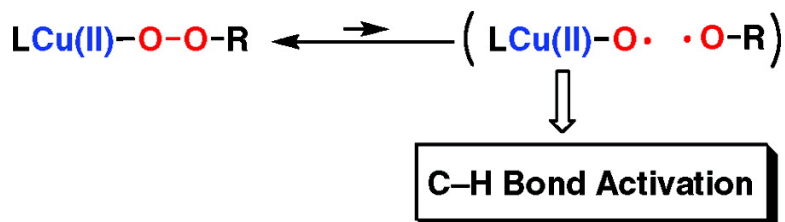Communication

Reactivity of Mononuclear Alkylperoxo Copper(II) Complex. O–O Bond Cleavage and C–H Bond Activation

Atsushi Kunishita, Hirohito Ishimaru, Satoru Nakashima, Takashi Ogura, and Shinobu Itoh

More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 4 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

Reactivity of Mononuclear Alkylperoxo Copper(II) Complex. O−O Bond Cleavage and C−H Bond Activation

Atsushi Kunishita,† Hirohito Ishimaru,‡ Satoru Nakashima,‡ Takashi Ogura,‡ and Shinobu Itoh*,†

Department of Chemistry, Graduate School of Science, Osaka City University, 3-3-138 Sugimoto, Sumiyoshi-ku, Osaka 558-8585, Japan, and Picobiology Research Center, Graduate School of Life Science, University of Hyogo, 3-2-1 Koto, Kamigori-cho, Ako-gun, Hyogo 678-1297, Japan

Received January 19, 2008; E-mail: shinobu@sci.osaka-cu.ac.jp

Mononuclear copper-active oxygen species play important roles as reactive intermediates in many biological and industrial catalytic oxidation processes.[1−3] For copper monooxygenases such as peptidylglycine α-amidating monooxygenase (PAM) and dopamine β-monooxygenase (DβM), a mononuclear hydroperoxo copper(II) species LCu(II)−OOH, which is formally generated by the reaction of LCu(I) and O_2 and subsequent addition of H• (or H⁺ + e⁻), has been suggested as the reactive intermediate for the aliphatic hydroxylation of the substrates.[4] More recently, a mononuclear superoxo copper(II) species LCu(II)−OO•, initially formed intermediate of the reaction between LCu(I) and O_2, has also been proposed as a possible reactive intermediate.[5−8] Furthermore, a recent QM/MM calculation study has suggested that a copper(II)−oxyl radical species LCu(II)−O•, which can be generated by O−O bond homolysis of LCu(II)−OOH, is the most reactive species among the intermediates.[9] To gain insight into the dioxygen activation mechanism at the mononuclear copper active sites, a great deal of effort has been made in model chemistry to evaluate the structure, spectroscopic features, and reactivity of the mononuclear copper-active oxygen species.[1−3,10−18]

On the other hand, alkylperoxo iron(III) complexes LFe(III)−OOR have been studied extensively in model systems to provide significantly important insights into the catalytic mechanism of non-heme iron monooxygenases.[19−21] In this respect, studies of mononuclear alkylperoxo copper(II) complexes LCu(II)−OOR may also afford important information about the dioxygen activation mechanism at the mononuclear copper reaction centers. However, little is known about the reactivity of LCu(II)−OOR complexes.[22−24]

We herein report the reactivity study of a new mononuclear alkylperoxo copper(II) complex **2**, which is generated by the reaction of copper(II) starting material **1**[24] and cumene hydroperoxide (CmOOH) in CH_3CN (Scheme 1). The cumylperoxo copper-

Scheme 1

(Y = ClO₄⁻, S = CH₃CN)
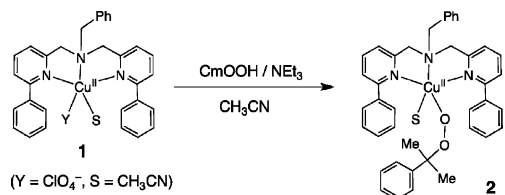
(II) complex **2** has been found to undergo homolytic cleavage of the O−O bond and induce C−H bond activation of exogenous substrates, providing important insight into the catalytic mechanism of the copper monooxygenases.

Treatment of **1** with cumene hydroperoxide in the presence of triethylamine in acetonitrile at −40 °C gave cumylperoxo copper-
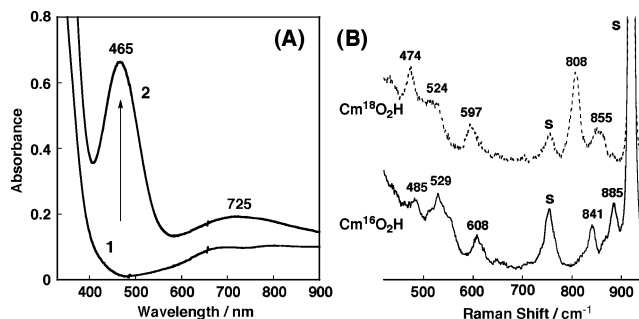
† Osaka City University.
‡ University of Hyogo.

