Ligand Effects on Dioxygen Activation by Copper and Nickel Complexes: Reactivity and Intermediates

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ABSTRACT

Copper and nickel complexes having various active-oxygen species $M_n–O_2$ ($n = 1$ or 2), such as *trans*-(μ-1,2-peroxo)Cu^{II}_2, bis(μ-oxo)M^{III}_2, bis(μ-superoxo)Ni^{II}_2, and ligand-based alkylperoxo-M^{II}_m, can be produced by a series of tetradentate tripodal ligands (TMPA analogues) containing sterically demanding 6-methyl substituent(s) on the pyridyl group(s), where TMPA = tris(2-pyridylmethyl)amine. Roles of the methyl substituent(s) for the formation of the active-oxygen species and their oxidation reactivities are reported.

Introduction

Dioxygen-activating nonheme transition-metal centers in metalloenzymes have structural diversity. They use a variety of donor atoms provided by proteins together with exogenous ligands, such as H_2O, OH^-, O^{2-}, and need structural flexibility and/or change during the catalytic cycles. To mimic such structural flexibility and/or change, a variety of ligands have been developed. Recent advances in synthetic model chemistry have provided a chemical basis for structures and physicochemical properties of various active-oxygen species $M_n–O_2$ (M = Fe,[1–3] Co,[4] Ni,[4] and Cu,[5–11] and $n = 1$ or 2). Although metalloenzymes use mainly manganese, iron, and copper ions, the chemistry of other transition-metal complexes is also important not only to provide an additional chemical basis for understanding the reaction mechanisms of the metalloenzymes but also to develop the artificial oxidation catalysts. Among those metal complexes, nickel and copper ions are capable of producing similar $M_n–O_2$ species in the oxidation states of II and III as shown in Figure 1. Systematic studies of the structures and reactivities of those nickel and copper complexes depending upon the change in the d electron configurations and the d orbital energies are of particular importance to gain the fundamental basis for dioxygen-activation chemistry mediated by metal complexes. In this Account, we focus on the formation of the nickel and copper complexes having
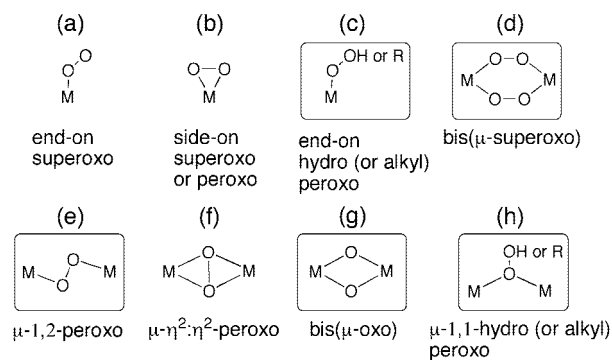
Masatatsu Suzuki was born in Kanazawa, Japan, in 1948. He received his Ph.D. degree under the supervision of Prof. S. Kida from Kyushu University in 1975. Then, he joined Kyushu University as an Assistant Professor (1975–1983). During that period, he spent a year (1980–1981) as a postdoctoral fellow in Prof. Kazuo Nakamoto's group at Marquette University, Milwaukee, WI. Then, he moved to Kanazawa University and became an Associate Professor in 1988 and a Professor in 1994. His research interest is centered on syntheses of functional models for various dioxygen-activating metalloenzymes.

FIGURE 1. Representative $M_n–O_2$ (M = Cu and/or Ni, and $n = 1$ or 2) species. The framed species are structurally characterized species derived from TMPA analogues.

active-oxygen species supported by the N_4 tetradentate tripodal ligands, tris(2-pyridylmethyl)amine (TMPA) analogues, containing 6-methyl substituents on the pyridyl groups.

Since Karlin et al. synthesized the first structurally characterized copper–dioxygen complex, *trans*-(μ-1,2-peroxo)dicopper(II) (Figure 1e), using a tetradentate tripodal ligand TMPA,[12,13] a variety of $Cu_n–O_2$ complexes have been developed. Kitajima et al. synthesized the first example of the peroxo-dicopper(II) models for the O_2 transport protein (hemocyanin) and aromatic ring oxidation enzyme (tyrosinase), which have a (μ-η^2:η^2-peroxo) coordination mode (Figure 1f), using sterically demanding tridentate Tp derivatives (Tp = hydrotris(pyrazolyl)borate).[5,14,15] Since then, many (μ-η^2:η^2-peroxo)dicopper(II) complexes of bi- and tridentate ligands have been developed.[6–11] Furthermore, Tolman et al. discovered the making and breaking of the dioxygen O–O bond performed by copper complexes; they demonstrated that some (μ-η^2:η^2-peroxo)-dicopper(II) complexes of sterically demanding tridentate N,N',N''-trisubstituted tacn (tacn = 1,4,7-triazacyclononane) undergo facile interconversion with bis(μ-oxo)dicopper(III) species (Figure 1g),[16,17] which involves a reversible two-electron redox process. The relative stability between (μ-η^2:η^2-peroxo)dicopper(II) and bis(μ-oxo)dicopper(III) species depends upon various factors, such as steric and electronic effects as well as solvents, counteranion, temperature, and so on.[18–22] In addition to copper complexes, Hikichi et al. expanded the bis(μ-oxo)dimetal chemistry to the cobalt and nickel complexes.[4,23,24] They synthesized bis(μ-oxo)M^{III}_2 complexes (M = Co and Ni) of the Tp derivatives in the reaction of bis(μ-hydroxo)M^{II}_2 complexes with H_2O_2, which is in marked contrast to the formation of the (μ-η^2:η^2-peroxo)dicopper(II) complexes having the same ligand system.[15]

In addition to the bi- and tridentate ligands, a wide variety of N_4 tetradentate tripodal ligands have been

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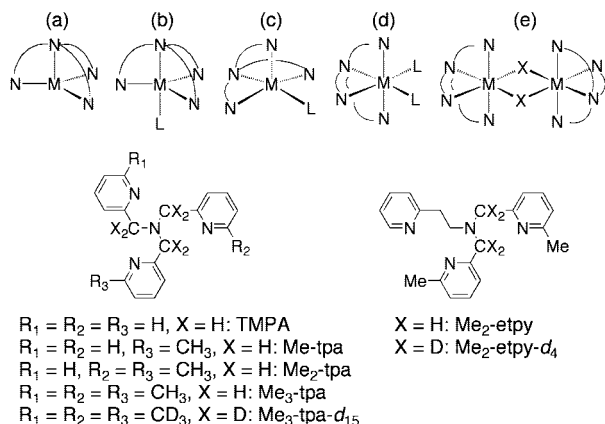
FIGURE 2. Stereochemical diversity of metal centers and tetradentate tripodal ligands.

