III. BECKMANN REARRANGEMENT IN POLYMER MATRICES

The polymeric backbone of the functionalized polymer has been found to induce specific effects, often termed the 'polymer effect', which are unique and characteristic of the solid or gel-phase system. The macromolecular structural features of the polymeric support material have also been proved to contribute significantly to the reactivity of the functional groups.

The course, rate and stereospecificity of molecular rearrangements are influenced by a number of factors characteristic of the rearranging substrate and its environment. The incorporation of the rearranging molecular system in a polymer support provides a unique microenvironment for the rearranging functional groups. The polymer support material can significantly influence the mechanistic and kinetic behaviour of the functional groups by virtue of its characteristic chemical and steric structure.

Since its discovery in the 1880s, the Beckmann rearrangement of a ketoxime to form an amide, or in cyclic system to form a lactam, has been extensively studied. The process has been utilized in the synthesis and proof of structure of numerous organic compounds. A large number of reagents, both acidic and basic have been reported as suitable for the reaction. The reaction is now recognized as the prototype of a class of rearrangements involving migration to an electron-deficient nitrogen. It has been the subject of numerous kinetic and mechanistic studies including applications of tracer
techniques using the oxygen isotope $^{18}\text{O}$. Considering the familiarity of and the extent of investigations that have been carried out on the Beckmann rearrangement, it was thought of interest to study the effects of possible macromolecular features on this rearrangement when carried out in a polymeric environment or on a polymer support.

This chapter deals with the investigation of the Beckmann rearrangement undergone by polymer-bound ketoximes. The preparation of polymeric analogues of benzophenone oximes from the corresponding ketone polymers and the preparation of polymeric benzyl phenyl ketoximes via a new route involving a Grignard reaction, are treated in detail. The investigation is centred mainly on the Beckmann rearrangement undergone by the above two types of polymeric oximes when subjected to rearrangement conditions.

The time course and rate of the rearrangement were traced using a new chemical method of analysis. This was followed by the study of the effect of the nature of the polymer backbone, crosslink density and other structural parameters of the polymer matrix on the rate of rearrangement. Finally the effect of the solvent was investigated in detail. The molecular character and the degree of the crosslinking of the polymer and compatibility with the solvent used were some of the factors which merited a thorough investigation in these cases. The migratory aptitude under different reaction conditions was studied to assess the extent of the 'polymer effect' on the rearrangement reaction.
RESULTS AND DISCUSSION

The role of the polymer matrix is to serve as a support for immobilizing the rearranging systems and to provide a particular hydrophobic or hydrophilic environment for the functional groups attached to it. The physical and chemical participation of the polymer matrix in the rearrangement reaction would be related to the 'polymeric effect' which in turn has its origin in the molecular character of the monomers. Important properties such as the polarity and hydrophilic-hydrophobic balance are related to the molecular properties of the monomers. Therefore, a proper choice of different monomers can produce polymer supports with varying physicochemical properties. Thus structurally different polymer supports can impart different microenvironmental effects on the rearranging functional groups. In order to study the effect of the nature of the polymeric backbone on the rearrangement reaction, two different polymeric support systems with differing polarity and hydrophobic/hydrophilic effect were chosen: (1) Divinylbenzene (DVB)-crosslinked polystyrene and (2) Tetraethyleneglycol diacrylate (TTEGDA)-crosslinked polystyrene.

III.1 Polymer synthesis

Suspension polymerization has been proved to be the most useful technique for synthesising crosslinked polymeric supports, principally because of the extremely convenient physical form of the beaded product which lends itself to further conversions.121-123
III.1.1 Divinylbenzene (DVB)-crosslinked polystyrene

Styrene-DVB polymers (1A) of different crosslink densities were prepared using suspension polymerization technique. The stabiliser was first removed from styrene and commercial divinylbenzene (~ 55 per cent w/w divinylbenzene in ethylstyrenes) by washing samples with an excess of 1 per cent aqueous sodium hydroxide and twice with water. The monomers in the required ratio were dissolved in toluene and it was suspended in a solution of polyvinylalcohol (molecular weight ~ 72,000) in water. Benzoyl peroxide was added to initiate the free radical polymerization. Since the size of the polymer beads formed depend on the extent of dispersion of the monomers in solution, the rate of stirring and the temperature, these factors were carefully controlled. When the polymerization is over, tough, insoluble and almost spherical crosslinked beads of the polymer precipitates out. Since DVB is a rigid and non-polar crosslinking agent, the polymer produced by the copolymerization of styrene and DVB is hard, rigid and hydrophobic (Scheme III.1).

\[
\begin{align*}
\text{CH} &= \text{CH}_2 \\
\text{CH} &= \text{CH}_2 \\
\text{CH}_2 &= \text{CH} \\
\text{CH}_2 &= \text{CH} \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2
\end{align*}
\]

\[
\begin{align*}
\text{CH} &= \text{CH}_2 \\
\text{CH} &= \text{CH}_2 \\
\text{CH}_2 &= \text{CH} \\
\text{CH}_2 &= \text{CH} \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2
\end{align*}
\]

\[
\begin{align*}
\text{CH}_2 &= \text{CH}_2 \\
\text{CH} &= \text{CH}_2 \\
\text{CH}_2 &= \text{CH} \\
\text{CH}_2 &= \text{CH} \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2 \\
\text{CH} &= \text{CH}\text{CH}_2 \\
\text{CH}_2 &= \text{CH}\text{CH}_2
\end{align*}
\]

Scheme III.1. Preparation of DVB-crosslinked polystyrene 1A.
By using appropriate mole per cent of the monomer (styrene) and crosslinking agent (divinylbenzene), polymers with 2, 5, 10 and 15 per cent crosslink densities were prepared. These "crosslink density" percentages are not absolute; the figures indicate only the relative amount of the crosslinking agent in the polymerization mixture. It is not easy to exactly determine the amount of built-in crosslinking agent in the crosslinked polymers. As mentioned earlier, commercial DVB contains only about 55% w/w polymerizable divinylbenzene and the remainder is mainly 3- and 4-ethylvinylbenzenes. This factor was taken into account in the calculation of the weight of DVB required for the preparation of polymers with different crosslink densities.

The polymer samples obtained by the suspension polymerization were washed thoroughly with water and then subjected to Soxhlet extraction overnight using acetone as the solvent. Finally they were dried at 70°C in an air oven to produce a virtually quantitative yield of dry beads. The beads were weighed, and the IR spectrum was recorded using KBr pellets. The spectrum was compared with that of an authentic sample. The yields of the polymers obtained are given in Table III.1.

