Schiff base ligand containing copper(II) complexes: Synthesis, characterization and binding properties with phosphate

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Two mononuclear copper(II) complexes of a phenol-based Schiff base ligand, 2-[(2-dimethylamino-ethylimino)-methyl]-phenol (HL) have been synthesized and characterized. In methanol, the reaction of stoichiometric amounts of CuCl₂·2H₂O, Cu(OAc)₂·H₂O and the ligand HL in the presence of Et₃N at ambient temperature afforded mononuclear copper(II) complexes, [Cu(L)(H₂O)Cl] (1) and [Cu(L)(H₂O)(OAc)] (2), respectively. Complexes 1 and 2 have been characterized by elemental analysis, molar electrical conductivity, FTIR, UV-Vis and mass spectrometry. DFT calculation has been performed to optimize molecular structures of 1 and 2 to find the structural parameters and overall geometry around the copper centers. Both complexes 1 and 2 are investigated for their binding affinity towards the phosphate ion in aqueous-methanol (3:1; v/v) solution at pH ~7.5 using UV-Vis spectroscopy. The phosphate ion binds to the metal complexes in 1:1 molar ratio. The binding constants of the phosphate-bound mononuclear copper(II) complexes have been determined from UV-Vis titration experiments.

Keywords: Schiff base ligand, copper(II) complex, phosphate binding, UV-Vis titration.

Introduction

Schiff bases are an important class of compounds in both the medicinal and pharmaceutical fields1–3 with a broad range of biological activities such as antifungal, antibacterial, antimalarial, anti-inflammatory, antiviral, and antipyretic properties4–7. The non-bonding electron pair on the nitrogen atom in these compounds makes them prone to coordinate to metal ions in a form of very important Schiff base complexes. In recent decades, the coordination chemistry of Schiff bases has been extraordinarily developed in many aspects8–16. Based on a variety of Schiff base ligands with different numbers of coordination sites (starting with the bi compartmental N₂O₂ types up to the polydentate NₓOᵧ structures), a large number of molecular structures with targeted properties (optical, magnetic or electrical) have been reported. Copper is familiar as an essential bio-element for sometime and its biological role(s) has been known only in the last decades due to the rapid development of bioinorganic chemistry17. Copper(II) complexes efficiently treated with Menkes and Wilson diseases18. Copper is a crucial segment of redox dynamic metalloenzymes, where it takes an interest in redox responses by cycling amongst +1 and +2 oxidation states. Example of these metalloenzymes is cytochrome oxidase, superoxide dismutase, ceruloplasmin and dopamine-β-hydroxylase etc. As is well known, the p-block oxo-anion, such as phosphate ligand can coordinate one, two or more metal ions through the oxygen donor sites, yielding various mononuclear to polynuclear complexes19,20. In spite of their potential binding capability, a large number of transition metal complexes involving inorganic phosphate are still sparse, mainly due to the difficulties in preparation, tendency to form layered complexes, and low crystalline properties of such reaction products. In view of all these observations, herein we report the synthesis, characterization, and phosphate binding affinity of Schiff base containing two copper(II) complexes.

Results and discussion

Synthesis and general characterization:

The phenol-based Schiff base ligand, 2-[(2-dimethylamino-ethylimino)-methyl]-phenol (HL) has been synthesized according to the previously published procedure (Scheme 1)21. The synthesis of ligand HL was accomplished by the condensation of stoichiometric amounts of salicylaldehyde and N,N-dimethylmethylenediamine in methanol under refluxing conditions for 30 min. The ligand was characterized by
elemental analysis, FTIR (Fig. S1, Supplementary file) and $^1$H NMR spectroscopy.

