A simple Cu(II) complex of phenolic oxime: synthesis, crystal structure, supramolecular interactions, DFT calculation and catecholase activity study

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ABSTRACT

A copper (II) complex [Cu(4-MeO-salox)2](I) based on saloxime ligand was synthesized and characterized using single crystal X-ray diffraction studies. The geometry was further emphasized by DFT optimization. The complex was found to be pseudo-macrocyclic mononuclear having square planer geometry. The complex I shows two types of supramolecular hydrogen bonding interactions and forms the multi-dimensional framework with the help of CH⋯O, OH⋯O and s⋯s(chelate) interactions. The complex I performs as efficient catalyst in catecholase activity having good turnover number (TON), kcat = 22.97 h−1 where TON is the number of catechol molecules converted into quinone by catalyst molecule i.e 1 in a unit time.

1. Introduction

Phenolic oximes are widely used in industrial copper extraction process from waste streams, and as corrosion protectors in protective coatings. They exhibit selective preference for copper (II) over the other metals, particularly over iron present in pregnant leach solutions. The large selectivity for copper (II) is due to the fact that it perfectly fits in the cavity created by two hydrogen bonded ligands, producing a stable pseudo-macrocyclic monomer (Scheme 1). Mononuclear complexes of Co(II), Ni(II), Cu(II), and Zn(II) with these phenolic oximes are also known to be formed. One more important aspect of phenolic oximes is their capability to form polynuclear complexes since both the oximate and oximato groups simultaneously coordinates to the metal center [5, 6, 7, 8]. Formation of pseudo-macrocyclic monomer complex with Cu(II) is also one of the most attention grabbing features of phenolate oximes [9].

Moreover, enzymes containing Cu(II) [10] like tyrosinase, hemocyanin, and catechol oxidase control numerous biochemical reactions rate in alive systems. The active sites of these type-III copper proteins contain magnetically coupled binuclear Cu(II) centers. These metallo-enzymes take vital part in the selective oxidation of organic compounds promoting the activation of dioxygen [11]. Tyrosinase regulates the oxidation of phenols into catechols (catecholase activity), followed by catechols into o-quinones (catecholase activity). On the other hand, the enzyme catechol oxidase oxidizes catechols to o-quinones, highly reactive compounds that undergo auto-polymerization to generate a brown pigment melanin, that protects the tissues of higher plants from damage against insects and pathogens [12].

The oxidase (oxygenase) activity of model coordination complexes for metalloenzymes are of picy interest for the progression of bioactive catalysts for oxidation reactions [13]. In this perspective, the type-3 dicopper enzyme catechol oxidase employs aerobic dioxygen to attain the specific oxidation of catechols to orthoquinones [14]. A range of

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The pseudo-macrocyclic cavity created via Hydrogen-bonding between phenolic oximes in 2:1 metal complex. M (Cu and Co) is in the +2 oxidation state.

Scheme 1. The pseudo-macrocyclic cavity created via Hydrogen-bonding between phenolic oximes in 2:1 metal complex. M (Cu and Co) is in the +2 oxidation state.

In the present endeavor, we are projected to reveal synthesis and crystal structure of the stable complexation of oxime with Cu(II) in MeOH in presence of triethylamine (TEA) as a base and supramolecular interactions like CH⋯O, OH⋯O and π⋯π(chelate) interactions are capable of forming the multi-dimensional framework. For I, the supramolecular assemblies i.e. π⋯π stacking interaction forms a 1D array which is further expanded through two different types of C–H⋯O and OH⋯O hydrogen bondings to ensure a 2D framework. This Cu(II) complex also shows efficient catalytic efficacy towards catecholase activity.

dinuclear copper-contain functional models of this metalloenzyme have been progressed during the last decades [15, 16, 17].

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2. Experimental

2.1. Materials and methods

The starting materials 4-methoxy-salicylaldehyde was procured from Lancaster. Hydroxylamine hydrochloride, sodium azide, anhydrous Na2SO4, and CuCl2.2H2O were purchased from Merck, India. Tetraethylammonium hydroxide was of SRL, India. Solvents like methanol, diethylether, and acetonitrile were of reagent grade and dried before use.

2.2. Physical measurements

A Nicolet Magna IR 750 FTIR spectrometer (series-II) was used to record the Infrared spectra (400–4000 cm⁻¹) in liquid state. Bruker NMR spectrometer (300 MHz) was utilised for recording ¹H-NMR spectra. The absorption spectra were carried out on a Jasco V660 spectrophotometer (Jasco, Hachioji, Japan) using quartz cuvettes of 10 mm path length.

