An oxamato bridged trinuclear copper (II) complex with 5-nitro-1,10-phenanthroline : Synthesis, reactivity, DNA and BSA binding study

Sanjoy Dhara[a] and Sandipan Sarkar[b*]

[a]*Department of Chemistry, Santipur college, Nodia-741401*
[b]*Department of Applied Science and Humanities, Durgapur Institute of Advanced Technology &
Management, Rajbandh, Durgapur-713212, India*

Abstract: A new trinuclear oxamato bridged copper(II)complex was isolated from the reaction mixture of $Na_2[Cu(pba)]3H_2O$, copper perchlorate hexahydrate and 5-nitro-1,10-phenanthroline(np) in methanol. The structure of complex has been confirmed through elemental, magnetic susceptibility, and molar conductivity analysis. IR, UV-Vis. It shows that the complex has composition of $[Cu_3(pba)(np)_2)](ClO_4)_2(pbaH_4 = $ 1,3-propanediylbis (oxamic acid), np = 5-nitro-1,10-phenanthroline)type. The hydrolysis of complex in basic medium and thermo-gravimetric analysis also confirmed the presence of three copper ions in the complex. Binding ability of the complex with calf thymus-DNA (CT-DNA) and bovine serum albumin (BSA) were studied by measuring the effects of absorption, emission spectral and viscosity measurement studies. All the results suggest that the complex interacts strongly with calf thymus-DNA (CT-DNA) and bovine serum albumin (BSA) with a binding constant (K_b) of 4.01×10^4 and 4.5×10^5 and linear Stern–Volmer quenching constant (K_{sv}) of 6.9×10^4 and 3.7×10^5 respectively. Electrochemical equivalency of three copper(II)ions in complex was identified by getting only one quasi reversible cyclic voltammogram.

Keywords: Copper complex; Nitrogen–sulfur ligand; DNA binding, BSA Binding

Introduction

Polynuclear copper(II)[1] complexes are the great deal of interest because on one hand, copper is an essential bioelement responsible for numerous catalytic processes in living organisms, on the other hand, to the possibility provided by copper(II) polynuclear complexes of exploration of magneto-structural correlations[2-4].Multinuclear Cu sites in metalloproteins are inportent for a wide range of functions, including oxygen transport (hemocyanin),[5] electron transfer (CuA from cytochrome *c* oxidase [C*c*O] and nitrous oxide reductase [N2-OR]), [6, 7] oxidases and oxygenases (catechol oxidase, ascorbate oxidase, and particulate methane monooxygenase [pMMO], for example),[8,9] and the reduction of nitrous oxide to dinitrogen (CuZ from N2OR). [7] Depending on the ligands used, trinuclear Cu(II) complexes have shown to possess different arrangements of metal atoms, namely equilateral-, isosceles-scalene-triangular beside linear clusters [10].

Y. Journaux et al. [11] have emphasized on the synthesis of polynuclear complexes as the following synthetic schemes: (i) the self-assembly method, (ii) the use of polynucleating ligands, and (iii) the use of complexes as ligands.

In this paper We have used the strategy "complexes as ligands" for the preparation of trinuclear copper complex. Copper-oxamate, $[Cu(pba)]^{2-}$ complex has been used as the ligand in the preparation of trinuclear complex. This paper deals with the synthesis, spectroscopic characterization and biological activities of an oxamato-bridged linear trinuclear copper(II) complex, $[Cu_3(pba)(np)_2(H_2O)(ClO_4)]ClO_4H_2O$ (1), where $pbaH_4$ = 1,3-propylenebis(oxamic acid) and np= 5-Nitro-1,10-phenanthroline. Several homo-trinuclearcopper(II) complexes or hetero-bimetallic transition metal complexes have been synthesized using

the coordination capability of metallo-ligands [12–18] in search of new magnetic material. But still no attention has been paid on the biological reactivity of this type of complex except our group [19]. The biological activity of the trinuclear complex towards CT-DNA and BSA have been explored and the interaction studied by means of absorption and emission spectra to obtain the binding constant (K_b) and the linear Stern–Volmer quenching constant (K_{sv}).

