Chapter 1

1.1 Need of Catalysis

Catalysis plays a vital role in the selective oxidation of both saturated and unsaturated hydrocarbons to useful products [1]. Use of catalysts for the oxidation of petroleum based feed-stocks to important chemicals like alcohols, carbonyl compounds, epoxides etc. is a very important technology. In fact catalytic oxidation is the single most important technology for the conversion of hydrocarbon feedstock (olefins, alkanes and aromatics) to industrially important oxygenated derivatives [2]. However, there are very few practical processes for converting them to more valuable products, because of their chemical inertness which arises from the presence of strong and localized C–C and C–H bonds [3]. There are hundreds of different reagents and methods available for the oxidation of organic chemicals. Even though these methods exist, most of them share some common disadvantages. The traditional methods of oxidation use stoichiometric reagents such as permanganate and dichromate which produce toxic wastes in large quantities. Nitric acid is also used as it is cheap, but it produces various unwanted nitrogen oxides. Moreover, it is very corrosive. When reactions are scaled up to tones instead of grams, the use of such oxidants are no longer remains an attractive option. Therefore, in the recent years, environmental and economic considerations have provided a strong motivation to redesign commercially important processes so that the use of harmful chemicals and the generation of toxic wastes may be avoided. One major goal of green chemistry is to find out new routes to organic synthesis which are environmentally friendly. Thus, development of cleaner processes with high atom economy and low E-factor (mass of waste per mass unit of product) is a pressing need of current research [4-6]. The methods should aim at 100% atom utilization, increase product selectivity and replace stoichiometric reagents. The goal of today’s research is to devise new methods of synthesis which consume lesser amount of energy and minimize the emission of harmful gases. Target is to use innocuous oxidants such as O₂, H₂O₂ or alkyl peroxides as oxidants instead of HNO₃, K₂Cr₂O₇; KMnO₄ etc. Catalysts play a vital role in achieving these goals [7,8]. To make the processes greener, catalyst recovery and reuse are further important goal.
Oxidation reaction may be defined as a process in which concerted elimination of hydrogen from inorganic or organic substrates and addition of an electronegative element takes place in a chemical reaction. The substrate losing the electron(s) gets oxidized and the reagent which causes oxidation is called oxidant or oxidizing reagent [9]. Oxidation reactions are among the most useful industrial processes. However, these reactions are very polluting and hazardous as these reactions deliver considerable amounts of toxic wastes. Therefore, catalysis is strongly encouraged. Development of metal-based catalytic systems, which allow these oxidations to take place under mild conditions with benign oxidants (O$_2$, H$_2$O$_2$ and peroxides), is a much sought after goal for both bulk and fine chemical synthesis [6]. Although both vapour and liquid phase processes are in operation, recent trends indicate a shift over to liquid phase processes, gradually from the 1950s. Two very important processes viz. Wacker process and Hock process were commercialized during this period. Wacker process was for the conversion of terminal olefins to carbonyl compounds, whereas by Hock process phenol was produced from cumene. Today oxidation of hydrocarbons in the liquid phase is of great importance due to their role in converting petroleum hydrocarbon feed stocks such as alkanes, olefins etc. into industrially important organic chemicals. Some examples are the oxidation of p-xylene to terephthalic acid, of cyclohexane to cyclohexanol and cyclohexanone, of cumene to cumene hydroperoxide etc. Since oxidation of hydrocarbon ultimately gives carbon dioxide and water, thus partial oxidation is only industrially important. This type of oxidation processes depend on proper control of the reaction conditions. In general hydrocarbon oxidation gives multiple products. In many hydrocarbon oxidations the desired intermediates have tendency to react further. Therefore to achieve better selectivity is a very important goal in hydrocarbon oxidation.

The oxidation of alcohols to the corresponding carbonyl products is a vital process in synthetic organic chemistry. Raw materials for the synthesis of Nylon-6 and Nylon-6,6 are obtained from cyclohexane oxidation [3]. Oxidation processes are also used in large scale production of many commercial pharmaceuticals. Oxidation of carbon-carbon bonds is frequently used in the synthesis of pharmaceutical agents as the resulting products such as epoxides, carbonyl compounds; vicinal diols etc. are useful as valuable synthetic intermediate [10].
The oxidation reactions can be carried out either heterogeneously or homogeneously.

1.1.1 Homogeneous Catalysis

Homogeneous catalysis is a reaction system in which the catalyst and the reactant are in the same phase. This type of catalysis has played an important role in the field of liquid phase oxidation. Systematic study of homogeneous liquid phase oxidation was started in the 1950s [11]. Oxidation of \( p \)-xylene to terephthalic acid was discovered in this period. There are many advantages of using homogeneous catalysis over heterogeneous catalysis. Two such advantages are high activity and high selectivity as the reactants and catalyst co-exist in the same phase. Most of the homogeneous catalysts synthesized so far are biomimetic [12]. Some currently used industrial processes to produce millions of tons of important chemicals have no counterpart in heterogeneous catalysis. Homogeneous catalysis is used for the industrial production of adipic acid from cyclohexane, of acetaldehyde from ethylene (Wacker oxidation), of terephthalic acid from \( p \)-xylene, of propylene oxide from propene etc. Homogeneous catalysis is extensively used for the production of epoxide intermediates from which many medicines and other useful chemicals can be obtained [13].

Mechanism of homogeneous oxidation may be depicted as follows which is a radical oxidation.

