CHAPTER 4

Epoxidation with In Situ Prepared Manganese Based Homogeneous Catalysts

An apical ligand approach

4.1 Introduction

In the past 15 years considerable progress has been made in the field of homogeneous catalyzed epoxidations of unfunctionalized olefins. Epoxidation is an important methodology for preparation of highly functionalized organic compounds; optically active epoxides especially are important intermediates. From many olefins it is now possible to create in only one step optically active epoxides in nearly enantiomerically pure form. A few systems have been shown to be extremely useful in this field, and have reached the stage of synthetic applicability. These were discussed in chapter 1.

As mentioned in chapter 1, for industrial purposes, manganese catalysts are preferred since manganese itself is a relatively non-toxic metal. Iron can also be considered but manganese complexes are superior so far in selective epoxidation of olefins, chiefly because they show fewer side reactions than iron complexes.

The synthesis of most ligands used in the catalytic epoxidation reactions discussed here is described in chapter 2. The structure and properties of the manganese complexes used in catalytic experiments were described in chapter 3.

4.1.1 Epoxidation reactions using Mn-Oxo transfer catalysts

The results of the epoxidation reactions catalyzed by the newly developed Mn catalysts described in this chapter show some resemblance to the outcome of reactions catalyzed by Mn-salen complexes and Mn-porphyrins (Figure 4.1).

Manganese porphyrins and salen complexes are capable of catalyzing the epoxidation of olefins with high efficiency using bleach or iodosylbenzene as well as hydrogen peroxide as oxidants.[1,5] For porphyrins, turnover numbers can be as high at 30,000, in particular using chloro-substituted porphyrin complexes such as **2**,[2] but the enantioselectivity with chiral analogues of such catalysts leaves room for improvement.[3,5] Another disadvantage of Mn-porphyrin chemistry is the difficulty of synthesizing the chiral ligands themselves as lengthy syntheses and difficult purification steps are often needed.

Mn-salen systems, however, show high enantioselectivity but rather low turnover numbers in epoxidation reactions. A number of research groups have tried to rigorously improve catalyst stability by making robust ligands.[4]

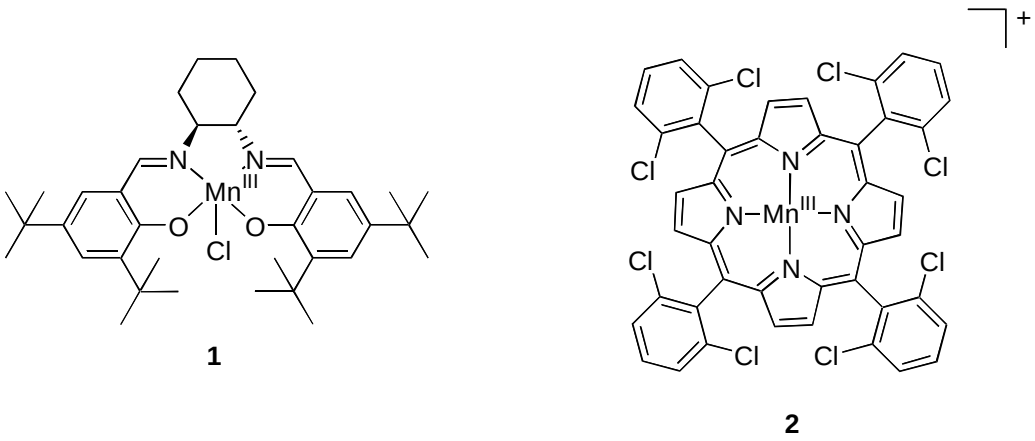
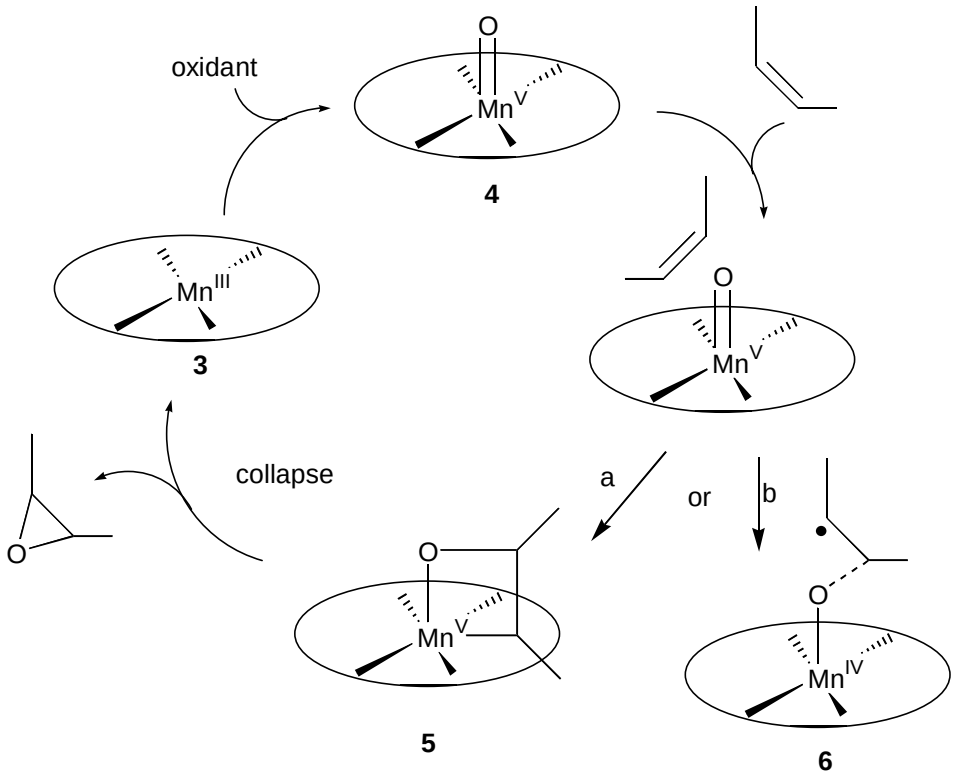


Figure 4.1 *Mn-salen and Mn-porphyrin complexes **1** and **2***

The mechanism of epoxidation with **2** is believed to be similar to the mechanism in Mn-salen **1** catalyzed epoxidations (Scheme 4.1).[5,6] First, from the oxidant and Mn-salen or Mn-porphyrin complexes **3** a Mn^{V}-oxo species **4** is formed,[1,5] which, in the case of a salen based Mn complex, has been detected by electro spray ionization mass spectrometry.[7]



Scheme 4.1 *Catalytic cycle involved in manganese porphyrin and salen epoxidations*

Subsequently, the oxygen atom is transferred to the olefin in a concerted or two step mechanism and a Mn^{III}-species is released under formation of the epoxide.[8]

The existence of Mn-oxo intermediates **4** is well established now.[7,8] Two possible pathways have been proposed, as shown in Scheme 4.1 (route a or b) and the matter of concerted vs non-concerted reaction mechanisms has been the subject of discussion.[7,8] If a

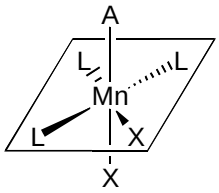
stepwise mechanism (route b) operates, rotation around the former double bond (in **6**) can cause isomerization during reaction leading to the obtainment of *trans*-epoxides from *cis*-olefins. This is the case with manganese-salen catalyzed epoxidation of cinnamate esters with electron withdrawing substituents at para positions.[9]

4.1.2 Hypothesis on a generally valid apical ligand effect

We noticed a few common features concerning epoxidations catalyzed by manganese complexes using hydrogen peroxide as oxidant.

a) In the case of manganese salen catalyzed epoxidations with H_2O_2, phenol moieties and imine moieties are present in the ligand.
b) In the manganese salen catalyzed epoxidations with hydrogen peroxide as the oxidant there is the requirement of an additional axial ligand/base.[10]
c) Salen systems can be partially reduced and the resulting ligand with an amine moiety present in the ligand as well as an intramolecular attached imidazole moiety, is still able to give a manganese-based catalyst, which can catalyze epoxidations with hydrogen peroxide. In this case no additional axial ligands are necessary.[11]
d) Additional (axial) ligands have a beneficial effect in Mn-porphyrin catalyzed epoxidations.[12]
e) As is the case in Mn-salen catalyzed epoxidations, intramolecular apical ligands in porphyrin systems improve catalyst performance.[13]
f) In the Mn-TMTACN complex (see Chapter 1), each of the three nitrogen atoms is trans to any labile coordination site on Mn. This results in a catalyst which is able to epoxidize olefins with high turnover numbers.[14]
g) A possible reason for the rather low turnover numbers of Mn-salen systems in epoxidation reactions is the hydrolysis of the imine bonds. Elimination of the imine bond by reduction or by stabilizing it via incorporation in an aromatic system like pyridine could possibly give a more stable catalyst.

