Structure and antioxidant superoxide dismutase activity of copper(II) hydrazone complexes

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ABSTRACT : Three new mixed ligand hydrazone complexes viz., [Cu(L)(neocuprin)]NO₃.H₂O **1**, [Cu(L)(HL)]ClO₄ **2** and [Cu₂(2-(2-pyridyl)benzimidazole)₂(L)₂](ClO₄) **3** (L = *N'*-(*E*)-phenyl(pyridin-2-yl)methylidene]furan-2-carbohydrazide) have been synthesized by the biomimetic synthesis strategy and their structures were determined by single crystals X-ray analysis. The effect of differing contiguous, as well as the rotational conformational versatility of HL, was demonstrated by the difference in structures of complexes **1-3**. These complexes exhibited the antioxidant superoxide dismutase enzymatic activity. The geometry of copper(II) atom in complex **1** is distorted square pyramidal while in complexes **2** and **3** the geometries around copper(II) atoms are distorted octahedral. Magnetic measurements and epr spectroscopy of binuclear complex **3** have shown antiferromagnetic exchange interaction with a coupling constant (*J*) = -10.87 cm⁻¹. Electronic and spectral properties of these newly synthesized hydrazone complexes (**1-3**) are interpreted by DFT and TDDFT calculations. The results reveal that molecular structures have significant effect on antioxidant superoxide activity. Such biological experimental values (antioxidant SOD activity data) are indicative of the promising application of these complexes into the bioinorganic chemistry of superoxide dismutase.

1. Introduction

Antioxidant superoxide dismutases (SOD) are endogenous and first line defense enzymes that contain either Cu-Zn, Fe, Mn or Ni at the active site of these metalloenzymes. A large number of mononuclear Cu^{II}, dinuclear Cu^{II}-Cu^{II} or Cu^{II}-Zn^{II} low molecular weight complexes have been synthesized as superoxide dismutase mimics to emulate the structure and function of metal binding sites[1-15]. The synthesis of low molecular weight model compounds to mimic the active site of metalloenzyme has been an active area of research in the last few decades. However, these model complexes in homogeneous solution are still somewhat sensitive to the environments and they show lower activity and selectivity than the corresponding natural metalloenzymes. The main function of the metalloprotein backbone plays important roles in site-isolation, nanoconfinement and substrate duct to facilitate a specific catalytic function. Therefore, further integration of a scaffold with a model metal complex catalytic system would be most desirable to better mimic the structure and reactivity of metalloenzyme. For the ongoing integration of appropriate ligation with metal complex, site-isolation and confinement can be

achieved by appropriate design of the periphery of ligands allowing for effective catalysis to be tethered to a scaffold to achieve site-isolation and introduction of neighboring functionality to simulate the local environment of active center of the metalloenzyme[16]. All living organisms consume molecular oxygen as the ultimate oxidant supporting cellular respiration, but a considerable portion of molecular oxygen is metabolized through the one electron reduction product, superoxide anion ($O_2^{\cdot-}$). Respiring organisms have involved a system of defense against these dangerous metabolites which allows them to enjoy the benefits of living in an oxygen-rich environment. As a part of this protective arsenal, antioxidant superoxide dismutase are present in aerobes to catalyze the conversion of superoxide anion into H_2O_2 and O_2 (eq. 1,2 and Scheme I).

(ME = copper containing metalloenzyme)

Scheme I Half reactions for the dismutation of superoxide radical mediated by Cu-SOD enzyme.

This deleterious oxygen-derived free radical ($O_2^{\cdot-}$) has been demonstrated to be a mediator of reperfusion diseases, such as those following acute myocardial ischemia-reperfusion injury [17-20], inflammation [21-24] and cerebral ischemia reperfusion injury [25-27], neuronal apoptosis [28-32], cancer [33,34] and AIDS[33,34]. In light of clinical data surrounding the use of SOD metalloenzymes, low molecular weight mimics of the metalloenzymes (SOD models) have been proposed for treatment of several diseases. This aroused our interest in the synthesis of low molecular weight structural and functional model of antioxidant superoxide dismutase enzymes using biological ligands such as Schiff bases and benzimidazole. The importance of Schiff base complexes for bioinorganic chemistry, biomedical applications, supramolecular chemistry, catalysis and material science, separation and encapsulation processes and formation of compounds with unusual properties and structures has been well recognized and reviewed. Benzimidazole is an interesting heterocyclic ring because it is present in various naturally occurring drugs, such as omeprazole, astemizole and emedastine difumarate[35]. Interest in exploring metal complexes with ligands has continually increased, since the recognition that many of these materials may serve as models which mimic both the structure and reactivity of metal ion sites in complex biological systems[36,37] and possess a broad spectrum of biological activity[38,39]. So herein, we report three new copper mono- and binuclear complexes of *N*-

[(*E*)-phenyl(pyridin-2-yl)methylidene]furan-2-carbohydrazide. But, only a little attention has been paid to the structure–activity of the copper(II) complexes regarding their biological activity[40]. Structures of these complexes have been determined by single crystal X-ray analysis. DFT calculations have been done to compare the bond lengths and bond angles. Antioxidant superoxide dismutase assay was carried out by NBT methods[41,42].

2. Experimental

All the chemicals were reagent grade and used without further purification. The ligand *N'*-[(*E*)-phenyl(pyridin-2-yl)methylidene]furan-2-carbohydrazide (HL) was synthesized as described previously[40,43-45]. Water was purified using a millipore deionizing system to keep resistivity

2.1. Syntheses of mixed ligand copper(II) complexes.

2.1.1. Syntheses of [Cu(L)(neocuprin)]NO₃·H₂O **1**

To a methanol solution (20 ml) of neocuproin (0.217 g 1.0 mmol) was added drop wise Cu(NO₃)₂·3H₂O (0.241g, 1 mmol) in methanol (20 ml). The resulting mixture was allowed to stir for 15 min and then 20 ml of methanol solution of HL (0.291 g, 1 mmol) was added with stirring. Afterward, the resultant deep-blue solution was stirred for 1h at RT and filtered. After the filtration, solution was left to stand for few days at room temperature. Suitable crystals for X-ray analysis were obtained upon slow evaporation of a methanol solution. The crystals were collected by filtration and dried over fused CaCl₂. (Yield ~75%). Anal., Calcd. and X-ray for C₃₁H_{26.79} Cu N₆ O_{6.40} (*M* = 649.24 g mol⁻¹): Anal. C, 57.27; H, 4.14; N, 12.81 % Calcd.; C, 57.89; H, 4.19; N, 13.07; O, 14.93; Cu, 9.88; % X-ray; C, 57.29; H, 4.13; N, 12.94; O, 15.77; Cu, 9.79 %. FAB Mass (m/z) Anal.: 562.23, Calcd.: 562.11, X-ray 562.1. IR (KBr), cm⁻¹: 3453, 3068, 3007, 2922, 2415, 2167, 2014, 1596, 1564, 1495, 1442, 1391, 1318, 1263, 1200, 1154, 1088, 937, 860, 788, 701, 622, 549, 436 (See detail in Fig. S1).

2.1.2. Syntheses of [Cu(L)(HL)]ClO₄ **2**

A methanol solution (20 ml) of HL (0.582 g, 2 mmol) was added drop wise to methanol solution (20 ml) of Cu(ClO₄)₂·6H₂O (0.370g, 1 mmol) and the resulting solution was stirred for 3 h. The resulting green solution was filtered, suitable crystals for single crystal X-ray analysis were obtained upon slow evaporation at room temperature. The crystals were collected by filtration and dried over fused CaCl₂. (Yield ~73%). Anal., Calcd. and X-ray (%) for C₃₄H₂₅ Cu N₆ O₈ Cl (*M* = 744.60 g mol⁻¹): Anal. C, 54.83; H, 3.37; N, 11.25 % Calcd.; C, 54.84; H, 3.38; N, 11.26; O, 17.18; Cu, 8.52, Cl, 4.73 % X-ray; C, 54.85; H, 3.36; N, 11.29; O, 17.19; Cu, 8.53, Cl, 4.76 %; FAB MASS(m/z) Anal.: 645.14, Calcd.: 644.59, X-ray 644.95. IR (KBr), cm⁻¹: 3440, 3149, 2927, 2361, 1645, 1565, 1502, 1399, 1322, 1199, 1092, 1012, 971, 885, 790, 696, 621, 526, 432 (See detail in Fig. S2).

