CLUSTER ISSUE

Too Many Cooks Spoil the Broth – Variable Potencies of Oxidizing Mn Complexes of a Hexadentate Carboxylato Ligand

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Given the hexadenticity of the monoanionic ligand in the procatalyst [Mn(tpena)(H$_2$O)](ClO$_4$) {tpena$^-$ = N,N,N'-tris(2-pyridylmethyl)ethylenediamine-N'-acetate}, it is perhaps surprising that this complex can catalyze the epoxidation of alkenes. When peracetic acid is used as terminal oxidant, the selectivity and rates of reactions are comparable with those reported for the manganese complexes of the commonly employed neutral tetradentate N4 ligands under analogous conditions. Cyclooctene conversion rates are similar when *tert*-butyl hydroperoxide (TBHP) is used; however, the selectivity is greatly diminished. In the absence of organic substrates, [Mn^{II}(tpena)]$^+$ catalyzes water oxidation by TBHP (initial rate ca. 23 mmol/h when [Mn] = 0.1 mM, at room temp.). To ex-plain the variations in the selectivity of catalytic epoxidations and the observation of competing water oxidation, we propose that several metal-based oxidants (the "cooks") can be generated from [Mn^{II}(tpena)]$^+$. These embody different potencies. The most powerful, and hence least selective, is proposed to be the isobaric isomer of [Mn$^{IV}_2$(O)$_2$(tpena)$_2$]$^{2+}$, namely an oxylic radical complex, [(tpena)Mn^{III}(μ_2-O)-Mn^{IV}(O$^{\cdot}$)(tpena)]$^{2+}$. The formation of this species depends on the catalyst concentration, and it is favoured when TBHP is used as the terminal oxidant. The generation of the less potent [Mn^{IV}(O)(tpena)]$^+$, which we propose as the direct oxidant in epoxidation reactions, is favoured in non-aqueous solutions when peracetic acid is used as the terminal oxidant.
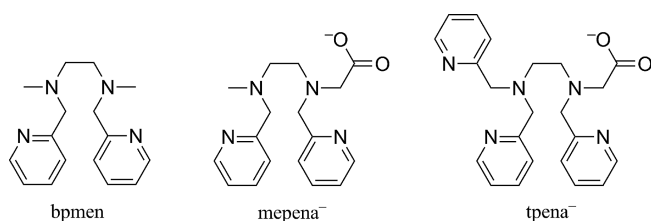
Introduction

One or more carboxylate donors (Glu, Asp) are a ubiquitous presence in the first coordination spheres of most non-heme metalloenzymes capable of the O$_2$ activation needed in biological catalytic oxidations.[1] This is also the case for the manganese-containing enzymes superoxide dismutase,[2] oxalate decarboxylase[3] and the oxygen evolving centre[4] where O$_2$ evolution occurs. It seems therefore obvious to explore the use of supporting ligands that furnish monodentate carboxylato donors in the context of discovering efficient catalysts for biomimetic catalytic oxidation reactions. Anionic weak-field carboxylato ligands are expected to be suitable for accessing high-valent metal states, and active roles involving non-coordinated carbonyl O atoms

can be envisaged in the usually requisite accompanying proton transfers. Coordination flexibility for carboxylato ligands in terms of monodentate, bidentate, μ_2-η^1-, μ_2-η^2-, μ_3-$\eta^1\eta^2$-, μ_4-$\eta^2\eta^2$-bridging coordination modes is well known, and "carboxylate shifts" between some of these extremes are assumed to be important for the mechanisms of metalloenzymes. Finally, transient percarboxylato functions generated by insertion of an O$_2$-derived oxygen atom into M–Asp/Glu bonds are worth appraising as metal-based oxidants for potential in vivo reactions. Speculations concerning these species can be extended to the possibility that parallel mechanisms are at play when peracetic acid is employed as the terminal oxidant. Although it is not explicit in much of the literature, the reason for the extensive use of this oxidant in catalytic oxidations is likely to stem from observations of comparatively better selectivity. It is plausible, but perhaps unconsidered, that improved selectivity over, for example, reactions using H$_2$O$_2$, might be due to an active role of acetic acid. Could it be that in Nature these groups can generate an "internal peracetic acid" concomitant with the activation or, conversely, with release of O$_2$?