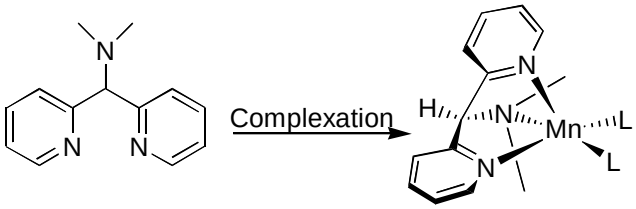
From this we concluded that phenol, imine and/or amine moieties are necessary in a good ligand and for best performance of the catalyst, an apical ligand, preferably intramolecular i.e. covalently attached to the remaining part of the ligand, should be present during epoxidation reactions using hydrogen peroxide as the oxidant. This is what can be denoted as the ‘apical donor atom effect’. We suspect a manganese complex with a ligand that has permanently a donor group present in an apical position could be an excellent catalyst when hydrogen peroxide is used as the oxidant.



L= N or O donor atom
A= apical N or O donor atom
X= N or O donor atom or free site

Figure 4.2 *Proposed coordination environment for a good Mn epoxidation catalysts*

Fortunately, we have developed in our group a ligand system which fulfills most of the requirements. N-[di(2-pyridyl)methyl]-N,N-bis(2-pyridylmethyl)amine **9** (Figure 4.3), meets the requirement of both pyridine donor atom and 'apical donor atom effect'. The lower half of the ligand, as shown in Scheme 4.2, has the ability to introduce an apical nitrogen donor atom to the metal center, in about a 90 degree angle to the plane of the metal and the two other nitrogen donor atoms. Moreover, we concluded after model studies that this is the only sterically allowed binding mode of this moiety. On could also view it from another perspective by considering the two pyridine nitrogen atoms and the metal center as being in one plane and the aliphatic nitrogen atom as the apical donor atom. In addition, more donor atoms of arbitrary nature can be coupled to this moiety by connecting them to the aliphatic nitrogen atom.



Scheme 4.2 *Complexation mode of the di(2-pyridyl)methylamine moiety*

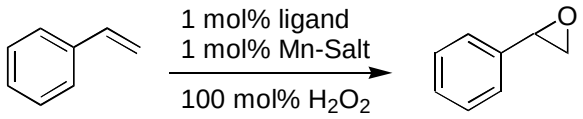
Based on these considerations, we focussed on the design of new ligands for selective catalytic epoxidation. The aim of the research described in this chapter is to develop a manganese based epoxidation catalyst that is able to use H_2O_2 as oxidant. Steric constraints of the ligands, reaction conditions, manganese sources and the tolerance of systems towards various substrates and functional groups in these substrates were investigated.

4.2 Reaction conditions

Screening of suitable ligands and catalysts in metal catalyzed epoxidation usually proceeds by applying standard reaction conditions. To 1 mL of a stock solution of substrate (1 M) and bromobenzene (~ 0.5 M, internal standard) in acetone was added 1 mL of a stock solution of catalyst, (0.01 M in acetone). To the reaction mixture was subsequently added in one portion 100 μl of 30% H_2O_2 (1 mmol). The reaction mixtures remained homogeneous at allt times.

Aliquots (0.15 mL) of the reaction mixtures were taken at appropriate times. The samples were filtered over a plug of silica and eluted with ether. The clear solutions were analyzed by GC, using automated injection. Control experiments showed that no epoxide was lost during filtration, product ratios did not change during sampling or workup and bromobenzene, the internal standard, was not oxidized. Reported yields were determined after 30 minutes unless noted otherwise.

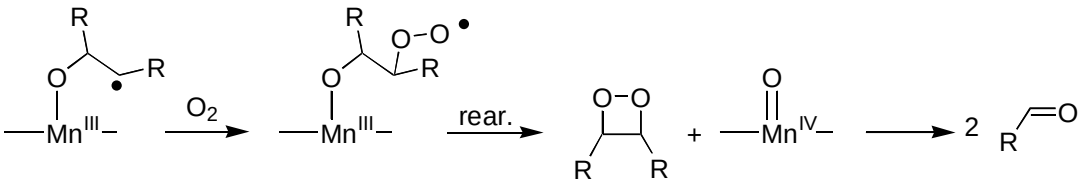
Besides the isolated complexes, the free ligands and $Mn(ClO_4)_2.6H_2O$ were also used as catalyst. ClO_4^- is a non-coordinating anion, leaving room at the metal center for substrates and oxidants. Complexes with ClO_4^- as the counterion can often be induced to crystallize, which makes it possible to study isolated species.



7 **8**

Scheme 4.3 *Catalytic test reaction*

A common side reaction in the catalyzed epoxidation of styrene is formation of benzaldehyde. A possible mechanism of formation of benzaldehyde involves the reaction of the Mn^{III}-species, as depicted in Scheme 4.4, with molecular oxygen and subsequent rearrangement of the adduct.[15] We found, however, no indication that the amount of oxygen present in the reaction mixture, had influence on the amount of benzaldehyde formed during the epoxidation reaction. Initial reactions performed under nitrogen atmosphere or air produced similar amounts (in all cases less than 1.5 %) of benzaldehyde. Catalytic epoxidations were accordingly performed under air atmosphere.



Scheme 4.4 *Possible formation of benzaldehyde by reaction with oxygen*

4.2.1 Pentadentate nitrogen donor atom ligands

The ligands N4Py **9** and 5Py **11** are described in chapter 2 and their manganese complexes are described in chapter 6. The complexes **10** and **12** dissolve well in acetone and were tested in the catalytic epoxidation reaction of styrene, as were the free ligands in combination with $Mn(ClO_4)_2.6H_2O$. The results are summarized in Table 4.1.

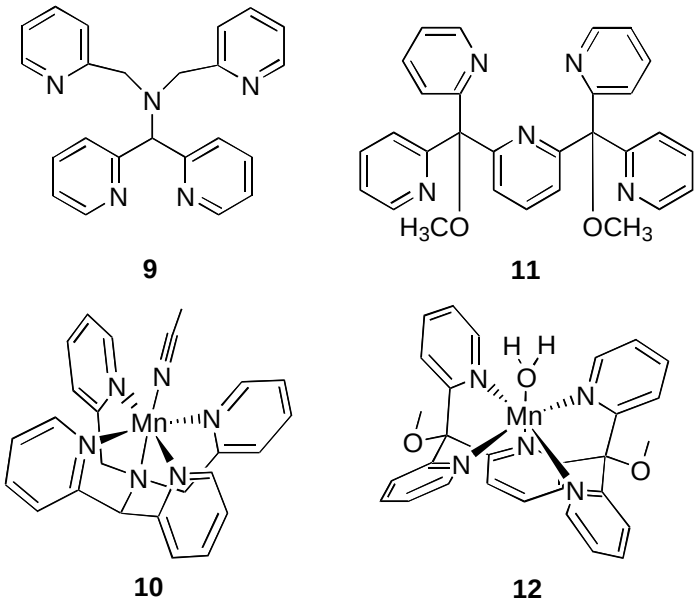


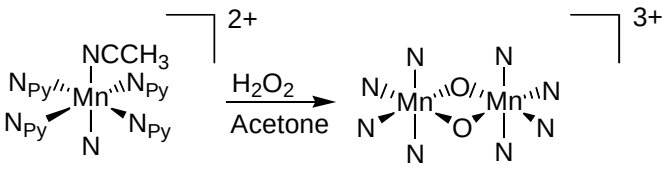
Figure 4.3 *Pentadentate nitrogen donor atom ligands **9**,**11** and their manganese complexes **10** and **12***

Table 4.1 *Epoxidation of styrene using pentadentate nitrogen donor atom ligands*[a]

Entry	Catalyst	Yield (%)
1	$Mn(ClO_4)_2.6H_2O$/N4Py **9**	<1
2	$[MnN4PyCH_3CN](ClO_4)_2$ **10**	<1
3	$Mn(ClO_4)_2.6H_2O$/5Py **11**	<1
4	$[Mn5Py(H_2O)] (ClO_4)_2$ **12**	<1

a) Reaction performed at ambient temperature
b) Yields based on substrate, using 1 equivalent of H_2O_2

As can be seen from entries 3 and 4, no reaction took place using 5Py as the ligand. Moreover, no color change took place indicating that H_2O_2 does not give rise to an oxidized manganese species. In contrast, when N4Py **9** was used as the ligand (entries 1 and 2) a rapid color change occurred to dark green and evolution of oxygen was observed. Dark green manganese complexes are known from the literature and the color is an indication of a Mn^{III}/Mn^{IV} di μ-oxo species.[16] Details of this complex and the reaction will be discussed in chapter 6. Although a new high valent dinuclear manganese complex was formed, we found no indications that epoxidation takes place.



