Modulation of the Copper-Dioxygen Reactivity by Stereochemical Effect of Tetradentate Tripodal Ligands

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Dioxygen reactivity of a copper(I) complex having a sterically hindered Me_3-tpa and monooxygenase activity of its oxygenated species toward the ligand were significantly modulated by the presence of the 6-methyl group onto pyridyl group.

It has been shown that some (μ-$\eta^2 : \eta^2$-peroxo)dicopper(II) complexes are converted to high valent bis(μ-oxo)dicopper(III) species, which have a monooxygenase activity for the coordinating ligand as substrate.[1] Previously, we found that introduction of methyl group(s) into tpa[2] had a significant influence on the dioxygen reactivity of copper(I) complexes $[Cu(Me_n\text{-tpa})]^+$ (n = 0–3); the copper(I) complexes of tpa[3] and Me-tpa[4] generated trans-μ-1,2-peroxo species upon oxygenation, while $[Cu(Me_2\text{-tpa})]^+$ (**1a**) reacted with O_2 to give a bis(μ-oxo)dicopper(III) species, $[Cu_2(Me_2\text{-tpa})_2(O_2)]^{2+}$ (**1b**) which could be reversibly converted to **1a** by N_2 bubbling and showed a regioselective monooxygenase activity for the supporting ligand.[5] Herein we report the dioxygen reactivity of a copper(I) complex having a sterically more hindered Me_3-tpa ($[Cu(Me_3\text{-tpa})]^+$ (**2a**)) which can also greatly modulate the dioxygen reactivity of a copper(I) species and the monooxygenase activity of the dicopper/dioxygen species toward the ligand. In the previous study,[4] we were not aware of the oxygenation of **2a** in various organic solvents at −70 °C, since the oxygenation is very slow and the formation of the oxygenated species (bis(μ-oxo)dicopper(III) and/or (μ-$\eta^2 : \eta^2$-peroxo)dicopper(II)) is poor compared to those of the Me_n-tpa (n = 0–2) complexes (*vide infra*). A careful reexamination of the oxygenation of **2a** and $[Cu(Me_3\text{-tpa-}d_{15})]^+$ (**2a**-d_{15})[2] in acetone at −80 °C showed the formation of a bis(μ-oxo)$Cu(III)_2$ species which was identified by resonance Raman spectroscopy.

Such a low dioxygen reactivity of **2a** seems to be attributable to the stabilization of the copper(I) oxidation state and/or the destabilization of the copper(II) oxidation state, and a steric requirement of three methyl groups. $E_{1/2}$(Cu(II)/Cu(I)) values of the copper(I) complexes $[Cu(Me_n\text{-tpa})]^+$ are highly dependent on the numbers of the methyl groups; $E_{1/2}$ in CH_3CN measured by cyclic voltammetry are −0.32 for tpa, −0.26 for Me-tpa, −0.14 for Me_2-tpa, and 0.07 V for Me_3-tpa vs $Ag/AgNO_3$. Crystal structure of **2a**[6] revealed that the copper(I) ion was buried in a hydrophobic pocket consisting of three methyl groups of the pyridyl pendants (Figure 1). These factors may be responsible for the observed low dioxygen reactivity of **2a**.

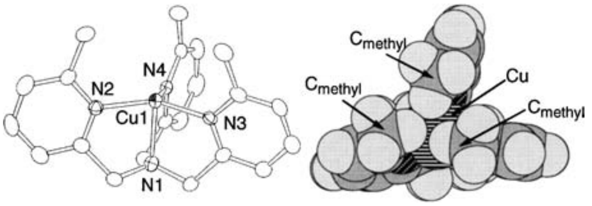


Figure 1. ORTEP drawing (50% probability) (hydrogen atoms are omitted for clarity) and space filling view of a complex cation of **2a**. Selected bond lengths (Å): Cu1-N1 2.191(4), Cu1-N2 1.971(3), Cu1-N3 1.978(3), Cu1-N4 2.081(4).

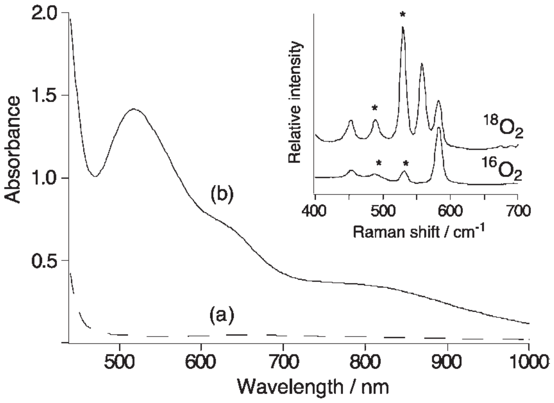


Figure 2. Electronic spectra of **2a**-d_{15} under Ar (a) and under O_2 (b) in acetone at −80 °C ([Cu] = 19.73 mM, light path length = 1.08 cm). Inset: Resonance Raman spectra of **2b**-d_{15} in acetone at ∼ − 90 °C (∼1 mM) with 406.7 nm laser excitation. The asterisk bands are solvent bands.