Figure 1. (A) Spectral change for the reaction of **1** (0.6 mM) with CmOOH (1.2 mM) in the presence of NEt₃ (0.6 mM) in CH₃CN at −40 °C. (B) Resonance Raman spectra of **2** generated by using Cm¹⁶O¹⁶OH (solid line, below) and Cm¹⁸O¹⁸OH (dotted line, above) obtained with λ_{ex} = 488.0 nm in CH₃CN at −40 °C; s denotes the solvent bands.

(II) complex **2**, the formation of which was confirmed by the following experimental data. Thus, complex **2** exhibited a relatively intense absorption band at 465 nm (ϵ = 1100 M⁻¹ cm⁻¹) due to the peroxo−to−copper(II) charge transfer transition (LMCT) together with a weak d−d band at 725 nm (ϵ = 320 M⁻¹ cm⁻¹) as shown in Figure 1A. Complex **2** also gave isotope-sensitive resonance Raman bands at 885, 841, 608, 529, and 485 cm⁻¹, which shifted to 855, 808, 597, 524, and 474 cm⁻¹ upon ¹⁸O-substitution using Cm¹⁸O¹⁸OH instead of Cm¹⁶O¹⁶OH (Figure 1B). Appearance of the multiple resonance Raman bands and their associated isotope shifts (Δn = 30, 33, 11, 5, and 11 cm⁻¹) are similar to those reported from the resonance Raman studies of the cumylperoxo copper(II) complex supported by the hydrotrispyrazolylborate ligand and the cumylperoxo iron(III) complex of 6-Me₃-TPA [tris(6-methyl-2-pyridylmethyl)amine].[23,25] By analogy to those detailed Raman studies, the bands in the 800 cm⁻¹ region of **2** can be assigned to mixed O−O/C−O/C−C vibrations of the cumylperoxo group and the band at 608 cm⁻¹ to the Cu−O stretching vibration. Then, the additional 529 and 485 cm⁻¹ bands of **2** can be assigned to C−C−C and C−C−O deformation modes of the alkylperoxo moiety.[23]

The ESR spectrum of **2** (Figure S1, g_1 = 2.250, g_2 = 2.065, g_3 = 2.030, A_1 = 160, A_2 = 7, A_3 = 5 G), which is different from that of the starting material **1** (Figure S2), reflected a distorted tetragonal geometry of **2**, and its mononuclearity was confirmed by spin quantification using the ESR spectrum (99% spin remained). Unfortunately, instability of **2** precluded us from getting ESI-MS data even at the low temperature.

The cumylperoxo copper(II) complex **2** gradually decomposed, obeying first-order kinetics even at −40 °C (k_{dec} = 2.2 × 10⁻³ s⁻¹, Figure S3) to give bis(μ-hydroxo)dicopper(II) complex **4** in a 64% isolated yield, where no ligand hydroxylation took place (see Supporting Information). Notably, acetophenone (PhC(O)CH₃) was obtained in a 92% yield from the final reaction mixture. This clearly

Scheme 2
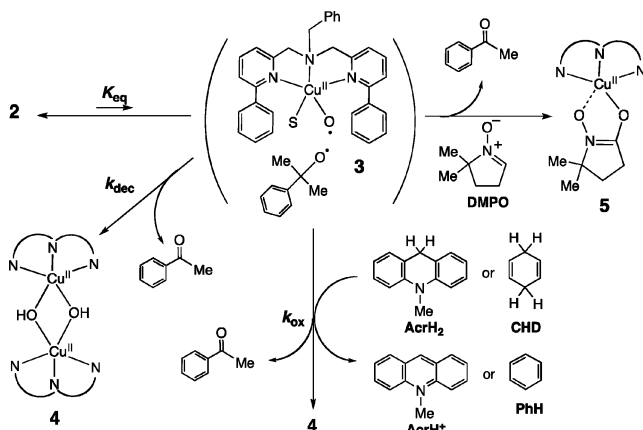
demonstrates that O−O bond homolysis of the peroxo moiety of **2** occurred since it is well-known that cumyloxyl radical quickly undergoes β-scission to give acetophenone ($k = 6.3 \times 10^5$ s^{-1} at 30 °C).[26] In fact, LCu(II)−O$^\bullet$ species **3**, generated by the O−O bond homolysis of **2**, was trapped by the reaction with 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO), a well-known radical trap reagent,[16,17,27] where formation of a 1:1 adduct **5** between **3** and DMPO was confirmed by the ESI-MS and ESR measurements (a possible structure of **5** is indicated in Scheme 2).[28]

