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Binuclear macrocyclic and macrobicyclic complexes for dioxygen activation and transport

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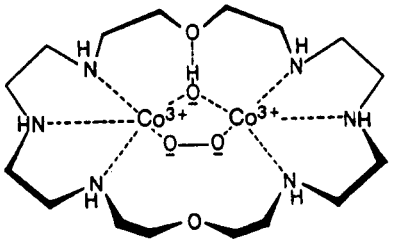
Abstract. The binuclear cobalt(II) complexes of OBISTREN and OBISDIEN are excellent oxygen carriers because their dioxygen complexes do not undergo ligand degradation and can give up their coordinated oxygen when subjected to a change of pressure or temperature. The additional coordination positions in OBISDIEN recognize and coordinate bridging reducing ligands which then undergo redox reactions with coordinated dioxygen. When isophphalaldehyde condenses with diethylenetriamine, the resulting Schiff base macrocyclic ligand forms a binuclear Cu(I) complex which reacts with dioxygen to form a complex which rapidly hydroxylates an adjacent phenyl ring. When furan or pyridine is used in place of benzene the resulting dioxygen complexes may be used to oxidize substrates such as phenols, catechols, and aromatic amines. A catalytic cycle for the oxidation of 3,5-ditertiarybutylcatechol is shown.

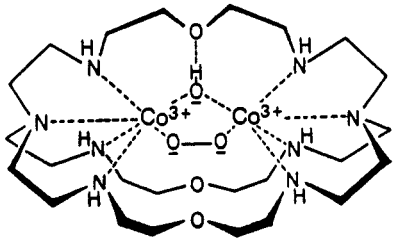
DIOXYGEN TRANSPORT

The formulas of the dinuclear hydroxo-bridged cobalt dioxygen complexes formed from OBISDIEN and OBISTREN[1,2] are indicated by formulas **1** and **2**. The oxygenation constant is fairly normal for OBISDIEN but considerably below what is expected for OBISTREN. The OBISDIEN dioxygen complex has three basic nitrogens per cobalt while the corresponding complex formed from OBISTREN with an additional basic nitrogen per metal ion has a stability which is almost three order of magnitude lower. Many examples have been given in the literature to indicate that the stabilities of dioxygen complexes increase with an increase in the number of basic nitrogens coordinated to the cobalt. The stabilities of these two oxygen carriers are just the opposite of what one would predict, indicating that the OBISTREN complex is much lower in stability than would be expected. The effect is probably a steric one because the oxygen complexes formed are quite normal in both cases, with strong charge transfer bands around 370 nm and, as indicated by the formulas, are diamagnetic in character, showing that the metal centers have the characteristics of cobalt(III) and the bridging oxygen has the characteristics of a peroxo group.



1 μ-hydroxo-μ-peroxo dicobalt(II) OBISDIEN dioxygen complex

$$K_{O_2} = \frac{[Co_2(OH)O_2L][H]}{[Co_2L]P_{O_2}} = 10^{-3.29}\ M\ atm^{-1}$$



2 μ-hydroxo-μ-peroxo dicobalt(II) OBISTREN dioxygen complex

$$K_{O_2} = \frac{[Co_2(OH)O_2L][H]}{[Co_2L]P_{O_2}} = 10^{-6.00}\ M\ atm^{-1}$$

The oxygenation constants shown above together with the stability constants of the metal complexes and the pK's of the ligands can be used for setting up the distribution curves indicated

in Figures 1a and 1b. For the distribution curves of the OBISDIEN oxygen complex (Figure 1a) it is seen that the oxygen complex reaches its maximum concentration at a little over pH 7 and at higher pH is converted from the monohydroxo to the dihydroxo and trihydroxo noxygen species. In the case of OBISTREN, however, only one dinuclear cobalt dioxygen species is formed having a maximum concentration at about pH 8. The coordination number of cobalt in this complex is 6 so that there is no tendency to form the dihydroxo and trihydroxo species that is observed for the OBISDIEN dioxygen complex.