Scheme 4.5 *Formation of a dinuclear mixed valent Mn^{III}/Mn^{IV} complex*

4.3 Towards salen mimics with intramolecular apical donor atoms

4.3.1 Pentadentate salen-like ligands

The construction of ligands with intramolecular apical donor atoms seemed crucial for good catalysis in epoxidation reactions with manganese complexes. From the former paragraphs it can be concluded that ligands containing only nitrogen donor atoms give unsatisfactory results in catalyzed epoxidation with H_2O_2 as the oxidant. We therefore decided to synthesize analogues with phenol moieties present in the ligand. The synthesis of these ligands is described in chapter 2.

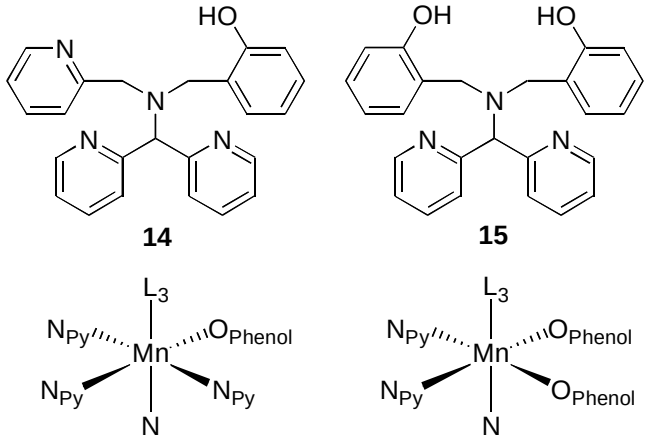


Figure 4.4 *Proposed coordination modes of new ligands*

The ligands were designed to bind to manganese as indicated in Figure 4.4. The sixth coordination site on manganese remains unoccupied by the ligand, leaving room for oxidant or substrate. The aliphatic nitrogen atom is in an apical position with respect to the plane of manganese and the other coordinating atoms. Model studies indicated that the geometry of the ligand, in case of formation of a mononuclear manganese complex, ensures that it can only bind to the metal in the way depicted in Figure 4.4.[17] Salen ligands contain 2 imine bonds and 2 phenol moieties. The imine bonds have been replaced in ligands **14** and **15** with pyridine moieties, in the expectation of higher stability towards hydrolysis during epoxidation reactions. Unfortunately we were not able to isolate well defined complexes and catalytic epoxidation reactions were performed using in situ prepared catalysts.

Table 4.2 *Epoxidation using pentadentate phenol containing ligands*[a]

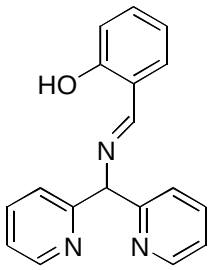
Entry	Catalyst	Substrate	Yield (%)[b]
1	$Mn(ClO_4)_2.6H_2O$/ ligand **14**	Cyclohexene	10
2	$Mn(ClO_4)_2.6H_2O$/ ligand **15**	Cyclohexene	32
3	$Mn(ClO_4)_2.6H_2O$/ ligand **15**	Styrene	15

a) Reactions performed at ambient temperature.
b) Yields based on substrate, using 1 equivalent of H_2O_2

As predicted from our ‘apical donor atom’ hypothesis, the system with pentadentate ligands was active in the epoxidation reaction when hydrogen peroxide was used as oxidant. Yields were low but clearly the in situ prepared complexes catalyzed the epoxidation reaction. In addition to cyclohexene epoxide also some allylic oxidation products were obtained. The use of the in situ prepared catalyst from ligand **14** resulted in formation of 2% cyclohexenol and 17 % cyclohexenone. Only 1% cyclohexenone and 2% cyclohexenone were formed using ligand **15**. Apparently the ligand containing one phenol moiety results in formation of a less active but much more selective catalyst.

4.4 Imine ligands

Intermediates in the synthesis of the pentadentate ligands **14** and **15** described in the former paragraph are imines. Ligand **16** contains an imine moiety, two pyridine moieties and a phenol moiety all capable of coordinating to a manganese ion. Also in this case we were not able to isolate well defined Mn complexes to use in catalytic experiments and therefore the ligand was employed to prepare catalysts in situ. The same test reaction and conditions were used as before.



16

Figure 4.5 *Imine* **16** *used as ligand*

A stock solution of the catalyst was prepared by adding equimolar amounts $Mn(ClO_4)_2.6H_2O$ to a suspension of the imine in acetone. The undissolved imine rapidly dissolved upon addition of $Mn(ClO_4)_2.6H_2O$. Usually the bright yellow solution turned colorless within minutes indicating complexation or degradation of the ligand. Within 10 min the stock solutions were used in catalytic epoxidation experiments and the yields indicated in Table 4.3 were reached. Upon addition of H_2O_2 the solutions turned red-brown and the color vanished during ca 10 min and reaction mixtures turned light yellow. In the initial stage of these reactions very fast formation of epoxide was observed. With disappearance of the color, catalytic activity also decreased.

In contrast to the reactions performed in acetone, almost no epoxidation activity was observed when reactions were performed in methanol or acetonitrile. Similar solvent effects were observed in epoxidation reactions catalyzed by the Mn-TACN system and were ascribed

to the formation of a perhemiketal from acetone and H_2O_2 and the slow release during the epoxidation reaction of H_2O_2 from the perhemiketal.[18]

Table 4.3 *Catalytic epoxidation using imine **16** as ligand*[a]

Entry	Salt	Time (min.)	Solvent	Yield[b] (%)
1	$Mn(ClO_4)_2.6H_2O$	15	Acetone	18
2	$Mn(ClO_4)_2.6H_2O$	15	MeOH	2
3	$Mn(ClO_4)_2.6H_2O$	15	MeCN	2
4	$Mn(NO_3)_2.6H_2O$	15	Acetone	6

a) Reactions performed at ambient temperature
b) Yields based on substrate, using 1 equivalent of H_2O_2.

Difficulties arose when catalytic epoxidation reactions were performed in duplo. When the same stock solution (acetone) was used the next day, almost no catalytic activity was observed. We suspected degradation of the ligand in this case and catalytic epoxidation using a 1 h old stock solution of catalyst showed less than 5 % epoxide formation. We were able to unravel the main course of the catalyst degradation as described in the next paragraph.

4.4.1 Isolation of the degraded catalyst and its characterization

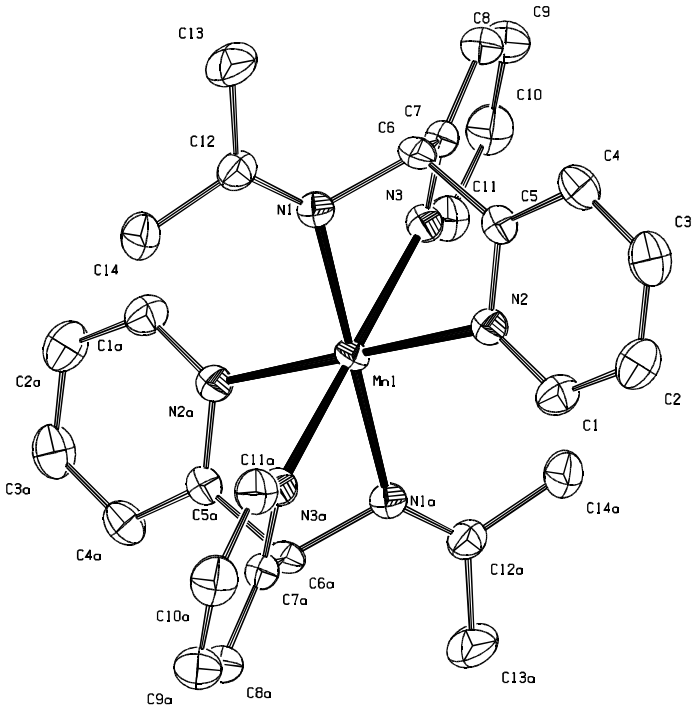
A stock solution of $Mn(ClO_4)_2.6H_2O$ and ligand **16** in acetone was stored at 4^{o}C for several weeks and crystals were obtained. The crystals were suitable for X-Ray analysis and the molecular structure of complex **17** is shown in Figure 4.6. Bond distances and angles are summarized in Table 4.4.

