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Synthesis, structural characterization, superoxide dismutase and antimicrobial activities studies of copper (II) complexes with 2-(*E*)-(2-(2-aminoethylamino) methyl)-4-bromophenol and (19*E*, 27E)-N^1, N^2-*bis* (phenyl (pyridine-2-yl)-methylene)-ethane-1, 2-diamine as ligands

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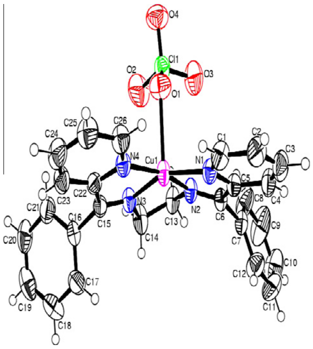
HIGHLIGHTS

- Design of new ligands (HL/L^1) and copper (II) complexes.
- Single crystal X-ray analysis.
- Superoxide dismutase activity determination.
- Magnetic susceptibility measurements.
- Antimicrobial activity.

GRAPHICAL ABSTRACT

Three new copper (II) complexes, $[Cu(L)(H_2O)]ClO_4$ (**1**), $[Cu(L^1)(ClO_4)]^+$ (**2**) and $[Cu(L^1)]^{2+}$ (**3**), derived from 2-(*E*)-(2-(2-aminoethylamino)methyl)-4-bromophenol (HL) and (19*E*, 27*E*)-N^1,N^2-bis(phenyl (pyridine-2-yl)-methylene)-ethane-1, 2-diamine(L^1), were synthesized and characterized by using various physic-chemical and spectroscopic methods. The solid-state structures of complexes **1** and **2** (Fig. 4) were determined by single crystal X-ray crystallography which revealed distorted square pyramidal geometry around Cu (II) ion.



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ABSTRACT

Three new copper (II) complexes, $[Cu(L)(H_2O)]ClO_4$ (**1**), $[Cu(L^1)(ClO_4)]^+$ (**2**) and $[Cu(L^1)]^{2+}$ (**3**), where HL = 2-(*E*)-(2-(2-aminoethylamino)methyl)-4-bromophenol, L^1 =(19*E*, 27*E*)-N^1,N^2-*bis(*phenyl(pyridine-2-yl)-methylene)-ethane-1, 2-diamine, have been synthesized and characterized by using various physic-chemical and spectroscopic methods. The solid-state structures of **1** and **2** were determined by single crystal X-ray crystallography. Infrared spectra, ligand field spectra and magnetic susceptibility measurements agree with the observed crystal structures. The molecular structure of copper complexes showed that the ligands occupies the basal plane of square pyramidal geometry with the H_2O of **1** or the ClO_4 of **2** occupying the remaining apical position. Complexes **1** and **2** crystallize in the monoclinic system of the space group $P2_{1/c}$, a = 10.5948(6)Å, b = 19.6164(11)Å, c = 8.6517(5)Å, α = 90°, β = 108.213(2)°, γ = 90° and Z = 4 for **1**, a = 9.5019(3)Å, b = 11.3 801(3)Å, c = 25.3168(14)Å, α = 90°, β = 100.583(4)°, γ = 90°, and Z = 4 for **2**. The synthesized Schiff base (HL/L^1) was behaves as tetradentate ON_3/N_4 ligands with donor groups

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suitable placed for forming 2 or 3 five membered chelate rings. Copper (II) complexes display X-band EPR spectra in 100% DMSO at 77 K giving $g_{||} > g_{\perp} > 2.0023$ indicating $d_{x^2-y^2}$ ground state. The half-wave potential values for Cu (II)/Cu (I) redox couple obtained in the reaction of the copper (II) complexes with molecular oxygen and superoxide radical (O_2^-) electronegated in DMSO are in agreement with the SOD-like activity of the copper (II) complexes. In *vitro* antimicrobial activities of the complexes against the two bacteria (*Escherichia coli*, *Salmonella typhi*) and the two fungi (*Penicillium*, *Aspergillus sp.*) have been investigated comparing with the Schiff base ligands.

Introduction

Transition metal complexes with Schiff base ligands have been widely investigated since such ligands can bind metal centers at more than one site and thus allow the successful synthesis of metal complexes with interesting stereochemistry and model enzymes/biological systems. The Schiff base of 5-bromo-2-hydroxybezaldehyde with *N*-(2-aminoethyl) ethane-1, 2-diamine has created a well-known class of metallo-biomolecules [1,2]. Similarly, a heterocyclic nucleus, namely pyridine base ligands has also been reported in many biochemical reactions to design and develop molecular systems of biological and medicinal importance. Benzoyl pyridine derivatives are important compounds in organic chemistry because of their application in heterocyclic synthesis and such ligating species on coordination with metal ions may emerge as a metal-mediated drugs. A 2-benzoyl pyridine derived Schiff base (19*E*, 27*E*)-*N*^{1}, *N*^{2}-*bis* (phenyl (pyridine-2-yl)-methylene)-ethane-1, 2-diamine has been used as a good chelating agent with 3d-metal ions [3–8].

