CHAPTER-I

INTRODUCTION
The study of polymer-supported (PS) reactions has been an area of considerable interest in recent years due to many attractive features of these reactions\cite{1}. Several of these arise from the fact that the polymer-supported species can easily be separated from the other reaction products, usually, the polymer is a resin and separation is achieved simply by filtration or centrifugation. Occasionally non cross-linked polymers have been used and separation in that case is made by membrane filtration or by addition of a solvent that precipitates the polymer. The easy separation simplifies the work-up procedure and makes it feasible to automate the process. If the polymer can be recycled it becomes practicable to prepare and use quite complex PS species. In favourable cases it may be possible to carry out the reactions and the recycling process using a column of the PS species in much the same way as column of ion-exchange resins are used.

Another attractive feature concerns the possibility of selecting 'high concentration' or 'high dilution' reaction conditions for the PS species\cite{2}. The former are favoured by the use of a low cross-linked resin in which a high percentage of the repeated units bear a reactive group. The latter are favoured by using highly cross-linked (20\%) or macroporous (inflexible) resins and a low percentage of substitution. 2\% cross-linked polystyrene resins have been employed in some cases in order to obtain high dilution conditions, but a
substantial proportion of the groups in such resins can interact even when only 0.5% of the phenyl residues are functionalized\cite{3}.

The polymer-supported resins have been used in many ways in polymer-supported reactions, such as PS substrate, PS reagents, PS catalysts, and PS enzymes.

There are two main areas where organic chemists have used synthetic macromolecules in the laboratory. One is chromatography, the other is polymer-supported reactions. The two areas are not unrelated. Ion-exchange resins, for instance, may be used in chromatography or as polymer-supported catalysts and certain materials used in affinity chromatography may also be used as polymer-supported reagents. Most applications use resins because of their insolubility in all solvents. Non cross-linked polymers which are soluble, are occasionally used. These have the advantage that the reactions or processes occurring on the polymer do not encounter the problem of diffusion and reactions occur in a homogenous phase. In both cases the polymers are prepared by modification of preformed polymers or directly by copolymerization. The most widely used synthetic macromolecules are based on cross-linked polystyrene, polyacrylates, polymethacrylates, and polyacrylamides. Various natural polysaccharides (e.g. agarose) or modified natural polysaccharides (e.g. sephadex) are also used, especially when a hydrophilic material is
required.

Insoluble polymer-supports have been widely used as 'handles' to facilitate the synthesis of polypeptides[4-6], polynucleotides[7] and even polysaccharides[8]. Merrifield in 1963 employed the use of insoluble polymer support to facilitate the synthesis of polypeptides. The solid-support used in the latter case was chloromethylated cross-linked polystyrene. Similar kinds of polymeric supports have been used to synthesize polynucleotide and polysaccharides. The scope of the insoluble polymer support method of preparing large peptides was demonstrated in the synthesis of Ribonuclease A in an automated synthesis procedure[9]. The use of polymer-supports in repetitive 'sequential-type' organic synthesis of above mentioned macromolecules, is essentially based on the joining of a few simple monomer units, has been adequately discussed by Marshall and Merrifield[10], in Biochemical Aspects of Reactions on Solid Supports' in 1971.

It is only recently that insoluble polymers have been used in general organic synthesis different from the repetitive 'sequential-type' synthesis of polypeptides, polynucleotides, and polysaccharides. It has now been found that insoluble polymers can be used for a wide variety of purposes to solve specific synthetic problems. Before discussing reactions that have been successfully carried out with the help of solid-supports, we must look towards the essential features of
a useful support. These are as follows:

1. It must contain reactive sites at which the substrate can be attached and removed easily. It should also be stable to the physical and chemical conditions of the synthesis.

2. It must allow rapid, unhindered contact between the support-bound molecule and the reagents.

3. The support should provide enough points of attachment to give a good yield of the product.

4. It must be readily separable from the liquid phase at every stage of the synthesis.

Several kinds of materials have now been examined as supports. Polystyrene resins have been most extensively studied, but polysaccharides and especially silica supports have found to be more useful. Soluble polymers have also been explored, either alone or in conjunction with a solid support. The physical forms of the supports have ranged from amorphous gels and rigid glasses to linear macromolecules. Separation of the liquid and solid phases has been accomplished by simple filtration, ultrafiltration, gel-filtration, decantation, or centrifugation. A brief discussion of the various supports including their method of preparation and properties is given below:
(A) **Polystyrene supports:**

The first successful supports for solid-phase peptide synthesis were copolymers of styrene and divinylbenzene \[11\]. They were suspension polymers in the form of small beads and consisted of amorphous gels with a random network of cross-linked chains Fig. 1.

Fig. 1: Partial structure of copoly(styrene-m-divinylbenzene)

The extent of swelling, the effective pore size, and the physical stability of the beads are all determined by the degree of cross-linking. The polystyrene-supports containing 0.2% to 16% divinylbenzene have been studied, for their swelling capacity, chemical reactivity, and their physical stability.
Beads containing too low-cross-links (0.2% to 0.5%) of divinylbenzene were quite fragile, whereas highly cross-linked resins were too rigid to allow ready diffusion of reagents within the beads.

At present, one to two percent cross-linked beads 50-100 μm in diameter are considered to be most satisfactory. The various advantages of this resin are:

(a) They can be easily manipulated and readily separated from solvents and reagents by filtration and washing.

(b) They readily undergo aromatic substitution reactions, generally at the para-position of the pendant phenyl rings.

(c) With this type of support the chemical reactions are not limited to the outer surface of the beads but occur throughout the gel matrix (Merrifield and Littau, 1968).

(d) The high resorption of solvent by the dried beads enhances diffusion of reagents to the interior and produces a large effective surface for the synthesis.

(e) The resin swells nicely in solvents like DMF, dioxane, tetrahydrofuran, chloroform and dichloromethane. Swelling is negligible in very polar solvents like methanol or very nonpolar ones like methanol or very nonpolar ones like hexane.
B. Synthetic resin supports:

Inukai et al. found an amorphous polymer prepared from phenol, s-trioxane, and a catalytic amount of 4-toluenesulfonic acid to be a useful solid support (Eq. 2.)\textsuperscript{13}.

\[
\text{C}_6\text{H}_5 - \text{OH} + \begin{array}{c}
\text{O} \\
\text{O}
\end{array} + \text{H}^+ \rightarrow \left[ \begin{array}{c}
\text{HO} \\
\text{CH}_2
\end{array} \right]_n
\]

Eq. 2.

