CATALYSIS BY POLYMER SUPPORTED DENDRIMERS, THEIR METAL COMPLEXES AND NANOPARTICLE CONJUGATES

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CERTIFICATE

This is to certify that the thesis entitled **"Catalysis by Polymer Supported Dendrimers, their Metal Complexes and Nanoparticle Conjugates"** submitted for the award of the Degree of Doctor of Philosophy of the Cochin University of Science and Technology, is a record of original research work carried out by Mr. Rajesh Krishnan G. under my supervision and guidance in the Department of Applied Chemistry, and further that it has not formed the part of any other thesis previously.

Kochi-22
Date 27-06-2008

Dr. K. Sreekumar
(Supervising Teacher)

DECLARATION

I hereby declare that the thesis entitled **"Catalysis by Polymer Supported Dendrimers, their Metal Complexes and Nanoparticle Conjugates"** submitted for the award of Ph.D. Degree, is based on the original work done by me under the guidance of Dr. K. Sreekumar, Reader, Department of Applied Chemistry, Cochin University of Science and Technology and further that it has not previously formed the basis for the award of any other degree.

Kochi-22

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ITHACA

When you start on your journey to Ithaca
Then pray that the road is long,
Full of adventure, full of knowledge,
Do not fear the Lestrygonians
And the Cyclopes and the angry Poseidon.
You will never meet such as these on your path,
If your thought remain lofty, if a fine
Emotion touches your body and your spirit.
You will never meet the Lestrygonians,
The Cyclopes and the fierce Poseidon,
If you do not carry them with in your soul,
If your soul does not raise them up before you.

Then pray the road is long.
That the summer mornings are many,
That you will enter ports seen for the first time
With such pleasure, with such joy!
Stop at Phoenician markets,
And purchase fine merchandise,
Mother-of pearl and corals, amber and ebony,
And pleasurable perfumes of all kinds,
Buy as many pleasurable perfumes you can:
Visit hosts of Egyptian cities,
To learn and learn from those who have knowledge.
Always keep Ithaca fixed in your mind.
To arrive there is your ultimate goal.
But do not hurry the voyage at all.
It is better to let it last for long years;
And even to anchor at the isle when you are old,
Rich withal that you have gained on the way,
Not expect that Ithaca will offer you riches.

Ithaca has given you the beautiful voyage.

Without her you would never have taken the road.
But she has nothing more to give you.

And if you find her poor, Ithaca has not defrauded you.
With the great wisdom you have gained, with so much experience,
You must surely have understood by then what Ithacas mean.

C. P. Cavafy

PREFACE

Catalysts are used in the manufacture of a vast variety of chemicals and fuels, and as such significantly contribute to our economy and high living standards. Catalysts are used in the production of over 7000 compounds worth over $3 trillion globally. Catalyst-based manufacturing accounts for about 60% of chemicals production and 90% of processes. These figures will likely increase in the future as a result of increasing pressures for the development of environmentally friendly manufacturing processes. The economic benefits of an efficient catalyst are enormous: catalytic processes are less capital intensive, have lower operating costs, produce higher purity products and fewer by-products. In addition, catalysts provide important environmental benefits, such as catalytic converters for automobiles.

Nanoscience is at the forefront of scientific and technological developments of the XXI century. Nanochemistry occupies a place of choice in this discipline and can be regarded as the use of synthetic chemistry to make nanoscale building blocks of different size and shape, composition and surface structure, charge and functionality. These building blocks may form, or can be used to make, even more sophisticated architectures having different properties and particular uses.

Dendrimers, monodisperse nanosized polymeric molecules composed of a large number of perfectly branched monomers that emanate radially from a central core, can be considered as one of the most fascinating molecules arising from this area of research. Dendritic molecules are repeatedly branched species that are characterized by their structure perfection. The latter is based on the evaluation of both symmetry and polydispersity. They are considered as the

fourth major macromolecular architecture after linear, crosslinked and branched polymers. The name comes from the Greek term "δενδρον"/*dendron*, meaning "tree". The ability to easily tune the size, topology, molecular weight and consequently the properties of these nanoobjects has led to their widespread use in a variety of applications from biology to material science, i.e., at the interface of many disciplines. Their unique branched topologies lead to properties that differ frequently from those of linear polymers, thus exciting the interest and curiosity of thousands of researchers worldwide. Dendritic architecture is one of the most pervasive topologies observed in nature at the macro- and micro dimensional length scales. At the nanoscale (molecular level), there are relatively few natural examples of this architecture. Most notable are glycogen and amylopectin, the two proteins used for energy storage in many higher organisms. This also adds curiosity to these molecules as a totally new synthetic molecular architecture that is new to the nanoworld, but has so many potentials.

Among the two areas of research consecrated by dendrimers, the most vital one is catalysis and the other is biotechnology and medicine. Dendrimers are considered to fill the gap between homogeneous catalysts and heterogeneous catalysts and they show many advantages over conventional catalysts. In principle, dendritic catalysts can provide systems that

(1). show the kinetic behavior and thus the activity and selectivity of a conventional homogeneous catalyst. Catalysts supported on heterogeneous systems show diminished activity compared to the homogeneous analogues, which is because of reduced accessibility,

(2). can easily be removed from the reaction mixture by membrane or nanofiltration technique because of their large size compared to the products (an advantage of heterogeneous catalysts),

(3). allow mechanistic studies, because of the monodisperse, uniform character of their catalytic sites and the symmetry of the molecules (an advantage of homogeneous catalysts),

(4). allow fine-tuning of their catalytic centers by precise ligand design (an advantage of homogeneous catalysts),

(5). require relatively low metal loading (an advantage of homogeneous catalysts over heterogeneous catalysts).

The advantages of dendrimer catalysts arise from their unique properties as a result of their peculiar structure. Since dendrimers generally contain three distinguishable parts in their structure, one can distinguish periphery functionalized, core functionalized and focal point functionalized catalytic systems. All these systems show their own activity and selectivity. After the introduction of dendrimer-based catalysts, a new term was coined in dendrimer chemistry and it was 'the dendrimer effect'. The special properties that may result from catalyst incorporation onto these macromolecules can be described as a "dendrimer effect." This term has been generally invoked in the literature to explain phenomena that arise as the generation of dendrimer increases. This may be positive or negative depending on the dendrimer platform, the placement of catalysts, the reaction conditions and the mechanism of reactions.

The biggest stumbling block in the widespread application of dendrimers in catalysis even in the midst of all these advantages is the lengthy and complicated synthetic procedure of dendrimer based catalysts. Any attempt to create a perfect harmony between these advantages and disadvantages is valuable in dendrimer research.

The scope of the present thesis lies in checking the viability of solid phase synthesis of dendrimers on insoluble polymer supports and investigating the possibility of applying these supported dendrimers in heterogeneous catalysis.

Objectives of the present Study

- Solid phase synthesis of poly(amido amine) and poly(propylene imine) dendrimers.
- Evaluation of the organocatalytic properties of polymer supported dendrimers
- Synthesis and characterization of polymer supported dendrimer-metal complexes
- Evaluation of the catalytic properties of polymer supported dendrimer-metal complexes

- Synthesis and characterization of polymer supported dendrimer-metal nanoparticle conjugates
- Evaluation of the catalytic properties of polymer supported dendrimer-metal nanoparticle conjugates.

The thesis is divided into six chapters.

Chapter 1 - Introduction

The first chapter is an introduction to the current scenario of solid phase organic synthesis, polymer supported catalysts and dendrimers in catalysis. The first section of this chapter gives an introduction to solid phase organic synthesis. The history of solid phase organic synthesis is briefly described covering the pioneering work of Merrifield followed by the works of Leznoff, Neckers, Frechet and Ellman due to which solid phase organic synthesis secured the current status. This section is followed by the protocols for the selection of the solid support and a small description of supports used in the present work. The second section deals with polymer supported catalysts. In this part, the present status of polymer supported catalysts is reviewed covering the literature from 1998 to April 2008. Both organocatalysts and metal based catalysts are discussed. The third section deals with dendrimers giving special emphasis on dendrimer based catalysts. In the beginning, a brief description of the history of dendrimers is given followed by a detailed picture of the dendritic structure and general methods of synthesis. This is followed by an elaborate review of dendrimers in catalysis covering the literature from 1991 to April 2008. The literature before this period is also mentioned under special circumstances depending on their importance.

Chapter 2 - Solid Phase Synthesis of Dendrimers

The second chapter discusses the solid phase synthesis of poly(propylene imine) (PPI) and poly(amido amine) (PAMAM) dendrimers. Solid phase synthesis of the dendrimers were carried out on aminomethyl polystyrene, 3-nitro-4-aminomethyl polystyrene (DVB crosslinked) and aminated poly(methyl

methacrylate) (DVB crosslinked) resins. The synthesis of dendrimers began from the primary amino pendant groups on the polymer supports. The primary amino group functioned both as the core of the dendrimer and the linker that connected the support and the dendrimer. The dendrimers were synthesized up to third generation by adopting the divergent approach used in their solution phase synthesis with suitable modification so that they could be successfully transformed to the solid phase. Poly(propylene imine) dendrimers were synthesized by an acetic acid catalyzed double Michael addition of acrylonitrile to the amino groups of the supports followed by reduction of the nitrile groups to amino groups using $LiAlH_4$ in THF. Poly(amido amine) dendrimers were synthesized by double Michael addition of methylacrylate to the amino groups of polymer supports in methanol followed by transamination using large excess of ethylene diamine. The progress of the solid phase synthesis was followed by FTIR spectroscopy, qualitative ninhydrin test, quantitative estimation of amino groups and solid state CP-MAS ^{13}C NMR spectroscopy. After the synthesis, the dendrimers were detached from the polymer supports and analyzed using NMR spectroscopy and MALDI-TOF MS. The spectral data revealed that dendrimers up to third generation were synthesized on the supports without defects. Synthesis of dendrimers above third generation on the solid phase failed. The effect of degree of crosslinking of the supports and spacers on the synthesis was studied.

Chapter 3 - Polymer Supported Dendrimers as Organocatalysts

Since the supported dendrimers described in this thesis are highly basic and the first, second and third generation dendrimers carry two, four and eight primary amino groups on the periphery respectively, it was assumed that they could act as heterogeneous basic organocatalysts. The PAMAM and PPI dendrimers attached to the supports were screened as catalysts in a number of reactions and found that the supported dendrimers were efficient catalysts for Knoevenagel condensation, ring opening of epoxides and Mannich reaction. Two reactions for which the catalysts showed better activity were selected for further study. They are Knoevenagel reaction and desymmetrisation of epoxides.

Knoevenagel condensation between various carbonyl compounds and active methylene compounds were carried out in the presence of the supported dendrimers. Various factors affecting the catalysis like amount of catalysts, solvent, temperature and electronic and steric nature of the substrates were studied in detail. The dendrimer catalysts showed excellent activity. Only one mole percent of catalyst was required to obtain excellent yield with in a short interval of time. About thirty styrene derivatives were prepared and all the reactions proceeded to completion with in a short period of time. The most important aspect of the catalysis by supported dendrimers was that high yields were obtained in polar protic solvents like ethanol and water. All the products were obtained in excellent yield, purity and 100% selectivity. Since no side reactions were observed and the reaction proceeded to complete conversion, no additional purification of the products was required. All products were characterized by PMR, FTIR and melting points. The catalysts were recycled ten times with no loss of activity. The effect of generation of the dendrimer and the nature of the support on catalysis was also studied. It was found that, third generation dendrimers were better catalysts and better results were obtained when lightly crosslinked supports were used.

Ring opening of epoxides with anilines was efficiently catalyzed by supported-dendrimers. Various 2-amino alcohols were synthesized from different epoxides and anilines in the presence of catalytic amount of the supported-dendrimers. The influence of reaction conditions and nature of substrates were studied in detail. The reaction proceeded effectively in polar solvents including water at 50 °C. But polar solvents like water, ethanol etc. may act as a competing nucleophile and so the use of these solvents were avoided and the reaction was carried out in dioxan. Only 1 mol% of the third generation dendrimer was required for completion of the reaction. Lower generation dendrimers showed poor activity as well as third generation dendrimers attached to highly crosslinked resins. The amino alcohols were isolated by column chromatography on silica gel and characterized by various spectral methods.

Chapter 4 - Synthesis and Characterization of Polymer supported Dendrimer Metal Complexes

The polymer supported dendrimers were used as ligands for preparation of polymer-supported dendrimer-metal complexes by ligand exchange method in aqueous medium. The metal complexes of Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Pd(II), Ag(I) and Zr(IV) were prepared. The influence of various factors like reaction time, temperature and pH of the reaction medium, presence of a co-solvent and the degree of crosslinking of the polymer support were studied. From these experiments, suitable reaction conditions were optimized. Generally, complex formation was effective at room temperature, at natural pH of the reaction mixture in the presence of acetone as co-solvent with in a period of 12 h. It was observed that, PAMAM dendrimers were more efficient in complex formation compared to the PPI dendrimer of the same generation. The complexes prepared in this manner were characterized by various analytical techniques like FTIR, UV-Vis, TG-DTA, ICP AES, EPR and Solid state NMR. From these analytical data structure of the complexes was predicted.

Chapter 5 - Polymer Supported Dendrimer Metal Complexes as Heterogeneous Catalysts

The polymer supported dendrimer metal complexes prepared were screened as heterogeneous catalysts in a number of reactions. Many complexes gave promising results as catalysts for reactions like oxidation of alcohols, aldol reaction, epoxidation, Diels-Alder reaction, Heck coupling, Kharasch addition, diaryl methanol synthesis, benzodiazepine synthesis, xanthene synthesis and N-arylation of aromatic amines. Among these reactions, two were selected for detailed studies.

Polymer-supported dendrimer-Mn(II) complexes were found to be highly efficient catalysts in the oxidation of secondary alcohols to ketones under mild conditions. Compared to many previously reported polymer supported catalysts, the present complex showed high activity. Only 5 mol % of the catalyst was required to drive the reaction to completion.As described in the case of earlier

catalysts, the catalytic activity was maximum in polar solvents like acetone, water, dioxan etc. Oxidation of various alcohols was carried out in the presence of different oxidants like $K_2Cr_2O_7$, $KMnO_4$ and urea-hydrogen peroxide adduct (UHP). The problems observed during the application of strong oxidizing agents could be effectively overcome when the mild oxidizing agent UHP was used. In many cases, the ketones were isolated in excellent yields. The catalyst was recycled up to four times with out considerable loss of activity. PAMAM-Mn(II) complex showed better activity and stability compared to PPI-Mn(II) complexes.

Polymer-supported dendrimer-Pd(II) complexes were used as heterogeneous catalysts in the three component Mannich reaction between aldehydes, ketones and anilines to give β-amino ketones. Various factors influencing the reaction were studied and the condition for the maximum yield was optimized. The reaction proceeded well in ethanol in the presence of 2 mol% of the catalyst. A number of β-amino ketones were synthesized and isolated with excellent yields. The products were characterized using FTIR and PMR spectroscopies. The catalyst after washing with ethyl acetate was recycled six times without considerable loss of activity. In the case of Pd(II) complex also, better activity was shown by the PAMAM complex.

Chapter 6 - Polymer Supported Dendrimer Encapsulated Nanoparticles-Synthesis, Characterization and Catalysis

The possibilities offered by dendrimers as templates for metallic nanoparticles are already proved by many research groups. The last chapter of this thesis deals with synthesis and characterization of polymer supported dendrimer encapsulated metal nanoparticles and their use in heterogeneous catalysis. Polymer supported PAMAM dendrimer nanoparticle conjugates of Pd, Cu, Ag, Ni and Co were prepared by chemical reduction of the corresponding supported dendrimer-metal complexes using hydrazine-hydrate in methanol.

The supported dendrimer-metal nanoparticle conjugates were characterized by UV-Vis spectroscopy, TG/DTA, SEM, AFM and TEM. The Pd, Cu, Ag and Ni nanoparticles were stable and showed long shelf life. But Co

nanoparticles were oxidized back to the higher oxidation state on contact with air during a short period of time. So it was difficult to handle and analyze them. It was observed that the nanoparticles prepared using first and second generation dendrimers were of larger size and agglomerated while the nanoparticles prepared using the third generation dendrimers were well separated and of smaller size.

The Pd-nanoparticle conjugate prepared was used as catalyst in Suzuki coupling between aryl boronic acid and aryl halides. By varying the reaction conditions, the most suitable condition required to get better yield was arrived at. The efficiency of the catalyst was proved by preparing various biphenyls. Better results were given by the third generation dendrimer-nanoparticle conjugates as the nanoparticles were of smaller size and well-separated; they offered more surface area for heterogeneous catalysis. The catalyst was recycled four times without loss of activity. On further recycling a gradual loss of metal ions was observed and this may be due to the decomposition of the dendrimer backbone during the course of the reaction.

In general, the thesis describes the synthesis, characterization and environmental friendly catalysis by different polymer-supported dendrimers, their metal complexes and nanoparticle conjugates. The possibilities of recycling of the catalysts were explored along with chances to avoid the use of aromatic and halogenated solvents.

The last chapter gives a brief summary of the work done and provides scope for further improvements in the study of catalysis using polymer supported dendrimers. References are given at the end of each chapter.

CONTENTS

Chapter 1

INTRODUCTION

1. 1. SOLID PHASE ORGANIC SYNTHESIS

1. 1. 1. Historical Background

After the 1963 seminal paper by Merrifield[1], solid phase synthesis found a boom in academia and industrial labs because of the advantages it offers and the beauty of the concept. The rediscovery of polymers as organic molecules and their use in organic synthesis was made by Merrifield when he introduced his "solid-phase technique" for the synthesis of peptides, in which an insoluble cross-linked macromolecule was used as a protecting group, simultaneously providing a facile method for isolating and purifying the product of each condensation step. Since that announcement, functionalized polymers have found widespread application in organic synthesis and related fields. They have been employed as stoichiometric reagents, as catalysts, as protecting groups, as substrate carriers, in analytical chemistry, in ion exchange, in the detection of reaction intermediates, in chromatography, in biologically and pharmacologically active systems, in the immobilization of enzymes and cells, in the application of dyes and colorants, and in the field of agricultural chemicals. For a long time the solid phase synthesis meant only synthesis of peptides and nucleic acids. Although there was considerable advancement in peptide chemistry using solid phase technique, application of polymer-supported approach to traditional organic molecules did not go far in the earlier days. Some work appeared in the early 1970s. Later successful works by Leznoff [2], Neckers[3], Frechet[4], and others clearly showed that polystyrene bead supported organic chemistry worked well. But the science community lost interest in this technique soon because of the difficulty in analyzing the compounds attached to the polymer support and also due to wide variety of solution phase chemistry available at the time. The situation changed in 1992 with the report by Bunin and

Ellman of the preparation of combinatorial libraries of organic molecules.[5] The report of solid phase synthesis of diversomers by the Parke- Davis group[6] shortly thereafter simulated considerable interest in re-examination of solid phase organic synthesis. With in the past few years, a number of reports have appeared which established the great potential of solid phase organic synthesis. A number of reviews appeared in the literature describing solid phase organic synthesis[7, 8] along with many classical books dealing with solid phase organic synthesis and solid phase combinatorial chemistry[9-13]. The importance of solid phase synthesis is so high that it accounts for approximately 75% of all combinatorial efforts in industry and academia.[14]

The most important part in starting a solid phase organic synthesis is the selection of a functionalized polymer as support and the success of the synthesis is mainly determined by the nature of the resin. A functionalized polymer in the present context is a synthetic macromolecule to which functional groups are chemically bound, which can be utilized as reagents, catalysts, protecting groups, etc. The following section deals with the choice of support, the features to be consider to select a support, the advantages and disadvantages of supports and supported synthesis, and the common polymer supports used now-a-days.

1. 1. 2. The Choice of Polymer Support

From the beginning, the advantage of synthesizing a molecule attached to a solid support has been clear: a) purification process is reduced to a simple filtration step; b) reactions can be driven to completion through the use of an excess of reagents; c) site isolation or, at least apparent site isolation through an appropriate choice of polymer characteristics and reaction conditions; d) the resin acting as a protecting group for a given functionality and e) the possibility of automation and therefore, its great potential for combinatorial synthesis. All these advantages make the solid phase synthesis a versatile tool for both academic and industrial laboratories. In addition to solid phase organic synthesis of peptides and small molecular libraries, polymer supported catalysts and reagents could achieve wide attention. The backbone of these processes includes

a macromolecule with a suitable functional group. The macromolecule can be a linear species capable of forming a molecular solution in a suitable solvent, or alternatively a crosslinked species, or so-called resin, which though readily being solvated by a suitable solvent, remains macroscopically insoluble. Of the two approaches, the use of resins has been more widespread because of the practical advantages accruing from their insolubility. Active functional groups may be incorporated into polymer chains (i) by direct polymerization and copolymerization of monomers containing the desired functional groups, (ii) by chemical modification of a preformed polymer, and (iii) by a combination of (i) and (ii).

A difficulty with the first method is that considerable manipulation of the copolymerization procedure may be necessary to ensure a good yield of the required copolymer and, in the case of resins, to ensure also a satisfactory physical form. In the second method commercially available resins of high quality are normally employed and the desired functional groups introduced by using standard organic synthetic procedures.

The ease of chemical modification of a resin, and indeed the level of success in its subsequent application as a reagent or a catalyst, can depend substantially on the physical properties of the resin itself. Functionalized polymeric supports must possess a structure which permits adequate diffusion of reagents into the reactive sites, a phenomenon which depends on the extent of swelling or solvation, the effective pore size and pore volume, and the chemical and mechanical stability of the resins under the conditions of a particular chemical reaction or reaction sequence. These in turn depend on the degree of crosslinking of the resin and the conditions employed during preparation of the resin. This solid support is considered as being analogous to a cosolvent.[15] Thus, when a reaction is carried out on a polystyrene support, it can be considered that, toluene is a cosolvent in the reaction. The solid support is therefore an integral part of the reaction, and, in addition to being suitable for the reaction; need to be optimized for any particular reaction. For this reason, the translation of organic reactions from solution phase to solid phase often requires some work

to optimize the overall process. In general, reactions that tolerate excess of reagents can be transferred more easily to the solid phase than those require stoichiometric amount of reagents. The latter situation rarely works well on solid supports due to the fact that the solid phase approach is based on the use of large excess of reagents to drive the reactions to completion.[16]

An optimal solid support has the following characteristics:

1. Mechanically robust: batchwise and flow – continuous modes.
2. Stable to variation in temperature
3. Mobile, well solvated and reagent accessible sites
4. Acceptable loading
5. Good swelling in a broad range of solvents
6. Acceptable bead size
7. Stable in acidic, basic, reducing and oxidizing conditions
8. Compatible with radical, carbene, carbanion and carbenium ion chemistry
9. Biocompatible and swelling in aqueous buffer
10. Little nonspecific binding to biomolecules.

But obtaining a support with all these properties is only a dream and so the most suitable support should be chosen for a specific purpose.

1. 1. 3. Types of Supports

Polymer supports are mainly classified in to three and they are (a) microporous or gel-type resins; (b) macroporous resins, and (c) macroreticular resins.

Microporous species are prepared from a vinyl monomer and a difunctional vinyl comonomer in the absence of any additional solvating media. In the dry state they are microporous, with polymer chains being separated by typical solid-state intermolecular distances. On contact with a good solvent, a soft gel network is formed with the generation of considerable porosity depending on the degree of crosslinking. When the degree of crosslinking is very low, swollen resins generally have low mechanical stability and readily fragment

even under carefully handling. Increasing the degree of crosslinking can increase mechanical stability, but this results in poor swelling that give rise to acute diffusional limitations resulting in slow and incomplete reactions. In practice, resins of 1-2% crosslink ratio provide a satisfactory compromise generally allowing adequate penetration by most reagents and yet retaining sufficient mechanical stability to provide ease of handling.

Very similar properties can arise with macroporous resins. These are prepared as before but with the inclusion of an inert solvent. Where the solvent solvates both monomer and polymer, a fully expanded network is formed with a considerable degree of porosity. Removal of the solvent causes a reversible collapse of the matrix, and in the dry state, such materials are similar to microporous resins. In order to achieve mechanical stability in the solvent swollen state, it is usual to employ larger quantities of bifunctional comonomer in the preparation. When the solvent employed during polymerization is a good solvent for the monomers, but a precipitant for the polymer, the term macroreticular is generally employed to describe the product. The latter is a highly porous rigid material which retains its overall shape and volume when the precipitant is removed. Again it is normal to use a larger quantity of bifunctional comonomer, and this enables such products to be subjected to high pressures, and find applications in high-performance liquid chromatography. The structure of these resins is quite different from the previous two. They have a large and permanent pore volume, and reaction sites may be regarded as being located on a permanent interior surface of the resin. Macroporous species have also been prepared in the presence of large inert molecules which subsequently can be washed away to create permanent voids.

The choice of using a microporous or macroreticular resin in preparing a functionalized polymer can be a difficult one and depends very much on the application in question. In a swelling solvent, microporous species can often be loaded or functionalized to higher levels than macroreticular ones. However, the latter are generally much less sensitive to the choice of solvent, which is not always a readily variable parameter in some chemical reactions. Swollen

microporous resins are less sensitive to sudden shock but cannot be subjected to steady and high pressures. Conversely, rigid macroreticular species are brittle and fracture under sudden stress, but can withstand considerable steady pressures.

The role of a solvent in the application of a functionalized resin is complex. Ideally it should interact with the polymer matrix to optimize the diffusional mobility of reagent molecules. It should have the correct solvating characteristics to aid any chemical transformation being carried out. It should not limit the reaction conditions which are to be applied (e.g., the temperature), and in the case of bound photosensitizers, for example, it should encourage translucence and not opacity. Naturally it is difficult to satisfy all of these criteria simultaneously, and the selection of a solvent is often a compromise. With those applications involving the assembly or modification of a polymer bound substrate, the final cleavage step releasing the product into solution can be incomplete, or the vigorous conditions employed in cleavage may result in degradation of the polymer. The overall chemical and mechanical stability of the support can often be limiting, the ultimate capacity of a functionalized polymer is also restricted, and may be important in preparative organic chemistry involving stoichiometric quantities of supported reagents.

One of the major differences between inorganic supports and polymers is the lower loading capabilities of the former which, while being suitable for the attachment of catalysts and in polypeptide and oligonucleotide synthesis, is totally unsuitable for high-capacity demand. Difficulty in the characterization of reactions on polymers can also arise. These are maximized in the case of resins, where those techniques relying on the formation of a true homogeneous solution, at best, may be rendered inadequate or insensitive and, at worst, can be completely useless. Finally in the use of functionalized polymers, there always exists the additional chemical option of a side reaction with the polymer itself. A number of classic crosslinking side reactions have been identified, associated with intrapolymeric reactions, which have never been recognized, let alone characterized. Despite these potential drawbacks, a large number of systems

have been developed, and considerable scope now exists for their exploitation in routine synthetic chemistry.

Macroporous resins have a permanent well developed porous structure even in the dry state. This type of resins can be prepared by using an appropriate porogen along with the monomer and crosslinker mixture used in suspension polymerization. The polymer matrix is rather heterogeneous or non- uniform. Some area contains impenetrable crosslinked and entangled polymer chains, other areas devoid of polymer. These materials have much more surface area than gel type resins, typically ranging from 50 to 1000 m^2/g. Unlike gel type resins, these materials do not need to swell in a solvent to allow access to the interior because they possess permanent porous structure. The dimension of pores can be manipulated by precise polymerization conditions.[17] The polymeric supports can be further classified depending on the chemical constitution[18] and such a discussion is avoided here.

The supports used in the present research work are discussed in the coming section.

1. 1. 3. a. DVB Crosslinked Polystyrene

Lightly crosslinked polystyrene (1-2% DVB) was Merrifield's resin of choice for the synthesis of the tetrapeptide and it remains the most commonly used support for solid phase organic synthesis due to its ready availability and low cost. It is prepared by suspension polymerization of styrene and divinylbenzene (Figure 1-1). They can be substituted with a wide variety of functionalities, although, chloromethylation or aminomethylation are more common. Loading can vary from 0.3 to 3 mmol/g. The resin show best swelling behavior in toluene or dichloromethane. The preparation, characterization and applications of 1-2 mol% of divinylbenzene crosslinked polystyrene is extensively reviewed.[17,19] Eventhough this resin possesses many characteristics required for a good support, it has some disadvantages and that include poor swelling in polar organic solvents, low loading and poor accessibility of reaction sites.

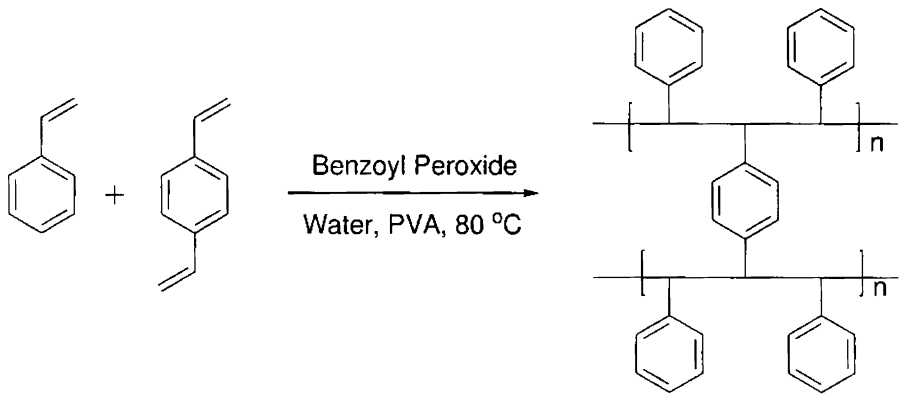


Figure 1-1. DVB crosslinked polystyrene

1. 1. 3. b. Poly (methyl methacrylate) Supports

Akelah et. al. prepared DVB crosslinked poly (methyl methacrylate) resin by suspension polymerization of methyl methacrylate and DVB (Figure 1-2).[20]

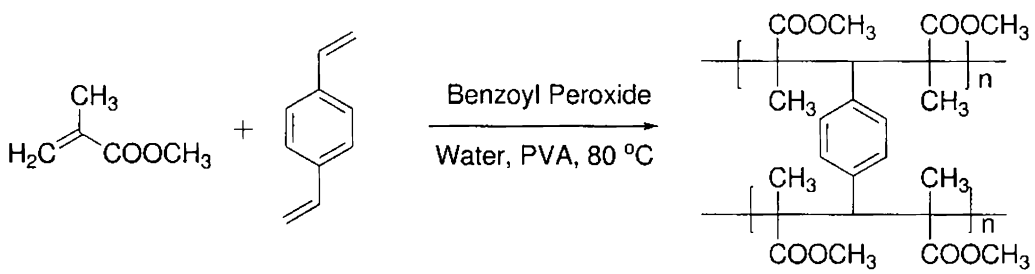


Figure 1-2. DVB crosslinked poly(methyl methacrylate)

The polymer composition and polymerization conditions were optimized to produce a wide range of structural characteristics desirable for various types of chemical applications. The resin was functionalized with ethylene diamine under phase transfer conditions to obtain polymer containing primary amine functional groups. In another attempt, the ester groups of the resin were reduced with $LiAlH_4$ to attain hydroxyl group containing resin. These kinds of resins also find applications in solid phase organic synthesis and in the development of polymer supported catalysts and reagents.[21]

In addition to these resins, there are a number of polymer-supports used in solid phase organic synthesis and in the development of polymer-supported

catalysts and reagents. The important ones are PEG crosslinked PS[22-25], Janda Jel[26-29], Tenta gel[30,31], Argo gel[32,33], Rasta resin[34-36], ROMP gel[37], CLEAR resin[38], polyacrylamides[39-41], POEPOP resin[42], SPOCC resin[43], crosslinked NVP[44], crosslinked PVA[45,46], polyalkanes and their fluorinated derivatives etc.[47-49]

Other materials have also been investigated to use in solid phase organic and peptide synthesis. For example, cellulose paper disks, an inexpensive and easy to handle support have been used in peptide synthesis.[50] Beaded cellulose also has been employed in Fmoc solid phase peptide synthesis of fragments ranging from 5 to 34 amino acids.[51] A cotton thread wrapped around a cylinder has been used as a support for the preparation of a combinatorial library of peptides where the identity of each member of the library was determined by its position along the cotton thread allowing combinatorial synthesis and screening of the peptides.[52]

1. 2. POLYMER SUPPORTED CATALYSTS

Recent interest in the development of environmentally benign synthesis has evoked a renewed interest in developing polymer-bound catalysts and reagents for organic synthesis that maintain high activity and selectivity.[53,54] A polymeric catalyst or polymer-supported catalyst is a conventional catalytic species attached to a macromolecular backbone. The polymer species may be a linear or a crosslinked entity, and again the latter have proved particularly useful. Polymeric catalysts are generally used in catalytic quantities relative to reaction substrates, and can often be reused many times. The attachment of a catalyst to a support may improve its stability and selectivity. On the other hand, increased experimental convenience arising with a polymeric catalyst may be offset by a significant reduction in reactivity associated, for example, with diffusional limitations imposed by resin supports. A wide variety of catalysts have been supported in this way, ranging from strong acids and bases (ion-exchange resins), transition-metal complexes, organic catalysts and photosensitizers right through to the highly specific enzyme catalysts.

Probably the most important advantage in using a functionalized polymer as support of a catalyst is the simplification of product work-up, separation, and isolation. In the case of crosslinked polymer resins, simple filtration procedures can be used for isolation and washing, and the need for complex chromatographic techniques can be eliminated. Scarce and/or expensive materials can be efficiently retained when attached to a polymer and, if appropriate chemistry is available, they can in principle be recycled many times and this in metal-based catalysis means using precious metal catalysts several times. Odorous and harmful substances can be handled easily by attaching them to polymers and they can be easily separated from the final product easily. In addition, polymer supported catalysts can be manipulated easily and large number of diversity can be introduced by techniques of combinatorial chemistry like mix and split method.[4] Due to these advantages, polymer supported catalysts are widely used in combinatorial library preparation and pharmaceutical industry.[7, 55] Resins, in addition, provide the possibility of automation in the case of repetitive stepwise synthesis and the facility of carrying out reactions in flow reactors on a commercial scale. Moreover, immobilization of catalysts on an insoluble polymer has significant influence on the activity and selectivity. The reactivity of an unstable reagent or catalyst may be attenuated when supported on a resin, and the corrosive action of, for example, protonic acids can also be minimized by this effective encapsulation.

In addition to these factors, a number of potentially important reactivity changes may be induced by the use of a functionalized polymer. When the latter is crosslinked, restricted interaction of functional groups may be achieved. A high degree of cross-linking, a low level of functionalization, low reaction temperatures, and the development of electronic charges near the polymer backbone tend to encourage this situation, which may be regarded as mimicking the solution condition of "infinite dilution". In these circumstances, intermolecular reaction of bound molecules is prevented, and such attached residues can be made either to react intramolecularly or to react selectively with

an added soluble reagent. Polymer supported metal complexes with vacant coordination sites can be regarded as fulfilling this description, with the resin inhibiting the normal solution oligomerization processes of such species. Under certain circumstances, it is also possible to achieve the complementary state of "high concentration" by heavily loading a flexible polymer matrix with one particular moiety in an attempt to force its reaction with a second polymer-bound species. Another advantage is due to the unique microenvironment created for the reactants within the polymer support. Improved catalyst stability within the polymer matrix, increased selectivity for intramolecular reactions, enhanced regioselectivity due to steric hindrance, and the superior activity of some supported chiral catalysts due to site cooperation have all been reported.

Balancing the above advantages, there are also a number of important disadvantages. Probably the most important of these is the likely additional time and cost in synthesizing a supported reagent or catalyst. This may well be offset by the potential advantages, and certainly in the case of regenerable and recyclable species, this objection essentially disappears. The occurrence of slow reactions and poor yields, however, can seldom be accommodated, and this can be a problem. Appropriate choice of support and reaction conditions can overcome these difficulties.

Eventhough, a large number of polymer supports were developed in the last fifty years, the most widely used support for the preparation of polymer-supported catalysts is polystyrene. The synthesis and applications of polymer-supported catalysts were widely reviewed.[56-70]

1. 2. 1. Polymer-Supported Catalysts for C-C Bond Formation

One of the most studied areas in polymer-supported catalysts is the development of novel catalysts for carbon-carbon bond forming reactions. Colacot et al. reported a novel polymer supported catalyst for Suzuki coupling reaction in which palladium complexes of commercially available polymer (FibreCat™-1001) containing triphenyl phosphine ligand was treated with palladium salts and the resulting catalyst was used for catalyzing Suzuki

coupling. The reaction proceeded well within a short period of time compared to many previously reported catalysts.[71] There was no metal leaching observed, but the catalyst turned black after the first run and so no recycling studies were described. In the same year, another group developed a catalyst for Suzuki coupling from triphenyl phosphine ligand supported on DVB crosslinked polystyrene and palladium chloride. The catalysts performed well under a given set of conditions and could be recycled many times with out considerable leaching.[72] Phan et al. used polystyrene supported salen type palladium catalyst for Suzuki coupling. The catalyst was so efficient that all the substrates attempted gave 100% yield and the catalyst was recyclable.[73] Another interesting example to mention is polystyrene supported palladium –N-heterocyclic carbene reported by Lee and co-workers.[74,75] A short and versatile synthesis of reusable diarylphosphinopolystyrene-supported palladium catalyst for Suzuki coupling was described by Schweizer et al.[76] In this method, nucleophilic substitution of the chlorine atoms of a Merrifield resin by diarylphosphinolithium followed by introduction of palladium with a soluble palladium salt gave the catalyst. Ten different catalysts were prepared by varying the substitution on the aryl groups on the phosphino groups and all these catalysts were screened in the cross coupling between 4-bromoacetophenone and benzene boronic acid. All these catalysts gave quantitative yield with considerably lower amount of catalyst. A β-ketoester complex of palladium was prepared and used as a recyclable catalyst for Heck reaction between aryl iodides and bromides and alkenes by Dell'Anna et al.[77] The catalyst was stable in air and water and gave good to excellent yields. Polymer supported N-methylimidazolium-palladium complex and polymer supported N-heterocyclic carbene-palladium complex were developed by Altaya et al.[78] and Shokouhimehr et al.[79] respectively for Heck reaction. The latter catalyst gave good yield with all the substrates attempted while the yield varied from 10%-100% in the case of the former. Polymer supported palladium catalyst for Stille coupling was reported by Dell'Anna et al.[80] The coupling between aryl iodides and bromides with organostannanes has been investigated in the presence of a polymer supported palladium catalyst. The reaction could be

performed in air without any activating ligand and with non-dried solvents. The catalyst, which acts by releasing controlled amounts of soluble active species, could be recycled several times in the coupling between $Sn(CH_3)_4$ or nBu_3SnPh with iodoarenes or activated bromoarenes. In a recent report, Bai and Wang used polymer-supported triphenyl phosphine-Pd complex as reusable catalyst for atom efficient coupling reaction of aryl halides with sodium tetraphenylborate in water under microwave irradiation to give polyfunctional biaryls in excellent yields (Figure 1-3).[81]

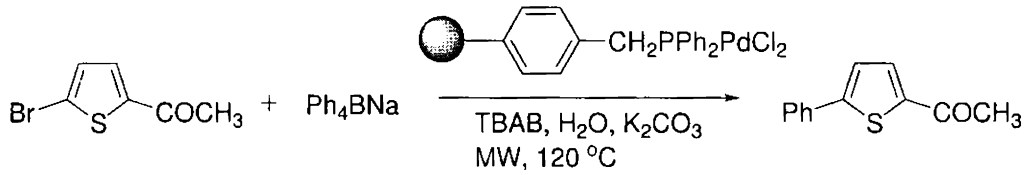


Figure 1-3. Polymer-supported triphenyl phosphine-Pd complex catalyzed coupling reaction of aryl halides with sodium tetraphenylborate in water.

There are few examples of polymer-supported catalysts for aldol reaction in literature. Itsuno et al. developed a chiral catalyst for asymmetric Mukaiyama aldol reaction.[82] Chiral *N*-sulfonylated α-amino acid monomer derived from (*S*)-tryptophan was copolymerized with styrene and divinylbenzene under radical polymerization conditions to give a polymer-supported *N*-sulfonyl-(*S*)-tryptophan. Treatment of the polymer-supported chiral ligand with 3,5-bis(trifluoromethyl)phenyl boron dichloride afforded a polymeric Lewis acid catalyst effective for asymmetric Mukaiyama aldol reaction of silyl enol ethers and aldehydes. Various aldehydes were allowed to react with silyl enol ethers in the presence of the polymeric chiral Lewis acid to give the corresponding aldol adducts in high yield with high levels of enantioselectivity.[78] Catalytic efficiency of polymer-supported sulphonic acid in cross aldol condensation between arylaldehydes and cycloketones to afford α,α′-bis(substituted benzylidene)cycloalkanones was shown by An et. al.[83]

Madhavan and Weck described polymer-supported (*R,R*)-(salen)AlCl complexes that were immobilized on poly(norbornene)s that displayed excellent activities and enantioselectivies as catalysts for the 1,4-conjugate addition of

cyanide to α,β-unsaturated imides (Figure 1-4).[84] These supported catalysts could be recycled up to 5 times without compromising catalyst activities or selectivities. Furthermore, the catalyst loadings could be reduced from 10-15 mol%, the common catalyst loadings for non-supported (salen)Al catalysts, to 5 mol%, a decrease of metal content by 50-66%, without lowering product yields or enantioselectivities. Kinetic studies indicated that the polymer-supported catalysts are significantly more active than their corresponding unsupported analogues.

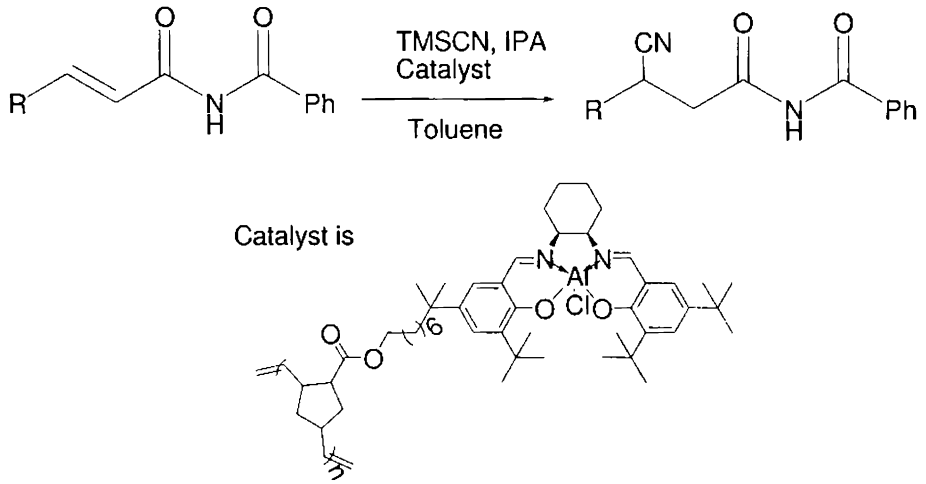


Figure 1-4. Polymer supported Al catalysts for the 1,4-conjugate addition of cyanide to α,β-unsaturated imides.

Liu and Jiang showed that Janda Jel supported tertiaryphosphine was an efficient green organocatalyst for α-addition of carbon nucleophile to α,β-unsaturated compounds under mild conditions.[85]

1. 2. 2. Polymer-Supported Catalysts for Oxidation and Epoxidation

Another type of polymer-supported catalyst developed to maturity is catalyst for oxidation and epoxidation. Polymer supported oxidation catalysts attain great attention because of their resemblance with enzymatic catalysts in action.[86,87]

Divinyl benzene crosslinked polystyrene supported β-diketone linked complexes of Mn(II) have been prepared, characterized and used as

heterogeneous catalyst in the oxidation of secondary alcohols to ketones in the presence of $K_2Cr_2O_7$ as oxidants.[88]

The preparation of a series of polymer supported chiral Schiff bases derived from salicylic aldehyde and optically active amino alcohols were reported by Barbarini et al.[89] These heterogeneous ligands have been complexed with $VO(acac)_2$ and employed to catalyze the enantioselective oxidation of sulfides to sulfoxides with hydrogen peroxide as an environmentally acceptable oxidant (Figure 1-5). The procedure afforded the sulfoxides in good yield and selectivity and with enantiomeric excess values comparable to those obtained with the homogeneous counterparts. The catalyst can be used for at least four cycles without any significant decrease in both efficiency and enantioselectivity.

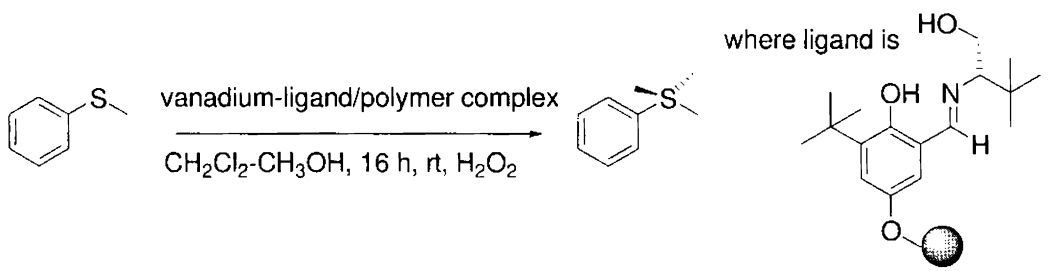


Figure 1-5. Polymer supported chiral Schiff base-vanadium complex catalyzed oxidation of sulphides.

Anchoring of the amino acid L-valine on chloromethyl polystyrene in the presence of a base gave a fresh ligand for polymer-supported catalyst as described by Valodkar and co-workers.[90] Reaction of cupric acetate with this polymeric ligand resulted in chelate formation with Cu(II) ion. The supported Cu(II) complexes behaved as versatile catalysts in the oxidation of various substrates such as benzyl alcohol, cyclohexanol and styrene in the presence of *t*-butyl hydroperoxide as oxidant. The effect of reaction conditions on conversion and selectivity to products has been studied in detail. Preliminary kinetic experiments revealed that the Cu(II) complexes attached to polymer matrix can be recycled about four times with no major loss in activity. Kang et al. used polystyrene supported 1,10-phenanthroline as the ligand for the development of a new ruthenium based oxidation catalyst.[91] 5-amino-1,10-phenanthroline

prepared according to a standard procedure was attached to DVB crosslinked chloromethyl polystyrene. The polymer-supported metal complex prepared from this ligand and $RuCl_3$ was used as heterogeneous catalyst in the oxidation of primary and secondary alcohols in the presence of iodosyl benzene as oxidizing agent. The conversion was from moderate to excellent. The catalyst was recycled five times, but after the third cycle the efficiency was lost considerably. Benaglia and co-workers prepared a new oxidation catalyst by anchoring TEMPO on PEG chains.[92] This system was used as catalyst in the aerobic oxidation of alcohols in the presence of $Co(NO_3)_2$ or $Mn(NO_3)_2$ as co-catalyst. Primary and benzylic alcohols were converted to carbonyl compounds with an yield of up to 99%. The authors showed that introduction of a spacer between the catalyst and the polymer considerably increased the activity of the catalyst. The catalyst was recycled six times with out loss of activity. Lie *et al* used polystyrene supported 2-iodobenzamide as an efficient organic catalyst for the oxidation of alcohols.[93] The catalyst prepared from aminomethyl polystyrene and 2-iodobenzoic acid in a single step was used in the oxidation of both primary and secondary alcohols in CH_3CN-H_2O mixture and the oxidizing agent selected was Oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$). The conversion was moderate to excellent and the catalyst was reused four times without any loss of activity.

Sreekumar and co-workers have reported a number of polymer supported catalysts for epoxidation of olefins.[94-97] Metal complexes of polymer supported β-diketones were used effectively as heterogeneous catalysts in the epoxidation of various olefins by H_2O_2. Both DVB crosslinked polystyrene and poly(methyl methacrylate) were used as supports. Better results were obtained with poly(methyl methacrylate) supported catalyst under similar conditions.

Saldino et al. reported a novel catalyst for the epoxidation of alkenes by H_2O_2. Methylrhenium trioxide (CH_3ReO_3, MTO) was supported on poly(4-vinyl pyridine) 25% crosslinked with divinylbenzene and on poly(4-vinyl pyridine-N-oxide) 2% crosslinked with DVB. In addition, microencapsulated MTO with polystyrene 2% crosslinked with DVB or a mixture of PS and PVP (both 2% crosslinked with DVB) were also studied. A detailed characterization of the

catalyst was done with FTIR, SEM and WAXS which revealed a distorted, octahedral rhenium coordination geometry in the supported catalyst and the reticulation grade of polymer was shown to be linked to surface morphology.[98] All these catalysts showed good activity and the yield of the epoxide was above 90% in many cases. Moreover, the formation of the diol as a side product from epoxide was diminished considerably. The same group also reported a convenient and efficient synthesis of monoterpene epoxides by application of heterogeneous poly(4-vinyl pyridine)/methylrhenium trioxide (PVP/MTO) and polystyrene/methylrhenium trioxide (PS/MTO) systems.[99] Even, highly sensitive terpenic epoxides were obtained in excellent yield. The epoxidation was carried out with H_2O_2 and the catalysts were stable systems for at least five recycling experiments.

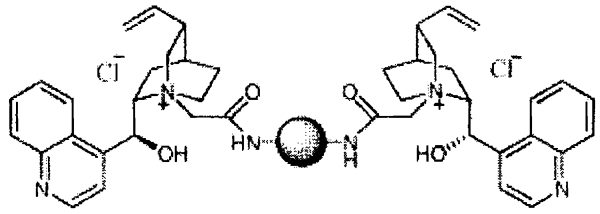
Lu and co-workers attached dimeric cinchonine, cinchonidine, and quinine via nitrogen to long linear PEG chains to afford soluble polymer-supported chiral ammonium salts, which were employed as phase-transfer catalysts in the asymmetric epoxidation of chalcones.[100] The highest enantiomeric excess obtained was 86%. The structures of the catalysts are shown in Figure 1-6.

Polymer-supported $Co^{II}LCl_2$ {L = 2-(alkylthio)-3-phenyl-5-(pyridine-2-ylmethylene)-3,5-dihydro-4*H*-imidazole-4-one} complex has been synthesized and employed as a catalyst for the epoxidation of alkenes using iodosylbenzene and hydrogen peroxide as oxidants by Beloglazkina et al.[101] The epoxides were obtained in 10 to 85% yield.

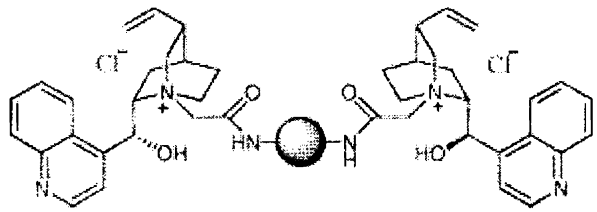
1. 2. 3. Polymer-Supported Catalysts for Ring Opening Reactions

β-amino alcohols found wide-spread applications in pharmaceutical synthesis and fine chemical industry. The most successful method for their synthesis is nucleophilic ring opening of epoxides by amines in the presence of a catalyst. Bandini et al. developed a polymer-supported Indium Lewis acid catalyst for the ring opening of epoxides to give β-amino alcohols.[102] This new heterogeneous Amberlyst 15/Indium complex effectively catalyzed (20 mol % based on indium) the formation of new C-C as well as C-S bonds through the

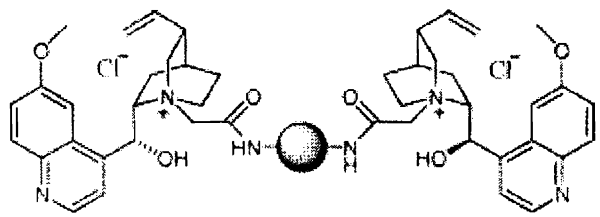
highly regio and stereoselective ring-opening reaction of enantiomerically pure epoxides. The easily prepared Amberlyst 15/Indium Lewis acid did not require inert atmosphere conditions or anhydrous media and could be easily recovered and recycled for several times without loss of activity.