Experimental

Materials and physical measurements

All chemicals used were analytical reagent and were commercially available. Solvents were distilled from an appropriate drying agent. Calf thymus-DNA, Tris–HCl buffer solution from Bangalore-Genie and BSA, ethidium bromide (EB) from Sigma were used as received. The metallo-ligand, $Na_2[Cu(pba)]_3H_2O$ was prepared following the reported procedure [20] with a little modification. The elemental analyses (C, H and N) were performed on a Perk in Elmer model 2400 elemental analyzer. Copper analyses were carried out by Varian atomic absorption spectrophotometer (AAS) model-AA55B, GTA equipped with graphite furnace. IR spectra were obtained on JASCO FT-IR model 460 plus spectrometer with KBrdisk, electronic absorption spectra on a JASCO UV–Vis/NIR spectrophotometer model V-570, and the fluorescence spectra on a Fluorometer Hitachi-2000. The magnetic susceptibility measurements were performed at room temperature by using a vibrating sample magnetometer PAR 155 model. Molar conductance (L_M) was measured in a Systronics conductivity meter 304 model using solutions 10^{-3} mol L^{-1} in appropriate solvents. Thermo-gravimetric analysis was performed on a Perkin-Elmer Diamond TG/DTA Thermal Analyzer from room temperature to 330 °C at a heating rate of 20°C min^{-1} using platinum crucibles. Electrochemical measurements were recorded on a computer controlled EG&G PAR model 270 VERSTAT electrochemical instruments with TEAP as supporting electrolyte, a Pt-disk as working electrode and a Pt-wire as auxiliary electrode. All the measurements were made at 298 K with acetonitrile as solvent.

Synthesis of trinuclear complex

A solution of 5-nitro-1,10-phenanthroline (2.0 mmol, 0.45 g) in methanol was added dropwise upon starring to a solution of copper perchlorate hexahydrate (2.0 mmol, 742 mg) in methanol (25 mL) and the mixture was stirred for 4.0 h at ambient temperature. Then an aqueous solution of metallo-ligand, $Na_2[Cu(pba)]_3H_2O$ (1.0 mmol, 378 mg) was added dropwise to the resulting mixture at stirring condition. The mixture was filtered and the clear filtrate was kept aside. After a few days, deep blue colored crystalline complex was obtained by filtration followed by washing with water, methanol and dried in vacuo.

Yield: 80–85%

DNA binding experiments

All the experiments involving CT-DNA and BSA, which were studied by UV absorbance and fluorescence displacement of ethidium bromide (EB), were performed following our previously reported method [29].

Results and discussion

Synthesis and characterization

In this work the copper(II) complex of 1,3-propylenebis (oxamide) of formulation $Na_2[Cu(pba)]3H_2O$ was prepared according to th literature method[20] and was used as metallo-ligand to react with copper(II) perchloratehex ahydrateandnp for the synthes is of the trinuclear copper(II) complex in methanol medium at ambient temperature. The novel complex was characterized by physico-chemical and spectroscopic tools. The complex is stable in air and soluble in methanol, DMF and DMSO and insoluble in hexane, ether and dichloromethane. The conductivity measurement in methanol showed a conductance of 104 Ko mol1 cm1 at 300 K suggesting that in solution complex exists as 1:1 electrolyte and it has the same structure both in solution and solid state.

Spectral characterization

The IR spectrum of the complex (fig. 1) showed a broad intense band at 1100 cm^{-1} and another splitted band at 610 cm^{-1} assigned to ν_{ClO4}^- symmetricand asymmetric stretching, which suggests the presence of coordinated ClO_4^- to one of the copper atoms. A characteristic band at 1472 cm^{-1}is assignable to the $\nu_{C=N}$ stretching frequency. Another characteristic band at 1600 cm^{-1} indicates the presence of C=O group in complex. The ring skeletal vibrations (C=C) were consistent in the region of 1440–1465 in the complex [30]. In the lower frequency region medium-weak bands observed at 551–563 and 435–458 cm^{-1} have been assigned to (M–N) and (M–O) vibrations, respectively [31, 32].
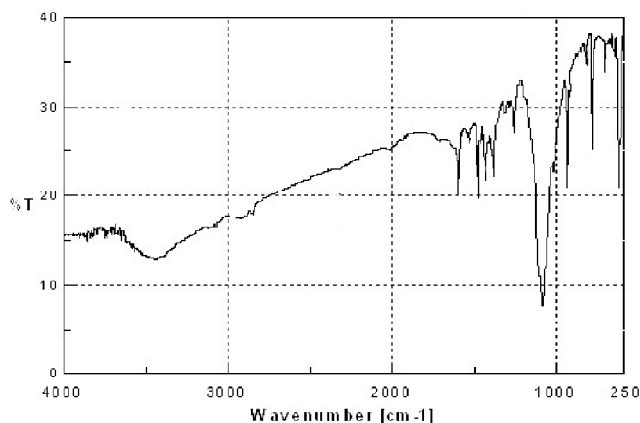
Figure 1: IR spectrum of the complex **1**