2.1.3. Syntheses of $[Cu(L)_2(2-(2\text{-pyridyl})\text{benzimidazole})_2]ClO_4$ **3**

Complex **3** was prepared by a method similar to that of complex **1**, except that 2-(2-pyridyl)benzimidazole (0.195g, 2 mmol) was added instead of neocuproin and metal salt was taken $Cu(ClO_4)_2 \cdot 6H_2O$ (0.740g, 2 mmol) in place of $Cu(NO_3)_2 \cdot 3H_2O$ in the molar ratio 2 : 2 : 2 in 20 ml of methanol. Diffraction quality single crystals were obtained after a few days by slow evaporation of dark green methanol solution of complex **3** in air at room temperature. The crystals were collected by filtration and dried over fused $CaCl_2$. (Yield ~75%). Anal., Calcd. and X-ray (%) for $C_{58}H_{42}Cu_2N_{12}O_8Cl$ ($M = 1197.59 \text{ g mol}^{-1}$): Anal. C, 51.19; H, 3.89; N, 13.42 % Calcd.; C, 58.17; H, 3.53; N, 14.04; O, 10.68; Cu, 10.60; Cl, 2.96 % X-ray; C, 58.16; H, 3.51; N, 14.05; O, 10.69; Cu, 10.61; Cl, 2.96 %; FAB MASS(m/z) Anal.: 1098.10, Calcd.: 1098.12, X-ray 1098.14. IR (KBr), cm^{-1} : 3421, 3063, 2923, 2856, 1595, 1481, 1437, 1389, 1358, 1321, 1209, 1091, 1013, 886, 789, 750, 702, 623, 483, 441 (See detail in Fig. S3).

Caution: Metal perchlorate salts are potentially explosive. They should be handled with great care.

2.2. Physical measurements

Elemental analyses were carried out on Euro Vector EA3000 elemental analyzer. FAB mass spectra were carried out on JEOL SX 102/DA 6000 Mass Spectrometer using xenon (6 kV, 10 mA) as the FAB gas. The accelerating voltage was 10 kV and the spectra were recorded at RT with m-nitrobenzyl alcohol as the matrix. Infrared (IR) spectra were recorded on a Bruker Spectrophotometer at normal temperature preparing KBr pellets by grinding the sample with KBr (IR grade), in the range of 400 to 4000 cm^{-1} . The molar ion exchange were measured using a Systronics digital conductivity meter (TDS-308) using a 10^{-3} M solution in DMSO. Electronic absorption spectra in the 300-900 nm range were recorded at 25°C on a Shimadzu UV-Vis recording Spectrophotometer UV-1601 in solution. Magnetic susceptibility measurements for **1**, **2** at room temperature and for **3** were collected at low temperature. The magnetic susceptibilities of powder sample of **3** were measured over a temperature range of 2-300 K with a field of 100 MT, using a Quantum Design SQUID magnetometer MPMS-XL5. All experimental data were corrected for diamagnetism estimated from Pascal constants and temperature-independent paramagnetism (TIP). Electron paramagnetic resonance (epr) spectra were recorded using a Varian E-line Century Series epr spectrometer equipped with a dual cavity and operating at the X-band of the 100 kHz modulation frequency. Tetracyanoethylene (TCNE) was used as a field marker ($g = 2.00277$). Cyclic voltammetry (CV) measurements were carried out with a BAS-100 Epsilon electrochemical analyzer having an electrochemical cell employed as a standard three-electrode configuration: Ag/AgCl was used as reference electrode, glassy carbon as working electrode and platinum wire as an auxiliary electrode. Tetrabutylammonium perchlorate (TBAP) (0.1 mol L^{-1}) was used as the supporting electrolyte in DMSO. All measurements were carried out at 298 K under nitrogen. The solution was deoxygenated by purging nitrogen gas. The

antioxidant SOD activities were evaluated using alkaline DMSO as a source of superoxide radicals ($\text{O}_2^{\bullet -}$) and nitro blue tetrazolium chloride (NBT) as a scavenger[41-43].

2.3. X-ray crystallography

X-ray quality single crystals for complexes **1**, **2** and **3** were selected and crystallographic analysis was carried out with an Bruker APEX-II CCD diffractometer equipped with graphite monochromated $\text{MoK}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$ for **1** and **2** and $1.54182 \text{ \AA}$ for **3**) operating at 50 kV and 30 mA. Intensity data were collected at 100 K for **1** and **2**, 150 K for **3** using ω -2 θ scan technique. Cell refinement, indexing and scaling for the data set were carried out using Bruker Saint Packages [46]. Structures were solved by direct methods and subsequent Fourier analyses [47] and refined by the full-matrix least square method based on F^2 with all observed reflections [47], absorption correction were applied using SADABS [48]. All structures were solved by direct methods by using the SHELXS package [49] and refined with SHELXL-2014 [49]. All the non-hydrogen atoms were refined anisotropically and all the hydrogen atoms were fixed by HFIX and placed in ideal positions. All calculations were performed using the SHELXL97, PLATON and WinGx system-version 1.80.05 [50]. In complex **1** a nitrate anion and crystalline water molecule are found disordered over two positions at half occupancy with an oxygen atom of nitrate and water molecule. In complex **3** the furane ring and perchlorate anion were found were found disordered over two positions, thus the furane carbon were isotropically refined. SQUEEZE [51] was used to correct the data and a potential value of 2821.9, 3100.0 and 6365.15 $\text{\AA}^3$ for **1**, **2** and **3**, respectively. The refinement with (without) the model treatment gives R values of 0.0672(0.2006), 0.0637(0.1836) and 0.0480(0.1517) for **1**, **2** and **3**, respectively, thus improving this parameter by 60%. Crystallographic data are summarized in Table 1. CCDC 1480500, 1480515 and 1480516 contain the supplementary crystallographic data for the present paper.

2.4. Computational method

Full geometry optimizations were carried out using density functional theory (DFT) method at the B3LYP level [52,53] for **1**, **2** and **3**. All elements except Cu were assigned 6-31G(d) basis set[54,55]. LANL2DZ with effective core potential for Cu atom was used [56]. The vibrational frequency calculations were performed to ensure that the optimized geometries represent the local minima and that there is an only positive Eigen value. In the computational model, the mono cationic complexes were taken into account. All calculations were performed with GAUSSIAN09 program package [57] with the aid of the Gauss View visualization program. Vertical electronic excitations based on B3LYP optimized geometries were computed using the time-dependent density functional theory (TDDFT) formalism [58] in DMSO using a conductor-like polarizable continuum model (CPCM) [59].

