Chapter 1

Redox state dependent ligand exchange in manganese based oxidation catalysis

Manganese based oxidation catalysis plays a central role both in nature, in the oxidation of water in photosystem II (PS II) and the control of reactive oxygen species, as well as in chemical processes, in the oxidation of organic substrates and bleaching applications. The focus of this chapter is to survey efforts made to explore and elucidate the redox dependent coordination chemistry of these manganese based systems in solution. The mechanisms by which their catalytic redox reactions proceed is discussed to draw correlations with the behaviour and activity of complexes developed and used as model compounds for the active sites of the corresponding enzymes or used as catalysts in the oxidation of organic substrates. Due to the increase in attention to the environmental and economic impact of chemical processes, manganese catalysts that use $\text{H}_2\text{O}_2$ as oxidant are the primary focus of this chapter.

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Introduction

Oxidation catalysis, especially that involving oxygen, plays a central role in both biochemical and industrial processes. The oxidation of organic substrates to highly functionalized organic compounds, e.g., oxidation of olefins to the corresponding diols or epoxides, alcohols to aldehydes, ketones or carboxylic acids, the oxidation of alkanes and the bleaching of stains and raw materials are of enormous economic importance. Among the many oxidants available, H$_2$O$_2$ and O$_2$ are preferred since they are inexpensive, readily available, have a high oxygen content and are environmentally benign, with usually only water as a waste product. Although these oxidants are appealing for synthetic chemistry and bleaching applications, their intrinsic activity is kinetically limited under ambient conditions, and especially at room temperature and atmospheric pressure. Indeed, the reaction of dioxygen (O$_2$) with closed shell organic compounds is spin-forbidden despite being a highly exergonic reaction and proceeds through the formation of free radical intermediates.

The chemistry of oxygen is dominated by its relatively unreactive forms water (H$_2$O, the fully reduced state) and dioxygen (O$_2$, the fully oxidized state), while the intermediate forms, i.e. the hydroxyl radical (OH$^-$), hydrogen peroxide (H$_2$O$_2$) and the superoxide radical (O$_2^-$), are highly reactive. Nature has evolved numerous redox enzymes based on a wide range of transition metals, including iron, copper and manganese, to harness the remarkably rich redox chemistry of oxygen. The paramount examples are, almost certainly, the oxidation of water to dioxygen by the oxygen evolving complex (OEC) of photosystem II (PSII) and the disproportionation of H$_2$O$_2$ and superoxide by catalases and superoxide dismutases, respectively, which mitigate the oxidative stress placed on living cells by reactive oxygen species (ROS). Despite this, biological systems are able to activate dioxygen for controlled chemical synthesis via electron and proton transfer at the transition metal based catalytic sites in enzymes. Achieving such control in synthetic systems requires an understanding of the redox controlled coordination chemistry of metal complexes.

The presence of manganese at the active sites of many of the enzymes, such as arginases, responsible for these key biochemical processes has stimulated the synthesis and characterization of manganese complexes to functionally and/or structurally mimic the active sites of these metalloenzymes. The coordination chemistry of manganese is complex given the ready accessibility of a wide range of oxidation states that are stable under ambient conditions (Mn$^{II}$ to Mn$^{VII}$), complicated further by its propensity to form well defined mono- and multi-nuclear complexes. For dinuclear systems, depending on the ligands present, all oxidation states from Mn$^{II}$Mn$^{II}$ to Mn$^{IV}$Mn$^{IV}$ have been observed in aqueous media. $\mu$-Oxido and $\mu$-carboxylato bridged multinuclear manganese complexes (especially in the Mn$^{III}$ and Mn$^{IV}$ oxidation states) are an important class in regard to redox chemistry and the occurrence of these structural motifs in the active sites of various manganese containing redox enzymes. Furthermore, such complexes are ubiquitous in regard to their application in oxidation catalysis. The study of such complexes has therefore been a highly active research area over the last decades.

Direct spectroscopic data on the structure of the reactive intermediates formed by manganese complexes is, however, often limited and therefore mechanistic
understanding is based largely on inferences made from catalytic activity, in particular the analysis of reaction products, reactivity with various terminal oxidants and the effect of additives on catalyst performance, etc.\(^5\) In addition, the lability of manganese complexes when in low oxidation states, in particular \text{Mn}^{II}, increases the complexity of speciation analysis, especially in aqueous solutions.

The paradigm in manganese oxidation catalysis is by and large that \text{Mn}^{IV} and \text{Mn}^{V} species,\(^{29,30,31,32,33}\) in particular mononuclear complexes, are the reactive intermediates that engage in substrate oxygenation.\(^{34,35,36,37}\) However, in cases where such species have been observed, they serve to reinforce Halpern’s premise that if a species can be observed in a catalytic system, then it is at most a resting state. Furthermore, the widespread use and variety of, so-called, additives in manganese oxidation catalysis reflects the complexity in the roles they play, over and above their roles as potential ligands.

In this chapter, the solution chemistry of manganese based complexes of interest to oxidation catalysis in both biological as well as chemical processes will be discussed. The focus is on understanding the mechanisms by which the redox reactions proceed when catalysed by manganese complexes, developed and used as model compounds for the active sites of the corresponding enzymes or used as catalysts in the oxidation of organic substrates. The interplay between changes in redox state and coordination chemistry will be highlighted as well as how these processes are affected by the presence of oxygen in its various forms (\textit{i.e.} water, hydroxyl radical, hydrogen peroxide, superoxide and/or dioxygen) and other agents present in solution (\textit{e.g.}, co-catalytic additives). The importance of a diverse range of experimental parameters in controlling the reactivity and selectivity observed in the preparation of fine chemicals with manganese catalysed oxidations has been discussed in depth elsewhere.\(^5,6\) In addition, with respect to increased attention to the environmental and economic impact of chemical processes, systems that use \text{H}_2\text{O}_2 as an oxidant will be the primary focus of this chapter rather than those in which oxidants such as peracids, hypochlorite, Oxone etc. are employed.\(^{38,39,40,41}\)

The goal of this chapter is to survey the approaches that have been taken to understand, first and foremost, the coordination chemistry of manganese based catalysts in solution and, secondly, to draw correlations with the behaviour and activity of complexes under reaction conditions. First, a brief overview is provided of the most extensively used techniques to study the coordination chemistry of manganese complexes in solution and speciation analysis, followed by discussion of the redox dependent exchange of two common ligands in manganese complexes, \textit{i.e.} carboxylato and oxido ligands. Model complexes of three classes of manganese containing metalloenzymes, which are responsible for the catalytic oxidation of water, the disproportionation of \text{H}_2\text{O}_2 and the dismutation of superoxide, respectively, are discussed in more depth. This is followed by selected examples of reactions involving manganese containing catalysts employing \text{H}_2\text{O}_2 for the oxidation of substrates in organic and in aqueous media in which insight into mechanisms has been gained.
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Spectroscopy and electrochemistry of manganese complexes

The transient nature of the species that are directly responsible for the oxidation of substrates makes their spectroscopic observation highly challenging, if not, in many cases impossible. Nevertheless, spectroscopic and electrochemical methods have been essential in elucidating overall reaction mechanisms, especially where a multi-technique approach is applied under catalytically relevant conditions. It is pertinent, therefore, to discuss briefly the more commonly applied analytical techniques available for the study of manganese catalysts and highlight a key challenge; i.e. that the sensitivity of a particular technique is highly dependent on the oxidation state and nuclearity of the species present and hence quantitative analysis is often as important as qualitative analysis.

UV/Vis absorption spectroscopy is perhaps the most widely applied technique to study manganese complexes in solution. The absorption spectra are comprised of two major contributions, broad absorption bands typically in the visible/near-infrared, arising from metal centred electronic transitions that are sensitive to the coordination sphere, and narrower transitions in the UV region arising from ligand to metal charge transfer (LMCT, typically Mn-O) and ligand centred transitions, $\pi$ to $\pi^*$ and $\sigma$ to $\pi^*$. Notwithstanding contributions in the UV region from ligand centred transitions, in general the absorptivity of MC and LMCT bands is highly dependent on the oxidation state of the manganese ion with absorptivity increasing as the oxidation state of the manganese ions increases. Indeed high spin mono- and multinuclear Mn$^\text{II}$ complexes are typically colourless with very low intensity visible absorptions ($10^{-100}$ M$^{-1}$ cm$^{-1}$) and usually no low energy LMCT transitions. By contrast, manganese complexes in higher oxidation states are generally highly coloured, the most famous of which is permanganate (Mn$^{\text{VII}}$) which shows strong absorption in the blue region with a pronounced vibrational progression.

FT-IR absorption and Raman spectroscopy are a key asset in the study of manganese complexes, especially in the case of carboxylato bridged multinuclear complexes, where direct evidence for a coordination mode can be obtained through the frequencies of the C–O stretching of carboxylato ligands. Changes in coordination and redox state have a pronounced effect on both frequencies, shapes and intensities of vibrational bands. Although perfectly suited to studies in the solid state, a key challenge lies in the sensitivity of both FTIR and Raman spectroscopies, which limits their application in solution to typically $> 50$ mM. Such concentrations are well above those used conventionally under catalytic conditions and hence the interpretation of vibrational data must be done with caution due to possible concentration dependent changes in nuclearity and coordination chemistry. A notable exception to this limitation is where the laser used to obtain the Raman spectrum is coincident with an electronic transition in the complex studied and a phenomenon called resonance enhancement occurs. In this case spectra can be obtained from even optically dilute solutions ($< 1$ mM). The approach is referred to as resonance Raman (rR) spectroscopy. It should be noted, however, that the enhancements in band intensity achieved with rR spectroscopy are selective in that only modes associated with changes in bond length associated with the electronic transition are enhanced substantially. The spectra obtained therefore provide detailed information on the electronic structure for complexes.
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Electron spin resonance (ESR) spectroscopy or electron paramagnetic resonance (EPR) spectroscopy\(^{50}\) is useful in the elucidation of the detailed structure of manganese complexes and although not universally applicable, many oxidation states can be probed readily even at 77 K and at less than 1 mM concentrations, making it a highly valuable technique to study systems under catalytically relevant conditions. By and large, the primary use of EPR spectroscopy has been in the determination of oxidation state, coordination environment and especially nuclearity. Mononuclear high spin Mn\(^{II}\) and Mn\(^{IV}\) complexes show 6 line (s = 5/2) spectra typically at g = 2 and 4, respectively, although they are not often clear due to the line broadening. Antiferromagnetically coupled Mn\(^{IV}\)Mn\(^{IV}\) and Mn\(^{III}\)Mn\(^{III}\) complexes are EPR silent however, Mn\(^{II}\)Mn\(^{III}\) and Mn\(^{IV}\)Mn\(^{IV}\) complexes show rich EPR spectra such as the characteristic 16 line spectrum at g = 2 for Mn\(^{III}\)Mn\(^{IV}\) complexes. Mn\(^{III}\) complexes are a special case\(^{50}\) in that, although they are paramagnetic, they are not observed by X-band EPR spectroscopy and high field EPR spectroscopy at low temperature is required to reveal these species.

NMR spectroscopy\(^{51}\) is, despite the paramagnetic nature of many manganese complexes, useful in their study since many bi- and multi-nuclear complexes show strong antiferromagnetic interactions, in particular Mn\(^{III}\)Mn\(^{III}\) and Mn\(^{IV}\)Mn\(^{IV}\) complexes.\(^{52}\) Importantly, the technique compliments EPR spectroscopy as species that are EPR silent can often be observed by NMR spectroscopy and vice versa.

Cyclic Voltammetry (CV)\(^{53,54,55}\) The wide range of redox states accessible with manganese complexes means that electrochemical methods can provide thermodynamic data (redox potentials) on single- or multi electron oxidation and reduction processes. Furthermore, techniques such as cyclic voltammetry can provide a wealth of information both in terms of speciation analysis and in understanding redox driven changes in the coordination sphere of complexes.

Spectroelectrochemistry\(^{56,57}\) in which a sample undergoing electrolysis is characterised in situ with a spectroscopic technique (e.g. UV/Vis, FTIR, Raman or EPR spectroscopy), is a valuable approach to characterising the changes that occur in their coordination environment of the complexes upon changes in redox state. Indeed, the combination of electrochemistry and spectroscopy allows for access to and characterisation of often highly reactive species.

Electrospray ionisation mass spectrometry (ESI-MS)\(^{58,59,60,61,62}\) is perhaps the most important of the mass spectrometric techniques with regard to the characterisation of manganese complexes, especially since reaction mixtures can be sampled directly. Mass spectrometry exhibits its own limitations that are especially important in the present context. Complexes in lower oxidation states, which are highly labile, present problems due to the potential for redox reactions to occur due to the (high) voltages used and the difficulty in controlling pH, dilution and/or the high temperatures encountered within the mass spectrometer. For example, in the case of more kinetically stable complexes, i.e. in Mn\(^{III}\) and Mn\(^{IV}\) oxidation states, facile reduction coupled with ligand exchange can easily occur giving rise to erroneous results. Hence, drawing firm conclusions with regard to speciation from ESI-MS data is highly challenging. Recent innovations in cryo-ESI-MS\(^{63}\) however, should go a considerable way to improving the applicability of the technique in understanding the solution chemistry of manganese complexes.
In addition, X-ray based techniques, over and above X-ray crystallography, although not yet easily accessible, are making an increased impact in the study of manganese complexes. Indeed X-ray absorption techniques (e.g., EXAFS, EXANES etc.) are key tools in determining electron density (oxidation state) at the metal centres in both synthetic complexes and enzymes.

Redox state dependent exchange of acetate and oxido ligands in multinuclear manganese complexes

As mentioned above, over the last decades, synthetic manganese complexes bearing oxido and carboxylato ligands have been of particular interest in efforts to mimic the functional and spectroscopic properties of bioinorganic complexes such as the water oxidation complex (WOC) in photosystem II (PSII) and manganese superoxide dismutases. A key aspect of the functionality of these biological systems is that redox changes can affect the coordination mode, in particular binding and dissociation of carboxylato and oxido ligands. In this section several examples will be discussed in which ligand exchange processes have been studied and in particular how changes in redox state can drive changes in coordination.

A highly accessible method to assess the lability of ligands is to use $^{18}$O-labelled water to monitor exchange by ESI-MS. Tagore et al. have employed ESI-MS to determine the rates of $\mu$-oxido exchange in acetonitrile, in the presence of trace water, by ESI-MS for several bis-$\mu$-oxido dimanganese complexes including: $[(\text{mes-terpy})_2\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}(\mu-\text{O})_2](\text{H}_2\text{O})_2](\text{NO}_3)_3$ (1, mes-terpy = 4′-mesityl-2,2′:6′,2′′-terpyridine), $(\text{bp}_{\text{a}})_2\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}(\mu-\text{O})_2][\text{ClO}_4]_3$ (2, bpy = 2,2′-bipyridine), $(\text{phen})_2\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}(\mu-\text{O})_2][\text{ClO}_4]_3$ (3, phen = 1,10-phenanthroline), $[(\text{bpea})_22\text{Mn}^{\text{III}}\text{Mn}^{\text{IV}}(\mu-\text{O})_2(\mu-\text{OAc})][\text{ClO}_4]_2$ (4, bpea = bis(2-pyridyl)ethylamine), $[(\text{bpea})_2\text{Mn}^{\text{IV}}\text{Mn}^{\text{IV}}(\mu-\text{O})_2(\mu-\text{OAc})][\text{ClO}_4]_3$ (4$^{\text{ox}}$, terpy $=$ 2,2′:6′,2′′-terpyridine), and $[(\text{tacn})_2\text{Mn}^{\text{IV/IV/IV/IV}}(\mu-\text{O})_6]\text{Br}_3\text{SO}(\text{OH})_{0.5}\cdot\text{H}_2\text{O}$ (5, tacn = 1,4,7-triazacyclononane).

