Chapter 2

Polymer-Bound Reagents: A Retrospect
POLYMER BOUND REAGENTS: A RETROSPECT

2.1. Introduction

In the forty four years since Merrifield’s first report on solid-phase peptide synthesis\(^1\), organic and polymer chemists have worked to extend the various benefits that result from using reactants bound to crosslinked and therefore insoluble supports\(^2,3\) to other areas of organic synthesis. Recent years have seen polymer-supported reagents and catalysts become common tools for organic synthesis and screening of a large number of organic compounds.\(^4,5\) The use of polymer-supported reagents and scavengers provides an attractive and practical method for the clean and efficient preparation of novel chemical libraries with potential application in the pharmaceutical or agrochemical industries\(^6\).

Scheme II. 1. Schematic representation of the reaction between a polymeric reagent and a reactant

Polymeric reagents are reactive functional polymers, which are used to effect the chemical transformation of a reaction substrate to afford the reaction product, the polymeric reagent itself forming the polymeric by-product\(^7\) (Scheme II. 1). It is a novel type of substance possessing a combination of the physical properties of a high polymer and the chemical properties of the attached reagent. They may be used as reactants in
conventional or unconventional chemical or biochemical processes. Interests in the field is being enhanced by the possibilities of creating systems that combine the unique properties of conventional active moieties and those of high molecular weight polymers. Reactions which are possible only at extreme high dilutions in solution may be carried out at relatively high concentrations on polymeric carriers. The polymer may be organic or inorganic and reagent attachment may be via chemical bonds or physical interactions. The polymeric backbone may be chosen or tailor made to provide a special microenvironment for reactions of the pendant reactive group. Special electronic and steric conditions, significantly different from those existing in the bulk solution, may be created in the close vicinity of the reacting species. The special features of polymeric reagents make their chemistry both unique and useful in chemical practice. Polymeric reagents have developed over the past decade from a somewhat exotic and esoteric research activity into a fast growing field in biochemistry, organic synthesis, specific separations, and analysis.

2.2. Advantages and disadvantages of polymer-supported reactions

Solid-phase method can be considered as a relatively green technology having more advantages and wider applicability compared to the conventional oxidation methods in solution phase. There is now widespread recognition of the advantages of performing chemistry either on polymer supports or with polymer-supported reagents or catalysts. Crosslinked polymers are insoluble and non-volatile; they are odourless and non-toxic and are therefore more environmentally friendly. Highly toxic chemicals can be rendered inert and harmless through attachment to a polymer support. The initial cost of a reagent may be higher than the cost of waste disposal but the advantages in purification of reaction products,
shelf stability and the possibilities for automation of sequential reactions easily out-weigh the initial costs. They have the potential for automated synthesis and testing using high-throughput screens. Another key advantage is that it is possible to use excess reagent to drive reactions to completion, without incurring a penalty in the work up procedure. The reactivity of an unstable reagent or catalyst may be attenuated when supported on a polymer and the corrosive action of protonic acids can be minimised by effective encapsulation. In addition, a number of potentially important reactivity changes may be induced by the use of functionalised polymers. When the latter is crosslinked, restricted interaction of functional groups may be achieved.

A high degree of crosslinking, a low level of functionalisation, low reaction temperature and the development of electronic charges near the polymer backbone encourage the interaction which may be regarded as mimicking the solution conditions of infinite dilution. In these circumstances, intermolecular reaction of bound molecule is prevented and such attached residues can be made either to react intermolecularly or to react selectively with an added soluble reagent. Polymer matrix can provide selectivity in asymmetric synthesis either due to the steric constraints imposed by the macromolecular matrix or due to microenvironmental effects. The great advantage of solid-phase technique is that it has the potential to synthesise compounds faster than classical organic synthesis.

An important aspect of the benefits associated with polymer-supported synthesis is the relative site-site isolation envisioned when a reactive moiety is attached to a solid support. Many reagents undergo irreversible reactions intramolecularly. So site-site interaction must be
reduced to assure facile regeneration of the active site. New methodology for analysis of insoluble polymers must evolve, particularly if multi-step solid-phase synthesis of complex organic substrates is considered. These problems are challenging but the potential applications of polymer-bound reagents dictate further efforts in this field.

Although considerable improvements have been made in this area in recent years, the existing techniques still do not provide the same quality of analysis as rapidly and conveniently as conventional solution-phase techniques. Another fundamental disadvantage of this approach is that additional steps are required to attach and detach products from the polymers: often a vestigial part (the point of attachment of the molecule to the solid support) of the linker unit is found in the final product and linker compatibility with the reagents used can be a source of problems or limitations. It is also not possible to undertake convergent syntheses using this methodology and the polymer loading and swelling characteristics can be poor, necessitating the use of solvents, which are perhaps not optimal for the chemistry being carried out. However, the most frustrating aspect of this type of chemistry is usually the time consuming process of attempting to optimise solution-phase chemistry on a polymer-supported substrate, particularly where a long synthetic sequence is required.

2.3. Chemical modification of the polymer support

A functionalised polymer is a synthetic macromolecule to which reactive functional groups are attached by polymer analogues which can be utilised as reagents, catalysts, protecting groups etc. The macromolecule can be a linear species capable of forming a molecular solution in a suitable solvent or alternatively a crosslinked species, which though readily being solvated by a suitable solvent remains macroscopically insoluble. Of the
two approaches the use of crosslinked polymers has been more widespread because of the practical advantages occurring from the insolubility.

Three methods\textsuperscript{19} have been used for incorporating the active functionality into the substrate (i) preparation of the reactant as a vinyl monomer that can be homopolymerised or copolymerised with another vinyl monomer, then used in the reaction as is or after further modifications, (ii) attachment of the active group to a preformed polymer by reaction with a functional group on the polymer and (iii) entrapment of the reactive compound within the polymer by means other than covalent bonding.

The two most versatile routes in chemical modification of styrene polymers are via chloromethylation and lithiation. Together these two provide a method for attaching a wide variety of both electrophilic and nucleophilic species\textsuperscript{20} (Scheme II. 2).

![Scheme II. 2. Chemical modification of polystyrene](image-url)
A difficulty with the first method is that considerable manipulation of the copolymerisation procedure may be necessary to ensure a good yield of the required polymer in a satisfactory physical form. In the second method, chemical modification is done by using a standard organic synthetic procedure and it must be free of side reactions. Even so the polymers prepared in this way rarely have every repeat unit functionalised and distribution of groups may not be uniform. Different methods provide different functional group distributions. Standard elemental analysis with supporting IR absorption spectra generally provides satisfactory evidence for chemical modifications and allows calculation of the degree of substitution or functionalisation of a polymeric species, quoted in milliequivalents/g of polymers. However, a major problem with the preparation of polymer supports by polymer derivatisation is the possibility of side reactions taking place on the polymer. Indeed very few aromatic substitution reactions are expected to proceed without the formation of any side product. On a polymer support, the side products of the reaction cannot be removed from the derivatised polymer, and they remain as all-time contaminants on the polymer. Aminofunctionalised polystyrenes provide indispensable platforms for attachments of handles and linkers, spacer arms and other moieties for facilitation of solid-phase mediated organic transformations.

2.4. Factors affecting the efficiency of polymer-supported reactions

It is increasingly recognised that, when polymers are used as supports for catalysts or organic reagents, the reactivity and selectivity of the supported catalysts or reagents may be seriously changed by polymer effects, the origin of which may be physical like viscous diffusion effects, steric effects, site separation effects and local concentration effects or
chemical like microenvironmental interactions and coordination unsaturation etc.\textsuperscript{24,25} Apart from the effect of possible heterogenisation, polymer attachment gives system containing several active species macromolecules which can behave differently from the low molecular weight analogue, because of cooperative interactions\textsuperscript{26}. It has been established that the facilitation of reactions using polymeric reagents and the reactivity of functional groups attached to the polymeric network are influenced by a number of characteristic features of the polymer matrix like the nature of the polymer support, microenvironmental effect, site-site interaction, diffusional and molecular sieving effects, swelling, spacer effects and nature and degree of crosslinking.\textsuperscript{27}

\textbf{2.4. a. Nature of the polymer support}

The performance of a polymeric reagent is influenced by the physical and chemical properties of the support. Many copolymers of hydrophilic and hydrophobic monomers with amphiphilic characteristics were found to have compatibility in a wide range of solvents,\textsuperscript{28,29} which is significant in polymer-supported reactions. A list of monomers commonly used is given below (Fig. II. 3).