Initiation:
\[
\text{In}_2 \rightarrow 2\text{In}^* \\
\text{In}^* + \text{RH} \rightarrow \text{InH} + \text{R}^*
\]

Propagation:
\[
\text{R}^* + \text{O}_2 \rightarrow \text{RO}_2^* \\
\text{RO}_2^* + \text{RH} \rightarrow \text{ROOH} + \text{R}^* \\
\text{(Rate controlling step)}
\]
Termination:

\[ \text{RO}_2^* \rightarrow \text{RO}_4 \rightarrow \text{O}_2 \ + \ \text{non radical products} \]

Here, \( \text{In}_2 \) is an organic radical initiator. Transition metal complexes may also take part in the initiation step and in certain cases their involvement becomes absolutely necessary. In such cases the reaction steps may be depicted as follows.

\[ \text{RH} + \text{M}^{(n+1)+} \rightarrow \text{R}^* + \text{H}^+ + \text{M}^n \]

\[ \text{ROOH} + \text{M}^n \rightarrow \text{RO}^* + \text{OH}^- + \text{M}^{(n+1)+} \]

\[ \text{ROOH} + \text{M}^{(n+1)+} \rightarrow \text{ROO}^* + \text{H}^+ + \text{M}^n \]

Thus there is another possibility for the propagation step

\[ \text{RO}^* + \text{RH} \rightarrow \text{ROH} + \text{R}^* \]

[13].

1.2 Role of Transition Metals in Catalysis

The use of transition metal complexes as catalysts in various oxidation reactions is quite widespread because these catalysts can facilitate the selective oxidation of various substrates under mild conditions, and also in understanding reactions of biological importance [1,14]. Transition metal complexes also play a significant role in functional group transformation and organic synthesis. Many transition metal catalyzed reactions are now common in organic synthesis [15]. Transfer of peroxy-O atom from an alkyl hydro-peroxide to an olefinic substrate is hard without prior activation. This activation is made possible by various metal complexes such as complexes of Mo(VI), Ti(IV), V(V), Co(III), Pd(II) etc. Such O-atom transfer processes become possible due to interaction between the activated
oxygen atom and the olefin. For $\text{H}_2\text{O}_2$ also transfer of the oxygen atom does not take place unless it is activated [13].

Many transition metal complexes are known to catalyze various other organic transformations \textit{viz.} condensation, isomerisation, rearrangement, hydrogenation, dehydrogenation, reduction etc. along with oxidation. In these complexes metal ions may be present in more than one oxidation states. In general homolytic oxidation reactions are catalyzed by the first-row transition metals e.g., $\text{Co}^{III}/\text{Co}^{II}$, $\text{Mn}^{III}/\text{Mn}^{II}$, $\text{Fe}^{III}/\text{Fe}^{II}$, $\text{Ni}^{II}/\text{Ni}^{I}$, $\text{Cu}^{II}/\text{Cu}^{I}$, $\text{Cr}^{VI}/\text{Cr}^{V}$ and $\text{V}^{V}/\text{V}^{IV}$ whereas heterolytic oxidation reactions are usually catalyzed by second-row transition metals, e.g., $\text{Ru}^{VII}$, $\text{Os}^{VI-VII}$, $\text{Rh}^{III}/\text{Rh}^{II}$ and $\text{Ir}^{III}/\text{Ir}^{II}$. [16]. Among the first row transition metal complexes, the copper complexes occupy an important position in oxidation chemistry as these complexes are readily available and they have biological relevance [4]. Copper catalyzes the aerobic oxidation of primary alcohols [12]. Copper catalyzes the biological synthesis of lignin [17]. Many proteins containing copper act as redox catalysts in many important biological processes. For example, galactose oxidase oxidizes primary alcohols to corresponding aldehydes with simultaneous reduction of $\text{O}_2$ to hydrogen peroxide. This reaction involves a two-electron reduction of dioxygen to hydrogen peroxide, with concomitant oxidation of alcohol to aldehyde. Galactose oxidase has a broad substrate specificity which allows the enzyme to metabolize a wide range of alcohols.

$$\text{RCH}_2\text{OH} + \text{O}_2 \rightarrow \text{RCHO} + \text{H}_2\text{O}_2$$
Figure 1.1 Some biological functions performed by copper proteins [18].

Tyr 495
His 496
HN

\[
\text{His 581} \\
\text{NH} \\
\text{OH}_2 \\
\text{O} \\
\text{N} \\
\text{Cu} \\
\text{O} \\
\text{S} \\
\text{Tyr 272}
\]

Figure 1.2 Active centre of galactose oxidase.

Tyr = tyrosinate
His = Histidine

The active centre of galactose oxidase contains mononuclear copper(II) species with a distorted square pyramidal geometry [18]. Coordination chemists have synthesized many copper complexes with a view to examining if this reaction can be
carried out with such model complexes. We shall discuss examples of such complexes in a latter section in this chapter.

