Chemical Activation of a Mononuclear Non-Porphyrinic Manganese Complex using Water as Oxygen Source for the Oxygen Atom Transfer Reaction

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Oxidation reactions are among the most widely studied chemical transformations, given their importance in both biological and industrial processes.[1] Nature has developed a wide range of metalloproteins that use dioxygen to generate highly oxidized metal–oxo species as reactive intermediates.[2] In these processes electrons and protons are required to cleave the O—O bond, liberating a water molecule and yielding a highly oxidized metal–oxo species responsible for the oxygen atom transfer in a variety of organic substrates.[3] In developing bioinspired models of these enzymes, chemists commonly employ oxygen-containing oxidants to generate the reactive metal-oxo species through an oxygen atom transfer reaction to the metal center.[4]

An alternative pathway towards such metal-oxo species resides in activating a metal-bound water molecule through a two electron-, two proton-abstraction, with the metal-oxo species transferring an oxygen atom to an organic substrate. Such a process is in sharp contrast with the reductive O_2 activation pathway as electrons and protons are products of the reaction. In fact, highly oxidized manganese-oxo species are proposed as the reactive species at the heart of photosystem II,[5] the oxygen-evolving complex (OEC) prior to the formation of the O—O bond.[6] Such a reactive species is reached after a first water molecule coordinated to a manganese ion has been converted to an electrophilic oxygen atom through deprotonation and oxidation of the manganese ion. This metal-bound oxygen atom will then endure so-called nucleophilic attack from another water molecule to create the O—O bond. It is therefore appealing to generate these highly active intermediates using water as a renewable source of oxygen to drive oxidation of organic compounds.[7] Recently Nam and Fukuzumi reported on the generation of a manganese(IV)-oxo species by oxidation of a manganese(II)–aquo complex with Ce^{IV} as chemical oxidant.[8] The authors showed that the Mn^{IV}-O species was able to perform hydrogen abstraction reactions. An important piece of information from this study comes from the theoretical calculations that support the stabilization of the Mn^{IV}-oxo species in aqueous solution through a cluster of water molecules in the second coordination sphere of the metal ion.

Recently, some of us have reported on the electrochemical generation of the mononuclear Mn^{IV}-hydroxo species with a pentadentate ligand.[9] We have clearly shown that water molecules in the second coordination sphere are crucial to inhibit the deleterious formation of μ-oxo manganese complexes. Our finding, therefore, brings experimental support to the theoretical proposal by Nam et al. In the present study we are interested in using the powerful one-electron oxidant Ce^{IV} to generate a highly oxidized manganese-oxo species through the chemical activation of a bound water molecule. We also report on the catalytic oxidation of alkenes through the oxygen atom transfer reaction, where the oxygen atom stems from a substrate water molecule.

The syntheses of the ligand (abbreviated as tBuLH; see Supporting Information, Scheme S1) and the corresponding manganese complexes were realized following reported procedures. The crystal structure of the [tBuLMn^{III}OH]ClO$_4$ was described in a recent paper.[8] We have successfully isolated crystals of 2[tBuLMnCl]MnCl$_4$ of sufficient quality to perform X-ray analysis. A view of the monocationic unit is shown in Figure 1. The pentadentate ligand, bearing four nitrogen atoms and one oxygen atom, is distributed at the apex and the four positions in an equatorial plane, describing a distorted square planar geometry around the manganese(III) ion, leaving the sixth position of the coordination sphere for the chloride ligand. The metal–ligand bond distances are reminiscent of those of a typical Mn^{III} (see Table S1). The typical Jahn–Teller distortion for the Mn^{III} ion is situated on the axis containing the two pyridines.

Cyclic voltammograms of both manganese complexes reveal the presence of two oxidation processes (see Figure S1). The Mn$^{IV/III}$ couple for both complexes was found to be reversible in nature in an acetonitrile/water mixture (Figure 2a).[10] A second irreversible oxidation process was also observed for both derivatives at around 1.8 V vs. SCE (see Figure S1). Interestingly, the addition of water leads to an increase of the anodic current together with a shift of the anodic wave to

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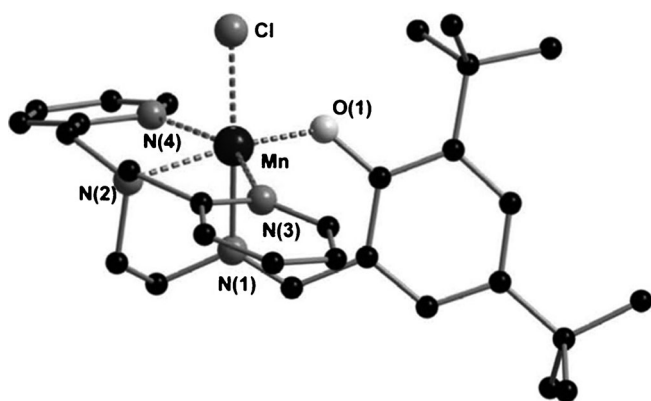Supporting Information for this article is available on the WWW under http://dx.doi.org/10.1002/cssc.201200440.