A polymeric reagent may have a quite different reactivity from the conventional reagent due to the effects of several factors like steric hindrance by the polymer to the attachment of reactants to the reactive sites, incompatibility of the reactants and the polymer or adsorption of the products onto the polymer support.
Fig. II. 1. Monomers commonly used for the preparation of polymer supports (a) styrene (b) methacrylic acid (c) N-vinyl pyrrolidone (d) acrylamide (e) methyl methacrylate (f) 4-vinyl pyridine (g) vinlycarbazole (h) maleic anhydride (i) acrylonitrile

The hydrophilic or hydrophobic character and solvent compatibility of the polymer can be changed by variations in the nature and ratio of the comonomer units. The commonly used supports are based on polystyrenes, polyacrylamides, polyvinyl pyrrolidones or other inorganic supports like silica or alumina.
**Polystyrene based polymer supports**

Polystyrene fulfills the major criteria for a support, i.e., it is chemically stable in a variety of commonly used solvents, both polar and apolar. Polystyrene\(^\text{30}\) is still one of the most popular polymeric materials used in synthesis due to its inexpensiveness, ready availability, mechanical robustness, chemical inertness and facile functionalisation. Among the polystyrenes, the one crosslinked with divinylbenzene (2 mol%) has been the most popular to date because this polymer swells strongly in several solvents and its reactions are carried out mainly in solvents like benzene, methylene chloride and dimethylformamide. A number of different strategies have been employed to prepare alternative supports that avoid the limitations of PS-DVB\(^\text{31}\). Predominant in this area has been the grafting of polyethylene glycol (PEG) onto the polystyrene backbone.\(^\text{32,33}\) Tenta Gel and Argo Gel\(^\text{30}\) are two commercially available examples of this, where the incorporation of PEG chains dramatically increases polymer compatibility with polar solvents. Hydrophobic properties of crosslinked polystyrene have been substantially offset by carrying out a graft polymerisation of ethylene oxide inside the beads.\(^\text{34,35}\) All PEG derivatised polystyrenes undergoes better swelling and hence better synthetic reactivity. In other cases N, N-dimethacrylamides are used and the poor physical properties of these polymers overcome by depositing them inside rigid supports. One way forward is to investigate beads prepared using longer, more flexible crosslinking agents than DVB like ethyleneglycol dimethacrylate (EGDMA) and tetraethyleneglycol diacrylate (TTEGDA) in order to give different solvation properties.
The relatively rigid, macroporous (macroreticular) gel is another type of styrene polymer that, once solvate, does not appreciably change dimensions as a function of solvent polarity. These polymers have the advantages of ease of filtration from the reaction medium after reaction, more accessible reactive groups and large pore sizes which offer less hindrance to the diffusion of the reactant. The drawbacks of these polymers are lower reactivity than the microporous polymers and brittleness, which makes reuse somewhat difficult. Microporous polymers have poor swelling especially in protic highly polar media and poor site accessibility.

A new microgel that has promising utility for organic synthesis was investigated by Spanka et al.\textsuperscript{36} which forms solutions that exhibit lower viscosity even at high concentrations when compared with linear polymers. In addition, the outcome of each individual reaction step can be easily monitored by simple proton NMR, an option not available when using insoluble polymers. Varieties of polystyrene-based supports are widely used as recyclable materials for both catalysis\textsuperscript{37,38} and reagents and cover a broad range of chemical transformations. The development of a wide range
of polystyrene-supported oxidants for the oxidation of a range of primary and secondary alcohols\textsuperscript{39,40} are reported. Polystyrene supports have been widely used as a support for peptide synthesis.\textsuperscript{41,42} Some groups have studied the use of linear polystyrene as a soluble solid support\textsuperscript{43}, the aim being to make the heterogeneous species more solution like.

**Polyacrylamide based polymer supports**

The design of synthetic polar polymeric supports such as polyacrylamide is a significant advance\textsuperscript{44} in the field of metal complexation,\textsuperscript{45,46} dye binding\textsuperscript{47} and for the preparation of a number of polymer-supported reagents\textsuperscript{48}. The polyacrylamide polymers represent the extreme of hydrophilic nature.\textsuperscript{49}

After Tomoi and co-workers\textsuperscript{50} discovered that polystyrene-supported phosphoric triamides catalysed phase-transfer reactions polyacrylamides, either as such\textsuperscript{51} or properly substituted and quaternised, were employed to promote ethers, azidohydrins, halohydrins, and thiocyanohydrins formation. The quaternised derivative of polyacrylamides crosslinked with 2\% DVB proved to be an efficient recoverable and recyclable catalyst for the nucleophilic ring opening of epoxides in water.\textsuperscript{52,53} The reagents based on crosslinked polyacrylamide polymers were used for oxidations\textsuperscript{25,54} and ester hydrolysis\textsuperscript{55}.

![Polyacrylamide-supported ammonium salt](image)

**Fig. II. 3. Polyacrylamide-supported ammonium salt**
Polyacrylamide and its modified forms have been used as cosolvent-type catalysts for nucleophilic displacement reactions under biphasic and triphasic conditions. Also, modified polyacrylamide grafted onto the surface of a porous nylon capsule membrane was used as a phase-transfer catalyst\textsuperscript{56}. These supported systems were found to have different characteristics in terms of polarity, solvation, and reactivity compared to commonly used polystyrene-supported species.

Recently Tamami and Mahdavi\textsuperscript{52} have reported the use of quaternised amino functionalised crosslinked polyacrylamide as an efficient polymeric phase transfer catalyst.\textsuperscript{57} Acrylamide copolymerised with N,N'-methlene-bis-acrylamide (NNMBA), tetaeryleneglycol diacrylate (TTEGDA), triethyleneglycol dimethacrylate (TEGDMA) and divinylbenzene (DVB) in different proportions afford crosslinked polyacrylamides with varying nature and extent of crosslinking.\textsuperscript{58}

**Polyvinyl pyrrolidone based polymer supports**

While crosslinked polystyrene has held a dominant position as the support for a variety of uses, several other polymers have also been used advantageously in a number of applications\textsuperscript{59}. These include for example polyvinylpyridine, polyacrylamide, polyvinyl pyrrolidone and various acrylic polymers. Of particular interest in the context are the nitrogen containing heterocyclic polymers having good ligand properties and can be used for the preparation of a variety of oxidising or reducing agents and catalysts.

Polyvinyl pyrrolidones find wide application in the field of polymer-supported reagents\textsuperscript{60} and is also capable of binding different dyes\textsuperscript{61}. They are used in toiletries, cosmetics, and a variety of pharmaceuticals, including the manufacture of tablets and micro-
encapsulated materials and also as a blood plasma substitute. Linear polyvinyl pyrrolidone is a hygroscopic, amorphous polymer and is the soluble homopolymer of N-vinyl pyrrolidone. Povidone is the generic name for polyvinyl pyrrolidone in pharmaceutical grade. On complexing with PVP the toxicity of iodine is reduced and retains the antiseptic properties of iodine and hence the PVP-iodine complexes are widely used as house-hold antiseptic.

**Miscellaneous supports**

Vinyl group polymerisation has been used to prepare polymers incorporating heterocyclic systems such as pyridine, quinoline and imidazole rings. They have been prepared by polymerisation of the respective monomers either alone or as copolymer with DVB, 2- or 4-vinyl pyridine and N-vinyl pyrrolidone. These heterocyclic group bearing polymers have been functionalised to give polymeric reagents for synthesis. Vinyl polymers incorporating acrylamide, ethylene-maleic anhydride etc. have also been prepared and functionalised to serve as polymeric supports in organic synthesis.