The reaction of the ligand HL with CuCl$_2$·2H$_2$O in 1:1 molar ratio in methanol in the presence of Et$_3$N produced a greenish blue mononuclear complex [Cu(L)(Cl)(H$_2$O)] (1) (Scheme 2). Similarly, the reaction of the ligand HL with Cu(OAc)$_2$·H$_2$O in 1:1 molar ratio in methanol in the presence of Et$_3$N yielded a greenish blue mononuclear complex [Cu(L)(OAc)(H$_2$O)] (2) (Scheme 2). The role of Et$_3$N in the synthesis of 1 and 2 is to deprotonate the phenolic -OH of ligand HL during complexation with copper(II) ion. The complexes 1 and 2 are characterized by the elemental analysis, solution molar electrical conductivity, FTIR, UV-Vis and mass spectroscopic analyses. The molar conductivity values of complexes 1 and 2 in MeOH are 37 and 23 Ω$^{-1}$ cm$^2$ mol$^{-1}$ at room temperature, indicating their non-electrolytic formulations, respectively$^{22}$. The metal complexes, being the light-absorbing species, their binding interactions with phosphate can easily be investigated by UV-Vis spectroscopic technique. In the present investigation, the phosphate binding studies of the complexes were performed using UV-Vis spectroscopic technique in aqueous-methanol (3:1; v/v) solution at pH ~7.5.

**FTIR and UV-Vis studies:**

The FTIR spectra of solid samples of the complexes were recorded and analyzed. In the FTIR spectra, the characteristic stretching vibrations appeared at 1606 and 1605 cm$^{-1}$, are attributable to the metal-bound imine (C=N) functionalities of complexes 1 and 2, respectively$^{23,24}$. Additionally, the FTIR spectrum of complex 2 shows a strong asymmetric stretching vibration ($\nu_{\text{as}(\text{COO}^-)}$) and a strong symmetric stretching vibration ($\nu_{\text{s}(\text{COO}^-)}$) at 1575 and 1400 cm$^{-1}$, respectively. The difference of $\Delta$ value ($\Delta = \nu_{\text{as}(\text{COO}^-)} - \nu_{\text{s}(\text{COO}^-)}$), of 175 cm$^{-1}$ between the asymmetric and symmetric stretching vibrations is ascribed to the monodentate terminal coordination of exogenous acetate group$^{25}$. The spectra of 1 and 2 also exhibit the broad absorption bands at 3355 and 3354 cm$^{-1}$,
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typically of \( \nu_{\text{O-H}} \) band for the coordinated water molecule. The FTIR spectra of both complexes 1 and 2 are displayed in Figs. S2 and S3 (Supplementary file), respectively.

The solution behavior of complexes 1 and 2 was analyzed using UV-Vis spectroscopy. The UV-Vis spectra of the complexes were run in aqueous-methanol (3:1; v/v) solution. The spectra of complex 1 display a broad absorption band at 668 nm (\( \varepsilon \), 115 M\(^{-1}\) cm\(^{-1}\)) due to the d-d transition and copper(II) ion bound ligand-based charge transfer transitions at 356 nm (\( \varepsilon \), 6632 M\(^{-1}\) cm\(^{-1}\)), 261 (\( \varepsilon \), 27506 M\(^{-1}\) cm\(^{-1}\)), and 240 nm (\( \varepsilon \), 28118 M\(^{-1}\) cm\(^{-1}\)). Similarly, the spectra of complex 2 show a broad absorption band at 667 nm (\( \varepsilon \), 108 M\(^{-1}\) cm\(^{-1}\)) due to the d-d transition and copper(II) ion bound ligand-based charge transfer transitions at 358 nm (\( \varepsilon \), 5543 M\(^{-1}\) cm\(^{-1}\)), 263 nm (\( \varepsilon \), 21237 M\(^{-1}\) cm\(^{-1}\)) and 240 nm (\( \varepsilon \), 23894 M\(^{-1}\) cm\(^{-1}\)). The UV-Vis spectra of complexes 1 and 2 are presented in Figs. 1 and 2, respectively.