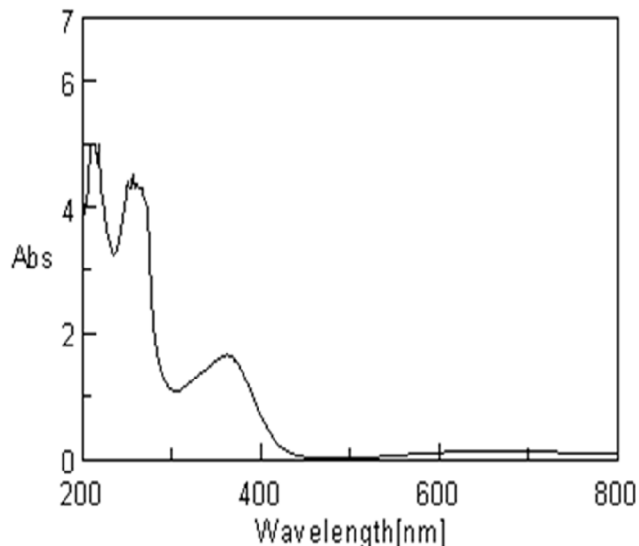**Figure 2:** A UV-Vis spectrum of copper(II) complex **1** in acetonitrile

The electronic spectrum of the copper(II) complex was recorded in the UV–Vis region using methanol as solvent. Three absorption bands with varied intensity were observed. An intense bands at 230 nm (s, e = 19 151 dm^3 mol^{-1} cm^{-1}) and at 316 nm (s, e = 10 122dm^3 mol^{-1} cm^{-1}) may be attributable to the spin exchange interaction between the copper(II) ions through the p-path orbital set up by the oxamato bridge [33]. It has been also observed that regular and distorted square-pyramidal copper(II) complexes exhibit a *d-d* transition band in the region 550-670 nm, whereas trigonal bipyramidal ones show a maximum absorption at > 670 nm [34-36]. A broad band observed at the 627 nm (b, e = 119dm^3 mol^{-1} cm^{-1}) is in agreement with the d–d transition for the two terminal copper(II) ions in the square pyramidal geometry.
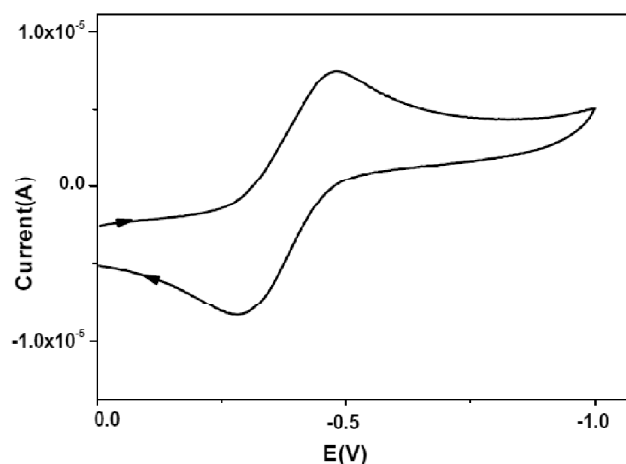
Thermal analysis

The thermal behaviour of the complex was investigated using thermal gravimetric analysis. In compound, an initial mass loss of 3.7% was observed in the range from room temperature to 110°C. It corresponds to the release of the lattice and the coordinated water molecules (Calc. 4.0%). After this temperature, the observed plateau suggested the thermal stability of the anhydrous species up to270 C. The second weight loss of 10.5% in the range 270–311 C, corresponds to the removal of perchlorate ion.

DNA-binding studies

The binding mode of complex with calf thymus DNA was examined by electronic absorption titration (Fig. 4) and ethidium bromide (EB) fluorescence displacement experiments (Fig. 6). Complex showed a significant hyper chromism effect centered at the 313 nm absorption maximum. The intrinsic binding constant K$_b$ was
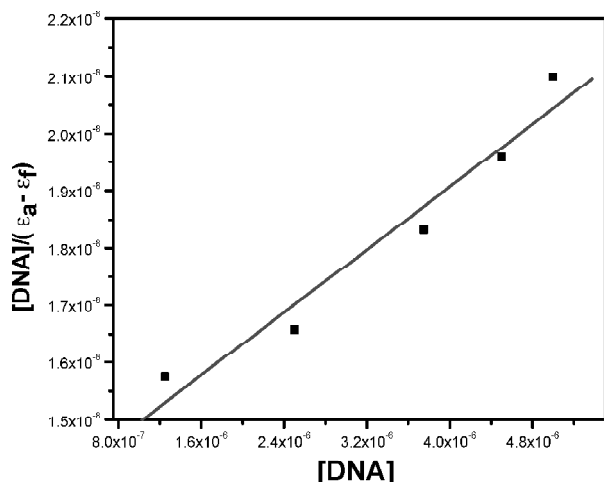

