INTRODUCTION AND OBJECTIVES

The chemistry of polymer supports is an area which gained popularity in the late sixties with an impetus originated from the solid phase peptide synthesis (SPPS). The chemistry and technology of reactive functionalised polymers achieved rapid progress in the early eighties. It continues to be an active area of research with its wide range of applications in medicine, agriculture and synthetic organic chemistry. Wider prospects are open in the field due to the possibility of combining the unique structural features of the macromolecular system with the functional features of the attached moiety. The solid phase technique offers a great promise in solving the problems accompanying the conventional chemical reactions and for providing the possibility of automation by carrying out the reaction in flow reactors.

Functional polymers are systems in which the reactive functional groups are attached to a macromolecular backbone. The chemistry and applications of these functionalised polymers depend largely on the characteristics of the specific active functional groups. The most important advantage of these reagents is the insolubility leading to filterability which makes it possible to be recycled for reuse. The general advantage has
been exploited and extensively reviewed. These polymers are used in organic synthesis either as passive or active supports. In passive support the polymer functions as a heterogeneous matrix to which a low molecular weight substrate is attached and is allowed to react with various reagents and finally cleaved from the polymeric support in a modified form. In active supports the reagent or a catalyst attached to the insoluble polymer effects a synthetic or catalytic transformation on a soluble substrate. This group includes polymer bound reagents in which the active site is consumed during the course of the reaction and the polymer bound catalyst in which the active site catalyses numerous chemical transformations.

Polymeric reagents are easily separable from low molecular weight compounds. With crosslinked polymers, simple filtration is usually sufficient. Ultrafiltration and selective precipitation removes the soluble polymers. This feature enables one to use a large excess of either the low molecular weight substrate or the polymeric reagent in order to increase the reaction rate and yield. The soluble reactants and products can be easily cleaned off from a crosslinked polymer. This permits the use of polymeric reagents in either column or batch process and they can be regenerated several times. The attachment to the insoluble macromolecular matrix can also solve the problems of lability, toxicity or odour. In addition, the polymer matrix can be so selected or tailor-made
to provide a specific microenvironment that may induce specificity at the reaction site.\textsuperscript{10}

Polymer-based solid phase synthesis is amenable to many of the synthetic techniques normally associated with the homogeneous analogous allowing its application to be extended beyond traditional areas of peptide and nucleic acid synthesis to the synthesis of more structurally diverse molecules.\textsuperscript{11-14} The solid phase technique has the potential for regeneration and reuse,\textsuperscript{15} which offset their initial expense and for providing the possibility of automation by carrying out the reactions in flow reactors.

Solid phase peptide synthesis involves the attachment of a C-terminal amino acid to a solid support and the addition of subsequent amino acids in stepwise fashion till the desired sequence is completed. A reagent can be applied to cleave the product from the support in the modified form. In solid phase peptide synthesis all the reaction steps are heterogeneous. It is between the soluble reagent in the solution phase and the growing peptide chain in the solid support. The most important advantage of the polymer support is that, it simplifies and accelerates the multistep synthesis because of the possibility of carrying out the reaction in a single vessel. It also avoids large loss that occurs during the isolation and purification of intermediates. The yield can be improved through the
use of excess reactants forcing the individual reaction to completion and decreasing the aggregation of intermediate products.\textsuperscript{16}

When polymers are used as catalyst or organic reagent, the reactivity and selectivity of the supported moiety may be changed by the so-called 'polymer effects' the origin of which may be physical or chemical. Though the crosslinked polymers are insoluble in common organic solvents, polymers with low degree of crosslinking swell extensively exposing the inner reactive groups to the soluble reagents.\textsuperscript{17-18} In contrast to crosslinked polymeric systems, reactions with linear polymers that are soluble in organic solvents are carried out in a homogeneous reaction condition. But here, the separation from the low molecular weight contaminants may be difficult.

An extensive study was done on the variation of structural features of the polymer matrix with the conditions of polymerisation such as monomer-diluent ratio, temperature and stirring speed. The correlation of structure and reactivity in polymer supported solid phase reactions and the development of new flexible hydrophilic support PS-NVP-HDODA for an efficient solid phase peptide synthesis forms the overall thrust of the thesis.

After a brief introduction in Chapter 1 emphasising the objectives of the work presented in the thesis, current trends in polymer supported solid phase reactions are summarised in Chapter 2. Major thrust has been given to the various types of polymer supports used in polymer aided reactions.
The interdependence of morphology and reactivity of the polymeric beads and the factors such as diluent, temperature, crosslinker and concentration affecting the structural features such as porosity and bead size are illustrated in Chapter 3.

Based on the observed factors affecting the reactivity of the polymer bead, a new and flexible polymer bead was prepared by suspension polymerisation method. The development of new flexible hydrophilic support, its characterisation and use in the synthesis of biologically active peptides form the basis of Chapter 4. Chapter 5 gives the summary and outlook of the work presented in this thesis.
REFERENCES


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