FIGURE 3. Formation, molecular structure, and decomposition of $[Cu_2(O)_2(Me_2-tpa)_2]^{2+}$ (**3**$^{Me2-tpa}$). Atoms are colored by atom type (copper, green; oxygen, red; nitrogen, dark blue; and carbon, gray).

developed,[5–10,25,26] which are capable of accommodating the stereochemical diversity of metal complexes as shown in Figure 2. Among them, TMPA is one of the most widely used tetradentate tripodal ligands in inorganic chemistry. As mentioned, Karlin et al. first demonstrated that copper(I) complexes of TMPA and its analogues, $[Cu(L)(CH_3CN)]^+$, produce *trans*-(μ-1,2-peroxo)dicopper(II) complexes in a trigonal bipyramidal structure via the formation of end-on superoxo-copper(II) complexes ($[Cu(L)(O_2)]^+$).[12,13,27,28] Such tetradentate tripodal ligands tend to form trigonal bipyramidal *trans*-(μ-1,2-peroxo)dicopper(II) complexes. However, the introduction of the methyl substituent(s) into the 6 position of the pyridyl group(s) can modulate the stereochemical and electronic effects, which influence the stereochemistry and reactivity of metal complexes having active-oxygen species. The 6-methyl groups can play various roles, such as (1) controlling the stereochemistry of metal centers and modulating the donor properties by steric requirement, (2) constructing the hydrophobic cavity around the active-oxygen center, which protects the active-oxygen center from unfavorable decomposition reactions, and (3) acting as an oxidation substrate to probe the oxidation ability of the active-oxygen center. In this Account, we report how stereochemical and electronic effects of a series of TMPA analogues, Me_n–tpa (n = 1–3) and Me_2–etpy, shown in Figure 2, influence the formation and reactivity of the nickel and copper complexes having active-oxygen species (M_n–O_2). Such systematic studies for the Fe_n–O_2 species using Me_n–tpa ligands have also been reported by Que et al.[1,2,29]

Formation and Characterization of Bis(μ-oxo)dicopper(III) Complexes

TMPA forms an acetonitrile adduct, $[Cu(TMPA)(CH_3CN)]^+$ (**1**^{TMPA}), whereas, Me_2–tpa, Me_3–tpa, and Me_2–etpy do not form the adducts but form a four-coordinate trigonal pyramidal $[Cu(L)]^+$ (Figure 2a).[30–32] It has been shown that, in the metal complexes having more sterically crowded five- and six-coordinate environments, the M–N(6-methylpyridyl) distances are longer than the M–N(pyridyl) distances, owing to the steric interaction between the
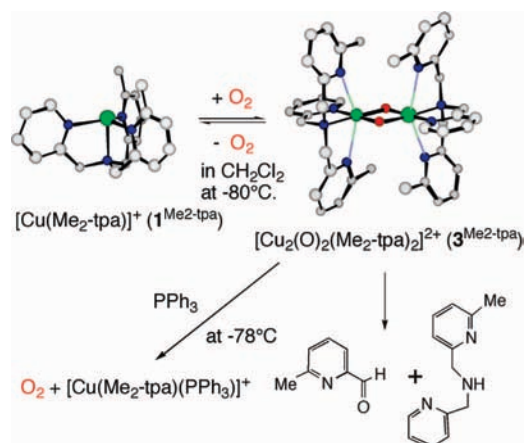
6-methyl group and adjacent donor atom.[29,33,34] However, no significant elongation of the Cu–N(6-methylpyridyl) distances relative to the Cu–N(pyridyl) distances is observed in the present trigonal pyramidal copper(I) complexes, indicating that the 6-methyl group(s) has no significant influence on the steric interaction in the four-coordinate trigonal pyramidal structure.

The reaction of $[Cu(Me-tpa)]^+$ (**1**$^{Me-tpa}$) with dioxygen generated a *trans*-(μ-1,2-peroxo)dicopper(II) complex $[Cu_2(O_2)(Me-tpa)_2]^{2+}$ (**2**$^{Me-tpa}$) similar to the TMPA complex.[35] This peroxo complex decayed rapidly compared to the TMPA complex. Although the ν_{O-O} of **2**$^{Me-tpa}$ (833 cm^{-1}) is comparable to that of the TMPA complex (832 m^{-1}), the ν_{Cu-O} (550 cm^{-1}) is significantly lower than that of the TMPA complex (561 cm^{-1}),[36] suggesting some stereochemical change in the Me–tpa complex because of the steric interaction between a 6-methylpyridyl group and peroxide, which seem to be responsible in lowering the thermal stability of **2**$^{Me-tpa}$. Such observations were also made for some *trans*-(μ-1,2-peroxo)dicopper(II) complexes of sterically demanding ligands, such as Me_3Bz_3–tren (tris(N-benzyl-N-methylaminoethyl)amine).[37]

Unlike **1**$^{Me-tpa}$, the introduction of more 6-methyl-2-pyridylmethyl pendant(s) and/or a 2-pyridylethyl pendant significantly influences the reactivity with O_2. The copper(I) complex $[Cu(Me_2-tpa)]^+$ (**1**$^{Me2-tpa}$) generates a bis(μ-oxo)dicopper(III) complex $[Cu_2(O)_2(Me_2-tpa)_2]^{2+}$ (**3**$^{Me2-tpa}$) at ~ −80 °C, as shown in Figure 3.[30] Although the copper(I) complexes of the Me_2–etpy and Me_3–tpa also generate bis(μ-oxo)dicopper(III) complexes, $[Cu_2(O)_2(Me_2-etpy)_2]^{2+}$ (**3**$^{Me2-etpy}$) and $[Cu_2(O)_2(Me_3-tpa)_2]^{2+}$ (**3**$^{Me3-tpa}$), the reactions are slow compared to that of **1**$^{Me2-tpa}$ and, during the formation, significant oxidative N-dealkylation of Me_2–etpy occurs for **3**$^{Me2-etpy}$,[32] and oxidative N-dealkylation and oxidation of the 6-methyl group of the 6-methyl-2-pyridylmethyl pendant of Me_3–tpa take place for **3**$^{Me3-tpa}$.[31] In addition, they did not fully oxygenate even at −80 °C under 1 atm of O_2 (vide infra).

However, the decomposition of $3^{Me2–etpy}$ can be significantly suppressed (stable for days at −80 °C) using a deuterated ligand Me_2–etpy-d_4, in which four hydrogen atoms of the methylene groups are deuterated, and in the case of the Me_3–tpa complex, a perdeuterated Me_3–tpa-d_{15} was needed for the formation of bis(μ-oxo) species ($3^{Me3–tpa}$-d_{15}), which is stable for 1 day at −80 °C. The results indicate that the decompositions of these complexes involve the C–H bond cleavage of the methylene and/or 6-methyl groups and significant kinetic isotope effects for those C–H bond cleavages.