Figure 3: CV diagram of copper complexes in acetonitrile for complex **1**using TBAP as supporting electrolyte at the scan rate of 100 mVs^{-1} at room temperature
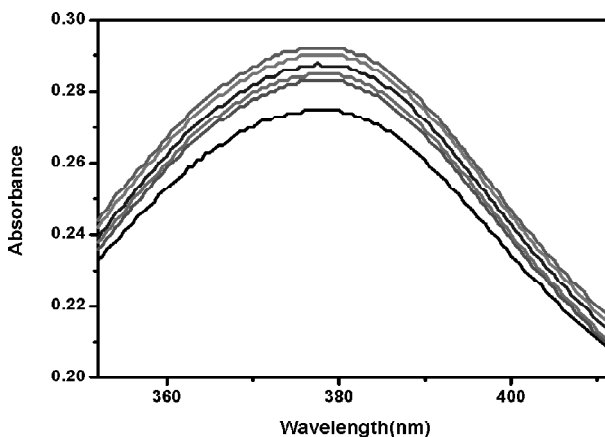
Figure 4: Electronic spectral of the complexthrough titration with CT-DNA in tris-HCl. The increase of DNA concentration is indicated by arrow mark put it

Figure 5: Plot of [DNA]/(ε_a-ε_f) *versus* [DNA] for the titration of CT-DNA with complex **1** in tris HCl buffer; binding constant $K_b = 1 \times 10^5 M^{-1}$ (R = 0. 0.95469 for five points).
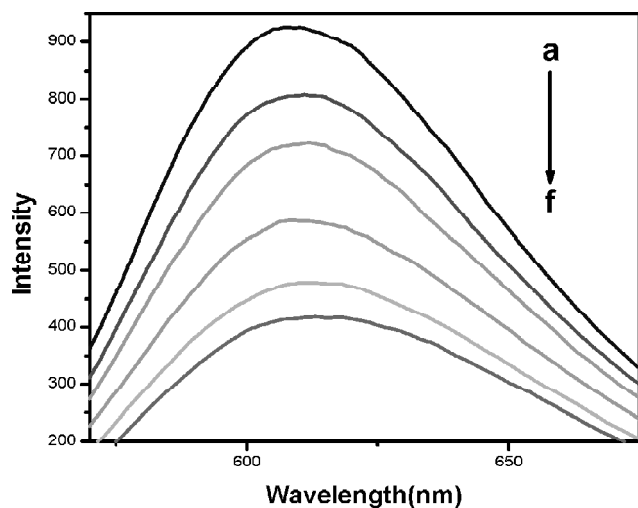
Figure 6: Emission spectra of the CT-DNA-EB system in tris–HCl buffer based on the titration of complex.l_{ex} = 522 nm.

calculated to be $4.01\times10^4 M^{-1}$, from the slope to intercept ratio of the graph obtained by plotting the [DNA]/(ε_a-ε_f) versus [DNA] (Fig. 5, R = 0.89527, 5 points), by using the following equation[37]

$$[DNA]/(\varepsilon_a- \varepsilon_f) = [DNA]/(\varepsilon_b - \varepsilon_f) +1/[K_b(\varepsilon_b-\varepsilon_f)]$$

where [DNA] is the DNA concentration, ε_a, ε_b and ε_f symbolize the extinction coefficient for each addition of DNA to the complex, for the copper complex in the fully bound form and for the free copper complex, respectively.

The linear Stern–Volmer quenching constant K_{sv} has been calculated from the linear Stern–Volmer equation, [38] by considering the quenching of EB bound to DNA due to the presence of the complex:

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

where I_0 and I represent the fluorescence intensities in the absence and presence of quencher, respectively, and Q is the concentration of quencher. Here, the value of K_{sv} (6.9×10^4, R = 0.97556 for five points) (viz. Fig. 7) is comparable to that of the well-established groove binding rather than classical intercalator agent [39].

