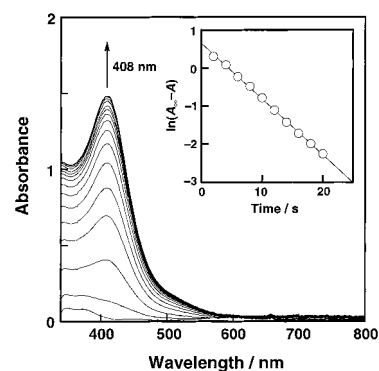# Aliphatic Hydroxylation by a Bis(μ-oxo)dinickel(III) Complex

Shinobu Itoh,*,† Hideki Bandoh,† Shigenori Nagatomo,‡
Teizo Kitagawa,*,‡ and Shunichi Fukuzumi*,†

Department of Material and Life Science
Graduate School of Engineering, Osaka University
2-1 Yamada-oka, Suita, Osaka 565-0871, Japan
Institute for Molecular Science
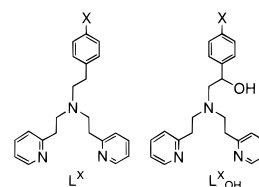*Myodaiji, Okazaki 444-8585, Japan*

Received April 26, 1999

The structure and reactivity of transition-metal complexes of active oxygen species have long been among the most important and attractive subjects not only in bioinorganic chemistry but also in synthetic organic reactions.[1−7] Among several types of mono-, di-, and polynuclear transition-metal active oxygen complexes, high-valent bimetallic bis(μ-oxo) complexes [M(μ-O)$_2$M] have recently attracted particular attention as possible reaction intermediates in oxygen metabolism, such as dioxygen activation for substrate hydroxylation and for tyrosyl radical formation by non-heme metalloenzymes and dioxygen evolution in photosystem II.[8−12] The structures of high-valent bimetallic bis(μ-oxo) complexes have been well characterized by X-ray crystallographic analyses on M(μ-O)$_2$M complexes where M = Fe, Cu, Mn, and Ni.[11,13−17] The reactivities of M(μ-O)$_2$M complexes where M = Fe, Cu, and Mn have also been explored in relation with aliphatic C−H bond activation.[14c,18−20] Such C−H bond activation by M(μ-O)$_2$M complexes is currently receiving increased attention as the key step in reactions of methane monooxygenases (MMO) and related enzymes.[9b,12] To elucidate the C−H bond activation mechanism, it is highly desired to explore C−H bond activation by different types of active oxygen−metal complexes, the

