Synthesis and characterization of μ-phenoxo-bridged binuclear copper(II) complexes derived from binucleating ligands

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The new pentadentate binucleating symmetrical ligand 2,6-bis [N-(3,5-dichloro-2-hydroxybenzyl)-N-cyclohexylamino-methyl]-4-methylphenol (H₃L¹) has been prepared and its binuclear copper(II) complexes of the general formula [Cu₂L(X)], where X = OH (perchlorato counter ion complexes), OAc, NO₃ have been prepared. Their spectral properties and catecholase activities were studied. New unsymmetrical ligands and their complexes have also been synthesized. The phenolate oxygen atom of the binucleating ligands behaves as a bridging group. Conductivity studies showed that all the complexes are neutral. ESR spectra of the complexes show a broad band centred at 3500 G with no hyperfine splittings. The observed room temperature magnetic studies were found to be less than spin only value for d⁹ system. The rate constants of the complexes for the oxidation of catechol to o-quinone were in the range of 0.72×10⁻³ to 15.0×10⁻³ min⁻¹.

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The study of binuclear copper(II) complexes is a topic of considerable current interest¹ because of their use as models for a number of important biological systems containing a coupled binuclear copper active site². The development of highly pre-organized macrocyclic and acrylic ligands has enhanced the success in molecular recognition promoting selective bonding, transformation and transfer of large variety of substrates³. Although, several metalloproteins undertake various functions, they do have similar chemical properties at the bicopper active site, such as antiferromagnetism, EPR inactivity and the ability to transfer two or more electrons reversibly and simultaneously at positive potential⁴. Their large size and complexity make it difficult to have better understanding on the exact structure and functions of these proteins. As an approach towards this goal, several researchers have attributed wide varieties of simple binuclear copper complexes as models for these metalloproteins and studied their properties. These studies offered more information about the mechanism of exchange interaction between the paramagnetic metal centers, which is useful in finding appropriate building units for the construction of new magnetic materials⁵ and in the development of new redox catalysis for reaction other than biologically important ones.

There is a growing interest in binuclear transition metal complexes derived from binucleating ligands⁶,⁷. The impetus for the study of these complexes derives from three areas of interest. First, it is of interest to see whether the coupled (i.e. interacting) metal ions in such complexes exhibit chemical relaxivities that are different from mononuclear complexes. Several metalloenzymes, such as cytochrome oxidase and nitrogenase have coupled metal centers and catalyze important reactions under mild conditions. Second, it is important to ascertain whether complexes of binucleating ligands have electronic structural features that reflect the interaction between the metal ions. Third, metal complexes of binucleating ligands can provide interesting cases for the study of magnetic exchange interactions⁸,⁹. The catecholase activity of copper co-ordination compounds with different structural parameters has been investigated to some extent¹⁰. Nishida and co-workers have found that square-planar mononuclear copper(II) complexes exhibit little catalytic activity while non-planar mononuclear copper(II) complexes show a high catalytic activity.

The aim of this work is the synthesis and characterization of binuclear copper(II) complexes as structural and functional models for catechol oxidase. For obtaining a short metal-metal distance, which has been determined for catechol oxidase by EXFAS, binucleating ligands are used with a bridging alcoholase or phenolate oxygen atom. To obtain

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functional models it is necessary to have free co-
coordination sites on the metal atom. Therefore, ligands
with a low number of donor atoms seem to be of great
support. Furthermore, the behaviour of the copper
complexes formed were studied towards catecholase
activity by UV-Vis spectroscopy. Based on this,
special types of binucleating ligands and their
complexes have been synthesized and their spectral
and catalytic studies have been reported here.

Experimental Procedure
All the chemicals and reagents used were obtained
from commercial sources and used without further
purification. Catechol was used after recrystallization.
All the samples were thoroughly dried prior to
elemental analysis.

IR studies were recorded as KBr pellets on
Shimadzu FT-IR spectrometer. 1H NMR spectra of
the ligands were recorded in CDCl3 using varian XL
300 Fourier Transfer NMR spectrometer. The
electronic spectra of all the complexes were recorded
on Hitachi 320 double beam spectrophotometer.
Acetonitrile and DMF were used as solvent for
different complexes. Conductivity measurements
were done using freshly prepared solution in DMF.
Room temperature solid state magnetic susceptibility
data were obtained from Guoy balance using
Hg[Co(SCN)4] as the calibrant. Diamagnetic
corrections were obtained using pascal’s constants11.

