Inorganica Chimica Acta, 198–200 (1992) 359–367

A classification scheme for homogeneous metal catalyzed oxidations by O_2

Russell S. Drago and Robert H. Beer

Department of Chemistry, University of Florida, Gainesville, FL 32611 (USA)

Abstract

The metal complex catalyzed oxidation of organic substrates is an important area of chemistry with relevance to biological and industrial processes. The immense literature in the area can be overwhelming with considerable speculation concerning the role metals play in the process. In this article, the reactions metal complexes undergo in the activation of O_2 are divided into five classes. The classification serves as a guide for the selection of metal complexes to catalyze the oxidation of organic substrates. It also provides a summary of established reaction types for an investigator to consider before proposing a new mechanism.

Introduction

The study of metal complex activation of O_2 is being pursued actively in many laboratories because of its importance in industrial and biological chemistry. In the course of discovering new reactions that involve metal catalyzed oxidations in our laboratory, we often propose mechanisms that are working hypotheses to guide further experimentation. Though numerous oxidation reactions and mechanisms have been reported, systematic patterns that organize them are lacking, making it difficult to compare new discoveries with established ones. In an attempt to systematize metal catalyzed oxidation reactions, we offer a general scheme based on the role the metal plays in O_2 activation and oxidation reactions using examples from the literature and the author's laboratory.

The activation of O_2

The reactivity of O_2 is governed by its preference to react as a two electron oxidant rather than a one electron oxidant. When O_2 is reduced by one electron to form O_2^- or by a hydrogen atom to form HO_2, the electron is added to a doubly degenerate π^* orbital, where O_2 has the molecular orbital (MO) configuration $\sigma_{2s}^2\pi^4\pi^{*2}$. The addition of an electron to either of the half filled π^* orbitals results in a loss of orbital exchange energy. The difference in the reduction potential [1] and O–H bond energy [2] between HO_2 (0.12 V, 59 kcal/mol) and H_2O_2 (0.78 V, 41 kcal/mol) underscores that one electron reduction versus two electron reduction of O_2 is energetically unfavorable. The loss of exchange energy accounts for the lack of reactivity of O_2 with diamagnetic organic molecules that can only provide one electron or one hydrogen atom per molecule. The reactions of O_2 with homogeneous metal catalysts described in the following five classes however, lead to oxidants that react readily with organic compounds.

Classes of metal catalyzed reactions

Five classes are defined by the role of the metal atom in the activation of O_2 and the metal O_2, oxo, peroxo or high oxidation state metal oxidants they form:
(I) Metal bound O_2
(II) Metal oxo via dioxygen
(III) Metal oxo via peroxides
(IV) Metal peroxo systems
(V) Metal centered oxidizing agents

A reaction in a class may function to oxygenate organic substrates as a monooxygenate or dioxygenate. These terms are defined by the number of O_2 oxidizing equivalents used productively in the desired substrate oxidation reaction (monooxygenate = one oxygen atom to oxide/a $2e^-$ oxidation; dioxygenate = both oxygen atoms to oxide/a $4e^-$ oxidation). This definition includes, but is not to be confused with, the mono- and dioxygenase enzymes which incorporate one or both atoms of O_2 into an organic substrate, respectively.

0020-1693/92/$5.00

Product selectivity, regioselectivity, retention of configuration, kinetic isotrope effects and structure reactivity correlations can all be used to obtain mechanistic information to aid in classification. In addition, radical chain initiators and inhibitors as well as radical traps can be employed. Based on these results, classes that include radical chain processes can be distinguished from classes that do not involve radicals. Assigning some reactions to classes may require an in depth study of the metal catalyst. These studies often reveal that the metal complex plays multiple roles in a catalytic system, and such a system would involve a combination of classes.

I. Metal bound O_2

The coordination of O_2 to transition metals can be described with the spin pairing model [3]. An electron in a d_{z^2} orbital of a low spin five-coordinate cobalt(II) complex pairs with an electron in the π^* orbital of oxygen to form a sigma bond*. Bonding to other metals involves a similar interaction [3c]. The basicity [4] and radical character [5] of O_2 increase upon coordination of O_2 to cobalt(II). These features help explain why metal bound O_2 complexes react with organic compounds while O_2 alone does not.

Equations (1) and (2) show the reaction of cobalt bound O_2 with an organic substrate, S–H. Cobalt bound O_2 abstracts a hydrogen atom from the substrate to form a cobalt(III) hydroperoxide, which dissociates into Co(II) and HO_2, and a substrate radical. The substrate radical can then react with O_2 or $LCoO_2$, where L indicates an unspecified ligand(s).

$$\text{S–H} + LCoO_2 \longrightarrow \text{S}^{\cdot} + LCo(III)O_2H \longrightarrow Co(II) + HO_2 \quad (1)$$

$$\text{S}^{\cdot} + LCoO_2 \longrightarrow LCoO_2S \quad (2)$$

The subsequent reactivity of $LCoO_2S$ to form oxidized products and regenerate the catalyst is discussed as a Class IV reaction.