The polymer swells nicely in DMF but not in chloroform, dioxane, benzene, or pyridine. Losse et al. prepared a similar resin from phenol and formaldehyde, methylated the phenolic hydroxyl groups with diazomethane, and chloromethylated the methoxy benzene rings in the usual manner\textsuperscript{14}. This support was found to be comparable to the styrene-divinylbenzene resin for the synthesis of gramicidin S\textsuperscript{15}. Wissmann et al. prepared a modified phenolic resin\textsuperscript{16}. Inman and Dintzis\textsuperscript{17} introduced beaded polyacrylamide. This support was further modified by Atherton and Sheppard which swelled well in polar organic solvents\textsuperscript{18}.

Carbohydrate supports:

Because of the successful use of cellulose derivatives
for fractionation and purification of peptides and proteins, Merrifield in 1959 examined cellulose as the first solid support for peptide synthesis. This support swells both in water and in organic solvents. The support however, could not gain much ground because of its low chemical stability.

D. Silica supports:

Among the most promising new supports for solid-phase synthesis are those based upon porous glass beads. The silanol groups on the surface can be derivatized in various ways with organic substituents\cite{19,20}. The silica support was porasil-C which has a surface area of $50 \text{ m}^2 \text{g}^{-1}$ and an average pore diameter of 20-40 nm. This support was used by Bayer et al for peptide synthesis\cite{21}.

The solid supports described above permit a wide range of synthetic reactions. Virtually any chemical reaction is possible in a heterogenous liquid-solid system. The rates of reactions are usually somewhat slower, but the types of reactions are not seriously restricted by the solid-support. Different types of insoluble supports can be used for a variety of purposes to solve specific synthetic problems. Polymeric supports have been used in organic synthesis in two distinct ways. Used as a polymeric reagent, the method involves a one step process and the functionalized polymer reacts to transform a low molecular weight substrate to the
product. Used as a polymeric protective group, the method involves a multistep process. The polymer acts as a protecting group binding a low molecular weight substrate by a cleavable covalent linkage while transformations are done on the polymer bound substrate at some other functional group. In the former category the spent polymeric reagents are usually converted back into the polymeric reagent itself by simple chemical reactions, while in the latter the recovery is not so important.

**Polymeric reagents:**

In many chemical reactions, a chemical reagent is used, which after the reaction, forms a byproduct, sometimes very difficult to separate from the desired product. If the chemical reagent is covalently attached to an insoluble polymer carrier, the byproduct will remain attached to the polymer and can be separated from the desired product by simple filtration. This principle has been employed in designing polymeric reagents for performing certain specific reactions. Leznoff was first to study these reactions in detail. Some of the reactions where the polymeric support has been used as a reagent, are described below.

A. **Peracid reagents**:

Insoluble peracid reagents have been used in the
epoxidation of olefins\textcite{22}. A cross-linked poly(methacrylic acid) on treatment with $\text{H}_2\text{O}_2$ in presence of a sulfonic acid gives a polymer containing $0.005 \text{ ml}$ of peracid/g of polymer. This insoluble peracid, on reaction with olefins, gives epoxides in high yield. The polymer can be reused until all the peracid groups have been exhausted and can then be reconverted into the peracid as before. The advantage of using this reagent in epoxidation reactions lies in the fact that the product can be obtained by simple evaporation of the solvent, the acid byproduct remaining attached to the polymer.

B. Acylating and similar reagents:

The reagent has been prepared by the co-polymerization of styrene, divinylbenzene, and benzoyl-isomaleimide, which on reaction with acid and acetic anhydride contain succinyl acetate groups\textcite{23}. The polymer on reaction with cyclohexylamine gives N-acetylcyclohexylamine in quantitative yield. Letsinger prepared 'popcorn' polymer from styrene, p-vinylbenzoic acid and divinylbenzene\textcite{24}. The polymer after derivatization contains benzoic anhydride groups. The reagent converted aniline or ethanol to their acylated products in high yields.
C. Ylide reagents:

It is well known that, in the Wittig reaction, a complication that sometimes arises is the difficulty of separation of the Wittig product from the usual byproduct, triphenylphosphine oxide. By attaching the Wittig reagent to an insoluble polymer, the triphenylphosphine oxide remains attached to the polymer after reaction and can be easily separated from the product by simple filtration. Polymer-bound Wittig reagents can be readily synthesized by the co-polymerization of styrene, divinylbenzene, and p-styryldiphenyl phosphine shown in Scheme 2\cite{25,26}.
D. Condensation reagents

Carbodiimide is an excellent condensing reagent used in the synthesis of peptides and nucleotides. Polymer-bound reagent was first prepared by Fridkin et al. and was used in
peptide synthesis\textsuperscript{27}. Scheme 3, represents the synthesis of this reagent prepared according to Weinshenker and Chen, and later used for the synthesis of anhydrides, and in Moffat oxidation\textsuperscript{28,29,30}.

\begin{align*}
\text{P} & \xrightarrow{(i) \text{Potassium phthalimide}} \text{P} \\
\text{P} & \xrightarrow{(ii) \text{NH}_2\text{NH}_2} \text{Pr}^\text{i-NCO} \\
\text{P} & \xrightarrow{\text{A}} \text{TsCl - (Et)}_3\text{N;} \\
\text{Stearic anhydride} & \xrightarrow{\text{Stearic acid}} \text{P} \\
\end{align*}

\textbf{Scheme 3}

D. Disulfide reducing agent:

Gorecki and Patchornik synthesized polymers, based on sephadex, sepharose, cellulose, and polyacrylamide containing 1,3-dithiol groups\textsuperscript{31}. The polymer reacts with disulfides to give the reduced product, the thiol (Scheme 4). The spent polymer can be reduced for reuse.
Chemical applications:

Some of the important applications of the use of polymeric supports in organic reactions are described below:

(1) As polymeric catalysts:

Inorganic catalysts bound to or generated within a solid-support are generally more selective than the same catalysts in solution. Grubbs and Kroll attached rhodium to tertiary phosphine sites on copoly (styrene-2% divinylbenzene) beads.\(^3\)

The latter was found to function as Wilkinson hydrogenation catalyst and prompted hydrogenation of cyclohexene, styrene and nitrobenzene. Scheme 5, shows the preparation of the polymer catalyst, later modified by Collman and coworkers Scheme 6.\(^3\)
(Scheme 5.)