Fig. 1. UV-Vis spectra of complex 1 at (a) \( 10^{-3} \) (M) and (b) \( 10^{-4} \) (M) in aqueous-methanol (3:1; v/v) solution.

Fig. 2. UV-Vis spectra of complex 2 at (a) \( 10^{-3} \) (M) and (b) \( 10^{-4} \) (M) in aqueous-methanol (3:1; v/v) solution.
Mass spectrometry:

In order to further characterize the complexes using ESI mass spectrometric technique, the aqueous solutions of 1 and 2 were positive-ion electrosprayed into a quadrupole ion-trap mass spectrometer and subjected to collision-induced dissociation. The mass spectrum of complex 1 exhibits the signals at m/z = 315 and 304 that correspond to the \{[Cu(L)(Cl)(H$_2$O)]$^+\text{Li}$\} and \{[Cu(L)(CH$_3$OH)(H$_2$O)]$^+$\} species, respectively, confirming the mononuclear identity of complex 1 in solution. The species \{[Cu(L)(Cl)(H$_2$O)]$^+\text{Li}$\} is a monopositive ion formed when one Li$^+$ ion coming possibly from reaction vessel/container during the experiment is trapped with [Cu(L)(Cl)(H$_2$O)]. The species \{[Cu(L)(CH$_3$OH)(H$_2$O)]$^+$\} is also a monopositive ion formed when Cl$^-$ ion in [Cu(L)(Cl)(H$_2$O)] is replaced by CH$_3$OH during the experiment. The mass spectrum of complex 2 indicates the signals at m/z = 331 and 304 that correspond to the \{[Cu(L)(OAc)(H$_2$O)]$^+\text{H}$\} and \{[Cu(L)(CH$_3$OH)(H$_2$O)]$^+$\} species, respectively, suggesting the mononuclear identity of complex 2 in solution. The species \{[Cu(L)(OAc)(H$_2$O)]$^+\text{H}$\} is a monopositive ion produced when one H$^+$ ion is trapped with [Cu(L)(OAc)(H$_2$O)] during the experiment. The species \{[Cu(L)(CH$_3$OH)(H$_2$O)]$^+$\} is also a monopositive ion produced when OAc$^-$ ion in [Cu(L)(OAc)(H$_2$O)] is replaced by CH$_3$OH.

The representative mass spectrum of complex 1 is shown in Fig. S4 (Supplementary file).

**DFT optimized structures of complexes 1 and 2:**

Despite our great efforts, we didn’t succeed to obtain the single crystals of complexes 1 and 2, suitable for X-ray diffraction analysis. So, the DFT calculation has been performed to optimize their molecular structures to find the structural parameters and overall geometry around the copper centers. Views of the DFT optimized structures of 1 and 2 are presented in Figs. 3 and 4. Bond parameters of 1 and 2 are given in Table 1. The optimization was accomplished without any symmetry restrictions. The vibrational frequencies were examined to authenticate the identity of the stationary point, and this was found to be a minimum (without any negative frequency).

The DFT optimized structure of complex 1 shows that the copper(II) center displays a distorted trigonal bipyramidal geometry (trigonality factor, $\tau = 0.649$)\(^{26}\). The trigonal bipyramidal coordination geometry around copper(II) is completed by an exogeneous monodentate water oxygen (O31), exogeneous monodentate chloride (O34), phenoxo oxygen (O23), a secondary amine nitrogen (N8), a tertiary amine nitrogen (N20), and a water oxygen atom in the axial position and the secondary amine nitrogen, tertiary amine nitrogen, phenoxo oxygen, and the acetate oxygen atom in the equatorial positions. In both complexes 1 and 2, the ligand (L$^-$) is coordinated to the copper(II) ion in a tridentate (N,N,O) mode. The Cu-O and Cu-N bond distances are comparable to those found in similar mononuclear copper(II) complexes\(^{27-29}\). The six- and five-membered chelate rings are also non-planar with bite angles of N(8)-Cu(30)-O(23) = 98.694 and N(8)-Cu(30)-N(20) = 83.891° in 1, respectively. Similarly, in com-
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### Table 1. Selected bond lengths (Å) and angles (deg) in complexes 1 and 2