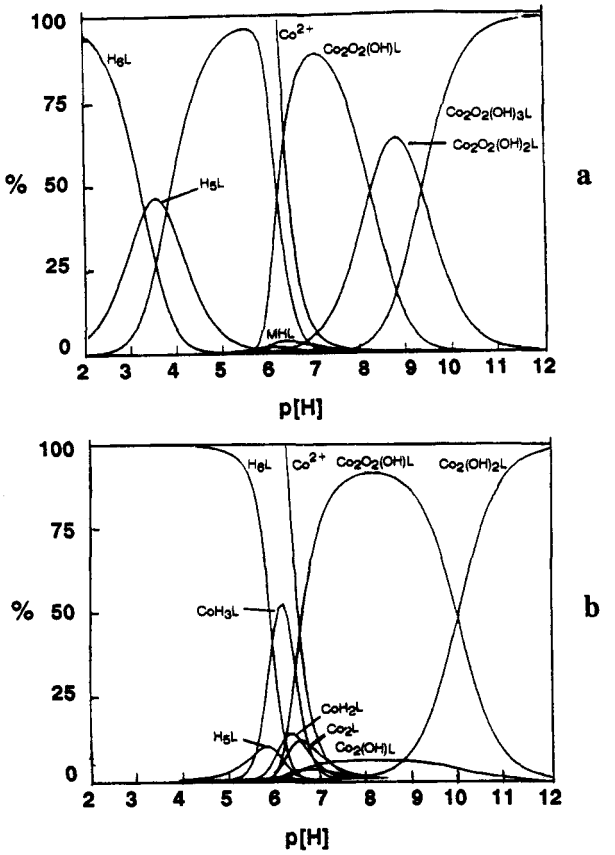


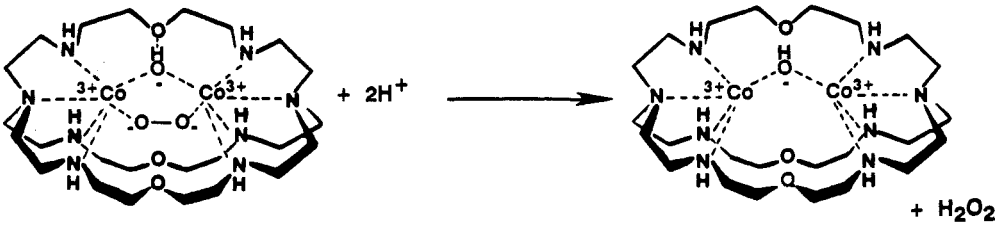
Figure 1. Distribution of species as a function of p[H] in a solution containing a 1:2 molar ratio L:Co(II) at 25.0 °C, μ = 0.100 M under 1 atm oxygen; A: OBISDIEN-Co(II), [OBISDIEN] = 0.00100 M; B: OBISTREN-Co(II), [OBISTREN] = 0.00100 M.

An important feature of a good dioxygen carrier is the ability to undergo oxygenation and deoxygenation many times without an appreciable degree of degradation. Many macrocyclic and macrobicyclic ligands have been used to form dicobalt dioxygen complexes which carry oxygen but in almost all cases the rates of degradation are too rapid for commercial use as an oxygen carrier (a half-life of a day or a even week is much too rapid). The oxygen carriers derived form OBISTREN and OBISDIEN, however, are notable in that the rates of degradation of the oxygen complexes is very slow. The half-life of OBISTREN has been estimated as about six months while that of the OBISDIEN oxygen complex seems to be three or four months. In addition to its high resistance to degradation the OBISTREN dicobalt peroxo bridge complex has a relatively low thermodynamic stability, with about 90% formation at pH 8 at room temperature. At slightly higher temperature the degree of formation is somewhat less, therefore the oxygen can be removed from the dioxygen complex by a moderate elevation temperature or a moderate decrease in pressure, making it fairly easy to recover the oxygen from the oxygen complex. For these reasons the oxygen complex derived form the dicobalt(II) complex of OBISTREN seems to be the best oxygen carrier described in the literature thus far.[3,4]

Several kinds of degradation of dioxygen complexes have been reported and Figure 2 illustrates three of the most common routes. In metal centered degradation the cobalt is converted to cobalt(III) and hydrogen peroxide is released. There is no change in the ligand itself. Also, the oxygen complex may undergo ligand centered degradation in which the ligand is attacked by the dioxygen. This attack may take the form of a dehydrogenation reaction, indicatd by A of Figure 2.