(R) -CH₂Cl + Ph₂PLi ➔

(R) -CH₂PPh₂ ➔

\[ \left[ \left( \text{C}_6\text{H}_5 \right)_3\text{P} \right]_3\text{RhCl} \]

\[ \text{P(C}_6\text{H}_5)_3 \]

\[ \text{P(C}_6\text{H}_5)_3 \]

\[ \text{cyclohexane} \]

(Scheme 6.)
(2) **Monoprotection of a bifunctional compound:**

It is very difficult to selectively block one functional group of a completely symmetrical difunctional compound. Partial protection will generally provide a statistically distributed mixture of unprotected, monoprotected, and diprotected derivatives, difficult to separate. The problem has been solved by the use of a resin-bound protecting group\([34]\). The latter on treatment with a very large excess of the bifunctional reagent and recovering the excess reagent by filtration, results into a resin bearing essentially only the monoprotected difunctional reagent. After reaction of the unprotected functional group and cleavage from the resin a compound with only one functional group is obtained. A series of monotriphenylmethyl \(1,\omega\)-alkanediols have been prepared in this manner Scheme 7\([34]\).

\[
\begin{align*}
\text{R} & \quad \text{CH}_2 - \text{C} - \text{Cl} + \text{HO} - (\text{CH}_2)_n - \text{OH} \\
\text{R} & \quad \text{CH}_2 - \text{C} - \text{O} - (\text{CH}_2)_n - \text{OH} \\
& \quad \text{Ph}_3\text{CCl} \\
\text{R} & \quad \text{CH}_2 - \text{C} - \text{O} - (\text{CH}_2)_n - 0 - \text{CPh}_3 \\
& \quad \text{NH}_4\text{OH}
\end{align*}
\]
Similarly, the solid-support has been used in preparing desired monoacylated or monoalkylated esters. Generally, an attempt to monoacylate or monoalkylate an ester gives diacylated or dialkylated product by self-condensation of the ester, a common competing reaction. Patchornik and Kraus studied this reaction in detail presented in Scheme 8 [35, 36].
3. Polymers in synthetic applications

Besides the use of a polymer-support as a reagent and as a catalyst, it can be used in synthesizing certain compounds which otherwise are very difficult to prepare and if formed are in a very low yield. Some of the applications of the polymer in synthesizing such compounds are discussed below:

(a) Synthesis of threaded macrocycle (or Accumulation of a Low Yield Product):

The synthesis of stable topological molecules such as catenanes has been the goal of chemists[37]. Although Schill and Wolovsky tried to synthesize such compounds, the yields were found to be extremely low[38,39]. Harrison and Harrison
realised the potential of insoluble polymer supports in solving this problem. If a macrocyclic ring could be attached to an insoluble polymer, then a series of reactions could be tried to thread the macrocycle to give stable topological compounds. Even if only a small percentage of macrocyclic rings were threaded, undesirable, nonthreaded byproducts could simply be washed out from the polymer by filtration. The procedure could be repeated several times and in the end threaded macromolecule was cleaved from the polymer. The entire procedure is outlined in scheme 9.

\[ \text{Scheme 9} \]

\[
\begin{align*}
\text{(I)} & \quad \text{Ph}_3\text{C} - \text{O} - \text{C} - \text{CH} - (\text{CH}_2)_{28} \\
\rightarrow & \quad \text{Ph}_3\text{C} - 0 - \text{C} - \text{CH} - (\text{CH}_2)_{10} - 0 - \text{CPh}_3 \\
\text{i} & = \text{HO} - (\text{CH}_2)_{10} \text{OH, Tr-Cl,}
(\text{1,10 decanediol})

\text{ii} & = \text{repeat 70 times.}

\text{NaHCO}_3, \text{MeOH.}

\text{III} & \quad \text{Ph}_3\text{C} - \text{O} - \text{C} - \text{CH} - (\text{CH}_2)_{10} - 0 - \text{CPh}_3
\end{align*}
\]
The threaded macrocule (III) obtained as an oil in 6% yield by first esterifying the cyclic acyloin (I) to a carboxy-resin (II) and treating portions of the diol with triphenylmethyl chloride in presence of the resin bound macrocycle 70 successive times followed by cleaving the macrocycle from the resin.

(b) Enhancement of asymmetric induction:

The asymmetric synthesis of \( \text{R} - 2\)-hydroxy-2-phenylpropionic acid when performed on a solid support, improved the optical yield from 53% to 65%\(^1\). 0\(^1\),0\(^2\)-Cyclohexylidine-\( \text{D} \)-xylofuranose was attached to triphenylmethyl chloride sites on copoly (styrene-2% divinylbenzene) and phenylglyoxylic acid, was esterified to the 3-hydroxyl group of the sugar.

The resin bound \( \text{D} \)-ketoester was treated with Grignard reagent and the resulting \( \text{D} \)-hydroxy ester was saponified from the resin to release \( \text{R} - 2\)-hydroxy-2-phenylpropionic acid Scheme 10.
(c) **Dieckman cyclization reaction of mixed esters**

The use of polymer support in the Dieckman condensation of mixed esters affords two advantages\[42\]. The cyclization step gives higher yields by intramolecular rather than intermolecular reaction owing to the "diluent" effect of the polymer. Secondly, the mixture of ketoesters formed, automatically separates out as a ketoester into the solution and the other remaining attached to the insoluble polymer.
Scope and limitations of insoluble polymer-supported methods in organic synthesis are summarized thus:

A. **Scope**: (1) Some of the main advantages of synthesis on insoluble polymeric supports have been demonstrated in polypeptide synthesis, that is, the normal procedures of organic chemistry, especially solvent extraction and separating flask manipulations, are omitted [42]. It also allows excess of reagents and substrates to be separated from
the reaction product by simple filtration, thus avoiding complex chromatographic procedures.

(2) The automatic removal of a byproduct of a chemical reagent by virtue of the reagent's attachment (and hence also the byproduct) to an insoluble polymer is exploited. This byproduct can often be reconverted into the original valuable reagent.

(3) The flexibility of attaching and interconverting a wide variety of functional groups on a preformed insoluble polymer has been used to advantage for attaching many different types of substrates to the polymer[41].

(4) The advantage of using a functionalized insoluble polymer to 'fish out' a desired minor component from the bulk of a reaction product, as illustrated in the synthesis of a threaded macrocycle[40].

(5) The use of insoluble functionalized polymers as an alternative means of carrying out reactions under conditions simulating high dilution is an important advantage, for example synthesis of cyclic peptides and the Dieckman condensation[43,42].

B. Limitations: (1) One of the major limitations of solid phase synthesis is that the reaction does not necessarily proceed to 100% completion[44]. In repetitive type synthesis this leads to delayed sequences.
(2) The cleavage of the reaction product from the polymer is sometimes incomplete, possibly due to the steric hindrance of the polymer. To avoid this vigorous conditions are required for cleavage that may decompose the product.