2.3. Synthesis and characterization

2.3.1. Synthesis of the 4-OMe-H3salox (H2L)

The solution of 4-methoxy-salicylaldehyde (3.04 g, 20 mmol) (Scheme 3) in ethanol (60 mL) was stirring with NH2OH.HCl (2.76 g, 40 mmol) in 20 mL of water. After that 20 mL of aqueous solution of Na2CO3 (4.00 g, 40 mmol) was then added in the resulting mixture and was refluxed at 80 °C. The reaction progression was tailored by TLC (solvent: 1/1 hexanes/EtOAc). The solid product was precipitated out from reaction mixture which was then filtered with celite bed and was collected by washing with cold water. The needle like crystalline material (4-MeO-H3salox) was obtained after recrystallization from methanol. Yield: 2.17g (65%). M.P.:133–134.5 °C. ¹H NMR (δ, ppm; 300 MHz, DMSO-d6): 3.73 (3H, m, aromatic protons), 6.86–7.38 (3H, m, aromatic protons), 8.12 (1H, s, methyne), 9.68 (1H, bs for Phenolic OH proton). 10.21 (1H, s, N–OH proton).

2.3.2. Synthesis of complex [Cu(4-MeO-salox)2](1)

The reaction between 4-MeO-H3salox and CuCl2 in presence of TEA in MeOH gives complex [Cu(4-MeO-salox)2](1) [18]. The pale yellow solution of 4-MeO-H3salox (0.167g, 1.0 mmol) in 30 mL of DMSO: DCM (2:1; v/v) was stirred and the solid [Cu(bpy)Cl2] (0.290 g, 1.0 mmol) (Scheme 3) was stirred after adding to it. The resulting solution was then stirred continued for 2h with the addition of TEA (triethylamine) (0.202 g, 2.0 mmol) and the colour of the resulting solution became green. After completion of the reaction, the filtrate without any precipitation was kept aside uninterrupted for slow evaporation. The green block-shaped crystals were formed after 5 days, and collected them by filtration. Yield 0.25g (65%) based on copper content. IR analysis: 3125 b cm⁻¹ for ν(OH), 1625 cm⁻¹ for ν(N=C). Elemental analysis for molecular formula C16H16CuN2O6 (M.W. 395.86) Calc.C 48.55%, H 4.07%, N 7.08% Found C 48.59 %, H 4.05%, N 7.10%.

2.3.3. Crystallographic analysis

A Bruker SMART APEX-II CCD diffractometer equipped with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å) was used to collect the single crystal X-ray data of the complex was on using. Data collection, reduction, structure solution, and refinement were carried out by employing Bruker APEX-II suite (v2.0-2) program [19]. All resultant reflections correspond to 2θmax were collected and corrected for Lorentz and polarization factors with Bruker SAINT plus. After that corrections for absorption, inter frame scaling, and other systematic errors were corrected with SADABS [20]. The structures were resolved using direct methods and refinement was computed by means of full matrix least-square technique with SHELX-97 software package [21] based on F². by HFIX command were performed to fix all the hydrogen atoms geometrically and positioned at the ideal positions. Calculations were computed with the WinGX system Ver-1.80 [22]. The other non-hydrogen atoms were refined with the thermal anisotropic parameters. Mercury 3.1 programme was employed to generate the drawing of resultant molecules. The crystallographic data are listed and summarised Table 1.

2.3.4. Computational details

Density functional theory (DFT) was employed to optimize the ground state electronic structure of I in gas phase [23]. The method was coupled with the conductor-like polarizable continuum model (CPCM) [24]. Becke’s hybrid function [25] along the Lee-Yang-Parr (LYP) correlation function [26] was utilised all over the theoretical study. The absorbance spectral properties in DMSO medium was calculated by Time-dependent density functional theory (TDDFT) [27] linked with the CPCM model was used for calculation. Calculation for the transitions...
with lowest 40 doublet – doublet (as Cu(II) is d^9 system, S = 1/2) was carried out for obtaining the theoretic UV-Vis spectral transitions and results of the TD calculations were qualitatively very similar with experimental.

For the DFT calculations 6–31g basis set was used for C, H, N, O, and Cu atoms and performed with the Gaussian 09W software package [28]. The molecular orbital contributions from groups or atoms were computed by the Gauss Sum 2.1 program [29].

