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RESEARCH ARTICLE

Binuclear copper (II) complexes containing pyN_4O moiety as a model for catechol oxidase; synthesis, characterization and catechol oxidase activity

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Abstract

A new series of copper (II) complexes, $[(Me\text{py}N_4O)Cu_2^{II}(\mu\text{–}SO_4)]_2SO_4$ (**1**), $[(Me\text{py}N_4O)Cu_2^{II}Br_2]Br$ (**2**), $[(Me\text{py}N_4O)Cu_2^{II}(NO_3)_2]NO_3$ (**3**), $[(Br\text{py}N_4O)Cu_2^{II}(\mu\text{–}SO_4)]_2SO_4$ (**4**), $[(Br\text{py}N_4O)Cu_2^{II}Br_2]Br$ (**5**), $[(Br\text{py}N_4O)Cu_2^{II}(NO_3)_2]NO_3$ (**6**) and $[(Br\text{py}N_4O)Cu_2^{II}Cl_2]Cl$ (**7**) were synthesized and completely characterized. Catalytic activity towards the oxidation of catechol and 4-*tert*-butylcatechol by copper complexes ***1-7*** has been investigated and correlated with the structure. The complexes bearing $Me\text{py}N_5OH$ moiety have less catechol oxidase activity in respect to complexes containing $Br\text{py}N_4OH$ moiety. The rate of oxidation of substrate depends strongly on the anionic ligands. For instance, the activity of complexes containing $Br\text{py}N_5OH$ moiety was found to be in the following order: $Br^- > NO_3^- > SO_4^{-2} > Cl^-$. For complexes containing $Me\text{py}N_5OH$ moiety, the catalytic activity follows the order of $NO_3^- > SO_4^{-2} > Br^-$ for oxidation of 4-*tert*-butylcatechol, whereas, the order of activity for oxidation of catechol is $Br^- > SO_4^{-2} > NO_3^-$. In a general, complexes ***5*** was found to be the most efficient catalysts due to the perfect match between the copper (II) centers and the incoming substrate (catecholate) to get bound effectively for subsequent redox reaction. The oxidation of 4-*tert-buty*lcatechol is easier than catechol because of the presence of the electron-donating tert-butyl group in the 4-*tert-buty*lcatechol.

INTRODUCTION

Binuclear metalloenzymes are prevalent in nature, performing a range of functions on various substrates [1]. Dimeric copper sites play an important role in the activation of biological oxygen [2–4]. The study of structural and functional aspects of copper metalloenzymes via model systems is a subject of intense research [5–10].

Catechol oxidases are type III dicopper proteins with two proximate copper ions coordinated primarily by histidine donors [11–13]. It catalyzes a two-electron transfer reaction during the oxidation of a wide range of o-diphenols, such as caffeic acid, to the corresponding quinones by molecular oxygen in a process known as a catecholase activity. Quinone compounds undergo an auto-polymerization leading to the formation of a brown polyphenolic pigment, i.e. melanin, a process thought to protect a damaged tissue against pathogens or insects [14].

In 1998, Krebs and co-authors have reported the crystal structures of catechol oxidase from Ipomoea batatas (sweet potato) which reveals a nitrogen-rich coordination environment, with three histidine donors to each copper [15]. In addition to three histidine residues, a bridging solvent molecule, most likely hydroxide anion was refined in a close proximity to the two metal centers, completing the coordination sphere of the copper ions to a trigonal pyramid. The metal–metal distance is 2.9 Å in the oxidized Cu^{II}–Cu^{II} met form. Upon reduction of the Cu^{II} ions to Cu^{I} oxidation state, the distance Cu^{I}–Cu^{I} increases to 4.4 Å, while the histidine residues move only slightly, and no significant change was observed for other residues of the protein [16, 17, 18].

Design and study of model complexes for catechol oxidase and other type III copper centers has been an area of much interest [6–10, 19-21]. For this reason some of the biomimetic models reported recently use nitrogen-containing binucleating ligands to produce unsymmetric dicopper complexes [6, 22-27]. Many of them have been employed to model catechol oxidase and structure–activity relationships have been reported. [28-32]

Hydroxo-bridged dicopper(II) complexes of five-coordinate acyclic diazadiamine NNNNO-ligands, was employed previously as a model for catechol oxidase [33] providing a nitrogen-rich coordination set similar to that of the enzyme (three nitrogen donors). The catecholase activity of several other dicopper complexes has been investigated, allowing correlation between activity and structural parameters [34-39].

