OXIDATION OF ORGANIC SUBSTRATES WITH DIOXYGEN COMPLEXES AS INTERMEDIATES

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Abstract - Reactions are described in which oxygen complexes of cobalt, iron, and copper may be involved in the oxidation of organic substrates by electron transfer (oxidase models) and oxygen insertion (oxygenase models). Examples are given of oxidation reactions in which dioxygen complexes are inferred by kinetics and proposed reaction mechanisms. Oxidative degradations of dioxygen complexes to inert species are described in some detail. Kinetics and proposed mechanisms are presented for the oxidation of ditertiarybutylphenol by cobalt dioxygen complexes. The results suggest that a dioxygen complex intermediate is required for oxygen insertion, but not for the coupling (dehydrogenation) reaction.

INTRODUCTION

The high level of research activity on dioxygen complexes over the past two decades has been concerned primarily with the equilibria and kinetics of formation, and studies of their electronic and vibrational spectra, magnetic properties, and crystal structures. These developments have been thoroughly described and evaluated in many reviews, a few of which are cited here (Ref.1-4). In spite of these major developments, relatively little work has been done on the chemical reactions that dioxygen complexes undergo, and there is now a remarkable opportunity to determine how structure and bonding of dioxygen complexes influence their reactivity as oxidants for a wide variety of substrates. The breadth of such investigations could be further extended by the large number of dioxygen complexes that are now known, - including mononuclear and binuclear complexes in which the coordinated oxygen may be considered to exist primarily as a superoxo or peroxo moiety. In addition, a large number of transition metal ions are now known to form dioxygen complexes, and hundreds of their complexes have been found to combine with dioxygen.

Scope
Because of space limitations this paper will be restricted primarily to the first row transition metals - mainly cobalt, iron, and copper. Two types of reactions will be considered: simple electron transfer oxidase models in which oxygen is reduced to water, and oxygen atom transfer to the substrate (oxygenase models). These oxygen insertion reactions may be further classified in accordance with whether one or both oxygen atoms become part of the organic molecule being oxidized (partial insertion reactions or monooxygenase models and complete insertion reactions or dioxygenase models). Several of the reactions of dioxygen complexes to be discussed below involve a dioxygen complex as the primary oxidant. Under certain conditions such reactions become catalytic in the presence of a small amount of the metal precursor complex, which may undergo many cycles of oxygenation and reduction and the reactive dioxygen complex is regenerated as long as the supply of oxygen holds up. There are many reactions of the latter type in which the intermediate dioxygen complexes have not been isolated or identified but their presence has been inferred from the reaction kinetics or other chemical evidence. Such reactions will be considered below under a separate classification.

PART I

Reaction systems in which dioxygen complexes may be present as unstable but reactive intermediates
Oxidation of ascorbic acid. The oxidation of ascorbic acid by molecular oxygen in the presence of copper(II) ion as catalyst was found to be first order in the concentrations of copper ion, the mono anion of ascorbic acid, and over a limited concentration range, of dioxygen itself (Ref.5). These observations, especially the oxygen dependence, led to the postulation of a ternary ascorbate-copper-dioxygen complex as a reactive intermediate in which two successive electron transfers occurred from the ascorbate ligand to the coordinated dioxygen, resulting in the formation of dehydroascorbic acid and hydrogen peroxide. The same type of behavior was observed with Fe(III) ions as catalysts (Ref.5). This work

was extended to catalytic systems involving vanadyl (Ref.6) and uranyl (Ref.7) ions. In the presence of metal chelates of copper(II) and iron(III) such as those of nitrilotriacetic acid (NTA) and ethylenediaminetetraacetic acid (EDTA), catalytic effects were found to be considerably lower and independent of oxygen concentration. For these systems it was concluded that one-electron transfers occur between the ascorbate monoanion and the higher valent form of the metal chelate. The resulting ascorbate radical anion is then oxidized in a second step by the Cu(II) or Fe(III) chelate. In such systems the function of the dioxygen is considered to be merely to reoxidize the catalytic chelate complex from the lower valent state to the reactive higher valent form (Ref.8).

Recently a reinvestigation of the Cu(II) ion-catalyzed oxidation of ascorbic acid led Jameson and Blackburn (9,10,11) to postulate a binuclear Cu(II) complex containing ascorbate monoanion and dioxygen as ligands. Their observance of half order dependence on the concentration of molecular oxygen led to their suggestion that a binuclear dioxygen complex is the intermediate in which the rate determining electron transfer takes place. It was also suggested that the dioxygen complex is stabilized by the formation of a Cu(III) species through donation of electrons from the metal ions to coordinated dioxygen (Ref.10 & 11). It was subsequently suggested (Ref.12) that the observed half order dependence on dioxygen concentration might represent a reaction mechanism transition between the first order dependence observed at high dioxygen concentration and the lack of oxygen dependence and hence lack of dioxygen complex formation at low oxygen concentration. Because of the special requirements concerning the nature of the ligand necessary to stabilize Cu(III) (Ref.13), the Cu(III) species must be present, if at all, at extremely low concentrations, and hence would be undetectable as a reactive intermediate. While the question of mononuclear vs. dinuclear complex formation is still undecided, the presence of some kind of intermediate dioxygen complex seems to be indicated. At extremely low concentrations of catalytic metal ions or complexes it seems that equilibrium conditions would mitigate against formation of polynuclear complexes and so under such conditions it would seem that the formation of mononuclear dioxygen complex intermediates would be more reasonable.