Such a reaction is quite likely when there is an aromatic ring in the organic ligand so that a Schiff base can be formed in which the double bond of the Schiff base is conjugated with the ring. Ligand-centered degradation may also take the form a hydroxylation reaction, as indicated in B of Figure 2. An example of this kind of degradation will be shown below. Both the OBISDIEN and OBISTREN dinuclear cobalt dioxygen complexes undergo metal centered degradation and the ligand in each case is not affected. The Co(III) complex produced by such degradation may be reduced to the original Co(II) complex, which is the original oxygen carrier.

Metal-centered degradation



Ligand-centered degradation

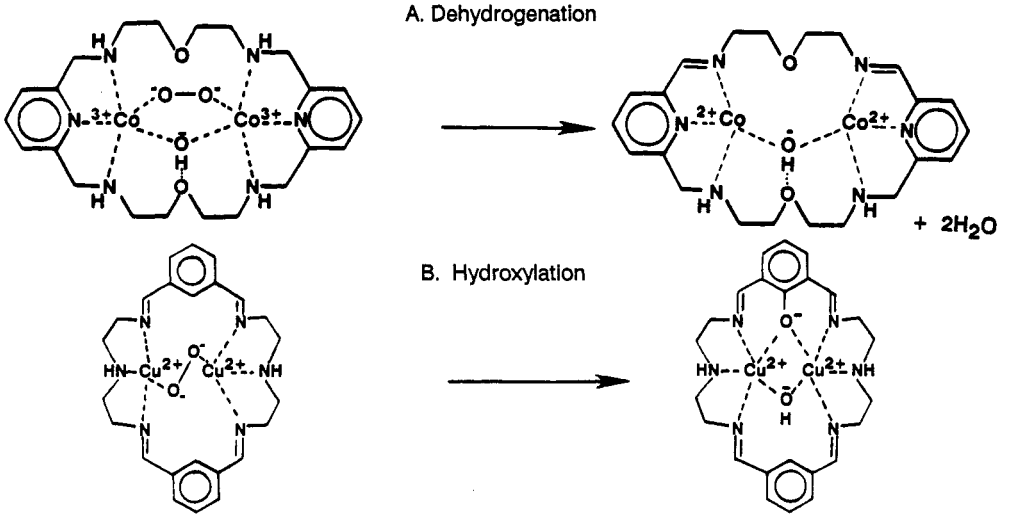
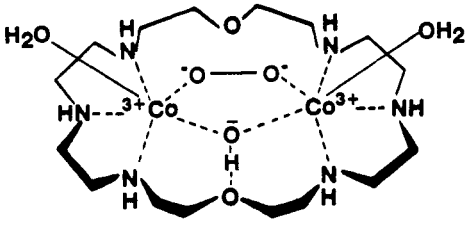


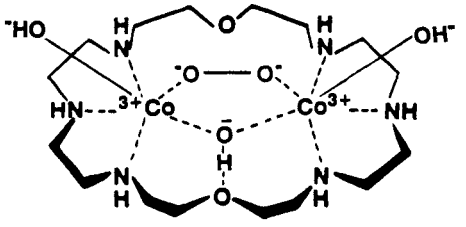
Figure 2. Degradation of dioxygen complexes.

Molecular Recognition

The fact that the dioxygen complex of OBISDIEN has two aquo donors, one on each cobalt center, which are converted to hydroxo groups at high pH, 3 and 4, suggests the possibility of adding a third bridging group which would coordinate both metal centers simultaneously. Such a