Kinetic studies were performed using Hitachi 320
double beam spectrophotometer. The catalytic
oxidation of catechol to \( o \)-quinone by the complexes
was studied in a 10−3 M methanol solution. The
reaction was followed spectrophotometrically by
choosing the strongest absorbance at 400 nm and
monitoring the increase in the absorbance at this
wavelength as a function of time. A plot of \( \log(\frac{A}{A_0-A}) \)
versus time was drawn for each of the
complexes and the rate constant for the catalytic
oxidation was calculated.

Synthesis of precursor compound and ligand

2-Formyl-6-[methyl aminomethyl-2,4-dichloro]-4-methylphenol
(PCI)
To 2-methylenedi-4,6-dichlorophenol (1.101 g, 5
mmol) in tetrahydrofuran (30 cm³), 3-chloromethyl-5-
methyl salicylaldehyde (1 g, 5 mmol) was added and
stirred well, followed by the addition of triethylamine
(0.8 cm³, 5 mmol). After stirring for one hour, the
whole reaction mixture was refluxed for 3 h and then
cooled. To this, water was added and the compound
was extracted from chloroform and recrystallized
from tetrahydrofuran (m.p. 130°C, yield 2 g, 50%).

1H NMR (CDCl3): \( \delta \approx 2.2-2.3 \) (two like peaks, Ar-
CH and N-CH3), \( \delta \approx 3.6 \) (benzyl group protons), \( \delta \approx 6.8 \)
(Ar-H), \( \delta \approx 9.4 \) (aldehyde protons).

2,6-Bis[N-3,5-dichloro-2-hydroxybenzyl]-N-cyclohexylamino-
methyl]-4-methyl phenol (H₂L₁)
2 - Cyclohexylenaminomethyl - 4, 6-dichlorophenol
(13.6 g, 50 mmol) was added to paraformaldehyde
(1.8 g, 60 mmol) in 50 cm³ of glacial acetic acid and
stirred well at room temperature for 24 h. Then 4-
methylphenol (2.6 cm³, 25 mmol) was added and
stirred for 72 h. The reaction mixture was neutralized
with solid Na₂CO₃ and the residue was extracted with
CH₂Cl₂ (3×75 cm³). To this extract 75 cm³ of distilled
methanol was added and the white solid separated
was filtered and removed. The filtrate was completely
evaporated and the residue was dissolved in n-butanol
(75 cm³). The resulting solution was kept at room
temperature for several days. Colourless crystalline
solid separated was filtered and recrystallized from
chloroform – methanol (1:1) mixture (m.p. 120°C,
yield 5.2 g, 30%).

1H NMR (CDCl3): \( \delta \approx 2.1 \) (cyclohexyl -CH₂), \( \delta \approx 2.3 \)
(Ar-CH₃), \( \delta \approx 2.5 \) (N-CH), \( \delta \approx 3.6-3.7 \) (benzyl group
protons), \( \delta \approx 6.8 \) (Ar-H).

Synthesis of complexes

\[ Cu₂L₁(OH) \cdot H₂O \]
To the ligand H₂L₁ (0.456 g, 0.06 mmol) in
methanol (30 cm³), copper perchlorate hexahydrate
(0.5 g, 1.3 mmol) in methanol (25 cm³) was added
and refluxed on water bath for 4-6 h. Solvent was
evaporated at room temperature. Green solids
separated were filtered, washed with diethyl ether,
dried and collected.

\[ Cu₂L₁(X) \cdot H₂O, \text{where } X = OAc, NO₂ \]
The above procedure was followed using the
corresponding copper(II) salts instead of copper(II)
perchlorate hexahydrate. Green solids separated were
dried and collected.

\[ Cu₂L₂(OH) \cdot H₂O \]
Sodium hydroxide (0.31g, 7.7 mmol) was added to
PC1 (0.69 g, 2.5 mmol) in chloroform (30 cm³). To this
2-aminophenol (0.28 g, 2.5 mmol) in methanol
(25 cm³) was added, followed by the addition of copper(II)
perchlorate hexahydrate (1.02 g, 5.0 mmol)
in methanol (30 cm³) \textit{in situ} and refluxed for 5-6 h.
The brown coloured complex obtained was filtered, dried and collected.

