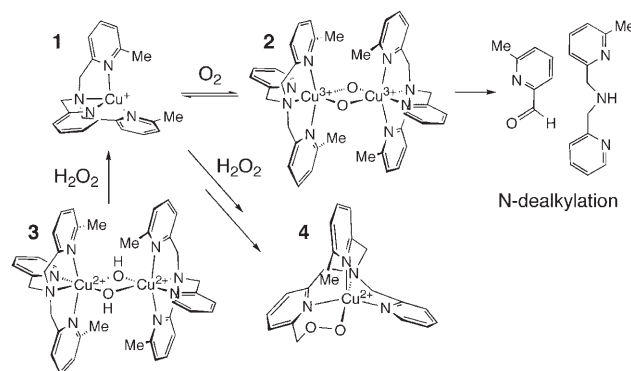


A Mononuclear Alkylperoxocopper(II) Complex as a Reaction Intermediate in the Oxidation of the Methyl Group of the Supporting Ligand**

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Functionalization of aliphatic C–H bonds by using active oxygen species mediated by copper complexes is of great interest because of its biological significance and industrial applicability. Various types of $\text{Cu}_n\text{--O}_n$ complexes have been developed and extensively investigated to elucidate possible reaction intermediates that play an essential role in the functionalization of aliphatic C–H bonds.^[1] Previously, we have found that the reaction of a copper(I) complex bearing the tetradentate tripodal ligand $\text{Me}_2\text{-tpa}$ (bis(6-methyl-2-pyridylmethyl)(2-pyridylmethyl)amine), namely $[\text{Cu}(\text{Me}_2\text{-tpa})]^+$ (**1**), with O_2 generates the bis(μ -oxo)dinickel(III) complex $[\text{Cu}_2(\text{Me}_2\text{-tpa})_2(\text{O})_2]^{2+}$ (**2**), which undergoes regioselective N-dealkylation of the $\text{Me}_2\text{-tpa}$ ligand by H-atom abstraction from a methylene group upon decomposition (Scheme 1).^[2] We also found that reaction of the bis(μ -hydroxo)dinickel(II) complex $[\text{Ni}_2(\text{Me}_2\text{-tpa})_2(\text{OH})_2]^{2+}$ with H_2O_2 produces a bis(μ -oxo)dinickel(III) complex. Unlike **2**, under O_2 this bis(μ -oxo)dinickel(III) complex oxidizes one of the 6-methyl groups of the $\text{Me}_2\text{-tpa}$ ligand to generate the bis(μ -alkylperoxo)dinickel(II) complex $[\text{Ni}_2(\text{Me-tpa-CH}_2\text{OO})_2]^{2+}$ (**5**) together with N-dealkylation of the $\text{Me}_2\text{-tpa}$ ligand.^[3,4] A similar bis(μ -alkylperoxo)dinickel(II) complex (**6**) has been reported by Tolman and co-workers in the reaction of the (μ - η^2 : η^2 -peroxo)dinickel(II) complex $[\text{Cu}_2(\text{L}^{\text{IPr}_3})_2(\text{O}_2)]^{2+}$ (L^{IPr_3} = 1,4,7-triisopropyl-1,4,7-triazacyclononane) with 2,4-*tert*-butylphenol in the presence of O_2 .^[5] Herein we report the formation of the novel mononuclear alkylperoxocopper(II) complex $[\text{Cu}(\text{Me-tpa-CH}_2\text{OO})]^+$ (**4**)



Scheme 1. Reactions of the copper species, see text for details.

by the regioselective oxidation of a methyl group of $\text{Me}_2\text{-tpa}$ in the reaction of $[\text{Cu}(\text{Me}_2\text{-tpa})]^+$ (**1**) or $[\text{Cu}_2(\text{Me}_2\text{-tpa})_2(\text{OH})_2]^{2+}$ (**3**) with H_2O_2 , its structural and spectroscopic characterization, and its reactivity. Complex **4** is the first example of a structurally characterized alkylperoxocopper(II) complex that is a reactive intermediate and provides a fundamental basis for the functionalization of aliphatic C–H bonds by $\text{Cu}_n\text{--O}_n$ species.

