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2-Benzoylpyridine and copper(II) ion in basic medium: Hydroxide nucleophilic addition stabilized by metal complexation, reactivity, crystal structure, DNA binding study and magnetic behavior

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ABSTRACT

On reaction of 2-benzoylpyridine (Bzpy) with copper(II) ion, different types of copper(II) complexes have been isolated in pure form depending upon the counter anion of the copper(II) salts used as reactant and the pH of the medium. Mono-nuclear copper(II) complexes of formula $[Cu(Bzpy)_2(ClO_4)_2]$ (1) and $[Cu(Bzpy)_2(H_2O)_2](NO_3)_2$ (2) were formed with copper(II) perchlorate and nitrate, respectively. On the other hand, following a similar reaction type in presence of alkali, we obtained the dinuclear copper(II) complex $[Cu_2(Bzpy)_2(BzOpy)_2(H_2O)](ClO_4)_2$ (3) containing the hydroxy-2-pyridylphenylmethanolato $(BzOpy)^-$ anion, achieved through the nucleophilic addition of the hydroxide to the carbonyl group of Bzpy, which is stabilized by metal complexation. However, this behavior was not recorded with copper(II) nitrate. The complexes were characterized by physicochemical and spectroscopic tools along with structural characterization by single crystal X-ray diffraction analysis. The interaction of dinuclear copper(II) complex **3** with calf thymus DNA (CT-DNA) has been investigated by using absorption and emission spectral studies and the binding constant (K_b) and the linear Stern–Volmer quenching constant (K_{sv}) have been determined. Complex **3** was active to oxidize the catechol to the corresponding quinone in MeCN medium *via* complex-catechol intermediate. Magnetic behavior for **3** is typical for uncorrelated spins down even up to 2 K.

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1. Introduction

The design of binuclear metal complexes incorporating suitable bridging ligands has attracted considerable research interest in recent years [1–4], primarily due to their relevance for biological processes, molecular electronics and for theoretical studies of electron transfer processes [5–9]. In addition binuclear copper(II) complexes are of interest for availing magnetostructural correlations and as useful model systems for catalysis. As far as biochemistry is concerned, catechol oxidases are ubiquitous plant enzymes, belonging to the oxidoreductase class and containing a dinuclear copper center, which catalyse the two-electron oxidation of a broad range of *o*-diphenols (catechol) to the corresponding quinones coupled with the reduction of molecular oxygen to water [10]. The synthesis and investigation of functional model

* Corresponding author. *E-mail address:* pabitracc@yahoo.com (P. Chattopadhyay). complexes for metalloenzymes that mimics the oxygenase activity is therefore of great promise for the development of new and efficient catalysts for oxidation reactions [11]. Moreover, compounds showing the property of cleaving double stranded DNA under physiological conditions are of importance since these could be used as diagnostic agents in medicinal and genomic research [12]. Several efficient cleaving agents have been developed over the course of time, however, most of the studies deal with macrocyclic mononuclear copper(II) complexes [13–15] indicating greater DNA cleaving efficiency of the macrocyclic binuclear copper(II) complexes than mononuclear ones [16].

Considering the above fact, with the use of 2-benzoyl pyridine (Bzpy) as ligand moiety we have synthesized the mononuclear copper(II) complexes $[Cu(Bzpy)_2(ClO_4)_2]$ (1) and $[Cu(Bzpy)_2(H_2O)_2]$ (NO₃)₂ (2), and one dinuclear copper(II) complex, $[Cu_2(Bzpy)_2(BzO-py)_2(H_2O)]$ (ClO₄)₂ (3) in alkali medium. The dinuclear one (3) contains the hydroxy-2-pyridylphenylmethanolato (BzOpy)⁻ monoanion *in situ* formed through the nucleophilic addition of the hydroxide to the ketone group of the 2-benzoyl pyridine. The

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new ligand results stabilized upon coordination and to the best of our knowledge it represents the first structurally characterized report of this species. The interaction of complex **3** with DNA (CT-DNA) along with the oxidation of catechol to its corresponding quinone *via* complex-catechol intermediate has been investigated using spectral studies. The magnetic properties of complex **3** are also reported, here.