3. Results and discussion

3.1. Structural descriptions

The reaction between 4-MeO-saloH2 and CuCl2 in presence of TEA in MeOH gives complex [Cu(4-MeO-saloH)2(1)], in quantitative yield but if this reaction takes place in MeCN then one tridentate iminoacylated ligand may form by the nucleophilic attack of oxime-O atom (-C¼NOH) on –C¼N centre of acetonitrile to form monodentate iminoacylated complex [5, 6, 7, 8, 9].

The structural analyses from single-crystal X-ray diffraction studies shows that complex 1 is a CuII mononuclear species that comprises of one CuII ions and two tridentate NO2 donor 4-MeO-saloH2 ligands. It is crystallized in a monoclinic system with space group P21/n. The structure consists of a discrete [CuII(4-MeO-saloH)2] as a neutral species in which the ligand is mono-deprotonated, presented in Figure 1a. The CuII atom is coordinated with two tridentate 4-MeO-saloH2 ligands specifically through N1 and O2 and their symmetry related counter atoms to form tetracoordinated complex which adopted square planer geometry. The bond lengths around the Cu atom are Cu1–Ni (N1 and N1a)~1.932Å and Cu1–Oi (O2 and O2a)~1.898Å (i¼inversion center). The selective bond angles and bond lengths are enlisted in Table 2. Here, free protonated oxime –OH groups are also in bonding distances though it is not capable of forming octahedral geometry as in planer way. In the asymmetric unit, the monomer is intramolecularly H-bonded (1.955Å) by the phenolate oxygen and oxime proton (-C¼NOH) (Figure 1) to structure a stable pseudo-macrocyclic framework. The nearest Cu/C15/C15/C15/Cu internuclear distance is 6.414Å. The mean deviation between Cu1 and well defined planes around Cu1 (Cu1 N1 N1i O1 O1i) is 0.000Å and it shows that the complex is perfect square planar.

From the single crystal X-ray diffraction studies, it was shown that there were various types of supramolecular interactions present in the crystal exhibit a crystallographic arrangement. By inspection of molecular assemblies through supra-molecular interactions on 1 showed that 1 forms two types (A and B) of hydrogen bonding interaction. The Type A: the intermolecular H-bonding (Table 3) is between oxime-OH (O3) and oxime-OH(O3a) of neighbor’s and vice-versa; O3–H3⋅⋅⋅O3a = 2.619Å (Figure 1b) with molecular synthon R2^2(4) in graph set motif and likewise, Type B: the intermolecular H-bonding is CH⋅⋅⋅O interactions.
between azomethine proton (C7–H7) and oxime–OH (O3; C7–H7–O3 = 2.480 Å with supramolecular synthon R22(8) in graph set motif and form 1D network crystallographic b axis. The conception of the supramolecular synthons is a very crucial step to understand the association of molecular crystals. It is nothing but a retrosynthetic route where fragmentation of the crystal structures can be done into supramolecular synthons [30].

Simultaneously, the CH...O, OH...O and π...π(chelate) interactions are capable of forming the supramolecular tetramer in crystallographic ac plane in 1 (Figure 1d). In this tetramer, the non-covalent π...π(chelate) (3.740 Å) (Figure 1d) between the centroid of benzene ring and the centroid of chelation with copper atom and NO donor of oxime. In the transition metal complexes, the non covalent π...π interactions take part in an important role in the construction of a supramolecular architecture. This π...π interaction requires an appropriate geometrical conformation by which the π orbitals lobes of ligands to position either face to face or to somewhat parallel maintaining distance up to 3.8 Å [31]. In this particular case, the said distance is 3.740 Å.

The combinatorial effect of hydrogen bonding: Type-A and Type-B are extended in an one dimensional (1D) network (Figure 2) along crystallographic c axis. This 1D supramolecular assembly is further expanded with the help of CH...O, OH...O and π...π(chelate) interactions to 2D framework in crystallographic ac plane and with inversion of plane (Figure 3 a, b). Hydrogen bonding parameters are tabulated in Table 3.

Symmetry operator a = 2-x,-y,1-z.