† Osaka University.
‡ Institute for Molecular Science.
(1) Valentine, J. S., Foote, C. S., Greenberg, A., Liebman, J. F., Eds. *Active Oxygen in Biochemistry*; Chapman and Hall: London, 1995.
(2) Foote, C. S., Valentine, J. S., Greenberg, A., Liebman, J. F., Eds. *Active Oxygen in Chemistry*; Chapman and Hall: London, 1995.
(3) Kitajima, N.; Moro-oka, Y. *Chem. Rev.* **1994**, *94*, 737−757.
(4) Feig, A. L.; Lippard, S. J. *Chem. Rev.* **1994**, *94*, 759−805.
(5) Pecoraro, V. L.; Baldwin, M. J.; Gelasco, A. *Chem. Rev.* **1994**, *94*, 807−826.
(6) Solomon, E. I.; Tuczek, F.; Root, D. E.; Brown, C. A. *Chem. Rev.* **1994**, *94*, 827−856.
(7) Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879−2932.
(8) Valentine, A. M.; Lippard, S. J. *J. Chem. Soc., Dalton Trans.* **1997**, 3925−3931.
(9) (a) Que, L., Jr. *J. Chem. Soc., Dalton Trans.* **1997**, 3933−3940, (b) Shu, L.; Nesheim, J. C.; Kauffmann, K.; Munck, E.; Lipscomb, J. D.; Que, L., Jr. *Science* **1997**, *275*, 515−518.
(10) Tommos, C.; Babcock, G. T. *Acc. Chem. Res.* **1998**, *31*, 18−25.
(11) Ruttinger, W.; Dismukes, G. C. *Chem. Rev.* **1997**, *97*, 1−24.
(12) Elliot, S. J.; Zhu, M.; Tso, L.; Nguyen, H.-H. T.; Yip, J. H.-K.; Chan, S. I. *J. Am. Chem. Soc.* **1997**, *119*, 9949−9955.
(13) Hsu, H.-F.; Dong, Y.; Shu, L.; Young, V. G., Jr.; Que, L., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 5230−5237.
(14) (a) Halfen, J. A.; Mahapatra, S.; Wilkinson, E. C.; Kaderli, S.; Young, V. G., Jr.; Que, L., Jr.; Tolman, W. B. *Science* **1996**, *271*, 1397−1400. (b) Mahapatra, S.; Halfen, J. A.; Wilkinson, E. C.; Pan, G.; Wang, X.; Young, V. G., Jr.; Cramer, C. J.; Que, L., Jr.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11555−11574. (c) Mahadevan, V.; Hou, Z.; Cole, A. P.; Root, D. E.; Lal, T. K.; Solomon, E. I.; Stack, T. D. P. *J. Am. Chem. Soc.* **1997**, *119*, 11996−11997.
(15) (a) Que, L., Jr.; True, A. E. *Prog. Inorg. Chem.* **1990**, *38*, 97−200. (b) Lal, T. K.; Mukherjee, R. *Inorg. Chem.* **1998**, *37*, 2373−2382 and references therein.
(16) Limburg, J.; Vrettos, J. S.; Liable-Sands, L. M.; Rheingold, A. L.; Crabtree, R. H.; Brudvig, G. W. *Science* **1999**, *283*, 1524−1527.
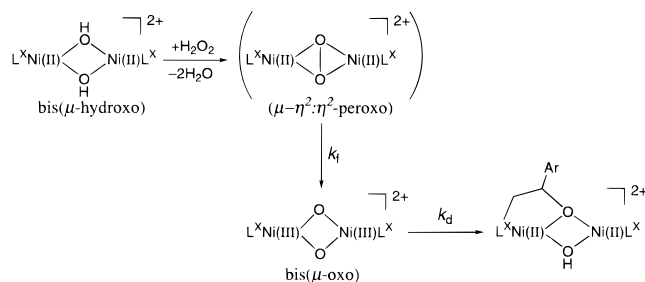(17) Hikichi, S.; Yoshizawa, M.; Sasakura, Y.; Akita, M.; Moro-ka, Y. *J. Am. Chem. Soc.* **1998**, *120*, 10567−10568.
(18) Kim, C.; Dong, Y.; Que, L., Jr. *J. Am. Chem. Soc.* **1997**, *119*, 3635−3636.
(19) Mahapatra, S.; Halfen, J. A.; Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11575−11586.
(20) Wang, K.; Mayer, J. M. *J. Am. Chem. Soc.* **1997**, *119*, 1470−1471.

Figure 1. Spectral change observed upon addition of 1 equiv of H_2O_2 into an acetone solution of $[(\mathbf{L^H}Ni^{II})_2(\mu\text{-OH})_2](ClO_4)_2$ (2.5×10^{-4} M) at −90 °C in a 1-cm path length UV cell; 2-s interval. Inset: First-order plot based on the absorption change at 408 nm.

Chart 1

reactivity of which can be finely tuned by varying the metals and the ligands. In addition, the formation mechanism of M(μ-O)$_2$M complexes has yet to be elucidated. We report herein the first aliphatic ligand hydroxylation by a Ni^{III}(μ-O)$_2$Ni^{III} complex, the formation and decay of which were directly followed by spectroscopy.[21] We have previously reported the same type of aliphatic hydroxylation of the ligand sidearm in the reaction of the Cu(I) complex with O$_2$, where a (μ-η^2:η^2-peroxo)dicopper-(II) complex rather than a bis(μ-oxo)dicopper(III) complex was observed as a reaction intermediate.[22] Thus, this study provides an excellent opportunity to disclose the actual role and reactivity of bis(μ-oxo) vs (μ-η^2:η^2-peroxo) bimetallic complexes in the C−H bond activation process.