The exchange of the $\mu$-oxido ligands in 2 and 3 with $\text{H}_2^{18}$O was originally reported by Cooper and Calvin to occur only at higher temperatures in aqueous solutions. In acetonitrile with trace water, however, Tagore et al. noted that exchange was as rapid as for the other complexes albeit with an uncertainty due to the inability to observe the intact complexes by ESI-MS. The rate of the exchange of $\mu$-OAc bridges with $\text{CD}_3\text{CO}_2\text{D}$ for complexes 4 and 4$^{\text{ox}}$, which is of relevance to the reported inhibition of PSII by acetate, is much greater than $\mu$-O exchange. From comparison of the rate constants of the ligand exchange, it was concluded that $\mu$-O exchange for $\text{Mn}^{\text{IV}}$ complexes is slower than for $\text{Mn}^{\text{III}}$ complexes and also slower than for a manganese centre that can switch between the $\text{Mn}^{\text{IV}}$ and $\text{Mn}^{\text{III}}$ oxidation states rapidly compared with the rate of exchange. This difference in exchange rate was rationalized by the Jahn-Teller distortion present in a high-spin octahedral $\text{Mn}^{\text{III}}$ ($d^5$) ion that is absent in an octahedral $\text{Mn}^{\text{IV}}$ ($d^3$) ion. The availability of a labile coordination site serves to enhance the rate of exchange of $\mu$-oxido ligands also. Notably the tetranuclear $\text{Mn}^{\text{IV}}$ complexes 5 and 6 showed no evidence of exchange even over extended periods.

The availability of sites that can coordinate water was proposed to be key to achieving catalytic activity. Tagore et al. have explored the mechanism of $\mu$-O exchange in 1 and...
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3, *i.e.* with and without terminal water-binding sites, respectively, in further detail. The order in respect to complex is 1 in both cases excluding bimolecular reactions, however, the order in $H_2^{18}O$ for the μ-O exchange was 1 and < 1 for 1 and 3, respectively. Addition of an acid, such as HNO$_3$ or HClO$_4$ to 1 and 3, respectively, increased the rate of μ-O exchange in acetonitrile for 1 and decreased it for 3, indicating a difference in the mechanisms for exchange. In addition, the insensitivity to (Bu$_4$N)(NO$_3$) and (Bu$_4$N)(ClO$_4$) or ionic strength confirmed that the effects were due to pH. Notably, addition of excess phen ligand slowed down the exchange rates and indicated that phen dissociation is important in the case of 3, whereas dissociation of the mes-terpy in 1, if it is necessary, has no effect on the exchange rate. Voltammetry indicated pK$_a$'s of ca. 2.4 and 4 for the μ-O bridge and terminal aqua ligand in 1, respectively. The absence of a solvent (kinetic isotope effect) KIE (H/D) on the rate of μ-O exchange indicated that proton transfer was unlikely to be involved in the rate-determining step. DFT calculations indicated that the bridge opened form was less stable than the bridged closed form. The proposed mechanism of exchange in 1 (Scheme 1) indicated that protonation of the μ-O bridge by the water coordinated to the Mn$IV$ ion, which is more acidic, occurs. Based on the pK$_a$ of the complex, reported oxido-exchange in aluminium–oxido clusters$^{77}$ and bridge opening in manganese dimers due to protonation,$^{69,78,79}$ it was suggested that protonation followed by bridge opening is energetically favourable for 1. In the case of 3, dissociation of a phen ligand, which is followed by coordination of water occurs prior to exchange of the μ-O bridge. A deprotonation of the water trans to the oxido bridge was proposed to increase the sigma donating strength of the hydroxido.

Scheme 1 Proposed dissociative mechanism of μ-O Exchange in 1, involving sequential oxido-bridge opening and coordination of labelled water.$^{75}$

The absolute $^{16/18}$O isotope exchange rates determined for 1 may provide insight into empirical data for kinetic isotope effects (KIE) observed in various steps and states of the OEC.$^{80}$ The exchange rates measured for the S0, S2, and S3 states of the OEC are ca. 800-4000 times greater than for 1 and are considered to be due to μ-O exchange. However, the μ-O exchange rate for 1 approaches (~8 times slower) the slow exchange rate in the S1 state of the OEC. The absence of terminal water-binding sites on manganese inhibits
μ-O exchange in the S1 state, and dissociation of chelating ligands is necessary for μ-O exchange when terminal water-binding sites are unavailable.

In the case of carboxylate bridged complexes based on the tmtacn ligand (1,4,7-trimethyl-1,4,7-triazacyclononane), e.g., [Mn<sup>II</sup>Mn<sup>III</sup>(μ<sup>-16</sup>O)(μ-CH<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>(tmtacn)]<sup>2+</sup> (7), de Boer et al. have shown, by ESI-MS, that the rate of exchange of the μ-O bridge is dependent on the substituent on the carboxylate ligands. For example, whereas for 7 in CH<sub>3</sub>CN/H<sub>2</sub>O (9:1), μ-O equilibration was complete within 8 min, for [Mn<sup>II</sup>Mn<sup>III</sup>(μ-16-O)(μ-2,6-dichloro-benzoate)]<sub>2</sub>(tmtacn)]<sup>2+</sup> (8) equilibration was complete within 4 min and within 1 min for [Mn<sup>II</sup>Mn<sup>III</sup>(μ-16-O)(μ-CCl<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>(tmtacn)]<sup>2+</sup> (9). These data indicate that reducing the electron density at the manganese ions increased the μ-oxido ligand exchange rate.

For complexes of the type [Mn<sup>II</sup>Mn<sup>III</sup>(μ-OH)(μ-RCO<sub>2</sub>)<sub>2</sub>(tmtacn)]<sup>2+</sup> and [Mn<sup>III</sup>Mn<sup>III</sup>(μ-O)(μ-RCO<sub>2</sub>)<sub>2</sub>(tmtacn)]<sup>2+</sup>, the stretching bands of the μ-carboxylato bridge undergo a shift to higher wavenumber with increasing electron withdrawing character of the R group. For example, the carboxylato stretching band of 9 is at 1659 cm<sup>-1</sup> in both the solid state and in solution whereas for the analogous acetato bridged complex it is at 1568. Furthermore, in acetonitrile, addition of CCl<sub>3</sub>COOH to [Mn<sup>II</sup>Mn<sup>III</sup>(μ-OH)(μ-CCl<sub>3</sub>CO<sub>2</sub>)<sub>2</sub>(tmtacn)]<sup>2+</sup> (9c) results in the disappearance of the band at 1695 cm<sup>-1</sup> and the appearance of a band at 1720 cm<sup>-1</sup>. Addition of D<sub>2</sub>O resulted in a partial recovery of the band at 1695 cm<sup>-1</sup>. Based on this and comparison with data reported by Wieghardt et al., the absorption at 1720 cm<sup>-1</sup> was assigned by de Boer et al. to the complex [Mn<sup>II</sup>Mn<sup>III</sup>(μ-CCl<sub>3</sub>CO<sub>2</sub>)<sub>3</sub>(tmtacn)]<sup>2+</sup>. The observation of the tris-μ-trichloroacetato bridged complex indicates that exchange of carboxylato bridges may be via the same pathway as for exchange of the μ-oxido bridges, i.e. opening of the μ-oxido bridge is followed by coordination by H<sub>2</sub>O or a carboxylato ligand.

The relation between manganese oxidation state and carboxylato stretching bands of monodentate coordinated carboxylates was studied by Berggren et al. in the dinuclear manganese complexes (10) [Mn<sup>IV</sup>Mn<sup>IV</sup>(μ-O)<sub>2</sub>(L<sub>1</sub>)<sub>2</sub>]<sup>2+</sup> (H<sub>L1</sub> = 2-((2-(bis(pyridin-2-ylmethyl))amino)ethyl)(methyl)amino)acetic acid) and (11) [Mn<sup>III</sup>Mn<sup>IV</sup>(μ-O)<sub>2</sub>(L<sub>2</sub>)<sub>2</sub>]<sup>+</sup> (H<sub>L2</sub> = N,N-bis(2-pyridylmethyl)glycine) (Figure 1). Both complexes showed similar cyclic voltammetry in acetonitrile with two quasi-reversible reduction waves assigned to Mn<sup>IV</sup>Mn<sup>IV</sup>/Mn<sup>III</sup>Mn<sup>IV</sup> and Mn<sup>III</sup>Mn<sup>IV</sup>/Mn<sup>III</sup>Mn<sup>III</sup> redox couples, respectively. The oxidation state of the Mn<sup>IV</sup>Mn<sup>IV</sup> and Mn<sup>III</sup>Mn<sup>IV</sup> complexes in solution was confirmed by EPR spectroscopy.

Comparison of the FTIR spectra of complexes 10 and 11 in CD<sub>3</sub>CN in different oxidation states showed that all of the carboxylato bands were affected by the reduction and/or
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the overall change in charge of the complexes, with the Δ value (Δ = ν_a(COO) – ν_s(COO)) changing for the Mn^{IV}Mn^{V} to Mn^{III}Mn^{IV} reduction by 70–125 cm^{-1} and to a lesser extent (60–80 cm^{-1}) for the Mn^{III}Mn^{IV} to Mn^{III}Mn^{III} reduction. In contrast to that observed for monodentate carboxylates, for the complex [(Mn_2(μ-O)(μ-OAc)_2(tacn)]_n^+ (where n = 3) to the Mn^{III}Mn^{III} state (n = 2) for the bridging μ-carboxylato ligands in the latter complexes. The data indicated that significant changes in the IR active carboxylato stretching modes can be expected for monodentate carboxylato ligand upon a change in the oxidation state of the manganese ion.

As part of an effort to understand the effect of water on the redox properties of synthetic OEC mimics, Kurz et al. studied the redox behaviour of the dinuclear complex, [Mn^{III}Mn^{III}L(μ-OAc)_2] (12) (where L is the trianion of 2,6-bis[[[3,5-di-tert-butyl-2-hydroxybenzyl][2-pyridylmethyl]amino]methyl]-4-methylphenol). The presence of up to 0.5 M water in acetonitrile was found to not affect the coordination of acetate ligands to the complex significantly based on ESI-MS data. Cyclic voltammetry of 12 showed that its oxidation was made less positive by the presence of water, however. With 5 M water, part of 12 re-reduced at a potential 0.2 V lower indicating the presence of a prior rapid equilibrium. Bulk electrolysis in the presence of water followed by UV/vis absorption spectroscopy showed that one-electron reduction to the Mn^{II}Mn^{III} state resulted in a hypochromic shift and decrease in absorbance and the appearance of a ca. 2000 G wide multiline signal centred at g ≈ 2 with ca. 150 G line spacing assigned to a Mn^{II}Mn^{III} species. A further one electron reduction resulted in only a broad absorption remaining at greater than 350 nm and a change to a 25-line signal at g ≈ 2, ascribed to a Mn^{II}Mn^{II} or to a Mn^{II}Mn^{III} species that had undergone significant structural changes compared to one-electron reduced 12. The changes were reversed fully upon reoxidation to the Mn^{III}Mn^{III} state.

As expected 12 (Figure 2) is EPR silent in acetonitrile at 5 K, however, after oxidation in the presence of 0.5 M water a 16-line spectrum centred at g = 2, typical for a Mn^{III}Mn^{IV} species with a single (μ-oxido)-bridge, is observed. Comparison of the EPR spectrum of 12 in anhydrous acetonitrile with that of 12 with water present (at ~ 0.5 M) indicated that water stabilized the Mn^{III}Mn^{IV} state. At higher concentrations of water (> 5 M), monomeric Mn species were observed, manifested by the presence of a 6-line signal, attributed to monomeric Mn^{II} species, superimposed on the 16-line signal. It was concluded that reduction of 12 in CH_3CN/H_2O did not result in a change in coordination mode with only a fraction of the Mn^{III}Mn^{IV} species undergoing ligand rearrangement to yield the species responsible for the 25-line EPR signal). Oxidation of 12 lead to formation of a Mn^{III}Mn^{IV} complexes, which, in the presence of water, undergoes
replacement of one or both of the acetato ligands to form $\mu$-oxido bridge(s) between the manganese centres and thereby stabilize the higher oxidation states. These changes in coordination mode can be induced by chemical oxidation and reduction also.

Eilers et al. have studied the structural rearrangements that the complex $[\text{Mn}^{\text{II}}\text{Mn}^{\text{II}}(\text{bpmp})(\mu-\text{OAc})_2]^+$ (13, bpmp = 2,6-bis[bis(2-pyridylmethyl)amino]methyl-4-methylphenol anion) undergoes in the presence of water. In anhydrous acetonitrile, 13 undergoes two quasi-reversible oxidations (Figure 3). Addition of water (10 % v/v) resulted in a broadening of the second oxidation wave, together with a loss of reversibility and the appearance of an additional reduction wave at 0.2 V (vs Fc$^{+/0}$) on the return cycle. The irreversibility was assigned, to a charge compensating ligand-exchange reaction where one of the $\mu$-OAc was replaced by $\mu$-O bridge and the new reduction wave to the reduction of one of the products formed. The additional reduction wave was irreversible also indicating that the initial product converts to the original complex rapidly and quantitatively. It should be noted that the first oxidation wave was essentially unperturbed by addition of water indicating that the Mn$^{\text{II}}$Mn$^{\text{III}}$ state is stable towards ligand exchange.

![Figure 3 Cyclic voltammograms (0.100 V s$^{-1}$) of 13 (2 mM) in CH$_3$CN with 10% (v/v) of water (a) and neat CH$_3$CN (b) with 0.1 M (n-C$_4$H$_9$)N][ClO$_4$] as supporting electrolyte. Inset: Second cycle. Reproduced with permission from ref 90. Copyright RSC (2005).](image)

From FTIR spectroscopy, in CH$_3$CN with D$_2$O, it was apparent that the Mn$^{\text{II}}$Mn$^{\text{II}}$ and Mn$^{\text{II}}$Mn$^{\text{III}}$ complexes show less tendency to undergo exchange of the acetato ligands with water than does the complex in its Mn$^{\text{III}}$Mn$^{\text{III}}$ oxidation state. Furthermore The absence of IR absorption from acetic acid indicated that water binds as aquo rather than in the hydroxido or oxido form.
Anderlund et al.\textsuperscript{92} reported a di-μ-acetato bridged dinuclear manganese complex, \((\text{Mn}^\text{II}\text{Mn}^\text{III}L(\mu-\text{OAc})_2)^+\) (14), with an non-symmetric ligand, \(L = 2-\{\text{bis(2-pyrid-2-ylmethyl)amino}3\text{methyl}\}_6-\{\text{bis(3,5-di-tert-butyl-2-hydroxybenzyl)2-pyrid-2-ylmethyl)amino}3\text{methyl}\}_{4-\text{methylphenol}}\), that provided \(N_3O_3\) and \(N_2O_4\) coordination at the \(\text{Mn}^{n+}\) and \(\text{Mn}^{(n+1)+}\) centres, respectively (Figure 4).