All reported metal reactions [6, 7] involve substrates that are capable of hydrogen bonding to the bound O_2, e.g. substituted phenols. Hydrogen atom abstraction can occur only when the OH bond energy of $LCo(II)O_2$–H is greater than that of S–H. The O–H bond energy in Co(SMDPT) (where SMDPT is bis(salicylidene-γ-iminopropyl)methyl amine) is estimated [6] to be about 87 kcal mol^{-1}. Comparable values are found for the bond energy of HOO–H (88 ± 1 kcal mol^{-1}) and for $(CH_3)_3CO_2$–H (89 ± 0.2 kcal mol^{-1}). The LCo–O_2 adduct reacts with substrates to form an OH bond with a strength comparable to that obtained when HO_2 reacts to form H_2O_2 (90 kcal mol^{-1}). As a consequence of this thermodynamic barrier, oxidation of substrates with S–H bond energies greater than 90 kcal mol^{-1} are not observed.

II. Metal oxo via dioxygen

Formation of high valent metal oxo species from O_2 can proceed via a μ-peroxo dinuclear complex formed by two spin pairing interactions of O_2 (eqn. (3)). The μ-peroxo complex undergoes O–O bond scission to form two metal oxo oxidants.

$$M^{II}L + O_2 \longrightarrow LM^{III}\text{–}O_2 \xrightarrow{ML} LM^{III}\text{–O–O–}M^{III}L \longrightarrow 2LM^{IV}\text{–O} \quad (3)$$

This reaction has been observed [9, 10] in the conversion of M(II)(TMP) to M(IV)O(TMP) (where TMP is *meso*-tetramesityl porphyrinate and M is Fe or Ru). The Ru(IV)O species disproportionates into *trans*-Ru(VI)$(O)_2$(TMP) and Ru(II)(TMP).

Metals in higher oxidation states III and IV do not form stable enough O_2 adducts to be converted to metal oxo species. These high oxidation state metal complexes react with oxygen to form M(V) and M(VI) oxo complexes via unstable O_2 intermediates or with ion paired O_2^- and O_2^{2-} species generated by metal to O_2 electron transfer reactions. Alternatively, the conversion of a metal aquo moiety to a metal oxo can be accomplished with oxidizing equivalents provided by the reduction of O_2 to water (eqns. (4) and (5)).

$$M(II)(H_2O) \xrightarrow{-e^-} M(III)(OH) + H^+ \quad (4)$$

$$M(III)OH \xrightarrow{-e^-} M(IV)O + H^+ \quad (5)$$

Class II reactions use all four oxidizing equivalents furnished by O_2 – a case of dioxygenate activity.

Oxygen atom transfer reactions [11a] are the most common of several oxidation mechanisms used by metal oxo complexes [11]. Semi-empirical INDO/1 molecular orbital calculations provide considerable insight as to how these reactions may occur [12]. In the epoxidation of alkenes by the Ru(IV)O moiety, the alkene undergoes a non-concerted (2 + 1) cycloaddition to Ru(IV)O leading to a bound epoxide [12] (Fig. 1). Initially a weak complex is formed as the π orbital of ethylene donates electron density into the Ru–O group (where Ru(IV)O has a $\sigma^2\pi^4\pi^{*2}$ MO configuration like O_2). As the distance from the alkene to the Ru–O group decreases, an off-center canted pathway is favored in which the plane formed by the carbon and hydrogen atoms in ethylene is not perpendicular to the Ru–O bond vector. A weak oxygen–carbon bond forms by pairing up a Ru–O π^* electron with a π electron of ethylene producing an average of the structures shown in brackets

---

*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 unpaired electron.

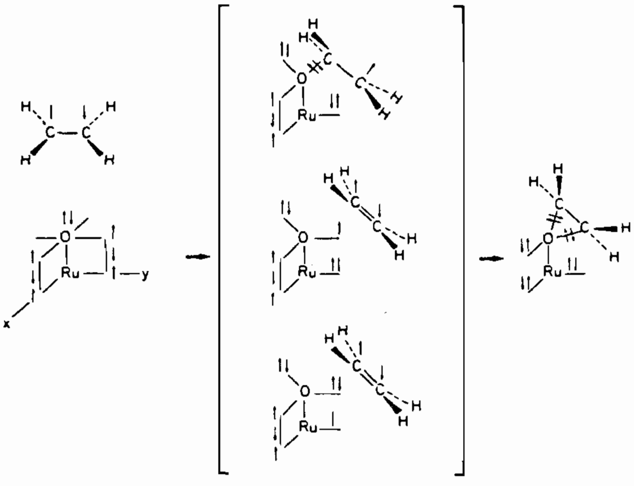


Fig. 1. A valence bond interaction diagram representing the formation of a bound epoxide.

in Fig. 1. The radical carbon of the bound ethylene then pairs up with the second unpaired electron of the electron rich Ru–O system forming a bound epoxide.

Experimentally both *cis* and *trans* β-methylstyrene retain stereochemistry [13]. Theoretical calculations suggest that stereochemistry is largely maintained because of the partial carbon–carbon double bond character in the intermediate shown in brackets. To complete a catalytic cycle, the epoxide is displaced by solvent and the reduced metal complex is reoxidized by O_2 to the metal oxo.

INDO/1 calculations show that the reaction of a *trans*-Ru(IV)$(O)_2$ complex with ethylene is similar to the Ru(IV)O system which yields a bound epoxide [14a]. In contrast, a *cis*-Ru$(O)_2$ complex undergoes a concerted (3+2) cycloaddition [14a] with alkenes leading to a Ru(IV) dioxometallocycle intermediate, $\overline{\text{RuO(IV)OCH}_2\text{CH}_2}$. This intermediate undergoes carbon–carbon bond cleavage forming two carbonyl containing products and Ru(II). This reaction pathway accounts for the benzaldehyde and acetaldehyde observed in catalytic oxidation of *trans*-β-methylstyrene by *cis*-$[Ru(O)_2(dmp)_2]^{2+}$ (where dmp is 2,9-dimethyl-1,10-phenanthroline) [15].