Diacetamido-PEG2000 N-bound cinchoninium chloride



Diacetamido-PEG_{2000} N-bound cinchonidinium chloride



Diacetamido-PEG_{2000} N-bound quininium chloride

Figure 1-6. Polymer supported chiral ammonium salts used as phase transfer catalysts

Polymer supported copper sulphate was used as heterogeneous catalyst for the ring opening of epoxides with amines. An alkylamine functional,

insoluble and crosslinked polymer support was prepared by reacting a glycidyl group containing polymer with ethylenediamine. Copper complex of this polymer was prepared. This complex could be used as a heterogeneous catalyst to afford a rapid, efficient and mild method for synthesis of β-amino alcohols by aminolysis of epoxides. The reaction proceeded in a short time and the yields of the amino alcohols vary from 60 to 100%.[103] Lee and co-workers reported another novel catalyst for ring opening of epoxides. Polymer-supported metal (Fe or Ru) complexes for epoxide ring opening reactions were successfully prepared by anchoring the bis(2-picolyl)amine ligand onto the polymer poly(chloromethylstyrene- co-divinylbenzene); they showed heterogeneous catalytic activity and easy recyclability in the ring opening reaction of various epoxide substrates with methanol or H_2O at room temperature under mild and neutral conditions. The catalyst was recycled ten times with out loss of activity.[104]

1. 2. 4. Polymer-Supported Catalysts for Reduction

A number of polymer-supported catalysts for reduction and hydrogenation of functional groups can be found in the literature. Saluzzo et al. reported polymer supported catalysts for asymmetric heterogeneous reduction of a C=O bond by hydrogen transfer or molecular hydrogen.[105] Hydrogen transfer reduction was performed with amino alcohol derivatives of enantiopure poly((S)- glycidyl methacrylate-co-ethyleneglycol dimethacrylate) (poly(GMA-co-EGDMA)) and poly((S)-glycidyl methacrylate- co-divinyl benzene) (poly(GMA-co-DVB)) for solid–liquid catalysis. Finally, hydrogenation with molecular hydrogen was employed both in solid–liquid and in liquid–liquid biphasic catalysis. The first one was performed with BINAP grafted onto a polyethylene glycol and the second one with polyureas containing the BINAP structure. All the catalysts gave excellent yield with more than 99% enantiomeric excess. *N*-Methyl-α,α-diphenyl-L-prolinol derivatives with *para*-bromo substituents in one or both of the phenyl rings are easily bound to crosslinked polystyrene beads containing phenylboronic acid residues using Suzuki reaction.

When the products were used as catalysts for the reaction of aldehydes with diethylzinc in toluene at 20 °C, the alcohols were produced in chemical yields >90% and with ees of up to 94%. The best of the two supported catalysts gave ees only 0–9% lower than those obtained with the corresponding soluble catalyst. One of the supported catalysts was recycled successfully nine times.[106] The same catalysts were used to catalyze reductions of several prochiral ketones with borane in tetrahydrofuran at 22 °C. The expected secondary alcohols were obtained in high chemical yields and ees were generally in the range 79–97 %. The catalyst was recycled 14 times without loss of stereochemical performance.[107]

Zarka et al. reported the synthesis of new amphiphilic block copolymers with (2S, 4S)-4-diphenylphosphino-2- (diphenylphosphinomethyl) pyrrolidine (PPM) units in the side chain and their application in the asymmetric hydrogenation.[108] The polymers prepared were used as macroligands for the rhodium catalyzed hydrogenation of two prochiral enamides, acetamido cinnamic acid and its methyl ester. Additionally, catalyst recovery and reuse was possible by simple extraction of the substrate/product from the aqueous polymer phase after each cycle.

Attaching a homogeneous rhodium catalyst to a fluoroacrylate copolymer backbone developed a novel hydrogenation catalyst soluble in supercritical carbon dioxide.[109] The polymer was synthesized by the polymerization of 1*H*,1*H*,2*H*,2*H*-heptadecafluorodecyl acrylate monomer (zonyl TAN) and *N*-acrylosuccinimide (NASI), the former increasing the solubility in supercritical carbon dioxide and the latter providing attachment sites for the catalyst. Diphenylphosphinopropylamine, $NH_2(CH_2)_3PPh_2$ (DPPA), was used to exchange the NASI groups in the polymer, which was then reacted with $[RhCl(COD)]_2$ to obtain the catalyst. The catalyst was soluble in supercritical carbon dioxide and its hydrogenation activity was evaluated using 1-octene and cyclohexene hydrogenation as model reactions. The synthesis route for the catalyst is reproducible, as shown by reaction activity studies on different

batches of catalyst. The catalyst was evaluated at different substrate-to-rhodium molar ratios and at different temperatures.

Amphiphilic PS-PEG resin dispersed palladium nanoparticles were used as catalysts for the hydrogenation of olefins and hydrodechlorination of chloroarenes was developed by Nakao and co-workers.[110] In many cases of the substrates attempted, up to 99% yield was obtained in both reactions. The catalyst was recycled ten times with out considerable loss of activity.

1. 2. 5. Polymer-Supported Catalysts for Olefin Metathesis

In the last thirty years, olefin metathesis have become one of the indispensable synthetic tool.[111] Because of this importance of metathesis reaction, many groups have developed polymer-supported catalysts for metathesis reaction. Schrock and Hoveyda reported the first recyclable chiral polymer supported catalyst for olefin metathesis.[112] A chiral bis(styrene) derivative was co-polymerized with styrene under the conventional suspension polymerization conditions and this polymer-supported ligand was complexed with a molybdenum triflate to get the respective catalyst. The catalyst performed well in asymmetric ring closing metathesis and an ee as high as 98% was obtained. Even if the catalyst exhibited less activity than the homogeneous counter part, the stability of the polymer-supported system was very high as observed from the low metal leaching. Akiyama and Kobayashi reported a linear polystyrene supported arene-ruthenium catalyst for ring closing olefin metathesis for the synthesis of various heterocycles (Figure 1-7).[113] The products were obtained from 50 to 100% yield. The authors have also described the catalyst recycling.

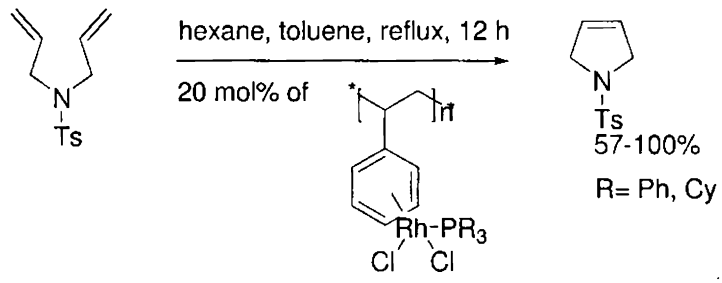


Figure 1-7. Polystyrene supported arene-ruthenium catalyst for ring closing olefin metathesis

Another interesting example of polymer supported metathesis catalyst was reported by Jafarpour et al.[114] They have attached a number of metal complexes to the macroporous poly(DVB). Under the reaction conditions, the metal complexes undergo cross metathesis with poly-DVB and exchange their carbene moiety for the unbound vinyl groups of the supporting polymer, giving rise to polymer supported catalysts.

1. 2. 6. Miscellaneous Polymer-Supported Catalysts

There are a number of polymer-supported catalysts of which only one reference can be found in the literature. These miscellaneous catalysts are reviewed in the following section.

Li et al. used the polymer-supported bimetallic catalyst system PVP–$PdCl_2$–$NiCl_2$/TPPTS/PPh_3 in the hydroxycarbonylation of styrene under aqueous–organic two-phase condition.[115] The reaction proceeded to 100% conversion and with a selectivity of up to 64% to the branched acid. The catalyst was recycled three times with out loss of activity. Zhang reported a silica-supported chitosan (CS)–palladium complex CS–$PdCl_2$/SiO_2, which showed good conversion and higher regioselectivity in carbonylation of 6-methoxy-2-vinylnaphthalene.[116] The high selectivity of the catalyst was achieved by the synergic effect of Pd–Ni bimetallic system and by polymer protection. Effects of reaction variables have been studied to optimize the reaction conditions. The hydroesterification of various substrates were also investigated. XPS and TEM showed that the catalytically active species were composed of particles of nanometric size and the polymer would serve as a ligand. Recycling of the catalyst was also studied.

Trost and co-workers reported polymer supported C_2-symmetric ligands for palladium catalyzed asymmetric allylic alkylation reactions.[117] In the presence of 25 mol% of ligand and 5 to 10 mol% palladium, the reaction proceeded with up to 97% yield and 68-99% ee. Homochiral 2,2'-bis(oxazolin-2-yl)-1,1'-binaphthyl (boxax) ligands were anchored on various polymer supports including PS-PEG, PS, PEGA, and MeO-PEG via selective monofunctionalization

at the 6-position of the binaphthyl backbone by Hocke and Uozumi. Palladium(II) complexes of these supported boxax ligands catalyzed Wacker-type cyclization of 2-(2,3-dimethyl-2-butenyl)phenol to give 2-methyl-2-isopropenyl-2,3-dihydrobenzofuran with up to 96% ee.[118] The scheme of the reaction and structure of the catalyst are given in Figure 1-8.

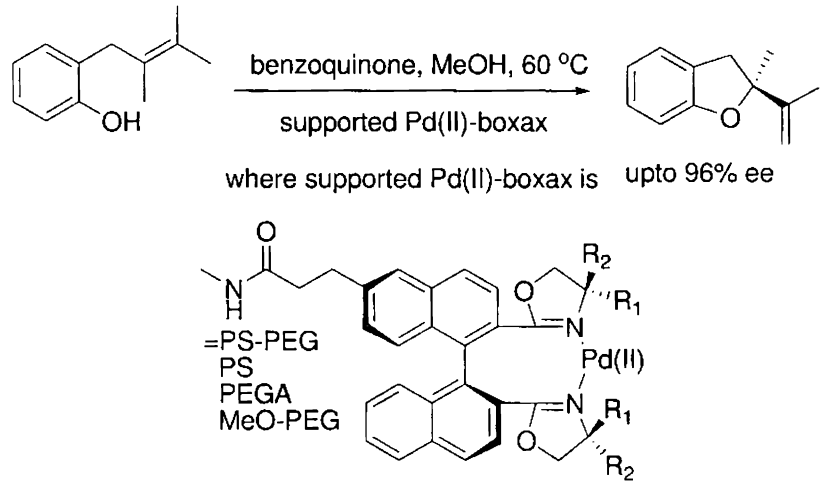


Figure 1-8. Polymer supported palladium(II) complexes catalyzed Wacker-type cyclization

A novel polymer supported BisBinol ligand was prepared by Sekiguti *et al* for the preparation of bimetallic catalysts for various organic transformations.[119] The polymer was prepared by co-polymerization of MMA and a monomer containing the BisBinol moiety in the presence of AIBN. A bimetallic complex of this polymeric ligand with Al and Li was found to be efficient catalysts in the formation of Michael adduct between 2-cyclohexen-1-one with dibenzyl malonate with up to 96% ee. The same ligand was used in the preparation of a bimetallic titanium catalyst, which promoted the asymmetric carbonyl-ene reaction of methyl glyoxylate with α-methyl styrene in high yield with excellent enantioselectivity.

Iimura et al. showed that polystyrene sulphonic acid containing a long alkyl chain on the aromatic ring was a highly efficient catalyst for many organic transformations in water.[120] The authors showed that, with the increase in the

length of the alkyl chain, the efficiency of the catalyst increased and very low loading of the sulphonyl group was required to get excellent results. Only 1 mol% of the catalyst was required for getting excellent yield in reactions like hydrolysis of thioesters, deprotection of ketals, transthioacetalization of acetal and hydration of epoxides with in a very short reaction time under mild reaction conditions in water as the solvent.

Montchamp and co-workers described a reusable polymer-supported hydrophosphinylation catalyst for the preparation of H-phosphinic acids.[121] Reaction of excess commercially available polystyryl isocyanate with nixantphos in refluxing toluene directly produced the desired urea-linked ligand with a loading of 0.1 to 0.3 mmol of ligand per gram of resin. The active catalyst was prepared by treating the ligand with Pd_2dba_3. The catalyst was successfully employed in the hydrophosphinylation of alkenes with H_3PO_2. The same catalyst was used for allylation of H_3PO_2 with allylic alcohols by the same group.[122] It was observed that the polymer supported catalyst showed less efficiency than the homogeneous counter part in both reactions.

A series of polar group functionalized polystyrene-supported phosphine reagents were examined as catalysts in the aza-Morita–Baylis–Hillman reaction of *N*-tosyl arylimines and a variety of Michael acceptors with the aim of identifying the optimal polymer/solvent combination by Toy et al.[123] For these reactions *J*anda*J*el-PPh_3 (1 mmol PPh_3/g loading) resin containing methoxy groups (*JJ*-OMe-PPh_3) on the polystyrene backbone in THF solvent provided the highest yield of all the catalyst/solvent combinations examined. The methyl ether groups were incorporated into *JJ*-OMe-PPh_3 using commercially available 4-methoxystyrene, and thus such polar polystyrene resins were easily accessible and found utility as nucleophilic catalyst supports. Up to 81% yield was reported by the authors.

In another interesting report, polymer-supported palladium catalysts prepared from commercially available phosphine-functionalised polymers (PS-PR_2), $Pd_2(dba)_3$ and P(*t*-Bu)$_3$ were used as heterogeneous catalysts in the amination of aryl halides.[124] Four commercially available resins were used and

the Pd species generated insitu from $Pd_2(dba)_2$ and $P(t\text{-}Bu)_3$ were attached to the resin to get the corresponding catalyst. Catalyst stability was investigated using ^{31}P NMR spectroscopy. One of the catalysts was reused in the amination of bromobenzene and chlorotoluene, up to three times, without loss in yield. Recyclability of the catalyst was dependent on the method of preparation and the nature of the polymer-bound phosphine.

Commercially available polystyrene supported triphenyl phosphines were found to be highly active catalyst in the Trost's γ-addition of various pro-nucleophiles with methyl 2-butynoate in water-toluene mixture.[125] The catalyst was recyclable up to three times with gradual loss in activity. Eventhough, this was considered as a green route for Trost's addition, the requirement of large amount of catalyst and a large variation in the yield of products with various substrates limited its practical application.

Two polymer-supported chiral ligands were prepared based on Noyori's (1*S*,2*S*)- or (1*R*,2*R*)-*N*-(*p*-tolylsulfonyl)-1,2-diphenylethylenediamine by Li et al.[126] The ligand prepared by the standard procedure was coupled to aminomethyl polystyrene in the presence of DCC. The combination of this supported ligand with $[RuCl_2(p\text{-cymene})]_2$ has shown to exhibit high activities and enantioselectivities for heterogeneous asymmetric transfer hydrogenation of aromatic ketones with formic acid–triethylamine azeotrope as the hydrogen donor, whereby affording the respective optically active alcohols, the key precursors of chiral fluoxetine, a drug used for the treatment of depression and anxiety. The catalysts can be recovered and reused in three consecutive runs with no significant decline in enantioselectivity. The procedure avoids the plausible contamination of fluoxetine by the toxic transition metal species.

A poly(vinyl pyrrolidone) supported catalyst was reported by Chari and Syamasundar.[127] Condensation of o-phenylenediamine with ketones under solvent free conditions to afford the corresponding 1,5-benzodiazepine derivatives in high yield was catalyzed by this PVP supported ferric chloride catalyst.

A novel polymer-supported *N*-heterocylic carbene (NHC)–rhodium complex was prepared from chloromethyl polystyrene resin using a simple procedure by Yan et al.[128] This polymer-supported NHC–rhodium complex was used as a catalyst for the addition of arylboronic acids to aldehydes affording arylmethanols in excellent yields.

Huisgen's [3+2] cycloaddition reaction between azides and alkynes was catalyzed by a polymer-supported catalyst prepared from CuI and Amberlyst A-21.[129] The catalyst prepared by simple stirring of polymer and copper salt followed by filtration and washing showed high efficiency and the triazole derivatives were obtained in excellent yield.

Zhao and Li showed that polymer supported sulfonamide of N-glycene was a highly efficient and selective catalyst for allylation of aldehydes and imines (generated in situ from aldehydes and amines) with allytributyltin.[130] Commercially available polystyrene-DVB resin was chlorosulphonylated followed by grafting of glycene ethyl ester. Saponification of this resin gave the active catalyst. The allylation proceeded with small amount of catalyst with in a short time interval. The allylic alcohols and amines were produced in good to excellent yield.

Polymer-bound *p*-toluenesulfonic acid was shown to catalyze efficiently the direct nucleophilic substitution of the hydroxy group of allylic and benzylic alcohols with a large variety of carbon- and heteroatom-centered nucleophiles.[131] The reaction conditions were mild, the process was conducted under an atmosphere of air without the need for dried solvents, and water was the only side product of the reaction and up to 90% conversion was observed.

Sulfenylphosphinoferrocene (Fesulphos) ligand carrying an alcohol linker was attached to Wang resin or Merrifield resin via an ether linkage and used in heterogeneous catalysis by Martin-Matute et al.[132] This ligand was used in Cu(I) catalyzed asymmetric 1,3-dipolar cycloaddition of imines and N-phenylmaleimide. Among the catalysts, the Merrifield resin supported one showed better activity and up to 99% ee was obtained in many cases. The same ligand was also used in the enantioselective Pd catalyzed allylic substitution. It

was observed that, even if the yield was little lower compared to the homogeneous counterparts, the enantioselectivity was higher for the polymer-supported ligand. The recycling experiments failed because of the oxidation of the ligand. The structure of the ligand is shown in Figure 1-9.

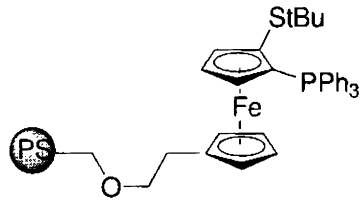


Figure 1-9. Polymer supported sulfenylphosphinoferrocene ligand

Oxidative conversion of ketones and alcohols using a polymer supported catalyst was studied by Yamamoto et al.[133] Various ketones were converted to the corresponding α-tosyloxyketones with *m*CPBA and *p*-toluenesulfonic acid in the presence of a catalytic amount of poly(4-iodostyrene). Moreover, secondary alcohols were directly converted to the corresponding α-tosyloxyketones using *m*CPBA and catalytic amounts of iodobenzene and potassium bromide, followed by treatment with *p*-toluenesulfonic acid in a one-pot manner. Both linear poly(4-iodostyrene) and macroporous crosslinked poly(-iodostyrene) were used and better results were obtained by the linear one. The catalysts were compared with the simple iodobenzene and the results showed that the polymer supported versions were less efficient and the efficiency was very low in the case of latter reaction.

A polymer supported triazole[134] prepared by Cu (I) catalyzed Huisgen 1,3-dipolar cycloaddition between trans-4-hydroxyproline and Merrifield type resin was used as highly efficient catalyst for α-aminoxylation of aldehydes and ketones by Font et al.[135] The enantioselectivity of the catalyst was so high that the product obtained in up to 99% ee. The catalyst was recycled three times with out considerable loss of yield and enantioselectivity.

Linear polystyrene supported sulphonamide [10-(4-perfluorobutylsulfonamino sulfonylphenyl)decyl polystyrene] was developed by Zhang et al.[136] A long alkyl chain separated the polymer support and the

catalytically active species. This strongly acidic catalyst performed well in esterfication of carboxylic acids in water. In contrast to other catalysts, no excess of alcohol was required and the reaction proceeded well with equimolar quantities of acids and alcohols. The authors compared the catalyst with Nafion NR50 and NKC-9, two conventional solid acid catalysts and found that the reported catalyst was much more active than the former in esterification under the same condition. The catalyst was recycled five times with out appreciable loss of activity.

Merrifield resin supported cinchona ammonium salts bearing 2′-fluorobenzene, 2′-cyanobenzene and 2′-*N*-oxypyridine groups were prepared and applied to the phase-transfer catalytic alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester for the enantioselective synthesis of α-amino acids by Shi et al.[137] Various α-amino acids were obtained in good yield (60-87%) and good enantiomeric excess (76–96%).

(Dimethylamino)methyl polystyrene supported CuI was used as an efficient and environmentally benign heterogeneous catalyst for the cyclization of propargyl alcohols with CO_2 to alkylidene cyclic carbonates under supercritical conditions by Jiang et. al.[138]

As this review has shown, a large number of supported ligands and corresponding metal complexes have been prepared and used as catalysts for synthetic organic chemistry along with many polymer supported phase transfer and organocatalyst. This is an area of growing interest due to the pressure from pharmaceutical and fine chemical industry because of the potential advantages the supported catalysts have.

1. 3. DENDRIMERS

Nanoscience is at the forefront of scientific and technological development and is the science of the 21st century. Nanochemistry occupies a place of choice in this discipline and can be regarded as the use of synthetic chemistry to make nanoscale building blocks of different size and shape, composition and surface structure, charge and functionality. These building

blocks may form, or can be used to form, even more sophisticated architectures having different properties and particular uses.[139]

Dendrimers, monodisperse nanosized polymeric molecules composed of a large number of perfectly branched monomers that emanate radially from a central core, can be considered as one of the most fascinating molecules arising from this area of research. Dendritic molecules are repeatedly branched species that are characterized by their structure perfection. The latter is based on the evaluation of both symmetry and polydispersity. They are considered as the fourth major macromolecular architecture after linear, cross-linked and branched polymers. The name comes from the Greek "δενδρον"/*dendron*, meaning "tree". The ability to easily tune the size, topology, molecular weight and consequently the properties of these nano-objects has led to their widespread use in a variety of applications from biology to material science, i.e. at the interface of many disciplines. Remarkably, their unique branched topologies lead to properties that differ frequently from those of linear polymers, thus exciting the interest and curiosity of thousands of researchers worldwide. Dendritic architecture is one of the most pervasive topologies observed in nature at the macro- and microdimensional-length scales. At the nanoscale (molecular level), there are relatively few natural examples of this architecture. Most notable are glycogen and amylopectin, the two proteins used for energy storage in many higher organisms. This also adds curiosity to these molecules as a totally new synthetic molecular architecture that is new to the nanoworld, but has so many potentials.[140]

1. 3. 1. Historical Background

The history of dendrimers goes back to 1952 when Flory first made theoretical prediction of the possibility of existence of such architecture among polymers.[141, 142] But it took another twenty five years for the chemists to synthesize such a molecule successfully and the first report on the synthesis of dendrimers was published by Vogtle[143] who reported the synthesis of molecules with novel architecture in his primary communication and he represented these

molecules as 'cascade' molecules. They were prepared by exhaustive Michael addition of acrylonitrile to an amine core followed by reduction of the nitrile groups to amino groups. Later Denkewalter et. al. reported the synthesis of poly(L-lysine) dendrimers using the techniques of peptide chemistry.[144-146] But scientific community failed to recognize the potential of these molecules and this novel molecular systems remained unnoticed for few more years. Dendrimers became a hot topic in science after the discovery of poly(amidoamine) dendrimers (PAMAM) by Tomalia et. al.[147,148] These dendrimers were prepared by exhaustive Michael addition of methyl acrylate to ammonia or a diamine followed by the amidation of the resulting ester with an excess amount of ethylene diamine. Repetition of these two steps led to higher generation dendrimers. The synthesis of polymers with up to 10 so called generations have been reported with yields of the order of 98-100% at every step. Around the same time, Newkome and co-workers started developing a series of highly branched molecular components, where in each layer (or generation) had a different constitution. Branching was derived from tetrahedral carbon atoms by using units such as pentaerythritol- leading to very compact arborol structures.[149] The systems developed by Newkome were initially known as arborols where as Tomalia's molecules were called dendrimers and the latter term became popular because of their structural features. The era of dendrimers slowly started to flourish. Few years later, Hawker and Frechet reported the synthesis of polyarylether dendrimers by a novel synthetic strategy which is now a days known as the convergent method.[150,151] Another important type of dendrimer which gathered wide spread attention was also reported at this time and they are the phenyl acetylene dendrimers.[152,153] Another historical stage in dendrimer chemistry was the reinvention of poly(propyl imine) dendrimers by two different research groups simultaneously. Mulhaupt[154] reported the synthesis of these dendrimers by Michael addition of acrylonitrile to ethylene diamine followed by reduction of the nitrile groups to primary amines with hydrogen in the presence of Raney Ni catalyst while Meijer[155] reported the synthesis of the same type of dendrimers by Michael addition of acrylonitrile to

1,4-diaminobutane in water followed by reduction of nitrile groups by hydrogen in the presence of Raney Co catalyst. These two methods are well known for their utility in large-scale synthesis of PPI dendrimers. Another important class of dendrimers is peptide dendrimers and these molecules are expected to find their own role in medicine and biology in future.[156] In addition to these six classes of dendrimers which are synthesized to higher generations and found wide spread applications, there is an estimate amount of one hundred different dendrimers reported but many of them only have negligible role today.

1. 3. 2. The Dendritic Structure

Dendrimers are highly ordered, regularly branched, globular macromolecules prepared by stepwise iterative approach. A higher generation dendrimer can be considered as a three dimensional sphere with nanoscale dimensions. Their structure is divided into three distinct architectural regions: (i) a core or focal moiety, (ii) layers of branched repeat units emanating from this core and (iii) end groups on the outer layer of repeat units as shown in Figure 1-10.

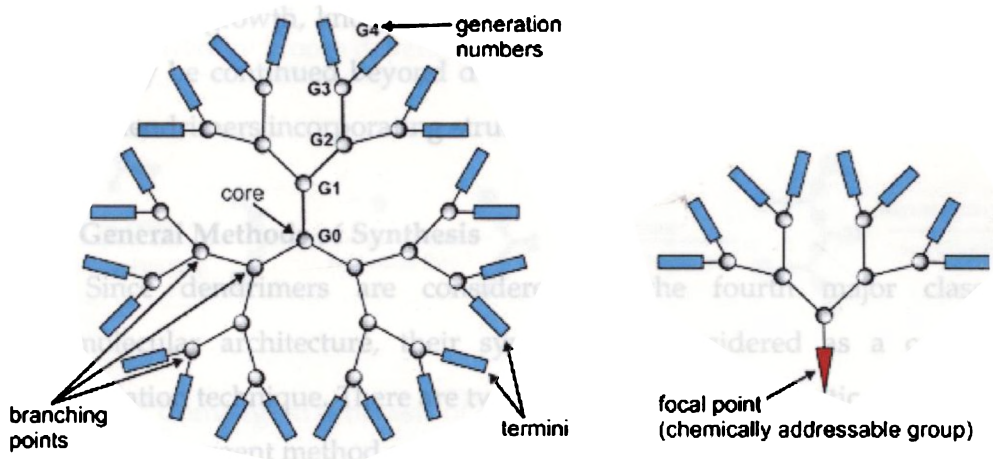


Figure 1-10. The dendritic structure

At least three characteristic features of dendrimers are in sharp contrast to those of traditional linear polymers because of their characteristic structure. (i)

A dendrimer can be isolated as an essentially monodisperse single compound, unlike most linear polymers whose synthesis affords a range of molecular species differing in molecular weight (MW). Size monodispersity results from a well-designed iterative synthesis that allows reactions to be driven to completion, side-reactions to be avoided, and in some cases, the dendritic products to be purified at intermediate steps during their growth. (ii) As their molecular weight increases, the properties of dendrimers (e.g., solubility, chemical reactivity, glass transition temperature) are dominated by the nature of the end groups. Unlike linear polymers that contain only two end groups, the number of dendrimer end groups increases exponentially with generation, and therefore the end-groups frequently become the primary interface between the dendrimer and its environment. (iii) In contrast to linear polymer growth that, theoretically, can continue ad infinitum barring solubility issues, dendritic growth is mathematically limited. During growth of a dendrimer, the number of monomer units increases exponentially with generation, while the volume available to the dendrimer only grows proportionally to the cube of its radius. As a result of this physical limitation, dendritic molecules develop a more globular conformation as generation increases. At a certain generation, a steric limit to regular growth, known as the De Gennes dense packing[157] is reached. Growth may be continued beyond de Gennes dense packing, but this leads to irregular dendrimers incorporating structural flaws.

1. 3. 3. General Methods of Synthesis

Since dendrimers are considered as the fourth major class of macromolecular architecture, their synthesis is considered as a controlled polymerization technique. There are two widely accepted synthetic methods and they are the divergent method and convergent method.[158]

In divergent method, the synthesis starts from a core, which is generally a molecule having three or four reactive sites like ammonia or ethylene diamine. In this method, molecules are added to a core with a fixed number of reactive sites. The resulting molecule contains surface groups which will be activated by

a chemical reaction so that they will be ready for further growth. The first step will be repeated so that the number of surface groups will be multiplied. Repetition of the above steps will finally give a dendrimer with fixed molecular weight of required generation. Divergent method was pioneered by Tomalia and Newkome. This method can be represented as in Figure 1-11.

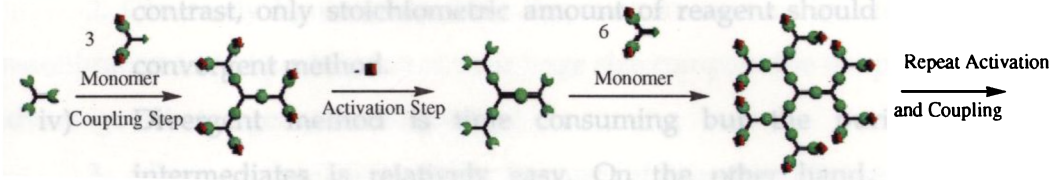


Figure 1-11. Divergent synthesis of dendrimers

In convergent method, small dendrons were prepared and purified initially to get molecules with a reactive group at the centre known as focal point and the periphery of the molecules will be unreactive under the set of conditions used. After preparing the small dendrons, they were attached to a core molecule with three or four reaction centers by using a chemical reaction. This will give dendrimers with very narrow molecular weight distribution (Figure 1-12). Frechet followed by Moore developed this method.

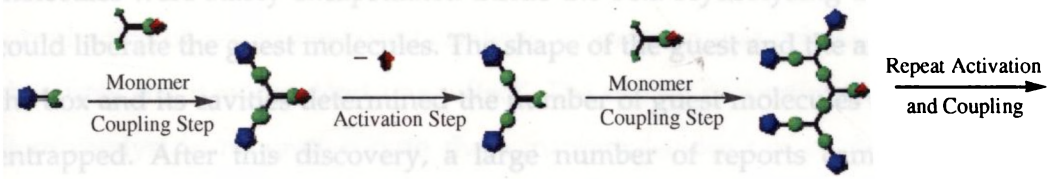


Figure 1-12. Convergent synthesis of dendrimers

On comparing these two methods some merits and demerits for each can be found and they are summarized below.

i) Divergent approach allows the synthesis of very large dendrimers (M.W > 100,000). Convergent method is used for dendrimers with

lower molecular weight but with accurate placement of functional groups.

ii) In convergent method, unwanted reactions and incomplete reactions are less; but in divergent method, the problem of incomplete reactions is high.

iii) Large excess of reagents can be used in divergent approach. In contrast, only stoichiometric amount of reagent should be used in convergent method.

iv) Divergent method is time consuming but the purification of intermediates is relatively easy. On the other hand, convergent method is fast but all the dendrons used for this purpose should be extensivly purified for getting uniform weight distribution.

1. 3. 4. Applications of Dendrimers

Scientific community recognized the potential of dendrimers after the discovery of 'the dendritic box' by Meijer and coworkers in 1994. [159,160] Meijer and co-workers trapped small molecules like rose bengal or p-nitrobenzoic acid inside the 'dendritic box' of poly(propylene imine) dendrimer with 64 branches on the periphery. A shell was formed on the surface of the dendrimer by the reaction of the terminal amines with an amino acid (L-phenylalanine) and guest molecules were stably encapsulated inside the box. Hydrolysing the outer shell could liberate the guest molecules. The shape of the guest and the architecture of the box and its cavities determined the number of guest molecules that could be entrapped. After this discovery, a large number of reports came describing various applications of dendrimers in chemistry, biology and material science.[161-175]

1. 3. 5. Dendrimers in Catalysis

Among the two area of research consecrated by dendrimers, the most vital one is catalysis and the other is biotechnology and medicine. Dendrimers are considered to build the gap between homogeneous catalysts and

heterogeneous catalysts and they show many advantages over conventional catalysts.[176] In principle, dendritic catalysts can provide systems that

1. Show the kinetic behavior and thus the activity and selectivity of a conventional homogeneous catalyst. Catalysts supported on heterogeneous systems show diminished activity compared to the homogeneous analogues, which is because of reduced accessibility.

2. Can easily be removed from the reaction mixture by membrane or nanofiltration technique because of their large size compared to the products (an advantage of heterogeneous catalysts).

3. Allow mechanistic studies, because of the monodisperse, uniform character of their catalytic sites and the symmetry of the molecules (an advantage of homogeneous catalysts).

4. Allow fine-tuning of their catalytic centers by precise ligand design (an advantage of homogeneous catalysts) and

5. Require relatively low metal loading (an advantage of homogeneous catalysts over heterogeneous catalysts).

The advantages of dendrimer catalysts arise from their peculiar structure and the properties arise due to this structure. Since dendrimers generally contain three distinguishable parts in their structure, one can distinguish periphery functionalized, core functionalized and focal point functionalized catalytic systems. All these systems show their own activity and selectivity. After the introduction of dendrimer-based catalysts, a new term was coined in dendrimer chemistry and it is 'the dendrimer effect'. The special properties that may result from catalyst incorporation onto these macromolecules can be described as a "dendrimer effect." This term has been generally invoked in the literature to explain phenomena that arise as the generation of dendrimer increases.[177] This may be positive or negative depending on the dendrimer platform, the placement of catalysts, the reaction conditions and the mechanism of reaction.

The biggest stumbling block in the wide spread application of dendrimers in catalysis even in the midst of all these advantages is the lengthy and complicated synthetic procedure of dendrimer based catalysts. Any attempt

to create a perfect harmony between these advantages and disadvantages are valuable in dendrimer research.

1. 3. 5. a. Periphery Functionalized Dendrimers in Catalysis

Periphery-functionalized dendrimers have their ligand systems, and thus the metal complexes, at the surface of the dendrimer. The catalytic sites will be directly available for the substrate, in contrast to the other two systems, in which the substrate has to penetrate the dendrimer prior to reaction. This accessibility allows reaction rates that are comparable with homogeneous systems. On the other hand, the periphery functionalized systems contain multiple reaction sites and ligands, which results in extremely high local catalyst and ligand concentration. In reactions where excess ligand is required to stabilize the catalyst, this local concentration effect can indeed result in stable systems. Furthermore, if a reaction proceeds by a bimetallic mechanism, the dendritic catalysts might show better performance than the monomeric species. Periphery functionalized dendrimer catalyst can be represented as in Figure 1-13.

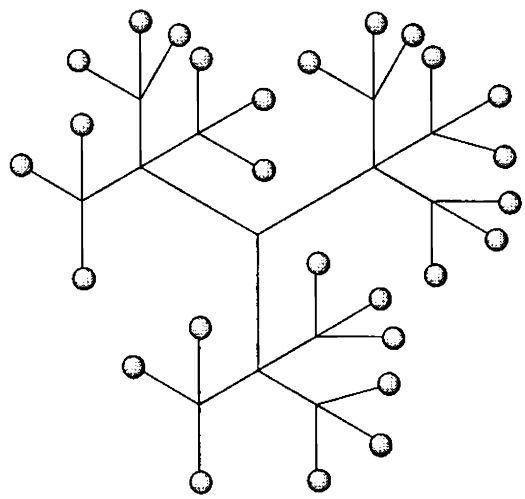
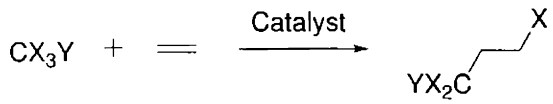


Figure 1-13. Schematic structure of periphery functionalized dendrimer

First example of a dendrimer-based catalyst was reported by Keijsper and co-workers.[178] A hexaphosphine catalyst containing a benzene core was used in the palladium catalyzed polyketone formation by alternating polymerization

of CO and alkene. By using this catalyst, it was observed that, fouling was reduced to 3% compared to the 50% given by monomeric version under similar conditions. A possible explanation is that, in the dendritic catalysts, the palladium remains attached to the surface of the growing polymer and do not go into solution during the chain-transfer reaction (which may lead to fouling). This is the first example of a dendrimer effect observed in catalysis.

Another classical example of dendritic catalyst was reported by Knapen *et al* who functionalized generation zero and one carbosilane dendrimers with up to twelve pincer like NCN-nickel(II) groups.[179] These dendrimers were applied as catalysts for the Kharasch addition of CX to alkene (Figure 1-14). The catalytic activity of the dendritic catalysts was slightly lower than that of the monomeric parent compound. A negative dendrimer effect was observed and the activity decreased with increase in generation of the catalyst.



where catalyst is

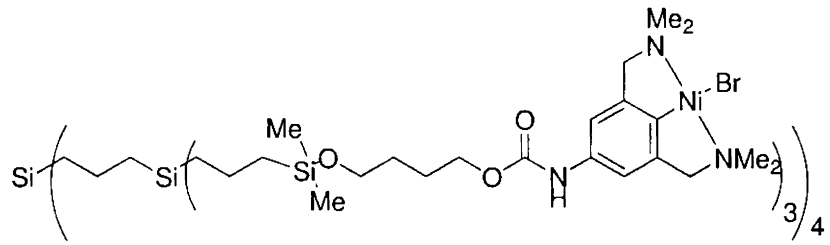


Figure 1-14. Carbosilane dendrimers carrying pincer like NCN-nickel(II) groups catalyzed Kharash addition

Molecular modeling showed that the accessibility of the catalytic sites was similar for dendrimers and monomer, and it was proposed that the lower rates were because of the high local concentration of nickel centers and interaction between the neighboring Ni(II) and NI(III) sites. A similar effect was observed by Miedaner et al. in palladium-functionalized dendrimers when used as catalysts in the electrochemical reduction of CO_2 to CO.[180]

Catalyst for carbon-carbon bond formation is another area of interest in which periphery functionalized dendrimers found wide spread applications. Several groups have prepared systems that were functionalized with phosphine ligands at the periphery of the dendrimer. Commercially available DAB dendrimers were equipped with diphenylphosphane groups at the periphery by Reetz *et al* by a double phosphination of the amines with diphenylphosphine and formaldehyde.[181] The palladium complexes of these dendrimers were prepared and used as catalysts in the Heck reaction of bromobenzene and styrene to form stilbene (Figure 1-15). Interestingly the dendrimers showed larger turnover number than the monomeric parent compounds, which was ascribed to the higher thermal stability of the dendritic palladium complexes. No palladium black formation was observed when dendrimer catalysts were used. After the reaction, the dendritic catalyst was completely precipitated upon addition of diethyl ether. In this way, the catalysts were recycled and a second catalytic run gave similar results with out loss of activity.

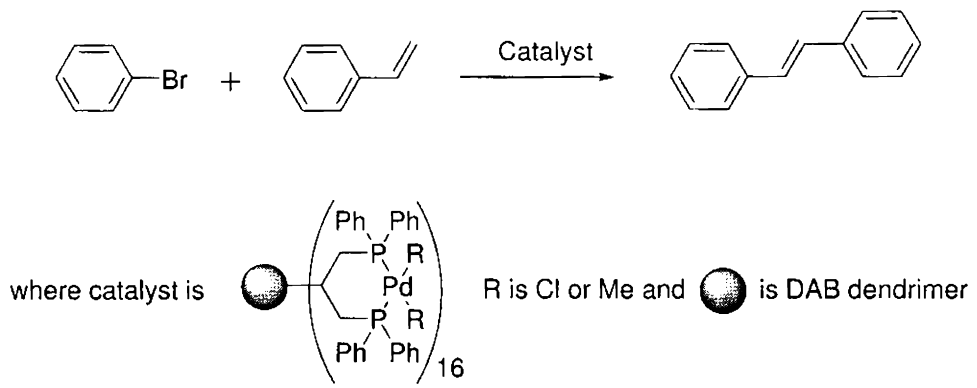


Figure 1-15. Heck reaction catalyzed by palladium complexes of DAB dendrimer with diphenylphosphine groups at the periphery.

Brinkmann and co-workers also used the palladium-dendrimer complex described above as catalyst in allylic substitution.[182] But the catalyst was not stable under the reaction conditions tested and palladium leaching was observed. The catalyst showed better stability with higher generation dendrimer and fourth generation dendrimer-palladium complex showed the highest activity.

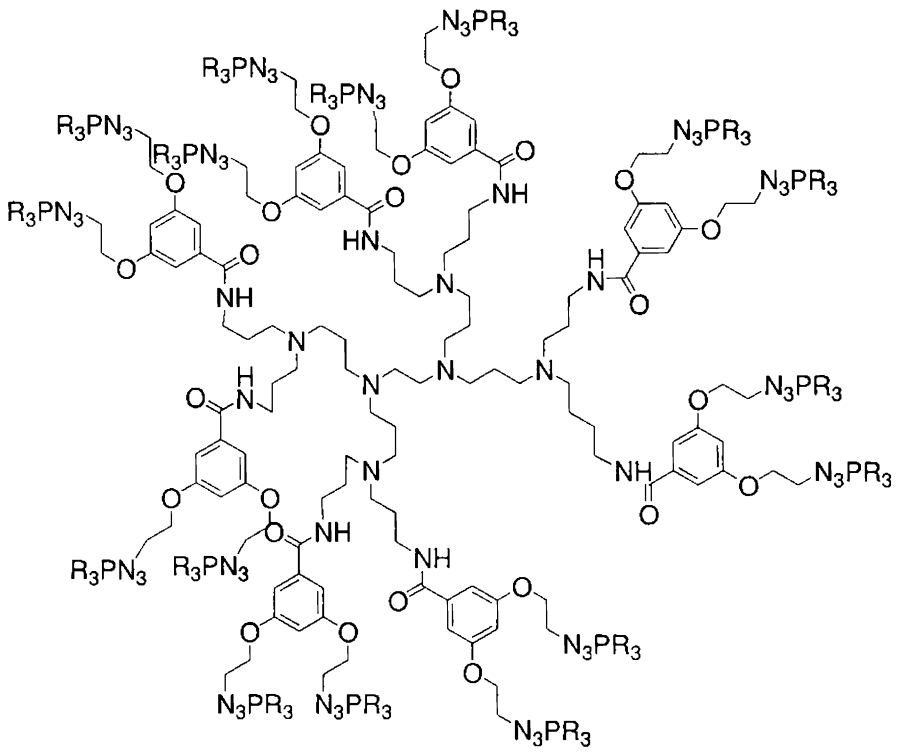
De Groot *et al* prepared a similar catalyst but with a different dendritic backbone and in this case, the DAB dendrimer was replaced by a carbosilane dendrimer. But this catalyst too did not perform well in allylic substitution and metal leeching was observed in considerable amount.[183]

Later, Astruc and co-workers showed that palladium complexes of DAB dendrimer containing bis-phosphines on the periphery are highly efficient catalysts in Sonogashira coupling between aryl halides and terminal alkynes.[184-186] The two catalysts developed were so effective that the reaction proceeded with out the presence of copper whereas conventional processes required both palladium and copper to catalyze the reaction effectively. In addition, the catalyst was effective even at –40 °C. But a negative dendrimer effect was observed and the rate of reaction decreased with increase in dendritic generation.

Another interesting example of dendrimer catalyst used for carbon-carbon bond formation was that reported by Sarkar et al.[187] A second generation DAB dendrimer surface functionalized with highly basic bicyclic azido phosphine moiety was used as base catalyst for Michael addition and Henry reaction. The catalyst showed good performance and was considered due to the co-operative effect of sixteen azido phoshine units in each dendrimer. The structure of the catalyst is shown in the Figure 1-16. This study proved the ability of dendrimers to act as organocatalysts also, in addition to their role as multidentate ligands in metal complex based catalysts.

A classical example of dendrimer catalyst is the one reported by Mizugaki et al.[188] A third generation DAB dendrimer was funtionalized with diphenylphosphane and palladium complex of this dendrimer was used as catalyst in the hydrogenation of cyclopentadiene. The catalyst showed better activity than the corresponding monomeric complex and soluble polystyrene supported complex. The dendrimer backbone was proposed to act as a base to capture HCl, there by accelerating the formation of catalytically active (diphosphine)PdHCl species. Gade and Findeis reported another dendrimer catalyst in which tripodal phosphane ligands were attached to a dendrimer

periphery and rhodium complex of this dendrimer was used as catalyst in the hydrogenation of alkenes in THF.[189]



where R_3P is $P(iBuNCH_2CH_2)_3$

Figure 1-16. DAB dendrimer surface functionalized with highly basic bicyclic azido phosphine moiety.

Many dendritic catalysts for polymerization were reported by various groups and the important ones are described here. Seyferth et al. synthesized carbosilane dendrimers with 4, 8, and 12 peripheral zirconocene, hafnocene and titanocene groups.[190,191] The zirconocene containing dendrimer was used as catalyst in the methylaluminoxane (MAO) activated olefin copolymerization and in silane polymerization. The active form of the metallocene catalyst used for α-olefins was cationic and was typically generated by a co-catalyst. Industrially, this is usually methylaluminoxane or perfluorophenylborane. The interaction between the ion pair affects the overall activity, steroregularity, chain transfer, termination rate and lifetime of the metallocene catalyst. Less nucleophilic

counter ions are particularly desirable; this has, in the past, been achieved through charge delocalization or steric shielding.

However, in their work, Mager and co-workers achieved this through steric crowding at the surface of a peripherally modified carbosilane dendrimer.[192] Co-catalysts G0 to G2 were synthesized with 4, 12, and 36 alkyl-tris- (pentafluorophenyl)borates at the periphery (Figure 1-17). When employed with $[(Ind)_2ZrMe_2]$ metallocene co-catalysts, these non-coordinating dendrimer polyanions were highly active in ethylene polymerization and copolymerization with propylene or 1-hexene, although activity was not generation-dependent. Unlike non-coordinating small molecule anions resulting from $B(C_6F_5)_3$, the dendrimer polyanions gave high activities even in aliphatic solvents, with no apparent loss in activity at reaction times greater than 40 min. This positive dendrimer effect was thought to arise from the specific and unique interaction between the active cationic metallocene co-catalyst and the crowded anionic surface of the dendrimer.

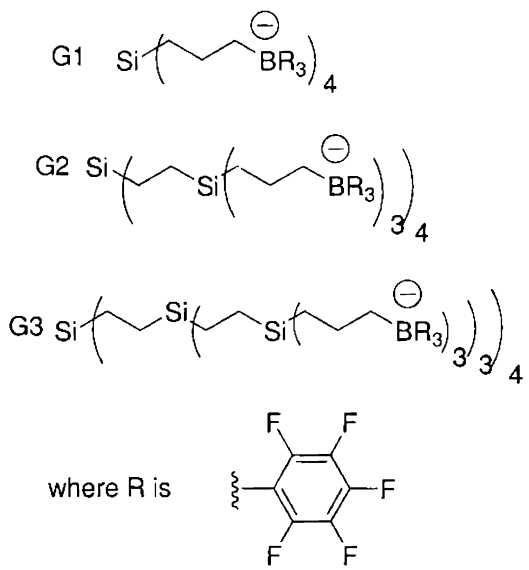


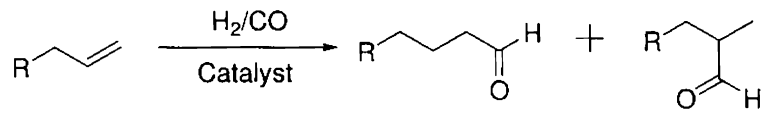
Figure 1-17. Polycarbosilane dendrimers used as polymerization catalysts.

In a similar study relating the nature of the interaction between a dendritic polymerization catalyst with a conventional anionic co-catalyst, Zheng and coworkers prepared first and second generation carbosilane

metallodendrimers bearing bis(imino)pyridyl iron(II) catalyst precursors at their periphery.[193] After activation with modified methylaluminoxane (m-MAO) at a ratio of Al/Fe>1200, the rate of ethylene polymerization for either of the multivalent dendrimer catalyst was comparable to the parent Fe catalyst. However, at lower Al/Fe ratios (<1000), the activities of both dendrimer catalysts were superior to the small molecule catalyst. In addition, the molecular weight and the melting temperature (Tm) of the polyethylene obtained increased with the generation of the dendrimer catalyst: Tm=127.9, 133.9 and 134.1 8 °C for the parent, G1 and G2 catalysts, respectively. Again, this positive dendrimer effect was generally thought to involve a fundamentally different interaction of the dendritic periphery with the polymeric counter ion derived from m-MAO than was experienced with the small molecule catalyst system. Benito et al. synthesized a series of carbosilane dendrimers with surface Ni(II)pyridylimines.[194] These were used as catalysts in the polymerization of α-olefins. They reported a strong generation dependence on the molecular weight and topology of the final product. With an increase in generation of the dendrimer catalyst, there was a strong preference for oligomerization and hence chain transfer, over polymerization.

Cole-Hamilton and coworkers showed that Rh-phosphine-terminated dendrimers based on polyhedral silsesquioxane cores with 16 PPh_2 arms gave much higher linear selectivities (14: 1) than their small molecular analogues (3.4: 1) in the hydroformylation of cyclooct-1-ene.[195,196] The scheme of the reaction and the structure of the catalyst used are given in Figure 1-18.

The peptide dendrimers for ester hydrolysis described by Delort show a positive dendrimer effect.[197] Four generations of a dendrimer containing His-Ser in all branches were synthesized by the techniques of solid phase peptide synthesis and after cleavage from the support these dendrimers were screened for their catalytic activity in a ninety-six well plate set up. It was observed that the rate of hydrolysis of pyrene trisulfonate esters increased with increase in generation. The dendrimers displayed enzyme like Michaelis-Menten kinetics.



where catalyst is Rh complex of

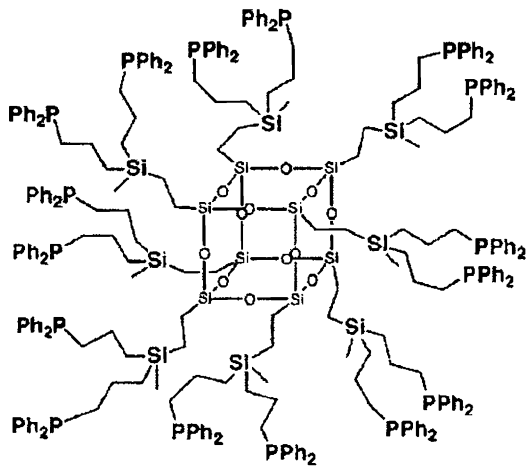


Figure 1-18. Hydroformylation catalyzed by Rh complex of phosphine-terminated dendrimers based on polyhedral silsesquioxane cores.

