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Dioxygen Activation

$[Mn(tmc)(O_2)]^+$: A Side-On Peroxido Manganese(III) Complex Bearing a Non-Heme Ligand**

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The chemistry of metal–O_2 complexes has attracted much interest in the biological and bioinorganic chemistry communities, as such species are generated as key intermediates in the activation of dioxygen by metalloenzymes and corresponding model compounds.[1] In biomimetic studies, a number of metal–O_2 adducts have been synthesized and characterized with various spectroscopic methods, and their reactivities in the oxidation of organic substrates have been extensively investigated.[2] For example, peroxidoiron(III) complexes with heme and non-heme ligands have been synthesized as chemical models of cytochrome P450 aromatase and Rieske dioxygenases, and their reactivities have been demonstrated in various nucleophilic reactions, such as aldehyde deformylation.[3,4] Peroxidocopper(III) and -nickel(III) complexes have been synthesized and characterized recently, but their reactivities have not been well established in oxidative nucleophilic reactions of organic substrates.[2d,e,5]

Peroxidomanganese(III) complexes are also invoked as reactive intermediates in the reactions of Mn-containing enzymes, such as manganese superoxide dismutase, catalase, and the oxygen-evolving complex of photosystem II.[6] In biomimetic studies, a number of Mn–peroxido complexes have been synthesized and characterized with a variety of spectroscopic methods including X-ray crystallography. A notable example is the first X-ray crystal structure of a side-on peroxido manganese(III) porphyrin complex ($[Mn^{III}(tpp)(O_2)]^-$; tpp = *meso*-tetraphenylporphyrin), reported by Valentine and co-workers.[7] The second crystal structure of a monomeric side-on peroxido manganese(III) complex bearing a non-porphyrinic ligand was reported by Kitajima et al.[8] However, reactivities of the peroxidomanganese(III) complexes have been rarely investigated in oxidation reactions. In the present work, we synthesized a peroxidomanganese(III) complex bearing a macrocyclic tetradentate N_4 ligand, $[Mn^{III}(tmc)(O_2)]^+$ (**1**; tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane). The X-ray crystal structure of **1** shows the binding of a peroxido ligand in a side-on η^2 fashion. We have also demonstrated that **1** is capable of conducting aldehyde deformylation by a nucleophilic reaction in which cyclohexanecarboxaldehyde is deformylated to give cyclohexene as a sole product.

Addition of 5 equivalents of H_2O_2 to a solution containing $[Mn(tmc)(CF_3SO_3)_2]$ and triethylamine (TEA; 2.5 equiv) in CH_3CN at 25 °C afforded a green intermediate **1** with absorption bands at 453 nm ($\varepsilon = 490\,\mathrm{M^{-1}\,cm^{-1}}$) and 630 nm ($\varepsilon = 120\,\mathrm{M^{-1}\,cm^{-1}}$; Figure 1 a, see the Supporting Information for experimental details). The intermediate persisted for several hours ($t_{1/2} \approx 5$ h) at 25 °C. The electrospray ionization mass spectrum (ESI-MS) of **1** exhibits a prominent ion peak at a mass-to-charge ratio (*m*/*z*) of 343.1 (Figure 1 b) whose mass and isotope distribution pattern corresponds to $[Mn(tmc)(O_2)]^+$ (calculated *m*/*z* 343.2; Figure 1 b, inset). When the reaction was carried out with isotopically labeled $H_2{}^{18}O_2$, a mass peak corresponding to $[Mn(tmc)(^{18}O_2)]^+$ appeared at *m*/*z* 347.1 (calculated *m*/*z* 347.2; Figure 1 b, inset). The 4-mass-unit increase upon the substitution of ^{16}O with ^{18}O