Related theoretical calculations on the hydroxylation of a C–H bond by metal oxo complexes indicate the reaction pathway depends upon the electrophilicity (acceptor properties) of the metal oxo bond [14b]. The mechanism of alkane hydroxylation involves varying contributions of two extreme paths – hydrogen atom abstraction A and oxygen atom transfer, B and one of several possible concerted paths, C, as shown in Fig. 2.

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. The oxygen atom transfer path, B, involves C–O bond formation resembling an S_N2 transition state. 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. 2, 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 electrophilic has a greater contribution from path A and is more radical in nature. Hydrocarbon oxidations with cytochrome P-450 model complexes, e.g. MnO(P)Cl (where P is a porphyrin) [16, 17] are less concerted and resemble path A. The oxidations of the more electrophilic complex, $MnOP^+$, with no auxiliary donor, is more concerted (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 are observed [16], belying the importance of the strength of donors to the reaction pathway in metal oxo catalyzed oxidations.

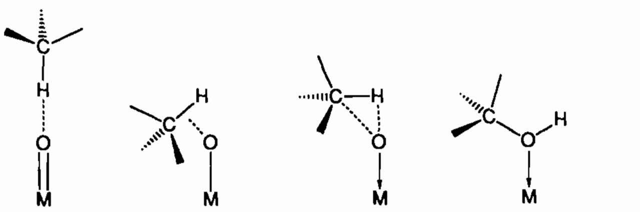


Fig. 2. Paths for the oxidation of alkanes: A, hydrogen atom abstraction; B, oxygen atom transfer; C, concerted path; D, the product-bound methanol.

Specific examples of Class II reactions utilizing O_2 are relatively few. As noted earlier, a Ru(II) porphyrin complex reacts with O_2 to form Ru(IV)O and *trans*-Ru(VI)$(O)_2$ complexes [10]. The latter species catalyzes the aerobic oxidation of norbornene. Mn(TPP)N_3, where TPP is *meso*-tetraphenylporphyrinate, and the pentafluoro analogue, Mn(TFPP)N_3, are reported [18] to catalyze the reaction of O_2 with isobutane to produce isobutanol. The Fe(III)(TFPP) analogues, Fe(TFPP)N_3, $[Fe(TFPP)]_2O$ or Fe(TFPP)OH, are active catalysts for the oxidation of isobutane and propane by O_2. Additional mechanistic data will allow this reaction to be assigned definitively to Class II or Class IV (*vide infra*).

III. Metal oxo via peroxides

For reactions in this class, kinetic or thermodynamic barriers prevent the facile activation of O_2 by a metal complex. Metal catalyzed oxidations can occur, however, with a O_2 derived oxidant, i.e. hydrogen peroxide or alkyl hydroperoxide. If a sacrificial reducing agent is used to convert oxygen to hydrogen peroxide or an alkyl hydroperoxide, these oxidants can react with a metal complex to form the high oxidation state metal oxo species discussed in the Class II section. These reactions take advantage of the stronger oxidizing ability of H_2O_2 (1.78 V) versus O_2 (1.23 V) [2a] to oxidize lower valent metal complexes to metal oxo species. Class III reactions monooxygenate organic substrates since only two of the four oxidizing equivalents of O_2 are available following its reduction to a peroxide. Monooxygenase enzymes that form metal oxo intermediates are candidates for this class.

Class III reactions can be divided formally into two steps: (i) the reaction to form the peroxide and (ii) the reaction of the peroxide with metal complexes. The reduction of O_2 to form hydrogen peroxide occurs with a variety of reducing agents or metal complexes. The reductants BH_4^-, NADH and anthraquinol derivatives are used to produce H_2O_2 for metal catalyzed oxidations. Anthroquinol forms the basis for commercial production of H_2O_2 from H_2 and O_2 by catalytically reducing the quinone back to the quinol [19]. Transition metal ions with accessible oxidation states that differ by two, e.g. Co(I), Co(III), can reduce O_2 to metal bound peroxo complexes which react with water or acid leading to H_2O_2 or M–OOH species [20]. Metal–hydrido species can also insert [21] O_2 to form MOOH complexes. Alternatively, metal–O_2 adducts can be reduced to H_2O_2 or M–OOH species with one-electron reducing agents [6, 22].

Organic compounds can react with O_2 at elevated temperatures to form alkylhydroperoxides, e.g. isobutane and ethylbenzene [23]. The hydroperoxide of *N*-methylpyrrolidinone [24] forms readily at 75 °C under a pressure of a few atmospheres of O_2. The insertion of O_2 into a metal alkyl ($MR + O_2 \rightarrow MOOR$) [25], the alkylation of metal–peroxo compounds [26], and the reaction of CoO_2 with a substituted phenol [6] all lead to metal alkylperoxo complexes. If the metal alkyl peroxide forms metal oxo complexes, then the reaction is assigned to Class III.

