Chapter – 4

Study of Mononuclear Mn(III) Complexes of Schiff’s Bases with Long Side Chains
The catalytic oxygen atom transfer reactions, mediated by transition metal complexes, have been receiving considerable attention, as models for enzyme catalyzed oxygenation reactions. Studies are directed, towards the development of the models, mimicking enzymatic activity, for selective catalytic oxygenation of the organic compounds (1 – 4).

**Catalytic activity of enzymes as oxygenases**

The oxygenase enzymes catalyse reactions of dioxygen with organic substrates, in which the oxygen atoms of the dioxygen are incorporated into the final oxidised, products. These enzymes are divided into two types’ viz., dioxygenase and monooxygenase. Dioxygenase enzymes direct both the atoms of the dioxygen molecule into the substrate, while in case of monooxygenase enzymes, one oxygen atom of the dioxygen molecule is inserted into the substrates and the other oxygen atom is reduced to water (5)

**Monooxygenase**

There are several monooxygenase enzymes, containing heme iron, nonheme iron, or copper sites, as the prosthetic groups. However, the following three monooxygenase enzymes are better known. They are as follows.

1. **cytochrome P – 450**, a heme containing protein, whose active site resembles the dioxygen binding site of the myoglobin or haemoglobin, in many respects, except that the axial ligand to the iron is a thiolate side chain from cysteine, instead of an imidazole side chain from histidine, as in haemoglobin.

2. **tyrosinase**, this enzyme protein contains two copper ions, in close proximity, in its active site. It closely resembles hemocyanin, in it's spectroscopic properties.

3. **methane monooxygenase**, This protein contains two nonheme iron ions, in close proximity and resembles hemerythrin, in many of it's spectroscopic properties.

The resemblance in structure of the monooxygenase, with the dioxygen carrying proteins, suggest the binding of the dioxygen to the metalloenzymes, as an essential first steps in the enzymatic activity, presumably followed by other steps, leading to the oxygenation of the substrate.
More detailed mechanistic information are available for the cytochrome P - 450. The types of oxidation reactions which are catalysed by cytochrome P - 450 are following:

1. Hydroxylation of aliphatic compounds —

\[ \begin{array}{c}
\text{C–H} \\
\quad \rightarrow \\
\text{C–OH}
\end{array} \]

2. Hydroxylation of aromatic ring —

\[ \begin{array}{c}
\text{H} \\
\quad \rightarrow \\
\text{OH}
\end{array} \]

3. Epoxidation of olefins —

\[ \begin{array}{c}
\text{O}
\end{array} \]

4. Amine oxidation to amine oxides —

\[ \begin{array}{c}
\text{N} \\
\quad \rightarrow \\
\text{N}^+\text{O}^-
\end{array} \]

5. Sulfide oxidation to sulfoxide —

\[ \begin{array}{c}
\quad \rightarrow \\
\text{S} \quad \rightarrow \quad \text{S}
\end{array} \]

6. Oxidative dealkylation of heteroatoms —

\[ \begin{array}{c}
\text{Ph–O–CH}_3 \\
\quad \rightarrow \\
\text{Ph–OH} + \text{HCHO}
\end{array} \]

**Mechanism of oxygenation**

It has been suggested that an iron(V)-oxo complex is the most probable candidate, as the "active intermediate", in cytochrome P - 450 catalysed oxygenation reaction. Studies of the reactivity of the synthetic metalloporphyrin complexes, in oxygen transfer reactions and characterisation of the intermediate species, observed during the course of the reaction, have been invaluable in evaluating the potential intermediates and the reaction pathway of cytochrome P - 450. This knowledge helps to develop the efficient catalysts for the oxidation of the
organic substrates Logically, it would be most desirable, if one could mimic the enzymatic oxygenation reactions of organic substrates using iron porphyrins, dioxygen and the reducing agents. However, studies of such iron-porphyrin catalysed reactions have failed to produce meaningful results, and this could be related back to the mechanism of the mono-oxygenation reaction by the cytochrome P–450. This may be attributed to the natural design of the enzyme. It can direct the electrons, from a reducing agent into the iron-dioxygen-substrate complex, to reduce one of the oxygen atoms of the bound oxygen molecule, and thus can generate the "active oxidant", within the confines of the enzyme active site, in the immediate proximity of the bound substrate. Without the constraints imposed by the enzyme, however, iron porphyrins generally will either (1) catalyse the oxidation of the reducing agent by dioxygen, leaving the substrate untouched, or (2) initiate free radical autoxidation reaction.

