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Binuclear copper(II) complexes: synthesis, structural characterization, DNA binding and in silico studies

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Abstract: Two new binuclear Cu(II) complexes represented by the general formula \{(dmso)Cu(µ-L)\textsubscript{4}Cu(dmso)\} (1) and \{(Phen)(L)Cu(µ-L)\textsubscript{2}Cu(L)(Phen)\} (2) where dmso = dimethyl sulfoxide, L = 2-bromophenyl acetate and Phen = 1,10-phenanthroline have been synthesized, isolated quantitatively and characterized by UV/Visible and FT-IR spectroscopic techniques, Thermogravimetry/Differential Thermal Analysis and X-ray single crystal XRD studies. Complex 1 is paddlewheel with 1,2-O,O-bridging while 2 has 1,1-O-bridging. The values of the intrinsic binding constants with DNA were found out to be 2.0\times10\textsuperscript{3} and 1.1\times10\textsuperscript{3} M\textsuperscript{-1}, respectively for compound 1 and 2. The mode of interaction of complexes with DNA was also evaluated through computational study by molecular docking (in silico) study using MOE (molecular operating environment) software. The synthesized complexes are structurally as well as biologically important.

Keywords: crystal structures; DNA interaction; molecular docking

INTRODUCTION

The wide range application of copper compounds and their role as micronutrients beneficial to organisms have attracted the inorganic chemists for the synthesis of their complexes.\textsuperscript{1} The copper complexes play an important role as catalyst in the synthesis of optically active compounds.\textsuperscript{2} The polynuclear copper complexes found applications in photoluminescence behaviors\textsuperscript{3}, synthesis of organic compounds\textsuperscript{4}, and anti-inflammatory activity.\textsuperscript{5} The deficiency and excess of copper in the body is responsible for disorders, for example Wilson’s and Menkes diseases, respectively.\textsuperscript{6} Copper complexes also plays an important
role in the proper functioning of several enzymes and proteins responsible for energy metabolism, respiration and DNA synthesis.\(^7\)

Copper complexes incorporating carboxylate ligands are used in the production of thin film in semiconductor industry involving chemical vapor deposition method.\(^8\) The copper complexes bearing carboxylate functionality and phenanthroline ligands show DNA binding affinity.\(^9\) The small changes in the structure of ligands around copper greatly alter the electronic and magnetic behaviors of the resulting complexes.\(^10\) The phenanthroline bearing copper complexes show chemical nuclease activity and are used in DNA oxidative cleavage in the presence of a reducing agent.\(^11\) Phenanthroline and its derivatives are used as chelating agents for metal determination in analytical chemistry.\(^12\)

The molecular docking is used to model the interaction of the synthesized complexes with DNA, which gives information about the conformational changes in ligand and DNA when interact with each other.\(^13\)

Bromophenyl acetate is the derivative of the general class of phenyl acetic acid, which plays an important role in the growth of plants like auxin.\(^14\) It is also used in the synthesis of non-steroidal anti-inflammatory drugs like Diclofenac (Voltaren), which have analgesic, antipyretic, and anti-inflammatory effect through cyclooxygenase inhibition.\(^15\) The dinuclear copper(II) complexes containing planar aromatic heterocyclic ligands show pronounced DNA cleavage activities as compared to the corresponding mononuclear copper(II) complexes.\(^16\) The mononuclear copper(II) complexes with phenanthroline ligand also show DNA binding activities but their DNA binding affinities are lesser than dinuclear copper(II) complexes.\(^17\) The phenanthroline ligand, due to presence of aromatic ring in their chemical structure and hydrophobic nature, enhances the DNA binding affinities of the complexes.\(^18\) The high level of copper in human body can promote cancer, metastasis, and angiogenesis. As a strategy, scientists have synthesized the copper chelator to remove the excess copper from body.\(^19\)

Keeping in view the above mentioned applications and uses of copper complexes in various fields, we have synthesized binuclear copper complexes with carboxylate ligands and 1,10-phenanthroline. The complexes were structurally characterized through various spectroscopic techniques and their DNA binding affinities were determined experimentally through absorption spectroscopy and theoretically through computational approach of molecular docking.