2. Experimental

2.1. Materials and physical measurements

All chemicals and reagents were obtained from commercial sources and used as received. Solvents were distilled from an appropriate drying agent. Tris-HCl buffer solution and CT-DNA were purchased from Bangalore-Genie, ethidium bromide (EB) from Sigma. Microanalyses were performed with the use of a Perkin–Elmer 2400 CHN elemental analyzer. Copper analyses were carried out by Varian atomic absorption spectrophotometer (AAS) model-AA55B, GTA using graphite furnace. Infrared spectra were obtained by a JASCO FT-IR model 420 using KBr disk. Electronic spectra were recorded on the JASCO UV-Vis/NIR model V-570. Magnetic moments (μ , B.M.) were obtained from vibrating sample magnetometer PAR 155 model. The magnetic measurements were carried out with a Quantum design MPMS-5S SQUID susceptometer. Molar magnetic susceptibility was recorded between 300 and 2 K with an applied field of 1 kOe. Data have been corrected for the sample holder and for the diamagnetic contribution of all atoms by using Pascal's tables [17]. The field dependence of the magnetization was recorded at 2 K up to 50 kOe. All measurements have been performed on crushed crystals, the powder (46.5 mg) was mixed to grease and hold in a gelatin capsule.

2.2. Reactions of 2-benzoylpyridine with copper(II) ion

2.2.1. Synthesis of $[Cu(Bzpy)_2(ClO_4)_2]$ (1)

To a methanolic solution of 2-benzoyl pyridine (2 mmol, 366 mg) copper(II) perchlorate hexahydrate (1 mmol, 370 mg) in methanol was added dropwise and the mixture was stirred for 4 h at ambient temperature. Then the reaction mixture was filtered off and the green single crystals, suitable for X-ray diffraction, were obtained from the filtrate through slow evaporation at room temperature. Yield: 80–85%.

(1): Anal. Calc. for $C_{24}H_{18}Cl_2CuN_2O_{10}$: C, 45.78; H, 2.74; N, 4.48; Cu, 10.37. Found: C, 45.82; H, 2.89; N, 4.45; Cu, 10.11%. IR (cm⁻¹): $v_{C=N}$, 1472; $v_{(3)ClO_4}$, 1135, 1060. Magnetic moment (μ , B.M.): 1.71.

2.2.2. Synthesis of $[Cu(Bzpy)_2(H_2O)_2](NO_3)_2$ (2)

It was prepared following a similar procedure as for **1** by replacing only the copper(II) perchlorate with the nitrate salt.

(2): *Anal.* Calc. for $C_{24}H_{22}CuN_4O_{10}$: C, 25.78; H, 1.60; N, 2.48; Cu, 10.97. Found: C, 48.84; H, 3.76; N, 9.50; Cu, 10.77%. IR (cm⁻¹): $v_{C=N}$, 1473; v_{NO_3} , 1379. Magnetic moment (μ , B.M.): 1.74.

2.2.3. Synthesis of $[Cu_2(Bzpy)_2(BzOpy)_2(H_2O)](ClO_4)_2$ (3)

To a methanolic solution of 2-benzoyl pyridine (2.0 mmol 366 mg) copper(II) perchlorate hexahydrate (1.0 mmol, 370 mg) was added dropwise and the mixture was stirred for 4 h at ambient temperature. Then KOH (1.0 mmol, 56 mg) in methanol was added and the final mixture was stirred for another 2 h. The solution was kept aside and after a few days, deep green colored crystalline complex was obtained by filtration followed by washing with water, methanol and dried in a vacuum arrangement. Single crystals suitable for X-ray diffraction were also obtained from this solution. Yield: 70–75%.

(**3**): Anal. Calc. for $C_{48}H_{40}Cl_2Cu_2N_4O_{15}$: C, 51.72; H, 3.68; N, 4.98, Cu, 11.32. Found: C, 51.88; H, 3.63; N, 5.04, Cu, 11.45%. IR (cm⁻¹): $\nu_{C=0}$, 1750; ν_{CI0_4} , 1084.

2.3. X-ray crystal structure analyses

Diffraction data were collected at room temperature on a Nonius DIP-1030H system (complex 1) and at 173 K on a Stoe Mark II-Image Plate Diffraction System [18] equipped with a two-circle goniometer for complex **3**. The radiation used was Mo K α graphite monochromatized ($\lambda = 0.71073$ Å) in both cases. Cell refinement, indexing and scaling of the data sets were performed using programs Denzo, Scalepack [19] and CrysAlis [20]. An empirical absorption correction was applied to the data of compound **3** using the MULscan ABS routine in PLATON [21].