The complex $[C_{28}H_{30}MnN_6]\cdot(ClO_4)_2\cdot 2C_3H_6O$ crystallized in the triclinic spacegroup $P\overline{1}$ with Z=1. Each asymmetric unit contains one formula unit, consisting of nine moieties: a cationic Mn complex, two ClO_4^- anions and two acetone molecules. The structure is that of a six coordinated mononuclear compound in an octahedral geometry. The axis through the planes of N1-N2-N3 and N1a-N2a-N3a is slightly elongated resulting in a trigonal antiprismatic distortion. The steric constraints of the ligands cause a *fac* coordination of the ligand.[19,20]Acetone is present in the crystal lattice and evaporates upon standing. The Mn-N bond lengths are in the 2.21 – 2.26 Å and in agreement with literature data for related Mn complexes.[20,21]

Table 4.4 *Selected bond distances (Å) and angles (^{o}) of* **17**[a]

Mn1-N1	2.2149(16)	Mn1-N3	2.2597(17)
Mn1-N2	2.2542(16)		
N1-Mn1-N1a	180.0(5)	N1-Mn1-N3	74.25(6)
N2-Mn1-N2a	180.0(3)	N2-Mn1-N3	83.09(6)
N3-Mn1-N3a	180.0(5)	N1-Mn1-N2a	106.04(6)
N1-Mn1-N2	73.96(6)		

a) standard deviations in parenthesis



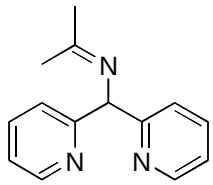


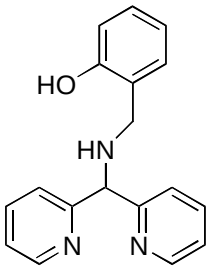
Figure 4.6 *Left: ORTEP representation of the cation of* **17** *(hydrogen atoms omitted for clarity) right: the ligand in complex* **17**

From the structure it is clear that the initial imine bonds have dissappeared and the amine has been converted into a new imine. A new ligand has been formed, which consists of the bis-(2-pyridyl)methyl amine moiety and the solvent acetone. The trans-imination of ligand **16** occurs without the presence of H_2O_2 and is catalyzed by $Mn(ClO_4)_2.6H_2O$ since a solution of ligand **16** in acetone is stable.

Attempts to crystallize the same complex from a solution of bis-(2-pyridyl)methyl amine and $Mn(ClO_4)_2.6H_2O$ in acetone were unsuccessful.

4.5 Secondary amine ligands

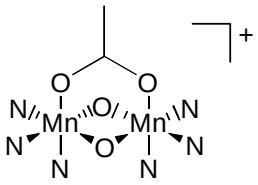
From the former paragraph it is clear that imine bonds are easily hydrolyzed upon dissolving the ligand and $Mn(ClO_4)_2.6H_2O$ in acetone. Hence, it is almost certain that the ligand **16** is not stable under the reaction conditions. We therefore decided to test the analogous amine **18**, easily prepared by reduction of the imine bond by $NaBH_4$.



18

Figure 4.7 *Secondary amine used as ligand in epoxidation reactions*

Again we were not able to isolate well defined mononuclear complexes and used a catalyst prepared in situ from the ligand and $Mn(ClO_4)_2.6H_2O$. Also the dinuclear acetate bridged complex **19** (Figure 4.8) prepared from this ligand (see chapter 3) has been tested under the same standard conditions as mentioned before.



19

Figure 4.8 *Complex **19** prepared from ligand **18***

The results of the catalytic epoxidations are summarized in Table 4.5. Although yields are still moderate, the in situ prepared complexes are active in the epoxidation reaction. Addition of a second equivalent of H_2O_2 at the time that epoxidation activity was no longer observed did not give rise to further epoxidation and so we can conclude that the catalyst has decomposed when epoxidation stops. Catalyst activity is substantially lower, especially at the start of the reaction but the efficiency and catalyst stability are substantially higher using the in situ prepared catalysts from ligand **18** compared to the epoxidation reactions using the corresponding imines **17**. Moreover, the results of the reactions were reproducible.

In the case of the epoxidation of styrene a 40 % yield was obtained. Changing the solvent to methanol decreased the yield to 2 %. Changing the counterion to acetate further decreased the yield to less than 1 %, which is comparable to yields obtained when complex **19** was used. Acetate is known to promote formation of multinuclear complexes.[22] Complex **19** (entries 7,8) was barely active as a catalyst in the epoxidation of styrene. High catalase activity was observed using complex **19** or the in situ prepared catalyst from $Mn(OAc)_2.4H_2O$ and ligand **18**. Pretreatment of the complex with H_2O_2 did not result in better yields.[23] In all cases catalase activity was observed but only in the case of complex **19** the decomposition stopped after about 5 min, indicating that all H_2O_2 had been consumed. In all other cases decomposition of H_2O_2 was observed until epoxidation activity was no longer observed,

Besides styrene, *trans*-β-methylstyrene and cyclohexene (entries 5,6) were epoxidized in 21% and 24% yield respectively. Only traces of benzaldehyde were found and in the case

of cyclohexene only trace amounts of the allylic oxidation products cyclohexenol and cyclohexenone were formed. Allylbenzene was a poor substrate and only 5% of the epoxide was obtained.

From the results obtained so far we concluded that ligand **18** is able to form with the appropriate salt $Mn(ClO_4)_2.6H_2O$, an active catalyst for the epoxidation of olefins. The results are reproducible indicating that the active species is reasonably stable. The best solvent for this type of epoxidation is acetone and aliphatic terminal alkenes appear to be poor substrates.

Table 4.5 *Catalytic epoxidation reactions using secondary amine ligand **18**[a]*

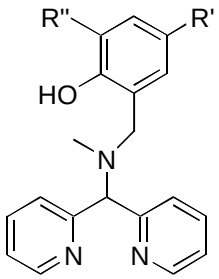
Entry	Catalyst	Substrate	Time (min.)	Solvent	Yield[c] (%)
1	**18** / $Mn(OAc)_2.4H_2O$	Styrene	15	Acetone	<1
2	**18** / $Mn(ClO_4)_2.6H_2O$	Styrene	71	Acetone	40
3	**18** / $Mn(ClO_4)_2.6H_2O$	Styrene	15	MeOH	2
4	**18** / $Mn(ClO_4)_2.6H_2O$	Allylbenzene	15	Acetone	5
5	**18** / $Mn(ClO_4)_2.6H_2O$	*tr*-β-Me-styrene	60	Acetone	21
6	**18** / $Mn(ClO_4)_2.6H_2O$	Cyclohexene	30	Acetone	24
7	Complex **19**	styrene	60	Acetone	5
8	Complex **19**	styrene	40	Acetone	0[b]

a) Reactions performed at ambient temperature. b) The catalyst was treated before addition of substrate with 100 equivalents of H_2O_2 and stirred for 10 min. Fast decomposition of H_2O_2 was observed. c) Yields based on substrate, using 1 equivalent of H_2O_2.

4.6 N-Methyl amine ligands

Since the secondary amine **18** described in the former paragraph was successfully employed in our catalyzed epoxidation reaction, we decided to enhance steric hindrance and change amine donor properties. Various N-methylated ligands were employed using para and ortho/para substituted phenols. From the unsubstituted ligand, **20a** we were able to isolate various well defined complexes **21**-**24** as described in chapter 3. The topology of these complexes is depicted in Figure 4.10. Both in situ prepared catalysts and isolated complexes were used in the catalytic epoxidation reaction. The results are summarized in Table 4.6. Since the reactions were found to stop after about 20 min, a second equivalent of H_2O_2 was added at this point and epoxidation continued.

Unfortunately, all isolated complexes **22**-**24** (entries 2-4) were inactive as catalysts in the epoxidation reaction except for complex **21**. Employing complex **21** (entry 1) in the epoxidation reaction resulted in a 34 % yield of styrene epoxide. The activity of the complex is, however, low, probably due to the poor solubility of the complex in the reaction mixture. Moreover, in the case of catalysis using the isolated complexes, 1 mol% of complex with respect to the substrate was used which implies that in the case of the di- and trinuclear complexes two and three times as much ‘manganese’ was present.

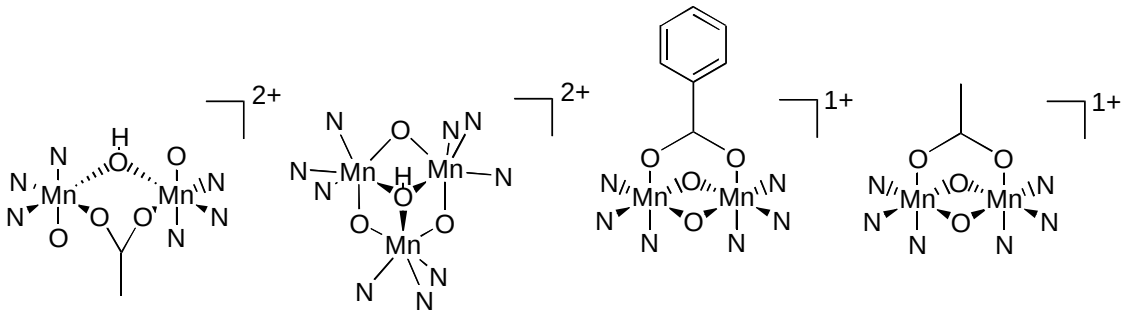


20

Compound	R'	R''
a	H	H
b	Cl	H
c	NO_2	H
d	MeO	H
e	t-Bu	t-Bu

Figure 4.9 *Various substituted N-methyl amines used as ligands in epoxidation reactions*

The activity and efficiency of complex **21** as a catalyst was found to be rather low for this reason. Although the reaction mixture containing the trinuclear complex **22** showed a color change from colorless to brown, only trace amounts of epoxide could be detected. In the case of complexes **23** and **24** we observed fast decomposition of H_2O_2 as was the case employing complex **19**. Only trace amounts of epoxide were found.



