Coordination Chemistry Reviews, 117 (1992) 185–213
Elsevier Science Publishers B.V., Amsterdam

Homogeneous metal-catalyzed oxidations by O_2

Russell S. Drago
Department of Chemistry, University of Florida, Gainesville, FL 32611 (USA)

(Received 31 October 1991)

CONTENTS

A. INTRODUCTION

The role of transition metal complexes in the activation of oxygen is complicated by the many different reaction pathways that are available. Widely differing conditions are required to oxidize selectively different substrates [1] to desired products, often with no discernible patterns in the role the metal plays. Detailed mechanisms generally are not known. In those cases where kinetic studies have been carried out, complicated reaction mechanisms are often needed to account for the reactivity. Thus, oxidation chemistry can appear to be a series of facts which one applies to the oxidation of new substrates in an Edisonian fashion.

Research in our laboratory on the selective activation of O_2 has led to an attempt to systematize the different fundamental pathways whereby transition metal complexes can catalyze the selective oxidation of organic substrates. Reactions will be grouped into classes based on the role of the transition metal complex without concern for the detailed reaction mechanisms of the particular substrates discussed. The ensuing classification can provide direction in the choice of metal complex catalysts for selective oxidations.

0010-8545/92/$15.00

One of the key features to understanding the reactivity of O_2 is its greater tendency to react as a two-electron oxidant rather than a one-electron oxidant. This reactivity is quantitatively manifested in its redox potentials [1] in acidic aqueous solution (0.12 V vs 0.78 V, Table I(a)) and in the OH bond energies [2] of HO_2 and H_2O_2 (Table I(b)). With an m.o. configuration of $\sigma_{2s}^2\pi^4\pi^{*2}$, the electron added in reducing O_2 to O_2^- or paired up in forming HO_2, in a hydrogen atom abstraction reaction, involves the doubly degenerate π^* orbital. In both types of reaction, the exchange energy of the half-filled π^* orbital is lost, leading to an endothermic contribution to the reactivity. As a result, O_2 is a poor initiator of reactions with diamagnetic organic substrates that can only provide one electron or one hydrogen atom per molecule. This property makes O_2 kinetically unreactive. When the substrate is a radical, e.g. $C_nH_{2n+1}\cdot$ or $H\cdot$, oxygen becomes very reactive as rapid spin pairing of electrons occurs, leading to the radicals $C_nH_{2n+1}O_2\cdot$ or $HO_2\cdot$.

Metal complexes can overcome this kinetic obstacle in a variety of ways. In this article, an attempt will be made to place the results of studies on oxidation reactions with O_2 reported in the literature and carried out in the author's laboratory into a general scheme. Oxidations that can be achieved with O_2 have been divided into five classes that are based on the role of the metal in the mechanism. This classification should help in choosing catalysts to carry out selective oxidations. No

TABLE I

Reduction potentials and bond energies

(a) *O_2 reduction potentials (standard state is O_2 (aq))*

Half-reaction (acid)	E^0 (V)		
	Acid		Base
$O_2 + H^+ + e^- \rightarrow HO_2$	0.12	0.78	−0.16
$HO_2 + H^+ + e^- \rightarrow H_2O_2$	1.44		+0.20
$H_2O_2 + e^- \rightarrow HO^- + HO\cdot$	0.71	1.76	0.87
$\cdot OH + e^- + H^+ \rightarrow H_2O$	2.81		
$O_2 + 4e^- + 4H^+ \rightarrow 2H_2O$	1.27		0.45

(b) *Bond energies*

Reaction	ΔH (kcal mol^{-1})
$O_2 + H \rightarrow HO_2$	59 (47)
$HO_2 + H \rightarrow H_2O_2$	90
$O_2^- + H \rightarrow HO_2^-$	80

attempt will be made to review the extensive literature in this area. Instead, reactions will be selected for discussion to provide the reader facility with the classification.

B. CLASSES OF METAL-CATALYZED REACTIONS

(i) Class I: metal-bound O_2

The discovery of cobalt(II) coordination compounds that reversibly bind dioxygen stimulated efforts to find substrates that react with the bound O_2. Substituted phenols are converted to quinones [3] as well as diphenoquinone, 3-substituted indoles are converted to ketoamides [4], flavanols are oxidized readily to CO and ring-opened products [5], while lignosulfonate and isoeugenol are converted to vanillin [6] by these systems.

The coordination of oxygen to cobalt, in our view, involves the spin pairing model [7]. An unpaired electron in an essentially d_z^2 orbital of a low spin*, five-coordinate cobalt(II) complex couples to an electron in the π^* orbital of oxygen to form a sigma bond, ψ_1, as shown in Fig. 1. The negative charge on the coordinated oxygen can vary from ~ 0.1 to ~ 0.8, depending on the ligand field strength of the attached ligands. As the ligand field strength increases, the energy of the cobalt d_z^2 orbital increases, the cobalt contribution to ψ_1 decreases and the oxygen contribution increases. This makes the bound O_2 more negative. The unpaired electron remains in a molecular orbital that is largely composed of oxygen a.o. coefficients independent of the charge on oxygen.

The basicity of the coordinated oxygen was demonstrated by measuring [8] the change in the OH stretching frequency of trifluoroethanol upon hydrogen bonding to the bound O_2. With Co(SMDPT) [SMDPT = bis(salicylidene-γ-iminopropyl)-methylamine], the terminal oxygen of the coordinated O_2 was found to be about as basic as the carbonyl oxygen of *N*,*N*-dimethylacetamide. This is a very considerable enhancement in basicity over that of free O_2, which is not basic enough to hydrogen bond to the alcohol. The basicity of the bound O_2 is considerably less than that of the superoxide ion, indicating that it is not an ionically bound superoxide ion. By spin trapping cobalt-bound O_2, it was shown [9] that the radical reactivity of oxygen is also enhanced by metal coordination. These experiments show that coordination of oxygen to cobalt(II) enhances both its nucleophilicity and radical reactivity.

The increased basicity and increased radical reactivity are key features for understanding [10,11] oxidations catalyzed by cobalt-bound O_2. The established reaction paths for this class involve hydrogen atom abstraction to initiate the reaction

---

* High-spin five-coordinate complexes also form O_2 adducts. These can be viewed in a thermodynamic cycle as proceeding through an endothermic step that converts the high-spin to a low-spin complex. The O_2 adduct contains one unparied electron.

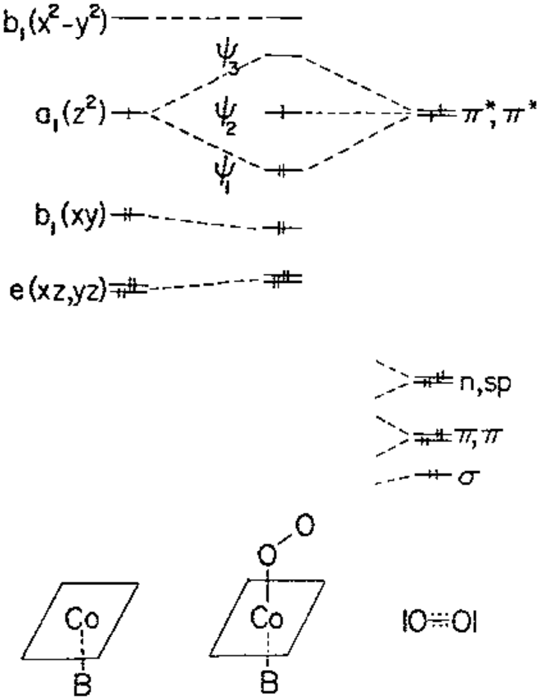


Fig. 1. The spin pairing model for bonding O_2 to Co(II) complexes.

and is shown in the equation

$$S{-}H + L_5CoO_2 \rightarrow S\cdot + L_5Co(III)O_2H \tag{1}$$
$$\hookrightarrow L_5Co(II) + HO_2$$

L will be used to indicate an unspecified ligand and S–H for hydrogen-containing substrates. After hydrogen atom abstraction by the metal bound O_2, $L_5Co(III)O_2H$ dissociates HO_2, regenerating the catalyst. HO_2 disproportionates rapidly into O_2 and H_2O_2. Reaction of the radical in eqn. (1) with L_5CoO_2 (or, in some cases, O_2) then occurs. The former is shown in the equation

$$S\cdot + L_5CoO_2 \rightarrow L_5CoO_2S \tag{2}$$

All known reactions involve substrates that are capable of hydrogen bonding to the bound O_2, e.g. substituted phenols. In the case of substituted phenol oxidation, enhanced radical reactivity of bound O_2 leads to a faster rate for eqn. (2) than that for radical coupling to form S_2. The subsequent reactivity of L_5CoO_2S to yield the observed products and regenerate the Co(II) complex is covered in Class IV. Thus, the full reaction involves a combination of Class I and Class IV chemistry for all known substrates. Many of the catalyzed oxidations that will be discussed involve a combination of classes because the metal complex plays more than one role.

In order for hydrogen atom abstraction to occur, the OH bond energy of $L_5Co(II)O_2{-}H$ must be greater than that of S–H. The O–H bond energy in $Co(SMDPT)O_2{-}H$ is estimated [3] to be about 87 kcal mol^{-1}. This can be compared with the 88 ± 1 kcal mol^{-1} bond energy of HOO–H and 89 ± 0.2 for $(CH_3)_3CO_2{-}H$. Coordination of O_2 to the metal removes the degeneracy of the oxygen π-system (i.e. the exchange energy is lost) and the $L_5Co{-}O_2$ reacts with substrates to form an OH bond with a strength comparable with that obtained when HO_2 reacts to form H_2O_2 (see Table 1). Table 2 lists S–H bond energies [11] for substrates that could be considered for an oxidation reaction. For many substrates with bond energies greater than 90 kcal mol^{-1}, thermodynamic considerations rule out oxidation by this path.

Oxidative stability of the catalyst for 300–500 turnovers can be attained, making this catalytic air oxidation a feasible synthetic reaction for a high-value product. Extension of this reaction type to substrates with stronger bonds requires that L_5MO_2 complexes be found that form stronger $L_5MO_2{-}H$ bonds. The possibility that metals other than cobalt(II) can form diamagnetic O_2 adducts that impart singlet oxygen-type reactivity to the bound O_2 also constitutes an area for future investigation.

(ii) Class II: metal oxo via dioxygen

Class II systems involve formation of a high-valent metal oxo species by reaction of a metal complex with O_2. Both oxygen atoms of O_2 are used productively to oxidize the substrate. We shall refer to catalysts that productively use both oxygen atoms of O_2 to oxidize the substrate as *dioxygenates*. The metal oxo complex undergoes oxygen atom transfer or other type reactions in the oxidation of organic substrates, regenerating the lower oxidation state of the metal. Formal oxidation state cycles of the metal from two to four, three to five and four to six are commonly involved.

