CHAPTER 2

POLYMER-SUPPORTED REAGENTS: AN OVERVIEW
2.1. Introduction

Functional polymers are considered as organic molecules and their application in organic synthesis was pioneered by the introduction of "solid-phase technique" for the synthesis of peptides by R. B. Merrifield in 1963. Before this invention, polymers were used as ion exchangers and find application as acid and base catalysts. It was thought that polymer support does not have any significant effect on the reactions of the attached reactive species and considered as an inert medium. But later it was found that the macromolecular matrix has a definite influence on the reactions of the bound species. The influence of the macromolecular matrix on the reactions of the bound species is important not only in designing new efficient and specific polymeric reagents, but also in understanding the fundamental nature of the reactions occurring in such organised assemblies.

A polymeric reagent is considered as a reactive group attached to a three-dimensional polymer support and chemical reactions can be carried out with these reactive groups. The exhausted reagent can be easily removed by simple filtration from the reaction mixture and can be regenerated without reduction in its reactivity. Based on the advantages of the functional group and the properties of the polymer backbone, reactive functional polymers have found application as reactive materials in biology and chemical technology. Functional polymers are used in organic oxidations.
Polymer-supported Reagents: An Overview

reductions,\textsuperscript{33,34} halogenations,\textsuperscript{35} peptide condensation,\textsuperscript{36,37} ion-exchangers,\textsuperscript{38,39} chelating agents,\textsuperscript{40} synthesis of hetrocycles,\textsuperscript{7,41} catalyst,\textsuperscript{42-46} media for trapping unstable reaction intermediates\textsuperscript{47,48} and a number of other specific organic reactions.\textsuperscript{49-52} Organometallic polymers are having potential semiconducting properties.\textsuperscript{53}

Polystyrene is used as the support material for most of the polymeric reagents due to the following advantages: (i) easy functionalisation of the aromatic ring,\textsuperscript{54} (ii) degree of crosslinking can be controlled, (iii) being hydrocarbon, these are compatible with organic solvents, (iv) polymers are not degraded by most chemical reagents under ordinary conditions,\textsuperscript{2} and (v) commercial availability. The other types of supports commonly used are based on pyridine polymers,\textsuperscript{55} heterocyclic systems other than pyridine\textsuperscript{56} and organic polymers containing nitrogen.\textsuperscript{57} A highly polar polymeric system such as polyacrylamide have been used as passive supports for the step-wise synthesis of peptide\textsuperscript{58,59} and also used as support material for organic reagents.

This review is an attempt made to rationalise the observations in the development of various polymeric reagents especially polymer-supported oxidising agents. The reagents are classified according to the fundamental molecular character of the polymer support and the nature of the oxidising functionality. The literature has been presented in such a way as to get more insight into the structural environments of the reagent functions.

2.2. Advantages and limitations of reactive polymers

The major advantages of polymeric reagents are due to its insolubility. The immobilised attached species makes the product work-up easy. In
chemical synthesis, the product separation from excess low molecular weight reactants and catalyst is a tedious process and the chance of product loss is high. This can overcome by the use of polymer-supported strategy. In the case of soluble polymers, ultrafiltration or selective precipitation removes soluble polymers. In insoluble crosslinked polymers simple filtration is usually sufficient for the separation. The crosslinked polymer can be easily cleaned off from soluble reactants and products by simple filtration. This provides the use of polymeric reagent in column or batch process. In some cases, by-products remain attached to the polymer thus the product purification is also possible.

The reactivity of the unstable reagent or catalyst may be altered when supported on a polymer. This is due to the restricted mobility of the functional groups in the reaction medium. The polymer matrix can be so selected or tailor-made to provide a specific microenvironment that may induce some specificity at the reaction site.

Polymeric reagent can be regenerated and reused several times hence it is economically very useful. Volatility, odour and toxicity usually occur with low molecular compounds can be reduced by incorporating this into a polymer support. Expensive reagents can be efficiently retained when attached to a polymer and can be recycled by suitable means. Polymeric reagents can provide the possibility of automation in the case of repetitive step-wise synthesis and the facility of carrying out reactions in flow reactors on a commercial scale. Due to the increased shelf life of the polymeric reagent, the supported analogues can be stored under ordinary conditions for a long period. The general representation of the utilisation of polymeric reagent is shown in Scheme 2.1.
There are several drawbacks associated with the use of polymer-supported reagents. The most important among them is the additional time and cost in synthesising a supported reagent. The attachment to or detachment from the polymeric support needs prolonged reaction time resulting in comparatively poor yield. It is difficult to separate the impurities from the functionalised polymer. The reaction conditions should be mild and non-destructive to the polymer backbone or to the product and selective so that only the bond between the polymer and reagent may be formed or cleaved as desired. In the use of functionalised polymer, there always exist the possibility of side reaction with the polymer itself. In some cases intrapolymeric reactions like cyclisations have also been observed as side reactions. Finally, monitoring of the chemical reactions taking place on the polymer is difficult using the usual chemical methods applicable to homogeneous solutions. Some of these drawbacks can overcome by the proper choice of the support.
2.3. Design of polymer-supported reagents

The attachment of functional groups to a polymer is the first method towards the preparation of a reactive polymer which can be utilised as reagent, catalyst, or protecting group. There are two approaches which have been used for the introduction of active functional group in the polymer matrix: (i) by polymerisation of the monomers containing the desired functional group, and (ii) by chemical modification of the non functionalised, preformed polymer. This is explained in Schemes 2.2 and 2.3. Using the former method many functional linear polymers can be prepared by cationic, anionic or free radical polymerisation. But crosslinked polymers are more useful than the linear ones. The crosslinked polymers can be prepared in good physical form by suspension polymerization.\textsuperscript{52,63} The ability to control the loading and distribution of reactive groups is difficult in the second method.

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\includegraphics[width=\textwidth]{polymer-supported_reagents.png}};
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.2.} Preparation of polymeric benzoic acid by the polymerisation of its monomer

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {\includegraphics[width=\textwidth]{polymer-supported_reagents.png}};
\end{tikzpicture}
\end{center}

\textbf{Scheme 2.3.} Preparation of polymeric benzoic acid by chemical modification of the preformed polymer
The introduction of a particular functional group into a support by chemical modification is the most commonly employed method. The merit of this method is the possibility to avoid the synthesis of a complex monomer. Generally after the chemical modification, the final functionalised polymer has the same physical form as the original polymer.\textsuperscript{64,65} The reactivity and accessibility of the reaction site in the polymeric reagent depends on the extent of swelling of the polymer matrix. The reaction conditions used must be carefully chosen to ensure that the reagent can penetrate into the crosslinked matrices throughout the reaction sequence. There should not be any side reaction. The ease of chemical modification of a resin and the success in its application as a reagent or a catalyst depends on the physical properties of the resin itself. In the case of a crosslinked polymer the attachment of a functional group into a polymer support changes the original pore volume. But this is not the case with linear polymers which have the facility to expand or contract their hydrodynamic volumes.

