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Water Oxidation Catalyzed by a Dinuclear Mn Complex: A Functional Model for the Oxygen-Evolving Center of Photosystem II**

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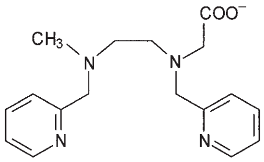
Multinuclear manganese complexes have played an important role in the search for structural analogues of the active site of the oxygen-evolving complex (OEC) of photosystem II.[1] However, the discovery of a functional biomimetic manganese complex that catalyzes the oxidation of water to dioxygen remains a challenge with enormous scientific implications. Reported here is the discovery that a dimanganese complex of the ligand *N*-methyl-*N′*-carboxymethyl-*N*,*N′*-bis(2-pyridylmethyl)ethane-1,2-diamine (mcbpen$^-$) catalyzes the oxidation of water by *tert*-butylhydrogenperoxide (TBHP) or cerium nitrate to dioxygen. Furthermore, we have directly measured the evolved O_2 concentration in solution by using the relatively new method of membrane inlet mass spectrometry (MIMS). The isotopomer distribution is quantified with this method and shows that the reaction is highly specific: One oxygen atom in the evolved dioxygen comes from water, and the other is derived from the oxidant.

It did not escape our attention that a series of dinuclear manganese complexes of the new pentadentate ligand mcbpen$^-$,[2] for which we have identified complexes with the oxidation states Mn^{II}/Mn^{II}, Mn^{III}/Mn^{III}, Mn^{III}/Mn^{IV}, and Mn^{IV}/Mn^{IV}, is highly relevant as a model system for the OEC. Two molecules of water are coordinated in the stable, crystallographically characterized $[Mn^{II}_2(mcbpen)_2(H_2O)_2](ClO_4)_2$ (**1**-$(ClO_4)_2$). The X-ray crystal structure of **1**-$(ClO_4)_2$ shows two seven-coordinate Mn^{II} atoms with the carboxylate arms of mcbpen bridging the metal centers through one of the oxygen atoms to give a Mn⋯Mn separation of 4.0914(9) Å in the dinuclear structure. Manganese complexes of mcbpen$^-$ with a formal metal oxidation state higher than Mn^{II} are unstable, but have sufficiently long lifetimes in solution for spectroscopic (ESR and UV/Vis), spectrometric (ESIMS), and electrochemical characterization.[2] A plausible precursor for dioxygen, two oxides in a Mn_2O_2 rhombus, is present in an unstable Mn^{IV}/Mn^{IV} complex $[Mn^{IV}_2(O)_2(mcbpen)_2]^{2+}$, which has been identified in solutions of **1**-$(ClO_4)_2$ treated with TBHP in acetonitrile. The present work arose from our efforts to delineate the decomposition pathway of $[Mn^{IV}_2(O)_2(mcbpen)_2]^{2+}$: Does this occur through release of O_2? In this scenario, $[Mn^{II}_2(mcbpen)_2(H_2O)_2]^{2+}$ can be considered a low-valent complex with a substrate (H_2O) coordinated, and $[Mn^{IV}_2(O)_2(mcbpen)_2]^{2+}$ the appropriate higher formal oxidation state species with the product precursors coordinated. As such, the mcbpen$^-$ dinuclear system is unique in manganese chemistry and pertinent to modeling the OEC.



mcbpen$^-$

We have now used both a Clark electrode and MIMS[3–6] to prove that O_2 is evolved from aqueous solutions containing **1**-$(ClO_4)_2$ and two separate chemical oxidants. The complex catalyzes the oxidation of water. When **1**-$(ClO_4)_2$ is mixed with 5–100 equivalents of TBHP in water, the initially pale solutions turn dark brown and bubbles are observed with the higher amounts of TBHP. The solutions generally bleach within 24 h and **1**-$(ClO_4)_2$ can be reisolated. Figure 1 shows the profiles of the O_2 evolution in the reaction of an aqueous solution of **1**-$(ClO_4)_2$ treated with periodic additions of TBHP (20 equivalents). The evolution of O_2 ceases approximately 25 min after each addition, and essentially the same amount of O_2 is repeatedly produced on each addition. The pH value of the system was 4.75 and did not change during the experiment. Control experiments in which an aqueous solution of manganese(II) perchlorate at the same pH value is used produces no O_2 on addition of 20 or more equivalents of TBHP. The shape of the traces in the MIMS experiments indicates evolution of O_2 rather than a surge, for example, from its introduction by the syringe.[7] The fact that there is little decay in the response to each TBHP addition implies convincingly that the system is turning over.[8] To date, evolution of 10–20 equivalents of O_2 has been recorded with no detectable catalyst decomposition or inhibition.

