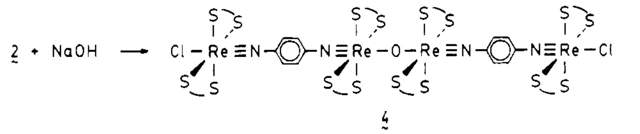
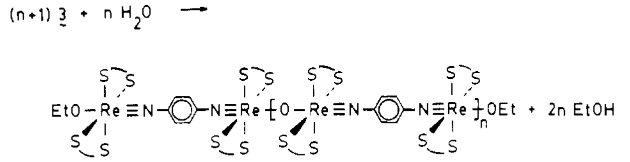


(4)

symmetric ν(Re–O–Re) stretching mode. Similarly, when a CH_2Cl_2 solution of **3** is treated with H_2O, the original yellow color is discharged in favor of deep purple and a black precipitate is formed. This black precipitate is again insoluble in common organic solvents and displays an IR spectrum that retains all of the characteristic dithiocarbamate absorptions of **3** but that also shows a strong broad band at 694 cm^{-1}, assignable as ν(Re–O–Re). Repeating the above experiment with H_2O enriched in both ^{17}O and ^{18}O affords a product displaying additional IR bands at 679 and 660 cm^{-1}; calculated values for ν(Re–^{17}O–Re) and ν(Re–^{18}O–Re) modes are 675 and 658 cm^{-1}, respectively. The hydrolytic coupling reaction of **3** has also been monitored by ^{1}H NMR spectroscopy. When an excess of H_2O is added to a $CDCl_3$ solution of **3**, the peaks due to the rhenium complex disappear as the precipitate forms, while signals due to free ethanol increase in intensity. No intermediates could be observed, and there was no evidence for other decomposition products being formed. Thus, we formulate the coupling reaction as shown in eq 5. Over a 2-h period at 298 K, the amount of ethanol formed corresponded to approximately 80% of the ethoxide ligands originally present in the sample; this result implies an average value of 4 for n in eq 5. We have attempted to prepare oligomers of greater solubility by employing a dicyclohexyldithiocarbamate analogue of **3** in the coupling reaction, but the resulting oxo-bridged material (ν(Re–O–Re) = 692 cm^{-1}) was again insoluble.



(5)

This study has demonstrated that, by the proper choice of coligands, phenylenediimido complexes can be used as reactive "monomers" in the construction of novel extended-chain inorganic materials. With proper modifications, such as varying the bridging ligands and tuning of oxidation states, such species may be expected to display novel conducting properties, and we are now pursuing this line of investigation.

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Structure of an L-Tyrosyl-L-histidine–Copper Complex Involving an Axial Copper(II)–Phenol OH Bonding. Implication for Substrate Binding at the Active Site of Tyrosinase

Tyrosinase is a copper-containing monooxygenase that catalyzes the hydroxylation of phenols to catechols (cresolase activity) and the two-electron oxidation of catechols to *o*-quinones (catecholase activity).[1,2] On the basis of the structural similarity of oxytyrosinase to oxyhemocyanin and the associative ligand substitution mechanism, Solomon et al.[1,3-5] proposed the molecular orientations for the hydroxylation and oxidation reactions through systematic chemical and spectroscopic studies. Very recent X-ray crystal structure analyses have revealed the coordination mode of the binuclear copper center in hemocyanin[6] and the O_2^{2-}-bridged binuclear structure of a Cu(II) complex.[7] Although Cu(II)–phenolic substrate interactions are reasonably required for the enzymatic hydroxylation mechanism, it remains unclear whether the phenol group coordinates to the Cu(II) ion in the phenolate (O^-) form or in the protonated (OH) form because of the lack of structural information on Cu(II)–phenol bonding.