The generation of polar environment in an originally non-polar support (and vice versa) by the introduction of appropriate functional groups can alter significantly the solvent compatibility of the system. An example for this is the sulphonation of hydrophobic DVB-crosslinked polystyrene to hydrophilic ion exchanger.\textsuperscript{66,67} Generation of an ionic groups on a lightly crosslinked, non polar support can actually aggregate or cluster into charged nuclei, with considerable increase in the rigidity of the resin matrix.\textsuperscript{68}

Crosslinked polystyrene was widely used as the support because polystyrene meets many of the requirements of a solid support. The accepted methods for the chemical modification of polystyrene are chloromethylation, bromination and lithiation followed by the necessary polymer analogous reactions for the incorporation of the required reagent function (Scheme 2.4).
Drawbacks of the functionalisation of the polymer support is the difficulty to control accurately the loading of the resin and the adequate characterisation of the structural changes taking place during the functionalisation.

2.4. Characterisation of functional polymers

The analysis applicable for soluble linear functional supports is more or less same to those in low molecular chemistry. But insoluble crosslinked polymer cannot be detected by this method. The techniques used for the characterisation of the functional polymers are summarised below.
2.4.1 Chemical analysis

The functional groups are detected qualitatively by the titration method. The groups which can be detected by this method are usually polymer-bound oxidising and reducing agents, acids, phenols and bases. The volumetric analysis is independent on the nature of the polymer support. Chloromethylated polystyrene can be analysed by modified Volhard's method. Nitrogen and phosphorous can be detected by Kjeldahl method and Messenger's method respectively. Polymer bound oxidising agents such as peracids can be readily estimated by iodometry.

Gravimetric analysis is useful for functional group detection, if the reactions were carried out with reasonable degree of weight change. Reliable measurements of transformed functional groups could be detected from the difference in mass obtained during chemical transformations. Important factors required for this analysis is the physical stability of the polymer matrix. The drying and recovering of the functional polymers should be done with care. Elemental analysis is useful for the detection and estimation of elements such as carbon, hydrogen, halogen, nitrogen, sulphur and phosphorous which are introduced or lost in chemical transformations.

2.4.2 Instrumental analysis

Crosslinked polymers can be analysed using solid state high resolution NMR technique. The technique comprises multiple phase sequences (MP) dipolar decoupling (DD) and magic angle sample rotation (MAR). To enhance weak \(^{13}\text{C}\) resonance, cross-polarisation (CP) was used. This technique provides dynamic and structural information, also to give a detailed description of molecular behaviour at the monomeric level. Highly swollen, lightly crosslinked polymers can give excellent \(^{13}\text{C}\)-NMR spectra, but the \(^{1}\text{H}\)-NMR spectra are of very limited use. Proton NMR is found to be useful for
investigating the relaxation properties of solid polymers.\textsuperscript{74,75} \textsuperscript{1}H- and \textsuperscript{13}C-NMR spectra could be used for the determination of chloromethylation levels in the case of 1-2\% crosslinked chloromethylated polystyrene gels.\textsuperscript{76} Generally low-crosslinked gels gave narrow line spectra due to polymer solutions. But in high crosslinked gels broad line spectra similar to that of amorphous solids were obtained. This can be sharpened by dipolar decoupling and magic angle spinning. It was found that aliphatic band appears to be less broaden than the aromatic band as crosslinking increases, but the aliphatic signal area decreases markedly.\textsuperscript{77-80} \textsuperscript{13}C spin-lattice relaxation times and nuclear overhauser effects have been determined for toluene in crosslinked gel beads substituted with tri-n-butyl phosphonium chloride groups.\textsuperscript{81,82}

Considerable success has been achieved with ESR spectroscopy\textsuperscript{83-85} by the use of nitroxide spin labels bound to the polymeric support or added to the solvents used to swell the samples. This method was used for measuring molecular mobility\textsuperscript{86} but not for evaluating structure. In the soluble polymers structure determination can be achieved by this method.

IR spectroscopy was most widely used for the characterisation of functional polymers. This technique can be used for structural determination of the polymers and also for following the course of the reactions of polymers. The sensitivity of this method has been enhanced by the introduction of Fourier Transform Infrared (FTIR) spectrometers, due to their ability to measure difference spectra.

SEM is used to determine the presence of reactive groups within the polymer beads. This technique gives an idea about the bead size, shape and surface of the polymer bead. In ion-exchange resins, the porosity can be determined by using this technique. It has been found that reaction of lithium
diphenyl phosphide with 2% chloromethylated crosslinked polystyrene beads gives uniform distribution of phosphorous.87

In thermal analysis techniques, thermogravimetry (TG) is one in which the change in sample mass (mass-loss or gain) is determined as a function of temperature and/or time.88 Three modes of thermogravimetry are commonly used as: (a) isothermal thermogravimetry, in which the sample mass is recorded as a function of time at constant temperature, (b) quasi-isothermal thermogravimetry, in which the sample is heated to constant mass at each of a series of increasing temperatures, and (c) dynamic thermogravimetry, in which the sample is heated in an environment whose temperature is changing in a predetermined manner, preferably at a linear rate. The resulting mass-change versus temperature curve provides information concerning the thermal stability and composition of the initial sample, the thermal stability and composition of the residue, if any.

2.5. Factors affecting the reactivity of polymer-supported reagents

2.5.1 Nature and type of the polymer support

The first requirement for the development of a solid-phase reagent is the selection of a suitable support. The nature of the polymer support plays an important role in determining the reactivity of the reagent attached to the polymer support. The support may be linear or crosslinked. A linear species is capable of forming molecular solutions in suitable solvents.89 Hence high conversions can be obtained because of the homogenous accessibility of the functional groups. These advantages of linear polymers were demonstrated by the use of N-chloronylons90 for oxidation and chlorination. It has been observed that the binding of a reactive function into a polymer support altered the macrostructure of the polymer chain.91 But they have the
disadvantage of the difficulty in separation from the reaction mixture. This limits the automation of the technique and the possibility of side reactions producing unwanted crosslinks during reactions. Gel formation is another potential problem with the linear polymers. These problems can overcome by using crosslinked polymers.

Crosslinked polymer consists of infinite networks in which linear chains are interconnected and hence they are macroscopically insoluble in almost all the solvents.\textsuperscript{23} It can be separated from the reaction mixture by simple filtration. The network structures are of two types, having random distribution of crosslinking sites throughout the polymer particle and having an unpenetrable core where there is an accumulation of crosslinking sites. The structures of linear, lightly crosslinked and highly crosslinked polymer are shown in Figure 2.1.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{polymer_structures.png}
\caption{Schematic representation of linear and crosslinked polymers}
\end{figure}
Crosslinked polymers are usually prepared by suspension polymerization and also called 'bead' or 'pearl' polymerisation. The physical form of the polymer beads obtained by this method depends on several factors like the speed of stirring, the shape of the reaction vessel and stirrer, the droplet density, the volume fraction of the dispersed phase and the temperature. Another method for the preparation of crosslinked polymer is popcorn polymerisation in which mixture of a monovinyl and small amount of divinyl species are mixed together and warmed gently in the absence of any initiator and solvent, resulting in white and opaque glassy polymer with characteristic 'popcorn' appearance. A small amount of 'popcorn' polymer itself can be used to seed the polymerisation of another monomer mixture. Due to permanent voids, they are able to absorb large quantities of solvents.