3. Results and discussion

3.1. Synthesis and characterization

The ligand (HL) was synthesized from the condensation reaction between 2-benzoyl pyridine and 2-furoic acid hydrazide in ethanol medium. The ligand HL was obtained with sufficient purity and used without further purification in the synthesis of the copper(II) complexes **1-3**. Corresponding copper(II) hydrazone complexes were synthesized by the direct reaction of ligand with copper(II) salts, $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ or $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ (Scheme II). The Schiff base (HL) acts as a mononegative (L) donor for the present three complexes, whereas in mononuclear octahedral complex **2**, one part of HL acts as a neutral tridentate ligand. A methanol solution of copper(II) nitrate was added to a methanol solution of ligand, followed by the addition of methanol solution of neocuprin with constant stirring for 1h to prepare complex **1**. The copper(II) complex **2** was obtained by the direct reaction of HL ligand with $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ in a methanol in 2:1 molar ratio. Complex **3** was also synthesized by the direct reaction of HL ligand with $\text{Cu}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ in methanol followed by methanol solution of 2-(2-pyridyl)benzimidazole was added in a 2:2:2 molar ratio. The IR peaks most useful for determining the mode of coordination of the ligands are the $\nu(\text{C-N})$ and $\nu(\text{C=O})$ vibrations. All the complexes, exhibit IR bands due to C=N stretch in the range $1595\text{-}1645\text{ cm}^{-1}$ and the skeletal vibration in the range $1481\text{-}1565\text{ cm}^{-1}$. In complex **1**, the band centered at 1442 , 1318 and 860 cm^{-1} are exhibited due to the presence of free nitrate ion[60]. A broad band at 3453 cm^{-1} indicates the presence of lattice water molecule in complex **1**. Four bands in the region of $2900\text{-}3100\text{ cm}^{-1}$ are attributed to the presence of methyl group in complex **1**[60]. The presence of bands at 1092 , 1012 , 790 and 696 cm^{-1} for complex **2** and 1091 , 1013 , 789 and 702 cm^{-1} for complex **3**, indicate a T_d symmetry of ClO_4^- , suggest the presence of ClO_4^- outside[61,62] in the coordination sphere of the complex **2** and **3**. The $-\text{N-H}$ stretching frequency appeared at 3440 and 3421 cm^{-1} for complex **2** and **3**, respectively, thus inducing the coordination of ligand to metal ion in deprotonated form [63] in **2** and deprotonation of substituted imidazole moiety in complex **3**. The in-plane deformation mode of the pyridine ring $621 \pm 1\text{ cm}^{-1}$ in all the present copper(II) complexes, suggests the coordination of the pyridine nitrogen[64, 65]. The experimental values of μ_{eff} 1.82 and 1.91 B.M. for **1** and **2**, respectively revealed the presence of +2 oxidation state of copper. Variable temperature magnetic measurements of complex **3** showed antiferromagnetic interactions in between two copper atoms. The molar conductance (λ_m) of these complexes in DMSO ($3.0 \times 10^{-3}\text{ mol L}^{-1}$) are 111, 108 and $115\text{ }\Omega^{-1}\text{ cm}^2\text{ mol}^{-1}$ for complexes **1**, **2** and **3**, respectively. Thus, these complexes suggest 1:1 electrolyte in DMSO.

Scheme II Synthetic routes of copper(II) complexes 1-3.

3.2. Structural characterization

All the present complexes **1-3** crystallized as single black, red and blue crystals belonging to the monoclinic crystal system with space group $P2_1/c$. ORTEP views of the asymmetric unit of these complexes (**1-3**) with atom labels are shown in Fig. 1, 2 and 3, respectively. Details of the data collection and the parameters of refinement process are given in Table 1. Selected bonding parameters for present complexes are listed in Table 2, 3 and 4, respectively.

In complex **1**, the asymmetric units contain one neutral bidentate ligand (neocuprin) and one monoanionic Schiff base (L). The copper(II) atom is chelated by the neocuprin pyridine nitrogen N(4) and N(5), the amino nitrogen (N(1)), pyridine nitrogen (N(2)) and hydrazone oxygen (O(1)) of Schiff base (L). The stereochemistry of the penta-coordinated Cu is best described as the distortion parameter $\tau = \beta - \alpha / 60$, in which β and α are the two largest L–M–L angles of the coordination sphere (Table 2)[66,67]. The $\tau = 0.5-1$ indicates that geometry is distorted trigonal-bipyramidal and $\tau = 0-0.5$ indicates that geometry is distorted square-pyramidal. For this complex τ value is 0.143, indicating that the geometry of coordination around the copper atom is distorted square-pyramidal (Fig. 1). In addition, the copper(II) atom slightly deviates from the equatorial plane by 0.44 Å in the direction of the pyridine nitrogen (N(4)). The copper atom is displaced from its least-square basal plane (mean deviation 0.056 Å) by 0.44 Å toward the apical oxygen atom. The coordination geometry in **1** around the copper(II) atom is distorted square-pyramidal, with the copper ion being surrounded by one azomethine nitrogen, one pyridine nitrogen moiety and one hydrazone oxygen of L tridentate ligand. Other coordination sides are occupied by pyridine group of neocuprin bidentate ligand. The axial position of square pyramidal is occupied by hydrazone oxygen with ligand. Cu–N(1) = 2.008 Å, Cu–N(2) = 1.945 Å and Cu–O(1) = 1.995 Å and neocuprin N of the pyridine ring Cu–N(4) = 2.213 Å and Cu–N(5) = 2.005 Å. In the five-coordinated structure, the basal plane is formed by nitrogen atoms (L and neocuprin). The sum of the planar angles N(2)–Cu–N(1), N(1)–Cu–N(5), N(5)–Cu–N(4) and N(2)–Cu–N(4) is 360°. The two bond lengths Cu–O(1) (1.9915(18) Å) and Cu–N(2) (1.949(2) Å) are shorter than the three Cu–N (2.008(2), 2.009(2) and 2.212(2) Å) bond lengths in the square-pyramidal complex. These bond lengths and angles are in good agreement with that recently reported for analogous square-pyramidal Cu(II) species [62,68–72]. In the outer sphere of complex the nitrate anion was found to be disordered. The position of all the oxygen atoms (O(11), O(12) and O(13)) were shared by both orientations, thus disorder was found along the C_3 rotation axis. In addition, crystalline water molecules were also disordered. Disorder was not observed in nitrogen atom N(11) of nitrate anion. The crystal packing of **1** (Fig. S4) is stabilized by a three dimensional hydrogen bonding network. The pyridine hydrogen and imine nitrogen of L group are in intermolecular hydrogen bonding with the neighboring NO_3^- ion and crystalline water molecule with the distance varies from 2.390–3.516 Å (Table S1) and bond angles are varies from 128.4° to 158°.

Complex **2** consists of a discrete centro symmetrical $[\text{Cu}(\text{L})(\text{HL})]^+$ cation and one perchlorate (ClO_4^-) anion. The copper(II) coordination environment of the complex

$[\text{Cu}(\text{L})(\text{HL})]^+$ is depicted in Fig. 2. As shown in Fig. 2 each molecule of the same type is in the trans position to another. The central copper(II) atom adopts a trans-octahedral geometry, being linked to four basal atoms, three nitrogen atoms [N(1A), N(2A) and N(2B)] and one oxygen atom O(1A), the two apical atoms N(1B) and O(1B). Sum of the basal angles [N(1A)-Cu-N(2A), N(2A)-Cu-O(1A), O(1A)-Cu-N(2B) and N(2B)-Cu-N(1A)] is 360° . These basal angles [74.43, 74.28, 117.34 and 93.99] are not close to ideal octahedral value 90° . The L and HL use two nitrogen and one oxygen donor atoms acting as a tridentate chelating ligand to form a five membered Cu-N-C-C-N and Cu-N-N-C-O metallocycle with a coordinated copper. Interatomic distances and angles are shown in Table 3. The basal plane bond distances vary from 1.94 to 2.88 Å and two equatorial plane bond distances are Cu-N(1B) (2.03 Å) and Cu-O(1B) (2.007 Å) [73-75]. This axial elongation could be attributed to the Jahn-Teller distortion of copper(II) ion [76,77]. There is one non coordinated ClO_4^- counter anion attached to the complex via hydrogen bond with the furan ring H of ligand L. The C-H.....O separation is 3.501 Å (Table S1), falling into the normal range of such separation [74,75] and the C-H.....O angle is 151.6° , leading to the construction of a three-dimensional network structure (Fig. S5).