Inorganic matrix supports like silica, alumina, celite and montmorillonite clay have been developed for anchoring reactive groups. It is claimed that such groups are more accessible to the reagents in solution compared with those embedded in the polymer bead because on such supports the reactive groups are mainly confined to the surface. Silica gel supported Jones reagent is found to be capable of oxidising a wide range of benzyl alcohols efficiently and selectively to the corresponding benzaldehydes. Iodic acid supported on wet montmorillonite K10 and silica gel was used for the oxidation of benzyl alcohols under microwave irradiation without solvent. This method offers some advantages in term of
simplicity of performance, solvent-free condition, no side product formation, very low reaction time and a wide range of benzyl alcohols can be converted to their corresponding aromatic aldehydes and ketones.

2.4. b. Microenvironmental effect

It has been found that the microenvironment surrounding the active site in a polymer-supported reagent can play an important role in determining the rate and yield of product formation and can be tailored to a given reaction in order to optimise performance. For eg. the catalytic activities of polymer-supported sulphonic acid catalysts are influenced by the microenvironment surrounding the acid ligands. The microenvironment in a bead may alter the concentrations of low molecular weight reactants present relative to those in the surrounding solution. The microenvironment in the vicinity of the polymer backbone can be expected to be sterically crowded. This is the reason why reactions at the phenyl residues of polystyrene occur mainly at the $m$- and $p$- positions and not the $\alpha$- positions. The steric effects will be greatest when a reactive functional group is directly attached to the polymer backbone, but as the functional groups are separated from the backbone by spacer groups, steric effects would be expected to disappear rapidly and functional group accessibility and mobility to increase.

The support might be expected to influence the course of the reactions greatly if polarities are such that a substrate moiety bound to a polymer support prefers to interact with the support itself rather than with the solvent. By immobilising reactive functional groups onto polymer supports, mutual inaccessibility of the functional groups can be achieved which is rather difficult in homogeneous conditions and a situation approaching infinite dilution can be attained while the actual concentration
may be relatively high. The monoacylation of esters having more than one α-hydrogen atom under homogeneous conditions occurs with side reaction such as self condensation and diacylation. Both these unwanted side reactions could be avoided by immobilising the ester enolate onto a suitable polymer support, thus separating them from each other and from unionised ester molecules.69

2.4. c. Site-site interactions

With a crosslinked polymer the mobility of the polymer chains and hence the attached functional groups is restricted.19 With lightly crosslinked polymers such as 1% or 2% crosslinked polystyrenes the mobility is not reduced significantly, but as the crosslinking increases a point is eventually reached where a small but significant fraction of the functional group cannot reach others. At this stage a degree of permanent site isolation is achieved. The stage at which it occurs depends on the degree of functionalisation and the distribution of the functional groups, the type and distribution of the crosslinks, the extent of crosslinking, the extent of swelling of the polymer matrix and the type of the polymer.

Crucial factors in site-site interaction are the functional group loading and nature of the solvent. In most of the polymer-supported reagents studied the overall concentration of the reactive groups in the beads is reasonably high70. For example with a loading of reactive functional groups of 1mmol/g on a lightly crosslinked gel that swells in the reaction solvent by a factor of 3, the concentration of the reactive groups is 0.33mol/dm³. With a loading of 0.5mmol/g on a highly crosslinked macroporous support which swells only moderately in the reaction solvent, the overall concentration of the reactive species will be 0.5mmol/dm³, but if the functional groups were introduced by chemical modification of preformed
beads they will be located mainly in the pores and there the local concentration will probably be in excess of 1mmol/dm$^3$. When loadings beyond 1mmol/g are employed, then intra-resin reactions can become dominant.$^7$1

If it is desired to allow low molecular mass species in solution reacting with a polymer-supported site to compete effectively with reactions between supported sites the one way to achieve this would be to use moderately loaded lightly crosslinked polymer supports which swell extensively in the reaction solvent. This will reduce the concentration of the supported sites and make it relatively easy for the species in solution to diffuse into the beads. The solvent and the microenvironment in the beads encourage the low molecular mass reactive species to concentrate in the beads.

Clearly increasing the percentage of crosslinking would be expected to reduce chain mobility and thus be a major factor in decreasing the ease of site-site interactions. Changes in the loading of the reactive sites are expected to have a significant but less dramatic effect. Compared to the analogous reaction systems in solution, polymer-supported reagents can show substrate selectivity, be slower or faster, follow a different course or give a different stereochemical result.

2.4. d. Access of soluble reactants to supported reagents

For reactive species in solution to gain access to the reactive sites in the beads, these beads must be swollen by the reaction solvent. Functionalities attached to the beads can significantly affect the swelling properties, especially with highly functionalised beads and that during chemical reactions, the swelling properties may change considerably as one functionality is transformed into another. Reactions in the swollen beads
take place in a gel phase and not as commonly described as in a solid-phase.

In polymer-supported reactions solvent restriction may sometimes be overcome by using macroporous or macroreticular polymers. Various types of internal structure are possible depending on the amount and type of porogen used. Such beads have a rigid porous structure that scarcely swells in most solvents. The open texture allows a wide variety of solvents to enter the pores but not necessarily the highly crosslinked near rigid framework of the bead. An effect relating to access arises if the polarity of the microenvironment within the beads differs significantly from that of the solvent outside the beads. If the diffusion barriers are not too high, equilibrium may be set up between the soluble reactant in the beads and those outside the beads.

2.4. e. Diffusional and Molecular sieving effects

The rate of a supported reaction is highly influenced by the diffusion of low molecular weight reagents through the polymer matrix. In soluble polymers the problem is not so prominent. However, with crosslinked polymers and inorganic supports such limitations always remain a real possibility. The classic criterion for diffusion control in polymer supports is rate dependence on 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.

With many polymers, there exists a significant pore volume and interior surface which is readily accessible to the substrate molecules, from where diffusion may occur not only from the geometric exterior, but also
from this interior surface. The pore volume of a polymer support can be increased by the incorporation of diluents during preparation, and considerable enhancement in rates of reaction, can be brought about\(^74\). In the addition reactions of olefins using polymeric benzyl triethyl ammonium dihaloiodate, a significant dependence on the molecular size of the alkene substrate and solvent employed was observed\(^75\). 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. As the size of the substrate is increased, a retardation effect is observed in the reaction rates\(^76\). These molecular sieving effects influence the kinetics of the supported reaction. The mechanism of diffusion of the supported reagents is quite different from the low molecular weight reactions.\(^77\)

**2.4. f. Swelling of the polymer support**

One of the most important properties of lightly crosslinked polymer beads for solid-phase synthesis is the ability to swell in the reaction solvent.\(^78\) The extent of swelling is determined not only by the chemical characteristics of the beads but also by the degree of crosslinking. The mobility of the polymer chains will depend upon crosslink density, solvent, temperature, flexibility of the chain segments and the free volume generated by randomly distributed substituents.\(^79\) Effective penetration of reagents occurs in swollen systems only. Accordingly, a compromise must usually be found in practice between handling convenience and maximum site accessibility.

For successful design of new polymer-supported reagents, particularly in the context of combinatorial chemistry and automation, it is important to consider the properties and the role of the polymeric support\(^80\). Most of the reactants in solution have to enter the beads and react in a gel
phase. The swelling of the polymers with organic solvents is one method of affording better access to the reactive sites of the polymer prior to its use. Swollen crosslinked polymers are the solvents in which solid-phase organic reactions are performed. The choice of reaction solvent is therefore crucial in polymer-supported reactions and the best solvent may not be the one commonly applied in the analogous reaction using low molecular mass reactants. The thermodynamic interactions between the polymer and the reaction medium must be favourable or the polymer and the reaction medium must be compatible. The diffusion of the soluble substrate into the polymer beads is rate limiting and therefore, in some cases, can result in the supported reactant displaying a pronounced size selectivity. The selectivity arises because a more bulky molecule diffuses more slowly to the reactive sites in the beads. Another effect that needs consideration occurs when the polarity of the microenvironment within the beads differs significantly from that of the solvent outside. This difference can either facilitate or prevent a low molecular mass reactant from approaching the active sites.