Protien (Bovine serum albumin) binding experiments

#### *Absorption characteristics of BSA–Cu(II) complex*

The absorption spectra of BSA in the absence and presence of Cu(II) complex at different concentrations were studied. (Fig. 8) From this study we observed that upon increasing the concentration of the complex the absorption of BSA increases regularly. It is may be due to the adsorption of BSA on the surface of the complex. From these data the apparent association constant (K_{app}) determined of the complexes with BSA has been determined using the following equation, [24].

$$1/(A_{obs} - A_0) = 1/(A_c - A_0) + 1/ K_{app}(A_c - A_0)[comp]$$

Where,A_{obs} is the observed absorbance of the solution containing different concentrations of the complex at 280 nm, A_0 and A_c are the absorbances of BSA and the complex at 280 nm, respectively, with a concentration of C_0, and K_{app} represents the apparent association constant. The enhancement of absorbance at 280 nm was due to absorption of the surface complex, based on the linear relationship between $1/(A_{obs}- A_0)$ *vs* reciprocal
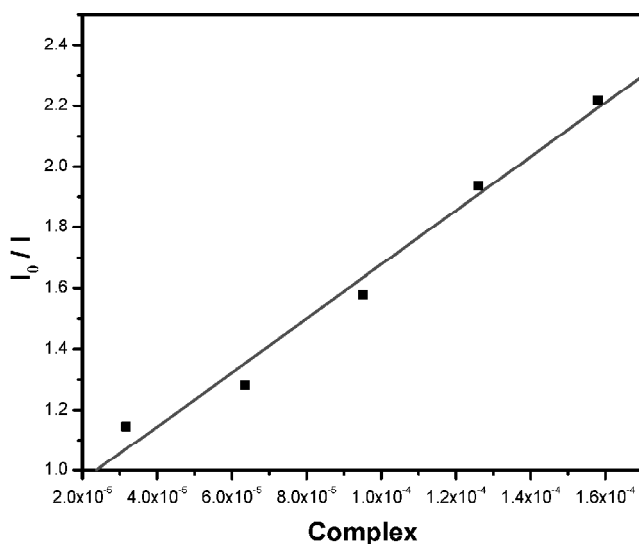
Figure 7: Plot of I_0/I *versus* [complex] for the titration of CT-DNA–EB system with complexusingspectrofluorimeter; linear Stern–Volmer quenching constant (K_{sv}) for complex **1** = 1.125×10^4; (R = 0.99023 for five points)
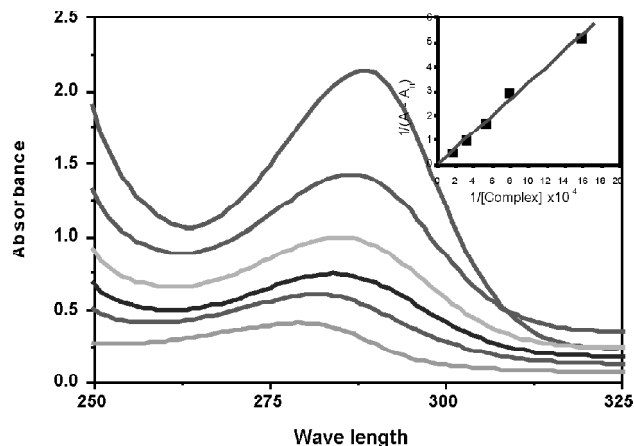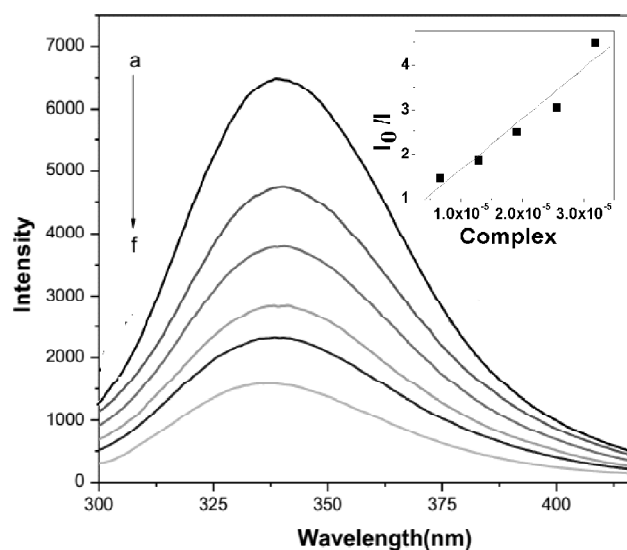
Figure 8: Absorption spectrum of BSA in the presence of complex in the concentration range 0-6.34 × 10^{-5} M. Inset is the linear dependence of 1/A- A$_0$ on the reciprocal concentration of complex.

concentration of the complex with a slope equal to 1/K$_{app}$(A$_c$ - A$_0$) and an intercept equal to 1/(A$_c$ - A$_0$) (Fig. 8, inset). The value of the apparent association constant (K$_{app}$) determined from this plot is 4.5 × 10^5 M^{-1}.

