Chapter 5

Manganese Catalysts for Alcohol Oxidation

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Abstract

In this chapter new manganese complexes and their use as catalyst in the oxidation of alcohols is described. The in situ prepared manganese complexes based on ligands 2.2 - 2.8 were applied in the catalytic oxidation of alcohols to aldehydes or ketones. Highly active and selective catalysts were found with excellent turnover numbers (up to 900) using aqueous hydrogen peroxide as oxidant at ambient temperatures. Electron paramagnetic resonance spectroscopy (EPR) and electrospray mass spectrometry (ES/MS) indicated that dinuclear species may be involved in the catalytic oxidations. Comparing the rate of oxidation of benzyl-d₇ alcohol with that of benzyl alcohol by the different catalysts yielded isotope effects \( (k_{H}/k_{D}) \) of 2.2 - 4.3. Although the exact nature of the oxidising species has not been elucidated, these results indicate that hydroxyl radicals are not involved in these processes.

5.1 Introduction

The oxidation of alcohols to the corresponding carbonyl compounds is a key reaction in organic synthesis. Many traditional procedures are based on strong oxidising (metal-based) reagents like KMnO₄, MnO₂, SeO₂, RuO₄ or chromium(VI) compounds. Recently, a number of catalytic alcohol oxidation methods using cheap and environmental friendly oxidants like oxygen or hydrogen peroxide have been reported. Stack et al. reported a mimetic system (complex 5.1, Figure 1) for the mononuclear copper enzyme galactose oxidase (GOase), which catalyses the aerobic oxidation of benzylic and allylic alcohols to the corresponding carbonyl compounds with the formation of H₂O₂. The studied Cu-model complexes are based on diimine diphenolate ligands containing a binaphthyl backbone unit to enforce a non-square planar geometry preferred by the CuII-ion. Furthermore, the substituents on the phenolate moieties are necessary in order stabilise the CuI-phenoxyl radical species. Benzyl alcohol and 1-phenyl ethanol are readily converted to the corresponding carbonyl compounds with the concomitant formation of H₂O₂, using O₂ as oxidant at room temperature. Under neat reaction conditions turnover numbers over 1000 were readily achieved. When the catalytic oxidation experiments where performed in acetonitrile, the reactions occur however, much less efficiently. Another attractive GOase model based on a novel dinuclear CuII-phenoxyl radical species was described by the group of Wieghardt (5.2, Figure 1). High yields could be obtained for the conversion of primary and secondary alcohols. In addition to aldehydes, ketones and/or 1,2-diols were also formed (formed by oxidative C - C coupling). In all cases the reduction product is H₂O₂. More details about reaction mechanisms have been discussed in Chapter 1.
Figure 1 Structural models for the galactose oxidase enzyme (GOase).4,6

Another selective catalyst for oxidation of alcohols to the corresponding carbonyl compounds on a multigram scale employing O₂ as oxidant was disclosed by Markó et al.7 High conversions and yields were obtained with high tolerance to a variety of functional groups using a 5 mol% phenanthroline Cu¹-complex and 5 mol% of a dialkylazodicarboxylate as a hydrogen transferring agent. Oxygen could also be replaced by air after intensive efforts to optimise the catalytic oxidation reaction.8 Although evidence for a number of postulated intermediates was not obtained, a dehydrogenation mechanism was proposed as given in Scheme 1. Mechanisms involving an oxo transfer process were excluded, because sulfides and alkenes were found to be inert towards oxidation using this procedure.8 The envisioned mechanism involves the conversion of the copper complex (CuCl.Phen, Phen = 1.10-phenanthroline, 5.3) to complex 5.4 by the addition of diethylhydrazinodicarboxylate (DEAD-H₂) as the co-catalyst and base. In the presence of O₂, complex 5.4 is subsequently converted to the µ²-peroxo bis copper(II) intermediate 5.5. Upon heating, homolytic O - O bond cleavage provides the copper oxy radical 5.6, followed by intramolecular hydrogen atom abstraction generating radical 5.7 (= azo-substituted copper(I) hydroxyl species 5.8). Ligand exchange and release of H₂O leads to species 5.9. Subsequently intramolecular hydride shift and elimination of the carbonyl compound closes the catalytic cycle. The role of the azo additives is besides to transfer hydrogen atoms also believed to stabilise several reactive copper intermediates formed in this catalytic cycle e.g. complex 5.8.⁸b