21 **22** **23** **24**

Figure 4.10 *Complexes used in epoxidation reactions (molecular and crystal structures, see chapter 3)*

Table 4.6 *Catalytic epoxidation reactions using N-methylated ligand **20a**[a]*

Entry	Catalyst	Substrate	Time (min.)	Yield[b] (%)
1	**21**	Styrene	60	34
2	**22**	Styrene	60	<1
3	**23**	Styrene	60	<1
4	**24**	Styrene	60	<1
5	$Mn(ClO_4)_2.6H_2O$/**20a**	Styrene	60	80
6	$Mn(ClO_4)_2.6H_2O$/**20a**	Dihydronaphthalene	56	58
7	$Mn(ClO_4)_2.6H_2O$/**20a**	1-Decene	60	14
8	$Mn(ClO_4)_2.6H_2O$/**20a**	*tr*-β-Me-styrene	60	52
9	$Mn(ClO_4)_2.6H_2O$/**20a**	*cis*-β-Me-styrene	60	c:40,tr:20
10	$Mn(ClO_4)_2.6H_2O$/**20a**	Cinnamyl alcohol	70	81

a) Reactions performed at 0°C, second equivalent of H_2O_2 added after 20 min.
b) Yield based on substrate

In contrast to the epoxidation reactions with ligand **16**, previously described, which turned red, reaction mixtures turned green upon addition of H_2O_2 and subsequently turned via greenish brown to pale yellow. Although the yellow color was an indication that almost all H_2O_2 was consumed, the catalytic activity was retained at low levels. Addition of more H_2O_2 gave rise to a green/brown colored homogeneous reaction mixture again. At the end of the reactions white fine precipitates were observed.

The in situ prepared catalysts (entries 5-10) were very active. After 20 min a second equivalent of H_2O_2 was added. Styrene was epoxidized in 80 % yield (entry 5) but again 1-decene was epoxidized only in low yield (entry 7). Dihydronaphthalene and *trans* and *cis*-β-methylstyrene were epoxidized in 58%, 52% and 60 % yield, respectively. When the in situ prepared catalysts were used, addition of the second equivalent of H_2O_2, in all cases except for 1-decene, full conversion of substrates was reached within 60 min.

Cis-β-methylstyrene gives besides the desired *cis* epoxide also a considerable amount of *trans* epoxide. The isomerization does not occur with *trans*-β-methylstyrene as a substrate. Hence, it is likely that at least in the epoxidation of c*is*-β-methylstyrene a non-concerted pathway is involved.

An excess of H_2O_2 is necessary since H_2O_2 is also decomposed by the in situ prepared catalysts. The catalase activity was, however, much higher when complexes **23** and **24** where used as a catalyst. When H_2O_2 was added slowly in portions (Figure 4.11) within 80 min full conversion of styrene was observed. The total amount of added H_2O_2 was only 1.5 equivalents. Thus it can be concluded that by keeping the H_2O_2 concentration low, the decomposition of H_2O_2 is suppressed.

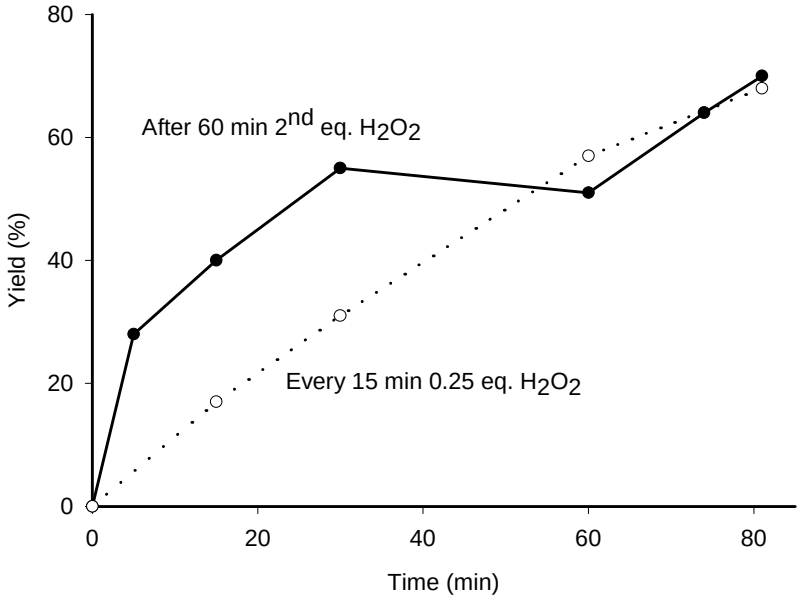


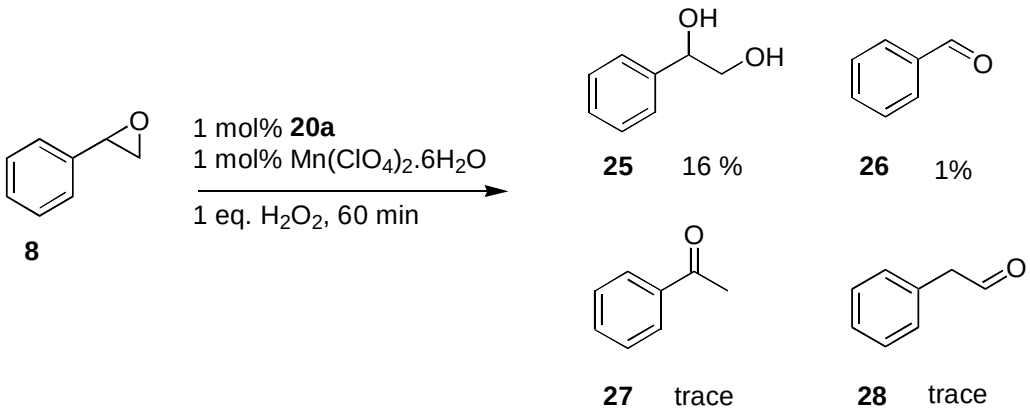
Figure 4.11 *Influence of portion-wise H_2O_2 addition on the yield of the epoxidation reaction of styrene*

In the case of the epoxidation of styrene, 80% epoxide was obtained when the second equivalent of H_2O_2 was added after 20 min. The remaining 20% was found to be mainly 1-phenyl-1,2-ethanediol. As is illustrated in Figure 4.11, during the reaction the amount of epoxide is decreasing until a second portion of H_2O_2 is added. In the latter, illustrative experiment, the second equivalent of H_2O_2 was added after 60 min and 72 % yield of styrene oxide was obtained.

4.6.1 Epoxide decomposition

The hydrolysis of styrene oxide seems to be the main pathway to the diol. This was confirmed by an experiment employing the usual conditions and using styrene oxide as the substrate. When styrene oxide is treated with H_2O_2 in acetone, no epoxide is degraded. In the presence of 1 mol% of ligand **20a** and 1 mol % of $Mn(ClO_4)_2.6H_2O$, after 1 h, 18 % of the initial amount of epoxide is degraded (Scheme 4.6). The amount of degradation is of the same order when styrene is catalytically epoxidized. GC-MS analysis of reaction mixtures showed that the major part (16 %) of the epoxide is converted into the corresponding diol. Benzaldehyde is formed in 1 % yield. Trace amounts of phenylacetaldehyde were also detected.

Addition of base ($NaHCO_3$ or triethylamine) did not lead to improved catalytic activity or suppression of epoxide hydrolysis. Instead, addition of base increased the decomposition of H_2O_2 and yields dropped dramatically (< 5%). Hydrolysis of epoxides is a common problem in epoxidations using H_2O_2.[24] Therefore pyridine is used as additional base and ligand in rhenium catalyzed epoxidations.[25]



Scheme 4.6 *Decomposition of styrene oxide under conditions employed in catalytic epoxidation reactions*

4.6.2 Electronic and steric effects of ligand substitutions

To optimize the epoxidation reaction we decided to introduce substituents at the 4 and 6 positions of the phenol moiety of the ligand (Figure 4.9). Although we were not able to

introduce other groups than methyl at the aliphatic nitrogen moiety as explained in chapter 2, substituted salicylaldehydes are readily available. Various N-methyl amine ligands **20** have been synthesized and tested in the epoxidation reaction. Styrene was chosen as the substrate and 0.4 mol% of catalyst and 1 eq of H_2O_2 with respect to the substrate was used.