The crystal structure of the bis(μ-oxo) Me_2–tpa complex revealed that each copper ion has a square planar structure composed of a N_2O_2 donor with two 6-methyl-2-pyridylmethyl pendant arms, which interact weakly with copper ion in the axial positions [2.48(1) and 2.55(1) Å].[30] The average Cu–O (1.803 Å) and Cu $\cdots$ Cu [2.758(4) Å] distances are comparable to those of the bis(μ-oxo)dicopper(III) complexes of tri- and bidentate ligands, such as $[Cu_2(O)_2(Bn_3–tacn)_2]^{2+}$ (tacn = 1,4,7-triazacyclononane; 1.806 and 2.794 Å)[38] and $[Cu_2(O)_2(L_{ME})_2]^{2+}$ (1.806 and 2.743 Å) (L_{ME} = N-methyl-N-ethyl-N'-methyl-N'-ethyl-1,2-cyclohexanediamine).[39] The crystal structure of $[Cu_2(O)_2$-$(Me_2$–etpy-$d_4)_2]^{2+}$ ($3^{Me2–etpy}$-d_4) is similar to that of $3^{Me2–tpa}$.[32] Thus, the presence of two 6-methylpyridyl groups prevents the formation of *trans*-(μ-1,2-peroxo)dicopper(II) species in a trigonal bipyramidal structure because of a steric interaction and generates bis(μ-oxo)dicopper(III) complexes.

The electronic spectrum of $3^{Me2–tpa}$ in dichloromethane at −80 °C showed intense absorption bands at 258 nm ($\varepsilon = \sim36\,000$ M^{-1} cm^{-1}), with a shoulder at 300 nm, and at 378 nm ($\varepsilon = \sim19\,000$ M^{-1} cm^{-1}) and a weak band at $\sim$490 nm ($\varepsilon = \sim330$ M^{-1} cm^{-1}).[30] The spectral features of $[Cu_2(O)_2(Me_3$–tpa-$d_{15})_2]^{2+}$ ($3^{Me3–tpa}$-d_{15}) and $[Cu_2(O)_2$-$(Me_2$–etpy-$d_4)_2]^{2+}$ ($3^{Me2–etpy}$-d_4) are similar to that of $3^{Me2–tpa}$.[31,32] The spectral features of these complexes are somewhat different from those of the bis(μ-oxo)dicopper(III) complexes of the bi- and tridentate ligands, which exhibit two intense absorption bands at $\sim$300 and $\sim$400 nm assigned to the ligand-to-metal charge transfer (LMCT) transitions from the bridging oxides to Cu^{III} centers (π_σ^* → d$_{xy}$ and σ^* → d$_{xy}$, respectively) by Solomon et al.[40] The absorption bands at $\sim$300 and 378–390 nm of the present complexes can also be assigned to the π_σ^* → d$_{xy}$ and σ^* → d$_{xy}$ transitions, respectively. The energies of the latter σ^* → d$_{xy}$ transitions of the present complexes are higher than those of the bis(μ-oxo)Cu$^{III}_2$ complexes of the bi- and tridentate ligands (390–448 nm).[7] This high energy shift seems to be attributable to high denticity of the present complexes, which increases the d orbital energy, although the interaction from the apical positions is weak. The resonance Raman (rR) spectra of $[Cu_2(O)_2(Me_2$–tpa)$_2]^{2+}$ ($3^{Me2–tpa}$), $[Cu_2(O)_2(Me_3$–tpa-$d_{15})_2]^{2+}$ ($3^{Me3–tpa}$-d_{15}), and $[Cu_2(O)_2(Me_2$–etpy-$d_4)_2]^{2+}$ ($3^{Me2–etpy}$-d_4) showed the bands at 590–579 cm^{-1}, assignable to the symmetric breathing mode of the Cu_2O_2 core,[40,41] which are almost at the lowest end of those observed for the bis(μ-oxo)dicopper(III) complexes (630–580 cm^{-1}).
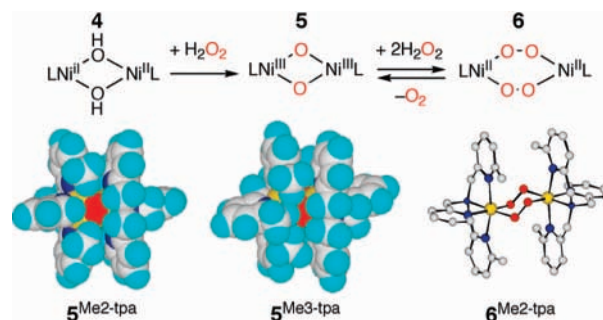

FIGURE 4. Formation pathway of bis(μ-oxo)Ni$^{III}_2$ (**5**) and bis(μ-superoxo)Ni$^{II}_2$ (**6**) in the reaction of bis(μ-hydroxo)Ni$^{II}_2$ (**4**) with H$_2$O$_2$ and molecular structures of $[Ni_2(O)_2(Me_2$–tpa)$_2]^{2+}$ (**5**$^{Me2–tpa}$), $[Ni_2(O)_2(Me_3$–tpa)$_2]^{2+}$ (**5**$^{Me3–tpa}$), and $[Ni_2(O_2)_2(Me_2$–tpa)$_2]^{2+}$ (**6**$^{Me2–tpa}$). Atoms are colored by atom type (nickel, yellow; oxygen, red; nitrogen, dark blue; carbon, gray; and hydrogen, light blue).

Formation and Characterization of Bis(μ-oxo)dinickel(III) Complexes

As mentioned already, Hikichi et al. first synthesized bis(μ-oxo)dinickel(III) complexes of Tp derivatives in the reaction of bis(μ-hydroxo)dinickel(II) complexes with H$_2$O$_2$.[4,23,24] Similar bis(μ-oxo)dinickel(III) complexes of tridentate ligands having N$_3$ and S$_3$ (thioether) donors have also been reported.[42–44] Me_2–tpa and Me_3–tpa also produce the bis(μ-oxo)dinickel(III) complexes, $[Ni_2(O)_2(Me_2$–tpa)$_2]^{2+}$ (**5**$^{Me2–tpa}$) and $[Ni_2(O)_2(Me_3$–tpa)$_2]^{2+}$ (**5**$^{Me3–tpa}$), in the reactions of the bis(μ-hydroxo)dinickel(II) complexes (**4**) with H$_2$O$_2$.[45,46]