A strength of the MIMS technique is that ^{18}O labeling experiments can be carried out to investigate the source of the O atoms in the evolved O_2. The $^{18}O^{16}O$ isotopomer is produced exclusively when ^{18}O-labeled water (min. 95% ^{18}O) is used. No significant levels of $^{16}O_2$ and $^{18}O_2$ are detected. Thus, one oxygen atom in the O_2 evolved in the **1**-$(ClO_4)_2$ catalyzed oxidation of water by TBHP is derived from water. The reaction was carried out in pure water, and the measuring cell was purged with Ar, so the only other source of oxygen atoms was the oxidant, TBHP.[9] In these experiments, the concentration of one substrate, water, is in large excess (172-fold) of the other substrate TBHP. It is not realistic to change these ratios such that the reaction stoichiometry might

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Supporting information (ESI mass spectra of reaction solutions containing TBHP and $(NH_4)_2[Ce(NO_3)_6]$ in water, labeled water, and acetonitrile; further MIMS traces) for this article is available on the WWW under http://www.angewandte.org or from the author.

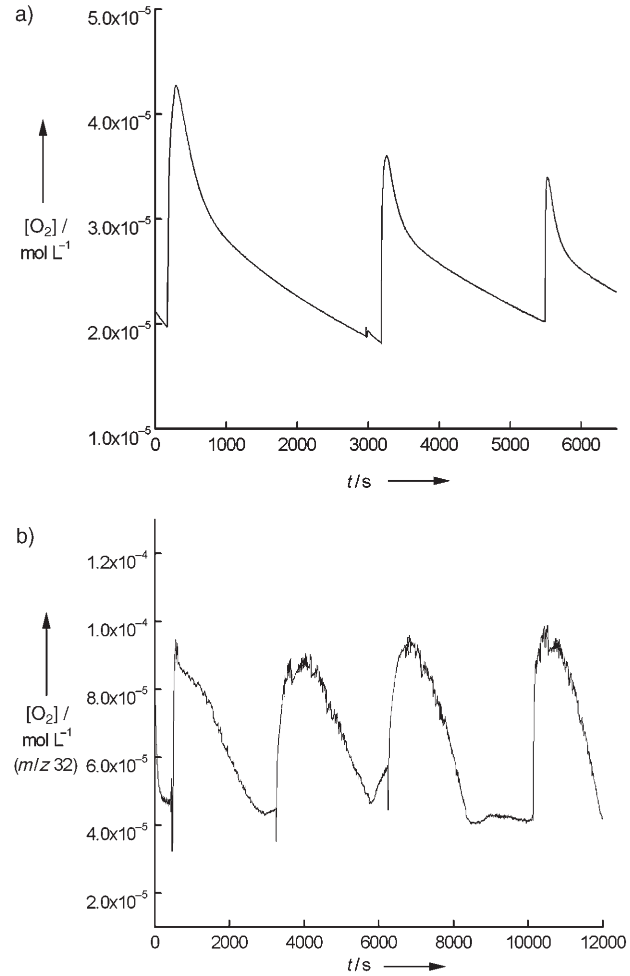
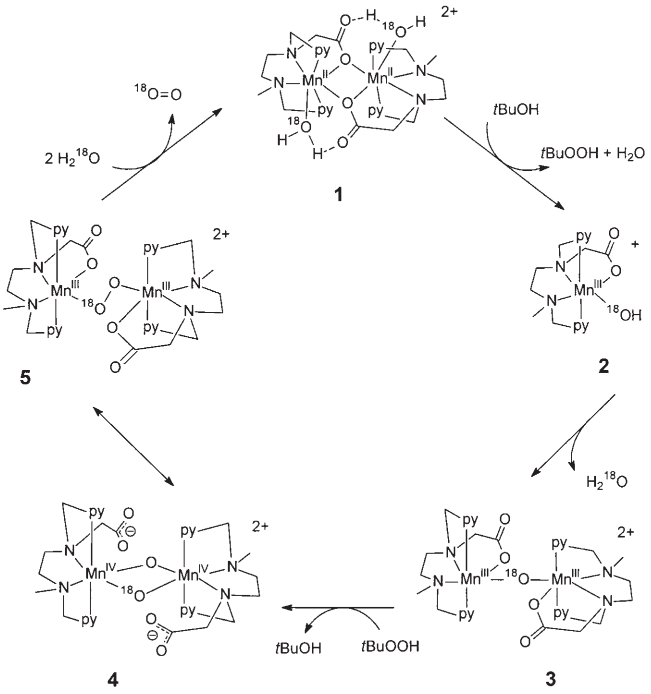