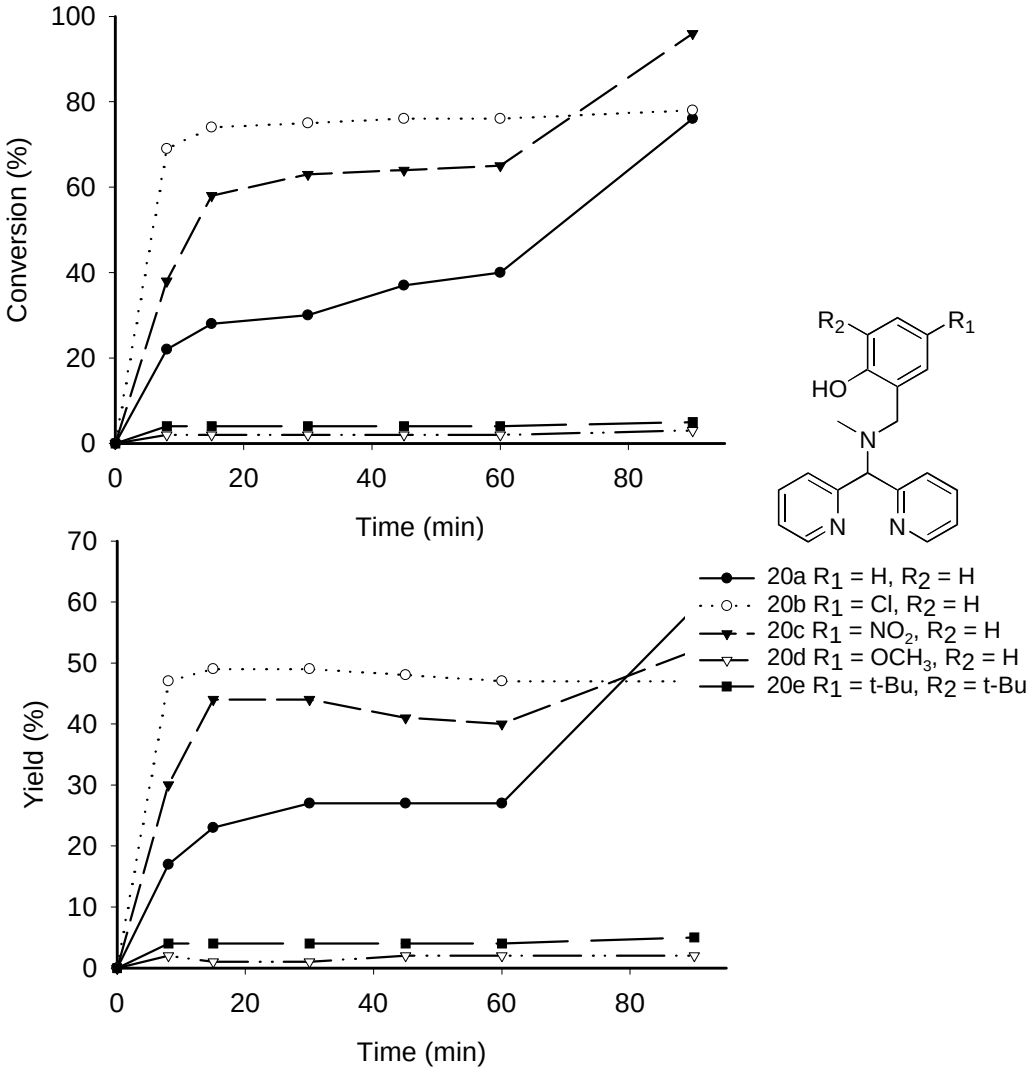


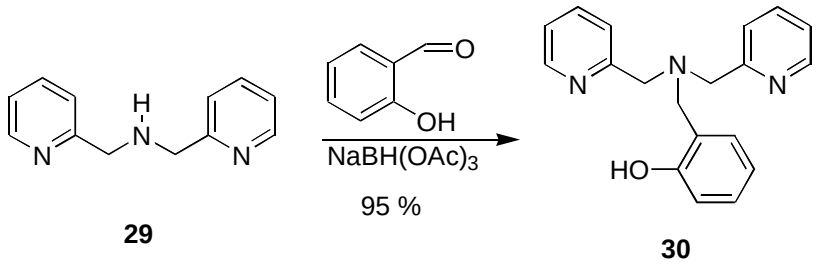
Figure 4.12 *Yield of epoxide (lower figure) and conversion (upper figure) of styrene in epoxidation reactions using substituted ligands: Ratio catalyst : styrene : H_2O_2 = 1: 250 : 250. Reactions were performed at room temperature. At t = 60 min a second equivalent of H_2O_2 was added.*

The influence of the substituents on both reaction rate and efficiency is considerable as illustrated in Figure 4.12. Tert-butyl groups in ortho and para positions with respect to the phenolic OH are not tolerated at all (ligand **20e**). Less than 5% conversion to the epoxide was observed. Prolonged stirring with a second eq of H_2O_2 had no effect on conversion and yield in this case, indicating that catalase activity is not a problem using this ligand. The same applies for the methoxy substituted ligand **20d**.

The highest efficiency is reached using the unsubstituted ligand **20a**. After addition of a second equivalent H_2O_2 the catalysis continues and 59 % yield of epoxide is obtained. The conversion reached at this point is 76%. Although total conversion is higher (96 %) when the nitro substituted ligand **20c** is used, more epoxide is decomposed as can be seen from Figure 4.12. After 20 min the total amount of epoxide begins to decrease while conversion still increases. Addition of a new portion of H_2O_2 leads to a further increase of the yield (52%). The chloro substituted ligand **20b** provides the most active catalyst. Within 8 min 47% epoxide is formed corresponding to 118 turnovers. At this point the catalyst has degraded, since no additional epoxide was formed after a second equivalent H_2O_2 was added. After the catalyst is no longer active, degradation of epoxide virtually stops. This last observation is an indication that product degradation is catalyzed by the same species that is responsible for epoxidation.

4.6.3 Effects of ligand architecture

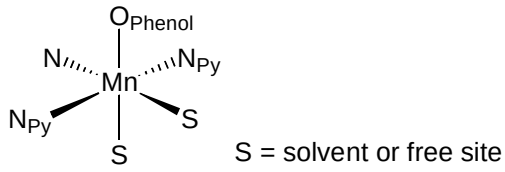
Thus far we have seen that in the new catalytic system ligands based on pyridine and phenol donor groups and manganese salts with non coordinating counter ions can be used in catalytic epoxidation. Still a major question is whether the bispyridyl-methylamine moiety is essential, i.e. whether the apical donor atom hypothesis applies. Since catalysts based on ligands **14, 15** and **20a** are all active in epoxidation reactions we can conclude that at least one phenol moiety has to be present and at least two pyridine moieties. An easier accessible ligand is compound **30** and it was synthesized as depicted in Scheme 4.7. The characteristic methylene ^{1}H-NMR resonances at δ 3.73 ppm and δ 3.83 ppm integrate for two and four protons respectively.



29 **30**

Scheme 4.7 *Synthesis of ligand* **30**

Ligand **30** was tested in catalytic epoxidations, using the catalyst formed in situ with $Mn(ClO_4)_2.6H_2O$ and with styrene as the substrate. Under standard conditions (vide supra) we did not observe any epoxide formation. This observation is in accordance with our apical donor atom hypothesis although other explanations cannot be excluded for the lack of reactivity. Ligand **30** has about the same stereochemistry as ligand **20a**, except that it is possible that chelation of the ligand provides a conformer in which both pyridine nitrogen atoms and tertiary amine are in the same equatorial plane, which means that in this case the phenol moiety acts as an apical ligand. Ligand **20a** can never chelate in such a fashion in which all three nitrogen atoms are coordinated in an equatorial plane.



Scheme 4.8 *Presumed complexation of ligand* **30**

4.7 Discussion and Conclusions

The epoxidation of alkenes using manganese based catalysts has been investigated and various ligands have been tested. The pentadentate nitrogen donor atom ligands **9** and **11** do not give rise complexes that are active as a catalyst in the epoxidation reaction. In contrast, the pentadentate ligands with at least one phenol moiety (**14** and **15**) yield active catalysts. A prerequisite for a good ligand appears to be the presence of a phenol group.

Imine containing ligand **16** (Figure 4.5) yields an active catalyst in the epoxidation reaction using H_2O_2 as oxidant. However, imine **16** is easily hydrolyzed and the product resulting from this hydrolysis has been isolated and found to be not active as catalyst.