### 3.2. Electronic spectra

UV-vis spectra can be a good detector of geometry for complexes of copper Schiff base [25, 26]. Electronic spectra of complex 1 shown in Figure 4 were recorded in MeOH (4 × 10⁻⁵ (M)) solution. The one band at 323 nm (ε = 2.4 × 10⁴ M⁻¹ cm⁻¹) in the electronic spectrum is due to intra-ligand transition. The another lower intensity band at 397 nm (ε = 1.4 × 10⁴ M⁻¹ cm⁻¹) is the indication of a tetra coordinated square planer Cu(II) center [32] and generally recognized as ligand to metal charge transfer transition (LMCT).

### 3.3. Geometry optimization and electronic structure

The optimized geometry of complex 1 is similar with molecular structure obtained from SCXRD in Figure 5. The difference of energy between HOMO and LUMO is 4.18 eV (Figure 5a). The diagram of

| Bond Distances (Å) | Cu1–O2 | Cu1–O2a | Cu1–O3 | Cu1–O3a |
|-------------------|--------|---------|--------|---------|
| Cu1–O2            | 1.898 (15) | Cu1–O2a | 1.898 (15) |
| Cu1–O3            | 2.859 (2) | Cu1–O3a | 2.859 (2) |
| Cu1–N1            | 1.932 (2) | Cu1–N1a | 1.932 (2) |

| Bond Angles (°) | O2–Cu1–O3 | O2–Cu1–N1 | O3–Cu1–N1a | O3–Cu1–N1 |
|----------------|-----------|-----------|-------------|-----------|
| O2–Cu1–O3      | 117.59 (6) | 91.92 (7) | 154.28 (8) | 154.28 (8) |
| O2–Cu1–N1      | 180.00    | 180.00    | 180.00      | 180.00    |
| O2–Cu1–O3a     | 62.41 (6) | 62.41 (6) | 62.41 (6)   | 62.41 (6) |
| O2–Cu1–N1a     | 88.08 (7) | 88.08 (7) | 117.59 (6)  | 117.59 (6) |
| O3–Cu1–N1      | 25.72 (8) | 25.72 (8) | 25.72 (8)   | 25.72 (8) |
| O3–Cu1–O3a     | 25.72 (8) | 25.72 (8) | 25.72 (8)   | 25.72 (8) |

Symmetry operator a = 2-x,-y,1-z.

### Table 3. Hydrogen bonds for 1 (Å and °).

| D–H...A | d (D...A) | d (D–H) | d (H...A) | (DHA) |
|---------|-----------|---------|-----------|-------|
| Cu7–H7–O3 | 2.480 | 3.308 (3) | 148.00 |
| Cu3–H3–O3a | 2.619 | 3.049 (2) | 65.73 |

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frontier molecular orbitals (FMOs) with their corresponding positive and negative regions for the optimization of 1 has been depicted in Figure 5. The positive and negative lobes are shown by green and orange colour, respectively.

The experimental absorption bands have been explained by of TD-DFT calculations [33]. In the ground state optimized structure of 1, the electron cloud remains mostly on HOMO-1, LUMO and LUMO+2 orbitals presents at the benzene ring with –OMe groups while the electron density on HOMO, HOMO-2, LUMO+1 and LUMO+3 orbital resides at π and π* orbitals involvement of benzene ring of ligand alongside with metal’s d orbital contribution.

The UV-Vis spectra of the 1 were performed at room temperature in MeOH. The complex (1) showed two well determined absorption bands are situated at 320 and 399 nm, having ILCT and LMCT transitions feature respectively, which are in well corroborate with experimental results of 323 and 397 nm. These two absorption peaks can be predicted as the S0→S5 and S0→S3 electronic transitions (Figure 5b) with oscillator strengths $f = 0.1426$ and $f = 0.0719$ (Table 4) respectively.

Figure 2. The H-bonding interactions with the combination of Type-A and Type-B form 1D supramolecular network along crystallographic c axis for 1. Some H-atoms are omitted for clarity.