The structures were solved by direct methods [22] and subsequent Fourier analyses and refined by the full-matrix least-squares method [22] based on F^2 with all reflections. The H-atoms were included at calculated positions and treated as riding atoms using SHELXL default parameters, those of the coordinated water in **3** were located on ΔF map. In compound **3** the two perchlorate anions are positionally disordered with large thermal displacement parameters. Oxygen atoms of Cl(1) are disordered over two positions (occupancies 0.72/0.28), while the other anion is located over two positions (0.6/0.4) sharing two O atoms. Moreover two adjacent residuals were interpreted as partially occupied water molecules (occupancy of 0.2 each). In the final cycles of refinement the perchlorate anions and the water molecules were held fixed.

All the calculations were performed using the WinGX System, Ver. 1.80.05 [23]. Crystal data and details of data collection and refinement for the structures reported are summarized in Table 1.

2.4. DNA binding experiments

The Tris–HCl buffer solution (pH 8.0), used in all the experiments involving CT-DNA, was prepared by using deionized and sonicated HPLC grade water (Merck). The CT-DNA was sufficiently free from protein, being the ratio of UV absorbance of the DNA in Tris–HCl solution at 260 and 280 nm ($\Lambda_{260}/\Lambda_{280}$) of *ca.* 1.9 [24].

Table 1 Crystal data and details of structure refinement for complex 1 and 3.

	1	3 ·0.4(H ₂ O)
Formula	$C_{24}H_{18}Cl_2CuN_2O_{10}$	$C_{48}H_{40}Cl_2Cu_2N_4O_{15} \cdot 0.4(H_2O)$
Formula weight	628.84	1118.03
Crystal system	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/n$
a (Å)	6.848(3)	18.6204(13)
b (Å)	13.889(4)	14.1696(8)
c (Å)	13.211(4)	18.7372(13)
β(°)	92.98(3)	102.195(5)
V (Å ³)	1254.8(8)	4832.1(6)
$\rho_{\rm calc} ({\rm g/cm^3})$	1.664	1.536
Ζ	2	4
F(000)	638	2288
θ Range (°)	2.13-23.25	1.4-25.70
μ (Mo K $lpha$) (mm $^{-1}$)	1.146	1.066
Reflections collected	5693	65 242
Independent reflections (R_{int})	1752	9143
R merge	0.0973	0.0502
Reflections $I > 2\sigma(I)$	781	7198
Goodness-of-fit (GOF) on F ²	0.798	1.037
Final <i>R</i> indices $[I > 2\sigma(I)]$	$R_1 = 0.0440$ $wR_2 = 0.0898$	$R_1 = 0.0461$ $wR_2 = 0.1155$
R indices (all data)	$R_1 = 0.1098$ $WR_2 = 0.1008$	$R_1 = 0.0630$ $wR_2 = 0.1231$

The concentration of DNA was determined with the help of its extinction coefficient ε of 6600 L mol⁻¹ cm⁻¹ at 260 nm [25]. Stock solution of DNA was always stored at 4 °C and used within 4 days. Concentrated stock solution of complex 3 was prepared by dissolving the copper(II) complex in DMSO and diluting suitably with Tris-HCl buffer to the required concentration for all the experiments. Absorption spectral titration experiment was performed by keeping constant the concentration of the copper(II) complex with varying the CT-DNA concentration. To eliminate the absorbance of DNA itself, equal solution of CT-DNA was added either to the copper(II) complex solution and to the reference one. In the fluorescence displacement experiment with ethidium bromide (EB), 5.0 mL of EB solution $(1.0 \text{ mmol } L^{-1})$ in Tris-HCl were added to 1.0 mL of DNA solution at saturated binding levels [26], and stored in the dark for 2.0 h. The copper(II) complex solution was titrated into the DNA/EB mixture and then diluted in Tris-HCl buffer to 5.0 mL making the solutions with the varied mole ratio of the copper(II) complex to CT-DNA. Prior to measurements, the mixture was shaken up and incubated at room temperature for 30 min. The fluorescence spectra of EB bound to DNA were obtained at an emission wavelength of 584 nm.