Addition of 10 equivalents of 1M H_2O_2 , prepared by dilution of 30% H_2O_2 with acetonitrile, to an acetonitrile solution of **3**^[2,6] at -40°C resulted in a rapid color change from pale blue to green. The ESI-TOF mass spectrum of the green solution shows a prominent signal at m/z 412.1, which can be assigned to the mononuclear complex **4** (see Supporting Information). Stepwise addition of H_2O_2 to an acetonitrile solution of **3** at -40°C under N_2 revealed that **3** is reduced to the copper(I) complex $[\text{Cu}(\text{Me}_2\text{-tpa})]^+$ (**1**),^[2] as confirmed by the ESI-TOF mass spectrum. Compound **1** then reacts with further H_2O_2 to give the selective formation of **4** (Supporting Information). This result clearly shows that the oxidation of the methyl group of $\text{Me}_2\text{-tpa}$ starts with the reaction of **1** with H_2O_2 . For the maximum yield of **4** from the reaction of **1** with H_2O_2 under N_2 , no more than about three equivalents of H_2O_2 is needed (Figure S2 in Supporting Information).

We succeeded in isolating single crystals of **4** from the reaction of an acetonitrile solution of **1** with five equivalents of H_2O_2 at -40°C under N_2 . The crystal structure clearly shows that one of the 6-methyl groups of $\text{Me}_2\text{-tpa}$ has been oxidized to a ligand alkylperoxide group (Figure 1). The structure is best described as an intermediate between a square pyramid and a trigonal bipyramid, with an N_4O donor set. The O–O bond length is 1.477(5) Å, which is comparable to those in $[\text{Cu}\{\text{HB}(3,5\text{-iPr}_2\text{pz})_3\}(\text{OOCMe}_2\text{Ph})]^+$ (1.460(6) and 1.454(6) Å)^[7] and the closely related dinuclear alkylperoxodinickel(II) complex **5** (1.458(4) Å).^[3] Thus, the alkylperoxocopper(II) complex can be produced as well as the corresponding nickel complex **5**, although the formation process is quite different.

The electronic spectrum of **4** in acetonitrile at -40°C shows two absorption bands at about 379 ($\epsilon = 2000$) and 636 nm ($\epsilon = 190\text{ M}^{-1}\text{ cm}^{-1}$), as shown in Figure 2, which can be assigned to the $\pi^*(\text{OOR})$ -to- Cu^{II} ligand-to-metal charge transfer (LMCT) and d–d transitions, respectively, by analogy with the features of **6** ($\lambda_{\text{max}} = 380\text{ nm}$ ($\epsilon = 2800\text{ M}^{-1}\text{ cm}^{-1}$))^[5]

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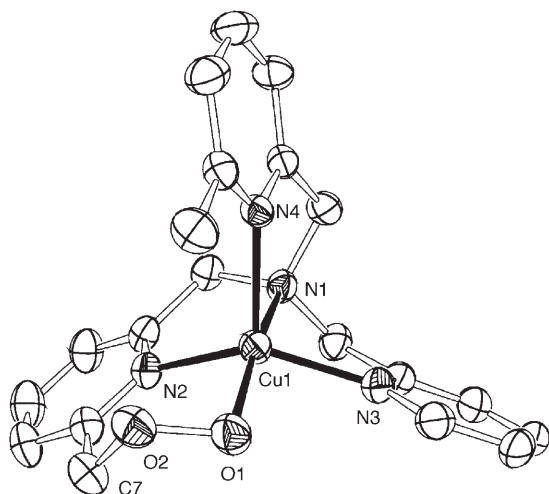


Figure 1. ORTEP drawing (thermal ellipsoids set at 50% probability) of $[\text{Cu}(\text{Me-tpa-CH}_2\text{OO})]^+$ (**4**). Hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°]: Cu1–O1 1.887(4), Cu1–N1 2.031(4), Cu1–N2 2.026(3), Cu1–N3 2.022(4), Cu1–N4 2.197(3), O1–O2 1.477(5); O1–Cu1–N1 165.9(2), O1–Cu1–N2 92.3(1), O1–Cu1–N3 93.0(2), N1–Cu1–N2 82.9(1), N1–Cu1–N3 81.4(2), N2–Cu1–N3 135.1(1), Cu1–O1–O2 107.4(2), O1–O2–C7 107.1(3).