The crystal structure of the complex showed that the terminal phenoxyl ligand coordinated to the \(\text{Mn}^\text{III}\) centre rather than the \(\text{Mn}^\text{II}\) centre. The assignment of \(\text{Mn}^\text{II}\text{Mn}^\text{III}\) redox state was confirmed by its magnetic moment of 7.20 BM at room temperature, which is slightly lower than the expected value of 7.6 BM, and at low temperature of 1.79 BM, which was close to the expected 1.73 BM. FTIR spectroscopy showed absorption bands at 1590 cm\(^{-1}\) (\(s, \nu_aC-O, \text{carboxylato}\)) and 1441 cm\(^{-1}\) (\(s, \nu_sC-O, \text{carboxylato}\)) in the solid state and the similarity with the spectrum of the complex in anhydrous \(\text{CD}_3\text{CN}\) confirmed that the di-μ-acetato bridging remained intact upon dissolution.

One electron reduction, by electrolysis at \(-0.93\) V, resulted in the appearance of an EPR spectrum (at 12 K) typical of a weakly coupled \([\text{Mn}^\text{II}\text{Mn}^\text{II}L(\mu-\text{OAc})_2]^+\) complex together with a loss of visible absorbance. The \(\text{Mn}^\text{II}\text{Mn}^\text{III}\) complex was recovered after reoxidation at 0.08 V. Bulk electrolysis at 0.57 V yielded an EPR silent product, which was assigned as \([\text{Mn}^\text{III}\text{Mn}^\text{III}L(\mu-\text{OAc})_2]^{2+}\). The product of the electrolysis at 0.82 V was not identified due to the instability of the oxidized complex, ascribed to oxidative degradation of the ligand and liberation of \(\text{Mn}^\text{II}\), as observed by EPR spectroscopy.

The redox properties of 14 were compared to those of the symmetric analogues \([\text{Mn}^\text{II}\text{Mn}^\text{II}(\text{bpmp})(\mu-\text{OAc})_2]^+\) (15, where BPMP is the anion of 2,6-bis\{N,N-di(2-pyridinemethyl)amino}3methyl\}_{4-\text{methylphenol}}\) and \([\text{Mn}^\text{III}\text{Mn}^\text{III}(\text{bhpp})(\mu-\text{OAc})_2]^+\) (16, where bhpp is 1,4-bis[2-hydroxybenzaldehyde]propyl)piperazine), which present \((N_3O_3)\) and \((N_2O_4)\) donor sets, respectively.\textsuperscript{87,93} Higher oxidation states were found to be stabilised by the increase in the number of oxygen donors, however, metal oxidation states higher than \(\text{Mn}^\text{III}\text{Mn}^\text{III}\) could not be obtained by bulk electrolysis in non-aqueous solvents.

The presence of the bridging acetato ligands in all three oxidation states \(\text{Mn}^\text{II}\text{Mn}^\text{II}\), \(\text{Mn}^\text{II}\text{Mn}^\text{III}\), \(\text{Mn}^\text{III}\text{Mn}^\text{III}\) was confirmed by FTIR spectoelectrochemistry with \(\Delta \nu = \nu_{\text{as}} - \nu_s\) for the acetato ligand of 120, 170 and 220 cm\(^{-1}\), respectively.\textsuperscript{90} Ligand exchange reactions for 14 and the oxidation states higher than \(\text{Mn}^\text{III}\text{Mn}^\text{III}\) were investigated in aqueous acetonitrile also. An increase in water concentration resulted in depletion and replacement of the bands of the bridging acetato ligands (\(\nu_{\text{as}}\), 1590 cm\(^{-1}\), \(\epsilon = 4170\) M\(^{-1}\) cm\(^{-1}\)) by the broader and weaker \(\nu_{\text{as}}\) band of unbound acetate ions at lower frequency (1574 cm\(^{-1}\), \(\epsilon = 840\) M\(^{-1}\) cm\(^{-1}\)). It was concluded that one of the acetate bridges was replaced readily by two terminal aqua ligands while the second acetate remained coordinated even at the highest concentrations of water (up to 30 M) employed. In
contrast, for the bpmp analogues both of the acetato ligands were replaced under these conditions together with formation of acetic acid and acetate demonstrating that the water undergoes deprotonation upon coordination. Electrolysis of 14 in acetonitrile/water at the 0.47 V (vs. Fe+/0) to form the MnIII-MnIV complex and subsequent oxidation at 0.72 V vs. Fe+/0 to generate the MnIII-MnIV state lead to the appearance of acetic acid (1725, 1380 and 1300 cm⁻¹), which confirmed that the water-derived ligands are at least partly deprotonated upon oxidation of the Mn centres. Hence, in higher oxidation states the water derived ligands are present as oxido- or hydroxido-bridges.

14 undergoes photooxidation to a MnIII-MnIV complex of in the presence of the [RuII(bpy)₃]³⁺ and the electron acceptor [CoIII(NH₃)₅Cl]²⁺, in aqueous organic solution. It was proposed that the product bears a di-µ-oxido or di-µ-oxido/hydroxido bridging motif in place of the µ-acetato ligands. Further photoinduced oxidation of this complex might result in the formation of a MnIV-MnIV or MnIII-MnIV product with a ligand-based radical. The estimated redox potential of the MnIII-MnIV/MnIII-MnIII couple of the MnIII-MnIV complex obtained was within a desirable potential range with respect to the average potential of 0.81 V vs. the normal hydrogen electrode (NHE) (at pH 7) required for water oxidation. Therefore, the ratio O/N ratio in 14 may achieve a near perfect balance between oxidation potential and stabilisation of higher oxidation states, although the ability of the complex to engage in water oxidation was not evaluated.

The key attraction of multinuclear manganese complexes based on the 1,4,7-triazacyclononane (tmtacn) family of ligands is their thermodynamic stability and extensive redox and coordination chemistry. In the mid-1980s, complexes based on this ligand and its analogues were studied spectroscopically and electrochemically by Wieghardt et al., with a focus on mimicking the structure and function of manganese based enzymes. The subsequent application to laundry cleaning, shifted attention towards aqueous media in the mid-1990s. Hage et al. reporting on the pH dependence of the physical and electronic properties of [MnIV,MnIV(µ-O)]₃ (tmtacn)₂]²⁺ (17) in CH₂CN and water. 17 undergoes protonation only with concentrated strong acids (e.g., H₂SO₄, HClO₄), The νas (670 cm⁻¹) and νs (701 cm⁻¹, λex = 488 nm) Mn-O-Mn vibrational modes in the IR and Raman spectra of 17, respectively were identified by¹⁸O-labelling. Protonation resulted in a shift in both bands to 683 cm⁻¹ with an increase in the Mn-O-Mn angle (78° to 81°). The reduction potential of 17 is surprisingly negative, given that the complex is in the MnIV-MnIV oxidation state, was attributed to the strong σ-donor properties of the three µ-oxido ligands. The EPR spectrum of the MnIII-MnIV species generated using the one electron reductant Co(Cp)₂ showed the characteristic 16–line spectrum with a hyperfine coupling constant (½) of ca. 69 G at 77 K. In acetonitrile, it was proposed that the reduced species contained either a MnIII-MnIV(µ-O)₃ core or a MnIII MnIV(µ-O)₂(µ-OH) core with similar Mn-O-Mn angles as the parent compound on the basis of FTIR and UV/Vis spectrophotometry. The band at 668 cm⁻¹ (νas(Mn=O-Mn)) reflects the Mn-O-Mn bond angle (vide supra) and does not change upon reduction. The bands at 791, 990 and 1007 cm⁻¹ decreased in intensity and a new band at 1016 cm⁻¹ appeared. Similarly, in aqueous solution reduction of 17 leads to a complex with a MnIII-MnIV(µ-O)₂(µ-OH) core also, however, in citrate buffer a positive shift in reduction potential is observed below pH 4, consistent with a 1e-/1H⁺ coupled reduction. As would be expected, in the one electron reduced state (i.e. MnIII-MnIV), the pKₐ (protonation of one of the µ-oxido ligands) increased to ca. 4. Notably however,
Redox state dependent ligand exchange in manganese based oxidation catalysis

Reductive bulk electrolysis of **17** in aqueous citrate buffer at pH = 3.5 resulted in the appearance of two absorption bands at 485 and 515 nm and a weak band at 725 nm, which are characteristic of a $[\text{Mn}^{\text{III}}\text{Mn}^{\text{III}}(\mu-O)(\mu-\text{RCO}_2)\_2(\text{tmtacn})\_2]^{2+}$ species$^{85}$ rather than **17** in the Mn$^{\text{III}}$Mn$^{\text{IV}}$ oxidation state.

Although these complexes were shown to be catalytically active in oxidations with H$_2$O$_2$, (*vide infra*), already in the mid-1990s$^{95}$ and later it was discovered that certain additives$^{101,102,103,104,105}$ can play a role in enhancing their catalytic performance which prompted renewed interest in the complexes redox and solvent dependent coordination chemistry. One such class of additives were carboxylic acids (*vide infra*). As will be discussed below, the conversion of the *tris*-µ-oxido bridged complex **17** to *bis*-µ-carboxylato complexes such as **7**-**9** was found to be central to the catalytic activity observed in several cases.$^{106,107}$ This reaction requires reduction of **17** from a Mn$^{\text{IV}}$Mn$^{\text{IV}}$ oxidation state to a Mn$^{\text{III}}$Mn$^{\text{III}}$ state, together with exchange of two µ-oxido ligands with two µ-carboxylato ligands. In an effort to understand this process in detail, de Boer *et al.*$^{81,108}$ investigated the redox dependent coordination chemistry of both **17** and *bis*-µ-carboxylato species, such as **9a**, under conditions employed in the catalytic oxidation of alkenes. A relatively complex interplay was noted between redox state, pH, carboxylic acid and water in determining both the initial conversion of **17** and the species present under catalytic conditions (Scheme 2).

![Scheme 2](image-url)

Scheme 2 Summary of redox chemistry of **9** and **9a-c** in 0.1 M TBAPF$_6$/CH$_3$CN in the presence of CCl$_3$CO$_2$H (L = tmtacn).

As noted by Hage *et al.*$^{52}$ the one electron reduction of **17** at -600 mV (vs SCE) undergoes a shift and becomes an irreversible four-electron reduction at ca. -0.2 V in the presence of a carboxylic acid in water. de Boer *et al.*$^{81}$ observed a similar effect of carboxylic acid in acetonitrile (Figure 5). Notably the species formed initially upon reduction is the colourless Mn$^{\text{II}}$Mn$^{\text{II}}$ complex **9a**, which can undergo subsequent oxidation to form
initially the Mn$^{III}$ complexes 9b followed by a loss of H$_2$O to form 9 (Figure 6). In contrast to trichloroacetic acid, when acetic acid is present the μ-oxido bridged dinuclear complex 17 is formed immediately upon oxidation, which is consistent with ESI-MS data for the effect of the carboxylato ligand on $^{18}$O exchange (vide supra).

Figure 5 Cyclic voltammogram of 17 in CH$_3$CN (0.1 M KPF$_6$) a) with 10 equiv CCl$_3$CO$_2$H 0.1 V s$^{-1}$ in CH$_3$CN/0.1 M KPF$_6$, before (i) and after (ii) bulk reduction at –0.2 V. b) after reoxidation at 1.10 V, initial scan direction anodic (thin line) and cathodic (thick line). Reproduced with permission from ref 90. Copyright ACS (2007).

Figure 6 UV.Vis spectroscopy of 17 (1 mM) with CCl$_3$CO$_2$H (10 mM) in CH$_3$CN/0.1 M KPF$_6$. a) UV.Vis spectrum, b) expansion of visible region) before (thick line) and after (dotted line) bulk reduction at -0.2 V, and after bulk reoxidation at 1.1 V (thin line). Reproduced with permission from ref81. Copyright ACS (2007).

The redox chemistry of complex 9 highlights the interplay of both redox state, H$_2$O and pH in controlling the coordination chemistry of manganese complexes. The μ-oxido bridged Mn$^{II}$Mn$^{II}$ complex 9c undergoes reversible one-electron oxidation to $[\text{Mn}^{II}\text{Mn}^{III}(\mu-O\text{H})(\mu-\text{CCl}_3\text{CO}_2)_2(\text{tmtacn})_2]^{2+}$ at 0.53 V (Figure 7). Addition of carboxylic acid, however, results in the immediate opening of the μ-oxido bridge to form the $[\text{Mn}^{II}\text{Mn}^{III}(\mu-O_2\text{H}_3)]$ complex 9a. In the absence of CCl$_3$CO$_2$H, 9a undergoes a two electron oxidation at $E_{p,a} = 1.03$ V (vs SCE) to a de $[\text{Mn}^{III}\text{Mn}^{III}(\mu-O_2\text{H}_3)]$, which is more acidic and undergoes deprotonation to form the $[\text{Mn}^{III}\text{Mn}^{III}(\mu-O\text{H})_2]$ species 9b.
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Figure 7 (left) Cyclic voltammetry of 9c (1 mM) in CH₃CN/0.1 M (TBA)PF₆ in the (a) absence and (b) presence of 10 mM CCl₃CO₂H. Initial scan direction from the open circuit potential is cathodic in each case. Scan rate: 0.1 V s⁻¹. (right) Cyclic voltammetry of 9 (1 mM) in CH₃CN/0.1 M (TBA)PF₆ (a) in the absence (i) and presence (ii) of 10 mM CCl₃CO₂H. Reproduced with permission from ref 81. Copyright ACS (2007).

The Mn^{III}Mn^{III} complex 9, which is the primary species observed under catalytic conditions, undergoes a reversible oxidation to the Mn^{III}Mn^{IV} to Mn^{IV}Mn^{IV} oxidation states and reversible reduction to the Mn^{II}Mn^{III} oxidation state. Addition of 1 eq. or more of carboxylic acid resulted in the reduction changing to an irreversible two electron process. Thin layer voltammetry demonstrated that the product of the reduction was 9a.

Overall it can be concluded that the rates of exchange of bridging oxido and carboxylato ligands, which are of particular relevance to biological systems, are heavily affected by both oxidation state and the electron donating ability of the ligands. Lower oxidation states, in addition to higher exchange rates, also tend to favour the less strongly sigma-donor carboxylates over oxido and hydroxido ligands. The mechanism of exchange appears to follow a general trend of protonation of the oxido bridging ligands followed by nucleophilic attack of water or carboxylates. Understanding the intimate relation between changes in redox state and changes in the coordination environment of multinuclear manganese complexes, as will be shown, essential to elucidation of mechanistic pathways in the oxidation catalysis that such complexes engage in.

