# SYNTHESIS AND CHARACTERIZATION OF COPPER(II) COMPLEX OF A NEW AMINOPHENOL LIGAND AS A MODEL FOR GALACTOSE OXIDASE METALLOENZYME ACTIVE SITE AND ITS APPLICATION IN AERIAL ALCOHOL OXIDATION

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In this work, we have synthesized a copper(II) complex of 6,6'-(propane-1,3-diylbis(azanediyl))bis(2,4-di-tert-butylphenol) due to its structural similarity to galactose oxidase active site. The electrochemical oxidation of $K_2[Cu(L^{DAP})Cl_2]$ complex shows that the oxidation process is ligand-centered due to the oxidation of phenolate to the phenoxyl radicals. The $K_2[Cu(L^{DAP})Cl_2]$ complex also undergoes an electrochemical metal-centered reduction. The difference in oxidation and reduction peaks considered as the stability of the mentioned complex, which has been estimated in the presence of various coordinating ligands such as acetate and chloride. Also, a highly efficient and eco-friendly oxidation of alcohol to the aldehyde with air as oxidant and $K_2[Cu(L^{DAP})Cl_2]$ complex as a catalyst was performed.
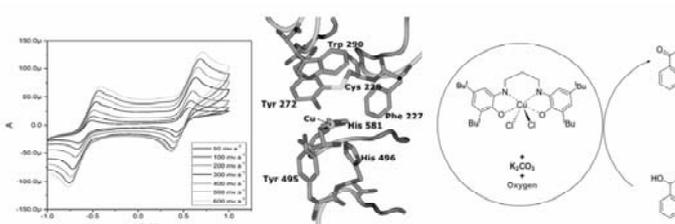
INTRODUCTION

Designing a redox active metal complex with collating the electronic property of metal ion and electronic and structural trait of ligands is an elegant template for tuning the electronic and magnetic property of bio-inspired catalyst.[1] Non-innocence arises when the frontier orbitals of the metal and the ligand are close enough in energy for mixing to occur and is therefore dependent on both the ligand and the metal. This phenomenon has been observed in the active site of metallo-enzymes.[2] Since the biomimetic models can provide valuable information to better understand the biodegradation mechanisms of enzymes so transition-metal complexes containing proradical phenolate ligands are so an interesting class of model complexes for galactose oxidase (GAO).[3-7] The active site of this enzyme contains a Cu(II) ion, cysteine, water and redox active tyrosine moieties.

Non-innocent complexes catalyzed a series of very important organic reactions such as Negishi-type C–C bond formation,[8] cyclopropanation,[9] N–N coupling,[10] C-H amination,[11] water oxidation,[12-18] water reduction,[12,19] ethylene oxidation[14,20] and alcohol oxidation.[21-22] It should be noted that the control of the radical centers in the design of biomimetic models that are containing redox active phenoxyl radicals is so difficult. This control, which involves stability, magnetic properties and reactivity, depends on interdependent factors such as protonation of the phenolic moieties, geometry and electronic properties.[23]

In this paper, we report the synthesis, characterization and electrochemical redox properties of $K_2[Cu(L^{DAP})Cl_2]$ complex containing a novel

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synthesized [N-O]-donor aminophenol ligand (H₂L^{DAP}) (Scheme 1) which provides the coordination sphere around Cu(II) center. Also, a highly efficient and eco-friendly oxidation of alcohol to the aldehyde with air as oxidant and K₂[Cu(L^{DAP})Cl₂] complex as a catalyst was performed.
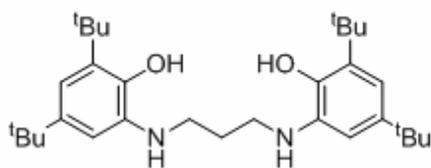
Scheme 1 – The structure of H₂L.^{DAP}

EXPERIMENTAL

Materials and Methods

Reagents and analytical grade materials were obtained from commercial suppliers and used without further purification, except those for electrochemical measurements. Elemental analyses (C, H, N) were performed by the Elementar, Vario EL III. Fourier transform infrared spectroscopy on KBr pellets was performed on a FT IR Bruker Vector 22 instrument. NMR measurements were done on a Bruker 400 instrument. UV-Vis absorbance digitized spectra were collected using a CARY 100 Bio spectrophotometer. Cyclic voltammetry was performed using Autolab potansiostat/galvanostat 101. The working electrode was a glassy carbon disk (2.0 mm diameter) and Pt wire was used as counter electrode. The working electrode potentials were measured *versus* a quasi-reference electrode of Silver wire (all electrodes from Azar Electrode). The Ag quasi-reference electrode was calibrated using a ferrocene/ferrocenium redox couple (0.41 V) as an external standard. The GC analysis was carried out using a VARIAN CP 3800 with dihydrogen carrier gas.