The formation of high-valent metal oxo species from O_2 can proceed via several

TABLE 2

Substrate bond dissociation energies, ΔH_D (kcal mol^{-1})

$H{-}C_2H_5$	100 ± 1	$H{-}NHC_6H_5$	88 ± 2
$H{-}CHCH_2$	106	$H{-}OC_2H_5$	104 ± 1
$H{-}CH_2CHCH_2$	86 ± 1.5	$H{-}OC_6H_5$	87 ± 2
		$H{-}OC_6H_3(CH_3)_2$	87 ± 2
$H{-}C_6H_5$	111 ± 2	$H{-}SC_6H_5$	83 ± 2
$H{-}COCH_3$	86 ± .8	$H{-}CH_2OH$	94 ± 2
$H{-}CH_2C_6H_5$	88 ± 1	$H{-}CH(CH_3)OH$	93 ± 2

paths. A μ-peroxo dinuclear complex formed by two spin pairing interactions of O_2 with two metal complexes (eqn. (3)) decomposes to form the metal oxo as shown by the equation

$$M^{II}L_5 + O_2 \rightarrow L_5M^{III}{-}O_2 \xrightarrow{ML_5} L_5M^{III}{-}O{-}O{-}M^{III}L_5 \rightarrow L_5M^{IV}{-}O \tag{3}$$

This sequence of reactions has been observed [11] in the conversion of Fe(II)(TMP) to FeO(TMP)L where TMP is meso-tetramesityl porphyrinate. A similar reaction has also been shown [13] to form Ru(IV)O, which disproportionates to Ru(VI) dioxo complexes with tetramesityl porphinate ruthenium(II).

Complexes with III and IV oxidation states do not form stable O_2 adducts. These complexes are converted by oxygen to V and VI oxo complexes, respectively, by reactions other than eqn. (3). Possibilities include unstable O_2 intermediates or reactions of ion paired $O_2^{\cdot-}$ and O_2^{2-} species generated by metal to O_2 electron transfer. Another possibility involves oxidation of the metal by electron transfer, converting coordinated water to metal hydroxo and metal oxo systems.

$$M(H_2O)^{n-} \xrightarrow{-e^-} M(OH)^{(n+1)-} + H^+ \tag{4}$$

$$MOH^{(n+1)+} \xrightarrow{e^-} MO^{(n+2)+} + H^+ \tag{5}$$

In this dioxygenate class of reactions, all four electrons required to reduce O_2 are used productively in forming metal oxo compounds. In later sections, reactions will be discussed that utilize both oxygens in dioxygenate-type reactivity, but do not involve metal oxo species.

Several different reactions of high-valent metal oxo compounds with organic substrates can occur. Oxygen atom transfer from these high oxidation state complexes to alkenes can lead to epoxides. Transferring an oxygen atom off a metal center is an unusual reaction and semi-empirical INDO/1-type molecular orbital calculations were carried out to gain insight as to how this reaction may occur with Ru(IV)O complexes. Glyoxal diimine was used in the calculation to model phenanthroline, pyridyl and porphyrin ligands. The Ru(IV)O system is proposed [14] to be an inorganic analogue of O_2 with the higher energy metal oxo m.o.s having a $\sigma^2\pi^4\pi^{*2}$ configuration. Alkenes act as nucleophiles and undergo a non-concerted $(2+1)$ cycloaddition reaction leading to a bound epoxide [14], as shown in Fig. 2.

In the initial approach, the π orbital of ethylene donates electron density into Ru—O, forming a weak complex. As the distance decreases, the favorable pathway involves an off-center, canted approach such that the molecular plane of ethylene is not perpendicular to the Ru—O bond vector. An oxygen—carbon bond forms by pairing up a Ru—O, π^* electron with a π electron of ethylene. The structure of the system at this point is most easily visualized as an average of the structure in brackets in Fig. 2.

After the first bond is nearly completely formed, the partially positive charged,

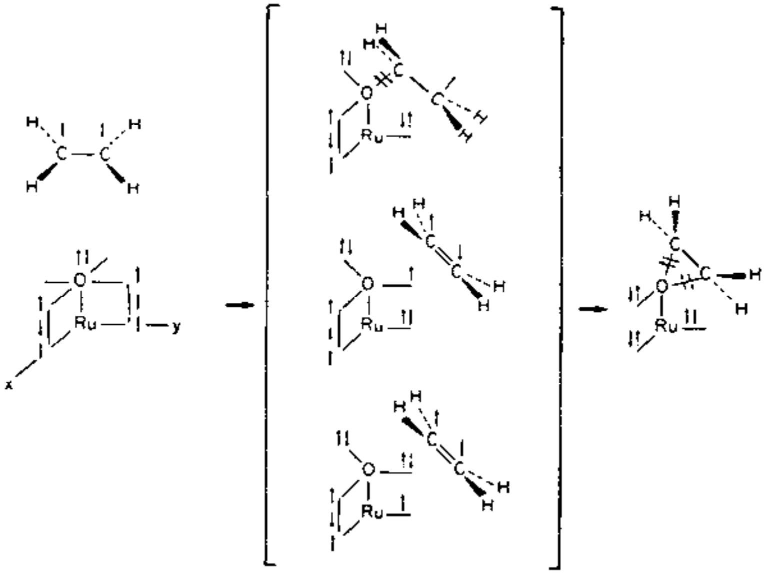


Fig. 2. A valence bond interaction diagram representing the formation of a bound epoxide.

radical carbon of the bound ethylene bonds to the second unpaired electron of the electron-rich Ru–O system, forming the second bond of the bound epoxide. The metal center is reduced to ruthenium(II) and *facilitates the reaction by acting as a receptor of the two electrons left over when the epoxide forms.* To complete the catalytic cycle, epoxide is eliminated and the reduced metal complex is reoxidized to the metal oxo by O_2. Stereochemistry is largely maintained in this mechanism because of the partial carbon–carbon double bond remaining in the species formed after the first carbon–oxygen bond forms. Retention of stereochemistry is observed experimentally in the epoxidation of both cis and trans β-methyl styrene.

The concerted (2+1) cycloaddition and the (2+2) oxometallocycle are calculated to be very energetically unfavorable pathways. The MO results are consistent with the application of Woodward–Hoffman rules to this system [14(b)].

Dioxoruthenium(VI) complexes may have the two oxygens in a cis or trans orientation in six-coordinate complexes with the trans usually being more stable. The reaction of the *trans*-$Ru(O)_2$ complex with ethylene is found by INDO/1 to proceed in a similar fashion [15(a)] to the Ru(IV)O system, leading to a bound epoxide. With Ru(IV)O being analogous to O_2, the *cis*-dioxo complex is analogous to ozone. The *cis*-$Ru(O)_2$ complex is found to undergo a concerted (3+2) cycloaddition [15(a)] with alkenes, leading to a Ru(IV) dioxometallocycle, intermediate $\overline{ORu(IV)OCH_2CH_2}$. As shown in the correlation diagram in Fig. 3, this is an allowed reaction. The dioxo metallocycle is in a deep potential well relative to ruthenium-oxo-epoxide. Thus, this intermediate reacts by cleaving the carbon–carbon bond, forming two carbon–oxygen double bonds and reducing the metal

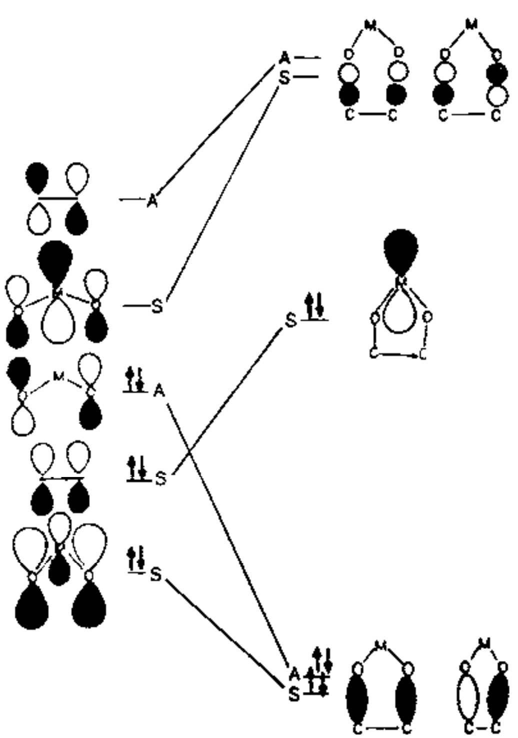


Fig. 3. Orbital correlation diagram for the [3+2] addition (or 1,3-dipolar addition) of ethylene to a cis-RuO_2^{2+} fragment. S and A correspond to symmetric and antisymmetric orbitals.

oxidation state by two. This accounts for the large amount of benzaldehyde and acetaldehyde observed in the catalytic oxidation of *trans-β*-methylstyrene by *cis*-$[-Ru(dmp)_2(O)_2]^{2+}$, where dmp is 2,9-dimethyl-1,10-phenanthroline. Cleavage products are observed in the non-catalytic oxidation of alkenes with RuO_4.

The path followed [15(b)] in the oxidation of alkanes by metal oxo complexes depends upon the electrophilicity (acceptor properties) of the metal oxo bond. The mechanism involves varying contributions of two extreme paths which involve hydrogen atom abstraction (A) and oxygen atom transfer (B). These two paths and one of several possible concerted paths (C) are shown in Fig. 4.

The hydrogen atom abstraction path (A) involves formation of a radical pair [M—O—H, $\cdot CH_3$], which collapses to a bound methanol by radical attack on the oxygen [15(b)]. The oxygen atom transfer path (B) involves C—O bond formation resembling an S_N2 transition state [15(b)]. For the same reasons that protonation occurs perpendicular to the sigma bond when CH_5^+ is formed, electrophilic M—O bonds interact perpendicular to the C—H sigma bond (Fig. 4, B). A linear structure results when C—H bonds (e.g. $CHCl_3$) react with nucleophiles to form three-center, four-electron hydrogen bonds. For this reason, an M—O bond that is not as electro-

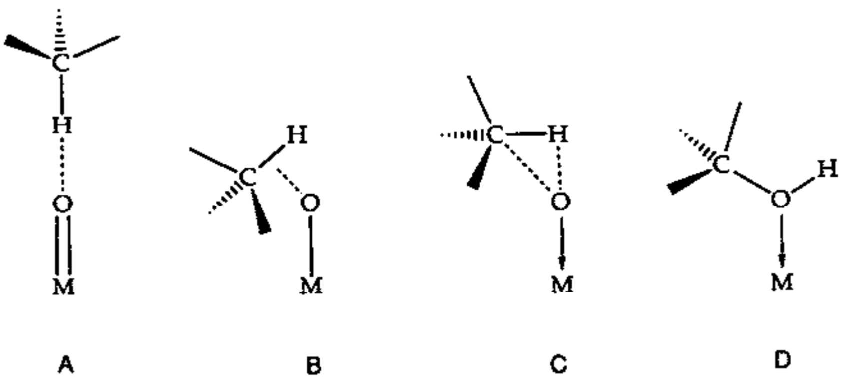


Fig. 4. Paths for the oxidation of alkanes. A, Hydrogen atom abstraction; B, Oxygen atom transfer; C, a concerted path; D, the product-bound methanol.

philic has a greater contribution from path A, and is more radical in nature [15(b)]. The porphyrin complexes FeO(P)(SH) and MnO(P)Cl, where P is a porphyrin, are generated from oxygen atom transfer reagents [16,17]. Hydrocarbon oxidations with these complexes are less concerted and resemble path A. The more electrophilic $MnOP^+$ is more concerted, resembling path C. As the strength of the axial ligand is increased in MnOPX, the reaction becomes more like path A, and more products from radical reactions with the solvent or axial ligand are observed [16]. The oxygen of M–O must be very electrophilic for either of these reactions to occur. The differences discussed here represent slight changes in oxygen electrophilicity.