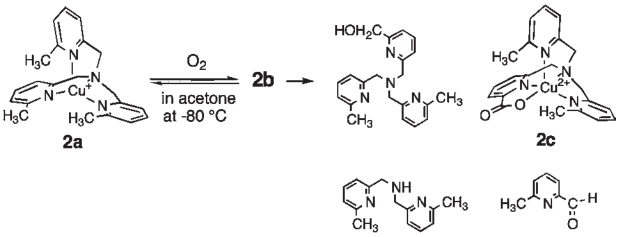
Complex **2a** ([Cu] = ∼10 mM) in acetone at −80 °C reacts slowly with dioxygen to produce a brown species (**2b**; $\lambda_{max} = 517$ nm). The electronic spectral change showed that the formation and decay of **2b** occurred simultaneously. Therefore, it was difficult to accumulate the brown species under the conditions. However, a deuterated ligand (Me_3-tpa-d_{15}) can greatly stabilize the brown species (**2b**-d_{15}) which is stable for at least 1 day (Figure 2), indicating that the rate determining step of the thermal decomposition includes the C-H bond scission of the methyl and methylene groups (*vide infra*).

It was found that the formation ratio of the brown species monitored at 517 nm was highly dependent on the concentrations of **2a**-d_{15}; ε values change from 67 $M^{-1}\,cm^{-1}$ ($[Cu]_{total}$ = 19.7 mM) to 27 $M^{-1}\,cm^{-1}$ ($[Cu]_{total}$ = 3.9 mM), where ε values are calculated based on the total copper concentration. The results indicate that **2b**-d_{15} is not fully formed under these conditions and suggest the following equilibrium (eq 1). The equilibrium constant estimated by assuming eq 1 is 40 ± 10 $M^{-1}\,atm^{-1}$ at −80 °C, indicating that the dioxygen affinity of **2a** is very low.[7]

$$2Cu(I) + O_2 \overset{K}{\rightleftharpoons} Cu(III)_2(O)_2 \quad (\text{or } Cu(II)_2(O_2)) \qquad (1)$$

The resonance Raman (rR) spectra of **2b**-d_{15} ([Cu] = ~1 mM) in acetone at −90 °C with a 406.7 nm laser excitation showed an intense band at 583 cm^{-1}, which is shifted to 558 cm^{-1} ($\Delta^{18}\mathrm{O} = 25\,\mathrm{cm}^{-1}$) upon $^{18}O_2$ substitution (Figure 2 (inset)).[8] These spectral features are characteristic of those of the bis(μ-oxo)dicopper(III) complexes (577–619 cm^{-1} ($\Delta^{18}\mathrm{O} = 20$–$29\,\mathrm{cm}^{-1}$)),[9] indicating the formation of a bis(μ-oxo)dicopper(III) species. Although there is no rR evidence for the presence of (μ-$\eta^2 : \eta^2$-peroxo)dicopper(II) and/or trans(μ-1,2-peroxo)-dicopper(II) species which are expected to exhibit the $\nu_{\mathrm{O\text{–}O}}$ band at 720–765 cm^{-1} and 800–900 cm^{-1}, respectively,[10–12] the formation of a small amount of those species may not be ruled out only from the rR experiments, since the intensity of the $\nu_{\mathrm{O\text{–}O}}$ band of (μ-$\eta^2 : \eta^2$-peroxo)dicopper(II) species is generally low.[13] It has been shown that the bis(μ-oxo)dicopper(III) and the (μ-$\eta^2 : \eta^2$-peroxo)dicopper(II) species have an intense absorption band at 375–450 nm and 340–370 nm, respectively.[9,10] The electronic spectrum of **2b**-d_{15} ($[\mathrm{Cu}]_{\mathrm{total}}$ = ~5 mM) in acetone at −80 °C, however, did not show a distinct absorption band in the UV region due to a poor formation of **2b**-d_{15} under the conditions,[14] whereas a difference spectrum revealed an appearance of a new absorption band at ~390 nm upon oxygenation similar to that of **1b**, supporting the presence of a bis(μ-oxo)dicopper(III) species. There are additional absorption bands at ~630 nm (sh, $\varepsilon = 34\,\mathrm{M}^{-1}\,\mathrm{cm}^{-1}$) and ~810 nm (sh, $\varepsilon = 16\,\mathrm{M}^{-1}\,\mathrm{cm}^{-1}$). The assignments of those bands are not clear and there is a possibility of the presence of additional species not identified at present.