The present study aimed at the synthesis, characterization and catecholase activity of dicopper complexes of NNNNO-bonded ligands with terminal, rather than bridging, ligands. To achieve this goal, spectroscopic techniques, such as IR, UV-Vis, conductance and magnetic measurement were employed in conjugation with quantum chemical calculations.

2. Results and discussions

2.1. Synthesis and Characterization

The copper (II) complexes, $[(Me\text{pyN}_4\text{O})\text{Cu}_2^{\text{II}}(\mu\text{–SO}_4)]_2\text{SO}_4$ (**1**), $[(Me\text{pyN}_4\text{O})\text{Cu}_2^{\text{II}}\text{Br}_2]\text{Br}$ (**2**), $[(Me\text{pyN}_4\text{O})\text{Cu}_2^{\text{II}}(\text{NO}_3)_2]\text{NO}_3$ (**3**), $[(Br\text{pyN}_4\text{O})\text{Cu}_2^{\text{II}}(\mu\text{–SO}_4)]_2\text{SO}_4$ (**4**), $[(Br\text{pyN}_4\text{O})\text{Cu}_2^{\text{II}}\text{Br}_2]\text{Br}$ (**5**), $[(Br\text{pyN}_4\text{O})\text{Cu}_2^{\text{II}}(\text{NO}_3)_2]\text{NO}_3$ (**6**) and $[(Br\text{pyN}_4\text{O})\text{Cu}_2^{\text{II}}\text{Cl}_2]\text{Cl}$ (**7**) were prepared by reacting 2,6–diformyl–4–methylphenol or 2,6–diformyl–4–bromophenol with 1,3–diaminopropane in the presence of the appropriate copper(II) salt in 1:2:2 ratio (see scheme 1 and experimental section for further details). The addition of diethyl ether to the reaction solution afforded colored crystals.

The addition of one mole of dialdehyde to two moles of the diamaine in the absence of copper ions viscous oiled product(s) was obtained. The IR (KBr) spectra of the product showed absorption at ca 1650 cm^{-1} characteristic of the –C=N– (imine) group, indicating that Schiff base condensation had occurred, but also a strong absorption at ca 1700 cm^{-1} characteristic of C=O, indicating the presence of residual keto-functions, presumably the terminal groups of open chain oligomers [19].

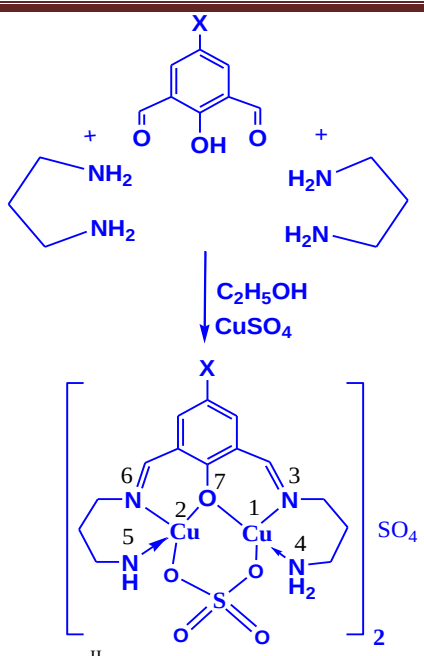
We attempted to demettalate the copper (II) complexes by addition of dil HCl in dichloromethane to obtain the NNNO ligands but to no avail, leading usually to regeneration of the dialdehyde and diamine again.

The elemental analysis, IR and UV-Vis spectroscopic techniques, conductance and magnetic measurements were used for structural characterization of the synthesized complexes. Evidence for the formation of the complexes comes from elemental analysis which is consistent with the condensation of dialdehyde, diamine and copper(II) salts in 1:2:2 molar ratio. IR (KBr) spectra of all complexes **1**-**7** proved to be invaluable to confirm the presence of the imine-linkage at ca. 1611-1657 cm^{-1}, but no absorption peak for carbonyl groups was observed, indicating that the products were free from the starting materials. Characteristic bands arise in the region 3200–3300 cm^{-1} are attributed to symmetric and asymmetric N–H stretching. Characteristic bands in the region 1565–1528 cm^{-1} assigned to the ν(C–O) vibration of phenol group. This assumes partial double–bond character as a consequence of delocalization of the double bonds in the chelate rings containing C=N linkage [40]. The vibration spectra of the complexes exhibit new peaks at 1470, 1450, 830 and 750 cm^{-1} attributed to the end–capping amine coordinated to the terminal metal ion [41].