The role of transition metal complexes in oxidative reactions are either through direct involvement of the metal centre in the oxidative reactions or in the form of preformed complexes that participate in the organic reactions. The molecular oxygen, hydrogen peroxide and organic peroxides are the most commonly used oxidants in association with transition metal complexes for organic oxidation reactions. These metal catalyzed reactions are important alternatives to traditional methods of oxidation. In traditional methods stoichiometric amounts of metal oxides or metal salts are used for such oxidations. But these methods generate heavy metal wastes. A third type of method as alternative to the traditional methods has been developed. These reactions are often called oxidative dehydrogenation rather than oxidation [8].

\[
R_1^1R_2^2\text{CHOH} + OM^n \rightarrow R_1^1R_2^2\text{C} = O + M^{n-2} + H_2O
\]

\[
R_1^1R_2^2\text{CHOH} + M^nX_2 \rightarrow R_1^1R_2^2\text{C} = O + M^{n-2} + 2HX
\]

\[
R_1^1R_2^2\text{CHOH} + M^n \rightarrow R_1^1R_2^2\text{C} = O + M^{n+2}H_2
\]

1.3 Importance of Copper

Copper is one of the most abundant elements in the earth’s crust. It occurs in the first-row transition metals in the periodic table. It occurs in several oxidation states and the ions readily form complexes yielding a wide variety of coordination compounds. The oxidation states cover the range of Cu(0) in the metal, Cu(I) in the cuprous compounds, Cu(II) in the cupric compounds, Cu(III) and Cu(IV). Of these, Cu(0) and Cu(IV) states are rare. Although Cu(III) is known with certainty, it has been clearly characterized only in a handful of compounds. Cu(I) and Cu(II) are the most common oxidation states of copper. Cu(II) is more stable than Cu(I) under normal conditions. It forms a large number of compounds. Most Cu(I) compounds are readily oxidized to Cu(II) compounds [19]. The chemistry of copper(II) apparently receives more attention because of the relative ease in the synthesis of its new compounds. Moreover these compounds are very important in various fields of research such as
magnetism, basic coordination chemistry, catalysis, biomimetics, liquid crystals, etc. [20-22]. The d$^9$ configuration of Cu(II) makes it subject to Jahn-Teller distortion which influences the stereochemistry of copper(II) complexes [23]. The geometries of Cu(II) species may be mononuclear [24,25], dinuclear [26], trinuclear[27] and tetranuclear [28], although many polymeric species including metal-organic frameworks (MOFs) based on copper(II) are also known [27,29].

A very important part of coordination chemistry is the understanding of copper-dioxygen species, which may be of many types. The research on copper-dioxygen complexes as catalysts is driven by the diversity of the active-site structure of copper-based O$_2$ carriers. Enzymes with active site with one, two, three or four copper ions are known and there is wide variation in ligand environment and reactivity patterns. Attempts to generate Cu(II)$\text{–OOR}$ complexes are inspired by the biological reactions performed by dopamine $\beta$-monooxygenase. The active site of catechol oxidase also has a dicopper(II) active site which converts $\text{o-catechol}$ to $\text{o-quinone}$ [30].

![Chemical reaction](image)

Therefore, it seems that copper is an essential metal for living organisms, since they are present in active sites of many oxygen activating enzymes. Most ligands used in copper complex catalysts have nitrogen as donor atoms [31-33]. The mononuclear complexes are more common in oxidation catalysis research.

### 1.4 Copper Carboxylates

Transition metal complexes with carboxylates are an important class of coordination compounds, which may be mono-, oligo-, or poly-nuclear. The transition metal carboxylates are important for their capabilities of gas storage, ion exchange, catalytic activity etc. Depending on the various ways in which a carboxylate ion bind
to a metal center, these metal carboxylates differ in their properties such as structural, 
magnetic, catalytic, etc. Metal carboxylates play important roles in synthetic chemistry 
because of the versatile coordination modes of carboxylate group. Therefore the field 
of coordination complexes with carboxylates as ligand is a very important subject of 
research. In previous studies from this laboratory, methods for synthesizing Cu(II) 
tetracarboxylates were established, their structures were described [22] and a few 
complexes of this type were examined as catalyst in selective oxidation of various 
alcohols with aq. TBHP. The authors took the oxidation of benzyl alcohol as the 
model reaction, where a maximum yield of 82% benzaldehyde was obtained in 3 h 
under the optimized condition [33]. A microporous copper(II) carboxylate complex, 
trans-1,4-cyclohexane dicarboxylate \([\text{Cu}_2(\text{OOCC}_6\text{H}_{10}\text{COO})_2]\) has been reported to act 
as a biomimetic heterogeneous catalyst for selective oxidation of various alcohols 
with H₂O₂ [34].

Carboxylate complexes of copper(II) are of special chemical and biological 
interest and accordingly their preparation, structure and properties have been 
extensively studied [21,22,35]. M. MELNÍK reported that in copper carboxylates the 
Cu–Cu distance increases with the increasing strength of the acid and the Cu–L axial 
distances have a tendency to contract [36]. At the same time, there is a movement of 
the copper atom out of the square basal plane of its square pyramidal coordination 
sphere. The Cu–Cu and Cu-basal plane distances are increased from 2.61 and 0.19 Å 
in Cu(CH₃COO)₂.H₂O to 2.89 and 0.32 Å in Cu(F₃CCOO)₂.quin respectively. Here 
‘quin’ means quinone. The authors also concluded that the axial ligand also plays a 
role in determining both the Cu–Cu and Cu–basal plane distances [36].

Structurally, compounds of carboxylic acid derivatives can be broadly divided 
into five groups depending upon the bonding modes (Table 1) [37]. Out of these 
modes only syn-syn configuration brings metal atoms close enough to form a clustered 
structure. The anti-anti and anti-syn configurations form polymeric structures.
### Table 1 Different modes of coordination of carboxylate anions.