Addition of AcrH$_2$ (10-methyl-9,10-dihydroacridine) into the acetonitrile solution of **2** at −40 °C resulted in formation of AcrH$^+$ (*N*-methylacridinium ion) as an oxidation product. Figure S7 shows the spectral change for the reaction, where the characteristic absorption band at 465 nm due to **2** decreases with a concomitant increase in the absorption bands at 358, 395, 415, and 440 nm due to AcrH$^+$. From the absorption intensity at 440 nm ($\epsilon = 2150$ M^{-1} cm^{-1}),[29] the yield of AcrH$^+$ was determined as 49% based on **2**.[30] The reaction obeyed first-order kinetics in the presence of a large excess of AcrH$_2$ as shown in the inset of Figure S7. Plot of the first-order rate constant k_{obs} against the substrate concentration gave a linear line, from which the second-order rate constant k_2 ($= k_{ox}K_{eq}$) was determined as 6.7 M^{-1} s^{-1} (Figure S8).[31] In addition, a significantly large kinetic deuterium isotope effect of $k_2^H/k_2^D = 19.2$ was obtained at −40 °C when AcrD$_2$ (AcrD$_2$/9,9-dideuterated derivative) was used in place of AcrH$_2$ (Figure S8). Existence of such a large kinetic deuterium isotope effect clearly indicates that a hydrogen transfer process is involved in the rate-determining step of the C−H bond activation of AcrH$_2$ by **2**. Similarly, oxidation of 1,4-cyclohexadiene (CHD) proceeded smoothly ($k_{ox} = 0.25$ M^{-1} s^{-1}, Figures S9 and S10), and the formation of benzene product was confirmed by GC−MS.

Apparently, the oxidation of exogenous substrates (AcrH$_2$ and CHD) by **2** proceeds via the O−O bond homolysis since acetophenone was also produced in these reactions as in the case of the self-decomposition of **2** (Scheme 2). Although the mechanism involving stepwise O−O bond cleavage and C−H bond activation of the substrate (rate $= k_{ox}K_{eq}$[**2**][substrate]) and its concerted variant could not be distinguished by the kinetic data, the present results suggest a possible contribution of a mononuclear copper(II)−oxyl radical species LCu(II)−O$^\bullet$ (**3**) to the C−H bond activation process.[32] In summary, the reactivity (the O−O bond homolysis and the C−H bond activation of the exogenous substrates) of the alkylperoxo copper(II) complex has been explored for the first time to provide important insights into the catalytic mechanism of copper monooxygenases.