Figure 1. Measurement of O_2 concentration in an Ar-purged aqueous solution of **1**-$(ClO_4)_2$ with TBHP additions followed over time. a) Evolution measured by using a Clark electrode with injections of TBHP (2.7 μL, 1 M) at $t=0$, 50, and 90 min to **1**-$(ClO_4)_2$ (0.2 mM, 3.2×10^{-7} mol) b) Evolution of $^{16}O_2$ measured by means of MIMS with injections of TBHP (10 μL, 0.323 M, 3.2×10^{-6} mol) at $t=8$, 54, 104, and 169 min to **1**-$(ClO_4)_2$ (0.5 mM, 1.67×10^{-7} mol). $^{18}O^{16}O$ (*m/z* 34) and $^{18}O_2$ (*m/z* 36) concentrations were followed but are not present in detectable amounts. The first, second, third, and fourth additions of TBHP generate 2.52×10^{-7}, 2.9×10^{-7}, 2.58×10^{-7}, and 2.62×10^{-7} mol of $^{16}O_2$ respectively (total: 1.062×10^{-6} mol $^{16}O_2$). Note: The relative concentrations of TBHP and **1**-$(ClO_4)_2$ in the two experiments are different, therefore, the measurement scales of the two experiments cannot be directly compared.

be experimentally verified because increasing the oxidant concentration will give an unreliable measurement, as MIMS, similar to an O_2 electrode, detects only the oxygen dissolved in the liquid and not the oxygen expelled as bubbles. Thus, with water as the solvent we were limited to using the concentrations of the THBP and **1**-$(ClO_4)_2$ shown in Figure 1 in the quantitative experiments. It is likely that greater yields are achievable.

On the basis of our earlier characterization of the transient mononuclear and dinuclear Mn^{III} and dinuclear Mn^{IV} complexes of mcbpen$^-$ generated by oxidation of **1**-$(ClO_4)_2$ with TBHP in acetonitrile and water (see Supporting Information and ref. [2]), we propose the speculative reaction mechanism outlined in Scheme 1. Oxidation of **1**-$(ClO_4)_2$ with TBHP cleaves the bridging carboxylate-O ligands of **1**[10] and produces the transient mononuclear hydroxide $[Mn^{III}(mcbpen)OH]^+$ (**2**). ESIMS studies of the reaction in both



Scheme 1. A speculative mechanism for water oxidation by *t*BuOOH catalyzed by **1**-$(ClO_4)_2$.

