ELSEVIER

Catalysis Today 44 (1998) 183–188

CATALYSIS TODAY

# Reductive activation of dioxygen: A new concept for the catalytic oxidation

Munetaka Akita, Yoshihiko Moro-oka*

*Research Laboratory of Resources Utilization, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503, Japan*

**Abstract**

Transition metal–dioxygen complexes, which have been studied intensively in relevance to the active species of oxygenation with dioxygen molecule, are classified according to the extent of electron transfer from the metal center(s) to the $O_2$ ligand. A new $O_2$-activation method via a higher valent bis(μ-oxo) dimetal species resulting from extensive electron transfer is proposed on the basis of the results of our bioinorganic studies on the dioxygen complexes supported by the hydrotris(3,5-diisopropylpyrazolyl)borate ligand ($Tp^{iPr}$). © 1998 Elsevier Science B.V. All rights reserved.

*Keywords:* Dioxygen complex; Aliphatic oxidation; O–O cleavage

## 1. Introduction

Oxygenation with molecular oxygen is an essential transformation in chemical and biological processes, most of which are associated with transition metal catalytic species (catalysts and metalloproteins, respectively) [1]. The role of the transition metal species ranges widely from (i) incorporation of dioxygen and substrates into the coordination sphere (molecular recognition) to (ii) chemical transformations (bond formation, redox process, etc.) leading to oxygenated products. One of the key features which influences the above aspects is the variety of coordination modes of dioxygen molecule to the metal component, which are characterized by spectroscopic and crystallographic studies of isolated discrete transition metal–dioxygen complexes [2]. The coordination mode is also closely related to *how dioxygen molecule is activated by a transition metal species*.

In this paper we are going to display examples where dioxygen molecule is activated by electron transfer from the metal center, in other words, *reductive activation*,[1] and the system to be discussed will be focused on bioinorganic systems related to metalloproteins. At first sight, reductive activation of dioxygen molecule sounds inconsistent with the function as an oxidant, because increase of electron density at the oxygen atom causes reduction of its electrophilicity toward a substrate to be oxidized (e.g. hydrocarbon). However, a new possibility of oxygenation by way of another species, which results from extensive electron

---

*Corresponding author. Tel.: 00 81 45 924 5228; fax: 00 81 45 924 5226; e-mail: ymorooka@res.titech.ac.jp

[1] In general, the term "reductive oxidation" stands for the process shown: $O_2 + 2H^+ + 2e^- \rightarrow [O] + H_2O$. Action of protons and electrons (two equivalents each) to a dioxygen molecule results in elimination of the thermodynamically very stable water molecule to leave a highly reactive oxygen atom, which is so electrophilic as to oxygenate C=C double bonds and C–H bonds (even the C–H bond in methane). A group of enzymes called "monooxygenases" employs this process within the coordination sphere of an active metal site for generation of highly reactive species. Cytochrome *P*-450 is raised as a typical example.

*PII* S0920-5861(98)00189-8

transfer from the metal center(s), has been developed recently.

## 2. Classification of transition metal–dioxygen complexes

In Fig. 1, the O–O stretching vibrations and the coordination structures of isolated transition metal–dioxygen complexes are summarized along with the data for metalloenzymes relevant to oxygen transport and oxygenation. The dioxygen complexes are classified according to:

1. the extent of electron transfer from the metal center to the $O_2$ moiety, and
2. nuclearity of the metal component, though these two aspects are closely related to each other as will be discussed below.

One electron transfer to the $O_2$ ligand forms a superoxide anion $(O_2^-)$, and transfer of two electrons leads to a peroxide ligand $(O_2^{2-})$. Because the electrons are