Complex **3** exhibits two bands at 1240 and 1380 cm^{-1} attributed to the coordinated and ionic nitrate groups, respectively. Characteristic bands at 1216 and 1465 were observed for complex **6**, assigned for coordinated nitrate [42], whereas, the ionic nitrate was observed at 1383. Complex **1** exhibits two bands at 780 and 686 cm^{-1} attributed to the coordinated sulphate group [43]. Characteristic bands for complexes **4**-**7** appear in the region 620–616 cm^{-1} assigned to the ν(C–Br) vibration.

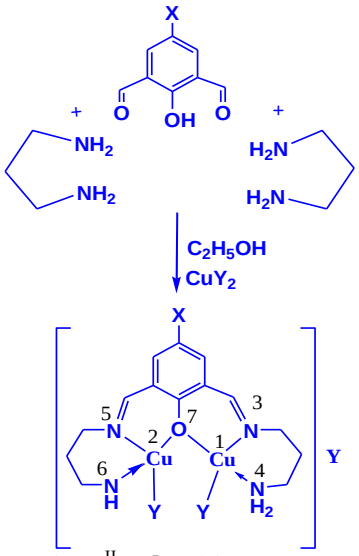
Electrical conductivity measurements in DMF showed that all complexes are 1:1 electrolytes, and this is in good agreement with the suggested structure.

The electronic spectra of the compounds were measured in DMF solution. In the visible region, all complexes exhibit a single weak absorption band between 570 and 600 nm, assigned for d-d transition. In the UV-vis region all complexes, except for **1** and **6**, exhibit an intense absorption between and 370 and 395 nm, assigned to C=N chromophores (π–π* transition). Complexes **1** and **6** display absorption maxima at 360 and 259 nm. The relatively weaker absorption appears to be due to ligand to metal (N→Cu) charge transfer which probably is swamped in complexes **2**–**5** and **7** by the intense π–π* transition of the C=N groups.



$[(MepyN_4O)Cu_2^{II}(\mu–SO_4)]_2SO_4$ (**1**), X = Me
$[(BrpyN_4O)Cu_2^{II}(\mu–SO_4)]_2SO_4$ (**4**), X = Br

Scheme 1. Syntheses and structures of dinuclear copper complexes **1** and **4**.



$[(MepyN_4O)Cu_2^{II}Br_2]Br$ (**2**), X = Me, Y = Br
$[(MepyN_4O)Cu_2^{II}(NO_3)_2]NO_3$ (**3**), X = Me, Y = NO_3
$[(BrpyN_4O)Cu_2^{II}Br_2]Br$ (**5**), X = Br Y = Br
$[(BrpyN_4O)Cu_2^{II}(NO_3)_2]NO_3$ (**6**), X = Br, Y = NO_3
$[(BrpyN_4O)Cu_2^{II}Cl_2]Cl$ (**7**), X = Br, Y = Cl

Scheme 2. Syntheses and structures of dinuclear copper complexes **2**, **3**, **5, 6 and 7**.

2.2. Catechol oxidase biomimetic of Copper (ll) Complexes.

4-tert-butylcatechol is the most widely used substrate among the different catechols that used in catechol oxidase model studies because of its low redox potential. Another advantage is the presence of bulky non-polar substituents that prevent further oxidation reactions, such as ring opening reactions and/or cyclization/tautomerization reactions [44, 45]. The aerobic oxidative transformation of 4-tert-butylcatechol and catechol to the corresponding light-absorbing 4-tert-butylquinone and quinone were followed spectrophometerically by monitoring the formation of 4-tert-butyl quinone and quinone, respectively [56-48]. The metal complex and a solution of substrate (catechol or 4-tert-butylcatechole) added together in the spectrophotometer cell at 25˚C. Formation of quinone and 4-tert-

butylquinone was monitored by the increase in absorbance at 390 nm as a function of time, Figure 1. Experimental studies showed that the catalytic activity depends strongly on many factors such as the nature of the ligand either organic or inorganic and the substrate. Study of all these factors has been done as shown in the following section:

2.2.1 Effect of ligand structure:

Controlling the geometry around a metallic center is of fundamental importance in many areas of chemistry. The choice of ligands which force metal ions into unusual geometries or which stabilize special oxidation states are of interest in designing catalytic systems or in bioinorganic chemistry[49]. The introduction of various electron-acceptor and/or bulky and steric substituents to benzene ring can be used for tuning the electron density on the ring [50]. The impact of different groups is visible on the oxidative catechol reaction rate. The oxidation reaction rates examined by complexes **1-7** are shown in the following Table **9** and Figures 2 and 3.

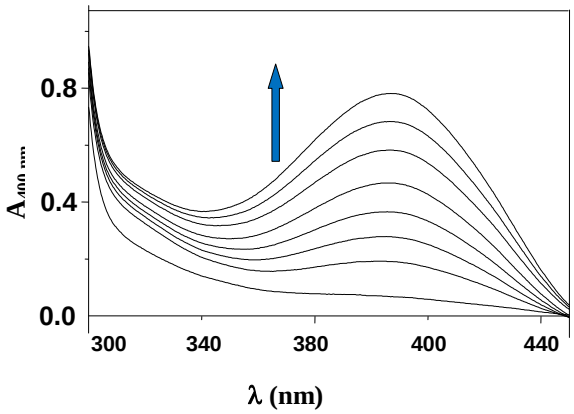


Figure 1: UV spectrum upon addition of 0.01 M of catechol to a solution of complex **1** in aerobic conditions; the spectra recorded each 30 min after catechol addition to complex. The arrow shows the increase in absorption vs. time.

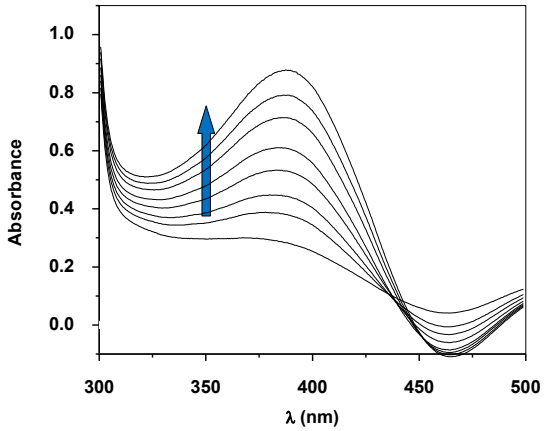


Figure 2: UV spectrum upon addition of 0.01 M of catechol to a solution of complex **5** in aerobic conditions; the spectra recorded each 30 min after catechol addition.

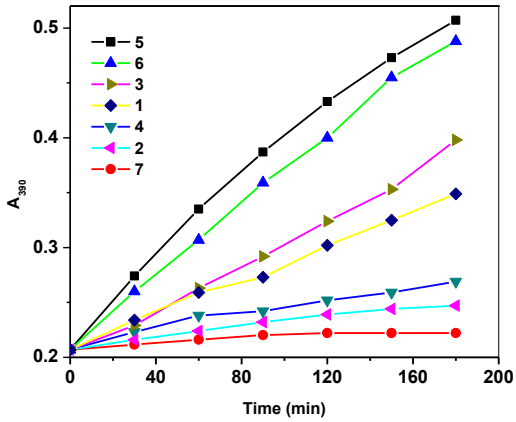


Figure 3 The change of absorbance of the test complexes together with TBC at 390 nm versus time.

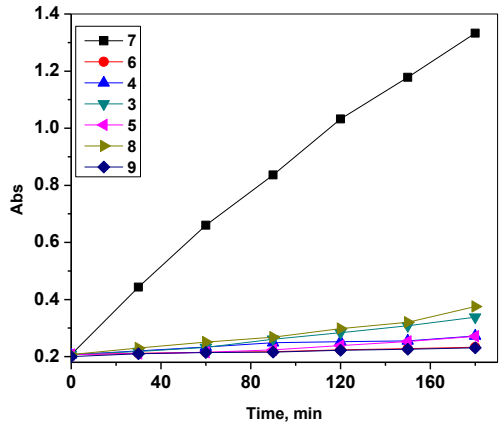


Figure 4. The change of absorbance of the test complexes together with catechol at 390 nm versus time.