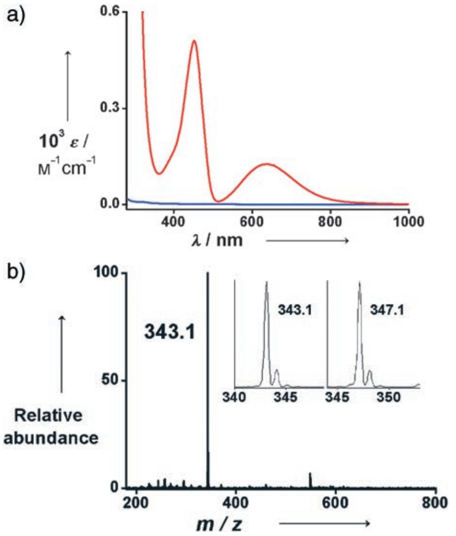

Figure 1. a) UV/Vis spectra of $[Mn(tmc)]^{2+}$ (blue) and **1** (red). b) ESI mass spectrum of **1**. Insets show the observed isotope distribution patterns for $[Mn(tmc)(^{16}O_2)]^+$ (left) and $[Mn(tmc)(^{18}O_2)]^+$ (right).

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indicates that **1** contains an O_2 unit. The X-band EPR spectrum of the starting $[Mn(tmc)]^{2+}$ complex exhibits an intense six-line hyperfine signal at $g = 2.0$ (see the Supporting Information), which is a typical EPR signal for a high-spin ($S = 5/2$) Mn^{II} species.[9] In contrast, **1** is EPR-silent (see the Supporting Information), which suggests that **1** is either a high-spin ($S = 2$) or low-spin ($S = 1$) d^4 species. The spin state of **1** in CH_3CN was then determined by using the ^1H NMR spectroscopic method of Evans;[10] the room-temperature magnetic moment of $5.4\mu_B$ clearly indicates a high-spin state ($S = 2$) of the Mn^{III} species. Taken together, the spectroscopic data provide strong evidence that the intermediate **1**, generated in the reaction of $[Mn(tmc)]^{2+}$ and H_2O_2 in the presence of base, is a high-spin Mn^{III} complex bearing an O_2 ligand, namely $[Mn^{III}(tmc)(O_2)]^+$.[11,12]

The greater thermal stability of **1** allowed the isolation of single crystals suitable for X-ray crystal structural analysis. Green platelike crystals were obtained upon addition of diethyl ether to a solution of **1** derived from the reaction of $[Mn(tmc)(CF_3SO_3)_2]$ and H_2O_2 in the presence of TEA in CH_3CN at −20 °C (50 % yield), and the crystallographic analysis of the single crystals clearly establishes that **1** contains a monomeric six-coordinate side-on peroxido Mn^{III} cation ($[Mn(tmc)(O_2)]^+$) with space group *C*2/*c* (Figure 2a; see the Supporting Information for crystallographic data). The O–O bond length of 1.403(4) Å is typical for a peroxide ion bound to a transition-metal ion, but is slightly shorter than those found in $[Mn(tpp)(\eta^2\text{-}O_2)]^-$ (O–O bond length of 1.43 Å) and $[Mn(Tp^{Pr})(3,5\text{-}Pr_2pzH)(\eta^2\text{-}O_2)]$ (O–O bond length of 1.421 Å; Tp^{Pr} = hydrotris(3,5-diisopropyl-1-pyrazolyl)borate; 3,5-Pr_2pzH = 3,5-diisopropylpyrazolyl).[7,8] The peroxido ligand is symmetrically bound to a manganese ion in a side-on η^2 fashion with an Mn–O bond length of 1.884(2) Å. The four N atoms of the tmc ligand coordinate to the metal center, and the average Mn–N bond length is 2.265(4) Å, which is in good agreement with those of other monomeric peroxido Mn^{III} complexes.[7,8] The geometry around the Mn^{III} ion is a very distorted octahedral in which the $O1/O1^i/N1/N1^i$ plane bisects the tmc ligand (Figure 2b). All four *N*-methyl groups of the tmc ligand point toward the peroxido ligand,[13] which is different from the situation in $[Fe^{IV}(tmc)(O)]^{2+}$.[14] In the latter case, the four *N*-methyl groups point away from the oxido ligand. The high thermal stability of **1** is ascribed to the fact that the peroxido ligand is placed in the pocket of the four methyl groups so that the access of external substrates to the peroxido group is restricted (Figure 2c).