Perhaps surprisingly, and arguably because of synthetic bottlenecks, the manganese complexes of chelating ligands

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furnishing monodentate carboxylato ligands have not been as extensively examined as systems based on neutral aminopyridyl chelating ligands.[5] Manganese complexes of neutral N4 tetradentate ligands are effective as catalysts in homogeneous epoxidation.[6] The complexes of *N*,*N*′-bis(2-pyridylmethyl)ethylenediamine (bpmen)[7] (Scheme 1) are representative. In recent years, we have modified the ethylenediamine scaffold of bpmen by the inclusion of carboxylate groups in efforts towards the discovery of improved catalysts. We discovered that the manganese complex of the pentadentate ligand *N*-methyl-*N*,*N*′-bis(2-pyridylmethyl)-ethylenediamine-*N*′-acetate (mepena⁻) and an analogue containing a benzyl group in the place of the methyl group are sufficiently powerful to catalyze the oxidation of water using *tert*-butyl hydroperoxide (TBHP) as the terminal oxidant.[8] A 2-methylpyridyl arm in place of the methyl group gives the hexadentate ligand *N*,*N*,*N*′-tris(2-pyridylmethyl)-ethylenediamine-*N*′-acetate (tpena⁻, Scheme 1). Using the iron complex of tpena⁻, we have achieved rapid and selective catalysis of sulfoxidation by iodosylbenzene reactions.[9] Since "coordinative unsaturation" is commonly perceived as desirable for the construction of catalysts, this latter reaction might seem surprising given the potential hexadenticity of tpena⁻. More commonly, procatalysts are based on chelating ligands with lower donor numbers (mostly four N donors). Important roles as auxiliary ligands by solvents are often ignored, and an increasing reliance on ESI mass spectrometry for the identification of solution-based species may have reinforced a misconception that solvent adducts, which usually do not survive ionization, are irrelevant. Further seven-coordination, especially for d⁵ Fe^III and Mn^II and N/O donor sets, is reasonable.[10]

zation of a colourless air-stable manganese(II) complex, [Mn(tpena)(H₂O)]ClO₄ ([**1**]ClO₄). The ESI mass spectrum of this material shows that the [Mn^II(tpena)]⁺ ion at *m/z* 445.13 is dominant in an otherwise clean spectrum. There are no traces of ions with a higher metal oxidation state. The structure of the intercationic hydrogen-bonded pairs in [**1**]ClO₄·4.5H₂O, determined by single-crystal X-ray analysis, is shown in Figure 1. Selected parameters are listed in Table 1. The manganese(II) atom is seven-coordinate, similar to the manganese(II) ions in complexes of pentadentate mepena⁻,[10c] and hexadentate edta[11] and tpen.[10d] Seven-coordination is known to stabilize the +2 oxidation state of the manganese centre,[10e] and this structure will presumably prevent spontaneous oxidation of **1** in both solid and solution states. [**1**]ClO₄·4.5H₂O crystallizes in the Sohncke space group[12] *P*2₁, and the same enantiomeric form in each monomer implies that it undergoes spontaneous resolution.[13] The crystallization of [**1**]ClO₄·4.5H₂O therefore constitutes a rare example where a seven-coordinate complex is isolated as a pure enantiomer.[14] The two molecules
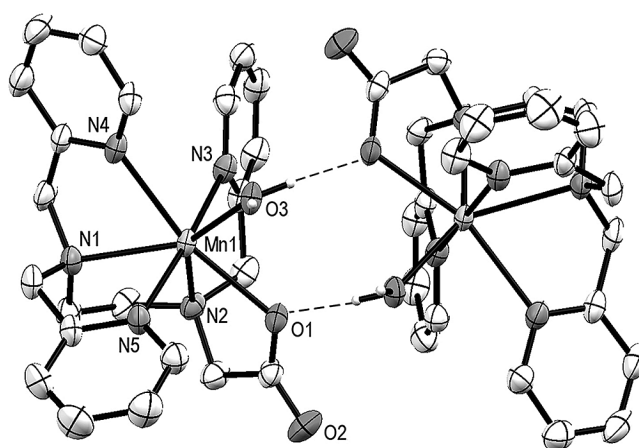

Figure 1. The H-bonded [Mn(tpena)(H₂O)]⁺ (**1**) cations in the asymmetric unit of [**1**]ClO₄·4.5H₂O. All H atoms, except those at the aqua ligand are omitted for clarity. Hydrogen bonds are indicated by dashed lines. Displacement ellipsoids are drawn at the 50% probability level.

Scheme 1. N4, N4O and N5O ligands based on an ethylenediamine backbone.

The use of chelating ligands with relatively high donor numbers like the N4O and N5O ligands mepena⁻ and tpena⁻, will limit the number of solution-state solvent-derived species, potentially simplifying metal catalyst speciation in reaction mixtures. Our studies show that this is not counter-beneficiary, since the catalysis of oxidation reactions is not blocked. Furthermore the less complicated solution-state metal-ion speciation has allowed for consideration of the reaction mechanism.

Results and Discussion

The reaction of manganese(II) perchlorate with *N*,*N*,*N*′-tris(2-pyridylmethyl)ethylenediamine-*N*′-acetic acid (tpenaH) in a water/methanol mixture results in crystalli-

Table 1. Average selected distances (Å) and bond angles (°) for [**1**]ClO₄·4.5H₂O.