Table 1. Comparison of catalytic parameters of selected catechol oxidase model systems and catechol oxidase from Ipomoea batatas.

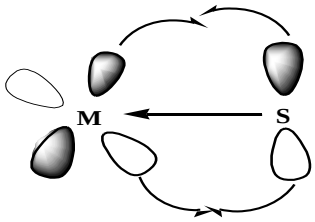
Complex	Activity (μmol mg^{-1} min^{-1}) Catechol	3,5-di-tert-butylcatechol
[(*Me*pyN$_4$O)Cu$_2^{II}$(μ–SO$_4$)]$_2$SO$_4$ (**1**)	0.360	0.47
[(*Me*pyN$_4$O)Cu$_2^{II}$Br$_2$]Br (**2**)	0.280	0.16
[(*Me*pyN$_4$O)Cu$_2^{II}$(NO$_3$)$_2$]NO$_3$ (**3**)	0.017	0.59
[(*Br*pyN$_4$O)Cu$_2^{II}$(μ–SO$_4$)]$_2$SO$_4$ (**4**)	0.010	0.30
[(*Br*pyN$_4$O)Cu$_2^{II}$Br$_2$]Br (**5**)	2.820	1.00
[(*Br*pyN$_4$O)Cu$_2^{II}$(NO$_3$)$_2$]NO$_3$ (**6**)	0.360	0.94
[(*Br*pyN$_4$O)Cu$_2^{II}$Cl$_2$]Cl (**7**)	0.008	0.01
Catechol oxidase from I. batatas [12]	2.293	-

In this study, a correlation between the catalytic activity for oxidation of catechol and 4-tert-butylcatechol using complexes containing two different ligands was carried out. Generally, the rate catalytic oxidation of both substrates by complexes (**2** and **3**) that contain toluene moiety is relatively lower than those containing bromobenzene moieties (**5-7**), except in the case of complexes containing sulphate anions (**1** and **4**). These difference in reactivity could be traced to two reasons; 1) the presence of methyl group at the benzene ring leads to the absence of the conjugation (poor in electron and stability) and consequently returns the complex weaker in the oxidation reaction [50]; 2) It may also be due to the easier reduction of the Cu (II) to the Cu (I) ions on increasing the electron

withdrawing nature of the p-bromo on the phenolic ring [51, 52]. These results are in line with recently published results with other systems [53].

2.2.2 Effect of the anionic ligand:

The rate of oxidation of catechol and 4-tert-butylcatechol is dependent on the anion. The activity for complexes containing *Br*pyN_4OH moiety was found to be in the following order: $Br^- > NO_3^- > SO_4^{-2} > Cl^-$. This is in a line with literature [54]. This is attributed to the relatively strong bonding with the cation and consequently slow cycle of chelating. Thus, the coordination of the substrate to the metallic center is relatively more difficult [54]. The catalytic activity of complexes bearing NO_3^- (**3** and **6**) is more than those containing SO_4^{-2} (**1** and **4**). This could interpret based on two reasons; i) the Cu-N bond is weaker than Cu-S bond, as result of the π–back bonding of metal lone pair to the sulpher empty d-orbital [55]; ii) steric effect of SO_4^{-2} anion hinders the coordination of the substrate with the metallic center [56].



For complexes containing *Me*pyN_4OH moiety, the catalytic activity follows the order of $NO_3^- > SO_4^{-2} > Br^-$ for oxidation of 4-tert-butylcatechol, whereas, the order of activity for oxidation of catechol is $Br^- > SO_4^{-2} > NO_3^-$ and this because of the methyl substituent which increase the electron density on the metal center.

2.2.3 Effect of substrate:

Generally, the rate of the oxidation of 4-tert-butylcatechol is more than that of the oxidation of catechol, except in the case of complex **5** as shown in Table 1. The results described here are in agreement with literature, [57] that the oxidation of 4-*tert*-butylcatechol is easier than catechol. Owing the presence of the electron-donating group (*tert*-butyl) in 4-*tert*-butylcatechol, the electron density at hydroxyl oxygen in the *para*-position increases facilitating the binding to the metallic centers. [57].