Figure 3. (a) and (b) 2D framework composed of π⋯π(chelate) interactions, CH⋯O and OH⋯O interactions in crystallographic ac plane for 1. Some H-atoms are omitted for clarity.
3.4. Catechol oxidase mimicking activity and kinetic studies

In order to investigate the biomimicking catecholase activity of 1, 3,5-di-tert-butylcatechol (3,5-DTBC) was taken as substrate. The low redox potential of 3,5-DTBC helps for easy oxidation and the bulky tert-butyl substituents protects from over-oxidation [34]. The oxidized product 3,5-di-tert-butylquinone (3,5-DTBQ) (Scheme 4) is very stable and exhibits an absorption maximum at 401 nm in methanol [35]. The capability of the Cu(II) complex to mediate the oxidation of 3,5-DTBC was investigated UV/Vis spectroscopy. A 10⁻⁴ M solution of 1(1/2 10⁻⁴ mol⋅dm⁻³) was treated with 100 equivalents of 10⁻³ M solutions of 3,5-DTBC (1/2 10⁻³ mol⋅dm⁻³), under aerobic conditions in methanol. On incremental addition of the substrate 3,5-DTBC, the absorption band around 400 nm showed 70% hyperchromicity, which indicates of the production of the corresponding quinone 3,5-DTBQ during the experiment, the quinone absorbance band was found to be increased with time (Figure 6).

The kinetics studies of 3,5-DTBC oxidation to form 3,5-DTBQ catalyzed by 1 was measured by the initial rate method, monitoring the increase in the absorbance band at 400 nm at 25 °C. The rate constant was calculated from the plot of log (A₀/(A₀−Aₜ)) versus time. The dependence of substrate concentration on the rate of oxidation was investigated keeping the Cu(II) complex concentration constant as 10⁻⁴ M and increasing the substrate from 1 × 10⁻⁴ to 1 × 10⁻² mol⋅dm⁻³. At low concentrations of substrate, the first order dependence was observed. Whereas, saturation kinetics was observed at higher concentrations of substrate (Figure 7).

Michaelis–Menten theory for enzymatic kinetics was utilized and the Lineweaver–Burk (double reciprocal) plot [11] was constructed to analyze the results obtained from the plot of rate constants vs. substrate concentration. From the Lineweaver–Burk graph: 1/V vs. 1/[S] (Figure 7), using equation 1/V = (K_M/V_max)⋅(1/[S]) + 1/V_max, the Michaelis–Menten constant (K_M), maximum initial rate (V_max), and rate constant (k_cat) are extracted for 1. The turnover number (k_cat) was calculated by dividing the V_max values by the concentration of the complex. The turnover number (k_cat,TON) is the number of catechol molecules converted into quinone by catalyst molecule (here 1) in a unit time. The kinetic parameters are presented in Table 5. The obtained data from the Lineweaver–Burk plot are reasonable for catalytic activity measurements though the actual mechanism of this reaction may be quite complicated. The calculated k_cat (22.97 h⁻¹) value for complex 1 is almost similar to the reported value by Krebs et al. [36] (4 h⁻¹ to 214 h⁻¹).

Therefore in literatures, a lot of copper (II) complexes showed excellent catecholase activities [37, 38, 39] but Cu(II) complexes [40]

Table 4. The comparable calculated absorbance λ_max with experimental values for the complex 1.

| Theoretical (nm) | Experimental (nm) | Composition            | CI      | Electronic Transition | Energy (eV) | f  |
|------------------|-------------------|------------------------|---------|-----------------------|-------------|---|
| 320              | 323               | HOMO→LUMO              | 0.0259  | S₀→S₁                 | 4.1652      | 0.1426 |
|                  |                   | HOMO→LUMO              | 0.3149  |                       |             |    |
| 399              | 397               | HOMO→LUMO              | 0.2017  | S₀→S₁                 | 3.8063      | 0.0719 |
|                  |                   | HOMO→LUMO              | 0.8161  |                       |             |    |
obtained through the use of the dioxime ligand and as co-ligand 1, 10-phenanthroline exhibited the catecholase activity in very mild rate. Here in this report, the Cu(II) complex of oxime ligand shows excellent efficacy of catecholase activity so far.

4. Conclusions

The synthesis, structural as well as catecholase activity of a mononuclear square planer Cu(II) complex was demonstrated. The copper (II) complex exhibits numerous interesting characters in the single crystal X-ray structure analysis process. The stable complexation of oxime with Cu(II), in MeOH form pseudo-macrocyclic mononuclear complex and also capable of forming the multi-dimensional framework by the help of CH⋯O, OH⋯O and π⋯π(chelate) interactions. The Cu(II) complex performed as efficient catalyst and display good efficacy towards catecholase activiy having TON, \( k_{\text{cat}} = 22.97 \) h\(^{-1}\).

Declarations

Author contribution

Statement Malay Dolai: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Urmila Saha: Performed the experiments; Analyzed and interpreted the data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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Appendix A. Supplementary data

CCDC 900538 contains the supplementary crystallographic data for 1. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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