Mn1–O1	2.2903(19)	Mn1–N3	2.299(2)
Mn1–O3	2.1784(19)	Mn1–N4	2.394(2)
Mn1–N1	2.394(2)	Mn1–N5	2.272(3)
Mn1–N2	2.399(2)	Mn1–Mn2	5.482(2)
O1–Mn1–N3	98.54(8)	N1–Mn1–N2	73.78(9)
O1–Mn1–N1	129.21(8)	N3–Mn1–N1	101.69(9)
O1–Mn1–N4	160.39(8)	N3–Mn1–N2	72.86(9)
O1–Mn1–N2	68.61(8)	N3–Mn1–N4	83.16 (9)
O3–Mn1–N5	93.97(8)	N4–Mn1–N2	129.77(9)
O3–Mn1–O1	78.85(7)	N5–Mn1–O1	83.51(8)
O3–Mn1–N3	92.25(8)	N5–Mn1–N3	173.69(9)
O3–Mn1–N4	81.56(8)	N5–Mn1–N1	72.63(9)
O3–Mn1–N1	145.09(8)	N5–Mn1–N4	96.93(9)
O3–Mn1–N2	141.14(8)	N5–Mn1–N2	102.60(9)
N1–Mn1–N4	68.76(8)		

in the asymmetric unit have indistinguishable conformations[15] and are associated by O–H···O interactions involving the aqua ligands and the coordinated oxygen atoms of the carboxylate groups with O···O distances of 2.646(3) and 2.660(3) Å. These interactions give rise to a six-membered ring including the two manganese atoms and containing two H-bonds, with a chiral twisted-boat conformation. The structure comprises stacks of cations parallel to the *a*- and *b*-axes respectively, separated by ClO_4^- anions and H_2O molecules (Figure S1).

Complex **1** catalyzes the epoxidation of alkenes by peracetic acid (PAA). Conversion and selectivities are listed in Table 2. No diol byproducts are detected. Catalytic activity drops with decreasing catalyst loadings, and at 0.15% the conversion and yield can be attributed to the background reaction. Since bpmen (Scheme 1) possesses the same ethylenediamine backbone, for comparison, catalysis experiments were repeated under the same conditions with the procatalyst $[Mn_2(bpmen)_2(\mu_2\text{-}CH_3CO_2)_2](ClO_4)_2$ ([**2**]2ClO$_4$) as an N4 representative. The conversions for catalytic oxidation of cyclooctene using PAA as terminal oxidant are not strikingly different for the two systems, except that the selectivity in the reactions catalyzed by **1** is significantly higher under more dilute conditions (i.e. the concentration of all of the catalyst, oxidant and substrate are decreased, but they remain in the same proportion). Conversion rates for the catalytic oxidation of cyclooctene using *tert*-butyl hydroperoxide (TBHP) as the terminal oxidant were similar; however, a significant loss of selectivity was observed, and several unidentified products appear on the GC chromatogram (Figure S2). Differences, over acceptable experimental loss, between alkene conversion and epoxide yield can be translated into a measure of selectivity; the smaller the difference, the greater the selectivity. The Mn complex of the bpmen analogue N,N'-dimethyl-N,N'-bis(2-pyridylmethyl)-(1R,2R)-(+)-cyclohexane-1,2-diamine has been reported to give better results for epoxidation reactions in terms of catalyst loadings (down to 0.1%), conversion and selectivity compared to those we see with both **1** and **2**.[7] One could speculate that the non-sterically restricted ethylenediamine backbones of **1** and **2** compared with the rigidifying cyclohexane backbone make the systems floppier and that this may be one reason for their slightly lower efficiencies.

We can exclude oxidative breakdown of tpena$^-$ with formation of catalytically competent Mn–picolinate complexes[16] during the reactions with both peracetic acid and TBHP on the basis of the facts that the reactions start without any lag time and the post-catalysis ESI mass spectra of reaction mixtures still show $[Mn^{II}(tpena)]^+$ at *m/z* 445.13 as a dominant ion. No ions attributable to oxidative decomposition of the ligand can be discerned. More specifically, no peaks are found in common with the ESI mass spectrum of a mixture of manganese perchlorate and picolinic acid where Mn–picolinato complexes, for example $[Mn^{II}(pic)_2 + H]^+$ at *m/z* 299.99, and other derivatives are detected (Figure S3).