The crosslinked polymers with considerable difference in properties are prepared by changing the method of preparation and degree of crosslinking. Depending on the pore size, the crosslinked polymers are classified as gel polymers and macroporous resin. Gel polymers are also called microporous resins, and appear as translucent and have no permanent porosity, but swell to varying degrees in many organic solvents. The mobility inside the microporous resin is restricted due to the high viscosity of the solutions. These polymers are lightly crosslinked (1-5%) and prepared by suspension polymerisation. As the degree of crosslinking increased, the mobility of the polymer chain reduced. Macroporous crosslinked polymers are prepared by suspension polymerisation using higher amount of crosslinking agent (5-6%) and are swellable in good solvent. Due to large interior surface area, the reagents can easily permeate through these permanent pores. Another advantage of macroporous resin is its physical stability which makes it ideally suitable for column applications.
The nature of the polymer support may be hydrophilic or hydrophobic. Poly(methyl methacrylate), poly(vinyl alcohol) and cellulose are not used as polymer supports due to the inherent synthetic inconveniences associated with them. The most utilised matrices for polymeric reagent are lightly crosslinked DVB-polystyrene\(^{98}\) synthesised by Merrifield. But later it was found that due to the strong hydrophobic nature, it appears to be incompatible with polar solvents and substrates. Copolymers of styrene with ethyleneglycol dimethacrylate, tri- and tetra-ethyleneglycol diacrylate\(^{99}\) were introduced in peptide synthesis.\(^{100,101}\) Polyamide supports and multidetachable polystyrene-polyethyleneglycol grafted supports were also introduced as more hydrophilic supports.\(^{102}\) Reagents based on polyamides, poly(acrylamide)\(^{103}\) poly(vinyl pyridine)\(^{104,105}\) and poly(N-acryl pyrolidones)\(^{106}\) were found to be superior than polystyrene due to better hydrophobic-hydrophilic balance they could provide.\(^{107-109}\) NNMBA-crosslinked poly[1-vinyl(2-pyrrolidonium permanganate)]\(^{110}\) and NNMBA-crosslinked polyacrylamide permanganate\(^{111}\) reagents were used for the oxidation of alcohols. Some results of the oxidation are given in Table 2.1. Here, the reaction rate is high in the case of crosslinked poly(vinyl pyrrolidone) (PVP) matrix than crosslinked polyacrylamide (PAA) matrix. This is due to more polar and hydrophilic nature of poly(vinyl pyrrolidone) support.

**Table 2.1. Effect of polymer matrix on the oxidation reaction**

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Substrate</th>
<th>Time (h)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNMBA-crosslinked PVP-MnO(_4)</td>
<td>Benzoin</td>
<td>2</td>
<td>Benzil</td>
</tr>
<tr>
<td></td>
<td>Benzhydril</td>
<td>7</td>
<td>Benzophenone</td>
</tr>
<tr>
<td>NNMBA-crosslinked PAA-MnO(_4)</td>
<td>Benzoin</td>
<td>8</td>
<td>Benzil</td>
</tr>
<tr>
<td></td>
<td>Benzhydril</td>
<td>10</td>
<td>Benzophenone</td>
</tr>
</tbody>
</table>
Recently, for organic synthesis new supports were developed. These are polymer-supported chiral(salen)Mn(III)complex,\textsuperscript{112} polymer-bound rhodium catalyst for mediation of enantioselective hydride transfer,\textsuperscript{113} polymer-supported o-phenylene(diphosphine) ligands,\textsuperscript{114} polyimide supported molybdenum(IV) epoxidation catalyst\textsuperscript{115} and crosslinked poly(acenaphthylene).\textsuperscript{116}

The ease of chemical modification of a resin, and success of its subsequent application as a reagent or a catalyst, are depend substantially on the physical properties of the resin. Lightly crosslinked polymers are most widely used as polymeric reagents because of the easy diffusion of the low molecular weight substrate through the polymer network. Due to the rigidity of the highly crosslinked polymer, the low molecular weight substrate can not penetrate into the interior of the network and hence the reaction rate is low.

In addition to the organic polymers, a large number of inorganic supports based on alumina, silica and glasses have been widely used as catalyst for chromatographic applications\textsuperscript{117,118} and in organic synthesis. The effectiveness of the inorganic supports is due to the high surface area and high porosity. But its application is limited due to its low loading capacities, insolubility in suitable solvents and the possibility of biological and chemical degradation.

2.5.2 Swelling nature of functional polymers

The accessibility of the attached function to the substrate in continuous phase for chemical modification is necessary for deciding its utility.\textsuperscript{119,120} The swelling studies has an important role to understand the effect of solvent on
the physical and chemical nature of the immobilised species in the heterogeneous system.\textsuperscript{121} In solution, expansion or contraction of the polymer chain depends on the thermodynamics of polymer-solvent interaction. Generally in good solvents, polymer chain forms expanded coil conformations and in poorer one, the coil contracts and eventually precipitation takes place. The ability of a given solvent depends on the chemical nature of the polymer backbone, the nature of the solvent, crystallinity, the polymer - solvent interaction forces and temperature.\textsuperscript{122} But crosslinked polymers which are macroscopically insoluble in almost all solvents can expand by absorbing considerable amount of solvents and become extremely porous forming a pseudo gel.

If the degree of crosslinking is low (less than 2\% crosslinks), such gel networks can absorb large amount of solvents with only a small fraction of the total mass being polymer backbone. As the degree of crosslinking is increased, the polymer backbone becomes more rigid. Then the ability of the network to expand in 'good' solvent becomes reduced\textsuperscript{123} and penetration of reagents to the interior may become impaired. When the crosslink ratio is higher the swollen volume would be less.\textsuperscript{124,125} In the oxidation of benzoin to benzil using DVB-crosslinked polystyrene-\textit{t}-butylchromate reagent, as the crosslink density increased, the yield of the product decreased.\textsuperscript{126} As the crosslink density increases the swelling character of the polymer decreases resulting in low accessibility of the reactive groups to low molecular weight substrate in the solution phase. In the oxidation of cyclohexanone to cyclohexanone using DVB-, NNMBA- and TTEGDA-crosslinked poly(vinyl pyrrolidone) (PVP)-iodine complexes, the rate of reaction is highly dependent on the swelling nature of the polymer support.\textsuperscript{127} Some of the results of the oxidations are given in Table 2.2
Table 2.2. Effect of crosslinking density on the oxidation of cyclohexanol catalysed by crosslinked PVP-iodine complex