Manganese catalysts in water oxidation reactions

Water oxidation, a key reaction in nature, is carried out at low overpotential by the CaMn₄ cluster that lies at the heart of the oxygen-evolving complex (OEC) of photosystem II. In the OEC, the catalytic tetrannuclear Mn₄ core cycles through five oxidation states to accumulate sufficient redox potential and equivalents to oxidise water (2 H₂O → O₂ + 4 H⁺ + 4 e⁻). Despite being the focus of intense study for decades, only recently was the detailed structure of the OEC revealed by X-ray crystallography. It has been, however, the lack of crystallographic evidence for the structure of the OEC that has stimulated the synthesis of a wide range of structural, and more recently functional, models for the OEC. Although, the entire cycle is still not clear in detail, the
model for its function as described by Kok et al.\textsuperscript{112} is widely accepted and involves a cycle comprised of five flash-induced transitions between the so-called S-states, denoted as S\(_0\)-S\(_4\), with the S\(_0\) state being the most reduced and the S\(_4\) state the most oxidised. The S\(_2\)→S\(_2\) transition is considered as primarily an oxidation step, \textit{i.e.} without an accompanying change in the coordination environment, whereas the other transitions between the S-states involve removal of an electron and proton from the OEC.\textsuperscript{113} The S\(_4\) state decays spontaneously to recover the S\(_0\) state with concomitant release of dioxygen. It is clear that the structural changes, \textit{i.e.} changes in the coordination of the ligands bound to the manganese ions, that accompany changes in redox state, are central to the operation of the OEC.\textsuperscript{75,114}

Spectroscopic, structural and electrochemical data garnered over the last decades from synthetic manganese complexes\textsuperscript{31,115,116} have provided an important basis to understand the highly complex chemistry of the OEC.\textsuperscript{12,24,25,117} By and large, the primary focus has been on structural mimicry, however several synthetic complexes have been shown to be able to oxidize water.\textsuperscript{115,116,6j,118}

The first report on water oxidation chemistry by synthetic manganese complexes was with [Mn\textsuperscript{III}Mn\textsuperscript{IV}(μ-O)\textsubscript{2}(terpy)\textsubscript{2}(H\textsubscript{2}O)\textsubscript{2}]\textsuperscript{3+} in aqueous solution by Crabtree, Brudvig and co-workers.\textsuperscript{31,115} Later Yamazaki et al.\textsuperscript{119} reported the catalytic properties of 18 towards water oxidation when adsorbed on mica. It was demonstrated that the activity of the catalyst was dependent on the amount of complex adsorbed on layered compounds and also the cation exchange capacity of the layered structure. A series of derivatives of 18 (\textit{i.e.} [(Mn\textsuperscript{III}Mn\textsuperscript{IV}(μ-O)\textsubscript{2}(R-terpy)\textsubscript{2}(OH\textsubscript{2})\textsubscript{2})(NO\textsubscript{3})\textsubscript{3}, Figure 8) allowed for the influence of variation at the 4´-position of the terpy ligand on water oxidation activity to be probed and spectroscopic and electrochemical properties.

\textbf{Figure 8} [(H\textsubscript{2}O)(terpy)Mn\textsuperscript{III}Mn\textsuperscript{IV}(μ-O)\textsubscript{2}(terpy)(H\textsubscript{2}O)\textsubscript{2}]\textsuperscript{2+} complexes 18 R = H and 18a-g (R = Cl, MeS, Me, EtO, PrO, MeO, BuO) studied as water oxidation catalysts.\textsuperscript{119}

The similarity of the absorption spectra in the visible region of 18 and 18a-g in water indicates that the electronic structure of the Mn\textsuperscript{III}Mn\textsuperscript{IV}(μ-O)\textsubscript{2} core is scarcely affected by the nature of the 4´-substituent. The absorption bands at ca. 551 nm (ε = 605–623 M\textsuperscript{-1} cm\textsuperscript{-1}) and 650–658 nm (ε = 598–610 M\textsuperscript{-1} cm\textsuperscript{-1}) were assigned to d–d transitions and an oxygen to manganese charge-transfer band, respectively.\textsuperscript{69,120} The FTIR absorption at ca. 700 cm\textsuperscript{-1} was assigned to the asymmetric stretch (ν\textsubscript{as}) of a Mn–O–Mn bond.\textsuperscript{69} The g values obtained from magnetic susceptibility measurements, were close to 2 consistent with a Mn\textsuperscript{III}Mn\textsuperscript{IV}(μ-O)\textsubscript{2} dimer.\textsuperscript{121} Cyclic voltammetry showed a one electron oxidation (Mn\textsuperscript{III}Mn\textsuperscript{IV} to Mn\textsuperscript{IV}Mn\textsuperscript{IV}) and three reductions of (i) Mn\textsuperscript{IV}Mn\textsuperscript{IV} to Mn\textsuperscript{III}Mn\textsuperscript{IV} at 0.92 V vs SCE, (ii) a tetranuclear Mn\textsuperscript{IV\textsubscript{4}} species\textsuperscript{78,122} (which was formed from the Mn\textsuperscript{IV}Mn\textsuperscript{IV} dimer) to the Mn\textsuperscript{III}Mn\textsuperscript{IV} dimer at 0.80 V, and (iii) Mn\textsuperscript{III}Mn\textsuperscript{IV} to the Mn\textsuperscript{II} monomer at 0.62 V.
Comparison of the voltammetry of 18 with 18d (R = EtO−) showed a shift to lower potentials due to electron-donating character of the ethoxy moiety.

The oxidation of water to O₂ was catalysed by 18 when adsorbed on mica using CeIV as terminal oxidant. The second order rate constant (k₂/Μ⁻¹ s⁻¹) was varied moderately from 2.4 to 69 M⁻¹ s⁻¹ Depending on the substituent. Variation in local catalyst concentration was excluded as a factor by X-ray diffraction, which confirmed a negligible influence of the substituents on the interspace distance between the mica layers. Furthermore, inhibition of cooperative catalysis due to steric hindrance can be excluded as k₂ for 18e (R = PrO) and 18g (R = BuO) were significantly greater than for 18d (R = EtO). E₁/₂ for the MnIII/MnIV/MnIV/MnV redox couple with E₁/₂ (18, H > 18e, PrO > 18g, BuO > 18f, MeO > 18c, Me > 18d, EtO) correlated with an increase in k₂. It was suggested that the oxidizing power of the active species, assumed to be a MnIV/MnV species would likely correlate also with E₁/₂ for the MnIII/MnIV redox couple.

The formation of reactive electrophilic high-valent Mn−oxo species requires careful balancing of electron donating strength of the ligand environment. Ligands that are particularly strong donors have been shown to support higher oxidation states, such as the tetra-amido macrocyclic ligands (TAML) with tetrakiscarboxamido ligands reported by Collins et al. or tris-carboxamido ligands reported by Borovik and co-workers, which promote the formation of a high-spin MnV−oxido complex. However, these species are unreactive toward nucleophilic attack. Similarly, Lomoth et al. reported a MnIII/MnIII dimer with three phenolato ligands that stabilize the MnIV/MnIV oxidation state.

As shown by McKenzie and co-workers and Berggren et al. dinuclear and tetranuclear manganese complexes, respectively, of a ligand with a dangling carboxylate group showed oxygen evolution from water with the oxidants tert-butyl hydrogen peroxide, oxone or CeIV. Although the precise role of the carboxylate moiety remains unclear, it has been proposed that coordination of this anionic ligand may stabilize the high-valent manganese species that is the reactive intermediate. Brudvig et al. have reported the activity of [MnIII(PaPy₃)(NO₃)](ClO₄) (19) (PaPy₃H = N,N-bis(2-pyridylmethyl)-amine-N-ethyl-2-pyridine-2-carboxamide), [MnIII(PaPy₃)(μ-O)(PaPy₃)MnIII][ClO₄] (20), and [MnV(PY₃)(OH₂)]ClO₄ (21) (PY₅ = 2,6-bis(bis(2-pyridyl)methoxymethane)-pyridine) with a carboxamido donor group and [MnIII(NOPyOTf)(OTf)] (22) (NOPy = N,N-bis(2-pyridylmethyl)-N-bis(2-pyridyl)methylamine), which does not bear a carboxamido group, as water-oxidation catalyst using the terminal oxidants oxone or H₂O₂. The UV/vis absorption spectra of 19 and 20 in water are similar, which is consistent with MnIII in either monomeric or oxido-bridged dimeric form. In contrast, in non-aqueous solvents the UV/vis absorption spectra of the complexes are different. The effect of addition of water to 19 and 20 in acetonitrile showed that it is more difficult to displace the nitrate group than to break the μ-O bridge of the complex, since only 2% water in acetonitrile is required for 20 to undergo complete conversion to the species found in water while for 19, 12 vol% of water is needed.

Isosbestic points are maintained upon titration of 19 between pH 2 and 7, with an apparent pKₐ of 5.0 and approximately 9.9, assigned to the first deprotonation of the Mn-bound water to form [MnIII(PaPy₃)(OH)] followed by a second deprotonation of the Mn-bound water and subsequent dimerization to form an oxido bridged...
species\([\text{PaPy}_3]\text{Mn}(\mu-\text{O})\text{Mn}\text{(PaPy}_3\text{)}\text{]}^{2+}\), respectively. Dissociation of the pentadentate ligand occurs below pH 2 and above pH 10.5, MnO\(_2\) precipitated from solution.

\[
\begin{align*}
\text{pK}_a & = 5.0 \\
[Mn^{II}\text{(PaPy}_3\text{)(OH}_2\text{)}]^{2+} & \rightleftharpoons [Mn^{II}\text{(PaPy}_3\text{)(OH)}]\text{]}^+ \\
\text{pK}_a & = 9.9 \\
[Mn^{II}\text{(PaPy}_3\text{)(OH)}]\text{]}^+ & \rightleftharpoons [(\text{PaPy}_3\text{)}\text{Mn}^{II}(\mu-\text{O})\text{Mn}^{II}(\text{PaPy}_3\text{)}\text{]}^{2+}
\end{align*}
\]

Scheme 3 Equilibria established by 19 in solution

The initial rates of oxygen evolution by 19 and 20 upon addition of Oxone\(^{129,130}\) were similar while that of 22 was significantly lower. Although the actual catalytically active species has not been identified, the authors proposed that reaction with oxone to generate a high-valent manganese species is involved. Therefore, the greater reactivity of 19 and 20 compared to that of 22 may be due to stabilisation of the high-valent species by the anionic N-donor ligands.

An increase in absorbance was observed upon the addition of Oxone to both 19 and 20, which is consistent with oxidation to a higher redox state.\(^{131}\) 19 is EPR-silent in perpendicular mode, consistent with a Mn\(^{III}\) species. Upon the addition of Oxone, some mononuclear Mn\(^{II}\) signals were observed but the remainder of the manganese present was EPR silent consistent with a Mn\(^{III}\) or Mn\(^{IV}\)Mn\(^{IV}\) dimer and excluded formation of Mn\(^{III}\)Mn\(^{IV}\) or mononuclear Mn\(^{IV}\) species. 19 showed two quasi-reversible redox waves between +0.2 and +1.5 V, with only the first redox wave showing a pH dependence. It was postulated, based on the equilibria shown in Scheme 3 that if the equilibria were fast compared to the electrochemical time scale, the second oxidation may be the oxidation of a Mn\(^{III}\)Mn\(^{III}\)(\mu-\text{O}) complex to a Mn\(^{III}\)Mn\(^{IV}\)(\mu-\text{O}) complex with no net deprotonation.

A similar increase in absorbance, albeit much slower, was observed for 21 and 22. It is conceivable that achieving a stable high-valent state required formation of a \(\mu\)-oxido bridge between the metal centres. In the case of 19 and 20, the anionic ligand supports rapid formation and exchange of the \(\mu\)-oxido bridge. The cyclic voltammetry of 22 showed the decomposition of the complex to MnO\(_2\) upon electrochemical oxidation. Since 19 did not undergo similar decomposition, it was suggested that the PaPy3–ligand is more strongly bound than the N4Py ligand. Furthermore, the orientation of the carboxamido group trans to the site of water coordination should facilitate ligand exchange in 19 and 20 compared to that in 21 or 22. The possibility that manganese oxides catalyse oxygen evolution was excluded as they were relatively poor catalysts in the presence of oxone.\(^{132}\) The rate of the oxygen evolution catalysed by 19 and 20 was less than that observed for related manganese based catalysts, however,\(^{31}\) which is possibly due to the lack of readily exchangeable coordination sites due to the pentadentate nature of the ligand.

**Manganese catalysed disproportionation H\(_2\)O\(_2\)**

Catalase enzymes protect cells both from oxidative stress by disproportionation of H\(_2\)O\(_2\) into O\(_2\) and H\(_2\)O, which requires oxidation and reduction of H\(_2\)O\(_2\). Many catalase
enzymes are based on iron, however, several enzymes that utilise manganese have been found. Manganese based catalases have been isolated from *L. plantarum*[^133], *Thermus thermophilus*[^134], *Thermoleophilum album*.[^135,136] Catalases containing a bimetallic manganese active site were proposed to have a MnMn(μ-RCO₂)(μ-O/OH) structural unit with coordination by histidine and glutamate side chains and a range of Mn⁹Mn^(II), Mn⁹Mn^(III) and Mn⁷Mn^(IV).[^137] H₂O₂ disproportionation, is achieved by catalases through changes in the bridging ligands and redox state, *i.e.* in *T. Thermophilus* catalase, a μ-carboxylate ligand (Glu), a μ-OH, and a μ-OH₂ are present in the Mn⁹Mn^(II) oxidation state but a μ-oxidio bridge in the Mn³⁺Mn^(III) oxidation state.[^138] The design of manganese complexes that engage in catalase activity has received considerable attention over the last decades, focusing on the effect of redox state, redox potential, nuclearity, coordination asymmetry and inner-sphere ligand rearrangements.[^99,139,140] A series of six coordinate Mn⁹Mn^(II) and Mn⁷Mn^(III) complexes with binucleating salen type ligands and alkoxide bridges were reported as functional models for catalases.[^99,131,141,142,143] These complexes have shown catalytic efficiency, albeit approximately 575 and 3160 times less than that of *L. plantarum*[^144,145] and *T. thermophilus* enzymes.[^146] respectively. [Mn⁴⁺salpn(μ-O)]₂ (salpn = 1,3-bis(salicylideneamino)propane) is one of the most efficient MnCAT functional mimic, however, in contrast to enzymatic systems, they cycle between Mn⁹Mn^(IV) and Mn⁷Mn^(III) oxidation states.[^147,148] Indeed only a few of the reported synthetic catalase mimics operate via a Mn⁹Mn^(II) ↔ Mn⁷Mn^(III) redox cycle.[^99,139,142,143,146,149,150] It was also demonstrated by reactions with deuterium peroxide, that proton dissociation/association plays an important role for both complex formation and in the rate-limiting step.[^151]

Dismukes *et al.*[^152] have studied the effect of the bridging μ-hydroxide on μ-carboxylato coordination of manganese complexes as a functional model of dimanganese catalases (Figure 9). Two Mn⁹Mn^(II) complexes and their corresponding Mn⁷Mn^(III) complexes, based on ligands containing N-alkylated benzimidazoles, were studied in solution in presence of O₂ under basic conditions to understand better the mechanism of disproportionation of H₂O₂.

The pH dependence of the UV/Vis absorption spectra of complexes 23-26, in the Mn⁹Mn^(II) oxidation state, were studied in methanol under argon and under air. Under an argon atmosphere the absorption spectra of the complexes were unaffected by addition of hydroxide, however, in the presence of oxygen, three absorption bands at 425, 472, 760 nm appeared, which were assigned to ligand field transitions of Mn^(III) or Mn⁷Mn^(III) complexes in low symmetry environments (or possibly LMCT transitions) based on earlier studies of the reaction between 23 and H₂O₂.[^131] With 25, in which the ligand contains the N-alkylated benzimidazoyls, the same changes in the absorption spectrum as for 23 and 24 are observed indicate that the hydroxide induced changes are not due to deprotonation of the benzimidazole groups. The EPR spectrum of 23 in acetone is similar to that of manganese catalase from *T. thermophilus* in its Mn⁹Mn^(II) oxidation state.[^153] In the presence of 5 vol% water, however, a characteristic six line signal of a mononuclear Mn^(II) species at g = 2 and a broad low field signal at 1100-1600 G were observed for 23. These signals are attributed to a spin–uncoupled dinuclear Mn⁷Mn^(II) species. The six line signal disappeared upon the addition of NaOH under argon, while the signals of the spin-coupled species increased. In the presence of oxygen, the signals related to the Mn⁷Mn^(II) species diminished, consistent with formation of dinuclear
Mn$^{\text{III}}$Mn$^{\text{III}}$ species. The reversible protonation of the alkoxide moiety of the ligand in the presence of water was proposed based on EPR data. Protonation of the alkoxide moiety resulted in the formation of a spin-un coupled Mn$^{\text{II}}$Mn$^{\text{II}}$ complex through the dissociation of one of the Mn centres from the alkoxide moiety.