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 (eqn. (6)).

$$2H_2O_2 \longrightarrow 2H_2O + O_2 \qquad (6)$$

Metals that have two stable oxidation states that differ by one, i.e. Mn^{2+}/Mn^{3+}, Fe^{2+}/Fe^{3+}, Cu^+/Cu^{2+}, are very effective catalysts for the decomposition of hydrogen peroxide. The metal functions as both an oxidizing and reducing agent in the decomposition mechanism (eqns. (7) and (8)).

$$2H^+ + H_2O_2 + 2M(II) \longrightarrow 2M(III) + 2H_2O \qquad (7)$$

$$H_2O_2 + 2M(III) \longrightarrow 2M(II) + O_2 + 2H^+ \qquad (8)$$

When H_2O_2 is decomposed by metals in the presence of organic substrates, hydroxyl radicals produced by the H_2O_2 decomposition oxygenate the substrate. This reaction, called the Fenton reaction [27], belongs to Class IV. More efficient use of H_2O_2 occurs if it produces high valent metal oxo species instead of reducing the one electron oxidized metal complex in eqn. (8). Efficient utilization of H_2O_2 is observed in the oxidation of $[Ru(II)(dmp)_2(H_2O)_2]^{2+}$ to mono- and dioxo complexes [28].

Oxidation of metal complexes to metal oxo species with H_2O_2 can proceed through the oxidation of coordinated water (eqns. (4) and (5)) or by ligand substitution (eqn. (9)) [11c]. The dinuclear μ-peroxo species can then decompose to two high valent metal oxo species as shown in eqn. (3).

$$2M\text{–}OH + H_2O_2 \longrightarrow 2H_2O + M\text{–}O\text{–}O\text{–}M \qquad (9)$$

Sodium borohydride, ascorbic acid, H_2/colloidal Pt [29a, b] and Fe^{3+}/Zn/methyl viologen [30b] are reported [29] to reduce O_2 and form porphyrin iron–oxo cytochrome P-450 analogues [29–31]. Most articles [30, 31] on the reactions of cytochrome P-450 and its model compounds suggest a Class III reaction mechanism for O_2 activation. The Fe(II) center binds O_2 and is then reduced with a sacrificial reducing agent to form a Fe(III) peroxo species. The peroxo complex decomposes a porphyrin (P) cation radical oxidant, $(P^{\cdot+})Fe(IV)O$. After oxidation of a substrate, the resulting Fe(III) is reduced to Fe(II) by an additional electron.

If H_2O_2 is used instead of O_2, the sacrificial reducing agent is not required for catalytic oxidation. In the case of the enzyme, this reaction is referred to as the hydrogen peroxide shunt [30, 31]. This observation suggests an alternative mechanism to the commonly accepted O_2 activation mechanism for cytochrome P-450 [29–31]. It is possible that O_2 is reduced first to H_2O_2 in a separate two electron reduction and then reacts with the metal to produce a metal oxo species. In both the model and enzyme chemistry, it is difficult to ascertain which of the two above reaction pathways lead to the high valent metal oxo complex.

Alkyl hydroperoxides generated during the catalytic oxidation of alkenes by *cis*-$[Ru(dmp)_2(H_2O)_2]^{2+}$ react with the Ru(II) complex to form Ru(IV)O and *cis*-$Ru(VI)(O)_2$ species [28b]. The *cis*-$Ru(VI)(O)_2$ species epoxidizes the alkene, S, and is reduced to Ru(IV)O (eqn. (10)). The Ru(IV)O complex is converted back to the *cis*-$Ru(VI)(O)_2$ with O_2. The Ru(IV)O species can also epoxidize alkenes by an oxygen atom transfer reaction (eqn. (12)). The resulting Ru(II) complex requires additional alkyl hydroperoxide to regenerate the Ru(IV)O and *cis*-$Ru(VI)(O)_2$ catalysts (eqns. (10) and (11)). Because the peroxide produces an oxidized product, SOH, upon reaction with the Ru(II) complex and the ensuing ruthenium oxo complexes produce epoxide, this catalytic system constitutes a dioxygenate reaction. This is an example of a combination of classes; a Class III reaction to form Ru(IV)O species, followed by a Class II reaction type to form the *cis*-$\mathrm{Ru(VI)(O)_2}$ complex with O_2.

$$\mathrm{S+Ru(VI)(O)_2 \longrightarrow SO+Ru(IV)O} \qquad (10)$$

$$\mathrm{SOOH+Ru(II) \longrightarrow SOH+Ru(IV)(O)} \qquad (11)$$

$$\mathrm{Ru(IV)(O)+S \longrightarrow SO+Ru(II)} \qquad (12)$$

IV. Metal peroxo systems

The difference between this class of reactions and Class III is the involvement of metal peroxo complexes instead of high valent metal oxo complexes as reactive intermediates in substrate oxidation. Metal hydroperoxo (MOOH) and alkyl peroxo (MOOR) complexes of the early transition metals are well characterized [32]. They can be generated by the reactions discussed in the previous section.