Different from previous complexes, the molecular structure of complex **3** is shown in Fig. 3. Important bond distances and angles are listed in Table 4. In the structural unit of the complex it is seen that the Cu_2O_2 core consists of two hydrazone bridged copper atoms. The two metal ions are related by the crystallographic two fold screw axis in the direction of [0,1,0] at 0,y1/4 with screw component (0,1/2,0) passing through the middle of Cu1-Cu2. The asymmetric unit thus consists of the half of the binuclear complex. The complex **3** is formed by two unsymmetrical tridentate ligand (L) and bidentate neutral ligand (2-(2-pyridyl)benzimidazole) chelating the metal ions and forming a hydrazone bridged Cu(II) dimer. An ORTEP view of **3**, the possesses an octahedral coordination sphere (4+1+1) with hydrazone bridged oxygen and pyridine nitrogen occupying the axial positions at longer distances and an two pyridine nitrogen, one imine nitrogen and a hydrazone oxygen located in the equatorial planes. Sum of the planar angles in both copper(II) centers are 360° . These planar angles deviate from ideal octahedral planar angles 90° . The mutual disposition of the ligands deviates noticeable from perpendicularly which is indicated by deviate values of the trans angles, N(2A)-Cu(1)-N(4A) = $177.32(9)^\circ$, N(1A)-Cu(1)-O(1A) = $157.83(7)^\circ$ and N(5)-Cu(1)-O(1B) = 160.09° for Cu(1) and N(2B)-Cu(2)-N(4B) = $177.46(9)^\circ$, N(1B)-Cu(2)-O(1B) = $158.79(8)^\circ$ and N(5B)-Cu(2)-O(1A) = $158.26(8)^\circ$ for Cu(2) center. The basal bond distances for both copper centers are varies from 1.928-2.051 Å, while the apical distances Cu(1)-N(5A) = 2.302(3) Å and Cu(1)-O(1B) = 2.613 Å for Cu(1) and Cu(2)-N(5B) = 2.295 Å and Cu(2)-O(1A) = 2.608 Å for Cu(2) [71, 75, 78,79] are the longest As expected for an axially elongated geometry with a Jahn-Teller distortion which is typical for Cu(II) d^9 system. The Cu(1)...Cu(2) separation is 3.582 Å and bridging angles are Cu(1)-O(1B)-Cu(2) = 99.70° and Cu(1)-O(1A)-Cu(2) = 99.78° . Two such monomeric $[\text{Cu}(\text{L})(2\text{-(2-pyridine)benzimidazole})]^+$ entities eventually interconnect through the hydrazone oxygen to produce the binuclear polyhedron. A monomeric labeled representation of the chelating modes of the L and 2-(2-pyridyl)benzimidazole ligands connected to copper atom is shown in Fig. 4a

and b . In Fig. 4, consists of two molecular units, namely Cu(1) and Cu(2) molecular units. In the Cu(1) molecular unit, each hydrazone oxygen acts as a bridging atom and coordinates to the Cu(2) atom of the neighboring Cu(2) molecular unit. Each copper atom is five-coordinate and basal plane consist of N(1A), N(2A) and O(1a) of the mononegative (L). The fourth coordination site is occupied by the imidazolato nitrogen N(4A), while the fifth apical site is occupied by the pyridine nitrogen of natural ligand. Both Cu(II) polyhedron unit can be described distorted square pyramidal (4+1), with their trigonality parameter (τ) [67] values are 0.287 and 0.32 for Cu(1) and Cu(2), respectively. In ligand L, the furane ring was disordered. The position of the one oxygen and four carbons atom were shared by both orientations. In addition, anionic perchlorate was also disordered. All oxygen was shared by both orientations, no disorder was observed in chlorine atom, as a result of its involvement in general and bifurcated hydrogen bonding. The H-bonding scheme is comparable in the two structures (Fig. 5 and Unit cell diagram) leading to a 3D network. A detail of the H-bond interactions involving perchlorate anion, imidazolato nitrogen, pyridine hydrogen and hydrazone oxygen is shown in Fig. 5. The D...A distances and angles are shown in Table S1. The nature of bifurcated (or three centered) hydrogen bonds (Fig. 5) has been investigated along with the normal hydrogen bonds. The hydrogen atom (H6a) of the imidazolato nitrogen N(6a) forms bifurcated hydrogen bonds with the perchlorate oxygen atoms (O12 and O13). Such type of hydrogen bonds have been already investigated by earlier workers[80-82]. Moreover, the complexes are paired in the crystal about a center of symmetry giving rise to a double H-bond (Fig. 5) for complex **3**. The double hydrogen bond distances C(19b)-H(19b).....O(1a) = 2.510 Å and C(19a)-H(19a).....O(1b) = 2.552 Å and bond angles C(19b)-H(19b)-O(1a) = 132.89°. The crystal packing showing perchlorate anion H-bond connected by the furane ring hydrogen, the supramolecular motif generated from the intermolecular H-bonds (Fig. S6). These interactions propagate, leading to the formation of 3D supramolecular structure along the a-axis. Supramolecular structure in turn, self-assemble via electrostatic and Van der Waals interactions to construct a three-dimensional network. No significant C-H--- π interaction is observed in the crystal packing in spite of the presence of several planar moieties within the molecular structure.

3.3. UV-vis. Spectra

The electronic spectra of the complexes in DMSO solution exhibit characteristic absorption bands corresponding to the square-pyramidal for complex **1** and distorted octahedral geometry for complexes **2** and **3** (Fig. 6). It has been established that six coordinate copper(II) complexes possess elongated tetragonal or rhombic distortions in the octahedral field and display three spin allowed transitions assigned to are expected [83,84], viz., $^2B_{1g} \rightarrow ^2A_{2g}$ ($d_{x^2-y^2} \rightarrow d_{z^2}$), $^2B_{1g} \rightarrow ^2B_{2g}$ ($d_{x^2-y^2} \rightarrow d_{xy}$) and $^2B_{1g} \rightarrow ^2E_g$ ($d_{x^2-y^2} \rightarrow d_{xz,yz}$). It is rather difficult to resolve these bands because they are very close in energy. In TD-DFT calculations all bands are resolved. Six vertical excitation energies, oscillator strength and tentative nature of transitions are summarized in Table S2. The absorption bands around ~400 nm for the complexes **1-3** are due to the $\pi \rightarrow \pi^*$ transitions. The composition of two excitations at 2.5401 eV ($\lambda = 395$ nm and f

= 0.0009) and 2.5046 eV ($\lambda = 457$ nm and $f = 0.0010$), 1.9585 eV ($\lambda = 433$ nm and $f = 0.0012$) and 2.3132 eV ($\lambda = 535$ nm and $f = 0.0002$) and 1.7566 eV ($\lambda = 405$ nm and $f = 0.0513$) and 1.7512 eV ($\lambda = 508$ nm and $f = 0.0059$) for complexes **1**, **2** and **3**, respectively, which may be attributed to a combination of LMCT/ILCT/LLCT charge transfer transitions. Similarly, d-d bands are contributed to four excitations states, tentative nature of transitions, oscillator strengths and energies are shown in Table S2. Fig. 6 indicates a broad d-d band at 611 nm ($\epsilon = 62.5$ M⁻¹), 688 nm ($\epsilon = 56.2$ M⁻¹) and 690 nm ($\epsilon = 85.5$ M⁻¹) for complex **1**, **2** and **3**, respectively. Octahedral complexes (**2** and **3**) gave similar features but extinction coefficient (ϵ) of **3** is higher than mononuclear copper(II) complexes **1** and **2**. Observed higher excitation coefficient of **3** may be ascribed to the presence of two copper nuclei. Similar spectra were reported for other square-pyramidal and octahedral copper(II) complexes [85,86]. All the present copper(II) complexes exhibit a moderately intense band in the range between 384 to 407 nm which may be assigned to metal-to-ligand charge-transfer transitions [87,88].