Alcohols are oxidized with Ru(IV) oxo complexes [18(a)]. Calculations [18(b),(c)] indicate that the alcohol coordinates to the metal, expanding the coordination number to produce a d^4, seven-coordinate complex. For coordination number seven, the d-orbitals consist of two low-energy d orbitals and a higher energy set of three d orbitals. The CH_n group bound to oxygen of the coordinated alcohol can be oriented so as to form a five-membered ring, RuO···HCO, with a weak RuO···HC bond (see Fig. 5). With alcohol activation by coordination, this configuration undergoes H atom transfer concurrent with or followed by electron transfer and proton loss to form the aldehyde. A calculated [18(b),(c)] activation energy of 16 kcal mol^{-1} for this step agrees with the experimental value of 14 ± 2 kcal mol^{-1}. The proton reacts with the metal hydroxide formed from H atom transfer to produce coordinated

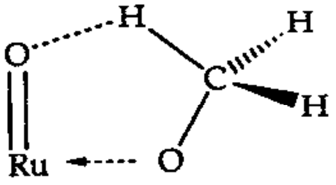


Fig. 5. The coordinated methanol intermediate in metal oxo alcohol oxidation.

water. The aldehyde is eliminated from the reduced metal complex because d^6 is not a favorable electronic configuration for coordination number seven and the aldehyde is a poor ligand. This mechanism combines alcohol coordination with the C–H activation mechanism discussed for hydrocarbons.

Different subtleties will exist in the mechanistic details of these reactions as the substrate varies. The above schemes gloss over these details, are intended to generalize metal function and lead to working models for catalyst selection.

Specific examples of reactions utilizing O_2 that fall into Class II are relatively few. Groves et al. [13] report a ruthenium(II) porphyrin complex that reacts with O_2 to form the Ru(IV)O and *trans*-Ru(VI)(O)$_2$ complex. This system is a catalyst for the selective aerobic oxidation of norbornene to epoxide. Ellis and Lyons [19] have reported that Mn(TPP)N_3, where TPP is meso-tetraphenylporphyrinate, and the pentafluoro analogue, Mn(TFPP)N_3, catalyze the reaction of O_2 with isobutane to produce isobutanol with dioxygenate results. The TFPP ligand forms iron(III) complexes, Fe(TFPP)N_3, [Fe(TFPP)]$_2$O or Fe(TFPP)OH, that are active catalysts for the oxidation of isobutane and propane by O_2. Further work is needed to verify the assignment of these systems to Class II. They may well belong to Class IV(a). In later sections, we will discuss other paths for obtaining dioxygenate activity that do not involve high valent oxo species.

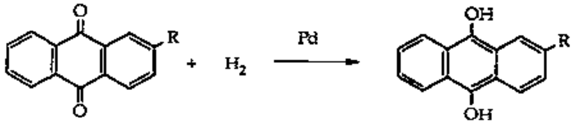
(iii) *Class III: metal oxo via peroxides*

For reactions in this class, either kinetic or thermodynamic factors prevent O_2 from converting the low oxidation state complex $M(N)$ to the high oxidation state $M(N+2)$. However, the oxidation does occur with the stronger oxidants hydrogen peroxide or alkyl hydroperoxides. Thus, if a sacrificial reducing agent is available to convert oxygen to hydrogen peroxide or an alkyl hydroperoxide (often, but not necessarily, metal-complex catalyzed), the high oxidation state metal oxo species can form and undergo the oxidation reactions with organic substrates discussed in the Class II section. With two oxidizing equivalents of the O_2 molecule reacting with the sacrificial reducing agent to form the peroxide, only one of the oxygen atoms (two oxidation equivalents) of O_2 is available for productive substrate oxidation. The system functions as a monooxygenate. These reactions take advantage of the stronger oxidizing ability of H_2O_2 than O_2 (Table 1), to oxidize lower-valent metal complexes to metal oxo species. The monooxygenase enzymes are thus candidates for this class, if they involve metal oxo oxidants.

We shall first consider reactions to form hydrogen peroxide and alkyl hydroperoxides, followed by their reactions with metals. Oxygen is converted to H_2O_2 directly by a variety of reducing agents, BH_4^-, NADH and substituted anthraquinol (eqn. (6)). The latter forms the basis for commercial, catalytic production of H_2O_2 from H_2 and O_2 by catalytically reducing the quinone back to the quinol (eqn. (7)) [20]. DuPont has recently patented [21] a process for the direct conversion of H_2 and

O_2 to H_2O_2 with Pd on an adsorbent carbon support. These reactions provide a way to activate O_2 by forming H_2O_2.

(6)



(7)

Transition metal ions with accessible oxidation states that differ by two, e.g. Ru(I), Ru(III); Co(I), Co(III), can also reduce O_2, leading to metal-bound peroxo complexes. These O_2 adducts react with water or acid, leading to H_2O_2 or M−OOH species [22,23]. Metal-hydrido species can also insert [24] O_2 to form MOOH complexes. It is also possible to reduce metal–O_2 adducts to H_2O_2 or M−OOH species with one-electron reducing agents [3,25]. All of these reactions represent possible reaction types for the catalytic reduction of O_2 in Class III systems.

Several organic substrates react with O_2 at elevated temperatures to form alkylhydroperoxides, ROOH. Isobutane [26], ethylbenzene [26] and *N*-methyl pyrrolidone [27] are examples. The latter reaction occurs at 75°C under a few atmospheres pressure of O_2. Metal-catalyzed oxidations of amides and lactams with O_2/H_2 mixtures [27(b)] or peroxides [27(c)] form amide hydroperoxides. Insertion of O_2 into a metal alkyl ($MR + O_2 \rightarrow MOOR$) [28], alkylation of metal-peroxo compounds [29] and the reaction of CoO_2 with a substituted phenol [3,30] all lead to metal alkylperoxo complexes. If the peroxides, once formed, react with the metal to produce oxo complexes, the reaction is assigned to Class III. As we shall see, Class IV-type reactions can lead to metal catalysis of alkylhydroperoxide formation, making some of these reactions a combination of Class III and Class IV.

Most first row transition metal ions in aqueous solution react with H_2O_2 by catalyzing the decomposition of H_2O_2 into H_2O and O_2.

$$2H_2O_2 \rightarrow 2H_2O + O_2 \qquad (8)$$

The enthalpy for hydrogen peroxide decomposition into water and oxygen (eqn. (8)) is 25 kcal mol^{-1}. The reduction potentials [30] for H_2O_2 behaving as an oxidizing and reducing agent in acidic solution are given in Table 3 as

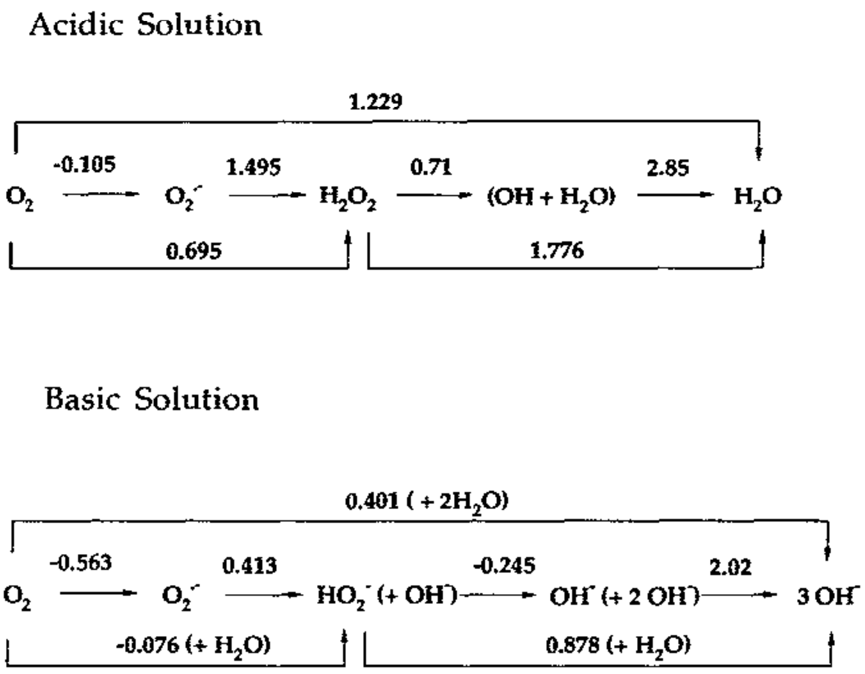
$$H_2O_2 + 2H^+ + 2e^- \rightarrow 2H_2O \qquad E^0 = 1.78\ V \qquad (9)$$

$$O_2 + 2H^+ + 2e^- \rightarrow H_2O_2 \qquad E^0 = -0.70\ V \qquad (10)$$

Metals that have stable oxidation states that differ by one (Mn^{2+}, Fe^{3+}, Cu^{2+}) are

TABLE 3

Redox potentials for oxygen species[a]



[a] From ref. 2. These values differ from those in Table 1 because of standard state differences.

very effective catalysts for the decomposition of hydrogen peroxide. The metal functions as both an oxidizing and reducing agent in the catalyzed decomposition mechanism

$$2H^+ + H_2O_2 + 2M(II) \rightarrow 2M(III) + 2H_2O \tag{11}$$

$$H_2O_2 + 2M(III) \rightarrow 2M(II) + O_2 + 2H^+ \tag{12}$$

Redox potentials involving other species formed in the reduction of O_2 are shown in Table 3. The detailed mechanism for H_2O_2 decomposition involves forming these species and hydroxyl radicals.

When H_2O_2 is decomposed by metals in the presence of organic substrates, some of the hydroxyl radicals react with the substrate. This reaction, called Fenton chemistry [31], belongs to Class IV. More effective utilization of H_2O_2 occurs if H_2O_2 can be used efficiently to form high-valent metal oxo species instead of the oxidized metal being reduced by H_2O_2 in the second step of the decomposition cycle (eqn. (12)). For example, in acetonitrile solution, H_2O_2 is reported [32] to convert $Fe(ClO_4)_2$ into Fe(IV)O. Surprisingly, no reaction is reported [33] when H_2O_2 is added to $[Ru(II)(bipy)_2(H_2O)_2]^{2+}$. A macrocyclic complex of ruthenium(II) is converted [34] to the dioxo complex by H_2O_2. Efficient utilization of H_2O_2 is observed in the oxidation of $[Ru(II)(dmp)_2(H_2O)_2]^{2+}$ to the mono-oxo and dioxo complex [35]. Cr(TPP)Cl reacts with hydrogen peroxide or alkyl peroxides to form CrO(TPP)Cl [36]. Reviews on the generation of high-valent metal oxo species with hypochlorite, iodosobenzene, amine oxides and peracids also exist [37].

One can envision oxidation paths with H_2O_2 that lead to metal oxo species as proceeding through the oxidation of coordinated water according to eqn. (4) and (5). Another path involves formation of a μ-peroxo species.

$$2M{-}OH + HOOH \rightarrow 2H_2O + M{-}O{-}O{-}M \tag{13}$$

As described in the Class II discussion, the μ-peroxo complex can decompose into high-valent metal oxo compounds.