Catechol oxidation. Metal ions of the first row transition series such as Mn(II), Co(II), Fe(III), and Cu(II), and their metal complexes, catalyze the oxidation of catechols to ortho-quinones by molecular oxygen (Ref. 14).   The observed reaction rates are dependent on dioxygen concentration in these systems, leading to the suggestion of an intermediate ternary dioxygen complex in which the electron transfer from coordinated catecholate anion to coordinated oxygen occurs in successive one electron steps. Since the metal ions tend to precipitate at the pH values employed, an additional (carrier) ligand is usually present, thus leading to the formation of a quarternary intermediate. More recent work by Rogic and coworkers (15 & 16), however, has shown conclusively that catechols may be oxidized to quinones, with subsequent rupture of the aromatic ring to give the half ester of cis,cis-muconic acid in the presence of copper complexes and molecular oxygen. The complex system employed was the so-called "Cu-reagent" which consists of cuprous chloride dissolved in pyridine and methanol. This work proved conclusively that dioxygen is not necessary for the oxidation of the catechol to the quinone and for the subsequent carbon-carbon bond fission reaction since the same reaction was observed in the absence of molecular oxygen. The conclusions of Rogic et al. (15 & 16) are supported by the work of Speier and Tyeklar (17) who also found that the oxidation of ditertiarybutylcatechol and the corresponding quinone by molecular oxygen is catalyzed by cuprous chloride in methanol, or in acetonitrile and pyridine. They demonstrated that oxygen complexes are not necessary by preparing the cupric chloro catecholate complex and observing its conversion to the quinone under nitrogen, and that under certain conditions ring splitting and formation of the muconate occurs in the absence of oxygen. However, in the presence of oxygen the reaction appeared to be much more vigorous and to occur by an entirely different mechanism.

Some recent papers have indicated the possible involvement of copper dioxygen complexes in systems involving copper catalysis under conditions whereby the copper dioxygen complex is not formed in sufficient concentration to be isolated or identified. Thus Lever and coworkers (18) have found that catechol is oxidized to quinone in the presence of a binuclear copper phthalazine complex as catalyst. Observation of reaction sequences and rates indicated the possibility of formation of a reactive dioxygen adduct of the copper(II) phthalazine complex.

Brown and coworkers (19) recently reported a copper assisted endodiol ring cleavage reaction which is clearly oxygen dependent. The Cu(II)-mixed ligand complex of 1,10-phenanthroline and catechols such as ditertiarybutylcatechol react with oxygen to give the usual oxidation product, cis,cis-muconolactone. The reaction occurring in these systems appears to differ considerably from those reported by Rogic (15 & 16). Molecular oxygen is clearly necessary for the reaction to occur and the nature of the counter ligand seems to be important in determining the course of the reaction.

From the above it appears that catalytic systems involving the Cu(I)-Cu(II) cycle may oxidize catechols to quinones and rupture the aromatic ring by more than one mechanism:- one in

which under certain conditions the Cu(II)-Cu(I) reagent seems to suffice, while there may be another parallel reaction in which an intermediate Cu(I) or Cu(II) dioxygen complex is clearly required. It is apparent that much more work needs to be done on these systems to determine the nature of these various types of reaction mechanisms. In the discussion of the properties and reactivities of dioxygen complexes described below, further examples will be given of dioxygen complexes containing copper as a catalyst for the activition of molecular oxygen.