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Crosslink density (mol%)</th>
<th>Cyclohexanone (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVB-crosslinked</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>NN MBA-crosslinked</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>TTEGDA-crosslinked</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>82</td>
<td></td>
</tr>
</tbody>
</table>

2.5.3 Effect of spacer handles

One of the serious disadvantages of the polymeric reagent is the slow conversion rate compared with the homogeneous reactions. This decrease in reactivity may be due to the close proximity of the polymer backbone. This effect is predominant in crosslinked polymers where the reactive sites are either flanked by the crosslinker or buried within the interior of the polymer networks. Hence these groups are not accessible to reagents and substrates in the continuous phase. It has been observed that the rate of a reaction involving a supported reagent is enhanced when reactive groups are anchored to the support using spacer arms.\(^\text{128-131}\) Hence the reactivity of functional groups is increased when these groups are separated from the backbone by flexible spacer arms.\(^\text{132}\) In most cases a few methylene\(^\text{133}\) or ethyleneoxide\(^\text{134}\) groups will serve the purpose of the spacer handles. These
handles make the active function protrude from the polymer matrix into the solution phase where they are more accessible to low molecular weight species and solvents.

The increased reactivity of the functional group on a support with spacer arm increases with increasing length of the spacer arm. This is due to the less steric effect imposed by the three-dimensional polymer matrix with increasing length of the spacer arm. It was found that, using 2% DVB crosslinked polystyrene support, the extent of immobilisation of enzymes increased with the length of the spacer.\textsuperscript{135} In the oxidation of alcohols carried out using DVB-crosslinked polystyrene-supported hypohalite reagent,\textsuperscript{136} and polystyrene-supported \textit{t}-butyl chromate reagents,\textsuperscript{126} the oxidising efficiencies of these reagents were found to be significantly greater with increasing the number of spacer methylene groups between polymer support and reagent functions.

\begin{equation}
\text{P-}\text{(CH}_2\text{n-}C\text{-OX)}_\text{CH}_3
\end{equation}

\text{X = Cl/Br} \quad (a)

\begin{equation}
\text{P-}\text{(CH}_2\text{n-COCR}_2\text{(OH)}_\text{CH}_3
\end{equation}

\text{b)

\(n = 0, 1, 2, 3, 4 \text{ and } 5\)

The catalytic activity of phase transfer catalyst based on polystyrene-supported phosphonium salt and crown ethers was high when the catalyst
site was separated by a long spacer.\textsuperscript{137-142} By the presence of spacers the reaction site is exposed to the solution and hence it is more solvated due to the more hydrophobic-hydrophilic balance of the support and the handles.

BDDMA-crosslinked polyacenaphthylene supported t-butyl chromates (a) with, and (b) without spacer are used for the oxidation of alcohols.\textsuperscript{126}

![Chemical structures](image)

The absence of spacer methylene group between the polymer matrix and the t-butyl chromate function is responsible for the low reactivity of resin (b). The presence of spacers allow more accessibility of the reactive groups to the substrate in the reaction medium for oxidation.\textsuperscript{143}

\subsection*{2.5.4 Nature and degree of crosslinking}

The nature and extent of crosslinking agent has significant influence on the chemical reactivity of attached functional group.\textsuperscript{144} The reactivity of the functional group is dependent on the distribution and accessibility of the reactive site on the polymer backbone. In good solvents, linear polymers
form macromolecular solutions and hence their functional groups are freely accessible in solution. Due to the insolubility of the crosslinked polymers, the accessibility of the immobilised functional groups is diffusion-controlled and penetrant transport causes some sort of molecular relaxations making the functional group buried deep in the polymer matrix available to low molecular weight species.\textsuperscript{145,146} In crosslinked polymer networks the distribution of the functional groups on the polymer backbone is non-homogeneous and there is some extent of non-equivalence of the functional groups. It might be expected that groups placed in the vicinity of the crosslinking points are very less accessible to reagents and solvents than groups situated away from the crosslinks.\textsuperscript{23} The degree of swelling is inversely proportional to the crosslink density. At high degree of crosslinking, the polymer matrix become more rigid and the penetration of the solvent and substrate molecules into the interior sites of the polymer is difficult.

A polymeric reagent should have porous structure to allow diffusion of substrates and solvents into the interior of the polymer matrix, thus leading to high reactivity of the polymeric reagent. The diffusion of the substrate into the matrix depends on the physical parameters such as total surface area, total pore volume and the average pore diameter of the polymer matrix. It is observed that polymers with very low crosslink density would be more suitable as a reagent due to increased swelling. This would result in high accessibility through enhanced diffusion properties.\textsuperscript{23} It is possible to increase the reactivity of the attached function by introducing hydrophilic and flexible crosslinking agent in the polymer matrix. The structures of the polymers with rigid and flexible crosslinking agents are represented in Figure 2.2.
DVB-, NNMBA- and TTEGDA-crosslinked poly(vinyl pyrrolidone) (PVP)-bromine complexes were used for the bromination of alkenes. Time required for the addition of bromine are given in Table 2.3. From the results, it is clear that the reactivity of the reagent increases with decreasing the rigidity of the polymer support. Hence highly flexible TTEGDA-crosslinked reagent shows maximum conversion than rigid DVB-crosslinked reagent.

Table 2.3. Nature of crosslinking on bromination reactions catalysed by bromine complexes of crosslinked PVP

<table>
<thead>
<tr>
<th>Crosslinking</th>
<th>Substrate</th>
<th>Time (h)</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVB</td>
<td>C₆H₅CH=CH₂</td>
<td>10</td>
<td>C₆H₅CHBr-CH₂Br</td>
</tr>
<tr>
<td></td>
<td>C₆H₅CH=CHC₆H₅</td>
<td>12</td>
<td>C₆H₅CHBr-CHBrC₆H₅</td>
</tr>
<tr>
<td></td>
<td>C₄H₄CH=CHCCCH₃</td>
<td>9</td>
<td>C₄H₄CHBr-CHBrCOCH₃</td>
</tr>
<tr>
<td>NNMBA</td>
<td>C₆H₅CH=CH₂</td>
<td>5</td>
<td>C₆H₅CHBr-CH₂Br</td>
</tr>
<tr>
<td></td>
<td>C₆H₅CH=CHC₆H₅</td>
<td>6</td>
<td>C₆H₅CHBr-CHBrC₆H₅</td>
</tr>
<tr>
<td></td>
<td>C₄H₄CH=CHCCCH₃</td>
<td>6</td>
<td>C₄H₄CHBr-CHBrCOCH₃</td>
</tr>
<tr>
<td>TTEGDA</td>
<td>C₆H₅CH=CH₂</td>
<td>4</td>
<td>C₆H₅CHBr-CH₂Br</td>
</tr>
<tr>
<td></td>
<td>C₆H₅CH=CHC₆H₅</td>
<td>3</td>
<td>C₆H₅CHBr-CHBrC₆H₅</td>
</tr>
<tr>
<td></td>
<td>C₄H₄CH=CHCCCH₃</td>
<td>3</td>
<td>C₄H₄CHBr-CHBrCOCH₃</td>
</tr>
</tbody>
</table>
DVB-, NN MBA- and EGDMA-crosslinked poly(methyl methacrylate) (PMMA)-supported isoxazolinium chromate and chlorochromate reagent have been developed for the oxidation of the alcohols. The NN MBA-crosslinked resin showed high reactivity in terms of reaction period and yield of the product. The presence of hydrophilic and flexible NN MBA in the polymer matrix reduced rigidity of the system and hence enhanced the swelling property with increasing reactivity of NN MBA-crosslinked PMMA-supported species.