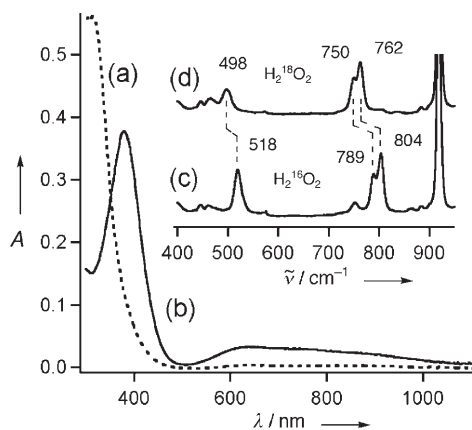


Figure 2. Electronic spectra of a) $[\text{Cu}(\text{Me}_2\text{-tpa})]^+$ (**1**) and b) $[\text{Cu}(\text{Me-tpa-CH}_2\text{OO})]^+$ (**4**) in acetonitrile at -40°C (optical path length = 0.427 cm, $[\text{Cu}] = 0.38\text{ mM}$). The inset shows the resonance Raman spectra of c) **4** and d) $\text{4-}^{18}\text{O-}^{18}\text{O}$ prepared from $\text{H}_2^{18}\text{O}_2$ in acetonitrile at -40°C (laser excitation at 406.7 nm).

and hydroperoxocopper(II) complexes.^[8] The LMCT energy of **4** is in the range of those of the mononuclear square-pyramidal and trigonal-bipyramidal hydroperoxocopper(II) complexes and significantly higher than the tetrahedral complex $[\text{Cu}\{\text{HB}(3\text{-}i\text{Bu-5-}i\text{Prpz})_3\}(\text{OOR})]^+$ (570–610 nm)^[9] owing to the lower Lewis acidity of the five-coordinate copper(II) center of **4**. The resonance Raman spectrum of **4** given in Figure 2 shows the isotope-sensitive bands at 804, 789, and 518 cm^{-1} for a $^{16}\text{O}_2$ sample (762, 750, and 498 cm^{-1} for an $^{18}\text{O}_2$ sample). The bands at 804 and 789 cm^{-1} can be assigned to the $\nu(\text{O-O})$ vibrations on the basis of their $^{16}\Delta\text{--}^{18}\Delta$ values of 42 and 39 cm^{-1} , respectively, and the band at 518 cm^{-1} to the $\nu(\text{Cu-O})$ vibration on the basis of its

$^{16}\Delta\text{--}^{18}\Delta$ value of 20 cm^{-1} . Such large isotope shifts and similar band shapes of the $\nu(\text{O-O})$ vibrations upon ^{18}O substitution in **4** suggest that mixing of the $\nu(\text{O-O})$ and $\nu(\text{O-C}$ and $\text{C-C})$ stretching vibrations of the alkylperoxo ligand is not significant, in contrast to those observed for $[\text{Cu}\{\text{HB}(3\text{-}i\text{Bu-5-}i\text{Prpz})_3\}(\text{OOR})]^+$.^[9] Although the origin of the two $\nu(\text{O-O})$ bands around 800 cm^{-1} is not known at present, because there is no significant change in the relative intensities of those two bands upon $^{18}\text{O}_2$ substitution suggests that they are not due to a Fermi doublet; there is a possibility that they are due to the presence of two geometrical and/or conformational isomers, as proposed for $[\text{Cu}\{\text{HB}(3,5\text{-}i\text{Pr}_2\text{pz})_3\}(\text{OOCMe}_2\text{Ph})]^+$.^[9]

As mentioned already, the selective oxidation of the methyl group of $\text{Me}_2\text{-tpa}$ starts with the reaction of **1** with H_2O_2 . To clarify the formation pathway of **4**, we investigated the source of the oxygen in $\text{Me-tpa-CH}_2\text{OO}^-$. The ESI-TOF mass spectrum of **4** produced in the presence of a mixture of H_2O_2 and $\text{H}_2^{18}\text{O}_2$ (1:1) under N_2 shows the formation of a mixture of **4** and $[\text{Cu}(\text{Me-tpa-CH}_2^{18}\text{O}^{18}\text{O})]^+$ ($\text{4-}^{18}\text{O-}^{18}\text{O}$) in a 1:1 ratio. No isotope scrambled species ($\text{4-}^{16}\text{O-}^{18}\text{O}$) was detected (Supporting Information). These findings indicate that the oxygen atoms of $\text{Me-tpa-CH}_2\text{OO}^-$ come from the same molecule of hydrogen peroxide. We also found that the reaction of an acetonitrile solution (10 mL in a 20-mL vial) of **1** (0.02 mmol) with five equivalents of $\text{H}_2^{16}\text{O}_2$ (0.1 mmol) in the presence of $^{18}\text{O}_2$ (ca. 6.4 mL, 0.27 mmol) at -40°C produces a mixture of $\text{4-}^{16}\text{O-}^{16}\text{O}$ (67%) and $\text{4-}^{18}\text{O-}^{18}\text{O}$ (33%), as shown in Figure 3.^[10] This result indicates that