Amino acid oxidation. Alpha amino acids are oxidized by molecular oxygen to alpha-keto acids with pyridoxal and first row transition metal ions as catalysts (Ref.20,21,22). This reaction is similar to the well known vitamin B_6-catalyzed transamination reaction except that the pyridoxal moiety is not reduced to a pyridoxamine derivative but is maintained in its oxidized form. Since the rate of reaction is dependent on the concentration of molecular oxygen it has been proposed (Ref. 22) that a ternary metal ion-dioxygen-Schiff base complex is formed as a reactive intermediate as indicated in Scheme I. The regeneration of pyridoxal makes possible additional reaction cycles resulting in the conversion of amino acid to keto acid with molecular oxygen as the primary oxidant, and with pyridoxal and metal ions as catalysts. In model systems Mn(II) seems to be the most effective metal ion, while in the parallel enzyme systems (amino acid and diamine oxidases) Cu(II) seems to be required.
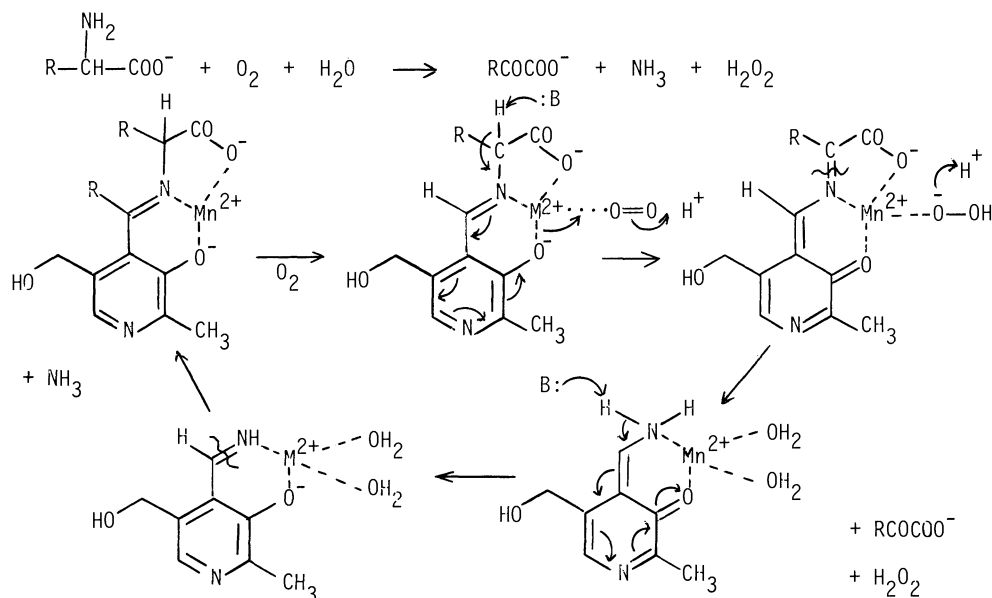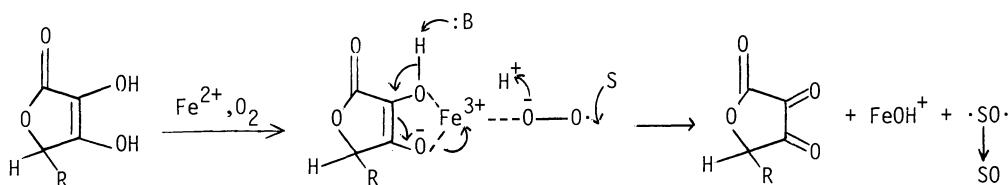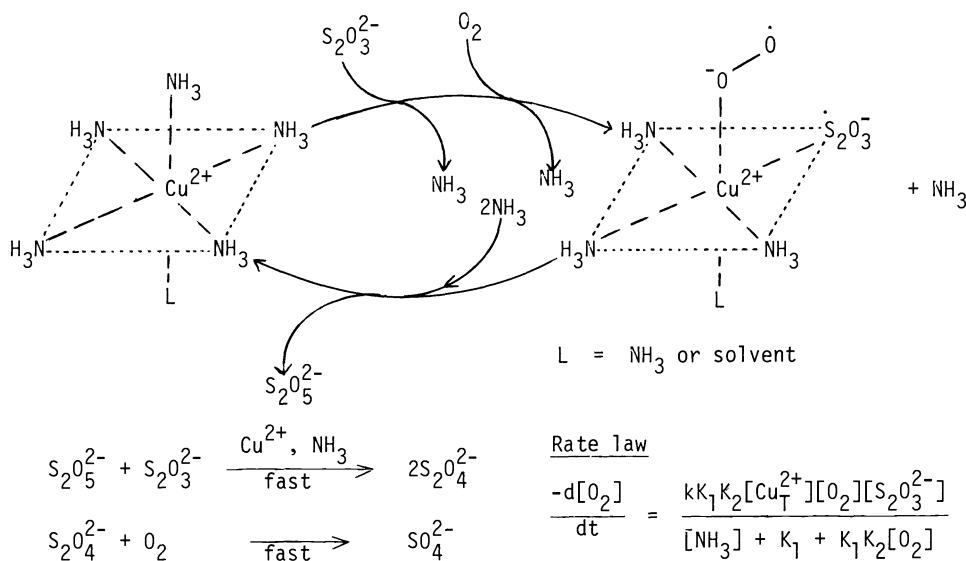

Scheme I. Oxidation of amino acids

Udenfriend's system. Reaction systems consisting of ferrous ion, a chelating agent such as EDTA, and a reducing agent such as ascorbic acid, promote the catalytic insertion of dioxygen into aromatic compounds containing activating substituents, such as anisole, phenols and salicylic acid (Ref.23,24,25). In such systems half of the oxygen is inserted into the substrate and the other half is reduced to water while the ascorbic acid or other reductant undergoes a two electron oxidation. A free radical mechanism was first suggested by Udenfriend and coworkers (23,24,25). Later Hamilton (26) proposed a mechanism involving attack of the substrate by a metal dioxygen complex intermediate, illustrated in Scheme II. In the proposed reactive intermediate O-O bond fission occurs so as to transfer one oxygen atom to the organic substrate while the other remains coordinated to the metal ion. Two successive electron transfers from the reductant to the metal complex are necessary to regenerate the ferrous ion, thus continuing the catalytic cycle. An interesting aspect of the proposed mechanism is that the electron transfer from reductant to dioxygen is suggested as occurring in the coordination sphere of the metal ion and that the partial reduction of dioxygen converts it to a more reactive intermediate capable of insertion of an oxygen atom into the substrate.

Oxidation of thiosulfate. The oxidation of thiosulfate by molecular oxygen in the presence of a copper-ammonia catalyst has been shown by Byerley et al. (27) to be first order in copper-ammonia catalyst concentration, molecular oxygen, and substrate, suggesting that the rate determination electron transfer step occurs in a Cu(II)-ammonia thiosulfate-dioxygen complex, illustrated in Scheme III. The reaction rate is lowered by an excess of ammonia, as one would expect, because excess ligand would tend to displace the dioxygen and possibly the thiosulfate from the coordination sphere. The binding of the dioxygen shown in the Scheme is indicated as a resonance form which is dependent on the simultaneous coordination

of the thiosulfate.

Scheme II. Proposed mechanism for Udenfiend's system.

L = NH$_3$ or solvent

$$S_2O_5^{2-} + S_2O_3^{2-} \xrightarrow[\text{fast}]{Cu^{2+},\ NH_3} 2S_2O_4^{2-}$$

$$S_2O_4^{2-} + O_2 \xrightarrow[\text{fast}]{} SO_4^{2-}$$

Rate law

$$\frac{-d[O_2]}{dt} = \frac{kK_1K_2[Cu_T^{2+}][O_2][S_2O_3^{2-}]}{[NH_3] + K_1 + K_1K_2[O_2]}$$

Scheme III. Copper(II) ammine-catalyzed oxidation of thiosulfate.