(3) The stability of the polymer used in synthetic schemes and as polymeric reagents is at times a troublesome problem.

(4) Ideally, the polymer should be recovered after use and regenerated in simple manner but this capability has been achieved in only a few cases and degeneration of the polymer occurs in many ways \[22, 45, 46, 31, 34\] \[29, 47\].

(5) The difficulty of determining exactly the course and extent of a chemical reaction on an insoluble polymeric support is a serious limitation \[48\].

Despite these shortcomings the polymer-supported reactions have become an area of exciting research in recent years.

**Functionalization of polymeric supports**

For carrying out different types of reactions a polymer should possess desired functionality. In each case a special functionalized polymer may be required for attaching the reagent covalently. One way to prepare a functionalized polymer is to begin with a monomer having the desired functionality. This monomer is then copolymerized with
another monomer without that functionality and a cross-linking monomer. The amount of the first monomer controls the reactive ends and the cross-linking reagent gives the polymer its insoluble character. Thus vinylbenzyl chloride, styrene and divinylbenzene on copolymerization give chloromethylated copoly(styrene-divinylbenzene). Another and more convenient method is to derivatize a preformed polymer. This can be done either through conventional chemical reactions or through grafting. Both linear polymers and resins can be modified. An important example of the former is the hydrolysis of the ester functionality in poly(vinylacetate), which yields poly(vinyl alcohol)|49|. The latter can be treated with aldehydes to give the poly(vinylacetal)|49|. Modification of cross-linked polymers or resins is not experimentally as easy as the modification of linear polymers because these resins are insoluble in all solvents. With conventional resins the reaction solvent must, therefore, be a solvent in which the resin will swell so that the soluble reagent can gain access to the interior of the network. Primary functionalization of cross-linked polystyrene which are available in convenient beaded form begins with one of the following reactions:

Friedel Craft alkylation; It is one of the most convenient and important method of introducing chloromethyl functionality onto the polymer|4,5|. A variety of other functional groups
can be deduced conveniently from the chloromethylated functionality.

\[
P + \text{ClCH}_2\text{OCH}_3 + \text{SnCl}_4 \xrightarrow{0^\circ, 30 \text{ min}} \text{ClH}_2\text{C} -
\]

**Friedel Craft acylation:**

This has been used for introducing phenacyl or benzoyl groups. These are quite reactive functional groups and can be used for further modification.

\[
P + \text{BrCH}_2\text{COCl} \xrightarrow{\text{i. } \text{AlCl}_3} \xrightarrow{\text{ii. } \text{DMF}} \text{C} - \text{CH}_2\text{Br}
\]

\[
P + \text{COCl} \xrightarrow{\text{AlCl}_3} \text{C} - \text{C}_6\text{H}_5
\]

**Lithiation:**

Lithium can be introduced by taking n-BuLi in presence of TMEDA. It is a very reactive group and can be replaced by a number of other functional groups.

\[
\text{(ii) BULi - TMEDA} \xrightarrow{\text{Cyclohexane } 15h; 60^\circ} \text{Li}
\]
One of these primary functionalized polymer is the starting point for secondary functionalization. The primary functional group is amenable to a variety of reactions, resulting, in the introduction of the desired functionality on the polymer as can be seen from the following scheme 12.

Scheme 12
Scheme 12 (Contd.)
Grafting:

Grafting is an important technique of modification of a preformed polymer. A suitable functional group can be introduced onto the preformed polymer by taking a monomer of desired functionality. Grafting can be achieved by the reaction of a 'monomer' onto a backbone polymer bonded at active sites along its chains or by fitting the reactive monomer species at initiating sites of the polymer backbone. The chemistry of grafting involves essentially the generation of active sites on the polymer backbone. Therefore a method of activation which generates maximum active sites on polymeric backbone, is expected to be more efficient in the production of graft. The generation of active sites on polymeric backbone is accomplished by a number of methods which include:

1. Physical activation
2. Chemical activation
3. Physico-mechanical method,
4. Generation of active sites by radiation.

The use of radiations for the generation of active sites on the polymer backbone has totally revolutionized the field of polymer chemistry. Chemical bonds are ruptured in organic materials when they are irradiated with electromagnetic radiation of 100-ev or more. Commonly used energy source is cobalt-60 (γ-rays). Free radicals have been detected in irradiated organic systems, and if organic monomers are irradiated, polymerization occurs via a free-radical mechanism. Irradiation in the presence of oxygen, an effective free
radical scavenger, produces peroxides and hydroperoxides within the polymer. The free radicals or peroxides formed on the polymer backbone by radiations can be used to initiate the polymerization of different monomers. Radiation synthesis is experimentally accomplished by:

a) The mutual irradiation in inert atmosphere of a polymer swelled by or dissolved in another monomer.

b) The preirradiation of a polymer in air to yield peroxo groups or trapped radicals on the backbone and subsequent contact with a monomer in the absence of air, accompanied by heating.

The formation and initial concentration of the free-radicals produced within any irradiated system depends upon the type of radiation, the total energy absorbed (dose, in rad), the rate at which energy is absorbed (dose rate; in rad./sec.) and the radiation sensitivity of the material.

The present chapter deals with the derivatization and functionalization of the commercially available polymer copoly (styrene-2% divinylbenzene) in beaded form. As has already been discussed, this polymer possesses all the desirable properties needed to make it an ideal polymeric support.

There are organic reactions which are carried out only in aqueous medium. There are others that should be carried out in organic medium alone. It is evident that if polymer-
supported reagents are to be used they should be compatible with the medium in which the reaction is being carried out. The present work, therefore, includes the designing of polymer-supported reagents compatible with both kinds of media. In the work done under the project the following insoluble polymeric reagents, have been designed and described:

1. Copoly(styrene-2% divinylbenzene)-g-poly(peracrylic acid) (Reagent I),
2. Copoly(styrene-divinylbenzene)-persulfonic acid, (Reagent II)
3. Copoly(permethacrylic acid-glycol diacrylate), (Reagent III).
4. Copoly(styrene-divinylbenzene)-g-poly(vinyl mercaptan), (Reagent IV).
5. Copoly(styrene-divinylbenzene-g-poly(N-hydroxyglutarimide) (Reagent V).

For the preparation of 1, 4 and 5 the monomers were grafted onto the swollen polymeric backbone by a mutual irradiation method. \( \gamma \)-Radiations were selected as a source of energy for the generation of free radicals. The grafted polymer thus obtained were converted into desired polymeric reagents by manipulating the functional groups introduced through the graft.