Sodium borohydride, ascorbic acid, H_2/colloidal Pt [38(a),(b)] and Fe^{3+}/Zn/methyl viologen [40(b)] are reported [38] to reduce oxygen and form metal oxo, cytochrome P-450 type intermediates [37–39], which would put the reactions in Class III. In both the model and enzyme [39] chemistry, it is difficult to determine which of the above paths lead to the high-valent, metal oxo complex. Most articles [39,40] on P-450 and its models utilize a path that follows eqn. (14)–(17) of Scheme 1. An iron(II) complex first binds O_2, and then is reduced with a sacrificial reducing agent such as NADH (nicotinamide adenine dinucleotide) to form an iron(III) peroxo complex (eqn. (14)). Decomposition of the peroxo complex occurs to form a porphyrin cation radical (P·) iron(IV) oxo species (eqn. (15)) that oxygen atom transfers to substrate forming iron(III) (eqn. (16)). The iron(III) complex is reduced to iron(II) (eqn. (17)) which binds O_2 and repeats the cycle.

$$Fe(II)(P) + O_2 \rightarrow Fe(P)O_2 \xrightarrow[H^+]{+e^-} Fe(III)(P)O_2H \tag{14}$$

$$Fe(III)(P)O_2H \xrightarrow[-H_2O]{+H^+} Fe(IV)O(P\cdot)^+ \tag{15}$$

$$Fe(IV)O(P\cdot)^+ + S \rightarrow SO + Fe(III)(P)^+ \tag{16}$$

$$PFe(III)^+ \xrightarrow{+e^-} PFe(II) \tag{17}$$

Scheme 1. For clarity, the porphyrin ligand is abbreviated by the symbol P and S refers to substrate.

If H_2O_2 is used instead of O_2, the sacrificial reducing agent is not required for catalytic oxidation. This reaction [38,39], referred to as the hydrogen peroxide shunt, involves conversion of $Fe(III)(P)^+$ complex to $Fe(IV)O(P\cdot)^+$ by H_2O_2 (eqn. (18) in place of eqns. (14) and (17) in Scheme 1).

$$Fe(III)(P)^+ + H_2O_2 \rightarrow Fe(IV)O(P\cdot)^+ + H_2O \tag{18}$$

If, in the P-450 reaction, the O_2 were reduced to H_2O_2 in a separate two-electron reduction in the enzyme, then formation of the metal oxo by eqn. (18) would lead to an alternative P-450 mechanism, eliminating eqn. (14), (15) and (17). Excellent reviews of extensive research in this area of O_2 activation exist [38,40].

The $Ru(dmp)_2L_2^{2+}$ complex (where L is H_2O) is oxidized to metal oxo complexes through the III to the IV and VI oxidation states by alkyl hydroperoxides generated during the induction period in the oxidation of an alkene. The resulting VI oxidation state catalyst reacts with substrate and is reduced to the IV oxidation state (eqn. (19)). The Ru(IV)O is converted back to $Ru(VI)(O)_2$ oxidation state with dioxygen.

$$S + M(VI)(O)_2 \rightarrow SO + M(IV)O \tag{19}$$

If oxygen atom transfer to substrate occurs from the IV oxidation state, to generate a ruthenium(II) complex, alkyl hydroperoxides are needed to regenerate the IV oxidation state. This is a very interesting combination of a Class III reaction to form Ru(IV)O species followed by a Class II reaction to form the dioxo complex with O_2. Substrate oxidation occurs according to eqn. (19). When the hydroperoxide used to generate Ru(IV)–O gives the same product as that from substrate oxidation by $Ru(VI)(O)_2$, dioxygenate type activity results.

$$ROOH + M(IV)O \rightarrow ROH + M(VI)(O)_2 \tag{20}$$

$$M(VI)(O)_2 + R{-}H \rightarrow ROH + M(IV)O \tag{21}$$

(iv) Class IV: metal peroxo systems

This class of reaction differs from Class III because metal peroxo complexes are involved as reactive intermediates instead of high-valent metal oxo complexes. Hydroperoxo (MOOH) and alkyl peroxo (MOOR) complexes of the early transition metals are well characterized [41]. They can be generated from substrates by the reactions discussed in the previous section. In the case of cumene, *N*-methylpyrrolidinone, ethers and alkenes with allylic hydrogens, uncatalyzed reactions with O_2 lead to slow formation of alkyl hydroperoxides. The reactions to form alkyl hydroperoxides are catalyzed by metal complexes through radical chain mechanisms which belong to Class IV. Initiation can occur by an outer sphere electron transfer to produce the radical cation which then loses a proton to solvent or substrate to form R·.

$$M(III) + R{-}H \rightarrow M(II) + R{\cdot}H^+ \tag{22}$$

$$R{\cdot}H^+ \xrightarrow[B]{} R\cdot + BH^+ \qquad \text{(B = solvent, substrate or base)} \tag{23}$$

$$R\cdot + O_2 \rightarrow RO_2\cdot \tag{24}$$

$$RO_2\cdot + RH \rightarrow RO_2H + R\cdot \tag{25}$$

The subsequent reactions of R· shown in eqns. (24) and (25) lead to the hydroperoxide with the reduced M(II) being oxidized back to M(III) by O_2.

The initiation reactions shown in eqn. (26) can be eliminated on thermodynamic grounds. While typical R -H bonds in hydrocarbons are about 95 kcal mol^{-1}, metal–hydrogen bond strengths are generally less than 80 kcal mol^{-1}.

$$\mathrm{M(IV) + R{-}H \rightarrow M{-}H + R\cdot} \tag{26}$$

The alkyl hydroperoxide, metal alkylhydroperoxo complex or the metal peroxo complex can undergo three main types of reaction that constitute a further subdivision of this class of reaction. These are:

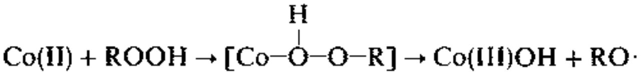
(1) Metal-catalyzed peroxide decomposition (Haber–Weiss or Fenton chemistry).

(2) Nucleophilic attack on peroxo or alkylperoxo complexes.

(3) Other reactions of metal peroxo intermediates.

(a) Metal-catalyzed peroxide decomposition

Alkylperoxides are decomposed by transition metal ions according to the Haber-Weiss mechanism [42] shown in Scheme 2.



$$\mathrm{Co(II) + ROOH \rightarrow [Co{-}\overset{\overset{H}{|}}{O}{-}O{-}R] \rightarrow Co(III)OH + RO\cdot} \tag{27}$$

$$\mathrm{Co(III)OH + ROOH \rightarrow Co(II) + ROO\cdot + H_2O} \tag{28}$$

$$\mathrm{RO\cdot + ROOH \rightarrow ROH + ROO\cdot} \tag{29}$$

$$\mathrm{Co(II) + ROO\cdot \rightarrow Co(III)OOR} \tag{30}$$

$$\mathrm{Co(III)OH + ROOH \rightarrow Co(III)OOR + H_2O} \tag{31}$$

$$\mathrm{2Co(II) + 3ROOH \rightarrow 2Co(III)OOR + ROH + H_2O} \tag{32}$$

$$\mathrm{Co(III)OOR \rightarrow Co(II) + ROO\cdot} \tag{33}$$

$$\mathrm{\longrightarrow \text{"}Co(III)O\cdot\text{"} + RO\cdot} \tag{34}$$

$$\mathrm{RO\cdot + RO_2H \rightarrow ROH + RO_2\cdot} \tag{35}$$

$$\mathrm{2ROO\cdot \rightarrow [RO_4R] \rightarrow O_2 + R'_2C{=}O + H^+} \tag{36}$$

Scheme 2. For clarity, the ligands on cobalt are not shown. R is a primary or secondary alkyl.

Equation (37) is proposed here as an alternative to eqn. (36).

$$\mathrm{Co(II) + ROO\cdot \rightarrow Co(III){-}O{-}OCHR'_2 \rightarrow Co(III)OH + R'_2C{=}O} \tag{37}$$

The Haber-Weiss mechanism can utilize various metal ions that undergo one-electron oxidation and reduction reactions.

The decomposition of a cobalt(III) *t*-butylperoxo complex was studied in the unreactive solvent benzene and in reactive hydrocarbon solvents [42(a)]. The former system indicated that thermal decomposition of the metal alkylperoxo complex leads to alcohol and ketone in a 1.8 : 1 ratio. Smaller amounts of the dialkylperoxo compound, one of the several minor products observed in metal-catalyzed peroxide decomposition, are found but not shown in the Haber–Weiss mechanism.

When the decomposition of Co—OOR is studied in reactive hydrocarbon solvents, oxidation of the hydrocarbon does not occur at an appreciable rate until 60°C, the temperature at which the cobalt alkylhydroperoxo complex decomposes. The main products of the decomposition of *t*-butylperoxo Co(III) in cyclohexane are cyclohexanone, cyclohexanol (~2 : 1 ratio) and substantial amounts of the dialkylperoxide, $C_6H_{11}O{-}OC(CH_3)_3$.

The homogeneous catalyzed oxidation of cyclohexane is an important commercial reaction from this class because the resulting ketone and alcohol are precursors for the synthesis of adipic acid, a nylon intermediate. Recently, it has been shown [42(b)] that this reaction can be initiated at lower temperatures than are possible with the commercial catalyst, cobalt(II)(octoate), by using cobalt trifluoroacetate. This led to studies whose results, in conjunction with those from the stoichiometric cobalt alkylperoxo decomposition [42(a)], support the following mechanism to account for the alcohol and ketone in the cyclohexane oxidation.

$$Co^{2+} \rightarrow Co[OX]$$

$$Co[OX] + C_6H_{12} \rightarrow C_6H_{11}\cdot + H^+ + Co^{2+}$$

$$C_6H_{11}\cdot + O_2 \rightarrow C_6H_{11}O_2\cdot$$

$$C_6H_{11}O_2\cdot + C_6H_{12} \rightarrow C_6H_{11}O_2H + C_6H_{11}\cdot$$

$$C_6H_{11}O_2H + Co^{2+} \rightarrow C_6H_{11}O\cdot + Co(III)OH$$

$$\begin{tikzcd}
Co(III)OH + C_6H_{11}O_2H \arrow[r] & Co(III)O_2H_{11}C_6 + H_2O \arrow[dl] \arrow[d] \arrow[dr] & \\
Co^{2+} + C_6H_{11}O_2\cdot & Co(III)OH + C_6H_{10}O & Co(III)O\cdot + C_6H_{11}O\cdot
\end{tikzcd}$$

$$C_6H_{11}O\cdot + H \rightarrow C_6H_{11}OH$$

$$Co(III)O\cdot + RH \rightarrow [Co(III)OH, R\cdot] \rightarrow Co(II) + ROH$$

Scheme 3. For simplicity, the ligands on cobalt are not shown. Co[OX] is an unknown oxidized cobalt species.

The reaction is carried out at low conversions because the alcohol and the ketone are more susceptible to oxidation in this system than cyclohexane.