D_2O and $H_2{}^{18}O$ clearly show that the oxygen atom in **2** is derived from water and not the oxidant, as the major ion generated is $[Mn^{III}(mcbpen)OD]^+$ (*m/z* 386.5) and $[Mn^{III}(mcbpen)^{18}OH]^+$ (*m/z* 387.3) in D_2O and $H_2{}^{18}O$, respectively. The next step in the catalytic cycle is dimerization and dehydration of **2** to give $[Mn^{III}_2(mcbpen)_2(O)]^{2+}$ (**3**). The dehydration in aqueous solution of manganese(III) and iron(III) complexes containing terminal hydroxides to give dinuclear mono-oxide bridged complexes is well documented. We have shown that reaction of **1**-$(ClO_4)_2$ with TBHP in water and acetonitrile produces the very short lived **3** as verified by ESIMS and UV/Vis spectroscopy.[2] A facile oxidation of **3** on the basis of the known instability of such species to oxidation is expected, and differs from the first oxidation step, in that the TBHP may in this case act as an oxygen atom donor to give the dimeric $[Mn^{IV}_2(O)_2(mcbpen)_2]^{2+}$ (**4**). It is likely that during the **3**→**4** reaction step the carboxylate arms are concomitantly displaced to accommodate the two μ-oxo ligands. Thus, an arrangement similar to other, known bis(μ-oxo)-dimanganese complexes of linear N_4 bispicen-based[11] ligands (Mn···Mn = 2.7 Å)[12–14] is achieved. The anticipated facile oxidation of **3** (oxidase activity) can be invoked to explain the slightly different curve shape in the first evolution step (the front of the peak shows a spike, which indicates an initial rapid reduction in O_2 concentration). This spike might be caused by an initial trace amount of O_2 in the solution which oxidizes **3** in the first cycle.

Spontaneous collapse of **4** followed by release of dioxygen and coordination of two molecules of water will result in reformation of **1** in aqueous solution. We imagine that the carboxylate arms of mcbpen$^-$ are not innocent in the O_2-elimination reaction; by swinging in and recoordinating the manganese atoms, as depicted in the resonance structures **4** and **5** (Scheme 1), the formation of a bond between the two oxide bridges might be favored as a Mn–O(Mn) bond at each Mn atom is displaced. Similar resonance in copper bis(μ-oxo)/μ-peroxo systems has been proposed.[15,16] Oxygen release from the μ-peroxo-Mn^{III}_2 complex **5** to give a Mn^{II}_2 species would then ensue. A notable feature of this mechanism is the involvement of the coordinatively flexible carboxylate arm of the mcbpen$^-$ ligand: Bridging, terminal, and noncoordinated modes support the various dinuclear and mononuclear structures proposed, and the oxidation states deduced experimentally, in a chemically logical fashion. This is analogous to the so-called "carboxylate shift" proposed to be important in the mechanisms of several non-heme iron enzymes. Of course any mechanistic proposal is speculative; however, we have spectroscopic evidence for all the species in Scheme 1 except **5**. Furthermore, the species are all chemically reasonable, comprising water/hydroxo/oxo ligands on metal centers of the appropriate oxidation state.

The overall reaction for the mechanism proposed in Scheme 1 including an ^{18}O label is described by Equation (1).[17]

$$2\,t\mathrm{BuOOH} + 2\,\mathrm{H_2}^{18}\mathrm{O} \xrightarrow{\mathbf{1}\text{-}(\mathrm{ClO_4})_2} 2\,t\mathrm{BuOH} + {}^{18}\mathrm{O}^{16}\mathrm{O} + \mathrm{H_2O} + \mathrm{H_2}^{18}\mathrm{O} \quad (1)$$

Equation (1) simplifies to Equation (2):

$$2\,t\mathrm{BuOOH} + \mathrm{H_2}^{18}\mathrm{O} \xrightarrow{\mathbf{1}\text{-}(\mathrm{ClO_4})_2} 2\,t\mathrm{BuOH} + {}^{18}\mathrm{O}^{16}\mathrm{O} + \mathrm{H_2O} \quad (2)$$