3.4. Epr Spectra

The epr spectra of the complexes **1-3** have been recorded in polycrystalline samples at room temperature and in DMSO solution at 77K. Representative epr spectra of complexes **1** and **3** are shown in Fig. 7 and 8, respectively and derived epr parameters are presented in Table 5. Spectra of the mononuclear complexes **1** and **2** are almost identical and show the usual features of a mononuclear copper center. A set of spectra of complex **1** is shown in Fig. 7. Epr spectra recorded on polycrystalline samples of both complexes show evidence of magnetic exchange between metal centers. But the nature of magnetic exchange is pseudo dipole-dipole interaction due to hydrogen bonding as interaction is lost in solution. Spectra of both complexes **1** and **2** in polycrystalline state show weak half-field signals near 1575 G, which are associated with $\Delta M_s = \pm 2$ transitions arising from coupling between $S = \frac{1}{2}$ metal ions. Frozen solution epr spectra of both mononuclear complexes **1** and **2** are consistent with monomeric structures and observed trend in the spin Hamiltonian parameters ($g_{\parallel} > g_{\perp} > 2.04$ and $|A_{\parallel}| \approx 149 \times 10^{-4}$ cm⁻¹ indicates a $d_{x^2-y^2}$ ground state with tetragonal site symmetry for copper(II) in both mononuclear complexes **1** and **2**[89]. Half-field signals are not observed in frozen solution epr spectra of **1** and **2**.

Polycrystalline room temperature spectrum of binuclear complex **3** is quite different in appearance than spectra of polycrystalline samples of mononuclear complexes (Fig. 8). A strong well-defined half-field signal (1540 G) is observed at the $g \cong 4.3$, which is associated with $\Delta M_s = \pm 2$ transitions from coupling between $S = \frac{1}{2}$ metal ions, a molecules (intra dipole-dipole interaction). This kind of observation suggests that the two copper(II) centers are coupled antiferromagnetically as evidenced by magnetic measurements. The polycrystalline epr spectrum of this complex shows features associated with the distorted geometry about both metal centers. Exchange interaction parameter G gave the value $G = 2.83$, indicating strong interaction in polycrystalline state. In frozen DMSO solution spectrum shows the evidence of exchange between metal ions (Fig. 8). The spectrum, which is markedly different from that of

mononuclear complexes[90], exhibits both $\Delta M_s = \pm 2$ signal at half-field and a high-field feature at $g_{\text{eff}} \sim 1.89$ that are characteristic of the hydrazido-bridged dicopper(II) centers. Similar observations were made on imidazolate-bridged copper(II) complexes [3,5,91]. The half-field signal exhibits a seven line pattern due to presence of two copper nuclei ($2 \times 2 \times \frac{3}{2} + 1 = 7$). Binuclear structure has already been established by single crystal analysis. Frozen solution spectra are very similar to that of Cu-ZnSOD having $f = g_{\parallel}/A_{\parallel}$ value are 146, 181 and 143 cm^{-1} for **1**, **2** and **3**, respectively [9].

3.5. Magnetic Properties of copper(II) complexes

The magnetic susceptibility measurements of **1** and **2** in polycrystalline state show that the present complexes are paramagnetic at room temperature. The observed magnetic moments at room temperature of complexes **1** and **2** are in the range expected for spin free d^9 ($S = \frac{1}{2}$) systems. The observed magnetic moment values 1.73 BM for complex **1** and complex **2** for 1.71 BM are quite close to the value except for complex having one copper ion is in fair arrangement with the spin system $S = \frac{1}{2}$ and $d_{x^2-y^2}$ orbital[92]. Variable temperature magnetic susceptibilities of complex **3** have been measured in the temperature range of 2-300K at 100 Oe and the plots of χ_M and μ_{eff} vs T are shown in Fig. 9. The magnetic susceptibility obeys the Curie-Weiss law ($\chi_M = C/(T - \Theta)$) with the Weiss constant $\Theta = 0.06$ K and the Curie constant $C = 0.91 \text{ cm}^3 \text{ K mol}^{-1}$. The value of $0.90 \text{ cm}^3 \text{ K mol}^{-1}$ for $\chi_M T$ at 300 K is in agreement with two $S = \frac{1}{2}$ spin and g parameter deviating from 2.12 as usually found for Cu(II) ions (vide infra). χ_M (per Cu ion) very slowly increase from $0.000014 \text{ cm}^3 \text{ mol}^{-1}$ at 300 K to $0.00011 \text{ cm}^3 \text{ mol}^{-1}$ at 33 K and then rapidly increase $0.00126 \text{ K cm}^3 \text{ mol}^{-1}$ at 2 K. Such results indicate weak antiferromagnetic interaction between the two copper atoms in this complex. For this complex the value of J is -10.87 cm^{-1} . The small values of the magnetic exchange coupling constant (J) found can be understood in terms of the geometrical distortions, which affect the copper coordination spheres, the geometries of the bridges and the planarity on the bridged core (Cu...O). To estimate a magnitude of magnetic exchange interaction (J) between the two copper(II) ions ($S = \frac{1}{2}$ spins) the isotropic Heisenberg-Dirac-Van-Vleck isotropic Hamiltonian formalism was used.

$$\hat{H} = -J\hat{S}_1\hat{S}_2 \quad \dots\dots\dots(i)$$

The magnetic data was analyzed using a classical Bleaney-Bowers equation[93].

$$\chi_{MT} = \frac{N\beta^2}{3k_B} \frac{2g^2}{1 + \exp(-J/k_B T)/3}$$

where N_A , k , β and g are the Avogadro number, the Boltzmann constant, the Bohr magneton and g-factor, respectively. This law gives the magnetic susceptibility as a function of temperature per atoms for dimeric nature of copper(II) complexes. The best of the data gives $J = -10.87 \text{ cm}^{-1}$ and $g = 1.99$ for **3**. This complex belongs to the well documented family of derivatives for two copper centers and is linked through oxygen atoms of hydrazido-bridged structure.

3.6. Electrochemistry of the copper(II) complexes

The electrochemical behavior of these complexes was studied using cyclic voltammetry (CV) and differential pulse voltammetry (DPV) and the data is tabulated in Table 6. The CV and DPV pictures are shown in Fig. 10. The biochemical reactions (enzymatic reactions) between superoxide dismutase and superoxide anion are redox reactions. The oxidized form of copper(II) SOD mimics oxidize the superoxide anion to O_2 and reduced [94] from of SOD mimics reduces superoxide to H_2O_2 . From this kind of half biochemical reaction it is clear that a requirement for SOD activity be that the redox potentials for reduction and oxidation of superoxide anion, e.a. $EO_2^{\bullet-}/O_2 < E_M^{II}/M^I < EO_2^{\bullet-}/HO_2^{\bullet-}$ (-0.3 to +0.9 V)[94,95]. From the electrochemical data presented in Table 6 the copper coupled involved in this process are very close to this range. Electrochemical methods have been most effective in characterizing these complexes. Both experiments have been recorded in DMSO solution containing 0.1 M [n Bu) $_4$ N]ClO $_4$ as a supporting electrolyte over the potential range 0.400 to -0.800V at 20°C at scan rate 400 mVs $^{-1}$ using a glassy carbon working electrode, a platinum wire counter electrode and an Ag/AgCl reference electrode. The mononuclear complexes **1** and **2** showed a irreversible wave at $E_{1/2} = -0.055$ V and 0.064 V (vs Ag/AgCl), respectively, which may be assigned to a Cu(II)/Cu(I) redox process[96](Fig. 10). The pair of oxidation-reduction peaks corresponds to the oxidation reduction couples Cu(II)/Cu(I), $E_{pa} = 0.248$ V, $E_{pc} = -0.358$ V, with the average formal potential [$E_{1/2} = E_{pc} + E_{pa}/2$] is -0.055V. The reduction is irreversible with little or no anodic peak. In case of complex **2** an irreversible redox process with $I_{pc}/I_{pa} \ll 1$ was observed, which is typical of Cu(II)/Cu(I) reduction in many mononuclear complexes [72,97-99]. Other CV data are tabulated in Table 6.