Two series of dendritic compounds functionalized at the periphery with polyoxometalate (POM) units were synthesized using two synthetic strategies by Nlate et al.[198] The first series involved the [CpFe]+- induced functionalization of polymethylarenes, leading to dendrimers in which the dendronic tripod was directly bonded to the arene core. In the second procedure, dendrimers with a spacer group of six atoms between the arene core and the tripod units were synthesized through a coupling reaction between the phenol dendron and bromobenzyl derivatives. These polyallyl dendrimers were functionalized at the periphery to give quaternary poly-ammonium salts. Reactions of the latter with $H_3PW_{12}O_{40}$ in the presence of hydrogen peroxide led to dendrimers containing $\{PO_4[WO(O_2)_2]_4\}^{3-}$ species at the periphery. These compounds are efficient catalysts for the selective oxidation of alkenes, sulfides and alcohols in an aqueous–$CDCl_3$ biphasic system, using hydrogen peroxide as the primary oxidant. The structures of these dendrimers are given in Figure 1-19.

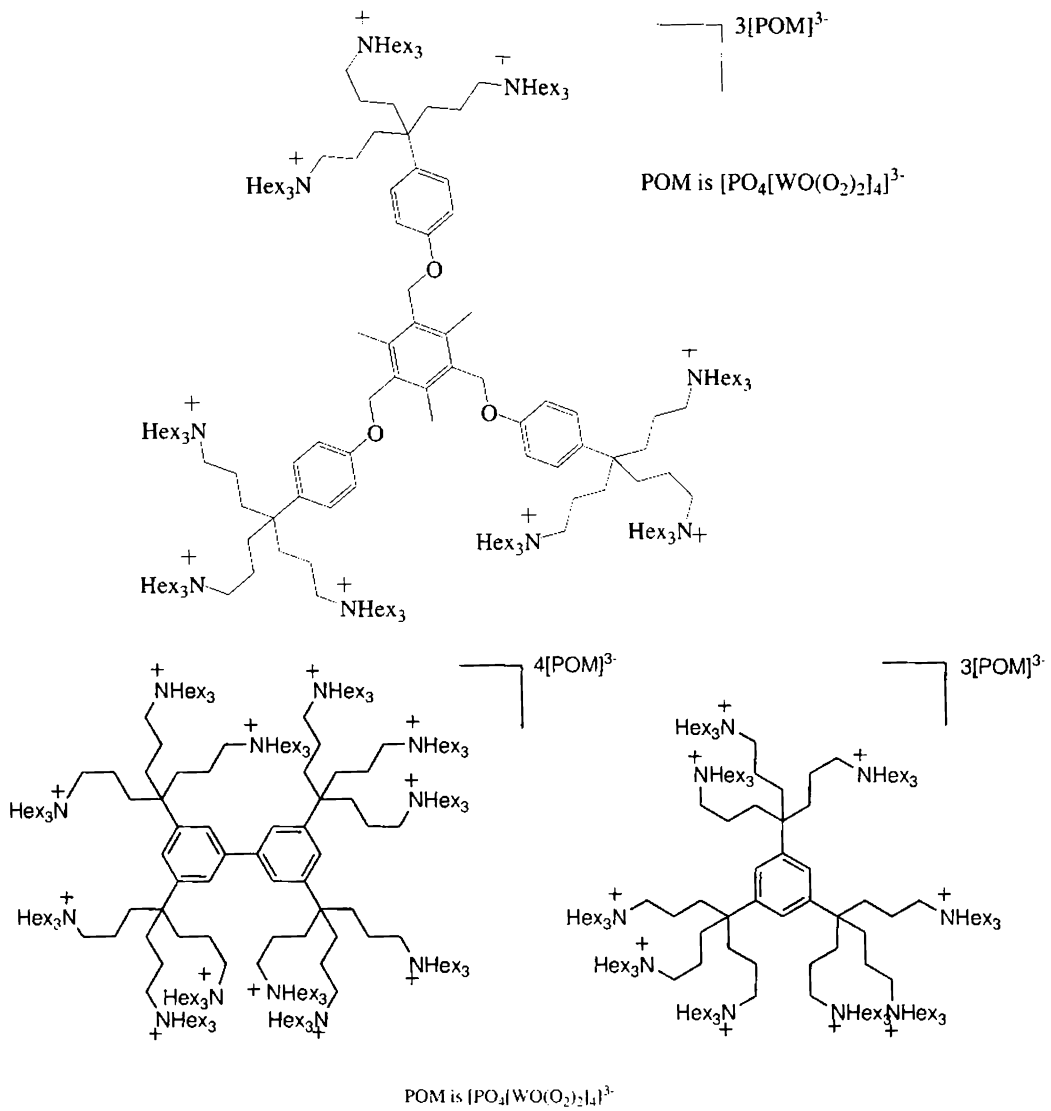


Figure 1-19. Dendrimers functionalized at the periphery with polyoxometalate (POM) units.

Rodriguez and coworkers explored the catalytic properties of a series of carbosilane dendrimer containing the P-stereogenic phosphine fragments [P(2-biphenylyl)PhCH$_2$] at the periphery in the hydrovinylation of styrene in scCO$_2$.[199] The reaction proceeded with good selectivity and enantiomeric excess. A negative dendrimer effect was observed and the monomeric species gave the better result followed by lower generation dendrimers.

Recently Niu et al. reported the preparation of few C3-symmetric 1,2,3-triazole linked dendrimers by Cu(I) catalyzed azide-alkyne click chemistry between arylether dendrimers carrying terminal alkynes on the periphery and ((2R,4S)-4-azidopyrrolidine-2-yl)diphenylmethanol (Figure 1-20).[200] The dendrimer carrying chiral 1,2,3-triazole on the periphery were used as organocatalysts for the asymmetric borane reduction of prochiral ketones. The catalysts show good activity and the product were isolated in good to excellent yields and good enantioselectivity.

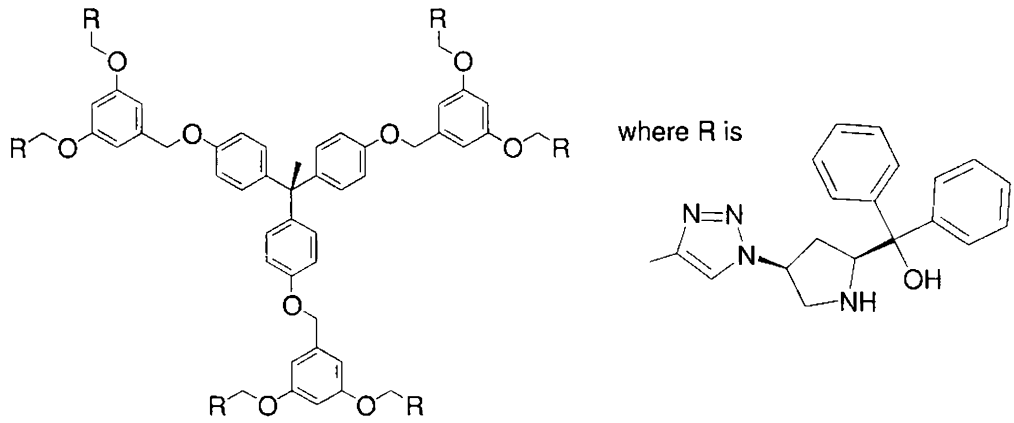


Figure 1-20. C3-symmetric 1,2,3-triazole linked dendrimers used as organocatalysts for the asymmetric borane reduction of prochiral ketones.

1. 3. 5. b. Core or Focal Point Functionalized Dendrimers

In core or focal point functionalized dendrimers the catalytic species is placed either in the core of the dendrimer or in the focal point of the dendrimer. A schematic representation of these two conditions is given in Figure 1-21.

Core functionalized Focal point functionalized

Figure 1-21. Schematic representation of core and focal point functionalized dendrimers.

In core or focal point functionalized dendrimers, the catalyst could benefit especially from the site isolation created by the dendritic environment.[176,177] For reactions that are deactivated by excess ligand or in cases in which bimetallic deactivation mechanism is operative, core-functionalized systems can specifically prevent such deactivation pathway, whereas periphery functionalized systems might suffer from relative low activity. Core functionalized dendrimers may benefit from the local catalyst environment created by the dendrimer. Effect of solvation of the substrate during the penetration of the dendrimer is another important factor. Another significant difference between core and periphery functionalized dendrimers is the molecular weight per catalytic site. Much higher costs will be involved in the application of core-functionalized systems and application can also be limited by the solubility of the system. On the other hand, solubility of the core-functionalized dendritic catalyst can be tuned by changing the end groups.

The first example of a catalytic reaction at the core of the dendrimer was provided by Gitsov et al. using dendritic alcoholates as macro-initiatores for anionic ring opening polymerization of ε-caprolactone.[201] The structure of the dendrimer catalyst and reaction schemes are given in Figure 1-22 and 1-23.

The dendritic catalyst shown above (Figure 1-23 A) exhibited high catalytic activity compared to conventional alkali metal alcoholates used for the polymerization of ε-caprolactone. The G4 alcoholate acted as a highly effective catalyst producing high M_w polymers with a narrow M_w distribution of 1.07. The catalysts showed a positive dendrimer effect and the best results were given by G4 dendrimer. G1 dendrimer gave only low molecular weight oligomers. The explanation for this behavior is that the large dendrimers prevent termination of the polymerization by shielding the growing tip from reaction with a chain of another growing tip.

Similarly, dendritic wedges were designed for use in the synthesis of living polymers and living block copolymers by controlled radical polymerization.[202] A nitroxyl radical was attached to the focal point of G1 to G3 aryl ether dendrimers (figure 1-23 B). In polymerization reaction, low

polydispersities were obtained using the high generation dendrimers because of the irreversible release of the growing chains and slow recombination. Unfortunately, insolubility of the polymer –dendrimer complexes limited the growth of the chains.

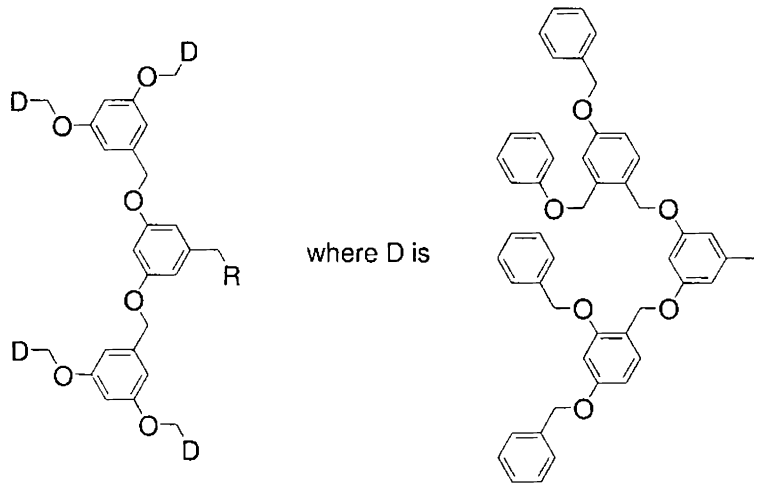


Figure 1-22. Dendritic alcoholate macro-initiators for anionic ring opening polymerization of ε-caprolactone.

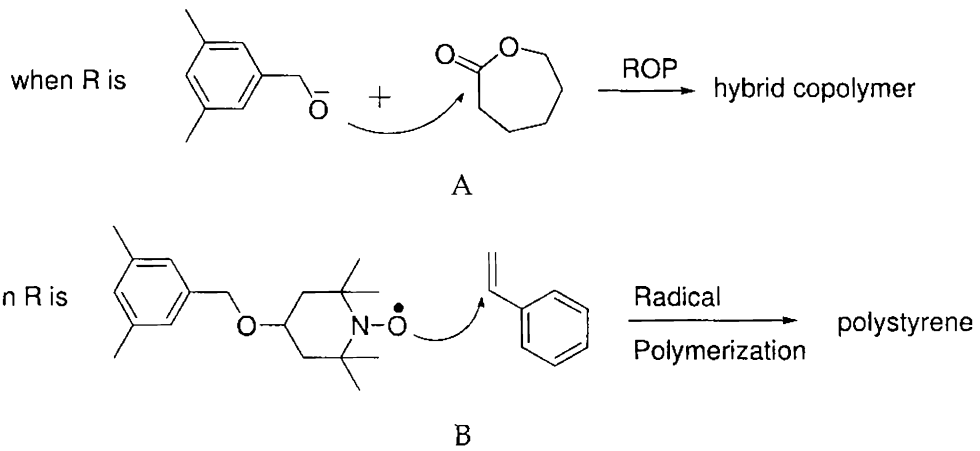


Figure 1-23. Ring opening polymerization of ε-caprolactone catalyzed by dendritic alcoholate macro-initiators

Chow et al. reported the synthesis of a series of poly(alkyl aryl ether) dendrons (G0-G3) functionalized at the focal point with dendritic biz(oxazoline) ligands.[203,204] Cu(II) complexes of these dendrimers catalyzed the Diels- Alder reaction between cyclopentadiene and N-2-butenoyl-2-oxazolidinone (Figure 1-24). A detailed study revealed that the reaction followed enzyme like Michaelis-

Menten kinetics. A reversible formation of the copper-dienophile complex is followed by the rate limiting conversion into the Diels-Alder adducts. The association constants of the catalyst-dienophile complex decreased slightly with the higher generation dendrimer. The G0-G2 systems showed almost similar activity, but the activity dropped dramatically in the case of the G3 dendrimer systems. Upon complexation of the dienophile at the focal point, it was observed that, the geometry of the metal center was changed. This resulted in an increase in steric repulsion between the dendritic wedges, which was more pronounced for the larger systems, and this resulted in the drop in activity.

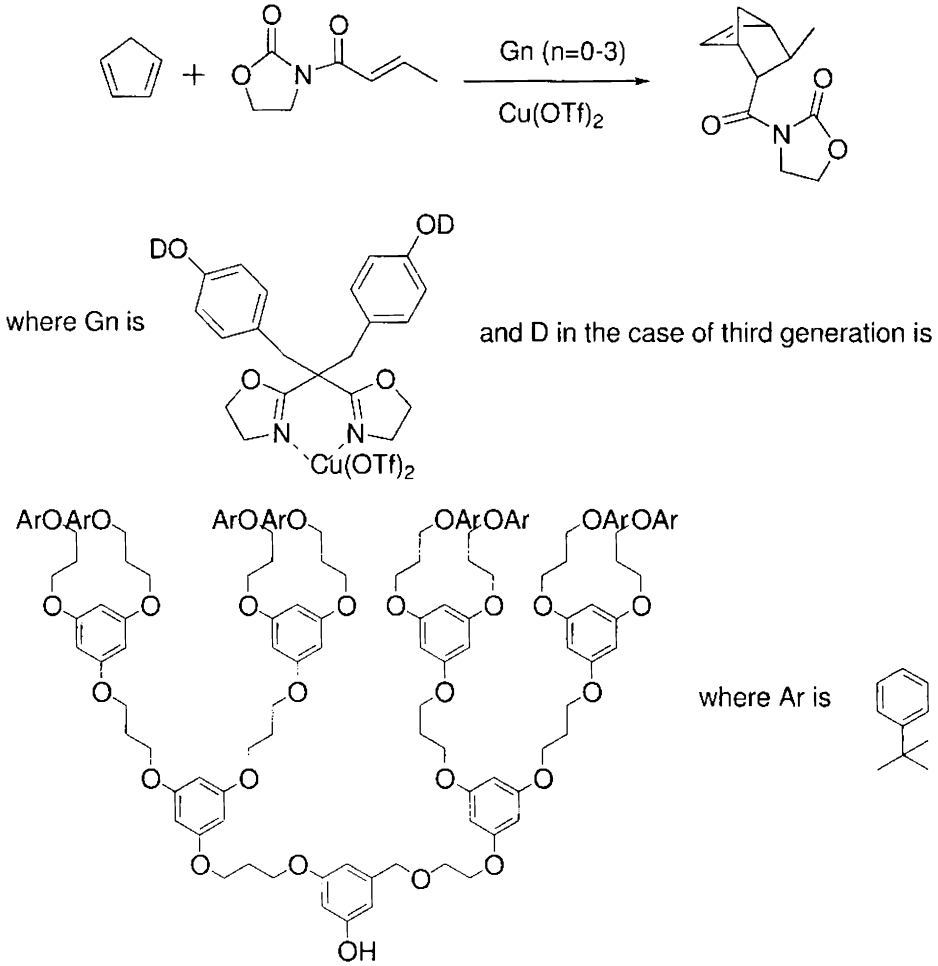


Figure 1-24. Diels- Alder reaction catalyzed by Cu(II) complexes poly(alkyl aryl ether) dendron functionalized at the focal point with dendritic biz(oxazoline) ligands.

Introduction of dendritic wedges on metalloporphyrins resulted in core functionalized dendrimers in which the porphyrin unit was shielded from the bulk solution. Bhyrappa et al. used steric shielding of the porphyrin units to establish regio and shape selective catalysis.[205,206] Eight bulky G1 and G2 poly(aryl ester) dendrons were connected to the porphyrin core to give the manganese(III) porphyrin complex (Figure 1-25). These complexes were used as catalysts in epoxidation and it was observed that they showed greater preference for the least hindered double bond than less sterically hindered porphyrins do.

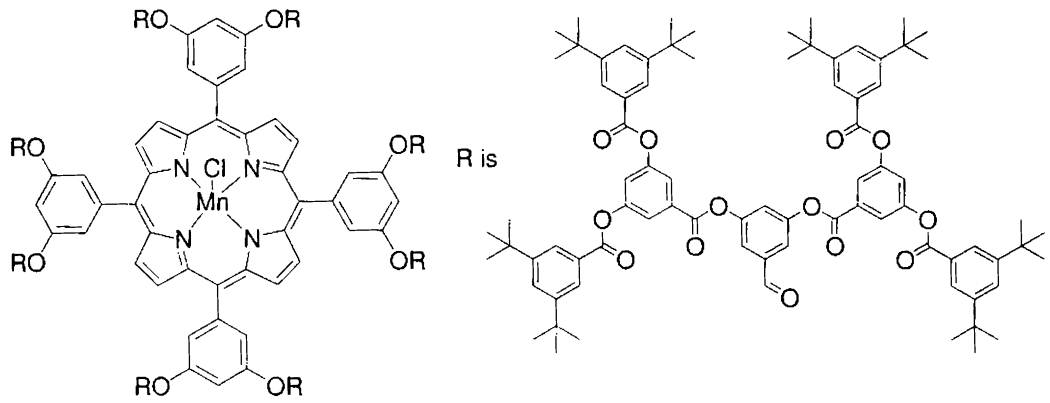
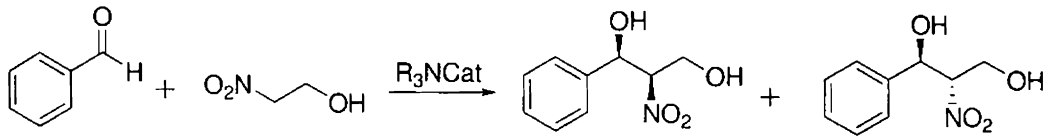


Figure 1-25. Dendritic metalloporphyrins

Another important core functionalized dendrimer catalyst to mention is the tertiary amine catalyst prepared by Zubia et al.[207] In their work, a single tertiary amine catalyst for the Henry reaction was encapsulated by different generations of aryl ether dendrimers (Figure 1-26). It was shown that the catalytic ability of a single active site in this reaction decreased both with higher generation and with higher branching multiplicity.

Due to their strong bond with metals, N-heterocyclic carbene (NHC) ligands are very desirable and have been shown to be extremely versatile in their applicability to a variety of organic transformations.[208] Fujihara et al. have reported the use of dendritic NHC ligands in the Rh(I)-catalyzed hydrosilylation of acetophenone and cyclohexanone (Figure 1-27).[209] A positive dendrimer effect resulting in an increase in the yield with increasing generation of the RhI

complex was observed. This effect was attributed to the folding of the dendrimer around the active site that led to greater stability and hence greater overall turnover during the course of the reaction.



where catalyst are first(**1**), second(**2**) and third(**3**) generation aryl ether dendrimers

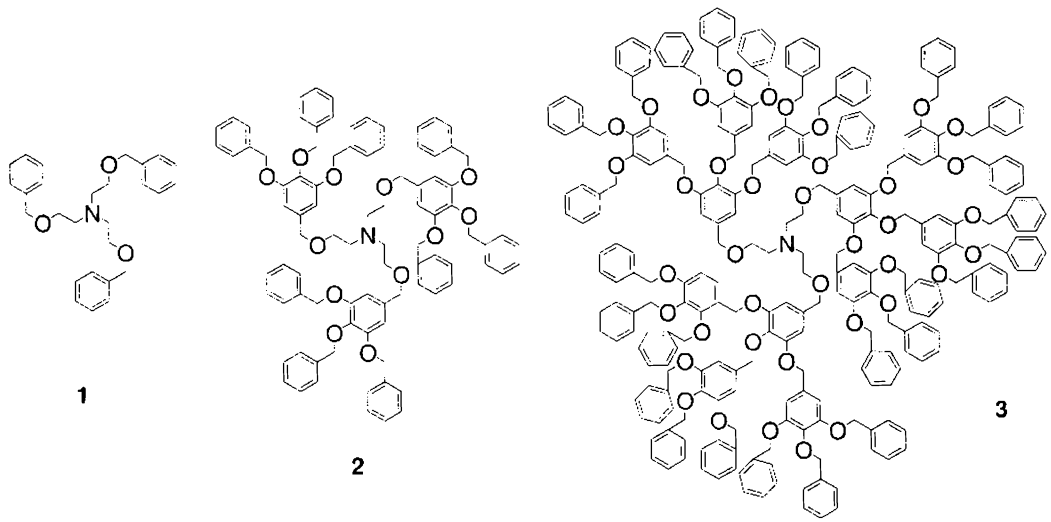
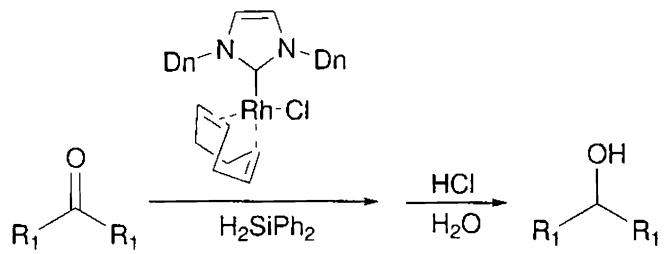


Figure 1-26. Henry reaction catalyzed by aryl ether dendrimers with tertiary amine core



where Dn is aryl ether dendrimer

Figure 1-27. Hydrosilylation of ketones catalyzed by Rh complex of dendritic NHC ligand

Nickel complexes bearing P,O ligands, such as o-phenylphosphinophenols, have been used widely in industry, for example, in the Shell higher olefin process.[210]

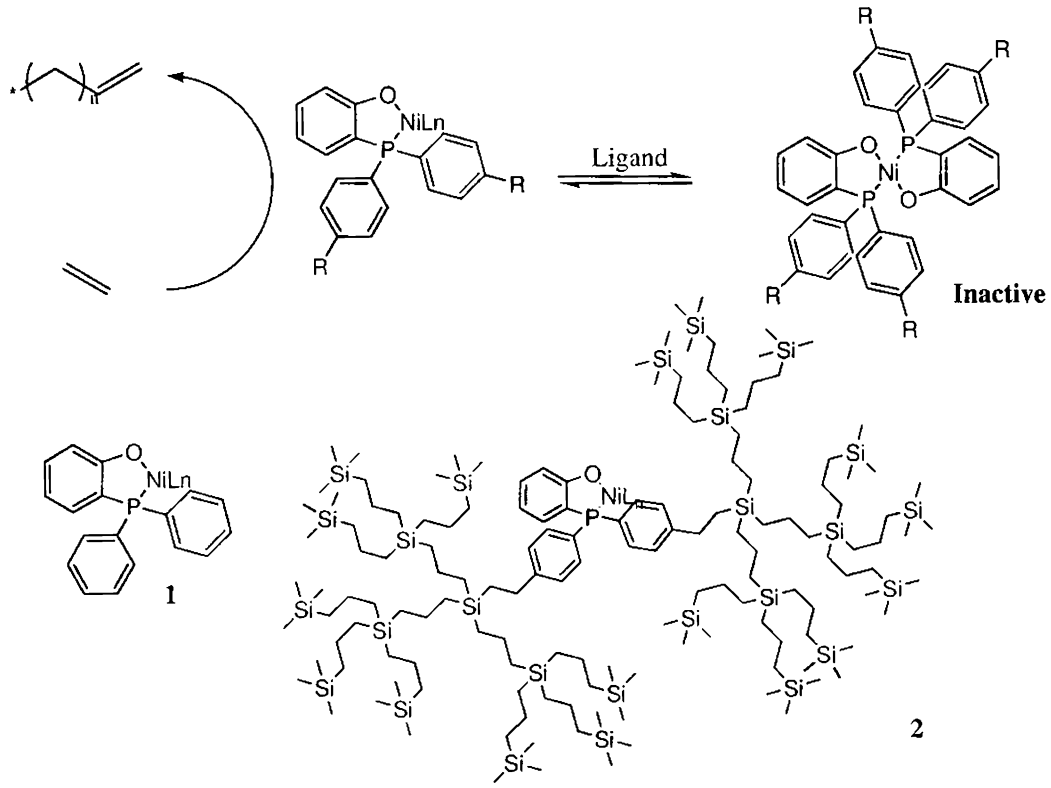


Figure 1-28. Shell higher olefin process catalyzed by Ni complex of dendritic ligand.

Reactions involving these nickel complexes are usually carried out in non-polar solvents such as toluene, although the use of more environmentally benign media has also been explored. However, in polar solvents like alcohols or water, there is a strong tendency for the formation of a bis-(P,O)nickel complex which is inactive. Muller and co-workers have constructed a second generation dendritic P, O ligand based on a carbosilane platform that was effective in preventing undesirable bis(P,O)nickel complexes in toluene (Figure 1-28).[211] As a consequence of this site isolation, the dendritic ligand 2 (TOFavg=7700 h^{-1}) outperforms the parent ligand 1 (TOFavg=3600 h^{-1}) in ethylene oligomerization

leading to higher yields of oligoethylene. The site isolation provided by the dendritic ligand 2 is mitigated in methanol as bis (P, O) nickel complexes are observed. However, the second P, O ligand appears to be labile at higher reaction temperatures in dendritic catalyst, which is not the case with the ligand and its bis (P, O) nickel complex of the monomric form. As a result, the nickel catalyst based on the dendritic ligand shows good activity (TOFavg=3242 h^{-1}) in methanol whereas the parent ligand itself does not produce any higher olefins. This is a classical example of site isolation provided by dendrimers in catalysis.

Apart from providing site isolation, the globular dendritic architecture around a catalytically active site also functions to bind guest molecules, another important factor for achieving efficient catalysis. This aspect of catalysis with dendrimers is reminiscent of molecular transformations achieved by enzymes in which substrate binding features prominently in determining the substrate selectivity and the extent of product inhibition.[212] The simple model describing the active site of an enzyme as a hydrophobic binding pocket for substrates held in close proximity to moieties that perform the transformation has often been applied, with mixed success, to hydrophobic, sometimes amphiphilic, dendrimers. Steric congestion resulting from the encapsulation of reactive groups within the dendrimer frequently leads to slower kinetics; however, there are notable exceptions: for instance, when substrate binding ability and nanoenvironment effects are paramount to achieving reactivity. In this respect, binding pockets with the desired characteristics will be found only in larger dendrimers. A nice example of this phenomenon was reported recently by Zhang et al. with a series of Frechet-type poly(benzyl ether) dendrimers with a diselenide core that demonstrated generation-dependent glutathione peroxidase (GPx) activity (Figure 1-29).[213]

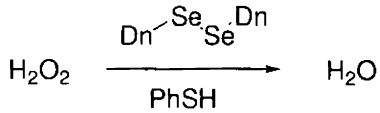


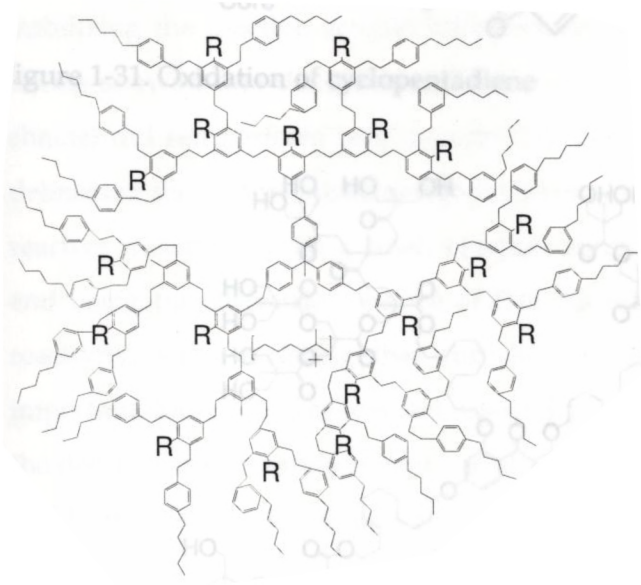
Figure 1-29. Reduction of hydrogen peroxide catalyzed by dendrimer with diselenium core.

The catalytic cycle involved the reduction of hydrogen peroxide by benzenethiol in the presence of dendrimer with diselenium core. Substrate binding was found to increase with dendrimer generation (Ka=16.4, 39.4 and 252.7M^{-1} for G1, G2 and G3, respectively) and the third generation catalyst performed much better than smaller molecules that catalyzed the same reaction.

Higher activities for the dendrimers were achieved upon the introduction of small amounts of water into the reaction medium, presumably as a result of stronger binding of the substrate to the dendrimer due to the hydrophobic effect. This study points to the importance of nanoenvironment effects in dendrimer catalysts where substrate binding requires larger dendrimers that are able to provide the more hydrophobic environment best suited for the reaction.

The dielectric nature of the nanoenvironment generated by the dendritic polymers also has a great role in catalysis. Piotti and co-workers reported an early example on the subject of nanoenvironment effects in catalysis with dendrimers. In this work, third and fourth generation unimolecular dendritic reverse micelles were prepared with a radial polarity gradient consisting of a nonpolar corona resembling the reaction solvent and more polar ester or alcohol functionalities at predetermined locations throughout the interior (Figure 1-30).[214] These dendrimers were specifically designed to catalyze reactions in which a nascent positive charge was developed during the transition state: for example, the simple unimolecular dehydrohalogenation of 2-iodo-2-methylheptane, which proceeded via an E1 elimination mechanism. Dendrimers with polyol interiors outperformed those with polyester cores. In addition, yields were significantly improved using the larger G4 dendrimer. One of the most striking features of this catalyst system was its ability to achieve high turnover even at very low catalyst loadings. The authors attributed this result to a kinetic but thermodynamically driven "concentrator effect" whereby the polarity gradient inherent to the dendrimer had driven the relatively polar substrates into the macromolecule's core leading to its accumulation in a constrained nanoenvironment that was more suitable for the E1 elimination than

the external reaction medium, hexane. Higher generation dendrimers showed better efficacy for the reaction due to a larger internal reaction volume that could accommodate a higher concentration of substrate molecules. In addition, the non-polar alkene product had a greater affinity for the hydrophobic surrounding medium thereby achieving the necessary turnover. The authors have described this latter phenomenon as a free-energy driven "catalytic pump."



where R is CO_2Me or CH_2OH

Figure 1-30. Dendrimer catalyst for E1 elimination reaction.

This concept, of a "concentrator effect" to accumulate substrates near a catalytically active site and a "catalytic pump" to prevent product inhibition, has been broadly applied to other dendrimer catalysts with amphiphilic designs. Hecht and Frechet reported the first results on light-driven catalysis at the core of the dendrimers via photosensitization.[215] In their design, a $^1O_2$-sensitizing benzophenone core was incorporated into globular dendrimers having a radial polarity gradient consisting of a hydrophobic interior and a hydrophilic surface exposed to the polar solvent. The resulting nanoscale photoreactors were created and applied to the oxidation of cyclopentadiene (CP) with dioxygen. The non-polar core was designed both to favor substrate accumulation of the CP substrate and to increase the lifetime of the photogenerated $^1O_2$. The rate of the reaction

and the stability of the catalyst increased with increase in generation of the catalyst. The scheme of the reaction and the structure of the third generation catalyst are given in Figure 1-31 and 1-32.

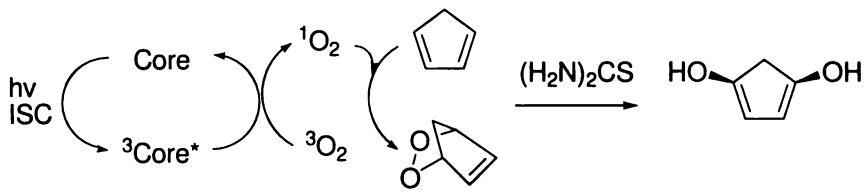


Figure 1-31. Oxidation of cyclopentadiene

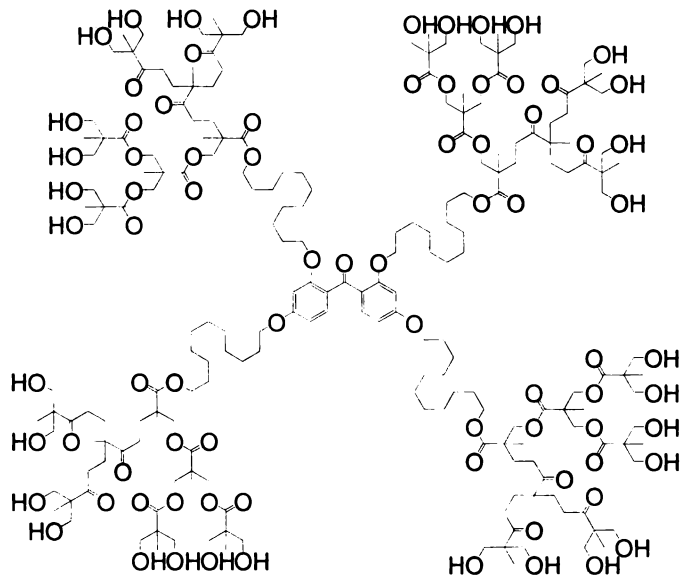


Figure 1-32. Dendritic photoreactor for the oxidation of cyclopentadiene with dioxygen.

In order to study the effect of steric shielding on the kinetics of dendrimer catalysts, Mizugaki functionalized the periphery of a third generation PPI dendrimer with either C10 or C16 acyl chains.[216] Their interiors were quaternized with iodomethane to afford lipophilic tetraalkylammonium iodide dendrimers. These dendrimers were used as Lewis base catalysts (via iodide ions) for the Mukaiyama aldol reaction of 1-methoxy-2-methyl-1-(trimethylsilyloxy)propene with various aldehydes in toluene. This study showed that dendritic iodides were remarkably more effective than other "small

molecule" sources of iodide, such as tetrabutyl- or tetrahexylammonium salts. The authors argued that the higher activity of the dendrimers over the discrete small molecule iodides stemmed from the high polarity of the nanoenvironment encapsulating the iodide in the macromolecular catalysts. The reactions were promoted to a greater extent in polar solvents such as DMF as opposed to toluene. Thus, the concentration of multiple cationic charges within the nanoscopic confines of the dendritic interior appears uniquely capable of stabilizing the reactive anionic intermediate. In addition, a study of the steric effects showed that dendrimer with a more crowded periphery (i.e., with C16 chains) did not perform well as with C10 peripheral chains. This work clearly delineated the opportunistic design features of a dendritic catalyst concentrating reactive moieties within a small reaction volume at the core of the dendrimer and using the dielectric constant of this discrete nanoenvironment to enhance reactivity, while stressing that sufficient access to that environment is also important. The control of reaction selectivity through dielectric effects exerted by the dendrimer nanoenvironment has also been observed by Ooe and co-workers in Pd catalyzed Heck reactions and allylic aminations.[217]

Another salient feature of dendrimers bearing one or more catalytically active sites at their core are their ability to achieve substrate selectivity through steric restriction. In the literature, this has often been referred to as "shape selectivity." The pioneering work with shape selective catalysts was performed by Bhyrappa et al. with dendritic manganese porphyrins.[205,206]

The kinetic behavior of various guest molecules with different steric constraints was investigated using distance- dependent excited state quenching through photoinduced electron transfer.[218] Anthracene-cored dendrimers were prepared from Frechet-type dendrons up to the fourth generation. Core accessibility was probed using trialkylamines, which are known to quench the photoexcited state of the anthracene chromophore through electron transfer. Various trialkylamines of different sizes and rotational degrees of freedom were used as quenchers. Each of these amine-based quenchers gave smaller Stern–Volmer bimolecular quenching rate constants, k_q, with increasing dendrimer

generation. This is consistent with the greater site isolation achieved with the increasing larger dendritic shells at higher generations. In addition, geometrically constrained molecules were found to have better access to the dendrimer cores than their more flexible counterparts.

Core-modified dendrimers have also been used as biomimics. Liu and Breslow prepared a series of PAMAM dendrimers with pyridoxamine residues at their core.[219] The pyridoxamine PAMAM dendrimers, G1 to G6, were used as catalysts in the transamination of pyruvic acid and phenylpyruvic acid in aqueous buffer The pyridoxamine PAMAM dendrimers displayed Michaelis–Menten kinetics and superior efficacy when compared to the simple pyridoxamine. Interesting positive dendrimer effects were drawn from the observed Michaelis–Menten parameters i.e., the second order rate constant k_2, the binding constant K_M, and the ratio k_2/K_M – as they changed with increasing generation. The larger dendrimers were much more efficient at facilitating general acid-base reactions along the catalytic pathway leading to a net increase of k_2.

Aryl ether dendrimers containing a proline core was used as a chiral catalyst for the reduction of ketones to secondary alcohols with borane (Figure 1-33). Five different catalysts were prepared and screened for their catalytic properties. Alcohols were obtained in excellent yield with ee ranging from 49 to 98%. One of the catalysts was reused five times with out any loss of catalytic and stereochemical activity.[220]

The same catalyst with suitable modification on the proline core was used for asymmetric Michael addition also[221] and in the enantioselective synthesis of (+)-sertraline[222]. The direct aldol reactions catalyzed by chiral dendritic catalysts derived from N-prolylsulfonamide and the same dendritic backbone mentioned above gave the corresponding products in high isolated yields (up to 99%) with excellent anti diastereoselectivities (up to >99:1) and enantioselectivities (up to >99% ee) in water. In addition, the catalyst may be recovered by precipitation and filtration and reused for at least five times without loss of activity.[223]

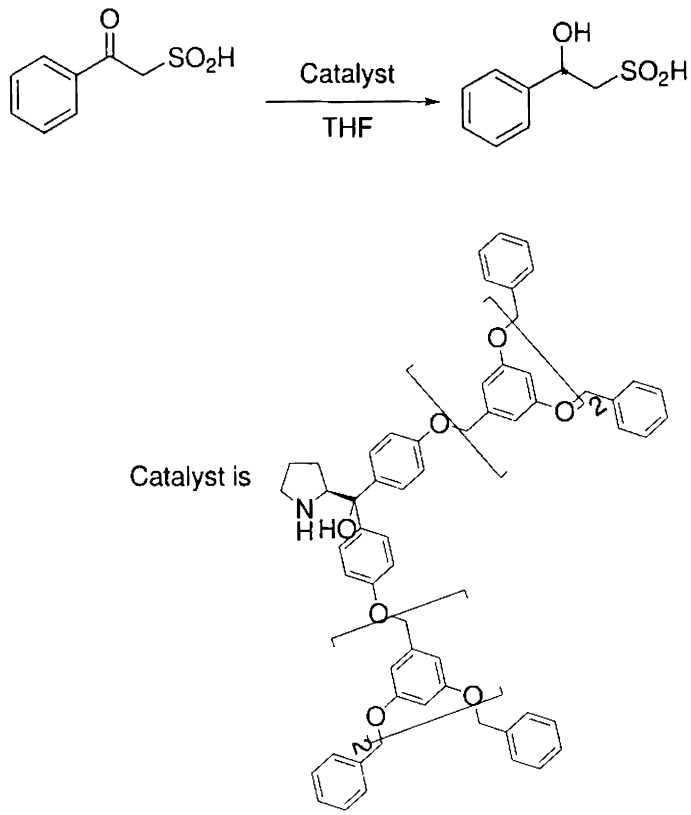


Figure 1-33. Reduction of ketones to secondary alcohols with borane catalyzed by aryl ether dendrimer with proline core

Muraki et al. reported a novel dendritic catalyst for three-component Mannich reaction in water.[224] The dendrimer contains a 2,2'-bipyridine core around which an aryl ether type dendrimer was constructed. The catalyst was prepared by treatment of $Cu(OTf)_2$ and the dendrimer in dichloromethane. The catalyst showed excellent activity compared to the $Cu(OTf)_2$ alone in the three component mannich reaction between aldehydes, amines and silyl enolates in water. A positive dendrimer effect was observed and the third generation catalyst gave better results. The yield of the product was low in all the cases because of the decomposition of the silyl enols in water.

Recently Wang and co-workers reported a new dendritic catalyst for the asymmetric hydrogenation of quinolines (Figure 1-34).[225]

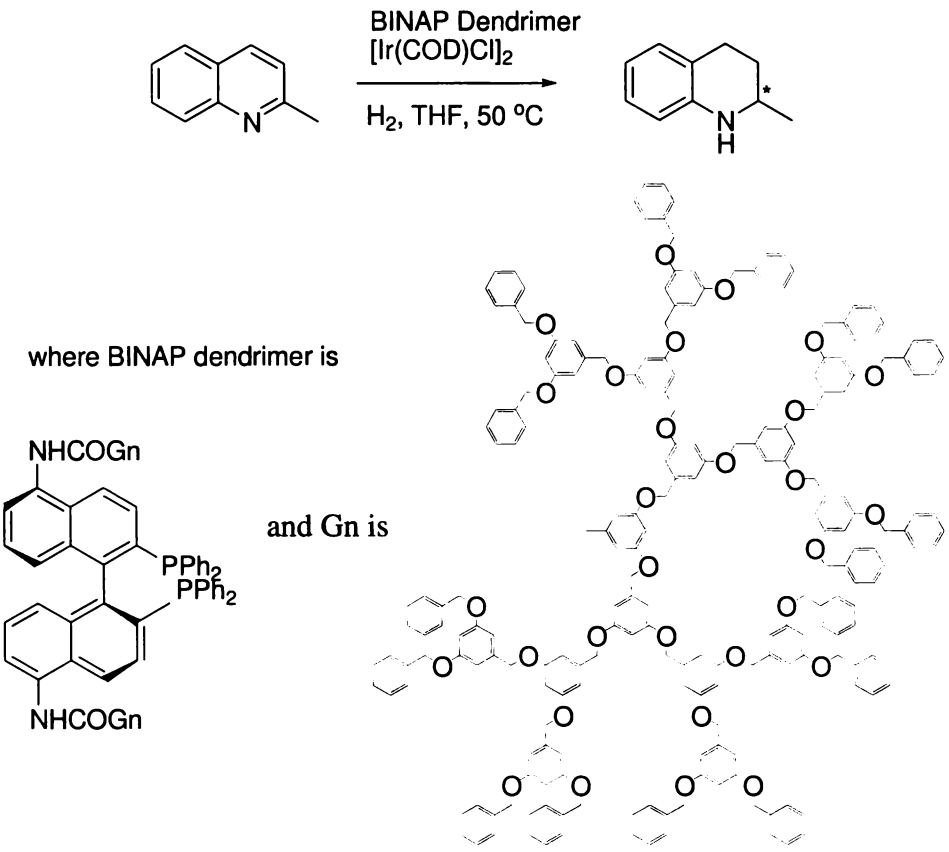


Figure 1-34. Asymmetric hydrogenation of quinolines catalyzed by dendrimer with Ir-BINAP core

The chiral dendrimer ligands were synthesized by condensation of the Frechet type aryl ether dendritic wedges carrying a COOH at their focal point with (*S*)-5,5′-diamino BINAP in the presence of triphenylphosphite, pyridine, and calcium chloride in *N*-methyl-2-pyrrolidone (NMP). The catalyst generated in situ from the dendrimer and $[Ir(COD)Cl]_2$ was used in the hydrogenation of the quinolines in THF. More than 75% of conversion was obtained with all the substrates used and the ee was also high. A positive dendrimer effect was observed and the third generation dendrimer gave better results.

A series of polyether dendritic chiral phosphine Lewis bases were synthesized by Liu and Shi (Figure 1-35).[226]

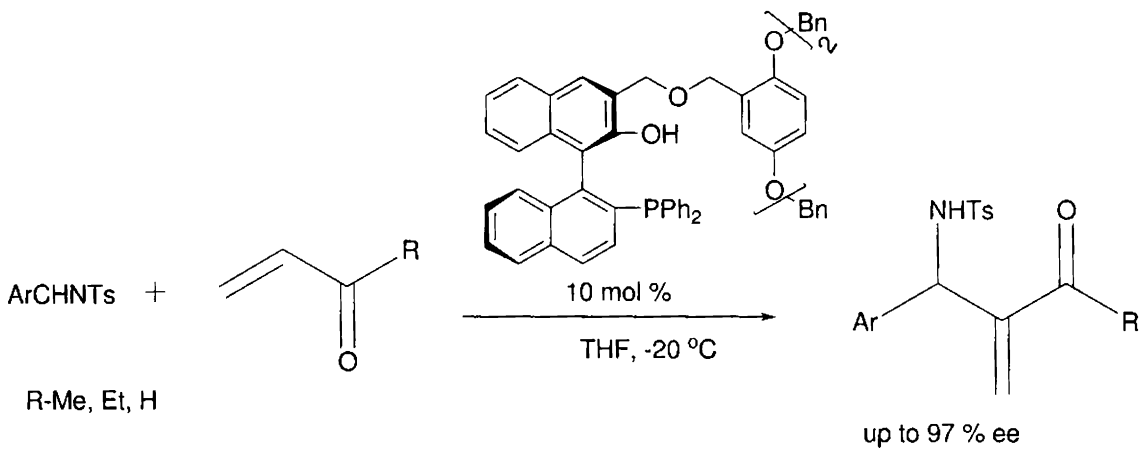


Figure 1-34. Aza-Morita-Baylis-Hillman catalyzed by dendritic chiral phosphine Lewis bases

These dendrimers carrying the chiral group at the core were successfully applied as reusable organocatalysts in the asymmetric aza-Morita-Baylis-Hillman reaction of *N*-sulfonated imines (*N*-arylmethylidene-4-methylbenzene sulfonamides) with methyl vinyl ketone, ethyl vinyl ketone, and acrolein to give the adducts in good to excellent yields along with up to 97 % ee. The enantioselectivity was higher for the dendritic catalyst compared to the original chiral phosphine Lewis bases.

Two other kinds of dendrimer catalysts, which find their role in organic reactions, are dendrimer encapsulated metal nanoparticles and dendrimer catalysts supported on insoluble supports like silica or crosslinked polymers. These two materials will be discussed in the respective chapters.

Since the first report dendrimers have been involved in many aspects of catalysis especially during the last ten years. There is much more than the aesthetic attraction in the use of dendrimers in the field. The perfect definition of catalytic sites and the clear possibility to recover the dendritic catalysts have been fully demonstrated. In short catalysts based on core and periphery functional dendrimers offer wide potential and this is described in a number of timely reviews and books.[227-236]

The following chapters will provide a detailed discussion on the use of polystyrene and poly(methyl methacrylate) supported PAMAM and PPI dendrimers, their metal complexes and metal nanoparticle conjugates as catalysts in various organic reactions.

1. 4. MATERIALS AND METHODS

Cholоromethyl ether, furoin, α-phenyl ethanol, 4-bromo α-phenyl ethanol, 4-methoxy α-phenyl ethanol and iodobenzene were prepared according to the standard procedures. All other chemicals were purchased from various chemical manufacturers and used as received unless otherwise stated. Benzaldehyde, anisaldehyde, salicyladehyde, acrylonitrile, acetic acid and methyl acrylate were purified according to the standard procedures. Absolute ethanol obtained from s.d. fine India Ltd. was used as received. All other solvents were purified according to standard procedure prior to use. THF was dried two times using sodium wire and distilled prior to use. FTIR measurements were done on a JASCO FTIR spectrometer as KBr pellets. NMR spectra were recorded on Bruker 300 MHz or 400 MHz instrument with TMS as internal standard using $CDCl_3$, D_2O, CD_3OD or $(CD_3)_2SO$ as solvent (NMR research centre, IISc. Bangalore, India, Bharathidasan University, Trichy) .Solid state CP- MAS ^{13}C- NMR spectra were recorded on a Bruker 400 MHz instrument with a spinning rate of 7 K (NMR research centre, IISc. Bangalore, India). GC/MS was taken on a Varian 1200 L single quadrapole GC/MS with capillary column. MALDI TOF MS was done on a Schimadzu Kratos compact analytical MALDI TOF MS using an Nd-YAG laser with an operating wave length of 354 nm (RGCB, Thiruvananthapuram, Kerala, India). The matrix used was α- cyano- 4-hydroxy cinnamic acid. Angiotensin II and insulin were used as internal standards. Melting point determination and TG-DTA analysis were done on Perkin Elmer Diamond model TG/DTA system using platinum as a standard. EPR spectra were recorded on a Varian E112 model spectrometer operating at an X band microwave frequency of 9.5 GHz and sensitivity 5 x 10^{10} ΔH spins at room temperature and at liquid nitrogen temperature in the solid

state (SAIF, IIT, Mumbai).SEM micrograph was recorded with JEOL JSM 840 microscope (Department of Materials Engineering, IISc. Bangalor). TEM images were taken on a JEOL 3010 HRTEM operating at electron beam energy of 300 KeV (DST unit of Nanoscience, IIT, Chennai). A suspension of the sample in methanol was loaded to the TEM copper coated carbon grid and the solvent was allowed to evaporate at room temperature before the images were taken. The AFM measurements were performed using a Digital Instruments Nanoscope IV model scanning probe microscope (Chemistry and Physics of Materials Unit, JNCASR, Bangalore).

REFERENCES

1. Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, 85, 2149.
2. Leznoff, C. C. *Acc. Chem. Res.* **1978**, 11, 327.
3. Neckers, D.C. *Chemtech*, **1978**, 108.
4. Frechet, J. M. J. *Tetrahedron*, **1981**, 37, 663.
5. Bunin, B. A.; Ellman, J. A. *J. Am. Chem. Soc.* **1992**, 114, 10997.
6. DeWitt, S. H.; Kiely, J. S.; Stankovic, C. J.; Schroeder, M. C.; Reynolds Cody, D. M.; Pavia, M. R. *Proc. Natl. Acad. Sci. USA*, **1993**, *90*, 6909.
7. Kobayashi, S. *Chem. Soc. Rev.* **1999**, 28, 1.
8. Wendeborn, S.; De Mesmaeker, A.; Brill, W. K. D.; Berteina, S. *Acc. Chem. Res.* **2000**, 33, 215.
9. *Handbook of Combinatorial Chemistry; Drugs, Catalysts, Materials;* Nicolaou, K. C., Hanko, R., Hartwig, W., Eds.; Wiley-VCH: Weinheim, **2002**.
10. Kshirsagar, T.; *High-Throughput Lead Optimization in Drug Discovery;* CRC Press: Boca Raton; **2008.**
11. Dorwald, F. Z.; *Organic Synthesis on Solid Phase; Supports, Linkers, Reactions;* Wiley-VCH: Weinheim, **2002**.
12. *Solid-Phase Organc Synthesis;* Burgess, K., Ed.; Wiley Interscience: New York, **2000**.