Relative rates of substrate oxidation for this reaction type are, in general, proportional to bond strengths: tertiary CH > secondary CH_2 > primary CH_3. Alkenes with allylic hydrogens are readily oxidized by this mechanism. The stability of the allyl radical facilitates hydrogen atom abstraction. Reaction proceeds as shown above to form and decompose the alkylhydroperoxide of the alkene. The principal products are the allylic ketone and alcohol.

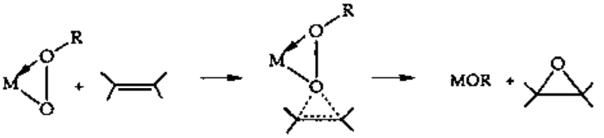
Recently, Shukla and Kahn have reported [42(c)] the specific oxidation of cyclohexane to cyclohexanol. Extensive thermodynamic and kinetic studies lead to a mechanism in which an M-peroxo dimer $(Ru(IV)EDTA)_2O_2$ abstracts a hydrogen atom from cyclohexane. The intermediate $[Ru(IV)OHEDTA] \cdot C_6H_{11}{}^+$ transfers a hydroxyl group to the radical to form the cyclohexanol.

The Mid-Century/Amoco process [43] for producing terephthalic acid involves air oxidation of *p*-xylene in acetic acid solvent. Mixed cobalt(II) and manganese(II) acetate complexes are used with a bromide promoter. The reaction is Class IV, involving benzylhydroperoxide decomposition to benzylalcohols and benzaldehydes with subsequent oxidation of these products to carboxylic acids.

As mentioned earlier, Fenton chemistry [31] generates hydroxyl radicals that react unselectively with organic substrates. Yields based on H_2O_2 are relatively low because of the competing decomposition reactions leading to O_2 and water.

(b) *Nucleophilic attack on peroxo and alkylperoxo complexes*

Reactions in this class involve substrate attack on a coordinated peroxo or alkylperoxo ligand and occur with high selectivity. High oxidation state, early transition metal catalysts, e.g. Mo(VI), lead to epoxides as products and late transition metals, e.g. Rh(III) lead to aldehyde or ketones. The former system forms the basis for the commercial production of propylene oxide from the reaction of propylene with alkyl hydroperoxides. Both homogeneous [28(a)] and heterogeneous [26(b)] catalysts are employed. Two alternative mechanisms have been proposed. One [44] involves nucleophilic attack of the olefin on the coordinated peroxo oxygen (eqn. (38)). A metal alkoxide and epoxide result with no change in the metal oxidation state.

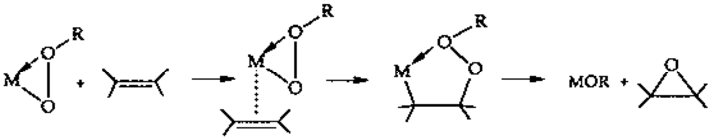


(38)

The metal peroxo species is regenerated via eqn. (39).

$$MOR + ROOH \rightarrow MOOR + ROH \qquad (39)$$

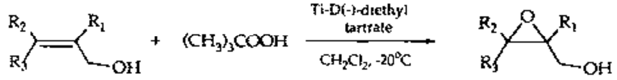
The other mechanism [45] involves a dipolar addition to form a peroxometallocycle which decomposes to an epoxide (eqn. (40)). The catalyst is again regenerated according to eqn. (39).



(40)

The epoxidation is stereoselective with cis-olefins yielding exclusively cis-epoxides and trans-olefins yielding trans-epoxides.

Optically active titanium diethyltartrate catalysts and *t*-butylhydroperoxide, *t*-BuOOH, effect asymmetric epoxidation of prochiral allylic alcohols in 70–87% yield with 90% or more enantiomeric excess. Interaction of the allylic alcohol functional group with titanium is important and alkyl- or aryl-substituted alkenes do not react.



(41)

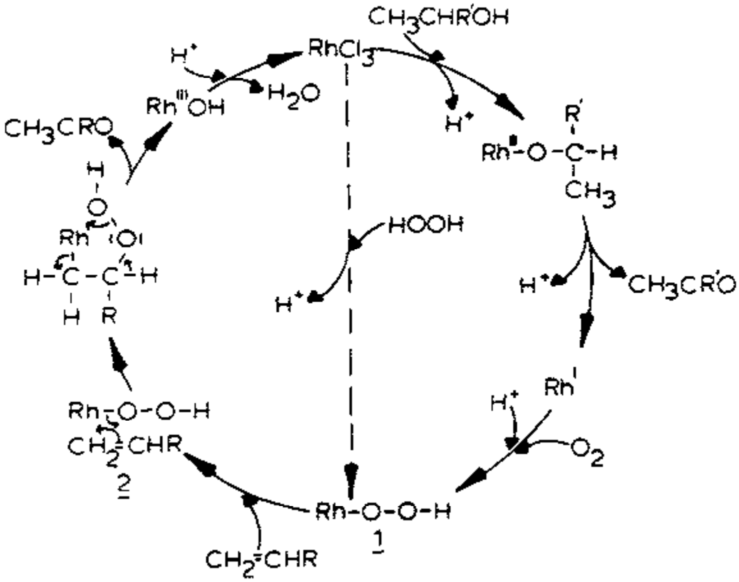
Alkyl hydroperoxides, with d^0 transition metal catalysts, can oxidize sulfides to sulfoxides or sulfones [46], tertiary amines to *N*-oxides [47] and primary amines to oximes [48].

Chiral, Schiff base, manganese complexes catalyze [49] the epoxidation of prochiral alkyl- and aryl-substituted olefins with high enantioselectivities. Iodosomesitylene was employed as the oxidant.

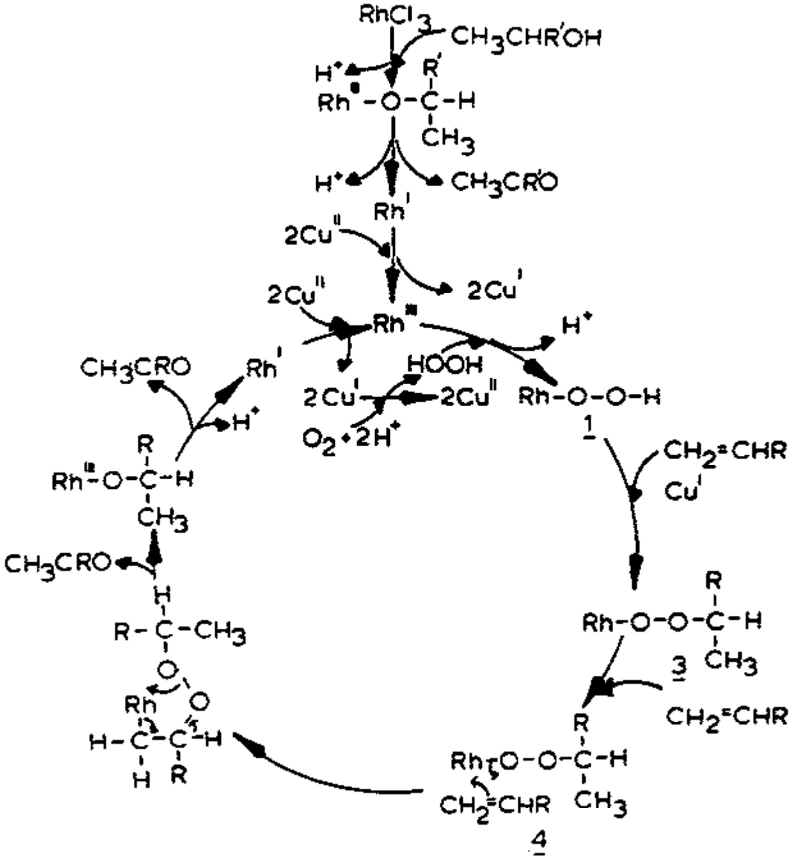
The selective oxidation of alkenes to ketones by O_2 is catalyzed by rhodium(I) or (III) in the presence of sacrificial reducing agents triphenylphosphine [50(a)] or reducing alcohol solvents [51] (i.e. monooxygenate activity). The mechanism [51] is shown in Scheme 4.

Mimoun et al. [51(b)] discovered that a copper(II)–rhodium trichloride co-catalyst led to selective oxidation of the alkene to ketone at room temperature without the need of a sacrificial reducing agent. Both oxygen atoms of O_2 are used to form product, leading to a novel dioxygenate-type reaction. Mechanistic investigations [51] led to the mechanism proposed in Scheme 5.

An alternate path [51] to Scheme 5 involves RhOOH reacting with alkene to generate aldehyde and Ru(III)OH. The latter undergoes Wacker-type chemistry (vide infra) to generate rhodium(I) and the second ketone.



Scheme 4.



Scheme 5.

Theoretical investigations have been carried out [52] aimed at answering the question, why do d^0 metal systems lead to epoxides and the late metal d^n systems lead to aldehydes or ketones? The problem was approached by considering similar peroxometallocycle intermediates for both reactions. As the peroxometallocycle, shown in eqn. (40), rotates to form an epoxide, interaction of the oxygen becoming the epoxide with the vacant t_{2g} orbitals of the d^0 metal provides a low-energy path for forming the new carbon–oxygen bond. This stabilization does not occur when the t_{2g} orbitals are filled in the late transition metals and ketone formation is a more favorable reaction pathway.

Several palladium, rhodium and ruthenium complexes catalyze reactions using peroxides or alkylhydroperoxides as the oxidant [53]. Anthracene, alkenes and alcohols are converted to ketones in rhodium(I)-catalyzed reactions with *t*-BuOOH [54]. Alkanes can be oxidized to ketones and alcohols [55]. Ru(bipy)$_2$(Ph$_3$P)(H$_2$O)$^{2+}$, where bipy is 2,2-dipyridyl, catalyzes the oxidation of cyclohexene by O$_2$ mainly to the allylic alcohol and ketone in a Class III or IV type reaction. Not enough information is available to classify these reactions as belonging to either Class III or IV.

(c) Other reactions of metal peroxo intermediates

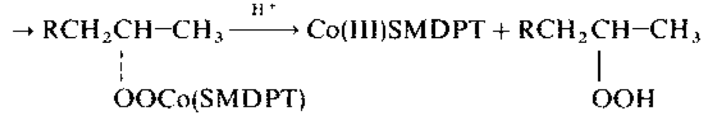
In Co(SMDPT)-catalyzed reactions [57] of alkenes with O_2 in reducing solvents, ketones and alcohols arising from oxidation of the internal carbon of the double bond are formed.

$$RCH_2CH{=}CH_2 \xrightarrow{O_2} RCH_2C(O)CH_3 \text{ and } RCH_2CH(OH)CH_3 \qquad (42)$$

Surprisingly, no products arising from oxidation of the allylic carbon are observed, i.e. $RCH(OH)CH{=}CH_2$ is not seen. One mole of solvent is oxidized per mole of product formed. The reaction does not occur with O_2 in a non-reducing solvent, but does occur in non-reducing solvents if H_2O_2 is used as the oxidant. This suggests a mechanism in which Co(III)SMDPTOOH forms, undergoes Markonikov addition across the double bond of an alkene and forms the metal alkylperoxo complex, $RCH_2{-}CH(CH_3)OOCo$ (eqns. (43) and (44)).

$$Co(III)SMDPT + H_2O_2 \rightarrow Co(OOH)SMDPT + H^+ \qquad (43)$$

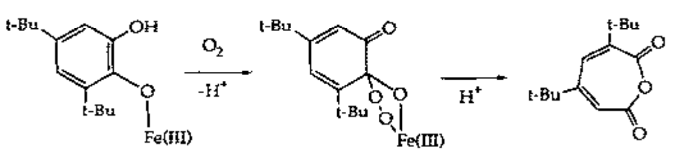
$$RCH_2CH{=}CH_2 + Co(OOH)SMDPT$$



$$\rightarrow \underset{\displaystyle OOCo(SMDPT)}{RCH_2\underset{|}{CH}{-}CH_3} \xrightarrow{H^+} Co(III)SMDPT + \underset{\displaystyle OOH}{RCH_2\underset{|}{CH}{-}CH_3} \qquad (44)$$

Haber–Weiss decomposition of the alkyl hydroperoxide leads to the observed products.