Sheldon et al. recently reported a water soluble palladium(II) bathophenanthroline complex.⁹ This Pd-system is a stable and recyclable catalyst for the selective oxidation of terminal olefins to the corresponding 2-alkanones, under neutral, copper and chloride free conditions.⁹ The same catalyst also proved to be suitable for the oxidation of alcohols using O₂ as oxidant.³b
Scheme 1 Proposed mechanism for the oxidation of alcohols by the Cu-phenanthroline complex (5.3). 

High conversions with high selectivities for both primary and secondary alcohols to the corresponding carbonyl compounds was obtained. However, high temperatures and pressures were necessary (100°C, 30 bar air pressure). As the catalyst precursor a dinuclear Pd-intermediate 5.10 (Scheme 2) containing two bridging hydroxy ligands was postulated. Upon addition of the substrate it presumably converts into mononuclear species 5.11. Next, the carbonyl compound and water are released after β-hydride elimination. The postulated zero-valent Pd-species 5.13 is subsequently oxidised with O₂ to a Pd-peroxide intermediate 5.14. The latter species reacts with one equivalent of the Pd⁰-species 5.13 to give the starting Pd-dimer 5.10. Using this water soluble palladium(II) bithophenanthroline catalyst, a wide scope of substrates can be oxidised, including primary and secondary allylic, benzylic and aliphatic alcohols. Turnover numbers of 400 were achieved with yields exceeding 90% for the conversion of secondary alcohols. For the oxidation of primary alcohols longer reaction times were necessary and lower turnover numbers were observed. An attractive feature of this water-soluble catalytic system is the possibility to re-use the Pd-complex maintaining high reactivity and selectivity.
5.2 Oxidation of primary and secondary alcohols with Mn-complexes

The dinuclear manganese(IV) complex \((\text{Mn}_2\text{O}(\text{tmtacn})_2)(\text{PF}_6)_2\)\(^{11,12,13}\) was studied as catalyst for e.g. the oxidation of a range of substituted benzylic alcohols to benzaldehydes.\(^{14}\) Turnover numbers in the range of 80 up to 1000 were readily reached with high selectivities employing \(\text{H}_2\text{O}_2\) as oxidant. From the 16-line spectrum obtained from EPR experiments, it was concluded that the Mn-tmtacn complex is reduced to a dinuclear Mn\(^{\text{III}}\)-Mn\(^{\text{IV}}\) mixed-valent species in the presence of oxidant. Ultimately a 6-line spectrum was obtained, indicative of mononuclear Mn\(^{\text{II}}\)-species.\(^{14}\)

In the course of our studies on novel ligands featuring three N-donor sets for each Mn-centre in dinuclear Mn-complexes we explored the dinucleating ligands\(^{15}\) \(\text{N,N,N',N'}\)-tetrakis(2-pyridylmethyl)-1,2-ethanediadmine (tpen, \(\text{2.2a}\)) and \(\text{N,N,N',N'}\)-tetrakis(2-pyridylmethyl)-1,3-propanediadmine (tptn, \(\text{2.2b}\), Figure 2) in catalytic epoxidation reactions.\(^{16}\)
Advantages of this type of ligand are their easy accessibility and the possibility for ligand modification as described in Chapter 2. Screening the corresponding dinuclear manganese complexes in a number of different catalytic epoxidation reactions showed that the complexes based on tpen (2.2a) were unreactive, in sharp contrast to the Mn-complexes based on tptn (2.2b), containing a two-carbon or a three-carbon spacer, respectively.\textsuperscript{16b,c}

In this chapter the use of tpen (2.2a), tptn (2.2b) and related ligands 2.5 - 2.8 in Mn-catalysed oxidation of a variety of primary and secondary alcohols employing H\textsubscript{2}O\textsubscript{2} as oxidant will be discussed.