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![Figure 9](image-url) Structure of manganese complexes 22-28 and 30, R = H or Ethyl, X = H or Cl.

The addition of NaOD to a solution of 27 in MeOD resulted a decrease in the $^1$H NMR signal at 22.8 ppm assigned to the methyl group of the bridging acetate and appearance of a new signal at 1.90 ppm, consistent with the conversion of the μ-bridging acetato ligand to a labile monodentate coordination mode. This monodentate ligand is in equilibrium with unbound acetate, which appeared at 1.89 ppm, hence the signal at 1.90 ppm showed a large coupling constant ($J = 24$ Hz). The conversion of 25 from the Mn$^{\text{II}}$Mn$^{\text{II}}$ to the Mn$^{\text{III}}$Mn$^{\text{III}}$ oxidation state in methanol is reversed upon addition of DCl. The same behaviour was observed with 26, in which a μ$_{1,3}$-chloroacetate bridging ligand is present instead of a μ-acetate bridge. In the case of 23 only six broad signals were observed by $^1$H NMR spectroscopy of upon addition of NaOD, which are assigned to the D$_2$O exchangeable protons on the benzimidazole moieties. The coordination mode of the carboxylate group of the complexes was determined by FTIR spectroscopy. 23 showed two modes at 1564 and 1427 cm$^{-1}$ assigned to the asymmetric and symmetric stretching mode of a symmetrical μ-bridging acetate ($\Delta \nu = 137$ cm$^{-1}$). The FTIR spectrum of the Mn$^{\text{III}}$Mn$^{\text{III}}$ form of 23 showed absorptions at 1564 cm$^{-1}$ disappeared and a new strong absorption at 1627 cm$^{-1}$ appeared, which was assigned to the monodentate coordination of acetate (the absorption from non-coordinated carboxylate appears at 1578 cm$^{-1}$). The 63 cm$^{-1}$ shift of the $\nu_{as}$ stretches confirmed the monodentate coordination of acetate. In the case of 24-26, a shift to higher wavenumber was observed as well upon oxidation from the Mn$^{\text{II}}$Mn$^{\text{II}}$ to the Mn$^{\text{III}}$Mn$^{\text{III}}$ oxidation state. The asymmetric carboxylato stretch increased from 1596 to 1629 (24), 1564 to 1632 (25) and 1592 to 1624 cm$^{-1}$ (26). Furthermore a new absorption band appeared between 583-590 cm$^{-1}$, which was assigned to a $\nu_3$ (Mn–O–Mn) stretch.
Although signals were not observed for 23 and 24 by ESI-MS, signals were observed for 25 and 26 with a base signal at \( m/z = 989 \) for 25 assigned to \([\{L^2 \text{Mn}^{II} \text{Mn}^{II}(\mu-\text{OAc})\}\text{ClO}_4]\)^+. Its intensity decreased upon addition of NaOH and two new signals appeared at \( m/z = 1048 \) and 949 assigned to \([\{L^2 \text{Mn}^{III} \text{Mn}^{III}(\mu-\text{O})\}\text{ClO}_4]\)^2^+ and \([\{L^2 \text{Mn}^{III} \text{Mn}^{III}(\mu-\text{O})\}\text{ClO}_4]\)^2^+ appeared. Notably, no evidence for an acetate bound to the Mn^{III}Mn^{III}(\mu-\text{O}) complex was obtained in the presence of more than 2 equiv. of NaOH, while for the Mn^{II}Mn^{II} complexes of 23 and 25, a bound acetate was observed. It was suggested that there is an unbound or weakly bound acetate, which dissociated under the conditions of the ESI-MS for the oxidized complex Mn^{III}Mn^{III}, since a bound monodentate acetate was observed with \(^1\)H NMR spectroscopy (\textit{vide supra}).

Scheme 4 Structural changes occurring upon addition of NaOH to complexes 23-26 in acetone.

In acetone (Scheme 4), in the absence of dioxygen, 23 is oxidized at \( E_{1/2} = 0.745 \) V in a quasi-reversible two electron process, with a second one electron oxidation at \( E_{1/2} = 1.25 \) V (Mn^{III}Mn^{III} \( \leftrightarrow \) Mn^{III}Mn^{IV}). Addition of NaOH resulted in the appearance of three new redox waves, two of which are irreversible, at 0.35 and 0.50 V, and overlap followed by a quasi-reversible oxidation at \( E_{1/2} = 0.98 \) V. The effect of NaOH on the redox chemistry of 23, which is in the Mn^{II}Mn^{II} redox state, is to change the two electron oxidation (Mn^{II}Mn^{II} \( \leftrightarrow \) Mn^{III}Mn^{III}) to two one-electron oxidation steps (Mn^{II}Mn^{II} \( \leftrightarrow \) Mn^{II}Mn^{III} \( \leftrightarrow \) Mn^{III}Mn^{III}) indicating an increase in the interaction between the two manganese centres, that are relatively isolated redox centres, through binding of the first equivalent of hydroxide to 23. The addition of a second equivalent of hydroxide resulted in a change of the two one electron processes to an irreversible two electron process at higher potential \( E_{1/2} = 0.6 \) V, which was rationalized by the binding of the second hydroxide to
form a symmetrical Mn$^{II}$Mn$^{II}$($\mu$-acetato)($\mu$-OH)(OH) complex with two terminal hydroxido ligands. Bulk electrolysis at 1.4 V vs SCE in the presence of 2 equiv. of hydroxide resulted in the appearance of a new species with an absorption maximum at 490 nm ($\varepsilon_{\text{max}} = 330$ M$^{-1}$ cm$^{-1}$) and a silent EPR spectrum as expected for an antiferromagnetically coupled Mn$^{IV}$Mn$^{IV}$ complex. The changes observed were reversed by addition of HClO$_4$. It was proposed that the stabilization of the higher oxidation states of 23, i.e. Mn$^{III}$Mn$^{III}$, Mn$^{II}$Mn$^{IV}$, and Mn$^{IV}$Mn$^{IV}$ was due to hydroxide coordination rather than deprotonation of the NH groups of the benzimidazoles, based on comparison with 25, in which the ligand is alkylated. Furthermore, addition of a non-coordinating base 2,6-di(t-butyl)pyridine to 23 resulted in changes to its cyclic voltammetry, in contrast to 25, for which no effect was observed confirming that the hydroxide acts as a ligand rather than simply a base.

In summary, carboxylate and hydroxido ligands undergo relatively facile exchange when the complex is in the Mn$^{II}$Mn$^{II}$ oxidation state, with both monodentate and bridging coordination modes observed in both cases. These changes in coordination mode of the carboxylato ligand, from bidentate to monodentate, are central to allowing other small molecules to bind to the manganese ions, a process referred to as a carboxylate shift, to provide the free site on the manganese centre for coordination. Importantly, as the oxidation state is increased, the exchange of carboxylato ligands for oxido ligands and especially bridging oxido ligands becomes increasingly pronounced, and driven in part by the stabilization that these more electron rich ligands provide.

In methanol by 23 is characterized by a lag phase, which is decreased by pre-equilibration of the complex with ~2% water. In addition, the reaction rate was increased by 5-6 fold by addition of water. Assuming a Michaelis-Menton model, the $k_{\text{cat}}$ and $K_M$ for 23 showed $10^5$−$10^6$ lower catalytic efficiency ($k_{\text{cat}}/K_M$) compared to the catalase enzymes from T. thermophilus and from T. album. Further reductions in lag time or increase in reaction rate were not observed upon further increases in the water content. The effect of water was proposed to be due to dissociation of the $\mu$-acetato ligand and indeed addition of excess acetate resulted in an increase in the lag phase and reduction in reaction rate. Notably addition of 1 equiv. of NaOH removed the lag phase completely and resulted in an increase in reaction rate with the observed rate constant ($k_{\text{obs}}$) of 1 M$^{-1}$ s$^{-1}$ increasing to 92 M$^{-1}$ s$^{-1}$ (with 5 equiv. of NaOH) and to 100 M$^{-1}$ s$^{-1}$ (with 8 equiv. of NaOH). The increase in reaction rate was ascribed to the deprotonation of the H$_2$O$_2$.

**Scheme 5** Activation and catalytic cycling between Mn$^{II}$Mn$^{II}$ and Mn$^{III}$Mn$^{III}$ redox states.
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\[ [\text{LMn}^{\text{II}}\text{Mn}^{\text{II}}(\mu-\text{OH})(\mu-\text{OAc})]^+ \text{(28a)} \] and the (inactive) \[ [\text{LH Mn}^{\text{II}}\text{Mn}^{\text{II}}(\mu-\text{OAc})]^3^+ \text{(29)} \] (the neutral ligand (LH) with a protonated alkoxide group (alcohol)), which was observed by EPR spectroscopy as a spin-uncoupled Mn\(^{\text{II}}\) species and shows lower activity towards \(\text{H}_2\text{O}_2\) disproportionation. Hence, only a partial elimination of the lag phase was observed in the presence of water. In contrast to the decrease in the reaction rate upon the addition of more than 2% water without hydroxide, increasing the amount of water from 98/2 v/v methanol/water to 11/89 v/v methanol/water for 23 and presence of 5 equiv. of NaOH resulted in an increase in the \(k_{\text{obs}}\) from 9.2 M\(^{-1}\) s\(^{-1}\) to 24.8 M s\(^{-1}\), which was attributed to enhancement of the rate of proton exchange. In the presence of the non-coordinating base 2,6-di(tertbutyl)pyridine, no change in the lag phase nor in \(\text{O}_2\) evolution rate was observed for complexes 23-26, confirming that ligand deprotonation is not involved.

The \(^1\text{H}\) NMR spectrum of 30 (which was generated by addition of 4-5 equiv. of NaOH to 25) in CD\(_3\)OD was similar to that of 27 (which was obtained by addition of 1 equiv. of NaOH to 25) after addition of 10 or 20 equiv. of \(\text{H}_2\text{O}_2\). The dependence of reaction rate on the concentration of 30 indicated that it is the resting state in the catalytic cycle. \(^1\text{H}\) NMR spectra obtained under catalytic conditions indicated that only one Mn\(^{\text{III}}\)Mn\(^{\text{III}}\) complex is present with two pairs of non-equivalent N-H protons and a monodentate acetato ligand on one of the manganese ions. It was also suggested that 27 and 30 are in equilibrium in aqueous solvents, and that the substitution of the hydroxido ligand by \(\text{H}_2\text{O}_2\) is facilitated by protonation. The rate limiting step in the \(\text{H}_2\text{O}_2\) disproportionation was proposed to be the oxidation of Mn\(^{\text{II}}\)Mn\(^{\text{II}}\) to Mn\(^{\text{III}}\)Mn\(^{\text{III}}\) species. Hence, for 28a, which is oxidized at lower potentials than 23-26, the 6.5-fold increase in \(k_{\text{cat}}\) was rationalised as due to a lowering of the activation energy in the oxidation step.

![Scheme 6](image)

**Scheme 6** Catalytic cycle for disproportionation of \(\text{H}_2\text{O}_2\) by 23-26
Based on the kinetic studies of the catalysed decomposition of H$_2$O$_2$ and also previous speciation analysis of these complexes, the mechanism shown in Scheme 6 was proposed for the disproportionation of H$_2$O$_2$ catalysed by the hydroxide containing derivatives of complexes 23 and 25.

28a, which bears three µ-bridging anions, is in equilibrium with species 28a', which bears a terminal acetate and an aqua ligand. The increase in the rate of the reaction with complex 28a and 28a' was proposed to be due to the lower activation barrier to the oxidation step compared with 23 and 25, which do not bear an OH group. This hypothesis requires that the rate limiting step is oxidation of 28a or 28a' to a Mn$^{III}$Mn$^{III}$ species such as 30. The thermodynamically favourable displacement of H$_2$O by H$_2$O$_2$ (steps A to B) is facilitated by the presence of the hydroxide bridge, and the propensity for the acetato ligand to switch between bridging and monodentate coordination. In the next steps (C and D), the cleavage of the hydroperoxide was proposed to be coupled with oxidation of the Mn$^{II}$Mn$^{II}$ complex to the Mn$^{III}$Mn$^{III}$ state. The oxidation of 28a under aerobic conditions shows direct formation of 30. Binding of a second molecule of H$_2$O$_2$ occurs in step D with stabilization of 31 proposed to be via intramolecular H-bonding between the terminal hydroperoxide and acetato ligand. The last step included the re-formation of complex 28a/28a' by protonation and reduction of 31 and formation of O$_2$.

Singorella et al. reported a water-soluble Mn$^{III}$Mn$^{III}$ mimetic of the active site of manganese catalases: Na[Mn$^{III}$Mn$^{III}$]-{3-Me-5-SO$_3$-salpentO)(µ-OAc)(µ-OMe)(H$_2$O)}-4H$_2$O (32), where 3-Me-5-SO$_3$-salpentOH = 1,5-bis(3-methyl-5-sulphonatosalicylideneamino)pentan-3-ol and its catalase activity in protic and aprotic solvents. The IR spectrum of 32 showed absorptions at 1558 and 1432 cm$^{-1}$, characteristic for the asymmetric and symmetric stretching vibrations of a µ-OAc ligand. The paramagnetic $^1$H NMR spectrum of 32 in CD$_2$OD confirmed that this complex retained its dinuclear structure in solution. Addition of NaOH (from 1 to 5 equiv.) did not result in a change to the aromatic hydrogen signals, but the intensity of the hydrogen signals of the bridging acetate decreased and disappeared upon addition of 5 equiv. of base. These observations, together with ESI-MS, suggested that in basic solution the bridging acetate converted into a monodentate terminal ligand and remains connected to the complex.

32 showed one quasi-reversible wave at $E_{1/2}$ 0.095 V, assigned to the Mn$^{III}$Mn$^{III}$/Mn$^{III}$Mn$^{II}$ redox couple. An irreversible reduction was observed at $E$ = −0.570 V assigned to the Mn$^{III}$Mn$^{II}$/Mn$^{II}$Mn$^{II}$ couple, by analogy with related complexes. Addition of base (Et$_3$N) did not affect the cyclic voltammetry of 32, which excluded the formation of a Mn$^{III}$Mn$^{III}$ (µ-O) complex in agreement with the $^1$H NMR spectral data. The activity of 32 in the disproportionation of H$_2$O$_2$ (150 equiv) was highest in DMF, and lowest (70 equiv) in water. It was suggested that the bridging ligands of the complex act as internal bases and promote deprotonation of the H$_2$O$_2$. However, in protic solvents, protonation of these ligands can lead to the inactivation of the catalyst and dissociation of the ligand. The catalytic activity of 32 in basic water showed generation of O$_2$ but the initial rate of H$_2$O$_2$ disproportionation decreased after each addition. Addition of excess H$_2$O$_2$ resulted in a loss in absorbance at 375 nm, indicative of partial decomposition of the catalyst, which is in agreement with ESI-MS data that showed a decrease of the peak related to Na$_2$[Mn$^{III}$Mn$^{III}$]{µ-OAc}{µ-OMe}L$^+$ (m/z 755.3) and an increase of peaks...
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corresponding to Na₃[Mn³⁺L⁺] (m/z 633.0) and H₂[L(MeOH)]⁺ (m/z 546.1). EPR spectroscopy confirmed the presence of the Mn³⁺(aq) ion (α = 90 G).