2.5. Reactivity of complex 3: oxidation of catechol

To record the reactivity of complex **3** towards stable organic compound, the oxidation of catechol to the corresponding quinone under dinitrogen atmosphere has been studied by treating an appropriate amount of 10^{-4} mol dm⁻³ solutions of **3** in acetonitrile with 10^{-2} mol dm⁻³ (100 eq.) of catechol and recording the UV–Vis spectra.

3. Results and discussion

3.1. Synthesis and characterization

The copper(II) complexes 1-3 were obtained in good yield by the reaction of the corresponding copper(II) salts with 2-benzoylpyridine in methanol. The dinuclear complex [Cu₂(Bzpy)₂(BzO $py_{2}(H_{2}O)](ClO_{4})_{2}$ (3) was collected to stir the reaction mixture (obtained from the reaction of copper(II) perchlorate and 2-benzoylpyridine in 1:2 M ratio) in alkaline (KOH) medium. It is noteworthy that the complex 3 was also obtained if the methanolic solution of complex, 1 was stirred in alkaline KOH medium as given in Scheme 1. The probable reaction path has been shown in Scheme 2. This may be taken place due to the presence of the two large perchlorate ions in the axial position of the octahedral coordination sphere of copper(II) ion in complex 1 (supported by the crystal structure described in Section 3.2). This is an unusual situation for copper(II) ion to accommodate two perchlorate ions in the coordination sphere. And as a result of sterically hindered condition, this was occurred in case of the complex 1, but similar phenomena was not observed in case of complex 2 where two water molecules was comfortably present in the coordination sphere of copper(II) ion as usual.

All the complexes are soluble in methanol, DMF and DMSO. In the solid state the complex is fairly stable in air so as to allow performing physical measurements. The room temperature magnetic moment (μ) of complex **1** and **2** are 1.71 and 1.74 B.M., equivalent to one unpaired electron. In case of the complex **3**, [Cu₂(Bzpy)₂(BzOpy)₂(H₂O)](ClO₄)₂, two Cu(Bzpy) fragments are bridged by oxygen of the new hydroxy-methanolato ligand formed by nucleophilic addition of hydroxide to carbonyl group. The variable temperature magnetic moment of **3** was measured and will discuss in details at Section 3.6.



Scheme 1. Reactions of 2-benzoylpyridine with copper(II) ion.

3.2. Structural description of complexes

The ORTEP view of complex $[Cu(Bzpy)_2(ClO_4)_2]$ (1) with the atom numbering schemes is illustrated in Fig. 1 and a selection of bond distances and angles is reported in Table 2. The molecular structure of the complex is centrosymmetric with the N, O chelating Bzpy ligands located in the equatorial plane (Cu–O and Cu–N bond distances of 1.988(4) and 1.956(4) Å, respectively) and completing the coordination sphere by two perchlorate ions at considerably longer distance (Cu–O(4) = 2.451(4) Å) as expected for the Jahn–Teller distortion. The chelating angle N–Cu–O angle is 82.08(18)°. The crystal packing shows complex molecules well separated that do not exhibit short contacts.

The molecular structure of complex **2** consists of centrosymmetric $[Cu(Bzpy)_2(H_2O)_2]^{2+}$ cations and nitrate ions. Since its structural characterization has been already reported [27], it is not discussed in detail. The Cu–O and Cu–N bond distances of the chelating Bzpy ligands are 2.068(2), and 1.965(2) Å, respectively. The former being longer than the value measured in **1**, but conversely the axial Cu–OH₂ is significantly shorter (2.256(3) Å).

The molecular structure of complex **3** together with the atom numbering is illustrated in Fig. 2 and the crystal packing in Fig. 3. A selection of bond distances and angles are listed in Table 2. The X-ray structural determination confirms the presence in the dinuclear complex $[Cu_2(Bzpy)_2(BzOpy)_2(H_2O)]^{2+}$ of the $(BzOpy)^-$ anion formed by the nucleophilic addition of the hydroxide to the ketone group of Bzpy.