PART II

Redox reactions of dioxygen complexes and organic substrates
Irreversible redox conversion of dioxygen complexes to inert species. A reaction that is
believed to be characteristic of nearly all dioxygen complexes is intramolecular redox re-
arrangement to produce inert species in which the metal ion is converted to a higher valence
form which is no longer capable of combining with dioxygen. This reaction takes various
forms depending on the metal ion and the coordinated ligand. Nearly all dioxygen complexes
of iron are rapidly converted in protic solvents to the familiar Fe(III) μ-oxo dimers.
Co(II) complexes in which the coordinated ligands are resistant to oxidative attack are con-
verted to the corresponding Co(III) complexes with the release of hydrogen peroxide. In many
cases, however, hydrogen peroxide is not formed but the ligand itself is attacked by oxygen
insertion or through a dehydrogenation reaction. The irreversible formation of inert
species may occur rapidly or very slowly depending on the nature of the ligand and the reac-
tion conditions. Many reactions of this nature in which the ligand undergoes oxidative attack
are quite complex and have not been thoroughly studied.

A reaction of this type which has been subjected to detailed studies is the irreversible
redox rearrangement of cobalt-dioxygen complexes of dipeptides (Ref.28,29,30). The peroxo
bridged binuclear cobalt complexes of dipeptides such as glycylglycine, glycylalanine, etc.
are converted to the very stable Co(III) bis-dipeptide complexes with the release of an
oxidized product formed by two-electron oxidation of the dipeptide. The reaction sequence in
Scheme IV represents activation of dioxygen by the metal ion since oxidation of the dipeptide
would not occur outside of the coordination sphere of the cobalt ion.

If dioxygen complexes of various metal ions are to be employed for the study of catalytic
oxidation and oxygenation reactions or for the study of stoichiometric redox reactions it is
necessary to first measure the rate of the intramolecular redox conversion to inert species
of the kind described above. Such studies are necessary to make sure that the lifetime of
the dioxygen complex will be sufficient for the proposed studies under the reaction condi-
tions to be employed. Only when such interferences can be ruled out it is possible to carry
out quantitative kinetic studies of the reactions of dioxygen complexes in solution.

$$Co^{2+} + 2\,L^- \;\rightleftharpoons\; CoL_2 \;\xrightarrow{2OH^-}\; Co(H_{-1}L)_2^{2-} \;\rightleftharpoons{\;O_2\;}\; [(H_{-1}L)_2CoO_2Co(H_{-1}L)_2]^{4-}$$

$$LOX^- + Co(H_{-1}L)_2^- \;\xleftarrow{\;L^-\;}\; Co(H_{-1}L)(LOX)^- + Co(H_{-1}L)_2^-$$

$$HL \;=\; H_2N\overset{\displaystyle R}{C}HCONH\overset{\displaystyle R}{C}HCHCOOH$$

$$HLOX \;=\; HN{=\!\!=}C\overset{\displaystyle R}{C}ONH\overset{\displaystyle R}{C}HCHCOOH$$

$$(R = H)$$

$$Co(H_{-1}L)_2^- \;=\;$$
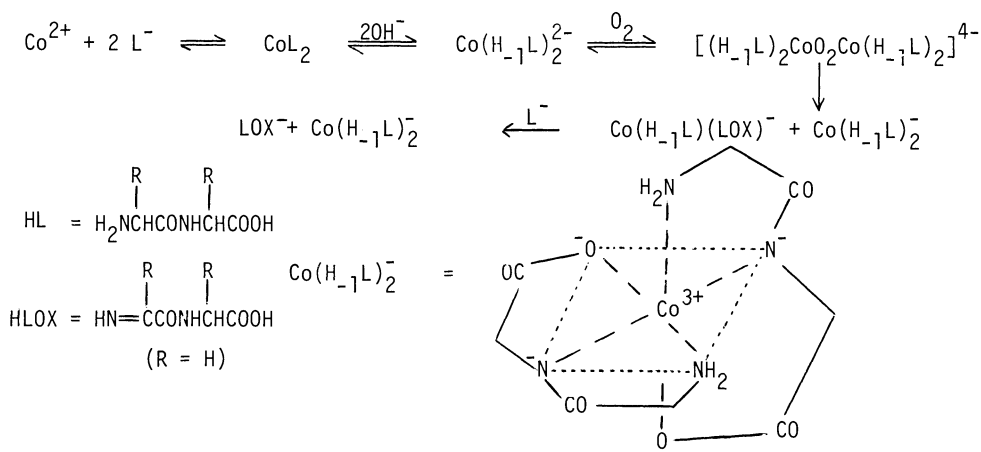
Scheme IV. Formation and redox rearrangment of cobalt dipeptide dioxygen complexes

Three types of reactions involving the dehydrogenation of coordinated ligands through dioxy-
gen complex formation are listed in Table 1. In addition to imine formation of coordinated
Co(II) dipeptides described above, the macrocyclic Co(II) Schiff base complex reported by
Black and Hartshorn (31) is converted by molecular oxygen to the corresponding corrinoid com-
plex by successive dehydrogenation reactions involving the removal of four hydrogen atoms
from the ligand. The two double bonds thus formed complete the conjugation between the
aromatic rings and thereby provide a macrocycle which is entirely conjugated with the excep-
tion of the ethylene bridge between adjacent donor nitrogen atoms.