13. *Polymeric Materials in Organic Synthesis and Catalysis*; Buchmeiser, M. R., Ed.; Wiley-VCH: Weinheim, **2003**.
14. *Combinatorial Chemistry on Solid Phase*; Brase, S., Ed.; Topics in Current Chemistry Vol.278; Springer-Verlag: Berlin, Heidelberg, **2007**.
15. Czarnik, A. W. *Biotechnol. Bioeng.* **1998**, 61, 77.
16. Hudson, D. *J. Comb. Chem.* **1999**,1, 333.
17. Sherrington D. C. *Chem. Comm.* **1998**, 2275.
18. Delgado, M.; Janda, K. D. *Curr. Org. Chem.* **2002**, 6, 1031.
19. Yan, B. *Comb. Chem. High Throughput Screening*, **1998**, 1, 215.
20. Akelah, A.; Hassanein, M.; Selim, A.; Kenway, E. R. *Eur. Polym. J.* **1986**, 22, 983.
21. Akelah, A. *React. Polym.* **1988**, *273*, 284.
22. Itsuno, S.; Moue, I.; Ito, K. *Polym. Bull. (Berlin, Ger)*, **1989**, 21, 365.
23. Wilson, M. E.; Paech, K.; Zhou, W. J.; Kurth, M. J. *J. Org. Chem.* **1998**, 63, 5094.
24. Auzanneau, F. I.; Meldal, M.; Bock, K. *J. Pept. Sci.* **1995**, 1, 31.
25. Renil, M.; Nagaraj, R.; Pillai, V. N. R., *Tetrahedron*, **1994**, 50, 6681.
26. Toy, P. H.; Janda, K. D. *Tetrahedron Lett.* **1999**, 40, 6329.
27. Toy, P. H.; Reger, T.S.; Garibay, P.; Garno, J. C.; Malikayil, J. A.; Liu, G. Y.; Janda, K. D. *J. Combi. Chem.* **2001**, 3, 117.
28. Garibay, P.; Toy, P. H.; Hoeg-Jensen, T.; Janda, K. D. *Synlett*, **1999**, 1438.
29. Vaino, A. R.; Janda, K. D. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, 97, 7692.
30. Rapp, W.; In *Combinatorial Peptide and Non- peptide libraries*; Jung, G., Ed. VCH, New York, 1996, 425.
31. Bayer, E.; Hemmasi, B.; Albert, K.; Rapp, W.; Dengler, M. *Peptides, Structures and Function, Proceedings of the Eighth American Peptide Symposium*; Hruby, V. J. Rich, D. H. Eds; Pierce Chemical Company: Rockford, IL, **1983**, 87.
32. Labadie, J. W.; Deegan, T. L.; Gooding, O.W.; Heissler, K.; Newcomb, W.S.; Porco J. A. Jr.; Tran. T. H.; van Eikeren, P. *Proc. Am. Chem. Soc.* **1996**, *75*, 389.

33. Gooding, O.W.; Baudart, S.; Deegan, T. L.; Heissler, K.; Labadie, J. W.; Newcomb, W.S.; Porco J. A. Jr.; van Eikeren, P. *J. Comb. Chem.* **1999**, 1,113.
34. Hodges, J. C.; Harikrishnan, L.S.; Ault- Justus, S. *J. Comb. Chem*, **2000**, 2, 80.
35. Lindsley, C. W.; Hodges, J. C.; Filzen, G. F.; Watson, B. M.; Geyer, A. G.; *J. Comb. Chem.* **2000**, 2, 550.
36. McAlpine, S. R.; Lindsley, C. W.; Hodges, J. C.; Leonard, D. M.; Filzen, G. F. *J. Comb. Chem.*, **2001**, 3, 1.
37. Barrett, A. G. M.; Cramp, S. M.; Roberts, R. S. *Org. Lett.* **1999**,1, 1083.
38. Kempe, M; Barany, G. *J. Am. Chem. Soc.* **1996**, 118, 7083.
39. Arshady, R.;Artherton, E.; Clive, D. L. J.; Sheppard, R. C.; *J. Chem. Soc. Perkin Trans.1*, **1981**, 538.
40. Meldal, M. *Tetrahedron Lett.* **1992**, 33, 5077.
41. Delgado, M.; Spanka, C.; Kerwin, L. D.; Wentworth, P. Jr.; Janda, K. D.; *Biomacromolecules*, **2002**, 3, 262.
42. Renil, M.; Meldal, M. *Tetrahedron Lett.* **1996**, 37, 6185.
43. Rademan, J.; Grotli, M.; Meldal, M.; Bock, K. *J. Am. Chem. Soc.* **1999**, 121, 5459.
44. Engstrom, J. U. A.; Helgee, B. *J. Comb. Chem.* **2006**, 8, 3, 355.
45. Wan, Y.; Huang, W.; Wang, Z.; Zhu, X. X. *Polymer*, **2004**, 45, 71.
46. Luo, J.; Pardin, C.; Zhu, X. X.; Lubell, W. D. *J. Comb. Chem.* **2007**, *9*, 4, 582.
47. Berg, R. H.; Almdal, K.; Pederson, W. B.; Holm, A.; Tam, J. P.; Merrifield, R. B. *J. Am. Chem. Soc.* **1989**, 111, 8024.
48. Daniels, S. B.; Bernatowics, M.S.; Coull, J.M.; Koster, H. *Tetrahedron Lett.* **1989**, 30, 4345.
49. Wang, Z.; Laursen, R.A. *Peptide Res.* **1992**, 5, 275.
50. Frank, R.; Doring, R. *Tetrahedron*, **1988**, 44, 6031.
51. Englebresten, D. R.; Harding, D. R. K. *Int. J. Peptide. Protein. Res.* **1994**, 43, 546.

52. Schwabacher, A.W.; Shen, Y: Johnson, C. W. *J. Am. Chem. Soc.* **1999**, 121, 8669.

53. *Solid-Phase Synthesis and Combinatorial Techniques*; Seneci, P., Ed.; John Wiley: New York, **2001**.

54. *Catalysis by Polymer-Immobilized Metal Complexes*; Pomogailo, A. D., Ed.; Gordon and Breach: Australia, **1998**.

55. Kobayashi, S. *Curr. Opin. Chem. Biol.* **2000**, *4*, 338.

56. Akelah, A.; Sherrington, D. C. *Chem. Rev.* **1981**, *81*, 557.

57. Shuttleworth, S. J.; Allin, S. M.; Sharma, P. K. *Synthesis* **1997**, *11*, 1217.

58. Shuttleworth, S. J.; Allin, S. M.; Wilson, R. D.; Nasturica, D. *Synthesis* **2000**, *8*, 1035.

59. Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach,A. G.; Longbottom, 62. D. A.; Nesi, M.; Scott, J. S.; Storer, I.; Taylor,S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3815.

60. de Miguel, Y. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4213.

61. de Miguel, Y. R.; Brule´, E.; Margue, R. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3085.

62. Clapham, B.; Reger, T. S.; Janda, K. D. *Tetrahedron* **2001**, *57*,4637.

63. Eames, J.; Watkinson, M. *Eur. J. Org. Chem.* **2001**, *7*, 1213.

64. Leadbeater, N. E.; Marco, M. *Chem. Rev.* **2002**, *102*, 3217.

65. McNamara, C. A.; Dixon, M. J.; Bradley, M. *Chem. Rev.* **2002**, *102*, 3275.

66. Dickerson, T. J.; Reed, N. N.; Janda, K. D. *Chem. Rev.* **2002**, *102*, 3325.

67. Bergbreiter, D. E. *Chem. Rev.* **2002**, *102*, 3345.

68. Benaglia, M.; Puglisi, A.; Cozzi, F. *Chem. Rev.* **2003**, 103, 3401.

69. Benaglia, M.; *New. J. Chem.* **2006**, *11*, 1525.

70. Cozzi, F. *Adv. Synth. Catal.* **2006**, *348*, 1367.

71. Colacot, T. J.; Gore, E. S.; Kuber, A. *Organometallics*, **2002**, 21, 16.

72. Shieh, W. C.; Shekhar, R.; Blacklock, T.; Tedesco, A. *Synth. Commun.* **2002**, 32, 1059.

73. Phan, N. T. S.; Brown, D. H.; Styring P. *Tetrahedron Lett.*, **2004**, 45, 7915.

74. Kim, J. H.; Jun, B. H.; Byun, J. W.; Lee, Y. S. *Tetrahedron Lett.*, **2004**, *45*, 5827.

75. Byun, J. W.; Lee, Y. S. *Tetrahedron Lett.*, **2004**, *45*,1837.

76. Schweizer, S.; Becht, J. M.; Drian, C. L. *Adv. Synth. Catal.* **2007**, *349*, 1150.

77. Dell'Anna, M. M.; Mastrorilli, P.; Muscio, F.; Nobile, C. F.; Suranna, G. P. *Eur. J. Inorg. Chem.*, **2002**, 5, 1094.

78. Altaya, B.; Burguete, M. I.; Verdugo, E. G.; Karbass, N.; Luis, S. V.; Sans, P. V. *Tetrahedron Lett.* **2006**, *47*, 2311.

79. Shokouhimehr, M.; Kim, J. H.; Lee, Y. S. *Synlett*, **2006**, 618.

80. Dell'Anna, M. M.; Lofu, A.; Mastrorilli, P.; Mucciante, V.; Nobile, C. F. *J. Organomet. Chem.* **2006**, *691*, 131.

81. Bai, L.; Wang, J. *Adv. Synth. Catal.* **2008**, *350*, 315.

82. Itsuno, S.; Arima, S.; Haraguchi, N. *Tetrahedron*, **2005**, 61,12074.

83. An, L. T.; Zou, J. P.; Zhang, L. L. *Catal. Commun.* **2008**, *9*, 349.

84. Madhavan, N.; Weck, M. *Adv. Synth. Catal.* **2008**, *350*, 419.

85. Liu, H. L.; Jiang, H. F. *Tetrahedron* **2008**, *64*, 2120.

86. Sherrington, D. C. *Pure & Appl. Chem.* **1988**, 60, 401.

87. Vinodu, M. V.; Padmanabhan, M. *Proc. Indian Acad. Sci. (Chem. Sci.)*, **2001**, 113, 1.

88. Nair, V. A.; Mustafa, S. M.; Sreekumar, K, *J. Polym. Res.* **2003**, *10*, 267.

89. Barbarini, A.; Maggi, R.; Muratori, M.; Sartori, G.; Sartorio, R. *Tetrahedron Asymmetry*, **2004**, 15, 2467.

90. Valodkar, V. B.; Tembe, G. L.; Ravindranathan, M.; Ram, R. N.; Rama, H. S. *J. Mol. Catal, A. Chem.* **2004**, 208, 21.

91. Kang, Q.; Luo, J.; Bai, Y.; Yang, Z.; Lei, Z. *J. Organomet. Chem.* **2005**, *690*, 6309.

92. Benaglia, M.; Puglisi, A.; Holczknecht, O.; Quici, S.; Pozzi, G. *Tetrahedron*, **2005**, *61*, 12058.

93. Lei, Z.; Yan, P.; Yang, Y. *Catal. Lett.* **2007**, *118*, 69.

94. Nair, V. A.; Sreekumar, K. *Curr. Sci.* **2001**, *81*, 194.

95. Nair, V. A.; Sreekumar, K. *J. Polym. Mater.* **2002**, *19*, 155.

96. Nair, V. A.; Suni, M. M.; Sreekumar, K. *Proc. Indian Acad. Sci. (Chem. Sci.)* **2002**, *114*, 481.

97. Nair, V. A.; Suni, M. M.; Sreekumar, K. *Designed Monomers and Polymers* **2003**, *6*, 81.

98. Saladino, R.; Neri, V.; Pelliccia, A. R.; Caminiti, R.; Sadun, C. *J. Org. Chem.* **2002**, *67*, 1323.

99. Saladino, R.; Neri, V.; Pelliccia, A. R. Mincione, E. *Tetrahedron*, **2003**, *59*, 7403.

100. Lu, J.; Wang, X.; Liu, J.; Zhang, L.; Wang, Y. *Tetrahedron Asymmetry*, **2006**, *17*, 330.

101. Beloglazkina, E. K.; Majouga, A. G.; Romashkina, R, B.; Zyk, N. V. *Tetrahedron Lett.* **2006**, *47*, 2957.

102. Bandini, M.; Fagioli, M.; Melloni, A.; Umani-Ronchi, A. *Adv. Synth. Catal.* **2004**, 346, 573.

103. Yarapathy, V. R.; Mekala, S.; Rao, B. V.; Tammishetti, S. *Catal. Commun.* **2006**, *7*, 466.

104. Lee, S. H.; Lee, E. Y.; Yoo, D. W.; Hong, S. J.; Lee, J. H.; Kwak, H.; Lee, Y. M.; Kim, J.; Kim, C.; Lee, J. K. *New J. Chem.* **2007**, *31*, 1579.

105. Saluzzo, C.; Lamouille, T.; Herault, D.; Lemaire, M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1841.

106. Kell, R. J.; Hodge, P.; Nisar, M.; Watson, D. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1803.

107. Kell, R. J.; Hodge, P.; Snedden, P.; Watson, D. *Org. Biomol. Chem.* **2003**, *1*, 3238.

108. Zarka, M. T.; Nuyken, O.; Weberskirch, R. *Chem. Eur. J.* **2003**, *9*, 3228.

109. Lopez-Castillo, Z. K.; Flores, R.; Kani, I.; Fackler Jr, J. P.; Akgerman, A. *Ind. Eng. Chem. Res.* **2002**, *41*, 3075.

110. Nakao, R.; Rhee, H.; Uozumi, Y. *Org. Lett.* **2005**, *7*, 163.

111. Grubbs, R. H. *Nobel Lecture*, **2005.**

112. Hultzsch, K. C.; Jernelius, J. A.; Hoveyda, A. H.; Schrock, R. R. *Angew. Chem. Int. Ed. Engl.***2002**, *41*, 589.

113. Akiyama, R.; Kobayashi, S. *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 2602.
114. Jafarpour, L.; Heck, M. P.; Baylon, C.; Lee, H. M.; Mioskowski, C.; Nolan, S. P. *Organometallics*, **2002**, *21*, 671.
115. Li, F. W.; Xu, L. W.; Xia, C. G. *Appl. Catal. A.* **2003**, *253*, 509.
116. Zhang, J.; Xia, C. G. *J. Mol. Catal. A. Chem.* **2003**, *206*, 59.
117. Trost, B. M.; Pan, Z.; Zambrano, J.; Kuiat, C. *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 4691.
118. Hocke, H.; Uozumi, Y. *Synlett*, **2002**, 2049.
119. Sekiguti, T.; Lizuka, Y.; Takizawa, S.; Jayaprakash, D.; Arai, T.; Sasai, H. *Org. Lett.* **2003**, *5*, 2647.
120. Iimura, S.; Manabe, K.; Kobayashi, S. *Org. Biomol. Chem.* **2003**, *1*, 2416.
121. Deprele, S.; Montchamp, J. L. *Org. Lett.* **2004**, *6*, 3805.
122. Bravo Altamirano, K.; Montchamp, J. L. *Org. Lett.* **2006**, *8*, 4169.
123. Zhao, L. J.; Kwong, C. K. W.; Shi, M.; Toy, P. H. *Tetrahedron*, **2005**, 61, 12026.
124. Guino, M.; Hii, K. K. *Tetrahedron Lett.* **2005**, *46*, 7363.
125. Skouta, R.; Varma, R. S.; Li, C, J. *Green Chem.* **2005**, *7*, 571.
126. Li, Y.; Li, Z.; Li, F.; Wang, Q.; Tao, F. *Org. Biomol. Chem.* **2005**, *3*, 2513.
127. Chari, M. A.; Syamasundar, K. *Catal. Commun.* **2005**, 6, 67.
128. Yan, C.; Zeng, X.; Zhang, W.; Luo, M. *J. Organomet. Chem.* **2006**, *691*, 3391.
129. Girard, C.; Onen, E.; Aufort, M.; Beauviere, S.; Samson, E.; Herscovici, J. *Org. Lett.* **2006**, *8*, 1689.
130. Li, G. L.; Zhao, G. *Org. Lett.* **2006**, *8*, 633.
131. Sanz, R.; Martinez, A.; Miguel, D.; Alvarez-Gutierrez, J. M.; Rodriguez, F. *Adv. Synth. Catal.* **2006**, *348*, 1841.
132. Martin-Matute, B.; Pereira, S. I.; Pena-Cabrera, E.; Adrio, J.; Silva, A. M. S.; Carretero, J. C. *Adv. Synth. Catal.* **2007**, 349, 1714.
133. Yamamoto, Y.; Kawano, Y.; Toy, P. H.; Togo, H. *Tetrahedron*, **2007**, 63, 4680.
134. Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.

135. Font, D.; Bastero, A.; Sayalero, S.; Jimeno, C.; Pericas, M. A. *Org. Lett.* **2007**, *9*, 1943.

136. Zhang, Z.; Zhou, S.; Nie, J. *J. Mol. Catal. A. Chem.* **2007**, *265*, 9.

137. Shi, Q.; Lee, Y. J. Kim, M. J.; Park, M. K.; Lee, K.; Song, H.; Cheng, M.; Jeong, B. S.; Park, H. G.; Jew, S. S. *Tetrahedron Lett.* **2008**, *49*, 1380.

138. Jiang, H. F.; Wang, A. Z.; Liu, H. L. Qi, C. R. *Eur. J. Org. Chem.* **2008**, *2008*, 2309.

139. Majoral, P. J. *New. J. Chem.* **2007**, *31*, 1039.

140. Tomalia, D. A. *Porg. Polym. Sci.* **2005**, *30*, 294.

141. Flory, P. J. *J. Am. Chem. Soc.* **1952**, *74*, 2718.

142. Flory, P. J.; *Principles of Polymer Chemistry*, Cornell University Press: Ithaca, New York, **1953**,

143. Buchleier, E.; Wehner, W.; Vogtle, F. *Synthesis*, **1978**, 155.

144. Denkewalter, R. G.; Kolc, J.; Lukasavage, W. J. U. S. Pat. 4, 289, 872, Sept. 15, **1981**.

145. Denkewalter, R. G.; Kolc, J.; Lukasavage, W. J. U. S. Pat. 4, 360, 646, Nov. 23, **1982**.

146. Denkewalter, R. G.; Kolc, J.; Lukasavage, W. J. U. S. Pat. 4, 410, 688, Oct. 18, **1983**.

147. Tomalia, D. A.; Baker, H.; Dewald, J. R.; hall, M.; Kallos, G.; Martin, S.; Roeck, J.; Ryder, J.; Smith, P. *Polym. J. (Tokyo)*, **1985**, *17*, 117.

148. Tomalia, D. A.; Baker, H.; Dewald, J. R.; hall, M.; Kallos, G.; Martin, S.; Roeck, J.; Ryder, J.; Smith, P. *Macromolecules*, **1986**, *19*, 2466.

149. Newkome, G. R.; Yao, Z. Q.; Baker, G. R.; Gupta, K. J. *J. Org. Chem.* **1985**, *50*, 2003.

150. Hawker, C. J.; Frechet, J. M. J. *J. Chem. Soc. Chem. Commun.* **1990**, 1010.

151. Hawker, C. J.; Frechet, J. M. J. *J. Am. Chem. Soc.***1990**, *112*, 7638.

152. Moore, J. S.; Xu, Z. *Macromolecules*, **1991**, *24*, 5893.

153. Xu, Z.; Moore, J. S. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 246.

154. Worner, C.; Mulhaupt, R. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1306.

155. De Brabander-van den Berg, E. M. M.; Meijer, E. W. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1308.

156. Crespo, L.; Sanclimens, G.; Pons, M.; Giralt, E.; Royo, M.; Albericio, F. *Chem. Rev.* **2005**, *105*, 1663.

157. De Gennes, P. G.; Hervet, H. J. *Phys. Lett.* **1983**, *44*, 351.

158. Grayson, S. M.; Frechet, J. M.J. *Chem. Rev.* **2001**, *10*, 3819.

159. Jansen, J. F. G. A.; de Brabander van den Berg, E. M. M.; Meijer, E. W. *Science*, **1994**, *266*, 1226.

160. Jansen, J. F. G. A.; Meijer, E. W. *J. Am. Chem. Soc.* **1995**, *117*, 4417.

161. *Dendrimers and Other Dendritic Polymers*; Frechet, J. M. J., Tomalia, D. A., Eds.; John Wiley & Sons, UK, **2001**.

162. *Dendrimers*; Vogtle, F., Ed.; Topics in Current Chemistry Vol. 197; Springer-Verlag: Berlin Heidelberg, **1998.**

163. *Dendrimers II: Architecture, Nanostructure and Supramolecular Chemistry*; Vogtle, F., Ed.; Topics in Current Chemistry Vol. 210; Springer-Verlag:Berlin Heidelberg, **2000**.

164. *Dendrimers III: Design, Dimension, Function*; Vogtle, F., Ed.; Topics in Current Chemistry Vol. 212; Springer-Verlag: Berlin Heidelberg, **2001**.

165. *Dendrimers IV: Metal Coordination, Self Assembly, Catalysis*; Vogtle, F., Schalley, C. A., Eds.; Topics in Current Chemistry Vol. 217; Springer-Verlag:Berlin Heidelberg, **2001**.

166. *Dendrimers V: Functional and Hyperbranched Building Blocks, Phtotophysical Properties, Applications in Materials and Life Sciences*; Vogtle, F., Schalley, C. A., Eds.; Topics in Current Chemistry Vol. 228; Springer-Verlag:Berlin Heidelberg, **2003**.

167. Boas, U.; Christensen, J. B.; Heegaard, P. M. H. *Dendrimers in Medicine and Biotechnology: New Molecular Tools*; The Royal Society of Chemistry: UK, **2006**

168. Newkome, G. R.; Shreiner, C. D. *Polymer*, **2008**, *49*, 1.

169. Vohs, J. K.; Fahlman, B. D. *New J. Chem.* **2007**, *31*, 1041.

170. Lo, S. C.; Burn, P. L. *Chem. Rev.* **2007**, *107*, 1097.

171. Hwang, S. H.; Shreiner, C. D.; Moorefield, C. N.; Newkome, G. R. *New J. Chem.* **2007**, *31*, 1192.

172. Guillot-Nieckowski, M.; Eisler, S.; Diederich, F. *New. J. Chem.* **2007**, *31*, 1111.

173. Frechet, J. M. J. *Proc. Nat. Acad. Sci.* **2002**, *99*, 4782.

174. Matthews, O. A.; Shipway, A. N.; Stoddart, J. F. *Prog. Poym. Sci.* **1998**, 23, 1.

175. Tomalia, D. A.; Naylor, A. M.; Goddard III, W.A. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 138.

176. Oosterom, G. E.; Reek, J. N. H.; Kamer, P. C. J.; Van Leeuwen, P. W. N. M. *Angew. Chem. Int. Ed. Eng.* **2001**, *40*, 1828.

177. Helms, B.; Frechet, J. M. J. *Adv. Synth. Catal.* **2006**, *348*, 1125.

178. Keijsper, J. J.; Van Leeuwen, P. W. N. M.; Van der Made, A. P.; EP 0456317, **1991**; Shell Int. Research, US 5243079, **1993** (*Chem. Abstr.* **1992**, 116, 129870).

179. Knapen, J. W. J.; Van der Made, A. P.; De Wilde, J. C.; Van Leeuwen, P. W. N. M.; Wijkens, P.; Grove, D. M.; Van Koten, G. *Nature*, **1994**, *372*, 659.

180. Miedaner, A.; Curtis, C. J.; Barkley, R. M.; DuBois, D. L. *Inorg. Chem.* **1994**, *33*, 5482.

181. Reetz, M. T.; Lohmer, G.; Schwickardi, R. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1526.

182. Brinkmann, N.; Giebel, D.; Lohmer, G.; Reetz, M. T.; Kragl, U. *J. Catal.* **1999**, *183*, 163.

183. De Groot, D.; Eggeling, E. B.; De Wilde, J. C.; Kooijman, H.; Van Haaren, R. J.; Van der Made, A. W.; Spek A. L.; Vogt, D.; Van Leeuwen, P. W. N. M. *Chem. Commun.* **1999**, 1623.

184. Mery, D.; Heuze, K.; Astruc, K. *Chem. Commun.* **2003**, 1934.

185. Heuze, K.; Mery, D.; Astruc, K. *Chem. Commun.* **2003**, 2274.

186. Heuze, K.; Mery, D.; Gauss, D.; Blais, J. C.; Astruc, K. *Chem. Eur. J.* **2004**, *10*, 3936.

187. Sarkar, A.; Ilankumaran, P.; Kisanga, P.; Verkade, J. G.; *Adv. Synth. Catal.* **2004**, 346, 1093.

188. Mizugaki, T.; Ooe, M.; Ebitani, K.; Kaneda, K. *J. Mol. Catal. A.* **1999**, *145*, 329.

189. Findeis, R. A.; Gade, L. H. *Eur. J. Inorg. Chem*, **2003**, *1*, 99.

190. Seyferth, D.; Wyrwa, R.; Franz, U. W.; Becke, S. (PCT Int. Appl.) WO 9732908, 1997 [Chem. Abstr. 1997, 127, 263179p].

191. Seyferth, D.; Wyrwa, R. WO 9732918, 1997 [Chem. Abstr. 1997, 127, 263180g].

192. Mager, M.; Becke, S.; Windisch, H.; Cenninger, U. *Angew. Chem. Int. Ed. Engl.* **2001**, 40, 1898.

193. Zheng, Z. j.; Chen, J.; Li, Y. S. *J. Organomet. Chem.* **2004**, 689, 3040.

194. Benito, J. M.; de Jesus, E.; de La Mata, F. J.; Flores, J. C.; Gomez, R. *Chem. Commun.* **2005**, 5217.

195. Ropartz, L.; Morris, R. E.; Foster, D. F.; Cole-Hamilton, D. J. *Chem Commun.* **2001**, 361.

196. Ropartz, L.; Morris, R. E.; Foster, D. F.; Cole-Hamilton, D. *J. Mol. Catal. A: Chem.* **2002**, *182-183*, 99.

197. Delort, E.; Darbre, T.; Reymond, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 15642.

198. Nlate, S.; Plault, L.; Astruc, D. *New J. Chem.* **2007**, *31*, 1264.

199. Rodriguez, L. I.; Rossell, O.; Seco, M.; Orejon, A.; Bulto, A. M. M. *J. Organometallic Chem.* **2008**, *693*, 1857.

200. Niu, Y. N.; Yan, Z. Y.; Li, G, Q.; Wei, H. L.; Gao, G. L.; Wu, L. Y.; Liang, Y. M. *Tetrahedron Asymmetry*, **2008**, *19*, 912.

201. Gitsov, I.; Ivanova, P. T.; Frechet, J. M. J. *Macromol. Rapid Commun.* **1994**, *15*, 387.

202. Matyjaszewski, K.; Shigemoto, T.; Frechet, J. M. J.; Leduc, M. *Macromolecules*, **1996**, *29*, 4267.

203. Mak, C. C.; Chow, H. F. *Macromolecules*, **1997**, *30*, 1228.

204. Chow, H. F.; Mak, C. C. *J. Org. Chem.* **1997**, *62*, 5116.

205. Bhyrappa, P.; Young, J. K.; Moore, J. S.; Suslick, K. S. *J. Am. Chem. Soc.* **1996**, *118*, 5708.

206. Bhyrappa, P.; Young, J. K.; Moore, J. S.; Suslick, K. S. *J. Mol. Catal. A. Chem.* **1996**, *113*, 109.

207. Zubia, A.; Cossio, F. P.; Morao, I.; Rieumont, M.; Lopez, X. *J. Am. Chem. Soc.* **2004**, *126*, 5243.

208. Herrmann, A. W. *Angew. Chem. It. Ed. Engl.* **2002**, *41*, 1290.

209. Fujihara, T.; Obora, Y.; Tokunaga, M.; Sato, H.; Tsuji, Y. *Chem. Commun.* **2005**, 4526.

210. Singleton, D. M. (Shell Oil Corp.), US Patent4, 472,522, **1985**; *Chem. Abstr.* **1985**, *102*, 46405.

211. Muller, C.; Ackerman, L. J.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2004**, *126*, 14960.

212. Liang, C.; Frechet, J. M. J. *Prog. Polym. Sci.* **2005**, *30*, 385.

213. Zhang, X.; Xu, H.; Dong, Z.; Wang, Y.; Liu, J.; Shen, J. *J. Am. Chem. Soc.* **2004**, *126*, 10556.

214. Piotti, M. E.; Rivera, Jr. F.; Bond, R.; Hawker, C. J.; Frechet, J. M. J. *J. Am. Chem. Soc.* **1999**, *121*, 9471.

215. Hecht, S.; Frechet, J. M. J. *J. Am. Chem. Soc.* **2001**, *123*, 6959.

216. Mizugaki, T.; Hetrick, C. E.; Murata, M.; Ebitani, K.; Amiridis, M. D.; Kaneda, K. *Chem. Lett.* **2005**, *34*, 420.

217. Ooe, M.; Murata, M.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2004**, *126*, 1604.

218. Aathimanikandan, S. V.; Sandanaraj, B. S.; Arges, C. G.; Bardeen, C. J.; Thayumanavan, S. *Org. Lett.* **2005**, *7*, 2809.

219. Liu, L.; Breslow, R. *J. Am. Chem. Soc.* **2003**, *125*, 12110.

220. Wang, G.; Liu, X. Y; Zhao, G. *Synlett*, **2006**, *8*, 1150.

221. Li, Y.; Liu, X. Y; Zhao, G. *Tetrahedron: Asymmetry*, **2006**, *17*, 2034.

222. Wang, G.; Zheng, C.; Zhao, G. *Tetrahedron: Asymmetry*, **2006**, *17*, 2074.

223. Wu, Y.; Zhang, Y.; Yu, M.; Zhao, G.; Wang, S. *Org. Lett.* **2006**, *8*, 4417.

224. Muraki, T.; Fujita, K.; Terakado, D. *Synlett*, **2006**, *16*, 2646.

225. Wang, Z. J.; Deng, G. J.; Li, Y.; He, Y. M.; Tang, W. J.; Fan, Q. H. *Org. Lett.* **2007**, *9*, 1243.

226. Liu, Y. H.; Shi, M. *Adv. Synth. Catal.* **2008**, *350*, 122.

227. *Dendrimer Catalysis;* Gade, L. H., Ed.; Topics in Organometallic Chemistry Vol. 20; Springer-Verlag: Berlin Heidelberg, **2006**.

228. Astruc, D.; Chardac, F. *Chem. Rev.* **2001**, *101*, 2991.

229. Kreiter, R.; Kleij, A.; Klein Gebbink, R. J. M.; van Koten, G. *Top. Curr. Chem.*, **2001**, *217*, 163.

230. van Heerbeeck, R.; Kamer, P. C. J.; van Leeuwen, P.W.N.M.; Reek, J. N. H. *Chem. Rev.* **2002**, *102*, 3717.

231. Reek, J. N. H.; de Groot, D.; Oosterom, G. E.; Kamer, P. C. J.; van Leeuwen, P.W.N.M. *Rev. Mol. Biotechnol.* **2002**, *90*, 159.

232. Twyman, L. J.; King, A. S. H.; Martin, I. K. *Chem. Soc. Rev.*, **2002**, *31*, 69.

233. Astruc, D.; Heuz´e, K.; Gatard, S.; M´ery, D.; Nlate, S.; Plault, L. *Adv. Synth. Catal.* **2005**, *347*, 2005.

234. M´ery,D. Astruc, D *Coord. Chem. Rev.* **2006**, *250* 1965.

235. Andre´ s, R.; Jesu´ s, E.; Flores, J. C.; *New J. Chem.* **2007**, *31*, 1161.

236. Caminade, A. M.; Servin, P.; Laurent, R.; Majoral, J. P. *Chem. Soc. Rev.* **2008**, *37*, 56.

Chapter 2

SOLID PHASE SYNTHESIS OF DENDRIMERS

2. 1. INTRODUCTION

Dendrimers and dendrons, highly branched and ordered oligomers, offer -in addition to their aesthetic beauty- a variety of interesting architecture-dictated properties for a wide range of applications.[1] These properties include high degree of structural control, well-defined shape, molecular weight and size, multivalency, high loading and proximity of the peripheral groups, and specific, isolated microenvironment in the interior. Among the various materials, fully or partially based on the dendritic architecture, the share of hybrids composed of dendritic molecules and insoluble organic or inorganic support has notably increased during the past decade.[2] These composite materials are used today in chemistry, material sciences, biology and medicine for such applications as synthesis, catalysis, chromatographic separation, drug design and vaccine development. Whereas the dendritic fragments of these materials constitute usually only a minor part of the total volume, these components can significantly alter the support properties, imparting entirely new features and functions on the hybrid composites. There are a number of modes for conjugation of the dendritic moiety to a support. Dendritic wedges can be coupled to the support through the focal point[2,3] or through the peripheral functionalities[4-6], whereas dendrimers are usually immobilized through the peripheral functional groups[7-11]. In this chapter, the focus is on the synthesis of dendritic structures branching outwards from the support (i.e., hybrid materials in which the dendrons are connected to the support via their focal point).

Solid phase synthesis of dendrimers are really a challenge because of the large number of reactions that take place simultaneously during the building up

of each generation and the number increase exponentially with increase in generation. Conversely, solid phase synthesis provides some inherent advantages over orthodox solution synthesis.[12] Syntheses of dendrimers need large excess of reagents for obtaining high purity and defect free products and solid phase synthesis usually use large excess of reagents. Purification of intermediates is easy in solid phase synthesis, which is the most painstaking and time-consuming process in solution phase synthesis of dendrimers. In addition, the polymeric resins on which the dendrimer is synthesized can be used as a high load resin for combinatorial library synthesis, with particular emphasis on one bead one compound approach.[13,14] The dendronised resins found applications in heterogeneous catalysis, which will be discussed, in the forthcoming chapters. These materials can also be used in bioassays in which the polymer supported dendrimers with suitable surface groups act as multivalent ligands for various biological receptors.[15]

In conventional solution synthesis of dendrimers two strategies were generally employed and they are divergent synthesis and convergent synthesis, the details of which are given in the first chapter. But divergent synthesis is more suitable and widely employed for solid phase synthesis of dendrimers with few exceptions.

The first example of solid phase dendrimer synthesis was reported by Tam and coworkers in 1988.[16,17] They had synthesized polylysine dendrimers on phenylacetamidomethyl polystyrene with a β-alanine spacer by a divergent approach through a conventional solid phase peptide synthesis. Polymer-bound polylysine dendritic cores have been widely used as synthetic intermediates and, both the Boc SPPS method[16,18-20] and the Fmoc SPPS method[21-24] were reported for their synthesis. Tentagel and polyethylene glycol polyacrylamide copolymer (PEGA) resins, equipped with a range of linkers, have also been adopted as supports for polylysine synthesis.[25-27] A variety of conjugate types incorporating polylysine dendrons have been generated on these supports. The first structures synthesized were those with peptides decorating the dendron periphery. Later, peptides were introduced between the support and the dendritic focal point. In

later works, carbohydrates were introduced as peripheral functionalities on the dendrons.[28,29] A number of natural amino acids were used in the synthesis of peptide dendrimers on solid phase along with artificial branching units including some unnatural amino acids.[30-44] Polyamide dendrons, based on 3,5-diaminobenzoic acid branching units, were prepared to the third generation on a polystyrene support (Rink amide MBHA resin) via the divergent, Fmoc chemistry-based approach by Alper and co-workers.[45-47] Chan and co-workers used a non-symmetric triamino acid, 4-azalysine, to prepare first and second-generation peptide like dendrons on polystyrene using Boc-chemistry.[48,49] The dendrons prepared divergently by Lee and co-workers on Tentagel and PS-co-PEG-NH_2 resins are based on symmetric, TRIS-derived triamino acid monomer and were constructed up to the formal fifth and seventh generations, respectively.[50]

The most widely studied dendrimer attached to insoluble support is poly(amidoamine) dendrimer. In 1997 Bradley and co-workers introduced the solid phase synthesis of PAMAM dendrimers on organic polymer support.[51] Initially, these dendrons were prepared on Tentagel up to the fourth generation. The assembly of the dendrons followed the divergent synthetic strategy developed by Tomalia et al. for PAMAM dendrimers in solution and was based on alternating steps of double Michael addition of terminal primary amines to methyl acrylate and aminolysis of the formed terminal esters with α,ω-alkanediamines (e.g., 1,3-propanediamine). Later, the approach was extended to PAMAM dendrons on polystyrene beads equipped with a short PEG spacer.[52,53] First to fourth generation poly(amidoamine) dendrimers were synthesized on the polymer. The reaction proceeded smoothly for the synthesis of first and second generation dendrimers but third and fourth generation dendrimers showed defected structure as observed from ESI MS data. These defects may be due to the steric hindrance and increased number of reactions that had to take place for this synthesis. These dendronised resins were used as high load resins for the synthesis of various molecules.[53]

PAMAM dendrimers were also prepared on silica, as early as 1998, by Tsubokawa et al. and by many other groups, among them those of Arya and Alper, Kunitake, Rhee, Bu and Qiu.[54-67] Usually, 3-aminopropyl functionalized silica was employed as the parent support. In most studies, ethylenediamine based PAMAM was constructed via the approach developed in solution by Tomalia et al. and pioneered on solid support by Bradley and co-workers. Almost all the attempts to grow PAMAM dendrimers on silica resulted in defected structures. This observed deviation most likely resulted from incomplete propagation reactions, which are caused by the increased steric hindrance in the pores and on the surface of the silica, accompanying the dendrimer growth. In a number of cases, PAMAM dendrons were also prepared from other polymer particle cores, such as chitosan, zirconia–urea–formaldehyde resin, silica-coated magnetite, and carbon nanotubes.[68-71] Like the silica support (vide supra), at least in the case of the chitosan, the theoretically predicted propagation of the dendrons was not achieved, presumably due to the steric hindrance in the support pores. In all these cases the generation of dendrimer was so assigned that the primary amino group of the support was the zero generation.

Triply branched polyamidourea dendrons were developed by Bradley and co-workers.[72,73] The TRIS derived monomer, an AB_3-type symmetrical isocyanato-triester, was prepared in three steps. The dendrimer growth involved attachment of the monomer to a resin-bound primary amine (thus converting the isocyanate into urea) followed by ester reaction with a propane-1,3-diamine spacer, forming an amide and restoring a primary amine terminus. Synthesis of this type of dendrimers included fewer steps and the dendrimer contained more number of branches compared to PAMAM. But the resin beads started to break when dendrimer generation was increased. This is due to the branches trying to position themselves as far apart as possible in order to minimize electronic repulsions (the so-called "umbrella effect"). These dendronised resins were found to be more stable towards strong reaction conditions and more compatible

to polar solvents compared to resins to which the PAMAM dendrimer was attached.

Frechet and co-workers demonstrated the synthesis of polyester dendrons on solid support.[74] These dendrons, based on 2,2-bis(hydroxymethyl)propanoic acid units, were assembled up to the fourth generation on poly(2-hydroxyethyl methacrylate-co-ethylene dimethacrylate) resin and decorated with chiral proline derivatives

The supported dendritic molecules, described thus far, have all been based on carbonyl-containing connecting groups (amides, ureas, esters). These groups are vulnerable to a variety of reaction conditions (reductive, hydrolytic, nucleophilic) and, therefore, are unsuitable for a wide range of synthetic and catalytic applications. In order to find a solution to the problems associated with above mentioned dendrimers, solid phase synthesis of aryl ether dendrimers was reported by Basso et al.[75] followed by Dahan and Portnoy.[76] Basso et al. carried out the synthesis on hydroxymethyl polystyrene using a two-step iterative procedure consisting of a Mitsunobu coupling followed by ester hydrolysis while Dahan and Portnoy carried out the synthesis on Wang resin using Mitsunobu coupling and ester reduction. The advantage of these dendrimers is that they are more robust to chemical reactions, because the ether bonds connecting the monomers are stable to many chemical reactions. These dendronised polymers were used as support for the synthesis of peptide libraries. Polythioether dendrons, the sulfur analogues of the poly(aryl benzyl ether) dendrons, were assembled by Portnoy *et al* to the fourth generation.[77] Portnoy and Dahan also prepared polyamine dendrons, analogous to the aryl benzyl ether and thioether dendrons, via a repetitive reduction, oxidation and reductive amination sequence.[78] The "classic" poly(propylene imine) dendrons were prepared on silica gel by Liu et al. via a divergent approach that was based on a repeating sequence of amine Michael addition to acrylonitrile and nitrile reduction.[79] Synthesis of fourth-generation dendrons was reported, though the publication lacked the characterization details to support the formation of truly dendritic architecture.

A number of research groups exploited use of substituted triazine units, and particularly the stepwise selective substitution pattern of triazine chlorides (e.g., cyanuric chloride), to prepare a range of support-dendron composite materials. Marsh et al. prepared first- and second-generation dendrons, assembled divergently from cyanuric chloride and bis(3-hydroxypropyl) amine on Wang polystyrene.[80] The same group extended the method to the synthesis of melamine based dendrons on polystyrene, PEGA and SynPhase resins, as well as silica gel.[81] Synthesis of triazine dendrimers on silica was also demonstrated by Wu et al.[82] and Acosta et al.[83]

Solid-phase synthesis of poly(phenyl acetyelne) dendrimer was reported initially by Moore and co-workers[84] followed by Wang and co-workers[85]. Both synthesis used the Sonogashira coupling to assemble the next dendritic shell and MeI-induced cleavage of aryl triazenes for cleavage of the dendritic building blocks from the support. The dendrons in both cases were prepared up to fourth generation.

In this chapter, solid phase synthesis of poly(amidoamine) (PAMAM) and poly(propylene imine) (PPI) dendrimers is described. First to third generation of these dendrimers were synthesized on insoluble polymer supports carrying primary amino groups. The supports used were aminomethyl polystyrene (DVB crosslinked) and aminated poly(methyl methacrylate) (DVB crosslinked). The preparation method involved multiple reaction steps for both dendrimers under various solvent and temperature conditions and the resins were generally exposed to the reagents for a long time. Moreover the preparation of PPI dendrimers involved a reduction step using metallic hydrides. Due to similar reasons other crosslinking agents cold not be used. The progress of the synthesis was monitored using various spectral and chemical methods generally used in solid phase combinatorial chemistry.[86-88] In addition, after synthesis; the dendrimers were cleaved from the resin and analyzed using various spectral methods.

2. 2. RESULTS AND DISCUSSION

2. 2. 1. Solid Phase Synthesis of Poly(amidoamine) (PAMAM) Dendrimers

Solid phase synthesis of the poly(amidoamine) dendrimers were carried out on aminomethyl polystyrene, 3-nitro 4-aminomethyl polystyrene (DVB crosslinked) and aminated poly(methylmethacrylate) (DVB crosslinked) resins. The synthesis of dendrimers began from the primary amino pendant groups on the polymer supports. The primary amino group functioned both as the core of the dendrimer and the linker that connected the support and the dendrimer. Poly(amidoamine) dendrimers were synthesized by double Michael addition of methyl acrylate to the amino groups of polymer supports in methanol followed by transamination using large excess of ethylene diamine.

2. 2. 1. 1. Preparation of Polystyrene Supported PAMAM Dendrimer

The preparation of polystyrene supported PAMAM dendrimers is a multi step process. The polystyrene resin was prepared with DVB as the crosslinking agent. They were properly functionalised to get the resin as the starting point of the synthesis.

2. 2. 1. 2. Preparation of DVB Crosslinked Polystyrene with Variable Degree of Crosslinking

DVB crosslinked polystyrene with varying degrees of crosslinking were prepared by suspension polymerization of the mixture of monomers in water containing the initiator, benzoyl peroxide and the stabilizer, poly(vinyl alcohol) at 80 °C according to the standard procedure.[89] The mole percentage of crosslinking agent was calculated based on the fact that commercial DVB contained 55% of p-DVB. Resins with different degrees of crosslinking viz. 1%, 2 %, 4% and 6% were prepared by taking appropriate quantities of monomers. The reaction is shown in Figure 2-1.

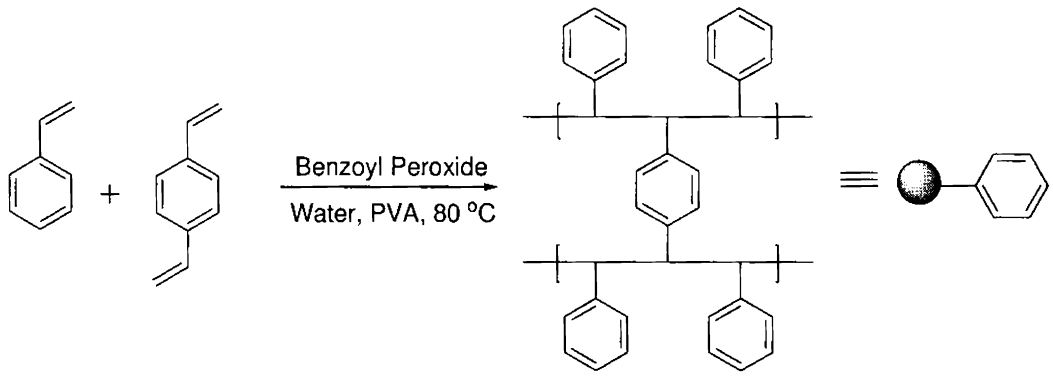


Figure 2-1. Preparation of DVB crosslinked Polystyrene

2. 2. 1. 3. Preparation of Chloromethyl Polystyrene

The polystyrene prepared as above was chloromethylated by a Friedel Crafts procedure.[90] The resin was chloromethylated using chloromethyl ether using anhydrous $AlCl_3$ as catalyst in a solvent mixture containing dicloromethane and carbon disulphide (4:1) at 0-5 °C as shown in Figure 2-2. FTIR spectrum of the resin showed a band at 720 cm^{-1} due to C-Cl stretching. Chlorine capacity was determined by Volhards method and the variation of chlorine capacity with degree of crosslinking is shown in table 2.1.

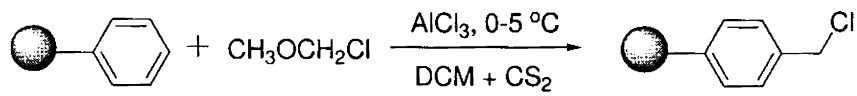


Figure 2-2. Preparation of chlorormethyl polystyrene

Table 2.1: Chlorine capacity of polystyrene: Effect of degree of crosslinking

Entry	Degree of crosslinking	Chlorine capacity (mmol/g)
1	1%	1.60
2	2%	1.60
3	4%	1.47
4	6%	1.45

2. 2. 1. 4. Preparation of 3-Nitro 4-Chloromethyl Polystyrene

Chlorormethyl polystyrene was nitrated with fuming nitric acid at 0-5 °C (Figure 2-3).[91] Introduction of a nitro group ortho to the chloromethyl group makes the resin photoactive. FTIR spectrum showed the appearance of peaks at 1539 cm^{-1} and 1380 cm^{-1} due to the asymmetric and symmetric stretching of the nitro group.

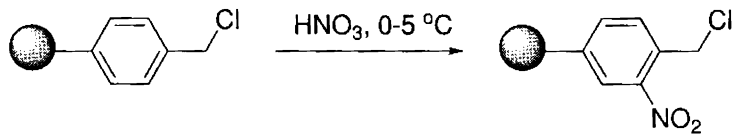


Figure 2-3. Preparation of 3-nitro 4-chloromethyl polystyrene

2. 2. 1. 5 Preparation of 3-nitro 4-aminomethyl Polystyrene

The nitrated chloromethyl polystyrene was converted into aminomethyl polystyrene so that the resin can act as the core of the dendrimer. The synthesis include two steps.[92]

In the first step, the chloromethyl resin was converted into phthalimidomethyl polystyrene by treating the resin with potassium phthalimide in dry DMF at 50 °C for 24 hours. The product resin showed FTIR bands at 1710 cm^{-1} and 1774 cm^{-1} due to the phthalimide group. The reaction is shown in Figure 2-4.

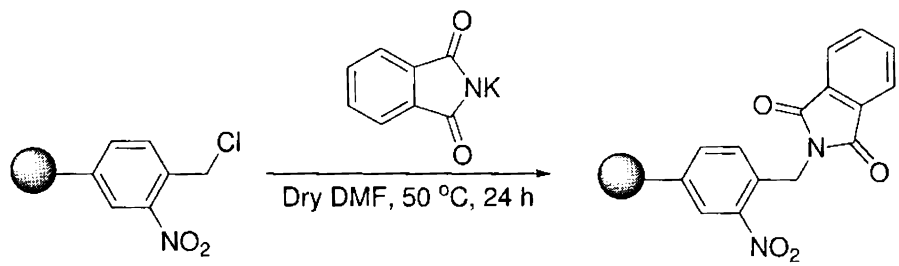


Figure 2-4. Synthesis of phthalimidomethyl polystyrene

The second step involves hydrazinolysis of the phthalimidomethyl polystyrene with hydrazine hydrate in absolute ethanol (Figure 2-5). The

reaction proceeded smoothly with in 24 hours and the FTIR spectrum of the final polymer shows the bands at 3393 cm^{-1} and 3303 cm^{-1} due to the asymmetric and symmetric stretching of the primary amino group. The bands due to the phthalimide groups disappeared completely. The variation of amino group capacity with degree of crosslinking is shown in table 2.2.

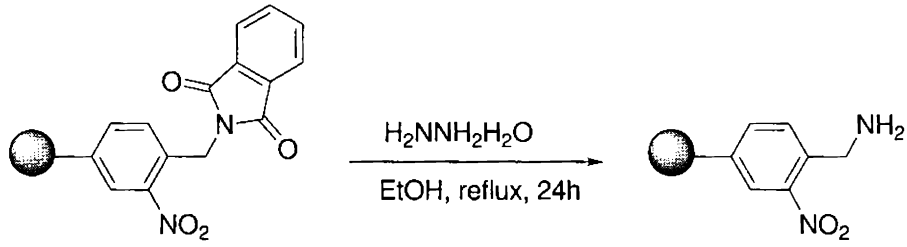


Figure 2-5. Synthesis of 3-nitro 4-aminomethyl polystyrene

Table 2.2: Amino group capacity of polystyrene. Effect of degree of crosslinking

Entry	Degree of crosslinking	Amino group capacity(mmol/g)
1	1%	1.55
2	2%	1.52
3	4%	1.37
4	6%	1.33

2. 2. 1. 6. Solid Phase Synthesis of G 0.5 PAMAM Dendrimer

The 0.5 generation PAMAM dendrimer was prepared by a double Michael addition of methyl acrylate to the primary amino group of the resin. The resin beads were suspended in an excess of methyl acrylate in methanol and stirred for four days at room temperature in an atmosphere of nitrogen. The molar ratio of the amino groups on the resin and methyl acrylate was taken as 1:250 to ensure complete reaction and to avoid the formation of defected dendrimer. At regular intervals, few resin beads were withdrawn and analyzed by FTIR spectroscopy and Kaiser ninhydrin test. The appearance of a sharp band at 1735 cm^{-1} due to the ester groups of the acrylate moiety gave the proof of the progress of reaction. Also, the disappearance of amino groups as observed from Kaiser test and FTIR spectra showed the completion of the reaction. Solid state

NMR spectrum of the resin shows peaks at δ 173 ppm arising from the C=O carbon atom of the methyl ester group of the acrylate moiety, which also gave evidence for the progress of the reaction. The reaction scheme is shown in figure 2-6.