Metal catalyzed reactions that form alkyl peroxides by radical chain mechanisms also belong to this class. Initiation of the radical chain can occur by outer sphere electron transfer to produce a radical cation which then loses a proton to solvent or substrate to form $R^{\cdot}$. Subsequent reactions of $R^{\cdot}$ with O_2 lead to the hydroperoxide RO_2H (eqns. (13)–(16)).

$$\mathrm{M(III)+R\text{–}H \longrightarrow M(II)+R^{\cdot}H^+} \qquad (13)$$

$$\mathrm{R^{\cdot}H^+ \xrightarrow[B]{} R^{\cdot}+BH^+} \qquad (14)$$

$$\mathrm{R^{\cdot}+O_2 \longrightarrow RO_2^{\cdot}} \qquad (15)$$

$$\mathrm{RO_2^{\cdot}+RH \longrightarrow RO_2H+R^{\cdot}} \qquad (16)$$

The reduced M(II) is oxidized back to M(III) by O_2. Hydrogen atom abstraction by the metal, eqn. (17), can be eliminated because R–H bonds in hydrocarbons ($\sim$95 kcal $\mathrm{mol^{-1}}$) are stronger than metal–hydrogen bonds ($\sim$60 kcal $\mathrm{mol^{-1}}$).

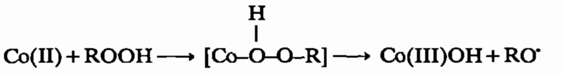
$$\mathrm{M+R\text{–}H \longrightarrow M\text{–}H+R^{\cdot}} \qquad (17)$$

The alkyl hydroperoxide, metal alkylhydroperoxo complex or metal peroxo complex can undergo three principal reactions that form subdivisions of this class:

(A) metal catalyzed peroxide decomposition (Haber–Weiss or Fenton chemistry),
(B) nucleophilic attack on metal peroxo or alkylperoxo complexes,
(C) other reactions of metal peroxo intermediates.

(A) Metal catalyzed peroxide decomposition

Alkylperoxides are decomposed by transition metal ions by the Haber–Weiss mechanism [33] shown for cobalt in Scheme 1.



$$\mathrm{Co(II)+ROOH \longrightarrow [Co\text{–}\overset{\overset{\displaystyle H}{|}}{O}\text{–}O\text{–}R] \longrightarrow Co(III)OH+RO^{\cdot}} \qquad (18)$$

$$\mathrm{Co(III)OH+ROOH \longrightarrow Co(II)+ROO^{\cdot}+H_2O} \qquad (19)$$

$$\mathrm{RO^{\cdot}+ROOH \longrightarrow ROH+ROO^{\cdot}} \qquad (20)$$

$$\mathrm{Co(II)+ROO^{\cdot} \longrightarrow Co(III)OOR} \qquad (21)$$

$$\mathrm{Co(III)OH+ROOH \longrightarrow Co(III)OOR+H_2O} \qquad (22)$$

$$\mathrm{2Co(II)+3ROOH \longrightarrow 2Co(III)OOR+ROH+H_2O} \qquad (23)$$

$$\mathrm{Co(III)OOR \longrightarrow Co(II)+ROO^{\cdot}} \qquad (24)$$

$$\mathrm{\longrightarrow \text{'}Co(III))O^{\cdot\prime}+RO^{\cdot}} \qquad (25)$$

$$\mathrm{RO^{\cdot}+RO_2H \longrightarrow ROH+RO_2^{\cdot}} \qquad (26)$$

$$\mathrm{2ROO^{\cdot} \longrightarrow [RO_4R] \longrightarrow O_2+R'_2C{=}O+H^+} \qquad (27)$$

Scheme 1. The ligands on cobalt are not shown; R is a primary or secondary alkyl.

Equation (28) is proposed here as an alternative to eqn. (27).

$$\mathrm{Co(II)+ROO^{\cdot} \longrightarrow Co(III)\text{–}O\text{–}OCHR_2' \longrightarrow Co(III)OH+R_2'C{=}O} \qquad (28)$$

The decomposition of a cobalt(III) t-butylperoxo complex was studied in both inert and reactive hydrocarbon solvents [33b]. In benzene, an inert solvent, thermal decomposition of the metal alkylperoxo complex results in a 1.8:1 alcohol:ketone product ratio. Small amounts of the dialkylperoxide are also observed. The dialkylperoxide is one of the several minor products observed in metal catalyzed peroxide decomposition not accounted for by the Haber–Weiss mechanism given in Scheme 1.

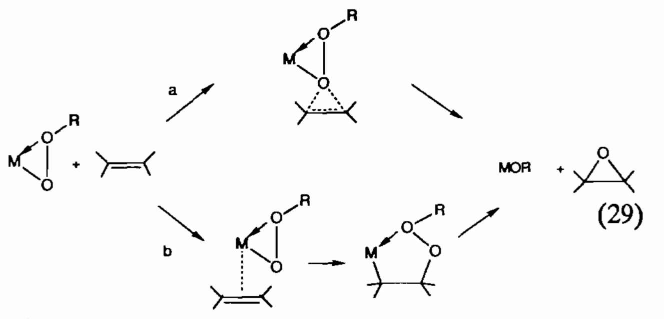
When the decomposition of Co–OOR is studied in a reactive solvent, oxidation of the hydrocarbon does not occur at an appreciable rate until 60 °C, the temperature at which the cobalt alkylhydroperoxo complex decomposes. The main products of the decomposition of the t-butylperoxo Co(III) complex in cyclohexane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

Relative rates of substrate oxidation for this reaction type are generally proportional to C–H bond strengths in order of decreasing bond strength: tertiary > secondary > primary. Alkenes with allylic hydrogens are readily oxidized by this mechanism since the stability of the allyl radical facilitates hydrogen atom abstraction. For alkenes, the reaction proceeds as shown in Scheme 1 with the allylic ketone and alcohol being the major oxygenated products.