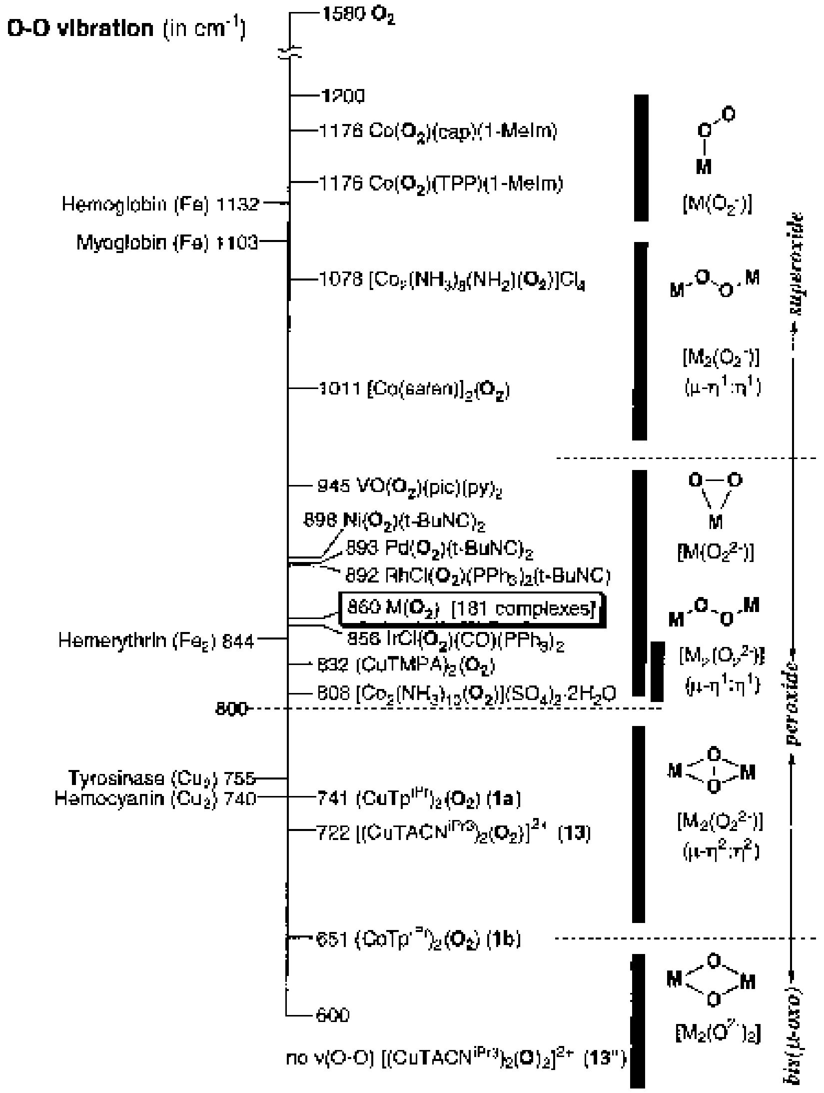
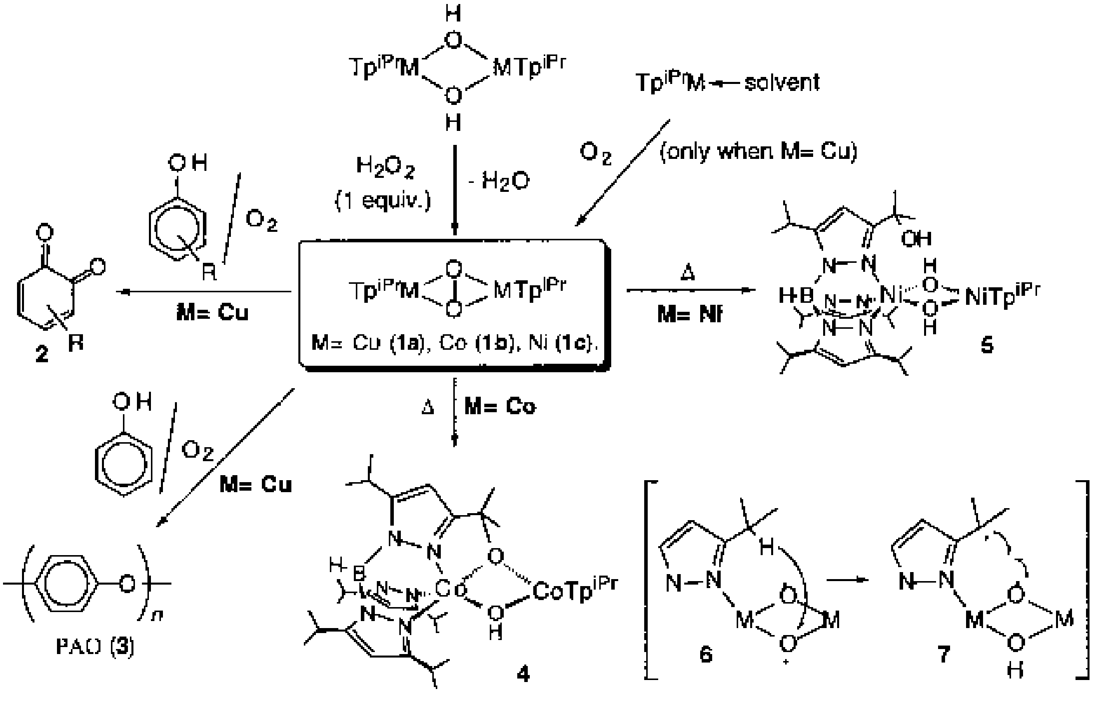


Fig. 1. Comparison of ν(O–O) values and coordination structures of transition metal–dioxygen complexes.

accommodated in the $\pi^*$-orbitals of the O–O moiety, the electron transfer causes not only reduction of the O–O bond order as is consistent with the increase of the O–O stretching vibrations, but also increase of the electron density at the oxygen atoms. Therefore, the dioxygen species thus incorporated in a transition metal species is rather nucleophilic owing to electron transfer from the metal center and therefore is sluggish with respect to oxygenation reactions, which intrinsically need electrophilic species to remove electron(s) from a substrate. In order to realize an efficient oxygenation reaction further activation is essential.