Fluorescence quenching of BSA by the complex

The effect of increasing the concentration of the complex on the fluorescence emission spectrum of BSA were studied and represented in (Fig. 9). With the addition of complex BSA fluorescence emission is quenched. The fluorescence quenching is described by the Stern–Volmer relation [25]:
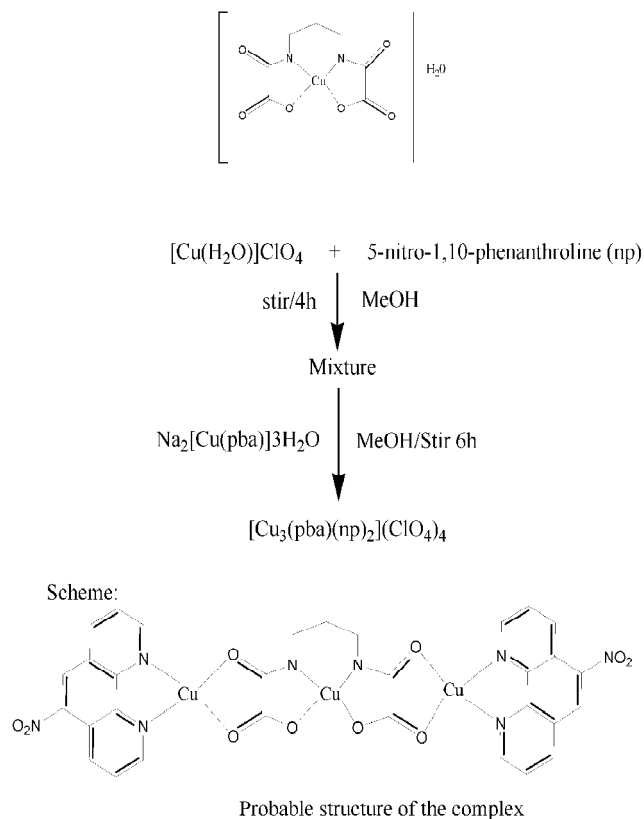
$$I_0/I = 1 + K_{SV} [complex]$$

where I$_0$ and I represent the fluorescence intensities of BSA in the absence and presence of quencher, respectively. K$_{SV}$ is the linear Stern–Volmer quenching constant and [complex] the molar concentration of the quencher. A linear plot (Inset, Fig. 9) between I$_0$/I against [complex] was obtained and from the slope we calculated the K$_{SV}$ as 3.7 × 10^5 suggesting strong interaction between Cu(II) complex and BSA.

Electrochemistry

Redox properties of complex 1 was examined by cyclic voltammetry using a Pt-disk working electrode and a Pt-wire auxiliary electrode in dry MeCN and in presence of [Et$_4$N]ClO$_4$ as supporting electrolyte. The potentials are expressed with reference to saturated KCl electrode. In solution the compound displayed a quasi reversible voltammogram having ipc/ipa = 1, Epc at 1.31 V and Epa 1.05 V with DE = 260 mV. Though the electrochemical analysis of complex 1, which has three copper(II) ions in different coordination environment and geometries (as observed in solid state), showed only one reduction point, indicating that the three metal centers are electrochemically equivalent in solution.

Figure 9: Fluorescence Quenching of BSA in the presence of various concentrations of the complex **1**, [complex] = 0, 1, 2, 3, 4 and 5 × 6.35 ×10^{-6} M. Insert shows the Stern–Volmer plot.

[Cu(H$_2$O)]ClO$_4$ + 5-nitro-1,10-phenanthroline (np)

stir/4h | MeOH

Mixture

Na$_2$[Cu(pba)]3H$_2$O | MeOH/Stir 6h

[Cu$_3$(pba)(np)$_2$](ClO$_4$)$_4$

Scheme:

Probable structure of the complex

Conclusion

A new trinuclear copper(II) complex, $[Cu_3(pba)(np)_2 (H_2O)(ClO_4)]ClO_4 H_2O$ having an almost linear arrangement of three electrochemically equivalent Cu(II) ions bridged by oxamato ligand has been synthesized and structurally characterized. Complex interacts with CT-DNA and the investigation indicates a tendency for this complex to be bound within the groove of DNA.

References

[1] Solomon E I, Sundaram U M, Machonkin T E, Multicopper Oxidases and Oxygenases, Chem. Rev. 96(7), 1996, 2563-2606.

[2] Kahn O, Competing spin interactions and degenerate frustration for discrete molecular species, *Chem. Phys. Lett. 265*, 1997, 109-114.