It has been demonstrated that substitution of some styrene units by acrylic esters can change the swelling behaviour, and Arshady and co-workers made an important contribution to the use of this type of polymer. Introduction of a carboxylic group into the polymer matrix can dramatically change the properties of the carrier; its internal polarity, and swelling capacity being the most important amongst them (hydrophilic-hydrophobic interactions). Swelling behaviour also aids in the maintenance of the physical integrity of the beads under a variety of reaction condition. While there may always be some inaccessible reaction sites, judicious choice of solvent should in principle lead to optimal utilisation of the polymer-bound functionality.
2.4. g. Effect of spacer handles

The feasibility of a polymer-supported reaction involving a crosslinked polymer support depends on the accessibility of the reactive groups in the polymer matrix, which in turn depends on the proximity of the macromolecular backbone. For a given polymeric reagent, the mobility of the bound functionality depends on whether the group is attached directly to the polymer or whether the group is attached through a spacer handle between the polymer backbone and the functional groups\textsuperscript{84,85}. In most cases, a few methylene groups will serve the purpose of the spacer arm which makes the active function protrude away from the polymer matrix into the solution-phase where they can become accessible to low molecular weight species and solvents.

It was reported that there was an increase in catalytic activity by insertion of spacer groups between polystyrene backbone and the catalytic centre\textsuperscript{86,87}. A sharp increase in the rate of acyl transfer reactions using polymer-supported hydroxamic acylating agents was observed as the length of the spacer arm was increased from zero methylene spacer to five methylene spacers\textsuperscript{88}.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig2_c.png}
\caption{DVB-crosslinked PS-supported hypohalite and t-butyl chromate}
\end{figure}

In the oxidation of alcohols carried out using DVB-crosslinked polystyrene-supported hypohalite\textsuperscript{89} and t-butyl chromate,\textsuperscript{90} (Fig. II. 4) the
oxidising efficiencies were found to be significantly increasing with the number of spacer methylene groups between polymer support and reagent function.

The effect of spacer arm becomes prominent as the degree of crosslinking is increased. Regen et al.\textsuperscript{91, 92} have reported that penetration of the soluble substrates occurs only upto three carbon atoms near the crosslinks and this region is significantly controlled by the polymer backbone. Increasing the spacer chain length will increase the site-site interaction. A crosslinked polystyrene-supported solid-phase analogue of t-butyl hypochlorite containing a trimethylene spacer group between the polymer matrix and the t-butyl hypochlorite function was prepared and used as a recyclable oxidising reagent for alcohols\textsuperscript{4}. The oxidising efficiency of this reagent was found to be significantly greater than those of the reagents containing only one spacer and no spacer between the reagent function and the polymer support.

Chung and coworkers\textsuperscript{93} found that spacer play a significant role in the oxidation of alkyl alcohols using polymer-supported IBX-amide reagents. The introduction of the spacer between the polymer support and IBX-amide group improved the initial conversion rate (up to 60\% conversion). Heterogeneous phase transfer catalysts like crown ethers immobilised on a polystyrene matrix show an increase in activity when they were bonded with long spacer chain to the polymer support.\textsuperscript{94} Such spacers allow the reaction site to get solvated due to hydrophilic-hydrophobic balance and the approach by the soluble substrate was more facilitated. Much attention has recently focused on the use of the immobilised enzymes supported on ion exchange polymers as biocatalysts.
for asymmetric synthesis\textsuperscript{95}. Ion exchange was facilitated by an increased distance between the active site and the polymer backbone.

\textbf{2.4. h. Nature and degree of crosslinking}

The most important factors governing the heterogeneity of the network are the nature and degree of crosslinking. The characteristics of the polymer matrix like mechanical stability and integrity of the polymer beads are dependent on the crosslink ratio. Lightly crosslinked polymers are extremely fragile with low mechanical stability and are not stable enough for recyclisation. Increased physical stability can be achieved with increased crosslinking, but there always exists a balance between the required mechanical properties and reactivity. At very high degree of crosslinking, the steric factors imposed by the polymer network adversely affect the reactivity.

The predominant method used to prepare a crosslinked polymer support\textsuperscript{96} is to polymerise a monovinyl compound with small amount of divinyl compound by radical initiators. This enables the use of suspension techniques and spherical particles are therefore available. Chemically different polymers polymerised with equal amounts of crosslinking agent may differ in pore structure because of the efficiency of the divinyl compound in crosslinking and a change in solvation. The proper pore size is achieved by the inert compound composed of a mixture of two solvents: one is good solvent for the polymer, the other a precipitant. Good solvents produce small pores, bad solvents large pores. Highly crosslinked networks are unsuitable as supports since they are very difficult to functionalise, due to the presence of dense crosslinking and inaccessible domains; even if functionalisation is achieved, the access of reactants to the active sites is slow and typically diffusion controlled.
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Fig. II. 5. Crosslinking agents commonly used for the preparation of polymer supports R=H, Oligo ethyleneglycol diacrylate, R=CH₃, Oligo ethyleneglycol dimethacrylate (b) Oligo alkanediol diacrylate (c) triethyleneglycol divinylether (d) N,N’-methylene-bis-acrylamide (e) divinylbenzene (f) 1,4-bis(acryloyl) piperazine (g) 1,4-phenylene diacryloyl chloride

The nature of the crosslinking agent is important in deciding the net polarity of the polymeric reagent system. Different crosslinking agents varying widely in their relative rigidity and polarity are available (Fig. II. 5). Divinylbenzene (DVB) is very rigid and hydrophobic, ethyleneglycol dimethacrylate (EGDMA) and N,N’-methylene-bis-
acrylamide (NNMBA) are semi-rigid and hydrophilic, hexanediol diacrylate (HDODA), is flexible and hydrophilic, triethylene glycol dimethacrylate (TEGDMA) and tetraethylene glycol diacrylate (TTEGDA) are extremely hydrophilic and flexible crosslinking agents. By choosing appropriate crosslinking agents, the hydrophilic/hydrophobic nature of the polymeric support can be changed.

2.5. Analysis and characterisation of functional and reactive polymers

2.5.1. Chemical Analysis

The concentration of functional groups in a polymeric reagent gives an idea of the maximum amount of reagent available in the polymer. The quantitative determination of polymer bound functional groups is restricted due to the fact that nothing is known of the degree of accessibility of the sites in the polymer. Chemical methods for the determination of functional groups in a polymer are applicable where the functional group can undergo straightforward reaction and if all of the functional groups are readily available to the reagents in solution. When the functionalised polymer contains amide or basic groups, the acid-base titration methods are most suitable. Hydroxyl and amino group in polymer are easily determined by acylation method. The groups like phenols, oxidising and reducing agents are usually detected by titration method. Chloromethylated polystyrene can be analysed by modified Volhard’s method. Polymer-supported oxidising agents such as peracids and chromates 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 that are introduced or lost in chemical transformations.

2.5. 2. Instrumental Analysis

One of the most important disadvantages of using polymer supports is the rather limited range of analytical techniques available. Techniques such as elemental analysis, chemical titration, atomic absorption, plasma analysis, EDAX-semi-quantitative analysis, IR and electron microscopy are mainly used to characterise the structures of the functional sites in polymeric reagents and catalysts, and there is a continuous need for the development of new analytical tools.

a. IR Spectroscopy

IR Spectroscopy is the most versatile and widely used technique for the characterisation of functional polymers. IR spectroscopy has mainly been used as a qualitative tool to show the presence of certain functional groups in a polymer or the extent to which a chemical transformation has taken place. The IR spectra of polymers containing hydroxyl or carboxyl groups can provide additional information about the hydrogen bonding in the polymers, which purely chemical methods fail to do. Since the concentration of the functional groups in polymers is relatively low compared to low molecular weight reagents, the power of the method can be enhanced by using Fourier Transform infrared spectrometers.
Reactive site isolation within the polymer matrix and intra-resin reactions within crosslinked polystyrene has been studied by IR spectroscopy\textsuperscript{98}. Varying the amount of crosslinking in the resin and thus the polymer rigidity did not affect the amount of intra-resin reaction\textsuperscript{99}.