3- Conclusion

In a conclusion, the oxidation of catechol and 4-tert-butylcatechol by copper complexes **1-7,** showed these complexes have catalytic activity towards both substrates. The complexes showed a significant change in their characteristics by varying the nature of the p-substituent of the phenolic ring. Evidently, the complexes bearing *Me*pyN_4OH moiety have less catecholase activity in respect to complexes containing *Br*pyN_4OH moiety. The rate of oxidation of substrate depends strongly on the anionic ligands. For instance, the activity of complexes containing *Br*pyN_4OH moiety was found to be in the following order: $Br^- > NO_3^- > SO_4^{-2} > Cl^-$. For complexes containing *Me*pyN_4OH moiety, the catalytic activity follows the order of $NO_3^- > SO_4^{-2} > Br^-$ for oxidation of 4-tert-butylcatechol, whereas, the order of activity for oxidation of catechol is $Br^- > SO_4^{-2} > NO_3^-$. We could conclude that the catalytic activity of complexes bearing NO_3^- (**3** and **6**) is more than those containing SO_4^{-2} (**1** and **4**). In a general, complexes **5** was found to be the most efficient catalysts due to the perfect match between the copper (II) centers and the incoming substrate (catecholate) to get bound effectively for subsequent redox reaction [58]. The oxidation of 4-tert-butylcatechol is easier than catechol because of the presence of the electron-donating tert-butyl group in the 4-tert-butylcatechol.

4- Experimental Part

4.1. Materials and general methods:

Unless noted otherwise, all procedures were carried using Schlenk techniques. Spectra were recorded on the following instruments: IR (KBr) discs or CaF_2 cuvettes, solvent bands were compensated): FT-IR Bruker Vector 22 spectrometer, Germany in the range 400-4000 cm^{-1}. Around 1.0 mg of a substance in the form of fine powder was mixed and ground well with about 100 mg of a spectroscopically pure KBr powder (Merck). The mixture was pressed then in a special disc under vacuum at pressure of about 150 Kg/cm^{-1} using a hydraulic press. The disc produced was 1.2 cm in diameter and of about 0.7 mm thickness. Spectra were recorded at 25 °C; -Elemental analyses: Elementary III CHNS Analyzer, Germany. Thermogravimetric analysis was performed using Shimadzu Stand-Alone Thermal Analyzer Instruments (TGA 50H) Japan. About 5 mg of pure sample was subjected to dynamic TGA scans at a heating rate 10 ºC/min in the temperature range of ambient to 900 ºC under a dynamic atmosphere of dry nitrogen gas

(flow rate = 10 ml/min). The TGA curves were analyzed as percentage weight loss as a function of temperature. The dehydration and composition steps were identified using a derivative of the TGA (D-TGA) curves. All UV-visible absorptions of coordinated compounds in solution state were recorded by UV- 2040 spectrophotometer Shimadzue, Japan and quartz cuvette. Hexamethylentetraamine, p–bromophenol, p–metylphenol and p–chlorophenol were purchased from Merch Schuchardt company and copper nitrate, copper sulphate were purchased from Adrich and copper chloride, copper bromide were purchased from Cambrian chemical company.

4.2.Catecholase assays

Catecholase activity was measured against catechol (Cat) and 3,5-di-tert-butylcatechol (3,5-DTBC). Kinetic assays were conducted in DMF (saturated with 1 atm O_2) at 298 K and formation of product was monitored at 390 nm (e = 1,900 M^{-1} cm^{-1}) [19]. Under these conditions no formation of quinone was observed in the absence of the copper complexes.

4.3. Synthesis

4.3.1. (*Me*pyN$_4$O)Cu$_2^{II}$Br$_2$]Br (**2**)

To 1, 3–diaminopropane (0.267 g, 3.6 mmol) in ethanol (30 mL), was added 2, 6–diformyl–4–methylphenol (dfmp) (0.295 g, 1.8 mmol) and the mixture was stirred for 30 min. $CuBr_2$ (0.804 g, 3.6 mmol) was added and the mixture was heated under reflux in water bath for 12 h, it was filtered while hot and dried to give brown solid. Yield (35 %); IR(KBr, cm^{-1}): 3418 (b, O–H), 3029 (v, C–$H_{aromatic}$), 2870 (v, C–$H_{aliphatic}$), 1451 (v, phenyl), 1564 (v,C–O $_{phenolate}$), 1634 (v, C=N), 3219 (w, N–H), 1273(v, C–N); Elemental analysis: calcd. for $C_{15}H_{23}Br_3Cu_2N_4O \cdot H_2O$ (660.91): C 27.29, H 3.82, N 8.49; Found C 26.82, H 3.96, N 8.67.