<table>
<thead>
<tr>
<th>Mode of coordination</th>
<th>Type</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Ionic" /></td>
<td>Ionic</td>
<td>Na(HCOO)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mn(CH₃COO)₂,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fe(CH₃COO)₂ etc.</td>
</tr>
<tr>
<td><img src="image" alt="Monomeric" /></td>
<td>Monomeric, with each RCOO group using only one of the two O-atoms to form a bond to metal atom</td>
<td>Co(O₂CCH₃)₂.4H₂O, Li(O₂CCH₃)₂.2H₂O</td>
</tr>
<tr>
<td><img src="image" alt="Syn-anti or anti-anti" /></td>
<td>Syn-anti or anti-anti forms; there is no possibility of M–M bond formation</td>
<td>Cu(O₂CH)₂.4H₂O (anti-anti)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cu(O₂CH)₂ (anti-syn)</td>
</tr>
<tr>
<td><img src="image" alt="Syn-syn" /></td>
<td>Syn-syn. M–M bond formation is possible</td>
<td>[Cu(O₂CCH₃)₂. H₂O]₂</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[Cr(O₂CCH₃)₂. H₂O]₂</td>
</tr>
<tr>
<td><img src="image" alt="Bidentate ligand" /></td>
<td>Bidentate ligand forming four membered ring</td>
<td>Zn(O₂CCH₃)₂.2H₂O</td>
</tr>
</tbody>
</table>

Metal carboxylates of transition elements are mainly of three types:

I. Ionic.

II. Tetrabridged dimmers.

III. Oligo- and poly-nuclear compounds giving various structural varieties.
Type II compounds have received extensive attention during the last four decades. [21,22,38]. Reedijk et al. have done some studies on various binuclear paddle wheel copper(II) carboxylates [39].

1.5 Catalytic Oxidation Reactions with Nitroxyl Radicals

A broad range of oxidative transformations can be accomplished using nitroxyl radicals. These radicals either may be stable (persistent) or reactive. TEMPO is a stable tetraalkyl nitroxyl radical (2,2,6,6-tetramethylpiperidine-1-oxyl). The unpaired electron is delocalized over the nitrogen–oxygen bond which accounts for its high stability for long periods of time without decomposition. It is well known as an oxidation catalyst in the oxidation of alcohol, sulfides etc., but particularly used in the oxidation of alcohols [40]. Usually such reaction systems are not prone to over oxidation. In catalyzed reactions involving TEMPO, an oxoammonium cation is formed from it, which selectively oxidizes a variety of alcohols. To generate the cation, TEMPO is usually oxidized with hypochlorite. Instead of hypochlorite, O₂ along with active metal catalysts such as Ru²⁺, Mn²⁺, Co²⁺ and Cu⁺ etc. can also be used to generate the oxoammonium cation [41]. Other than TEMPO, there are also some other radicals such as NHPI, PINO, SINO etc. which are used to oxidize alcohols [40].

Along with the oxidation of the alcohols, TEMPO also inhibits further oxidation of the aldehydes and ketones to acid. Since TEMPO is a persistent radical it has the ability to react immediately with other radicals and thus breaks free radical chains [42,43].
1.6 Various Oxidants Used in Oxidation Reactions

Some important examples of oxygen-donating oxidants are hydrogen peroxide, \textit{tert}-butyl hydroperoxide (TBHP), nitric acid etc. Nitric acid is corrosive and it produces various nitrogen oxides. Due to economical and environmental factors dioxygen, hydrogen peroxide, alkyl peroxides such as TBHP are mostly preferred as oxidants in organic transformation.

![Structure of TBHP](image)

Some advantages of TBHP are:

a) It can be used as a free radical initiator over a wide temperature range as it has good thermal stability.

b) It easy to handle in comparison to \( \text{H}_2\text{O}_2 \) or \( \text{CH}_3\text{C(O)OOH} \) (peracetic acid).

c) It is not very corrosive.

d) On activation by an appropriate transition metal complex, it leads to selective oxidations.

e) TBHP can be used as oxidizing agent in aqueous as well as non-aqueous media as it is soluble both in hydrocarbon solvents as well as water.
f) The co-product that TBHP forms is tert-butanol. This product is easy to separate by distillation and can be recycled or used for other industrial processes like synthesis of methyl tertiary butyl ether (MTBE) which is a gasoline additive for improving anti-knocking behavior [13].

Important physical and chemical properties of TBHP are listed in Table 2.

**Table 2** Physical and chemical properties of TBHP:

<table>
<thead>
<tr>
<th>Physical State</th>
<th>Clear liquid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula</td>
<td>$(\text{CH}_3)_3\text{COOH}$</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>90.14</td>
</tr>
<tr>
<td>Boiling point</td>
<td>89°C</td>
</tr>
<tr>
<td>Specific Gravity</td>
<td>0.93-0.94</td>
</tr>
<tr>
<td>Flash point</td>
<td>43°C</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble in water as well as common organic solvents</td>
</tr>
<tr>
<td>Stability</td>
<td>Stable under ordinary conditions</td>
</tr>
<tr>
<td>Active oxygen %</td>
<td>17.8</td>
</tr>
<tr>
<td>Product generated after decomposition</td>
<td>tert-butanol</td>
</tr>
</tbody>
</table>

For industrial application, the main methods for epoxidation of substituted alkenes involve use of peracids. However, the use of peracids is not clean, as peracids produce equivalent amounts of acid waste. Moreover, peracids are not very safe in handling. Therefore it is of utmost importance to develop methods for epoxidation of alkenes using safer oxidants and producing less waste. Hydrogen peroxide is a good option as it is cheap and produces only water as by-product [5,44]. It is worth mentioning that in the production of organic and inorganic peroxides, hydrogen peroxide is the starting material. Many catalytic systems using hydrogen peroxide with different metal complexes as catalysts have been reported. However, hydrogen peroxide is to be handled with care as it is corrosive to skin and subject to self-decomposition. Generally it is not as reactive as organic peroxides. Moreover, in most cases the achievable conversions are low [45-49].