**Scheme 1**—Synthesis of $H_3L_1$ and its complexes

**Scheme 2**—Synthesis of $H_3L_2$ and its complexes

**Scheme 3**—Synthesis of $H_3L_3$ and its complexes

The brown coloured complex obtained was filtered, dried and collected.

$[Cu_2L_1'(X)].H_2O$, where $X = OAc$, NO$_3$

The above procedure was followed using the corresponding copper(II) salts instead of copper(II) perchlorate hexahydrate. The complex $[Cu_2L_1'(OAc)].H_2O$ was brown in colour while the complex $[Cu_2L_1'(NO_3)].H_2O$ was green in colour.

$[Cu_2L_3'(OH)].H_2O$

PC1 (0.227 g, 0.08 mmol) was dissolved in chloroform (30 cm$^3$) and to this was added sodium hydroxide (0.1 g, 2.4 mmol). To this glycine (0.06 g, 0.08 mmol) in methanol (25 cm$^3$) was added, followed by the addition of copper(II) perchlorate hexahydrate (0.60 g, 1.6 mmol) in methanol (30 cm$^3$) in situ and refluxed for 5-6 h. The solid obtained was filtered, dried and collected.

$[Cu_2L_3'(X)].H_2O$, where $X = OAc$, NO$_3$

The above procedure was followed using the corresponding copper(II) salts instead of copper(II) perchlorate hexahydrate.

**Results and Discussion**

Some of the complexes synthesized were characterized by elemental analysis and the results are in good agreement with theoretical values. The elemental analysis data are given in Table 1.

**Molar conductivity**

Molar conductivity of the freshly prepared solution of the complexes in DMF shows the conductance value in the range of $10^{-16}$ $\Omega^{-1}$cm$^2$/M$^{-1}$, which indicates that the complexes are neutral$^{12}$. 

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Observed (%)</th>
<th>Calculated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C$</td>
<td>$H$</td>
<td>$N$</td>
</tr>
<tr>
<td>$[Cu_2L_1'(OAc)].H_2O$</td>
<td>50.64</td>
<td>5.06</td>
</tr>
<tr>
<td>$[Cu_2L_1'(NO_3)].H_2O$</td>
<td>47.98</td>
<td>4.80</td>
</tr>
<tr>
<td>$[Cu_2L_2'(OAc)].H_2O$</td>
<td>46.84</td>
<td>3.46</td>
</tr>
<tr>
<td>$[Cu_2L_2'(NO_3)].H_2O$</td>
<td>43.12</td>
<td>3.02</td>
</tr>
<tr>
<td>$[Cu_2L_3'(OAc)].H_2O$</td>
<td>41.72</td>
<td>3.44</td>
</tr>
<tr>
<td>$[Cu_2L_3'(NO_3)].H_2O$</td>
<td>37.48</td>
<td>2.86</td>
</tr>
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</table>
IR spectra
The IR spectra of all the complexes show broad bands in the range of 3415-3580 cm\(^{-1}\) due to the presence of co-ordinated or lattice water molecule. The absence of characteristic peaks due to perchlorate groups in the corresponding complexes indicates that the complexes are only hydroxo bridged and not perchlorato bridged, as there are no more perchlorate ions existing in the complexes. The band due to nitrate groups in the range of 1377-1382 cm\(^{-1}\) and agrees with the coordination of these groups toward the central metal ions. The band due to acetate group is in the range of 1540-1560 cm\(^{-1}\) in acetato bridged complexes. IR spectral data of the complexes are given in Table 2.

Electronic spectra
All the complexes exhibited a broad d-d band in the range of 612-660 nm characteristics of five coordinated square pyramidal structure. All the complexes show almost three intense bands in the UV range due to LMCT transition. Among all these, acetato bridged complexes show d-d band at longer wavelength as compared to other complexes. This may be due to the distortion of geometry upon coordination of acetate group to copper ions and this deviation from planarity provides the release of rigidity. Electronic spectral data of the complexes are given in Table 3 and spectra of some complexes are shown in Fig. 1.