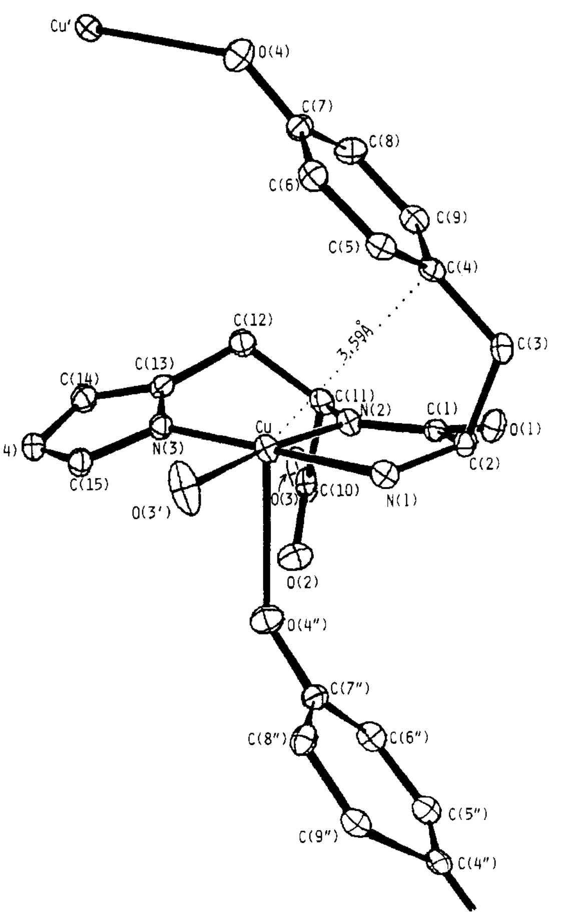

Figure 1. Computer-drawing model for [Cu(Tyr-His)]. Thermal ellipsoids are drawn at the 50% probability level; hydrogen atoms are omitted. The labeling scheme used for the atoms in the molecule is also shown. The atoms with and without primes are related by a screw axis. Selected bond lengths (Å) and angles (deg): Cu–N(1) = 2.022 (4); Cu–N(2) = 1.930 (4); Cu–N(3) = 1.961 (4); Cu–O(3′) = 1.938 (4); Cu–O(4″) = 2.601 (4); N(1)–Cu–N(2) = 83.6 (2); N(1)–Cu–N(3) = 177.0 (2); N(2)–Cu–N(3) = 93.9 (2); O(3′)–Cu–N(1) = 94.7 (1); O(3′)–Cu–N(2) = 174.8 (1); O(3′)–Cu–N(3) = 87.8 (1); O(4″)–Cu–N(1) = 87.8 (1); O(4″)–Cu–N(2) = 89.8 (1); O(4″)–Cu–N(3) = 90.6 (1); O(4″)–Cu–O(3′) = 85.3 (3); Cu–O(4″)–C(7″) = 136.8 (3).

In order to shed light on the tyrosine side chain interactions with Cu(II) bound with nitrogen donors including imidazole, we made an X-ray diffraction study of the copper(II) complex of L-tyrosyl-L-histidine (Tyr-His), [Cu(Tyr-His)] (**1**), as a model

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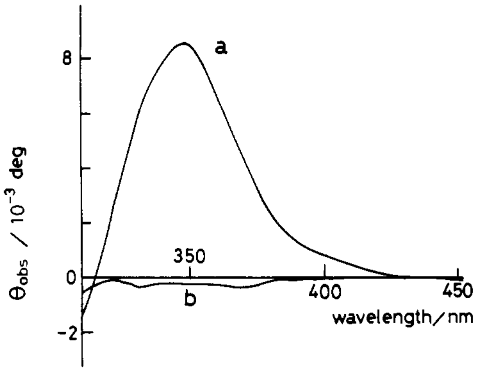

Figure 2. CD spectra of Cu(Tyr-His) (a) and Cu(L-tyrosine)$_2$ (b) in KBr disks.[16] The 350-nm peak disappeared in aqueous solution.

for the putative tyrosinase–substrate intermediate. To the best of our knowledge, this is the first structural evidence for phenolic oxygen coordination to Cu(II) without deprotonation.