ESI mass spectra of mixtures of **1** and 100 equiv. of TBHP or peracetic acid recorded within 3 min of mixing are shown in Figure 2. A minor ion assignable to $[Mn^{IV}O(tpena)]^+$ at *m/z* 461.1246 can be observed in both spectra; however, the proportion of this ion compared to that of $[Mn^{II}(tpena)]^+$ at *m/z* 445.1303 is much lower in the spectrum of the solutions containing peracetic acid. $[Mn^{II}(tpena)]^+$ is the base peak in this latter spectrum, and a minor peak corresponding to $[Mn^{II}(tpena)(HOAc)]^+$ is observed at *m/z* 505.1511. By contrast, the $[Mn^{II}(tpena)]^+$ ion is far less intense in the spectrum obtained with TBHP, where the base peak corresponds to $[Mn^{III}(OH)(tpena)]^+$ at *m/z* 462.1322. The second highest peak corresponds to $[(tpena)Mn^{III}(O)_2Mn^{IV}(tpena)]^+$ at *m/z* 922.2508. An expansion of the region *m/z* 460–462 shows that the peak for a doubly charged ion overlaps that for the singly charged $[Mn^{IV}O(tpena)]^+$ (*m/z* 461.1246, Figure S4). This is assigned to the dimeric species $[(tpena)Mn^{IV}(O)_2Mn^{IV}(tpena)]^{2+}$. A favourable reduction of $[(tpena)Mn^{IV}(O)_2Mn^{IV}(tpena)]^{2+}$ during ionization is a reasonable path for the formation of $[(tpena)Mn^{III}(O)_2Mn^{IV}(tpena)]^+$ {the opposite reaction, oxidation of $[(tpena)Mn^{III}(O)_2Mn^{IV}(tpena)]^+$, is not expected under MS conditions}. No trace of any oxo-bridged dinuclear manganese species is observed in the spectra with PAA.

Bubbles can occasionally be seen in mixtures of **1** and peracetic acid or TBHP in the presence of water. This suggests that water oxidation might be a competing reaction. For this reason, **1** was tested as a water-oxidation catalyst. This was carried out in the absence of organic substrates

Table 2. Conversion and selectivity in the catalytic oxidation of alkenes. The catalyst loading was 1.5 mol-% with respect to substrate in all reactions.

Substrate	Procatalyst	[Mn] (mM)[a]	Substrate concentration (mM)	PAA concentration (mM)	Conversion (%)	Selectivity (%)	Byproducts
Cyclooctene	[**1**]ClO$_4$	3	200	280	96	75	not detected
Cyclooctene	[**2**]2ClO$_4$	3	200	280	100	96	not detected
Cyclooctene	[**1**]ClO$_4$	0.3	20	28	98	92	not detected
Cyclooctene	[**2**]2ClO$_4$	0.3	20	28	89	84	not detected
Decene	[**1**]ClO$_4$	3	200	280	84	80	not detected
Decene	[**2**]2ClO$_4$	3	200	280	84	83	not detected
cis-Stilbene	[**1**]ClO$_4$	3	200	280	30	80	*trans*-epoxide
cis-Stilbene	[**2**]2ClO$_4$	3	200	280	31	86	*trans*-epoxide

[a] In terms of [Mn] concentration. Dry acetonitrile, 0 °C (cyclooctene) and room temp. (decene and stilbene); reaction quenched after one (cyclooctene and decene) and three (stilbene) hours with aluminium oxide.
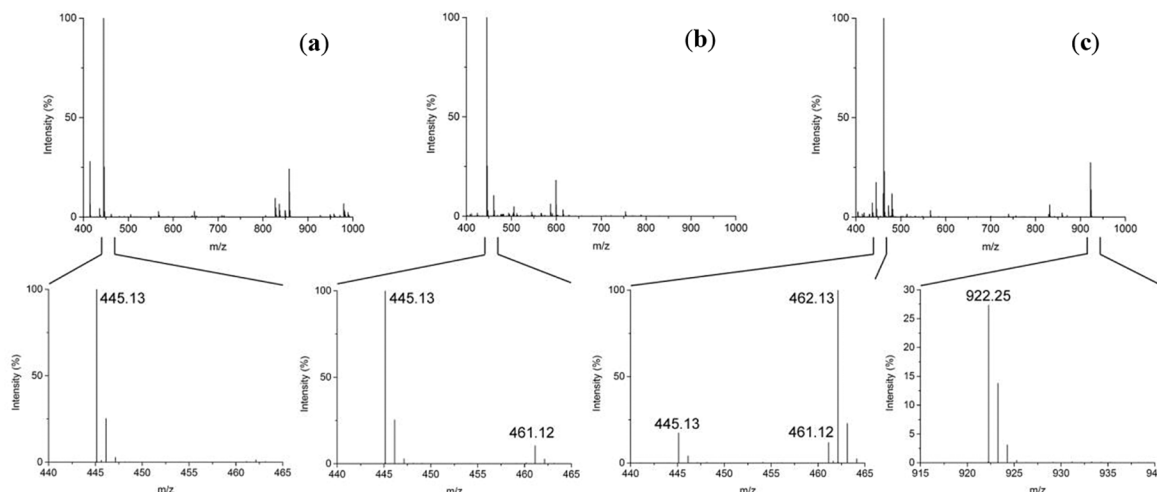
Figure 2. (a) The ESI mass spectra of [**1**]ClO$_4$. (b) After addition of 100 equiv. of peracetic acid. (c) After addition of 100 equiv. of TBHP. Assignments: m/z 445.1303 [Mn^{II}(tpena)]$^+$; m/z 505.1511 [Mn^{II}(tpena)(HOAc)]$^+$; m/z 461.1246 [Mn^{IV}O(tpena)]$^+$ and [(tpena)Mn^{IV}-(O)$_2$Mn^{IV}(tpena)]$^{2+}$, see text; m/z 462.1322 [Mn^{III}(OH)(tpena)]$^+$; m/z 922.2508 [(tpena)Mn^{IV}(O)$_2$Mn^{III}(tpena)]$^+$. Solvent: acetonitrile/water (9:1).