## 3. Reductive activation of dioxygen molecule through bis(μ-oxo) species

In our laboratory, bioinorganic studies on transition metal complexes supported by a series of hydrotrispyrazolylborates ($Tp^R$) are recent research subjects [3], and one of the notable results is synthesis of the dicopper $O_2$ complex $(CuTp^{iPr})_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-}O_2)$ **1a** (Scheme 1), which was studied as a model compound for the oxygenated form (*oxyhemocyanin*) of *hemocyanine* ($O_2$-transport proteins of invertebrates). The dicopper(II) complex **1a** was prepared by oxygenation of the reduced Cu(I) precursor or dehydrative condensation of the hydroxo complex with $H_2O_2$ [4]. Although its physicochemical properties such as O–O vibration and UV spectrum had been known and a number of model complexes with plausible geometries were prepared, none of them could reproduce the properties satisfactorily and no definite conclusion had been obtained. However, the striking similarity of the features of **1a** to those of *oxyhemocyanin* led to a prediction of the $O_2$-coordination mode as "$\mu\text{-}\eta^2\text{:}\eta^2$", which was later confirmed by X-ray crystallography of oxyhemocyanin of *Limulus polyphemus* [5]. One of the characteristic features is the O–O vibration appearing in the range as low as 741 $cm^{-1}$ (comparable to 740 $cm^{-1}$ for *oxyhemocyanin*), which is far below the O–O values of previous examples (>800 $cm^{-1}$). As

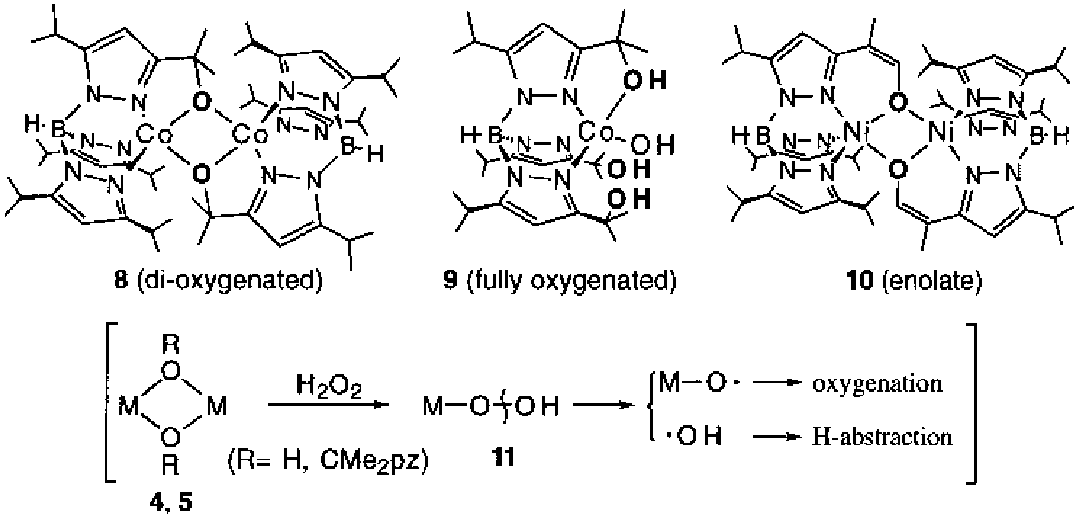


Scheme 1.

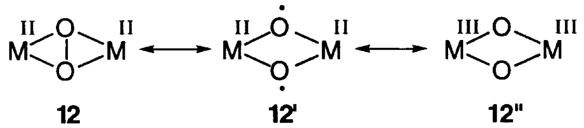
can be seen from Fig. 1, most of dioxygen complexes exhibit O–O vibrations above 800 cm$^{-1}$, and no example with O–O vibration below 800 cm$^{-1}$ was known before our report on the dicopper complex **1a** in 1989. The low value comes from the interaction with the two metal centers. Extensive back-donation to the $\sigma^*$-orbitals of the O–O bond, in addition to that to the $\pi^*$-orbitals generally observed for dioxygen complexes, causes weakening of the O–O bond [6].