The activity of low-molecular weight copper (II) complexes mimicking the superoxide dismutase (SOD) activity [9–11], provide models for metalloproteins active sites and lend insight toward the design of new catalysts. Copper is a biologically relevant element and many enzymes that depend on copper for their activity have been identified. Among these complexes, copper (II) complexes are known to play a significant role in naturally occurring biological systems [12], like (Cu, Zn-SOD) superoxide dismutase. Superoxide dismutase (SOD) which can destroy the superoxide very rapidly is nature's agent for protection of the organism from this radical burden. In fact native SOD enzymes have been shown in many studies to exhibit protection in animal models of inflammatory diseases [13]. Oberley and Buettner [14] have reported that cancer cells had less superoxide dismutase (SOD) activity than normal cells. The SOD shows bio-catalytic activity towards the superoxide ion (O_2^-) is toxic to cells; a defense mechanism must have been initiated by nature. All organisms, which use dioxygen and many that have to survive an oxygenated environment, present SOD in their metabolism. These SODs disproportionate the toxic O_2^- to molecular oxygen and hydrogen peroxide [15,16]. All SOD employ the two step Ping–Pong mechanism shown in Eqs. (1) and (2), where Cu is the redox active metal center capable of both oxidizing and reducing superoxide activity.

$$O_2^- + Cu^{II} - SOD \rightarrow O_2 + Cu^{I} - SOD \tag{1}$$

$$O_2^- + Cu^{I} - SOD + 2H^+ \rightarrow H_2O_2 + Cu^{II} - SOD \tag{2}$$

Copper complexes (II) complexes have a wider range of coordination geometries than any other transition metal ions [17]. Copper complexes have shown anti-inflammatory, antitumor, anticonvulsant, anti- diabetic, anticancer, anti- carcinogenic, anti- mutagenic, radio protectant, antibacterial and antifungal activities in animal models of diseased states [18–22]. In a previous paper [23], we have reported 5-bromo-2-hydroxybezaldehyde Schiff base copper (II) complexes namely $[Cu(L^1)(bipy)]\cdot 2H_2O$ **1,** $[Cu(L^1)(dmp)]\cdot CH_3CN$ **2** and $[Cu(L^1)(phen)]$ **3** where, L^1H_2 = 2-{[(*Z*)-(5-bromo-2-hydroxyphenyl)methylidene]amino}benzoic acid. The solid-state structures of **1** and **2** were determined by single crystal X-ray crystallography, which revealed distorted square pyramidal geometry around Cu (II) ion.

In continuation of our work on Schiff base copper (II) complexes [24], we describes the synthesis, structural characterization, superoxide dismutase and antimicrobial activities studies of three new copper (II) complexes with 2-(*E*)-(2-(2-aminoethylamino) methyl) -4-bromophenol and (19*E*, 27*E*)-*N*^{1},*N*^{2}-*bis* (phenyl (pyridine-2-yl)-methylene)-ethane-1, 2-diamine as ligands. The copper (II) complexes were formulated as $[Cu(L)(H_2O)]ClO_4$ (**1**), $[Cu(L^1)(ClO_4)]^+$ (**2**) and $[Cu(L^1)]^{2+}$ (**3**). The crystal structure of these complexes $[Cu\ (L)\ (H_2O)]\ ClO_4$ (**1**), $[Cu\ (L^1)\ (ClO_4)]^+$ (**2**), are described. The 2-(*E*)-(2-(2-aminoethylamino) methyl)-4-bromophenol and (19*E*, 27*E*)-*N*^{1},*N*^{2}-*bis(*phenyl(pyridine-2-yl)-methylene)-ethane-1, 2-diamine Schiff bases behaves as a tetradentate ON_3/N_4 donor ligands (Schemes 1 and 2) with donor groups suitable placed for forming 2 or 3 five membered chelate rings. The mononuclear complexes (**1**) and (**2**) show pentacoordiated copper (II) ion with distorted square pyramidal coordination geometry whereas complex (**3**) have square planar geometry. The SOD activities have been measured using alkaline DMSO as a source of superoxide radical (O_2^-) and nitro blue tetrazolium (NBT) as O_2^- scavenger.

Experimental

Materials used for synthesis

All the chemicals and solvents used were synthetic grade, purchased from the commercial source and used without further purification.

Synthesis of ligands

Schiff bases (HL/L^1) were prepared by standard literature procedure [23,24] and recrystallized from ethanol or methanol.

2.2.1 Synthesis of 2-(E)-(2-(2-aminoethylamino) methyl)-4-bromophenol (HL)

The 2-(*E*)-(2-(2-aminoethylamino)methyl)-4-bromophenol Schiff base was synthesized by the condensation of an equimolar ratio of 5-bromo-2-hydroxybezaldehyde (20.0 mmol, 4.02 g) and *N*-(2-aminoethyl) ethane-1, 2-diamine, (20.0 mmol, 2.16 mL) dissolved in ethanol (Scheme 1). The resulting reaction mixture was refluxed on a water bath for 4 h and then allowed to cool overnight. The colored crystalline solid of the obtained Schiff base was filtered, washed with cold ethanol several times and dried in air at room temperature and finally preserved under reduced pressure in a desiccator. Yield: 80%. Anal. Found (%): C, 46.12; H, 5.59; N, 14.67. Calcd for $C_{11}H_{16}BrN_3O$ (%): C, 46.15; H, 5.58; N, 14.69.