2.5.5 Microenvironmental effects

The attached functional groups present in polymers are in a different local environment than in free solution. The macromolecular network creates a particular microenvironment which mimic the ease of infinite dilution and hence changing the reaction mechanism. The bromination of cumene with poly(N-bromomaleimide) yield different products than those obtained with N-bromosuccinimide (NBS) in CCl₄. The bromination of cumene with NBS in carbon tetrachloride gave benzylic bromination product and a dibromo product. But with poly(N-bromomaleimide), completely different products were obtained. In poly-NBS, the neighbouring succinimide provide the polar medium, resulting different mechanism and the formation of different products. This is confirmed by the observation that the bromination with NBS in a more polar solvent like acetonitrile gave the same products. The polymeric N-chlorosuccinimide gave 100% aromatic substitution of chlorine in ethylbenzene but with monomeric N-chlorosuccinimide (NCS) only chain-substitution of ethylbenzene was observed. The presence of adjacent succinimide group in the polymeric reagent is responsible for high aromatic substitution (Scheme 2.5).
The chemical reactivity of the anchored functional group depends on its distribution and accessibility on the polymer backbone. The studies indicate that groups surrounding the active site can influence the product formation. It was found that in oxidation reactions with polyacrylamide-based reagents, the reactivity of the reagent function increased by crosslinking acrylamide with NN-MBA. In this case the incorporation of the crosslinking agent resulted in a better hydrophobic-hydrophilic balance. This makes the reagent more accessible to the substrates and solvent. But rigid and hydrophobic polystyrene-based N-haloamide was found to be less efficient in carrying out oxidation reactions.

The microenvironment effect can change the ionic properties of the reactive polymers. This also affects the binding constants of soluble molecules interacting with polymer-supported reagents. This effect was sensitively dependent on the nature of the reaction solvent employed. By changing the reaction medium, the direction and magnitude of the distribution effect changed significantly. Linear polymers are soluble in good solvents, but due to the insolubility of the crosslinked polymers, the accessibility of the functional groups are diffusion controlled.
2.5.6 Diffusional and molecular sieving effects

The macroscopic limitations associated with polymers can minimise or totally eliminate in the case of linear support by appropriate choice of the reaction solvent and concentrations. But, with crosslinked polymers and inorganic oxide supports such limitations always remain as a real possibility. Wheeler\textsuperscript{153} and Thiele\textsuperscript{154} proposed mathematical expression for the reactions involving simultaneous diffusion and chemical transformation of a substrate in a porous catalyst.

The classic criterion for diffusion control in resin supports is dependent on the particle size of the low molecular weight substrate. The diffusion of the substrate molecules into the polymer is dependent on pore size, pore volume, interior surface area and average pore diameter of the polymer networks. The amount of crosslinking agent determines the pore size and it will increase with decreasing amount of crosslinking agent. The pore volume can be increased by the incorporation of diluents during the synthesis of the polymer support. In the addition reactions of olefins using polymeric benzyl triethyl ammonium dihaloiodate, a significant dependence on the molecular size of the alkene substrate and the solvent employed was observed.\textsuperscript{155,156} Increasing the ring size of a cyclic olefin or going from a linear to a cyclic substrate with the same number of carbon atoms decreased the rate of reaction.

\[
P - \begin{array}{c} \text{CH}_2\text{N}^+(\text{C}_2\text{H}_5)_3\text{IX}^- \\
X = \text{Cl}_2/\text{Br}_2
\end{array}
\]
2.6. Polymer bound oxidising reagents

In the developmental stages of polymeric reagents, solid-phase synthetic strategy has been found useful in the synthesis of polypeptides, polynucleotides and other biomolecules. But later, they are found to be effective in carrying out the chemical conversion of a number of low molecular weight substances. Based on the mechanism of attachment, the development of the polymer-supported oxidising reagents can be classified into two. A cationic or anionic oxidising agent can associate with the polymer by electrostatic forces. In this case, polymer would contain chelating units or would carry ion exchange groups. Alternatively, oxidising agent can be covalently attached to the polymer. The advantage of immobilisation procedure is the recovery of the spent reagent. Many oxidants are environmentally hazardous and the attachment to a polymer allows the control of wastes. In the same way, an expensive reagent can be recovered and recycled. But the reactivity of the polymeric reagent may be less due to the diffusional problem, which can overcome by choosing suitable reaction medium.

Polymeric reagents are widely used to oxidise alcohols to carbonyl compounds, oxidation of catechols and phenols, epoxidation of olefins, and oxidation of thiols to disulphides. Most of the polymeric reagents have some interesting features regarding the rate of oxidation and the selectivity of substrate. It was found that, in some cases immobilised reagents were found to have greater reactivity than the homogenous analogues and in certain other cases entirely different products were obtained. Commonly polystyrene is used as a support for immobilising oxidising functions due to its readily availability and ease of functionalisation. Less reactivity of polystyrene can overcome by attaching a flexible and hydrophilic crosslinking agent. Recently, pyridine polymers are used as a support for immobilising the oxidising group.
through ionic bonding, providing greater polar atmosphere which can promote the reactions to be carried out with it.

2.6.1 **Redox polymers**

Polymeric redox reagents contain reactive functional groups of oxidation-reduction type. Reaction involves the loss of an equivalent number of protons or electrons from a functional group. This polymer can be prepared by addition polymerisation, condensation polymerisation or by the attachment of special functional groups onto a preformed polymer. Due to high voids, macroreticular polymers are found effective with the monomeric analogues while gel-type resins show weaker oxidising activities. In the case of lightly crosslinked polymers high yields of carbonyl compound were obtained, but found that yield decreased with increasing crosslinking density. This is due to the increased steric effect by the crosslinking interactions between the active site and substrate.

Hydroquinone and catechol incorporated polymers were used for the oxidation of hydrazobenzene to azobenzene. Styrene/divinylbenzene based redox polymers was developed by Kus. In the direct oxidation of alkyl halides to carbonyl compounds, polystyrene based amine was used. Disadvantages associated with this reagent are the presence of soluble counterpart, and the recyclability of polymeric by-product. Hydroquinone polymers were used for the oxidation of amines to ketones. Kamogawa prepared redox systems by attaching phenothiazine or methyleneblue like groups to polyacrylamide.