The formation of the $(BzOpy)^-$ anion was rather unexpected, although a similar reaction is frequently observed for the di-2-pyridylketone [(2-py)₂CO]. In fact when this ligand is coordinated to a number of metal ions, its carbonyl group easily undergoes addition of various nucleophiles, including water and methanol, forming the *gem*-diol [(2-py)₂C(OH)₂] and the hemiacetal form [(2-py)₂C(OR) (OH)], respectively. The former can function either as mono- or di-anionic and the presence of deprotonated hydroxy group(s) leads to a great coordinative flexibility [28–32]. The cited references report some selected examples of copper complexes, but hundreds of complexes containing other transition metal ions have been reported. On the other hand, structural result of **3** represents at our best knowledge the first report of the $(BzOpy)^-$ species stabilized upon coordination to the metal.



Scheme 2. Probable reaction path to form complex 3.



Fig. 1. ORTEP view (ellipsoids at 35% probability) of complex 1 with labeling scheme of independent atoms.

In complex **3** the metal ions Cu(1) and Cu(2) show an octahedral and a square pyramidal coordination geometry, respectively. In fact each (BzOpy)[–] anion is mono-coordinated to one copper ion through the pyridine N donor (Cu–N distances of 1.989(3) and 1.977(3) Å in Cu(1) Cu(2), respectively), whereas the methanolate oxygen acts as bridging donor towards the two Cu(Bzpy) fragments with Cu–O distances in between 1.916(2)–1.960(2) Å. These bridging oxygens, which form the Cu₂O₂ core of the complex, figure out Cu–O–Cu bond angles of 102.71(9)° and 103.58(10)°, and separate the metals at 3.028 Å.

Table 2	
Selected coordination bond lengths (Å) and angles (°) for ${\bf 1}$ and ${\bf 3}.$	

Complex 1			
Cu-N(1)	1.956(4)	Cu-O(1)	1.988(4)
Cu-O(4)	2.451(4)		
N(1)-Cu-O(1)#1	97.92(18)	O(1)-Cu-O(4)	89.76(16)
N(1)-Cu-O(1)	82.08(18)	O(1)-Cu-O(4)#1	90.24(16)
N(1)-Cu-O(4)#1	95.51(15)	C(6)-O(1)-Cu	113.5(4)
N(1)-Cu-O(4)	84.49(15)		
., .,	. ,		
Complex 3			
Cu(1)-N(3)	1.989(3)	Cu(2)-N(1)	1.977(3)
Cu(1)-N(4)	2.016(2)	Cu(2)-N(2)	1.991(2)
Cu(1) - O(1)	1.960(2)	Cu(2) - O(1)	1.916(2)
Cu(1)-O(4)	1.928(2)	Cu(2) - O(4)	1.925(2)
Cu(1)-O(1w)	2.450(2)	Cu(2)-O(3)	2.391(2)
Cu(1)-O(6)	2.499(2)		
N(3)-Cu(1)-N(4)	102.38(10)	O(6)-Cu(1)-N(3)	88.82(9)
O(1)-Cu(1)-O(1w)	88.79(9)	O(6)-Cu(1)-N(4)	73.01(9)
O(1)-Cu(1)-O(4)	76.22(9)	N(1)-Cu(2)-N(2)	100.64(10)
O(1)-Cu(1)-O(6)	97.49(9)	O(1)-Cu(2)-O(3)	105.99(8)
O(1)-Cu(1)-N(3)	157.47(10)	O(1)-Cu(2)-O(4)	77.33(9)
O(1)-Cu(1)-N(4)	100.16(9)	O(1)-Cu(2)-N(1)	82.24(10)
O(1w)-Cu(1)-O(4)	91.83(8)	O(1)-Cu(2)-N(2)	176.87(10)
O(1w)-Cu(1)-O(6)	165.83(9)	O(3)-Cu(2)-O(4)	102.15(8)
O(1w)-Cu(1)-N(3)	90.17(9)	O(3)-Cu(2)-N(1)	88.56(9)
O(1w)-Cu(1)-N(4)	93.43(9)	O(3)-Cu(2)-N(2)	75.44(9)
O(4)-Cu(1)-O(6)	101.99(8)	O(4)-Cu(2)-N(1)	158.86(10)
O(4)-Cu(1)-N(3)	81.32(10)	O(4)-Cu(2)-N(2)	99.68(9)
O(4) - Cu(1) - N(4)	173.56(9)		



Fig. 2. ORTEP view (ellipsoids at 50% probability) of complex **3**, C atoms not labeled for sake of clarity.