Bis(μ-hydroxo)dinickel(II) complexes of tridentate ligands $\mathbf{L^X}$ (X = OMe, Me, H, Cl; Chart 1) have been prepared as starting materials by treating the ligand and Ni(ClO$_4$)$_2$·6H$_2$O in the presence of triethylamine in a mixed solvent system of acetone/methanol/acetonitrile.[23] Addition of 1 equiv of H$_2$O$_2$ into an acetone solution of $[(\mathbf{L^H}Ni^{II})_2(\mu\text{-OH})_2]^{2+}$ at a low temperature (−90 °C) resulted in a spectral change, as shown in Figure 1, where a characteristic absorption band at 408 nm (ε = 6000 M^{-1} cm^{-1}) due to an intermediate readily developed. The same absorption intensity at 408 nm was obtained even when an excess amount of H$_2$O$_2$ was added (S1).[24] Thus, the stoichiometry of H$_2$O$_2$ to $[(\mathbf{L^H}Ni^{II})_2(\mu\text{-OH})_2]$ has been determined to be 1:1. The intermediate exhibited a resonance Raman band at 612 cm^{-1}, which shifted to 580 cm^{-1} when H$_2$^{16}O$_2$ was replaced by H$_2$^{18}O$_2$ (S2).[24] In addition, this intermediate was ESR silent.

(21) So far, only two examples of ligand hydroxylation of mononuclear Ni(II) complexes by dioxygen have been reported. However, the structure of the active oxygen intermediate has yet to be identified: (a) Kimura, E.; Sakonaka, A.; Machida, R. *J. Am. Chem. Soc.* **1982**, *104*, 4225−4227. (b) Chen, D.; Martell, A. E. *J. Am. Chem. Soc.* **1990**, *112*, 9411−9412.
(22) (a) Itoh, S.; Kondo, T.; Komatsu, M.; Ohshiro, Y.; Li, C.; Kanehisa, N.; Kai, Y.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 4714−4715. (b) Itoh, S.; Nakao, H.; Berreau, L. M.; Kondo, T.; Komatsu, M.; Fukuzumi, S. *J. Am. Chem. Soc.* **1998**, *120*, 2890−2899.
(23) Experimental details about the synthesis and characterization of the bis(μ-hydroxo)dinickel(II) complexes, the product analysis, and the kinetics are deposited in Supporting Information.
(24) See Supporting Information.

Scheme 1

The characteristic absorption band at 408 nm is fairly close to that of Hikichi's bis(μ-oxo)dinickel(III) complex (410 nm, ϵ = 4200 M^{-1} cm^{-1}).[17] The low-frequency resonance Raman band at 612 cm^{-1} is also very similar to those of $[Cu_2(\mu$-O)$_2]^{2+}$ complexes ($\sim$600 cm^{-1}).[14] In addition, the observed isotope shift of the resonance Raman band ($\Delta\nu$ = 32 cm^{-1}) agrees well with the expected shift of 28 cm^{-1} for diatomic Ni$-$O stretch. From these spectroscopic characteristics, together with the stoichiometry of H_2O_2 to $[(L^HNi^{II})_2(\mu$-OH)$_2]$ (1:1), the intermediate is most likely a bis(μ-oxo)dinickel(III) complex. The same absorption spectra with λ_{max} = 408 nm were obtained in other ligand systems (L^X).