Commercially available sulfonic acid cation-exchange polymer AG 50W-X8 (Bio-Rad) was the reformed polymer for the
preparation of a polymeric reagent. Cation exchange resins of this kind are extensively used in chemistry and biochemistry for derivatization and ion-exchange chromatography. These acidic resins have also been used for catalyzing a number of organic reactions. A brief description of these should therefore be in the fitness of things and is given below.

Sulfonic acid cation-exchange resins with porosity of 0.8 cm$^3$ g$^{-1}$, a specific surface not less than 60-70 m$^2$, and a pore radius not greater than 300 Å shows the maximum catalytic activity. For macroporous ion-exchange polymers, these conditions are usually fulfilled in the presence of 20-30% of divinylbenzene (DVB). Ion exchangers with this degree of cross-linking retain their porosity after many repeated swelling and drying operations and do not lose it as a result of conversion from one ionic form to another either. The porometric characteristics of the ion-exchangers influence not only their catalytic activity but also the effects due to blocking of the active centres by the components of the reaction mixture on which the stability of the operation of the catalyst depends.

The ion-exchange resins have been used not only in hydrogen or hydroxide forms, but also in salt forms, functioning as Lewis acids or bases. These catalysts are, as a rule, more thermostable and in some cases surpass cation exchangers in the H-forms and anion exchangers in the OH-forms as regards the
specificity of their action\[50\].

Applications of the cation-exchange resin as catalysts in reactions of organic compounds:

Esters of aliphatic acids and alcohols sucrose, acetals and \(\epsilon\)-caprolactone can be hydrolysed in the presence of sulfonic acid cation exchange resin\[51 to 53\]. Catalytic hydrolysis of esters in the presence of sulfonic acid cation-exchange resins is of greatest promise for industrial applications. This reaction is virtually unaccompanied by side processes. In a very few cases, ion-exchangers (H\(^+\)) have been used as hydration catalysts\[54\]. The use of sulfonic-acid cation exchangers have been successfully made in the dehydration of primary, secondary tertiary and dihydric alcohols under relatively mild conditions (\(t \leq 150^\circ\text{C}\))\[55 to 58\]. Primary alcohols under these conditions give rise to ethers only, but under severe conditions olefins can also be formed together with the ethers. Tertiary alcohols yield only olefins and secondary alcohols are dehydrated to a mixture of ethers and olefins at 100\(^\circ\)\[59\].

Isopropyl alcohol does not undergo dehydration with sulfuric acid at this temperature. A side reaction is often the polymerization of unsaturated hydrocarbons to oligomers. Sulfonic acid cation-exchange resins are the most effective and frequently used catalysts for the formation of esters
from various compounds. The replacement of soluble acids by sulfonic acid cation exchangers reduces the reaction time and increases the yield of the desired product in some cases. Esterifications, have been carried out between mono and dihydric alcohols and mono and dicarboxylic acids of several kinds.

Among several other cation-exchange resins only sulfonic acid resins have been used as alkylation catalysts. An improved yield of the desired products have been obtained as compared with aluminosilicates. The resin has definite advantages over the use of sulfuric acid. In contrast to sulfuric acid, they do not cause the formation of sulfoesters and sulfones\(^{60}\), are less complicated by side reactions involving the polymerization of olefins and transalkylation and ensure the preferential formation of monoalkylphenols. Sulfonated cation-exchangers have served as catalysts for the isomerization of hydrocarbons\(^{67}\), and for Beckmann rearrangement of cyclohexanone oxime to caprolactam, the rearranged products obtained in high yield in DMSO\(^{62}\). The condensation of 2-mercaptopethanol with hydrogen sulfide\(^{63}\), of alcohols with phenols,\(^{64}\) mesityl oxide\(^{65}\), trioxane\(^{66}\) and aldehydes\(^{67}\), of aldehydes with olefins\(^{68}\) etc. has been catalyzed with sulfonated cation exchangers. Cation-exchange resins have been shown to catalyze the addition reactions including hydrogenation, oxidation of several carboxylic acids,
cyclohexanone and derivatives of phthalic anhydride.

We have converted sulfonic acid groups of a cation-exchange resin into persulfonic acid functions by simple reactions. This persulfonic acid resin, Reagent II, could be used successfully for the oxidation of carboxylic acids, olefins and ketones to peracids, epoxides and esters respectively. The polymeric persulfonic acid has shown promise in several other oxidations. The spent resin can be reconverted into the active oxidant over and over again.

A water-compatible 'peracid' reagent, Reagent III was prepared from a hydrophobic resin 'hydrogel' which is essentially copoly(methacrylic acid-glycol diacrylate) 'Hydrogel' was gift from Dr. A. Jayakrishnan, of Sree Chitra Tirunal Institute for Medical Science and Technology, Trivandrum.

The Reagent I, compatible in nonaqueous media was prepared by grafting polyethylacrylate on preformed polymer copoly(styrene-2% DVB) followed by hydrolysis and peroxidation. Peroxidation of the carboxy groups was done with 30% hydrogen peroxide taking methanesulfonic acid as a solvent and as an acid, catalyst.

Polymeric reagent, Reagent IV, copoly(styrene-DVB)-g-poly(vinyl mercaptan), possessing 1,3-dithiol functionality, was prepared by starting form copoly(styrene-DVB)-g-polyvinyl
acetate in a multi-step process. The reagent was found to be an excellent polymeric reducing agent for compounds bearing disulfide linkages.

Copoly(styrene-DVB)-g-poly(N-hydroxyglutarimide), Reagent V, was prepared starting from copoly(styrene-DVB)-g-poly(ethyl acrylate) with a multi-step process. The reagent was successfully used in the synthesis of a dipeptide (Lev-Phe) and a tetrapeptide (Phe-Lev-Gly-Ala).
A General Note

1. The solvents used for the reactions were laboratory grade reagents and were distilled before use.
2. Anhydrous sodium sulfate employed as the drying agent was the product of Sarabhai M. Chemicals.
3. All melting points were recorded in sulfuric acid bath using capillary tube method at an altitude of 2000 meters and are uncorrected.
4. The homogeneity of the products were tested on plates made by silica-gel with 13% CaSO₄·1/2H₂O as binder.
5. Quantitative studies of the products were done on GLC/D.E.G.S. 15% column on 80/100 chromosorb Waw DMCS 6H x 1/8" SS, on a NUCON (5700) AIMIL Gas Chromatograph under the following conditions.