A different approach was suggested on the basis of the observation of the peroxide shunt reaction, using organic peroxide or single-oxygen-atom donors. The earliest successful studies demonstrated that Fe(TPP)Cl (TPP = tetraphenylporphyrin) would catalyse the epoxidation of olefins and the hydroxylation of the aliphatic hydrocarbons, by iodosylbenzene (5).

The homogenous catalytic activity of various metal complexes, of non-porphyrin ligands, in the oxygenation of organic molecules, using different mono-oxygen donors, has been reported by different groups and also from our laboratory. This includes Fe, Mn, Ru and Cr complexes, with different ligands like Schiff’s bases (6), amides (7), polypyridyl (8), amino carboxylates (9), macrocyclic ligands (10) etc.

Pathway of the catalytic reaction

The catalytic oxidation reaction has been proposed to proceed via the formation of a metal-oxo intermediate. The metal-oxo intermediate is formed by the reaction of the metal complex with the mono-oxygen donor oxidant. The oxygen atom of the metal-oxo intermediate is transferred to the organic substrate to form the oxygenated product, and thereby the metal complex is regenerated, completing the catalytic cycle.
The pathway, termed oxygen rebound mechanism, was suggested by Groves et al. (11)

**Role of the ligands in the catalytic activity of the complexes:**

The catalytic efficiency of a metal complex is dependent on the ease with which the metal-oxo is formed and also on its stability. The stability of the metal-oxo, in turn, is dependent on the electron density over the metal centre in the complex. The nature of the coordinated ligand controls the electron density over the metal centre in the complexes and hence the redox behaviour (12). When the metal-oxo intermediate is generated from an electron-rich metal centre, it is very stable and consequently, it's utility as the catalyst will be limited. The stable metal-oxo intermediate is reactive towards electron rich olefins only (13). Again, the complexes of an electron deficient metal ion will be either reluctant to form a metal-oxo intermediate, or will form a less stable metal-oxo intermediate, which is more reactive, and hence less selective towards the oxidation of organic substrates. The less stable metal-oxo species may lead to the formation of a large number of oxidised products from an olefinic substrate, via the intermediate formation of free radical (14).

Apart from the transfer of the oxygen atom of the metal-oxo intermediate to an organic substrate, the metal-oxo intermediate may react with another molecule of the same complex to form a μ-oxo complex, which is inactive as a catalyst, and hence causes the termination of the catalytic cycle (15).
The termination of the catalytic cycle may also be due to the oxidative degradation of the ligand part of the metal complex (16).

Thus, the nature of the ligand determines the catalytic activity of the complexes, and it is possible to tailor make metal complex systems, with optimum stability of the metaloxo intermediate, leading to maximum catalytic efficiency.

In the cyclic process of oxygen rebound mechanism, it has been proposed, that the combination of the reactive metal-oxo species with the alkenes may lead to the formation of following different intermediates, a) metallooxetane (17), b) carbon radical (18), c) carbocation (19), d) carbocation radical (20) and e) charge transfer complex (21) (Fig. 1). The most probable suggested intermediate is structure “c” (22, 23).