The attempt to establish the source of the O atoms in the evolved O_2 is clearly problematic where a terminal oxidant containing an O atom is used. We therefore tested $(NH_4)_2[Ce(NO_3)_6]$ as the oxidant. This Ce^{IV} source has been used in the studies of the oxidation of $[(bpy)_2(H_2O)RuORu(H_2O)(bpy)_2]^{4+}$ (bpy = 2,2′-bipyridine) by Meyer and co-workers[18,19] and recently in the report by Yagi and Narita that $[Mn_2O_2(terpy)_2(H_2O)_2](NO_3)_3{\cdot}6\,H_2O$ (terpy = 2,2′:6′,2″-terpyridine) adsorbed onto kaolin clay produces O_2 from water.[20] When $(NH_4)_2[Ce(NO_3)_6]$ was used as the oxidant, the evolution of O_2 from water catalyzed by **1**-$(ClO_4)_2$ was again detected, however, in lower yields than in the TBHP reaction. The pH value of the reaction mixture with $(NH_4)_2[Ce(NO_3)_6]$ drops rapidly to 1 and this is most likely the cause of the lower yields—at low pH values, the formation of high-valent oxo-bridged Mn species is not favored. Furthermore, ligand decoordination caused by competing protonation is suggested by the ESI mass spectra of reaction mixtures containing $(NH_4)_2[Ce(NO_3)_6]$ which show the presence of the free ligand mcbpenH_2^+ at m/z 315.4 in addition to $[Mn_2(mcbpen)_2]^{2+}$ at 368.3 and $[Mn^{III}(mcbpen)NO_3]^+$ at 430.2 (see Supporting Information). Figure 2 follows the concentration of the $^{18}O^{16}O$ isotopomer with time in experiments with $(NH_4)_2[Ce(NO_3)_6]$. Again, and initially surprisingly, the $^{18}O^{16}O$ isotopomer is produced exclusively in the ^{18}O labeling experiments with $(NH_4)_2[Ce(NO_3)_6]$.

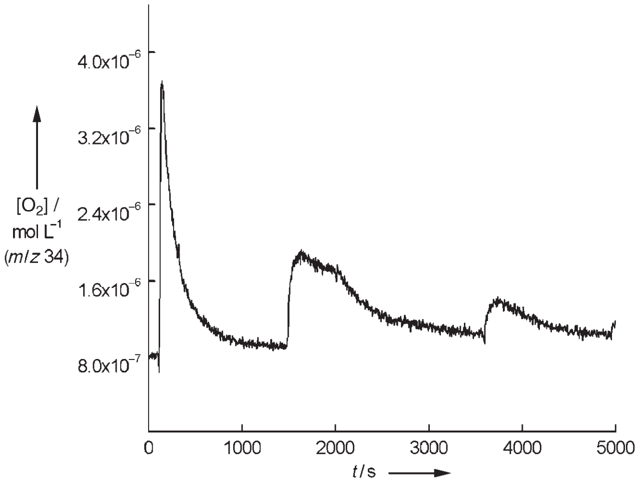


Figure 2. Trace of $^{18}O^{16}O$ evolution over time from a solution containing **1**-$(ClO_4)_2$ (2 mM, 7.1×10^{-7} mol) in 95% $H_2{}^{18}O$ after injections of $(NH_4)_2[Ce(NO_3)_6]$ (20 μL, 0.6 M) in 95% $H_2{}^{18}O$ at $t = 2$, 25, and 60 min. Total amounts of evolved oxygen are much lower, and the decrease in productivity with each addition of oxidant is evident from the comparison of the curve shape to that of Figure 1 b. The evolution of $^{16}O_2$ (m/z 32) and $^{18}O_2$ (m/z 36) was under detectable limits.

As the reaction is carried out in 95% $H_2{}^{18}O$ water, the only source of one ^{16}O atom is the nitrate[21] anion in the Ce^{IV} salt. Thus, the exclusive production of $^{18}O^{16}O$ in the reactions with Ce^{IV} as the oxidant can be only explained by the involvement of nitrate as an O-atom donor.[22] Thus, we propose that the water oxidation is coupled with both Ce^{IV} and nitrate reduction as shown in Equation (3). Inspection of the redox potentials of Ce^{IV} reduction and nitrite oxidation indicates any nitrite produced would be rapidly reoxidized to nitrate in the presence of excess Ce^{IV} [Eq. (4)].