However, the reactivity of the dicopper complex **1a** turned out to be still "nucleophilic" but some oxidation reactions were observed (Scheme 1). Addition of protic substrates resulted in hydrolysis of the ($\mu$-$O_2$)$Cu_2$ core. For example, phenols were found to be converted to *o*-quinone **2** under aerobic conditions probably via radical oxygenation of a phenoxo intermediate formed by the hydrolysis [7]. Since this reaction is also catalyzed by *tyrosinase*, the $O_2$-adduct of which also exhibits spectroscopic features characteristic of a ($\mu$-$\eta^2$:$\eta^2$-$O_2$)$Cu_2$ core [$\nu$(O–O) 755 cm$^{-1}$], **1a** can mimic not only the structural but also the functional aspects of *tyrosinase*. The reaction mechanism of *tyrosinase* may involve a radical one similar to that of **1a**, and the reaction mechanism involving a $\mu$-hydroperoxo–$\mu$-phenoxo-dinuclear species surrounded by the protein environment has been proposed for *tyrosinase*-catalyzed reactions [7]. An extension has led to the development of dehydrogenative condensation polymerization of phenol producing poly(1,4-phenylene oxide) (PAO: **3**) [8]. PAO is a useful engineering plastic when polymerized regiospecifially (*p*-conjunction) but most of the previous catalysts give polymers contaminated with *o*-linked isomeric structure. In this regard, complex **1a** is found to be an excellent regiospecific polymerization catalyst of phenol.

Recently a breakthrough via *reductive activation* has been found by us and another group. Introduction of a more electron-donating metal center in place of copper caused lowering or disappearance of the O–O vibration. The cobalt and nickel complexes ($\mu$-$O_2$)($MTp^{iPr}$)$_2$ (M=Co (**1b**), Ni (**1c**)) were accessible via the dehydrative condensation method [9]. The $\nu$(O–O) band for the cobalt complex **1b** was observed at 651 cm$^{-1}$, but that for the nickel complex **1c** could not be located, suggesting further weakening or breaking of the O–O bond. The $O_2$ species **1b,c** were thermally unstable, and analyses of the thermal decomposition products **4** and **5** revealed that the isopropyl groups in the $Tp^{iPr}$ ligand proximal to the metal center were oxygenated (Scheme 1). Although detailed information on the intermediates has not been obtained until now, homolytic O–O bond cleavage and H-abstraction by the resulting oxygen-radical species (**6**→**7**) followed by coupling with the remaining oxyl radical would result in oxygenation. When thermal



Scheme 2.



Scheme 3.

decomposition was carried out in the presence of an excess amount of $H_2O_2$, further oxygenated products **8** and **9** (M=Co) and **10** (M=Ni) were obtained (Scheme 2). Their formation may be explained in terms of O–O homolysis of a hydroperoxo intermediate **11** arising from protonolysis of the ($\mu$-OR)$_2$M$_2$ core in **4** and **5** with $H_2O_2$.

The high reactivity of the Co (**1b**) and Ni complexes (**1c**) may be ascribed to the contribution of the resonance forms **12**′ and **12**″ (Scheme 3). The di($\mu$-oxyl radical) form **12**′ arises from homolytic O–O bond cleavage, and concomitant electron-transfer from the metal centers forms the higher-valent bis($\mu$-oxo) species **12**″ resulting from formal 4e-reduction. The oxygen atoms in **12**′ and **12**″ may be electrophilic enough to abstract a proximal hydrogen atom via a radical or electrophilic mechanism, respectively. Thus extensive electron transfer from the metal center to the $\mu$-$\eta^2$:$\eta^2$-$O_2$ moiety in **12** finally produces an electrophilic oxygen species (**12**′ or **12**″) which is able to functionalize an aliphatic hydrocarbyl group. In this context, the higher valent form **12**″ may be regarded as a dimeric form of the oxo species [$M^{III}$=O], and it is well known that analogous oxo species are an active species for various oxygenation of hydrocarbons such as epoxidation and C–H oxygenation. Or the radical character of **12**′ may be responsible for the initiation of the oxygenation.

A similar concept (Scheme 3) was recently proposed by Tolman's group [10]. They prepared dicopper–$O_2$ complexes **13** analogous to **1a** supported by a series of $N_3$-donor ligands, substituted 1,4,7-triazacyclononanes (TACN). The coordination mode of the $O_2$-bridge is characterized to be "$\mu$-$\eta^2$:$\eta^2$" on the basis of the UV and vibrational data (Fig. 1). It is remarkable that the isopropyl derivative exhibited solvatochromism based on the reversible structural change between the $\mu$-$\eta^2$:$\eta^2$-$O_2$ form **13** and the bis($\mu$-oxo) form **13**″ (corresponding to **12**″) which was confirmed by X-ray crystallography. They also observed stoichiometric oxygenation of the substituents of the TACN ligand.