Another clean oxidant is ozone which is capable of selective oxidation. But it suffers from the disadvantage of requiring specialized equipments which is very expensive [5].
An ideal oxidant for any large scale oxidation reaction should be easily accessible, cheap and non-toxic. From this viewpoint dioxygen is the best oxidant. It is easily available since it is present in air and the only by-product produced from its decomposition is water. However, there are some disadvantages of using molecular oxygen such as 1) dioxygen is not very reactive towards organic molecules; 2) dioxygen is less selective. For better result appropriate catalyst which activates the dioxygen molecule is needed. The most promising solution to this challenge is homogeneous transition metal complexes which are able to catalyze selective oxidation reactions under mild conditions by using dioxygen [5].

1.7 Oxidation of Organic Substrates

1.7.1 Alcohols

Today there is a tremendous demand of environmentally benign oxidation processes in organic chemistry, especially on large-scale synthesis. A number of methods for metal-catalyzed aerobic oxidations of alcohols have been developed. Liquid phase oxidation of alcohols is potentially a very attractive reaction for the preparation of intermediates and fine chemicals [50]. There are many methods for oxidizing alcohols. Unfortunately most of the methods suffer from serious drawbacks like use of toxic oxidants or additive and forcing conditions. Any new method has to include mild reaction temperature, avoidance of costly and toxic oxidants, low catalyst loading, ability of chemoselective oxidation etc.

\[
\begin{align*}
R_1 \text{OH} & \xrightarrow{\text{catalyst}} R_1 \text{R}_2 \text{O} + \text{H}_2\text{O} \\
\text{O}_2 \text{or air} & \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad 
\end{align*}
\]

Many metals can be used under both homogeneous and heterogeneous condition for the oxidation of alcohols. The use of non-noble metals such as copper is the most important green development towards catalytic oxidation of alcohols in the 21st century. Copper would seem to be a metal for catalytic aerobic oxidation of
alcohols, since it comprises the catalytic centre in a variety of enzymes, e.g., galactose oxidase which catalyses oxidation of alcohols to aldehyde [18,51].

Scheme 1.1 Mechanism of galactose oxidase [40].

Semmelhack et al. first reported Cu catalyzed aerobic oxidation of alcohols. These authors initiated the use of Cu in combination with TEMPO as an attractive catalyst in DMF [52]. Subsequently, several reports on Cu catalyzed aerobic oxidation have appeared. A significant development of copper catalysts to oxidize alcohols has been pioneered by Marko and coworkers [53-56]. The oxidation method reported by Markó et al. which was published in 1996, used copper-phenanthroline complex as catalyst in the oxidation of primary, secondary, allylic and benzylic alcohols. In their system, carboxylate and hydrazine compounds were used as additives with copper(I) phenanthroline in order to enhance the rate and total TON of the reaction. The hydrazine additive acts as hydrogen acceptor. It receives a hydrogen atom from the substrate and donates it to oxygen during the catalytic reaction. Reactions were carried out under basic conditions in toluene [53].

Punniyamurthy et al. reported another catalyst involving TEMPO and a copper(II) complex for oxidation of alcohols under the atmosphere of O₂. They reported oxidation of both aromatic and aliphatic alcohols to their corresponding aldehydes. This procedure does not require an additive and the catalyst is recyclable without loss of activity. The reactions were carried out in toluene [57].

The catalytic system reported by Gamez et al. was based on [CuBr₂(2,2′-bipyridine)]-TEMPO system which catalyses the selective and very mild oxidation of primary alcohols to aldehydes. In their study the oxidation reactions were carried out
at room temperature under basic MeCN/water solution with air used as dioxygen source. The system uses TEMPO as a co-catalyst and was able to catalyze selectively the oxidation of benzylic, allylic and aliphatic alcohols to aldehydes. However, it was not successful in catalyzing the oxidation of secondary alcohols. The authors suggested that this was due to steric hindrance in the coordination of the secondary alcohols to copper [58].

Jiang et al. have reported another efficient four component system of acetamido-TEMPO/Cu(ClO$_4$)$_2$/TMDP/DABCO in DMSO for aerobic alcohol oxidation where 4 mol% Cu(ClO$_4$)$_2$, 4 mol% TMDP, 10 mol% DABCO and 6 mol% acetamido-TEMPO have been used. The oxidation was carried out at room temperature [59].

A dinuclear copper(II) complex was investigated as catalyst for aerobic oxidation of primary benzylic alcohols in presence of TEMPO and a base. All reactions were conducted in aqueous acetonitrile under aerobic conditions with 5 mol% of the catalyst in presence of TEMPO and NaOH. The products were the corresponding aldehydes. Oxidation of benzyl alcohol was complete in 15 h [60].