**Table III.1. Preparation of DVB-crosslinked polystyrene (1A).**

<table>
<thead>
<tr>
<th>DVB crosslink density (mole %)</th>
<th>Weight of the monomers (g)</th>
<th>Yield (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Styrene</td>
<td>DVB</td>
</tr>
<tr>
<td>2</td>
<td>10.21</td>
<td>0.47</td>
</tr>
<tr>
<td>5</td>
<td>9.89</td>
<td>1.18</td>
</tr>
<tr>
<td>10</td>
<td>9.37</td>
<td>2.37</td>
</tr>
<tr>
<td>15</td>
<td>8.85</td>
<td>3.55</td>
</tr>
</tbody>
</table>
III.1.2. Tetraethyleneglycol diacrylate (TTEGDA)-crosslinked polystyrene

In principle, the reactivity of a functional group should not be altered when it is attached to a polymeric backbone. However, the microenvironment created within the polymer matrix can create special effects and change the reactivity of the active site. In this case, to study the effect of the nature of the polymeric backbone on the reactivity, a polar polymeric support with TTEGDA as the crosslinking agent, reported earlier, was employed. The styrene-TTEGDA copolymer (1B) would provide a local environment different from that of the styrene-DVB copolymer, to the functional groups attached to it. Thus it facilitates a comparison of the effect of the molecular character of the two supports on the extent and rate of reactions of attached functional moieties. The styrene-TTEGDA copolymer system has a flexible network due to the extended length of the crosslinks.

Polystyrene samples with 2, 5, 10 and 15 mole per cent of TTEGDA were prepared by aqueous suspension polymerization of monomers and benzene as diluent at 80°C using benzoyl peroxide as initiator (Scheme 111.2).

High molecular weight (MW ~ 72,00) polyvinylalcohol (PVA) was used as the suspension stabiliser. Beads of convenient shape and size could be obtained under these conditions. The polymer beads were obtained in high yields and with particle size ranging from 100-500 mesh. They were freed from all low molecular weight and linear polymeric impurities by Soxhlet extraction and characterized by IR spectral analysis. They showed good mechanical properties and were obtained in easily filterable form. The results are given in Table III.2.
Scheme III.2. Preparation of TTEGDA-crosslinked polystyrene 1B.
Table III.2. Preparation of PS-TTEGDA (1B).

<table>
<thead>
<tr>
<th>TTEGDA crosslink density (mole %)</th>
<th>Weight of the monomers (g)</th>
<th>Yield (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Styrene</td>
<td>TTEGDA</td>
</tr>
<tr>
<td>2</td>
<td>10.21</td>
<td>0.60</td>
</tr>
<tr>
<td>5</td>
<td>9.89</td>
<td>1.51</td>
</tr>
<tr>
<td>10</td>
<td>9.37</td>
<td>3.02</td>
</tr>
<tr>
<td>15</td>
<td>8.85</td>
<td>4.53</td>
</tr>
</tbody>
</table>

III.2 Functionalization of polystyrene

Functionalization of polymers involves copolymerization of substituted monomers directly or functionalizing the preformed polymer by polymer-analogous reactions. Introduction of functional groups into styrene polymer by copolymerization of suitably substituted styrene monomers gives polymers of more uniform functionalization. In addition, they are not contaminated by a small proportion of other functional groups remaining from incomplete prior chemical transformation. However, in the case of functionalization of the preformed polymer the functional group will be more accessible to reactants for further chemical modification. In the present work, the second route for functionalization i.e., functionalizing the preformed polymer by polymer-analogous reactions, has been employed.
III.3 Chloromethylation of the polystyrene

There are two standard methods for chloromethylation of crosslinked polystyrene resins.125-127 A mixture of formaldehyde and gaseous hydrochloric acid in presence of Lewis acid catalyst (H₂SO₄, ZnCl₂) has been reported to effect the chloromethylation reaction. The second method utilizes chloromethylmethylether or dichloromethylmethylether in the presence of a catalyst such as AlCl₃, ZnCl₂ or SnCl₄. The advantage of this method is that chloromethylmethylether is a good swelling agent for the copolymer. The main disadvantage is the introduction of additional crosslinks in the polymer matrix.

It is therefore important to establish the optimum conditions for the chloromethylation reaction taking into account the various physicochemical characteristics of the polymer matrix. The ability of the macromolecular matrix to allow penetration of the reagent into it and the byproducts to escape out of the reaction sites is one of the factors necessary for achieving optimum conditions.128 When a sufficiently good swelling agent is used, the crosslinked network becomes extremely distended and gives a gel having low mechanical resistance making the reagent easily reach practically all the available reactive sites.

For comparatively smaller degrees of conversion, IR spectral studies show that more than 90% of chloromethylation takes place at the para-position and less than 10% at the ortho-positions.129,130 According to Greig and Sherrington, only the aromatic sites which do not belong to the crosslinked unit can be chloromethylated.131 Manatt and coworkers showed that the crosslinked and chloromethylated styrene-DVB copolymer, swollen by CDCl₃ can give 13C-NMR
spectra amenable to interpretation; 99% of the chloromethylation occurs at the 
para position.\textsuperscript{132}

The styrene-based copolymers (1A and 1B) were functionalized by 
electrophilic substitution of the aromatic ring. Chloromethylation of the styrene 
ring was carried out using chloromethylmethylether in the presence of Lewis acid 
and CH$_2$Cl$_2$ as the solvent.\textsuperscript{128,133} Chloromethylmethylether was conveniently 
prepared in good purity by passing dry HCl gas through methanol-formaldehyde 
mixture.\textsuperscript{134}

Even though anhydrous AlCl$_3$ can be used as an effective Friedel-Crafts 
catalyst, it incorporates into the polymer as a complex and cannot be washed 
away completely with common solvents. The product resin is darkly coloured and 
is of high chlorine capacity. Anhydrous SnCl$_4$ is found to be a better catalyst in 
chloromethylation reaction at low temperature (Scheme III.3).

\[
P - \bigcirc + \text{ClCH}_2\text{OCH}_3 \xrightarrow{\text{SnCl}_4, \text{CH}_2\text{Cl}_2} P - \bigcirc - \text{CH}_2\text{Cl}
\]

1A or 1B \hspace{2cm} 4A or 4B

\textbf{Scheme III.3.} Chloromethylation of the polystyrene resins.

The chloromethylated resins (4A and 4B) were purified by repeated 
washing and by Soxhlet extraction using suitable solvents. The degree of 
chloromethylation was determined from the chlorine content obtained by the 
Volhard's method.\textsuperscript{65} In this method of chlorine estimation, the resin was 
equilibrated with pyridine and the pyridinium chloride thus formed was treated
with silver nitrate solution in excess. AgCl was precipitated and the excess AgNO₃ was titrated with ammonium thiocyanate using ferric alum as the indicator. The results obtained are presented in Table III.3.

Table III.3. Chlorine capacity of PS-DVB and PS-TTEGDA resins.

<table>
<thead>
<tr>
<th>DVB crosslink density (mole %)</th>
<th>Chlorine capacity (mmol Cl/g)</th>
<th>TTEGDA crosslink density (mole %)</th>
<th>Chlorine capacity (mmol Cl/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>4.23</td>
<td>2</td>
<td>4.72</td>
</tr>
<tr>
<td>5</td>
<td>3.91</td>
<td>5</td>
<td>4.48</td>
</tr>
<tr>
<td>10</td>
<td>3.64</td>
<td>10</td>
<td>4.16</td>
</tr>
<tr>
<td>15</td>
<td>3.22</td>
<td>15</td>
<td>3.75</td>
</tr>
</tbody>
</table>

III.4 Preparation of crosslinked polystyrene-bound oximes

A series of polymer-bound ketoximes have been prepared for investigating the Beckmann rearrangement reaction.