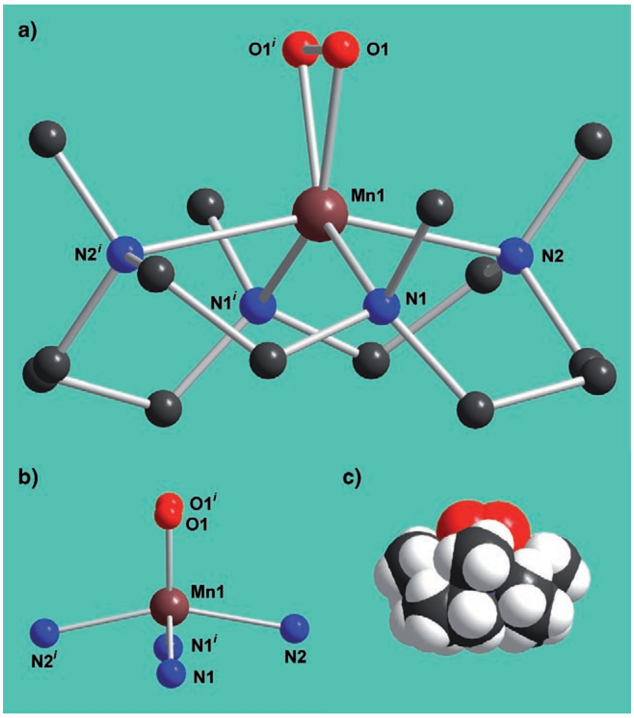


Figure 2. a) Structure of $[Mn^{III}(tmc)(O_2)]^+$ (**1**). b) View of the distorted octahedral $Mn(N_4O_2)$ moiety. c) Side view (space-filling representation) derived from the crystal structure determination. Selected bond lengths: Mn–O1 1.884(2), Mn–N1 2.215(2), Mn–N2 2.315(2), O1–O1^i 1.403(4) Å. Symmetry operation: *i* (−*x*+1, *y*, −*z*+1.5).

The reactivity of **1** was then investigated in electrophilic and nucleophilic reactions (see the Supporting Information for experimental conditions). First, the electrophilic character of **1** was tested in the oxidation of PPh_3, thioanisole, and cyclooctene. Upon addition of the substrates to the reaction solution of **1** in CH_3CN at 25 °C, the intermediate remained intact and showed no absorption spectral changes; analysis of the reaction solutions revealed that no oxygenated products were formed in the reactions. These results demonstrate that peroxidomanganese(III) species are not capable of conducting electrophilic two-electron oxidation reactions under our conditions. The nucleophilic character of **1** was then investigated in aldehyde deformylation, as it was known that peroxidoiron(III) complexes of heme and non-heme ligands react with aldehydes to give the corresponding deformylated products.[4] Upon addition of cyclohexanecarboxaldehyde (CCA) to **1** dissolved in CH_3CN at 0 °C, **1** disappeared with a first-order decay profile (Figure 3a). Fitting of the kinetic data to a pseudo-first-order rate equation allowed us to determine the k_{obs} value to be $2.2(2) \times 10^{-2}\,s^{-1}$ (Figure 3a, inset). Interestingly, analysis of the resulting solution revealed the formation of cyclohexene and formate as products (55 % based on **1** used; Scheme 1),[15] thus demonstrating that peroxidomanganese(III) species are capable of conducting aldehyde deformylation by attacking the carbonyl group in a nucleophilic reaction.[4] The formation of cyclohexene was not observed in the absence of the manganese complex. The pseudo-first-order rate constants increased proportionally with the aldehyde concentration, thus leading us to determine a second-order rate constant of $3.2(2) \times 10^{-1}\,\text{M}^{-1}\,s^{-1}$ (Figure 3b). By determining the first-order-rate constants for the deformylation of CCA by **1** between 263 and 278 K, we were able to calculate activation parameters of $\Delta H^{\neq} = 18(1)\,kJ\,mol^{-1}$ and $\Delta S^{\neq} = -200(10)\,J\,mol^{-1}\,K^{-1}$ (Figure 3c). Further, **1** reacted with other aldehydes (e.g., 2-phenylpropionaldehyde) to give the deformylated products (e.g., acetophenone). Furthermore, **1** disappeared at a fast rate in the reactions of other electrophiles (e.g., benzoyl chloride and acetic anhydride). As it has been shown that the reactions of peroxido iron(III) porphyrins with electrophiles generate high-valent oxido iron(IV) porphyrin intermediates[16] and

