Chapter 2

Copper-dioxygen complexes and their roles in biomimetic oxidation reactions

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**Abstract** Copper-dioxygen interactions are essential from both industrial and biological perspectives. This review will focus on recent advances in copper-dioxygen complexes with regard to their relevance to bioinorganic chemistry. New, room-temperature stable copper-peroxo compounds serve as models for the dioxygen transporting protein hemocyanin. Other copper-dioxygen complexes with formally-cleaved O-O bonds are also of interest as models for dioxygen activation. Interest in copper-dioxygen complexes which can oxidize organic compounds stems from their roles in biological substrate oxidation chemistry as well from their industrial utility. Copper-dioxygen complexes capable of hydroxylating arenes are reported which model tyrosinase, an enzyme which catalyzes the ortho-oxygenation of phenols. Synthetic copper compounds that catalyze the hydroxylation of aliphatic C-H bonds serve not only as models for industrial processes involving copper catalysts but also as mimics for copper monooxygenases such as dopamine β-monooxygenase, peptidylglycine α-amidating monooxygenase, and particulate methane monooxygenase. Copper-dioxygen compounds which oxidize benzylic C-H bonds as well as non-activated C-H bonds are reported, including recent studies where stereoselective hydroxylation occurs. Catechol oxidase models that catalyze the oxidation of o-diphenols to their corresponding o-quinones are also reported. Other copper oxidase models include mononuclear copper complexes which catalyze the two-electron oxidation of alcohols to aldehydes, coupled with the reduction of $\text{O}_2$ to $\text{H}_2\text{O}_2$ through a Cu(II) phenoxy-radical species, closely mimicking the mechanism of galactose oxidase. A dinuclear copper complex is reported which also catalyzes the aerobic oxidation of alcohols to the corresponding aldehydes and ketones. DNA as a substrate for oxidation by copper-phenanthroline compounds is overviewed.

**Key Words:** copper-O$_2$, bioinorganic chemistry, model compounds, dioxygen activation, binuclear copper, catalytic oxidation, alcohol and DNA oxidation

1. INTRODUCTION

In this review, we provide a bioinorganic perspective in overviewing recent advances in the chemistry of copper-dioxygen [dioxygen; molecular
oxygen, \( \text{O}_2 \)] complexes. Copper ions are among the most common and useful industrial and synthetic oxidation catalysts as well as one of the most ubiquitous redox active metals utilized by biological systems.

### 1.1 Practical Copper Oxidative Processes

Industrially,\(^1,^2\) copper has long been used as a catalyst in the Glaser process, which couples terminal acetylenes to give diacetylenes using cuprous chloride and molecular oxygen. This is a historically important (but now obsolete) catalytic process for producing the precursor to chloroprene, which is then used to produce neoprene rubber. Another important industrial process which utilizes copper/dioxygen chemistry is the oxidative coupling of 2,6-xylenol to form a para-phenylene oxide polymer by coupling an oxygen of one phenol molecule to the para carbon of another to form an aromatic polyether by the trade name PPO. This polyether is a high melting plastic that is extremely resistant to heat and to water, and it is useful as an engineering thermoplastic. Another less common process also uses copper(I) chloride to catalyze the analogous oxidation of 2,6-diphenylophenol to form an even more rigid and higher melting material than PPO. An important industrial process that indirectly utilizes copper/dioxygen chemistry is the Wacker process which produces acetaldehyde from ethylene.\(^3\) In this process, both palladium chloride and cupric chloride are used. Although the copper catalyst is not directly involved in the oxidation of the ethylene substrate, it is crucial for catalyzing the re-oxidation of \( \text{Pd}^0 \) to \( \text{Pd}(II) \) to sustain the catalytic cycle. Synthetically, copper/dioxygen reactivity has been utilized in a similar fashion in the osmium-catalyzed dihydroxylation of olefins. Cupric chloride/\( \text{O}_2 \) is used to catalyze the re-oxidation of osmium from a formal oxidation state of +6 to +8. Other synthetic uses of copper/dioxygen catalysts include the oxidation of various substrates such as aniline, aromatic diamines, alcohols, and thiols.\(^4\)

### 1.2 Copper in Biology

Copper ion is an essential trace element found in living systems, and its importance resides in its role as a protein or enzyme active-site constituent.\(^5-^9\) Recently described chaperone\(^10,^11\) proteins and metallothioneins\(^7\) aid the cell in the copper ion trafficking, and thus copper ion homeostasis. But the major role of copper proteins involves oxidation-reduction (i.e., ‘redox’) activity. Donors for copper ion complexes which are typically available in protein matrices include the side-chain imidazole group of histidine (His), the phenol oxygen donor of tyrosine, or the sulfur atom of the thiol group from cysteine (Cys). With these ligands, the Cu(I) and Cu(II) oxidation states are readily accessible and interconvertible under