**EXPERIMENTAL**

**Materials and methods**

Analytical grade anhydrous CuSO\(_4\), 2-bromophenyl acetate, 1-10 phenanthroline, sodium bicarbonate and potassium chloride were obtained from Fluka, USA, and were used as received. The solvent like methanol and dimethyl sulphoxide (DMSO) were of analytical grade. The water used in the experiment was singly distilled. The melting points were obtained in a capillary tube using a Gallenkamp, serial number C040281, U.K, electro-thermal
melting point apparatus. FT-IR spectra were obtained on a Nicolet-6700 FT-IR spectrophotometer, thermoscientific, USA, in the range from 4000 to 400 cm$^{-1}$.

**X-ray crystallographic studies**

The crystallographic data were obtained at 293 K using an Oxford diffraction Gemini ultra SCX CCD diffractometer using graphite monochromated Mo-Kα radiation ($\lambda = 0.071073$ nm). Data reduction and empirical absorption correction completed through CrysAlisPro (Oxford diffraction version 171.33.66). The structures of the complexes were solved by direct method with SHLEX-86 and refined by full matrix least square analysis against $F^2$ with SHLEX–9720 within WinGX package.21 ORTEP3 was used for drawing the structures of complexes.22

The data of both crystals has been deposited with CCDC 1880878 and 1880879 corresponding to 1 and 2, respectively.

**DNA interaction study by absorption spectroscopy**

Solutions of complexes were prepared with 8 mM concentration in aqueous DMSO (1:4) for UV-Visible analysis. The absorption spectra were determined by titrating the complexes against different concentrations of salmon sperm DNA (SSDNA). The solutions were allowed at ambient temperature to ensure the complete mixing of complexes with SSDNA. The cuvettes of 1 cm path length were used for recording the absorption spectra.

**Synthetic procedure for the complexes**

Complex 1 was prepared by treating 2-bromophenyl acetic acid (8 mmol, 1.72 g) with NaHCO$_3$ (8 mmol, 0.672 g) in distilled water at 50 °C. After completion of neutralization, aqueous solution of CuSO$_4$ (4 mmol, 0.636 g) was added and the reaction mixture was stirred for 2 h at 50 °C as shown in scheme S1. The final product was filtered, washed with distilled water, dried and recrystallized from dimethyl sulfoxide and characterized by FT-IR and single crystal analysis.

Complex 1: Dark blue color; m.p. 249-250 °C; yield (71 %). $\lambda_{max}$ = 651 nm. $\varepsilon$ = 48 L mol$^{-1}$ cm$^{-1}$. FT-IR: 1632 cm$^{-1}$ v(C=O)$_{asym}$, 1389 cm$^{-1}$ v(C=O)$_{sym}$, 416 cm$^{-1}$ v(Cu-O).

Complex 2 was prepared by treating 2-bromophenyl acetic acid (8 mmol, 1.72 g) with NaHCO$_3$ (8 mmol, 0.672 g) in distilled water at 50 °C. After completion of neutralization, aqueous solution of CuSO$_4$ (4 mmol, 0.636 g) was added and the reaction mixture was stirred for 2 hours at 50 °C; then solid 1,10-phenanthroline (4 mmol, 0.72 g) was added and stirred for another 2 hours as shown in scheme S2. The final product was filtered, washed with distilled water and air dried. The solid was recrystallized from methanol and was characterized by FT-IR and X-ray analysis.

Complex 2: Light blue color; m.p. 203-204 °C; yield (65 %). $\lambda_{max}$ = 671 nm. $\varepsilon$ = 39 L mol$^{-1}$ cm$^{-1}$. FT-IR: 1606 cm$^{-1}$ v(C=O)$_{asym}$, 1364 cm$^{-1}$ v(C=O)$_{sym}$, 429 cm$^{-1}$ v(Cu-N), 242 cm$^{-1}$ v(Cu-O).

Both the complexes are soluble in common solvents like methanol, ethanol, chloroform, acetone, DMSO, partially soluble in ether and insoluble in pure water.