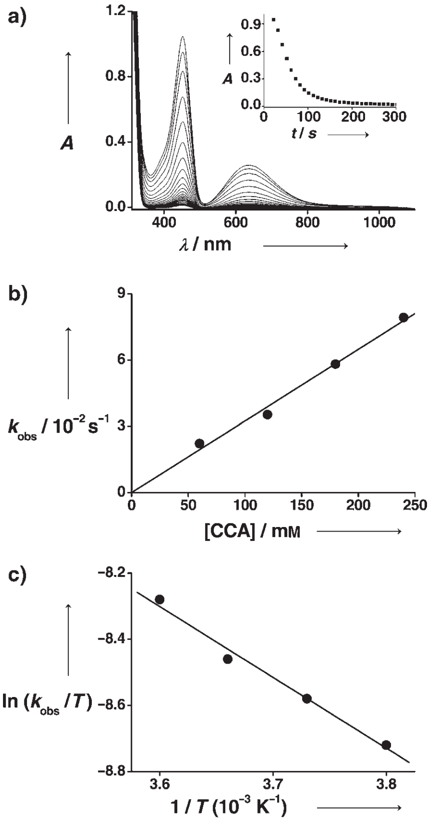
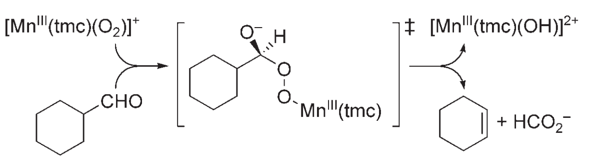


Figure 3. Kinetics of the reaction of **1** with cyclohexanecarboxaldehyde (CCA): a) UV/Vis spectral changes of **1** (2 mM) upon addition of CCA (30 equiv, 60 mM) in the presence of TEA (5 mM) at 0 °C. Inset shows the time course of the absorbance at 450 nm. b) Plot of k_{obs} against CCA concentration to determine a second-order rate constant at 0 °C. c) Plot of first-order rate constants against 1/*T* to determine activation parameters for the reaction of **1** (2 mM) and CCA (90 equiv, 180 mM).



Scheme 1. Proposed mechanism for the deformylation of CCA by $[Mn^{III}(tmc)(O_2)]^+$ (**1**).

that metal–peroxido complexes react with other metal complexes to form heterodinuclear bis(μ-oxido) or peroxido complexes,[17] detailed investigations for the reactions of nonheme peroxido manganese(III) complexes with various electrophiles and metal complexes are underway in this laboratory.

In summary, a Mn^{III}–peroxido complex bearing a macrocyclic tetradentate N_4 ligand was synthesized and characterized with various spectroscopic techniques, including X-ray crystallography. The crystal structure of the intermediate shows that the peroxido ligand is bound to a manganese ion symmetrically in a side-on η^2 fashion. We have also demonstrated that the Mn^{III}–peroxido complex is capable of deformylating aldehydes through a nucleophilic reaction but not capable of oxygenating substrates through an electrophilic reaction. The latter results indicate that Mn^{III}– and Fe^{III}–peroxido complexes show similar reactivities in nucleophilic and electrophilic reactions.[4e]

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[1] a) *Cytochrome P450: Structure, Mechanism, and Biochemistry*, 3rd ed. (Ed.: P. R. Ortiz de Montellano), Kluwer Academic/Plenum Publishers, New York, **2005**; b) *Comprehensive Coordination Chemistry II*, *Vol. 8* (Eds.: L. Que, Jr., W. B. Tolman), Elsevier, Oxford, **2004**; c) *Biomimetic Oxidations Catalyzed by Transition Metal Complexes* (Ed.: B. Meunier), Imperial College Press, London, **2000**.