$$\begin{aligned}&2\,\mathrm{Ce^{IV}} + 2\,\mathrm{H_2}^{18}\mathrm{O} + \mathrm{NO_3}^- \xrightarrow{\mathbf{1}\text{-}(\mathrm{ClO_4})_2}\\ &2\,\mathrm{Ce^{III}} + {}^{18}\mathrm{O}^{16}\mathrm{O} + \mathrm{H_2}^{18}\mathrm{O} + 2\,\mathrm{H^+} + \mathrm{NO_2}^-\end{aligned} \quad (3)$$

$$2\,\mathrm{Ce^{IV}} + \mathrm{H_2}^{18}\mathrm{O} + \mathrm{NO_2}^- \rightarrow 2\,\mathrm{Ce^{III}} + \mathrm{N}^{18}\mathrm{O}^{16}\mathrm{O_2}^- + 2\,\mathrm{H^+} \quad (4)$$

By combining Equations (3) and (4), the overall reaction for the **1**-$(ClO_4)_2$ catalyzed oxidation of water, including labels, by $(NH_4)_2[Ce(NO_3)_6]$ is that in Equation (5), which can be simplified to Equation (6).

$$\begin{aligned}&4\,\mathrm{Ce^{IV}} + 3\,\mathrm{H_2}^{18}\mathrm{O} + \mathrm{NO_3}^- + \mathrm{NO_2}^- \xrightarrow{\mathbf{1}\text{-}(\mathrm{ClO_4})_2}\\ &4\,\mathrm{Ce^{III}} + {}^{18}\mathrm{O}^{16}\mathrm{O} + \mathrm{H_2}^{18}\mathrm{O} + 4\,\mathrm{H^+} + \mathrm{NO_2}^- + \mathrm{N}^{18}\mathrm{O}^{16}\mathrm{O_2}^-\end{aligned} \quad (5)$$

$$4\,\mathrm{Ce^{IV}} + 2\,\mathrm{H_2}^{18}\mathrm{O} + \mathrm{NO_3}^- \xrightarrow{\mathbf{1}\text{-}(\mathrm{ClO_4})_2} 4\,\mathrm{Ce^{III}} + {}^{18}\mathrm{O}^{16}\mathrm{O} + 4\,\mathrm{H^+} + \mathrm{N}^{18}\mathrm{O}^{16}\mathrm{O_2}^- \quad (6)$$

Aqueous solutions of $[Mn_2O_2(terpy)_2(H_2O)_2](NO_3)_3{\cdot}6\,H_2O$, (**6**) have been shown to evolve dioxygen (without turnover) in the presence of aqueous sodium hypochlorite[23] and oxone.[24] In the presence of high concentrations of oxone ($KHS^{16}O_5$) (100:1 oxone:**6**) negligible amounts of labeled dioxygen were formed in the presence of $H_2^{18}O$, thus suggesting that oxone was the likely source of the O atoms in the O_2 produced under these conditions. However, by lowering the ratio of the oxone:**6** to 20:1, labeled dioxygen was detected, with the highest yielding mixtures containing doubly-labeled $^{18}O_2$ (12% ± 6%), mixed-labeled $^{18}O^{16}O$ (39% ± 15%), and $^{16}O_2$ (49% ± 19%).[24] Solutions of **6** in these reactions decompose rapidly to give permanganate. These results are in contrast to those we report for the Mn/mcbpen$^-$ system. In neither of the oxidation reactions with TBHP or Ce^{IV} as oxidant and **1**-$(ClO_4)_2$ as catalyst was permanganate produced as a decomposition product of the catalyst; the reaction is highly specific as only one isotopomer is produced, and there is turnover.

Notably, mcbpen$^-$ is mononegative and provides one carboxylate donor for each Mn ion, which is analogous to the protein donors for all the Mn atoms of the 3+1 OEC cluster.[25] The flexible carboxylate donor means that dinuclear manganese complexes of mcbpen$^-$ show the potential to change between 6 and 7 coordination as needed, depending on the Mn oxidation state and the presence of exogenous ligands. The Mn···Mn separations may vary between 4.0914(9) Å (Mn^{II}/Mn^{II}) and 2.7 Å (Mn^{IV}/Mn^{IV}). These features are a significant advance in ligand design for an OEC model and may in fact be crucial to the functionality of this system. The dinuclear complexes in the proposed catalytic cycle (Scheme 1) are all plausible intermediates and have structural precedents with either mcbpen$^-$ itself or related ligand systems. The highly specific and catalytic oxidation of water catalyzed by **1**-$(ClO_4)_2$ is a noteworthy advance in the mimicry of the activity of the OEC.