It will be shown that several \textit{in situ} prepared complexes with Mn(OAc\textsubscript{3}) based on tptn (2.2b) and tptn-derivatives are active and selective catalysts for the oxidation of a number of substituted primary benzyl alcohols to benzaldehydes and secondary alcohols to the corresponding ketones.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{ligands.png}
\caption{Ligands used for the manganese-catalysed alcohol oxidation.}
\end{figure}

5.3 Synthesis of ligands

The ligands 2.2a and 2.2b (Figure 2) were synthesised according to several (slightly modified) literature procedures\textsuperscript{15} and the corresponding manganese complexes were studied as epoxidation catalysts.\textsuperscript{16} Ligands 2.5 and 2.6 were provided by dr. Minze Rispens. Ligands 2.7 and 2.8 were prepared as described in Chapter 2. The general synthesis route is summarised in Scheme 3.
Catalysts prepared in situ from Mn(OAc)$_3$ and ligands 2.2 - 2.8 (Figure 2) were examined as catalysts in the oxidation of a number of substrates utilising H$_2$O$_2$ as oxidant.$^{17}$ The alcohol oxidation experiments were performed at 0°C under a nitrogen atmosphere using acetone as solvent. The manganese catalysts based on ligands 2.2a, 2.2b were made by mixing 1 equivalent of the selected ligands with 2 equivalents of Mn(OAc)$_3$, followed by addition of substrate (1000 equivalents). For the preparation of catalysts based on ligands 2.5 - 2.8, 1 equivalent of Mn-salt was used. The reactions were initiated by addition of oxidant and were monitored by GC. The results (turnover numbers and selectivities) for the oxidation of various alcohol substrates to the corresponding carbonyl compounds are summarised in Table 1. The in situ prepared Mn-catalyst based on tpen (ligand 2.2a) resulted in an unreactive oxidation catalyst, similar results were obtained during epoxidation experiments.$^{18}$ However, the in situ prepared Mn-catalyst based on ligand 2.2b (tptn) provided a highly active and selective alcohol oxidation catalyst.

Scheme 3 Synthesis of ligands 2.7 and 2.8.
<table>
<thead>
<tr>
<th>Substrate</th>
<th>2.2b</th>
<th>Sel.</th>
<th>2.5</th>
<th>Sel</th>
<th>2.6</th>
<th>Sel</th>
<th>2.7</th>
<th>Sel</th>
<th>2.8</th>
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<td>95</td>
<td>331</td>
<td>99</td>
<td>303</td>
<td>99</td>
<td>127</td>
<td>95</td>
<td>293</td>
<td>95</td>
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<td>270</td>
<td>75</td>
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<td>99</td>
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<td>6 2,5-dimethoxybenzyl alcohol</td>
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<td>99</td>
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<td>95</td>
<td>400</td>
<td>70</td>
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</table>