ESR spectra
The solid ESR spectra of the complexes at 298 K were obtained in the X-band and the g values were calculated using the relationship \(\hbar v = g\beta H\). The ESR spectra of all the complexes show a broad signal with no hyperfine splittings around 3500 G with g value of 2.1. The broad ESR spectra clearly reveal that there is strong antiferromagnetic interaction between two metal ions in the complexes. This antiferromagnetic coupling occurs due to the quenching of the spin of the electrons of one metal ion by the adjacent metal ion. The ESR spectra of the complex \([\text{Cu}_2L^3\text{(OAc)}]_2\text{H}_2\text{O}\) is shown in Fig. 2.

Magnetic studies
The magnetic susceptibilities measured at room temperature (298 K) are substantially lower than the spin only value of 1.73 B.M., which may be due to the presence of antiferromagnetic coupling. Room temperature susceptibilities gave \(\mu_{\text{eff}}\) values in the range of 1.55 to 1.62 B.M. The reason for such an

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>([\text{Cu}_2L^1\text{(OH)}]_2\text{H}_2\text{O})</td>
<td>3500, 1560, 500</td>
</tr>
<tr>
<td>([\text{Cu}_2L^1\text{(OAc)}]_2\text{H}_2\text{O})</td>
<td>3450, 1482, 1230</td>
</tr>
<tr>
<td>([\text{Cu}_2L^1\text{(NO}_3\text{)}]_2\text{H}_2\text{O})</td>
<td>3500, 1482, 1224</td>
</tr>
<tr>
<td>([\text{Cu}_2L^2\text{(OH)}]_2\text{H}_2\text{O})</td>
<td>3500, 1556, 542</td>
</tr>
<tr>
<td>([\text{Cu}_2L^2\text{(OAc)}]_2\text{H}_2\text{O})</td>
<td>3450, 1573, 499</td>
</tr>
<tr>
<td>([\text{Cu}_2L^2\text{(NO}_3\text{)}]_2\text{H}_2\text{O})</td>
<td>3430, 1482, 1226</td>
</tr>
</tbody>
</table>

Table 3—Electronic spectral data of the binuclear copper(II) complexes

<table>
<thead>
<tr>
<th>Complexes</th>
<th>(\lambda_{\text{max}}/\text{nm (}\varepsilon/M\text{-1 cm}^{-1}\text{dm}^3))</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>d-d</td>
</tr>
<tr>
<td>([\text{Cu}_2L^1\text{(OH)}]_2\text{H}_2\text{O})</td>
<td>630 (178) 408 (10200), 350 (12900), 300 (103900)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^1\text{(OAc)}]_2\text{H}_2\text{O})</td>
<td>660 (118) 480 (7600), 347 (12500), 294 (95600)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^1\text{(NO}_3\text{)}]_2\text{H}_2\text{O})</td>
<td>620 (156) 360 (9900), 286 (11300), 260 (15200)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^2\text{(OH)}]_2\text{H}_2\text{O})</td>
<td>620 (156) 420 (5800), 295 (14800), 230 (11300)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^2\text{(OAc)}]_2\text{H}_2\text{O})</td>
<td>660 (118) 480 (7600), 390 (14200), 294 (95600)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^2\text{(NO}_3\text{)}]_2\text{H}_2\text{O})</td>
<td>620 (150) 340 (8500), 286 (11300), 260 (15200)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^3\text{(OH)}]_2\text{H}_2\text{O})</td>
<td>620 (156) 408 (10200), 295 (11300), 230 (14800)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^3\text{(OAc)}]_2\text{H}_2\text{O})</td>
<td>600 (129) 390 (14200), 343 (18200), 295 (77600)</td>
</tr>
<tr>
<td>([\text{Cu}_2L^3\text{(NO}_3\text{)}]_2\text{H}_2\text{O})</td>
<td>612 (560) 340 (8500), 286 (11300), 260 (15200)</td>
</tr>
</tbody>
</table>
observation is due to the quenching of unpaired spin of the metal ion by the unpaired spin of the adjacent Cu(II) ion, coupled by super exchange interaction. The magnetic moments are listed in Table 4.

Kinetic studies of oxidation of catechol (catecholase activity)

All the synthesized complexes were subjected to the test for catecholase activity. In all cases oxidation of pyrocatechol to o-quinone by binuclear copper(II) complexes was studied. The product o-quinone is considerably stable and has a strong absorbance at 400 nm. Therefore, activities and reaction rates can be determined using electronic spectroscopy by following the appearance of the absorbance maximum of the quinone. The reactivity studies were performed in methanol solution because of the good solubility of the complexes as well as of the substrate and of its product. Prior to a detailed kinetic study, it is necessary to get an estimation of ability of the complexes to oxidize catechol. For this purpose, 10−3 mol dm−3 solutions of complexes in methanol were treated with 50 equivalents of pyrocatechol in the presence of air.