[2] a) M. Momenteau, C. A. Reed, *Chem. Rev.* **1994**, *94*, 659–698; b) E. I. Solomon, T. C. Brunold, M. I. Davis, J. N. Kemsley, S.-K. Lee, N. Lehnert, F. Neese, A. J. Skulan, Y.-S. Yang, J. Zhou, *Chem. Rev.* **2000**, *100*, 235–349; c) M. Costas, M. P. Mehn, M. P. Jensen, L. Que, Jr., *Chem. Rev.* **2004**, *104*, 939–986; d) L. M. Mirica, X. Ottenwaelder, T. D. P. Stack, *Chem. Rev.* **2004**, *104*, 1013–1045; e) E. A. Lewis, W. B. Tolman, *Chem. Rev.* **2004**, *104*, 1047–1076.

[3] a) D. L. Wertz, J. S. Valentine, *Struct. Bonding* **2000**, *97*, 37–60; b) D. T. Gibson, R. E. Parales, *Curr. Opin. Biotechnol.* **2000**, *11*, 236–243; c) A. Karlsson, J. V. Parales, R. E. Parales, D. T. Gibson, H. Eklund, S. Ramaswamy, *Science* **2003**, *299*, 1039–1042.

[4] a) D. L. Wertz, M. F. Sisemore, M. Selke, J. Driscoll, J. S. Valentine, *J. Am. Chem. Soc.* **1998**, *120*, 5331–5332; b) Y. Goto, S. Wada, I. Morishima, Y. Watanabe, *J. Inorg. Biochem.* **1998**, *69*, 241–247; c) K. Hashimoto, S. Nagatomo, S. Fujinami, H. Furutachi, S. Ogo, M. Suzuki, A. Uehara, Y. Maeda, Y. Watanabe, T. Kitagawa, *Angew. Chem.* **2002**, *114*, 1250–1253; *Angew. Chem. Int. Ed.* **2002**, *41*, 1202–1205; d) J. Annaraj, Y. Suh, M. S. Seo, S. O. Kim, W. Nam, *Chem. Commun.* **2005**, 4529–4531; e) M. J. Park, J. Lee, Y. Suh, J. Kim, W. Nam, *J. Am. Chem. Soc.* **2006**, *128*, 2630–2634.

[5] a) M. T. Kieber-Emmons, R. Schenker, G. P. A. Yap, T. C. Brunold, C. G. Riordan, *Angew. Chem.* **2004**, *116*, 6884–6886; *Angew. Chem. Int. Ed.* **2004**, *43*, 6716–6718; b) R. Schenker, M. T. Kieber-Emmons, C. G. Riordan, T. C. Brunold, *Inorg. Chem.* **2005**, *44*, 1752–1762.

[6] a) R. Tagore, H. Chen, R. H. Crabtree, G. W. Brudvig, *J. Am. Chem. Soc.* **2006**, *128*, 9457–9465, and references therein; b) A. J. Wu, J. E. Penner-Hahn, V. L. Pecoraro, *Chem. Rev.* **2004**, *104*, 903–938.

[7] R. B. VanAtta, C. E. Strouse, L. K. Hanson, J. S. Valentine, *J. Am. Chem. Soc.* **1987**, *109*, 1425–1434.

[8] N. Kitajima, H. Komatsuzaki, S. Hikichi, M. Osawa, Y. Moro-Oka, *J. Am. Chem. Soc.* **1994**, *116*, 11596–11597.