Supporting Information Available: Experimental details for the synthetic procedures and additional spectroscopic and kinetic data. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Itoh, S. *Curr. Opin. Chem. Biol*. **2006**, *10*, 115−122.
(2) Mirica, L. M.; Ottenwaelder, X.; Stack, T. D. P. *Chem. Rev*. **2004**, *104*, 1013−1045.
(3) Lewis, E. A.; Tolman, W. B. *Chem. Rev*. **2004**, *104*, 1047−1076.
(4) Klinman, J. P. *Chem. Rev*. **1996**, *96*, 2541−2561.
(5) Evans, J. P.; Ahn, K.; Klinman, J. P. *J. Biol. Chem*. **2003**, *278*, 49691−49698.
(6) Francisco, W. A.; Wille, G.; Smith, A. J.; Merkler, D. J.; Klinman, J. P. *J. Am. Chem. Soc*. **2004**, *126*, 13168−13169.
(7) Bauman, A. T.; Yukl, E. T.; Alkevich, K.; McCormack, A. L.; Blackburn, N. J. *J. Biol. Chem*. **2006**, *281*, 4190−4198.
(8) Chen, P.; Solomon, E. I. *J. Am. Chem. Soc*. **2004**, *126*, 4991−5000.
(9) Yoshizawa, K.; Kihara, N.; Kamachi, T.; Shiota, Y. *Inorg. Chem*. **2006**, *45*, 3034−3041.
(10) Wada, A.; Harata, M.; Hasegawa, K.; Jitsukawa, K.; Masuda, H.; Mukai, M.; Kitagawa, T.; Einaga, H. *Angew. Chem., Int. Ed*. **1998**, *37*, 798−799.
(11) Li, L.; Narducci Sarjeant, A. A.; Karlin, K. D. *Inorg. Chem*. **2006**, *45*, 7160−7172 and its Supporting Information.
(12) Fujisawa, K.; Tanaka, M.; Moro-oka, Y.; Kitajima, N. *J. Am. Chem. Soc*. **1994**, *116*, 12079−12080.
(13) Würtele, C.; Gaoutchenova, E.; Harms, K.; Holthausen, M. C.; Sundermeyer, J.; Schindler, S. *Angew. Chem., Int. Ed*. **2006**, *45*, 3867−3869.
(14) Maiti, D.; Sarjeant, A. A. N.; Karlin, K. D. *J. Am. Chem. Soc*. **2007**, *129*, 6720−6721.
(15) Maiti, D.; Lucas, H. R.; Sarjeant, A. A. N.; Karlin, K. D. *J. Am. Chem. Soc*. **2007**, *129*, 6998−6999.
(16) Fujii, T.; Yamaguchi, S.; Funahashi, Y.; Ozawa, T.; Tosha, T.; Kitagawa, T.; Masuda, H. *Chem. Commun*. **2006**, 4428−4430.
(17) Fujii, T.; Yamaguchi, S.; Hirota, S.; Masuda, H. *Dalton Trans*. **2008**, 164−170.
(18) Maiti, D.; Lee, D.; Gaoutchenova, K.; Würtele, C.; Holthausen, M. C.; Sarjeant, A. A. N.; Sundermeyer, J.; Schindler, S.; Karlin, K. D. *Angew. Chem., Int. Ed*. **2008**, *47*, 82−85.
(19) Costas, M.; Mehn, M. P.; Jensen, M. P.; Que, L., Jr. *Chem. Rev*. **2004**, *104*, 939−986.
(20) Shan, X.; Que, L., Jr. *J. Inorg. Biochem*. **2006**, *100*, 421−433.
(21) Seo, M. S.; Kamachi, T.; Kouno, T.; Murata, K.; Park, M. J.; Yoshizawa, K.; Nam, W. *Angew. Chem., Int. Ed*. **2007**, *46*, 2291−2294.
(22) Kitajima, N.; Katayama, T.; Fujisawa, K.; Iwata, Y.; Moro-oka, Y. *J. Am. Chem. Soc*. **1993**, *115*, 7872−7873.
(23) Chen, P.; Fujisawa, K.; Solomon, E. I. *J. Am. Chem. Soc*. **2000**, *122*, 10177−10193.
(24) Kunishita, A.; Teraoka, J.; Scanlon, J. D.; Matsumoto, T.; Suzuki, M.; Cramer, C. J.; Itoh, S. *J. Am. Chem. Soc*. **2007**, *129*, 7248−7249.
(25) Kim, J.; Zang, Y.; Costas, M.; Harrison, R. G.; Wilkinson, E. C.; Que, L., Jr. *J. Biol. Inorg. Chem*. **2001**, *6*, 275−284.
(26) (a) Avila, D. V.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc*. **1993**, *115*, 466−470. (b) Adachi, S.; Nagano, S.; Ishimori, K.; Watanabe, Y.; Morishima, I.; Egawa, T.; Kitagawa, T.; Makino, R. *Biochemistry* **1993**, *32*, 241−252.
(27) (a) Vicic, D. A.; Jones, W. D. *J. Am. Chem. Soc*. **1999**, *121*, 4070−4071. (b) Hetterscheid, D. G. H.; Bens, M.; de Bruin, B. *Dalton Trans*. **2005**, 979−984.
(28) The ESI-MS of **5** gave a set of peaks at 632.4 with Cm^{16}O$_2$H, which shifted to 634.4 with Cm^{18}O$_2$H (Figure S5). The mass distribution patterns and their associated isotope shift are fully consistent with the proposed structure of **5**. The ESR spectrum of **5** (Figure S6) indicated a distorted tetragonal structure of **5**, and spin quantification using the ESR technique revealed that the yield of **5** was 78%. Incorporation of ^{18}O into acetophenone was also confirmed by EI-MS using Cm^{18}O$_2$H.
(29) Itoh, S.; Kumei, H.; Nagatomo, S.; Kitagawa, T.; Fukuzumi, S. *J. Am. Chem. Soc*. **2001**, *123*, 2167−2175.
(30) Nearly 50% yield of AcrH$^+$ may indicate that intermediate **3** formally acts as a one-electron oxidant and that cumyloxyl radical does not participate in the oxidation reaction of the substrate.
(31) The intercepts of Figure S8 (2.2×10^{-3} s^{-1}) and Figure S10 (2.2×10^{-3} s^{-1}) are identical to the self-decomposition rate (2.2×10^{-3} s^{-1}).
(32) During the course of our research, a possible contribution of LCu(II)−O$^\bullet$ has been reported in some copper-dependent oxidation reactions.[18] (a) Hong, S.; Huber, S. M.; Gagliardi, L.; Cramer, C. J.; Tolman, W. B. *J. Am. Chem. Soc*. **2007**, *129*, 14190−14193. (b) Comba, P.; Knoppe, S.; Martin, B.; Rajaraman, G.; Rolli, C.; Shapiro, B.; Stork, T. *Chem.—Eur. J*. **2008**, *14*, 344−357.

JA800443S