Catecholase is an iron(III)-containing enzyme that cleaves catechol into a dicarboxylic acid. Studies of model compounds [58] indicate a mechanism that involves O_2 attack on a monodentate catechol bound to iron(III). The two electron oxidation of the catechol leads to the "peroxo-quinone" complex shown in the equation



(45)

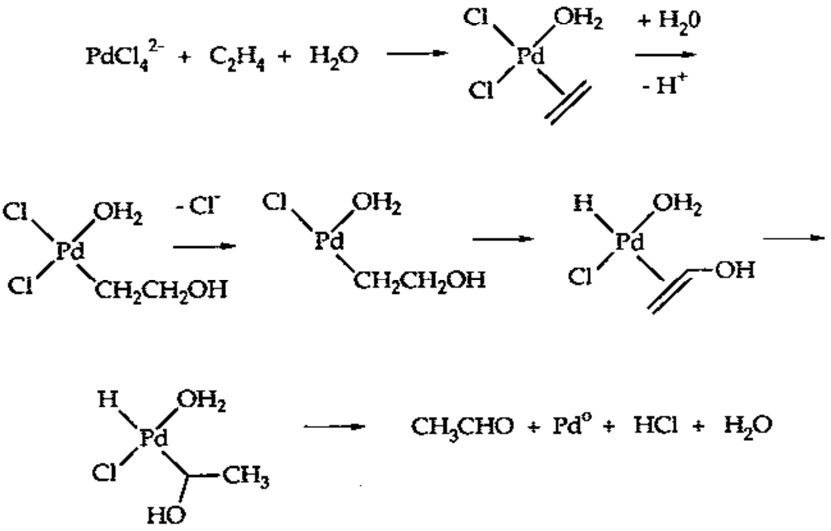
The muconic anhydride is then hydrolyzed to muconic acid. Other products are observed and the product distribution has been studied as a function of the Lewis acidity of the iron(III) center which can be modified by ligand variation. The reaction is similar to the Baeyer–Villiger lactonization of cyclic ketones by peroxo complexes of molybdenum [59].

Summaries [58,60(a)] of the extensive work that has been carried out on this system are available. A mechanism involving peroxide formation and an intermolecular mechanism for the oxidation of di-*tert*-butylcatechol is proposed [60(a)]. The solution and crystal structure of an iridium complex that is similar to the peroxo complex in eqn. (45), except that the semi-quinone is a bidentate ligand, has been achieved [60(b)]. The iridium complex does not catalyze the oxidative C—C cleavage of catechol but the rhodium analogue does.

This reaction is included in Class IV because it involves formation and reaction of a metal peroxo complex. Catecholase and the model systems provide interesting examples of ways to obtain dioxygenate activity out of peroxo intermediates. The substrate to be oxidized furnishes the two electrons to make peroxide, in contrast to phenol which can only furnish one, and the peroxide then carries out further oxidation.

(v) Class V: metal-centered oxidizing agents

A very important reaction in this category involves the Wacker process for oxidizing ethylene to acetaldehyde [61]. Nucleophilic attack on a coordinated alkene occurs to form a sigma-bonded hydroxyethyl.



(46)

$$2Cl^- + Pd^0 + 2CuCl_2 \rightarrow PdCl_4^{2-} + Cu_2Cl_2 \tag{47}$$

$$Cu_2Cl_2 + 2HCl + \tfrac{1}{2}O_2 \rightarrow 2CuCl_2 + H_2O \tag{48}$$

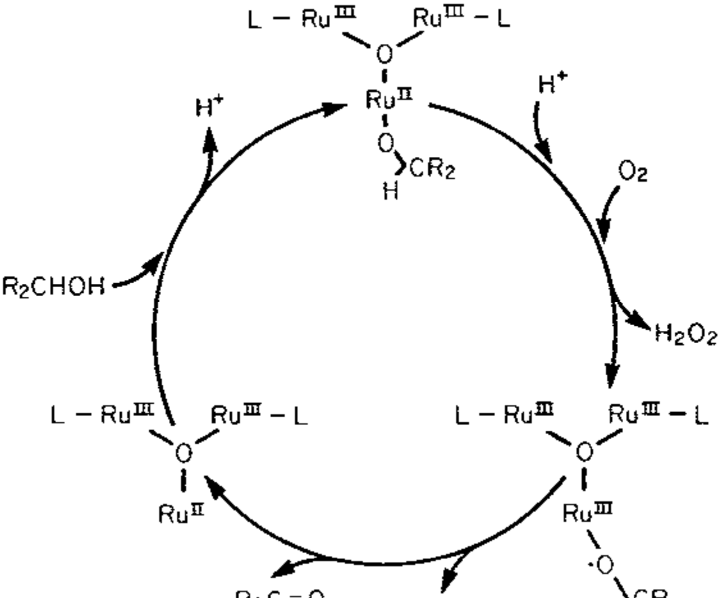
$$C_2H_4 + \tfrac{1}{2}O_2 \rightarrow CH_3CHO \tag{49}$$

Scheme 6.

With chloride dissociation, the hydroxyethyl undergoes a β-hydride elimination forming a π-bonded vinyl alcohol. At this point, the coordinated vinyl alcohol, which is a tautomer of acetaldehyde, can dissociate from the complex. It has also been proposed [61(b)] that re-addition of hydride to the vinyl alcohol gives the sigma-bonded complex, which β-eliminates to give the aldehyde. The hydrido-palladium complex reductively eliminates HCl to form Pd^0 (eqn. (46)). Before Pd^0 can aggregate to form the metal, it is reoxidized to Pd(II) by Cu^{2+} (eqn. (47)). Cu_2Cl_2 reacts rapidly with O_2 to reform Cu(II) (eqn. (48)). The net reaction is shown in eqn. (49). The reaction is assigned to Class V because the metal is doing the oxidation and the oxygen functions to regenerate the initial high oxidation state of the metal. Nucleophiles other than H_2O or OH^- can attack the coordinated alkene, making this a diverse reaction type. The stereochemistry of the nucleophilic addition has been studied in detail [62].

Methane has been oxidized [63] with H_2O_2 in a palladium-catalyzed reaction in trifluoroacetic acid. A Class IV mechanism has been ruled out in favor of an electrophilic attack on the C–H bond by Pd(II) forming $CF_3CO_2CH_3$ in CF_3CO_2H solvent. The role of H_2O_2 is to regenerate Pd(II), putting this reaction into the Class V category.

Another reaction that would be placed in this category involves the catalytic, selective oxidation of alcohols to aldehydes by O_2 using $Ru_3O(CH_3CH_2CO_2)_6(H_2O)_3{}^+$ as a catalyst [64]. The half-reaction for the oxidation of the alcohol to the aldehyde involves a two-electron oxidation with two protons liberated. The reaction is shown in Scheme 7.



Scheme 7.

In the second cycle involving another alcohol molecule, the H_2O_2 formed in the first cycle is the oxidant, instead of O_2, forming water as the product. Dioxygenate activity results. Oxidation occurs only when the ligand is in the coordination sphere of the metal. Normally, aldehydes are easier to oxidize than alcohols. Since alcohol is a better ligand than the corresponding aldehyde, selective oxidation to the aldehyde is attained.

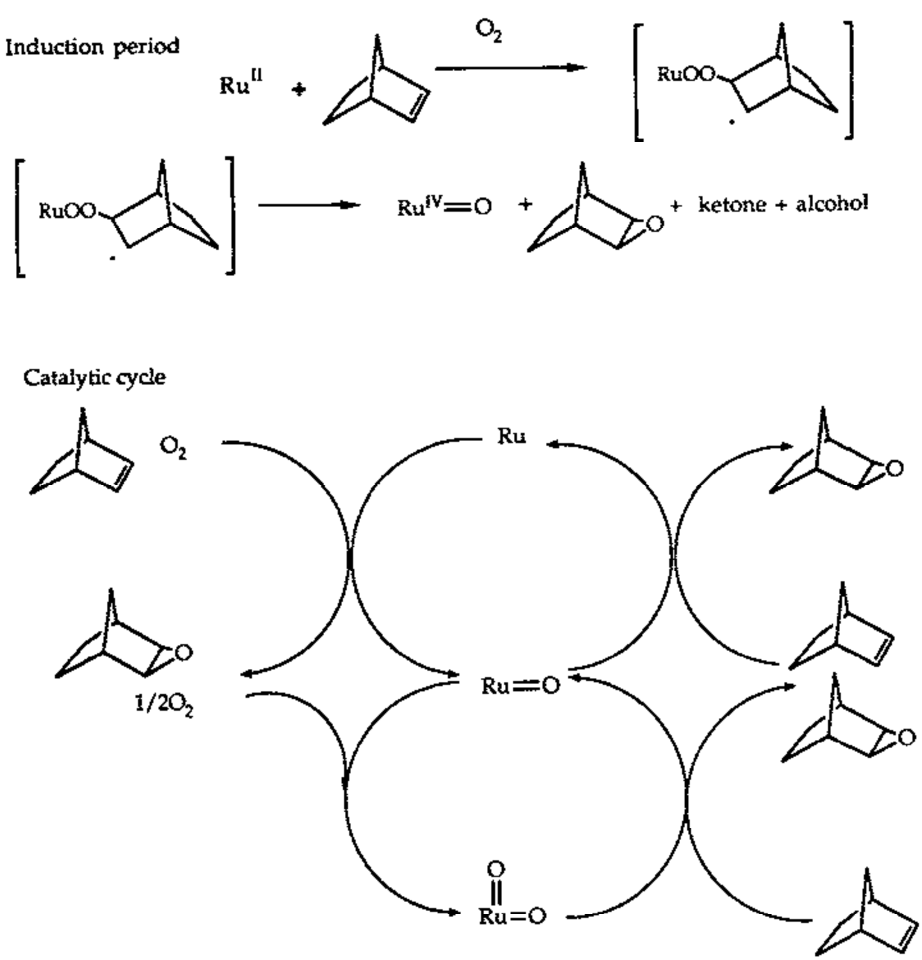
C. HOW TO CLASSIFY REACTIONS

One of the first steps in understanding an oxidation reaction involves distinguishing free radical mechanisms from non-free radical mechanisms. A number of tests have been proposed and discussed in detail [65]. They include product selectivity, regioselectivity, retention of configuration, kinetic isotope effects and structure reactivity correlations. In addition, radical chain initiators and inhibitors as well as radical traps can be employed. Based on these results, it is straightforward to distinguish radical chain processes, Class IV(a), from the other classes. Assigning reactions to the other classes involves an in-depth study of the reactivity of the inorganic catalyst. In many instances, the oxidation mechanism is a combination of classes. This discussion can be made more specific by applying these considerations to reactions that involve the oxidation of hydrocarbons.