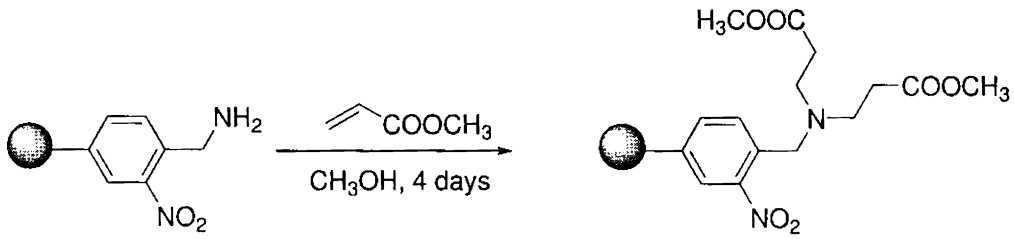


Figure 2-6. Solid phase synthesis of G 0.5 PAMAM dendrimer

2. 2. 1. 7. Solid Phase Synthesis of G 1 PAMAM Dendrimer

First generation PAMAM dendrimers were synthesized by transamination of the ester groups of the G 0.5 dendrimer. Polymer supported G 0.5 PAMAM dendrimer was slowly added to a solution of excess of ethylene diamine in methanol kept at 0 °C. Generally 125 times molar excess of ethylene diamine was taken compared to each ester group on the resin to ensure complete reaction and prevent cyclisation. The temperature was maintained at 0 °C for one hour and the reaction mixture was stirred at room temperature for four days for the completion of reaction. FTIR spectra of the resin bead showed peaks at 3390 cm^{-1} and 3344 cm^{-1} due to the primary amino groups. The carbonyl peak showed a shift and appeared at 1660 cm^{-1} since the ester group was converted to amide group. Kaiser test also showed the appearance of primary amino groups. Solid state NMR spectrum did not give much information because the chemical shifts of various carbon atoms in the first generation dendrimer are close to each other and also with that of the resin (except the C=O carbon). Estimation of amino groups showed that the amount of amino groups became almost double compared to the initial aminomethyl resin. The reaction scheme is shown in Figure 2-7.

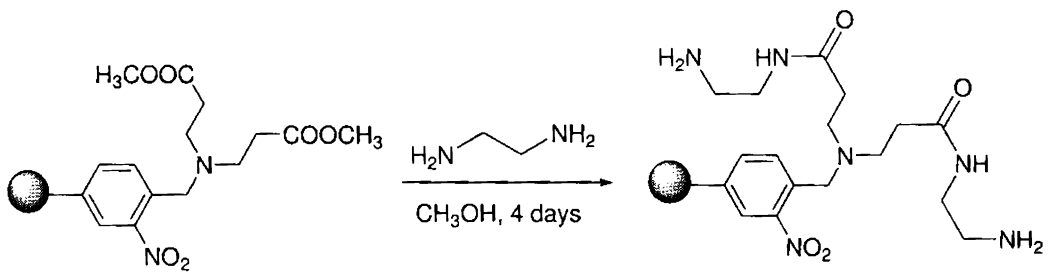


Figure 2-7. Solid phase synthesis of G 1 PAMAM dendrimer

Photolysis of the resin carrying G1 PAMAM dendrimer in methanol with 354 nm radiation released the dendrimer from the resin (Figure 2-8). Spectral analysis of this product showed that first generation dendrimer obtained was of high purity and defect free. The mechanism of photocleavage is given below. The G1 PAMAM dendrimer was characterized by various spectral methods.

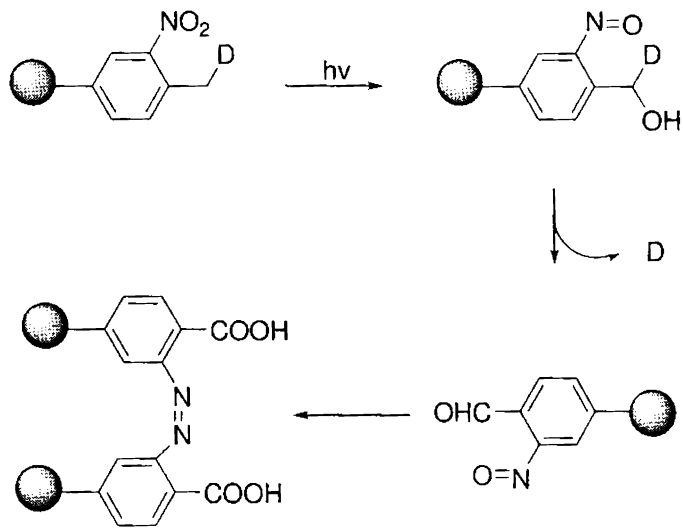


Figure 2-8. Mechanism of photolysis

The mechanism of photocleavage involves the conversion of the nitro group into a nitroso group and insertion of an oxygen atom into the C-H bond located at the benzylic position (Figure 2-8). The released product is accompanied by the o-nitrosobenzaldehyde photoproduct which is further

transformed through crosslinking into the azobenzene-2, 2'-dicarboxylic acid which, having a deep red color, act as an internal light filter, thereby reducing cleavage yields as well as crosslinking the resin and preventing compound diffusion. The aldehyde can also trap out the amine product.

2. 2. 1. 8. Solid Phase Synthesis of G 1.5 PAMAM Dendrimers

Solid phase synthesis of 1.5 generation PAMAM dendrimer starts from polystyrene supported first generation PAMAM dendrimer. The amino groups of the resin were subjected to a double Michael addition with methyl acrylate in methanol (Figure 2-9). The molar ratio of amino groups and methyl acrylate was maintained as above (1:250). The reaction was completed with in four days as observed from FTIR and Kaiser ninhydrin test.

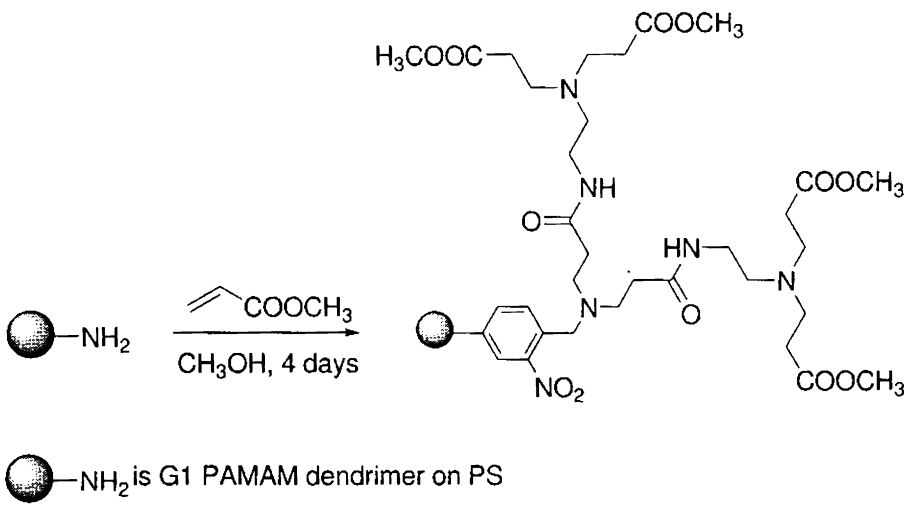


Figure 2-9. Solid phase synthesis of G 1.5 PAMAM dendrimer

2. 2. 1. 9. Solid Phase Synthesis of G 2 PAMAM Dendrimer

G1.5 PAMAM dendrimer attached to polystyrene was converted into second generation PAMAM dendrimer by transamination of the surface ester groups using ethylene diamine in methanol (Figure 2-10). The time required for the completion of the reaction was four days as observed from spectral and chemical derivetisation methods. Estimation of amino groups also showed that the second generation dendrimer was formed successfully on the resin.

Photolysis of the resin released the dendrimer from the resin and was characterized using spectral methods which proved that the dendrimer formed was homogeneous and of high purity.

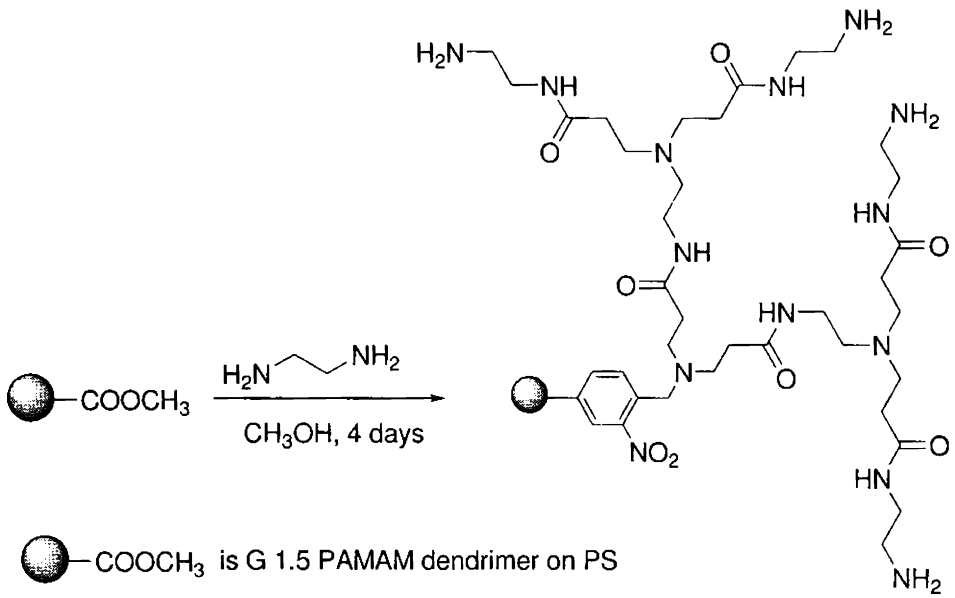


Figure 2-10. Solid phase synthesis of G2 PAMAM dendrimer

2. 2. 1. 10. Solid Phase Synthesis of G 2.5 PAMAM Dendrimer

Generation 2.5 PAMAM dendrimer was synthesized on the resin by a double Michael addition of methyl acrylate to the amino groups of second generation PAMAM supported on polystyrene. The reaction conditions were as described in the synthesis of G1 PAMAM dendrimer. The final resin showed a band at 1736 cm^{-1} in FTIR spectra, which was due to the ester groups, and almost complete disappearance of the bands due to amino groups. The reaction scheme is shown in Figure 2-11.

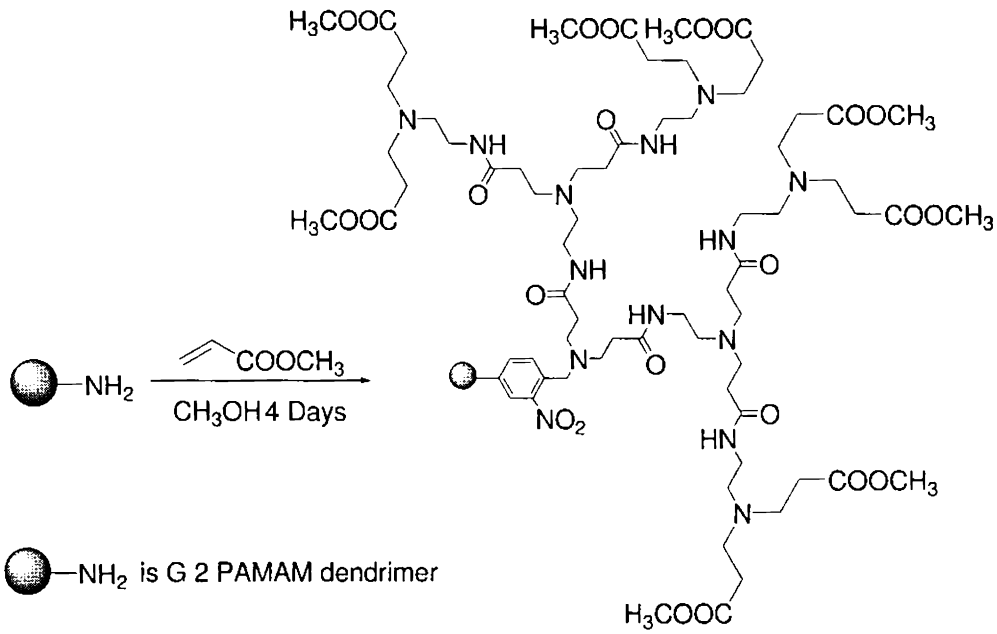


Figure 2-11. Solid phase synthesis of G 2.5 PAMAM dendrimer

2. 2. 1. 11. Solid Phase Synthesis of G 3 PAMAM Dendrimer

Third generation dendrimer synthesis on the solid phase began with the G 2.5 dendrimer attached to polystyrene beads. The ester groups of the dendrimer were subjected to transamination with ethylene diamine as described above (Figure 2-12). Photolytic cleavage of the dendrimer from the resin followed by spectral analysis of the product showed that the dendrimer was formed with good purity and was almost homogeneous.

G3 PAMAM dendrimer: Reddish brown oil; FTIR (KBr, ν_{max} (cm^{-1})) 3387, 3340, 1697, 1601, 1193; ^{1}HNMR (D_2O, 400 MHz): δ 2.1 (16H, s, NH_2), 2.27-2.3 (28H, m, CH_2), 2.6 (36H, m, CH_2), 2.8-3.0 (20H, m, CH_2), 3.2 (12H, m, CH_2), 3.5 (16H, m, CH_2); ^{13}CNMR (D_2O, 100 MHz): δ 174.2 (CO), 52.5 (CH_2), 52 (CH_2), 48 (CH_2), 41.2 (CH_2) 40.1 (CH_2), 38.8 (CH_2), 35. 7 (CH_2), 33.4 (CH_2); MALDI TOF MS m/z: 1615. 43 (100 % $[M]^+$), 1611 (30 % $[M-4H]^+$),

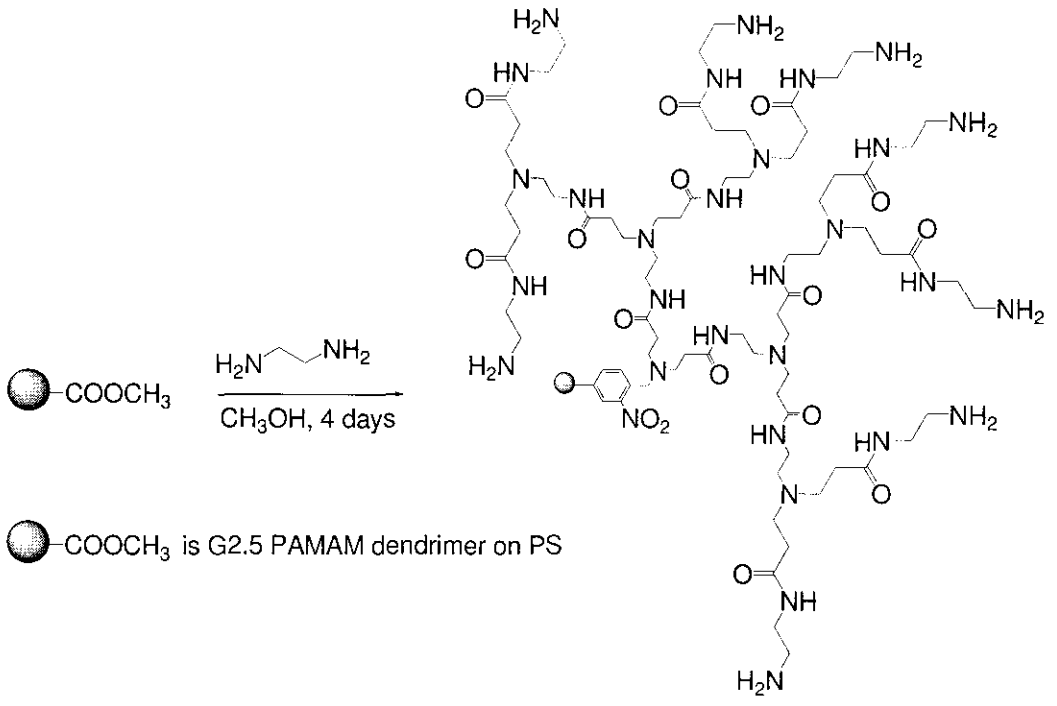


Figure 2-12. Solid phase synthesis of G3 PAMAM dendrimer

The attempts to synthesize dendrimers of higher generation on solid phase failed because of the slow and incomplete reaction as observed from FTIR spectra. The higher generation dendrimers formed were of many defects as observed from the spectral analysis of the cleaved products. The slow reaction may be due to the very large number of reactions that were to take place for the creation of each higher generation which increased exponentially with generation. So the third generation dendrimer was selected as the maximum possible defect free dendrimer that could be synthesized on polymer support in the present case.

The third generation PAMAM dendrimer has eight primary amino groups on the surface and seven tertiary amino groups at internal branching points. These make the system a strong organic base and offer a number of possible coordination sites. Along with the amino groups, there are fourteen amide groups. The amide bond gave the system stability towards many reaction conditions except strong acids and bases. Estimation of amino groups showed that the number of amino groups per gram of the resin increased after the

formation of each generation. The variation of amino groups with increase in the generation is shown in table 2.3.

Table 2.3: Number of NH_2 groups per gram of resin with increase in generation

Entry	Generation	Number of NH_2 groups in the resin with crosslinking (mmol/g)			
		1	2	4	6
1	0	1.55	1.52	1.37	1.33
2	1	3.06	3.00	2.60	2.50
3	2	6.00	5.84	4.86	4.10
4	3	11.80	10.00	8.00	6.93

2. 2. 1. 12. Preparation of Poly(methyl methacrylate) Supported PAMAM Dendrimers

Polystyrene resin offers many advantages, but there are some disadvantages also associated with these systems. These include poor swelling in polar solvents, low loading, steric hindrance from the aromatic rings and additional crosslinking arise from introduction of various functional groups in post polymerization steps. These are the driving forces for the development of new polymer supports for solid phase organic synthesis that do not contain styrene network. Of these, the most important one is poly(methyl methacrylate) with different crosslinkers. The advantages of poly(methyl methacrylate) resin are: higher compatibility towards polar solvents, long alkyl chains free from steric hindrance and high swelling behavior compared to polystyrene. But there are some disadvantages: limited number of options for the introduction of functional groups and instability of the ester group or its derivatives under various reaction conditions. In this part of the thesis, solid phase synthesis of first to third generation PAMAM dendrimer on aminated poly(methyl methacrylate) is described.

2. 2. 1. 13. Preparation of DVB Crosslinked Poly(methyl methacrylate) with Variable Degree of Crosslinking

DVB crosslinked poly(methyl methacrylate) with varying degrees of crosslinking were prepared by suspension polymerization of the mixture of

monomers in water containing the initiator, benzoyl peroxide and the stabilizer poly(vinyl alcohol) at 80 °C according to a standard procedure.[93] The mole percentage of crosslinking agent was calculated considering the fact that commercial DVB contains 55% of p-DVB. Resins with different degrees of crosslinking viz. 1%, 2 %, 4% and 6% were prepared by taking appropriate quantities of monomers. The FTIR spectra of the polymer showed a band at 1765 cm^{-1} due to the C=O stretching of the methyl ester groups. The reaction is shown in Figure 2-13.

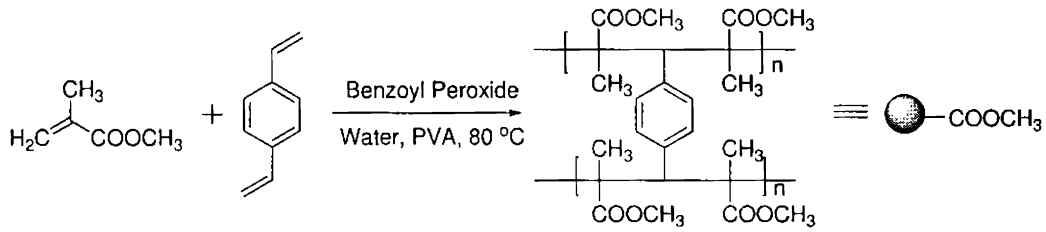


Figure 2-13. Preparation of DVB crosslinked poly(methyl methacrylate)

2. 2. 1. 14. Introduction of Amino Group on Poly(methyl methacrylate)

The methyl ester group of the poly(methyl methacrylate) was converted into an aminoethyl group with an amide bond through transamination of the ester groups with ethylene diamine in the presence of a phase transfer agent.[93] This gave the resin with an amino group with a small spacer of two carbon atoms in between the resin and the functional group. The FTIR spectra showed that the C=O stretching of the ester group was shifted towards 1650 cm^{-1}, since it was converted into an amide group. Additionally, there were two bands at 3400 cm^{-1} and 3339 cm^{-1} due to the asymmetric and symmetric stretching of the primary amino groups. The presence of amino groups was again confirmed by Kaiser test and amino group estimation. The amount of amino groups on the resin with varying amount of crosslinking agent is shown in table 2. 4.

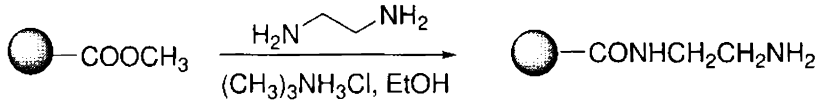


Figure 2-14 Introduction of amino group on poly(methyl methacrylate).

Table 2.4: Amino group capacity of PMMA resin:Effect of degree of crosslinking

Entry	Degree of Crosslinking	Amino group Capacity (mmol/g)
1	1%	2.30
2	2%	2.18
3	4%	1.94
4	6%	1.83

2. 1. 15. Solid Phase Synthesis of PAMAM Dendrimers on Poly(methyl methacrylate) Support

Solid phase synthesis of PAMAM dendrimers on poly(methyl methacrylate) resin was performed in the same way as the synthesis of these dendrimers was carried out on polystyrene resin. The general scheme of reaction involved a double Michael addition of methyl acrylate to the amino groups of the polymer followed by transamination of the ester groups with ethylene diamine. The reaction conditions were as described in the case of polystyrene resin. The progress of the reaction was checked by FTIR spectroscopy and Kaiser test as well as amino group estimation. FTIR spectroscopic studies showed that the appearance and disappearance of the bands at around 3395 cm^{-1} and 3350 cm^{-1} due to the asymmetric and symmetric stretching of the primary amino groups occurred due to the formation of various generations of dendrimers. Additionally, the appearance of a band around 1760 cm^{-1} from the methyl ester group of the methyl acrylate during the Michael addition step also confirmed the formation of dendrimer. Off bead analysis of the dendrimer was not possible as both the linker and dendrimer contain similar amide bonds, hydrolytic cleavage of dendrimer from resin resulted in the degradation of the dendrimer. Solid state NMR also failed because of poor resolution that prevented identification of the dendrimer carbon atoms from that of polymer support. Since the reaction proceeded well on more sterically hindered polystyrene, it was assumed that the reaction proceeded satisfactorily on poly(methyl methacrylate) also and it was confirmed by the amino group estimation and FTIR spectroscopy. The reaction scheme followed the same path as that in polystyrene resin and the structure of

the final product attached to the poly(methyl methacrylate) is shown in Figure 2-15.

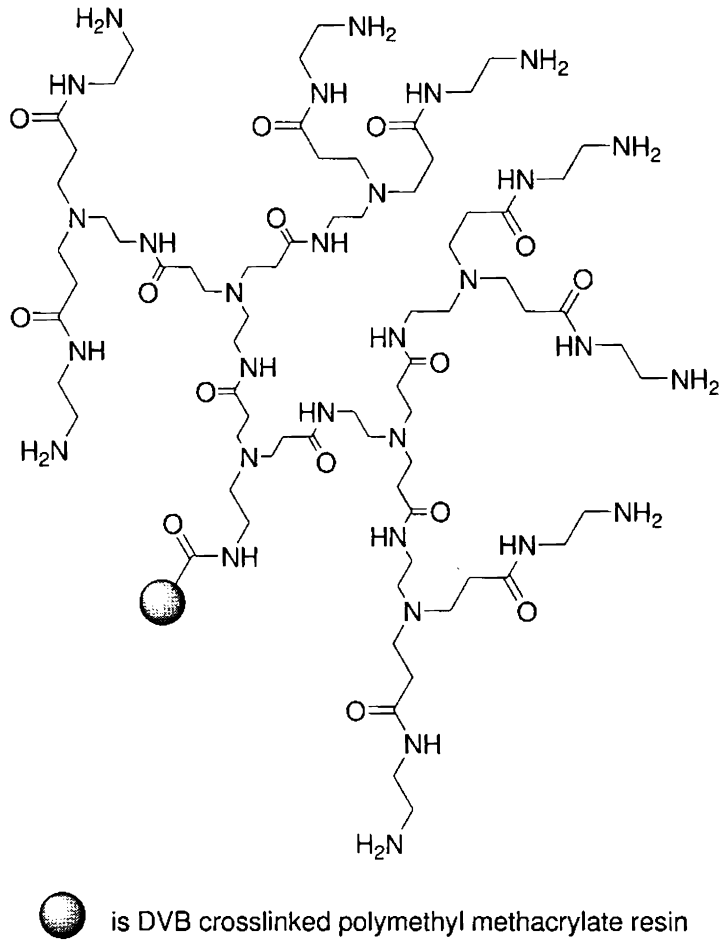


Figure 2-15. Poly(methyl methacrylate) supported G3 PAMAM dendrimer

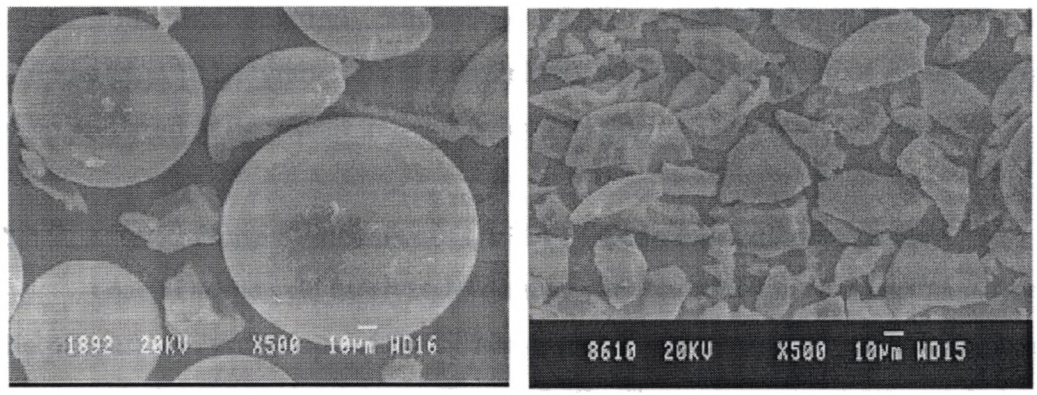
The structural details of the dendrimer are similar to that described in the case of polystyrene supported dendrimer. The only difference is the nature of bond which connects the dendrimer to the support. In the case of polystyrene supported system, the dendrimer is connected to the system through a methylne group while in the case of poly(methyl methacrylate) system, the dendrimer is connected to the support through an amide bond.

The time required for the completion of reaction was little less for PMMA resin. After the multi step synthesis under conditions of varying temperature and constant stirring, the PMMA beads got crushed to large extent compared to polystyrene as observed from scanning electron microscopic images (Figure 2-

16). It may be due to the poor mechanical stability of the PMMA beads. Also, the growing dendrimer chains may break down the resin beads in their attempt to position the growing branches free from electronic repulsion and this phenomenon is known as the 'umbrella effect' and it was observed by previous authors.[29] But this didn't create any difficulty in the progress of the reaction or further purification of the product and also in metal complexation and catalysis, which will be discussed, in the coming chapters. The amount of amino groups per gram of the resin after the formation of each generation as a function of degree of crosslinking is shown in table 2.5.

Table 2.5: Number of NH_2 groups per gram of resin with increase in generation

Entry	Generation	Number of NH_2 groups in the resin with crosslinking (mmol/g)			
		1	2	4	6
1	0	2.30	2.18	1.94	1.83
2	1	4.60	4.29	3.10	3.00
3	2	8.78	8.00	5.45	5.30
4	3	16.94	15.10	9.20	9.00



(a) (b)

Figure 2-16. SEM images of (a) polystyrene support (b) PMMA support

In both cases, it was observed that the formation of dendrimer was retarded as the degree of crosslinking of the resin was increased. This may be

due to poor swelling of the resin that prevents the movement of reactant molecules to the interior of the resin. Additionally, this poor swelling creates steric hindrance to the growing dendrimer in the internal voids of the resin, which will result in incomplete or structure with defects.

2. 2. 2. Solid Phase Synthesis of Poly(propylene imine) (PPI) Dendrimer

Solid phase synthesis of the poly(propylene imine) dendrimers were carried out on aminomethyl polystyrene (DVB crosslinked), 3-nitro 4-aminomethyl polystyrene (DVB crosslinked) and aminated poly(methyl methacrylate) (DVB crosslinked) resins. The synthesis of dendrimers began from the primary amino pendant groups on the polymer supports. The primary amino group functioned both as the core of the dendrimer and the linker that connected the support and the dendrimer. Poly(propylene imine) dendrimers were synthesized by double Michael addition of acrylonitrile to the amino groups of polymer supports in methanol followed by reduction of the nitrile groups to amino groups using lithium aluminum hydride.

2. 2. 2. 1. Preparation of Polystyrene Supported PPI Dendrimer

Both aminomethyl polystyrene (DVB crosslinked) and 3-nitro 4-aminomethyl polystyrene (DVB crosslinked) of various degrees of crosslinking were prepared as described in the previous section.

2. 2. 2. 2. Solid Phase Synthesis of G 0.5 PPI Dendrimer on Polystyrene

Glacial acetic acid catalyzed[94] double Michael addition was performed on the primary amino groups of the polystyrene by acrylonitrile to get polystyrene supported G 0.5 PPI dendrimer (Figure 2-17). The polymer was suspended in excess of acrylonitrile so that the molar ratio of primary amino group to that of acrylonitrile was 1:200. The progress of the reaction was followed by FTIR spectroscopy and Kaiser ninhydrin test. FTIR spectra showed the appearance of a peak at 2242 cm^{-1} which was due to the CN stretching vibrations. The disappearance of the peaks at 3393 cm^{-1} and 3303 cm^{-1}, due to the stretching vibrations of the primary amino groups of the polymer, gave an additional proof

to the progress and completion of the reaction. Kaiser test also proved the disappearance of primary amino groups. Solid state ^{13}C CP-MAS NMR spectrum of the polymer after reaction showed a peak at δ 114 ppm which was from the nitrile carbon atom.

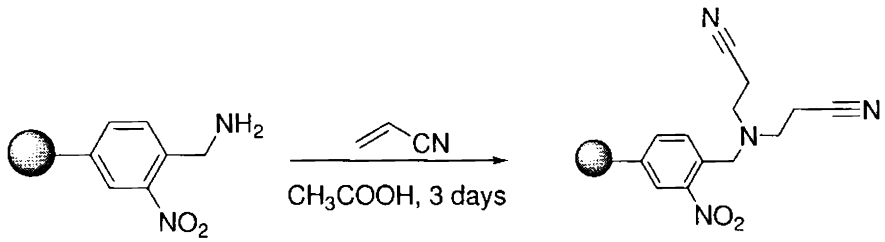


Figure 2-17. Solid phase synthesis of G 0.5 PPI on PS

2. 2. 2. 3. Solid Phase Synthesis of G1 PPI Dendrimer on Polystyrene

Solid phase synthesis of G1 PPI dendrimer was done by reducing the nitrile groups of polystyrene supported G 0.5 PPI dendrimer to primary amino groups. The reduction was done using $LiAlH_4$ in dry THF at 0 °C. The temperature was raised to 50 °C to ensure complete reduction. Generally, the reaction was completed with in 12 hours. The reaction was followed by FTIR spectroscopy and by Kaiser test. FTIR spectra showed the disappearance of the band at 2242 cm^{-1} and appearance of two bands at 3400 cm^{-1} and 3347 cm^{-1} due to the asymmetric and symmetric stretching of the primary amino groups produced due to reduction of nitrile groups. After the completion of reaction, the nitrile peak was completely disappeared. Solid state ^{13}C CP-MAS NMR spectrum showed a peak at 27 ppm, which was due to the carbon atom β to the primary amino group of the dendrimer. Quantitative estimation of amino groups showed that there was an increase in the number of amino groups per gram of the resin. The scheme of the reaction is given in Figure 2-18.

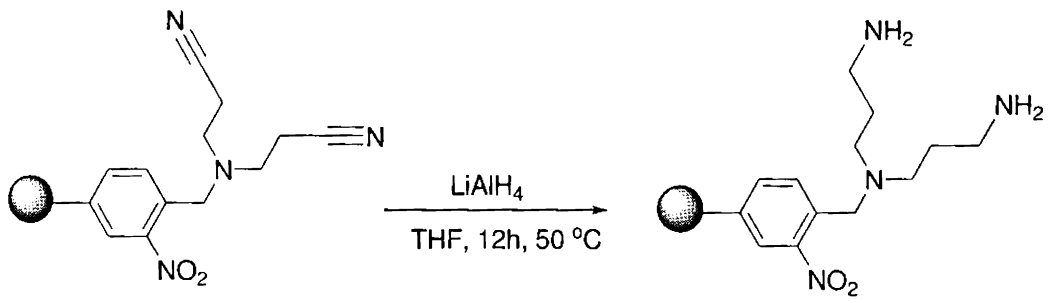


Figure 2-18. Solid phase synthesis of G1 PPI on PS

Photolysis of the resin carrying G 1 dendrimer in methanol released the dendrimer from the resin, which was isolated and characterized. The spectral data showed that the dendrimer was formed with high purity and was homogeneous.

Instead of THF, solvents like dioxan and ether were tried as the reaction medium. In dioxin, the reduction proceeded quantitatively, but was slow. This is due to the poor solubility of $LiAlH_4$ in dioxan compared to THF.[95] In ether, the reduction was slow and it may be due to poor swelling of the resin in ether and the swelling behavior will be poorer as the dendrimer grows to higher generations. The reduction was performed by $NaBH_4$ in the presence of $CoCl_2$. $6H_2O$. In this case also, the reduction was quantitative. But this method was avoided because of the possible complex formation of Co with higher generation dendrimer and also due to the precipitation of metal borides in the polymer matrix that will affect future reactions, applications and swelling behavior of the polymer. The reaction is slow at lower temperature but the reduction is complete at 50 °C.

2. 2. 2. 4. Solid Phase Synthesis of G 1.5 PPI Dendrimer on Polystyrene

The solid phase synthesis of G 1.5 dendrimer was done by acetic acid catalyzed double Michael addition of acrylonitrile to the amino groups of polymer supported G1 PPI dendrimer. The reaction conditions were as described in the synthesis of G 0.5 PPI dendrimer on polystyrene. The reaction was followed by FTIR spectroscopy. The appearance of a peak at 2238 cm^{-1} due

to the nitrile group and disappearance of the peaks due to amino groups proved the progress of the reaction. Kaiser test also proved the disappearance of amino groups. The scheme of reaction is given in Figure 2-19.

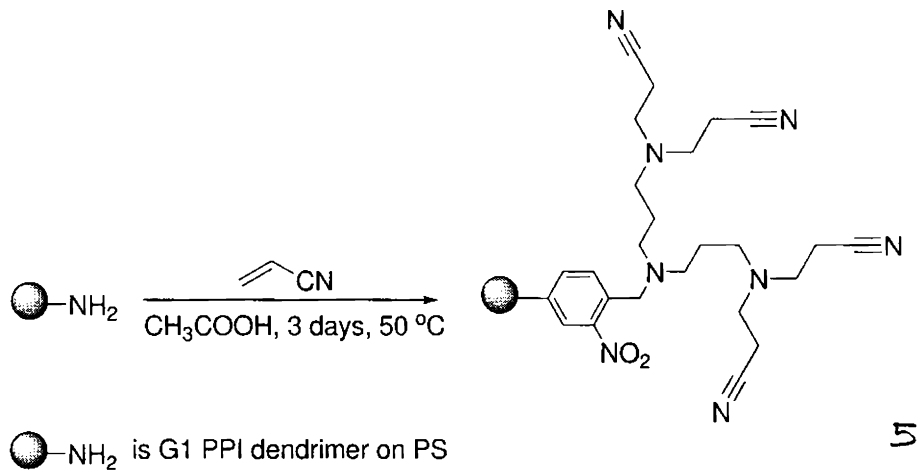


Figure 2-19. Solid phase synthesis of G 1.5 PPI dendrimer on PS

2. 2. 2. 5. Solid Phase Synthesis of G2 PPI Dendrimer on Polystyrene

Second generation PPI dendrimer was synthesized on polystyrene support by reduction of the nitrile groups of polystyrene supported G 1.5 dendrimer to primary amino groups using $LiAlH_4$ in THF at 50°C. FTIR spectral measurements showed the progress of the reaction. At the end of the reaction, the nitrile stretching peak was completely disappeared and peaks due to primary amino groups appeared. Estimation of amino groups also proved the progress of the reaction. The scheme of the reaction is shown in Figure 2-20.

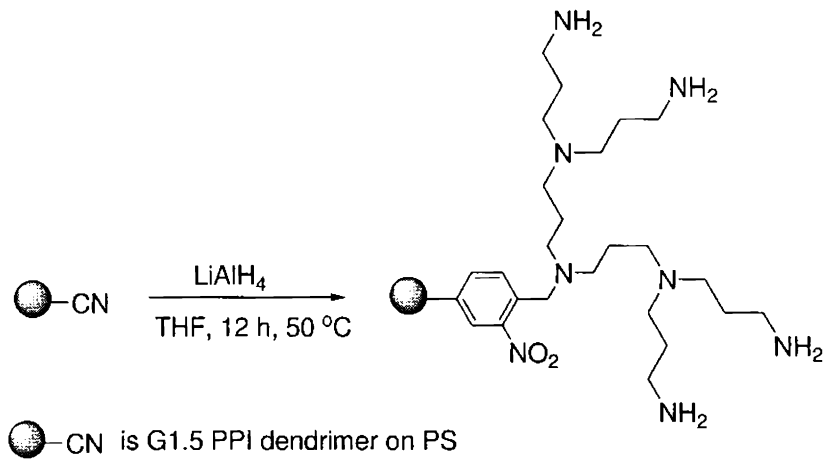


Figure 2-20. Solid phase synthesis of G2 PPI dendrimer on PS

Photolysis of the polymer carrying the dendrimer in methanol at 354 nm released the dendrimer from the resin. The purity of the product was good but yield was low. It may be due to the fact that the some of the nitro groups on the resin got reduced during the reduction of the nitrile groups and this prevented photolytic cleavage of a part of the dendrimer.

2. 2. 2. 6. Solid Phase Synthesis of G 2.5 PPI Dendrimer on Polystyrene

Acetic acid catalyzed Michael addition of acrylonitrile to the primary amino groups of the G2 PPI dendrimer supported on polystyrene gave polymer supported G 2.5 generation PPI dendrimer. The reaction proceeded smoothly under the given conditions. The progress of the reaction was followed by FTIR spectroscopy and the nitrile peak appeared at 2237 cm^{-1} and the peaks due to the amino group disappeared almost completely. The scheme of the reaction is given in Figure 2-21.

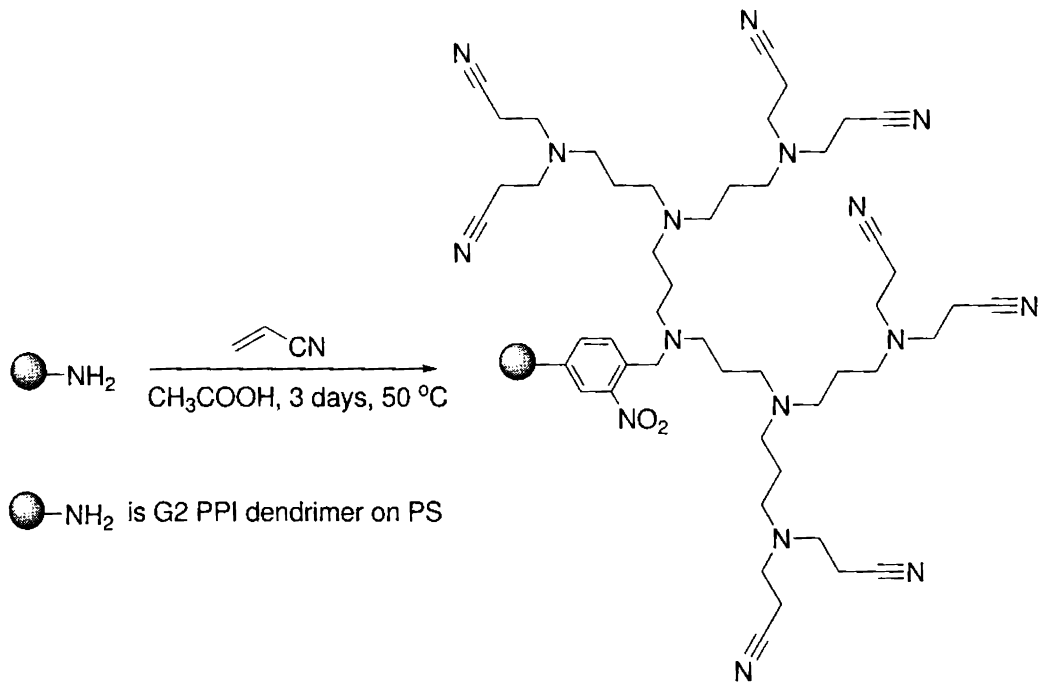


Figure 2-21. Solid phase synthesis of G2.5 PPI dendrimer

2. 2. 2. 7. Solid Phase Synthesis of G 3PPI Dendrimer on Polystyrene

Reduction of the nitrile groups of the G 2.5 PPI dendrimer supported on polystyrene beads to primary amino groups gave third generation PPI dendrimers supported on polystyrene (Figure 2-22) . The reaction was followed by FTIR and the appearance of amino group peaks and the disappearance of nirile peak confirmed the progress of the reaction. Kaiser test showed the appearance of the primary amino groups.

Estimation of amino groups confirmed the exponential increase of the amount of amino group per gram of the resin. The increase in the number of amino group with generation is shown in table 2.6.

Table 2.6: Number of NH_2 groups per gram of resin with increase in generation

Entry	Generation	Number of NH_2 groups of resin with crosslinking (mmol/g)			
		1	2	4	6
1	0	1.55	1.52	1.37	1.33
2	1	3.04	3.00	2.60	2.45
3	2	5.98	5.80	4.80	4.00
4	3	11.76	10.10	7.90	6.20

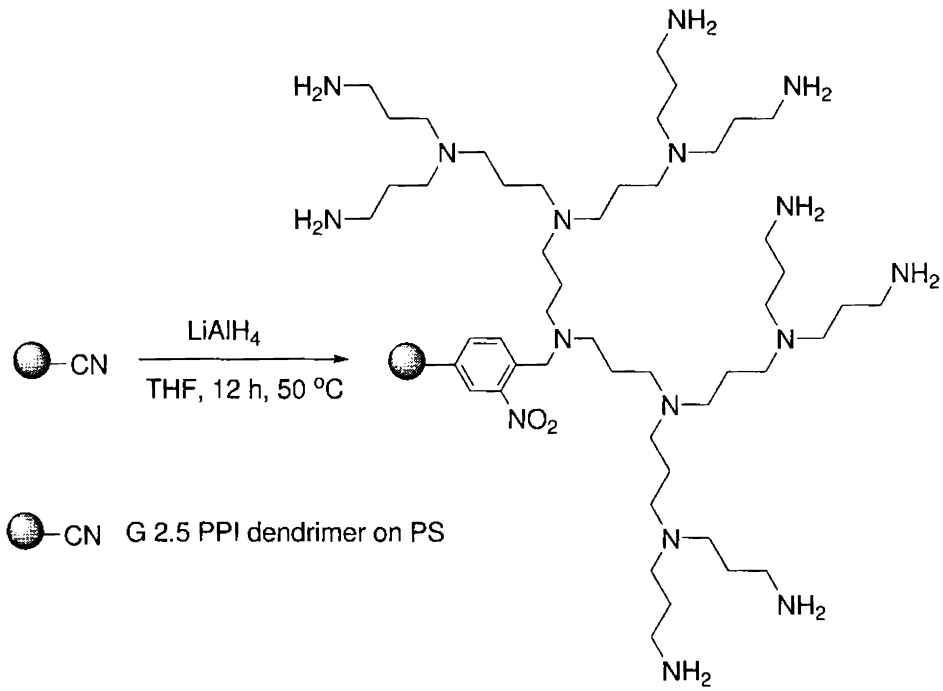


Figure 2-22. Solid phase synthesis of G 3 PPI dendrimer on PS

Photolytic cleavage of the dendrimer from the resin in methanol followed by its characterization also gave evidence for the formation of G 3 PPI dendrimer. But in this case, the yield was very low. It may be because of the reduction of more number of nitro groups during the reduction of nitrile groups and so only few o-nitro benzyl groups were available for final stage photolytic rearrangement and cleavage. The resin carrying the G3 dendrimer was analyzed by MALDI TOF MS in which the resin was irradiated with a laser beam of 354 nm which resulted in the cleavage of the dendrimer from the resin followed by its ionization. From this experiment molecular ion peak of the dendrimer with 100% intensity was obtained with out considerable other peaks which showed that the G3 dendrimer was free from defects.

G3 PPI dendrimer: Brown oil; FTIR (KBr, ν_{max} (cm^{-1})) 3397, 3340, 1609, 1198; ^{1}HNMR (CD_3OD, 300 MHz): δ 1.49-1.51 (12H, m, CH_2), 1.67 (16H, q, CH_2),2.1(17H,s, NH_2) 2.38,(36H, t, CH_2), 2.55-2.61 (20H, m, CH_2); ^{13}CNMR (CD_3OD, 75MHz): δ 53.4 (CH_2), 52 (CH_2), 47.9 (CH_2), 39.5 (CH_2), 29.8 (CH_2), 27.2

(CH_2), 25.2 (CH_2); MALDI TOF MS m/z: 820.07 (100 % $[M + 4 H]^+$), 821.42 (80 % $[M+5H]^+$), 828 (30% $[M+ Na]^+$).

SEM analysis of the resin beads showed that a part of the beads got crushed under this synthetic method. This may be due to the extreme reaction conditions and long term stirring employed during the synthesis. Additionally, the hydrogen gas bubbles trapped inside the bead during reduction may employ a pressure that will break down the bead. This breaking down of beads did not affect the synthesis or its further applications that will be described in the next section. Umbrella effect is not seemingly very pronounced in the case of PPI dendrimers because of its small size compared to PAMAM dendrimers.

2. 2. 2. 8. Solid Phase Synthesis of PPI Dendrimers on Poly(methyl methacrylate) Support

Solid phase synthesis of PPI dendrimers on PMMA support was performed in the same way as the synthesis was done on polystyrene support. The support selected was aminated poly(methyl methacrylate) which was synthesized as described in sections 2. 2. 1. 13 and 2. 2. 1.14. Solid phase synthesis of the dendrimer was done by a double Michael addition of acrylonitrile to the primary amino groups of the resin followed by the reduction of the nitrile groups to primary amino groups. The reaction conditions were same as that employed in the case of polystyrene. The reaction was followed by FTIR spectroscopy, Kaiser ninhydrin test and amino group estimation. The appearance and disappearance of peaks due to nitrile group at around 2235 cm^{-1} and the peaks due to amino groups in the range 3400- 3200 cm^{-1} gave evidence for the progress and completion of the reaction. The estimation of amino groups illustrated an exponential increase of amino groups, which was due to the formation of the dendrimer. The variation of amino groups with increase in generation is given in the table 2.7. Solid state ^{13}C NMR spectrum of the nitrile functionalised dendrimer gave a peak at δ 118 ppm, which was due to the nitrile carbon atom. Other peaks from the dendrimer and the resin could not be resolved from the solid state NMR spectra because of line broadening. The

structure of the third generation PPI dendrimer on PMMA support is given in Figure 2-23.

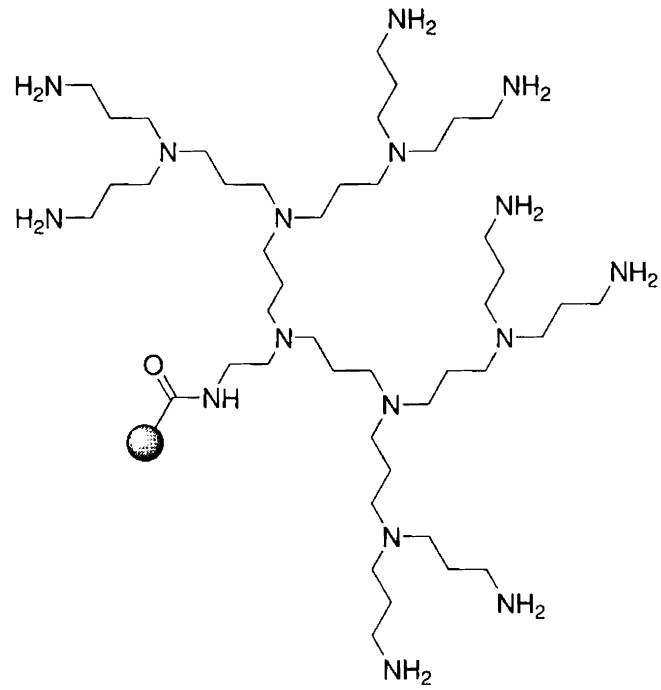


Figure 2-23. Structure of the G3 PPI on PMMA

Estimation of amino groups confirmed the exponential increase of the amount of amino group per gram of the resin. The increase in the number of amino group with generation is shown in table 2. 7.

Table 2.7: Number of NH_2 groups per gram of resin with increase in generation

Entry	Generation	Number of NH_2 of resin with crosslinking (mmol/g)			
		1	2	4	6
1	0	2.30	2.18	1.94	1.83
2	1	4.58	4.20	3.00	3.00
3	2	8.78	8.00	5.40	5.22
4	3	16.85	15.00	9.09	8.78

Hydrolysis of the amide bond that connected the dendrimer to the resin with a base released the dendrimer from the resin. But the yield of the

dendrimer decreased with higher generation dendrimers. This is due to the partial reduction of the amide bond to amino group by $LiAlH_4$ during the reduction of the nitrile groups. Attempts to separate the dendrimer released from the resin into the water medium, used for hydrolysis, by solvent extraction failed because of its poor solubility in common organic solvents that are immiscible with water. Removal of water by evaporation followed by extraction with an organic solvent also failed to a great extent because of the hygroscopic nature of the dendrimer and due to the presence of NaCl, which is a byproduct of the neutralization. But small amounts of the dendrimer was isolated and characterized by common spectral methods.

During the synthesis, the resin beads were crushed due to the severe reaction conditions and prolonged stirring; also due to, the hydrogen bubbles released during the reduction step. The percentage of resin beads crushed was higher in the case of PMMA resin because of the poor mechanical stability of the PMMA resin.