[3] Ferrer S, Haasnoot J G, Reedijk J, Muller E, BiaginiCingi M, Lanfranchi M, ManottiLanfredi A M, Ribas J, Trinuclear N,N-Bridged Copper(II) Complexes Involving a Cu_3OH Core: $[Cu_3(\mu_3-OH)L_3A(H_2O)_2]A\cdot(H_2O)_x$ {L = 3-Acetylamino-1,2,4-triazolate; A= CF_3SO_3, NO_3, ClO_4; x = 0, 2} Synthesis, X-ray Structures, Spectroscopy, and Magnetic Properties, *Inorg. Chem. 39*, 2000, 1859-1867.

[4] Ferrer S, Lloret F, Bertomeu I, Alzuet G, Borra´s, J, Garcia-Granda S, Liu-Gonzales M, Haasnoot J G, Cyclic trinuclear and chain of cyclic trinuclear copper(II) complexes containing a pyramidal Cu(3)O(H) core. Crystal structures and magnetic properties of [Cu(3)(mu(3)-H)(aaat)(3) (H(2)O) (3)](NO(3))(2).H(2)O [aaat = 3-acetylamino-5-amino-1,2,4-triazolate] and ([Cu(3)(mu(3)-OH)(aat)(3)(mu (3)-SO(4))].6H(2)O)(n) [aat = 3-acetylamino-1,2,4-triazolate]: new cases of spin-frustrated systems. *Inorg. Chem. 41*, 2002 5821-5830.

[5] Magnus K A, In *Handbook of Metalloproteins*; Messerschmidt, Huber A, Poulos R, Wieghardt T, Eds K, Wiley, New York, 2, 2001, 1303-1318.

[6] Iwata S, Ostermeier C, Ludwig B, Michel H, Structure at 2.8 A resolution of cytochrome c oxidase from Paracoccusdenitrificans, *Nature, 376*, 1995, 660-669.

[7] Brown K, Tegoni M, Prudeˆncio M, Pereira A S, Besson S, Moura J, Moura I, Cambillau C, A novel type of catalytic copper cluster in nitrous oxide reductase, *Nat. Struct. Biol. 7*, 2000, 191-195.

[8] Lieberman R L, Rosenzweig A C, Crystal structure of a membrane-bound metalloenzyme that catalyses the biological oxidation of methane, *Nature, 434*, 2005, 177-182.

[9] Messerschmidt A, In *Handbook of Metalloproteins*; Messerschmidt, Huber A, Poulos RT, Wieghardt K, Eds, Wiley, New York, 2,2001, 1345-1358.

[10] Bandyopadhyay S, Lo J M, Yao H H, Liao F L, Chattopadhyay P, A linear trinuclear complex of copper(II) with $N,N2$ -bis(2-hydroxy-5-methoxybenzelidene)-1,3-diiminopropane, J. Coord. Chem. 59, 2006, 2015 and references therein.

[11] Aukauloo A, Ottenwaelder X, Ruiz R, Journaux Y, Pei Y, Rivie're E, Munõz M C, Rational design of homo and hetero hexanuclear coordination compounds: Syntheses and magnetic properties of $[Cu^{II}_2M^{II}_4]$ (M = Cu ; Ni) species and the crystal structure of $\{[Cu(tmen)(H_2O)]_2[Cu(tmen)]_2 [Cu_2L](H_2O)\}(ClO_4)_2 \cdot 2 H_2O$, *Eur. J. Inorg. Chem.*, 5, 2000, 951-955 and references therein.

[12] Bandyopadhyay S, Lo J M, Yao H H, Liao F L, Chattopadhyay P, A linear trinuclear complex of copper(II) with $N,N2$ -bis(2-hydroxy-5-methoxybenzelidene)-1,3-diiminopropane, J. Coord. Chem. 59 2006, 2015-2021.

[13] Ruffer T, Brauer B, Powell A K, Hewitt I, Salvan G, Synthesis, characterization and magnetic properties of new homotrinuclear copper(II) complexes, Inorg. Chim. Acta 360, 2007, 3475-3483.

[14] Tercero J, Diaz C, Fallah M S E, Ribas J, Solans X, Maestro M A, Mahia J, Synthesis, Characterization, and Magnetic Properties of Self-assembled Compounds Based on Discrete Homotrinuclear Complexes of Cu(II), Inorg. Chem. 40, 2001, 3077-3083.

[15] Turner S, Kahn O, Rabardel L, Crossover between Three-Dimensional Antiferromagnetic and Ferromagnetic States in Co(II)Cu(II) Ferrimagnetic Chain Compounds. A New Molecular-Based Magnet with T_c = 38 K and a Coercive Field of 5.66×10^3 O, J. Am. Chem. Soc. 118, 1996, 6428-6432.