(a) Conditions, see experimental section. (b) All products were identical to independently synthesised samples and identified by GC and $^1$H-NMR. (c) Turnover number in mole product per mole ligand. (d) Selectivity in mole aldehyde (or ketone) per mole converted substrate.
The conversion of benzyl alcohol (entry 1) resulted in the selective formation of benzaldehyde with 326 turnover numbers. Subsequently a range of para-substituted benzyl alcohols were screened, achieving high t.o.n.’s in the range of 201 (Table 1, 4-methoxybenzyl alcohol, entry 2) to 449 (4-chlorobenzyl alcohol, entry 3). Although substrates with electron-donating substituents such as 4-methoxybenzyl alcohol (entry 2) react less efficiently compared to substrates containing electron-withdrawing groups like 4-trifluoromethyl benzyl alcohol (entry 4), rather small effects on the catalysis (t.o.n.’s) were found. However, a distinct steric effect was observed as ortho substituted substrates react more sluggishly and in fact 2,5-dimethoxybenzyl alcohol (entry 6) was found to be virtually unreactive. High conversions were also obtained when secondary alcohols were oxidised. For example, the oxidation of cyclohexanol (entry 7) resulted in 363 t.o.n.’s and also for cycloheptanol (entry 8) excellent results (894 t.o.n.’s) were found with selectivities up to 99% to the corresponding ketones. For 4-trifluoromethyl benzyl alcohol lower selectivities were observed (entry 4). Perhaps over-oxidation to benzoic acid takes place, however, this was not quantified. Other secondary alcohols like 2-octanol (entry 10) and sec-phenylethyl alcohol (entry 11) were selectively transformed to the corresponding ketones with high conversions. Although the oxidation of secondary alcohols proceeds with satisfactory conversions, the in situ prepared complexes gave only low conversions in the oxidation of 1-octanol (entry 9).

The Mn-complex prepared in situ using ligand 2.7 (Figure 2) resulted in dramatically lower t.o.n.’s for the oxidation of some substrates. With the substituted benzyl alcohols (entry 1 - entry 6) only low t.o.n.’s were reached, typically between 21 (entry 5) and 173 (entry 4), whereas employing secondary alcohols generally higher conversions were observed. However, the results with ligand 2.7 are inferior compared to those with the Mn-catalyst based on ligand 2.2b. Higher t.o.n.’s were reached by using the in situ prepared complex of ligand 2.8, containing a three-carbon spacer, and the observed results are comparable with the Mn-complex based on ligand 2.2b.

Suitable oxidation catalysts were also found by employing the Mn-complexes based on ligand 2.5 or ligand 2.6, resulting in high conversions and selectivities for primary and secondary alcohols. Generally the results even surpasses those found for ligand 2.2b, achieving turnover numbers easily over 700. In addition preliminary experiments with Mn(ClO$_4$)$_2$ resulted in only slightly lower conversions compared to Mn(OAc)$_2$.

Addition of a second amount of H$_2$O$_2$ (1 ml of a 30% solution in water, 9.8 equivalents with respect to substrate) resulted in some cases (ligand 2.2b and 2.7) in a considerable increase in aldehyde or ketone yield, indicating that the catalysts are robust under the conditions used. In a control experiment in which the ligand was omitted, strong peroxide decomposition and no oxidation products were found. In the absence of the manganese salt only substrate and no oxidation products were found.

The reaction time profiles were followed for the oxidation of cyclohexanol to cyclohexanone and the results are summarised in Figure 3. Turnover numbers up to 600 were easily reached for the Mn-complexes. Following the time course of the oxidation of cyclohexanol, a remarkable decrease in induction time was obtained for the complexes based on ligands 2.5 and 2.6, containing additional methyl groups at the 3-position of the pyridine
rings, compared to the Mn-complexes based on ligands 2.7 or 2.8. The striking influence of the additional methyl groups on the reactivity could be a result of either electronic or steric properties of the ligands; perhaps pointing to a change in coordination of the ligand as has been observed for Fe-tpa\textsuperscript{19} complexes.\textsuperscript{20} Notably, Mn-complexes derived from ligands related to 2.5 and 2.6 but with CH\textsubscript{3}-groups at the 6-position, were found to be completely inactive during alcohol oxidation experiments. Similar results were observed during epoxidation studies as discussed in Chapter 2.

![Figure 3](image)

**Figure 3** Time profile of the oxidation of cyclohexanol with Mn-complexes prepared *in situ* with ligands 2.2b - 2.8:
- ■ ligand 2.2b, ▼ ligand 2.5, ◆ ligand 2.6, ○ ligand 2.7, ▲ ligand 2.8.