Table 1. Dehydrogenation of coordinated ligands through dioxygen complex
          formation

Ligands	Metal complex or dioxygen adduct	Product
Dipeptides, HL $H_2N\overset{R}{C}HCONH\overset{R}{C}HCHCOOH$	$(H_{-1}L)_2Co^{3+}{-}\overset{^-O{-}O^-}{\cdots}{-}Co^{3+}(H_{-1}L)_2$	$HN{=\!\!=}C\overset{R}{C}ONH\overset{R}{C}HCHCOOH$ $Co(H_{-1}L)_2^-$
4-nitrogen macrocycle L = pyridine		
6-nitrogen-4-oxygen macro-cycle		

The six nitrogen, four oxygen macrocycle investigated by Nelson et al. (32) forms a bi-
nuclear Cu(I) complex which reacts with molecular oxygen to form a dioxygen adduct which
then undergoes four dehydrogenation reactions to produce four imine type double bonds in the
macrocylic ring. A reaction mechanism involving alternating aerobic and anaerobic steps was
suggested so that successive coordination of two oxygen molecules alternating with reduction
of each dioxygen through dehydrogenation steps yielded the final product indicated in Table
1. Evidence was also found for even further dehydrogenation beyond the formation of the
product shown, and it was suggested that some dehydrogenation of the ethylene bridging groups

also occurred, although this reaction was rather sluggish and incomplete.

Examples shown in Table 1 may very well be the beginning of a pattern of dehydrogenation reactions of coordinated ligands in dioxygen complexes. Apparently the building up of conjugated systems provides a low energy pathway for such dehydrogenation reactions and suggests additional ligands which probably should be examined for this type of behavior. Considerably more work is needed in this area of dioxygen complex chemistry.

Oxygen insertion in coordinated ligands of dioxygen complexes. Oxidative rearrangement of dioxygen complexes to form a higher valent metal complex species results in a two electron reduction of the coordinated dioxygen in binuclear complexes and in a one electron reduction of the dioxygen in the mononuclear complexes, resulting in the formation of coordinated peroxo and superoxo species respectively. It is these partially reduced dioxygen moieties that attack the coordinated ligands in cases where such ligands are susceptible to further oxidation. There are now a few examples that have been reported in which the attack involves insertion of an oxygen atom at a sensitive part of the ligand molecule. An interesting example of such a reaction is the oxidative rearrangement of the dioxygen complex which is formed by the reaction of oxygen with the meta-xylyl binucleating ligand N,N,N',N'-tetrakis[2-(2-pyridyl)ethyl]-α,α'-diimino-m-xylene[m-xyl(py)] reported by Karlin et al. (33). Although the oxygen complex was not isolated in this case the high probability of its formation is indicated by the fact that cobalt (Ref. 34) and copper (Ref. 35,36) complexes of related para xylyl systems react reversibly with dioxygen. The redox rearrangement of this binuclear dioxygen complex results in the formation of the bridging phenoxide group indicated in Table 2. It is suggested that part of the driving force for this reaction is the formation of a phenoxide oxygen donor at a position in which it strongly stabilizes the final Cu(II) dioxygen binuclear complex.

Table 2. Oxygen insertion in coordinated ligands through dioxygen complex formation

Ligand	Metal complex	Product
m-xylyl binucleating hexadentate ligand		
5,7,12,13-tetramethyl-2,3,9,10-dibenzo[14]-4,6,11,13-tetraene-N_4		
5,7-dimethyl-[14]4,7-diene-N_4		

Two additional examples of oxygen insertion into coordinated ligands involve oxidation of the oxygen complexes indicated in Table 2 to carbonyl derivatives (Ref. 37 & 38). In both cases the carbonyl formed is conjugated with double bonds already present in the molecule.

Oxidative rearrangement to inert complexes involving oxidation of central metal ions. An interesting exception to the patterns of behavior indicated in Tables 1 and 2 has been reported by Nelson (39). When the high spin $[Fe(II)-(2,2'-bi-2-imidazolylene)_3]^{2+}$ reacts with dioxygen in aprotic solvents the oxygen is reduced to water while four metal ions are oxidized to the ferric form with concomittant extraction of one proton from each of four coordinated ligands. The higher valent metal ion is stabilized by the additional charge formed through proton dissociation. The proposed reaction mechanism indicates donation of a proton from the coordinated ligand to the coordinated dioxygen moiety within the coordination sphere of the dioxygen complex. In this case the ligand is not actually oxidized but merely deprotonated, and four metal complexes are required for the conversion of a single dioxygen to water. Since the dioxygen complex formed is either mononuclear or binuclear it is obvious that several intermolecular proton transfers must take place to complete the reduction of one dioxygen complex.

Oxidation of organic substrates by dioxygen complexes
When the coordinated ligand in a dioxygen complex is more resistant to oxidation than an available substrate in the reaction mixture, the latter may be oxidized either through a dehydrogenation reaction or through oxygen insertion. This section describes a number of representative examples of this type of reaction.