<table>
<thead>
<tr>
<th>Bond lengths</th>
<th>Complex 1</th>
<th>Complex 2</th>
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<tr>
<td>Cu(30)-O(23)</td>
<td>1.8457</td>
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<td>Cu(30)-O(31)</td>
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<tr>
<td>Cu(30)-N(8)</td>
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<tr>
<td>Cu(30)-Cl(34)</td>
<td>2.1601</td>
<td>1.8301</td>
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<thead>
<tr>
<th>Bond angles</th>
<th>Complex 1</th>
<th>Complex 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>N(20)-Cu(30)-N(8)</td>
<td>83.891</td>
<td>85.105</td>
</tr>
<tr>
<td>Cl(34)-Cu(30)-N(20)</td>
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<td>O(33)-Cu(30)-N(30)</td>
<td>98.984</td>
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<td>O(31)-Cu(30)-O(23)</td>
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<td>O(31)-Cu(30)-Cl(34)</td>
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<td>96.863</td>
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<tr>
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<td>105.09</td>
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<td>N(8)-Cu(30)-Cl(34)</td>
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<tr>
<td>N(20)-Cu(30)-O(23)</td>
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<tr>
<td>N(20)-Cu(30)-O(31)</td>
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<tr>
<td>O(23)-Cu(30)-Cl(34)</td>
<td>120.46</td>
<td>119.30</td>
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</table>

Complex 2, the six- and five-membered chelate rings are non-planar with bite angles of 91.175 and 85.105°, respectively. In both complexes 1 and 2, the Cu-O<sub>aqua</sub> bond distances are same and it is 1.8301 Å, which is within the range of values previously reported in the literature.<sup>27-29</sup> The exogenous acetate group in complex 2 binds to the copper(II) ion in a terminal binding mode. This type of terminal binding of carboxylate is common in copper complexes.<sup>30</sup>

**UV-Vis spectroscopy and phosphate binding:**

The UV-Vis titration technique has been used to investigate the binding interactions of the complexes with phosphate ion in aqueous-methanol (3:1; v/v) solution in 30 mM Tris-HCl buffer (pH ~7.5). To obtain insight into the binding properties of 1 and 2 towards PO<sub>4</sub><sup>3-</sup>, the UV-Vis spectral changes upon the addition of substrate (Na<sub>2</sub>HPO<sub>4</sub>:2H<sub>2</sub>O) to aqueous/methanol solution of the complexes have been investigated. The binding with substrates leads to a gradual decrease in the absorption intensities accompanied by a red shift in the UV-Vis titration spectra, as the complex/substrate assembly via coordination is expected to perturb the ligand based. The UV-Vis spectra clearly show significant hypochromism in the charge transfer regions with a red shift of 2–6 nm of the absorption maximum of complex 1 ($\lambda_{max}(1) = 240$ nm, 261 nm, 356 nm) upon PO<sub>4</sub><sup>3-</sup> binding ($\lambda_{max} = 242$ nm, 267 nm, 359 nm) (Fig. 5). Similarly, the UV-Vis spectra clearly exhibit significant hypochromism in the charge transfer regions with a red shift of 2–4 nm of the absorption maximum of complex 2 ($\lambda_{max}(2) = 240$ nm, 263 nm, 358 nm) upon PO<sub>4</sub><sup>3-</sup> binding ($\lambda_{max} = 242$ nm, 266 nm, 362 nm) (Fig. 6). The significant hypochromism along with substantial red shift for the complexes revealed the active participation of PO<sub>4</sub><sup>3-</sup> ion during the binding events, in solution. Both the complexes bind with PO<sub>4</sub><sup>3-</sup> ion to yield 1:1 complex/substrate bound assemblies (Figs. 5 and 6 insets). The 1:1 stoichiometry of phosphate bound complex formed from the complex and phosphate is further confirmed by the linear fit of data as given in Figs. 7 and 8. If the system contains only one light absorbing species (i.e. metal complex), no complex/phosphate bound product formation takes place and the slopes of the linearly fitted data for corresponding wavelength pairs in systems containing complex or complex and phosphate would be alike. This is not observed here; therefore, the binding between complexes and phosphate takes place and the phosphate bound copper(II) complexes are produced (Figs. 7 and 8). The binding constants of the phosphate bound
mononuclear copper(II) complexes are determined from the UV-Vis titration experiments by the method of Rose and Drago and the values are found to be 3.290 \times 10^{-4} \text{ M} and 2.512 \times 10^{-4} \text{ M}, corresponding to complex 1/PO_4^{3-} and complex 2/PO_4^{3-} assemblies, respectively.