Hodgson *et al.* investigated the effects of methyl groups at the pyridine rings of bispicen\textsuperscript{21} ligands (e.g. 2.18a, Scheme 3) on the redox potentials of the corresponding manganese complexes.\textsuperscript{22} Structural studies revealed that the methyl groups at the 6-position are in close proximity of the metal center and therefore impose severe steric constraints.\textsuperscript{22} Furthermore, from electrochemical studies (cyclic voltammetry) showed that the difference in electrochemical properties between parent and methylated is entirely due to steric factors.\textsuperscript{22}

Based on the research of Hodgson, we tentatively propose that the additional methyl groups at the 6-postion in our ligand system prevent the approach of a H\textsubscript{2}O\textsubscript{2} molecule to the metal core, resulting in unreactive oxidation catalysts. On the contrary introduction of a methyl functionality at the 3-postions or increasing the spacer length, facilitates the reaction
with H$_2$O$_2$. However, additional research is necessary to elucidate the origin of these effects and to establish the relation between the effect of the methyl groups in the ligands and the observed enhanced reactivity.

5.5 Primary kinetic isotope effect

Primary kinetic isotope effects have been extensively studied in order to obtain more insight into oxidation mechanisms. The primary kinetic isotope ($k_{\text{H}}/k_{\text{D}}$) data found for many alcohol oxidation reactions by high-valent transition metal complexes usually indicate the involvement of an association/dissociation equilibrium of the alcohol to the metal complex prior to hydride or hydrogen transfer. The values of the kinetic isotope effects observed for the oxidation of benzyl alcohol catalysed by the manganese complexes based on ligands 2.2b, 2.5 - 2.8 were determined by competition experiments between benzyl alcohol and benzyl-d$_7$ alcohol (Scheme 4). Values in the range of $k_{\text{H}}/k_{\text{D}}$ 2.2 to 4.3 were observed, and these values ($k_{\text{H}}/k_{\text{D}} \geq 2$) strongly indicate that cleavage of the (benzylic) C-H bond is involved in the rate determining step. Higher values were found for the Cu-based galactose oxidase models studied by the groups of Stack ($k_{\text{H}}/k_{\text{D}} = 5.3$) and Itoh ($k_{\text{H}}/k_{\text{D}} = 6.8$). A primary kinetic isotope value of 7.7 was found for galactose oxidase itself by Maradufu et al. Similar values ($k_{\text{H}}/k_{\text{D}} = 4.0$) were found in our group for the oxidation of primary and secondary alcohols using a non-heme dinuclear iron catalyst. A $k_{\text{H}}/k_{\text{D}}$ value of 3.8 was calculated for the oxidation of alcohols by the [$\text{Mn}_2\text{O(tmtacn)}_2]\text{(PF}_6\text{)}_2$ catalyst. Based on the competition experiments it can be concluded that hydroxyl radicals are not involved in these processes, as due to the high reactivity of these radicals a much lower isotopic effect would be expected. Generally, isotope effect values of 1 - 2 are associated with radical oxidation reactions. In agreement with this, no indications for hydroxylation of aromatic rings for the various substrates employed, as listed in Table 1, have been obtained. Furthermore, no hydroxylation of benzene, which is also a substrate for hydroxylation using OH radicals, has been observed under the same conditions.

<table>
<thead>
<tr>
<th>Ligand</th>
<th>$k_{\text{H}}/k_{\text{D}}$</th>
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<tbody>
<tr>
<td>2.2b</td>
<td>3.2</td>
</tr>
<tr>
<td>2.5</td>
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</tr>
<tr>
<td>2.6</td>
<td>3.4</td>
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<td>2.7</td>
<td>2.2</td>
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<tr>
<td>2.8</td>
<td>4.3</td>
</tr>
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</table>

Scheme 4 Competition experiments used for isotope effect determination.
5.6 EPR and ES/MS experiments