Synthesis of H₂L^{DAP}

To a solution of 3,5-DTBQ(0.44 g, 2 mmol) in n-heptane (5mL) was added 1,3-diaminopropane (0.08 mL, 1 mmol), and the reaction stirred for 2h at room temperature in the presence of air. The yellow precipitate was formed. The pale yellowish microcrystals were grown from a 1:1 solvent mixture of dichloromethane/n-heptane (Scheme 2).

Yield: 0.220 g (45%). Anal. calcd. (found) for C₃₁H₅₀N₂O₂: C 77.13 (77.01), H 10.44 (10.39), N 5.80 (5.76).ν$_{max}$(KBr)/cm^{-1}: 3367 (O-H), 3291 (N-H), 2962, 2715, 2601 (C-H), 1593 (C=C), 1486 (C=N), 1141 (C-N), 884-596 (=C-H bending). ¹H NMR (400 MHz, deuterated DMSO, 298 K): δ 1.216 (s, 9H), 2.514, 2.519, 2.523, 2.528, 2.532, 2.546 (s, 9H), 3.216
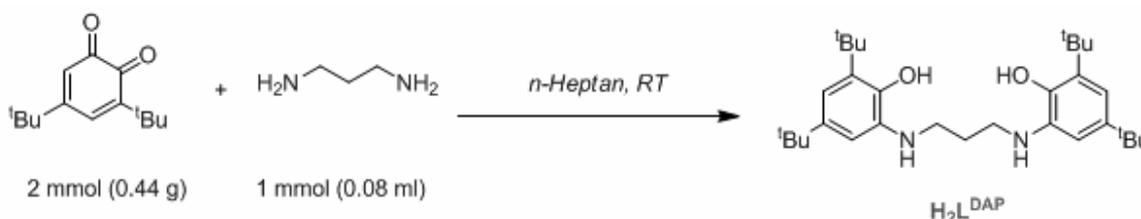
(sextet), 3.349 (s), 4.475 (s, 2H), 6.507, 6.513 (d, 1H), 6.597, 6.603 (d, 1H), 7.289 (s, 1H). ¹³C{¹H}NMR (100 MHz, deuterated DMSO): δ 30.34, 31.98, 34.22, 34.93, 38.97, 39.18, 39.39, 39.59, 39.80, 40.01, 40.22, 111.70, 112.06, 136.88, 137.34, 140.29, 142.07. m.p. 158-161 ˚C.

Synthesis of K₂[Cu(L^{DAP})Cl₂] complex

H₂L^{DAP} (0.485 g, 1 mmol) and Potassium hydroxide (0.112 g, 2 mmol) were dissolved in a 2:1 acetonitrile/dichloromethane mixture (45 mL), and then CuCl₂.6H₂O (0.238 g, 1 mmol) was added. The reaction mixture was stirred for 4 hours at room temperature in the presence of air. The dark violet microcrystals were grown from a 1:1 solvent mixture of dichloromethane/methanol. as previously described[24], Yield: 0.63 g (92%). Anal. calcd. (found) for C₃₁H₄₆Cl₂CuK₂N₂O₂: C53.86 (53.22), H 6.71 (6.95) N 4.05 (3.92), Cu 9.19 (9.1). ν$_{max}$(KBr)/cm^{-1}: 2962 (C-H), 1594 (C=C), 1486 (C=N), 1141 (C-N), 743 (=C-H bending).

Catalytic activity of K₂[Cu(L^{DAP})Cl₂] complex in oxidation of alcohols

The oxidation was carried out in an oxygen atmosphere at 80°C. In a typical experiment, alcohol (1 mmol), K₂[Cu(L^{DAP})Cl₂] (4 mol%) and K₂CO₃ (2 mmol) were added in 5 mL of oxygen saturated toluene in an equipped flask with an oxygen balloon. The solution was magnetically stirred for some hours and the mixture was filtered through a plug of silica, then diluted with toluene (2 mL). The progress of the reaction was monitored by gas chromatography. In a separate blank test, a 15-ml two-necked round-bottom flask was charged with the catalyst solution of copper(II) chloride or copper(II) acetate in a mixed medium of K₂CO₃ (2 mmol) in 5 mL of air or oxygen saturated toluene. Then the flask was equipped with an oxygen balloon. The progress of the reaction was monitored by gas chromatography.