Conclusion

Two copper(II) complexes have been synthesized using the ligand, 2-[1-(2-dimethylamino-ethylimino)-ethyl]-phenol (HL) and fully characterized by different analytical techniques including DFT optimization. Both of these complexes show the excellent binding interactions with phosphate ion in aqueous/methanol solution. The binding occurs most possibly, through the coordination of phosphate group with the copper(II) complexes. The binding constants from the interactions between both the complexes and phosphate, were determined from the UV-Vis titration experiment. The binding interaction between the various synthetic model complexes and inorganic phosphate is the topic of current research works in the field of inorganic chemistry. The coordination-cum-binding ability of PO_4^{3-} ion with copper(II) supported by the 2-[2-dimethylamino-ethylimino]-methyl]-phenol (HL) ligand will positively contribute to the field of coordination chemistry.
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Experimental

Materials and methods:

Salicylaldehyde and N,N-dimethylethylenediamine were purchased from Sigma-Aldrich Chemie GmbH, Germany. Copper chloride dihydrate, copper acetate monohydrate, triethyl amine and disodium hydrogen phosphate dihydrate were purchased from Merck, India. All other chemicals and solvents were reagent grade materials and used as received from commercial sources without further purification. Microanalyses (C, H, N) were carried out using a Perkin-Elmer 2400 CHNS/O Series II elemental analyzer. FTIR spectra were recorded on a Perkin-Elmer L120-000A spectrometer (200–4000 cm⁻¹). NMR spectra were obtained on a Bruker AC 400 NMR spectrometer. UV-Vis spectra were recorded on a Shimadzu UV 1800 (190–1100 nm) (1 cm quartz cell) spectrophotometer. The solution electrical conductivity was obtained with a METTLER TOLEDO Five EASYTM Plus FEP 30 digital conductivity meter with a solute concentration of about 10⁻³ M. Mass spectrometric experiments were performed using a Micromass Q-Tof Micro™ (Waters) mass spectrometer.

Synthesis of 2-[(2-dimethylamino-ethylimino)-methyl]-phenol (HL):

A solution of N,N-dimethylethylenediamine (2.093 mL, 19 mmol) in methanol (10 mL) was added to a solution of salicylaldehyde (2 mL, 19 mmol) in methanol (10 mL). A deep brown solution of Schiff base was obtained and refluxed at 60°C for 4 h. Then, the solution was cooled at room temperature. Then, the solution was evaporated to dryness under rotary evaporator. A yellowish orange highly viscous solution was obtained. The product was dried under vacuum over P₂O₅. The product is slightly hygroscopic and confirmed by elemental analysis. Yield: 2.2 g (60.27%). Anal. Calcd. for C₁₁H₁₅N₂O₂: C, 68.72; H, 8.39; N, 14.57. Found: C, 68.70; H, 8.35; N, 14.45. FTIR (cm⁻¹): ν 3379(b), 3060(s), 2942(s), 2832(s), 2771(s), 1681(s), 1663(s), 1633(s), 1582(s), 1496(s), 1462(s), 1279(s), 1210(s), 1151(s), 1040(s), 973(s), 757(s); ¹H NMR (400 MHz, CDCl₃, room temperature): 8.3 (1H, s), 7.2 (4H, m), 3.7 (2H, t), 2.8 (2H, t), 2.2 (6H, s).

