C–H Activation by $Cu(III)_2O_2$ Intermediate with Secondary Amino Ligand

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(Received November 18, 2002; CL-020976)

Reaction of Cu(I) complex having a newly designed tridentate ligand *i*-Bu_3CY with dioxygen has given an active bis(μ-oxo)dicopper(III) complex, which has exhibited a unique intramolecular hydroxylation of the β-methine carbon of isobutyl group of the ligand.

Development of new oxidation and oxygenation reactions of organic compounds is very important from a viewpoint of organic, catalytic and industrial chemistries. In stereo- and/or enantio-selective oxygenation catalysis, metal complexes play essential and key roles for many cases.[1] Therefore, preparation of a high-valent metal-oxo species causes us to take an interest as the intermediates in these reaction systems, which are especially proposed as important factors in enzymatic reactions, such as an iron(IV)-oxo porphyrin π-cation radical in cytochrome P450 and a bis(μ-oxo)diiron(IV) core in soluble methane monooxygenase (sMMO).[2] These high-valent metal-oxo species are afforded by the O–O bond cleavage of dioxygen molecule in metalloenzymes. Tolman et al. have found that in the study of μ-η^2:η^2-peroxodicopper(II) complex with 1,4,7-triisopropyl-1,4,7-triazacyclononane (*i*-Pr_3TACN), the peroxo species is converted to bis(μ-oxo)dicopper(III) species through the O–O bond cleavage.[3] After discovering $[Cu^{III}_2(i\text{-}Pr_3TACN)_2(\mu\text{-}O)_2]^{2+}$ species, several bis(μ-oxo)dicopper(III) species were prepared and their structures, spectroscopies, and reactivities toward organic compounds were investigated.[4] The coordinating atoms of the bis(μ-oxo)dicopper(III) complexes reported hitherto have been almost consisted of imines and/or tertiary amines. Recently, Karlin et al. have reported the bis(μ-oxo)dicopper(III) complex with donor sets having one secondary and two tertiary amines.[5] Then we have designed and prepared a new tridentate ligand with three secondary amine nitrogens, *cis*,*cis*-1,3,5-tris(isobutylamino)cyclohexane (*i*-Bu_3CY), which has a higher binding ability to copper and form a square-pyramidal geometry with a rigid six-membered chelate ring forced by cyclohexane framework. Using this ligand we prepared and characterized the bis(μ-oxo)dicopper(III) and discovered a unique hydroxylation of aliphatic hydrocarbon.

The starting materials, $[Cu^I(i\text{-}Bu_3CY)(MeCN)]SbF_6$ (**1**), were prepared by reaction of a tridentate ligand *i*-Bu_3CY with $[Cu^I(MeCN)_4]SbF_6$ in THF/Et_2O under Ar,[6] whose colorless crystals suitable for X-ray analysis were obtained from the solution on standing for a few days. The crystal structure of **1** revealed that the geometry around each copper ion forms a tetrahedron coordinated with three secondary amine nitrogens of *i*-Bu_3CY and an acetonitrile; Cu–N(*i*-Bu_3CY) = 2.080(2), 2.142(2), 2.140(2) Å and Cu–N(acetonitrile) = 1.900(2) Å.[7] The distance of Cu(1) from the trigonal plane defined by three secondary amine nitrogens is 1.114 Å; the Cu(I) ion in complex **1** comes close to the trigonal plane in comparison with the case of the Cu(I) complex with *i*-Pr_3TACN (1.40 Å).[8] The Cu–N bond lengths and displacement of Cu(I) ion from trigonal plane are shorter than those of $[Cu^I(i\text{-}Pr_3TACN)(MeCN)]SbF_6$, indicating that *i*-$Bu_3CY$ binds strongly to Cu(I) ion in comparison with *i*-Pr_3TACN. This may result from the structural factor that the five-membered chelate ring in the Cu(I) complex with *i*-Pr_3TACN has been replaced by the six-membered ring in complex **1** with *i*-Bu_3CY.

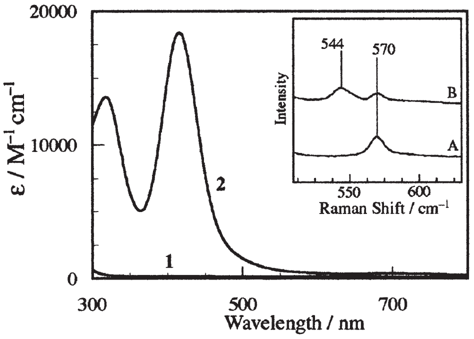

Figure 1. UV-vis spectra **1** and the product (**2**) generated by the reaction of **1** with O_2 in THF at −90 °C. Inset: Resonance Raman spectra of the reaction of **1** with $^{16}O_2$ (A) and $^{18}O_2$ (B) in THF at −100 °C ($\lambda_{ex} = 413.1$ nm).

The reaction of **1** with O_2 in THF gave bis(μ-oxo)dicopper(III) species (**2**) with two intense absorption bands at 318 nm ($\varepsilon = 13000\,M^{-1}cm^{-1}$ per 2Cu) and 416 nm ($\varepsilon = 18000\,M^{-1}cm^{-1}$ per 2Cu). The resonance Raman spectra of **2** in THF exerted a band characteristic to a Cu–O stretching vibration for the Cu_2O_2 core at 570 cm^{-1}, which shifted to 544 cm^{-1} using $^{18}O_2$ instead of $^{16}O_2$. The observed frequencies are in the lowest energy site among the bis(μ-oxo)dicopper(III) species reported hitherto,[9] indicating that the Cu–O bond strength for Cu_2O_2 core prepared in this system is weaker than them. In CH_2Cl_2, it exhibits similar spectroscopic features to those in THF, $\lambda_{max} = 319$, 412 nm and $\nu(Cu_2O_2) = 571$ ($^{16}O_2$), 546 ($^{18}O_2$) cm^{-1}, indicating that **2** is not affected by solvent in contrast to the case of $[Cu_2(\mu\text{-}O)_2(AN)_2]^{2+}$ with N–H groups that have been influenced by solvent mediums.[5] **1** predominately formed bis(μ-oxo)dicopper(III) species in the reaction with dioxygen in spite of a kind of solvents.