Cobalt(II)-Schiff base complexes as catalysts. The dioxygen complexes that have been most widely investigated as oxidants and as catalysts for the oxidation of organic substrates by molecular oxygen are the Co(II)-Schiff base complexes of the type first investigated by Calvin (40). The use of these dioxygen complexes as oxidants for a wide variety of organic substrates has been studied in detail by Nishinaga and coworkers (41,42,43), and by others (44-47). The catalytic complexes investigated contain pentacoordinated and tetracoordinated cobalt as indicated in Scheme V. Typical reactions involve the oxidation of hindered phenols to the corresponding p-quinones, substituted indoles to o-formylaminoacetophenone derivatives, and 3-hydroxyflavones to the corresponding depsides. The oxidation of phenols occurs with single oxygen insertion and dehydrogenation and may be considered as models for monooxygenase enzyme systems. The oxidation of indoles and hydroxy flavones involve the insertion of both oxygen atoms of dioxygen and have been proposed as models of dioxygenase enzymes. A recent survey of the literature indicates that about sixteen Co(II)-Schiff base complexes have been studied as catalysts for the oxidation by molecular oxygen of a wide variety of substrates. In all a total of about one hundred and twelve individual oxidation reactions of this type have been reported.
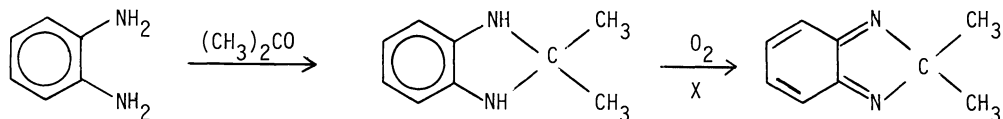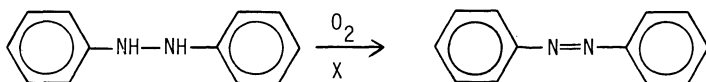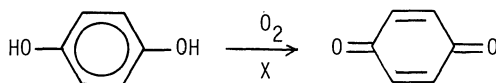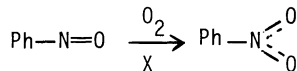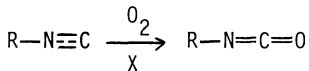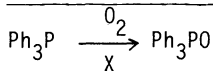
Cobaloxime(II)-catalyzed oxidations. Simandi and coworkers (48,49,50) have recently shown that cobaloxime(II) complexes show remarkable catalytic activity in the oxidation of organic compounds by molecular oxygen. The catalytic oxidation reactions reported thus far include both dehydrogenation and oxygen insertion reactions of the type indicated in Scheme VI. Cobaloxime(II) reacts with dioxygen in aprotic solvents to form mononuclear superoxo and binuclear μ-peroxo complexes (Ref.51). Although the exact species involved in the dehydrogenation reactions is somewhat in doubt, there can be no question about the involvement of cobaloxime(II) dioxygen complexes in this reaction. Simandi and coworkers (52) suggested the formation of an "oxenoid" species as the active intermediate in the oxygen insertion reactions indicated in Scheme VI. Although this is certainly a strong possibility, a reasonable alternative mechanism could involve the formation of the metal complex peroxo derivative of the substrate which would give rise to the final products by O-O bond fission, in accordance with the mechanisms of oxygen insertion described below.

Cobalt(II)-porphyrin complexes as catalysts. Recent work in the author's laboratory on the catalytic effects of metal porphyrins on the oxidation of di-t-butylphenol by molecular oxygen has revealed striking differences in the catalytic effects of cobalt(II) tetraphenylporphine and the corresponding complexes of Fe(III), VO(IV) and Mn(III). The kinetic data obtained (Ref.53) show that the cobalt(II)-TPP complex is much more effective as a catalyst than the corresponding complexes of other metal ions. The autocatalytic nature of the Co(II) complex, indicated by a very rapid increase in rate with time, indicates a possible free radical mechanism whereby the build-up of intermediate free radical species is necessary before the maximum rate is achieved. No such effects were observed for the porphyrin complexes of the other metal ions. The fact that the cobalt porphyrin complex is known to form a dioxygen adduct in solution, while the porphyrin complexes of the other metals would not form appreciable concentrations of such complexes, suggests that the difference in behavior may be due to formation of a dioxygen complex as the reactive intermediate. In addition to the formation of the quinone, there is a parallel reaction involving the formation of a coupling product from two phenoxide radicals, which involves a concomittant dehydrogenation to give diphenoquinone as the reaction product. The reaction mechanism proposed for this system is similar to the one previously suggested by Drago (45) for the oxidation of phenols by Co(II)-Schiff base complexes. The formation of the two oxidation products
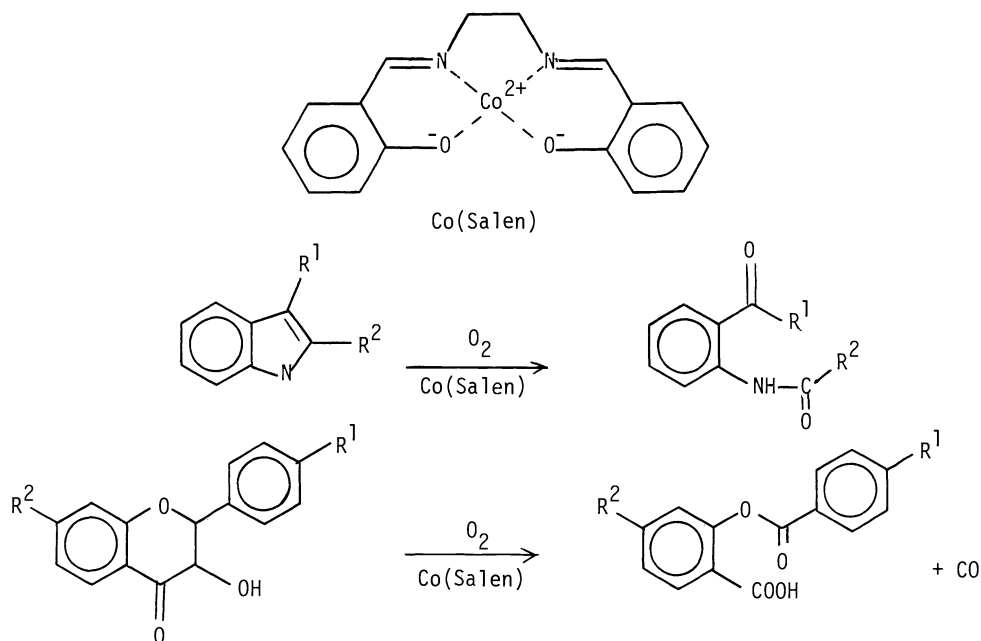
Co(Salen)