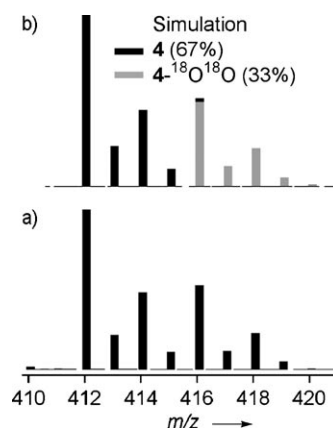


Figure 3. a) ESI-TOF mass spectrum of **4** generated from $\text{H}_2^{16}\text{O}_2$ in the presence of $^{18}\text{O}_2$ as described in the text; b) a simulated spectrum consisting of **4** (67%) and $\text{4-}^{18}\text{O-}^{18}\text{O}$ (33%).

exogenous O_2 can be incorporated into the alkylperoxo ligand. However, the amount of $\text{4-}^{18}\text{O-}^{18}\text{O}$ formed (33%) seems to be too low for these experimental conditions as the amount of $^{18}\text{O}_2$ present is significantly larger than that of $^{16}\text{O}_2$ (if present, at most 0.04 mmol), which can only be generated from H_2O_2 by reactions such as disproportionation. A combination of the above two experimental results suggests that both exogenous O_2 and some modified species derived from H_2O_2 , such as $\cdot\text{OOH}$ generated by radical chain reactions, act as oxygen sources of the $\text{Me-tpa-CH}_2\text{OO}^-$ and that some unidentified reactions proceed simultaneously. This

situation is in marked contrast to the formation of **5** and **6**, where exogenous O_2 is the sole oxygen source.^[3–5]

A possible reactive species derived from the Me_2 -tpa ligand and some modified species derived from H_2O_2 and O_2 is the ligand radical Me -tpa- CH_2^{\cdot} , which has also been proposed for the formation of **5** and **6**.^[3–5] This ligand radical may be generated as follows: **1** reacts with H_2O_2 to produce an active oxygen species by either O–O bond homolysis or heterolysis ($Cu^{II}-OH + \cdot OH$ or $Cu^{III}=O + H_2O$) that is capable of performing the selective H-atom abstraction from the methyl group to generate the ligand radical Me -tpa- CH_2^{\cdot} . This situation is in marked contrast with the reactivity of complex **2**, which selectively oxidizes the methylene group of Me_2 -tpa.^[2] Although the reaction of Me -tpa- CH_2^{\cdot} with a reactive species derived from H_2O_2 remains unclear, a possible reactive species is $\cdot OOH$, which can be generated by a radical-chain reaction and which produces the alkylperoxide directly. In the case of the reaction with O_2 , Me -tpa- CH_2^{\cdot} produces the ligand peroxy radical Me -tpa- CH_2OO^{\cdot} , as in the case of the formation of **5** and **6**.^[3–5] The conversion pathway from Me -tpa- CH_2OO^{\cdot} into Me -tpa- CH_2OO^- is not known at present.

The alkylperoxo ligand in **4** in acetonitrile at 20°C under N_2 undergoes O–O bond cleavage by either homolysis or heterolysis to generate a ligand aldehyde, as proposed for **5**.^[3,4] The ESI-TOF mass spectra of the resulting solution reveal the formation of the alkoxo- and carboxylatocopper(II) complexes $[Cu(Me-tpa-CH_2O)]^+$ (**7**) and $[Cu(Me-tpa-COO)]^+$ (**8**) together with the aldehyde and alcohol copper(I) complexes $[Cu(Me-tpa-CHO)]^+$ and $[Cu(Me-tpa-CH_2OH)]^+$,^[11] although the relative amounts of these complexes are not known at present. Thus, unlike the decomposition of **5**, decomposition of **4** proceeds by some rather complicated reactions. Complex **8** was characterized by comparison of an authentic sample prepared separately and X-ray crystallography (Figure 4). Further study of the decomposition pathways and products is under investigation.