RESULTS AND DISCUSSION

Synthesis and structural characterization of ligand HL^{DAP}

The ligand H₂L^{DAP} was synthesized *via* the condensation of 1,3-diaminopropane with one equivalent of 3,5-DTBQ. For more purifications, microcrystals of H₂L^{DAP} suitable for electrochemistry and catalytic studies were obtained by recrystallization from dichloromethane/n-hexane.
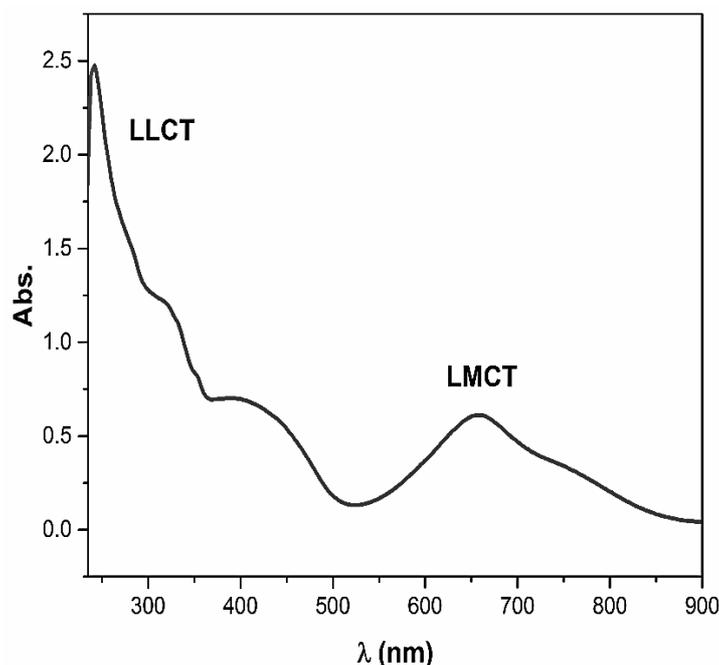

2 mmol (0.44 g)   1 mmol (0.08 ml)

Scheme 2 – Schematic reaction pathway for synthesis of H₂L^{DAP}.

Fig. 1 – UV/vis spectrum of $K_2[Cu(L^{DAP})Cl_2]$.

Synthesis and structural characterization of $K_2[Cu(L^{DAP})Cl_2]$ complex

Treating H_2L^{DAP} with $CuCl_2.6H_2O$ (0.238 g, 1 mmol) in the presence of 2 equivalents of Et_3N under aerobic conditions in acetonitrile at 298 K afforded a microcrystalline precipitate of $K_2[Cu(L^{DAP})Cl_2]$. Elemental analytical data of the copper complex correspond to the calculated values for a 1:1 copper/ligand ratio (The amount of copper: 9.1 %). In the IR spectra of the complex, the strong and sharp νO-H stretch of the ligand disappears, and the νC=N band is shifted to lower energy by 10–20 cm^{-1} as compared to the νC=N band of the free ligand. The absorption maxima observed in the near-UV regions is caused by $\pi\rightarrow\pi^*$ transitions involving the aminophenolate units (below 400 nm). The lowest energy bands (between 500 and 800 nm) are proposed to arise from charge-transfer transitions from the phenolate(π) to Cu(II)(dπ^*) (Fig. 1).

Electrochemistry studies

The electrochemical behavior of $K_2[Cu(L^{DAP})Cl_2]$ complex is studied by cyclic voltammetry in CH_2Cl_2 at low temperature (233 K).Two reversible redox peaks in cyclic voltammetry studies showed that the oxidation of this complex is ligand-centered and metal centered due to the oxidation of o-aminophenolate to the iminosemiquinone radicals and reversible oxidation of Cu^{II}/Cu^{I} ion couple. The stability of reversible electrochemical behavior in various scan rates confirms that the $K_2[Cu(L^{DAP})Cl_2]$ complex is completely stable in redox processes and it is a unique characteristic for application in catalytic reactions such as alcohol oxidation (Fig. 2). In voltammogram of $K_2[Cu(L^{DAP})Cl_2]$ one quasi reversible metal center peak in positive potential ($E_{1/2}$ = 0.51) and one quasi reversible ligand center peak in negative potential ($E_{1/2}$ = - 0.58) were observed (Figure 2).[25] Regarding oxidation potential of copper ion in the organic solvent, positive peak region can be related to redox of iminophenolate/iminosemiquinone species in reaction to the medium. On the other hand, a negative peak region can be related to redox of metal species.