Figure 1. Crystal structure of [*t*BuLMnCl]⁺. Hydrogen atoms and solvent molecules were omitted for clarity. Selected metric distances (Å): Mn–N(1) 1.9854(17), Mn–N(2) 2.1193(18), Mn–N(3) 2.2731(18), Mn–N(4) 2.2676(18), Mn–O(1) 1.8455(14), Mn–Cl 2.291(4).

lower potential. These features are reminiscent of the formation of a reactive species. All attempts to further characterize the doubly oxidized species were unsuccessful.

The chemical oxidation of the [*t*BuLMn^{III}OH]⁺ complex with cerium(IV) ammonium nitrate (CAN) was realized at −20 °C in a mixture of acetonitrile and water. Figure 2 B shows the evolution of the electronic absorption spectrum upon addition of up to 5 equiv of CAN. The spectral features are identical to the [*t*BuLMn^{IV}OH]$^{2+}$ species generated by the one-electron electrolysis of the [*t*BuLMn^{III}OH]⁺ complex (Figure 2C).[10] Electron paramagnetic resonance (EPR) measurements of the resulting solution also confirmed the formation of a high-spin Mn^{IV} species.[11] The mass spectrum of the chemically generated Mn^{IV} species also corroborated the chemical formulation of the deprotonated form of the [*t*BuLMn^{IV}OH]$^{2+}$ species in solution (see Figure S5 B).

We performed DFT calculations to gain insights into the electronic properties of the [*t*BuLMn^{III}OH]⁺ complex and the one-electron oxidized species. Methyl groups were added instead of the bulky *tert*-butyl groups to alleviate calculation time. In the first place we analyzed the effect of a second-sphere water molecule on hydrogen-bonding interactions with the axial hydroxy group on the Mn^{III} ion. The geometry of [LMn^{III}OH]⁺ and [LMn^{III}OH,H$_2$O]⁺ in their high spin $S=2$ ground state was fully optimized and the main calculated metric data fitted with experimental observations. The influence of the second-sphere water molecules was evidenced by a slight elongation of the Mn–OH bond in the hydrated system, from 1.81 to 1.84 Å, and a small increase of the electronic density of the hydroxylic oxygen (−0.63 to −0.66) in the presence of H$_2$O. The map of the spin density of [*t*BuLMn^{III}OH]⁺ is characteristic of a high-spin Mn^{III} ($S=2$) (see Supporting Information). In a second step, DFT calculations were performed on the singly oxidized form. No trend to deprotonation was observed during the geometry optimization. The locus of the first oxidation was located at the metal center and led to a high-spin ($S=3/2$) Mn^{IV} complex, as evidenced by the spin density map. This is pertained by the EPR data for the one-electron oxidized species. Our theoretical findings for the
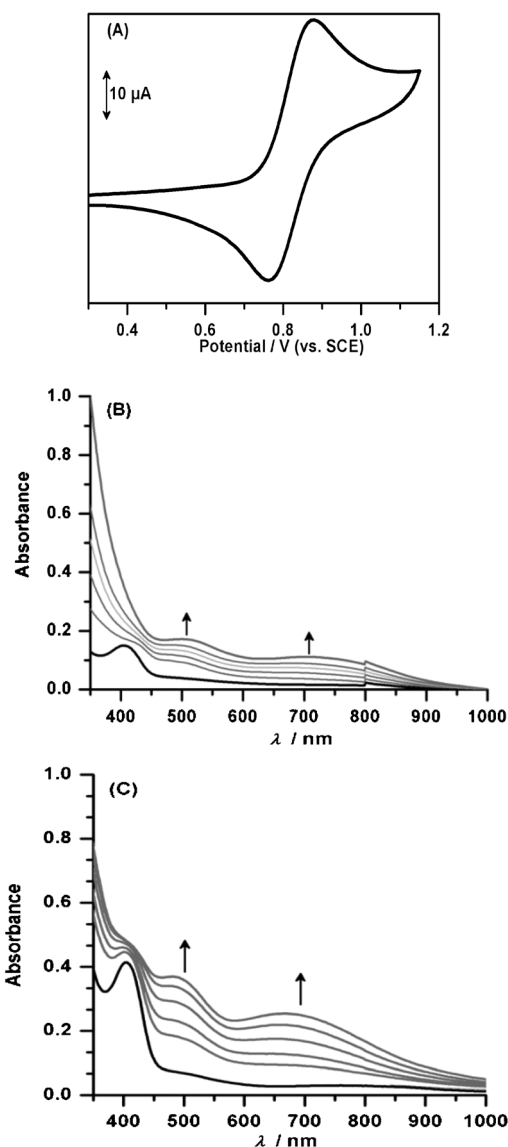