Unlike the bis(μ-oxo)dinickel(III) complexes of N$_3$ ligands, **5**$^{Me2–tpa}$ and **5**$^{Me3–tpa}$ are very reactive with H$_2$O$_2$ to oxidize H$_2$O$_2$ to superoxide, which produce bis(μ-superoxo)dinickel(II) complexes, $[Ni_2(O_2)_2(Me_2$–tpa)$_2]^{2+}$ (**6**$^{Me2–tpa}$) and $[Ni_2(O_2)_2(Me_3$–tpa)$_2]^{2+}$ (**6**$^{Me3–tpa}$), as shown in Figure 4. In the case of the Me_2–tpa complex, no **5**$^{Me2–tpa}$ was observed in the reaction of $[Ni_2(OH)_2(Me_2$–tpa)$_2]^{2+}$ (**4**$^{Me2–tpa}$) with even 0.2 equiv of H$_2$O$_2$, indicating that **5**$^{Me2–tpa}$ is extremely reactive with H$_2$O$_2$ compared to **5**$^{Me3–tpa}$. Such a high reactivity of **5**$^{Me2–tpa}$ toward H$_2$O$_2$ seems to be partly attributable to the structural feature of **5**$^{Me2–tpa}$, in which there is a space around the bis(μ-oxo)Ni$^{III}_2$ core to which H$_2$O$_2$ can access, as shown in Figure 4. However, **5**$^{Me2–tpa}$ can be isolated from the thermal decomposition of **6**$^{Me2–tpa}$ through disproportionation of the superoxo ligands (Figure 4). It is noted that such high reactivity toward H$_2$O$_2$ has not been reported for the bis(μ-oxo)dinickel(III) complexes of N$_3$ ligands. The origin of the high reactivity of the present complexes toward H$_2$O$_2$ compared to those of N$_3$ ligands is not known at present.

The crystal structures of **5**$^{Me2–tpa}$ and **5**$^{Me3–tpa}$ are similar to those of bis(μ-oxo)dicopper(III) complexes,[45,46] although the average Ni–N(axial) distance (2.27 Å) is significantly shorter than those in the copper complexes (2.51 Å), in the latter of which copper(III) ion having the d^8 electron configuration tends to adopt a square planar structure. However, the average Ni–N(axial) bond distance is significantly longer than the average Ni–N(equatorial) bond distance (2.004 Å), which is attributable to the

Jahn–Teller effect in a low-spin d^7 electron configuration and partly steric requirement of the 6-methyl substituents. The in-plane 6-methyl substituents of $5^{Me3-tpa}$ form a hydrophobic cavity around a Ni^{III}(μ-O)$_2$Ni^{III} core, which may suppress the oxidation of H$_2$O$_2$ compared to $5^{Me2-tpa}$ as described above. Bis(μ-superoxo)dinickel(II) complexes of Me$_2$–tpa and Me$_3$–tpa have a distorted octahedral structure, in which two Ni centers are linked by two μ-1,2-O–O bridges.

[Ni$_2$(O)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ ($5^{Me2-tpa}$) shows an intense absorption band at 376 nm ($\varepsilon = \sim$6000 M^{-1} cm^{-1}),[46] and [Ni$_2$(O)$_2$(Me$_3$–tpa)$_2$]$^{2+}$ ($5^{Me3-tpa}$) shows an intense absorption band at 394 nm ($\varepsilon = \sim$4000 M^{-1} cm^{-1}),[45] assignable to the O^{2-}-to-Ni^{III} charge-transfer transition [LMCT: (σ_g + d$_{x^2-y^2}$(+)) $\rightarrow$ (d$_{xy}$(–) + σ_u*)] based on theoretical calculations by Riordan and Brunold et al. for [(PhTt$^{t\text{Bu}}$)$_2$Ni$_2$(μ-O)$_2$] having a S$_3$ (thioether) tridentate ligand [PhTt$^{t\text{Bu}}$ = phenyltris((*tert*-butylthio)methyl)borate].[47] Such LMCT transitions have also been observed for the five-coordinate bis(μ-oxo)dinickel(III) complexes containing tridentate N$_3$ donor ligands ($\lambda_{max} \sim$ 405–414 nm).[23,24,42,43] As in the case of the bis(μ-oxo)dicopper(III) complexes, the LMCT transition energies of the present six-coordinate complexes are higher than those of the five-coordinate complexes, such as [Ni$_2$(O)$_2$(Tp^{Me3})$_2$] (λ_{max} = 410 nm), where Tp^{Me3} = hydrotris(3,4,5-trimethylpyrazolyl)borate.[24] This may also be ascribed to high d orbital energy because of the increased coordination number from five to six. In addition, the LMCT transition energy of $5^{Me2-tpa}$ is higher than that of $5^{Me3-tpa}$, which is also attributable to a stronger electron donation of Me$_2$–tpa compared to Me$_3$–tpa.

The rR spectra of $5^{Me2-tpa}$ and $5^{Me3-tpa}$ showed a characteristic intense band at 574 and 571 cm^{-1}, respectively, assignable to a symmetric breathing mode of the Ni$_2$O$_2$ core as observed for the Cu$_2$O$_2$ cores. These values are lower than those of the bis(μ-oxo)dinickel(III) complexes of the tridentate nitrogen ligands (599–612 cm^{-1}),[42,43] suggesting that the Ni–O bonds for the present six-coordinate complexes $5^{Me2-tpa}$ and $5^{Me3-tpa}$ are weaker than those of the five-coordinate complexes.

The bis(μ-superoxo)dinickel(II) complexes [Ni$_2$(O$_2$)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ ($6^{Me2-tpa}$) and [Ni$_2$(O$_2$)$_2$(Me$_3$–tpa)$_2$]$^{2+}$ ($6^{Me3-tpa}$) exhibit the ν_{O-O} vibration at 1080–1100 cm^{-1}.[45,46] Their electrospray ionization time of flight/mass spectrometry (ESI–TOF/MS) in acetone suggested the formation of a monomeric superoxo species in the solution state. However, ESR and X-ray absorption spectra of $6^{Me2-tpa}$ clearly indicated that the Ni^{II}(μ-OO)$_2$Ni^{II} core structure remains intact in solution. This is in marked contrast to a monomeric superoxo nickel(II) complex of a sterically bulky tridentate thioether ligand, [Ni(O$_2$)(PhTt^{Ad})], where the superoxo ligand has been proposed to bind to the nickel center in a side-on fashion.[48]

Reversible Four-Electron Redox Process of O$_2$ Performed by Copper Complexes

Interconversion between (μ-η^2:η^2-peroxo)dicopper(II) and bis(μ-oxo)dicopper(III) cores has been well-demonstrated for the complexes of various bi- and tridentate ligands.[6,7] The interconversion involves the reversible two-electron redox process. The most striking feature of the present complexes of the TMPA analogues having the 6-methyl substituents is the reversible cleavage and formation of the dioxygen O–O bond associated with the four-electron redox process. [Cu$_2$(O)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ ($3^{Me2-tpa}$) in dichloromethane at −80 °C exhibits reversible deoxygenation by bubbling N$_2$ to regenerate the copper(I) complex $1^{Me2-tpa}$, as shown in Figure 3.[30] This is the first example of the reversible four-electron redox of dioxygen mediated by the metal complex.