III.4.1 Preparation of polymeric benzophenone oximes via Friedel-Crafts acylation reaction

The polymeric benzophenone oxime 3a has been described earlier by Ontjes et al.135 and Pietta et al.136 as an intermediate in the preparation of the benzhydrylamine polymer support used in peptide synthesis. Oxime polymers 3b, 3c, 3d have been prepared by Kaiser and co-workers using similar procedures,
who employed the polymer-bound oxime esters as supports for solid-phase peptide synthesis.137,138

In the present work, oxime polymers 3a-3d have been prepared by similar experimental methods. As illustrated in Scheme III.4, oxime polymers 3a-3d were synthesised via the ketone polymers 2a,135,136,139 2b,139 2c139 and 2d,137 which in turn were obtained by Friedel-Crafts acylation of crosslinked polystyrene, using the appropriate acid chloride.

\[
\begin{align*}
\text{P} & \quad \text{P} - \text{XC}_6\text{H}_4\text{COCl} \\
\text{SnCl}_4 & \rightarrow \\
\text{P} & \quad \text{P} - \text{XC}_6\text{H}_4\text{COCl} \\
\text{NH}_2\text{OH.HCl} & \rightarrow \\
\text{pyridine} & \\
\text{NH}_2\text{OH.HCl} & \rightarrow \\
\text{pyridine} & \\
\end{align*}
\]

\[
\begin{align*}
\text{P} = \text{Polystyrene}; \ a, \ X=\text{H}; \ b, \ X=\text{OMe}; \ c, \ X=\text{Cl}; \ d, \ X=\text{NO}_2
\end{align*}
\]

Scheme III.4. Preparation of polymeric benzophenone oximes.

The resulting benzophenone polymers 2a-2d had strong carbonyl absorbances in their IR spectra between 1655 and 1665 cm\(^{-1}\), depending on the
nature of the substituent X. The benzophenone polymers obtained from the acylation reaction were quantitatively converted into corresponding oximes by reaction with hydroxylamine hydrochloride and pyridine in refluxing ethanol. The IR spectra of the oxime resins 3a-3d showed no carbonyl absorption and had strong absorption at 3500 cm$^{-1}$ (O-H str.). The capacities of the oxime resins were determined using N analysis and the acetylation method (Table III.4).

**Table III.4.** Capacity of the polymeric oximes 3a-3d.

<table>
<thead>
<tr>
<th>Oxime</th>
<th>Capacity (mmol N-OH/g)</th>
<th>Oxime</th>
<th>Capacity (mmol N-OH/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>1.20</td>
<td>3a</td>
<td>1.32</td>
</tr>
<tr>
<td>3b</td>
<td>1.15</td>
<td>3b</td>
<td>1.24</td>
</tr>
<tr>
<td>3c</td>
<td>1.08</td>
<td>3c</td>
<td>1.16</td>
</tr>
<tr>
<td>3d</td>
<td>0.91</td>
<td>3d</td>
<td>1.04</td>
</tr>
</tbody>
</table>

**III.4.2 Preparation of polymeric benzyl phenyl ketoximes via Grignard reaction**

Polymeric benzyl phenyl ketoximes were prepared via a new route involving a Grignard reaction with cyanomethyl polystyrene 5 (Scheme III.5).
P = Polystyrene; a, X=H; b, X=Me; c, X=OMe; d, X=Cl; e, X=NMe₂

Scheme III.5. Preparation of polymeric benzyl phenyl ketoximes.

Cyanomethyl polystyrene 5 was prepared from chloromethyl polystyrene 4 using KCN/DMF following literature procedures. The oxime polymers 7a-7e were synthesised via the ketone polymers 6a-6e which in turn were obtained by the Grignard reaction of cyanomethyl polystyrene 5 with the appropriate Grignard reagent.
The polymeric benzyl phenyl ketones 6a-6e had strong absorbance in their IR spectra between 1680 and 1700 cm\(^{-1}\) depending on the nature of the substituent X. They were converted into the corresponding oximes by reaction with hydroxylamine hydrochloride and sodium hydroxide in refluxing ethanol-DMF solvent mixture. The IR spectra of the oxime resins 7a-7e showed no carbonyl absorption and had strong absorption at 1660 cm\(^{-1}\) (C = N str.) and at 3450 cm\(^{-1}\) (O-H str.). By analogous procedures, the polymer-bound oximes 7f and 7g were also prepared using the appropriate Grignard reagents.

![Chemical Structures](image)

The capacities of the oxime resins were determined by using N analysis and by using the acetylation method. The capacities varied from 1.53 mmol N-OH/g to 1.92 mmol N-OH/g (Table III.5).

**Table III.5. Capacity of the polymeric oximes (7a-7f).**

<table>
<thead>
<tr>
<th>Oxime</th>
<th>PS-2% DVB resin Capacity (mmol N-OH/g)</th>
<th>Oxime</th>
<th>PS-2% TTEGDA resin Capacity (mmol N-OH/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>1.75</td>
<td>7a</td>
<td>1.92</td>
</tr>
<tr>
<td>7b</td>
<td>1.64</td>
<td>7b</td>
<td>1.82</td>
</tr>
<tr>
<td>7c</td>
<td>1.66</td>
<td>7c</td>
<td>1.85</td>
</tr>
<tr>
<td>7d</td>
<td>1.62</td>
<td>7d</td>
<td>1.77</td>
</tr>
<tr>
<td>7e</td>
<td>1.58</td>
<td>7e</td>
<td>1.76</td>
</tr>
<tr>
<td>7f</td>
<td>1.73</td>
<td>7f</td>
<td>1.90</td>
</tr>
<tr>
<td>7g</td>
<td>1.56</td>
<td>7g</td>
<td>1.74</td>
</tr>
</tbody>
</table>
In all the above steps of polymer-analogous conversions on the crosslinked macromolecular matrix, a remarkable dependence of the extent of conversion on the nature of the solvent and the extent of swelling was observed. Thus, in the Grignard reaction step, the extent of conversion of the cyano group to the keto group (determined by gravimetric analysis), increased significantly when the cyano resin 5 was allowed to pre-swell in THF-ether solvent mixture rather than in pure ether. In the case of the pre-swollen resin the reaction was more facilitated. These observations point to the role of organic solvents in the swelling of the hydrophobic polystyrene matrix and thereby permitting the soluble reactants to diffuse into the crosslinked macromolecular matrix for effective reaction.143-145

The configurations of the polymer-bound oximes were not determined, but it seemed probable that the oxime with the polymeric group in the anti-hydroxyl position would be formed almost exclusively due to steric reasons. This factor will be later dealt with.