## 4. Conclusions

Metal complexes supported by facially arranged $N_3$ donors such as $Tp^R$ and $TACN^R$ form dinuclear $\mu$-$\eta^2$:$\eta^2$-$O_2$-type dioxygen complexes **12**, which are not so active as oxidants. The $O_2$-moiety in **12** is rather nucleophilic and protic substrates such as phenols can be oxidized via a hydroperoxo intermediate arising from partial hydrolysis of the $\mu$-$\eta^2$:$\eta^2$-$O_2$-core with the substrates. However, upon introduction of electron-donating metals (e.g. Co and Ni) or ligands (e.g. $TACN^R$) the extensive electron transfer to the $\sigma^*$-orbital of the $\mu$-$\eta^2$:$\eta^2$-$O_2$-moiety causes O–O bond cleavage to form the bis($\mu$-oxyl) species **12**′ or the higher valent bis($\mu$-oxo) species **12**″, which potentially works as an oxidizing agent. At this moment, only *intramolecular*, *stoichiometric* oxygenation of aliphatic groups in the $N_3$-ligands is observed. But appropriate design of the ligand, for e.g., introduction of ligand-substituents resistant to the intramolecular oxygenation is expected to lead to a new phase of catalytic oxygenation.

## References

[1] The Thematic Issue of Chem. Rev. (metal dioxygen complexes), Chem. Rev. 94 (1994) 567–856; The Thematic Issue of Chem. Rev. (bioinorganic enzymology), Chem. Rev. 96 (1996) 2239–3042.

[2] J.A. Lyons, Aspects Homog. Catal. 3 (1977) 1; M.H. Gubelmann, A.F. Williams, Struct. Bonding 55 (1983) 1; N. Kitajima, M. Akita, Y. Moro-oka, in: W. Ando (Ed.), Organic Peroxides, Wiley, New York, 1992.

[3] N. Kitajima, W.B. Tolman, Progr. Inorg. Chem. 43 (1995) 419; S. Trofimenko, Chem. Rev. 93 (1993) 943.

[4] N. Kitajima, K. Fujisawa, C. Fujimoto, Y. Moro-oka, S. Hashimoto, T. Kitagawa, K. Toriumi, K. Tatsumi, A. Nakamura, J. Am. Chem. Soc. 114 (1992) 1277; N. Kitajima, Y. Moro-oka, Chem. Rev. 94 (1994) 737; N. Kitajima, Y. Moro-oka, J. Chem. Soc., Dalton Trans. (1993) 2665; N. Kitajima, Adv. Inorg. Chem. 39 (1992) 1.

[5] K.A. Magnus, B. Hazes, H. Ton-That, C. Bonaveture, J. Bonaveture, W.G.J. Hol, Proteins 19 (1994) 302; K.A. Magnus, H. Ton-That, J.E. Carpenter, Chem. Rev. 94 (1994) 727.

[6] E.I. Solomon, U.M. Sundaram, T.E. Machonkin, Chem. Rev. 96 (1996) 2563.

[7] N. Kitajima, T. Koda, Y. Iwata, Y. Moro-oka, J. Am. Chem. Soc. 112 (1990) 8833.

[8] H. Higashimura, K. Fujisawa, Y. Moro-oka, M. Kubota, A. Terahara, A. Siga, H. Uyama, S. Kobayashi, to be reported.

[9] S. Hikichi, H. Komatsuzaki, N. Kitajima, M. Akita, M. Mukai, T. Kitagawa, Y. Moro-oka, Inorg. Chem. 36 (1997) 266; S. Hikichi, H. Komatsuzaki, M. Akita, Y. Moro-oka, J. Am. Chem. Soc. 120 (1998) 4699.

[10] J.A. Halfen, A. Mahapatra, E.C. Wilkinson, S. Kaderli, V.G. Young, Jr., L. Que, Jr., A.D. Zuberbühler, W.B. Tolman, Science 271 (1996) 1397; A. Mahapatra, J.A. Halfen, E.C. Wilkinson, G. Pan, X. Wang, V.G. Young, Jr., C.J. Cramer, L. Que, Jr., W.B. Tolman, J. Am. Chem. Soc. 118 (1996) 11555; W.B. Tolman, Acc. Chem. Res. 30 (1997) 227.