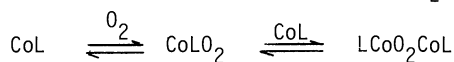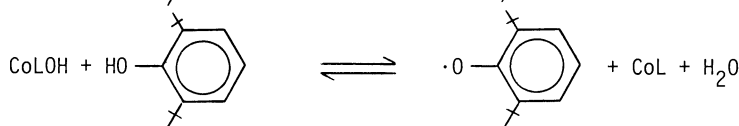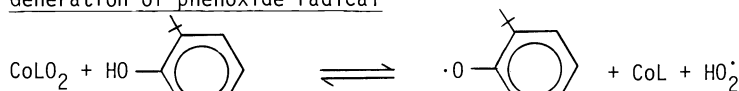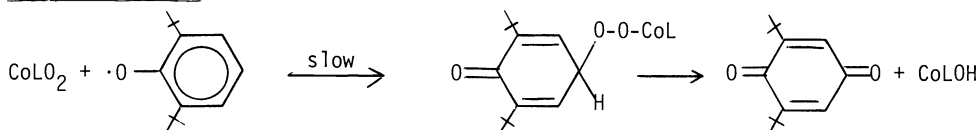Scheme V. Oxygenation of indoles and hydroxyflavones of Co(Salen)

Dimethylglyoxime, H_2L	Cobaloxime	Catalyst, X	Oxygen Complexes
H_3C, CH_3 (HO—N, N—OH)	$Co(HL)_2$	$Co(HL)_2B_n$ n = 1 or 2 B = Ph_3P, Py, Et_3N	$Co(HL)_2O_2B$ $B(HL)_2CoO_2Co(HL)_2B$

Dehydrogenation reactions

$$HO-\bigcirc-OH \xrightarrow[X]{O_2} O=\bigcirc=O$$

$$\bigcirc-NH-NH-\bigcirc \xrightarrow[X]{O_2} \bigcirc-N=N-\bigcirc$$

Insertion reactions

$$Ph_3P \xrightarrow[X]{O_2} Ph_3PO \qquad R-N\equiv C \xrightarrow[X]{O_2} R-N=C=O \qquad Ph-N=O \xrightarrow[X]{O_2} Ph-N\overset{O}{\underset{O}{\lessgtr}}$$

Scheme VI. Cobaloxime-catalyzed dehydrogenation and oxygen insertion

illustrated in Scheme VII indicates that the oxygen insertion reaction leading to the forma-
tion of the quinone requires a dioxygen complex as an intermediate whereas formation of the
coupling product does not require a dioxygen complex except for the initial formation of the
phenoxide radical. Further work on this system (Ref.53) showed that as the temperature is
increased there is very rapid decrease in the rate of formation of the quinone. It seems
reasonable to expect that increasing the temperature would decrease the concentration of
dioxygen complex intermediates present in solution because the dioxygen would tend to dissoc-
iate at higher temperature. This fact, and the observation that this kind of temperature
dependence was not observed for the coupling reaction, lends further support to the idea
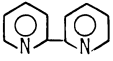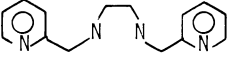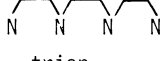that the dioxygen complex may provide the main pathway for oxygen insertion.
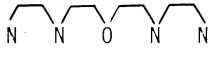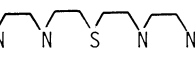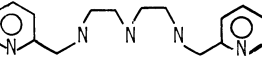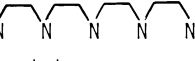
Dioxygen complex formation (TPP = H_2L)

$$CoL \rightleftharpoons[\quad]{O_2} CoLO_2 \rightleftharpoons[\quad]{CoL} LCoO_2CoL$$

Generation of phenoxide radical

$$CoLO_2 + HO-\text{(aryl)} \rightleftharpoons \cdot O-\text{(aryl)} + CoL + HO_2^{\cdot}$$

$$CoLOH + HO-\text{(aryl)} \rightleftharpoons \cdot O-\text{(aryl)} + CoL + H_2O$$

Oxygen insertion

$$CoLO_2 + \cdot O-\text{(aryl)} \xrightarrow{\text{slow}} \text{(dienone with O-O-CoL)} \longrightarrow \text{(quinone)} = O + CoLOH$$

Dehydrogenation (coupling)

$$2 \cdot O-\text{(aryl)} + \tfrac{1}{2} O_2 \longrightarrow \text{(coupled diquinone)} + H_2O$$
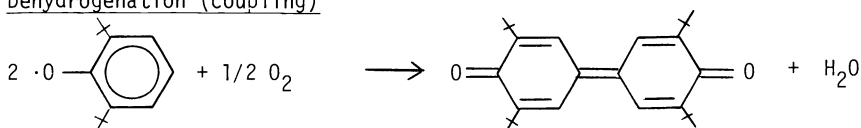
Scheme VII.   Co(II)-TPP-catalyzed oxidation of 2,6-di-_t_-butylphenol

Co(II)-polyamine complexes as catalysts. Oxygen complexes of a large number of polyamines and polyamino acid chelates of Co(II) are now known and their stabilities in aqueous solution have been measured (Ref.54). Recently the catalytic behavior of the bisdipyridyl cobalt(II)-dioxygen complex in the oxidation of ditertiarybutylphenol with molecular oxygen has been reported (Ref.55). The reaction was found to proceed through an intermediate dioxygen complex as illustrated in Scheme VIII to give the corresponding quinone (insertion) and the coupling (dehydrogenation) product. In this system the dioxygen complex is stable enough so that it may be isolated and studied separately; the kinetics of both stoichiometric and catalytic reactions were measured. The suggested reaction mechanism indicated in Scheme VIII is based partly on the kinetic data obtained and partially on other published work on the oxidation of phenols (Ref. 41 & 45). Although the mechanism indicated suggests that the reactive dioxygen complex is the μ-hydroxo-μ-peroxo dibridged species, the main form of the dioxygen complexes present, it is also possible that precursors of this complex could be the reactive starting materials for the oxidation process. The μ-peroxo complex without the additional hydroxo bridge may also be present in solution in appreciable amounts and is the main species present below pH 6. In addition, it would also be reasonable to consider a reaction mechanism involving dissociation of the binuclear dioxygen complexes to the mononuclear superoxo form as an initial step prior to the oxidation of the substrate.