Experimental Section

All solutions were prepared using doubly deionized water. $H_2^{18}O$ (95 atom%) was purchased from ISOTEC (Sigma Aldrich). All other chemicals were purchased from Aldrich and used without further purification. Solutions of *tert*-butylhydrogenperoxide (TBHP) in decane (6 M) or water (1 M and 0.32 M) were used. **1**-$(ClO_4)_2$ was synthesized as reported previously.[2] **Caution!** Perchlorate salts of metal complexes with organic ligands are potentially explosive!

Electrospray Ionization Mass spectra were obtained using a Finnigan TSQ 700 triple-quadrapole instrument equipped with a Finnigan API source in nanoelectrospray mode. The oxygen concentration was measured with an MI-730 oxygen electrode from Microelectrodes Inc., USA and by means of membrane inlet mass spectrometry (MIMS). In the MIMS experiment, the sample cell had a volume of 500 µL and was made of stainless steel. The solution was stirred with an impeller connected through a stirring shaft to an electric motor operating at 400 rpm. The sample cell was mounted on a vacuum flange, and the only separation between the liquid in the sample cell and the vacuum chamber of a single-quadrapole mass spectrometer (Balzers QMG 420) was a 51-µm thick silicone membrane (SIL-TEC Sheeting, Technical products Inc., USA). The inlet was thermostatically controlled at 30 °C. The concentration of O_2 was determined by using the calibration method described by Degn and Lauritsen.[26]

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[7] A deliberate injection of O_2 into the system does not invoke this response, rather the surge is recorded, and this immediately decays exponentially.

[8] We are currently designing a new cell so that a continuous supply of TBHP can be added in order to attain a steady state of catalytic activity. Visual inspection of the reactions indicates that the concentrations used in the MIMS experiments are not optimal and the system potentially produces much greater amounts of product.

[9] We have not found determinations of O-exchange between water and *t*BuOOH in the literature. However, the specific production of one isotopomer observed in our work is indirect evidence that any exchange of this nature is not kinetically relevant. If there was significant exchange then a distribution of isotopes, $^{16}O_2$, $^{18}O^{16}O$, and $^{18}O_2$, would be observed. Furthermore we have monitored the reaction solution at *m*/*z* 92, which corresponds to singly ^{18}O-labeled TBHP. No trace was detected (and we do see unlabeled TBHP at *m*/*z* 90). Therefore competing homolytic cleavage of the O–O bond in TBHP and consequent radical Haber–Weiss chemistry can be eliminated in mechanistic considerations. Furthermore oxidation is observed with the Ce^{IV} oxidant.

[10] The complex is dimeric in solution as well as in the solid state as evidenced by solution ESR spectroscopy.[2]

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[22] As mentioned in the text, the nitrate-containing $[Mn^{III}(mcbpen)NO_3]^+$ is in fact observed in the ESI mass spectra of the reaction solutions. This fact cannot be regarded as evidence for Mn activation for nitrate reduction. However, it does suggest a higher concentration of $[Mn^{III}(mcbpen)NO_3]^+$ than the isoelectronic $[Mn^{III}(mcbpen)OH]^+$, which is seen in the TBHP reactions. An attempt to verify the possible involvement of nitrate in the water oxidation was made by adding a 100-fold excess of sodium nitrate to the reaction. This resulted in complete inhibition of the reaction. This observation is not surprising if nitrate is capable of substituting the water ligands of **1**-$2(ClO_4)_2$ and consequently inhibiting the reaction. We have also attempted to detect the $N^{18}O^{16}O_2^-$ isotopomer by negative-ion ESIMS. Unfortunately, in the presence of such large excess of the unlabeled nitrate, this experiment was beyond the resolution capabilities of our instrument.

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