![Figure 1](image)

The change in the catalytic activity of the metal complexes, as function of change of ligand and change of substituents over ligand, has been well observed by Kochi & co-workers. They observed that substitution on the aromatic part of the Schiff’s base ligands by electron withdrawing groups; enhance the catalytic efficiency of a complex for epoxidation of olefins (24). It was observed that Schiff’s bases derived from 2-hydroxyacetophenone show greater catalytic activity, compared to those derived from salicylaldehyde (25), due to the electron releasing effect of the methyl groups. Studies were also carried out with different substitutions on the non – aromatic part the of salen type complex (25) and it was found that if hydrogen on the non – aromatic bridging part of a binuclear complex, is replaced by –OH, the yield of the epoxide is more.

Mn(III) Schiff’s base complexes (fig. 2) are known to be effective catalysts for oxidation reaction (26).
During recent years chiral salen–type transition metal complexes (salen = N,N'-bis(salicylaldehydo)ethylenediamine) have emerged as highly efficient catalysts for various important reactions, ranging from oxidations to carbon–carbon bond formations (27, 28).

As stated earlier, the hydrophobic substrate gets bound to the metal ion in the intermediate state. Hence, the hydrophobicity around the metal ion in the intermediate stage, should favour the binding of the hydrophobic substrate with the metal ion and this can control the rate of the catalytic reaction. In order to study the effect of non–coordinating hydrophobic side groups, present in the Schiff’s base ligands on the catalytic activity of its complexes, in this chapter, manganese(III) complexes of Schiff’s bases, with long side chains, e.g 2-hydroxy(4-n–alkoxy)benzaldimine and 2-hydroxy(4-n-alkoxy)benzaldiminopropane have been synthesized, characterized and their catalytic activities have been studied.

The alkoxy side chains at the 4–position of the Schiff’s base ligands have R = C_nH_{2n+1}, n = 6, 10, and 14. Since the OR group is at the 4–position of the 2-hydroxy(4-n–alkoxy)benzaldimino moiety of the tetradentate Schiff’s base ligands, it may be expected that they should provide hydrophobic environment around the metal centre, without causing steric hindrance to the substrates.

**Experimental**

**Physical Measurement & Materials**

The details of physical measurements & materials are, as described in the previous chapter.
Cyclic voltametric studies were carried out using a PC controlled EG&G/PAR 273A electro chemistry system. A glassy carbon working electrode, a platinum wire auxiliary electrode, and a Ag/AgCl reference electrode were used in three electrode configuration. TEAP was the supporting electrolyte and the concentration of the solution was \( \sim 10^{-3} \) M. Gas chromatography analyses were carried out on a Shimadzu GC 14B instrument, equipped with oracle 3 computing integrator, using 10% SE 30 with 1% QF on chromosorb column (2M). Nitrogen was used as carrier gas.

\[ \text{Mn (CH}_3\text{COO)}_2\text{4H}_2\text{O, was of S D Fine Chem, India make. All other chemicals and solvents were of reagent grade commercial materials and were used, as received.} \]

Syntheses of 4-n-alkoxy-2-hydroxybenzaldehyde

The ligands, 2-hydroxy-4-(n-alkoxy)benzaldehydes, were synthesized following a method reported by M. Marcos et. al. (29, 30), as mentioned in Chapter 1. The ligands L₁ and L₂ were prepared by condensing 2-hydroxy-4-(n-alkoxy)benzaldehydes with appropriate diamines, in 2:1 mole ratio, in dry methanol.

Synthesis of 1,2-bis(2-hydroxy-4-(n-alkoxy)benzaldimino)ethanemanganese(III) complexes: (series - I)

To a 50.0 mL ethanolic solution of Mn(CH₃COO)₂.4H₂O 0.245 g (0.1 mmol), the Schiff's base ligand 1,2-bis(2-hydroxy-4-(n-alkoxy)benzaldimino)ethane (0.1 mmol), in 10 mL dichloromethane, was added. The mixture was refluxed for 6 h. The resulting solution was subjected to distillation, to remove the solvents, till the solution was reduced to 5.0 mL volume. To this solution, excess of solid sodium perchlorate was added, followed by the addition of 100 mL water. The precipitate thus formed, was filtered, washed thoroughly with water, and dried in vacuum. The solid product was crystallized from dry ethanol.