3 Binuclear hydroxo-bridged cobalt dioxygen OBISDIEN complex

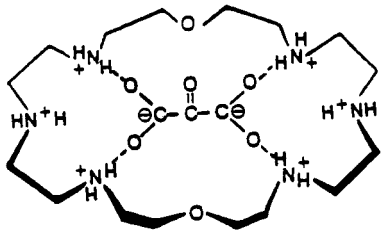


4 Binuclear trihydroxo cobalt dioxygen OBISDIEN complex

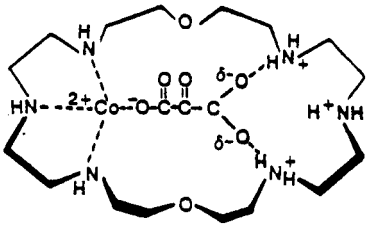
bridging group should have the correct size and shape to bridge the two metal ions and coordinate them simultaneously and thus be "recognized" by the macrocyclic complex. If such a third bridging group is also a reducing agent there is a possibility that it will react with the coordinated dioxygen within the macrocycle with the electron pathway from the reducing agent to the dioxygen through the metal ions. Bridging groups that meet these requirements are the oxalate anion, a two electron reductant, and the mesoxalate anion (often called ketomalonic acid), a four electron reductant.

The bridging equilibria by these donors have been described including the redox reactions in which the ligand is oxidized to CO_2 and the dioxygen is reduced to water.[5,6] The recognition by the dinuclear cobalt(II) dioxygen complex of OBISDIEN of a number of bridging molecules or anions has been reported.[7]

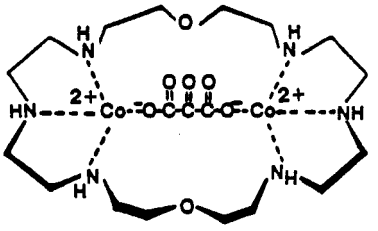
In order to determine the affinity of mesoxalate for the OBISDIEN dicobalt dioxygen complex it is first necessary to take into account a number of other reactions which may or may not compete with the reaction in question. Such interactions are the bonding of mesoxalate to the free ligand, **5**, to the mononuclear OBISDIEN cobalt complex, **6**, and to the dinuclear OBISDIEN dicobalt complex, **7**. Whether or not these are competing reactions will depend on the equilibrium constants determined. Finally, the interaction of the mesoxalate with the oxygen complex can be determined. It is noted that when the dioxygen complex, **8**, is formed a hydroxo bridge is also



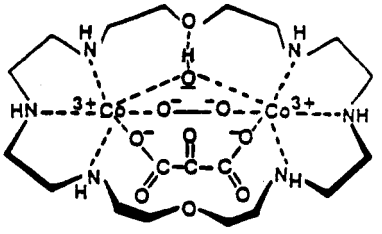
5 μ-Mesoxalatohexaprotonted OBISDIEN complex



6 μ-Mesoxalaltotriprotonated OBISDIEN complex



7 μ-Mesoxalatodicobalt(II) OBISDIEN complex



8 μ-Hydroxo-μ-peroxo dicobalt(III) OBISDIEN complex

formed because of the increase in charge on the cobalt and its consequent higher tendency to hydrolyze. The distribution of the dioxygen containing species in this system is shown in Figure 3 which indicates that the maximum concentration of the dioxygen complex in which mesoxalic acid is also found occurs a little above pH 8. When the temperature of the solution is raised to about 50 °C a redox reaction between the coordinated dioxygen and the mesoxalate occurs in which the mesoxalate is converted entirely to CO_2.The four electron oxidation which takes place matches the oxidizing power of dioxygen to water and the original Co(II) OBISDIEN complex is formed after the redox reaction has been completed. The complex is thus available for combination with more dioxygen which in turn can combine and react with more substrate. The reaction is therefore catalytic in nature, as is indicated by Scheme I. Thus we have a redox reaction which occurs within a macrocyclic complex whereby a reducing agent supplies electrons to coordinated dioxygen which in turn is reduced to water.