Hamilton *et al.* developed 'replica gel' (microcapillary type) polymers, having high surface area, for oxidising acetic acid to peracetic acid and to epoxidise oleic acid and cyclohexene. It was found that the efficiency of replica gel for this oxidation increased with dilution in methanol.
In weakly basic conditions, crosslinked polystyrene bound pyridodipyrimidine reagent, which may be considered to be NAD (P)\textsuperscript{*} models were found to oxidise alcohols.\textsuperscript{168} Flavin and various amine functionalised styrene-DVB copolymers were used as coenzyme models for catalysing oxidation reactions.\textsuperscript{169} It was believed that low molecular weight flavins are unable to oxidise thiophenol in non-enzymatic systems. But immobilised flavins oxidise thiophenol to diphenyl sulphide. This is due to the environmental effect of the immobilised-flavin reagent. In flavin enzyme most of the active sites are situated in hydrophobic regions. This hydrophobic environment plays the important role in the binding and activation of substrates. Kunitake \textit{et al.} found that flavin redox polymer can be used as models for coenzymes. They used it for the oxidation of dihydronicotinamide adenine dinucleotide (NADH).\textsuperscript{170}

![Structure of polymer-supported flavin reagent](image)

**Figure 2.3.** Structure of polymer-supported flavin reagent

Yoneda and co-workers converted benzyl alcohol to benzaldehyde and cyclopentanol to cyclopentanone using this polymer.\textsuperscript{168,171} Reaction of 2-vinyl pyrididine polymers with methyl bromide gives popcorn type \textit{N}-methyl-2-pyridinium bromide which permits reversible oxidation-reduction reactions.\textsuperscript{172}
2.6.2 Polymer-supported peracids

Helfrich and co-workers introduced peracids, prepared from a copolymer containing both carboxylic and sulphuric acid groups. This reagent was prepared by the reaction of hydrogen peroxide with polymeric carboxylic acid and was widely used in the epoxidation of olefins. In epoxidation reaction, carboxylic acid formed as by-product could be easily reconverted to peracids. The efficiency of this reagent in epoxidation reaction was found to be dependent on the swelling nature of the resins and its crosslink density. The extent of swelling was determined by the nature of the solvent. In non-polymeric reactions, chloroform or methylene chloride was found as good solvent but in polymeric analogue, THF or dioxane was found to be better. It was observed that the high conversion was obtained with large excess of the reagent, but there exists a problem of separation of the product from relatively large amount of the resin. Aliphatic polymeric peroxy acid was found to be explosive even though they are effective in epoxidation reactions.

(a) Peroxyarsonic acid

Polymer-supported arsonic acid was prepared by the reaction of lightly crosslinked polystyrene with lithium followed by triethoxyarsine and hydrogen peroxide (Scheme 2.6).

\[
\begin{align*}
\text{Scheme 2.6. Preparation of polymer-bound arsonic acid}
\end{align*}
\]
It was effectively used for Baeyer-Villiger oxidations of ketones in dioxane.\textsuperscript{180} In protic solvents reactivity of polymer-supported peracids was found to be decreased. But the reactivity of this reagent was found to be same with other peracids. Polymeric peroxyarsonic acid was also used for the oxidation of olefins.\textsuperscript{179}

(b) \textit{Perbenzoic acid}

Peroxybenzoic acid can be anchored to crosslinked polystyrene beads by a variety of methods. Frechet \textit{et al.}\textsuperscript{176} prepared peracid by reaction of polymer bound benzoic acid with 70\% H\textsubscript{2}O\textsubscript{2} in the presence of acid catalyst. Using the same procedure, the polymer bound acid chloride could be treated with sodium peroxide and 10\% H\textsubscript{2}O\textsubscript{2} (Scheme 2.7). It was observed that using 85\% H\textsubscript{2}O\textsubscript{2} high capacity (4 mmol/g) peroxybenzoic acid was obtained. Another alternative route to polymer-supported peracid involves the ozonolysis of the aldehyde function.

![Scheme 2.7. Preparation of polymeric perbenzoic acid and its use in epoxidation reaction](image)

Perbenzoic acid was used for the oxidation of olefins, penicillin derivatives and sulphides.\textsuperscript{177} Low capacity of this reagent was found to react with penicillins and deacetoxycephalosporins to give high yields of sulphoxides. On passing a solution of acetone containing penicillin \textit{G} through a column filled with peroxyacid resin, penicillin \textit{G} was oxidised to its \textit{S}-oxide form.\textsuperscript{181}
Polymer-supported Reagents: An Overview

Epoxidation reactions were also carried out by using polymeric aliphatic peroxy acids. But its use is limited because of its explosive nature in dry or nearly dry state.\textsuperscript{178,182-184} It was found that in epoxidation reaction, the rate of formation of the product depends on the distribution coefficient of the polymeric reagent.

(c) \textit{Peroxyseleninic} acid

Polymeric phenyl seleninic acid was successfully used in the oxidation of ketones and olefins due to its partial oxidation to selenonic acid, which is a powerful acid. This reagent was also used in Baeyer-Villiger oxidation of ketones.\textsuperscript{185,186} Polymer bound phenyl seleninic acid has been shown to be an effective catalyst for the oxidation of activated alcohols.

A yellow colour polymer was prepared by treating mercurated 2\% crosslinked polystyrene with selenium dioxide (Scheme 2.8).\textsuperscript{185} Disappearance of yellow colour was occurred by treating with 30\% H\textsubscript{2}O, due to the formation of peracids.

\[
\text{SeO}_2 + \text{P-HgCl} \rightarrow \text{P-SeO}_2\text{H}
\]

\textbf{Scheme 2.8.} Preparation of peroxyseleninic acid

2.6.3 \textit{Polymer-supported periodate}

Periodate form of macroporous anion-exchange resins is commercially available. These resins can be used either in protic or aprotic solvents to oxidise various quinols, catechols, glycols, triphenylphosphine, hydrazobenzene and benzhydroxamic acid. Commercially available periodate
form of macroporous anion exchange resins such as Amberlyst-A 26 and Amberlite-IRA 904 has the ability to oxidise catechols and quinols under anhydrous conditions to o- and p-quinones respectively.\textsuperscript{187,188} Due to the high mechanical stability of this polymer, this can be used in column for the oxidation of 2,5-di-t-butyl quinol in acetone at 20°C.\textsuperscript{189-191} Reaction of polymer-supported periodate with triphenylphosphine, hydrazobenzene and benzohydroxamic acid in chloroform gave triphenylphosphineoxide, azobenzene and nitrosocarbonylbenzene respectively. Recently, Liu et al.\textsuperscript{192} discovered that thioethers are oxidised to sulphoxides using alumina-supported sodium periodate in ethanol. Styrene-divinylbenzene supported polyvalent iodine compounds were used for the oxidation of alcohols, diols and amines.\textsuperscript{189,193}

2.6.4 Polymer-supported sulphur reagents

Polymer-supported sulphonium salts were used in epoxidation and also in the oxidation of primary and secondary alcohols. Disadvantages such as odour, difficulty to separate the by-products from the product associated with low molecular reactions could overcome by anchoring to a polymer. Successful oxidation-reduction process was carried out with polymeric thiol-disulphide systems.\textsuperscript{194} Insoluble polymeric sulphonium salts were found to be very effective in preparing epoxides by reaction of their ylid with carbonyl compounds.\textsuperscript{49,195,196} Regeneration of spent polymeric methyl sulphide to polymeric ylid was carried out on treatment with methyl bromide.