2. 3. CONCLUSION

Solid phase synthesis of poly(amidoamine) (PAMAM) dendrimers and poly(propylene imine) (PPI) dendrimers were performed. The supports selected were 3-nitro 4-aminomethyl polystyrene and aminoethyl poly(methyl methacrylate). The resins were prepared with different degree of crosslinking; the amount of functional groups estimated and characterized using spectral methods. The solid phase synthesis was performed under optimized conditions to get high purity and homogeneous dendrimer in good yield. The dendrimers formed were characterized with various on bead and off bead analytical methods. The behavior of the resin beads and linker groups during the synthesis were observed. The effect of degree of crosslinking was also studied. It can be concluded that solid phase synthesis of the PAMAM and PPI dendrimers were successful.

2. 4. EXPERIMENTAL

2. 4. 1. Preparation of DVB Crosslinked Polystyrene

The monomers were washed with 2% aqueous NaOH solution and water to remove the inhibitors and dried with $CaCl_2$. Styrene (20 mL), DVB (1 mL) and benzoyl peroxide (250 mg) were mixed in a 100 mL dropping funnel. This solution was added drop wise over a period of 45 minutes with constant stirring to a solution of Poly(vinyl alcohol) (5g) in distilled water (200 mL) kept at 80 °C in a water bath. The reaction mixture was stirred for 20 h using a mechanical stirrer and the temperature was maintained at 80 °C. The white colored polymer formed was filtered and washed well with hot water (20 mL x 5 times), dioxan (20 mL x 3 times), acetone (20 mL x 3times), methanol (20 mL x 3 times) and dichloromethane (20 mL x 3 times). It was dried at 50° C for 12 h. Yield, 16.30 g.

2. 4. 2. Preparation of Chloromethyl Polystyrene

Polystyrene beads (10 g) were suspended in a solvent mixture containing dichloromethane and carbon disulphide in the ratio 4:1 (50 mL) for 10 h. These preswollen beads were added to a mixture of anhydrous $AlCl_3$ (20 g, 0.15 mol) chloromethyl ether (10 mL, 0.13 mol) in DCM-CS_2 solvent mixture cooled to 0 °C in an ice bath with stirring. The addition is completed in 30 minutes. The reaction mixture was slowly brought to room temperature and to refluxing temperature. The reaction mixture was refluxed for 10 hours. The resin beads were collected by filtration, washed repeatedly with dioxan-water (1:1, 20 mL x 3 times), dioxan-HCl-water (1:1:1, 20 mL x 3 times), water (20 mL x 5 times), methanol (20 mL x 3 times), dichloromethane (20 mL x 3 times). The beads were washed in a soxhlet with methanol for 6 h. It was dreid at 50 ° C for 12 h. Yield 10.82g.

2. 4. 3. Estimation of Chlorine Capacity of the Resin

The chloromethyl resin (250 mg) was refluxed in pyridine (5 mL) for 1 h. Acetic acid (10 mL) and water (10 mL) was added to the reaction mixture. The

chloride ions were displaced by the addition of conc. HNO_3 (5 mL) and precipitated with a measured excess of standard $AgNO_3$ solution. The AgCl formed was coated with toluene (5mL). The excess of $AgNO_3$ was back titrated with standard NH_4SCN solution using ferric alum as indicator (1 mL, 40% freshly prepared solution of ferric alum in water was used). A red color due to the formation of $Fe(SCN)_3$ indicated the end point. The amount of chloride ions per gram of the resin was calculated from the titre value. The results are given in table 2. 1.

2. 4. 4. Preparation of 3-nitro 4-chloromethyl Polystyrene

Chloromethyl polystyrene (10 g) was added in small lots with stirring to fuming nitric acid (50 mL, 90%) taken in a 250 mL beaker and cooled to 0 °C. The addition was very slow that the temperature was not allowed to rise above 5 °C. After the completion of addition, the temperature was maintained at 0- 5 °C for 1 h with constant stirring. The temperature was slowly brought to room temperature with in a period of 2-3 h. The reaction mixture was heated slowly to 50 °C. It was poured over crushed ice. The polymer beads were recovered by filtration, washed with water (20 mL x 5 times), dioxan (20 mL x 3 times) and methanol (20 mL x 3 times) and dried at 50 °C for 12h. The nitrogen content of the resin was estimated as 6.35 mmol/g. Yield, 13.00 g.

2. 4. 5. Preparation of Phthalidomethyl Polystyrene

3-nitro 4-chloromethyl polystyrene (10 g) was suspended in dry DMF (150 mL) and (3.4 g, 17.8 mmol) of potassium phthalimide was added to it with stirring. The reaction mixture was kept at 50 °C for 24 h with constant stirring. The polymer beads were filtered, washed with dry DMF (20 mL x 3 times), methanol (20 mL x 3 times), water (20 mL x 5 times), and methanol (20 mL x 3 times). It was dried at 50 °C for 12 h. Yield, 11. 76g.

2. 4. 6 Preparation of Aminomethyl Polystyrene

The above resin was added to absolute ethanol (100 mL) taken in a 250 mL r. b. flask. Hydrazine hydrate (2 mL) was added and the reaction mixture

was refluxed with stirring for 24 h. The polymer beads were recovered by filtration and washed with ethanol (20 mL x 3 times), 5% aq. KOH (20 mL x 3 times), water (20 mL x 5 times), ethanol (20 mL x 3 times). Dried at 50 °C for 12 h. Yield, 10.50 g.

2. 4. 7. Estimation of Amino Groups

The aminomethyl resin (250 mg) was suspended in HCl (40 mL, 0.1 M) for 24 h with occasional stirring. The resin was filtered and washed well with distilled water. The filtrate and washings were collected. The unreacted HCl was estimated by titration against standard Na_2CO_3 solution using methyl orange indicator. A blank titration was also carried out. From these values, the amount of amino groups per gram of the resin was calculated.

2. 4. 8. Preparation of DVB Crosslinked PMMA Resin

The monomers were washed with 2% aqueous NaOH solution and water to remove the inhibitors and dried with $CaCl_2$. Methyl methacrylate (20 mL,), DVB (1 mL) and benzoyl peroxide (250 mg) were mixed in a 100 mL dropping funnel. This solution was added drop wise over a period of 45 minutes with constant stirring to a solution of PVA (5g) in distilled water (200 mL) kept at 80 °C in a water bath. The reaction mixture was stirred for 20 h using a mechanical stirrer and the temperature was maintained at 80 °C. The white colored polymer formed was filtered and washed well with hot water (20 mL x 5 times), dioxan (20 mL x 3 times), acetone (20 mL x 3times), methanol (20 mL x 3 times) and dichloromethane (20 mL x 3 times). It was dried at 50° C for 12 h. Yield, 17.00 g.

2. 4. 9. Preparation of Aminated PMMA

In a 250 mL r. b. flask a mixture of DVB crosslinked PMMA resin (10 g), ethylene diamine (17 mL, 250 mmol) and tetra-n-butylammonium bromide (3.2 g, 10 mmol) were mixed. The reaction mixture was stirred at 100 °C for 48 h. The resin was collected by filtration, washed with ethanol in a soxhlet extractor and then dried at 50 °C for 12 h. Yield 10.70 g.

2. 4. 10. Solid Phase Synthesis of PAMAM Dendrimer

Solid phase synthesis of PAMAM dendrimers includes two steps. The experimental procedure is as described below.

2. 4. 10. a. General Procedure for Michael Addition of Methyl Acrylate

The resin (5 g) was added in portions to a 250 mL round bottom flask containing methyl acrylate (110 mL, 1.25 mol) and methanol (100 mL) at room temperature with stirring. The reaction mixture was stirred at room temperature under an atmosphere of nitrogen for five days. After the reaction, excess reactants and solvent were removed under vacuum. The polymer was washed well with methanol (20 mL x 3 times), ethanol (20 mL x 3 times), ether (20 mL x 3 times) and acetone (20 mL x 3 times) and dried under vacuum for 24 h.

2. 4. 10. b. General Procedure for Transamination

The above resin was added in small fractions with stirring to a mixture of ethylene diamine (80 mL, 1.25 mol) and methanol (100 mL) taken in a round bottom flask and cooled to 0 °C in an ice-salt bath. The reaction mixture was stirred at 0 °C for 1 h and the temperature was allowed to rise to the room temperature (30 °C) and stirred at room temperature for four days to ensure complete reaction. After the completion of the reaction the resin beads were filtered under vacuum and washed well with DMF (20 mL x 3 times), DCM (20 mL x 3 times), methanol (20 mL x 3 times) and ether (20 mL x 3 times). The resin was dried under vacuum for 24 h. Amount of amino groups per gram of the resin was estimated after each generation.

2. 4. 11. Solid Phase Synthesis of PPI Dendrimers

Solid phase synthesis of PPI dendrimers includes two steps. The experimental procedure is as described below.

2. 4. 11. a. General Procedure for Michael Addition of Acrylonitrile

The aminated resin (5 g) was added in portions to a mixture of acrylonitrile (20.5 mL, 310 mmol) and acetic acid (4.5 mL, 77.5 mmol, 10 times

the number of amino groups on resin) with constant stirring. The reaction mixture was kept at 50 °C with stirring for three days. The polymer was recovered by filtration under vacuum and washed with methanol (20 mL x 3 times), water (20 mL x 3 times), methanol (20 mL x 3 times), acetone (20 mL x 3 times) and DCM (20 mL x 3 times) and dried under vacuum for 24 h.

2. 4. 11. b. General Procedure for the Reduction of Nitrile Group to Amino Group

The resin beads obtained from the above step was suspended in dry THF (20 mL) taken in a 100 mL r. b. flask kept at 0 °C in an ice bath. The reaction mixture was kept in the ice bath for one hour to cool the reaction mixture. A slurry of $LiAlH_4$ (1 mole for each mole of nitrile groups on the resin) in dry THF (20 mL) was added drop wise to the reaction mixture with stirring. The reaction mixture was kept at 0 °C for 1 h. The temperature was slowly brought to 50 ° C. It was stirred at 50 °C for 12 h to ensure complete reduction. Excess $LiAlH_4$ was removed by adding ethyl acetate (50 mL). It was filtered under vacuum, washed with ethyl acetate (20 ml x 3 times), THF (20 mL x 2 times), ether (20 mL x 3 times) THF- dil. HCl (1:1, 20 mLl x 3 times), dil. HCl (20 mL x 4 times), water (20 mL x 3 times), 5 % aq. NaOH (20 mLl x 3 times), water (20 mL x 5 times), methanol (20 mL x 3 times) and acetone (20 mL x 3 times). The resin was dried under vacuum for 24 h.

2. 4. 12. General Procedure for Photolysis

The polystyrene resin (1g) carrying the dendrimer was suspended in methanol (50 mL) in the reaction chamber of an immersion type photoreactor. The suspension was degassed for 1 h with dry nitrogen and irradiated with Philips HPK 125W medium pressure mercury lamp at 340-350 nm for 24 h with constant stirring. A solution of $CuSO_4$ was circulated through the outer jacket of the photochemical reactor to filter off light waves below 320 nm. After photolysis the resin was filtered and washed with methanol (20 mL x 3 times). Combined filtrate and washings were evaporated under vacuum. The product obtained was characterized by various spectral methods with out further purification.

2. 4. 13. General Procedure for Hydrolysis

The PMMA resin (1 g) carrying the dendrimer was suspended in NaOH (10 mL, 20%) and refluxed for 24 h. The resin beads were filtered and washed with water (20 mL x 3 times). The combined filtrate and washings were collected and evaporated to 20 mL. It was neutralized with conc. HCl. Water was removed under vacuum. The product was isolated by extraction with methanol and characterized using various spectral methods without further purification.

REFERENCES

1. *Dendrimers and Dendrons: Concepts, Synthesis and Applications*; Newkome, G. R., Moorefield, C. N., Vogtle, F. Eds.; Wiley-VCH, Weinheim, **2001**.
2. Kehat, T.; Goren, K.; Portnoy, M. *New J. Chem.* **2007**, *31*, 1218.
3. Dahan, A.; Portnoy, M. *J. Poly. Sci. Polym. Chem.* **2005**, *43*, 235
4. Cardona, C. M.; Jannach, S. H.; Huang, H.; Itojima, Y.; Leblanc, R. M.; Gawley, R. E.; Baker G. A.; Brauns, E. B. *Helv. Chim. Acta*, **2002**, *85*, 3532;
5. Choi, Y. S.; Yoon, C. W.; Lee, H. D.; Park M.; Park, J. W. *Chem. Commun.***2004**, 1316.
6. Oh, S. J.; Ju, J.; Kim, B.; C. Ko, E.; Hong, B. J.; Park, J. G.; Park, J. W.; Choi, K. Y. *Nucleic Acids Res.* **2005**, *33*, e90.
7. Miksa, B.; Slomkowski, S.; Chehimi, M. M.; Delamar, M.; Majoral J. P.; Caminade, A. M.; *Colloid Polym. Sci.* **1999**, *277*, 58.
8. Benters, R.; Niemeyer C. M.; Wohrle, D. *Chem. Bio Chem.* **2001**, *2*, 686
9. Mark, S. S.; Sandhyarani, N.; Zhu, C.; Campagnolo, C.; Batt, C. A.; *Langmuir*, **2004**, *20*, 6808.
10. Gruttner, C.; Bohmer, V.; Casnati, A.; Dozol, J. F.; Reinhoudt, D. N.; Reinoso-Garcia, M. M.; Ruderhausen, S.; Teller, J.; Ungaro, R.; Verboom, W.; Wang, P. *J. Magn. Magn. Mater.* **2005**, *293*, 559
11. Archer, M. J.; Lin, B.; Wang, Z.; Stenger, D. A. *Anal. Biochem.* **2006**, *355*, 285.
12. Fruchtel, S. M.; Jung, G. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 17.

13. Haag, R. *Chem. Eur. J.* **2001**, *7*, 327.
14. Lebreton, S.;Monaghan, S.; Bradley, M. *Aldrichimica Acta.* **2001**, *34*, 75.
15. Yang, M.; Tsang, E. M. W.; Wang, Y. A.; Peng, X.; Yu, H. Z. *Langmuir*, **2005**, *21*, 1858.
16. Posnett, D. N.; McGrath, H.; Tam, J. P. *J. Biol. Chem.***1988**, *263*, 1719.
17. Tam, J. P. *Proc. Natl. Acad. Sci. U. S. A.* **1988**, *85*, 5409.
18. Tam, J. P.; Zavala, F. *J. Immunol. Methods*, **1989**, *124*, 53.
19. Francis, M. J.; Hastings, G. Z.; Brown, F.; McDermed, J.; Lu, Y. A.; Tam, J. P. *Immunology*, **1991**, *73*, 249.
20. Rao, C.; Tam, J. P. *J. Am. Chem. Soc.*, **1994**, *116*, 6975.
21. Drijfhout, J. W.; Bloemhoff, W. *Int. J. Pept. Protein Res.* **1991**, *37*, 27.
22. McLean, G. W.; Owsianka, A. M.; Subak-Sharpe J. H.; Mardsen, H. S. *J. Immunol. Methods*, **1991**, *137*, 149.
23. Nardelli, B.; Lu, Y. A.; Shiu, D. R.; Delpierre-Defoort, C.; Profy, A. T.; Tam, J. P. *J. Immunol.* **1992**, *148*, 914.
24. Tam, J. P.; Lu, Y. A.; Yang, J. L. *Eur. J. Biochem.* **2002**, *269*, 923.
25. Grandjean, C.; Rommens, C.; Gras-Masse, H.; Melnyk, O. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 1068.
26. Melnyk, O.; Fruchart, J. S.; Gandjean, C.; Gras-Masse, H. *J. Org. Chem.* **2001**, *66*, 4153.
27. Kantchev, E. A. B; Chang, C. C.; Chang, D. K. *Biopolymers*, **2006**, *84*, 232.
28. Purohit, G.; Sakthivel, T.; Florence, A. T. *Int. J. Pharm.***2001**, *214*, 71.
29. Al-Jamal, K. T.; Sakthivel, T.; Florence, A. T. *J. Pharm. Sci.* **2005**, *94*, 102.
30. Esposito, A.; Delort, E.; Lagnoux, D.; Djojo, F.; Reymond, J. L. *Angew. Chem., Int. Ed. Engl.* **2003**, *42*, 1381.
31. Lagnoux, D.; Delort, E.; Douat-Casassus, C.; Esposito, A.; Reymond, J. L. *Chem. Eur. J.* **2004**, *10*, 1215.
32. Douat-Casassus, C.; Darbre, T.; Reymond, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 7817.
33. Clouet, A.; Darbre, T.; Reymond, J. L. *Adv. Synth. Catal.* **2004**, *346*, 1195.

34. Lagnoux, D.; Darbre, T.; Schmitz, M. L.; Reymond, J. L. *Chem. Eur. J.* **2005**, *11*,, 3941.

35. Clouet, A.; Darbre, T.; Reymond, J. L. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 4612.

36. Clouet, A.; Darbre, T.; Reymond, J. L. *Biopolymers*, **2006**, *84*, 114.

37. Clouet, A.; Darbre, T.; Reymond, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 15642.

38. Delort, E.; Nguyen-Trung, N. Q.; Darbre, T.; Reymond, J. L. *J. Org. Chem.* **2006**, *71*, 4468.

39. Kofoed, J.; Darbre, T.; Reymond, J. L, *Org. Biomol. Chem.* **2006**, *4*, 3268.

40. Crespo, L.; Sanclimens, G.; Royo, M.; Giralt, E.; Albericio, F. *Eur. J. Org. Chem.* **2002**, 1756.

41. Crespo, L.; Sanclimens, G.; Montaner, B.; Perez-Tomas, R.; Royo, M.; Pons, M.; Albericio, F.; Giralt, E., *J. Am. Chem. Soc.* **2002**, *124*, 8876.

42. Sanclimens, G.; Crespo, L.; Giralt, E.; Royo, M.; Albericio, F. *Biopolymers*, **2004**, *76*, 283.

43. Sanclimens, G.; Crespo, L.; Giralt, E.; Albericio, F.; Royo, M. *J. Org. Chem.* **2005**, *70*, 6274.

44. Sanclimens, G.; Crespo, L.; Pons, M.; Giralt, E.; Albericio, F.; Royo, M. *Tetrahedron Lett.* **2003**, *44*, 1751.

45. Arya, P.; Rao, N. R.; Singkhonrat, J.; Alper, H.; Bourque; S. C.; Manzer, L. E. *J. Org. Chem.* **2000**, *65*, 1881.

46. Alper, H.; Arya, P.; Bourque, S. C.; Jefferson, G. R.; Manzer, L. E.; *J. Am. Chem. Soc.* **2001**, *123*, 2889.

47. Lu, S. M.; Alper, H. *J. Am. Chem. Soc.* **2003**, *125*, 13126.

48. Mahajan, A.; Chhabra, S. R.; Chan, W. C. *Tetrahedron Lett.* **1999**, *40*, 4909.

49. Chhabra, S. R.; Mahajan, A.; Chan, W. C. *J. Org. Chem.* **2002**, *67*, 4017.

50. Cho, J. K.; Kim, D. W.; Namgung, J.; Lee, Y. S. *Tetrahedron Lett.* **2001**, *42*, 7443.

51. Swali, V.; Wells, N.J.; Langley, G.J.; Bradley, M. *J. Org. Chem.* **1997**, *62*, 4902.

52. Wells, N.J.; Basso, A.; Bradley, M. *Biopolymers (Peptide Science)*, **1998**, *47*, 381.

53. Wells, N.J.; Davies, M.; Bradley, M. *J. Org. Chem.* **1998**, *63*, 6430.

54. Tsubokawa, N.; Ichioka, H.; Satoh, T.; Hayashi, S.; Fujiki, K. *React. Funct. Polym.* **1998**, *37*, 75.

55. Tsubokawa, N.; Kotama, K.; Saitoh, H.; Nishikubo, T. *Compos. Interfaces*, **2003**, *10*, 609.

56. Taniguchi, Y.; Shirai, K.; Saitoh, H.; Yamauchi, T.; Tsubokawa, N. *Polymer*, **2005**, *46*, 2541.

57. Bourque, S. C.; Maltais, F.; Xiao, W. J.; Tardif, O.; Alper, H.; Arya, P. Manzer, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 3035.

58. Bourque, S. C.; Alper, H.; Manzer, L. E.; Arya, P. *J. Am. Chem. Soc.* **2000**, *122*, 956.

59. Reynhardt, J. P. K.; Alper, H. *J. Org. Chem.*, **2003**, *68*, 8353.

60. Zweni, P. P.; Alper, H. *Adv. Synth. Catal.* **2004**, *346*, 849.

61. Sakai, K.; Teng, T. C.; Katada, A.; Harada, T.; Uemura, S.; Asami, Y.; Sakata, M.; Kunitake, M.; Hirayama, C. *Chem. Lett.* **2001**, 510.

62. Sakai, K.; Teng, T. C.; Katada, A.; Harada, T.; Yoshida, K.; Yamanaka, K.; Asami, Y.; Sakata, M.; Hirayama, C.; Kunitake, M. *Chem. Mater.* **2003**, *15*, 4091.

63. Chung, Y. M.; Rhee, H. K. *Chem. Commun.* **2002**, 238.

64. Chung, Y. M.; Rhee, H. K. *C. R. Chim.* **2003**, *6*, 695.

65. Bu, J.; Judeh, Z. M. A.; Ching, C. B.; Kawi, S. *Catal. Lett.* **2003**, *85*, 183.

66. Bu, J.; Li, R.; Quah, C. W.; Carpenter, K. J. *Macromolecules*, **2004**, *37*, 6687.

67. Wang, C.; Zhu, G.; Li, J.; Cai, X.; Wei, Y.; Zhang, D. Qiu, S. *Chem. Eur. J.* **2005**, *11*, 4975.

68. Tsubokawa, N.; Takayama, T. *React. Funct. Polym.* **2000**, *43*, 341.

69. Lei, S.; Yu, S.; Zhao, C. *J. Chromatogr. Sci.* **2001**, *39*, 280.

70. Abu-Reziq, R.; Alper, H.; Wang, D.; Post, M. L. *J. Am. Chem. Soc.* **2006**, *128*, 5279.

71. Pan, B.; Cui, D.; Gao, F.; He, R. *Nanotechnology*, **2006**, *17*, 2483.

72. Fromont, C.; Bradley, M. *Chem. Commun.* **2000**, 283.

73. Lebreton, S.; How, S. E.; Buchholz, M.; Yingyongnarongkul, B.; Bradley, M. *Tetrahedron*, **2003**, *59*, 3945.

74. Ling, F. H.; Lu, V.; Svec, F.; Frechet, J. M. J. J. Org. Chem. **2002**, *67*, 1993.

75. Basso, A.; Evans, B.; Pegg, N.; Bradley, M. *Chem. Commun.* **2001**, 697.

76. Dahan, A.; Portnoy, M. *Macromolecules*, **2003**, *36*, 1034.

77. Dahan, A.; Weissberg, A.; Portnoy, M. *Chem. Commun.* **2003**, 1206.

78. Dahan, A.; Portnoy, M. *J. Am. Chem. Soc.* **2007**, *129*, 5860.

79. Liu, P.; Wu, X.; Pu, Q.; Su, Z. *Anal. Chim. Acta.* **2005**, *95*, 695.

80. Marsh, A.; Carlisle, S. J.; Smith, S. C. *Tetrahedron Lett.* **2001**, 42, 493.

81. Dilly, S. J.; Carlisle, S. J.; Clark, A. J.; Shepherd, A. R.; Smith, S. C.; Taylor P. C.; Marsh, A. *J. Polym. Sci. Part A: Polym. Chem.* **2006**, *44*, 2248.

82. Acosta, E. J.; Carr, C. S.; Simanek, E. E.; Shantz, D. F. *Adv. Mater.* **2004**, *16*, 985.

83. Acosta, E. J.; Gonzalez S.O.; Simanek, E. E.; *J. Polym. Sci. Part A: Polym. Chem.* **2005**, *43*, 168.

84. Bharathi, P.; Patel, U.; Kawaguchi, T.; Pesak, D. J.; Moore, J. S. *Macromolecules*, **1995**, *28*, 5955.

85. Chi, C.; Wu, J.; Wang, X.; Zhao, X.; Li, J.; Wang, F. *Tetrahedron Lett.* **2001**, *42*, 2181.

86. *Optimization of Solid- Phase Combinatorial Synthesis*; Yan, B., Czarnik, A. W., Eds.; Marcel Decker: New York, **2002**,.

87. *Combinatorial Chemistry: Synthesis, Analysis, Screening*; Jung, G., Ed.; Wiley-VCH: Weinheim, **1999**.

88. Kay, C.; Lorthioir, O. E.; Parr, N. J.; Congreve, M. McKeown, S. C.; Scicinski, J. J.; Ley, S.V. *Biotechnol. Bioeng. (Combi. Chem.)* **2001**, *71*, 110.

89. Braun, D.; Cherdron, H.Ritter, H.; *Polymer Synthesis: Theory and Practice. Fundamentals, Methods and Experiments, 3rd Ed.*; Springer: New York; **2001**

90. Sreekumar, K.; Ph. D. Thesis, Mahathma Gandhi University, Kottayam, Kerala, November **1988.**

91. Merrifield, R. B.; *J. Am. Chem. Soc.* **1963**, 85, 2149.

92. Sparrow, J. T.; *J. Org. Chem.* **1976**, *41*, 8, 1350.

93. Akelah, A.; Hassanein, M.; Selim, A.; Kenawy, E. R. *Eur. Polym. J.* **1986**, *22*,12, 983.

94. Buchleier, E.; Wehner, W.; Vogtle, F. Synthesis, **1978**, 155.

95. Hudlicky, M.; *Reductions in Organic Chemistry*, Ellis Horwood Ltd. England, **1984**, pp21.

Chapter 3
POLYMER SUPPORTED DENDRIMERS AS ORGANOCATALYSTS

3. 1. INTRODUCTION

Organocatalysis is the acceleration of chemical reactions with a substoichiometric amount of an organic compound, which does not contain a metal element.[1] It is man's approach to mimic nature in enzyme catalysis. Organic catalysts can be considered as minimalistic version of enzymes, from which they are conceptually derived and to which are often compared.[2] Even if, only in some cases, they display the remarkable selectivity peculiar of enzymes, organic catalysts are generally more stable, less expensive and enjoy wider applications under a variety of conditions unsustainable by enzymes. In addition, organic catalysts are more amenable than both metal- based and biocatalysts to anchoring on a support with the aim of facilitating catalyst recovery and recycling.[3,4] There may be loss of activity and selectivity when metal complexes and biocatalysts like enzymes are attached to polymer supports; but such an observation is rarely found in the case of organic catalysts. Some organocatalysts like proline and cinchona alkaloids may have the extraordinary capacity to mediate efficiently not only one but rather a variety of seemingly unrelated chemical transformations.[5] Such catalysts are called 'privileged catalysts' and this term was coined in analogy to pharmaceutical compound classes that are active against a number of different biological targets.[6] Other advantages include lower toxicity and the reactions can be performed under an aerobic atmosphere, with wet solvents; indeed, the presence of water is often beneficial to the rate and selectivity of the reaction.[5,7]

In this chapter, application of polymer supported poly(amidoamine) (PAMAM) and poly(propylene imine) (PPI) dendrimers as organic catalysts is

described. Polymer supported dendrimers were used as organocatalysts for two different reactions of synthetic importance. The reactions selected were Knoevenagel condensation of carbonyl compounds with active methylene compounds and ring opening of epoxides with nucleophiles.

As a carbon- carbon bond forming reaction, Knoevenagel condensation has found wide spread applications in the synthesis of polymerizable monomers with optical and electrical properties, natural products and pharmaceutically important molecules.[8-13] A large number of catalysts are used for this reaction from classical piperidine to ionic liquids to carbon nanotubes containing nitrogen.[14-24]. But many of these catalysts exhibit several problems. Some are time consuming, some contain metals, some need special laboratory techniques and inert atmosphere, some necessitate the use of halogenated or aromatic solvents etc. When polymer supported dendrimers were used as catalysts for Knoevenagel condensation, these problems were easily eliminated. Polymer supported PAMAM and PPI dendrimers were found to be highly efficient, selective, recyclable catalysts for Knoevenagel condensation.

Ring opening reactions of epoxides with various nucleophiles are of both biological and synthetic importance. In living cells, epoxides are removed by converting them to water soluble diols by the enzyme epoxide hydrolase.[25,26] The easy and common method to prepare 2-aminoalcohols is nucleophilic opening of epoxide rings by amines. 2-aminoalcohols represent a broad range of β-adrenergic blockers widely used in the management of cardiovascular disorders[27] including hypertension,[28,29] angina pectoris, cardiac arrhythmias, and also other disorders related to the sympathetic nervous system. The versatility of this transformation is recognized well as it constitutes the key step for synthesis of β_2-adrenoceptor agonists, novel anti-HIV agents,[30] 4-dimethoxydaunomycin,[31] protein kinase C inhibitor balanol,[32] glycosidase inhibitor,[33] antimalarial agents,[34] liposidomycin B class of antibiotics,[35] naturally occurring brassinosteroids,[36] diverse heterocycles, for example, benzodiazepinones/ benzoxazines/benzoxazepinones[37] and indoles[38] a vast range of biologically

active natural and synthetic products[39] unnatural amino acids[40] and chiral auxilaries[41].

Catalysts have found to play an important role in both stereo and enantioselective synthesis of 2-aminoalcohols.[42-52] But almost all catalysts used for this synthesis include at least one metal center as an integral part of the catalytic system. The problem with the metal complexes is the possibility of the metal leaching from the catalysts, which can contaminate the final products and also result in the deterioration of the catalytic activity. There are a handful of examples of organic catalysts used for the synthesis of 2-aminoalcohols. The classical example is the ring opening reaction of epoxides with various nucleophiles catalyzed by tributylphosphine in water.[53] Another example of oragnocatalysis is the one reported by Kleiner in which a thiourea derivative was used as the catalyst which gave excellent yield and selectivity when the reaction was carried out in water.[54] Polymer supported organocatalysts explored in the synthesis of 2-aminoalcohols are very few.[3]

Polymer supported PAMAM and PPI dendrimers were found to be highly efficient catalysts for both Knoevenagel condensation and nucleophilic ring opening of epoxides with amines. Various factors like degree of crosslinking of the polymer, generation of dendrimers, amount of catalyst, solvent, temperature etc. affecting the catalytic performance were also studied. Moreover a comparison was done on the catalytic nature of dendrimers under homogeneous and polymer supported conditions.

3. 2. RESULTS AND DISCUSSION

3. 2. 1. Knoevenagel Condensation

Both polymer supported PAMAM and PPI dendrimers were found to be highly efficient catalysts in Knoevenagel condensation. The scheme of the reaction is shown in Figure 3-1. Initially the reaction was carried out using polystyrene supported PAMAM and PPI dendrimers.

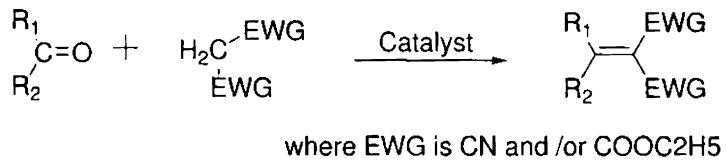


Figure 3-1. Knoevenagel condensation catalyzed by polymer supported dendrimer

In order to quantify the catalytic performance of the polymer supported dendrimers, a model reaction between benzaldehyde and malononitrile was carried out under various reaction conditions. The initial study focused on the optimization of the concentration of the catalyst. Molar equivalents of the carbonyl compound and active methylene compound were reacted in the presence of various amounts of both polystyrene supported PAMAM and PPI dendrimers in ethanol. The results are presented in table 3.1. It was found that, only 0.5 mole percent of the catalyst was required to drive the reaction to completion within a very short period of time. The high speed of the reaction with the present catalyst compared to other catalysts may be due to the local concentration of a large number of catalytic sites within a very small volume due to the dendritic backbone. Increase in the amount of catalyst did not show any positive effect in the reaction.

Table 3.1: Influence of the amount of catalyst on Knoevenagel condensation

Entry	Amount of catalyst (mol%)	% Yield [a, b]	
		PAMAM	PPI
1	0.1	80	83
2	0.2	88	92
3	0.5	100	100
4	1.0	100	100

[a] reaction conditions: 5 mmol benzaldehyde, 5 mmol malononitrile, 5 mL ethanol, room temperature, 15 minutes, [b] isolated yield

In the next step the role of solvent in the reaction was studied. As seen in table 3.2 the reaction proceeded very well in polar solvents including water. Normally, polystyrene-supported catalysts favor non-polar solvents. The opposite behavior observed here is because of the dendritic branches on the polymer surface, which are highly polar; make the polymer-supported system as a whole more compatible to polar solvents. The preference for polar solvents by dendrimers carrying polar surface groups was reported previously.[55,56] In a previous report, Kobayashi showed that polystyrene containing polar groups can act as highly efficient catalysts in water even if they contain strong hydrophobic groups attached to the benzene ring of polystyrene.[57] From these results it is assumed that such effects are pronounced in the case of the present catalysts also. This enables the Knoevenagel condensation to be carried out in a greener route, whereas, many of the conventional Knoevenagel condensations demand solvents like benzene, toluene, acetonitrile etc. in the presence of other catalysts.

Table 3.2: Knoevenagel condensation catalyzed by polymer supported dendrimers: solvent effect

Entry	Solvent	PAMAM		PPI	
		Time in Minutes	% Yield[a,b]	Time in Minutes	% Yield[a,b]
1	Ethanol	15	100	10	100
2	Methanol	15	100	10	100
3	Water	90	98	70	98
4	Benzene	360	70	300	75
5	THF	480	75	420	82
6	CH_3CN	600	70	540	70
7	$CHCl_3$	600	70	540	70

[a] reaction conditions: 5 mmol benzaldehyde, 5 mmol malononitrile, 0.5 mol% of catalyst (G3PAMAM or G3PPI on PS), 5 mL solvent, room temperature. [b] isolated yield

The reaction proceeded more smoothly with the PPI dendrimers. This is because, in the case of PPI dendrimers, the amino groups are more closely spaced because of the smaller chain length of the dendrimer and due to this, a large number of catalytic sites are confined to a nanoscopic volume, which enhances the catalytic activity. Additionally, the amide groups present in the PAMAM dendrimers may have some retarding effect on the nucleophilicty of the amino groups of the PAMAM dendrimer which slows down the reaction. But these effects are very small because, both the catalysts are highly active towards almost all substrates studied.

A comparison between the dendrimers attached to different supports was carried out and the result is presented in table 3.3.

Table 3.3: Effect of support on catalysis

Entry	% Yield [a,b]			
	PAMAM on PMMA	PAMAM on PS	PPI on PMMA	PPIon PS
1	100	100	100	100

[a] reaction conditions: 5 mmol benzaldehyde, 5 mmol malononitrile, 0.5 mol% of catalyst (G3PAMAM or G3PPI), 5 mL ethanol, room temperature, 15 minutes.
[b] isolated yield

From these data it can be seen that all the catalysts were equally efficient under the given set of conditions.

An investigation on the effect of generation of dendrimer on the catalytic activity (table 3.4) showed that the zero and first generation dendrimers gave products after a long reaction time and the yields were low. With second generation dendrimer the product formation was observed with in a relatively small interval of time and the yields were good. But the reaction was not so efficient with many aldehydes and ketones on comparison with the third generation dendrimer. Even if the loading of the lower generation dendrimers were increased, it was difficult to obtain similar results given by the third generation dendrimer. The variation of easiness of the reaction with the

generation of dendrimers is considered to be a dendrimer effect and similar behavior was observed with other dendrimer based catalysts.[38]

Table 3.4: Effect of generation of dendrimer on catalysis

Entry	Generation	Mol % of the catalyst	% Yield [a, b]	
			PAMAM	PPI
1	0	0.5	Nil	Nil
2	1	0.5	30	34
3	2	0.5	70	77
4	2	1.0	74	80
5	3	0.5	100	100

[a] reaction conditions: 5 mmol benzaldehyde, 5 mmol malononitrile, polystyrene supported catalyst, 5 mL ethanol, room temperature, 15 minutes. [b] isolated yield

The result showed that a positive dendrimer effect was observed in the catalysis. The higher activity of the third generation dendrimers was due to the more closed structure of the dendrimer which confined the surface amino groups to a smaller volume. Due to this, the catalysis is more efficient and such efficiency is not achieved even with twice the amount of the second generation dendrimer.

To get more insight on the effect of generation of dendrimer on catalysis, the reaction between benzaldehyde and malononitrile was carried out in the presence of various generations of dendrimers in such a way that the equivalence of amino groups was same in all cases. The results are summarized in table 3.5. The third generation catalyst gave better results under identical reaction conditions. From these experiments it is possible to assume that catalytic species situated at the periphery of a dendrimer exhibit co-operative interaction which can play a decisive role in catalysis. Due to this cooperative effect, the dendronized catalyst is more effective than individual catalyst of same quantity.

Table 3.5: Effect of generation of dendrimer under same concentration of amino groups

Entry	Generation	Milliequivalence of amino groups	% Yield [a, b]	
			PAMAM	PPI
1	0	0.2	Nil	Nil
2	1	0.2	Nil	Nil
3	2	0.2	70	74
4	3	0.2	100	100

[a] reaction conditions: 5 mmol benzaldehyde, 5 mmol malononitrile, polystyrene supported catalyst, 5 mL ethanol, room temperature, 15 minutes, [b] isolated yield

The generality of the reaction was established by preparing a number of different styrene derivatives with various substitutions. The product obtained after the completion of the reaction and on evaporation of the solvent is of high purity and need no further purification. This is an added advantage compared to other catalysts reported in literature used for the same reaction, where column chromatography is necessary for the purification of products. The products were characterized by FTIR and ^{1}HNMR spectroscopy. The reaction proceeded smoothly at room temperature when malononitrile was used as the active methylene compound. But for other active methylene compounds, slightly higher temperature was needed (50 °C). The results are summarized in table 3. 6. a and 3.6. b.

Acetophenone and cyclohexanone, which usually do not undergo Knoevenagel condensation, also gave products under similar conditions with excellent yield. Benzoin and benzil also gave the condensation product, but required more time for the completion of the reaction. This may be due to the steric hindrance offered by the two phenyl groups that are close to the carbonyl group. Benzophenone did not give the product even after prolonged time under similar conditions. The carbonyl group flanked between two phenyl rings is prevented from interacting with the dendrimer surface groups that block the molecule to undergo reaction. Similar selectivity of dendrimer based catalysts for smaller substrates was reported in literature.[59]

Table 3.6.a: Knoevenagel condensation catalyzed by polymer supported PAMAM dendrimer

Entry	Carbonyl Compound	Active Methylene Compound	Temp. °C	Time (minutes)	% Yields [a,b]
K1	C_6H_5CHO	$CH_2(CN)_2$	30	15	100
K2	$4\text{-}CH_3OC_6H_4CHO$	$CH_2(CN)_2$	30	15	100
K3	$4\text{-}ClC_6H_4CHO$	$CH_2(CN)_2$	30	20	99
K4	$4\text{-}(CH_3)_2NC_6H_4CHO$	$CH_2(CN)_2$	30	20	100
K5	$2\text{-}OHC_6H_4CHO$	$CH_2(CN)_2$	30	20	98
K6	$4\text{-}OHC_6H_4CHO$	$CH_2(CN)_2$	30	20	100
K7	$3\text{-}NO_2C_6H_4CHO$	$CH_2(CN)_2$	30	15	99
K8	$4\text{-}NO_2C_6H_4CHO$	$CH_2(CN)_2$	30	15	99
K9	$3CH_3O,4\text{-}OH\text{-}C_6H_3CHO$	$CH_2(CN)_2$	30	15	100
K10	$3,4(CH_3O)_2C_6H_3CHO$	$CH_2(CN)_2$	30	20	99
K11	C_4H_3OCHO	$CH_2(CN)_2$	30	10	99
K12	$C_6H_{10}O$	$CH_2(CN)_2$	50	15	99
K13	$C_6H_5COCH_3$	$CH_2(CN)_2$	50	40	98
K14	$C_6H_5COCHOHC_6H_5$	$CH_2(CN)_2$	50	90	97
K15	$C_6H_5COCOC_6H_5$	$CH_2(CN)_2$	50	120	100
K16	C_6H_5CHO	$(CN)CH_2COOC_2H_5$	50	15	99
K17	$4\text{-}CH_3OC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	15	99
K18	$4\text{-}ClC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	20	98
K19	$4\text{-}(CH_3)_2NC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	15	100
K20	$2\text{-}OHC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	20	99
K21	$4\text{-}OHC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	15	100
K22	$3\text{-}NO_2C_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	20	100
K23	$4\text{-}NO_2C_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	20	100
K24	$3CH_3O,4\text{-}OH\text{-}C_6H_3CHO$	$(CN)CH_2COOC_2H_5$	50	20	100
K25	$3,4(CH_3O)_2C_6H_3CHO$	$(CN)CH_2COOC_2H_5$	50	20	100
K26	C_4H_3OCHO	$(CN)CH_2COOC_2H_5$	50	15	98
K27	$C_6H_{10}O$	$(CN)CH_2COOC_2H_5$	50	20	98
K28	$C_6H_5COCH_3$	$(CN)CH_2COOC_2H_5$	50	45	95
K29	C_6H_5CHO	$CH_2(COOC_2H_5)_2$	50	60	95
K30	$4\text{-}CH_3OC_6H_4CHO$	$CH_2(COOC_2H_5)_2$	50	60	95

[a] reaction conditions: 5 mmol carbonyl compound, 5 mmol active methylene compound, 0.5 mol% of catalyst G3PAMAM on PS, 5 mL ethanol. [b] isolated yield of pure product. [c] yield from GCMS data

Table 3.6.b: Knoevenagel condensation catalyzed by polymer supported PPI dendrimer

Entry	Carbonyl Compound	Active Methylene Compound	Temp. °C	Time (minutes)	% Yields [a,b]
K1	C_6H_5CHO	$CH_2(CN)_2$	30	10	100
K2	$4\text{-}CH_3OC_6H_4CHO$	$CH_2(CN)_2$	30	10	100
K3	$4\text{-}ClC_6H_4CHO$	$CH_2(CN)_2$	30	17	99
K4	$4\text{-}(CH_3)_2NC_6H_4CHO$	$CH_2(CN)_2$	30	10	100
K5	$2\text{-}OHC_6H_4CHO$	$CH_2(CN)_2$	30	20	98
K6	$4\text{-}OHC_6H_4CHO$	$CH_2(CN)_2$	30	15	100
K7	$3\text{-}NO_2C_6H_4CHO$	$CH_2(CN)_2$	30	15	99
K8	$4\text{-}NO_2C_6H_4CHO$	$CH_2(CN)_2$	30	15	99
K9	$3CH_3O,4\text{-}OH\text{-}C_6H_3CHO$	$CH_2(CN)_2$	30	10	100
K10	$3,4(CH_3O)_2C_6H_3CHO$	$CH_2(CN)_2$	30	10	100
K11	C_4H_3OCHO	$CH_2(CN)_2$	30	10	99
K12	$C_6H_{10}O$	$CH_2(CN)_2$	50	15	99
K13	$C_6H_5COCH_3$	$CH_2(CN)_2$	50	30	98
K14	$C_6H_5COCHOHC_6H_5$	$CH_2(CN)_2$	50	90	98
K15	$C_6H_5COCOC_6H_5$	$CH_2(CN)_2$	50	120	100
K16	C_6H_5CHO	$(CN)CH_2COOC_2H_5$	50	10	99
K17	$4\text{-}CH_3OC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	10	99
K18	$4\text{-}ClC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	20	98
K19	$4\text{-}(CH_3)_2NC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	10	100
K20	$2\text{-}OHC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	20	99
K21	$4\text{-}OHC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	10	100
K22	$3\text{-}NO_2C_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	15	100
K23	$4\text{-}NO_2C_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	20	100
K24	$3CH_3O,4\text{-}OH\text{-}C_6H_3CHO$	$(CN)CH_2COOC_2H_5$	50	10	100
K25	$3,4(CH_3O)_2C_6H_3CHO$	$(CN)CH_2COOC_2H_5$	50	15	100
K26	C_4H_3OCHO	$(CN)CH_2COOC_2H_5$	50	15	100
K27	$C_6H_{10}O$	$(CN)CH_2COOC_2H_5$	50	20	98[c]
K28	$C_6H_5COCH_3$	$(CN)CH_2COOC_2H_5$	50	45	95[c]
K29	C_6H_5CHO	$CH_2(COOC_2H_5)_2$	50	45	95
K30	$4\text{-}CH_3OC_6H_4CHO$	$CH_2(COOC_2H_5)_2$	50	45	97

[a] reaction conditions: 5 mmol carbonyl compound, 5 mmol active methylene compound, 0.5 mol% of catalyst G3 PPI on PS, 5 mL ethanol. [b] isolated yield of pure product. [c] yield from GCMS data

When ethyl cyanoacetate was used for condensation, only E isomer of the product was formed except in the case of acetophenone. In the case of acetophenone, the formation of two isomers was confirmed by GCMS which showed two well separated peaks in the GC having the same molecular mass.

A possible mechanism of the reaction includes the formation of imines from the amino group of the dendrimer and carbonyl compounds, which reacts with the active methylene compound to give the corresponding olefins and it can be represented as in Figure 3-2.

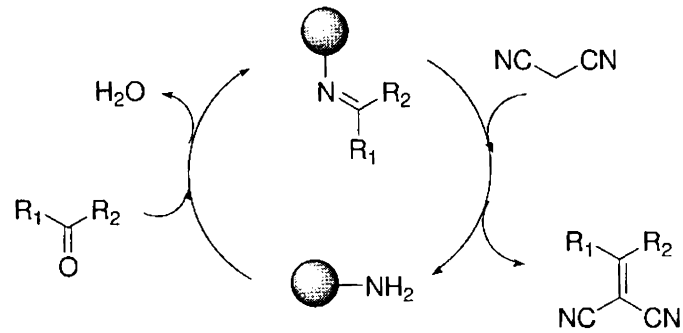


Figure 3-2. Possible mechanism of Knoevenagel condensation

The possibility of catalyst recycling was studied. For this purpose, the catalyst was washed extensively with ethyl acetate and dried under vacuum at room temperature. The color of the polymer supported catalyst was turned to light brown from yellow in the case of PAMAM dendrimers and from light brown to dark brown in the case of PPI dendrimers after the first run, but the catalytic activity remained the same for the subsequent runs. FTIR measurements showed that the catalyst did not undergo any chemical change and all the peaks corresponding to various functional groups in the catalysts remained unchanged after the reaction. The catalyst showed no reduction in activity even after the tenth run. The results are summarized in table 3. 7.

Table 3.7: Effect of recycling on catalysis

Entry	No. of recycling	%Yield [a, b]	
		PAMAM	PPI
1	1	100	100
2	2	100	100
3	5	100	100
4	7	97	97
5	10	94	95

[a] reaction conditions: 5 mmol benzaldehyde, 5 mmol malononitrile, 5 mL ethanol, room temperature, 15 minutes, G3 PAMAM or G3 PPI on PS, [b] isolated yield

In a similar way, both PAMAM and PPI dendrimers supported on poly(methyl methacrylate) also showed good catalytic properties under identical conditions (table 3.8).

Table 3.8: Knoevenagel condensation catalyzed by PMMA supported PAMAM dendrimer

Entry	Carbonyl Compound	Active Methylene Compound	Temp. °C	Time (minutes)	% Yields [a,b]
1	C_6H_5CHO	$CH_2(CN)_2$	30	10	100
2	4-$CH_3OC_6H_4CHO$	$CH_2(CN)_2$	30	10	100
3	4-ClC_6H_4CHO	$CH_2(CN)_2$	30	17	99
4	4-$(CH_3)_2NC_6H_4CHO$	$CH_2(CN)_2$	30	10	100
5	2-OHC_6H_4CHO	$CH_2(CN)_2$	30	15	98
6	4-OHC_6H_4CHO	$CH_2(CN)_2$	30	15	100
7	3-$NO_2C_6H_4CHO$	$CH_2(CN)_2$	30	15	99
8	4-$NO_2C_6H_4CHO$	$CH_2(CN)_2$	30	15	99
9	3CH_3O,4-OH -C_6H_3CHO	$CH_2(CN)_2$	30	10	100
10	3,4$(CH_3O)_2C_6H_3CHO$	$CH_2(CN)_2$	30	10	100
11	C_4H_3OCHO	$CH_2(CN)_2$	30	10	99
12	C_6H_5CHO	$(CN)CH_2COOC_2H_5$	50	10	99
13	4-$CH_3OC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	50	10	99
14	4-ClC_6H_4CHO	$(CN)CH_2COOC_2H_5$	50	15	98
15	C_6H_5CHO	$CH_2(COOC_2H_5)_2$	50	30	95

[a] reaction conditions: 5 mmol carbonyl compound, 5 mmol active methylene compound, 0.5 mol% of catalyst G3 PAMAM on PMMA, 5 mL ethanol. [b] isolated yield

The speed of the reaction under similar conditions was little higher for these catalysts because of the lesser steric hindrance offered to the approaching substrate by the polymer support. But due to the poor mechanical stability of the PMMA resin, the resin particles got powdered after few cycles of catalysis. Here also PPI dendrimers were observed to be more active.

The degree of crosslinking of the polymer support has little effect on the catalysts efficiency (table 3.9). The reaction became sluggish when the dendrimer supported on polystyrene of higher degree of crosslinking was used. This is due to the lower swelling capacity of the resin of higher degree of crosslinking. This prevents the reactants from interacting with the catalytic sites.

Table 3.9: Effect of support on the catalytic activity of the PAMAM dendrimer in Knoevenagel condensation

Degree of Crosslinking	% Yield [a,b]	
	PS	PMMA
1%	100	100
2%	100	100
4%	97	96
6%	90	90

[a] reaction conditions: 5 mmol benzaldehyde, 5 mmol malononitrile, 0.5 mol% PAMAM dendrimer, 5 mL ethanol, room temperature, 15 minutes, [b] isolated yield

3. 2. 2. Synthesis of 2-Aminoalcohols by Ring Opening of Epoxides with Amines

Various 2-aminoalcohols were synthesized from epoxides and amines using polymer supported dendrimers as heterogeneous organic catalysts. The scheme of the reaction is presented in Figure 3-3.

Initially cyclohexene oxide and aniline were allowed to react in THF in the presence of various amounts of third generation PAMAM dendrimer and

PPI dendrimer supported on polystyrene. The results are presented in table 3. 10. THF was selected because, from the previous experiment, it was noted that the dendrimer based catalysts were more active in polar solvents. It was observed that, only 2 mol% of the catalyst was required for obtaining good yield. The yield of the product was low when lower concentrations of the catalysts were used. An increase in the concentration of the catalyst had virtually no impact on the speed of the reaction and yield of the product.

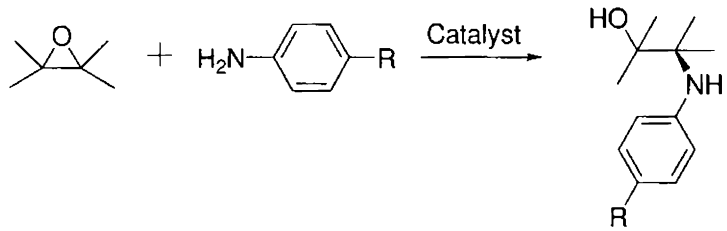


Figure 3-3. Ring opening of epoxides catalyzed by polymer supported dendrimers

Table 3.10: Influence of the concentration of catalyst on ring opening of epoxides

Entry	Mol% of the catalyst	% Yield [a, b]	
		PAMAM	PPI
1	0.5	Nil	Nil
2	1	40	35
3	1.5	79	74
4	2	90	87
5	2.5	90	87

[a] reaction conditions: 5 mmol cyclohexene oxide, 5.2 mmol aniline, polystyrene supported catalyst, 5 mL, THF, 50 °C, 12 h. [b] isolated yield.