Here the N, O chelating Bzpy ligands have the oxygen located at one axial position of the octahedral coordination sphere of Cu(1) and at the apical site of the square pyramid of Cu(2). Thus Cu–O(Bzpy) bond lengths of 2.499(2) Å (Cu(1)–O(6)) and 2.391(2) Å (Cu(2)–O(3)) are significantly elongated with respect the value measured in **1**, while the Cu(1)–N(4) and Cu(2)–N(2) are only sensibly longer (2.016(2) and 1.991(2) Å, respectively). The octahedral geometry of Cu(1) is completed by an aqua ligand with Cu(1)–O(1w) bond length of 2.450(2) Å.

Excluding the coordinated water molecule at Cu(1), the complex has an approximately 2-fold axis with the pseudo symmetry axis passing in between the metals, approximately normal to Fig. 2. The chiral C atoms in the $(BzOpy)^-$ anions of each complex have the same configuration.

The coordinated water molecule O(1w) and the hydroxyl groups, which are located on the same side of the equatorial plane



Fig. 3. Side view of complex **3** showing the hydrogen bond interactions with the perchlorate anions. Only oxygen atoms at higher occupancy (0.72) are shown for Cl(1) anion, while perchlorate Cl(2) is splitted over two positions (0.60/0.40).

of the complex, form hydrogen bonds with the perchlorate counterions giving rise to a discrete entity (Fig. 3). The positional disorder detected for the counter anions (see Section 2) could be a requirement to ensure these interactions, but due to this crystallographic feature a detailed analysis is meaningless.

3.3. Spectral characterization

In IR spectra, the point of interest for **1** and **3** is the band due to perchlorate. The perchlorate v_3 vibration of **1** splits into two stretching frequencies at 1135 and 1060 cm⁻¹, suggesting the unidentate function of the ClO₄⁻ ligand to Cu(II) ion in the solid state [33,34] and it is also supported by the X-ray crystallographic structure. But in the IR spectrum of complex **3** an intense absorption band at 1085 cm^{-1} along with a weak band at *ca*. 623 cm^{-1} due to the symmetric $(v_{s(C104)})$ and asymmetric $(v_{as(C104)})$ stretching vibration of non-coordinated perchlorate ion, respectively were observed. In addition to the characteristic band at *ca*. 1750 cm⁻¹ assignable to $v_{C=0}$ observed in the IR spectra of **1** and **3**, a weak band around 3350 cm⁻¹ attributable to v_{OH} was observed only in the IR spectrum of complex 3. The presence of an intense band at around 1379 cm⁻¹ (corresponding to v_{NO_3}) in the IR spectrum of complex 2 confirm the existence of the nitrate ion as counter anion; besides those observed in the range $1469-1478 \text{ cm}^{-1}$ for v_{NO_3} . Band attributable to $v_{(Cu-N)}$ at *ca*. 455 is present in IR spectra of the three complexes present.

The electronic spectra of **1** and **3** were recorded in acetonitrile at room temperature. The intraligand absorptions <400 nm are assigned to $\pi \rightarrow \pi^*$ (226 nm, $\varepsilon = 17,687 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ for **1** and 224 nm, $\varepsilon = 16\,902 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ for **3**) and $n \rightarrow \pi^*$ (258 nm, $\varepsilon = 7123 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ for **3**) and $n \rightarrow \pi^*$ (258 nm, $\varepsilon = 7123 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ for **1** and 261 nm, $\varepsilon = 6453 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ for **3**) transitions. The complex **1** exhibit the characteristic broad d–d absorption band at 540 nm (438 dm³ mol⁻¹ cm⁻¹) with a shoulder at low energy at *ca.* 695 nm (112 dm³ mol⁻¹ cm⁻¹) in solution along with an intense demonstrates square planar geometry around the copper ion in the solution state [35]. A characteristic broad d–d absorption band at *ca.* 597 nm (398 dm³ mol⁻¹ cm⁻¹) observed in the electronic spectra of the complex **3** demonstrates the square pyramidal geometry around the copper ion in the solution state and it is assignable to assigned to the envelope of ${}^{2}B_{1g} \rightarrow {}^{2}A_{1g}$, ${}^{2}B_{2g}$ and ${}^{2}E_{g}$ transitions [36].