Quite different electrochemical behavior was observed for the binuclear copper(II) complex **3**. As previously reported in literature[10,45, 100], two distinct reduction processes were seen for homo binuclear copper(II) complex **3** but this time quite large separation between the cathodic peaks (Fig. 10). The first reduction was irreversible and its peaks positions (cathodic and anodic) are well separated by 0.299 V. The second reduction was also irreversible, in this reduction the oxidation peak is little or no anodic peak[101]. In-fact, this wave had the same electrochemical characteristic as that found for mononuclear complexes **1** (Fig. 10). We interpret that both coppers centers (Cu(1) and Cu(2)) have been oxidized at 0.263 V. This type of redox feature is due to the effect of hydrazide bridge to destabilize the mixed valence species. These two waves of an one electron transfer correspond to Cu_2^{II} to $Cu^{II}Cu^I$ and Cu^ICu^I processes. The conproportionation constant for the equilibrium $Cu_2^{II} + Cu_2^I \xrightleftharpoons{K_{con}} 2Cu^{II}Cu^I$ was evaluated using the relationship $\log K_{con} = 16.9 (\Delta E_{1/2})$ [102-105]. The larger the separation between the potentials of the couple, the greater the stability of the mixed-valence species with respect to the conproportionation. The values of ΔE and K_{con} are listed in Table 6. Redox properties of these complexes were also measured by DPV. The measurements of reduction potentials by DPV yielded similar results where potentials agreed with those measured by other electrochemical techniques and are independent of scan rate. This method also helped to establish the

homobinuclear complex **3**. For this complex two sequential reduction processes were obtained as shown in Fig. 10 and two Cu(II)/Cu(I) potentials are tabulated in Table 6.

3.7. Electronic structure and DFT calculations

The geometries of the mentioned complexes are optimized in the singlet ground state. The coordination obtained from single crystal X-ray diffraction data for complexes **1-3** were optimized using the DFT/B3LYP (LANL2DZ/631G(d)) level of calculations. The calculated bond lengths and bond angles are well correlated with X-ray data (Table 2, 3 and 4 for complexes **1**, **2** and **3**, respectively). Counter plots of selected molecular orbitals for complexes **1-3** are shown in Fig. S7-S9. The energy and composition of selected molecular orbitals of the complexes are given in Table 7. In complex **1** and **3**, the contribution of Schiff base ligand in HOMO is 27 - 40% and $d\pi$ character of copper(II) is 45–60% (Table 7). The contribution of neocuprin is 15% and 2-(2-pyridyl)benzimidazole is 10% for complex **1** and **3**, respectively. On the other hand π L character of LUMO is reduced contribution of 0 and 8% for **1** and **3**, respectively. While the complex **2** is 100% π L LUMO character, but $d\pi$ character of HOMO is 100%.

3.8. Antioxidant (SOD) activity

To examine the antioxidant SOD like activity, the mononuclear Cu(II) (**1** and **2**) and Cu(II)-Cu(II) homobinuclear (**3**) complexes exhibit catalytic activity toward the dismutation of superoxide anions. The antioxidant SOD activities of the complexes **1**, **2** and **3** were investigated by the well-used NBT assay [41-43] using the reduction of NBT to MF^+ kinetically at 560 nm, as the source of superoxide. Superoxide dismutation is a redox process, IC_{50} value for SOD activity has been defined as the chromophore concentration required to yield 50% inhibition of the reduction of NBT at pH 7.4. The IC_{50} values obtained for SOD-like activity of the Cu(II) complexes are shown in Table 8. The IC_{50} values of the complexes **1**, **2** and **3** are 21, 49 and 17 μ M, respectively. All the present complexes showed SOD activity but are less active than the native SOD ($IC_{50} = 0.04 \mu$ M). Thus antioxidant SOD activities of present complexes were also compared with previously reported values[10,41, 42,106,107]. This is a clear demonstration that the antioxidant mimics exhibit a significant antioxidant SOD activity. The good activities of these complexes, may be attributed to the flexible nature of ligand used, which is able to accommodate the geometrical change from Cu(II) to Cu(I) [96] in catalytic process. The distorted geometry of the all complexes may favor the geometrical change (Fig. 1, 2 and 3), which is essential for the catalytic properties of the complexes. The antioxidant SOD activity of these complexes increase in order **2** < **1** < **3**. The fact that complex **3** acts as a better catalyst of $O_2^{\cdot -}$ dismutation compared to **1** and **2** which might be ascribed due to the presence of two copper ions. The subtle difference in these structures lead to different antioxidant SOD activities, The activity and catalytic rate constant (k_{McCF}) of these complexes were also evaluated. The kinetic catalytic constant k_{McCF} was obtained by the equation $k = k_{NBT} \times [NBT] / IC_{50}$, where $k_{NBT} = 5.94 \times 10^{-4} (\text{molL}^{-1})^{-1}\text{S}^{-1}$ is the second order rate constant for NBT[108], of these complexes

data are shown in Table 8, similar results have also been compared. The higher IC_{50} can only be accredited to the vacant coordination site, which facilitate the binding of superoxide anion, electron of aromatic ligands that stabilize Cu-O₂ interaction and not only to the partial dissociation of complex in solution.

3.9. Structure-activity relationship analysis

In order to further gain some insight into the structure-activity relationship for the Cu^{II} N₄O/O₂ mimics. These complexes further investigated by the electrochemical studies and density functional theory (DFT) calculations. We observed that electron-accepting abilities and coordination geometries around copper(II) ions of these complexes influenced by outer sphere substituents and have significant effects on the antioxidant SOD activity.

The mechanism of antioxidant SOD activity involves the conversion of O₂^{•-} to molecular oxygen (O₂) and simultaneously the copper(II) center accepts an electron from O₂^{•-} [109]. Therefore, it is supposed that the stronger the electron accepting ability of copper complex, the more favorable is the electron transfer from O₂^{•-} to copper(II) and antioxidant SOD activity would be better.

Redox behaviors of complexes **1-3** were evaluated by the cyclic and different pulse voltammetry, since it is known that redox properties of the metal complexes are correlated with their catalytic ability. The $E^{1/2}$ values of complexes **1** and **2** exhibited irreversible one electron reduction wave, which can be assigned to the Cu^{II}/Cu^I pair [110] whereas complex **3** yielded two irreversible waves. The E_{pc} values indicate that their electron accepting abilities are in the order **2** > **1** > **3**, which is consistent with antioxidant SOD activity. Similarly, the E_{pc} values observed by DPV have also exhibited almost similar trend in electron accepting abilities (**2** ≈ **1** > **3**). Therefore, based on the mechanisms of activities and the favorable relevance between enzyme mimic activity data and electrochemical data, it is proved that the electron accepting ability has an important influence on the antioxidant SOD activity of these complexes. Furthermore, difference in coordination geometries is also responsible for difference in enzyme mimetic activities of these complexes. Complexes **1** and **3** (monomeric unit of homobinuclear complexes) have same square pyramidal geometry, while complex **2** is distorted octahedral geometry. So there is a less change of attack of O^{•-} on complex **2** as compared to **1** and **3**.

In addition, DFT calculations were also performed to make the further analysis of the enzymatic activities of the complexes **1-3**. In complexes the important parameter is the energy gap (E_{gap}) between LUMO and HOMO. The less value of this descriptor means that molecules are more active [111]. According to the E_{gap} , the ranking of mentioned complexes should be **1** > **3** > **2**. Hence, it is to be noted that homo binuclear complex is supposed octahedral during geometry optimization and therefore octahedral geometries are less appropriate for activity of O₂^{•-}. Therefore, less antioxidant activity is suggested.