<table>
<thead>
<tr>
<th>Detector</th>
<th>FID/Instrumental Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>Column temperature</td>
<td>195°C</td>
</tr>
<tr>
<td>Carrier gas</td>
<td>Nitrogen</td>
</tr>
<tr>
<td>Flow rate</td>
<td>40 ml/min.</td>
</tr>
<tr>
<td>Sample volume</td>
<td>1 ul.</td>
</tr>
<tr>
<td>Chart speed</td>
<td>1.00 cm/min.</td>
</tr>
</tbody>
</table>

The peaks were identified with the retention times of reference compounds under the same set of conditions and the peak area was calculated by height-width method. In some cases the analysis of the reaction
product was done by HPLC using KONTRON HPLC System 600 under the conditions described with each experiment. HPLC system was equipped with a variable wavelength UV detector. Therefore analysis of the product absorbing in the UV region was conveniently carried out.

7. \( \gamma \)-Chamber-900 having cobalt-60 isotope obtained from (Bhabha Atomic Research Centre, Trombay, Bombay) was used as a source for \( \gamma \)-irradiations for grafting purposes.

8. The names of polymer-supported reagents have been given in accordance with the nomenclature generally followed for polymers.

9. DMF, DCC, THF, DNP, PEG, aliquat-336, BTEAC, Boc- and P are the abbreviations used in the text and stand for dimethylformamide, dicyclohexylcarbodiimide, tetrahydrofuran, 2,4-dinitrophenyl, polyethyleneglycol, tricaprylammonium chloride, tertiary butyloxy carbonyl, and copoly(styrene-2% divinylbenzene).

10. GLC, HPLC and TLC are the abbreviations given to gas-liquid chromatography, high pressure liquid chromatography and thin-layer chromatography.
Material and Methods:

Commercially available copoly(styrene-2% DVB) beads (Eastman Kodak Co. U.S.A.) were used as the backbone polymer for grafting. Ethyl acrylate (Fluka Chemie) was washed with 5% sodium hydroxide solution, dried over anhydrous sodium sulfate and was then distilled. Vinyl acetate (Fluka Chemie) was distilled before use. Benzene (Ranbaxy Laboratories) was shaken with concentrated H2SO4 until free from thiophene, then with water, dilute NaOH and again with water, followed by drying with calcium sulfate and finally distilled. DMF (Glaxo Laboratories) was dried by adding sodium hydroxide pellets, refluxed with calcium sulfate and distilled under reduced pressure. Dioxane (E. Merck) was purified by passing through a dry bed of activated alumina and stored over molecular sieves (4 Å). Ethyl alcohol (B.P.) (Bengal Chemicals and Pharmaceutical Ltd.) and carbon disulfide (SD's) were used directly without purification. p-Toluenesulfonyl chloride (Fluka AG) and p-toluenesulfonic acid (Loba Chemie) were recrystallized before use. Methanesulfonic acid (Fluka AG) was used as supplied.

Preparation of ethylxanthate:

Ethylxanthate was prepared according to the procedure given by Rao[69].
A specified amount of ethanol was measured into a wide mouth conical flask, to which a slight excess of saturated solution of potassium hydroxide in water was introduced. The flask was cooled in an ice bath and the temperature maintained below 10°. Then an excess of carbon disulfide was gradually added with constant stirring. The stirring was continued for 15 minutes after the addition of required amount of \( \text{CS}_2 \) during which ethyl xanthate separated as thick reddish brown mass. The reddish orange liquid containing polysulfide impurities was removed by suction. Ethyl xanthate thus prepared was purified by dissolving in acetone and precipitating with benzene or petroleum ether (40-60°). The compound was stored in vacuum desiccator.

**Preparation of potassium trithiocarbonate:**

Potassium trithiocarbonate was prepared by the method of Deskini[1]. A saturated solution of potassium hydroxide in absolute alcohol was taken in a conical flask and saturated with hydrogen sulfide. This was followed by the slow addition of \( \text{CS}_2 \) solution in absolute alcohol from a dropping funnel with constant stirring. The stirring was continued for 20 minutes after the addition. The orange coloured crystals of the compound separated out which were removed by filtration, washed with absolute alcohol, dried and kept in a vacuum desiccator. A standard solution of the compound was prepared by dissolving a little more than the calculated amount in doubly distilled
boiled water and standardized iodometrically.

A. Preparation of copoly(styrene-DVB)-g-poly(ethyl acrylate):

(a) By Mutual irradiation:

Accurately weighed polystyrene resin (0.2 g) taken in a 50 ml conical flask was allowed to swell for 10 minutes in 15 ml of distilled benzene. To the swollen polymer was added 1 ml of ethyl acrylate, and the flask was kept in the \( \gamma \)-chamber for 24 h. After irradiation, the grafted polymer was stirred with benzene for 3 h at room temperature on a magnetic stirrer for dissolving the homopolymer. The polymer was then taken in a weighed thimble and extracted with DMF in a soxlet extractor. At the end, the thimble containing the grafted polymer was taken out, washed with acetone, dried and weighed. Percentage of grafting was calculated from the weight of the grafted polymer which was found to be 100%.

(b) By thermal process:

Polystyrene beads (0.2 g) were taken in a 50 ml standard joint glass tube containing 15 ml of benzene. The swollen polymer was then irradiated with \( \gamma \)-radiation for 24 h in the \( \gamma \)-chamber. The polymer was removed from the chamber and ethyl acrylate (1 ml) was immediately added to activated polymer. Polymer, along with the monomer was then refluxed on the water bath for 3 h. The grafted polymer was taken in a weighed thimble and extracted with DMF in a soxlet extractor.
for 8h. The polymer was washed with acetone dried and weighed. Percentage of grafting was found to be 100%.

Preparation of copoly(styrene-DVB)-g-polyacrylic acid:

The grafted polymer was taken in a 250 ml round bottomed flask. To this was added distilled dioxane (20 ml) and 5-6 pellets of potassium hydroxide dissolved in minimum amount of distilled water. The reaction mixture was heated on a water bath for 5h and the resin was filtered out. Heating with KOH in dioxane was repeated twice to ensure complete hydrolysis of the ester groups. The polymer was then filtered and washed several times with distilled water until the filtrate became neutral. It was then washed with water, dioxane (50 : 50), dioxane, DMF and CH₂Cl₂. The polymer was then treated with 2M HCl in dioxane water and washed with aqueous dioxane. It was finally dried under vacuum.