[9] a) D. P. Kessissoglou, W. M. Butler, V. L. Pecoraro, *Inorg. Chem.* **1987**, *26*, 495–503; b) M. Maneiro, M. R. Bermejo, M. I. Fernández, E. Gómez-Fórneas, A. M. González-Noya, A. M. Tyryshkin, *New J. Chem.* **2003**, *27*, 727–733.

[10] a) D. F. Evans, *J. Chem. Soc.* **1959**, 2003–2005; b) D. F. Evans, D. A. Jakubovic, *J. Chem. Soc. Dalton Trans.* **1988**, 2927–2933.

[11] Although we have attempted to measure resonance Raman spectra of **1**, we failed to observe ν(O–O) and ν(Mn–O_2) vibrations when using 413- and 624.8-nm laser excitations. It is worth noting that no Raman vibrations of Mn^{III}–O_2 species have been reported yet, but O–O stretching bands have been

observed between 890 and 1000 cm^{-1} in infrared spectra. See reference [8] and M. W. Urban, K. Nakamoto, F. Basolo, *Inorg. Chem.* **1982**, *21*, 3406 – 3408.

[12] Other non-heme manganese(II) complexes, such as $[Mn(N4Py)]^{2+}$ (N4Py = *N*,*N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine), $[Mn(tpa)]^{2+}$ (tpa = tris(2-pyridylmethyl)amine), and $[Mn(bpmen)]^{2+}$ (bpmen = *N*,*N'*-dimethyl-*N*,*N'*-bis(2-pyridylmethyl)-1,2-diaminoethane), did not show the formation of peroxido manganese(III) complexes under the identical reaction conditions.

[13] A crystal structure of $[Mn^{II}(tmc)(Cl)]^{+}$ shows that the four *N*-methyl groups are located on the same side of the manganese ion and point toward the chloride ligand: C. Bucher, E. Duval, J.-M. Barbe, J.-N. Verpeaux, C. Amatore, R. Guilard, L. Le Pape, J.-M. Latour, S. Dahaoui, C. Lecomte, *Inorg. Chem.* **2001**, *40*, 5722 – 5726.

[14] J.-U. Rohde, J.-H. In, M. H. Lim, W. W. Brennessel, M. R. Bukowski, A. Stubna, E. Münck, W. Nam, L. Que, Jr., *Science* **2003**, *299*, 1037 – 1039.

[15] a) A. D. N. Vaz, S. J. Pernecky, G. M. Raner, M. J. Coon, *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 4644 – 4648; b) A. D. N. Vaz, E. S. Roberts, M. J. Coon, *J. Am. Chem. Soc.* **1991**, *113*, 5886 – 5887.

[16] a) E. McCandlish, A. R. Miksztal, M. Nappa, A. Q. Sprenger, J. S. Valentine, J. D. Stong, T. G. Spiro, *J. Am. Chem. Soc.* **1980**, *102*, 4268 – 4271; b) M. Schappacher, R. Weiss, *J. Am. Chem. Soc.* **1985**, *107*, 3736 – 3738; c) H. Furutachi, K. Hashimoto, S. Nagatomo, T. Endo, S. Fujinami, Y. Watanabe, T. Kitagawa, M. Suzuki, *J. Am. Chem. Soc.* **2005**, *127*, 4550 – 4551.

[17] a) N. W. Aboelella, J. T. York, A. M. Reynolds, K. Fujita, C. R. Kinsinger, C. J. Cramer, C. G. Riordan, W. B. Tolman, *Chem. Commun.* **2004**, 1716 – 1717; b) E. E. Chufán, K. D. Karlin, *J. Am. Chem. Soc.* **2003**, *125*, 16160 – 16161; c) N. W. Aboelella, E. A. Lewis, A. M. Reynolds, W. W. Brennessel, C. J. Cramer, W. B. Tolman, *J. Am. Chem. Soc.* **2002**, *124*, 10660 – 10661.