with TBHP as terminal oxidant under conditions similar to those implemented for the catalysis of water oxidation reactions using [Mn(mepena)]$^+$.[8] Figure 3 shows the amount of dioxygen evolved as a function of time in the absence of potential organic substrates, including solvent. For comparison, the same experiment was performed using [Mn$_2$(mepena)$_2$(H$_2$O)$_2$](ClO$_4$)$_2$ ([**3**]2ClO$_4$) and [Mn$_2$-(bpmen)$_2$(O)$_2$](ClO$_4$)$_3$ ([**4**]3ClO$_4$) as the procatalysts. It was interesting to observe that even the bpmen system catalyzes water oxidation; however, the complexes with the carboxylato N4O and N5O ligands, mepena$^-$ and tpena$^-$, show higher activity. As mentioned, we have previously reported **3** as a catalyst for this reaction, and this system shows the highest activity in the series reported here. A disproportionation of TBHP is not expected, and was eliminated, by ^{18}O-labelling experiments using **3**.[8] In these experiments, we also ascertained that one O atom from water and one from the TBHP ends in the product O$_2$. We have not performed these labelling experiments for reactions using **1** and **4**; however, it seems reasonable to assume that this would also be the case. The TONs (per [Mn]) measured after 70 min at room temp. are 3600, 7400 and 800, with initial rates of 2, 23 and 0.5 mmol/h, for **1**, **3** and **4** respectively.

On the basis of a catalyst concentration dependence in the rate of O$_2$ evolution, the detection of Mn^{II}, Mn^{III}OH, Mn^{IV}O and dinuclear Mn(O)$_2$Mn species, and DFT calculations, we have proposed a mechanism involving both mononuclear and dinuclear Mn species in the catalysis of water oxidation by **3**.[8a,10c] Crucially, we suggested that a dinuclear oxylic radical species [(mepena)Mn^{III}(μ$_2$-O)Mn^{IV}-(O·)(mepena)]$^{2+}$ was the oxidant capable of attacking water in the critical O–O bond formation step. Significantly also, the calculations inferred that the mononuclear Mn^{IV}O species were not capable of oxidizing water. Such a species may, however, be sufficiently potent to oxidize weaker C–H/C–C bonds and hence be capable of acting as a direct metal-
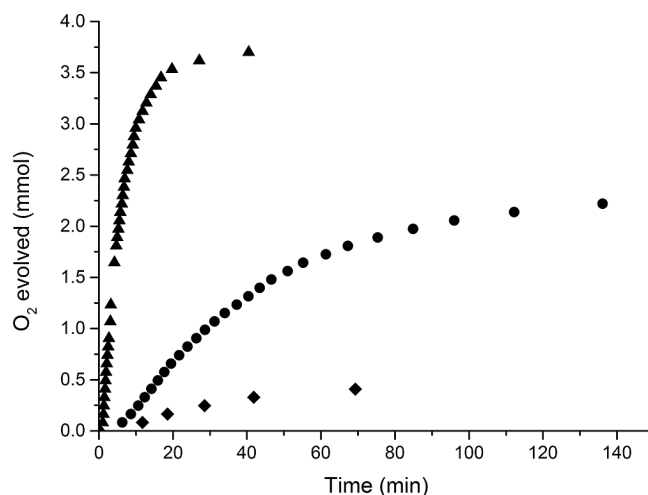

Figure 3. Amount of dioxygen evolved as function of time. [TBHP] = 2.56 M; [Mn] = 0.1 mM; (●) [Mn^{II}(tpena)(H$_2$O)]ClO$_4$, (**1**); (▲) [Mn$_2$(mepena)$_2$(H$_2$O)$_2$](ClO$_4$)$_2$ (**3**); (♦) [Mn$^{(III/IV)}_2$(bpmen)$_2$(O)$_2$]-(ClO$_4$)$_3$ (**4**). TON after 70 min: 3600 (●), 7400 (▲) and 800 (♦).

based oxidant in alkene epoxidation. The observation of ions assignable to [(tpena)Mn^{III}(O)$_2$Mn^{IV}(tpena)]$^+$ and [(tpena)Mn^{IV}(O)$_2$Mn^{IV}(tpena)]$^{2+}$ in ESI mass spectra suggest that, despite the potential hexadenticity of tpena$^-$, oxo-bridged dinuclear species are present in solutions. On the basis of our experience with both the N4O and N5O systems, these appear in somewhat lower abundances compared to the pentadentate mepena$^-$ system.[10c] A lower steady-state concentration of [(L)Mn^{IV}(O)$_2$Mn^{IV}(L)]$^{2+}$ would seem then to be the likely explanation for the lower TONs for water oxidation by TBHP for the N5O system relative to that of the N4O system. This situation is quite different for the neutral N4 system, where the dioxo-bridged ([(L)Mn^{III}(O)$_2$Mn^{IV}(L)]$^{3+}$) (**4**, L = bpmen) and homologues of its oxidized congener [(L)Mn^{IV}(O)$_2$Mn^{IV}-

