

Oxidation and Superoxide Dismutase Activities of Mononuclear Copper(II) Acetate with Imidazoles as Models for Copper Containing Enzymes.

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Copper plays an important role in a variety of enzyme-catalyzed reactions. Copper containing enzymes have mononuclear and binuclear structures. Over the years we have prepared and studied several mononuclear and binuclear Cu(II) carboxylate complexes with several nitrogen based ligands as biomimetics for copper containing enzymes. The mononuclear complexes have the formula, $\text{Cu(II)(L}_{2-6}\text{)(RCOO)}_2$, where L= imidazole type ligand. Most of imidazoles interact with copper(II) acetate or with other copper(II) carboxylates to produce mono-nuclear structures. Previously, we prepared and determined the molecular structures of copper acetate with imidazoles. While the interaction of copper acetate with imidazole produced *trans*- bis-adduct and tetrakis-adduct, the interaction with 2-methylimidazole and with 1,2-dimethylimidazole produced *cis*-bis-adducts. In the imidazole tetrakis-adduct (**1**) the four imidazole rings occupies coplanar positions with respect to Cu(II) and the two acetate anions coordinate axially through one of the acetate oxygen atoms to form tetragonally elongated $\text{CuN}_4\text{+O}_2$ chromophore. In bis-adducts the copper ion is coordinated to two 2-methylimidazole (**2**) or 1,2-dimethylimidazole (**3**) nitrogen atoms in *cis*-configuration and two carboxylate oxygen atoms from each acetate ligands. The second carboxylate oxygen atoms interact weakly in the axial position to form *cis*- $\text{CuN}_2\text{O}_2\text{+O}_2$ chromophore.

The biomimetic catalytic activities of these complexes as models for copper containing enzymes are reported. The superoxide dismutase (SOD) mimetic activities of complexes are determined using the indirect xanthine-xanthine oxidase –nitroblue tetrazolium method and compared to those for other Cu(II) carboxylate complexes. The results indicated that these complexes are potent SOD mimics, especially the tetrakis-imidazole adduct (**1**). The polyphenol oxidase activities of these complexes are studied and found to catalyze the oxidation of 3,5-di-tert-butylcatechol to the corresponding *o*-quinone and the oxidative dealkylation of 2,4,6-tri-tert-butylphenol to 2,6-di-tert-butyl-1,4-benzoquinone and 4,6-di-tert-butyl-1,2-benzoquinone as the main products. The catalytic oxidative coupling of two molecules of aromatic amines *o*-aminophenol to 2-aminophenoxazin-3-one and *o*-phenylenediamine to 2,3-diaminophenazine by these complexes will be also presented. These reactions are relevant to the action of type 2 copper-containing oxidase phenoxazinone synthase enzyme. Phenoxazinone chromophore is the final step in the biosynthesis of actinomycin D which is used clinically for the treatment of certain types of cancer. The formation of copper ion semiquinone species in the above oxidative reactions, which may be the catalytic intermediate that reacts with oxygen which leads to the formation of the respective product, will be discussed and is demonstrated spectrophotometrically.