The complexes, 1,3-bis(2-hydroxy-4-(n-alkoxy)benzaldimino)propane manganese(III) (series – II) were synthesized by following the same method, as described for the complexes of series – I, using 1,3-bis(2-hydroxy-4-(n-
alkoxy)benzaldimino)propane instead of 1,2-bis-(2-hydroxy-4-(n-alkoxy)benzaldimino)ethane.

As the perchlorate salts of metal complexes are potentially explosive, they were handled in small quantities.

**Procedure for catalytic oxidation reaction**

All the reactions were carried out in a schlenk tube, under dinitrogen atmosphere, olefin (4.0 mmol) and the catalyst (0.02 mmol) were dissolved in 5.0 mL dichloromethane. The reaction mixture was de-areated by flushing nitrogen for 10 min. Iodosyl benzene (0.4 mmol) was added and the reaction mixture was stirred for about 5 h. 2 μL aliquots were withdrawn from the reaction mixture, in 1 h intervals, and was analyzed by gas chromatograph, using FID detector. After 5 h of reaction time, there was no further increase in the yield of the epoxide, indicating that the reaction was complete within 5 h.

**Result and discussion**

![Scheme 1](image)

**Scheme 1**
In the present study, Schiff's bases of 2-hydroxy(4-n-alkoxy)benzaldehyde with two aliphatic diamines have been used to from manganese complexes. Individual ligands and their complexes with abbreviations are shown in Scheme - 1. The microanalytical data (C, H, N), as collected in Table 1, correspond to expected compositions of these complexes.

**Mass spectral studies**

The FAB mass spectra of two representative complexes, one from each of the two series, were recorded to establish the structure of the complexes, as shown in scheme 1. In the mass spectrum of 2 (fig. 3), the peak with maximum intensity, at \( m/z = 633 \), corresponds to the molecular ion, \([LiMn]^+\). The peak, at \( m/z = 493 \), corresponds to the fragment \([LiMn] - OC_{10}H_{21}\) and the peak, at \( m/z = 353 \), corresponds to \([LiMn] - (OC_{10}H_{21})_2\). In the mass spectra of 5 the peak with maximum intensity, at \( m/z = 647 \), corresponds to the molecular ion \([L_2Mn]^+\). The peak, at \( m/z = 507 \), corresponds to the fragment \([L_2Mn] - OC_{10}H_{21}\) and the peak at \( m/z = 367 \), corresponds to \([L_2Mn] - (OC_{10}H_{21})_2\). The fragmentation patterns in the mass spectra are in agreement with the proposed structure of the complexes.

**IR spectral studies**

The \( \nu_{C=\mathbf{N}} \) stretching frequency of the free ligands (ca. 1640 cm\(^{-1}\)) was found to be shifted to ca. 1609 cm\(^{-1}\), due to the coordination of the azomethine function to the metal ions (31). Further, the OH stretching band of the phenolic hydroxyl group, in the IR spectra of the free ligand, disappeared in the IR spectra of the complexes (fig 4), supporting the deprotonation of the phenolic hydroxyl groups of the ligand, during complexation. The strong bands near ca. 1122 and 625 cm\(^{-1}\) are observed in the IR spectra of all the complexes, due to the presence of noncoordinated perchlorate (32).

**Electronic spectral studies**

The complexes are highly soluble in ethanol, methanol, dichloromethane, acetonitrile, chloroform and benzene. The electronic spectra of the complexes, in
the UV-visible region, were recorded in dichloromethane solution of concentration $10^{-3}$ – $10^{-5}$ (M). The spectral data are collected in Table 1 and representative spectrum of a complex is shown in fig 5. In the electronic spectra of all the complexes a band of low intensity appears at ca. 495 nm. On the basis of the low value of the extinction coefficient, this band has been assigned to the electronic transition between the d-orbitals of the metal ion. In the UV region of the electronic spectra of all the complexes, two bands appear at ca. 300 & 355 nm. The values of the extinction coefficients of these bands are of the order of $10^5$. The same bands also appear in the electronic spectra of the free ligands. Therefore, these bands have been assigned to intraligand electronic transitions in the complexes. However, the positions of these bands get shifted in the electronic spectra of the complexes compared to the same in the ligands.