$Ru(dmp)_2L_2^{2+}$ (where L is the solvent, water or acetonitrile) catalyzes [35,66] the epoxidation of norbornene by O_2 after a 12–24 h induction period. Spectral studies show that solutions of the catalyst are not oxidized by O_2 and when solutions exposed to O_2 for 24 h are used in the catalytic reaction, no change is observed in the induction period. Norbornene solutions, without catalyst, can be exposed to O_2 for 24 h without shortening the induction period. When *t*-BuOOH is added to the reactants, the induction period is eliminated. Spectral studies show that $[Ru(dmp)_2S_2]^{2+}$ reacts with *t*-BuOOH to form monooxo and dioxo complexes. It is also found that, once the monooxo complex is formed from peroxides, O_2 converts it to the dioxo complex. These and other mechanistic studies led to the working hypothesis shown in Scheme 8.

The reaction is seen to be a Class III reaction during the induction period, becoming Class II after the induction period. The dioxo complex selectively oxidizes methane to methanol and formaldehyde [66].

The GIF systems [67] oxidize saturated hydrocarbons selectively to ketones and have an unusual selectivity order for C—H reactivity of sec > tert ≥ primary. The systems involve pyridine and acetic acid as solvent and either reduce O_2 with zinc dust, iron powder, or a cathode to form peroxides or use KO_2 or H_2O_2 as the oxidant. In "normal" attack of alkoxy radicals on adamantane, the tertiary position is most reactive, leading to a ratio of products resulting from attack of $C^2/C^3 = 0.15$. Oxidation of adamantane by a GIF system gives a C^2/C^3 ratio of 10–20 and at



Scheme 8. For simplicity, the two dmp ligands and water or CH_3CN to make the complex six-coordinate are omitted. Ketone and alcohol refer to 2-norbornanone and 2-norbornanol, respectively.

lower O_2 pressure the ratio can be as high as 100. The high ratio is in part due to the reaction of the tertiary radical with pyridine. When radicals are generated from adamantane, both the secondary and tertiary radicals react with pyridine [67(b)]. Since products expected from a C^2 radical reaction with pyridine are not observed in the GIF system, a different mechanism is proposed for the oxidation of the C^2 position of adamantane than the C^3. It is proposed that one reagent attacks both positions, generating radicals at the tertiary position but not the secondary. Extensive mechanistic work has been carried out on this most interesting system. The proposed mechanism involves high-valent metal-oxo species generated from iron(II), O_2 and reducing equivalents as in the P-450 mechanism. This would place the reaction into Class III. In order to account for selectivity to ketone, the intermediate formed from the alkane attack on M—O is proposed to lead to a metal–carbon bond instead of the carbon–oxygen bond shown in Fig. 4. This reactivity has been improved with ligand modification of the iron systems and has been extended to cobalt complexes [68].

The next system to be discussed involves methane monooxygenase, MMO, and its model compounds [40(b),69]. An oxygen atom is inserted into a C—H bond by the concerted reduction of O_2 by the MMO hydroxylase/reductase cofactors. Methane is oxidized to methanol at a rate 20 50 times faster than the P-450 catalyzed oxidation of hydrocarbons. The k_H/k_D ratio for oxidizing CH_4 and CD_4 is 5. The active center of MMO consists of two iron atoms in close proximity [69(f)] with a structure similar to hemerythrin [69(b)]. As more data accumulates, this reaction can be assigned to Class III or IV.

The oxidation of CH_4 to methyl trifluroacetate in CF_3CO_2H solvent by $Co(III)(CF_3CO_2)_3$ occurs [70] at 150–180°C and 10–40 atm CH_4 with yields of 90+% based on Co(III). The reaction becomes catalytic with O_2 recycling the $Co(II)(CF_3CO_2)_3$. This would be classified as a Class V reaction.

As we have seen, many of the oxidation reactions are a combination of classes. Although this complicates understanding the activation of O_2, it also adds an element of excitement for the creative research chemist seeking to obtain selectivity at milder conditions. A very novel system [71] carries out copper(II) and chloride-free Wacker-type chemistry faster and more efficiently than the standard system under mild conditions. A triple catalyst is employed with Pd(II) going to Pd(0) in a Class V-type reaction with the substrate. A benzoquinone–hydroquinone conversion regenerates Pd(II) and macrocyclic complexes catalyze the reaction of O_2 with hydroquinone to regenerate benzoquinone. The mechanism of the O_2 reaction is unknown and could involve Class I, II or III.

The scope of the chemistry covered by this classification is tremendous. An entire book would be required to do justice to all of the research that has been carried out in this area. The intent of this article is not to review the literature, but to provide examples to justify the classification scheme presented and to enable the reader to use the scheme. The author apologizes to those authors whose work is not covered. The reader should now be in a position to appreciate research in the area of oxidations in the context of this classification. More importantly, this start will stimulate attempts to find new classes or novel combinations of classes.

D. SUMMARY

Metal-catalyzed oxidations are classified according to the role the metal plays in the oxidation mechanism.

(i) Class I. Metal-bound O_2. The complex coordinates O_2, enhancing its basicity and radical reactivity. The substrate reacts with the coordinated O_2 molecule.

(ii) Class II. Metal oxo via dioxygen. High-valent metal oxo species are formed from O_2. Substrate reacts with the metal oxo complex. Both oxygens of O_2 are used productively in substrate oxidation. Thus, the system is a dioxygenate.

(iii) Class III. Metal oxo via peroxides. Metal oxo species are generated by reducing O_2 to peroxo complexes, alkylperoxo complexes, H_2O_2 or RO_2H. These systems are often monooxygenates, including the monooxygenase enzymes, but, in some cases, dioxygenate-type activity can occur. As in Class II, the substrate reacts with a high-valent metal oxo complex.

(iv) Class IV. Metal peroxo systems. Metal peroxo complexes are the reactive intermediates in this class. They can undergo several reactions with substrate leading to a further subdivision: (a) Radical species are formed from peroxide decomposition. Haber–Weiss and Fenton chemistry is included. (b) Substrate attacks a bound metal peroxo or alkylperoxo complex. (c) Other reactions of metal-bound peroxo complexes.

(v) Class V. Metal-centered oxidizing agents. The metal complex in a high oxidation state oxidizes the substrate. The reduced complex is reoxidized by O_2 or peroxide.

ACKNOWLEDGEMENTS

The author acknowledges several helpful discussions of this manuscript with Dr. Robert H. Beer and Douglas E. Patton. The author's research in this area has received support from the U.S. Army CRDEC, Army Research Office and the National Science Foundation.

REFERENCES

1 R.A. Sheldon and J.K. Kochi, Metal-catalyzed Oxidations of Organic Compounds, Academic Press, New York, 1981.
2 (a) H. Taube, Prog. Inorg. Chem., 34 (1986) 607.
  (b) D.T. Sawyer, J. Phys. Chem., 93 (1989) 7977.
3 C.L. Bailey and R.S. Drago, Coord. Chem. Rev., 87 (1987) 321 and references cited therein.
4 A. Nishinaga, Chem. Lett., (1975) 273.
5 A. Nishinaga, T. Tojo and T. Matsuura, J. Chem. Soc. Chem. Commun., (1974) 896.
6 R.S. Drago, B.B. Corden and C.W. Barnes, J. Am. Chem. Soc., 108 (1986) 2453.
7 (a) R.S. Drago, T. Beugelsdijk, J.A. Breese and J.P. Cannady, J. Am. Chem. Soc., 100 (1978) 5373.
  (b) R.S. Drago, Inorg. Chem., 18 (1979) 1408.
  (c) R.S. Drago and B.B. Corden, Acc. Chem. Res., 13 (1980) 353.
  (d) R.S. Drago, in I. Bertini and R.S. Drago (Eds.), ESR and NMR of Paramagnetic Species in Biological and Related Systems, Reidel, Dordrecht, 1979, pp. 289–298.
  (e) R.S. Drago, Coord. Chem. Rev., 32 (1980) 97.
8 R.S. Drago, J.P. Cannady and K.A. Leslie, J. Am. Chem. Soc., 102 (1980) 6014.

9 (a) D.E. Hamilton, R.S. Drago and J. Telser, J. Am. Chem. Soc., 106 (1984) 5353.
(b) R.S. Drago, in R.S. Drago, I. Bertini and C. Luchinat (Eds.), The Coordination Chemistry of Metalloenzymes, Reidel, Dordrecht, 1983, p. 247.

10 A. Zombeck, R.S. Drago, B.B. Corden and J.H. Gaul, J. Am. Chem. Soc., 103 (1981) 7580.

11 (a) A.L. Balch, Y.W. Chan, R.S. Cheng, G.N. LaMar, B. Latos, L. Grazynski and M.W. Denner, J. Am. Chem. Soc., 106 (1984) 7779 and references cited therein.

12 R.C. Weast (Ed.), Handbook of Chemistry and Physics, Chemical Rubber Publishing Co., Cleveland, 65th edn., 1985.

13 (a) J.T. Groves and R. Quinn, J. Am. Chem. Soc., 107 (1985) 5790.
(b) J.T. Groves and R. Quinn, Inorg. Chem., 23 (1984) 3844.
(c) J.T. Groves and K.H. Ahn, Inorg. Chem., 26 (1987) 3833.

14 (a) T.R. Cundari and R.S. Drago, Inorg. Chem., 29 (1990) 487.
(b) T.R. Cundari and R.S. Drago, Int. J. Quantum Chem., 36 (1989) 773.

15 (a) T.R. Cundari and R.S. Drago, Inorg. Chem., 29 (1990) 2303.
(b) T.R. Cundari and R.S. Drago, Int. J. Quantum Chem., 24 (1990) 666.

16 M.J. Nappa and R.J. McKinney, Inorg. Chem., 27 (1988) 3740.

17 (a) C.L. Hill and B.C. Schardt, J. Am. Chem. Soc., 102 (1980) 6374.
(b) C.L. Hill, J.A. Smegal and T.J. Henley, J. Org. Chem., 48 (1983) 3277.

18 (a) L. Roecker and T.J. Meyer, J. Am. Chem. Soc., 109 (1987) 746 and references cited therein.
(b) T.R. Cundari and R.S. Drago, Inorg. Chem., 29 (1990) 3904.
(c) T.R. Cundari and R.S. Drago, Int. J. Quantum Chem., 23 (1989) 489.

19 (a) P.E. Ellis, Jr. and J.E. Lyons, J. Chem. Soc. Chem. Commun., (1989) 1187.
(b) P.E. Ellis, Jr. and J.E. Lyons, J. Chem. Soc. Chem. Commun., (1989) 1189.
(c) P.E. Ellis, Jr. and J.E. Lyons, J. Catal. Lett. 3 (1989) 389.
(d) J.F. Lyons and P.E. Ellis, Jr., Catal. Lett. 8 (1991) 45.
(e) P.E. Ellis, Jr. and J.E. Lyons, Coord. Chem. Rev., 105 (1990) 181.