(L)]$^{4+}$ can be isolated.[17] Isolation obviously suggests that the oxo-bridged Mn$_2$(III/IV) and Mn$_2$(IV/IV) dimers of bpmen are less reactive (in other words, as we shall see, less readily form oxylic radical complexes). In the presence of oxidants, the Mn^{II} complexes of bpmen cannot be detected, let alone isolated. This is, as mentioned, not the case for the N4O and N5O systems.

By taking into account the observations reported here and previous results, we have set up a general mechanism for competing alkene epoxidation and water oxidation in Scheme 2. Mononuclear and oxo-bridged dinuclear species can be generated in solution with the ligands in Scheme 1. The concentrations of the various species will depend on the concentration of water, the presence of organic substrate and/or solvents, the nature of the terminal oxidant and the number and type of donor atoms in the spectator ligands bound to manganese. A reasonable assumption might be that any (hydr)oxo species with oxidation state of +3 or higher is potentially oxidizing, and Mn^{II}–oxidant adducts should not be excluded as potential direct oxidants. Direct oxidizing species for the alkenes could be both the mononuclear manganese(IV)oxo species [Mn^{IV}O(L)]$^{n+}$ (step *iii*) and the dinuclear [(L)Mn^{III}(μ$_2$-O)Mn^{IV}(O˙)(L)]$^{n+}$ (step *vii*). Complex [Mn^{IV}O(L)]$^{n+}$ is generated by heterolytic O–O cleavage in [Mn^{II}(H)OOR(L)]$^{n+}$ (steps *i* and *ii*); however, in the presence of excess acetic acid, as is the case for the reactions in which peracetic acid is terminal oxidant, step *i* shows greater reversibility than is possible for step *ii*. Thus,

steady-state concentrations of [Mn^{IV}O(L)]$^{n+}$ are lower in the peracetic acid reactions. Consequently, its condensation with Mn^{II} and Mn^{IV} species (steps *v* and *vi*) will be far less favoured compared to mixtures with TBHP and no acetic acid. Conversely, the steady-state concentration of [Mn^{IV}O(L)]$^{n+}$ will be significantly higher in the reactions using TBHP as terminal oxidant, thereby favouring formation of [(L)Mn^{III}(μ$_2$-O)Mn^{III}(L)]$^{2n+}$ or [(L)Mn^{IV}(μ$_2$-O)$_2$Mn^{IV}(L)]$^{(2n+1)+}$ ↔ [(L)Mn^{III}(μ$_2$-O)Mn^{IV}(O˙)(L)]$^{(2n+1)+}$ by its reaction with [Mn^{II}(L)]$^{n+}$ or another molecule of [Mn^{IV}O(L)]$^{n+}$, respectively. In the case of tpena$^-$ as the supporting ligand, the Mn^{II}–oxidant adduct complexes, [Mn^{II}(H)OOR(L)]$^{n+}$, R = –CMe$_3$, –C(O)CH$_3$, are presumably seven-coordinate, similar to the parent procatalyst **1**. Decoordination of pyridine donors is likely in the structures of the higher-valent d^4 and d^3, Mn^{III} and Mn^{IV} centres. This is entirely feasible, and several complexes in which the pyridyl arm of multidentate aminopyridine ligands are decoordinated have been crystallographically characterized, including some with tpena$^-$.[9,18] The presence of nucleophilic dangling pyridine groups should in fact assist the isomerization (step *viii*) towards the reactive oxylic radical form, furnishing a rationale for why water oxidation is favoured for the N4O and N5O ligands.