4. Conclusions

In this article three new copper(II) complexes were synthesized by the biomimetic synthetic strategy and their structures were determined by single crystal X-ray analysis. The exchange interaction is stronger in complex **3** and is antiferromagnetically coupled. The structure-activity relationship for these new antioxidant mimics was analyzed based on experimental and DFT calculations. Results reveal that antioxidant activities of these complexes are affected by the molecular geometries of the complexes. Interestingly, antioxidant property of complex **3** is best among these complexes. This study throws light on bioinorganic chemistry of SOD and could be a good examples of antioxidant SOD mimics.

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Fig. 1. X-ray crystal structure of $[\text{Cu}(\text{HL})(\text{Neopuprin})]^+ \mathbf{1}$ showing the atomic numbering scheme.

Fig. 2. X-ray crystal structure of $[\text{Cu}(\text{HL})(\text{L})]^+ \mathbf{2}$ showing the atomic numbering scheme.

Fig. 3. X-ray crystal structure of $[\text{Cu}_2(\text{HL})_2(2\text{-(2-pyridyl)benimidazole})_2]^+ \mathbf{3}$ showing the atomic numbering scheme.

Fig. 4. (a) and (b) are monomeric unit of copper(II) complex of homobinuclear copper(II) complex **3**.

Fig. 5. Structure of $[\text{Cu}_2(2\text{-(2-pyridyl)benzimidazole})_2(\text{L})_2]\text{ClO}_4 \cdot 3$ along with bifurcated hydrogen bonding.

Fig. 6. UV-visible spectrum of copper(II) complexes (0.25×10^{-3} M) in DMSO. [Inset: UV-visible spectrum of copper(II) complexes (3.0×10^{-3} M) in DMSO.]

Fig. 7. X-band epr spectra of $[\text{Cu}(\text{L})(\text{neocuprin})]\text{NO}_3 \cdot \text{H}_2\text{O}$ 1

Fig. 8. X-band epr spectra of $[\text{Cu}_2(2-(2\text{-pyridyl})\text{benzimidazole})_2(\text{L})_2]\text{ClO}_4 \mathbf{3}$. In caption $\Delta M_s = 2$ transation. Upper polycrystalline at RT. Lower solution epr spectra in DMSO at LNT 77K.

Fig. 9. A plot for complex **3** of temperature dependance of χ_M (o) vs. T and μ_{eff} (-----) vs T. The solid line correspond to the fit with Curie-Weiss equation.

Fig. 10. Top : Differential Pulse voltammogram of **1-3** using a scan rate 20 mVs^{-1} in DMSO, the pulse amplitude is 50 mV . Bottom : Cyclic voltammogram of **1-3** in DMSO at a Glassy carbon electrode with scan rate 400 mV s^{-1} .

Table 1

Crystal data and structure refinement parameters for copper(II) complexes.

	C ₃₁ H ₂₇ CuN ₆ O ₆ 1	C ₃₄ H ₂₅ ClCuN ₆ O ₈ 2	C ₅₈ H ₄₂ ClCu ₂ N ₁₂ O ₈ 3
Formula weight	649.24	744.59	1197.56
Temperature (K)	100(2)	100(2)	150(2)
Wavelength (Å)	0.71073	0.71073	1.54184
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	P2 ₁ /c	P2 ₁ /c	P2 ₁ /c
Unit cell dimensions			
a (Å)	12.210(2)	12.482(3)	14.6300(3)
b (Å)	8.9284(17)	12.131(3)	13.8202(2)
c (Å)	26.531(5)	20.473(6)	32.2223(5)
α (°)	90	90	90
β (°)	102.670(3)	90.509(5)	102.313(2)
γ (°)	90	90	90
Volume (Å ³)	2821.9(9)	3100.0(15)	6365.15(19)
Z	4	4	4
Density (calculated) (Mg/m ³)	1.528	1.595	1.250
Absorption coefficient (mm ⁻¹)	0.833	0.857	1.692
Crystal size (mm ³)	0.420 x 0.380 x 0.310	0.210 x 0.200 x 0.160	0.230 x 0.180 x 0.130
θ (°)	1.709 to 32.145	1.951 to 28.382	4.257 to 71.437
Index ranges	-18 ≤ h ≤ 18, -13 ≤ k ≤ 12, -38 ≤ l ≤ 38	-6 ≤ h ≤ 16, -15 ≤ k ≤ 16, -27 ≤ l ≤ 22	-17 ≤ h ≤ 11, -16 ≤ k ≤ 15, -39 ≤ l ≤ 39
Reflections collected	40742	14809	44647
Data / restraints / parameters	9246 / 36 / 431	7468 / 0 / 455	12234 / 164 / 776
Goodness-of-fit on F ²	1.044	1.031	1.018
Final R indices [I > 2σ(I)]	R1 = 0.0672, wR2 = 0.1842	R1 = 0.0637, wR2 = 0.1729	R1 = 0.0480, wR2 = 0.1410
R indices (all data)	R1 = 0.0862, wR2 = 0.2006	R1 = 0.0790, wR2 = 0.1836	R1 = 0.0577, wR2 = 0.1517

Table 2

Interatomic distances [Å] and angles [°] relevant to the copper coordination sphere in **1**.

	X-ray	DFT		X-ray	DFT
Cu-N(2)	1.945(2)	1.987	Cu-O(1)	1.9915(18)	1.967
Cu-N(1)	2.008(2)	2.102	Cu-N(5)	2.009(2)	2.032
Cu-N(4)	2.213(2)	2.234			
N(2)-Cu-O(1)	78.98(8)	78.90	N(2)-Cu-N(1)	80.53(10)	81.45
O(1)-Cu-N(1)	156.91(9)	157.10	N(2)-Cu-N(5)	165.51(10)	166.22
O(1)-Cu-N(5)	96.23(8)	97.32	N(1)-Cu-N(5)	101.03(10)	102.36
N(2)-Cu-N(4)	113.74(10)	114.12	O(1)-Cu-N(4)	89.90(8)	90.21
N(1)-Cu-N(4)	108.11(10)	1.9.32	N(5)-Cu-N(4)	79.68(10)	80.32

Table 3

Interatomic distances [$\text{\AA}$] and angles [$^\circ$] relevant to the copper coordination sphere in **2**.

	X-ray	DFT		X-ray	DFT
Cu-N(2B)	1.940(3)	1.976	Cu-O(1B)	2.007(2)	2.124
Cu-N(1B)	2.038(3)	2.236	Cu-N(2A)	2.074(3)	2.089
Cu-O(1A)	2.232(2)	2.198	Cu-N(1A)	2.280(3)	2.278
N(2B)-Cu-N(1B)	80.46(11)	81.12	O(1B)-Cu-N(1B)	159.33(10)	159.89
N(2B)-Cu-N(2A)	168.22(10)	168.98	O(1B)-Cu-N(2A)	102.53(10)	102.87
N(1B)-Cu-N(2A)	98.01(11)	98.07	N(2B)-Cu-O(1A)	117.34(10)	118.23
O(1B)-Cu-O(1A)	91.82(9)	91.89	N(1B)-Cu-O(1A)	91.46(10)	91.78
N(2A)-Cu-O(1A)	74.28(9)	74.91	N(2B)-Cu-N(1A)	93.99(10)	93.92
O(1B)-Cu-N(1A)	93.47(9)	93.89	N(1B)-Cu-N(1A)	94.29(10)	94.69
N(2A)-Cu-N(1A)	74.43(10)	74.85	O(1A)-Cu-N(1A)	148.67(9)	148.95
O(2)-Cl(1)-O(1)	110.27(17)	110.59	O(2)-Cl(1)-O(4)	108.89(19)	108.95
O(1)-Cl(1)-O(4)	109.8(2)	109.2	O(2)-Cl(1)-O(3)	110.38(18)	110.25
O(1)-Cl(1)-O(3)	109.13(17)	109.25	O(4)-Cl(1)-O(3)	108.35(19)	108.85

Table 4

Interatomic distances [$\text{\AA}$] and angles [$^\circ$] relevant to the copper coordination sphere in **3**.