**Molecular docking**

The three dimensional (3D) structures of the newly synthesized Cu-complexes were drawn by Molecular Operating Environment (MOE-2016) software.23 The hydrogen atoms were added to the synthesized compounds by 3D protonation followed by energy minimization using MOE. The crystal structure of the double stranded DNA dodecamer was
retrieved from the protein databank (PDB id: 1BNA) [www.rcsb.org/pdb]. Prior to molecular docking, all water molecules were removed from the retrieved crystal structure using the Molecular Operating Environment software. The 3D protonation and energy minimization of the retrieved DNA was carried out by using MOE software. The macromolecule (DNA) was allowed to dock to the synthesized copper complexes using MOE. For each ligand ten conformations were generated. The top-ranked conformation of each complex was used for further analysis.

RESULTS AND DISCUSSION

FT–IR data

Both the complexes were characterized by FTIR spectrophotometer, which shows all characteristic absorption bands in the spectrum.

The complex 1 showed peak at 1632 cm\(^{-1}\) corresponding to the asymmetric (C=O) stretching frequency and a symmetric stretching peak of (C=O) at 1389 cm\(^{-1}\). The Cu-O peak of carboxylate appeared at 416 cm\(^{-1}\).\(^{24}\) The IR spectroscopy is a powerful tool for determining the coordinating mode of COO moiety in metal carboxylate complexes, the difference between asymmetric and symmetric stretching frequencies, \(\Delta\nu \{\nu_{\text{asym}}(\text{OCO}) - \nu_{\text{sym}}(\text{OCO})\}\) less than 150 cm\(^{-1}\) corresponds to a chelate nature, greater than 250 cm\(^{-1}\) shows a monodentate carboxylate moiety and value between 150 and 250 cm\(^{-1}\) indicates a bridging behavior.\(^{25}\) The \(\Delta\nu\) value for complex 1 was 243 cm\(^{-1}\) which shows a bridging coordination mode of the carboxylate group which was further confirmed by the structural studies.

The complex 2 showed peak at 1606 cm\(^{-1}\) which corresponded to the asymmetric stretching of C=O and 1364 cm\(^{-1}\) which is symmetric stretching frequency of C=O functionality of the carboxylate ligand. The Cu-N bond vibration was found at 470 cm\(^{-1}\). The appearance of a Cu-O absorption band at 429 cm\(^{-1}\) is an indication for the coordination of carboxylate through oxygen. The \(\Delta\nu\) value of 242 cm\(^{-1}\) corresponds to the bridging behavior of carboxylate group in line with the XRD data.

Crystal structure description

The ORTEP diagram for the complex 1 is shown in Fig 1. The crystal refinement parameters and important bond lengths and angles are given in tables S1 and S2. The molecule belongs to space group P-1. The complex is in the dimeric form, in which each Cu is in five coordinated square pyramidal environment. The four oxygen atoms of the carboxylates around each Cu(II) occupy the square planar position while the DMSO oxygen occupies the apical position of the square pyramid. The Cu…Cu and average Cu-O (equatorial) bond distance are 2.649 and 1.965 Å, respectively, which are closely related to the bond distances of Cu(II) complexes reported in the literature.\(^{26}\) The Cu-O bond distances are asymmetrical in the equatorial plane and are shorter as compared to the axial Cu-O bond (2.153(2) Å) as are reported for the structurally similar dimeric Cu(II)
The axial Cu-O bond distance is 2.1529 (2) Å, which shows a weak interaction with copper. The elongation of apical bond is due to the occupancy of anti-bonding \(a_1\) orbital (\(d_{z^2}\)) by two electrons resulting in a high electron cloud along the Cu-O axial bond.\(^{28}\) The \(d_{x^2-y^2}\) orbital is singly occupied and therefore the ligands experience lesser repulsion from the metal electron and come closer to it in the equatorial plane. The \(O_1-Cu_1-O_3\) angle for the complex is 90.1(1)°, the \(O_1-Cu_1-O_5\) angle is 98.9(1)°, the \(O_1-Cu_1-O_2\) is 167.8(1)°, \(O_3-Cu_1-O_4\) angle is also 167.9(1)°. These data clearly show the square pyramidal geometry for the complex 1.