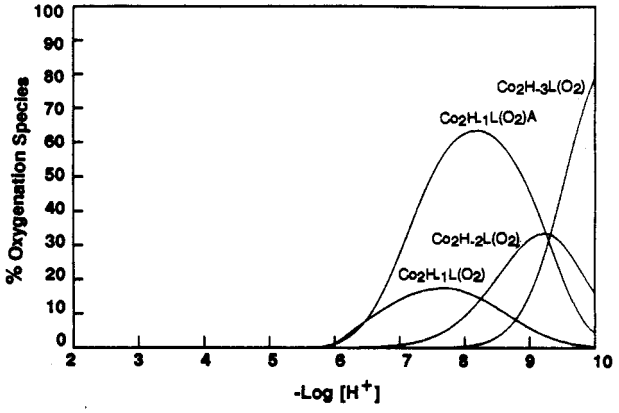
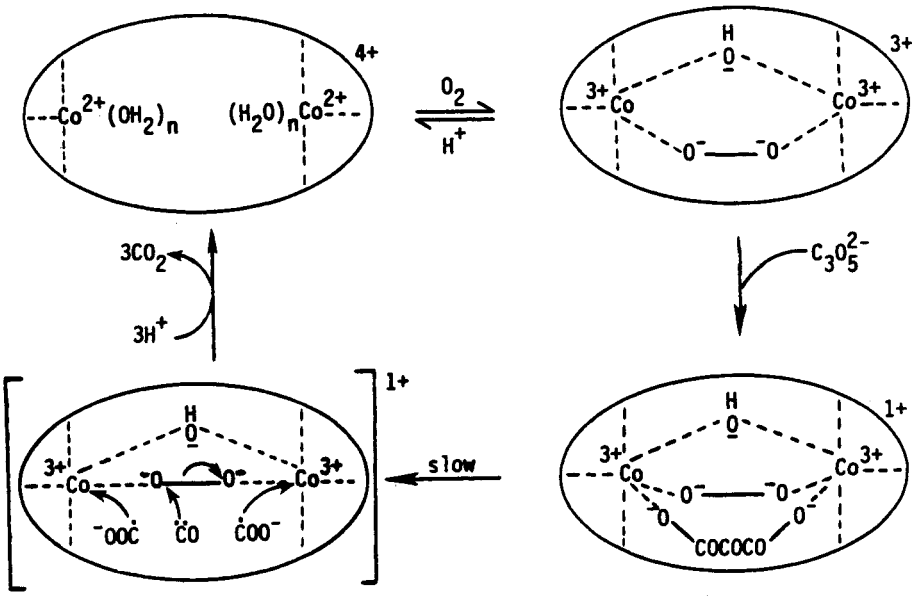


Figure 3. Distribution of dioxygen complex species present as a function of p[H] in a solution containing a 1:1:2 molar ratio of OBISDIEN (L) mesoxalic acid (H_2A), and Co(II), respectively, under 1.00 atm of dioxygen at 25.0 °C and μ = 0.100 M (KCl). $T_A = T_L = 1/2T_{Co(II)} = 2.00 \times 10^{-3}$ M. Non-dioxygen-containing species are omitted for clarity.

Scheme I

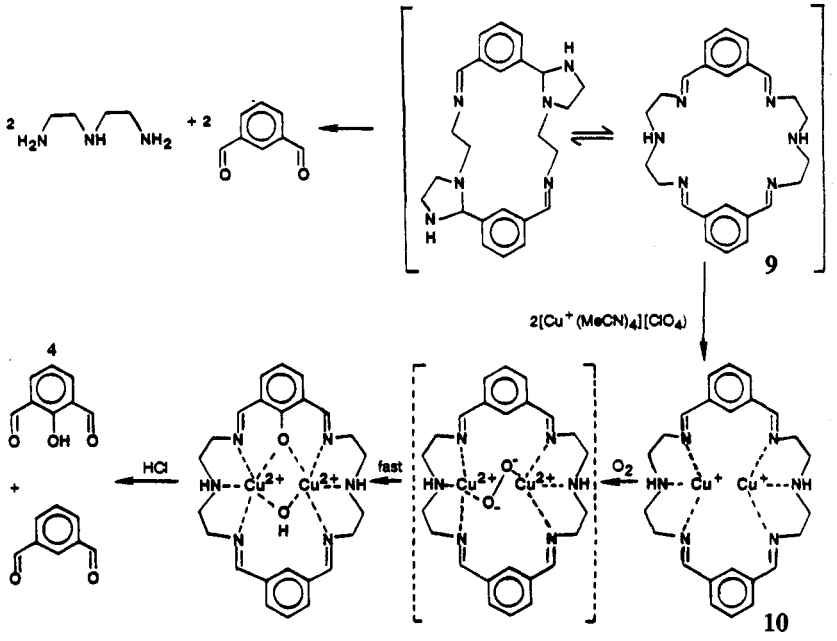


Dioxygen Activation

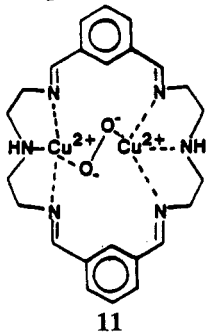
While the dinuclear cobalt OBISDIEN complex described above may be interpreted as an activator of dioxygen, in that the oxygen complex can oxidize the substrates that also bridge the metal ion, the copper(I) dioxygen complexes are much more reactive in this regard. This section deals with examples of this type of oxygen activation.