Catalytic oxidation in ionic liquids is a very effective method for oxidizing organic substrates as ionic liquids are usually inert towards auto-oxidation [61]. Ionic liquids are compounds that are generally liquid or close to liquid at room temperature and are highly polar. They are usually salts of organic cations. e.g., tetraalkylammonium, N-alkylpyridinium, 1,3-dialkylimidazolium and tetraalkylphosphonium. In order to be liquid at room temperature the cations should preferably be unsymmetrical, e.g., $R_1$ and $R_2$ in dialkylimidazolium should be different.
Many organic and organometallic compounds are soluble in ionic liquids. A mild and effective procedure for the oxidation of primary and secondary alcohols to the aldehydes and ketones using a catalyst mixture of TEMPO-CuCl in 1-butyl-3-methylimidazolium hexafluorophosphate [bmim][PF₆] was reported by Ansari et al. Various types of benzylic, allylic, and aliphatic alcohols, both primary and secondary, have been successfully oxidized by this method [62].

Sheldon et al. found that in stoichiometric experiments under inert atmosphere, copper(I) is oxidized by TEMPO in the Cu/TEMPO system to produce piperidinylxocopper(II). When one equivalent of benzyl alcohol was added to this solution, copper(I), benzaldehyde and the amine, TEMPH was formed in a 1:1:1 ratio [40].
Scheme 1.2 CuCl-catalyzed stoichiometric oxidation of an alcohol by TEMPO.

The corresponding carbonyl compound and TEMPOH were obtained by the oxidation of the alcohol by TEMPO, catalyzed by copper. The catalytic cycle has been shown in Scheme 1.3 The key step is the intramolecular hydrogen abstraction within an alkoxy copper(II)/TEMPO complex which generates a coordinated ketyl radical anion and TEMPOH.

Scheme 1.3 Mechanism of CuCl/TEMPO catalyzed aerobic oxidation of alcohols [40].

Semmelhack et al. reported the use of TEMPO in combination with cuprous chloride as a catalyst for the aerobic oxidation of benzylic and allylic alcohols. It was
proposed that copper(II) oxidizes TEMPO to the oxoa ammonium cation which is the actual oxidant. The copper(II) is regenerated by reaction of copper(I) with oxygen [52].

\[
\begin{align*}
4 \text{Cu(II)} & + 4 \text{N} \text{N} \text{O} \text{•} \\
2 \text{N} \text{O} \text{•} & + 2 \text{RCH}_2\text{OH} \\
2 \text{OH} & + 2 \text{RCHO} + 2 \text{H}^+ \\
4 \text{Cu(I)} & + 4 \text{H}^+ + \text{O}_2 \\
& \rightarrow 4 \text{Cu(II)} + 2 \text{H}_2\text{O}
\end{align*}
\]

Scheme 1.4 Semmelhack mechanism for CuCl/TEMPO catalyzed alcohol oxidation [52].

Minisci et al. reported aerobic oxidation of alcohols catalyzed by TEMPO with Mn(NO$_3$)$_2$ and Co(NO$_3$)$_2$ in which they concluded that in the absence of TEMPO the products, aldehydes and ketones are readily oxidized to carboxylic acids [42]. Dijksman used polymer immobilized TEMPO as a catalysts for alcohol oxidations. The author has referred to the catalyst as polymer-immobilized piperidinyloxyl (PIPO), which proved to be a very effective catalyst for the oxidation of aliphatic and benzylic alcohols with hypochlorite. In the absence of a solvent, PIPO was a very effective recyclable heterogeneous catalyst [63].

Sheldon et al. have reported the use of PIPO in an amount equivalent to 1 mol% of nitroxy radical with 1.25 equivalent of 0.35M NaOCl (pH 9.1) for the oxidation of a variety of alcohols. In the solvent-free system, aliphatic primary alcohols were oxidized to the corresponding carboxylic acids. The authors also used RuCl$_2$(PPh$_3$)$_3$/TEMPO system for the aerobic oxidation of a broad range of alcohols where primary and secondary alcohols were oxidized to the corresponding aldehydes.
and ketones. Primary allylic alcohols were converted to the corresponding α,β-
unsaturated aldehydes [40].

Naiwei Wang et al. have described the FeCl₃-TEMPO-NaNO₂ catalyst system
for aerobic oxidation of alcohols at room temperature where dichloromethane and
trifluorotoluene are superior solvents to acetonitrile and lead to a significant increase
in reaction rates. The conversions were 100% with selectivity >99% towards
corresponding aldehydes and ketones [64].

Ruthenium catalyzed aerobic oxidation of alcohols inspired by the biological
oxidation of secondary alcohols has also been reported [65]. There are more reports on
alcohol oxidation catalyzed by ruthenium complexes [66-72].

1.7.2 Styrene

In view of the importance of the epoxy compounds in the manufacture of
various valuable commodities such as polyurethanes, unsaturated resins, glycols,
surfactants and other products, epoxidation of alkenes is considered to be a highly
important reaction in industrial organic synthesis [73].