Fig. 2 represents the packing diagram for complex 1, which shows that the intermolecular interactions comprise mostly of C···H-C, O···H-C and S···H-C type interactions. These weaker linkages arise because the molecule has no polar hydrogen to result in true hydrogen bonding.

The ORTEP diagram for complex 2 is shown in Fig 3. The complex belongs to space group C2/c and is composed of dimeric units, where each copper atom is surrounded by five donor atoms adopting square pyramidal geometry. The two nitrogen atoms of phenanthroline and two oxygen atoms of two carboxylates occupy the equatorial position, while the third carboxylate containing bridging oxygen atom occupies the axial position.

The two Cu-N bonds in the plane are 2.037(2) Å each and the two Cu-O bonds from the two carboxylates moiety in the plane are 1.930(1) and 1.955(2) Å, while the apical Cu-O bond distance is 2.455(2) Å which is mostly similar to the dinuclear Cu(II) complexes reported in the literature.\(^{29}\) The geometry around copper is less distorted square pyramidal than that of...
the complex 1 owing partly to the asymmetric bridging nature of the 1,1-O-bridging oxygen atom. The elongation of axial bond along axial position is due to accommodation of two electrons in the $a_1 (d_{z^2})$ orbital, which does not allow the close approach of the ligands along $z$-axis while the $d_{x^2-y^2}$ orbital having $b_1$ symmetry is singly occupied and presents minimum repulsion to the approaching ligands along $x$- and $y$-axes. This results in closer ligand approach and consequently shorter bond length. The $O_1$-$Cu_1$-$O_3$ bond angle is 95.96(9)$^\circ$, the $O_1$-$Cu_1$-$N_1$ angle is 169.1(1)$^\circ$, the $O_3$-$Cu_1$-$N_3$ angle is 89.7(1)$^\circ$, $O_1$-$Cu_1$-$O_3$ angle is 88.10(8)$^\circ$, $O_3$-$Cu_1$-$N_1$
angle is 94.50(9)° and the O$_3$-Cu$_1$-N$_2$ angle is 168.4(1)°. These data indicate square pyramidal geometry for complex 2.

The axial bond elongation with respect to equatorial bond length is in close agreement with the already reported complexes. The greater separation in bond length between two Cu(II) ion with respect to Cu-O and Cu-N bond length is due to the nonexistence of actual bond between two Cu(II) ion. Each Cu(II) ion has unpaired electron in the d$_{x^2-y^2}$ orbital, which is not properly oriented for Cu-Cu bond formation. While the d$_{z^2}$ orbital on each copper ion are pointing the right way for Cu-Cu bond formation, however these orbitals are fully populated with electron pair. Therefore the Cu-Cu bond can’t exist in such dinuclear Cu(II) complexes.\textsuperscript{30}

The supramolecular structure of the complex 2 has been given in Fig. 4 showing that the molecules are held together through weak Br····H-C and O···H-C type linkages. Again here, there is no polar hydrogen and thus no H-bonding in the lattice of 2.

The copper atoms in both complexes are indicated as Cu1, because the geometry around each copper is same and hence both are chemically identical and the complex is centrosymmetric.

**Thermogravimetric analysis**

Figure S1 shows the thermogravimetric curve of complex 1 which contains three decomposition steps. The complex is stable below 80 °C and above this temperature water molecule is lost (weight loss: calculated, 16.55 %; observed 16.18 %). The decomposition of monodentate carboxylate ligands occurs in the range of 220-260 °C (weight loss: calculated, 42.48 %; observed, 42.43 %), while the most strongly bonded copper oxide decomposed between 500-710 °C corresponding to a total weight loss of 24.0 % (calculated 23.44 %). The accumulative observed weight loss was 82.25 %. The weight of the final residue
is 17.30% of the total weight. Thermogravimetric plot of complex 2 has been shown in Fig. S2 which shows two decomposition steps. The complex is stable upto 80°C and the loss of water molecule starts above 80°C and completed at 120°C (weight loss: calculated, 17%; observed, 16.70%). Monodentate carboxylate ligands decompose in temperature range 220-260°C (weight loss: calculated, 42.40%; observed 42.41%). However, more refractory copper oxide has been found to decompose between 500-710°C range corresponding to a total weight loss of 24.0% (calculated 23.41%). The accumulative observed weight loss was 82.60%. The final residue weight is 17.30% of the total weight.