The increase of the absorption band at 408 nm obeyed first-order kinetics, as shown in the inset of Figure 1. The rate constant (k_f) for formation of the bis(μ-oxo)dinickel(III) complex was determined as 0.14 s^{-1} at -90 °C.[25] The activation parameters for the formation process have been determined from the temperature dependence of k_f as $\Delta H^{\ddagger}$ = 5.6 ± 0.1 kcal mol^{-1} and $\Delta S^{\ddagger}$ = -30.9 ± 0.6 cal K^{-1} mol^{-1} (S3).[24] Since the isotope-labeled bis(μ-oxo) core was generated upon treatment with $H_2^{18}O_2$ instead of $H_2^{16}O_2$ (demonstrated by the resonance Raman spectrum),[26] the precursor of the bis(μ-oxo) intermediate may be a (μ-η^2:η^2-peroxo)dinickel(II) complex. The activation parameters of the k_f process are similar to those of the O$-$O bond homolysis in the (μ-η^2:η^2-peroxo)dicopper(II) complex of the same ligand ($\Delta H_H^{\ddagger}$ = 6.7 ± 0.2 kcal mol^{-1} and $\Delta S_H^{\ddagger}$ = -37.1 ± 1.2 cal K^{-1} mol^{-1}).[22b] Such a similarity of the activation parameters indicates that O$-$O bond homolysis of the peroxo species is the rate-determining step for formation of bis(μ-oxo)dinickel(III) complex, as shown in Scheme 1.[27] In such a case, the formation rate of the bis(μ-oxo)dinickel(III) complex should obey first-order kinetics in the equimolar reaction between $[(L^XNi^{II})_2(\mu$-OH)$_2]$ and H_2O_2, as observed experimentally (the inset of Figure 1).

The bis(μ-oxo)dinickel(III) complex is relatively stable at low temperature (below -80 °C) but gradually decomposes at higher temperature (above -50 °C) (S4),[24] leading to benzylic ligand hydroxylation to give L^X_{OH} (Chart 1), as obtained in the reaction of $[Cu^I(L^X)]^+$ with O_2 (96% based on $[(L^HNi^{II})_2(\mu$-OH)$_2]$).[22,23]

The oxygen source for the OH group in L^H_{OH} has been confirmed as hydrogen peroxide by the isotope labeling experiment using $H_2^{18}O_2$.[26] The ligand hydroxylation process obeyed first-order kinetics (S4),[24] and from the temperature dependence of the decay rate (k_d) (Eyring plot, line H in S5)[24] were obtained the activation parameters $\Delta H_H^{\ddagger}$ = 14.9 ± 0.2 kcal mol^{-1} and $\Delta S_H^{\ddagger}$ = -10.1 ± 0.8 cal K^{-1} mol^{-1}. Perdeuteration of the ligand sidearm (L^H-d_4; 1,1,2,2-tetradeuterated phenethylamine derivative) resulted in a significant decrease in the decay rate, as shown in S5 (line D), where the activation parameters were determined to be $\Delta H_D^{\ddagger}$ = 17.2 ± 0.1 kcal mol^{-1} and $\Delta S_D^{\ddagger}$ = -7.0 ± 0.4 cal K^{-1} mol^{-1}.[28] A very large kinetic deuterium isotope effect was obtained for the hydroxylation reaction (e.g., KIE = 21.4 at -20 °C). Furthermore, examination of the *para*-substituent effects (Hammett plot of k_d vs σ^+) gave ρ = -0.83 (R = 0.98) (S6),[24] which is nearly the same as the ρ value for the oxidative *N*-dealkylation in $[(L^{(p-R)Bn_3}Cu)_2(\mu$-O)$_2]^{2+}$ (ρ = -0.8, $L^{(p-R)Bn_3}$ = 1,4,7-tri(*para*-substituted-benzyl)triazacyclononane), where hydrogen atom abstraction by the bis(μ-oxo) complex is the rate-determining step.[19] Thus, ligand hydroxylation in $[(L^XNi^{III})_2(\mu$-O)$_2]^{2+}$ may proceed via the rate-determining hydrogen abstraction (k_d), followed by hydroxyl rebound.[29]

It is interesting to note that the nickel(II) complex affords a bis(μ-oxo)dinickel(III) complex, whereas the copper(II) complex of the same ligand gives (μ-η^2:η^2-peroxo)dicopper(II) in the reaction with H_2O_2.[22] The higher stability of the Ni(III) state as compared to that of the Cu(III) state may enhance O$-$O bond homolysis of the peroxo intermediate, although the origin of such a difference remains to be clarified in detail. We have also shown that the bis(μ-oxo)dinickel(III) species shows a reactivity in C$-$H bond activation similar to that of Tolman's bis(μ-oxo)dicopper-(III) complex: both species exhibit an electrophilic radical character in nature.[19,30] In the previous study, we proposed that a bis(μ-oxo)dicopper(III) complex is the real active intermediate for the benzylic ligand hydroxylation of L^X in the reaction of $[Cu^I(L^X)]^+$ with O_2, even though such an intermediate could not be detected directly.[22b] The present results, however, may suggest the validity of our proposed mechanism for the benzylic ligand hydroxylation, where the high-valent bimetallic bis(μ-oxo) species is involved as the real active species, as in the case of the nickel system.[31]