### b. FT-Raman Technique

FT-Raman technique\textsuperscript{100} provides structural information that is a complementary to that obtained from FT-IR experiment. It is considered that FT-IR is best suited for the characterisation of supported species since many functional groups are polar and give place to the appearance of strong absorption bands in the IR. Accordingly the presence or absence of those groups can be assessed, sometimes even quantitatively, by monitoring the corresponding bands. It has to be taken into account, however that some of those groups show all bands in the Raman spectra, even if they are of low intensity, and that some groups are more active in Raman than in IR. On the other hand the nature of the sampling techniques for Raman spectroscopy make it a no interfering and non-destructive technique very suited for the study of solid, insoluble materials. This analysis is necessary in order to understand the properties of polymer-supported reagents and catalysts and in particular, some of the changes occurring upon immobilisation. Additionally, the characteristics of some of the organic functional groups more active in Raman can provide a direct way for the study of the polymeric network that is acting as the support, in particular for PS-DVB polymers that are the most used. This is an important aspect in the study of polymer-supported species, as many works have shown how the polymeric matrix can play an essential role in determining the final properties of the supported reagents and catalysts.
A simple analysis of the FT-Raman spectra of the chloromethylated polymers is one of the more simple and fast methods to monitor how chloromethylation of PS-DVB is very often accompanied by additional crosslinking. Quantitative analysis of functional polymers can also be carried out with the use of FT-Raman spectroscopy.

c. Scanning Electron Microscopy

Characterisation of the microstructure of polymer fibers can provide insight into the fundamental structures present and into the relationship between structure and properties important for applications. Morphological characterisation provides information to understand the effects of processing history on mechanical and other physical properties. These techniques are used to observe features like structure, molecular orientation, size and distribution of molecular additives.

d. Atomic Force Microscopy (AFM)

Atomic force microscopy methods are used for the elucidation of the surface and near surface structure of polymeric solids. Conformational and chain order, crystalline order, polymer crystals, lamellar structures, lamellar surfaces, fold surfaces, fibers and films with highly oriented molecules all yield important information. Controlled deformation of polymer surfaces, both reversible and irreversible with the atomic force microscope provides a wealth of information about mechanical properties on a nanometer scale. The observation of phase separated regions and of polymer crystals lying below a smooth surface shows that not only topography but also elastic inhomogeneity can be observed in great detail with the atomic force microscope.
Self-assembly of macromolecules on a substrate takes place as the concentration of their solution increases. Domains of packed macromolecules on substrates can be easily observed in AFM. The structure-property relationship in multicomponent polymer materials is difficult to understand without microscopic analysis. AFM is very helpful in this analysis at scales from hundreds of microns to nanometers. The specific shapes of individual components as well as variations in their mechanical and electric properties allow them to be distinguished from one another in AFM images.

e. $^{13}$C CP-MAS NMR Spectroscopy

Nuclear Magnetic Resonance spectroscopy has become a method of a great importance for every aspect of the structure and properties of macromolecules\textsuperscript{102}. NMR techniques give detailed insight into the structure and the dynamics of a wide range of systems from classical polymers and site-specific information also becomes accessible. NMR analysis of polymers helps to understand: (i) polymer chain branching, (ii) monomer type, (iii) monomer level, (iv) monomer distribution, (v) molecular weight, and (vi) molecular end-groupings. High-resolution solid-state $^{13}$C NMR,\textsuperscript{103} typically based on the techniques of magic-angle spinning (MAS) and high-power proton decoupling and often combined with cross polarization (CP), has figured prominently among the investigative methods used in the study of polymer systems\textsuperscript{104}.

In many cases NMR technique might be most useful to study $^{13}$C nuclei within the polymer-bound functionality because the most crucial element in organic functionalities is typically carbon. Shea and Sasaki\textsuperscript{105} showed that $^{13}$C CP-MAS NMR can be an extraordinarily valuable technique in providing molecular level details of binding interactions in a
functionalised polymer, which in their case was prepared by a molecular imprinting method.\textsuperscript{106}

\textbf{f. Thermal Analysis}

Among the various thermal methods of analysis, thermogravimetry is a powerful analytical method extensively used to study the thermal stability and decomposition pattern of the crosslinked polymers in reactive and functional polymers.\textsuperscript{107} This is a tool which solves a number of application oriented problems and fundamental aspects of polymer structure, degradation, stability and reactivity.\textsuperscript{108,109} The characteristics of the polymer matrix like the nature of the polymer backbone, the chemical nature and extent of crosslinking can influence the thermal stability of the crosslinked polymers. In addition, the change in the macromolecular structure due to functionalisation is also an important factor affecting the thermal stability. From a single thermogravimetric trace, meaningful values may be obtained for parameters such as activation energy, pre exponential factor and reaction order. These parameters are useful in characterising particular polymer degradation and that the TG curve for each particular set of these parameters is unique and in some cases can be used for identification purposes. Thermogravimetric analysis\textsuperscript{110} is commonly used to determine the temperature range in which the polymer-supported catalysts can be used without destroying the polymeric network of the support. The routes by which polymers degrade can be categorised according to six main mechanisms.\textsuperscript{111} They are main-chain scission, side group scission, elimination, depolymerisation, cyclisation and crosslinking. In an inert atmosphere, some polymers give an almost quantitative yield of their parent monomers.\textsuperscript{112} In air complete oxidation of the sample to oxides of its constituent elements commonly occurs. Nitrogen containing polymers
usually generate some ammonia or hydrogen cyanide. Halogen-containing polymers yield the respective hydrogen halides.

g. Mass spectral analysis

Mass spectral analysis has been applied to identify intermediate species and catalytic reaction products. The difference in the mass spectra of the pyrolysed catalyst before and after successive catalytic cycles has been used to identify catalyst-substrate adducts and final products, and to determine their relative abundance. The results of mass spectral analysis supported by IR spectra served to elucidate the mechanism of the catalytic reaction. Mass spectroscopy has also been used to determine the percentage of crosslinking reagent in a series of polystyrene-DVB copolymers and to determine the degree of chloromethylation.

h. Photoemission spectroscopy

The texture (surface/mass, pore size and structure) of pure polymer supports and supported catalysts affects the rate of transport of reactants to and of products from the reaction centre. Photoemission spectroscopy is based on the analysis of electrons emitted by a sample irradiated with high energy photons. XPS is frequently used to determine the oxidation state of metals in heterogeneous catalysis and to study the chemical composition and structure of polymer support and in favourable cases information on the dispersion of the catalyst can also be obtained.

i. Electron Spin Resonance Spectroscopy

For supports in a well-swollen state, the electron spin resonance spectroscopy can be used for its characterisation. Considerable success has been achieved with ESR spectroscopy\textsuperscript{113} 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{114} but not for evaluating structure. In the soluble polymers structure determination can be achieved by this method.\textsuperscript{115}

2.6. Polymer-supported oxidising reagents

The oxidation of functional groups is one of the most fundamental reactions in organic chemistry but is often accompanied by complications. Ion-exchange polymers were used in organic chemistry long before the more sophisticated polymeric reagents were prepared. Polymer-supported reagents are being currently regarded as amenable alternatives to improve the efficiency of oxidations in that they allow reagent recovery and recycling. Special polymeric effects were observed already with these relatively simple polymeric reagents. These methods provide mild conditions for oxidation of alcohols and are viable alternatives to metal based oxidants. One of the most interesting classes of polymer-supported oxidising agents is polymer-bound anionic oxidising agents. Polymer-supported hypobromate\textsuperscript{116}, iodates, and periodates\textsuperscript{117} have been reported and are the polymeric analogues of the monomeric reagents. Poly(4-vinylpyridinium) bromates\textsuperscript{118} and poly(N-vinyl pyrrolidinium) permanganate\textsuperscript{119} were reported as efficient recyclable oxidising agents.