The appearance of a band at 528 nm, which showed a pronounced vibrational progression, and a strongly resonantly enhanced Raman band at 834 cm⁻¹ (λₑₓᶜ = 514 nm) in basic solution during the disproportionation of H₂O₂ are consistent with an oxido-Mn⁴⁺ LMCT transition and a Mn⁴⁺=O stretching vibration, respectively. The constant activity of the complex and the appearance of the spectral features of a Mn⁴⁺=O species upon successive additions of H₂O₂ indicated that the ligand remained coordinated to the manganese complex. Indeed the reaction rate was first order in catalyst and, since no lag phase was observed at the start of the reaction, it was proposed that 32 was responsible for the disproportionation of H₂O₂. The efficiency of the catalyst, expressed in terms of k₉cat/KM, was improved compared to other alkoxido- or phenoxido- bridged complexes reported until then. The complex showed higher affinity for the substrate which at pH 10.6 is HO₂⁻ vs H₂O₂. As noted above, the activity and affinity of the complex depended on the pH. Hence, in non-buffered solution of protic solvents the loss of activity of the complex was observed due to changes in pH as disproportionation proceeded.

The exchange of the carboxylato ligand with hydroxide and hydroperoxide in five complexes [Mn³⁺Mn⁴⁺(μ-4-RC₆H₄COO)₂(μ-O)(bpy)₂(H₂O)₂](NO₃)₂ [R = Me (33), F (34), CF₃ (35), MeO (36) and tBu (37)] was investigated by Corbella et al. Magnetic susceptibility data for the complexes showed behaviour typical of a ferromagnetically coupled Mn³⁺Mn³⁺ complex and the strength of the coupling correlated with the Hammett parameters (σ) with increasing coupling correlating with increasing electron-withdrawing character of the carboxylate ligand.

Complexes 33-37 showed activity towards the catalytic disproportionation of H₂O₂ in CH₃CN at 25 °C. The rate of the H₂O₂ decomposition increased as its concentration was increased and the efficiency of the complexes was found to correlate with Hammett parameters for the carboxylato ligands’ R groups: 36 (MeO) > 37 (tBu) > 33 (Me) > 34 (F) > 35 (CF₃). The small difference in the catalytic activity of 34 (F) and 35 (CF₃) was attributed to the difference in structure of these complexes. UV/vis absorption and EPR spectroscopy before and after addition of H₂O₂ indicated that Mn³⁺Mn⁺ complexes were formed upon addition of H₂O₂, with no evidence for mixed-valence species such as Mn³⁺Mn⁺⁺ or Mn³⁺Mn⁺. The integrity of the complexes towards ligand dissociation was confirmed by their activity over multiple cycles of addition of H₂O₂ compared with that of Mn³⁺(NO₃)₂.

Latour and co-workers have studied the reactivity of the complexes [Mn³⁺Mn⁴⁺(μ-O)₂(tpa)₂](ClO₄)₂ (38) and [Mn³⁺Mn⁴⁺(μ-O)₂(bpg)₂](ClO₄)₂ (39), [{Mn₂(pda)₂(O)₂}Na(H₂O)₆]₄ (40) and [Mn₂(O)₂(nita)₂]Na₃ (41) (where tpa=tris-picolylamine, H(bpg)=bispicolylglycylamine, H₂(pda)=picolyldiglycylamine, H₃(nita)=nitrolotriacetic acid) to explore the influence of the number of carboxylato moieties in the tripodal ligands on electronic properties and activity towards H₂O₂ disproportionation, mimicking the carboxylato-rich active site of the manganese catalase enzymes (vide supra). The corresponding Mn³⁺Mn³⁺(μ-O)₂ complexes were generated by one-electron reduction. ¹⁸O labelling allowed for assignment of the Mn-O oxido stretching band at 660 cm⁻¹. The results showed a trend in the exchange interaction, which became less antiferromagnetic in the
order $38 (J=161 \pm 5 \text{ cm}^{-1}) < 39 (J=142 \pm 5 \text{ cm}^{-1}) < 40 (J=133 \pm 9 \text{ cm}^{-1})$. This order is in agreement with the strengths of the Mn-O$_{\text{oxide}}$ bonds, as revealed by the structural and infrared studies, indicating that the carboxylato ligands affect the strength of the Mn-O-Mn bonds. The electronic absorption spectra of $38-40$ showed bands at ca. 380 nm assigned to $\pi \rightarrow \pi^*$ transitions of the pyridine moieties. The half-width at middle height of the EPR signals decreases by ca. 0.1–0.2 mT on going from $38$ to $40$ and more importantly (by ca. 0.35 mT), to $41$, which is consistent with the reduction in the number of nitrogen hyperfine couplings.

$38$ and $39$ showed two reversible redox couples ($i.e.$ reduction to the Mn$^{III}$Mn$^{III}$($\mu$-O)$_2$ species and oxidation to the Mn$^{IV}$Mn$^{IV}$($\mu$-O) species). Replacement of pyridine moieties by carboxylates lowered the oxidation potential of the Mn$^{III}$Mn$^{IV}$/Mn$^{IV}$Mn$^{IV}$ and Mn$^{III}$Mn$^{IV}$/Mn$^{IV}$Mn$^{IV}$ redox couples as expected due to stabilization of higher oxidation state by anionic carboxylato ligands. The exchange of the $\mu$-oxido ligands was determined in acetonitrile and acetonitrile/methanol (4:1) by ESI-MS and showed that replacement of pyridine moieties by carboxylates accelerated the rate of exchange. A similar effect was observed upon reduction of the [MnMn($\mu$-O)$_2$] core from the mixed-valent state [Mn$^{III}$Mn$^{IV}$] to [Mn$^{III}$Mn$^{III}$] for which the exchange rate of oxido ligands was increased by a factor of 84. Since oxido exchange involves the deprotonation of a molecule of water, it was suggested that the basic character of carboxylate moiety could play a significant role in the observed rate enhancement.

Addition of HClO$_4$ to $38$ in acetonitrile inhibited the disproportionation of H$_2$O$_2$ while addition of trimethylamine increased the reaction rate. These observations are consistent with the increase in H$_2$O$_2$ decomposition rate observed upon substitution of pyridine moieties by carboxylato moieties. In the case of the Mn$^{III}$Mn$^{IV}$ complexes, EPR spectroscopy showed that the 16-line spectrum was lost at the end of the reaction and was replaced by a poorly resolved six-line EPR spectrum typical of Mn$^{II}$. ESI-MS, together with H$_2^{18}$O$_2$ (3% in H$_2^{16}$O), showed that immediately after addition of H$_2$O$_2$, $39$ incorporates oxido ligands from H$_2$O$_2$, which are lost subsequently by exchange with the H$_2^{16}$O$_2$, which suggested that the $\mu$-oxido bridged complex is a stage in the catalytic cycle. It was proposed that the higher reaction rates observed for the carboxylate bearing complexes was related to the ability of carboxylate ligands to act as internal bases. This effect is important in the catalase reaction, as deprotonation of H$_2$O$_2$ provides protons for transfer to $\mu$-oxido ligands, which can dissociate as water.

Fernandes et al. reported a mononuclear water-soluble complex [Mn$^{IV}$]$_2$(HPCLNOL)(η$^1$-NO$_3$)(η$^2$-NO$_3$)], $42$ (where HPCLNOL is 1-(bis-pyridin-2-ylmethyl-amo)-3-chloropropan-2-ol), which can engage in H$_2$O$_2$ disproportionation, and proposed the formation of a dinuclear species under reaction conditions (vide infra). $42$ showed two redox processes at 0.65 V and 0.92 V assigned to oxidation of Mn$^{II}$ to Mn$^{III}$ and subsequently to Mn$^{IV}$ and, as expected for a Mn$^{II}$ complex, exhibited no absorption in the visible region, and only ligand based $\pi \rightarrow \pi^*$ transitions in the UV.$^{163}$ Addition of H$_2$O$_2$ resulted in the appearance of broad absorption bands and shoulders at ca. 410, 539, and 620 nm, which were similar to those observed for Mn$^{III}$/Mn$^{IV}$($\mu$-oxido)$_2$ complexes containing the tripodal ligands bpa, $^{164}$ tpa, bpg and pda.$^{161}$ The band at highest energy was attributed to an oxido $\rightarrow$ Mn$^{IV}$ charge-transfer transition (LMCT), while the others ($\lambda = 500–560$ nm, $\lambda = 590–600$ nm) were assigned to Mn$^{IV}$ d–d transitions.$^{92}$
The visible absorption decreased faster over time in non-buffered solutions than in buffered solutions, which was ascribed to the degradation of the Mn$^{IV}$Mn$^{III}$($\mu$-O)$_2$ core due to either protonation or reaction with Mn$^{II}$ to form Mn$^{III}$ species. Furthermore, in the non-buffered system a change in pH during H$_2$O$_2$ decomposition was observed, which correlated with the onset of catalytic activity. The second change (increase) in pH was suggested to be due to the protonation of the $\mu$-oxido group and finally the subsequent decrease in pH occurred, concomitant with the conversion of H$_2$O$_2$ to O$_2$ and water. The appearance of a peak at m/z 722 in the ESI-MS, immediately after the addition of H$_2$O$_2$ and its increase over the course of the reaction was consistent with the formulation [(PCINOL)Mn$^{III}$-(μ-oxido)$_2$-Mn$^{IV}$ (PCINOL)]$^+$ (species C in Scheme 7). The protonation of the $\mu$-oxido bridge in species C was suggested to be the rate limiting and the inactivation of complex F in the presence of excess of H$_2$O$_2$ resulted in a decrease in the amounts of species C present and hence dioxygen evolution.

Scheme 7 Catalytic cycle for the decomposition of H$_2$O$_2$ by 42.
Chapter 1

The catalytic activity of 42 in the oxidation of cyclohexane using $\text{H}_2\text{O}_2$ or tert-butylhydroperoxide (t-BuOOH) as oxidant was studied also. The activity of 42 in the oxidation of cyclohexane would require that the oxidised state of 42 react with the substrate faster that with $\text{H}_2\text{O}_2$. Higher yields were obtained with t-BuOOH as oxidant. There was no indication of formation cyclohexyl peroxides as products in the reactions between 42 and $\text{H}_2\text{O}_2$ at room temperature which supported that radical species are not formed under these conditions. In contrast, when t-BuOOH is sued alkyl peroxides were observed.

Overall it can be concluded that in the functional models for dinuclear manganese based catalases, carboxylato shifts as well as exchange of aqua ligands is key to the activity observed. Importantly, the changes in coordination mode as the redox state shuttles between Mn$^{\text{II}}$Mn$^{\text{II}}$ and Mn$^{\text{III}}$Mn$^{\text{III}}$ states make reduction and then oxidation of $\text{H}_2\text{O}_2$ thermodynamically possible.

**Manganese catalysed dismutation of superoxide**

Superoxide is a particularly toxic reactive oxygen species (ROS) and its dismutation *in vivo* is necessary to keep its concentration low (8-40 pM). Superoxide dismutases (SODs) are metalloenzymes that catalyse the conversion of superoxide radicals ($\text{O}_2^-$) to $\text{H}_2\text{O}_2$ and $\text{O}_2$. Manganese superoxide dismutase (MnSOD) is present in mitochondria where it protects cells under conditions of aerobic metabolism. The enzymatic reaction consists of two distinct reactions, an oxidative reaction in which the substrate, $\text{O}_2^-$, is oxidized to dioxygen and a reductive half-reaction in which $\text{O}_2^-$ is converted to $\text{H}_2\text{O}_2$.

\[
\text{O}_2^- + \text{Mn}^{\text{III}}\text{SOD} \rightarrow \text{O}_2 + \text{Mn}^{\text{II}}\text{SOD}
\]

\[
\text{O}_2^- + 2\text{H}^+ + \text{Mn}^{\text{II}}\text{SOD} \rightarrow \text{H}_2\text{O}_2 + \text{Mn}^{\text{III}}\text{SOD}
\]

Several complexes containing metals such as copper, iron, manganese, or cobalt ions have been prepared as functional mimics. Cisnetti and co-workers reported the activity of the dinuclear complex $\[(\text{L})\text{Mn}^{\text{II}}\text{Mn}^{\text{II}}(\text{L})\]_2[\text{PF}_6]_2$ [43] (where LH = $N$-(2-hydroxybenzyl)-$N,N'$-bis[2-(N-methylimidazolyl)methyl]ethane-1,2-diamine) in aqueous solution. The UV/Vis absorption spectrum of 43 showed ligand based absorption bands in the UV region ($\lambda_1 = 287 \text{ nm}$, $\epsilon_1 = 4909 \text{ M}^{-1} \text{ cm}^{-1}$) as expected for a dinuclear Mn$^{\text{II}}$Mn$^{\text{II}}$ complex. In acetonitrile, 43 underwent a two electron oxidation at $E_{1/2} = 0.485 \text{ V}$ vs. SCE (Mn$^{\text{II}}$Mn$^{\text{II}}$/Mn$^{\text{III}}$Mn$^{\text{III}}$) at potentials lower than the analogous complex bearing a pyridine-containing ligand, as expected for the greater electron-donating strength of the imidazole group in 43. The second and third redox waves at $E_{p} = 1.4, 1.7 \text{ V}$ were assigned tentatively to Mn$^{\text{III}}$Mn$^{\text{III}}$$\rightarrow$Mn$^{\text{IV}}$Mn$^{\text{III}}$ and phenolato oxidation, respectively.

Oxidation at 0.8 V resulted in the appearance of two new absorption bands at 403 and 672 nm, assigned to a phenolato to Mn$^{\text{III}}$LMCT transition and a d-d transition, respectively, and an EPR silent solution as expected for the formation of a Mn$^{\text{IV}}$ complex. The bis-$\mu$-phenolato bridge has been shown to be relatively unstable compared to a $\mu$-oxido bridge undergoing dissociation to form two mononuclear $\[(\text{L})\text{Mn}^{\text{III}}(\text{S})\]^{2+}$ complexes, where S is water or solvent. The second redox wave,
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$[(L)\text{Mn}^{\text{III}}(\text{OH}_2)]^{2+}/[(L)\text{Mn}^{\text{IV}}(\text{OH}_2)]^{3+}$, disappeared upon the addition of base (2,6-lutidine) with the concomitant appearance of a new redox wave at 1.02 V vs. SCE, $[(L)\text{Mn}^{\text{III}}(\text{OH})]^{+}/[(L)\text{Mn}^{\text{IV}}(\text{OH})]^{2+}$. Reduction of the mononuclear $[(L)\text{Mn}^{\text{III}}(\text{OH}_2)]^{2+}$ species to $[(L)\text{Mn}^{\text{II}}(\text{OH})]^{+}$, in aqueous solution with the non-coordinating buffer piperazine-$N,N'$-bis(2-ethanesulfonic acid) (PIPES), results in a six line EPR signal at $g = 2$, which is typical a mononuclear Mn$^{\text{II}}$ complex. Comparison of the cyclic voltammogram of complex 43$(\text{PF}_6)_2$ with Mn$^{\text{II}}$(ClO$_4$)$_2$ and Mn$^{\text{II}}$Cl$_2$ in PIPES (piperazine-$N,N'$-bis(2-ethanesulfonic acid) showed no similarity, which, together with EPR data, suggested that in aqueous solution the Mn$^{\text{II}}$ remained coordinated to L. Indeed ESI-MS in water showed an ion assigned to $[(L)\text{Mn}]^+$. The superoxide dismutation activity of mononuclear cation was determined using the McCord–Fridovich assay, and shown to be amongst the most active Mn$^{\text{II}}$ complex reported, which was attributed to the fact that the potential of the Mn$^{\text{II}}$/Mn$^{\text{III}}$ couple of $[(L)\text{Mn}^{\text{II}}]^{+}$ at ($E_{1/2} = 0.199$ V vs. SCE) is close to the optimum 0.12 V vs. SCE at pH 7.