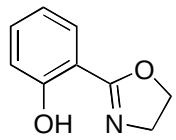
The imine **16** can be made more stable by reduction of the imine bond. The resulting secondary amine **18** act as suitable ligand for catalysts in the epoxidation reaction but the resulting -in situ formed- catalysts are not as active as the ones formed from imine containing ligands. The increased stability of the ligand accounts for higher efficiency of the corresponding catalyst.

Even more stable ligands were obtained by methylating the secondary amines. A more active catalyst was formed and efficiency increased: in the case of styrene 80% yield of styrene oxide was obtained using only 1 mol% of catalyst. All styrene was converted to oxygenated products, with only 2 equivalents of H_2O_2. In the latter case 40% of all H_2O_2 is efficiently converted to epoxide. Using 0.4 mol% of catalyst, 59% of epoxide was obtained, i.e. 148 turnovers/mol catalyst.

Substituents located at the phenol ring of the ligand have serious impact on the performance of the catalysts. Sterically demanding groups like t-butyl at the phenol moiety of the ligand inhibit catalysis. Also an electron donating methoxy substituent, located para to the phenolic oxygen, was found to prevent the oxidation.The ligands substituted with electron withdrawing moieties, like nitro and chloro substituents, provided the most active catalysts. The use of the nitro substituted ligand gave rise to almost full conversion (96 %) of styrene but the catalyst caused also the largest amount of decomposition of styrene oxide. By using the chloro substituted ligand, the most active catalyst was obtained. Within 8 min 47 % of styrene oxide is obtained. This catalyst is, however, also the most labile and addition of a second equivalent of H_2O_2 had no effect on the yield.

The effects of substituents positioned on the phenol ring of the ligand are thus remarkable. Electron withdrawing substituents seem to destabilize the actual reactive intermediate and fast reaction is observed. Electron donating substituents, like for instance methoxy, attenuate the catalyst. The same observations were made in the Mn-salen catalyzed

epoxidation using hypochlorite as oxidant.[26] Hoogenraad found similar substituent effects in the $Mn(Phox)_3$ catalyzed epoxidation using H_2O_2 as oxidant. The finding that conjugated olefins like styrene are more reactive in the epoxidation reaction than isolated olefins like 1-decene is in accordance with the observations in the Mn-salen catalyzed reaction[5] and the $Mn(Phox)_3$ system reported by Hoogenraad.[27]

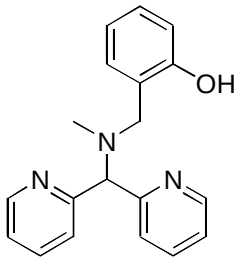


28

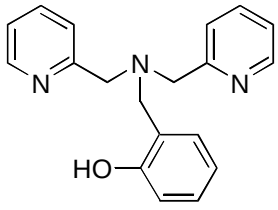
Figure 4.13 *Phox ligand* **28**

The results obtained using *cis*-β-methylstyrene as substrate clearly indicate that the mechanism of formation of the epoxidation itself is not concerted but at least in this case, a two step mechanism operates. The formation of *trans* epoxide is attributed to the formation of intermediates, which have enough time to isomerize. Related reactions in which the same isomerizations take place are known from the literature[9] and the epoxidation is often considered to proceed via Mn-oxo intermediates and alkenes, which are converted, in a non concerted mechanism, to the epoxide via a pathway involving radical intermediates (Scheme 4.1, path b).

The inability of ligand **30** to form active species capable of epoxidizing olefins in contrast to ligand **20a,** which forms very active species in the epoxidation reaction, is remarkable. It is not clear what the reason is for this observation but surely a conformational effect plays an important role. The unique binding properties of the lower half of ligand **20a**, enforcing a particular geometry (vide supra) are responsible for the creation of an active species in the epoxidation reaction. This might point to the effect of an apical ligand, which enhances the formation of Mn-oxo species for Mn salen and porphyrins in accordance with proposals in the literature.[1,5]



20a



30

Figure 4.14 *Activity and structure relationship?*

Ligand **20a** provides such an apical coordinating group intramolecularly, whereas ligand **30** is more flexible and the ligand can bind in several ways leaving more freedom to chelate the metal. For instance, the ligand can chelate in such a way that the pyridine moieties are bound in a *mer* configuration. The catalyst formed by ligand **20a** and $Mn(ClO_4)_2.6H_2O$ is

the first example of a non-salen or porphyrin system exhibiting the features consistent with an intramolecular apical ligand effect in epoxidation reactions, using H_2O_2 as oxidant.

Isolated di- and trinuclear complexes based on compound **20a** as the ligand are not active as epoxidation catalysts, and these results point to a mononuclear species as the active catalyst.

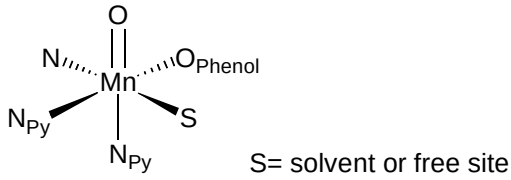


Figure 4.15 *Proposed active species in epoxidation reactions*

Furthermore, the characteristics of the epoxidation reaction (substituent effects, cis/trans isomerization and higher yields using conjugated olefins) resemble Mn-salen catalyzed epoxidations. Therefore the active species might have a ligand environment as depicted in Figure 4.15. We were, however, not able to detect such a mononuclear species with ES-MS.

4.8 Experimental Section

For general remarks, see chapter 3.

4.8.1 Materials

Cyclohexene, cyclohexene oxide, styrene, styrene oxide, trans-β-methylstyrene, dihydronaphthalene, 1-decene, cinnamyl alcohol, were obtained from Aldrich and Acros. *Cis*-β-methylstyrene was synthesized from phenyl-propyne by catalytic hydrogenation, using Lindlar's catalyst. Bispicolylamine was synthesized according to literature procedures.[28] Epoxides from the corresponding alkenes were prepared by epoxidation using *m*-CPBA (styrene, trans-β-methylstyrene, cis-β-methylstyrene, 1-decene, allylbenzene) and following a procedure described by Jacobsen[29] using a racemic catalyst (dihydronaphthalene).

4.8.2 Equipment and GC-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, or an a Hewlett Packard 5890 II Gas Chromatograph using a CP-wax 52 CB column or a CP-wax 57 CB column. Calibration was performed using authentic samples of the epoxide and alkene and independent samples of further byproducts. Conversions and yields were determined using bromobenzene as internal standard, and calculated using the Chemstation software.

4.8.3 Structure determination

Crystal structure determination of 17

$C_{28}H_{30}MnN_6 \cdot (ClO_4)_2 \cdot 2C_3H_6O$. 16587 Measured reflections, 4399 unique reflections (R_{int} = 0.0339). Analytical absorption correction (program PLATON, routine ABST, μ = 0.544 mm^{-1}, 0.84-0.93 transmission). R ($I > 2\sigma(I)$): R1 = 0.0433, wR2 = 0.1185. R (all data): R1 = 0.0472, wR2 = 0.1216. S = 1.038. Intensities were measured on a Nonius Kappa CCD diffractometer with rotating anode (Mo-K_α, λ = 0.71073 Å). The structure was solved with automated Patterson methods (program DIRDIF97[30]) and refined with the program SHELXL97[31] against F^2 of all reflections up to a resolution of $(\sin \vartheta/\lambda)_{max}$ = 0.65 $Å^{-1}$. Non hydrogen atoms were refined freely with anisotropic displacement parameters. Hydrogen atoms were refined as rigid groups. Structure calculations and checking for higher symmetry were performed with the program PLATON.[32]

Table 4.7 *Crystal data for $Mn[C_{14}H_{15}N_3]_2(ClO_4)_2.(C_3H_6O)_2$*

Formula	$C_{34}H_{42}Cl_2MnN_6O_{10}$
Formula weight	820.58
Crystal dimensions (mm)	0.15 x 0.30 x 0.39
Symmetry cell setting	Triclinic
Symmetry space group	P-1, 2
a (Å)	7.8380
b (Å)	11.1024
c (Å)	12.3543
Cell volume ($Å^3$)	962.99
Z	1
F(000)	427
D_{calc} ($g.cm^{-3}$)	1.415
μ (Mo Kα) mm^{-1}	0.54
T (K)	150
Min and max Residual density outside ($e^- Å^3$)	-0.46, 0.62

4.8.4 Synthesis

2-{[bis(2-pyridinylmethyl)amino]methyl}phenol (30)