Aqueous solutions of Tyr-His·HCl·0.5H$_2$O (0.55 mmol) and Cu(ClO$_4$)$_2$·6H$_2$O (0.55 mmol) were mixed and neutralized (pH 7) to make the final volume 150 mL.[8] Violet crystals of **1** suitable for X-ray diffraction studies separated from the solution after several days. The molecular structure of the complex is shown in Figure 1.[9] The central copper(II) ion, five-coordinated, has an approximate square-pyramidal geometry, where the three nitrogen atoms of Tyr-His and one carboxylate oxygen atom from the neighboring molecule constitute the square-planar base. Most important is the fact that the phenolic oxygen (O(4″)) of the neighboring complex occupies the apical position to complete the square pyramid. The basal coordination plane is planar to within 0.03 Å, and the Cu–O(4″) vector is almost perpendicular to this plane. Probably due to coordination of the phenol group, the Cu(II) ion moves out of the mean basal plane toward the apical ligand by 0.06 Å. The equatorial Cu–N and Cu–O bond lengths (Cu–N(1) = 2.022 (4) Å, Cu–N(2) = 1.930(4) Å, Cu–N(3) = 1.961 (4) Å, and Cu–O(3′) = 1.938 (4) Å) agree well with those generally found in square-planar Cu(II) complexes.[10-12] Although there is hitherto no direct information on Cu(II)–phenol bonding, the axial Cu–O(4″)(phenol) distance, 2.601 (4) Å, is considerably longer than the sum of the ionic radii for Cu(II) (0.72 Å) and –O$^-$ (1.40 Å)[13] and the axial Cu–O(water) bond length, 2.301 Å, reported for a similar five-coordinated pyramidal Cu(II) complex.[12] It is still within the range of 2.2–2.9 Å known for the axial Cu–O bond lengths,[14] and the O(4″) atom is considered to be weakly coordinated. No such coordination has been observed in [Cu(L-tyrosine)$_2$][10] and the ternary complexes [Cu(2,2′-bipyridine)(L-tyrosine)]$^+$ and [Cu(1,10-phenanthroline)(L-tyrosine)]$^+$.[15] Spectroscopic evidence supports the Cu(II)–OH(phenol) bonding; the circular dichroism (CD) spectra of **1** and Cu(L-tyrosine)$_2$ measured in the solid state (KBr disk)[16] revealed that **1** has a positive peak at 350 nm probably due to the Cu(II)–OH(phenol) bond, whereas the latter without such a bond does not have a peak around this wavelength (Figure 2). The equatorial Cu(II)–O$^-$(phenolate) bond in a dimeric complex gives rise to a negative peak at 390–400 nm in aqueous solution.[8] Solution equilibrium studies have shown that the phenol OH group of **1** has a macroscopic pK_a value of 9.18,[8] which is comparable with the microscopic constant (9.5) reported for the side chain phenol group in Cu(II)–glycyl-L-tyrosine[17] and indicates that the OH group is undissociated at neutral pH.

Another feature of the complex is the close contact between the Cu(II) ion and the carbon atom (C(4)) of the phenol ring (Cu···C(4) = 3.59 Å). Examples of similar and closer contacts (3.04–3.34 Å) between Cu(II) and aromatic rings have been reported for Cu(L-tyrosine)$_2$[10] and Cu(II)–peptide complexes[18,19] and are also found in the ternary complexes cited above. For steric reasons, the Cu(II)–aromatic ring interaction is considered to be cooperative with the intramolecular aromatic ring stacking.[20] The closest Cu···Cu distance in **1** is 6.725 (2) Å, which excludes magnetic interactions between the two Cu(II) centers.[21]

Although the axial Cu(II)–OH(phenol) bonding is not expected to be maintained in aqueous solution, it can probably exist in a hydrophobic environment in the absence of other ligating groups. The present finding suggests the possibility that the undissociated phenol group of tyrosine is initially bound at the axial position of the active site of tyrosinase and then undergoes facile deprotonation in the course of the enzyme action. The phenol ring–imidazole ring stacking[20] may assist the hydroxylation reaction.

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Supplementary Material Available: Listings of crystal data, atomic coordinates and isotropic temperature factors, hydrogen coordinates, anisotropic thermal parameters, bond lengths, bond angles, and torsion angles (6 pages); a listing of structure factor amplitudes (F_o, F_c) (6 pages). Ordering information is given on any current masthead page.

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(9) Crystal data: CuC$_{15}$H$_{16}$N$_4$O$_4$, M_r = 397.88, orthorhombic, space group $P2_12_12_1$, a = 17.388 (5) Å, b = 6.560 (1) Å, c = 13.060 (2) Å, V = 1489.7 Å^3, Z = 4, D_c = 1.774 g cm^{-3}, μ(Cu Kα) = 23.74 cm^{-1}, crystal dimensions 0.1 × 0.1 × 0.2 mm. Intensity data in the range $2\theta < 120°$ were collected by the ω–2θ scan technique using a Rigaku AFC-5RU automated diffractometer. The structure was solved by a direct method (MULTAN78) and was refined by least-squares techniques. The final R and R_w values were 0.033 and 0.033, respectively, for 1287 unique reflections with $|F_o| \geq 3\sigma|F_o|$. Full details are provided in the supplementary material.

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