	X-ray	DFT		X-ray	DFT
Cu(1)-N(2A)	1.937(19)	1.985	Cu(2)-N(2B)	1.928(2)	1.958
Cu(1)-N(1A)	2.016(2)	2.115	Cu(2)-N(4B)	1.957(2)	1.985
Cu(1)-N(5A)	2.302(3)	2.236	Cu(2)-N(1B)	2.014(2)	2.125
Cu(1)-N(4A)	1.968(2)	1.985	Cu(2)-O(1B)	2.048(17)	2.035
Cu(1)-O(1A)	2.051(17)	2.125	Cu(2)-N(5B)	2.295(3)	2.396
Cu(1)-O(1B)	2.614(19)	2.864	O(1A)-Cu(2)	2.608(19)	2.689
N(2A)-Cu(1)-N(4A)	177.32(9)	177.23	N(2B)-Cu(2)-N(4B)	177.46(9)	177.95
N(4A)-Cu(1)-N(1A)	98.02(8)	98.03	N(4B)-Cu(2)-N(1B)	98.17(9)	98.25
N(4A)-Cu(1)-O(1A)	103.46(7)	103.42	N(4B)-Cu(2)-O(1B)	102.76(7)	102.89
N(2A)-Cu(1)-N(5A)	100.42(9)	100.52	N(2B)-Cu(2)-N(5B)	100.08(10)	100.10
N(1A)-Cu(1)-N(5A)	102.89(9)	102.85	N(1B)-Cu(2)-N(5B)	102.10(10)	102.15
N(2A)-Cu(1)-O(1B)	89.07(7)	89.09	N(2B)-Cu(2)-O(1A)	90.59(8)	90.62
N(1A)-Cu(1)-O(1B)	95.88(7)	95.89	N(1B)-Cu(2)-O(1A)	98.31(8)	98.39
N(5A)-Cu(1)-O(1B)	160.09(7)	160.10	N(5B)-Cu(2)-O(1A)	158.26(8)	158.39
N(2A)-Cu(1)-N(1A)	80.50(8)	80.51	N(2B)-Cu(2)-N(1B)	80.42(9)	80.49
N(2A)-Cu(1)-O(1A)	78.24(7)	78.68	N(2B)-Cu(2)-O(1B)	78.80(7)	78.82
N(1A)-Cu(1)-O(1A)	157.83(7)	157.89	N(1B)-Cu(2)-O(1B)	158.79(8)	158.81
N(4A)-Cu(1)-N(5A)	77.68(9)	77.95	N(4B)-Cu(2)-N(5B)	78.11(10)	78.19
O(1A)-Cu(1)-N(5A)	87.16(8)	87.98	O(1B)-Cu(2)-N(5B)	85.72(9)	85.73
N(4A)-Cu(1)-O(1B)	93.31(8)	93.31	N(4B)-Cu(2)-O(1A)	91.71(7)	91.69
O(1A)-Cu(1)-O(1B)	77.62(7)	77.69	O(1B)-Cu(2)-O(1A)	77.78(7)	77.79

Table 5
Spin Hamiltonian and bonding parameters for copper complexes.

Complex	1	2	3
Polycrystalline			
$g_{\parallel}$	2.207	2.211	2.236
$g_{\perp}$	2.056	2.055	2.084
G	3.814	-	2.837
Frozen solution			
$g_{\parallel}$	2.181	2.341	2.134
$g_{\perp}$	2.0512	2.069	2.056
$A_{\parallel}$ (G)	160	138	160
G	3.634	4.323	2.453
f (cm ⁻¹)	146	181	143

Table 6
Electrochemical Data for reduction and oxidation of Cu(II) complexes.

Complex	CV									DPV				
	E_{pc}^1 (V)	E_{pa}^1 (V)	ΔE^1 (V)	$E_{1/2}^1$ (V)	E_{pc}^2 (V)	E_{pa}^2 (V)	ΔE^2 (V)	$E_{1/2}^2$ (V)	K_{con}	E_{pc}^1 (V)	I_{pc}^1	E_{pc}^2 (V)	I_{pc}^2	ΔE_{pc} (V)
1	-0.358	0.248	0.606	-0.055	-	-	-	-	-	-0.244	1.562			
2	-0.370	0.242	0.612	-0.064	-	-	-	-	-	-0.244	1.886			
3	-0.036	0.263	0.299	0.114	-0.422	0.263	0.685	-0.079	1.8×10^{-3}	0.064	1.605	-0.288	1.425	0.352

$\Delta E = E_{pa} - E_{pc}$, $E_{1/2} = E_{pc} + E_{pa} / 2$, $\log K_{con} = 16.9(\Delta E_{1/2})$, $\Delta E_{1/2} = E_{1/2}^1 - E_{1/2}^2$, $\Delta E_{pc} = E_{pc}^1 - E_{pc}^2$

Table 7

HOMO and LUMO molecular orbitals composition in the ground state for copper(II) complexes.

Complex	Molecular orbital	Energy (eV)	Contribution (%)		
			Cu	HL	X
1	LUMO+1	-1.8733	2	0	98
	LUMO	-1.9408	20	0	80
	HOMO	-3.1185	45	40	15
	HOMO-1	-4.6658	50	35	15
2	LUMO+1	2.3857	0	0	100
	LUMO	1.3753	0	100	0
	HOMO	-6.2805	100	0	0
	HOMO-1	-6.8386	100	0	0
3	LUMO+1	2.8534	10	25	65
	LUMO	2.7560	5	8	87
	HOMO	-3.6223	60	30	10
	HOMO-1	-4.4497	65	27	8

X = Neocuprin for **1**, HL for **2**, 2-(2-pyridyl)benzimidazole for **3**

Table 8

Antioxidant SOD activities (IC_{50} values, kinetic catalytic constant and SOD activity) of copper(II) complexes.

Compound	IC_{50} (μM)	k_{McCF} ($molL^{-1})^{-1}S^{-1}$	SOD activity (μM^{-1})	Reference
Native Cu Zn-SOD	0.04	-	25000	105
[Cu(Me ₄ bdpi)(H ₂ O) ₂](ClO ₄) ₃ ·4H ₂ O	1.1	-	909.09	10
[(PMDT)Cu-Ox-Zn(PMDT)]-(BPh ₄) ₂ ·2CH ₃ CN	205	1.62	4.88	41
[(Bipy) ₂ Cu-Im-Cu(Bipy) ₂](ClO ₄) ₃ ·CH ₃ OH	22	15.12	45.45	42
[Cu(idb)H ₂ O](NO ₃) ₂	1.02	-	980.4	106
[Cu(idb)H ₂ O](ClO ₄) ₂ ·H ₂ O	0.84	-	1190.5	106
[Cu(L)(neocuprin)]NO ₃ ·H ₂ O 1	21	15.84	47.62	This work
[Cu(L)(HL)]ClO ₄ 2	49	06.79	20.41	This work
[Cu ₂ (2-(2-pyridyl)benzimidazole) ₂ (L) ₂]ClO ₄ 3	17	19.57	58.82	This work

$$k_{McCF} = k_{NBT} \times [NBT] / IC_{50}, k_{NBT} = 5.94 \times 10^{-4} M^{-1} S^{-1}, [NBT] = 56 \mu mol$$

Graphical abstract

Three new copper(II) complexes have been synthesized and characterized using various physico-chemical techniques. The structures of the complexes have been determined by single crystal X-ray diffraction analysis. Antioxidant SOD activity tests showed that copper(II) complexes possess significant scavenging effect against free radicals.