Classic reagents for the oxidation of organic molecules are manganese dioxide (MnO\textsubscript{2}), potassium permanganate (KMnO\textsubscript{4}), chromium trioxide (CrO\textsubscript{3}), potassium chromate (K\textsubscript{2}CrO\textsubscript{4}) and potassium dichromate (K\textsubscript{2}Cr\textsubscript{2}O\textsubscript{7}).

2.6. a. Polymer-supported peracids

Peracids based on polymethacrylic acid have been prepared and used in epoxide reactions and the peracids were unstable and tended to
detonate. Peracids incorporated in polystyrene (Fig. II. 6) polymers were relatively more stable and did not explode on impact. Insoluble polymers containing vinyl perbenzoic acid units were prepared by chemical modification of two types of styrene-DVB copolymers. One was a hydrophobic swellable copolymer containing 1 or 2% DVB and the other was a rigid macroreticular polymer. The peracid containing copolymers prepared on the 1 or 2% crosslinked supports could be used at peak efficiency only after swelling of the polymer beads in solvents such as CCl₄, CHCl₃, dioxane and tetrahydrofuran. The macroreticular peracids, on the other hand, could be used in almost any solvent. In all cases the peracids were stable, could be stored in a refrigerator for long periods of time without appreciable loss of activity, and regenerated several times without degradation of the polymer matrix.

(a) \begin{center}
\begin{tikzpicture}
  \node[align=center,draw,circle] (A) at (0,0) {PS};
  \node[align=center,draw,circle] (B) at (0.5,0) {CO₂H};
  \node[align=center,draw,circle] (C) at (0,0.5) {\text{PS}};
  \node[align=center,draw,circle] (D) at (0.5,0.5) {\text{SeO₂H}};
  \draw[thick,-] (A) -- (B);
  \draw[thick,-] (A) -- (C);
  \draw[thick,-] (A) -- (D);
\end{tikzpicture}
\end{center}

(b)

\textbf{Fig. II. 6. Crosslinked Polystyrene-supported (a) perbenzoic acid and (b) peroxyseleonic acid}

2.6. b. Polymer-supported permanganates

Potassium permanganate (KMnO₄), an oxidising agent used in organic chemistry for over a century, is one of the most versatile and vigorous ones of the commonly used oxidants. Oxidations of organic substrates with KMnO₄ pose many problems. Most organic solvents are either readily oxidised by KMnO₄ or they do not dissolve the permanganate ion in appreciable amounts. These difficulties led to the use of heterogeneous conditions for permanganate oxidation and form the
basis of the study of Sreekumar and his coworkers on isoxazolinium\textsuperscript{124} (Fig. II. 7b) and pyrazolinium\textsuperscript{125} permanganate.\textsuperscript{126} KMnO\textsubscript{4} adsorbed on aluminium silicate is a reagent suitable for the selective oxidation of alcohols\textsuperscript{127}. Ability to complex metal salts with crown ethers is of interest because of the possibility of increased salt solubility and increased anion reactivity in organic solvents. In the absence of crown ether, potassium permanganate has no detectable solubility in benzene and is not reactive. Because of the high cost of crown ethers\textsuperscript{128,129} a pseudo-crown ether type heterogeneous permanganate oxidising agent was prepared. Polystyrene-supported polyoxyethylenes (Fig. II. 7a) is effective in carrying out the oxidation of primary and secondary alcohols to aldehydes and ketones and aldehydes to acids.

![Crosslinked polystyrene-supported (a) polyoxyethylene and (b) isoxazolinium permanganates](image)

**Fig. II. 7. Crosslinked polystyrene-supported (a) polyoxyethylene and (b) isoxazolinium permanganates**

Crosslinked poly-4-vinylpyridine, poly(4-vinylpyridine-co-styrene)\textsuperscript{123} and polystyrene-supported \( \beta \)-diketone\textsuperscript{130} were functionalised with permanganate group to afford the corresponding permanganate reagent and their role as catalysts in the oxidation of alcohols by Cr(VI) have been studied. Shaabani and Lee\textsuperscript{131} studied the oxidations of organic compounds by permanganate under solvent free conditions. Sherrington\textsuperscript{132} described manganese salen complexes attached to a variety of supports and found that
the polymethylmethacrylate-supported species displayed excellent enantioselectivities comparable to those of the homogeneous catalyst.

Shirini et al.\textsuperscript{133} developed a mild and efficient permanganate-supported oxidising agent using quaternary ammonium Dowex I-X8 and the reagent showed a high efficiency. Brunjes and coworkers\textsuperscript{134} prepared a polymer-bound reagent for the efficient oxidation of alcohols without racemisation in the presence of a catalytic amount of 2,2,6,6-tetramethyl-1-pipridinyl-oxyl (TEMPO).

2.6. c. Polymer-supported hypervalent iodine reagent

Hypervalent iodine reagents have attracted increasing interest during the past decades because of their high selectivity, mild nature and environment friendly properties as oxidising agents in organic synthesis\textsuperscript{135}. Much effort has been devoted to the synthesis and applications of polymer-supported IBX reagents for the oxidation of alcohols in recent years. A mild and efficient procedure for the oxidation of alcohols with polymer-supported IBX in the presence of \(N(CH_2CH_3)_3\) in \(CH_2Cl_2\) has been developed by Lei et al.\textsuperscript{136} This reagent has advantages over the traditional supported IBX reagents because of simplified preparation method and a high oxidation activity of 1.5 mmol/g. The oxidation protocol using this selective reagent is operational simplicity and provides good to excellent yields of carbonyl compounds. The reagent can be recycled at least four times without any obvious loss of activity.

Polymer-supported, recyclable hypervalent iodine(V) (Fig. II. 8) reagent for the efficient conversion of alcohols, carbonyl compounds and unsaturated carbamates in solution was prepared by Sorg and coworkers.\textsuperscript{137,138} The polymer was obtained with high loading (0.8mmol/g) and was capable of converting a diverse collection of alcohols including
complex and sensitive structures efficiently and in good to excellent yields into the respective carbonyl compounds\textsuperscript{139}.

![Figure II. 8. Polymer-supported hypervalent iodine reagents](image)

2.6. d. Polymer-supported bromine reagents

Polyvinyl pyrrolidone crosslinked with tetraethyleneglycol diacrylate was used as solid support for immobilising bromine function.\textsuperscript{140} Studies revealed that the extent of functionalisation as well as the reactivity of the oxidising function was highly dependent on the degree of crosslinking of the macromolecular matrix. Bromates have been used for oxidation of a variety of inorganic and a few organic compounds. Oxidation of alcohols by NaBrO\textsubscript{3} in the presence of cerium(IV) ammonium nitrate,\textsuperscript{141} bromine,\textsuperscript{142} NaHCO\textsubscript{3},\textsuperscript{143} HClO\textsubscript{4},\textsuperscript{144} NH\textsubscript{4}Cl\textsuperscript{145} and oxidation of different organic compounds by NaBrO\textsubscript{3} and AgNO\textsubscript{3} in the presence of Lewis acids\textsuperscript{146} are instances that have been reported. In addition, oxidation of different organic functional groups by bromate supported on commercial resin Amberlyst A-26 and polyvinyl pyridine, has been investigated. By using these polymeric oxidising agents it is possible to overcome many problems associated with the use of metal bromates, such as the necessity of having a strong acidic solutions or the presence of Lewis acids.
Polyvinyl pyrrolidone-bromine complex was prepared easily and used as a mild and convenient reagent for selective bromination of alkenes and bromination at the $\alpha$-hydrogen of active carbonyl compounds\(^{147}\). Selective oxidations of benzylic alcohols in the presence of aliphatic alcohols were also achieved at room temperature. In the presence of bromine and catalytic amount of Thallium(III) salt, polystyrene polymers are smoothly brominated and give homogeneous reactive polymers with a high reproducible degree of functionalisation.\(^{148}\) Kessat reported the synthesis of polymer-supported hydrotribromide\(^{149,150}\) (Fig. II. 9) polymers and were found to efficiently oxidise alcohols in the presence of aqueous NaOH to the corresponding carbonyl compounds in good yield. Interestingly, secondary alcohol oxidation was found to be preferred over primary.