Absorption spectroscopy

The absorption spectrum of the complex 1 is shown in Fig. 5A, which exhibits peak in the visible region having \( \lambda_{\text{max}} = 277 \text{ nm} \) corresponding to \( \pi-\pi \) transition due to the presence of aromatic ligand in the complex. The complex also shows a small peak in the in 498 nm visible region due to d-d transition. This absorption band is typical of distorted octahedral geometry in solution form, where the DMSO solvent molecule acts as ligand.  

Figure 5B shows the absorption spectrum of complex 2, showing an absorption band at \( \lambda_{\text{max}} = 289 \text{ nm} \) due to \( \pi-\pi \) electronic transition of the aromatic moiety in the complex and a weak absorption peak at 510 nm due to d-d transition in copper(II) ion. This also corresponds to distorted octahedral geometry where the solvent DMSO is attached at the sixth position to copper ion in the solution form.

![Figure 5. A, Absorption spectrum of pure complex 1 (\( \lambda_{\text{max}}=277 \text{ nm} \) absorbance = 0.91) and addition of DNA from 10-50 \( \mu \text{M} \) (b-f) in downward direction, causing a shift of \( \lambda_{\text{max}} \) to 289 nm and decrease of absorbance (0.91-0.81). B, Absorption spectrum of pure complex 2 (\( \lambda_{\text{max}}=289 \text{ nm} \) absorbance = 0.89) and addition of DNA from 10-50 \( \mu \text{M} \) in downward direction, causing a shift of \( \lambda_{\text{max}} \) to 294 nm and decrease of absorbance from 0.89 to 0.73.](image-url)
**DNA binding study through UV–Visible spectrophotometry**

UV-Visible spectrophotometer was used for monitoring the variation in $\lambda_{\text{max}}$ and absorbance of the complexes upon addition of DNA to the solutions of the complexes. The mode of interaction of the complexes with DNA can be judged from the shift in $\lambda_{\text{max}}$. A shift toward shorter wavelength (blue) is an indication of electrostatic interaction, while red shift (shift toward longer wavelength) is the consequences of intercalation.\(^{32}\) However, a very small blue shifts up to 5 nm and concomitant decrease in absorbance (hypochromism) is an indication of groove binding. The complex 1 showed a small red shift as well as hypochromism as evident form Fig. 5A, which corresponds to weaker intercalation mode of interaction of the complex with DNA helix. Similarly, the complex 2 showed a small red shift as well as hypochromism which according to the above discussion are a result of weaker intercalation mode of interaction with DNA as shown in Fig. 5B.

UV/Visible spectroscopy is commonly employed technique for DNA study and their interaction with drugs, the copper(II) complexes does not exhibit any intense d-d or charge transfer band to monitor their interaction with DNA, so the intense ligand base ($\pi-\pi$) absorption band is used to monitor the interaction of complexes with DNA.\(^{33,34}\) Both the complexes show a decrease in the intensity (hypochromism) as well as a small red shift (bathochromism), which according to the literature reflect intercalative mode of interaction, which result from the interaction between aromatic ligand and the DNA base pair through stacking interaction. The complex 1 gave peak at 277 nm with absorbance 0.91 in the UV-region due to aromatic moiety; similarly the complex 2 gave peak in UV-region due to phenanthroline at 289 nm with 0.81 absorbance.\(^{35}\)

The broad peak in the 500 nm range is due to d-d transition of Cu\(^{2+}\) ion as observed in other copper(II) complexes.\(^{32}\) There is decrease in the absorbance of the peak in UV region on addition of DNA owing to the formation of complex-DNA adduct and a consequent decrease in the concentration of the free complexes. Both the complexes show hypochromic effect as well as red shift, the extent of hypochromic effect and red shift is a measure of the degree of intercalation.\(^{36}\) The extent of interaction of the complexes with DNA was determined quantitatively from the binding constant $K_b$ values through the Benesi-Hildebrand equation\(^{33}\) as expressed below:

$$
\frac{A_0}{(A-A_0)} = \frac{\varepsilon_G}{(\varepsilon_{HG} - \varepsilon_G)} + \frac{\varepsilon_G}{(\varepsilon_{HG} - \varepsilon_G)} \frac{1}{K_b [C_{\text{DNA}}]} 
$$