III.5 Beckmann rearrangement of the polystyrene-bound oximes

The polystyrene-bound oximes (3a-3d and 7a-7g) prepared as above were subjected to Beckmann rearrangement conditions using phosphorus pentachloride or thionyl chloride as the reagent. The reaction was followed by determining the hydroxyl (N-OH) capacity of the oxime resin at fixed intervals of time, using the acetylation method. The final rearrangement product obtained showed absorbances near 3430 cm\(^{-1}\) and at 1695 cm\(^{-1}\) in the IR spectra characteristic of amides. This on hydrolysis gave an organic acid in addition to the polymeric product. The latter was tested for amino group using ninhydrin. Its IR spectra showed absorbances near 3400 cm\(^{-1}\) and at 1380 cm\(^{-1}\). The organic
acid was identified and characterised by comparison (mp, IR, NMR and MS) with an authentic sample. The following schemes (Schemes III.6 and III.7) are proposed to suit the above series of reactions, including the rearrangement step and hydrolysis of the product amide to yield the polymeric amine 9 or 12 and the organic acid 10a-10e.146

\[ \text{Scheme III.6. Beckmann rearrangement of the polystyrene-bound oximes 3a-3d and hydrolysis of the rearrangement products 8a-8d.} \]
Scheme III.7. Beckmann rearrangement of the polystyrene-bound oximes 7a-7e and hydrolysis of the rearrangement products 11a-11e.

The results of the above investigations indicated that 85-95% rearrangement is taking place in the case of polymeric analogues of ketoximes when subjected to Beckmann rearrangement conditions. It can also be inferred that the polymeric group 'migrates' even though it forms part of a bulky, high molecular weight crosslinked network system. This can be rationalised as due to the exclusive formation of the oxime with the polymeric group in the anti-hydroxyl position for steric reasons.
The crosslinked polystyrene support system of the above oximes offers the possibility of studying the effects of crosslink density and other structural parameters of the polymer matrix on the rate of the rearrangement. The results of such studies are discussed in sections III.7 to III.10.

III.6 Characterisation of the functionalized polystyrene resins

The adequate characterisation of the polymeric support and the functional group conversions carried out on the support is a major problem associated with polymer-supported chemistry. Crosslinked macromolecular supports are insoluble and methods such as UV and NMR present major problems for providing detailed structural information. The two most powerful techniques of analysis which are readily applicable are elemental analysis and infrared absorption spectroscopy.

IR spectroscopy is the most widely used technique for following the polymer supported reactions. Functional groups attached to polymer do not differ appreciably from those of small molecules and the techniques of taking the spectra of polymeric solids (film, mull or KBr pellet) is well-developed. Infrared spectroscopy has been particularly useful in following the polymeric transformations. The characteristic absorption due to a particular functional group often disappears completely on chemical transformation, with a simultaneous appearance of the characteristic absorption of the new group.
In the present work, DVB-crosslinked polystyrene and TTEGDA-crosslinked polystyrene, and the functional group conversions carried out on them have been characterised using IR spectroscopy. IR spectra were recorded in solid KBr pellets since all the polymers were insoluble.

DVB-crosslinked polystyrene resin 1A showed all the characteristic absorption peaks of polystyrene including the ones at 2850 cm\(^{-1}\), 1603 cm\(^{-1}\) and 906 cm\(^{-1}\), that are usually used to calibrate all spectra of polystyrene (Figure III.1).

![Figure III.1. IR spectrum (KBr) of DVB-crosslinked polystyrene resin 1A.](image)
In chloromethyl DVB-crosslinked polystyrene resin 4A, there are two sharp bands: one at 670 cm\(^{-1}\) corresponding to C-Cl stretching vibration and the other at 1260 cm\(^{-1}\) corresponding to H-C-Cl bending vibration (Figure III.2).

Fig. III.2. IR spectrum (KBr) of chloromethyl DVB-crosslinked polystyrene resin 4A.
TTEGDA-crosslinked polystyrene resin 1B shows an intense peak at 1720 cm$^{-1}$ of ester carbonyl and a band at 1150 cm$^{-1}$ of the ether linkages of the crosslinking agent besides the usual peaks of polystyrene (Figure III.3).
In chloromethyl TTEGDA-crosslinked polystyrene resin 4B, there is a sharp band at 1250 cm$^{-1}$ corresponding to H-C-Cl bending vibration (Figure III.4).

Fig. III.4. IR spectrum (KBr) of chloromethyl TTEGDA-crosslinked polystyrene resin 4B.
The IR spectra of polymeric benzophenone 2a showed a strong absorption peak at 1653 cm\(^{-1}\) corresponding to carbonyl absorption (Figure III.5). The IR spectra of the corresponding oxime 3a showed no carbonyl absorption and had strong absorption at 3500 cm\(^{-1}\) (O-H str.) (Figure III.6).

Fig. III.5. IR spectrum (KBr) of polymeric benzophenone 2a.
The IR spectrum of cyanomethylpolystyrene 5 had a very sharp peak at 2250 cm\(^{-1}\) corresponding to C = N stretching vibration. The polymeric benzyl phenylketone 6a, obtained by the Grignard reaction of cyanomethyl polystyrene with phenyl magnesium bromide, had strong absorbance in the IR spectra at 1690 cm\(^{-1}\) corresponding to C=O stretching vibration. The corresponding polymeric benzyl phenyl ketoxime 7a had strong absorptions at 1660 cm\(^{-1}\) (C=N str.) and at 3450 cm\(^{-1}\) (O-H str.) (Figure III.7).
Fig. III.7. Infrared spectra (KBr) of: cyanomethyl polystyrene 5; polymeric benzyl phenyl ketone 6a; polymeric benzyl phenyl ketoxime 7a.
Fig. III.8. IR spectra (KBr) of: polymeric oxime $\mathbf{\text{P}}$-$\text{C}_6\text{H}_5$-$\text{CH}_2$-$\text{C}(=\text{NOH})$-$\text{C}_6\text{H}_5$ 7a; polymeric amide $\mathbf{\text{B}}$-$\text{C}_6\text{H}_5$-$\text{CH}_2$-$\text{NHCO}$-$\text{C}_6\text{H}_5$ 11a.
IR spectra also provided valuable information regarding the Beckmann rearrangement reaction taking place. The polymeric product of the rearrangement step showed strong absorbances at 1695 cm$^{-1}$ (C=O str.) and near 3430 cm$^{-1}$ (N-H str.), whereas the strong C=N str. vibration band of the oxime at 1660 cm$^{-1}$ had completely disappeared. The disappearance of the C=N band and formation of the C=O stretching vibration band is clearly depicted in the overlay IR spectrum (Figure III.8). This is strong evidence for the Beckmann rearrangement reaction of the polymeric oxime to the corresponding amide.

The polymeric amines 9 and 12 obtained by the hydrolysis of the polymeric amides 8a-8d and 11a-11e respectively were also characterised using IR spectroscopy. The IR spectra showed absorbances near 3400 cm$^{-1}$ (O-H str.) and at 1380 cm$^{-1}$ (N-H str.) characteristic of amines (Figure III.9).