The copper(I) complex [Cu(Me$_2$–etpy-d_4)]$^+$ ($1^{Me2-etpy}$-d_4) was not fully oxygenated in acetone even at −80 °C under 1 atm of O$_2$. ^{1}H nuclear magnetic resonance (NMR) spectrum of $1^{Me2-etpy}$-d_4 ([Cu] = $\sim$19.0 mM) in the above conditions indicated that the formation ratio of [Cu$_2$(O)$_2$(Me$_2$–etpy-d_4)$_2$]$^{2+}$ ($3^{Me2-etpy}$-d_4) is 70%.[32] A thermodynamic study for the oxygenation (2[Cu(L)]$^+$ + O$_2$ → [Cu$_2$(O)$_2$(L)$_2$]$^{2+}$) showed that enthalpy and entropy changes are −53 + 2 kJ mol^{-1} and −187 ± 10 J mol^{-1} K^{-1}, respectively, which are significantly unfavorable compared to those of [Cu(AN)]$^+$ having a linear aliphatic triamine ligand (AN = 3,3′-iminobis(N,N-dimethylpropylamine) reported by Karlin et al.[21] Further introduction of a 6-methyl group into Me$_2$–tpa significantly lowers the dioxygen affinity of the copper(I) complex [Cu(Me$_3$–tpa-d_{15})]$^+$ ($1^{Me3-tpa}$).[31] The oxygenation constant (K= $\sim$3.8 × 10^3 M^{-2}) of $1^{Me3-tpa}$-d_{15} is about 10 times lower than that of $1^{Me2-etpy}$-d_4 (K = 4.0 × 10^4 M^{-2}) at −80 °C. Thus, the relative dioxygen affinity of the copper(I) complex is $1^{Me2-tpa} > 1^{Me2-etpy}$-$d_4 > 1^{Me3-tpa}$-$d_{15}$. This trend is well-correlated with the $E_{1/2}$(Cu^{II}/Cu^I) values (1^{TMPA} = −410, 1^{Me-tpa} = −350, $1^{Me2-tpa}$ = −230, $1^{Me2-etpy}$ = −90, and $1^{Me3-tpa}$ = −20 mV versus Fc$^+$/Fc).[32] Stepwise introduction of the 6-methyl-2-pyridylmethyl pendant and/or the 2-pyridylethyl pendant causes the positive shift of the $E_{1/2}$(Cu^{II}/Cu^I) values. Although the $E_{1/2}$(Cu^{II}/Cu^I) value is not a direct measure of the relative stability of copper(III) species, this seems to be also applicable to the copper(III) species. Thus, unlike bi- and tridentate ligands, the present type of the sterically demanding TMPA analogues preferentially form the bis(μ-oxo)dicopper(III) complexes and have a unique ability to stabilize both copper(I) and copper(III) oxidation states; they can take not only a square planar structure with weak ligation from the axial positions, which can fit to the copper(III) oxidation state with the d^8 electron configuration, but also a trigonal pyramidal structure suitable for the copper(I) oxidation state. Consequently, they are capable of performing reversible conversion between copper(I) and bis(μ-oxo)-dicopper(III) species involving a reversible four-electron redox process. The coexistence of copper(I) and bis(μ-oxo)dicopper(III) species implies that no appreciable redox reaction between these two species occurs in these systems. The hydrophobic cavities formed by the 6-methyl substituents of the pyridyl groups seem be responsible to prevent such a redox reaction.
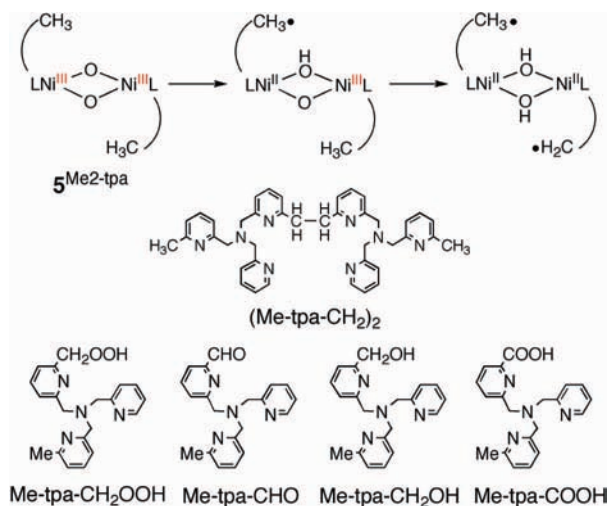
FIGURE 5. Formation pathway of the ligand-based coupling dimer [(Me–tpa–CH$_2$)$_2$] upon decomposition of $5^{Me2-tpa}$ under N$_2$ and the oxidation products of the 6-methyl group of Me$_2$–tpa upon decomposition of $5^{Me2-tpa}$ under O$_2$.

Oxidation Reactions by Bis(μ-oxo)dicopper(III) and Bis(μ-oxo)dinickel(III) Complexes

All of the bis(μ-oxo)dimetal complexes are reactive toward the supporting ligands as found for many bis(μ-oxo)dicopper(III) and dinickel(III) complexes. The reactivities highly depend upon the kind of metal ions and the supporting ligands. As mentioned already, the introduction of 6-methyl-2-pyridylmethyl pendant(s) and/or the 2-pyridylethyl pendant significantly suppresses dioxygen affinity, but the oxidation power of the bis(μ-oxo)dicopper(III) species toward the supporting ligands becomes stronger. As mentioned already, [Cu$_2$(O)$_2$(Me$_3$–tpa)$_2$]$^{2+}$ ($3^{Me3-tpa}$) and [Cu$_2$(O)$_2$(Me$_2$–etpy)$_2$]$^{2+}$ ($3^{Me2-etpy}$) are very reactive toward the supporting ligands compared to [Cu$_2$(O)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ ($3^{Me2-tpa}$). The order is $3^{Me3-tpa}$ > $3^{Me2-etpy}$ > $3^{Me2-tpa}$. Decomposition of $3^{Me2-tpa}$ and $3^{Me2-etpy}$ in acetone at low temperatures under N$_2$ causes the selective oxidative N-dealkylation of the 6-methyl-2-pyridylmethyl pendant.[30,32] However, decomposition of $3^{Me3-tpa}$ at −80 °C under O$_2$ caused hydroxylation of one of the 6-methyl groups of Me$_3$–tpa (Me$_2$–tpa–CH$_2$OH) and oxidative N-dealkylation of the 6-methyl-2-pyridylmethyl pendant.[31] In addition, a carboxylate complex [Cu(Me$_2$–tpa–COO)]$^+$, in which one of the 6-methyl groups of the Me$_3$–tpa is oxidized to carboxylate, was also isolated.