The binding constant $K_b$ values of the complexes were calculated from the intercept to slope ratio of the plots of $A_0/A-A_0$ vs. $1/[C_{\text{DNA}}]$, shown in Figs. 6 A and B. $K_b$ values were found out to be $2.0 \times 10^3$ and $1.1 \times 10^3 \text{M}^{-1}$ for complexes 1 and 2. These values are of comparable magnitude to those of other binuclear copper(II) complexes.\(^{9}\) This study indicated that the synthesized complexes bind efficiently with DNA.
The structural stability of synthesized complexes in solution was determined by preparing their 3 mM solution in aqueous DMSO (1:4) and scans their solution in 400-1100 nm after 1 hour, 3 hours, and 24 hours by UV-Visible spectroscopy for investigating their stability. It was observed from the figure 7 that no change is observed in their $\lambda_{\text{max}}$ for 24 hours, which suggest that their distorted octahedral geometry around each copper ion remain constant. However, a small increase in their absorbance was attributed to variation in temperature for 24 hours.

**Molecular docking studies**

To assess the interactions of the synthesized complexes with DNA, docking studies were carried out from which it was observed that the top ranked
conformations of both compounds were well interacted with the active residues of the DNA. Among the synthesized compounds, the most active compound is complex 1 on the basis of the docking scores. The docking results showed that the metal-complex derivatives bind to DNA by intercalation, which is the only interaction mode we obtained by docking. The result of docking of complex 1 with DNA is shown in Fig 8. As it can be seen that the complex 1 showed intercalation with DNA by forming five H-bonds with chain A, being the active residue of the DNA. The docking score of the DNA-complex adduct was -11.6946. The carbon atom of the ligand form H-π interaction with Adenine (DA5) and Guanine (DG16) residues of the DNA made π-H contact with 6-ring moiety of the inhibitor. Metal complexes which bind with DNA primarily by intercalation, are considered as the most effective class of molecules as an anticancer drug.

Figure 8. Docking orientation of complex 1 inside the active site of DNA

From the docking conformation of the complex 2 (docking score = -10.4301), it was observed that this compound established three polar interactions with active site residues DT7, DG14 and DC15 of DNA, respectively (Figure 9).

Figure 9. Docking orientation of complex 2 inside the active site of DNA
An excellent arrangement was obtained as the best docked pose showed important binding features mostly based on interactions due to various interacting moieties of derivatives, and phosphorus atom including its versatile structural features.

Both the copper complexes bind mainly through groove binding and partly through intercalation by hydrogen bonding with Adenine, Guanine and π-H contact with 6-ring moiety of the complexes as evident from a small red shift and a small hypochromism.

CONCLUSION

Two new binuclear copper(II) complexes have been synthesized from 2-bromomphenyl acetate and 1,10-phenanthroline and characterized by UV-Visible, FT-IR, TGA and X-ray studies. Both complexes have dinuclear structures, in which each Cu(II) is penta-coordinated and has square pyramidal geometry. Complex 1 is paddlewheel while 2 is oxygen bridged type. In both complexes the apical and equatorial Cu-O bond lengths are considerably different. The UV-Visible spectroscopy gave $K_b$ values $2.0 \times 10^3$ and $1.1 \times 10^3 \text{M}^{-1}$, respectively for complexes 1 and 2. The binding activity of both complexes with DNA was determined computationally by molecular docking through MOE software, in which the complex 1 intercalates with DNA by forming five H-bonds with chain A, as well as through H-π interaction with Adenine (DA5) and Guanine (DG16) residues of the DNA. The complex 2 established three polar interactions with active site residues DT7, DG14 and DC15 of DNA. Both results support each other which shows the biological relevance of the synthesized complexes.
REFERENCES

23. Molecular operating environment, Chemical Computing Group Inc, Montreal, QC, Canada, 2016