3.4. DNA-binding studies

3.4.1. Electronic absorption titration

The absorption spectra of complex **3** in the absence and presence of CT-DNA help to examine the binding mode of the copper complex with DNA helix. As shown in Fig. 4, when titrated by the CT-DNA, the copper complex showed a significant hyperchromism effect centered at the 270 nm absorption maximum, suggesting that a strong interaction is operative between the copper(II) complex and DNA. The observed spectral changes of the complex in the presence of CT-DNA might be indicative of groove binding mode interaction [37]. The literature survey shows that the interaction of the molecules having unfused aromatic ring systems linked by bonds that guarantee torsional freedom with DNA, allows the molecules to adopt appropriate conformation to closely match the helical turn of DNA grooves [38]. Here, the aromatic rings of the ligands in the copper(II) complex are likely to facilitate the formation of van der Waals contacts within the walls of groove or hydrogen bonds in DNA grooves. These spectral data helped us to calculate the intrinsic binding constant $K_{\rm b}$ of **3** with CT-DNA using the following equation [39] from the slope to intercept ratio of the graph obtained by plotting the $[DNA]/(\varepsilon_a - \varepsilon_f)$ versus [DNA] (Fig. 5).

$$[\text{DNA}]/(\varepsilon_{a} - \varepsilon_{f}) = [\text{DNA}]/(\varepsilon_{b} - \varepsilon_{f}) + 1/[K_{b}(\varepsilon_{b} - \varepsilon_{f})]$$

where [DNA] is the DNA concentration, ε_a , ε_b and ε_f symbolizes the extinction coefficient for each addition of DNA to the copper(II) complex, for the copper complex in the fully bound form and for the free copper complex, respectively. This binding constant K_b of **3** with CT-DNA was found to be 3.8×10^4 M⁻¹ (R = 0.99866, four regression points). This value compares well with that of the well-established groove binding agent [40].

3.4.2. Ethidium bromide fluorescence displacement experiments

The ethidium bromide (EB) fluorescence displacement experiments were also performed to investigate the interaction mode of **3** with CT-DNA. EB has been used to probe the interaction of metal complexes with DNA as the fluorescence intensity of EB is enhanced for its intercalation into the DNA and is quenched by the addition of another molecule being displaced in this case from DNA [41,42]. A significant decrease of the fluorescence intensity



Fig. 4. Electronic spectral titration of **3** with CT-DNA at 270 nm in Tris–HCl buffer; [complex] = 5.16×10^{-5} ; [DNA] $\times 10^{-6}$: (a) 0.0, (b) 0.94, (c) 2.00, (d) 4.82, and (e) 7.76 mol L⁻¹. The arrow indicates the increase of DNA concentration.



Fig. 5. Plot of [DNA]/(ϵ_a - ϵ_f) vs. [DNA] for the titration of **3** with CT-DNA in Tris–HCl buffer. Binding constant (K_b) = 3.8 × 10⁴ M⁻¹ (R = 0.99866). PABITRA if you report Plot of [DNA]/(ϵ_a - ϵ_f) × 10⁻¹⁰ vs. [DNA] × 10⁻⁶, CORRECT it would be more clear (just a suggestion).

of EB/DNA system is observed at 584 nm with the increasing concentration of **3** as reported in Fig. 6. The present observation leads us to guess that the copper complex may interact with DNA through a groove binding mode, releasing some EB molecules from the EB–DNA system. The quenching of EB bound to DNA due to the presence of the complex can be interpreted with the linear Stern– Volmer equation [43]:

$$I_0/I = 1 + K_{sv}[Q]$$

where I_0 and I represent the fluorescence intensities in the absence and presence of quencher, respectively. K_{sv} is the linear Stern–Volmer quenching constant and Q is the concentration of quencher. From the slope to intercept ratio in the plot of I_0/I versus [complex] (Fig. 7), the K_{sv} value was found to be 0.5×10^4 (R = 0.98775 for five points), which indicates a strong affinity of the copper(II) complex to CT-DNA.

3.5. UV–Vis spectroscopic study of reaction of complex 3 with catechol

First of all, the UV–Vis activities of pure catechol, dicopper(II) complexes and *o*-quinone in acetonitrile have been investigated.