In contrast to the selective oxidation of the methylene group in $3^{Me2-tpa}$, the corresponding bis(μ-oxo)dinickel(III) complex [Ni$_2$(O)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ ($5^{Me2-tpa}$) is capable of oxidizing both methylene and 6-methyl groups.[46] This seems to be attributable to the structural difference between copper and nickel complexes (vide infra). Thermal decomposition of $5^{Me2-tpa}$ in acetonitrile under N$_2$ afforded a coupling dimer of the Me$_2$–tpa ligand (Me–tpa–CH$_2$)$_2$, as shown in Figure 5, together with the oxidative N-dealkylation of the 6-methyl-2-pyridylmethyl pendant. The formation of (Me–tpa–CH$_2$)$_2$ clearly indicates the presence of a ligand-based radical (Me–tpa–CH$_2$•), which is stable enough for coupling with another Me–tpa–CH$_2$•. Isotope-labeling experiments using $5^{Me2-tpa}$ and [Ni$_2$(O)$_2$(Me$_2$–tpa-d_1)$_2$]$^{2+}$ ($5^{Me2-tpa}$-d_1) revealed that only an intramolecular ligand coupling occurs. The result strongly suggests the formation of a bis(Me–tpa–CH$_2$•)dinickel(II) species generated by stepwise hydrogen-atom abstractions from two methyl groups (Figure 5).

Thermal decomposition of $5^{Me2-tpa}$ under O$_2$ gave no coupling dimer of Me$_2$–tpa but gave ligand-based alcohol (Me–tpa–CH$_2$OH), carboxylate (Me–tpa–COO$^-$), and a trace amount of aldehyde (Me–tpa–CHO) together with a N-dealkylated ligand. Isotope-labeling experiments using ^{18}O$_2$ indicate that the oxygen source of the oxidized ligands is ^{18}O$_2$, suggesting that the ligand-based radical, Me–tpa–CH$_2$•, is very reactive with O$_2$ to produce a peroxyl radical (Me–tpa–CH$_2$OO•), and this reaction is much faster than the coupling of Me–tpa–CH$_2$• radicals and the oxygen rebound from the dinickel center. Although this conversion seems to involve some complicated reactions, such as radical chain reaction(s) and/or autoxidation, one of the reactive intermediates having a ligand-based alkylperoxide, [Ni$_2$(OH)(Me$_2$–tpa)(Me–tpa–CH$_2$OO)]$^{2+}$ ($7^{Me2-tpa}$), which can generate the oxidation products (Me–tpa–CHO, Me–tpa–COO$^-$, and Me–tpa–CH$_2$OH), was isolated upon decomposition of the bis(μ-superoxo)dinickel(II) complex [Ni$_2$(O$_2$)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ ($6^{Me2-tpa}$) under O$_2$ at −20 °C. A further oxidized complex [Ni$_2$(Me–tpa–CH$_2$OO)$_2$]$^{2+}$ ($8^{Me2-tpa}$) was also isolated in the reaction of [Ni$_2$(OH)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ ($4^{Me2-tpa}$) with a large excess of H$_2$O$_2$ at −40 °C.[49]

Although the conversion from the ligand-based peroxyl radical complex to the ligand-based alkylperoxo complex seems to involve some complicated reactions, such as radical chain reaction(s), a possible conversion pathway from $6^{Me2-tpa}$ is given in Figure 6: (1) disproportionation of the superoxo ligands in $6^{Me2-tpa}$ generates O$_2$ and $5^{Me2-tpa}$ as mentioned already; (2) $5^{Me2-tpa}$ generates a ligand-based alkyl radical (Me–tpa–CH$_2$•) by hydrogen-atom abstraction; (3) the resulting Me–tpa–CH$_2$• reacts with O$_2$ to produce a ligand-based alkylperoxyl radical (Me–tpa–CH$_2$OO•); and (4 and 5) the reaction of Me–tpa–CH$_2$OO• and a superoxo ligand of $6^{Me2-tpa}$ and/or hydrogen-atom abstraction of Me–tpa–CH$_2$OO• afford [Ni$_2$(OH)(Me$_2$–tpa)(Me–tpa–CH$_2$OO)]$^{2+}$ ($7^{Me2-tpa}$) and O$_2$.

The bis(μ-alkylperoxo)dinickel(II) complex [Ni$_2$(Me–tpa–CH$_2$OO)$_2$]$^{2+}$ ($8^{Me2-tpa}$) is capable of producing Me–tpa–COO$^-$ (∼62%) and Me–tpa–CH$_2$OH (∼37%).[49] Decomposition of $8^{Me2-tpa}$ in the presence of H$_2$^{18}O revealed that the oxygen atoms of both Me–tpa–COO$^-$ and Me–tpa–CH$_2$OH are scrambled with ^{18}O, suggesting the presence of some intermediate(s) that can react with water. A possible conversion pathway appears to involve the pathway shown in Figure 7: (1) the O–O bond cleavage of the peroxo ligand produces a ligand-based aldehyde; and (2) disproportionation of the aldehyde gives carboxylate and alkoxide via the Cannizzaro reaction, where the oxygen of aldehyde can be exchanged through acetal. Unusually facile disproportionation of aldehyde to car-
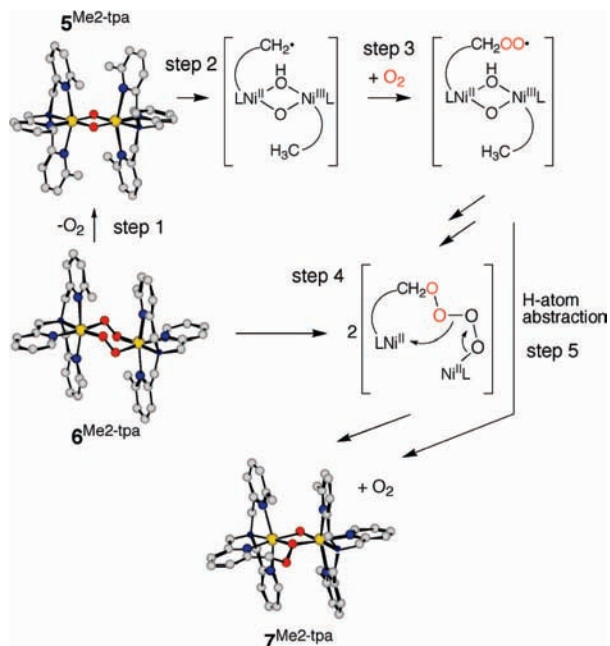
FIGURE 6. Possible sequential oxidation pathway of the 6-methyl group of $[Ni_2(O_2)_2(Me_2-tpa)_2]^{2+}$ ($6^{Me2-tpa}$) to $[Ni_2(OH)(Me_2-tpa)(Me-tpa-CH_2OO)]^{2+}$ ($7^{Me2-tpa}$). Atoms are colored by atom type (nickel, yellow; oxygen, red; nitrogen, dark blue; and carbon, gray).
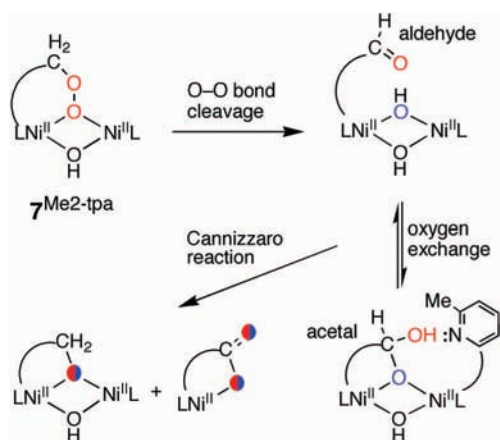

FIGURE 7. Possible formation pathway from a ligand-based alkylperoxo complex $[Ni_2(OH)(Me_2-tpa)(Me-tpa-CH_2OO)]^{2+}$ ($7^{Me2-tpa}$) to alkoxo and carboxylato complexes.

boxylate and alkoxide appears to be attributable to the presence of the 6-methyl-2-pyridylmethyl pendant, which may act as a base to facilitate the Cannizzaro reaction. However, formation of a larger amount of the carboxylate ligand than the alkoxide ligand probably suggests that some other side reaction(s) takes place at the same time.