Synthesis of [Cu(L)(Cl)(H₂O)] (1):

A solution of CuCl₂ 2H₂O (0.221 g, 1.30 mmol) in water (5 mL) was added to a solution of ligand (250 mg, 1.30 mmol) and triethylamine (0.18 mL, 1.30 mmol) in methanol (15 mL). The reaction mixture was stirred for 2 h resulting in a blue solution. The solution was filtered to discard the insoluble precipitate. The blue solid compound was isolated by adding excess diethyl ether to the clear filtrate. It was then filtered, washed and dried under vacuum to get the blue powder. Yield: 0.352 g (88%). Anal. Calcd. for C₁₁H₁₀N₂O₄ClCu: C, 42.86; H, 5.56; N, 9.09; Cu, 20.61. Found: C, 42.75; H, 5.38; N, 9.01; Cu, 20.72. Molar conductance, ΛM₁: (MeOH) = 37 Ω⁻¹ cm² mol⁻¹; FTIR (KBr, cm⁻¹): ν 3355(b), 3044(s), 1606(s), 1575(s), 1443(s), 1398(s), 1328(s), 1260(s), 1232(s), 1166(s), 1103(s), 1043(s), 984(s), 957(s), 887(s), 857(s), 756(s); UV-Vis (H₂O/MeOH): λmax (ε, M⁻¹ cm⁻¹) = 668 (115), 356 (6632), 261 (27506), 240 (28118).

Synthesis of [Cu(L)(OAc)(H₂O)] (2):

A solution of Cu(OAc)₂ H₂O (0.2216 g, 1.30 mmol) in water (5 mL) was added to a solution of ligand (250 mg, 1.30 mmol) and triethylamine (0.18 mL, 1.30 mmol) in methanol (15 mL). The reaction mixture was stirred for 2 h resulting in a dark blue solution. The solution was filtered to discard the insoluble precipitate. The blue solid compound was isolated by adding excess diethyl ether to the clear filtrate. It was then filtered, washed and dried under vacuum to get the blue powder. Yield: 0.3454 g (80%). Anal. Calcd. for C₁₃H₂₀N₂O₄Cu: C, 47.05; H, 6.07; N, 8.44; Cu, 19.15. Found: C, 47.10; H, 6.15; N, 8.41; Cu, 19.21. Molar conductance, ΛM₂: (MeOH) = 37 Ω⁻¹ cm² mol⁻¹; FTIR (KBr, cm⁻¹): ν 3354(b), 1606(s), 1575(s), 1534(s), 1468(s), 1443(s), 1400(s), 1351(s), 1329(s), 1260(s), 1232(s), 1167(s), 1144(s), 1043(s), 1022(s), 957(s), 856(s), 755(s); UV-Vis (H₂O/MeOH): λmax (ε, M⁻¹ cm⁻¹) = 667 (108), 358 (5543), 263 (21237), 240 (23894).

UV-Vis spectroscopy:

All experiments were performed on a Shimadzu UV 1800 spectrophotometer with 1 cm quartz cell at room temperature over a range of 200–900 nm. All experiments were done in water/methanol (3:1, v/v) solution in 30 mM Tris-HCl buffer (pH ~7.5) solution. The experiments were run by titrating fixed concentration of the complexes (1.00×10⁻³ M) with varying concentrations of phosphate (0–5×10⁻⁴ M). The UV-Vis absorbances and pH meter readings of the resulting solutions were measured immediately after mixing.

DFT calculations:

DFT calculation regarding the structure optimization of complexes 1 and 2 were carried out using the B3LYP method and 6-311G basis set.
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References