Supporting Information Available: Experimental details about the synthesis and characterization of the bis(μ-hydroxo)dinickel(II) complexes; the product analysis and kinetics of the ligand hydroxylation reaction; titration of $[(L^HNi^{II})_2(\mu$-OH)$_2]$(ClO$_4$)$_2$ with H_2O_2 (S1); resonance Raman spectra of $[(L^HNi^{III})_2(\mu$-^{16}O)$_2]^{2+}$ and $[(L^HNi^{III})_2(\mu$-^{18}O)$_2]^{2+}$ (S2); Eyring plot for the reaction of $[(L^HNi^{II})_2(\mu$-OH)$_2]$(ClO$_4$)$_2$ with H_2O_2 (S3); spectral change and the first-order plot of the benzylic ligand hydroxylation process (S4); Eyring plots for the ligand hydroxylation process (S5); and Hammett plot for the benzylic ligand hydroxylation process (S6) (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA991326E

(25) Nearly the same first-order rate constants (k_f = 0.14 ± 0.02 s^{-1}) for formation of the bis(μ-oxo)dinickel(III) complex were obtained even when the concentrations of the starting material, $[(L^HNi^{II})_2(\mu$-OH)$_2]$(ClO$_4$)$_2$, and H_2O_2 were varied {[bis(μ-hydroxo)dinickel(II)] = 1.7 × 10^{-4}–5.0 × 10^{-4} M, [H_2O_2] = 2.5 × 10^{-4}–1.0 × 10^{-3} M}. This result firmly demonstrates that the formation of the bis(μ-oxo)dinickel(III) complex is first-order with respect to the dinickel complex but zeroth-order in the H_2O_2 concentration.

(26) Judging from the peak areas of the resonance Raman peaks obtained for the reaction of $[(L^HNi^{II})(\mu$-OH)$_2]^{2+}$ with $H_2^{18}O_2$ at -80 °C (S2, Supporting Information), it has been confirmed that ca. 83% of ^{18}O is incorporated into the bis(μ-oxo)dinickel(III) core at the low temperature. In the product analysis using $H_2^{18}O_2$ at a higher temperature (-20 °C), however, only 42% of ^{18}O is incorporated into the hydroxylated ligand L^H_{OH}. We presumed that the oxygen atom of the bis(μ-oxo)dinickel(III) core was exchangeable with that of H_2O at the higher temperature. Que and his co-worker also reported that the oxygen atom of Fe$^{III}(\mu$-O)$_2$Fe^{IV} core is easily replaced by that of H_2O.[18]

(27) There could be another intermediate, such as a (μ-1,1-hydroperoxo)-(μ-hydroxo)dinickel(II) complex between the bis(μ-hydroxo)dinickel(II) complex (the starting material) and the (μ-η^2:η^2-peroxo)dinickel(II) complex, since neither the characteristic absorption band nor the resonance Raman band due to (μ-η^2:η^2-peroxo)dinickel(II) intermediate has been detected in the expected region (UV$-$vis, $\sim$350 nm; resonance Raman, $\sim$750 cm^{-1}).

(28) The ^{1}H NMR spectrum of the organic product showed that the ethylene group of the pyridine sidearms remained intact after the ligand hydroxylation of L^H-d_4.

(29) The hydrogen atom abstraction and the hydroxyl rebound can proceed in a concerted manner, as discussed for the copper system.[19]

(30) The radical character of the bis(μ-oxo)dinickel(III) complex has also been indicated by the reaction with phenol derivatives such as 2,4-di-*tert*-butylphenol and 2,6-di-*tert*-butylphenol and 1,4-cyclohexadiene.[23]

(31) Rapid preequilibration of the bis(μ-oxo)dinickel(III) species with a small amount of the more reactive species could not be ruled out completely.