2.6. e. Polymer-supported iodine reagents

Polymer-supported periodate can be used in a variety of solvents, and in many cases filtering off the polymer and evaporating the solvent gives clean oxidised product. Quinols are converted to quinones, 1,2-diols are cleaved to the corresponding carbonyl compounds, sulfides are oxidised to sulfoxides and triphenylphosphine is converted to triphenylphosphine oxide\(^{151}\). Silica gel-supported metaperiodate reagent was found to be useful for the oxidative cleavage of 1, 2-diols\(^{152}\). The reagent is easy to prepare, can be stored, and affords products in high yield and pure enough for
further synthetic operations and the reaction can be performed in dichloromethane.

Periodates oxidise various functional groups but due to solubility limitations these salts are typically only utilised in hydroxylic media. To overcome the solubility problem and also to make use of the advantages of polymeric reagents iodate and periodate supported on commercial anionic resin Amberlyst A-26 and also on polyvinyl pyridine (Fig. II. 10) were synthesised and reported to oxidise different organic functional groups in a range of solvents including aprotic solvents.

![Chemical Structures](image)

**Fig. II. 10. (a) Polystyrene-supported periodate, (b) PVP–supported hydrotriiodide**

Crosslinked poly(n-butyl-4-vinylpyridinium)periodate and iodate are easily synthesised and applied as new polymeric oxidising reagents by Tamami and coworkers. With these oxidants the oxidation of thiols to disulphides, hydroquinones to quinones, acyloins, oximes, allylic alcohols, and diols to their corresponding carbonyl compounds have also been carried out.

### 2.6. f. Polymer-supported hypohalites

Crosslinked polymer-supported analogues of t-butyl hypohalites (Fig. II. 11) were prepared by Pillai and coworkers. These reagents were found to oxidise primary and secondary alcohols to the
corresponding carbonyl compounds in high yields and are suitable for halogenation of carbonyl compounds and amides. The spent polymeric reagent after the oxidation or halogenation step can be recovered and regenerated many times by treating with sodium hypohalite without any loss of capacity.

2.6. g. Polymer-supported phase transfer catalysts

In polymeric phase transfer catalysts, in addition to mere insolubilisation, the polymer exerts a microenvironmental influence on the two reacting phases making the polymeric catalyst different from its soluble analogue. Many interesting polymer effects were observed with these heterogenised homogeneous catalysts. They promote reactions between soluble anions and organic substrates under triphase conditions. The catalytic functional groups anchored to the polymeric supports include crown ethers, cryptands, quaternary ammonium salts etc. Crosslinked chloromethyl polystyrene and silica gel were used as the supports and the catalyst groups were anchored either by the reaction with the corresponding amine or phosphine or by absorption. Spacer arms were used for linking the crown ether and cryptand. The catalytic activity of these anchored catalysts was lower than that of the corresponding non catalysed phase transfer catalysts. However, it was clearly indicated that the catalytic activity of the parent group was retained on binding to the polymer. Insertion of spacer arms has been found to improve catalytic activity. The catalysts recovered by filtration

![Fig. II. 11. Polystyrene-supported hypochlorite](image-url)
from the reaction mixture did not show any change in activity after several cycles. The crown polyethers form a complex with KMnO₄ (Fig. II. 12a) which is more efficient as an oxidising agent in non-aqueous media.¹⁵⁷

![Complex with KMnO₄](image)

**Fig. II. 12. (a) KMnO₄ complexed dicyclohexyl-18-crown-6 and (b) polystyrene-supported Ru(III)**

The Ru(III) salen complex was successfully heterogenised using the PS-DVB copolymer (Fig. II. 12b) by Dalal et al.¹⁵⁸ This catalyst was found to be active for oxidation of benzyl alcohol. The recycling efficiency of the catalysts was seen and it was found to be stable for four cycles. After that a decrease in rate was observed which may be due to leaching of the metal ions. Polymer anchored catalyst was found to be more effective than homogeneous counterpart. The formation of oxocomplex and the transfer of oxygen via this route might be responsible for the reaction.

### 2.6. h. Polymer-supported chromium oxidants

Chromium oxidations have been widely explored since the very beginning of organic chemistry. There has been a continuous interest in the development of new Cr(VI) reagent for the effective oxidation of organic substrates especially under mild aprotic conditions.¹⁵⁹ All forms of Cr(VI) are powerful oxidising agents and oxidise any CH bonds on a carbon with oxygen as far as possible without breaking any carbon-carbon bonds. For example secondary alcohols are converted to ketones, and aldehydes to
carboxylic acids. Chromic acid, acidified potassium dichromate and Jone’s reagent oxidise the activated CH bonds next to an aromatic ring, the benzyl hydrogens, so completely that they usually convert any alkyl benzene to a benzoic acid. Cr(VI) reagents are so powerful that they can also oxidise alkenes and alkynes, breaking the carbon-carbon bond as ozone does, but this reaction is not synthetically useful. Chromium-supported reagents avoid the need to use strong acid aqueous solutions. The chemo-, regio-, and stereoselective oxidation of alcohols to carbonyl compounds is one of the fundamental organic transformations not only from the synthetic point of view but it also enjoys significant biological and mechanistic interest.

Chromic acid is known to be a versatile oxidising agent reacting with almost all types of oxidisable groups. Chromic acid and permanganate unlike periodic acid, lead tetra acetate and phenyl iodosoacetate readily oxidise diols to α-hydroxy carbonyl compounds. The major use of chromic acid in synthetic chemistry is in the oxidation of primary and secondary alcohols to aldehydes and ketones respectively. Although a large number of reagents are known in the literature for such transformations there still appears a need either to improvise the existing oxidation methods or to introduce new reagents to obtain better selectivity under milder conditions.

Many years have passed from the introduction of pyridinium chlorochromate (PCC) as a reagent for oxidation of primary and secondary alcohols. Due to its mildness and high selectivity this oxidant has found wide applications in organic synthesis. Oxidative coupling of aromatic and aliphatic thiols is achieved efficiently by pyridinium chlorochromate in solution and solvent free conditions. Omitting the solvent does not change the reaction time and product yield significantly while the need of using the solvent makes the workup procedure easier.
There are a large number of chromates, chlorochromates, dichromates and fluorochromate immobilised on N-heterocycles (Fig. II.13) which can be used as inexpensive recyclable oxidants. Collin’s reagent (CrO$_3$ in CH$_2$Cl$_2$) and chromyl chloride (CrO$_2$Cl$_2$) are the most common reagents for partial oxidation. Crosslinked poly(n-butyl-4-vinylpyridinium) dichromate is a versatile and effective oxidising agent with which the oxidation of thiols to disulphides, hydroquinones to quinones, acyloins and allylic alcohols to the corresponding carbonyl compounds occurs at reflux condition without affecting the functional groups such as phosphines, oximes, sulphides and aromatic hydrocarbons. Chromium trioxide-3, 5-dimethyl pyrazole complex oxidises organic sulphides effectively. These reagents have many advantages over similar oxidising agents including ease of preparation involving a simple cation exchange, high yields of the oxidised species, shorter reaction times, good selectivity, lower oxidant/substrate ratio and lower solvent requirement.