A 2+2 condensation of isophthalaldehyde with diethylenetriamine produces a tetra Schiff base macrocyclic ligand, **9**, which combines with Cu(I) to give a complex, **10**, indicated in Scheme II. This dinuclear complex combines with oxygen to rapidly hydroxylate one of the phenol groups of the macrocyclic ligand as indicated in the Scheme.[8,9] The proof of hydroxylation was obtained by product analysis to indicate the formation of the phenolic derivative and by an ^{18}O tracer experiment in which all of the oxygen of the phenolic group was found to be derived from the original dioxygen. The oxygen insertion reaction is extremely rapid and the lifetime of the oxygen complex at room temperature is believed to be very short. However, Karlin[10] was able to obtain spectroscopic evidence for a number of dinuclear Cu(I) dioxygen complexes at -80 °C, but which rapidly underwent oxygen insertion reactions or other degradation reactions at more elevated temperatures.

Scheme II.



In view of the high reactivity of the dioxygen complex indicated by **11** it was thought that the use of a connecting group between the diethylenetriamine moieties in the macrocyclic ring that could not undergo insertion, as does an aromatic CH, would result in the formation of copper(I) dioxygen complexes that would have a greater lifetime, especially at room temperature. Accordingly the dioxygen complex with furan rings as bridging groups was prepared by Ngwenya[11] from the 2+2 condensation 2,5-dicarboxaldehyde and diethylenetriamine. The resulting dioxygen complex indicated by **12** has a lifetime of about 2 hours at room temperature (~ 25.0 °C) and can be used for the oxidation of various substrates. The Cu(I) dioxygen complex **12** and an analogous complex containing pyridine connecting groups, **13**, were investigated as oxidizing agents by Rockcliffe.[12,13,14] The corresponding Cu(II) complexes which did not form dioxygen adducts were also studied as oxidants. Table 1 lists the nine substrates that were investigated for reactivity with **13**, and the oxidation products that were obtained in each case. These reactions were carried out with an excess of dioxygen and an excess of substrate. Five of the substrates where oxidized catalytically by the Cu(I) dioxygen complex **13** while four substrates gave very low yields of oxidation products, with less than one turnover.



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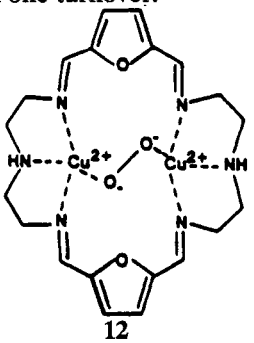
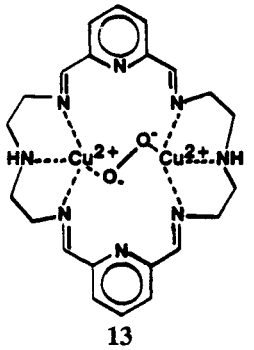


12



13

Table 1. Oxidations with $[Cu_2(PD)_2(DIEN)_2]^{2+}$ and Dioxygen

Substrate	% Conversion	Turnover	Product
2,6-dimethoxyphenol	46	3	3,3′,5,5′-tetramethoxydiphenoquinone
2,6-di-*t*-butylphenol	56	3	3,3′,5,5′-tetra-*t*-butyldiphenoquinone
2,4-di-*t*-butylphenol	< 1	< 1	3,3′,5,5′-tetra-*t*-butyl-2,2′-dihydroxybiphenyl
hydroquinone	43	5	benzoquinone
t-butylhydroquinone	38	4	*t*-butylbenzoquinone
3,5-di-*t*-butylcatechol	43	4	3,5-di-t-butyl-1,2-benzoquinone
4-*t*-butylcatechol	< 1	< 1	γ-lactone of 3-hydroxy-4-t-butylmuconic acid ester
4-methylcatechol	< 1	< 1	γ-lactone of 3-hydroxy-4-methylmuconic acid ester
3,4-dimethylaniline	6	< 1	3,3′,4,4′-tetramethylazobenzene