Davies et al.\textsuperscript{197} prepared a polymer-bound sulphide by the reaction of ethyl mercaptan with chloromethylated polystyrene. This reagent on oxidation with m-chloroperbenzoic acid (MCPBA) gives the sulphoxide which converts benzyl chloride into aldehyde as shown in Scheme 2.9.
The intermediate ion in this reaction is alkoxy sulphonium ion. The use of sulphoxide to oxidise an alcohol requires the conversion of that alcohol into a leaving group.

On lithiation, polymeric thioanisole gives polymeric phenyl thiomethyl lithium, which was used for the homologation of alkyl halide. Polymeric chlorinated thioanisole was prepared from polystyrene by treating with methylsulphide followed by chlorine in the presence of triethylamine. Lightly crosslinked thioanisole dichloride reagent act as selective oxidant for alcohols.

2.6.5 **Halogen containing reagents**

A number of quaternary ammonium polyhalide reagents have been reported as reagents for organic synthesis. Poly(N-haloamides) and poly(N-haloimides) were developed as efficient reagents for the oxidation of alcohols under mild conditions. Greater reactivity was found in imide type reagents. Frechet et al. prepared several N-chloroamides starting from crosslinked polystyrene and used for oxidation. Considering
Polymer-supported Reagents: An Overview

$N$-halopolyamides, $N$-bromopolyacrylamide was found to be very efficient than $N$-chloropolyacrylamide. This is because of its polar environment in the polyacrylamide support. The reactivity of this reagent was influenced by the nature and extent of crosslinking. Polymeric analogue of $t$-butylhypohalite was found to be a selective reagent for the oxidation of alcohols.\textsuperscript{129,213} The hypochlorite and hypobromite reagents are capable of oxidising primary and secondary alcohols to corresponding carbonyl compounds. In the case of acetyl polystyrene supported hypohalite reagent, the reactivity increased by separating the reagent function from the polymer matrix by the successive introduction of spacer methylene groups. The reactivity was also enhanced by the use of polar crosslinking agent such as tetraethyleneglycol diacrylate. Manecke et al.\textsuperscript{216} prepared poly($N$-chlorobenzotriazole) and used for the oxidation of hydrazocompounds and sulphides. Silica-alumina supported chromyl chloride was used as the selective reagent for the oxidation of alcohols to aldehydes and ketones.\textsuperscript{217}

Polymer-supported (viny pyridine)-bromine complex acts as an active source of halogen capable of oxidising thiols and thiol acids.\textsuperscript{218,219} Thiols of various types were shown to form disulphides in high yields. Polymer-supported hypobromite\textsuperscript{220,221} was prepared by treating crosslinked polyvinyl pyridinium hydrobromide with electric current in acetonitrile (Scheme 2.10).

![Scheme 2.10. Preparation of polymer-supported hypobromite reagent](image-url)

These polymeric reagents have the ability to oxidise secondary alcohols to ketones in high yield. The spent polymeric reagent was regenerated by
electrochemical oxidation. The resin could be used several times without loss of reactivity. Poly(vinylbenzyl)triphenyl phosphonium perbromide was used as a polymeric reagent for bromination. Poly(vinylpyrrolidone)-bromine complexes were used as selective oxidising agent. A mixture of polyvinyl pyridinium hydrobromide and hydrosulphate are effective in the electrochemical oxidation of alkyl side chains of aromatic compounds. Some examples are given in Table 2.4.

Table 2.4. Electrolytic side-chain oxidation of alkylbenzenes using polymeric electron carrier

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Substrate</th>
<th>Electricity (F/mol)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>C₆H₅CH₂C₆H₅</td>
<td>6.0</td>
<td>C₆H₅CO C₆H₅</td>
<td>78</td>
</tr>
<tr>
<td>2.</td>
<td>C₆H₅CH₃CH₃</td>
<td>4.0</td>
<td>C₆H₅CO CH₃</td>
<td>72</td>
</tr>
<tr>
<td>3.</td>
<td>p-CH₃OC₆H₄CH₂CH₃</td>
<td>4.0</td>
<td>p-CH₃OC₆H₄ COCH₃</td>
<td>54</td>
</tr>
<tr>
<td>4.</td>
<td>p-CH₃COOC₆H₄CH₂CH₃</td>
<td>6.0</td>
<td>p-CH₃COOC₆H₄COCH₃</td>
<td>60</td>
</tr>
</tbody>
</table>

Poly(vinyl pyrrolidone) iodine is used as a household antiseptic. Iodate and periodate ions supported on commercial ion exchange resins are used for the oxidation of sulphides and phosphines to the oxides. Hallensleben used (diacetoxy) iodopostyrene species in the oxidation of amines. The polymeric-iodyl species can be prepared by dichloriodopostyrene with peracetic acid (Scheme 2.11).

Scheme 2.11. Synthesis of polymeric iodyl reagent
This polymer is effective for the oxidation of anthracene to anthraquinone.

2.6.6 Polymer-supported chromium(VI) compounds

Polymeric chromium complex reagent was successfully used in the oxidation reactions. Allylic, benzylic, saturated primary and secondary alcohols were converted to the corresponding carbonyl compounds in high yield. Poly(benzimidazole chromate) was found to be very efficient reagent for oxidising alcohols. In this reaction, chromium complexes in the +2 or +3 oxidation state act as the polymeric by-product and easily converted to chromium(VI) species by treatment with low-molecular weight oxidising agent. The oxidation of alcohols to aldehydes and ketones were carried out by the use of chromic acid on anion exchange resin.225

Polymer-supported chromic acid is effective in the oxidation of 1,4-alkyl substituted benzene to dialdehyde.226 Using recyclable polystyrene-supported chromium trioxide reagent, selective oxidation of isoborneol to camphor was carried out.227,228 Reduced toxicity by immobilising chromium to a polymer support and also easy separation from the reaction mixture are the advantages of polymer bound chromium reagent.