In the second step, the influence of solvent on the catalytic activity of the polymer supported dendrimer was studied. The model reaction between cyclohexene oxide and aniline was performed in various solvents under identical conditions and the results are shown in table 3. 11. The reaction proceeded best in dioxan compared to other solvents. In water, the reaction proceeded as a

triphasic system and this resulted in the reduction of yield. When water was used along with an organic solvent miscible with water, the yield was increased. Solvents like ethanol, methanol etc., which gave good results in the previously discussed Knoevenagel condensation were omitted because of a possible competition from these nucleophilic solvents with the reactant nucleophile, i.e., the amine. The reaction did not perform well in chloroform, because in chloroform, it was expected that the dendrimer was not solvated well which prevented effective catalysis.

Table 3.11: Effect of solvent on ring opening of epoxides by amines

Entry	Solvent	% Yield [a, b]	
		PAMAM	PPI
1	Water	65	61
2	Dioxan	100	95
3	THF	90	87
4	Water + Dioxan (1:1)	89	85
5	Water + THF (1:1)	70	68
6	$CHCl_3$	60	60

[a] reaction conditions: 5 mmol cyclohexene oxide, 5.2 mmol aniline, 2 mol % of polystyrene supported catalyst, 5 mL solvent, 50 °C, 12 h. [b] yield by GC/MS.

Temperature of the reaction has significant effect on catalysis in the case of ring opening reaction. The reaction went to completion slowly at room temperature and the yield was low. But increasing the temperature to 50 °C had a remarkable impact on the speed of the reaction and the yield of the product was increased. The model reaction between cyclohexene oxide and aniline went to completion with in 12 h at 50 °C with 100 % conversion to the product as observed from GC/MS. The yield obtained at room temperature was also good compared to many other catalysts previously reported. Under refluxing condition, the reaction went to completion within 8 h but reaction at such high temperature was avoided considering the possible decomposition of dendritic backbone.

A comparison between the dendrimers attached to different supports was carried out and the result is presented in table 3. 12. It was observed that better results were obtained with dendrimers supported on polystyrene support. This may be due to the more hydrophobic nature of the polystyrene support. The polar dendritic catalysts situated in a nonpolar hydrophobic polystyrene network are supposed to act as catalysts through an enzyme mimicking mechanism in which the dendrimers playing the role of the enzyme's active site and the polymer that of an oversimplified peptide backbone not directly involved in the catalytic activity. Similar enzyme mimicking properties were shown previously by polymer supported aminoacids in which the amino acid acted as catalytic sites whereas the polymer support acted as the peptide backbone.[60,61]

Table 3.12: Effect of support on catalysis

Entry	% Yield [a, b]			
	PAMAM on PMMA	PAMAM on PS	PPI on PMMA	PPIon PS
1	95	100	91	95

[a] reaction conditions: 5 mmol cyclohexene oxide, 5.2 mmol aniline, 2 mol % of polystyrene supported catalyst, 5 mL solvent, 50 °C, 12 h. [b] yield by GC/MS.

An investigation on the effect of generation of dendrimer on the catalytic activity (table 3. 13) showed that dendrimers of higher generations were found to be catalytically more active. When the model reaction between aniline and cyclohexene oxide was carried out in the presence of dendrimers of various generations it was observed that a gradual increase in the yield of the product was observed with increase in the generation of the dendrimer and the third generation dendrimers are the most active catalysts. The variation of easiness of the reaction with the generation of dendrimers is considered to be a dendrimer effect and similar behavior was observed with other dendrimer based catalysts

Table 3.13: Effect of generation of dendrimer on catalysis

Entry	Generation	Mol % of the catalyst	% Yield [a, b]	
			PAMAM	PPI
1	0	2.0	20	20
2	1	2.0	51	49
3	2	2.0	90	87
4	3	2.0	98	91

[a] reaction conditions: 5 mmol cyclohexene oxide, 5.2 mmol aniline, 2 mol % of polystyrene supported catalyst, 5 mL solvent, 50 °C, 12 h. [b] isolated yield.

A number of 2-aminoalcohols were synthesized from various epoxides and amines for the generalization of the catalysts efficiency. The results are presented in table 3. 14.

The mechanism of the reaction involved activation of the epoxide by hydrogen bond formation with the catalyst followed by attack of the nucleophile. This can be represented as shown in Figure 3-4. A similar mechanism was reported earlier for the ring opening reaction catalyzed by hydroxyl compounds by Hine et al.[25,26] and by thiourea derivative reported by Kleiner and Schreiner[54]. The trans configuration of the product was confirmed from the determination of the $J_{H\text{-}H}$ coupling constants for CH-NH in the coresponding ^{1}HNMR spectrum. This configuration of the products also supports the presented mechanism.

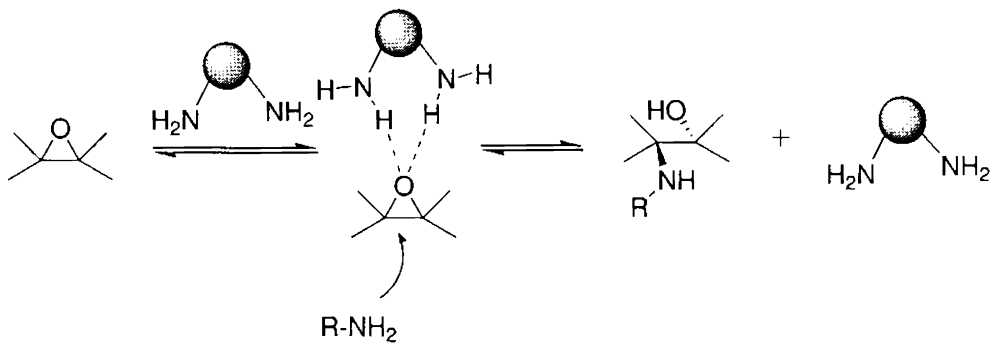


Figure 3-4. Possible mechanism of the ring opening of epoxides catalyzed by polymer supported dendrimers

Table 3.14: Ring opening of epoxides catalyzed by polstyrene supported dendrimers

Entry	Epoxide	Aniline	PAMAM		PPI	
			Time h	%Yield[a,b]	Time h	%Yield[a,b]
R1	Cyclohexene oxide	Aniline	12	98	12	95
R2	Cyclohexene oxide	4-bromoaniline	24	94	24	90
R3	Cyclohexene oxide	4-methoxyaniline	24	96	24	90
R4	Cyclohexene oxide	2-methylaniline	24	96	24	90
R5	Cyclohexene oxide	4-nitroaniline	24	90	24	80
R6	Cyclohexene oxide	3-chloroaniline	24	95	24	89
R7	Styrene oxide	Aniline	24	89	24	86
R8	Styrene oxide	4-bromoaniline	24	85	24	80
R9	Styrene oxide	4-methoxyaniline	24	90	24	84
R10	Styrene oxide	2-methylaniline	30	93	28	90
R11	Styrene oxide	4-nitroaniline	36	95	36	89
R12	2-butene oxide	Aniline	24	92	24	88
R13	2-butene oxide	4-bromoaniline	36	90	36	86
R14	2-butene oxide	4-methoxyaniline	24	93	24	86
R15	2-butene oxide	2-methylaniline	36	90	36	84
R16	2-butene oxide	4-nitroaniline	36	89	36	82

[a] reaction conditions: 5 mmol epoxide, 5.2 mmol aniline, 2 mol % catalyst, 5 mL dioxan, 50 °C, [b] isolated yield

PAMAM dendrimers were found to be more efficient catalyst than PPI dendriemr of the same generation. This may be due to the higher nucleophilicity of PPI dendriemrs. Due to the higher nucleophilicity, the conversion of the intermediate to the product may be difficult in the case of PPI dendrimers. Moreover due to this higher nucleophilicity some of the amino groups of the dendriemr may react with the epoxide. The presence of the amide bonds in the PAMAM dendriemer may reduce its nucleophilicity and due to this lower nucleophilicity, the conversion was more effective.

The reaction was slowed down with increase in the degree of crosslinking of the polymer support. This observation is due to the poor swelling of the resin that prevent diffusion of reactant molecules to the interior of the polymer where more than 90% catalytic sites are present. This effect is slightly higher in the case of PPI dendrimers because of lower chain length of the dendrimer, which reduce the distance between the surface amino groups and the polymer support and there by induce more steric hindrance to the reactants.

Poly(methyl methacrylate) supported dendrimers were also found to be good catalysts in the synthesis of 2-aminoalcohols (table 3.15). The time required for the completion of the reaction was almost similar to that of the polystyrene catalyst, but the yield was low as described earlier. Moreover the mechanical stability of polystyrene resin also make polystyrene supported dendrimers better catalysts.

Table 3.15: Ring opening of epoxides catalyzed by PMMA supported dendrimers

Entry	Epoxide	Aniline	PAMAM		PPI	
			Time h	%Yield[a,b]	Time h	%Yield[a,b]
1	Cyclohexene oxide	Aniline	12	90	12	86
2	Cyclohexene oxide	4-bromoaniline	24	87	24	82
3	Cyclohexene oxide	4-methoxyaniline	24	81	24	78
4	Cyclohexene oxide	2-methylaniline	24	86	24	70
5	Cyclohexene oxide	4-nitroaniline	24	79	24	70
6	Cyclohexene oxide	3-chloroaniline	24	81	24	72
7	Styrene oxide	Aniline	24	78	24	70
8	Styrene oxide	4-bromoaniline	24	75	24	71
9	Styrene oxide	4-methoxyaniline	24	73	24	68
10	Styrene oxide	2-methylaniline	30	75	28	75
11	Styrene oxide	4-nitroaniline	36	74	36	72
12	2-butene oxide	Aniline	24	72	24	68

[a] reaction conditions: 5 mmol epoxide, 5.2 mmol aniline, 2 mol % catalyst, 5 mL dioxan, 50 °C. [b] isolated yield

The catalyst recycling was also studied. The catalyst used in each run was washed well and reused in the subsequent runs. It was observed that the catalyst could be reused at least six times without considerable loss of activity (table 3.16). The FTIR spectra of the catalyst before and after the reaction showed that the peaks due to the primary amino groups of the dendrimer remained unaltered. This shows the stability of the catalyst under the given set of reaction conditions.

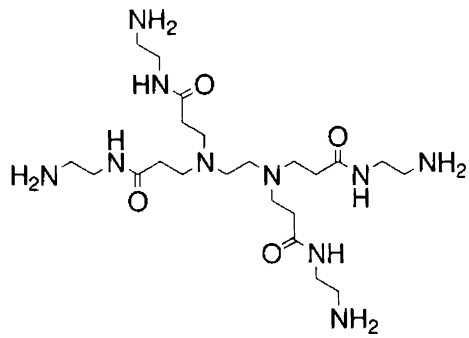
Table 3.16: Effect of recycling on catalysis

Entry	No. of recycling	%Yield [a, b]	
		PAMAM	PPI
1	1	98	95
2	2	98	95
3	5	92	89
4	6	91	86

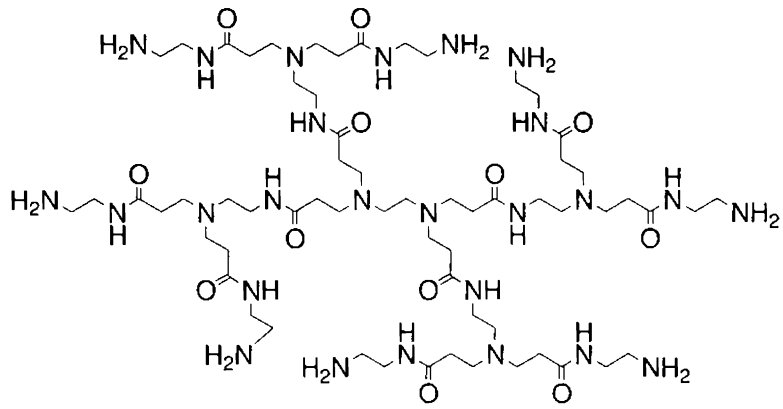
[a] Reaction conditions: 5 mmol cyclohexene oxide, 5.2 mmol aniline, 2 mol % of polystyrene supported catalyst, 5 mL dioxan, 50 °C. 12 h. [b] isolated yield.

3. 2. 3. Soluble Dendrimers as a Homogeneous Organic Catalyst

In order to compare the catalytic properties of polymer supported dendrimers with soluble dendrimers, zero and first generation PAMAM dendrimers were prepared and used as homogeneous catalysts in the above mentioned reactions. For this purpose, zero and first generation of PAMAM dendrimers were prepared according to the standard procedure that involved Michael addition of methyl acrylate to the ethylene diamine core followed by transamination of the ester groups with ethylene diamine.[62] The first generation dendrimer used here carry the same number of functional groups as that in the third generation supported dendrimer (Figure 3-5).



G 0 PAMAM dendrimer



G 1 PAMAM dendrimer

Figure 3-5. G0 and G1 PAMAM dendrimer

The dendrimers prepared were used as organic catalysts and the reaction medium selected was water for effortless separation of catalyst from the product.

Both zero and first generation dendrimers are highly efficient catalysts for Knoevenagel condensation. The reaction was carried out in the presence of 0.5 mol % of the catalyst and gave excellent yield at room temperature for most of the pairs of reactants tried. The reaction got completed with in a very short period of time and the products were isolated by simple filtration or extraction with a suitable organic solvent. The products obtained were of high purity and needed no further purification. The experimental results are summarized in the table 3. 17.

Table 3.17: Knoevenagel condensation catalyzed by PAMAM dendrimer

Entry	Carbonyl compound	Active methylene compound	Time (minutes)	Yield %
1	C_6H_5CHO	$CH_2(CN)_2$	2	100
2	4-$CH_3OC_6H_4CHO$	$CH_2(CN)_2$	3	100
3	2-OHC_6H_4CHO	$CH_2(CN)_2$	3	98
4	Furfural	$CH_2(CN)_2$	2	97
5	C_6H_5CHO	$(CN)CH_2COOC_2H_5$	15	95
6	4-$CH_3OC_6H_4CHO$	$(CN)CH_2COOC_2H_5$	10	90
7	2-OHC_6H_4CHO	$(CN)CH_2COOC_2H_5$	5	95
8	C_4H_3OCHO	$(CN)CH_2COOC_2H_5$	5	95
9	C_6H_5CHO	$CH_2(COOC_2H_5)_2$	10	95
10	4-$CH_3OC_6H_4CHO$	$CH_2(COOC_2H_5)_2$	5	97

[a] reaction conditions: 5 mmol carbonyl compound, 5 mmol active methylene compound, 0.5 mol% of catalyst (G1 PAMAM), 5 mL water. [b] isolated yield of pure product.

The reaction proceeded more quickly compared to the polymer supported systems and yields obtained were also equal or greater than that of the polymer supported systems. Additionally, the reaction proceeded at room temperature while certain reactants needed higher temperature when polymer supported dendrimers were used as catalyst. The better catalysis by PAMAM dendrimers in solution compared to the polymer supported system can be explained by considering the fact that in solution, better interaction is possible between the reactants and the catalyst. Furthermore, a phenomenon known as 'hydrophobic hydration' accelerates the reactions in water. [63-65] Although water does not dissolve organic components well, many organic transformations are significantly accelerated. The simple rationale is that water avoids mixing with organic solutes because this would lead to increased structuring and thus a loss of entropy of the water molecules around the solutes. Water avoids this situation by bringing the solutes together so that this so-called "hydrophobic hydration'

can lead to rate enhancement of reactions run with water-insoluble, or only partially soluble, substrates through minimization of the solute's volume.

Similarly unsupported soluble dendrimer (G0 and G1) were used to catalyzed the ring opening of epoxides by amines. The results are shown in table 3.18.

Table 3.18: Ring opening of various epoxides catalysed by amines

Entry	Epoxide	Amine	Time hours	Yield %
1	Cyclohexene oxide	$C_6H_5NH_2$	24	70
2	Cyclohexene oxide	4-$CH_3OC_6H_4NH_2$	24	63
3	Cyclohexene oxide	2-$CH_3C_6H_4NH_2$	24	65
4	Styrene oxide	$C_6H_5NH_2$	24	60
5	Styrene oxide	4-$CH_3OC_6H_4NH_2$	24	60
6	Styrene oxide	2-$CH_3C_6H_4NH_2$	24	56
7	2-butene oxide	$C_6H_5NH_2$	24	30
8	2-butene oxide	4-$CH_3OC_6H_4NH_2$	24	32
9	2-butene oxide	2-$CH_3C_6H_4NH_2$	24	36

a-reaction conditions: 5 mmol epoxide, 5.2 mmol aniline, 2 mol % catalyst, 5 mL water, 50 °C, [b] isolated yield

PAMAM dendrimer of both the generations are less efficient catalysts in the ring opening of epoxides. The supported dendrimers promoted the reaction efficiently and the yield of the product was high irrespective of the nature of the reactants. But such a performance was not observed with unsupported dendrimers. This lower activity can be explained by considering two factors. The reaction is performed in water. Water molecules may compete with the nucleophile i.e. anilines in this case. Since the concentration of water molecules is high there is always a chance that water molecules effectively replace the amine and thereby reduce the yield. But in the case of supported dendrimers the reaction was performed in dioxan and so this kind of retarding effect was not there. The second factor is that in the case of supported dendrimers an enzyme

like activity is expected to play a role to increase the activity of the catalyst. The hydrophilic dendrimers attached to a hydrophobic polymer network mimic an enzyme in activity which enhances the catalysis. This kind of effect which assist catalysis is also not there in the case of unsupported dendrimers.

The generation of dendrimer has considerable effect on the catalytic properties and this is more pronounced in the case of ring opening reaction. Both zero and first generation dendrimers were good catalyst for Knoevenagel condensation, but the reaction was slightly slower in the case of zero generation dendrimer. While considering the ring opening reaction first generation dendrimer was found to be far better catalyst than the zero generation one. The reaction was extremely slow and gave poor yield when zero generation dendrimer was used as catalyst and the rate and yield was higher when first generation dendrimer was used. This is due to the larger number of amino groups present in the first generation dendrimers compared to the zero generation one and the co-operative effect of these sites enhances the catalytic process.

The aqueous layer containing the dendrimer was separated after the first cycle of the reaction, which was used for another cycles. It was observed that the catalytic activity gradually decreased and after the third cycle the activity drastically dropped down in the case of both the reactions. Cloudiness was also formed in the aqueous layer at this stage. This is a serious set back compared to the polymer supported systems, which can be used a number of times with out loss of activity.

3. 3. CONCLUSION

To conclude, polystyrene and PMMA supported PAMAM and PPI dendrimers were found to be highly efficient and reusable organocatalysts. The supported dendrimers were used as organocatalysts in Knoevenagel condensation and in the nucleophilic ring opening of epoxides by anilines. Various factors affecting the catalytic activity like amount of catalyst, solvent, temperature, nature of the support and generation of dendrimers were studied

in detail. From these data the reaction conditions were optimized. The efficiency of these catalysts were proved by preparing various styrene derivatives and -amino alcohol derivatives. The catalysts were recycled and reused without considerable loss of activity. In short, polymer supported dendrimers were found to be highly active and green organocatalysts.

3. 4. EXPERIMENTAL

3. 4. 1 Synthesis of Soluble G0 Dendrimer

A solution of methyl acrylate (17.5 g, 0.203 mol) in methanol (20 mL) was prepared in a two necked round bottom flask fitted with a condenser and a dropping funnel. The flask was kept in an ice bath. A solution of ethylene diamine (2.5 g, 0.041 mol) in methanol (10 mL) was added drop wise with stirring over a period of 1 h. The resulting solution was stirred for further 30 min at the same temperature and allowed to warm to room temperature and stirred for further 48 h. The volatiles were removed under reduced pressure at 40 °C using a rotary evaporator to give the desired product and it was dissolved in methanol (10 mL) and evacuated as before. The product was dried under vacuum overnight. Yield= 13.52g (97%)

Ethylene diamine(37.56 g, 0.625 mol) was dissolved in methanol (50 mL) taken in a two necked round bottom flask fitted with a condenser and a dropping funnel kept in an ice bath. A solution of the above ester (5 g, 0.0125 mol) in methanol (20 mL) was added drop wise to it with constant stirring over a period of 1 h. The resulting solution was allowed to warm to room temperature and stirred for further 96h at room temperature. The volatiles were removed under reduced pressure using a rotary evaporator maintaing the temperature not higher than 40 °C and the excess 1,2 diaminoethane was removed using an azeotropic mixture of toluene and methanol (9:1 v/v) .The remaining toluene was removed by azeotropic distillation using methanol. Finally the remaining methanol was removed under vacuum to provide the amino-terminated product as yellow oil. It was dried under vacuum

overnight. Yield=6.32 g, 98% .

3. 4. 2 Synthesis of Soluble G 1 Dendrimer

A solution of methyl acrylate (8.26 g, 0.096 mol) in methanol (20 mL) was prepared in a two necked round bottom flask fitted with a condenser and a dropping funnel. The flask was kept in an ice bath. A solution of G0 dendrimer (5 g, 0.0096 mol) in methanol (10 mL) was added drop wise with stirring over a period of 1 h. The resulting solution was stirred for further 30 min at the same temperature and allowed to warm to room temperature and stirred for further 48 h. The volatiles were removed under reduced pressure at 40 °C using a rotary evaporator to give the desired product and it was dissolved in methanol (10 mL) and evacuated as before. The product was dried under vacuum overnight. Yield= 10.13g (98%)

Ethylene diamine(60 g, 0.625 mol) was dissolved in methanol (100 mL) taken in a two necked round bottom flask fitted with a condenser and a dropping funnel kept in an ice bath. A solution of the above ester (5 g, 0.004 mol) in methanol (20 mL) was added drop wise to it with constant stirring over a period of 1 h. The resulting solution was allowed to warm to room temperature and stirred for further 96 h at room temperature. The volatiles were removed under reduced pressure using a rotary evaporator maintaing the temperature not higher than 40 °C and then the excess 1,2 diaminoethane was removed using an azeotropic mixture of toluene and methanol (9:1 v/v) .The remaining toluene was removed by azeotropic distillation using methanol. Finally, the remaining methanol was removed under vacuum to provide the amino-terminated product as light brown oil. It was dried under vacuum overnight. Yield=5.60 g, 98%.

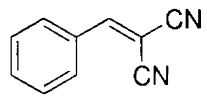
3. 4. 3. General Procedure of Knoevenagel Condensation Catalyzed by Polymer Supported Dendrimers

A 10 mL round bottom flask was charged with the carbonyl compound (5 mmol), active methylene compound (5 mmol), polymer supported catalyst (0.5 mol % of the substrates) and absolute ethanol (5 mL). The reaction mixture was stirred at the requisite temperature. The formation of the product was monitored

by TLC. After completion of the reaction, the reaction mixture was filtered. The catalyst was washed several times with ethyl acetate. The washings were collected and combined with the filtrate. The products were isolated by removing the solvent by evaporation. In general, no further purification method was required. All the products were previously reported ones and were characterized using FTIR and ^{1}HNMR spectroscopy. In the case of liquid products, GC/MS was used for characterization and yield determination.

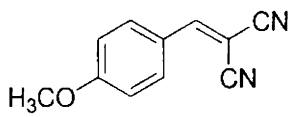
3. 4. 5. Characterization of Olefins

2-(Phenylmethylene)malononitrile (Entry K1)



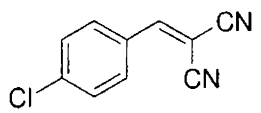
FTIR (KBr, ν_{max} (cm^{-1})) 2223, 1598; ^{1}HNMR ($CDCl_3$): δ 7.9 (d, phenyl, 2H, *J*=8.5 Hz), 7.8 (s, CH, 1H), 7.5–7.7 (m, phenyl, 3H).

2-[(4-Methoxyphenyl)methylene]malononitrile (Entry K2)



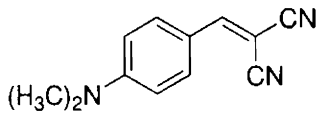
FTIR (KBr, ν_{max} (cm^{-1})) 2218, 1598; ^{1}HNMR ($CDCl_3$): δ 7.9 (d, phenyl, 2H, *J* =8.5 Hz), 7.6 (s, CH, 1H), 7.0 (d, phenyl, 2H, *J* =8.5 Hz), 3.9 (OCH_3, s, 3H,).

2-[(4-Chlorophenyl)methylene]malononitrile (Entry K3)



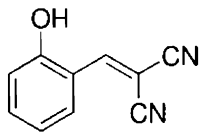
FTIR (KBr, ν_{max} (cm^{-1})) 2223, 1582; ^{1}H NMR ($CDCl_3$): δ 7.8 (d, phenyl, 2H *J* = 8.4 Hz), 7.7 (s, CH, 1H), 7.5 (d, phenyl, 2H, *J* = 8.4 Hz).

2-[(4-Dimethylaminophenyl)methylene]malononitrile (Entry K4)



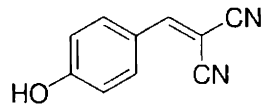
FTIR (KBr, ν_{max} (cm^{-1})) 2200, 1614; ^{1}HNMR ($CDCl_3$): δ 7.8 (d, phenyl, 2H, *J* = 9.0 Hz), 7.4 (s, CH, 1H), 6.6 (d, phenyl, 2H, *J* =9.0 Hz), 3.1 (s, CH_3, 6H).

2-[(2-Hydroxyphenyl)methylene]malononitrile (Entry K5)



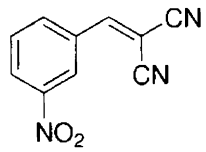
FTIR (KBr, ν_{max} (cm^{-1})) 3390 (OH), 2202, 1598; ^{1}HNMR ($CDCl_3$): δ 8.2 (s, CH, 1H), 7.9 (q, phenyl, 2H, *J* =3.1 Hz), 6.8 (q, phenyl, 2H, *J* =2.8 Hz), 5.0 (s, OH, 1H).

2-[(4-Hydroxyphenyl)methylene]malononitrile (Entry K6)



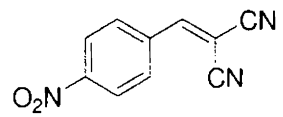
FTIR (KBr, ν_{max} (cm^{-1})) 3353, 2228, 1608; ^{1}HNMR ($CDCl_3$): δ 7.8 (d, phenyl, 2H, *J* = 8.3 Hz), 7.7 (s, CH, 1H), 6.9 (d, phenyl, 2H, *J* =8.7 Hz), 4.5 (s, OH, 1H).

2-[(3-Nitrophenyl)methylene]malononitrile (Entry K7)



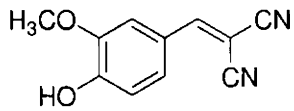
FTIR (KBr, ν_{max} (cm^{-1})) 2228, 1592, 1521, 1349; ^{1}HNMR ($CDCl_3$): δ 8.2 (s, CH, 1H), 7.4-8.1 (m, phenyl, 3H).

2-[(4-Nitrophenyl)methylene]malononitrile (Entry K8)



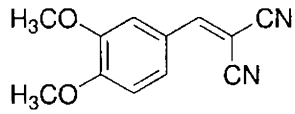
FTIR (KBr, ν_{max} (cm^{-1})) 2226, 1592, 1523, 1349; ^{1}HNMR ($CDCl_3$): δ 8.2–8.0 (d, phenyl, 2H, *J* =10.0 Hz), 7.8 (s, CH, 1H), 7.7–7.6 (d, phenyl, 2H, *J* =10.0 Hz).

2-[(3-Methoxy4-hydroxyphenyl)methylene]malononitrile (Entry K9)



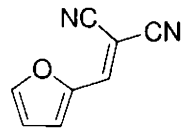
FTIR (KBr, ν_{max} (cm^{-1})) 3291, 2218, 1562; ^{1}HNMR ($CDCl_3$): δ 8.2 (s, CH, 1H), 7.0 (d, phenyl, 1H, *J* =8.6 Hz), 6.3 (d, phenyl, 1H, *J* =8.0 Hz), 6.1 (s, phenyl, 1H), 5.0 (s, OH, 1H), 3.9 (s, OCH_3, 3H).

2-[(3,4-Dimethoxyphenyl)methylene]malononitrile (Entry K10)



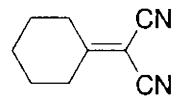
FTIR (KBr, ν_{max} (cm^{-1})) 2962, 2931, 2221, 1573; ^{1}HNMR (MeOD): δ 8.0 (s, CH, 1H), 7.7 (s, phenyl, 1H), 7.6 (d, phenyl, 1H, *J* =6.5 Hz), 7.1 (d, phenyl, 1H, *J* =8.5 Hz), 3.9 (s, OCH_3, 6H).

2-(Furylmethylene)malononitrile (Entry K11)



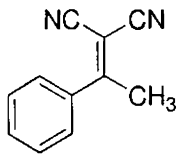
FTIR (KBr, ν_{max} (cm^{-1})) 2228, 1603; ^{1}HNMR ($CDCl_3$+MeOD): δ 7.8 (d, furyl, 1H, *J* =1.4 Hz), 7.5 (s, CH, 1H), 7.3 (d, furyl, 1H, *J* =3.6 Hz), 6.7 (q, furyl, 1H, *J* =1.6 Hz).

2-Cyclohexylidenemalononitrile (Entry K12)



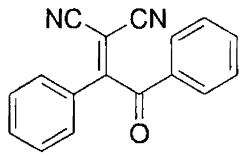
FTIR (KBr, ν_{max} (cm^{-1})) 2226, 1593; ^{1}H NMR (MeOD): δ 1.4-1.5 (m, cyclohexyl, 2H), 1.7-1.8 (m, cyclohexyl, 2H), 2.3-2.4 (q, cyclohexyl, 2H), 2.5-2.9 (q, cyclohexyl, 2H).

(2-Phenyl, 2-methylmethylene)malononitrile (Entry K13)



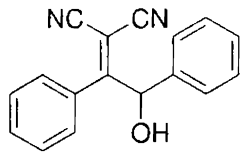
FTIR (KBr, ν_{max} (cm^{-1})) 2218, 1588; ^1H NMR (MeOD): δ 7.5-7.4 (m, phenyl, 5H), 2.6 (s, CH_3, 3H).

2-(2-oxo-1,2-diphenylethylidene)malononitrile (Entry K14)



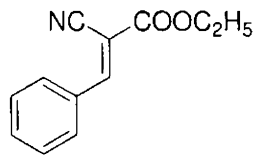
FTIR (KBr, ν_{max} (cm^{-1})) 2236, 1723, 1599; ^1H NMR (MeOD): δ 7.0-7.5 (m, phenyl, 10H).

2-(2-hydroxy-1,2-diphenylethylidene)malononitrile (Entry K15)



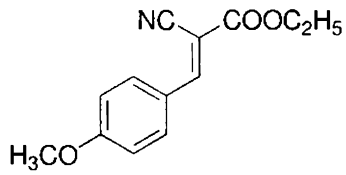
FTIR (KBr, ν_{max} (cm^{-1})) 3413, 2216, 1599; ^1HNMR (DMSO-d_6): δ 7.9 (s, phenyl, 2H), 7.5-7.2 (m, phenyl, 8 H), 3.3 (s, CH, 1H), 2.5 (s, OH, 1H).

Ethyl(E)-2-cyano-3-phenyl-2-propenoate (Entry K16)



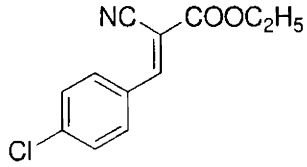
FTIR (KBr, ν_{max} (cm^{-1})) 2226, 1728, 1608, 1266, 1090; ^1HNMR ($CDCl_3$): δ 8.2 (s, CH, 1H), 7.9 (d, d, phenyl, 2H), 7.5 (m, phenyl, 3H), 4.3–4.4 (q, CH_2, 2H, J =7.0 Hz), 1.3–1.4 (t, CH_3, 3H, J =7.0 Hz).

Ethyl(E)-2-cyano-3-(4-methoxyphenyl)-2-propenoate (Entry K17)



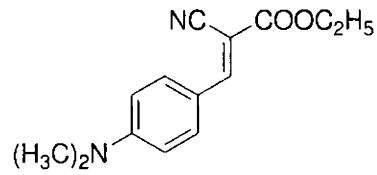
FTIR (KBr, ν_{max} (cm^{-1})) 2947, 2844, 2216, 1717, 1588, 1256, 1121; ^{1}HNMR ($CDCl_3$): δ 8.1 (s, CH, 1H), 8.0 (d, phenyl, 2H, *J* =7.0 Hz), 7.0 (d, phenyl, 2H, *J* =7.0 Hz), 4.3–4.4 (q, CH_2, 2H, *J* =7.0 Hz), 3.9 (s, OCH_3, 3H), 1.3–1.4 (t, CH_3, 3H, *J* =7.0 Hz).

Ethyl(E)-2-cyano-3-(4-chloropheny)l-2-propenoate (Entry K18)



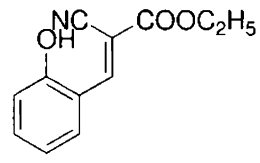
FTIR (KBr, ν_{max} (cm^{-1})) 2221, 1728, 1560, 1266, 1007, 753; ^{1}H NMR ($CDCl_3$): δ 8.1 (s, CH, 1H), 7.9 (d, phenyl, 2H, *J* = 8.5 Hz), 7.4 (d, phenyl, 2H, *J* =8.5 Hz), 4.3 (q, CH_2, 2 H, *J* = 7.1 Hz), 1.4 (t, CH_3, 3H, *J* = 7.1 Hz).

Ethyl(E)-2-cyano-3-(4-dimethylaminopheny)l-2-propenoate (Entry K19)



FTIR (KBr, ν_{max} (cm^{-1})) 2812, 2210, 1708, 1608, 1225, 1116; ^{1}HNMR ($CDCl_3$): δ 8.0 (s, CH, 1H), 7.9 (d, phenyl, 2H, *J* =8.8 Hz), 6.6 (d, phenyl, 2H, *J* =8.9 Hz), 4.3 (q, CH_2, 2H, *J* =7.1 Hz), 3.1 (s, $N(CH_3)_2$, 6H), 1.3 (t, CH_3, 3H, *J* =7.1 Hz).

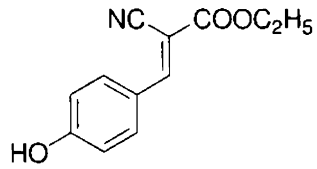
Ethyl(E)-2-cyano-3-(2-hydroxypheny)l-2-propenoate (Entry K20)



FTIR (KBr, ν_{max} (cm^{-1})) 3284, 2231, 1733, 1582, 1173, 1028; ^{1}HNMR ($CDCl_3$+MeOD): δ 8.1 (s, CH, 1H), 7.9 (q, phenyl, 2H, *J* =3.0 Hz), 6.8 (q, phenyl

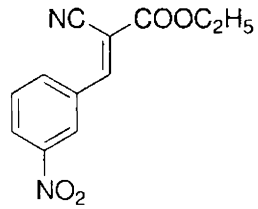
2H, *J* =2.8 Hz), 4.3 (q, CH_2, 2H, *J* =3.6 Hz), 4.0 (s, OH, 1H), 1.3 (t, CH_3, 3H, *J* =3.3 Hz).

Ethyl(E)-2-cyano-3-(4-hydroxypheny)l-2-propenoate (Entry K21)



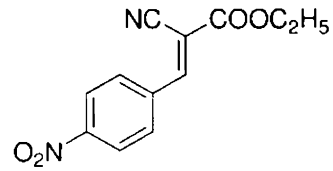
FTIR (KBr, ν_{max} (cm^{-1})) 3353, 2227, 1608, 1174, 1030; ^{1}HNMR ($CDCl_3$): δ 8.2 (s, CH, 1H), 7.9 (d, phenyl, 2H, *J* =8.0 Hz), 7.0 (d, phenyl, 2H, *J* =8.0 Hz), 4.4 (q, CH_2, 2H, *J* =7.0 Hz), 1.4 (t, CH_3, 3H, *J* =7.0 Hz).

Ethyl(E)-2-cyano-3-(3-nitropheny)l-2-propenoate (Entry K22)



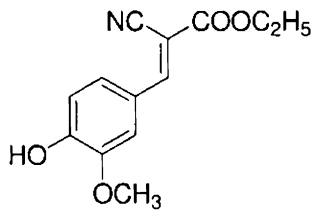
FTIR (KBr, ν_{max} (cm^{-1})) 2226; 1717, 1604, 1525, 1355, 1204, 1090; ^{1}HNMR ($CDCl_3$): δ 8.6 (s, CH, 1H), 7.2-8.6 (m, phenyl, 4 H), 4.4 (q, CH_2, 2H, *J* =7.1 Hz), 1.4 (t, CH_3, 3H, *J* =7.1 Hz).

Ethyl(E)-2-cyano-3-(4-nitropheny)l-2-propenoate (Entry K23)



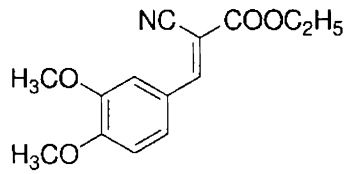
FTIR (KBr, ν_{max} (cm^{-1})) 2226, 1717, 1604, 1525, 1355, 1204, 1090; ^{1}HNMR ($CDCl_3$): δ 8.6 (s, CH, 1H), 7.2-8.6 (m, phenyl, 4 H), 4.4 (q, CH_2, 2H, *J* =7.1 Hz), 1.4 (t, CH_3, 3H, *J* =7.1Hz).

Ethyl(E)-2-cyano-3-(3-methoxy4-hydroxypheny)l-2-propenoate (Entry K24)



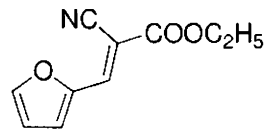
FTIR (KBr, ν_{max} (cm^{-1})) 3378, 2973, 2942, 2221, 1708, 1577, 1085, 1017; ^{1}HNMR ($CDCl_3$): δ 8.0 (s, CH, 1H), 7.8 (s, phenyl, 1H), 7.3- 6.9 (m, phenyl, 2H), 6.3 (s, OH, 1H), 4.3 (q, CH_2, 2 H, *J* =7.1 Hz), 3.9 (s, OCH_3, 3H), 1.4 (t, CH_3, 3H, *J* =7.1 Hz).

Ethyl(E)-2-cyano-3-(3,4-dimethoxypheny)l-2-propenoate (Entry K25)



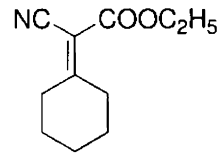
FTIR (KBr, ν_{max} (cm^{-1})) 2968, 2937, 2216, 1712, 1582, 1157, 1090; ^{1}HNMR (MeOD): δ 8.2 (s, CH, 1H),7.8 (d, phenyl, 1H, *J* =1.9 Hz), 7.6 (q, phenyl, 1H, *J* =2.0 Hz), 4.3 (q, CH_2, 2H, *J* =7.0 Hz), 1.4 (t, CH_3, 3H, *J* =7.1 Hz).

Ethyl(E)-2-cyano-3-furyl-2-propenoate (Entry K26)



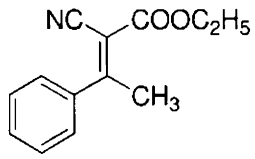
FTIR (KBr, ν_{max} (cm^{-1})) 2221; 1717, 1604, 1209, 1017; ^{1}HNMR ($CDCl_3$ +MeOD): δ 8.0 (s, CH, 1H), 7.7 (s, furyl, 1H), 7.4 (d, furyl, 1H, *J* = 3.2 Hz), 6.6 (t, furyl, 1H, *J* = 1.8 Hz), 4.3 (q, CH_2, 2 H, *J* = 1.9 Hz), 1.4 (t, CH_3, 3H, *J* = 2.0 Hz).

Ethyl 2-cyano 2-cyclohexylideneacetate (Entry K27)



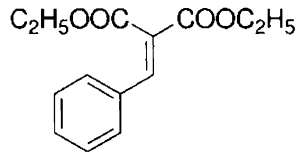
FTIR (KBr, ν_{max} (cm^{-1})) 2223, 1728; 1582, 1242, 1023; GC/MS calculated for $C_{11}H_{12}NO_2$ 193.24 (M^+), found 193 (M^+).

Ethyl(E)-2-cyano2-methyl-3-phenyl-2-propenoate (Entry K28)



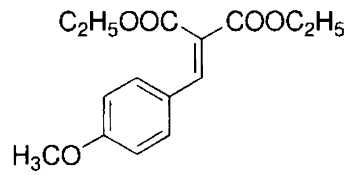
FTIR (KBr, ν_{max} (cm^{-1})) 2226, 1728, 1588, 1246, 1028; GC/MS calculated for $C_{13}H_{13}NO_2$ 215.25 (M^+), found 215 (M^+).

Diethyl 2-benzylidenemalonate (Entry K29)



FTIR (KBr, ν_{max} (cm^{-1})) 1725, 1280, 1112; ^{1}HNMR ($CDCl_3$): δ 7.8 (s, CH, 1H), 7.5–7.3 (m, phenyl, 5H,), 4.4 (q, CH_2, 2H, *J* =7.0 Hz), 4.3 (q, CH_2, 2H, *J* =7.0 Hz), 1.3 (t, CH_3, 3H, *J* =7.0 Hz), 1.2 (t, CH_3, 3H, *J* =7.0 Hz).

Diethyl 2-(4-methoxybenzylidene)malonate (Entry K30)



FTIR (KBr, ν_{max} (cm^{-1})) 1728, 1283, 1112; ^{1}HNMR ($CDCl_3$): δ 7.6 (s, CH, 1H), 7.3 (d, phenyl, 2H, *J* =8.0 Hz), 6.8 (d, phenyl, 2H, *J* =8.0 Hz), 4.4 (q, CH_2, 2H, *J* =7.0 Hz), 4.3 (q, CH_2, 2H, *J* =7.0 Hz), 3.8 (s, OCH_3, 3H), 1.4 (t, CH_3, 3H, *J* =7.0 Hz), 1.3 (t, CH_3, 3H, *J* =7.0 Hz).

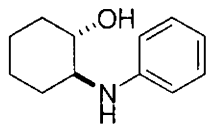
3. 4. 6. General Procedure for the Synthesis of 2-Aminoalcohols Catalyzed by Polymer Supported Dendrimers

A 10 mL round bottom flask was charged with epoxide (5 mmol) and amine (5.2 mmol) and polymer supported catalyst. The amount of catalyst taken was such that each reaction mixture contained 0.10 mmol of the corresponding dendrimer (2 mol % with respect to the epoxide). 5 mL of dry dioxan was added and the reaction mixture was kept in an oil bath with the temperature preset at

50 °C with constant stirring. The progress of the reaction was monitored by TLC on silica gel plate using hexane and ethyl acetate (25:1) as eluent. After the completion of the reaction, the catalyst was filtered off and washed with ethyl acetate. The filtrate and washings were combined and the solvent was removed under vacuum. The crude product was purified by column chromatography on silica gel using hexane-ethyl acetate (25:1) as eluent. All the products were previously reported compounds and were characterized using FTIR, and ^{1}H-NMR spectroscopy. The analytical data for representative compounds are given below.

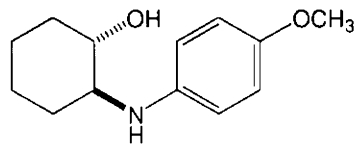
3. 4. 7. Characterization of 2-Aminoalcohols

trans-2-(phenylamino)cyclohexanol (Enrty R1)



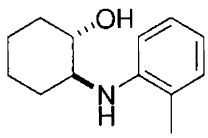
FTIR (KBr, ν_{max} (cm^{-1})) 3590, 3414, 2931, 2858, 1601, 1500, 1448, 1319, 1067; ^{1}HNMR ($CDCl_3$): δ 6.7–7.2 (m, phenyl, 5 H), 3.33 (ddd, *J* =4.2, 10.4 and 10.5, 1 H), 3.13 (ddd, *J*= 3.9, 10.0 and 10.1, 1 H), 2.9 (m, 2H), 2.10–2.16 (m, cyclohexyl, 2 H), 1.72–1.78 (m, cyclohexyl, 2 H) and 1.03–1.42 (m, cyclohexyl,4 H).

trans-2-(4-Methoxyphenylamino)cyclohexanol (Entry R3)



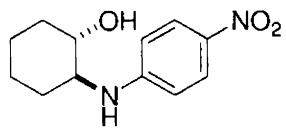
FTIR (KBr, ν_{max} (cm^{-1})) 3529, 3366, 3013, 2938, 2861, 1612, 1512, 1465, 1450, 1239, 1221, 1067; ^{1}HNMR ($CDCl_3$): δ 6.8 (d, *J* = 8 Hz, 2H), 6.7 (d, *J* = 8 Hz, 2H), 3.7 (s, 3H), 3.3 (ddd, *J* = 9.5, 9.3, 3.9 Hz, 1H), 3.0 (ddd, *J* = 10.9, 9.3, 3.8 Hz, 1H), 2.1 (m, 2H),1.72 (m, 2H), 1.3 (m, 3H), 1.0 (m, 1H).

trans-2-(2-Methylphenylamino)cyclohexanol (Entry R4)



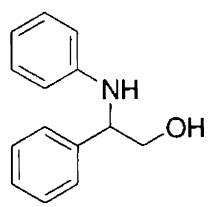
FTIR (KBr, ν_{max} (cm^{-1})) 3597, 3400, 2945, 2865, 1609, 1504, 1450, 1326, 1073; ^{1}HNMR ($CDCl_3$): δ 7.1 (m, 2H), 6.8 (d, *J* =7.9 Hz, 1 H), 6.7 (m, 1H), 3.4 (ddd, *J* = 10.5, 9.4, 4.8 Hz, 1H), 3.2 (ddd, *J* =10.9, 9.4, 3.8 Hz, 1H), 2.2 (s, 3H), 2.15 (m, 2H), 1.8 (m, 2H), 1.4 (m, 3H), 1.1 (m, 1H).

trans-2- (4-Nitrophenylamino)cyclohexanol (Entry R5)



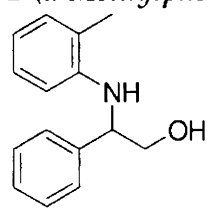
FTIR (KBr, ν_{max} (cm^{-1})) 3500, 3420, 2987, 2873, 1601, 1592, 1523, 1349, 1073, 890; ^{1}HNMR ($CDCl_3$): δ 7.98 (d, *J* = 9.3 Hz, 2H) 6.65 (d, *J* =9.3 Hz, 2H), 4.84 (s, 2H, N*H* & O*H*), 3.43 (ddd, *J* = 10.2, 10.2, 4.5 Hz, 1H), 3.29 (m, 1H), 2.00 (m, 2H), 1.75 (m, 2H),1.30(m, 4H).

2-Phenylamino-2-phenylethanol



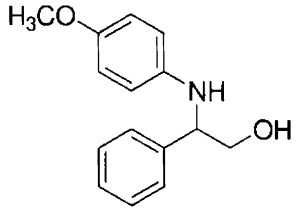
FTIR (KBr, ν_{max} (cm^{-1})) 3498, 3354, 2931, 2858, 1601, 1500, 1448, 1319, 1067; ^{1}HNMR ($CDCl_3$): δ 6.6-7.4 (m, 10H), 4.5 (dd, *J* =7.0, 4.0 Hz, 1H), 3.95 (dd, *J* =11.0, 4.0 Hz, 1H), 3.75 (dd, *J* = 11.0, 7.0 Hz, 1H).

2-(2-Methylphenyl)amino-2-phenylethanol



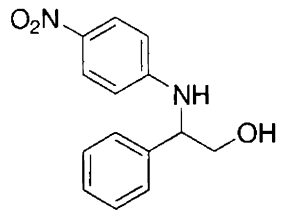
FTIR (KBr, ν_{max} (cm^{-1})) 3500, 3394, 2990, 2888, 1613, 1511, 1446, 1321, 1087; ^{1}HNMR ($CDCl_3$): δ 7.24-7.41 (m, 5 H), 7.06 (d, *J* =7.0 Hz, 1 H), 6.94 (t, *J* = 7.4 Hz, 1 H), 6.63 (t, *J* = 7.4 Hz, 1 H), 6.38(d, *J* = 8.1 Hz, 1 H), 4.53-4.57 (m, 1 H), 3.96-4.01 (m, 1 H), 3.77-3.83 (m, 1 H), 2.27 (s, 3 H).

2-(4-Methoxyphenyl)amino-2-phenylethanol



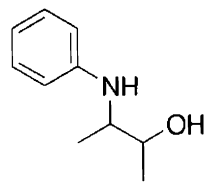
FTIR (KBr, ν_{max} (cm^{-1})) 3533, 3354, 2931, 2858, 1601, 1500, 1448, 1319, 1067; ^{1}HNMR ($CDCl_3$): δ 7.45-6.52 (m, 9 H, ArH), 4.87 (dd, *J* = 3.3, 9.2 Hz, 1 H), 3.73 (s, 3 H, OCH_3) 3.49 (dd, *J* = 14.0, 3.2 Hz, 1 H), 3.30 (dd, *J* = 14.0, 9.2 Hz, 1H).

2-(4-nitrophneylamino)-2-phenylethanol



FTIR (KBr, ν_{max} (cm^{-1})) 3500, 3354, 2931, 2858, 1601, 1500, 1448, 1319, 1067; ^{1}HNMR ($CDCl_3$): δ 7.95 (d, *J* = 9.2 Hz, 2 H, aryl), 7.38-7.27 (m, 5 H, aryl), 6.46 (d, *J* = 9.2 Hz, 2H, aryl),4.57 (dd, *J*= 4.1, 6.2 Hz, 1H), 4.00 (dd, *J* = 11.4, 4.1 Hz,1H), 3.81 (dd, *J* = 11.4, 6.2 Hz, 1 H).

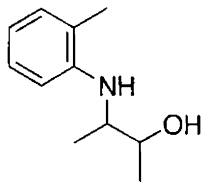
2-N-phenylamino-3-butanol



FTIR (KBr, ν_{max} (cm^{-1})) 3517, 3398, 3053, 2974, 2926, 1922, 1602, 1505, 1439, 1376, 1318 1254, 1005, 902, 751, 692; ^{1}HNMR (CDCl$_3$): δ 7.15-7.18 (m, 2H), 6.66-6.74 (m,

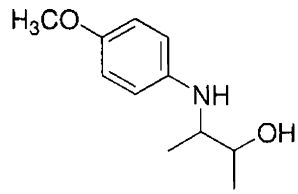
3H), 3.62 (m, 2H), 3.31 (m, 1H), 2.61 (brs, 1H), 1.25 (d, 3H, *J* = 6.8 Hz), 1.14 (d, 1H, *J* = 6.8 Hz).