![IR spectrum of the polymeric amine](image)

**Fig. III.9.** IR spectrum (KBr) of the polymeric amine $\text{C}_6\text{H}_5$-$\text{CH}_2$-$\text{NH}_2$ 12.
$^1$H, $^{13}$C and $^{19}$F - NMR spectroscopy have been used in monitoring polymer-supported reactions and in the characterization of the supports.\textsuperscript{148-150} High resolution $^{13}$C-NMR spectroscopy has been employed to study the additional crosslinking in chloromethyl DVB-crosslinked polystyrene resin.\textsuperscript{151,152} Gel-phase $^{13}$C-NMR has also been employed to monitor solid phase peptide synthesis on most commonly used polystyrene-based resins.\textsuperscript{153,154} This technique proved to be useful for characterising polystyrene-based starting supports as well as to determine the degree of functionality and purity. DVB-crosslinked phenyl acrylates have been characterized by solid state $^{13}$C-CP/MAS NMR method.\textsuperscript{155}

DVB-crosslinked polystyrene and TTEGDA-crosslinked polystyrene and the functional group transformation carried out on them have been characterised here by $^{13}$C-CP/MAS (solid-state) NMR spectroscopy. The $^{13}$C-CP/MAS solid state NMR measurements were conducted on a Bruker 300 MSL CP/MAS instrument operating at 75.47 MHz. The spectra were run with fine powder of polymer beads at room temperature and Kel-F rotor was employed for MAS. The samples were rotated with a spectral width of 25000 Hz, the CP time was 22 ms and number of scans was in the range of 200-300. Each sample was rotated with two different spin rates and by comparing the resultant spectra, the spinning side bands were eliminated.

The solid state $^{13}$C-NMR spectra of DVB-crosslinked polystyrene before and after chloromethylation are shown in Figure III.10. Prior to chloromethylation the spectrum shows overlapping resonances for the aliphatic carbon atoms of the polystyrene backbone (45.1-40.4 ppm) and discrete resonances for the protonated (128.1 ppm) and nonprotonated (145.8 ppm)
aromatic carbon atoms of the phenyl residues. After chloromethylation, new resonances appear due to the pendant benzylic carbon atom (46.3 ppm) and the quaternary carbon atom (135.9 ppm) of the aromatic residue which bears the pendant functionality.

**Fig. III.10.** $^{13}$C CP/MAS (solid-state) NMR spectra of:
DVB-crosslinked polystyrene resin 1A;
Chloromethyl DVB-crosslinked polystyrene resin 4A.
Solid state $^{13}$C-CP/MAS NMR spectrum of TTEGDA-crosslinked polystyrene resin (1B) showed an intense peak at 127.89 ppm which corresponds to protonated carbon atoms of the aromatic polystyrene rings and a small peak at 145.65 ppm arising from the non-protonated carbon of the polystyrene ring. The backbone methylene carbon of the polymer appears as a single peak at 40.34 ppm. The methylene carbon of the ether linkage of the crosslinking agent TTEGDA appears as a small peak at 70.65 ppm (Figure III.11).

Fig III.11. $^{13}$C-CP/MAS (solid-state) NMR spectra of TTEGDA-crosslinked polystyrene resin 1B.
Chloromethyl TTEGDA-crosslinked polystyrene resin was also characterized by $^{13}$C-CP/MAS NMR method. Chloromethyl resin 4B gave additional peak at 46.11 ppm due to the methylene carbon atom of the chloromethyl group and a small peak appears in the region 135.56 ppm corresponding to C-6 carbon of the polystyrene ring (Figure III.12).

Fig. III.12. $^{13}$C-CP/MAS (solid-state) NMR spectrum of chloromethyl TTEGDA-crosslinked polystyrene resin 4B.
The solid state $^{13}$C-NMR spectrum of cyanomethyl polystyrene 5, shows resonances due to both aliphatic (43.9, 40 ppm) and aromatic (145.2, 128.1 ppm) and a weak resonance at 119.4 ppm which is assigned to the cyanocarbons (Figure III.13).

$\text{CH}_{2}CN$

\[ \delta \text{ (ppm)} \]

Fig. III.13. $^{13}$C-CP/MAS (solid-state) NMR spectrum of cyanomethyl polystyrene 5.

$^{13}$C-CP/MAS NMR spectroscopy was also used to monitor the formation of ketones from cyanomethylpolystyrene; the conversion of the ketones into the corresponding oximes, and finally Beckmann rearrangement of the oximes into the corresponding amides. A typical set of solid state $^{13}$C-NMR spectra depicting the reaction sequence is given in Figure III.14.
Fig. III.14. $^{13}$C-CP/MAS (solid-state) NMR spectra of:
polystyrene-bound benzyl phenyl ketone 6a;
polystyrene-bound benzyl phenyl ketoxime 7a;
and polystyrene-bound amide 11a.
The $^{13}$C-NMR spectrum of polymeric benzyl phenyl ketone 6a shows two major resonance peaks at 127.6 (aromatic) and 39.93 (backbone methylene) ppm and also sidebands at 144.8, 125.7 (aromatic) and 43 (backbone methine) ppm, due to polymer backbone. In addition it shows a peak at 194.64 ppm which is assigned to the carbon atom of the carbonyl group. In the spectrum of the corresponding ketoxime 7a the peak at 194.64 is absent, but there is a new peak at 154.5 which is assigned to the carbon atom of the oxime group.

The Beckmann rearrangement of the ketoxime 7a into the corresponding amide 11a could also be followed using the $^{13}$C-NMR spectra. The peak at 176.92 ppm in the spectrum of 11a is entirely a new one and was not present in the oxime analogue 7a. This is assigned to the carbonyl carbon of the amide group.

Even though not much investigation has been carried out using $^{13}$C-CP/MAS solid-state NMR technique on crosslinked polymeric supports, there exists much scope for this method in the monitoring of reactions carried out on crosslinked functional polymers.

Elemental analysis of a polymer support gives an idea about the functional group capacity of polymer supports and their conversions. N analysis in the cyanomethyl polystyrene, ketopolystyrene, and oxime polystyrene gave information about the amount of functional group transformation. Volhard’s method was used in the estimation of chlorine in the chloromethyl polystyrenes. Other chemical methods include direct conversion of the functional groups which are freely accessible in solution, to quantify the reaction product. Hydroxyl group (-N-OH) capacity of the oximes was estimated by acetylation method.
Ninhydrin test was used to find out the presence of amino group in polystyrene resins. Acetylation method was used to estimate the amino group capacity in amino resins.

### III.7 Studies on reactivity

In principle, the reactivity of a functional group should not be altered when it is attached to a polymer.\(^{156}\) However special effects may be encountered when a reagent is attracted to a polymer or repelled from it, when the polymer-bound reactive group is activated or inhibited by a neighbouring group or when the local polarity of the polymer domain differs from that of the bulk solvent.\(^{157}\) Past studies have shown that chemically equivalent groups attached to a crosslinked-polymer are not equally reactive.\(^{158}\)

It has now been established that the success of the gel-bound reactions is highly dependent upon the accessibility of the resin bound reaction sites, as the diffusion of the reagents to the resin-bound reaction sites is not rate-limiting. The accessibility depends on the solvent used and the degree of crosslinking.\(^{159}\) Recently, attempts to optimise the structural parameters of macromolecular matrix with a view to design efficient polymer supports for peptide synthesis have been reported from this lab.\(^{160}\)

As mentioned earlier, the crosslinked polystyrene support system of the above oximes offers the possibility of studying the effects of solvent, crosslink density and other structural parameters of the polymer matrix on the rate of the rearrangement.
III.8 Reaction rate studies of the Beckmann rearrangement of polymeric oximes

The rates of the reaction of groups attached to a polymer can be studied with sufficient sensibility if the polymer-bound groups are exposed to react with a large excess of a reagent in the solvent which swells the polymer network and if the progress of the reaction is monitored by estimating the fraction of the polymer-bound reactant which has remained unchanged.161

In the present case, the rate of rearrangement was followed by determining the change in the hydroxyl (N-OH) capacity of the polymeric oximes at appropriate intervals of reaction time, using the acetylation method.162 Hence, the order of reaction and the rate constant were determined in each case. The method is reasonably sensitive and yields approximately first order plots. The experimental results obtained are presented in Table III.6.