Scheme 2 is entirely consistent with the facts that: (1) Epoxidation reactions using peracetic acid as terminal oxidant show the highest selectivity for all ligand systems we have tested; (2) while conversions are similar, the reactions
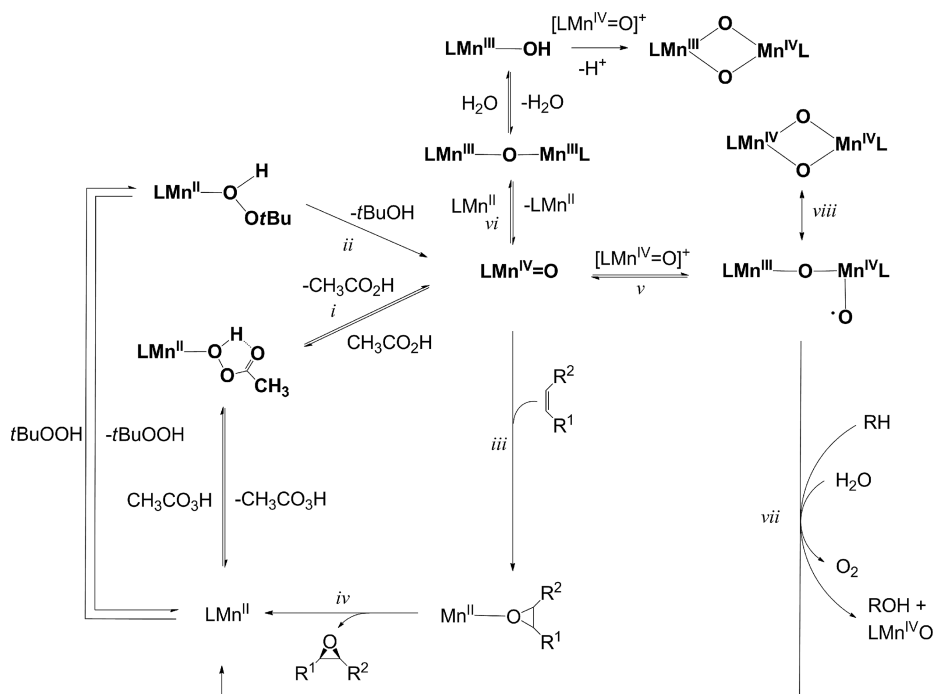
Scheme 2. Competing mechanisms for catalytic epoxidation of alkenes and oxidation of water by peracetic acid or TBHP as the terminal oxidant showing possible Mn-based oxidants (in bold). L = tpena$^-$, mepena$^-$, bpmen or other similar ligand. Complex charges are not drawn, since these will be dependent on the ligand, but they are related as indicated in the text. The species with bold lettering are potential oxidants. A reaction arrow is not drawn between the Mn^{II}–peroxyacid or Mn^{II}–alkylperoxide complexes and the Mn^{II}–epoxide, so that the scheme is not overcrowded. RH and ROH are general representations for an organic substrate and its oxidized product(s). The latter does not need to be an alcohol (e.g. ketones, C–C cleavage products, etc. can be produced).

using TBHP as terminal oxidant are less selective; (3) decreasing the concentration of all species (catalyst and substrates) improves selectivity in epoxidation (although rates are expected to decrease to the point where the uncatalyzed reaction dominates); (4) incorporation of a monodentate carboxylate donor into the ligand does not appear to alter efficiencies in any obvious way; (5) if it is not removed completely from reaction mixtures, water oxidation can be a competing reaction; this, however, may be compensated for by the judicial consideration of the equilibria in Scheme 2.

Conclusions

A common assumption in catalyst design is that "vacant sites" must be available for the coordination of substrates. In this work, we have shown that even a potentially hexadentate ligand does not quench catalysis of alkene epoxidation or water oxidation by its Mn complexes. Another hypothesis that we wanted to test was whether the presence of a monodentate carboxylato arm might play the role of an "internal peracetic acid" by allowing insertion of an O atom of an oxidant-derived O atom between itself and the manganese atom. We have found no evidence that this is the case and can thus not infer any special role, over that of spectator, for a carboxylate donor. We propose, however, that under certain conditions the carboxylate-containing N4O and N5O ligands favour formation of reactive dimanganese oxylic radical species that are too oxidizing to achieve a good selectivity towards the desired product in alkene epoxidations. They can even oxidize water. It is, however, possible to devise conditions for avoiding this competing reaction.

While the literature tends to focus on the choice of supporting ligands, and in limiting cases this will be important, we draw the conclusion that the choice of terminal oxidant, rate of addition, catalyst concentration and the presence or absence of water can be critical, but perhaps this has hitherto been less appreciated. The comparison of the results of catalysis experiments from different labs is always difficult, and this problem is only exacerbated if workers are not aware of potential pitfalls like competing water oxidation. These can be indicated by significant discrepancies in mass balance and conversions that appear high compared to product and by-product yields determined by traditional methods like GC. Dioxygen is usually not specifically monitored (and this is difficult), and these discrepancies appear often to be ignored. It is possible that Scheme 2 is relatively general and the position of the various equilibria will, however, depend on the choice of capping ligand. While under the right conditions the penta- and hexadentate N4O and N5O ligands can more easily promote oxo-bridge cleavage to form more selective oxidants $[Mn^{IV}O(L)]^+$, they can also generate the highly oxidizing dimanganese(III,IV) oxylic radical species. That low catalyst loadings down to 0.1 % or even less have been reported without loss of activity for the commonly used N4 catalysts is also consistent with our

scheme and the fact that the formation of stable dioxo bridged $Mn^{III/IV}$ species will be less favoured under these conditions.