Fig. 6. Emission spectra of the titration of the CT-DNA-EB system with complex **3** in Tris-HCl buffer. k_{ex} = 522 nm; [EB] = 0.96 × 10⁻⁶ mol L⁻¹; [DNA] = 2.07 × 10⁻⁵; [complex] × 10⁻⁶: (a) 0.0, (b) 0.82, (c) 1.64, (d) 2.46, and (e) 3.28 mol L⁻¹. The arrow indicates the increase of complex concentration.



Fig. 7. Plot of l_0/l vs. [complex] for the titration of **3** to the CT-DNA-EB system using spectrofluorimeter; linear Stern–Volmer quenching constant $K_{sv} = 0.5 \times 10^4$; (*R* = 0.98775, five regression points).



Fig. 8. Changes in UV-Vis spectra of catechol upon addition of complex 3.

Catechol is observed to be silent in the range of 350–800 nm, where o-quinone exhibits a band at 370 nm. To study the reaction of the dicopper(II) complex with catechol in acetonitrile medium, 5×10^{-5} mol dm³ solution of **3** was treated with 5×10^{-3} mol dm⁻³ (100 eq.) of catechol under aerobic condition. Immediately after the addition of the complex, the colorless solution becomes yellow. Then UV–Vis spectroscopic study (Fig. 8) was performed on this mixture. Change in intensity and band position was observed taking reading at intervals of 20 min during 2 h of the reaction course. No further change in intensity was detected after 2 h of the reaction completion. This result proves the oxidation of catechol to quinone catalyzed by complex **3**.

$$\begin{split} & [Cu_2^{II}(Bzpy)_2(BzOpy)_2(H_2O)](ClO_4)_2 + catechol \\ & \rightarrow [Cu_2^{I}(Bzpy)_2(BzOpy)_2(H_2O)] + orthoquinone \end{split}$$

3.6. Temperature dependence of magnetic susceptibility of complex 2

The temperature dependence of the molar magnetic susceptibility, χ_{M} , of complex **3** has been measured in the temperature range of 2–300 K. Results are plotted in the form of $\chi_{M}T$ versus *T* in Fig. 9. The value for $\chi_{M}T$ at 300 K is 0.80 cm³ mol⁻¹ K, which is



Fig. 9. Plot of $\chi_M T$ vs. *T* for complex **3**.

in good agreement with two non-interacting $S = \frac{1}{2}$ spin with g = 2.06. This value remains unchanged for lower temperatures with a slight decrease below 70 K to reach 0.78 cm³ mol⁻¹ K for 2 K. This behavior is typical for uncorrelated spins.

This behavior is rather surprising when the compound's structure is considered. Indeed, for two Cu(II) bridged by two alkoxo-oxygens sitting in equatorial position for both ions, with a Cu–O–Cu angle of *ca.* 103°, one would expect substantial antiferromagnetic interactions [44,45]. In the lack of any salient structural feature that may be invoked to account for the absence of exchange coupling, this behavior remains puzzling. More examples of related Cu dimers involving this bridging ligand will be required to conclude on the role of this peculiar ligand.

4. Conclusion

The reaction of 2-benzoylpyridine (Bzpy) with copper(II) salts leads to octahedral mononuclear complexes $[Cu(Bzpy)_2(ClO_4)_2]$ (1) and $[Cu(Bzpy)_2(H_2O)_2](NO_3)_2$ (2) By stirring the methanolic solution of complex **1** in alkaline medium or the by allowing a reaction with the reaction mixture of copper(II) perchlorate and Bzpy (1:2 M ratio) in alkaline medium a dinuclear complex, $[Cu_2(Bzpy)_2\{BzOpy\}_2(H_2O)](ClO_4)_2$, was obtained. The latter includes the monoanionic ligand BzOpy, obtained through the addition of a hydroxide to carbonyl group of Bzpy, which results stabilized upon metal coordination. This phenomenon of occurring the dinuclear copper(II) complexes 3 may be due to the presence of two perchlorate ions in the coordination sphere with a steric interactions. The dinuclear complex shows a biological activity, since it oxidizes the catechol to the corresponding quinone in MeCN medium and interacts with calf thymus DNA (CT-DNA) through a groove binding mode interaction.

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Appendix A. Supplementary material

CCDC 773466 and 773465 contain the supplementary crystallographic data for **1** and **3**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc. cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ica.2010.11.012.

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