Fortunately, by raising the temperature of the CH_2Cl_2 solution containing **2** from −80 °C to room temperature, a green single crystal was obtained as a decomposition product (**3**). Remarkably, the crystal structure of **3** (Figure 2) revealed the dinuclear copper complex with the two ligands that one β-methine carbon of the isobutyl groups of *i*-Bu_3CY was hydroxylated.[10,11] An insertion of an oxygen atom to the aliphatic β-carbon for the amino group by bis(μ-oxo)dicopper(III) species is the first time to the best of our knowledge, although it has been

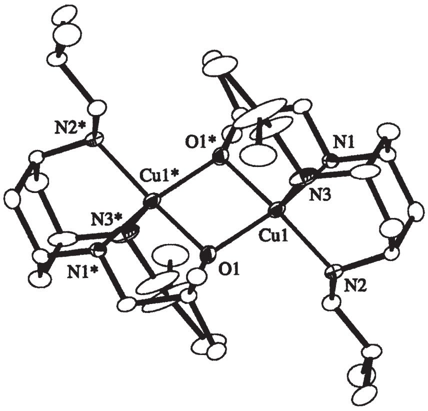

Figure 2. ORTEP view of the cation part of **3**, showing 30% probability thermal ellipsoids. The hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Cu(1)–O(1) 1.981(6), Cu(1)–N(1) 2.026(7), Cu(1)–N(2) 2.038(7), Cu(1)–N(3) 2.246(9); O(1)–Cu(1)–N(1) 155.4(3), O(1)–Cu(1)–N(2) 99.1(3), O(1)–Cu(1)–N(3) 108.6(3), N(1)–Cu(1)–N(2) 91.1(3), N(1)–Cu(1)–N(3) 93.5(3), N(2)–Cu(1)–N(3) 90.5(3).

previously reported that the α-carbon adjacent to an amino or phenyl group was hydroxylated by bis(μ-oxo)dicopper(III) species,[3,4c] and that the β-carbon was hydroxylated via different or ambiguous intermediate.[12,13] Moreover, the yield of isobutylaldehyde that was produced by hydroxylation of α-position was trace as examined by gas chromatography. The hydroxylation of β-position methine carbon of complex **2** under this condition was preferential. The decomposition rate of **2** in THF followed a first-order equation ($k = 7.6 \times 10^{-4}\,\mathrm{s}^{-1}$ at $-90\,^{\circ}\mathrm{C}$; $t_{1/2}$ (half-life) $= 9.1 \times 10^{2}\,\mathrm{s}$), and the activation parameters were $\Delta H^{\ddagger} = 34.0 \pm 2.0\,\mathrm{kJ\,mol^{-1}}$ and $\Delta S^{\ddagger} = -115 \pm 12\,\mathrm{J\,K^{-1}mol^{-1}}$. In CH_2Cl_2, the rate was $k = 2.0 \times 10^{-3}\,\mathrm{s}^{-1}$ at $-90\,^{\circ}\mathrm{C}$ ($t_{1/2} = 3.5 \times 10^{2}\,\mathrm{s}$), and the activation parameters were $\Delta H^{\ddagger} = 42.2 \pm 1.8\,\mathrm{kJ\,mol^{-1}}$ and $\Delta S^{\ddagger} = -62 \pm 10\,\mathrm{J\,K^{-1}mol^{-1}}$, which are similar to those of the bis(μ-oxo)dicopper(III) complexes reported previously.[4c,14] However, the consumption rate of **2** was much faster even at $-90\,^{\circ}\mathrm{C}$ in comparison with other bis(μ-oxo)dicopper(III) complexes reported previously,[4] suggesting the strong coordination of Cu(1) to nitrogen atoms of *i*-Bu_3CY. These findings suggest that the mechanism for hydroxylation of isobutyl group is the same as process reported previously:[4c,14] First, the reactions are initiated by an intramolecular hydrogen atom abstraction on the tertiary carbon of the isobutyl group by the active $Cu(III)_2(\mu\text{-}O)_2$ core. After the resultant carbon radical generated on the β-position is bound by the hydroxyl group, **3** is reconstituted by dimerization of a monomer complex with the hydroxylated ligand. It is quite unique that the aliphatic β-position, in which the C–H bond possesses the higher bond dissociation energy than those of aliphatic α-position,[15] has been hydroxylated.

In conclusion, the complex **1** with *i*-Bu_3CY ligand having a higher binding ability has exhibited high reactivity for dioxygen and has predominantly gave bis(μ-oxo)dicopper(III) species **2**. Furthermore, it is quite interesting that the complex **2** has exhibited a C–H activation which not the α-position but the β-one of the *i*-Bu_3CY ligand is intramolecularly hydroxylated to generate **3**. Using *i*-Bu_3CY ligand composed of secondary amine, we succeeded in the rise of oxidation ability of bis(μ-oxo)dicopper(III) species.

This work was supported by a Grant-in-Aid for Scientific Research (No. 11228203) from the Ministry of Education, Science, Sports and Culture, to which our thanks are due.

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