This is an important reaction in asymmetric cases. It is because from this
reaction two chiral carbons are obtained in one step. Since the epoxide group is very
reactive, epoxide intermediates can be readily transformed to various required organic
functional groups in a stereospecific manner. The selective epoxidation of alkenes is
successfully achieved in the fine chemicals industry by using stoichiometric amounts
of peroxo acids as oxidants [73]. However, the use of peracids is not a clean method
because this leads to the generation of an equivalent amount of acid waste. Moreover,
peracids are not safe in handling. Current green chemistry trends suggest the
development and implementation of catalytic processes which eliminate the use of
hazardous reactants and minimize waste generation. In line with the well-known utility
of transition-metal-based catalysts in various oxidation reactions, such systems have
also been found to be useful in the area of catalyzed oxidation of alkenes to produce
epoxides at enhanced rate, yield and selectivity. The use of cleaner oxidants such as hydrogen peroxide (H$_2$O$_2$), TBHP and cumyl hydroperoxide (CHP) rather than usual hazardous and costly organic peroxides (e.g., $m$-chloroperoxybenzoic acid, MCPBA) is believed to provide an environmentally friendly route to epoxides [13].

Styrene oxide (SO) is a commercially important intermediate used in the synthesis of fine chemicals, pharmaceuticals, UV-absorbers, perfumes, sweeteners etc. [74]. Conventional procedures for preparing SO make use of hazardous chemicals and at the same time generate undesirable products during the reactions [75]. In view of this, it is highly desirable to develop catalytic routes of styrene epoxidation which are environmentally friendly and relatively easy to implement. Cobalt complexes have been found to catalyze olefin epoxidation [76,77]. Earlier studies also made use of Mn complexes as catalysts with O$_2$ as the oxidant and TBHP as the initiator to obtain a maximum SO yield of 8.3% [78]. Benzaldehyde, phenylacetaldehyde and benzoic acid were often found to form as byproducts.

Maurya et al. had reported that under optimized conditions the oxidation of styrene gave five products namely styrene oxide, benzaldehyde, benzoic acid, phenylacetaldehyde, and 1-phenylethane-1,2-diol. Independent of the type of catalyst, the product selectivities follow the order: benzaldehyde > 1-phenylethane-1,2-diol > benzoic acid > styrene oxide > phenyl acetaldehyde. The formation of styrene oxide was low in all cases. The higher yield of benzaldehyde may be due to further oxidation of styrene oxide formed in the first step by a nucleophilic attack of H$_2$O$_2$ on styrene oxide followed by cleavage of the intermediate hydroperoxystyrene [79].

Vanadium silicalite with ferrierite has also been examined as catalyst in styrene oxidation with molecular oxygen as the oxidant and TBHP as the initiator. A
maximum selectivity of 59.18% for SO was observed by these authors at 373 K and 200 psi of pressure [80]. In a number of other reports [81-86], the selectivity towards styrene oxide is low because the major product is benzaldehyde. Oxidation of styrene over TS-1 catalyst has also been reported, where phenylacetaldehyde and benzaldehyde are the major products [87]. There are other reports on styrene oxidation over TS-1 as catalyst [88].

Many studies on epoxidation have made use of TBHP as the oxidant to produce epoxides in industry, particularly because of its lower sensitivity to metal contamination leading to safer handling compared with \( \text{H}_2\text{O}_2 \) or percarboxylic acids [89-92].

There are several reports on the catalytic use of copper in reactions including the oxidation of alkenes [93-95]. Maurya et al. has oxidized styrene with \( \text{H}_2\text{O}_2 \) using oxovanadium and copper complexes as catalysts. Five products were obtained in their process viz. styrene oxide, benzaldehyde, 1-phenylethane-1,2-diol, benzoic acid and phenyl acetaldehyde along with minor amounts of unidentified products.

![Scheme 1.6 Formation of all products in styrene epoxidation](image-url)

Scheme 1.6 Formation of all products in styrene epoxidation [95].
Oxidation of styrene with H$_2$O$_2$ in the presence of palladium chloride in several ionic liquids has been reported and has shown that the nature of the ionic liquid affects the selectivity and efficiency of the reaction. The product distribution in hydrophilic and hydrophobic ionic liquids is different. In case of hydrophilic ionic liquids phenylmethylketone was the main oxidation product accompanied by benzaldehyde and benzoic acid. Whereas in hydrophobic ionic liquids in addition to the already mentioned products, 1,3-diphenyl-1-butene and small amounts of polystyrenes was also observed [96].

1.7.3 Cyclohexane

The oxidation of cyclohexane is a very important process in the synthetic fiber industry. It is because a mixture of cyclohexanone and cyclohexanol known as K/A oil is obtained by cyclohexane oxidation. Cyclohexanol and cyclohexanone are important materials for producing adipic acid and caprolactam, which are intermediates in the manufacture of nylon-6 and nylon-66 polymers [97-99]. Today, adipic acid is produced by liquid phase oxidation of cyclohexane all over the world. [3]. Cyclohexanol and cyclohexanone also have some additional applications e.g. both are used as solvents for lacquers, varnishes as well as stabilizers and homogenizers for soaps and synthetic detergent emulsions [100]. The selective oxidation of cyclohexane requires activation of the relatively inert carbon hydrogen bond. In most of the cases cyclohexane oxidation requires extreme reaction conditions such as high temperature and pressure. Currently, most commercial production of adipic acid involves multiple steps starting from cyclohexane. The environmentally undesirable features of this multi-step mode of manufacture are

1) The generation of greenhouse gas N$_2$O.

2) The consumption of nitric acid as stoichiometric oxidant.

3) The use of Cr(III) salts and their disposal [100].