**Magnetic studies**

The magnetic moment values of the complexes were found to lie within the range 4.36 to 4.54 BM. This value corresponds to the expected spin only magnetic value for four unpaired electrons, on high spin Mn(III) centre, with $t_{2g}^3e_g^1$ configuration. Mn(II) undergoes aerial oxidation to Mn(III). The magnetic moment value is slightly less than the spin only value, 4.8 BM. This may be due to some intermolecular antiferromagnetic spin exchange interaction between the paramagnetic metal centres of the two molecules.

**ESR spectral studies**

The complexes, though paramagnetic, do not show ESR signal. This may be because, the zero field splitting is large and hence no allowed transition can take place (33).

Thus microanalytical data along with the IR, electronic spectral, mass spectral data and magnetic data, support the proposed structure of the complexes (scheme I).
Catalytic studies

The complexes were employed as the catalysts for the catalytic epoxidation of norbornylene and cis-cyclooctene, using iodosylbenzene as the monooxygen oxidant, in dichloromethane solution. Results of the oxidation studies, using the metal complexes of series – I and II as the catalysts, are shown in Table 2. A controlled experiment, using identical experimental condition, but excluding the metal complexes, gave insignificant yield of epoxide. The yield of epoxide, in the case of series – I complexes, was found to be very high, compared to the series – II complexes. The turnover numbers in the case of series – I and II were found to be ca. 10 for cyclooctene oxidation & ca. 7 for norbornene oxidation and ca. 7 for cyclooctene oxidation & ca. 4 for norbornene oxidation, respectively, indicating that the reactions are catalytic.

The metal complex catalysed oxygenation reaction is proposed to proceed via the formation of a metal-oxo intermediate, as suggested by Groves et al. The metal-oxo intermediate is formed by the reaction of the metal complex with the mono oxygen donor oxidant. The oxygen atom of the metal-oxo intermediate is transferred to the organic substrate, to form the oxygenated product and thereby the metal complex is regenerated, completing the catalytic cycle:

\[
ML^{n+} + AO \rightarrow [ML=O]^{(n+2)+} + A
\]

\[
[ML=O]^{(n+2)+} + S \rightarrow ML^{n+} + SO
\]

The complexes act as catalysts with moderate activity. The catalytic reaction terminated after few cycles. This is because, the metal-oxo intermediate may react with the parent metal complex to form a µ-oxo complex, which is inactive as a catalyst and hence the termination of the catalytic cycle (34)

\[
[ML=O]^{(n+2)+} + ML^{n+} \rightarrow LM^{(n+1)+} – O – ML^{(n+1)+}
\]

Alternatively, the termination of the catalytic cycle may also be due to the oxidative degradation of the ligand part of the metal complex (16, 35).

To suggest the mechanism of the oxidation reaction, the UV-visible spectra of the complexes were recorded in the presence of PhIO. It was found that after the addition of PhIO the colour of the Mn(III) complex solution turned to dark brown. In the spectrum of the reaction mixture, the peak at 495 nm of the original Mn(III) complex disappears. The spectrum shows absorption in the region 350 to 900 nm,
though no distinct new peak was observed in the visible region. This may be
because the tailing of the charge transfer transition masks the band due to the d-d
transition. The disappearance of the Mn(III) band, at 495 nm, and the appearance
of absorption in the lower energy region, on addition of PhIO, indicates formation of
Mn(V)=O. On addition of the substrate the peak of the original complex is revived in
the spectrum. It is thus indicated that the metal complex LM^m+ takes up one oxygen
from PhIO to form LM^m2=O intermediate, this transfers the oxygen to the substrate
and the catalyst is regenerated. Thus the catalytic reaction proceeds through the
oxygen rebound mechanism (11).