Recently this investigation has been extended to a study of the kinetics of oxidation of ditertiarybutylphenol by molecular oxygen in the presence of several polyamine cobalt-dioxygen complexes differing considerably in stability and in the strength of metal-dioxygen bonding. Preliminary results of these studies are indicated in Table 3 (Ref.56). Although it had been expected that the more stable dioxygen complexes would be less reactive toward the oxidation of organic substrates both with respect to dehydrogenation and oxygen insertion, the results in Table 3 reveal a much more complex pattern of behavior. The bis(dipyridyl)-cobalt-dioxygen complex, which is relatively low on the stability scale is a fairly reactive catalyst. On the other hand, the μ-peroxo dicobalttetraethylenepentamine complex, which is one of the most stable investigated thus far, turns out to be the most reactive oxidant of those listed. A possible pattern suggested by the rather meager data thus far available seems to indicate that the dibridged complexes are less reactive as oxidants than are the mono-bridged binuclear species. This could mean that steric effects are very important in the determination of reactivity of binuclear dioxygen complexes. On the other hand, such results could also be interpreted in terms of a mechanism whereby the mononuclear species is the reactive oxidizing agent, and that the monobridged binuclear complexes dissociate more readily to the mononuclear species than do the dibridged forms.

Table 3. PolyamineCo(II)-catalyzed oxidation of ditertiarybutylphenol

Ligand	Metal complex	Formula of dioxygen complex	Oxygenation constant		Rate $\dagger$ constant $M^{-1} s^{-1}$
bipy	CoL_2^{2+}	$\left[CoL_2 \overset{OH^-}{\underset{\bar{O}-\bar{O}}{<}} CoL_2 \right]^{3+}$	$\dfrac{[Co_2L_4(OH)O_2][H^+]}{[CoL_2]^2[O_2]}$	-2.6	4.6×10^{-3}
pyen	CoL^{2+}	$\left[CoL \overset{OH^-}{\underset{O^--\bar{O}}{<}} CoL \right]^{3+}$	$\dfrac{[Co_2L_2(OH)O_2][H^+]}{[CoL]^2[O_2]}$	$-4*$	2×10^{-3}
trien	CoL^{2+}			6.1	0.2×10^{-3}
tren	CoL^{2+}			4.4	0.09×10^{-3}
taotd	CoL^{2+}			2.20	$-$
tattd	CoL^{2+}	$[CoL-\bar{O}-\bar{O}-CoL]^{4+}$	$\dfrac{[Co_2L_2O_2]}{[CoL]^2[O_2]}$	8.40	$-$
pydien	CoL^{2+}			11.4	1×10^{-3}
tetren	CoL^{2+}			15.8	9×10^{-3}

* Estimated; $\dagger$ 35°C, 95 wt.% methanol
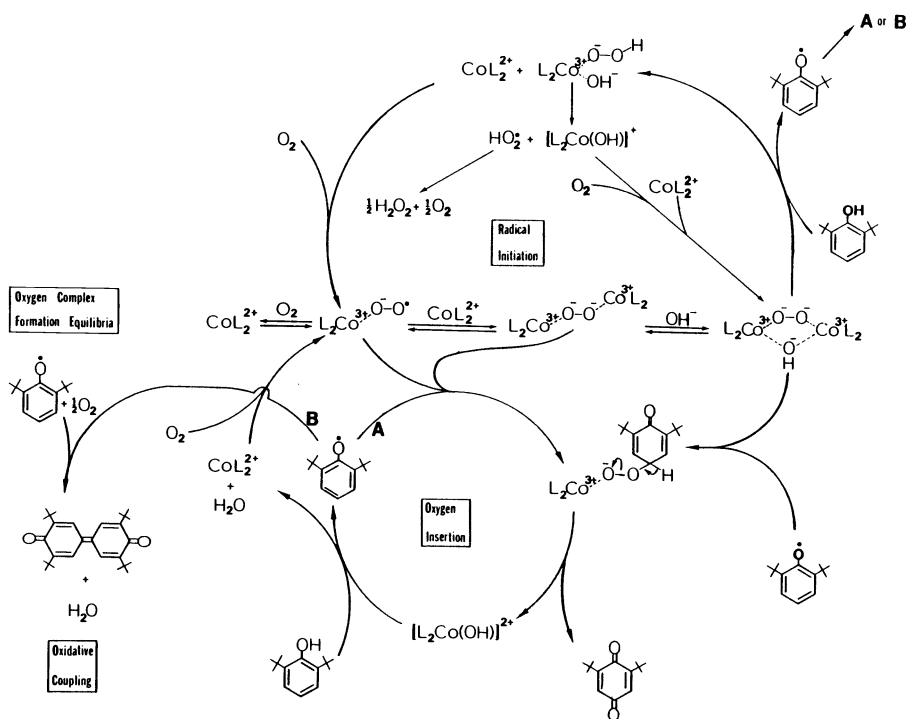
Scheme VIII. Proposed scheme for oxidation of 2,6-di-t-butylphenol by molecular oxygen, with tetrakis(dipyridyl)-μ-peroxo-μ-hydroxodicobalt(III) as a catalyst

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