Experimental Section

Elemental analysis was performed at the Chemistry Department at Copenhagen University. ATR-IR spectra were recorded as neat solids with a PerkinElmer Spectrum Two spectrometer. All spectra have been ATR- and baseline-corrected. UV/Vis spectra were recorded with an Agilent 8453 spectrophotometer using 1 cm quartz cuvettes. ESI mass spectra were recorded with a microspray LC-MS Bruker micrOTOF-Q II or for high resolution MS with a nanospray ThermoFisher Orbitrap XL mass spectrometer at a resolution greater than 10000. X-ray diffraction data were collected at 180(2) K with a Bruker–Nonius X8 APEX-II instrument (Mo-K_α radiation). Structure solution and refinement were carried out by using SHELXTL.[19]

N,N,N′-tris(2-pyridylmethyl)ethylenediamine-*N′*-acetic acid (tpenaH),[20] [Mn$_2$(bpmen)$_2$(CH$_3$CO$_2$)](ClO$_4$)$_2$ ([**2**]2ClO$_4$),[21] [Mn$_2$(mepena)$_2$(H$_2$O)$_2$](ClO$_4$)$_2$ ([**3**]2ClO$_4$)[10c] and [Mn$_2$(O)$_2$-(bpmen)$_2$](ClO$_4$)$_3$ ([**4**]3ClO$_4$)[17] were prepared according to previously reported procedures. Peracetic acid solution (39 % in acetic acid), *tert*-butyl hydroperoxide solution (5.5 M in decane) over molecular sieves 4 Å (catalysis experiments) and T-HYDRO solution (70 wt.-% in water for ESI-MS experiments) were purchased from Sigma–Aldrich and used without further purification. Acetonitrile was dried with activated 3 Å molecular sieves.

[Mn(tpena)(OH$_2$)]ClO$_4$·4.5H$_2$O ([1]ClO$_4$): Mn(ClO$_4$)$_2$·6H$_2$O (502 mg, 1.4 mmol) was added to tpenaH (543 mg, 1.3 mmol) in methanol (6 mL) and water (5 mL). Slow evaporation of the solvents afforded the product as a beige microcrystalline precipitate (98 mg, 12 %), which was characterized by elemental analysis, IR spectroscopy and ESI-MS. Overnight, a few colourless crystals of X-ray quality were deposited in the filtrate. ESI-MS (positive mode, CH$_3$OH): *m/z* (%) = 545.1(3) (100) [Mn(tpena)]HClO$_4^+$, 445.1 [Mn(tpena)]$^+$. IR (KBr): $\tilde{\nu}$ = 1605 (C=O, s), 1092 (ClO$_4^-$, bs) cm^{-1}. C$_{22}$H$_{32}$ClMnN$_5$O$_{10}$ ([Mn(tpena)(OH$_2$)]ClO$_4$·3H$_2$O) (616.91): calcd. C 42.83, H 5.23, N 11.35; found C 42.49, H 4.49, N 10.85.

CCDC-1050773 contains 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.

Epoxidation of Cyclooctene: The reactions were performed in dry acetonitrile in a total volume of 2.5 mL at 0 °C. Catalyst ([Mn] = 3 mM, 1.5 mol-%), substrate (200 mM) and oxidant (total concentration 280 mM) were added over 5 min with a syringe-pump. The reaction was quenched after one hour with aluminium oxide, and the products were analyzed by GC with biphenyl as internal standard. For the reactions run in diluted conditions, a similar mixture was prepared and diluted to a total volume of 25 mL.

Epoxidation of Decene: The reactions were performed in dry acetonitrile in a total volume of 2.5 mL at room temperature. Catalyst ([Mn] = 3 mM, 1.5 mol-%), substrate (200 mM) and oxidant (total concentration 280 mM) were added over 50 min with a syringe-pump. The reaction was quenched after one hour with aluminium oxide, and the products were analyzed by GC with biphenyl as internal standard.

Epoxidation of *cis*-Stilbene: The reactions were performed in dry acetonitrile in a total volume of 2.5 mL at room temperature. Cata-

lyst ([Mn] = 3 mM, 1.5 mol-%), substrate (200 mM) and oxidant (total concentration 280 mM) were added over 30 min with a syringe-pump. The reaction was quenched after three hours with aluminium oxide, and the products were analyzed by ^{1}H NMR spectroscopy with 1,2-dichlorobenzene as internal standard.

All the experiments were replicated at least three times and the values are within ±3%.

Measurement of Oxygen Evolution: An aqueous solution of the complex (1 mL, 0.5 mM in [Mn]) and acetonitrile (2 mL) was immersed in a water bath at 40 °C (controlled by using a Lauda ecoline RE104 thermostat). After 10 min, cold TBHP (6.4 M in water, 2 mL) was added. The test tube formed part of a closed system, and the gas evolved was led through a reflux condenser and collected in a low friction, air-tight glass syringe at room temperature. The amount of oxygen evolved was calculated by volume at ambient air pressure and temperature. All experiments were repeated at least twice.

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