The course of reaction was followed by UV-Vis spectroscopy, at regular interval, over the first 5 to 30 min. The first apparent result was that the reactivities of the complexes differ significantly from each other. The absorbance at 400 nm was measured as a function of time over the first 5 min. The slope was determined by the method of initial rates by monitoring the growth of 400 nm band of the product o-quinone. A linear relationship for initial rate and the complex concentration obtained for all the complexes, shows a first order dependence on the complex concentration for the systems.

A plot of log (A0/Ax−At) versus time for catecholase activity of the complexes are shown in Fig. 3 and the rate constant values are also reported in Table 4. In all these cases, acetato bridged complexes have higher activities than the hydroxo or nitrate bridged complexes. This may be attributed to the acetato ligand to be more susceptible for catechol substitution than the nitrate or hydroxo (perchlorato counter ion complexes) ligands. This flexibility was caused by the exogenous acetato bridge forming six-membered ring than four membered ring system formed by other systems, which was also promised by electronic spectroscopy. In the presence of alternative bridging co-ordination partners with a larger bond distance, the complex will adopt a relaxed conformation. Therefore, it may give up the acetato bridged structural moiety in favour of a bridging catechol co-ordination. In the case of other complexes catechol co-ordination may be assumed to be less favourable due to the stability of the complexes. Since, co-ordination of catechol is necessary condition for the electron transfer to the copper center, acetato bridged complexes show higher catalytic activity in catalysis than the other complexes. The higher catalytic activity of non-planar complexes was highly supported by several previous studies. It is also observed that the rate constant of the catecholase activity of the binuclear Cu(II) complexes is higher than the mononuclear Cu(II) complexes18-23.

Conclusion

Several binuclear copper(II) complexes have been synthesized. The efforts to obtain the crystals of these complexes by various methods such as mixture of solvents, slow evaporation and diffusion method, were unsuccessful. Conductivity studies confirm that all the complexes are neutral. Spectral studies were carried out for these complexes and from the electronic spectra of the complexes it was observed.

### Table 4—Rate constant values of catecholase activity and magnetic moment data

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Rate constant, Min−1</th>
<th>μ_eff (B.M.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Cu2L1(OH)2]H2O</td>
<td>9.09×10−3</td>
<td>1.62</td>
</tr>
<tr>
<td>[Cu2L1(OAc)2]H2O</td>
<td>15.0×10−2</td>
<td>1.55</td>
</tr>
<tr>
<td>[Cu2L1(NO2)2]H2O</td>
<td>2.60×10−3</td>
<td>1.58</td>
</tr>
<tr>
<td>[Cu2L2(OH)2]H2O</td>
<td>1.25×10−3</td>
<td>1.60</td>
</tr>
<tr>
<td>[Cu2L2(OAc)2]H2O</td>
<td>3.30×10−3</td>
<td>1.56</td>
</tr>
<tr>
<td>[Cu2L2(NO2)2]H2O</td>
<td>0.90×10−3</td>
<td>1.57</td>
</tr>
<tr>
<td>[Cu2L3(OH)2]H2O</td>
<td>6.00×10−3</td>
<td>1.61</td>
</tr>
<tr>
<td>[Cu2L3(OAc)2]H2O</td>
<td>6.20×10−2</td>
<td>1.56</td>
</tr>
<tr>
<td>[Cu2L3(NO2)2]H2O</td>
<td>0.72×10−3</td>
<td>1.59</td>
</tr>
</tbody>
</table>
that all the complexes have intense \(d-d\) band in the range of 612-660 nm and the acetato bridged complexes have distortion of the geometry and are shifted to higher wavelength. The ESR spectra of all the complexes have broad signal without hyperfine splittings due to spin-spin coupling. Antiferromagnetic coupling between the two copper centres is confirmed by the observed spin only magnetic moment data of the complexes in the range 1.55 to 1.62 B.M. The catecholase activities of these complexes were also performed and it was observed that the acetato bridged complexes have higher activity when compared to other complexes due to the deviation from planarity of the geometry, which makes them easy, to oxidize the pyrocatechol to \(o\)-quinone.

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**References**