20 W.C. Schremt, C.N. Satterfield and R.L. Wentworth, Hydrogen Peroxide, ACS Monograph No. 128, Reinhold, New York, 1955.

21 L.W. Gosser, U.S. Pat. 4,681,751 (1987).

22 B. Bosnich, W.G. Jackson, S.T.D. Lo and J.W. McLoren, Inorg. Chem., 13 (1974) 2605.

23 M. Nakajima, J.M. Latour and J.C. Morchon, J. Chem. Soc. Chem. Commun., (1977) 763.

24 J.H. Bayston and M.E. Winfield, J. Catal., 3 (1964) 123.

25 J.T. Groves, S. Krishnan, G.E. Avaria and T.J. Nemis, Adv. Chem. Ser., 191 (1980) 277.

26 (a) R. Landau, G.A. Sullivan and D. Brown, Chemtech., (1979) 602.
(b) R.A. Sheldon, J. Mol. Catal., 7 (1980) 107.

27 (a) R.S. Drago and R. Riley, J. Am. Chem. Soc., 112 (1990) 215.
(b) S.N. Gamagi and B.R. James, J. Chem. Soc. Chem. Commun., (1989) 1624.
(c) S.-J. Murahashi, T. Naota, T. Saito, H. Kumubayashi and S. Akutagawa, J. Am. Chem. Soc., 112 (1990) 7820.

28 G. Giannotti, C. Fontaine, A. Chiaroni and C. Riche, J. Organomet. Chem., 113 (1976) 57.

29 Y. Tatsumo and S. Otsuka, J. Am. Chem., Soc., 103 (1981) 5832.

30 N.N. Greenwood and A. Earnshaw, Chemistry of the Elements, Pergamon, New York, 1984.

31 (a) H.J.H. Fenton, J. Am. Chem. Soc., 65 (1984) 899.
(b) C. Walling, Acc. Chem. Res., 8 (1975) 125.

32 J.T. Groves and M. Van Der Puz, J. Am. Chem. Soc., 98 (1976) 5290.

33 C.M. Che, K.-Y. Wong, W.-H. Leung and C.-K. Poon, Inorg. Chem., 25 (1986) 345.

34 C.M. Che, T.F. Lai and K.Y. Wong, Inorg. Chem., 26 (1987) 2289.

35 A.S. Goldstein and R.S. Drago, J. Chem. Soc. Chem. Commun., (1991) 21.

36 L.C. Yuan and T.C. Bruice, J. Am. Chem. Soc., 107 (1985) 512.

37 (a) R.H. Holm. Chem. Rev., 87 (1987) 1401.
(b) J.M. Mayer and W.A. Nugent, Metal Ligand Multiple Bonds, Wiley, New York, 1988.
(c) T.J. Meyer, in A.E. Martell and D.T. Sawyer (Eds.), Oxygen Complexes and Oxygen Activation by Transition Metals, Plenum Press, New York, 1988, p.33.
(d) T.C. Bruice, Aldrichimica Acta, 21 (1988) 87.

38 (a) I. Tabushi and N. Koga, J. Am. Chem. Soc., 101 (1979) 6456.
(b) I. Tabushi, M. Kodera and M. Yokoyama, J. Am. Chem. Soc., 107 (1985) 4466.
(c) V.S. Kubhova, A.M. Khenkin and A.E. Shilov, Kinet. Katal. 29 (1988) 1278.
(d) D. Mansuy, M. Fontecave and J.F. Bartoli, J. Chem. Soc. Chem. Commun., (1983) 253.

39 (a) I. Tabushi, Coord. Chem. Rev., 86 (1988) 1 and references cited therein.
(b) J.H. Dawson, Science, 240 (1988) 433 and references cited therein.

40 (a) P.R. Ortiz de Montellano (Ed.), Cytochrome P-450, Plenum Press, New York, 1985.
(b) A.M. Khenkin and A.E. Shilov, New J. Chem., 13 (1989) 659.
(c) A.E. Shilov, in C.L. Hill (Ed.), Activation and Functionalization of Alkanes, Wiley, New York, 1989.

41 J.A. O'Connor and E.A.V. Ebsworth, Adv. Inorg. Chem. Radiochem., 6 (1969) 279.

42 (a) L. Saussine, E. Brazi, A. Robine, H. Mimoun, J. Fischer and R. Weiss, J. Am. Chem. Soc., 107, 3534 (1985) and references cited therein.
(b) A.S. Goldstein and R.S. Drago, Inorg. Chem., 30 (1991) 4506.
(c) R.S. Shukla and T.M.M. Kahn, J. Mol. Catal., 44 (1988) 85.

43 G.W. Parshall, Homogeneous Catalysis, Wiley, New York, 1980 and references cited therein.

44 (a) R.A. Sheldon, Recl. Trav. Chim. Pays Bas, 92 (1973) 253.
(b) A.O. Chong and K.B. Sharpless, J. Org. Chem., 42 (1977) 1587.
(c) R.A. Sheldon, in S. Patal (Ed.), The Chemistry of Functional Groups, Peroxides, Wiley, New York, 1983.

45 H. Mimoun, Angew Chem. Int. Ed. Engl., 2 (1982) 734.

46 O. Bartolini, F. Di Furia and G. Modena, J. Mol. Catal., 14 (1982) 53, 63 and references cited therein.

47 M.G. Sheng and J.G. Zajacek, J. Org. Chem., 33 (1968) 588.

48 G.N. Koskel, H.I. Faberov, L.L. Zalygin and G.A. Krushinskaya, J. Appl. Chem. USSR, 44 (1971) 885.

49 W. Zhang, J.L. Loebach, S.R. Wilson and E.N. Jacobsen, J. Am. Chem. Soc., 112 (1990) 2801.

50 (a) C. Dudley and G. Read, Tetrahedron Lett., (1972) 5273; J. Chem. Soc. Dalton Trans., (1977) 883; J. Mol. Catal., 7 (1980) 31.
(b) H. Mimoun, M.M.P. Machirant and I. Seree de Roch, J. Am. Chem. Soc., 100 (1978) 5437.

51 (a) E.D. Nyberg, D.C. Pribich and R.S. Drago, J. Am. Chem. Soc., 105 (1983) 3538.
(b) R.S. Drago, A. Zuzich and E.D. Nyberg, J. Am. Chem. Soc., 107 (1985) 2898.

52 K. Purcell, Organometallics, 4 (1985) 509.

53 H. Mimoun, in G. Wilkinson, R.D. Gildard and J.A. McCleverty (Eds.), Comprehensive Coordination Chemistry, Vol. 6, Pergamon, Oxford, 1987.

54 P. Miller and H. Idmoumaz, J. Organomet. Chem., 345 (1988) 187.

55 T.C. Lan, C.-M. Che, W.-O. Lee and C.-K. Poon, J. Chem. Soc. Chem. Commun., (1988) 1406.

56 R.A. Leising and K.J. Takeuchi, Inorg. Chem., 26 (1987) 4391.

57 D.E. Hamilton, R.S. Drago and A. Zombeck, J. Am. Chem. Soc., 109 (1987) 374.

58 L. Que et al., J. Am. Chem. Soc., 109 (1987) 5373; 110 (1988) 8085 and references cited therein.

59 S.E. Jacobson, R. Tang and F. Mares, J. Chem. Soc. Chem. Commun., (1978) 888.

60 (a) C. Biancini, P. Frediani, F. Laschi, A. Meli, F. Vizza and P. Zanello, Inorg. Chem., 29 (1990) 3402.
(b) P. Barbaro, C. Bianchini, C. Mealei and A. Meli, J. Am. Chem. Soc., 113 (1991) 3181.

61 (a) J. Schmidt, W. Jafner, R. Jira, J. Seldmeier, R. Sieber, R. Ruttinger and J. Kojer, Angew Chem. Int. Ed. Engl., 1 (1962) 80.
(b) J.-E. Bäckvall, B. Äkermark and S.O. Ljungren, J. Am. Chem. Soc., 101 (1979) 2411 and references cited therein.

62 (a) J.-E. Bäckvall, Pure Appl. Chem., 55 (1983) 1669.
(b) B. Äkermark, J.-E. Bäckvall and K. Zetterberg, Acta Chim. Scand. Ser B, 36 (1982) 577.

63 L.-C. Kao, A.C. Hutson and A. Sen, J. Am. Chem. Soc., 113 (1991) 700.

64 C. Bilgrien, S. Davis and R.S. Drago, J. Am. Chem. Soc., 109 (1987) 3786.

65 A.M. Kenkin and A.E. Shilov, New J. Chem., 13 (1989) 659.

66 C.L. Bailey and R.S. Drago, J. Chem. Soc. Chem. Commun., (1987) 179.

67 (a) D.H.R. Barton, in C.L. Hill (Ed.), Activation and Functionalization of Alkanes, Wiley, New York, 1989 and references cited therein.
(b) D.H.R. Barton, F. Halley, N. Ozbalik, M. Schmitt, E. Young and G. Balavoine, J. Am. Chem. Soc., 111 (1989) 7144.
(c) D.H.R. Barton, J. Bovin, K.M. Schwartzentruber, N. Ozbalik, D. Gaudin and J. Jankowski, Spectrosc. Lett., 20 (1987) 963.
(d) D.H.R. Barton, F. Halley, N. Ozbalik, E. Young, G. Balavoine, A. Gref and J. Boivin, Nouv. J. Chim., 13 (1989) 177.

68 (a) P. Cofre, S.A. Richert, A. Sobkowiak and D.T. Sawyer, Inorg. Chem., 29 (1990) 2645.
(b) C. Shen, A. Sobkowiak, S. Jeon and D.T. Sawyer, J. Am. Chem. Soc., 112 (1990) 879.
(c) C. Shen, S.A. Richert, P. Cofre, B. Ross, Jr., A. Sobkowiak, D.T. Sawyer and J. Kanofsky, J. Am. Chem. Soc., 112 (1990) 1936.

69 (a) H. Dalton, Adv. Appl. Microbiol., 26 (1980) 71.
(b) S.J. Lippard, Angew Chem. Int. Ed. Engl., 27 (1988) 344.
(c) J. Green and H. Dalton, Biochemistry 236 (1986) 155.
(d) A. Erickson, B. Hedman, K.O. Hodgson, J. Green, H. Dalton, J.G. Bentsten, R.H. Beer and S.J. Lippard, J. Am. Chem. Soc., 110 (1988) 2330.
(e) B.G. Fox, K.K. Surerus, E. Munch and J.D. Lipscomb, J. Biol. Chem., 263 (1988) 10553.
(f) M.P. Woodland, D.S. Patel, R. Cammack and H. Dalton, Biochem. Biophys. Acta, 873 (1986) 237.

70 M.N. Vargaftik, I.P. Stolarov and I.I. Moiseev, J. Chem. Soc. Chem. Commun., (1990) 1049.

71 J.-E. Bäckvall, R.B. Hopkins, H. Greunberg, M.M. Mader and A.K. Awasthi, J. Am. Chem. Soc., 112 (1990) 5160.