A major problem of cyclohexane oxidation is selectivity. This problem is due to higher reactivity of cyclohexanol and cyclohexanone than cyclohexane itself in the
oxidation medium. There are two industrial approaches to deal with this problem. In
the first one the conversion of the reaction is kept low so that the concentrations of the
products remain low in the oxidation mixture. But there is a disadvantage in this
approach. A large volume of unconverted cyclohexane is needed to be recycled in this
method. In the second approach boric acid is used to protect cyclohexanol as its boric
acid ester to prevent over-oxidation. This method also has a problem of recycling and
recovery of boric acid. In the further oxidation of ketone-alcohol mixture nitric acid is
used as the oxidant. But nitric acid is very corrosive and recovery of nitrogen oxides
that are produced is difficult [3]. In view of these problems, it is highly desirable to
develop catalytic routes of cyclohexane oxidation which are environmentally friendly
and relatively easy to implement. Extensive efforts have been dedicated to develop
transition metal complex catalysts for mild oxidation of cyclohexane. The use of
cleaner oxidants such as hydrogen peroxide (H$_2$O$_2$), TBHP and molecular oxygen
rather than metal oxides and usual hazardous organic peroxides (e.g., MCPBA) has
been emphasized to provide environmentally friendly routes [101].

Amorphous silicates containing Ce have been reported as catalysts for
cyclohexane oxidation where the products found were cyclohexanone, cyclohexanol
and cyclohexyl peroxide with a maximum conversion of 12.73% after 24 h at 343 K.
The oxidant used was TBHP [102]. Devika et al. studied the catalytic activity of
CeAlPO-5 molecular sieves in the vapour phase oxidation of cyclohexane in air where
cyclohexanone was obtained as main product (selectivity > 90%) [100].

Manganese(III) corroles have been found to catalyze cyclohexane oxidation at
room temperature in which a maximum conversion of 22% was found in 6 h where the
products were cyclohexanol and cyclohexanone. The oxidant used was TBHP and the
solvent was acetonitrile [103]. Oxidation of cyclohexane with H$_2$O$_2$ and Mn(IV) as the
catalyst at 298 K in presence of carboxylic acids as co-catalyst afforded cyclohexyl
hydroperoxide, cyclohexanone and cyclohexanol as products [104].

In a number of reports Co(III) complexes were used to catalyze cyclohexane
oxidation. [105-107]. Ken-ichi Shimizu et al. have reported the photo-oxidation of
cyclohexane with hydrogen peroxide promoted by Cu(II)-exchanged Y zeolite leading
to a maximum conversion of 14.7% in 6 h with selectivities of 8%, 1.2% and 5.5%
towards cyclohexanol, cyclohexanone and cyclohexyl hydroperoxide respectively. The
reaction was carried out at 300K [108]. 2,2’-bipyridil Cu(II) complexes were used as catalysts to give a total yield of 43.4% of cyclohexanol, cyclohexanone and cyclohexyl hydroperoxide at room temperature in 24 h. In this system a mixture of acetonitrile and water was used as solvent [109].

A Fe(III)-Schiff base complex in a Zn-Al layer double hydroxide (LDH) gave 45.5% conversion, yielding 72.3% and 27.7% selectivities towards cyclohexanone and cyclohexanol respectively at 343K in 8 h in acetonitrile [110].

Other iron complexes are also reported as catalysts for cyclohexane oxidation [111]. Under N₂ atmosphere the use of vanadium phosphorus oxide with hydrogen peroxide in acetonitrile gave 84% conversion yielding cyclohexanol and cyclohexanone at 338 K in 8 h [112]. Ruthenium-oxo complexes have been found to catalyze cyclohexane oxidation using TBHP as oxidant at room temperature, where products obtained were cyclohexanol and cyclohexanone [113].
1.8 Aims and Objectives of the Thesis

From the above discussion it is clear that catalysis is a vital process in the oxidation of organic substrates. From both economic and environmental points of view, target is to use O$_2$, H$_2$O$_2$ or alkyl peroxides as oxidants instead of stoichiometric reagents such as HNO$_3$, K$_2$Cr$_2$O$_7$, KMnO$_4$ etc. In this regard catalysis is a good option. In the present work it has been our aim to synthesize new copper complexes and examine them as catalysts in the oxidation of organic substrates such as alcohols, alkenes, cyclohexane etc. using air, O$_2$, H$_2$O$_2$, TBHP etc. as oxidants. One of the primary objectives was to prepare dicopper(II) tetracarboxylates of the type [Cu$_2$(µ-O$_2$CR)$_4$L$_2$] with a view to examining them as catalysts in oxidation processes mentioned above. Attempts were to be made to choose ligands in such a manner that the resultant complexes would be good for the applications in hand. To make the processes green we would try the reactions in solvent free conditions, wherever and whenever possible. The present work, in essence, was planned to be carried out in the following manner.

1) Following a detailed literature survey the metal complexes to be examined as catalysts are to be synthesized. Special emphasis will be put on the synthesis of dinuclear tetracarboxylate species of copper(II).

2) The isolated complexes will be characterized by IR, UV-vis-NIR, magnetic measurements and single crystal X-ray diffraction etc.

3) Detailed investigations will be undertaken to examine the metal complexes as homogeneous catalysts for catalytic oxidation of organic substrates such as alcohols, alkenes, cyclohexane etc. Efforts will be made to identify the catalytically active species by spectroscopic methods. The courses of the reactions will be followed by GC. Optimization of the reaction conditions will be done.
1.9 References


12) Zhan, B. Z.; Thompson, A. Tetrahedron 2004, 60, 2917-2935.