Figure 2. (A) Cyclic voltammetry of (1 mм) solution in acetonitrile (0.1 м NBu$_4$PF$_6$), $V=100$ mV s⁻¹, $T=20$ °C, on a glassy carbon electrode. (B) UV/Vis absorption spectra recorded in the course of the reaction of [*t*BuLMn^{III}OH]⁺ and [Ce(IV)(NO$_3$)$_6$](NH$_4$)$_2$ (5 equiv) in CH$_3$CN/H$_2$O (9.5:0.5) at −20 °C. (C) The inset shows UV/Vis absorption spectra recorded in the course of the electrochemical oxidation of [*t*BuLMn^{III}OH]⁺.

[LMn^{IV}-OH]$^{2+}$ species are in good agreement with collected experimental data.

Several substrates, including alkenes, alcohols, and thiols were subjected to oxidation in the presence of [*t*BuLMn^{III}OH]⁺ a 1:1 mixture of water and acetonitrile (Table 1) together with CAN.

For each substrate, control experiments using CAN and the MnBr$_2$/CAN combination (see Table S4) were performed. We have also chemically generated the Mn^{IV} species quantitatively and adding different alkenes did not lead to any chemical transformation. From these studies, we clearly established that the [*t*BuLMn^{IV}OH]$^{2+}$ species is not active towards the oxygen atom transfer reaction, leading us to propose that a second oxidation is necessary to yield the reactive species. Preliminary

Table 1. Selected [*t*BuLMn^{III}OH]$^{+}$-catalyzed oxidation of various substrates.

Entry	Substrate	Product[a]	Yield [%]	TON
1	cyclooctene	9-oxabicyclo[6.1.0]nonane	56	15
2	cyclooctene	9-oxabicyclo[6.1.0]nonane	56[b]	137
3	cyclooctene	9-oxabicyclo[6.1.0]nonane	56 (48)[c]	15
4	styrene	2-phenyloxirane	0	0
5	α-pinene	α-pinene epoxide	4	1
6	1-octene	octane-1,2-diol	10	3
7	benzyl alcohol	benzaldehyde	76[b] (85)[d]	n.d.
8	thioanisole	(methylsulfinyl)benzene	68 (87)[d]	n.d.
9	but-3-enoic acid	2-(oxiran-2-yl)acetic acid	0	0

[a] Conditions: substrate 0.4 mmol/1 mL acetonitrile; catalyst 0.004 equiv, CAN (0.25 equiv in 1 mL H$_2$O, RT, 0.5 h). [b] Conditions: substrate 0.4 mmol/1 mL acetonitrile; CAN (2 equiv in 1 mL H$_2$O, RT, 24 h). [c] Isolated yield, 1.5 h. [d] Catalyst-free reaction. n.d.: not determined.

DFT calculations were undertaken to gain insight into the electronic description of the doubly oxidized species. In this case, deprotonation of the axial hydroxyl group is more likely and our results point to the formation of a metalloradical species (see Supporting Information). We investigated the catalytic performance of [*t*BuLMn^{III}OH]$^{+}$ by using conditions similar to those used by Nam et al. previously (catalyst: 0.004 equiv; CAN 0.25 equiv). Interestingly, the catalytic run with cyclooctene showed after 0.5 h at room temperature the presence of the corresponding epoxide in 56% GC yield as the sole product (Table 1, entry 1). However, when the reaction was left for a longer time, the yield decreased (50% after 1 h and 30% after 2 h), probably due to the ring opening of the epoxide in the presence of excess water and a Lewis acid. Upon increasing the amount of oxidant up to 2 equiv, the analytical yield remained stable, but the TON increased by an order of magnitude, as the oxidant was not the limiting reagent anymore (entry 2). Unfortunately, using these conditions, the selectivity of the reaction decreased and the amount of by-products increased correlatively. Interestingly, increasing the catalytic charge did not appear beneficial. Indeed, when using 8 times more catalyst (0.02 equiv) the amount of epoxide remained in the 40% range, while the amount of byproducts increased drastically. Notably, when [*t*BuLMn^{III}Cl]$^{+}$ was used a milder epoxidation proceeded and the epoxide was detected in 46% yield after 1 h and 56% (48% isolated yield) after 1.5 h (see Table S4). We also noted that the ability of the [*t*BuLMn^{III}Cl]$^{+}$ complex for the catalytic oxidation is similar to that of the [*t*BuLMn^{III}OH]$^{+}$ complex. Such a chemical reactivity can be explained by the rapid exchange of the axial chloro ligand with a hydroxo group. This is supported by both the electrochemical behavior and the mass spectrum of the [*t*BuLMn^{III}Cl]$^{+}$ complex in the presence of water (see Figures S1 B, S2).

