginosa* (MIC 16–256 μg/mL) and *K. pneumoniae* (MIC 8–256 μg/mL) as compared to their corresponding ligand (with the exception for **2** and **5**, which exert a visible decrease of the action).

The high bactericidal activity of complex **1** against *S. aureus* is probably predetermined by its tetrahedral geometry in DMSO solution. Complex **3** was found to have better activity against all the bacterial species, probably due the axial symmetry (square planar) in DMSO solution. In case of **6**, the presence of the SO_4^{2-} moiety induced a visible increase of action against all the bacterial species taken in the study.

4. Conclusions

Physico-chemical analyses confirmed the composition and structures of the newly obtained complex combinations. Depending on the metal salt anion used, the ligand acts as mononegative bidentate (when reacted with $Cu_2(OAc)_4{\cdot}(H_2O)_2$) or mononegative tridentate (when reacted with $CuCl_2{\cdot}2H_2O$, $Cu(NO_3)_2{\cdot}3H_2O$, $CuSO_4{\cdot}5H_2O$ and $Cu(ClO_4)_2{\cdot}6H_2O$). The single crystal X-ray structure of **3**, being the first in the series of this type of compound, illustrates that the steric effect can have a profound influence on the Cu(II) geometry, rearranging into a distorted tetrahedral geometry. The anti-microbial activity was dependent on the microbial species tested and the metal salt anion used.

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Appendix A. Supplementary data

CCDC 742652 and 742653 contains the supplementary crystallographic data for $C_{19}H_{19}N_3O_3$ (**HL**) and $C_{38}H_{36}CuN_6O_6$ (**3**). These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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