Many examples of Class IVA reactions are known. The oxidation of cyclohexane [33, 34] to adipic acid (a nylon intermediate) and the Mid-Century/Amoco process [34] for producing terephthalic acid from *p*-xylene are important commercial reactions from this class. Recently [33c, e] cobalt(III) complexes, acting as strong oxidants, have been proposed to initiate similar C–H bond activation reactions under mild conditions. Shukla and Taqui Kahn [33d] have reported the selective oxidation of cyclohexane to cyclohexanol with $[Ru(IV)(L)]_2(O_2)$ (where L is an aminopolycarboxylate ligand), which initiates the reaction by abstracting a hydrogen atom from cyclohexane. The intermediate, $[Ru(IV)(O)(L)] \cdot C_6H_{11}{}^+$, transfers a hydroxyl radical to the cyclohexyl radical cation to form cyclohexanol. The Fenton reaction [27] which generates hydroxyl radicals that react unselectively with organic substrates also belongs to this class. Yields based on H_2O_2 are relatively low because of the competing metal catalyzed decomposition of H_2O_2.

(B) Nucleophilic attack on peroxo and alkylperoxo complexes

Reactions in this class involve attack on a coordinated peroxo or alkyl peroxo ligand by the substrate and occur with high selectivity. The use of high oxidation state, early transition metal catalysts such as Mo(VI) lead to epoxides. Both homogeneous [23a] and heterogeneous [23b] molybdenum catalysts are the basis for the commercial production of propylene oxide from propylene and alkyl hydroperoxide. Two alternative mechanisms have been proposed [35, 36]. One mechanism [35] involves nucleophilic attack of the alkene on the coordinated peroxo oxygen (eqn. (29a)). An epoxide and a metal alkoxide result with no change in the metal oxidation state. The other mechanism [36] involves the dipolar addition of the alkene to form a peroxometallocycle which eliminates the epoxide (eqn. (29b)).



(29)

The metal peroxo species is regenerated via eqn. (30).

$$MOR + ROOH \longrightarrow MOOR + ROH \qquad (30)$$

This reaction is remarkably stereoselective for *cis* and *trans* epoxides from their alkene precursors. Optically active titanium diethyltartrate catalysts and t-butylhydroperoxide effect the asymmetric epoxidation of prochiral allylic alcohols in 70–87% yield with 90% or more enantiomeric excess [37]. Alkyl and aryl substituted alkenes do not react. Alkyl hydroperoxides in combination with d^0 transition metal catalysts like Ti(IV) can oxidize sulfides to sulfoxides or sulfones [38], tertiary amines to *N*-oxides [39] and primary amines to oximes [40].

In contrast to high oxidation state, early transition metals, late transition metals catalysts, e.g. Rh(III), lead to aldehyde or ketone products. Selective oxidation of alkenes to ketones by O_2 can be accomplished with a Rh–OOH intermediate, but sacrificial reducing agents [41a, 42], indicative of monooxygenate activity, are required. Mimoun *et al.* [41b] discovered that by the addition of a copper(II) co-catalyst, both oxygen atoms of O_2 are used to form products. This is an example of catalyst modification that converts a monooxygenate system to dioxygenate activity. Mechanistic investigations [42] are consistent with this class.

Theoretical investigations attempt to explain why d^0 metal catalysts lead to epoxides and late metal d^n catalysts lead to aldehydes or ketones [43]. The problem was approached by considering the same peroxometallocycle intermediate for both reactions. As the peroxometallocycle forms the epoxide, an interaction between the oxygen atom and vacant t_{2g} orbitals of the d^0 metal provides a low energy pathway for forming the carbon–oxygen bond. This stabilization does not occur when the t_{2g} orbitals are filled, as in late transition metals, so the ketone product is more favored.

(C) Other reactions of metal peroxo intermediates

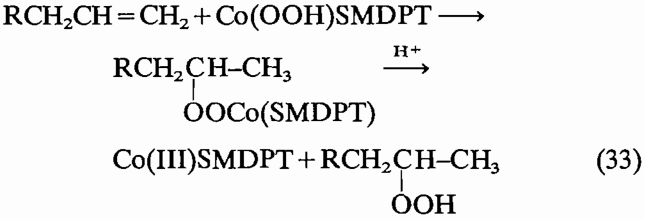
In the Co(SMDPT) catalyzed reactions [44] of alkenes by O_2, the oxidation of the internal carbon of the double bond forms the alcohol and ketone products shown in eqn. (31).

$$RCH_2CH{=}CH_2 \xrightarrow{O_2}$$

$$RCH_2C(O)CH_3 \text{ and } RCH_2CH(OH)CH_3 \qquad (31)$$

Surprisingly, no allylic oxidation products are observed. One mole of solvent is oxidized per mole of product formed. In t-butanol, an inert solvent, substitution of H_2O_2 for O_2 in this reaction is necessary to obtain the alcohol and ketone products. This reaction is consistent with the formation of Co(III)(OOH)SMDPT. The alkene undergoes Markonikov addition of the hydroperoxide complex to form $RCH_2{-}CH(CH_3)OOCo$ (eqns. (32) and (33)).

$$\mathrm{Co(III)SMDPT} + \mathrm{H_2O_2} \longrightarrow \mathrm{Co(OOH)SMDPT} + \mathrm{H^+} \qquad (32)$$



$$\mathrm{RCH_2CH{=}CH_2} + \mathrm{Co(OOH)SMDPT} \longrightarrow \underset{\displaystyle \mathrm{OOCo(SMDPT)}}{\mathrm{RCH_2CH{-}CH_3}} \xrightarrow{H^+} \mathrm{Co(III)SMDPT} + \mathrm{RCH_2}\underset{\displaystyle \mathrm{OOH}}{\mathrm{CH}}\mathrm{{-}CH_3} \qquad (33)$$

Haber–Weiss decomposition of the metal alkyl hydroperoxo complex leads to the observed products.