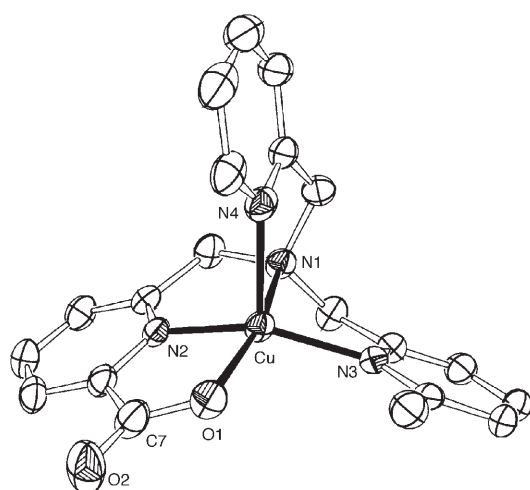


Figure 4. ORTEP drawing (thermal ellipsoids set at 50% probability) of $[Cu(Me-tpa-COO)]^+$ (**8**). Hydrogen atoms have been omitted for clarity.

In conclusion, we have succeeded in the selective formation of the mononuclear alkylperoxocopper(II) complex **4** derived from the reaction of the copper(I) complex **1** with H_2O_2 via the ligand radical Me -tpa- CH_2^{\cdot} . The reactivity of an active intermediate generated in the present reaction is quite different from that of the bis(μ -oxo)dicopper(III) species **2**. Decomposition of **4** gives alkoxo and carboxylato complexes together with aldehyde and alcohol complexes by O–O bond cleavage and subsequent reactions.

Experimental Section

4· PF_6 ·0.5 H_2O was prepared under N_2 using Schlenk techniques. 5 equivalents of 1M H_2O_2 , prepared by dilution of 30% H_2O_2 (4.3 mmol) with acetonitrile, was added to an acetonitrile solution (5 mL) of **1**· PF_6 (450 mg, 0.85 mmol) at $-40^\circ C$ to produce a green solution, which was stirred for 3 h at the same temperature. Diethyl ether (ca. 50 mL) was added to the resulting solution to yield a green powder, which was collected by filtration, washed with diethyl ether, and dried in vacuum at $-40^\circ C$. Single crystals suitable for X-ray crystallography were obtained by vapor diffusion of diethyl ether into an acetonitrile solution of the complex at $-40^\circ C$. UV/Vis (acetonitrile): λ_{max} (ϵ) = 379 (2000), 636 nm ($190 M^{-1} cm^{-1}$); elemental analysis (%) calcd for $C_{20}H_{22}CuF_6N_4O_{2.5}P$: C 42.37, H 3.91, N 9.88; found: C 42.81, H 4.15, N 9.63; ESI-TOF/MS (acetonitrile): m/z 412.1 $[M]^+$. Although the elemental analysis was satisfactory, the ESI-TOF mass spectra of the samples always showed additional unidentified signals at m/z 411.1 and 428.1 (relative intensities of 5–10% based on that of **4**). Repeated purification by addition of diethyl ether to an acetonitrile solution of **4** did not remove the impurity.

X-ray crystallographic data for **4** and **8** are given in the Supporting Information. CCDC-603442 (**4**) and CCDC-603443 (**8**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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- [10] Although addition of $^{18}\text{O}_2$ caused a slight color change from colorless to pale brown as a result of the formation of a small amount of **2**, its presence has no significant influence on the formation of **4**.
- [11] The ESI-TOF mass spectra of the solution after decomposition for 2 days revealed the formation of the copper(I) aldehyde and alcohol complexes $[\text{Cu}(\text{Me-tpa-CHO})]^+$ and $[\text{Cu}(\text{Me-tpa-CH}_2\text{OH})]^+$ (Supporting Information). Formation of copper(I) complexes was confirmed as follows: addition of 2,9-dimethyl-1,10-phenanthroline to the decomposed acetonitrile solution under N_2 generated $[\text{Cu}(\text{Me}_2\text{phen})_2]^+$. The total amount of copper(I) species was 20–25% (Supporting Information). We also found that these copper(I) complexes disappear upon addition of O_2 .