Similar observation was made in the cyclic voltammogram. The peak
corresponding to the redox couple Mn^{3+}/Mn^{2+} of the complex is not observed within
the solvent window. On the addition of PhIO, a new peak, due to reduction of the
high valent oxo-cation, Mn(V)=O, is observed at ca. ~0.633V. This observation further
supports the formation of the oxo-cation, on addition of PhIO.

The catalytic activity of 1,2-bis(2-hydroxybenzaldimino)ethanemanganese(III)
cation, i.e., the Schiff’s base complex without alkoxy side chain was determined,
under the same conditions, as the present catalytic studies. The percentage
epoxide yield was found to be 39.6 and 26.4 for cyclooctene and norbornene
respectively. Thus it is observed that the catalytic activity of the complexes with the
non-coordinating —OR groups do not differ significantly from the analogous
complex without alkoxy side chain. The complexes of Schiff’s bases with varying
chain length, also, do not exhibit significant difference in catalytic activity. This may
be because, the substituents, at the 4-position of the 2-hydroxy-(4-n-
alkoxy)benzaldimino moiety of the tetradentate ligands, may be far from the metal
centre and hence do not affect the hydrophobicity of the metal ion environment
significantly and consequently, the expected increase in catalytic activity is not
observed, in case of the metal complexes with long alkoxy chains.
Table 1: Characterization data

<table>
<thead>
<tr>
<th>Complex</th>
<th>Micro analytical data (%)</th>
<th>Electronic spectral data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>H</td>
</tr>
<tr>
<td>I</td>
<td>51.10</td>
<td>6.40</td>
</tr>
<tr>
<td></td>
<td>(51.21)</td>
<td>(6.09)</td>
</tr>
<tr>
<td>II</td>
<td>56.10</td>
<td>7.39</td>
</tr>
<tr>
<td></td>
<td>(56.25)</td>
<td>(7.55)</td>
</tr>
<tr>
<td>III</td>
<td>59.88</td>
<td>8.12</td>
</tr>
<tr>
<td></td>
<td>(60.0)</td>
<td>(8.40)</td>
</tr>
<tr>
<td>IV</td>
<td>51.94</td>
<td>6.56</td>
</tr>
<tr>
<td></td>
<td>(51.72)</td>
<td>(6.28)</td>
</tr>
<tr>
<td>V</td>
<td>56.25</td>
<td>7.40</td>
</tr>
<tr>
<td></td>
<td>(56.77)</td>
<td>(7.67)</td>
</tr>
<tr>
<td>VI</td>
<td>60.20</td>
<td>8.00</td>
</tr>
<tr>
<td></td>
<td>(60.40)</td>
<td>(8.40)</td>
</tr>
</tbody>
</table>

<sup>a</sup> calculated values are in parentheses, <sup>b</sup> in dichloromethane solution; <sup>c</sup> extinction coefficient.

Table 2: Results of Epoxidation

<table>
<thead>
<tr>
<th>Olefins</th>
<th>Product</th>
<th>Yield&lt;sup&gt;a&lt;/sup&gt; with catalyst (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I</td>
</tr>
<tr>
<td>Norbornene</td>
<td>Norbornene oxide</td>
<td>27.6</td>
</tr>
<tr>
<td>Cyclooctene</td>
<td>Cyclooctene oxide</td>
<td>38.99</td>
</tr>
</tbody>
</table>

Substrate: Oxidant: Catalyst mole ratio 200: 20: 1 Solvent CH<sub>2</sub>Cl<sub>2</sub>

<sup>a</sup> yield based on iodosyl benzene discharge
Figure 3: FAB mass spectrum of the complex 2.
Figure 4: IR spectrum of the complex III as KBr palette in the range 4000 to 500 cm$^{-1}$. 
Figure 5: Electronic spectrum of the complex 2 in dichloromethane
Reference:
3 K A Jorgensen and B Schoiett, Chem Rev., 1990, 90, 1483
4 R. H Holm, Chem Rev., 1987, 87, 1401