It was found that oxidation with the corresponding Cu(II) complex with the same substrates under catalytic conditions (excess dioxygen and substrate) occurred at appreciable rates only with the substrates which were found to be catalytic with the Cu(I) dioxygen complex. The substrates which were not catalytically oxidized by the Cu(I) dioxygen complexes were found to be oxidized very slowly or not at all by the Cu(II) complexes (Table 2). The pseudo first order rate constants of the substrates employed with the Cu(I) dioxygen complex and with the Cu(II) complex are given in Table 3.

Figure 4 gives a dramatic indication of the interdependence of Cu(I) dioxygen complex **13** and the Cu(II) complex **14** for a catalytic process to occur. In this figure the formation of 3,5-ditertiarybutyl-1,2-benzoquinone in the presence of the Cu(II) complex, indicated by **14** from 3,5-ditertiarybutylcatechol, is plotted as a function of time. The initial slow rate of formation of the product is characteristic of oxidation by Cu(II). The initial reaction, however, results in the formation of Cu(I) which then combines with dioxygen to form the more reactive Cu(I) dioxygen complex. This causes an increase in the rate of catalytic oxidation as is seen by the increased slope of the figure. The final higher slope of the rate of formation of oxidation product in Figure 4 is due to the presence of two catalysts, the Cu(II) complex **14** and the more reactive Cu(I) dioxygen complex **13**.

Table 2. Oxidations with the $Cu_2^{II}(PD)_2(DIEN)_2^{4+}$ Complex

Substrate	% Conversion	Turnover	Product
2,6-dimethoxyphenol	46	2	3,3′,5,5′-tetramethoxydiphenoquinone
2,6-di-*t*-butylphenol	39	3	3,3′,5,5′-tetra-*t*-butyldiphenoquinone
t-butylhydroquinone	64	6	*t*-butylbenzoquinone
2,4-di-*t*-butylphenol	0	0	-
hydroquinone	35	3	benzoquinone
3,5-di-*t*-butylcatechol	73	5	3,5-di-*t*-butyl-1,2-benzoquinone
4-*t*-butylcatechol	0	0	-
4-methylcatechol	< 1	< 1	γ-lactone of 3-hydroxy-4-methylmuconic acid ester
3,4-dimethylaniline	0	0	-

Table 3. Initial Rates for Cu(I)-Dioxygen and Cu(II) Oxidations

Substrate	Product	Initial Psuedo First Order Rate Constants, s^{-1}	
		Cu(I) + O_2	Cu(II)
2,6-dimethoxyphenol	3,3′,5,5′-tetramethoxydiphenoquinone	7.7×10^{-5}	1.5×10^{-5}
2,6-di-*t*-butylphenol	3,3′,5,5′-tetra-*t*-butyldiphenoquinone	6.7×10^{-5}	1.2×10^{-5}
2,4-di-*t*-butylphenol	3,3′,5,5′-tetra-*t*-butyl-2,2′-dihydroxybiphenyl	$<1.4 \times 10^{-10}$	0
hydroquinone	benzoquinone	8.3×10^{-4}	8.9×10^{-5}
t-butylhydroquinone	*t*-butylbenzoquinone	9.3×10^{-4}	1.9×10^{-4}
3,5-di-*t*-butylcatechol	3,5-di-*t*-butyl-1,2-quinone	3.8×10^{-4}	3.8×10^{-5}
4-*t*-butylcatechol	γ-lactone of 3-hydroxy-4-*t*-butylmuconic acid ester	5.6×10^{-7}	~0
4-methylcatechol	γ-lactone of 3-hydroxy-4-methylmuconic acid ester	~0	5.5×10^{-9}
3,4-dimethylaniline	3,3′,4,4′-tetramethylazobenzene	2.0×10^{-5}	~0