[16] Baron V, Gillon B, Sletten J, Mathoniere C, Codjovi E, Kahn O, Interchain interactions and three-dimensional magnetic ordering in Mn(II)Cu(II) chain compounds; crystal structure and metamagnetic properties of $MnCu(pbaOH)(H_2O)_3\cdot 2H_2O$, with pbaOH = 2-hydroxo-1,3-propylenebis (oxamato), Inorg. Chim. Acta, 235, 1995, 69-76.

[17] Nakatani K, Bergerat P, Codjovi E, Optimization of a molecular-based [manganese copper] magnet: $MnCu(pbaOH)(H_2O)_2$ (pbaOH = 2-hydroxy-1,3-propylenebis(oxamato)) with Tc = 30 K, Inorg. Chem. 30, 1991, 3977-3978.

[18] Kahn O, Pei Y, Verdaguer M, Renard J P, Sletten J, Magnetic ordering of manganese(II) copper(II) bimetallic chains; design of a molecular based ferromagnet, J. Am. Chem. Soc. 110, 1988, 782-789.

[19] Dey S, Sarkar S, Mukherjee T, Mondal B, Zangrando E, Sutter J P, Chattopadhyay P, An oxamato bridged trinuclear copper(II) complex: Synthesis, crystal structure, reactivity, DNA binding study and magnetic properties, Inorg. Chim. Acta, 376, 2011, 129–135 and references therein.

[20] Turner S, Kahn O, Rabardel L, Crossover between Three-Dimensional Antiferromagnetic and Ferromagnetic States in Co(II)Cu(II) Ferrimagnetic Chain Compounds. A New Molecular-Based Magnet with T_c = 38 K and a Coercive Field of 5.66×10^3 Oe, J. Am. Chem. Soc. 118, 1996, 6428.

[29] Dey S, Sarkar S, Paul H, Zangrando E, Chattopadhyay P, Copper(II) complex with tridentate N donor ligand: Synthesis, crystal structure, reactivity and DNA binding study, Polyhedron, 29, 2010, 1583-1587.

[30] Zhang Y L, Ruan W J, Zhao X J, Wang H G, Zhu Z A, Synthesis and characterization of axial coordination cobalt(III) complexes containing chiral Salen ligands, Polyhedron, 20, 2003, 1535-1545.

[31] Deacon G B, Phillips R J, Relationships between the carbon-oxygen stretching frequencies of carboxylato complexes and the type of carboxylate coordination, Coord. Chem. Rev. 33, 1980, 227-250.

[32] Nakamoto K, Infrared and Raman Spectra of Inorganic and Coordination Compounds, 3rd Edn, Wiley & Sons, New York, 1978.

[33] Vicente R, Escuer A, Ferretjans J, Stoeckli-Evans H, Solans X, Bardıa M F, J. Chem. Soc., Structurally alternating copper(II) chains from oxalate and azide bridging ligands: syntheses and crystal structure of $[Cu_2(\mu\text{-}ox)(deen)_2(H_2O)_2(ClO_4)_2]$ and$[\{Cu_2(\mu\text{-}N_3)(\mu\text{-}ox)(deen)_2\}_n][ClO_4]_n$(deen = $Et_2NCH_2CH_2NH_2$), Dalton Trans. 2, 1997, 167- 172.

[34] Golub G, Cohon H, Meyerstein D,*J. Chem. Soc., Chem. Commun*. The stabilization of monovalent copper ions by complexation with saturated tertiary amine ligands in aqueous solutions. The case of 2,5,9,12-tetramethyl-2,5,9,12-tetraazatridecane, Journal of the Chemical Society 5, 1992, 397.

[35] McLachlan G A, Fallon G D, Martin R L, Spiccia L,Synthesis, Structure and Properties of Five-Coordinate Copper(II) Complexes of Pentadentate Ligands with Pyridyl Pendant, *Inorg.Chem. 34*, 1995, 254-261.

[36] Bernhardt P V, Hayes E J,Copper(II) complexes of mono- and di-nucleating hexaamines, J. Chem. Soc. Dalton Trans. 6, 1998, 1037-1042.

[37] Wolfe A, Shimer G H, Meehan T, Polycyclic aromatic hydrocarbons physically intercalate into duplex regions of denatured DNA, Biochemistry, 26, 1987, 6392-6396.

[38] Stern O, VolmerM, Z. Phys. 20, 1919, 183-188.

[39] Strekowski L, Harden D B, Wydra R L, Stewart K D, Wilson W D, Molecular basis for potentiation of bleomycin-mediated degradation of DNA by polyamines. Experimental and molecular mechanical studies, J. Mol. Recognit. 2, 1989, 158-166.