From the results it was evident that: (i) the Beckmann rearrangement reaction in polymeric oximes follows approximately a course represented by the formula for a first order reaction, (ii) the rate of the reaction is increased by an increase in temperature, (iii) the rate of the rearrangement is almost the same under identical conditions for the different oximes (7a-7g) provided their polymeric part is the same. This is in keeping with the earlier observation that it is the polymeric part of the oxime that is 'migrating' in these Beckmann rearrangement reactions, (iv) the non-migrating low molecular weight part of the oxime does not exert much influence on the rate of the reaction, (v) the addition of a suitable solvent to the reaction mixture greatly facilitates the reaction.
Table III.6. Results of the reaction rate studies of the Beckmann rearrangement in polystyrene-bound oximes 7a-7g.

<table>
<thead>
<tr>
<th>Oxime resin</th>
<th>Hydroxyl capacity of the oxime (mmol N-OH/g)</th>
<th>Reagent</th>
<th>Temperature (°C)</th>
<th>Reaction time (h)</th>
<th>Hydroxyl capacity of the product (mmol N-OH/g)</th>
<th>% Rearrangement</th>
<th>Mean k (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>1.75</td>
<td>SOCl₂</td>
<td>30</td>
<td>24</td>
<td>0.51</td>
<td>70.8</td>
<td>0.05051</td>
</tr>
<tr>
<td>7a</td>
<td>1.66</td>
<td>SOCl₂</td>
<td>75</td>
<td>14</td>
<td>0.17</td>
<td>89.9</td>
<td>0.1659</td>
</tr>
<tr>
<td>7a</td>
<td>1.62</td>
<td>SOCl₂</td>
<td>75</td>
<td>8</td>
<td>0.23</td>
<td>85.8</td>
<td>0.2530</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C₆H₆</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7f</td>
<td>1.76</td>
<td>SOCl₂</td>
<td>30</td>
<td>24</td>
<td>0.52</td>
<td>70.5</td>
<td>0.0494</td>
</tr>
<tr>
<td>7f</td>
<td>1.73</td>
<td>SOCl₂</td>
<td>75</td>
<td>16</td>
<td>0.15</td>
<td>91.20</td>
<td>0.1557</td>
</tr>
<tr>
<td>7f</td>
<td>1.53</td>
<td>SOCl₂</td>
<td>75</td>
<td>8</td>
<td>0.10</td>
<td>87.6</td>
<td>0.2633</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C₆H₆</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7b</td>
<td>1.64</td>
<td>SOCl₂</td>
<td>75</td>
<td>16</td>
<td>0.13</td>
<td>92.07</td>
<td>0.1538</td>
</tr>
<tr>
<td>7c</td>
<td>1.66</td>
<td>SOCl₂</td>
<td>75</td>
<td>16</td>
<td>0.15</td>
<td>91.27</td>
<td>0.1527</td>
</tr>
<tr>
<td>7d</td>
<td>1.62</td>
<td>SOCl₂</td>
<td>75</td>
<td>16</td>
<td>0.12</td>
<td>92.59</td>
<td>0.1537</td>
</tr>
<tr>
<td>7e</td>
<td>1.56</td>
<td>SOCl₂</td>
<td>75</td>
<td>16</td>
<td>0.14</td>
<td>91.0</td>
<td>0.1513</td>
</tr>
<tr>
<td>7g</td>
<td>1.53</td>
<td>SOCl₂</td>
<td>75</td>
<td>16</td>
<td>0.14</td>
<td>91.1</td>
<td>0.1540</td>
</tr>
</tbody>
</table>
III.9 Effect of the polymer backbone

The macromolecular structural features of the polymeric support materials have been shown to contribute significantly to the reactivity of the functional groups. The specificity of the functional polymeric species is achieved by the unique interaction of the macromolecular support with the functional groups. The polymer support must possess a structure that permits enough diffusion of the substrates into the interior reactive sites. This is related to the swelling pattern of the matrix, effective pore size and pore volume, and to the rigidity or flexibility of the polymer matrix.163-165

In polymer-analogous Beckmann rearrangement, the migration process is initiated by the attack of the reagent on the oxime functionality. The rate and extent of the rearrangement are related to the accessibility of the attacking species, and this in turn is related to the molecular character and rigidity of the polymer matrix. These factors are subjected to investigation here using a series of polymeric oximes.

III.9.1 Effect of the nature of crosslinking

The molecular characteristics of the crosslinking agents, such as its polarity, hydrophobicity/hydrophilicity and rigidity contribute to the macromolecular structural features of the polymer matrix and thus should affect the migratory aptitude of the rearrangeable functions. For a comparative study, two different types of polymer supports were employed. Polystyrene (PS)-DVB resin is a typical hydrophobic polymer with rigid crosslinking units. On the other hand, PS-TTEGDA resin is a hydrophilic and polar polymer support with flexible
crosslinking. The oxime groups attached to both polymers were subjected to identical reaction conditions, and the percentage rearrangement was determined. The results are presented in Table III.7.

**Table III.7. Effect of the nature of the crosslinking on the extent of rearrangement**

<table>
<thead>
<tr>
<th>DVB-crosslinked polystyrene-bound benzophenone oxime</th>
<th>TTEGDA-crosslinked polystyrene-bound benzophenone oxime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Using PC15/solvent at 30°C for 5 h</td>
<td>Using PC15/solvent at 30°C for 5 h</td>
</tr>
<tr>
<td>DVB cross-link density (mole %)</td>
<td>TTEGDA cross-link density (mole %)</td>
</tr>
<tr>
<td>Percentage rearrangement in Cyclohexane Toluene Chloroform Toluene Chloroform THF</td>
<td></td>
</tr>
<tr>
<td>2 90.99 80.12 74.62 2 60.46 71.32 93.24</td>
<td></td>
</tr>
<tr>
<td>5 85.71 75.72 69.14 5 54.24 65.42 85.47</td>
<td></td>
</tr>
<tr>
<td>10 68.91 56.93 50.23 10 50.48 60.92 80.41</td>
<td></td>
</tr>
<tr>
<td>15 58.33 48.13 40.64 15 40.62 52.17 72.56</td>
<td></td>
</tr>
</tbody>
</table>

The results are best explained on the basis of the crosslinking pattern of the two polymer networks. The reactive sites are buried deep in the rigid polymer network in the case of PS-DVB resin and thus their accessibility to the attacking reagent is limited. But the reactive sites are more available to the reagent in the case of PS-TTEGDA resin owing to its less rigid nature. Therefore, the extent of rearrangement was higher in the case of TTEGDA-crosslinked polystyrene-bound oximes than in the case of DVB-crosslinked polystyrene-bound oximes, under identical reaction conditions.
III.9.2. **Effect of the degree of crosslinking**

The microenvironmental effect of the polymeric backbone on the extent of migration of the rearrangeable functional group attached to it is determined by the frequency of the crosslinking units within the matrix. A correlation between the percentage migration and extent of crosslinking was obtained from two different polymer supports with varying crosslink densities.