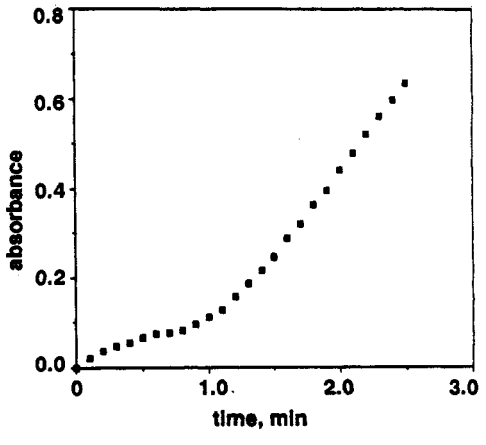
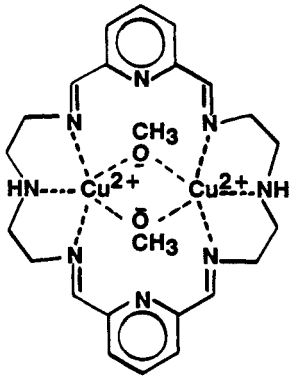


Figure 4. Time dependence of the catalytic formation of 3,5-d-*t*-butyl-1,2-benzoquinone in the presence of the binuclear Cu(II) macrocyclic complex (1.76×10^{-4} M) and excess dioxygen (P_{O_2} = 1 atm) monitored at 400 nm

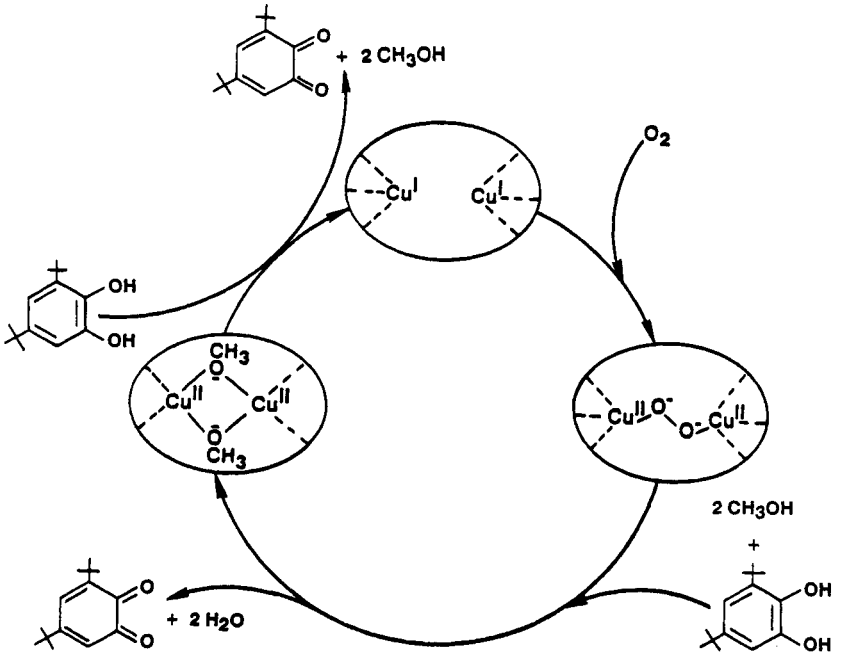


14 $Cu_2(PD)_2(DIEN)^{4+}$

Binuclear Cu(II) complex with pyridine bridging groups in the macrocyclic tetra Schiff base

The oxidation of 3,5-ditertiarybutylcatechol to 3,5-ditertiarybutyl-1,2-benzoquinone is illustrated by the cyclic process shown in Scheme III. If one starts with the dinuclear Cu(I) dioxygen complex, it is seen to combine with oxygen to form the peroxo bridged dinuclear Cu(I) complex in which the metal ion is indicated as Cu(II) with a bridging peroxo group. This combines with the substrate in the methanol-acetonitrile solvent to give the dimethoxy bridged Cu(II) complex and one mole of the quinone. The Cu(II) complex in turn oxidizes another mole of the substrate to the quinone forming the Cu(I) dioxygen complex and the cycle then repeats itself. A similar scheme can be written for all of the substrates in Table 1 that undergo catalytic oxidation.

Scheme III



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