Mechanistic studies in manganese catalysed alkene oxidation in organic solvents

Catalyst activation of H$_2$O$_2$ and O$_2$ has been a highly active area of research over the last decades with catalysts based on transition metals at the forefront of these efforts, in particular those based on titanium, vanadium, rhenium, and tungsten, primarily in their oxide forms and on iron, copper and cobalt, with carboxylate, amine and pyridyl based ligands. Manganese, the focus of the present chapter, and its complexes have seen widespread application in both fine and bulk chemical processes as catalysts for the activation of H$_2$O$_2$ especially. In the many oxidation reactions catalysed by manganese complexes, the active species involved in oxygen transfer and in C-H oxidation is frequently proposed to be a Mn$^{\text{V}}=$O moiety (e.g., LMn$^{\text{V}}=$O$^{36,37,181,182}$). Observing such active species is, however, highly challenging and indeed those Mn$^{\text{V}}=$O complexes that have been isolated from solution, have been found to be either incapable of converting olefins to epoxides or relatively unreactive at most.$^{124,125,183,184,185}$ Isotope labelling $^{18}$O has therefore proven invaluable in establishing Mn$^{\text{V}}=$O species as active intermediates in olefin epoxidation.$^{31,186,187}$

Manganese porphyrins and salen complexes have been studied intensively in epoxidations with a wide range of oxidants, primarily iodosylarenes, alkylhydroperoxides, meta-chloroperbenzoic acid ($m$CPBA) and hypochlorite.$^{7a}$ Activation of H$_2$O$_2$ is the primary focus of this chapter and a few examples of porphyrin complexes, employing H$_2$O$_2$ as terminal oxidant, have been reported also.$^{188}$ H$_2$O$_2$ disproportionation by manganese salen complexes usually competes with epoxidation, reducing efficiency in oxidant. However, additives with bulky groups, such as imidazoles and carboxylates which promote the formation of the Mn$^{\text{V}}=$O intermediates, as ascertained by ESI-MS as the actual epoxidising species, improved the performance of these catalytic systems. For a detailed discussion of manganese porphyrin, Schiff base and salen based systems and the reader is referred to several reviews covering these catalytic systems.$^4$ In this section, several examples of manganese based catalytic systems will be discussed in regard to mechanistic insights gained.
Busch and co-workers have studied the complex \([\text{Mn}^{II}(\text{Me}_2\text{EBC})]\)(\text{Cl})_2\) based on the cross-bridged cyclam ligand \(\text{Me}_2\text{EBC}\) (4,11-dimethyl-1,4,8,11-tetraazabicyclo[6.6.2]hexadecane), as a catalyst for oxidation reactions.\(^{190}\) UV/vis absorption spectroscopy of \(\text{Mn}^{II}\), \(\text{Mn}^{III}\) and \(\text{Mn}^{IV}\) complexes of this ligand upon reaction with \(\text{H}_2\text{O}_2\) or \(\text{t-BuOOH}\), in an aqueous solution, showed no evidence for the formation of a \(\text{Mn}^{V}\)-oxido species but rather \([\text{Mn}^{IV}(\text{Me}_2\text{EBC})(\text{OH})]\)^\(^{2+}\) has been confirmed to be the dominant species under neutral and acidic conditions. The absence of a stable \(\text{Mn}^{V}\) species is understandable considering that the ligand lacks the stabilising \(\pi\)-systems present in porphyrins and salen based ligands. It was proposed\(^{191}\) that the dominant mechanism for epoxidation by \(\text{Mn-Me}_2\text{EBC}\) employing \(\text{H}_2\text{O}_2\) is a Lewis acid activation pathway rather than a high valent \(\text{Mn}\)-oxo pathway; i.e. formation of \([\text{Mn}^{IV}(\text{Me}_2\text{EBC})(\text{O})(\text{OOH})]\)^\(^+\) from \([\text{Mn}^{IV}(\text{Me}_2\text{EBC})-(\text{O})(\text{OH})]\)^\(^+\). This peroxy complex is an inorganic peracid and transfers an oxygen atom directly to alkenes in a manner similar to that observed with organic peracids (Scheme 8). This mechanism was supported by ESI-MS under catalytic conditions by the detection of a signal assignable to \([\text{Mn}^{IV}(\text{Me}_2\text{EBC})(\text{O})(\text{OOH})]\)^\(^+\). Subsequent DFT studies by Haras and Ziegler, also support a mode of action of these complexes that involves a \(\text{Mn}^{IV}\)-OOH species.\(^{192}\)

**Scheme 8** Proposed Lewis acid mechanism for epoxidation of alkenes using \(\text{Mn}^{II}(\text{Me}_2\text{EBC})\text{Cl}_2\) and \(\text{H}_2\text{O}_2\).\(^{190}\)

### Manganese catalysed oxidations involving in situ generation of catalysts from well-defined manganese complexes

In many manganese based catalyst systems, especially for alkene oxidation, the use of additives to suppress \(\text{H}_2\text{O}_2\) disproportionation and to enhance catalytic activity has been widespread. Although this has increased dramatically the scope and activity of the catalysts, it has also raised many questions in regard to mechanism and the often complex roles the additives actually play. Furthermore, the initial form of the complex used as catalyst is not necessarily retained during catalysis and indeed different additives can lead to fundamentally different reaction pathways being followed by the one catalyst as will be highlighted in the following examples.

### Manganese aminopolypyridyl based oxidation catalysts

A rather extreme example of the changes that a catalyst undergoes in order to form the active catalytic species is found in a class of manganese complexes based on polyaminopyridyl based ligands.\(^{193}\) In early studies with this class of complexes it was concluded that high-valent manganese-oxido species were involved, however, as discussed above, such ligands are unlikely to stabilise such species (vide supra). A key
Redox state dependent ligand exchange in manganese based oxidation catalysis

to these systems with regard to mechanistic studies lay in the extensive disproportionation of \( \text{H}_2\text{O}_2 \) that competed with oxidation of substrates. The instability of this ligand class was first raised as an issue by Groni et al.\(^{194}\) in the identification of products arising from oxidation at the benzylic positions of these ligands, which Que\(^{195}\) and more recently Britovsek\(^{196}\) and coworkers have noted these pathways for iron complexes also.

Isolation of ligand degradation products by Pijper \textit{et al.}\(^{197}\) lead to the realisation that under certain conditions, \textit{i.e.} conditions used in several of the earlier studies\(^{193}\) dealing with the oxidation of alkenes and alcohols, oxidative ligand degradation to pyridine-2-carboxylic acid (PCA) was occurring rapidly under reaction conditions. Importantly, Pijper \textit{et al.} demonstrated that it was in fact the thus formed PCA that was the ligand responsible for the epoxidation activity observed and not the polypyridyl ligands used initially.

\textbf{Scheme 9} Oxidative decomposition of aminopolypyridyl ligands to pyridine-2-carboxylic, which was found to be the actually ligand responsible for the manganese based oxidation catalysis observed with \( \text{H}_2\text{O}_2 \) and alkenes.\(^{197}\)

The manganese pyridine-2-carboxylic acid system subsequently developed by Saisaha\(^{198}\) and Dong \textit{et al.}\(^{199}\) for the \textit{cis}-dihydroxylation and epoxidation of alkenes, as well as alcohol and alkane oxidation,\(^{200}\) presented a considerable challenge with regard to mechanistic studies due to the turn over frequencies (30 s\(^{-1}\)) and turn over numbers (>300,000) that could be achieved and the low catalyst concentrations employed (as low as 10 \( \mu \text{M} \)), which essentially precludes direct spectroscopic detection of reactive intermediates. This challenge, however, does not mean that insight into the mechanism by which oxidation takes place cannot be gained using spectroscopy. A key feature of the system is the \textit{in situ} formation of the catalyst from PCA, a manganese salt, a base (\textit{e.g.}, NaOH or NaOAc) and, most importantly, a ketone. The role of the ketone in the reaction was shown, by UV/Vis absorption and Raman spectroscopy, to be to form a hydroperoxide adduct together with the ketone present. The hydroperoxide formed was found to be the active oxidant, in the reaction and its formation was found to be rate controlling. The characteristic \( n-\pi^* \) absorption of butanedione, for example, was almost completely lost within several seconds of addition of \( \text{H}_2\text{O}_2 \) but recovered after the \( \text{H}_2\text{O}_2 \) concentration decreased below that of the butanedione. Formation of acetic acid by oxidative decomposition of butanedione was confirmed by \( ^{13}\text{C} \) NMR spectroscopy and constituted an important side reaction. The formation of peracetic acid was excluded under the reaction conditions employed, as peracetic acid does not react directly with electron deficient alkenes.\(^{199}\)

The formation of pyridine-2-carboxylic acid from aminopyridyl ligands in itself is of only secondary importance, \textit{i.e.} as a route to catalyst deactivation. However, although it is a very unlikely combination of conditions \textit{i.e.} the presence of a ketone solvent with
acetate, the catalytic systems obtained from the ligand degradation products is highly active in the oxidation of alkenes. This is perhaps an extreme example of a general challenge facing mechanistic studies – the identification of the catalyst, resting state and active species, actually engaging in the catalysis observed.

**Manganese tmtacn based oxidation catalysts**

As discussed above, the discovery of the catalytic activity of complexes based on the ligand 1,4,7-trimethyl-1,4,7-triazacyclononane (tmtacn), by Hage *et al.* in the mid-1990s, prompted interest in the capability of these complexes to engage the productive use of H₂O₂ in oxidation and bleaching catalysis. The application of manganese complexes of tnc ligands in oxidation catalysis was reviewed recently by Saisaha *et al.* and Watkinson *et al.* and hence only aspects with regard to the coordination and redox chemistry of the complexes and mechanisms will be discussed in this section.

Several studies in the late 1990s demonstrated that the catalytic activity of 17 increased with respect to catalytic oxidative transformations (such as alkene epoxidation) in the presence of certain additives, together with suppression of the disproportionation of H₂O₂. De Vos *et al.* demonstrated that efficient epoxidation of a wide range of alkenes with decreased H₂O₂ decomposition could be achieved by addition of carboxylic acids such as fumaric acid or the use of an oxalate buffered solution. Shortly after, Berkesser and Sklorz noted that addition of L-ascorbic acid and sodium ascorbate was also effective in both regards. Shul’pin and co-workers demonstrated that the addition of a large excess of acetic acid (w.r.t. substrate) was effective in promoting the C-H oxygenation activity of 17.

More recently, attention has focused on understanding the mechanism by which 17 catalyses reactions and in particular the role played by the various additives that were reported to enhance catalytic efficiency. de Boer *et al.* showed that carboxylic acids served multiple roles in facilitating the oxidation of alkenes by 17, *i.e.* to protonate 17 and thereby shifting its reduction potential positively to allow reduction, to suppress disproportionation of H₂O₂, to act as a ligand in, for example, 9 and to stabilise the complex under reaction conditions. Notably, a substantial lag period prior to the onset of substrate conversion was observed in reactions with 17 where H₂O₂ was added continuously. UV/Vis absorption spectroscopy confirmed that at the end of the lag period a sudden conversion of 17 to the bis-µ-carboxylato bridged complex 9 occurred concomitant with the onset of alkene oxidation. Although the precise origin of the lag phase is still unclear, cyclic voltammetry and spectroelectrochemistry confirmed that the reduction of 17 by H₂O₂ required prior protonation (by a carboxylic acid) of the complex and that, upon reduction, a rapid cascade of reactions lead ultimately to near quantitative conversion of 17 to 9 (*vide supra*). The assignment of 9 as a resting state of the catalyst was confirmed by the absence of a lag period when it was used as catalyst in place of 17.

Identifying the role the carboxylic acid plays as a ligand was key to understanding the effect that variation in the carboxylic acids had on both reactivity (increasing with an increase in the electron deficiency of the carboxylato ligand) and selectivity w.r.t to epoxidation/cis-dihydroxylation (with preference for the cis-diol product increasing with the steric bulk of the 2,6- position of benzoic acids).
A key question remains, however, as to the nature of the species that engages in oxygen transfer to the substrate. Regardless of its specific structure, with the exception of oxalic acid\textsuperscript{108} (\textit{vide infra}), the conversion of alkenes to both cis-diol and epoxide products began simultaneously at the end of the lag period, which suggested that a common active species is responsible for both cis-dihydroxylation and epoxidation. Furthermore, the oxidation activity of 17 (with CCl\textsubscript{3}CO\textsubscript{2}H) observed in solvents other than acetonitrile, \textit{e.g.}, acetone, \textsuperscript{1}BuOH/H\textsubscript{2}O and THF, correlated to the stability of 9 in those solvents, \textit{i.e.} the less stable 9 was found to be, the shorter the time for which reactivity was observed. A further point is that complex 9 was found to be relatively stable in the presence of H\textsubscript{2}O\textsubscript{2}, whereas is related complexes 9a-c underwent immediate conversion to 9 upon addition of H\textsubscript{2}O\textsubscript{2}. It is apparent therefore that 9 is a either a resting state in the cycle with its reaction with H\textsubscript{2}O\textsubscript{2} being the rate limiting step or it is a reservoir for the catalytically active species. Direct oxygen transfer from 9 was excluded also. The latter observation that moderate (>50\%) enantioselectivity in cis-dihydroxylation could be achieved using chiral carboxylic acids confirmed that the form of the catalyst engaged in oxygen transfer bears at least one carboxylato ligand.\textsuperscript{204}

Although, mononuclear high valent species are frequently proposed as the active species in regard to oxygen transfer to substrate, the data available support the involvement of dinuclear structures that are similar to 9. The model most consistent with the experimental data available is one in which a Mn\textsuperscript{III}(O−OH)Mn\textsuperscript{III}(OH) species is formed by reaction of 9 or 9b with H\textsubscript{2}O\textsubscript{2}. Such a first step is consistent with an associative mechanism for the exchange of the μ-oxido bridge with H\textsubscript{2}\textsuperscript{18}O (\textit{vide supra}) and is consistent with the increase rate of H\textsubscript{2}\textsuperscript{18}O exchange and catalytic activity observed with electron-deficient carboxylates such as μ-CCl\textsubscript{3}CO\textsubscript{2}. The presence of a proximal Mn\textsuperscript{III}-OH to the Mn\textsuperscript{III}-O-OH bond would be expected to polarized the O-O bond allowing for heterolytic rather than homolytic cleavage. For the cis-diol product one oxygen originated from H\textsubscript{2}O\textsubscript{2} and one from H\textsubscript{2}O. In contrast, for the epoxide, oxygen incorporation from both H\textsubscript{2}O\textsubscript{2} as well as from H\textsubscript{2}O was observed, the ratio dependent upon the μ-carboxylate bridging ligand, with increased electron withdrawing character favouring incorporation of oxygen from water.