![Fig. II.13. Polyvinylpyridine-supported chlorochromate and silver chromate](Image)

Sreekumar et al. have extensively reported the development of a wide range of reagents like polymer-supported isoxazolinium chromate and chlorochromate, polystyrene and polyacenaphthyene supported t-butyl chromate, pyrazolinium chromate, chlorochromate and pyrazole-CrO$_3$, polymethyl methacrylate-supported pyrazolinium chromate, chlorochromate and pyrazole-CrO$_3$ complexes capable of effective oxidation of alcohols. Cainelli and coworkers have found that it is possible to obtain a polymer-supported reagent very useful for the oxidation of alcohols utilising chloride form of Amberlyst A-26, a
commercial anion exchange polymer. Poly \([N-(4-pyridinium dichromate)-p\text{-styrene sulphonamide}]\)\(^{176}\) (Fig. II. 14a) is a stable, mild and efficient oxidising reagent that can oxidise both aliphatic and aromatic alcohols in good yield at a temperature of 38°C using \(\text{CH}_2\text{Cl}_2\) as solvent.

![Poly[n-(4-pyridinium dichromate)-p-styrene sulphonamide]](image)

**Fig. II. 14.** (a) Poly\([n-(4-pyridinium dichromate)-p\text{-styrene sulphonamide}]\) (b) Polystyrene-supported pyrazolinium chromate and chlorochromate

In the presence of quaternary ammonium species, chromium trioxide gave complex chromate salts \(X(\text{CrO}_3)_nQ^+\) which were soluble in methylene chloride\(^{177}\) and better efficiency was found under solid-liquid phase-transfer catalysis. Convenient, effective and simple method for the oxidation of alcohols to their corresponding carbonyl compounds in solution and under solvent free conditions using a combination of \((\text{NH}_4)_2\text{Cr}_2\text{O}_7\) and wet \(\text{SiO}_2\) is described by Shirini and his coworkers.\(^{178}\)

Quinolinium dichromate\(^{179}\) in water oxidises vicinal and nonvicinal diols to the corresponding \(\alpha\)-hydroxy carbonyl compound. Quinoxalinium dichromate\(^{180}\) oxidises benzyl alcohol and substituted benzyl alcohols smoothly in dimethyl sulphoxide and in the presence of acid to the corresponding aldehydes. Electron releasing substituents accelerate the reaction whereas electron withdrawing groups retard the reaction.
Quinoxalinium bromochromate is a new mild Cr(VI) oxidising and brominating agent which is effective in the oxidation of alcohols and bromination of aromatic compounds.

Several groups have reported the utility of chromium reagents supported on inorganic supports like silica gel, K-10 montmorillonite clay, Linde molecular sieves and neutral alumina. Silica gel-supported chromium trioxide reagent, prolinium, ammonium and caffenilium bound chlorochromate and chemisorbed chromyl chloride (CrO$_2$Cl$_2$ on Silica-Alumina) were stable that can be stored in the air at room temperature without losing activity and oxidised primary and secondary alcohols to their corresponding carbonyl compounds in good to high yields. In recent years, there has been an increasing interest in reactions that proceeds in the absence of solvents due to their reduced pollution, low costs and simplicity in process and handling. Hajipour and coworkers synthesised a chlorochromate reagent and used as an efficient and selective reagent for the oxidation of alcohols under solvent free conditions. Pyridinium and quinaldinium chlorochromate adsorbed on neutral alumina under solvent-free conditions has been found to oxidise primary aliphatic alcohols to alkyl alkanoates whereas primary benzylic and primary allylic alcohols produce the corresponding aldehydes.

Dowex I-X8, as a quaternary ammonium polymer, in which chloride ion is replaced by dichromate (Scheme II. 3) and bisulfate ions and polyvinyl pyridine-supported chromium peroxide reagents can be used as a stable and efficient oxidising agents for oxidative selection between benzylic alcohols according to their structures.
Scheme II. 3. Selective oxidation of allylic alcohols by PS-supported dichromate

Insoluble polymeric dichromate and chlorochromate reagents were prepared by modification of polymethyl methacrylate-co-divinylbenzene beads with ethylene diamine followed by treatment of the resulting polymer with excess methyl iodide and subsequent reaction with aqueous chromium trioxide or chromium trioxide and benzyltriethylammonium chloride respectively\textsuperscript{192}.

A brick red complex\textsuperscript{193} of CrO\textsubscript{3} with pyridine (CrO\textsubscript{3}.2C\textsubscript{5}H\textsubscript{5}N) is an effective reagent for the oxidation of primary and secondary alcohols to aldehydes and ketones. Primary and secondary alcohols with benzylically and allylically activated C-H bonds are chemoselectively oxidised to the corresponding carbonyl compounds by the (salen) Cr(III) complex as the catalyst iodosobenzene as the oxygen source and the oxidising species is the Cr(V) oxocomplex\textsuperscript{194}.

2.6. i. Miscellaneous polymer-supported oxidising agents

Sharma and his coworkers developed a facile method for the oxidation of alcohols to carbonyl compounds wherein montmorillonite K10
clay-supported iron(III) nitrate (clayfen) is used under solvent-free conditions. The process is accelerated tremendously by exposure to microwave irradiation and the reaction presumably proceeds via the intermediacy of nitrosonium ions. Butanediol dimethacrylate-crosslinked polystyrene-supported t-butyl hydroperoxide was employed in the oxidation of alcohols to carbonyl compounds. Sreekumar et al. developed polystyrene-bound dioxiranes (Fig. II. 15) which was found to oxidise a variety of organic substrates including alkenes to epoxides, pyridines to N-oxides and amines to nitro compounds.

![Fig. II. 15. Polystyrene-bound dioxiranes](image1)

The photooxidation property of polymer bound Rose bengal was investigated towards the oxidation of benzoin to benzil and it acts as an efficient heterogeneous photooxidising agent. A new cross-linked polystyrene-supported thioanisole reagent is reported by Toy and his coworkers which is an effective co-reactant for the sulfide-based oxidation of primary and secondary alcohols. The sodium ruthenate anchored onto polyvinyl pyridine (Fig. II. 16) reported by Friedrich et al. has been shown to catalyse the oxidation of a wide variety of alcohols under mild conditions, in the presence of a suitable co-oxidant.

![Fig. II. 16. Sodium ruthenate anchored on polyvinyl pyridine](image2)
Schiff-base complexes of copper supported on chloromethylated polystyrene as a catalyst have been studied in the oxidation of styrene with molecular oxygen\textsuperscript{203}. The main products are benzaldehyde and the epoxide of styrene. Compared with the unsupported copper complex the polymer supported complex has more effective catalytic activity and could be easily separated and reused.

Functionalised polymers have found increased use as supports on which molecular assembly can be carried out.\textsuperscript{204} They have also been employed as reagents,\textsuperscript{205} catalysts\textsuperscript{206} and for the preparation of transition metal complexes\textsuperscript{207}. The field of polymer-supported organic reactions is rapidly maturing and specific areas of application will no doubt continue to proliferate as experimentalists realise the advantages that polymer-supported species can bring to their own systems.\textsuperscript{208} The use in asymmetric syntheses will certainly be expanded as in their application in the synthesis of asymmetrically substituted symmetric molecules, e.g. porphoryns. With regard to polymeric reagents, the question of cheap and efficient regeneration remains a vital one. The use of electrochemical methods represents a novel step forward and highlights the close relationship with the developing field of polymer surface-modified electrodes.

In catalysis the use of the gas phase is particularly attractive, and the emergence of gas/solid phase transfer catalysis is a significant development. Supported transition metal complexes will also continue to attract considerable attention because of their tremendous industrial potential. Immobilised cluster compounds and coordinately unsaturated species with no true analogue under homogeneous conditions will probably prove of immense synthetic utility. More and more examples of the use of polar and/or hydrophilic supports are already in the pipeline, as the inherent
disadvantages of conventional polystyrene polymers are recognised. Such systems themselves have considerable potential disadvantages especially with regard to side reactions involving the support itself, and time may well prove the tremendous versatility of the styrene based systems.
Chapter II

References

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