Metal alkyl peroxo species are likely intermediates in the oxidation of catechol to muconic acid by catechol dioxygenase, an Fe(III) enzyme. Studies of model compounds [45] indicate a mechanism that involves the attack of O_2 on a monodentate catechol bound to Fe(III). The two electron oxidation of the catechol leads to a 'peroxo-quinone' complex which then forms muconic anhydride. The reaction is similar to the Baeyer–Villiger lactonization of cyclic ketones by peroxo complexes of molybdenum [46]. The crystal structure of an iridium complex related to the peroxo intermediate and proposed for catechol dioxygenase has been reported [47]. Catechol dioxygenase and its model complexes obtain dioxygenate activity from peroxo intermediates. This is possible because the substrate furnishes the two electrons to O_2, forming a peroxide which can undergo further oxidation reactions.

V. Metal centered oxidizing agents

Reactions in which the metal complex is the sole oxidant are assigned to Class V. The sole function of O_2 is to regenerate the high oxidation state of the metal. An example from this category is the Wacker reaction, an important industrial process for the Pd(II) catalyzed oxidation of ethylene to acetaldehyde [48]. In this reaction, nucleophilic attack of water on a Pd(II) ethylene π complex forms ethanol which remains coordinated by a Pd–C σ bond (Fig. 3). Upon the dissociation of a chloride ligand from the Pd(II) complex, hydride elimination from the ethanol forms a vinyl alcohol π complex. Vinyl alcohol, a tautomer of acetaldehyde, dissociates from the complex with the concomitant reduction of Pd(II) to Pd(O). Pd(O) is reoxidized to Pd(II) by a Cu(II) co-catalyst and the resulting Cu(I) species reacts rapidly with O_2 to reform Cu(II). 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 [48b, 49].

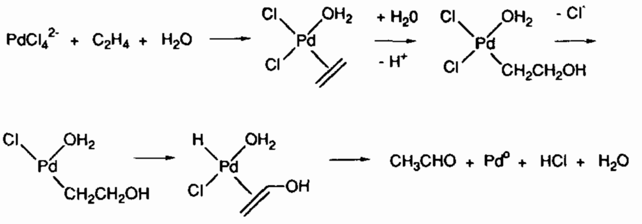


Fig. 3. The oxidation of ethylene to acetaldehyde by Pd(II) in the Wacker process.

Palladium catalysts have also been used successfully for the activation of C–H bonds in alkanes [30c]. Methane has been oxidized [50] with H_2O_2 in a palladium catalyzed reaction in trifluoroacetic acid. H_2O_2 regenerates the Pd(II) subsequent to the reduction of Pd(II) to Pd(O) by methane. In related work, ethanol can be oxidized to ethylene glycol in water [51]. This system displays interesting selectivity since a primary C–H bond is usually more difficult to oxidize than a C–OH bond.

Unusual selectivity is also observed in the $[Ru_3O(CH_3CH_2CO_2)_6(H_2O)_3]$ catalyzed oxidation of alcohols to aldehydes with O_2 [52]. Oxidation occurs only when the substrate can coordinate to the metal complex, displacing the axial water ligand. Since an alcohol is a better ligand than its corresponding aldehyde, selective oxidation to the aldehyde is attained. The half reaction for the oxidation of alcohol to aldehyde is a two electron oxidation accompanied by the loss of two protons. In the first cycle of the catalytic oxidation of alcohol by $[Ru_3O(CH_3CH_2CO_2)_6(H_2O)_3]$, O_2 is reduced to H_2O_2. H_2O_2 provides two additional oxidizing equivalents to the catalyst to convert another mole of alcohol to ketone. The two cycles enable the system to function as a dioxygenate.

Conclusions

The scope and complexity of metal catalyzed oxidation chemistry is tremendous. The mechanisms of these reactions are frequently unknown or controversial. In those cases where kinetic studies have been carried out, elaborate reaction mechanisms are often needed to account for the reactivity of the catalyst. The intention of this article is not to oversimplify this prolific area of research, but to enable the reader to appreciate oxidation chemistry in the context of the role of the metal catalyst [53].

Several examples of oxidation reactions with O_2 have been discussed to familiarize the reader with each classification which is summarized below. This classification scheme can be used to assign mechanisms of newly discovered reactions and to help choose metal catalysts for selective oxidations. It is hoped that this classification will stimulate efforts to find new classes of reactions [54].

Classification of metal catalyzed oxidations by O_2

Class I. Metal bound O_2. The metal coordinates O_2 enhancing its basicity and radical reactivity. The substrate reacts with the coordinated O_2 molecule.

Class II. Metal oxo via dioxygen. High valent metal oxo oxidants are formed by O_2 and a low oxidation state metal complex. Both oxygens of O_2 are used to oxidize the substrate with the metal oxo species.

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. As in Class II, a high valent metal oxo complex oxidizes the substrate. These systems are often monooxygenates but dioxygenate activity can occur.