The catalytic alcohol oxidation reactions were investigated by electron paramagnetic resonance spectroscopy (EPR). Initial experiments involved the in situ preparation of the Mn-complexes using ligands 2.2a, 2.2b and 2.5 - 2.8, under the same conditions as employed for the catalytic oxidation reactions (see paragraph 5.4). Samples of the catalytic oxidation reaction mixture at 0°C were taken in acetone and frozen to 77K for EPR studies. After mixing the ligands and Mn(OAc)\(_3\).2H\(_2\)O for 15 min no EPR signals were obtained at 77K, which may be caused by the formation of EPR-silent Mn\(^{III}\)-species or antiferromagnetically coupled Mn\(^{IV}\)-Mn\(^{IV}\) species. After addition of substrate (cyclohexanol) and oxidant (1.0 ml of 30% aq. H\(_2\)O\(_2\), 9.8 equivalents with respect to substrate) samples were immediately frozen to 77K for EPR analysis. Mixing ligand 2.6 with Mn(OAc)\(_3\).2H\(_2\)O yields immediately after addition of H\(_2\)O\(_2\) a strong 16-line signal with an A value of 78 G (Figure 4). Only weak 16-line signals were detected for the complexes based on ligands 2.2b and 2.8. For the complexes prepared with ligands 2.2a, 2.5 and 2.7 no EPR signals were detected. After 30 min the complexes derived from ligands 2.5 and 2.7 starts as well to display weak 16-line EPR signals comparable with catalysts prepared from ligands 2.2b and 2.8. However, after 90 min incubation at 0°C now also strong signals were obtained for the in situ prepared complexes based on ligands 2.2b, 2.5, 2.7, 2.8, whilst the intensity for the ligand 2.6 system remained constantly high. The obtained characteristic 16-line spectra represent mixed-valence Mn\(^{III}\)-Mn\(^{IV}\) complexes with an A value of 78 Gauss. After a reaction period of 4h, however, only the complexes based on ligands 2.2b and 2.7 still displayed a weak Mn\(^{III}\)-Mn\(^{IV}\) EPR signal (roughly 10% of the intensity observed after 90 min). The manganese complexes based on ligands 2.5, 2.7, 2.8 showed a 6-line EPR signal with an A value of 108 Gauss, typical for a mononuclear Mn\(^{II}\)-species. In sharp contrast to ligands 2.2b, 2.5 - 2.8, complexes with ligand 2.2a (tpen) remained EPR silent over the entire 4h reaction period.

Using electrospray mass spectroscopy (ES/MS) resulted in the observation of mainly mononuclear complexes after mixing the ligands 2.2a, 2.2b, 2.5 - 2.8 with Mn(OAc)\(_3\).2H\(_2\)O. Upon mixing ligand 2.2a with the Mn-salt, the ES/MS spectrum showed prominent peaks at m/z 425 and m/z 538, corresponding to protonated ligand 2.2a ([HL]\(^+\)) and a mononuclear complex identified as [LMn(OAc)]\(^+\), respectively. Similar species were obtained by preparing the complex in situ from ligand 2.2b, resulting in signals at m/z 439 and m/z 552. However, after mixing ligand 2.7 with Mn(OAc)\(_3\) signals for mononuclear complexes (m/z 537) were observed. Using ligand 2.8 containing a three-carbon spacer, a base peak of m/z 438 was found which was assigned to the free ligand. Mixing ligand 2.5 and 2.6 resulted in peaks at m/z 579 and at m/z 593 assigned to mononuclear species with the general structure [LMn(OAc)]\(^+\). After addition of substrate and H\(_2\)O\(_2\) to the in situ prepared Mn-complexes we found for the complex based on ligand 2.2a a base peak (at m/z 538), which was assigned to [LMn(OAc)]\(^+\).
Figure 4 Electron paramagnetic resonance spectrum of in situ prepared manganese complex based on ligand 2.6 immediately after addition of cyclohexanol and oxidant.