In order to study the effect of the degree of crosslinking on the extent of rearrangement, DVB-crosslinked polystyrene and TTEGDA-crosslinked polystyrene of different crosslink densities were prepared. They were converted into the oxime polymers by polymer-analogous reactions and subjected to the rearrangement conditions. The reaction was followed by determining the change in the hydroxyl capacity of the oxime, using the acetylation method. The results are given in Tables III.8 and III.9.

**Table III.8.** Effect of crosslink density on the rate and extent of Beckmann rearrangement of DVB-crosslinked polystyrene-bound benzophenone oxime 3a using PCl5/cyclohexane at 30°C for 5 h.

<table>
<thead>
<tr>
<th>DVB crosslink density (mole %)</th>
<th>Hydroxyl capacity of the oxime resin (mmol N-OH/g)</th>
<th>Hydroxyl capacity of the product resin (mmol N-OH/g)</th>
<th>Percentage rearrangement (%)</th>
<th>Mean k (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1.20</td>
<td>0.112</td>
<td>90.70</td>
<td>0.4591</td>
</tr>
<tr>
<td>5</td>
<td>0.98</td>
<td>0.140</td>
<td>85.71</td>
<td>0.3898</td>
</tr>
<tr>
<td>10</td>
<td>0.84</td>
<td>0.224</td>
<td>68.91</td>
<td>0.2758</td>
</tr>
<tr>
<td>15</td>
<td>0.43</td>
<td>0.177</td>
<td>58.33</td>
<td>0.1826</td>
</tr>
</tbody>
</table>
Table III.9. Effect of crosslink density on the rate and extent of Beckmann rearrangement of TTEGDA-crosslinked polystyrene-bound benzophenone oxime 3a using PCl5/THF at 30°C for 5 h.

<table>
<thead>
<tr>
<th>TTEGDA crosslink density (mole %)</th>
<th>Hydroxyl capacity of the oxime resin (mmol N-OH/g)</th>
<th>Hydroxyl capacity of the product resin (mmol N-OH/g)</th>
<th>Percentage rearrangement (%)</th>
<th>Mean k (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1.32</td>
<td>0.114</td>
<td>92.12</td>
<td>0.4894</td>
</tr>
<tr>
<td>5</td>
<td>1.20</td>
<td>0.123</td>
<td>89.75</td>
<td>0.4556</td>
</tr>
<tr>
<td>10</td>
<td>1.12</td>
<td>0.219</td>
<td>80.45</td>
<td>0.3263</td>
</tr>
<tr>
<td>15</td>
<td>0.95</td>
<td>0.365</td>
<td>61.58</td>
<td>0.1912</td>
</tr>
</tbody>
</table>

Ketoxime systems attached to PS-DVB and PS-TTEGDA resins show a regular decrease in the extent of rearrangement with increase in crosslink density. The results can be explained as arising from the increased rigidity of the polymer matrix and hence the poor accessibility of the reagent to the reactive sites, rather than from the steric participation of the polymer matrix in the course of the rearrangement.

The polymer supports used were in the bead form, with mesh size 200-400 and degree of crosslinking 2%, 5%, 10% and 15%. Beads with < 4% crosslinking are best described as gel phases while those with higher incorporation of DVB or TTEGDA, polymerised in the presence of solvents and emulsifiers, are large clusters of small beads with channels or pores. Both swell considerably in typical organic solvents, providing access of solvent-borne reagents to the interior of the beads. The degree of swelling decreases with increased crosslink density.
The reactivity of functional groups attached to a polymeric support is governed by their distribution and accessibility in the polymer matrix. Crosslinked resins are swollen to a considerable extent by good solvents to a pseudo-gel, and thus the attacking low molecular weight species can easily attack the reaction sites. But with increased crosslinking the access of the reactive species to the reaction sites on the highly crosslinked networks are considerably diminished as they are now flanked by a higher frequency of crosslinks, leading to a lesser extent of migration.

III.10 Effect of solvent

The effect of solvent on the extent and rate of Beckmann rearrangement was studied by using ketoxime systems bound to hydrophobic PS-DVB matrix and hydrophilic PS-TTEGDA matrix. A series of solvents with varying polarity were used for these investigations. The reaction was carried out under identical conditions in different solvents and the extent and rate of rearrangement were calculated.

In the case of ketoxime systems attached to PS-DVB matrix, the solvents used were cyclohexane, benzene, toluene, chloroform, dioxan, tetrahydrofuran and dimethylformamide. With an increase in solvent polarity, the rate of rearrangement was found to decrease. The typical case of the influence of solvent on the extent and rate of rearrangement of 2% DVB-crosslinked polystyrene-bound benzyl phenyl ketoxime \( 7a \) using \( \text{PCl}_5 \) as the reagent at 30°C is given in Table III.10 and is depicted in Figure III.15. The rate of rearrangement is enhanced by non-polar solvents like cyclohexane and benzene whereas more polar solvents retard it. The extent and rate of rearrangement could not be studied correctly in highly polar solvents like dimethylformamide.
Table III.10. Effect of solvent on the extent of Beckmann rearrangement of 2% DVB-crosslinked polystyrene-bound benzylphenylketoxime 7a using PCl₅ at 30°C for 5 h.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Hydroxyl capacity of the oxime (mmol N-OH/g)</th>
<th>Hydroxyl capacity of the product resin (mmol N-OH/g)</th>
<th>Percentage rearrangement (%)</th>
<th>Mean k (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexane (2.0)</td>
<td>1.61</td>
<td>0.04</td>
<td>97.52</td>
<td>0.7119</td>
</tr>
<tr>
<td>Benzene (2.3)</td>
<td>1.69</td>
<td>0.12</td>
<td>92.90</td>
<td>0.5038</td>
</tr>
<tr>
<td>Toluene (2.4)</td>
<td>1.63</td>
<td>0.16</td>
<td>90.18</td>
<td>0.4624</td>
</tr>
<tr>
<td>Chloroform (4.8)</td>
<td>1.61</td>
<td>0.36</td>
<td>84.48</td>
<td>0.2456</td>
</tr>
</tbody>
</table>

Fig. III.15. Effect of solvent on the extent of Beckmann rearrangement of 2% DVB-crosslinked polystyrene-bound benzylphenylketoxime 7a using PCl₅ at 30°C for 5 h.
In the case of the ketoxime systems attached to the PS-TTEGDA matrix, the solvents used were dioxan, tetrahydrofuran, toluene and benzene. With an increase in solvent polarity the rate of rearrangement was found to increase. The typical case of the influence of solvent on the extent and rate of rearrangement of 2% TTEGDA- crosslinked polystyrene-bound benzylphenylketoxime 7a using PCl5 as the reagent at 30°C is given in Table III.11. The rate of rearrangement is enhanced by polar solvents like dichloromethane and tetrahydrofuran, whereas non-polar solvents retard it.