Remarkably, when ^{18}O-labeled water (H$_2$^{18}O) was used in combination with acetonitrile as solvent the only product of the reaction was the isotopically labeled cyclooctene epoxide (see Figures S9–S10), bringing conclusive evidence that the oxygen atom originates from a water molecule being activated through a two-electron, two-proton process. More challenging substrates were also tested. Unfortunately, the electron-defi-

cient alkenes investigated appeared unreactive in our conditions (Table 1, entries 4, 5, and 9). In contrast, 1-octene appeared rather reactive. Indeed, when using 0.004 equiv of catalyst and 0.25 equiv of CAN, 1-octene was efficiently epoxidized and converted into the corresponding diol in situ upon ring-opening with water. The CAN-catalyzed nucleophilic attack of water on the epoxide was further demonstrated as stirring 1-octene with CAN (0.25 equiv) at RT in a 1:1 water/acetonitrile mixture afforded the corresponding diol in 61% isolated yield. In addition, a control reaction using H$_2$^{18}O afforded the bis ^{18}O-labeled compound as the only diol, again pertaining the fact that the inserted oxygen atoms come from water molecules activated in the coordination sphere of the manganese ion.

Other substrates, including benzyl alcohol and thioanisole, were also tested. In these cases, control reactions revealed that benzyl alcohol was equally oxidized to the corresponding aldehyde, regardless of whether the catalyst was present or not. Indeed, after 24 h at room temperature, benzaldehyde was present in 85% GC yield in the absence of catalyst and 76% GC yield in the presence of catalyst (Table 1, entry 7). A similar observation was made upon catalytic oxidation of thioanisole in the presence of 0.004 equiv of catalyst: the sulfoxide was evidenced in 68% GC yield, and 91% GC yield if 0.002 equiv of epoxide was used. In the absence of catalyst, the expected sulfoxide was isolated in 87% yield, definitely proving that the catalyst-free CAN-mediated oxidation proceeds efficiently.

We have described herein the chemical activation of a mononuclear manganese(III)-hydroxido complex with Ce^{IV} as oxidant. The resulting highly oxidized manganese species is capable to perform the oxygen atom transfer reaction to electron-rich alkenes. Experiments with isotopically labeled water clearly support that the oxygen atom originates from the water molecule. These results stand as a proof-of-concept for the use of water as oxygen source to perform the oxidation of organic substrates. Work on fine-tuning the electrochemical properties of manganese mononuclear complexes for the photochemical activation of a bound water molecule with the defining aim to exclude chemical oxidants is in progress.

Experimental Section

CAN-mediated oxidation: In a 10 mL round-bottom flask, 0.001 g (0.0016 mmol) of catalyst, 0.4 mmol of substrate (alkene alcohol or thiol), and 1 mL of acetonitrile were introduced. An aqueous solution of CAN [0.055 g (0.1 mmol) in 1 mL] was added dropwise and the reaction was allowed to stir for the appropriate amount of

time. Aliquots were taken on regular basis. For each sample, the reaction mixture was extracted with dichloromethane, dried over Na_2SO_4, and concentrated and purified by short-column chromatography packed with celite in order to remove the metallic salts. The non-polar fraction, eluted with a 1:1 mixture of Et_2O/cyclohexane, was directly analyzed by GC. The yield was calculated by GC analyses using diphenyl ether as internal standard. The filtrate was diluted in Et_2O and directly injected on the GC column (Zebron phase 2B1 from Phenomenex; $L = 30$ m, internal diameter 0.32 mm, di $= 0.25$ μm).

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