Preparation of copoly(styrene-DVB)-g-poly(oxoacrylic acid),

Reagent I:

Dichloromethane (15 ml), p-toluenesulfonylic acid (0.172 g, 1 mmol) and aliquat 336 (1 mmol) was added to copoly(styrene-DVB)-g-polyacrylic acid (2.0 g). To the stirred mixture hydrogen peroxide (20 ml) was added in instalments. After 8h of stirring, the resin was filtered out, washed with excess of water, water-DMF (1:1), DMF and CH₂Cl₂. Finally, the resin
was dried under suction. The activity of the resin was determined by potassium trithiocarbonate titration and was found to be 2.0 mE g\(^{-1}\). The resin was stored in a refrigerator for further use.

B. **Preparation of copoly(styrene-DVB)-persulfonic acid, Reagent II**:  

Polymeric sulfonic acid, cation exchange resin AG 50W-X8 (Bio-Rad), \(\text{P}-\text{SO}_3\text{H}\), was first cleaned and regenerated according to the following procedure:

The polymer (50 ml by volume) was taken in a glass column. 2N sodium hydroxide was run through the column until the eluent became alkaline. The column was then washed with distilled water until the eluent became neutral. 2N HCl was then run through the column until the eluent became acidic after which the column was washed with distilled water. The cleaned resin so obtained was used for the preparation of the title compound as follows:

(a) II\(^a\): To \(\text{P}-\text{SO}_3\text{H}\) (10 ml, wet volume) was added 50 ml of hydrogen peroxide in instalments with continuous stirring on a magnetic stirrer. The stirring was continued for 4h at 10\(^\circ\), after which the resin was filtered and washed thoroughly with distilled water until the washings were free of hydrogen peroxide (test with KI solution). The resin II thus obtained
was suction dried at room temperature and stored in a refrigerator. The resin was dried within the folds of filter paper immediately before use. The activity of the resin was determined by potassium trithiocarbonate titrations and was found to be 1.0 mE per ml.

(b) II\textsuperscript{b}: Potassium persulfate (0.02 mol; 5.4 g) dissolved in 20 ml of water was added to \( \text{P} - \text{SO}_3^\text{H} \) (10 ml, wet volume) in instalments with continuous stirring at 10°. After 4h the resin was washed thoroughly with distilled water until the washings were free of persulfate ions (test with KI solution). The resin II\textsuperscript{b} so obtained was suction dried and stored in a refrigerator. The activity of the resin was found to be in the same range (\(~\) 1.0 mE per ml.) as from the experiment under a, with the difference that slight discoloration of the product had taken place in this procedure.

C. Preparation of a water-compatible per-acidic reagent, copoly(permethacrylic acid -glycol diacrylate) Reagent III:

To the stirred solution of copoly(methacrylic acid-glycol diacrylate) 2.0 g, in methanesulfonic acid (15 ml) was added hydrogen peroxide (20 ml) in instalments. The stirring was continued for 8h, the resin was filtered off and washed with excess of water and suction dried. Its activity was determined by titration with potassium trithiocarbonate and
was found to be \(2.0 \text{ mE g}^{-1}\).

Potassium trithiocarbonate estimation of the peracid resins:

The activity of the resins I, II (from experiments a and b), and III were determined by the following procedure:

Water (25 ml) and potassium trithiocarbonate solution (6 ml) were added to the resin (wet weight 0.1 g) while stirring for 30 min. The excess of potassium trithiocarbonate was titrated against iodine solution using starch as an indicator.

The resin III which is hydrophobic in nature was estimated in a biphasic system using dichloromethane and water. Potassium trithiocarbonate was transferred to the organic phase for liberating the percarboxylic groups using a PTC.

The resin (100 mg) was taken in 10 ml of dichloromethane. To this was added 10 ml of water and BTEAC (100 mg). The mixture was stirred and excess of pot. trithiocarbonate solution was added. This solution was stirred for additional time to ensure complete transfer of \(K_2CS_3\) into organic layer and was then titrated with a standard iodine solution.

Effect of storage on the activity of \(\text{P} - \text{SO}_4\text{H}\):

Activity of a freshly prepared \(\text{P} - \text{SO}_4\text{H}\) was estimated by potassium trithiocarbonate titrations in terms of meq. of
peracidic groups per ml of the resin which was 1 mE per ml. A sample of the resin was stored in a refrigerator and the activity was determined after a week's storage. It was found that the activity remained almost unchanged.

A sample of $\text{P} - \text{SO}_4\text{H}$ was stored at room temp. (.18°C) for a period of 7 days after which it was titrated for the estimation of its peracidic content. It was found that the activity had decreased by about 25%.

Effect of drying on the activity of $\text{P} - \text{SO}_4\text{H}$:

In a conical flask 2.5 ml by volume of the $\text{P} - \text{SO}_4\text{H}$ resin II was taken. In another flask 2.5 ml by volume of the same resin II was lyophilized. In the third flask the same volume of wet resin II was dried under vacuum over $\text{P}_2\text{O}_5$ in a desiccator. Then the volume of the resin was made to 25 ml in each flask by adding distilled water and the peracidic content of the resins were estimated volumetrically by pot. thithiocarbonate titrations. The resin which was not dried had a peracid content of 1. mE per ml. The lyophilized resin had a peracid content of 0.7 mE per ml while the vacuum dried resin had the peracid content of 0.5 mE per ml only.

D. Preparation of polymeric Reagent IV $\text{P} - \text{CH} - \text{CH}_2 - \text{CH} - \text{CH}_2 - \text{SH} - \text{SH}$

The preparation of this reagent consisted of the following
different steps.

(a) **Preparation of copoly(styrene-DVB)-g-poly(vinyl acetate) (IVa)**:

Grafting of polyvinylacetate onto copoly(styrene-DVB) was done by both the methods, mutual irradiation of copoly (styrene-DVB) and vinyl acetate and pre-irradiation of copoly(styrene-DVB) followed by heating with vinyl acetate, in the same manner as described on page 41. The yield of the grafted product in each case was 100%.

(b) **Preparation of copoly(styrene-DVB)-g-poly(vinyl alcohol) (IVb)**:

Grafted polymer IVa taken in dioxane (20 ml) was hydrolysed with KOH dissolved in minimum quantity of water, by heating on a water bath for 5h. The resin was filtered and washed with water until the filtrate became neutral and then with water-dioxane (50:50), dioxane, DMF and CH₂Cl₂. Alkaline treatment was repeated twice after which the polymer was dried under vacuum.