![Scheme 10 Proposed catalytic cycle for 9 in the oxidation of alkenes.\textsuperscript{108}](image)

In contrast, several mechanistic studies on Mn-tmtacn catalysts have led to mono or dinuclear high valent oxidising species being proposed.\textsuperscript{205} Lindsay Smith and co-workers
studied the oxidation of a range of phenolic substrates and azo dyes by 17 in the presence and the absence of H₂O₂ in basic aqueous solution. A catalytically active mononuclear manganese species was proposed based on kinetic and EPR studies.²⁰⁶,²⁰⁷,²⁰⁸

The oxidation of phenols and epoxidation of cinnamic acid by a combination of tmtacn ligand and Mn²⁺ salt was studied by ESI-MS from which high-valent Mn⁴⁺=O and Mn⁵⁺=O species were proposed.²⁰⁷ Of particular interest was the effect of additives (and potential co-ligands) on the rate of conversion observed by loss in UV/vis absorption of the cinnamic acid at 260 nm and by ESI-MS, by following the disappearance of the signal at m/z 147 (cinnamate) and formation of a new signal at m/z 163 (epoxide product) in negative ion mode. In the absence of additives two signals appeared at m/z 277 and 259 in positive ion mode, which were assigned to the mononuclear Mn⁴⁺ ions [Mn⁴⁺(TMTACN)(OH)₃]⁺ (44) and [Mn⁴⁺(TMTACN)(O)(OH)₂]⁺ (45), respectively.

Figure 10 Complexes 44 and 45 proposed to be the active catalysts in the oxidation of phenolics and cinnamates²⁰⁷

ESI-MS studies did not yield evidence for the formation of manganese complexes with various additives, i.e. such complexes are either not formed or decomposed during MS analysis or were ESI-MS silent. The presence of peracids or manganese hydroperoxide complexes, such as those proposed for by Busch and coworkers¹⁹⁰ for related aza-ligand based complexes,(vide supra) was excluded since with peracetic acid, a longer lag phase and a lower rate of epoxidation was observed. Analogy with Mn³⁺ salens and tetraarylporphyrins, lead to the proposal that Mn⁵⁺=O species was the epoxidising agent and ¹⁸O-labelling experiments confirmed H₂O₂ as the source of oxygen in the product. 44 and 45 (Figure 10), which were detected by ESI-MS,²⁰⁷ form from a mixture of Mn³⁺SO₄, TMTACN and H₂O₂ and undergo one electron reduction by either H₂O₂ or an additive, to an ESI-MS silent Mn³⁺ complex (46, Scheme 11). Subsequent oxidation with H₂O₂ could yield [Mn⁵⁺(TMTACN)(O)(OH)₂]⁺, which in turn was proposed to be the species responsible for the epoxidation of cinnamate.
Watkinson et al.\textsuperscript{209} reported recently a study of the initial rates of epoxidation of styrene derivatives by H$_2$O$_2$ with a number of Mn-tmtacn catalysts and chiral BINOL based additives. It was noted that the method used to prepare the catalysts is likely to influence the mechanistic pathway followed. Indeed, this point can possibly be made more general, when one considers the earlier study by de Boer et al.\textsuperscript{108} where oxalic acid and ascorbic acid with \textsuperscript{17} were compared with other carboxylic acids as additives. In that study it was found that for oxalic acid a switch in the active species (and product distribution) was observed after several hours of reaction concomitant with the appearance of species similar to \textsuperscript{9}.

**Manganese catalysed oxidation of dyes in aqueous media (bleaching)**

Beyond the selective oxidations of organic substrates, the catalysed bleaching of bulk materials such as laundry, raw cotton and wood pulp are key industrial processes.\textsuperscript{210,211,212} Despite appearing diverse in general, the chromophores that need to be bleached in these bulk processes tend to be similar, in particular, polyphenolic substrates. In contrast to fine chemical processes the goal is primarily whitening either by oxidation of the chromophores so that they lose visible absorbance or that their water solubility increases sufficiently to allow their removal from the substrates.\textsuperscript{211} Primarily for economic reasons, the oxidants used in these processes are either chlorinebased, H$_2$O$_2$, ozone and/or peracetic acid, however, environmental demands have favoured the increasing use of chlorine free oxidants. The relative low reactivity of H$_2$O$_2$ requires, however, the use of either high temperatures and basic conditions or the use of catalysts, such as those based on manganese.\textsuperscript{213,214}
Eldik et al.\textsuperscript{215} have studied the ability of manganese catalysts to activate H$_2$O$_2$ to oxidise various azo and phenolic dyes in carbonate buffers by UV/vis spectroscopy.

\[
\begin{array}{c}
\text{dye} + \text{H}_2\text{O}_2 (10 \text{ mM}) \\
\text{Catalyst (0.02 mM),} \\
\text{Carbonate buffer,} \\
\text{pH 8.5-9, 25 C}^\circ
\end{array} \rightarrow \text{degradation products}
\]

\textbf{Scheme 12} Conditions used in catalytic dye oxidation with manganese catalysts.\textsuperscript{215}

The dyes examined generally showed $n \rightarrow \pi^*$ absorptions between 375-490 nm, depending on the substituents present, the $pK_a$ values of the dyes and pH.

The manganese complexes present at pH 8.5 was dependent on the bicarbonate concentration, with the appearance of a broad absorption at 300 nm upon addition of HCO$_3^-$ to Mn$^{II}$(aq), which increased with carbonate concentration. The formation of the Mn$^{II}$-HCO$_3^-$ complex showed a first-order rate constant ($k_{obs}$) prior to precipitation of Mn$^{II}$CO$_3$ in the absence of oxidisable substrates.

Coordination of bicarbonate to Mn$^{II}$-salt resulted in a shift in the oxidation potential from 0.52 V vs 0.48 V (vs Ag/AgCl). Notably, in the presence of the azo and polyphenolic dyes precipitation of manganese carbonate was not observed even at high concentrations of carbonate due to complexation between the dyes and manganese, manifested in changes to the UV/Vis absorption spectrum of the dye and a shift to less positive potentials of the first oxidation. Complexation energies for a series of different Mn-dye complexes, as calculated by DFT methods, indicated stabilization of the Mn$^{II}$ ion by hydroxyl containing ligands compared with nitrogen donor ligands. Notably, the activity towards dye bleaching was increased by the presence of a hydroxyl group in the dyes. The formation of high valent manganese oxido intermediates upon reaction of Mn$^{II}$ with H$_2$O$_2$ in bicarbonate solution was confirmed by UV/vis absorption spectroscopy, manifested in the appearance of a broad band at 460 nm. Furthermore, the six line ESR signal at $g = 2$, characteristic of Mn$^{II}$ in an octahedral environment, which was broadened upon addition of bicarbonate, was replaced by a broad signal at $g = 4$ which is characteristic of a high spin Mn$^{IV}$ species. In the absence of stabilizing ligands, the catalytically inactive species Mn$^{IV}$O$_2$ is formed instead. The formation of radicals was excluded by use of a radical scavenger, t-BuOH, by EPR and UV/vis spectroscopy and the absence of evidence for Mn$^{III}$ ions is consistent with the assumption that Mn$^{II}$ and Mn$^{IV}$ are the main species present during oxidation catalysis.

Kinetic analysis indicated that two equivalents of HCO$_3^-$ were required for catalysed oxidation with one equivalent needed for the formation of a complex with the Mn$^{II}$ ion and a second equivalent for the formation of peroxocarbonate in situ. Peroxocarbonate is a more reactive oxidizing agent than H$_2$O$_2$ itself, which was attributed to carbonate being a better leaving group compared to hydroxide. Maximum bleaching activity was observed between pH 8.2 and 8.5. At higher pH, a decrease in the rate of the reaction was observed, ascribed to deprotonation of the HOOCO$_2^-$ to form the less electrophilic oxidant CO$_4^{2-}$ and at still higher pH, the spontaneous decomposition of H$_2$O$_2$ and precipitation of the manganese salt (MnO$_2$) was observed.
The in situ formation of peroxocarbonate was assigned as the rate limiting step in the reaction, with the Mn$^{IV}$=O intermediate formed upon reaction of hydroperoxycarbonate reacting with the dye substrates rapidly to regenerate the Mn$^{II}$ species.

\[
\text{Mn}^{II} + \text{HOOCO}_2^- \rightleftharpoons \text{O} \quad \text{Mn}^{IV} + \text{HCO}_3^-
\]

**Scheme 13** Formation of a Mn$^{IV}$-oxido complex from the reaction of Mn$^{II}$ with in situ formed percarbonate.

The catalytic activity of Mn$^{II}$ ions towards bleaching of dyes was compared$^{216}$ with the catalytic activity of both [Mn$^{II}$(bpy)$_2$Cl$_2$] and [Mn$^{III}$$^{IV}$(μ-O)$_2$(bpy)$_4$](ClO$_4$)$_3$.2H$_2$O. Both complexes showed the maximum reactivity at ca. pH 8.7. The effect of carbonate concentration on the observed rate of oxidative was similar for both catalysts also, indicating a common reactive intermediate. Indeed, in the absence of carbonate, in CHES (N-cyclohexyl-2-aminoethanesulfonic acid) buffer, catalytic activity was negligible. Moreover, it was shown that monocarboxylate ions such as acetate, bicarbonate and formate, enhanced the activity of the catalyst towards olefin epoxidation with H$_2$O$_2$ while dicarboxylate ions, such as oxalate resulted in lower reactivity. EPR spectroscopy in aqueous bicarbonate showed that for both [Mn$^{II}$(bpy)$_2$Cl$_2$] and [Mn$^{III}$$^{IV}$(μ-O)$_2$(bpy)$_4$](ClO$_4$)$_3$.2H$_2$O, a broad weak signal at $g = 4-5$ was observed, which was attributed to a mononuclear Mn$^{IV}$ species, in addition to a six line signal at $g = 2$, characteristic of an octahedral mononuclear Mn$^{II}$ complex upon addition of H$_2$O$_2$. No evidence for the presence of mixed valent oxido-bridged manganese complexes or for radical species was obtained in the presence of either catalyst.

The key step was proposed to be a two electron oxidation of a monomeric Mn$^{II}$ precursor to a Mn$^{IV}$=O species, manifested in the appearance of an absorption band at 450 nm, assigned to a LMCT transition, upon addition of H$_2$O$_2$ for both catalysts. The authors concluded that ligand displacement by bicarbonate was not occurring in this system.

**Conclusions**

Although not as ubiquitous as iron based enzymes, the central role that manganese based enzymes play in the control of reactive oxygen species and of course in the OEC of PSII has driven the design and synthesis of a wide range of manganese complexes both as structural models and as functional mimics. These efforts have been stimulated further by the high activity that can be achieved with manganese catalysts in the selective oxidation of organic substrates. In contrast to iron complexes based on similar ligands, manganese based systems shows a remarkable propensity to form well defined multinuclear complexes with oxido and carboxylato bridging ligands. The activity of these catalysts, and activity of the enzymes that have inspired their preparation, is critically dependent on redox state dependent and redox driven changes in coordination mode. The most clear example being carboxylate shifts and opening of oxido bridges. It
is apparent, however, that although general trends are observed, i.e. that an increase in oxidation state favours oxido over carboxylato ligands and hence drives ligand exchange, even with relatively similar ligands, two complexes can show wildly different propensities to exchange oxido or carboxylato ligands to provide free coordination sites for binding to reactive oxygen species such as H$_2$O$_2$. From the perspective of oxidation catalysis, the variation in coordination chemistry seen with multinuclear manganese complexes poses considerable challenges to understanding both the nature of the species that engage in oxygenation of substrates and especially the key role played by additives in overall reaction mechanisms. Of course, such challenges are fertile ground for the discovery of new reactivity and in pushing the limits of our ability to develop highly active catalysts to study highly complex systems.

Overview of thesis

The goal of the research described in this thesis is to achieve a broad understanding of the mode of action of the manganese catalysts based around the tmtacn ligand system under a wide range of conditions in complex aqueous media. Achieving this aim requires the development of the necessary tools and techniques to probe complex systems at the molecular level to elucidate the mechanism by which the catalyzed reactions proceed. The first research line is focused on finding the appropriate model substrate and techniques to study oxidation and bleaching with manganese catalysts based on the tmtacn ligand. In second line the role of additives such as buffer, sequestrant, phase separation and pH on the activity of the catalyst will be explored.

Chapter 2 is focused on NIR Raman spectroscopy for offline analysis to monitor catalysis in aqueous media, specifically the epoxidation of water soluble alkenes. The potential of the DCDR (Drop coating deposition Raman) technique using hydrophobic surfaces to monitor reaction progress by off-line analysis was developed. The validation of the method and the development of a fitting procedure for analysis is discussed.

In chapter 3, the pH dependent aqueous and non-aqueous coordination chemistry of [Mn$^{III}$Mn$^{IV}$($\mu$-CH$_3$CO$_2$)(\mu-O)$_2$(Me$_4$dtne)](PF$_6$)$_2$, (which has been demonstrated as an exceptionally active catalyst in the bleaching of raw cotton and wood pulp at high pH (> 11), is explored by UV/vis absorption, Raman and electron paramagnetic resonance (EPR) spectrosopies, as well as cyclic voltammetry and ESI-MS. The effect of carboxylic acids on the speciation and eventually on catalytic activity is examined also.

Chapter 4 is focused on identifying a suitable model compound to allow for the study of the behaviour of catalysts under conditions relevant to cotton bleaching. Morin and its limitations as a model compound are discussed first followed by a discussion of chrysin as a more suitable model substrate. In addition, the challenge of studying reactions with substrate concentrations as low as $10^{-6}$ – $10^{-4}$ M is addressed through the use of UV/Vis absorption and UV resonance Raman spectroscopy.

Chapter 5 describes the activity of the manganese catalysts based on the ligand tmtacn in the oxidation of alkenes under two phase organic/aqueous reaction conditions. A central question in such processes, that is addressed here, is as to where, i.e. in which phase, the catalysed reaction takes place. Answering this question is important for the application of the catalysts as the use of phase transfer catalysts for example would
have a negative effect if the complexes are inactive in the organic layer. This goal is achieved by studying the activity of the Mn-tmtacn complexes in the oxidation of both hydrophilic and hydrophobic alkenes under two phase conditions and several approaches was taken to identify in which phase the catalytic reaction takes place.

In Chapter 6, the epoxidation of styrene sulfonate and oxidation of chrysin in water as model substrates in the pH ranges 6-9 and 10-11, respectively, catalysed by Mn-tmtacn complexes are compared and contrasted. The aim is to identify common effects of additives and pH that are often used with these catalyst systems.

Reference

Redox state dependent ligand exchange in manganese based oxidation catalysis


91  It should be noted that although the presence of ligand-exchange products in neat acetonitrile was confirmed by ESI-MS, this was ascribed to the presence of adventitious water.


Chapter 1


Redox state dependent ligand exchange in manganese based oxidation catalysis

146 M. Shank, V. V. Barynin, G. C. Dismukes, Biochemistry, 1994, 33, 15433-15436.
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