For the complexes based on ligand 2.2b, 2.6 and 2.8 signals at m/z 683, 724 and 682 were detected, corresponding to species like [LMn^{II}_{2}(OAc)_{2}(OH)]^{+}. It is noted that this is not the species observed with EPR. Whilst most Mn^{III}-Mn^{IV} species studied so far are magnetically strongly coupled due to two bridging oxygen atoms,\textsuperscript{30} dinuclear manganese(II) complexes with acetato bridges exhibit weak coupling and consequently exhibit very different EPR spectra.\textsuperscript{31} Although EPR experiments showed also dinuclear complexes after mixing ligands 2.5 and 2.7 with Mn(OAc)$_{3}$.2H$_{2}$O, these results could not be confirmed by the ES/MS experiments, perhaps due to redox chemistry or other side reactions in the mass spectrometer.

5.7 Conclusions

In conclusion, we have demonstrated that the \textit{in situ} prepared manganese complex based on tptn (ligand 2.2b) and the related ligands 2.5 - 2.8 are promising catalysts in a new alcohol oxidation procedure using H$_{2}$O$_{2}$ as the terminal oxidant. Main advantages of this catalytic system are the facile synthesis and possibility for ligand modification. In acetone and at ambient temperature the manganese complex of tptn is able to catalyse the selective oxidation of various alcohols to the corresponding aldehydes or ketones, with H$_{2}$O$_{2}$ as oxidant.

For the selected \textit{in situ} prepared Mn-complexes based on the discussed ligands, generally turnover numbers up to nearly 900 were found. Preliminary screening experiments of different catalytic alcohol oxidation reactions showed that the \textit{in situ} prepared manganese complex with the tpen 2.2a was unreactive, similar to ligand characteristics in previously described epoxidation studies.\textsuperscript{16b,c} The tptn-based modified ligands 2.7 and 2.8, containing a two-carbon spacer and a three-carbon spacer, respectively, were found to provide moderate
(complex based on ligand 2.7) to active catalysts (based on ligand 2.8), although long induction periods were observed. Using \textit{in situ} prepared complexes based on ligand 2.5 and ligand 2.6 excellent results were found and most remarkably, the induction period was strongly reduced particularly with complexes derived from ligand 2.6.

This may be linked with the observation that ligand 2.6 yields a strong 16-line EPR signal immediately after mixing the ligand with Mn-salt, H$_2$O$_2$ and substrate. Therefore we tentatively assign dinuclear species as being involved in the oxidation reactions. It needs to be emphasised that for the other ligands much longer induction times were observed before the oxidation reactions have been initiated. Furthermore, also longer incubation periods were necessary before strong 16-line EPR signals were detected.

ES/MS monitoring experiments also gave to some extent indications for the formation of dinuclear Mn-intermediates. The ligands with the three-carbon spacer yield in all cases much quicker active catalysts (showing shorter lag phases) than the two-carbon analogues, likely connected with a faster formation of dinuclear species.

Comparing the rate of oxidation of benzyl-d$_7$ alcohol with that of benzyl alcohol by the different catalysts showed isotope effects ($k_H/k_D$) of 2.2 - 4.3 and these results indicate that hydroxyl radicals are not involved in these processes. However, we cannot conclude which species exactly is involved in the oxidation reactions, \textit{e.g.} high-valent Mn=O species or Mn-OOH species. Based on the EPR experiments of the reaction mixtures we tentatively propose that by mixing the ligands with Mn-salts, subsequent addition of H$_2$O$_2$ gives rise to the formation of dinuclear Mn-species, which could be the intermediate precursors of the active intermediates for the oxidation of alcohols. During the oxidation reactions, these complexes are ultimately converted to mononuclear Mn$^{II}$-species.

5.8 Acknowledgements

Dr. Minze Rispens (University of Groningen) is gratefully acknowledged for providing several ligands described in this chapter. Dr. Ronald Hage (Unilever Research Vlaardingen) is gratefully acknowledged for helpful discussions and for the assistance with recording several EPR spectra.