4.3.2. [(*Me*pyN$_4$O)Cu$_2^{II}$(NO$_3$)$_2$]NO$_3$ (**3**)

To 1, 3–diaminopropane (0.267 g, 3.6 mmol) in ethanol (30 mL), was added 2.6–diformyl–4–methylphenol (dfmp) (0.295 g, 1.8 mmol) and the mixture was stirred for 30 min. $Cu(NO_3)_2 \cdot 3.5H_2O$ (0.902 g, 3.6 mmol) was added and the mixture was heated under reflux in water bath for 16 h, it was filtered while hot and dried to give green solid. Yield (30 %); IR(KBr, cm^{-1}): 3421(b, O–H), 3011(v, C–$H_{aromatic}$), 3209 (v, N–H), 2870 (v, C–$H_{aliphatic}$), 1564 (v, C–O $_{phenolate}$), 1637 (v, C=N), 1239(v, C–N), 1460(v ,phenyl); Elemental analysis: calcd. For $C_{15}H_{23}Cu_2N_7O_{10} \cdot 2H_2O$ (624.51) C 28.85, H 4.36, N 15.70; Found, C 29.08, H 4.20, N 14.52.

4.3.3. [(*Me*pyN$_4$O)Cu$_2^{II}$(μ–SO$_4$)]$_2$SO$_4$ (**1**)

To 1, 3–diaminopropane (0.267 g, 3.6 mmol) in ethanol (30 mL), was added 2.6–diformyl–4–methylphenol (dpmp) (0.295 g, 1.8 mmol) and the mixture was stirred for 30 min. $CuSO_4 \cdot 5H_2O$ (0.902 g, 3.6 mmol) was added and the mixture was heated under reflux in water bath for 16 h, it was filtered while hot and dried to give green solid. Yield (46.2%); IR(KBr, cm^{-1}): 3422 (b, O–H),3059(v,C–$H_{aromatic}$), 2878(v, C–$H_{aliphatic}$), 3209(v, N–H), 1458(v, phenyl), 1564(v, C–$O_{phenolate}$), 1611(v,C=N), 1278(v, C–N); Elemental analysis calcd. For $C_{30}H_{46}N_8Cu_4O_{14}S_3 \cdot 3H_2O$ (1147.16) C 31.41, H 4.57, N 9.77; Found, C 30.55, H 4.47, N 9.05.

4.3.4. Synthesis of 2, 6–diformyl–4–Bromophenol (*dfbp*)(**2**):

In a 3–necked round flask p–bromophenol (17.19 g, 0.1 mol), hexamethylenetetramine (urotropine) (28.2 g, 0.2 mol) and paraformaldhyde (30 g, 1.0 mol) were dissolved in 50 ml of acetic acid. This suspension was stirred gently until a light brown viscous solution formed which was then heated at 80° C for 2h. The mixture was allowed to cool to room temperature and sulphuric acid (10 ml) (Caution exothermic reaction) was then carefully added. The solution was heated again for 30 min before 400 ml distilled water was slowly added leading to the formation of a light yellow suspension. It was stored at 0° C over night and a pale yellow product was isolated by filtration, washed with a small amount of cold methanol, recrystalization from toluene. Yield (60%); M. p. 160° C; IR(KBr, cm^{-1}): 3423 (b, O–H), 3047 (v, C–$H_{aromatic}$), 2856 (v, C–$H_{aliphatic}$), 1600, 1442 (v, phenyl), 1670(v, C=O), 1559 (v, C–O $_{phenolate}$).