The thermal decomposition of **2b** at −80 °C under O_2 gave a hydroxylated ligand (Me$_2$-tpaCH$_2$OH in 19 ± 2% yield based on a dimer) and N-dealkylated products (bis(6-methyl-2-pyridylmethyl)amine in yield of 34 ± 4% and 6-methylpyridine-2-carbaldehyde), which were confirmed by ^{1}H NMR and MS analysis (Scheme 1). Isotope labeling experiment showed that the oxygen atoms of Me$_2$-tpaCH$_2$OH and 6-methylpyridine-2-carbaldehyde were derived from dioxygen. In addition, a complex [Cu(Me$_2$-tpaCOO)]$^+$ (**2c**) in which one of the methyl groups of the Me$_3$-tpa ligand was oxidized to carboxylate was isolated as blue crystals in yield of 29% based on a dimer from the reaction mixture, which was identified by FAB-MS and X-ray structural analysis.[15] The FAB mass spectrum of **2c** obtained under $^{18}O_2$ showed that two oxygen atoms of **2c** were derived from dioxygen, although partial isotope scrambling occurred. The possibility of the formation of Me$_2$-tpaCOO$^-$ due to the autooxidation of Me$_2$-tpaCH$_2$OH by a metal ion may be excluded, since the reaction of an acetone solution containing Me$_2$-tpaCH$_2$OH, $\mathrm{Cu(ClO_4)_2 \cdot 6H_2O}$ and Et$_3$N with O_2 did not give **2c**. The results are in marked contrast to the regioselective N-dealkylation of **1b** and the regioselective hydroxylation of the methyl group of a bis(μ-oxo)dinickel(III) complex having Me$_3$-tpa ([Ni$_2$(Me$_3$-tpa)$_2$(O)$_2$]$^{2+}$).[16] Thus the present results clearly showed that the reversible conversion between Cu(I) and bis(μ-oxo)Cu(III)$_2$ species and the monooxygenase activity of the dicopper/dioxygen species can be greatly controlled by a simple modification of stereochemical effect of the supporting ligand.



Scheme 1.

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2 Abbreviations of ligands used: tpa = tris(2-pyridylmethyl)amine; Me-tpa = (6-methyl-2-pyridylmethyl)bis(2-pyridylmethyl)amine; Me$_2$-tpa = bis(6-methyl-2-pyridylmethyl)(2-pyridylmethyl)amine; Me$_3$-tpa = tris(6-methyl-2-pyridylmethyl)amine; Me$_3$-tpa-d_{15}: all methyl and methylene groups are deuterated.

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6 Crystal data for **2a**: $\mathrm{C_{21}H_{24}N_4CuClO_4}$, $M = 495.44$, monoclinic, $P2_1/a$, $a = 12.093(1)$, $b = 14.898(1)$, $c = 11.8661(2)$ Å, $\beta = 98.0389(4)°$, $V = 2116.8(3)$ Å^3, $Z = 4$, $D_c = 1.554\,\mathrm{g\,cm^{-3}}$, $T = 123$ K, μ (MoKα) = 11.95 cm^{-1}, Of 20173 reflections collected, 4591 were unique ($R_{int} = 0.036$), refinement based on 3672 reflection ($I > 3\sigma(I)$). $R = 0.061$, $Rw = 0.099$.

7 The equilibrium constant was estimated by fitting the concentration dependency of the ε values to eq (1) (ε ($[\mathrm{Cu}]_{\mathrm{total}}$): 67 (19.7 mM), 55 (10.2 mM), and 27 (3.9 mM) and a partial O_2 pressure is 1 atm).

8 A similar rR spectrum is also observed with a 514.5 nm laser excitation.

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12 We also measured the rR spectra with 488.0 and 514.5 nm laser excitations, but there is no isotope sensitive band in those regions.

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14 Only ~20% of **2b**-d_{15} is formed under the conditions.

15 Crystal data for **2c**: $\mathrm{C_{21}H_{21}N_4CuClO_6}$, $M = 524.42$, monoclinic, $P2_1/c$, $a = 12.297(2)$, $b = 13.522(2)$, $c = 14.040(2)$ Å, $\beta = 104.52(1)°$, $V = 2259.8(5)$ Å^3, $T = 300$ K, $Z = 4$, $D_c = 1.541\,\mathrm{g\,cm^{-3}}$, μ (MoKα) = 11.30 cm^{-1}, Of 5158 reflections collected, 4936 were unique ($R_{int} = 0.013$), refinement based on 2394 reflection ($I > 3\sigma(I)$). $R = 0.054$, $Rw = 0.080$; Anal. Calcd for $\mathrm{C_{21}H_{22}N_4CuClO_{6.5}}$: C, 47.28; H, 4.16; N, 10.50%. Found: C, 47.32; H, 3.99; N, 10.69%. IR (cm^{-1}): ν_{as}(COO), 1660; ν_{s}(COO), 1344; $\nu(\mathrm{ClO_4})$, 1097. FAB-MS m/z: 424.1 (M$^+$).

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