Catalytic activity of $K_2[Cu(L^{DAP})Cl_2]$ complex in oxidation of alcohols

In continuation of our studies on the application of $K_2[Cu(L^{DAP})Cl_2]$, we were interested in using this complex for the oxidation of benzyl alcohols to corresponding aldehydes. With the optimized conditions (Scheme 3), we studied the efficiency of this complex for the oxidation of various alcohols in toluene using potassium carbonate as a base and oxygen as oxidant at 80 °C. The results are summarized in Table 1.
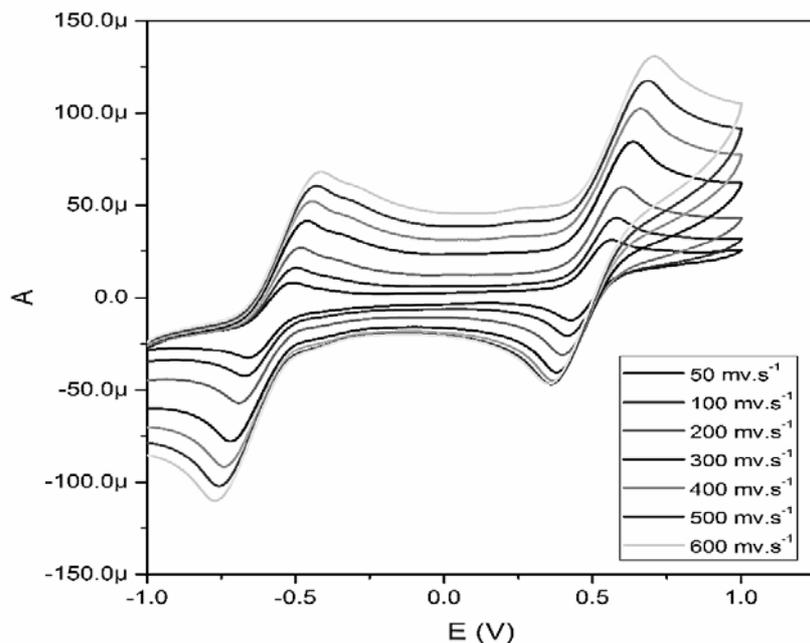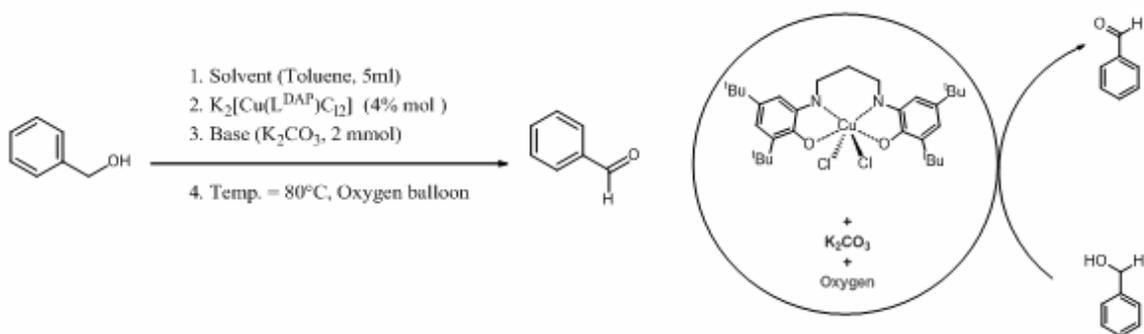
Fig. 2 – Cyclic voltammogram of $K_2[Cu(L^{DA}P)Cl_2]$ Conditions: 1 mM complex, 0.1 M NBu_4ClO_4, scan rate 50-600 mV/s, CH_2Cl_2, 233 K. Working electrode: Glassy carbon. The Ag quasi-reference electrode was calibrated using a ferrocene/ferrocenium redox couple.

Scheme 3 – Schematic representation of $K_2[Cu(L^{DAP})Cl_2]$ catalytic activity in the aerobic oxidation of alcohols.

Table 1

Alcohol oxidation results in toluene, catalysed by $K_2[Cu(L^{DAP})Cl_2]$ in the presence of K_2CO_3 as base and O_2 as oxidant at 80 °C

Entry	Substrate	Product	Time (h)	Yield (%)
1			6	91
2			8	87
3			8	80

CONCLUSIONS

In summary, we have prepared and characterized a novel non-innocent copper(II) complex with 1,3-diaminopropane based aminophenol ligand. Electrochemical oxidation of this complex showed that the redox behavior of HL^{DAP} in copper complex is quasi-reversible. In addition, highly efficient, and eco-friendly oxidation of alcohol to aldehyde was achieved with molecular oxygen as oxidant and $[Cu(L^{DAP})Cl_2]$-K_2CO_3 system as catalyst.

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