Class IV. Metal peroxo systems. Metals and peroxides form reactive intermediates. They undergo three principal reactions with substrates.

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.

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 authors acknowledge several helpful discussions of this manuscript with Douglas E. Patton. Russell S. Drago's research in this area has received support from the US 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; (c) N. N. Greenwood and A. Earnshaw, *Chemistry of the Elements,* Pergamon, New York, 1984.

3 (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.

4 R. S. Drago, J. P. Cannady and K. A. Leslie, *J. Am. Chem. Soc., 102* (1980) 6014.

5 (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, pp. 247.

6 C. L. Bailey and R. S. Drago, *Coord. Chem. Rev., 87* (1987) 321, and refs. therein.

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

8 *Handbook of Chemistry and Physics,* Chemical Rubber Publishing Co., Cleveland, OH, 65th edn., 1985.

9 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 refs. therein.

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

11 (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, New York, 1988, p. 33.

12 (a) T. R. Cundari and R. S. Drago, *Inorg. Chem., 90* (1990) 487; (b) *Int. J. Quantum Chem., 36* (1989) 773.

13 J. C. Dobson, W. K. Seok and T. J. Meyer, *Inorg. Chem., 25* (1986) 1514.

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

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

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

17 (a) C. L. Hill and B. C. Shardt, *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) P. E. Ellis, Jr. and J. E. Lyons, *J. Chem. Soc., Chem. Commun.,* (1989) 1187; (b) (1989) 1189; (c) *J. Catal. Lett., 3* (1989) 389.

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

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

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

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

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

24 (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.-I. Murahashi, T. Naota, T. Kuwabara, T. Saito, H. Kumobayashi and S. Akutagawa, *J. Am. Chem. Soc., 112* (1990) 7820.

25 C. Gianotti, C. Fontaine, A. Chiaroni and C. Riche, *J. Organomet. Chem., 113* (1976) 57.

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

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

28 (a) A. S. Goldstein and R. S. Drago, *J. Chem. Soc., Chem. Commun.,* (1991) 21; (b) A. S. Goldstein, R. H. Beer, R. S. Drago and A. Rheingold, submitted for publication.

29 (a) I. Tabushi and N. Koga, *J. Am. Chem. Soc., 101* (1974) 6456; I. Tabushi, *Coord. Chem. Rev., 86* (1988) 1, and refs. therein; (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.

30 (a) P. R. Ortiz de Montellano (ed.), *Cytochrome P-450,* Plenum, 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.

31 J. H. Dawson, *Science, 240* (1988) 433, and refs. therein.

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

33 (a) R. A. Sheldon, in S. Patai (ed.), *The Chemistry of Functional Groups, Peroxides,* Wiley, New York, 1983; (b) L. Saussine, E. Brazi, A. Robine, H. Mimoun, J. Fischer and R. Weiss, *J. Am. Chem. Soc., 107* (1985) 3534, and refs. therein; (c) A. S. Goldstein and R. S. Drago, *Inorg. Chem., 30* (1991) 4506; (d) R. S. Shukla and T. M. M. Kahn, *J. Mol. Catal., 44* (1988) 85; (e) H.-C. Tung and D. T. Sawyer, *J. Am. Chem. Soc., 112* (1990) 8214.

34 G. W. Parshall, *Homogeneous Catalysis,* Wiley, New York, 1980, and refs. therein.

35 (a) R. A. Sheldon, *Recueil, 92* (1973) 253; (b) A. O. Chong and K. B. Sharpless, *J. Org. Chem., 42* (1977) 1587.

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

37 M. G. Finn and K. B. Sharpless, *Asymmetric Synth., 5* (1985) 247.

38 O. Bartolini, F. Di Furia and G. Modena, *J. Mol. Catal., 14* (1982) 53; *14* (1982) 63, and refs. therein.

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

40 G. N. Koskel, M. I. Faberov, L. L. Zalygin and G. A. Kushinskaya, *J. Appl. Chem. USSR, 44* (1971) 885.

41 (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.

42 (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.

43 K. Purcell, *Organometallics, 4* (1985) 509.

44 D. E. Hamilton, R. S. Drago and A. Zombeck, *J. Am. Chem. Soc., 107* (1987) 374.

45 L. Que, Jr., R. C. Kolanczyk and L. S. White, *J. Am. Chem. Soc., 109* (1987) 5373, and refs. therein.

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

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

48 (a) J. Schmidt, W. Jafner, R. Jira, J. Seldmeier, R. Sieber, R. Ruttingcr and J. Kojer, *Angew. Chem., Int. Ed. Engl., 1* (1962) 80; (b) J. E. Bäckvall, B. Akermark and S. S. Ljunggren, *J. Am. Chem. Soc., 101* (1979) 2411, and refs. therein.

49 (a) J. E. Bäckvall, *Pure Appl. Chem., 55* (1983) 1669; (b) B. Äkermark, J. E. Bäckvall and K. Zetterberg, *Acta Chem. Scand., Ser. B, 36* (1982) 577; (c) J. E. Bäckvall, R. B. Hopkins, H. Grennberg, M. M. Mader and A. K. Awasthi, *J. Am. Chem. Soc., 112* (1990) 5160.

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

51 J. A. Labinger, A. M. Herring and J. E. Bercaw, *J. Am. Chem. Soc., 112* (1990) 5628.

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

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

54 R. S. Drago, *Coord. Chem. Rev.,* in press.