As in the case of the bis(μ-oxo)dicopper(III) complexes, the introduction of the 6-methyl-2-pyridylmethyl pendant destabilizes the nickel(III) oxidation state, leading to a stronger oxidant. This is in line with the successive positive shift of the $E_{1/2}$ (II,III/II,II) values of $[Ni_2(OH)_2(Me_n-tpa)_2]^{2+}$ (450, 550, 640, and 780 mV versus Fc/Fc$^+$ for TMPA, Me-tpa, Me$_2$-tpa, and Me$_3$-tpa, respectively).[46] $[Ni_2(O)_2(Me_3-tpa)_2]^{2+}$ ($5^{Me3-tpa}$) decomposes within 1 h at -40 °C, whereas $[Ni_2(O)_2(Me_2-tpa)_2]^{2+}$ ($5^{Me2-tpa}$) is

stable over 1 day under the same conditions. The high reactivity of $5^{Me3-tpa}$ may be partly due to the proximity effect between the in-plane methyl groups and the oxo groups and partly due to the higher oxidation power of $5^{Me3-tpa}$.

Correlation between Reactivities and Structures of Bis(μ-oxo)dicopper(III) and Dinickel(III) Complexes

Both bis(μ-oxo)dicopper(III) complexes $[Cu_2(O)_2(Me_2-tpa)_2]^{2+}$ ($3^{Me2-tpa}$) and $[Cu_2(O)_2(Me_2-etpy)_2]^{2+}$ ($3^{Me2-etpy}$) exhibited selective oxidation of the methylene group of the 6-methyl-2-pyridyl-methyl pendant in the apical position,[30,32] whereas $[Ni_2(O)_2(Me_2-tpa)_2]^{2+}$ ($5^{Me2-tpa}$) oxidized both methylene and methyl groups of the 6-methyl-2-pyridylmethyl pendant.[46] The differential reactivities of copper and nickel complexes are closely related to the $O_{oxo}\cdots H$ distances and their C–H bond energies. The molecular structure of $3^{Me2-tpa}$ suggests that the $O_{oxo}\cdots H$ distances for the methyl groups ($\sim$2.8–3.3 Å) are slightly longer than those for the methylene groups ($\sim$2.7 Å), as shown in Figure 8. The short $O_{oxo}\cdots H$ distances for the methylene groups together with a weaker C–H bond energy seem to be responsible for the selective oxidation of the methylene groups. In contrast, the $O_{oxo}\cdots H$ distances for the methyl groups in the nickel complex $5^{Me2-tpa}$ (2.3–3.5 Å) are shorter than those for the methylene groups (2.6–2.7 Å). Such relative $O_{oxo}\cdots H$ distances seems to be responsible for the parallel oxidation of the methyl and methylene groups in $5^{Me2-tpa}$. Thus, the oxidation reactivities are highly dependent upon the d-electron configuration, which can modulate the stereochemistry of the complexes. The relative oxidation powers of the copper complexes toward the supporting ligands are stronger than those of the corresponding nickel complexes. This is in line with the general trend that the nickel complexes can access a higher oxidation state compared to the corresponding copper complex, owing to a higher d-orbital energy of the nickel complexes. Selective oxidation of the methyl group in $[Ni_2(O)_2(Me_3-tpa)_2]^{2+}$ ($5^{Me3-tpa}$) seems to be due to the proximity effect of the in-plane methyl group in $5^{Me3-tpa}$ ($O_{oxo}\cdots H = 2.2$–2.7 Å).

Formation of the Mononuclear Ligand-Based Alkylperoxo-Copper(II) Complex

Various metal complexes having active-oxygen species have been synthesized in the reaction of bis(μ-hydroxo)dimetal complexes with ROOH (R = H, alkyl, and acyl) similar to nickel complexes mentioned above. The reaction of $[Cu_2(OH)_2(Me_2-tpa)_2]^{2+}$ in acetonitrile with H_2O_2 at -40 °C produced a ligand-based alkylperoxo complex, $[Cu(Me-tpa-CH_2OO)]^+$ ($9^{Me2-tpa}$), as shown in Figure 9.[50] The reaction of $[Cu_2(OH)_2(Me_2-tpa)_2]^{2+}$ with H_2O_2 under N_2 resulted in the reduction to the copper(I) complex $[Cu(Me_2-tpa)]^+$ ($1^{Me2-tpa}$), where no bis(μ-oxo)dicopper(III) species $[Cu_2(O)_2(Me_2-tpa)_2]^{2+}$ ($3^{Me2-tpa}$) was detected. $1^{Me2-tpa}$ further reacted with H_2O_2 to produce a monomeric
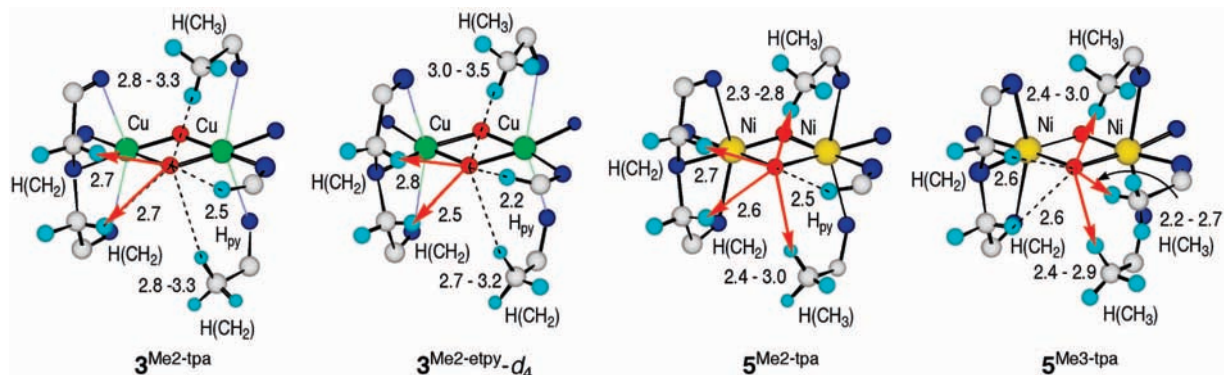
FIGURE 8. Molecular structures near the bis(μ-oxo)dimetal cores of [Cu$_2$(O)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ (**3**$^{Me2-tpa}$),[30] [Cu$_2$(O)$_2$(Me$_2$–etpy-d_4)$_2$]$^{2+}$ (**3**$^{Me2-etpy}$-d_4),[32] [Ni$_2$(O)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ (**5**$^{Me2-tpa}$),[46] and [Ni$_2$(O)$_2$(Me$_3$–tpa)$_2$]$^{2+}$ (**5**$^{Me3-tpa}$).[45] Reaction sites are shown by arrows. The H atoms are placed at the calculated positions with the C–H bond = 0.95 Å. Atoms are colored by atom type (copper, green; nickel, yellow; oxygen, red; nitrogen, dark blue; carbon, gray; and hydrogen, light blue).
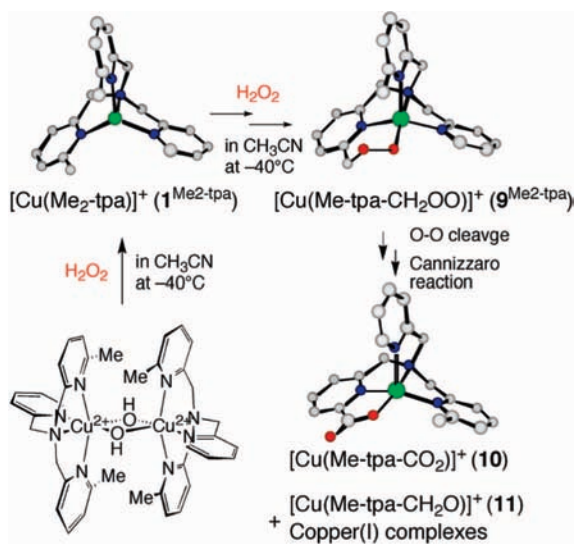