To a solution of bispicolylamine **29** (1.0 g, 5.0 mmol) in 30 mL 1,2-dichloroethane was added salicylaldehyde (0.92 g, 7.5 mmol) and $NaBH(OAc)_3$ (1.59 g, 7.5 mmol). The reaction mixture was stirred for 4 h and 20 mL 2M aq. HCl and 20 mL of water were added. The aqueous layer was separated and the organic layer was again extracted with 10 mL of water. The combined aqueous layers were made alkaline (pH = 8) with dil. aq. ammonia and extracted thrice with 30 mL of CH_2Cl_2. Drying and evaporation of the solvent yielded a light yellow oil which was purified by chromatography on silica (ether) and an off-white oil, which solidified on standing, was obtained. Yield: 1.45 g (4.8 mmol), 95%. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.73 (s, 2H), 3.83 (s, 4H), 6.74 (t, J = 7.3, 1H), 6.85 (J=8.1, 1H), 7.01 (d, J=7.3, 1H), 7.07 – 7.15 (m, 3H), 7.28 (d, J = 7.7, 2H), 7.56 (t, J = 7.7, 2H), 8.51 (d, J = 4.8, 2H), 10.9 (br, 1H). ^{13}C-NMR (75.4 MHz, $CDCl_3$) δ 53.43 (t), 56.57 (t), 114.04 (d), 116.35 (d), 119.72 (d), 120.30 (s), 120.72 (d), 126.55 (d), 127.66 (d), 134.28 (d), 146.39 (d), 155.06 (s), 155.74 (s). CI-MS: 306 ($M + H^+$)

4.8.5 Catalytic oxidation

Typical epoxidation procedure: 1 mL of a 1 M solution of styrene and 0.5 M bromobenzene in acetone was added to 1 mL of a 1 M solution of ligand and $Mn(ClO_4)_2.6H_2O$ in acetone. The solution was cooled to 0 ^oC and subsequently 100 µl of 30% H_2O_2 was added. Samples of 100 µl were taken at appropriate times using an automated Gilson pipette. The samples were filtered over a plug of silica, eluted with ca. 2 mL ether and stored in sealed bottles. GC analysis was performed within 12 h.

4.9 References

1 B. Meunier, *Chem. Rev*. **1992**, *92*, 1411 – 1456.

2 S. Banfi, M. Dragoni, F. Montanari, G. Pozzi, S. Quici. *Gazz. Chim. Ital*. **1993**, *123*, 431 – 436.

3 An example of significant enantioselective epoxidation: R.L. Halterman, S-T Jan, *J. Org. Chem*. **1991**, *56*, 5253 – 5254.

4 C.P. Horwitz, D.R. Fooksman, L.D. Vuocolo, S.W. Gordon-Wylie, N.J. Cox, T.J. Collins, *J. Am. Chem. Soc*. **1998**, *120*, 4867 – 4868; C-M. Che, W-K. Cheng, *J. Chem. Soc. Chem. Commun.* **1986**, 1443 – 1444; S-H. Zhao, P.R. Ortiz, B.A. Keys, K.G. Davenport, *Tetrahedron Lett.* **1996**, *37*, 2725-2728.

5 Excellent reviews have appeared: E.N. Jacobsen, Asymmetric Catalytic Epoxidation of Unfunctionalized Olefins in Catalytic Asymmetric Synthesis, Ojima, I. Ed.; VCH: New York, **1993**, 159; T. Katsuki, *Coord. Chem. Rev*. **1995**, *140*, 189 – 214.

6 A.W. van der Made, R.J.M. Nolte, W. Drenth, *Recl. Trav.Chim. Pays-Bas*, **1990**, *109*, 537 – 551; J.A.S.J. Razenberg, R.J.M. Nolte, W. Drenth, *Tetrahedron Lett.* **1984**, *25*, 789 – 792.

7 D. Feichtinger, D.A. Plattner, *Angew. Chem. Int. Ed.* **1997,** *36*, 1718 – 1719.

8 N.S. Finney, P.J. Pospisil, S. Chang, M. Palucki, R.G. Konsler, K.B. Hansen, E.N. Jacobsen, *Angew. Chem. Int. Ed.* **1997,** *36* 1720 – 1723; C. Linde, M. Arnold, P-O. Norrby, B. Akermark, *Angew. Chem. Int. Ed.* **1997,** *36* 1723 – 1725.

9 E.N. Jacobsen, L. Deng, Y. Furukawa, L.E. Martinez, *Tetrahedron*, **1994,** *50* 4323 - 4334.

10 P. Pietikainen, *Tetrahedron*, **1998**, *54*, 4319 – 326; P. Pietikainen, *Tetrahedron Lett.* **1994**, *35*, 941 – 944; R. Irie, N. Hosoya, T. Katsuki, *Synlett*, **1994**, 255 – 256.

11 T. Schwenkreis, A. Berkessel, *Tetrahedron Lett*. **1993**, *34*, 4785 – 4788.

12 F. Montanari, *Pure Appl. Chem*. **1994**, *66*, 1519 – 1526.

13 P.L. Anelli, S. Banfi, F. Legramandi, F. Montanari, G. Pozzi, S. Quici, *J. Chem. Soc. Perkin Trans. 1*, **1993**, 1345 – 1357.

14 D. de Vos, T. Bein, *Chem. Commun*. **1996**, 917 – 918.

15 R.D. Arasasingham, G-X. He, T.C. Bruice, *J. Am. Chem. Soc.* **1993,** *115*, 7985 -7991.

16 M. Suzuki, S. Tokura, M. Suhara, A. Uehara, *Chem. Lett*. **1988**, 477 – 480. T.K. Lal, R. Mukherjee, *Inorg. Chem*. **1998**, *37*, 2373 – 2382. M. Suzuki, H. Sneda, Y. Kobayashi, H. Oshio, A. Uehara, *Chem. Lett*. **1988**, *480*, 1763 – 1766; T. Ukono, Y. Nishida. *Polyhedron*, **1996**, *15*, 1509 – 1515; P.A. Goodson, D.J. Hodgson, J. Glerup, K. Michelsen, H. Weihe, *Inorg. Chim. Acta*, **1992**, *197*, 141 – 147; J. Glerup, P.A. Goodson, A. Hazell, R. Hazell, D. Hodgson, C.J. McKenzie, K. Michelsen, U. Rychlewska, H. Toftlund, *Inorg. Chem*. **1994**, *33*, 4105 – 4111.

17 M. Lubben, A. Meetsma, E.C. Wilkinson, B. Feringa, L. Que, Jr. *Angew. Chem. Int. Engl.* **1995**, *34*, 1512-1513.

18 D.E. de Vos, T. Bein, *J. Organomet. Chem.* **1996**, *520*, 195 – 200.

19 Inorganic Chemistry, J.E. Huheey, 3rd ed. **1983**, Harper and Row Publishers, New York, USA.

20 J. Glerup, P.A. Goodson, D.J. Hodgson, K. Michelsen, K.M. Nielsen, H. Weihe, *Inorg. Chem.* **1992**, *31*, 4611 – 4616.

21 D.J. Hodgson, K. Michelsen, E. Pedersen, *Acta. Chem. Scand.* **1990**, *44*, 1002 – 1005.

22 K. Wieghardt, U. Bossek, B. Nuber, J. Weis, J. Bonvoisin, M. Carbella, S.E. Vitols, J.J. Girerd, *J. Am. Chem. Soc*. **1988**, *110*, 7398 - 7411.

23 C. Zondervan, R. Hage, B.L. Feringa, *Chem. Commun*. **1997**, 419 – 420.

24 K. Sato, M. Aoki, M. Ogawa, T. Hashimoto, R. Noyori, *J. Org. Chem*. **1996**, *61*, 8310 – 8311; K. Sato, M. Aoki, M. Ogawa, T. Hashimoto, D. Panyella, R. Noyori, *Bull. Chem. Soc. Jpn*. **1997**, *70*, 905 – 915.

25 J. Rudolph, K.L. Reddy, J.P. Chiang, K.B. Sharpless, *J. Am. Chem. Soc.* **1997**, *119*, 6189-6190.
26 E.N. Jacobsen, W. Zhang, M.L. Güler, *J. Am. Chem. Soc*. **1991**, *113*, 6703 – 6704.
27 M. Hoogenraad, *Thesis: Manganese complexes as catalysts for homogeneous oxidation reactions*, **2000**, University of Leiden, The Netherlands, chapter 5.
28 D.W. Gruenwedel, *Inorg. Chem.* **1968**, *7*, 495 – 501.
29 W. Zhang, E.N. Jacobsen, *J. Org. Chem.* **1991,** *56*, 2296 – 2298.
30 P.T. Beurskens, G. Admiraal, G. Beurskens, W.P. Bosman, S. Garcia-Granda, R.O. Gould, J.M.M. Smits, C. Smykalla, **1997**, The DIRDIF97 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.
31 G.M. Sheldrick, **1997**. SHELXL-97. Program for crystal structure refinement. University of Göttingen, Germany.
32 A.L. Spek, **1998**. PLATON. A multipurpose crystallographic tool. Utrecht University, The Netherlands