5.9 Experimental section

\textbf{General procedure and methods}

For general information, see Chapter 2.
GC equipment and analysis

GC analyses were performed on a Hewlett Packard 6890 Gas Chromatograph equipped with an autosampler, using a HP-1 dimethyl polysiloxane column or a HP-5 5% phenylmethylsiloxane column. Calibration was performed using authentic samples of the alcohols and carbonyl compounds and independent samples. Conversions, yields and turnover numbers are the average of 2 - 3 runs (error ±10%) and were determined using bromobenzene as internal standard and calculated using the Chemstation software.

ES/MS and EPR experiments

The electrospray mass (ES/MS) experiments were performed at room temperature at a Micromass ZMD 2000, ESI(+), Vcone = 20V and Vcap = 3.25kV connected to an Alliance 2690 HPLC system, at the analytical department of the University of Groningen. EPR experiments were carried out at Unilever Research Vlaardingen, using a Bruker ECS 106 at 77K.

Catalytic oxidation reactions

Catalytic alcohol oxidation reactions were started by mixing 1.0 ml of a stock solution of Mn(OAc)$_3$.2H$_2$O in acetone and 1.0 ml of a stock solution of ligand 2.2b (or 2.2a). After stirring for 15 min, 1.0 ml of a stock solution of substrate and bromobenzene (internal standard) were added. After stirring for 2 min, excess of oxidant (1.0 ml of 30% aq. H$_2$O$_2$) was added. The concentrations of Mn(OAc)$_3$, ligand 2.2b (or 2.2a), substrate, hydrogen peroxide and internal standard were 2 mM, 1 mM, 1M, 9.8 M and 0.5 M, respectively. The progress of the reaction was monitored by GC, by taking a small sample of the reaction mixture and filtering over a short column of silica. To establish the identity of the alcohols and carbonyl compounds unequivocally, the retention times and spectral data were compared to those of commercially available or independently synthesised compounds. The same procedure as described for the catalytic reactions with 2.2b was followed with ligands 2.5 - 2.8 except that a 1M stock solution of Mn(OAc)$_3$.2H$_2$O was used.

Determination of primary kinetic isotope effect ($k_H/k_D$) for the catalytic oxidation of benzyl alcohol and benzyl-d$_7$ alcohol

For determination of the $k_H/k_D$ values, the same procedure as used in the previous described catalytic oxidation experiments was followed except that 1.0 ml of a stock solution (conc. 1 M) of benzyl alcohol, $p$-methylbenzyl alcohol and of bromobenzene (conc. 0.5 M, internal standard) were used. Another solution, using benzyl-d$_7$ alcohol, $p$-methylbenzyl alcohol and bromobenzene (internal standard) was also prepared and used as substrate.

The amounts of alcohols before and after the oxidation reaction were determined by GC analysis. The $k_H/k_D$ value was determined using the following the equations:32
\[ \frac{k_H}{k_{Me}} = \log \left( \frac{H_f}{H_i} \right) / \log \left( \frac{Me_f}{Me_i} \right) \] (1)

\[ \frac{k_D}{k_{Me}} = \log \left( \frac{D_f}{D_i} \right) / \log \left( \frac{Me_f}{Me_i} \right) \] (2)

then, \( \frac{k_H}{k_D} = \frac{\text{eq 1}}{\text{eq 2}} \)

\( H_i \) and \( H_f \) are final and initial quantities of benzyl alcohol.

\( D_i \) and \( D_f \) are final and initial quantities of benzyl alcohol \( d_7 \).

\( Me_i \) and \( Me_f \) are final and initial quantities of \( p \)-methylbenzyl alcohol.

### 5.10 References


17 Preliminary alcohol oxidation experiments employing catalysts based on e.g. ligand 2.13 resulted also in some activity, although long induction periods were obtained.

18 See Chapter 2.
19 tpa = \( N,N,N \)-tris(2-pyridinylmethyl)amine


21 bispicen = \( N^1,N^2 \)-bis(2-pyridinylmethyl)-1,2-ethanediamine