Table III.11. Effect of solvent on the extent of Beckmann rearrangement of 2% TTEGDA-crosslinked polystyrene-bound benzylphenylketoxime 7a using PCl5 at 30°C for 5 h.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Hydroxyl capacity of the oxime (mmol N-OH/g)</th>
<th>Hydroxyl capacity of the product resin (mmol N-OH/g)</th>
<th>Percentage rearrangement (%)</th>
<th>Mean k (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dichloromethane (8.9)</td>
<td>1.72</td>
<td>0.083</td>
<td>95.2</td>
<td>0.6062</td>
</tr>
<tr>
<td>Tetrahydrofuran (7.6)</td>
<td>1.73</td>
<td>0.142</td>
<td>91.8</td>
<td>0.4999</td>
</tr>
<tr>
<td>Toluene (2.4)</td>
<td>1.68</td>
<td>0.249</td>
<td>85.2</td>
<td>0.3803</td>
</tr>
<tr>
<td>Benzene (2.3)</td>
<td>1.70</td>
<td>0.258</td>
<td>84.8</td>
<td>0.3769</td>
</tr>
</tbody>
</table>

In the polymer-supported method, the functional groups are anchored or immobilized on the polymer support. These reactive sites are distributed on the surface of the polymer beads or they may be buried in between the crosslinks. Since the functional groups on the resin are not free to move, the surrounding low molecular weight substances must diffuse to the fixed reactive sites in the rigid-gel
structure, essentially by using solvents with good swelling properties. The primary function of the solvent is to affect the degree of swelling of the polymer lattice, which is an important factor in determining the chemical reactivity of immobilized molecules.

Hence favourable interaction between the polymer matrix and the solvent is an essential factor for the effective functional group transformation in polymer matrices. If the polymer and solvent are compatible, the movement of the reagent is facilitated by the good swelling behaviour of the backbone and hence the reaction rate increases. On the other hand, if the polymer and the solvent are incompatible, the reaction rate is retarded.

DVB-crosslinked polystyrene resin undergoes effective swelling in non-polar solvents like cyclohexane and benzene. In a good solvent swollen ketoxime analogue, the functional groups are highly accessible to the attacking low-molecular reagent, and hence the reaction is facilitated. PS-DVB resin does not show an effective swelling in polar solvents like THF and therefore the percentage rearrangement is reduced. PS-TTEGDA resin on the other hand, shows poor swelling property in non-polar hydrocarbon solvents like benzene. However, it undergoes good swelling in polar solvents like CH₂Cl₂ and THF. PS-TTEGDA resin immobilized ketoxime systems therefore undergo higher extents of rearrangement in these solvents.

The polarity of the solvent and that of the polymeric backbone are decisive in directing the extent and rate of the polymer-analogous reactions. The polarity of the polymer backbone is dependent upon the nature and extent of the crosslinking agent. It can be seen that the non-polar solvents like cyclohexane
and benzene have a pronounced positive effect on the reaction rate in the case of hydrophobic DVB-crosslinked polystyrene-bound oximes, while polar solvents like CH₂Cl₂ and THF show the same effect in the case of hydrophilic TTEGDA-crosslinked polystyrene-bound oximes. In other words, when the polarity of the solvent used and the polymer backbone were matching (i.e., the hydrophobic/hydrophilic balance) the rate of the reaction was maximum.

Crosslinked polymers are macroscopically insoluble in almost all the solvents. They can be solvated only to a limited extent. Even this limited solvation depends on the macromolecular characteristics of the polymer backbone. However by absorbing considerable amount of solvent, the crosslinked polymeric network can expand extensively and become extremely porous forming a pseudo-gel,166,167 providing access to the solvent-borne reagent to the interior of the polymer network.

DVB and TTEGDA-crosslinked polystyrenes represent two different types of polymer supports with entirely different macromolecular properties. The compatibility of the polymer matrix with different solvents is different depending on the polarity of the solvent. The migratory aptitude of the rearranging moiety is determined by the characteristics of the solvent which influence the swelling pattern of the matrix. In solvents which do not effectively swell the polymer network, movement of the reagent within the network to the reactive sites is difficult and hence the rate and overall extent of rearrangement are considerably decreased.
The above observations suggest that the rate and extent of rearrangement are largely controlled by the nature and degree of the crosslinking of the polymeric support and also by the reaction medium.

III.11 Comparison of the reaction rates of polymers and their low-molecular-weight analogues

There are no rates of rearrangement of benzophenone oximes in SOCl₂/C₆H₆ or PCl₅/C₆H₆ for comparison, but reaction rates of benzophenone oxime picrylether in C₆H₆ in the temperature range 50-80°C had been reported by Chapman and Howis.¹⁶⁸

<table>
<thead>
<tr>
<th>T (°C)</th>
<th>50</th>
<th>70</th>
<th>75</th>
<th>79</th>
</tr>
</thead>
<tbody>
<tr>
<td>k x 10⁻³ s⁻¹</td>
<td>0.24</td>
<td>3.1</td>
<td>5.7</td>
<td>8.8</td>
</tr>
</tbody>
</table>

Comparison of these set of data with those of their polymeric analogues reveals that the rate of rearrangement of the polymers are slower by factors of 10-80.

It had also been reported¹⁶⁸ that under similar conditions, the rate of the rearrangement increase in the same order as the dielectric constant of the solvent, i.e., the transformation is facilitated by an environment of polar molecules. But here, in the case of the DVB crosslinked polystyrene bound oximes the order is just the reverse.

Differences between the reactivity of polymers and analogous small molecules could be due to energetic interaction between the polymer and the second reagent, effects due to the local medium in the polymer domain and neighbouring group effects.¹⁶⁹
As crosslinked polymers are insoluble in all solvents and as, with the size of the beads used, more than 99% of the reactive groups are within the beads, it is clear that for reactions to take place the low molecular weight reactants must diffuse into the polymer beads. Due to a number of reasons related to the diffusion of the low molecular weight reactant into and out of the polymer beads, polymer supported reactions are often slower than that of their low molecular weight counterparts and longer reaction times may be needed. The same phenomenon is observed in the present case also.

In the case of the low molecular weight analogues, the rate of rearrangement is faster in polar than in non-polar solvents because the rate-determining step in the rearrangement is the ionisation of the intermediate formed between the oxime and the reagent used to effect the rearrangement. But when functional groups are within the dense and highly crosslinked regions of the polymer matrix the role of the reaction solvent is important in making the functional groups readily accessible and thus facilitating the reaction. The position of equilibrium, which in turn determines the reaction rates, depends on many factors such as polarity of the polymer and the polarity of the reaction solvent relative to the polarity of the substrate. The reaction solvent is crucial for this reason also. Thus in the present case of the rearrangement of the hydrophobic DVB-crosslinked polystyrene bound oximes, the rates were higher when non-polar solvents like cyclohexane and benzene were used.

The foregoing investigations indicate that a rearranging molecular system incorporated in a polymer matrix by polymer-analogous reactions, can undergo intramolecular migrations under suitable reaction conditions. The macromolecular properties and morphological characteristics of the polymer backbone are the
decisive factors in controlling the migratory aptitudes. However, the rearrangement can be effected in these macromolecular networks as in the case of the solution-phase low molecular weight analogues. The effects of the molecular level reaction parameters and physical and chemical nature of the polymeric matrix on the extent and rate of the rearrangement reaction can be investigated. A systematic analysis of the results offers a better understanding of the polymer effects and the mechanistic aspects of polymer-supported reactions.