A 2% crosslinked copolymer of 4-vinyl pyridine and divinylbenzene was treated with chromic anhydride and HCl to afford poly[vinyl (pyridinium chlorochromate)] and was used for the oxidation of alcohols to carbonyl compounds.107 The spent reagent was washed with acid to remove chromium salts and reused. Best conditions were obtained by wetting the reagent with a nonpolar solvent at about 70°C. In organic media neutral ligands complexed with chromium trioxide act as an efficient oxidising agent for alcohols.228,229
2.6.7 Supported permanganate reagents

A number of inorganic polymer-supported permanganates for the oxidation of alcohols to carbonyl compounds were developed.\textsuperscript{220-224} Regen \textit{et al.} discovered that potassium permanganate can activate alcohol oxidations in benzene by the simple impregnation into inorganic supports such as Linde Molecular Sieves, silica gel and certain clays.\textsuperscript{220} Potassium permanganate adsorbed on alumina is used to oxidise 1,4-cyclohexadienes to the corresponding aromatic compounds.\textsuperscript{225} The quaternary ammonium permanganates such as benzyl triethylammonium permanganate and tetra-\textit{n}-butyl ammonium permanganate have been used for the oxidation of organic substrates.\textsuperscript{226,227} But due to its explosive nature applications are limited. The cheaper and safer quaternary ammonium permanganate such as cetyl trimethyl ammonium permanganate is effective in \textit{cis}-hydroxylation of a variety of olefins in dichloromethane at room temperature.

Potassium permanganate is widely used as an oxidising reagent for organic substrates.\textsuperscript{228-230} The low solubility of the permanganate ion in organic solvents requires the use of oxidation resistant cosolvents such as acetic acid, acetone or \textit{t}-butyl alcohol. The permanganate oxidations in non aqueous solvents are reported.\textsuperscript{231} They used triphenyl methyl arsonium permanganate as a recyclable oxidising agent in organic solvents. Triphenyl methyl arsonium cation undergoes ion association compounds with anionic complex of a number of metals, permanganate, dichromate and triiodide ions. Isolated triphenyl methyl arsonium permanganate was soluble and stable in aprotic solvents like chloroform, nitrobenzene and are used as effective oxidising agents. Also the oxidations are found to be selective.

Ability to complex metal salts with crown polyethers are of interest because of the possibility of increased salt solubility and increased anion reactivity in organic solvents.\textsuperscript{242-244} Sam \textit{et al.}\textsuperscript{245} found that potassium permanganate can be solubilised in benzene by complexing with
dicyclohexyl-18-crown-6 (Figure 2.4) to provide a convenient and efficient oxidant for organic compounds under mild conditions.

![Figure 2.4. KMnO₄ complexed dicyclohexyl 18-crown-6](image)

In the absence of crown ether, potassium permanganate has no detectable solubility in benzene and is not reactive. Potassium permanganate complexed dicyclohexyl-18-crown-6 was used for the oxidation of olefins, alcohols, aldehydes and alkylbenzene. The oxidation of α-pinene to cis-pinonic acid using this complexed compound gave 90% yield (Scheme 2.12).

![Scheme 2.12. Oxidation of α-pinene using KMnO₄ complexed dicyclohexyl-18-crown-6](image)

But in aqueous potassium permanganate, oxidation of α-pinene to pinonic acid is only 40-60% yield. Some other oxidation reactions using KMnO₄ complexed dicyclohexyl 18-crown-6 are given in Table 2.5.
**Table 2.5.** Oxidation reactions using KMnO₄ complexed crownether

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Starting material</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>trans-Stilbene</td>
<td>Benzoic acid</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>Cyclohexene</td>
<td>Adipic acid</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>1-Heptanol</td>
<td>Heptanoic acid</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>Benzydrol</td>
<td>Benzophenone</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>Benzyl alcohol</td>
<td>Benzoic acid</td>
<td>100</td>
</tr>
</tbody>
</table>

Mechanism of oxidation in benzene is considered similar to that generally accepted for aqueous systems (Scheme 2.13).²⁴⁶-²⁴⁸

$$3RCH=CHR + 8KMnO_4 \rightarrow 6RCO_2K + 8MnO_2 + 2KOH + 2H_2O$$

![Scheme 2.13. Mechanism of potassium permanganate oxidation in benzene medium](image)

The reaction is initiated by [2 + 4] electrocyclic addition of permanganate ion to the olefinic π-bond to form the manganate ester ion (a). Rapid oxidation of (a) to (b) occurs by electron transfer.
Potassium permanganate in acetic anhydride is used for the oxidation of olefins to diketones. Oxidation of olefins to acids is by phase transfer catalyst. Crosslinked poly(4-vinyl pyridine) and poly(4-vinyl pyridine-co-styrene) functionalised with potassium permanganate species were found to be effective in selective oxidation of alcohols to corresponding carbonyl compounds. The oxidation of alcohols to the carbonyl compounds also takes place by using poly(1-vinyl (2-pyrrolidonium permanganate)).

Recently, poly(methyl methacrylate) supported pyrazolinium permanganate was used as an effective oxidising agent for the oxidation of primary and secondary alcohols to carbonyl compounds in high yield.

2.6.8 Miscellaneous oxidising reagents

Cu(II) complexes of polymer bound dimethylbenzylamine is used for the oxidative dimerisation of 2,6-disubstituted phenols (Scheme 2.14).

Scheme 2.14. Dimerisation of 2,6-disubstituted phenols

In this oxidation, active agent is a binuclear copper complex. Due to the increased local concentration of the active species, reactivity is higher than the monomeric species. Polymer-incorporated benzoquinone-hydroquinone system forms an important class of oxidation-reduction polymers. Co(II) complexes of bis (cyanoethyl amine) was used for the oxidation of 2,6-dimethyl phenol in air.
Suzuki\textsuperscript{253} and co-workers prepared bis(phosphonomethyl) amino and bis (2-hydroxyethyl) amino species. These ligands have been attached to microreticular or macroreticular polystyrene/DVB and coordinated to both oxo-vanadium (V), and oxo-molybdenum (VI). The expoxidation of (E)-geraniol with \( t\)-BuOOH was carried out using macroreticular oxo-vanadium(V) shown in Scheme 2.15.

\begin{center}
\includegraphics[width=0.8\textwidth]{ Scheme2.15.pdf}
\end{center}

\textbf{Scheme 2.15.} Epoxidation of (E)-geraniol using macroreticular oxo-vanadium(V)

Coordinated oxo-vanadium on polymer-bound acetylacetone group was used to oxidise sulphides, sulfoxides and cyclohexene.\textsuperscript{254} Oxidation of ascorbic acid with \( \text{H}_2\text{O}_2 \) was carried out using tetrapyridyliron(III) species anchored to D- or L-polyglutamate. The oxidation effect is stereospecific and the D-glutamate polymer oxidised L-ascorbate to a higher degree.\textsuperscript{255,256} Oxidation of thiols by immobilised phthalocyanines have been reported by both Schulten and Brouwer.\textsuperscript{257,258} Cobalt(III) derivatives of polymer attached metalloporphyrins oxidised thiols in air.\textsuperscript{259}
Polymer-supported reagents: An Overview

Scheme 2.16. Preparation of polymer-supported amine oxide reagent

Polymer-bound trimethylamine has been formed by the addition of dimethylamine to 1% crosslinked chloromethylated polystyrene. Oxidation with 30% hydrogen peroxide gave the amine oxide shown in Scheme 2.16. This polymer efficiently transforms primary halides and tosylates into the corresponding aldehyde.