FIGURE 9. Formation of [Cu(Me–tpa–CH$_2$OO)]$^+$ (**9**$^{Me2-tpa}$) and oxidation pathway. Atoms are colored by atom type (copper, green; oxygen, red; nitrogen, dark blue; and carbon, gray).

ligand-based alkylperoxo complex **9**$^{Me2-tpa}$ by the selective oxidation of a methyl group of Me$_2$–tpa. Although a detailed formation mechanism of **9**$^{Me2-tpa}$ is not known at present, a possible pathway involves a ligand-based radical Me–tpa–CH$_2$• as found for the nickel complex. The reaction of **1**$^{Me2-tpa}$ with H$_2$O$_2$ may generate an active-oxygen species (Cu^{II}–OH + •OH or Cu^{III}=O + H$_2$O) by either O–O bond homo- or heterolysis, which is capable of performing the selective hydrogen-atom abstraction from the methyl group to generate the ligand-based radical Me–tpa–CH$_2$•. This is in marked contrast to the reactivity of complex [Cu$_2$(O)$_2$(Me$_2$–tpa)$_2$]$^{2+}$ (**3**$^{Me2-tpa}$), which selectively oxidizes the methylene group of Me$_2$–tpa. Isotope-labeling experiments for the formation of [Cu(Me–tpa–CH$_2$OO)]$^+$ (**9**$^{Me2-tpa}$) using H$_2$^{16}O$_2$ under a large excess of ^{18}O$_2$ afforded both [Cu(Me–tpa–CH$_2$^{16}O^{16}O)]$^+$ and [Cu(Me–tpa–CH$_2$^{18}O^{18}O)]$^+$, indicating that Me–tpa–CH$_2$• reacts with not only O$_2$ but also a reactive species derived from H$_2$O$_2$. Although a further pathway for the formation of **9**$^{Me2-tpa}$ is not known at present, decomposition of **9**$^{Me2-tpa}$ gave the alkoxo- and carboxylato-copper(II) complexes, [Cu(Me–tpa–CO$_2$)]$^+$ (**10**)

and [Cu(Me–tpa–CH$_2$O)]$^+$ (**11**), together with some copper(I) complexes. The formation pathways for **10** and **11** may be similar to those observed for the corresponding nickel complexes (Figure 7) through the Cannizzaro reaction, as shown in Figure 9.

Concluding Remarks

A variety of nickel and copper complexes having active-oxygen species (M$_2$–O$_2$) can be generated by TMPA analogues that have 6-methyl substituents on the pyridyl groups. In the case of copper complexes, Me$_2$–tpa, Me$_2$–etpy, and Me$_3$–tpa destabilize the trigonal bipyramidal structure by the steric requirement of the methyl substituents and preferentially generate bis(μ-oxo)dicopper(III) complexes. They have a unique ability to stabilize copper(I) species in a trigonal pyramidal structure and copper(III) species in a square planar structure with weak ligation from the axial positions. Consequently, they are capable of performing reversible conversion between copper(I) and bis(μ-oxo)dicopper(III). Furthermore, dioxygen affinity of the copper(I) complexes can be modulated in the order **1**$^{Me2-tpa}$ > **1**$^{Me2-etpy}$-d_4 > **1**$^{Me3-tpa}$-d_{15} as successive introduction of the methyl group and/or pyridylethyl group. In contrast, the oxidizing powers of the bis(μ-oxo) species increase in the reverse order. These trends are well-correlated with the $E_{1/2}$(Cu^{II}/Cu^{I}) values by successive introduction of the methyl group.

The hydrophobic cavity formed by the 6-methylpyridyl group(s) seems to play an important role in suppression of some unfavorable decomposition reactions and stabilization of M$_n$–O$_2$ species. In the equilibrium between the copper(I) and bis(μ-oxo)dicopper(III) species, the hydrophobic cavity could be responsible for the suppression of the electron transfer between the copper(I) and bis(μ-oxo)dicopper(III) species. In addition, the hydrophobic cavity of the bis(μ-oxo)dinickel(III) complexes also plays an important role in the oxidation of H$_2$O$_2$ by the bis(μ-oxo)Ni^{III}$_2$ center. The stabilization of the M$_n$–O$_2$ species allows for isolation and structural characterization by X-ray crystallography at low temperatures. Structural information between the active center and substrate (the

methyl and methylene groups of the supporting ligand) provides additional understanding of the oxidation reaction.

The methyl group of the present ligands also functions as an oxidation substrate. For the bis(μ-oxo)dinickel(III) complexes, oxidation of a methyl group affords ligand-based alcohol and carboxylate. The oxidation starts from the hydrogen-atom abstraction by the oxo group of the bis(μ-oxo)Ni$^{III}_2$ center. A series of reaction intermediates and products, such as a ligand-based coupling dimer and a ligand-based alkylperoxo complex, have been detected and/or isolated, which allow for the elucidation of the oxidation mechanism.

Although simple modifications of the supporting ligands presented in this Account provided useful information for dioxygen-activation chemistry mediated by metal complexes, development of further functional groups, such as the reaction cavity, which can bind exogenous oxidation substrates, is needed as a future challenge.

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