4.3.5. [(*Br*pyN$_4$O)Cu$_2^{II}$Br$_2$]Br (**5**)

To 1, 3–diaminopropane (0.267 g, 3.6 mmol) in ethanol (30 mL), was added 2.6–diformyl–4–bromolphenol (dfbp) (0.412 g, 1.8 mmol) and the mixture was stirred for 30 min. $CuBr_2$ (0.804 g, 3.6 mmol) was added and the mixture was heated under reflux in water bath for 4h, it was filtered while hot and dried to give green solid. Yield: (20%); M. p.: 210° C; IR(KBr, cm^{-1}): 3420(b, O–H), 3128(v, C–$H_{aromatic}$), 2876(v, C–$H_{aliphatic}$), 3265(v, N–H),1594,1460(v, phenyl), 1634 (v, C=N), 1287(v, C–N), 650(v, C–Br), 1524 (v, C–O $_{phenolate}$). Elemental analysis: calcd. For $C_{14}H_{20}Br_4Cu_2N_4O \cdot 2H_2O \cdot$ (743.07) C 22.63, H 3.26, N 7.54; Found C 23.19, H 3.76, N 8.01.

4.3.6. [(*Br*pyN$_4$O)Cu$_2^{II}$(NO$_3$)$_2$]NO$_3$ (**6**):

To 1, 3–diaminopropane (0.266 g, 3.6 mmol) in ethanol (30 mL), was added 2.6–diformyl–4–bromophenol (dfbp) (0.412 g, 1.8 mmol) and the mixture was stirred for 30 min. $Cu(NO_3)_2 \cdot 3.5H_2O$ (0.902 g, 3.6 mmol), green precipitate was formed on cold, and the mixture was heated under reflux in water bath for 4h, it was filtered while hot and dried to give green solid. Yield: (35%); M. p.: 190° C; IR(KBr, cm^{-1}): 3422(b, O□ H), 3009(v, C–$H_{aromatic}$), 2892 (v, C–$H_{aliphatic}$), 3209(v, N–H),1597,1442(v, phenyl), 1634 (v, C=N), 1186(v, C–N), 678(v, C–Br); Elemental analysis calcd. For $C_{14}H_{20}BrCu_2N_7O_{10} \cdot 2H_2O$ (689.38): C 24.39, H 3.51, N 14.22; Found C 23.14, H 3.42, N 14.54.

4.3.7. [(*Br*pyN_4O)Cu_2^{II}(μ–SO_4)]$_2SO_4$ (**4**):

To 1, 3–diaminopropane (0.532 g, 6.8 mmol) in ethanol (30 mL), was added 2.6–diformyl–4–bromolphenol (dfbp) (0.824 g, 3.6 mmol) and the mixture was stirred for 30 min. $CuSO_4 \cdot 5H_2O$ (1.804 g, 6.8 mmol) was added and the mixture was heated under reflux in water bath for 4h, it was filtered while hot and dried to give green solid. Yield (50%); M. p. over 300° C; IR(KBr, cm^{-1}) : 3417(b, O–H), 3009(v, C–$H_{aromatic}$), 2893 (v, C–$H_{aliphatic}$), 3208(v, N–H),1598,1464(v, phenyl), 1631 (v, C=N), 1118(v, C–N), 617(v, C–Br)), 1563 (v, C–O $_{phenolate}$); Elemental analysis calcd. For $C_{14}H_{21}BrSCu_2N_4O_2 \cdot H_2O$ (598.42): C 28.10, H 3.87, N 9.36; Found C 28.14, H 3.42, N 8.96.

4.3.8. [(*Br*pyN_4O)$Cu_2^{II}Cl_2$]Cl (**7**):

To 1, 3–diaminopropane (0.266 g, 3.6 mmol) in ethanol (30 mL), was added 2.6–diformyl–4–bromophenol (dfbp) (0.412 g, 1.8 mmol) and the mixture was stirred for 30 min. $CuCl_2$ (0.484 g, 3.6 mmol), green precipitate was formed on cold, and the mixture was heated under reflux in water bath for 6h, it was filtered while hot and dried to give green solid. Yield (20%); IR (KBr, cm^{-1}): 3425(b, O–H), 3048(v, C–$H_{aromatic}$), 2962 (v, C–$H_{aliphatic}$), 3259(v, N–H), 1597, 1442 (v, phenyl), 1657 (v, C=N), 1097(v, C–N), 620(v, C–Br), 1564 (v, C–O $_{phenolate}$); Elemental analysis calcd. For $C_{14}H_{20}BrCl_3Cu_2N_4O \cdot H_2O$; C 26.79, H 4.17, N 8.93; found C 28.19, H 4.02, N 9.26.

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