(c) **Preparation of copoly(styrene-DVB)-g-poly(vinyl tosylate) (IVc)**:

\[
\text{P - CH - CH}_2 - \text{CH - CH}_2 - \text{OTs OTs}
\]

The resin (IVb) was taken in dry dioxane (10 ml). To
this was added pyridine (2 ml) and p-toluenesulfonyl chloride (0.83 g) and the reaction mixture was stirred for 72h at 40°. After cooling, the resin was filtered. The heating of the resin with pyridine and p-tolune sulfonyl chloride in dioxane was repeated twice. The polymer derivative was filtered, washed with dioxane, dioxane : water (1:1, 25 ml), water, water : ethanol (1:1, 25 ml) and ethanol.

(d) Preparation of copoly(styrene-DVB)-g-poly(vinyl xanthate) ester (IV^d) P - CH - CH₂ - CH - CH₂ -  
\[ \text{SCSOC}_2\text{H}_5 \quad \text{SCSOC}_2\text{H}_5 \]

Polymer IV^c was taken in DMF (10 ml) in a round bottom flask. To this was added ethyl xanthate (1 g) and the reaction mixture was stirred for 12 h under nitrogen. The resin was filtered and the reaction was repeated twice at the end of which it was filtered, washed with DMF, DMF - H₂O, H₂O (in this order), and dried.

(e) Preparation of copoly(styrene-DVB)-g-poly(vinyl mercaptan),

Reagent IV : P - CH - CH₂ - CH - CH₂ - CH -  
\[ \text{SH} \quad \text{SH} \quad \text{SH} \]

Polymer IV^d was taken in dioxane (10 ml) in a round bottom flask. To this was added concentrated solution of sodium hydroxide (0.1 N, 10 ml), at 75-80°C for 5 min under nitrogen. The mixture was agitated for 10 min at 50°C and
cooled. After neutralizing with 1 N HCl, ethanol was added and the product was removed by filtration, washed with ethanol, filtered, washed with hexane and vacuum dried at 50°C.

(f) **Estimation of -SH group**;

The thiolated polymer (IV, 20 mg) was treated with a solution of sodium borohydride in dioxane under nitrogen. It was then suspended in DMF (5 ml) and a solution of Ellman's reagent (2 ml) containing 40 mg of 5,5-dithiobis(2-nitrobenzoic acid) in 10 ml of 0.1 M sodium phosphate buffer, was added. Yellow colour was produced within one minute. The mixture was stirred under nitrogen for 30 minutes, centrifuged and the supernatant was read at 420 nm against a blank which was prepared exactly as above but in which the thiolated polymer was replaced by copoly(styrene-DVB). The activity of the resin in terms of thiol groups was 1.5 μE g⁻¹.

**Preparation of copoly(styrene-DVB)-g-poly(N-hydroxyglutarimide), Reagent V**;

Reagent V was prepared by the following two step process.

**Preparation of copoly(styrene-DVB)-g-polyacrylic acid**;

The polymer was prepared by the method given on page 42.
Preparation of copoly(styrene-DVB)-g-poly(glutaric anhydride):  

Copoly(styrene-DVB)-g-polyacrylic acid (2 g) was taken in dioxane (15 ml) and acetic anhydride (10 ml) was added to it. The mixture was heated on a water bath for 5h. At the end, the polymer was separated, washed with acetic acid followed by dioxane.

The reaction between polymer and acetic anhydride was repeated and the polymer washed with dioxane and dried.

Preparation of copoly(styrene-DVB)-g-poly(N-hydroxyglutarimide):  

Copoly(styrene-DVB)-g-poly(glutaric anhydride) 2 g was taken in DMF (20 ml). Hydroxylamine hydrochloride (1.5 g) was added to this and the reaction mixture was refluxed for 4h. At the end of the reaction the resin was filtered off, washed with water, water-DMF (1:1), DMF, dichloromethane and was suction dried.

Treatment with hydroxylamine HCl was repeated under the same conditions.
DISCUSSION

The first polymer-supported reagent of this class of peroxo acids poly(permethacrylic acid) was prepared on treatment of poly(methacrylic acid) with hydrogen peroxide in presence of methanesulfonic acid. The activity of the resin was 3.5 mmol per g. Later, polymer-supported peroxyacid resin was prepared by treating copoly(styrene-divinylbenzene) having carboxyl groups with 85% hydrogen peroxide in methanesulfonic acid at 25°C.

It was shown in each preparation that the conversion of carboxylated polymeric resin to its peracid is acid-catalyzed. (Strong acids like sulfuric acid or organic sulfonic acids were used). It was also suggested that sulfuric acid or its derivatives are first oxidized to their 'per-acids' by reaction with hydrogen peroxide. The 'per-acid' subsequently transforms the carboxyl group to percarboxylic group. This suggestion prompted us to synthesize a polymer-supported peroxy sulfonic acid reagent, copoly(styrene-DVB)-persulfonic acid. The resin was prepared by treating commercially available copoly(styrene-DVB)-sulfonic acid (AG 50W-X8, Bio-Rad) with 30% hydrogen peroxide. The polymer was stirred with H₂O₂ at room temperature (15°C) for 5h, followed by thorough washing with water. The activity of the resin as determined by potassium trithiocarbonate titration was found to be 1 mE per ml. indicating that 75%
of the sulfonic acid groups have been converted into persulfonic acid group. Further, it was seen that resin can be stored in the refrigerator for a month without any significant loss in its activity. The resin lost 50% of its activity on drying under vacuum over \( \text{P}_2\text{O}_5 \) and 30% after hyophilization. The persulfonated resin was also prepared by stirring the sulfonic acid resin with a solution of potassium persulfate. The resin prepared by using potassium persulfate was similar to that prepared by hydrogen peroxide method except that a slight discoloration of the polymer had taken place.

Carboxylic groups were introduced into the commercially available copoly(styrene-divinylbenzene) in two steps. Grafting of poly(ethyl acrylate) on the polymer was done by \( \gamma \)-ray induced copolymerization in 100% yield. The copolymer was then subjected to base-catalyzed hydrolysis. The resin was stirred with 30% hydrogen peroxide in presence of sulfuric acid. The oxidation could also be carried out in a two-phase system (water-methylene chloride) using Aliquat-336 as a phase-transfer catalyst. The resin prepared by the two-phase procedure had a higher activity.

A cross-linked polymer 'hydrogel' which was gifted to us by Dr. A. Jayakrishnan, of the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, was essentially copoly(methacrylic acid-glycol diacrylate).
This resin swells tremendously in water and is obtainable in beaded form. By treating these beads with hydrogen peroxide and methanesulfonic acid the resin was converted into the 'peroxy' form. Estimation showed that the activity of the resin was 2.0 mE per g.
REFERENCES


b) BRD, Appl. 2147739 (1973); Chem. Abs., 78, 158900 p (1973).

b) See Ref. 55a.