2-N-(2'-tolyl)amino-3-butanol



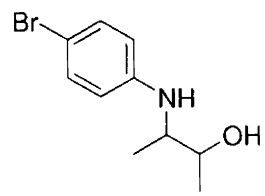
FTIR (KBr, ν_{max} (cm^{-1})) 3527, 3414, 2972, 2923, 1601, 1511, 1448, 1378, 1313, 1256, 1056, 748, 512; ^{1}HNMR ($CDCl_3$): δ 7.11 (d, 1H), 7.07 (d, 1H), 6.68-6.73 (m, 2H), 3.70 (t, 1H, *J* = 6.2 Hz), 3.40 (t, 1H, *J* = 6.2 Hz), 2.16 (s, 3H), 1.28 (d, 3H, *J* = 6.2 Hz), 1.18 (d, 3H, *J* = 6.2 Hz).

2-N-(4'-methoxyphenyl)amino-3-butanol



FTIR (KBr, ν_{max} (cm^{-1})) 3499, 3394, 2970, 1617, 1512, 1455, 1377, 1236, 1037, 822; ^{1}HNMR ($CDCl_3$): δ 6.83-6.86 (m, 2H), 6.71-6.75 (m, 2H), 3.81 (s, 3H), 3.63 (t, 1H, *J* = 6.6 Hz), 3.23 (t, 1H, *J* = 6.9 Hz), 1.32 (d, 3H, *J* = 6.0 Hz), 1.18 (d, 3H, *J* = 6.4 Hz).

2-N-(4'-bromophenyl)amino-3-butanol



FTIR (KBr, ν_{max} (cm^{-1})) 3577, 3400, 2973, 1593, 1492, 1390, 1315, 1080, 1006, 813, 453; ^{1}HNMR ($CDCl_3$): δ 7.23 (m, 2H), 6.53 (m, 2H), 3.65 (t, 1H, *J* = 6.2 Hz), 3.53 (s, 1H), 3.27 (t, 1H, *J* = 6.9 Hz), 2.45 (s, 1H), 1.24 (d, 3H, *J* = 6.2 Hz),1.14 (dd, 1H, *J* = 6.2 Hz).

3. 4. 8. General Procedure for Catalyst Recycling

After each run the catalyst filtered off from the reaction mixture was washed extensively with ethyl acetate in a soxhlet apparatus. It was then dried under vacuum for 24 hours and reused in the next cycle.

3. 4. 9. General Procedure for Catalysis with Water Soluble Dendrimers

Water solutions of G0 and G1 PAMAM dendrimers were prepared so that 1 mL of the solution contained 0.025 mmol of the corresponding dendrimer.

3. 4. 9. a. General Procedure of Knoevenagel Condensation

A 10 mL round bottom flask was charged with the water solution of the catalyst (1mL, 0.5 mol% of catalyst), 5 mmol carbonyl compound and 5 mmol active methylene compound. After adding water (4 mL) the reaction mixture was stirred at room temperature for the requisite time. The progress of the reaction was followed by TLC on a silica gel plate using hexane-ethyl acetate (10:1 v/v) mixture as eluent. The product was isolated by filtration (in the case of solids) or extraction with hexane. The solid products were washed with water and dried. In the case of liquid products, evaporation of the solvent gave the product in pure form. Generally, the products obtained were of high purity and required no further purification. All the products were known compounds and characterized using ^{1}HNMR and FTIR spectroscopy.

3. 4. 9. b. General Procedure for the Synthesis of 2-Aminoalcohols

A 10 mL round bottom flask was charged with the water solution of the catalyst (4mL, 2 mol% of catalyst), 5 mmol epoxide and 5.2 mmol aniline. After adding water (1 mL) the reaction mixture was stirred at 50 ^{o}C for the requisite time. The progress of the reaction was followed by TLC on a silica gel plate using hexane-ethyl acetate (25:1 v/v) mixture as eluent. After the completion of the reaction the organic layer was extracted with ethyl acetate. The final product was obtained by purification on a small column of silica using hexane, ethyl acetate mixture (25:1) as the eluent. All the products were known compounds and characterized using ^{1}HNMR and FTIR spectroscopy.

REFERENCES

1. Dalko, P. I.; Moisan, L. *Angew. Chem. Int. Ed. Eng.* **2004**, *43*, 5138.
2. Breslow, R. *Science*, **1982**, *218*, 532.
3. Benaglia, M.; Puglisi, A.; Cozzi, F. *Chem. Rev.* **2003**, *103*, 3401.
4. Cozzi, F.; *Adv. Synth. Catal.* **2006**, *348*, 1367.
5. *Enantioselective Organocatalysis*; Dalko, P. I. Ed.; Wiley-VCH: Weinheim, **2007.**
6. Yoon, T. P.; Jacobsen, E. N. *Science*, **2003**, *299*, 1691.
7. *Asymmetric Organocatalysis*, Berkessel, A., Groger, H. Eds; Wiley-VCH: Weinheim, **2005**
8. Zhang, X.R.; Chao, W.; Chuai, Y.T.; Ma, Y.; Hao, R.; Zou, D.C.; Wei, Y.G.; Wang, Y. *Org. Lett.* **2006**, *8*, 2563.
9. Kwak, G.; Fujiki, M. *Macromolecules*, **2004**, *37*, 2021.
10. Liao, J.; Wang, Q. *Macromolecules*, **2004**, *37*, 7061.
11. Nokami, J.; Kataoka, K.; Shiraishi, K.; Osafune, M.; Hussain, I.; Sumida, S. *J. Org. Chem.* **2001**, *66*, 1228.
12. Tietze, L. F.; Rackelman, N. In *Multicomponent Reactions*; Zhu, J., Bienayme, H., Eds.; Wiley-VCH: Weinheim, **2005**.
13. Cho, H.; Ueda, M.; Tamaoka, M.; Hamaguchi, Y.; Kazuo, A.; Kiso, T. Inoue, R. Ogino, T. Tatsuoka; Ishihara, T.; Noguchi, T.; Morita, I.; Murota, S. *J. Med.Chem.* **1991**, *34*, 1503.
14. Jones, G. *Organic Reactions*, Vol. XV Wiley: New York, **1967**.
15. Yamashita, K; Tanaka, T; Hayashi, M. *Tetrahedron Lett.* **2005**, *61*, 7981.
16. Cai, Y; Peng, Y; Song, G. *Catal. Lett.* **2006**, *109*, *1-2*, 61.
17. Reddy, K. R.; Rajagopal, K.; Maheswari, C. U.; Kantam, M. L. *New. J. Chem.* **2006**, *30*, 1549
18. Hangarge, R. K.; Jarikote, D. V.; Shingare, M. S. *Green Chemistry*; **2002**, *4*, 266.
19. van Dommele, S.; de Jong, K. P.; Bitter, J. H. *Chem. Commun.* **2006**, 4859.
20. Cao, Y. Q.; Rui Zhang, Z. D.; Chen, B. H. *Synth. Commun.* **2004**, 34, 16, 2965.

21. Narsaiah, A. V.; Nagaiah, K. *Synth. Commun.***2003,** 33, 21, 3825.

22. Hangarge, R. V.; Jarikote, D. V.; Shingare, M. S. *Green Chemistry*, **2002,** *4*, 266.

23. Berrue, F.; Antoniotti, S.; Thomas, O. P.; Amade, P. *Eur. J. Org. Chem.*, **2007**, *11*, 1743.

24. Xin, X.; Gou, X.; Duan, H.; Lin, Y.; Sun, H.; *Catal. Commun.* **2007**, *8 (2)*, 115.

25. Hines, J.; Linden, S. M.; Kanagasabapathy, V. M. *J. Am. Chem. Soc.***1985**, *107*, 1082.

26. Hines, J.; Linden, S. M.; Kanagasabapathy, V. M. *J. Org. Chem.* **1985**, *50*, 5096.

27. Connolly, M. E.; Kersting, F.; Bollery, C. T. *Prog. Cardiovasc. Dis.***1976**, *19*, 203.

28. Shanks, R. G.; Wood, T. M.; Dornhost, A. C.; Clark, M. L. *Nature;* **1966**, *212*, 88.

29. De Cree, J.; Geukens, H.; Leempoels, J.; Verhaegen, H. *Drug Dev. Res.* **1986**, *8*, 109.

30. Ruediger, E.; Martel, A.; Meanwell, N.; Solomon, C.; Turmel, B. *Tetrahedron Lett.* **2004**, *45*, 739.

31. Sekine, A.; Ohshima, T.; Shibasaki, M. *Tetrahedron* **2002**, *58*, 75.

32. Wu, M. H.; Jacobsen, E. N. *Tetrahedron Lett.* **1997**, *38*, 1693.

33. Lindsay, K. B.; Pyne, S. G. *Tetrahedron* **2004**, *60*, 4173.

34. Zhu, S.; Meng, L.; Zhang, Q.; Wei, L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1854.

35. Moore, W. J.; Luzzio, F. A. *Tetrahedron Lett.* **1995**, *36*, 6599.

36. Mori, K.; Sakakibara, M.; Okada, K. *Tetrahedron* **1984**, *40*, 1767.

37. Lieoscher, J.; Jin, S.; Otto, A. *J. Heterocycl. Chem.* **2000**, *37*,509

38. Schirok, H. *J. Org. Chem.* **2006**, *71*, 5538.

39. Erdeen, I. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C.W., Scriven, E. F. V., Eds; Pergamon: Oxford; **1996**; Vol. I A.

40. O'Brien, P. *Angew. Chem., Int. Ed. Eng.* **1999**, *38*, 326.

41. Ager, D. J.; Prakash, I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*,835.

42. Pasor, I. M.; Yus, M. *Current Org. Chem.* **2005**, *9*, 1.

43. Hodgson, D. M.; Gibbs, A. R.; Lee, G. P. *Tetrahedron*, **1996**, *52*, 14361.

44. Mai, E.; Schneider, C. *Chem. Eur. J.*, **2007**, *13*, 2729.

45. Shivani; Pujala, B.; Chakraborti, A. K. *J. Org. Chem.*, **2007**, *72*, 3713.

46. Kureshy, R. I.; Singh, S.; Khan, N. H.; Abdi, S. H. R.; Suresh, E.; Jasra, R.V. *J. Mol. Catal. A: Chem.*, **2007**, *264*, 162.

47. Kumar, S.P.; Leelavathi, P. *Can. J. Chem.*, **2007**, *85*, 37.

48. Azizi, N.; Saidi, M. R. *Tetrahedron*, **2007**, *63*, 888.

49. Yadav, J.S.; Reddy, A. R.; Narsaiah, A.V.; Reddy, B. V.S. *J. Mol. Catal. A: Chem.*, **2007**, *261*, 207.

50. Arai, K.; Salter, M. M.; Yamashita, Y.; Kobayashi, S. *Angew. Chem., Int. Ed. Eng.*, **2007**, *46*, 955.

51. Jeyakumar, K.; Chand, D. K. *Synthesis*, **2008**, 807.

52. Tabatabaeian, K.; Mamaghani, M.; Mahmoodi, N. O.; Khorshidi, A. *Tetrahedron Lett.*, **2008**, *49*, 1450.

53. Fan, R. H.; Hou, X. L. *J. Org. Chem.* **2003**, *68*, 726.

54. Kleiner, C. M.; Schreiner, P. R. *Chem. Commun.* **2006**, 4315.

55. Ooe, M.; Murata, M.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2004**, *126*, 1604.

56. Muller, C.; Ackerman, L. J.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2004**, *126*, 14960.

57. Iimura, S.; Manabe, K.; Kobayashi, S. *Org. Biomol. Chem.* **2003**, *1*, 2416.

58. Zheng, Z. J.; Chen, J.; Li, Y. S. *J. Organomet. Chem.*, **2004**, *689*, 3040.

59. Scot, R. W. J.; Wilson, O. M.; Crooks, R. M. *J. Phys. Chem. B*, **2005**, *109*, 692.

60. Benaglia, M.; Cinquini, M.; Cozzi, F.; Puglisi, A.; Celentano, G. *Adv. Synth. Catal.* **2002**, *344*, 533.

61. Benaglia, M.; Cinquini, M.; Cozzi, F.; Puglisi, A.; Celentano, G. *J. Mol. Catal. A: Chemical*, **2003**, *204–205*, 157.

62. Tomalia, D. A. *Polymer Chemistry A Practical Approach*, Davis, F. J. Ed.; Oxford University Press: UK, **2004**.

63. Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd Edn. Wiley-VCH: Weinheim, **2003**.

64. Franks, F. *Water–A Matrix of Life*, Royal Society of Chemistry: Cambridge, **2000**.

65. Blokzijl, W.; Engberts, J. B. F. N. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1545.

Chapter 4

SYNTHESIS AND CHARACTERIZATION OF POLYMER SUPPORTED DENDRIMER METAL COMPLEXES

4. 1. INTRODUCTION

Multidentate ligands have found wide applications in the area of functional supramolecular assemblies for molecular recognition, inclusion phenomenon, nanoscale molecular devices and catalysis.[1-7] Advances in macromolecular chemistry such as the invention of dendritic polymers are providing unprecedented opportunities to develop high-capacity nanoscale multidentate chelating agents with well-defined molecular composition, size, and shape.[8] Metal complexes of dendritic chelating agents have attracted the attention of many research groups not only because of the potential applications they offer, but also due to the complex structure they possess.

An early example of a detailed study on the complex formation properties of dendrimers was done by Ottaviani *et al.*[9] They have used electron paramagnetic resonance (EPR) spectroscopy to elucidate the structure and dynamics of Cu(II) complexes of different dendrimers. The initial studies were focused on the complex formation between Cu(II) ions and G n.5 PAMAM dendrimers (from G=0.5 to G=7.5) at different pH conditions. They observed that Cu(II) complexed with the oxygen atoms of the surface carboxylate groups as well as with the internal nitrogen atoms. The availability of both surface COO^- group and internal CO-NH and –N< binding sites makes possible the formation of different complexes, due to the distribution of Cu(II) at different sites, characterized by different ligands and /or different structural disposition of the ligands. Each of these complexes gave contribution to the EPR line shape. From a detailed EPR analysis of the aqueous solutions of half-generation PAMAM

dendrimers containing Cu (II), complexes with three different environments could be identified. The structure of the complexes is shown in Figure 4-1.

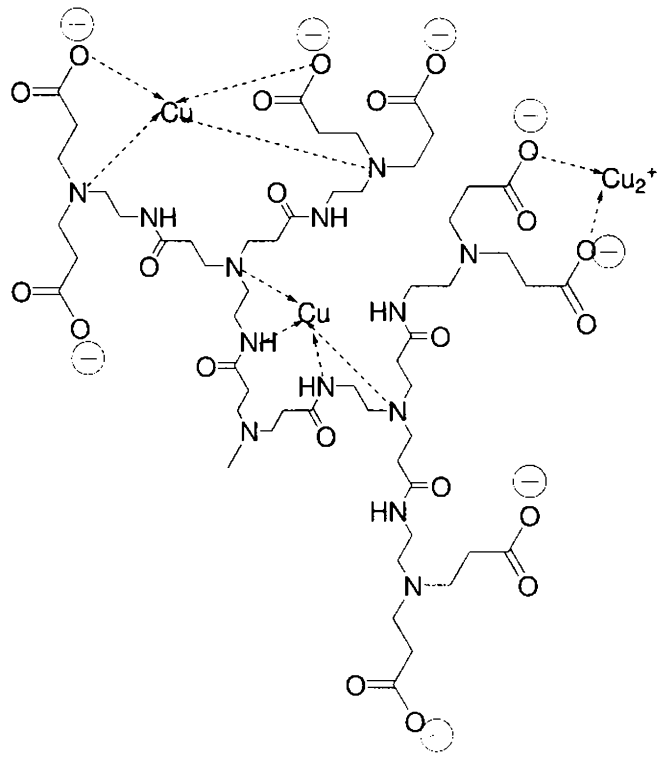


Figure. 4-1. Cu (II) complex of PAMAM dendrimer

The EPR line shape at room temperature indicates a variation in mobility of the Cu(II) complexes from 2.5th generation to 3.5th generation and is consistent with a change in the dendrimer morphology which results in a change in the motion of the Cu(II) complexes. At room temperature, for the early generation dendrimers, the complexes show fast mobility and suggest an openness of binding of the dendrimers. However for the later generations, even at room temperature, the complexes present slow motion, indicating a binding to a more compact dendrimer structure. Complexation involving both the external carboxylic groups and internal nitrogen sites is favored for dendrimers at lower generations in a large range of pH. The EPR results support the classification into "earlier" generations, characterized by an open structure, and "later" generations, with a more spheroidal, close-packed structure. At low pH, copper ions interact only with the surface carboxylate groups whereas at high pH, only

the internal nitrogenous ligands are available for bonding This latter complex forms simultaneously with a transient radical with the electron spin centered on a nitrogen atom and coupling with two CH_2 groups. This allows the identification of at least one of the ligand groups as an amide in the complex, as shown in the above figure (Figure 4-1).

The same authors later investigated the complexation behavior of Cu(II) ions in the presence of poly(amidoamine) starburst dendrimers carrying primary amino groups at the periphery.[10] As mentioned above the carboxylate groups at the surface of the half-generation dendrimers are available for complexation to Cu(II) over a large range of pH. Conversely, the amino groups at the surface of the full-generation dendrimers allow for Cu (II) complexation only at pH > 3.5. An intermediate species, existing only between pH 4 and 5 was formed by Cu (II) coordinating two external NH_2 groups. The Cu (II) ions may penetrate the dendrimer structure but are localized in the packed external structure of the dendrimer, showing complete quenching of motion at 228 K. Only at high pH, the Cu (II) ions are allowed to enter the internal voids of the dendrimer. In this case also, EPR analysis provided information on the morphology changes from the open structure of the earlier generation dendrimers ($G < 4$) to the packed external structure of the later generation dendrimers ($G > 4$). From these observations they proposed the following structures for the complexes as shown in Figure 4-2. The EPR analysis also confirmed that almost complete decomposition of the dendrimers in the constituent monomers occurred at pH > 5.5.

In another interesting work, Diallo *et al* showed the efficiency of PAMAM dendrimers as a multidentate ligand and their superiority over conventional ligands used in co-ordination chemistry.[11] PAMAM dendrimers carrying surface amino groups of third to eighth generation were allowed to complex with Cu(II) ions and the intake of Cu(II) ions were measured using AAS. From the amount of metal ion intake, a detailed picture of complex formation was drawn by the authors. It was estimated that G3, G4, G5, G6, G7 and G8 dendrimers were able to capture 8 ± 1, 13 ± 1, 29 ± 3, 46 ± 9, 83 ± 9 and 153 ± 20 Cu(II) ions per

dendrimer respectively. This observation clearly showed that dendrimers override conventional ligands which could normally intake one or two metal ions. The metal intake was maximum at a pH range between 5.9-6.1. At lower pH, the surface amino groups get protonated and so they are unable to take up metal ions.

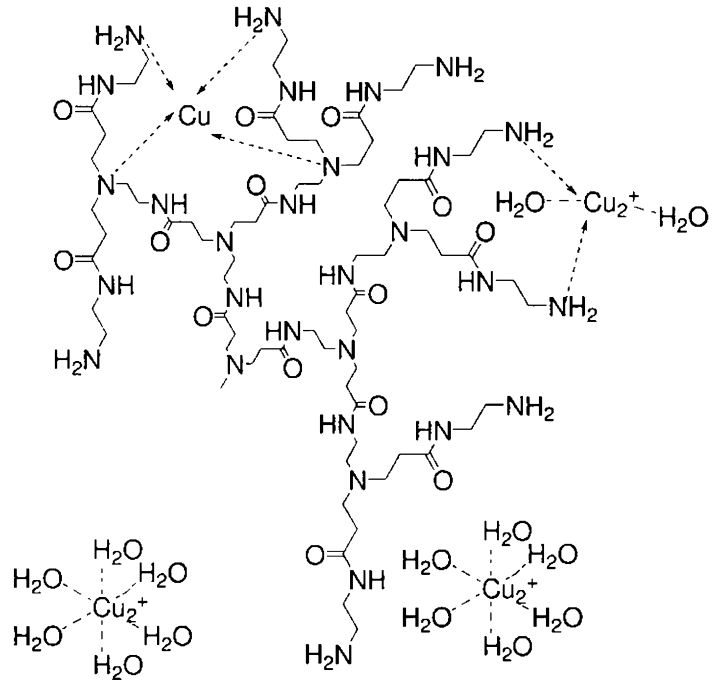


Figure 4-2 Another structure of Cu(II) complex of PAMAM dendrimer

An investigation of Cu(II)- poly(propylene imine) dendrimer complexes with a diaminobutane core (DAB-Am$_n$-Cu(II)$_x$, n=4 to 64, x=n/2) by means of extended X-ray absorption fine structure (EXAFS) and X-ray absorption near-edge structure (XANES) spectroscopies was carried out by Mc Carley *et al.*[12] By studying the EXAFS and XANES spectra of DAB-Am*n*- Cu(II)*x* at the copper K-edge the authors were able to determine the geometry of the dendrimer end-group complex about the Cu ion and parameters such as bond distances, coordination numbers, and nature of the ligands contributing to the copper coordination sphere. The results from this analysis fully support a structure that has the Cu(II) surrounded by three nitrogen atoms in the equatorial plane and an oxygen atom at 1.92 Å at the base of the pyramid. An axial oxygen atom at

approximately 2.6 Å completes the square-based pyramid. The oxygen atom in the equatorial plane and the other oxygen atom in the axial position are expected to be associated with solvent or other counter ions, as the ligands do not contain any oxygen atom. The structure of the complex was proposed as shown in Figure 4-3.

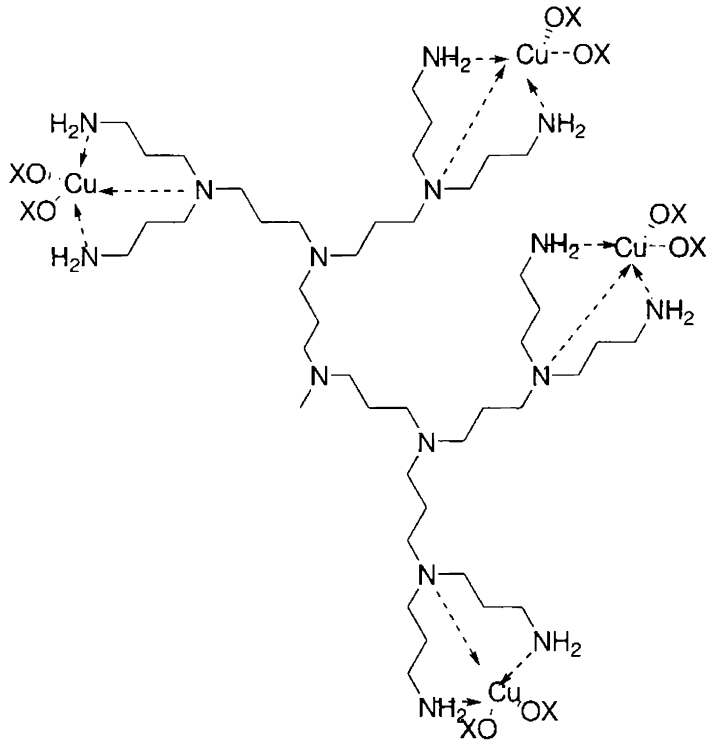


Figure 4-3. Structure of Cu(II) complex of PPI dendrimer

Crooks and Russell used MALDI-TOF MS combined with UV-visible spectroscopy to elucidate the structure of the dendrimer metal complexes.[13] They have measured the uptake of Cu (II) ions by G2, G3, G4, and G6 PAMAM dendrimers with ethylene diamine core and terminal OH groups in aqueous solution. While their spectroscopic data indicated maximum binding of 4, 8, 16, and 64 Cu(II) ions per molecule for the G2-OH, G3-OH, G4-OH, and G6-OH PAMAM dendrimers, respectively, the MALDI-TOF mass spectra suggested additional binding [up to 12 Cu(II) ions per molecule] for the G3-OH PAMAM dendrimer as the metal ion-dendrimer loading was increased to 32. The authors

attributed this additional uptake of Cu(II) to the presence of nonspecific metal ion binding sites for Cu(II) within the dendrimers.

Ottaviani, in a later work, explored the structure of PAMAM dendrimer-Ag(I) complexes and PAMAM-Ag(0) nanoparticle conjugates using EPR spectroscopy.[14] Since Ag does not have a measurable signal in EPR, Cu (II) ions were used as a probe to obtain useful information about the structure of the dendrimer metal complex. The results support the conclusions made by the authors about the structure of dendrimer-metal complexes in their previous works.

Diallo *et al* used titration methods, EXAFS and molecular modeling methods to investigation of the uptake of Cu(II) by ethylenediamine (EDA) core PAMAM dendrimers in aqueous solution.[15] The titration measurements of proton and metal ion binding evaluated the effects of (i) metal ion-dendrimer loading, (ii) dendrimer generation/ terminal group chemistry, and (iii) solution pH on the extent of binding of Cu(II) in aqueous solutions of PAMAM dendrimers. G3-NH_2, G4-NH_2, and G5-NH_2 EDA core PAMAM dendrimers and G4 EDA core PAMAM dendrimers with succinamic acid, glycidyol, and acetamide terminal groups were evaluated in this study. The overall results of the proton and metal ion binding measurements suggest that the uptake of Cu(II) by EDA core PAMAM dendrimers in aqueous solutions involves both the dendrimer tertiary amine and terminal groups. However, the extent of protonation of these groups control the ability of the dendrimers to bind Cu(II). When these groups are neutral at pH 9, the extent of binding of Cu(II) increases linearly with metal ion-dendrimer loading within the ranges of the tested metal ion-dendrimer loadings. In all cases, 100% of the Cu(II) ions are bound to the dendrimers. When these groups become fully/predominantly protonated at pH 5.0, no significant binding of Cu(II) is observed. A more complex metal ion uptake behavior is observed at pH 7.0. The extent of binding of Cu (II) goes through a series of two distinct binding steps as metal ion-dendrimer loading increases and this behavior was attributed to the presence of sites with different Cu (II) binding affinity and capacity within the dendrimers. To gain insight into

metal ion coordination with the amino groups of PAMAM dendrimers, EXAFS spectroscopy was employed to probe the structures of aqueous complexes of Cu(II) with G1-NH_2 and G5-NH_2 EDA core PAMAM dendrimers at pH 7.0. Analysis of the EXAFS spectra of the Cu (II) complex with the G5-NH_2 PAMAM dendrimer suggests that the first binding step involved the formation of octahedral complexe in which a Cu (II) central metal ion is coordinated to 2-4 dendrimer tertiary amino groups and 2 axial water molecules. To account for the Cu (II) ions that are not specifically bound to the dendrimers' tertiary amino groups at pH 7.0, it was hypothesized that the second binding step involved the formation of octahedral complexes of Cu(II) with water molecules trapped inside the G*x*-NH_2 PAMAM dendrimer. Finally, the results of experiments were combined with molecular modeling to propose a structure of the dendrimer-metal complex shown in Figure 4-4.

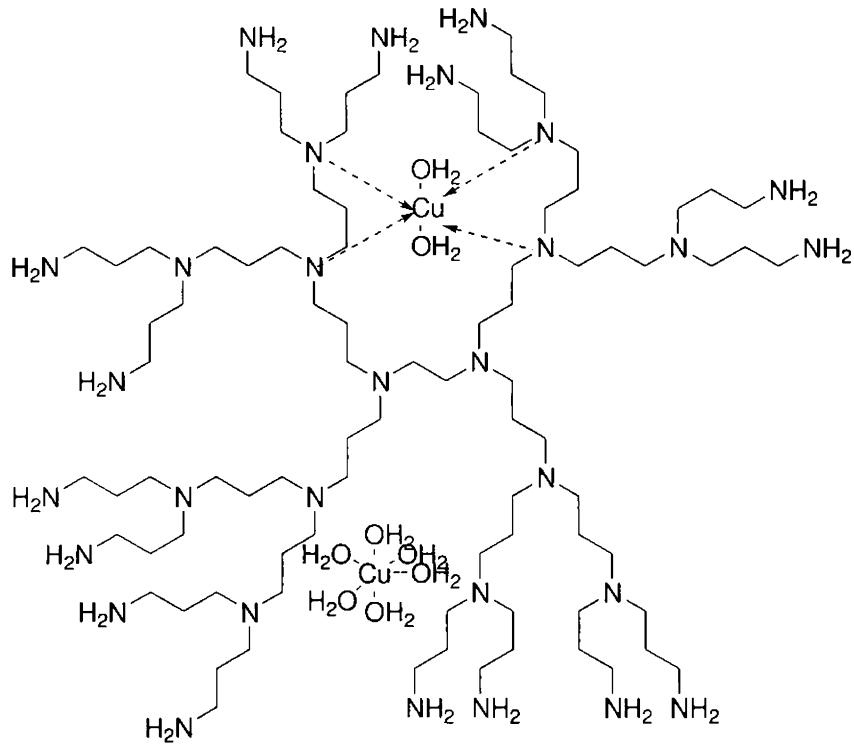


Figure 4-4. A structure of PPI-Cu(II) complex

Inspired from the results obtained from EXAFS analysis of Cu (II) complexes of DAB dendrimers, Tran et. al studied Cu (II) complexes of PAMAM dendrimers using EXAFS in combination with NMR spectroscopy.[16] The model of the complex proposed by analyzing these data showed that primary amine, amide and tertiary amine nitrogen atoms are involved in bonding with the Cu (II) ion to form five- and six membered rings. This result implies that Cu (II) forms complexes within the PAMAM dendrimer structure and not just at the periphery. The presence of nearby paramagnetic Cu (II) ions resulted in broadening of the ^{13}C and ^{1}H NMR signals associated with $-CH_2NH_2$, $CONHCH_2CH_2NH_2$, and CONH moieties, indicating binding to these nitrogen sites.

Electrochemical methods were used to explore electrostatic binding of metal complexes with G1.0-G5.0 PAMAM dendrimers as a function of pH by Kulczynska *et al.*[17] A simple titration between solutions containing an electroactive probe and dendrimers leads to binding ratios from potential shifts and binding constants from current measurements. The results suggest that the binding ratios obtained from CV potential shifts are an indicator of charge density for the PAMAM dendrimer series. According to the authors, only the outermost amines (the terminal amines) are charged at a pH of 7 where as lowering the pH causes the interior shells (the tertiary amine branching points) to become charged.

Eventhough few attempts were made to propose a satisfactory model of dendrimer-metal complexes using various experimental methods, none of these can successfully explain all the experimental results and a large number of contradictions have occurred when various experimental methods were used than similarities. To solve this problem some molecular modeling studies were performed with little success. Balbuena and Tarazona-Vasquez used classical molecular dynamics simulations and density functional theory calculations to obtain insights about the attachment of the Cu (II) ion to the lowest generation poly(amidoamine) dendrimer with hydroxyl periphery functionality, G0-OH, in aqueous solutions.[18] Various initial configurations of the ion relative to the

dendrimer sites were tested and it was concluded that both the solvent as well as -in a lesser degree for low generation dendrimers- the folding of the dendrimer branch played an important role in Cu(II) ion complexation. The presence of solvent and branch folding retain the ion close to the atomic binding sites consisting mainly of amide oxygen as well as hydroxyl oxygen but also tertiary amine nitrogen. Later the same authors extended their theoretical calculations to Pt (II) complexes of PAMAM dendrimers with hydroxyl groups at the periphery and showed that Pt (II) preferred tertiary amino groups at the branching points for binding than the –OH groups on the periphery or amide oxygen or nitrogen atoms on the branches.[19,20] Density functional theory (DFT) calculations have been used to predict the structures and EPR spectra of the Cu(II)-dendrimer complexes by Street and Dixon[21]and the results were compared with experimental EPR spectra. The results showed that the sites bonded to the Cu (II) ion were significantly different at different pH values. DFT calculations predicted that at pH 3, the hydrated ion complexes $Cu(H_2O)_6^{2+}$ or $Cu(H_2O)_5^{2+}$ were present. At pH 7.8, a chelating complex with two tertiary amine sites with or without two amide oxygen sites was present. At pH 11, the Cu (II) ion was bound to either the primary amine and amide oxygen sites on a single branch or to two tertiary amines and four amide oxygen sites on all four branches. These results showed the importance of the amide sites in Cu (II)-dendrimer complexes in neutral and basic solutions.

Eventhough the attempts to elucidate the structure of dendrimer metal complexes and identify the binding sites of metal ions to dendrimer were not so successful and gave contradictory results the efforts to identify the potential properties of these complexes gave many promising results and the exploration is going on very effectively by many research groups.

One of the most studied applications of dendrimer metal complexes is their photochemical and photophysical property. Serroni *et al* prepared a luminescent and redox active dendrimer which contained bipyridyl units in the core and branches. The core of the dendrimer was allowed to complex with Os(III) ions while the branches were allowed to complex with Ru(II) ions.[22]

Electroluminescent properties of poly(amidoamine) dendrimers containing pendant $[Ru(bpy)_3]^{2+}$ chromophores was investigated by Abruna and co-workers.[23,24] They compared devices made using indium tin oxide (ITO) and gold electrodes with devices made from $[Ru(bpy)_3]^{2+}$ films. The use of these systems in OLEDs elucidated the role of the concentration and density of the chromophore play in transport and luminescence, the effect the supramolecular architecture has on device performance and the role that the dendrimer structure played on the photophysics of $[Ru(bpy)_3]^{+2}$ in a solid-state environment. Dendrimers can act as a nanoscale antenna for transferring of electromagnetic radiations and this effect was experimentally verified by Kitagawa et. al. using a poly(aryl ether) dendrimer chloroiron(III) porphyrin complexes.[25] Kawa and Takahagi explored practical applications of the unique green fluorescence of terbium (III) cored poly(benzyl ether) dendrimer complexes for luminescence polymeric materials.[26] Initially, the influence of the isomerism in the dendron skeleton, both at the focal point and the hyperbranch repeating unit on the fluorescence ability was studied. Next, a 4-vinylphenyl group was successfully introduced at the terminal of the dendron subunit for radical polymerization. The terminal vinyl groups enabled the copolymerization of the terbium (III)-cored dendrimer complex with *N*-isopropylacrylamide, resulting in a green-fluorescent, clear hydrogel. A number of other examples of dendrimer-metal complexes can be found in the literature which shows promising optical or photophysical properties.[27-30]

Dendrimer-metal complexes are able to recognize their role in biology and medicine. PAMAM dendrimer silver complexes were found to be highly active antimicrobial agents. Their antimicrobial activity was better than silver nitrate solution and a possible explanation was the higher local concentration of silver ions and greater solubility of these complexes[31]. Gd (III) complexes of various dendrimers are found to be highly efficient contrast agents in MRI.[32]

A number of examples of dendrimer-metal complexes can be found in the literature of which no potential applications were recognized but their exotic structures made them interesting. [33-37]

Dendrimer metal complexes have a great number of applications in catalysis and as precursors of dendrimer-nanoparticle conjugates.

The present chapter deals with the synthesis and characterization of polymer-supported dendrimer-transition metal complexes. Both polymer-supported PAMAM and PPI dendrimers were used as ligands for complexation with metal ions. The metal ions selected were Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Pd(II), Ag(I) and Zr(IV) due to their availability, low cost and catalytic properties. The polymer supported metal complexes were prepared by ligand exchange method. Various factors influencing the complex formation were studied and conditions were optimized to get metal complexes of suitable loading. Eventhough, few supported dendrimer-metal complexes were reported in the literature, no successful attempts were done to characterize them. The metal complexes described here are characterized using various spectral and thermal methods. On comparing the characterization data with available models of non-supported dendrimer-metal complexes, possible structures of the supported dendrimer-metal complexes were proposed.

4. 2. RESULTS AND DISCUSSION

4. 2. 1. Preparation of Polymer-Supported PAMAM Dendrimer Metal Complexes

Definite volumes (20mL, 0.02 M) of the solutions of the respective metal ions were stirred with 500 mg of the polymer-supported dendrimer at room temperature in aqueous medium and at natural pH for different intervals of time. The metal intake capacity in each case was estimated by suitable methods and the results are furnished in table 4. 1. and 4. 2. The mode of complexation of metal ion with the dendronized resin is shown in the Figure 4-5. Standard solutions of the metal ions were prepared from the water-soluble salts of the metals and they were appropriately diluted to get solutions of required strength and its pH was taken as the natural pH of the reaction medium.

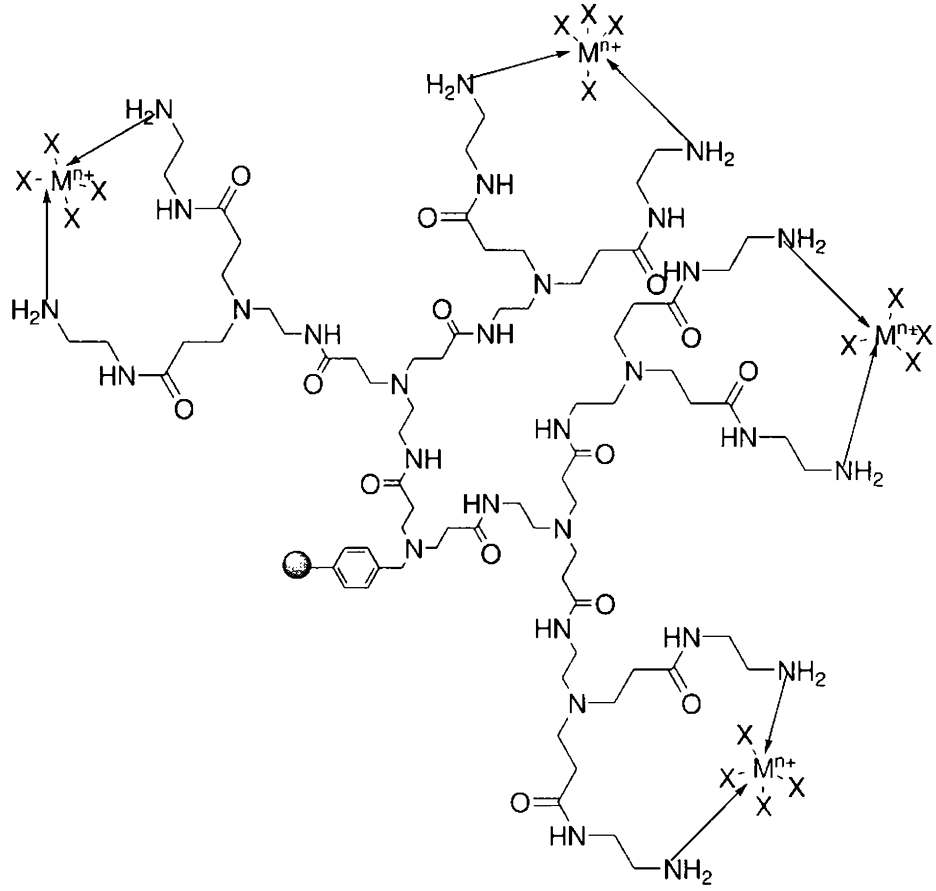
Table 4.1: Metal intake capacity of polystyrene-supported G3-PAMAM dendrimer

Time	Metal intake capacity (m. equiv./g)							
(h)	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
6	1.31	0.69	1.34	1.00	1.42	1.00	1.10	1.20
12	1.33	0.72	1.35	1.19	1.49	1.12	1.12	1.21
18	1.33	0.72	1.34	1.19	1.47	1.12	1.11	1.22
24	1.32	7.75	1.34	1.21	1.47	1.14	1.12	1.12

Table 4.2: Metal intake capacity of poly(methyl methacrylate)-supported G3-PAMAM dendrimer

Time	Metal intake capacity (m. equiv./g)							
(h)	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
6	4.71	2.66	4.52	4.00	4.90	3.25	3.89	3.34
12	5.10	2.90	5.12	4.93	5.72	3.73	3.90	3.92
18	5.10	2.91	5.11	4.92	5.72	3.75	3.91	3.91
24	5.10	2.90	5.12	4.92	5.70	3.74	3.91	3.93

The metal intake was found to be better for 12 h in both cases and hence for further studies on different aspects of complexation, the resin samples were equilibrated with the corresponding metal ion solutions for 12 h.



where ● is the poymer support, X is either water molecules or counter ions

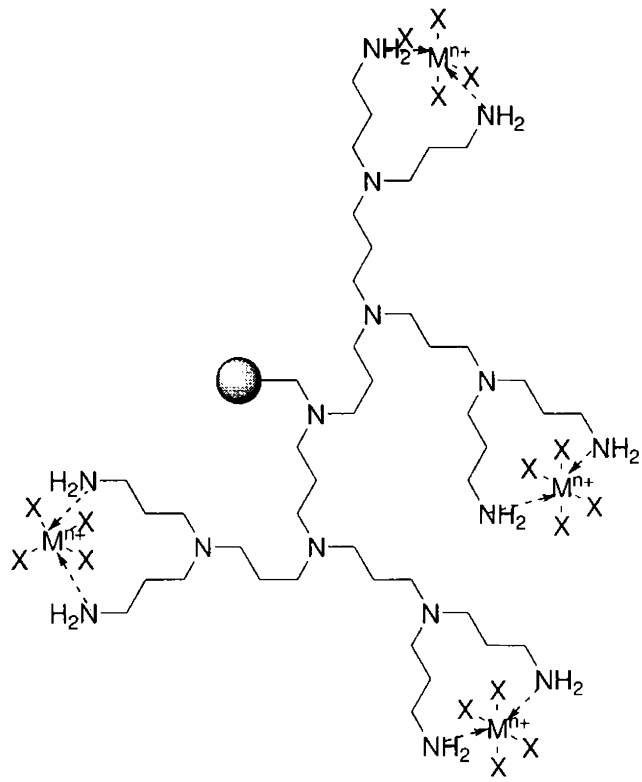
Figure 4-5. Proposed structure of the polymer supported PAMAM-metal complex

4. 2. 2. Preparation of Polymer-Supported PPI Dendrimer Metal Complexes

Polymer-supported metal complexes of PPI dendrimers were prepared using the same method as described in the case of PAMAM dendrimers. The supports used were DVB crosslinked polystyrene and poly(methyl methacrylate). The structure of the polymer-supported PPI metal complexes is given in Figure 4-6.

As described in the case of polymer-supported PAMAM dendrimers, the various factors affecting the complexation was studied by estimating the metal intake capacity by the polymer-supported ligand under various preset reaction conditions. Initially, the influence of time on complexation was determined by

carrying out the reaction under different intervals of time followed by determination of metal intake. The results are presented in tables 4. 3. and 4. 4.



where ● is the poymer support, X is either water molecules or counter ions

Figure 4-5. Proposed structure of the polymer supported PPI-metal complex

Table 4.3: Metal intake capacity of polystyrene-supported G3-PPI dendrimer

Time	Metal intake capacity (m. equiv./g)							
(h)	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
6	0.92	0.71	1.00	0.93	1.34	0.89	0.82	1.00
12	1.01	0.76	1.03	1.00	1.35	0.92	0.93	1.03
18	1.00	0.77	1.03	1.00	1.34	0.91	0.94	1.02
24	0.99	0.75	1.01	1.00	1.34	0.92	0.94	1.02

Table 4.4: Metal intake capacity of poly(methyl methacrylate)-supported G3-PPI dendrimer

Time (h)	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
6	3.00	1.66	3.58	3.71	3.90	2.90	3.00	3.00
12	3.67	2.00	3.92	3.71	4.12	3.00	3.10	3.21
18	3.68.	2.05	3.92	3.72	4.12	3.01	3.09	3.20
24	3.67	2.05	3.92	3.67	4.12	3.00	3.08	3.20

As observed in the case of PAMAM dendrimers, metal intake was found to be better for 12 h in this case also and hence for further studies on different aspects of complexation, the resin samples were equilibrated with the corresponding metal ion solutions for 12 h.

4. 2. 3. Factors influencing complexation

Complexation of metal ions with the polymer-supported dendrimers was regulated by various factors and they include nature of the polymer-support, generation of dendrimers and reaction conditions of complexation like time, temperature, co-solvent etc. A detailed study of these factors was done by varying the factors in a regular manner and estimating the metal intake capacity of the supported dendrimers. The efficiency of complexation determined from the metal ion capacity is used in further studies to prepare well-defined polymer-supported metal complexes. These factors are discussed in detail in the following section.

4. 2. 3. a. Nature of the Polymer-Support

The polymer-support plays an important role in determining the properties and efficiency of polymer-supported catalysts. In addition to acting as an insoluble support for the catalysts, the polymer backbone behaves as a co-solvent and a regulator which determines the interaction between the catalyst and reactants, the diffusion of reactants and products etc. In order to study the effect of the nature of the support, the complexation was carried out with

dendrimers attached to supports of different crosslink density. The results are presented in tables 4. 5. to 4. 8.

Table 4.5: Metal intake by G3 PAMAM dendrimer supported on PS-DVB with different degree of crosslinking

Degree of crosslinking	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
1	1.33	0.72	1.35	1.19	1.49	1.12	1.12	1.21
2	1.31	0.70	1.32	1.18	1.49	1.10	1.09	1.10
4	1.17	0.59	1.20	1.00	1.31	-		
6	1.00	0.42	0.91	0.87	1.09	-		

Table 4.6: Metal intake by G3 PAMAM dendrimer supported on PMMA-DVB with different degree of crosslinking

Degree of crosslinking	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
1	5.10	2.90	5.12	4.93	5.72	3.73	3.90	3.92
2	5.00	2.72	5.00	4.74	5.70	3.69	3.71	3.74
4	4.72	2.20	4.31	4.00	5.00	3.10		
6	4.21	1.89	4.00	3.78	4.75	2.95		

Table 4.7: Metal intake by G3 PPI dendrimer supported on PS-DVB with different degree of crosslinking

Degree of crosslinking	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
1	1.01	0.76	1.03	1.00	1.35	0.92	0.93	1.03
2	1.01	0.72	1.00	1.00	1.23	0.90	0.90	0.91
4	0.91	0.63	0.90	0.92	1.20	0.83		
6	0.81	0.49	0.84	0.84	0.92	0.70		

Table 4.8: Metal intake by G3 PPI dendrimer supported on PMMA-DVB with different degree of crosslinking

Degree of crosslinking	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
1	3.67	2.00	3.92	3.71	4.12	3.00	3.10	3.21
2	3.60	1.91	3.90	3.68	4.10	3.00	3.00	3.09
4	3.41	1.53	3.61	3.51	3.89	2.81		
6	3.29	1.00	3.32	3.00	3.59	2.77		

It was observed that 1 and 2% crosslinked supports showed good metal intake compared to other supports. As the degree of crosslinking increases, the swelling of the support decreases, which prevents the diffusion of metal ions into the polymer network and so, the metal intake decreases. Based on this observation, polymer-supports with 1 or 2% degree of crosslinking was chosen for further studies.

4. 2. 3. b. Generation of Dendrimer

First, second and third generations of polystyrene-supported PAMAM dendrimers were complexed with the metal salt solutions of different metals for a period of 12 h. The residual metal ion concentrations were determined and the metal intake by the resins were estimated and are furnished in tables 4. 9 and 4. 10.

Table 4.9: Metal intake by PAMAM dendrimer of various generations supported on PS-DVB

Generation of dendrimer	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
1	0.91	0.57	0.91	0.80	1.00	0.83	0.71	0.75
2	1.00	0.71	1.01	0.89	1.19	0.95	0.89	0.91
3	1.33	0.72	1.35	1.19	1.49	1.12	1.12	1.21

Table 4.10: Metal intake by PPI dendrimer of various generations supported on PS-DVB

Generation of dendrimer	Metal intake capacity (m. eq./ g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
1	0.84	0.50	0.78	0.78	0.92	0.70	0.69	0.71
2	0.91	0.69	0.91	0.88	1.01	0.81	0.84	0.89
3	1.01	0.76	1.03	1.00	1.35	0.92	0.93	1.03

The maximum metal intake capacity was shown by third generation dendrimer and this is due to the larger number of functional groups and due to the more closed structure of the dendrimer.

4. 2. 3. c. Effect of Temperature

Temperature is another factor influencing the metal complexation. For understanding the effect of temperature on complexation of metal ions, studies were conducted at various temperatures. The metal ion sorption capacities of various polymer-supported ligands were estimated for a definite period of time. Effect of temperature on the extent of metal complexation is an important measure of the interaction between metal ion and the polymeric ligands. Generally, metal sorption by resin from an aqueous solution of metal ions increases with an increase in temperature. The higher metal sorption at elevated temperatures is due to the increase in the number of molecules attaining the requisite activation energy. The observed metal ion intake by different polymeric ligands at various temperatures is given in tables 4. 11 and 4. 12.

Table 4.11: Metal intake by G3 PAMAM dendrimers supported on PS-DVB at various temperatures

Temperature (°K)	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
303	1.33	0.72	1.35	1.19	1.49	1.12	1.12	1.21
323	1.35	0.75	1.36	1.20	1.52	1.12	1.17	1.24
373	1.38	0.76	1.39	1.24	1.56	1.14	1.19	1.27

Table 4.12: Metal intake by PPI dendrimers supported on PS-DVB at various temperatures

Temperature (°K)	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
303	1.01	0.76	1.03	1.00	1.35	0.92	0.93	1.03
323	1.01	0.76	1.06	1.02	1.37	0.94	0.94	1.07
373	1.17	0.79	1.13	1.11	1.40	0.99	0.99	1.10

It was observed that there was no considerable increase in metal intake by the dendrimers with temperature. This may be due to the high complexing nature of the dendrimers due to their particular structure and larger number of surface functional groups which form stable complexes with the metal ions. The small decrease in the metal intake by PAMAM dendrimers at higher temperatures may be due to the slight decomposition of this dendrimer at higher temperature.

4. 2. 3. d. Effect of pH

Another major factor influencing the complexation capacity of the polymer-supported dendrimers is the pH of the reaction medium. For studying the effect of pH on complexation, experiments were conducted at various pH in aqueous medium. The experiments were conducted at three different pH. Acetic acid-sodium acetate buffer was used to adjust the pH at 5. Hydrochloric acid was used to adjust the pH at 2. Metal sorption was estimated for a definite period of time. The results are presented in tables 4. 13 and 4. 14.

Table 4.13: Metal intake by G3 PAMAM dendrimers supported on PS-DVB at various pH

pH	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
Natural pH	1.33		1.35	1.19	1.49	1.12	1.12	1.21
5	1.00		1.01	0.89	0.91	0.91	0.90	0.99
3	0.70	0.72	0.67	0.60	0.70	0.69	0.72	0.80

Table 4.14: Metal intake by PPI dendrimers supported on PS-DVB at various pH

pH	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
Natural pH	1.01		1.03	1.00	1.35	0.92	0.93	1.03
5	0.82		0.89	0.85	0.89	0.78	0.79	0.84
3	0.67	0.76	0.71	0.78	0.76	0.61	0.67	.078

The metal intake decreases with lowering of pH. This observation can be explained as follows. As pH decreases the surface amino groups of the dendrimer get protonated and this protonation prevents them from further complexation. From this data the pH of the reaction medium was taken as natural pH for further studies except in the case of iron, where slightly acidic medium was used.

4. 2. 3. e. Effect of Solvent on Metal Chelation

The lightly crosslinked resins can change in to a gel by swelling in the presence of good solvents. While swelling, the solvents interact with the polymer chains and the functional groups become more accessible to the metal ions. In the presence of a good solvent, the polymer network expands and becomes porous. The polar nature of the solvent influences the swelling of the polymer. The metal sorption by different polymeric ligands is heterogeneous in nature since it takes place in two distinct phases. The important factor which, controls the extent of complexation, is the compatibility of the two phases. For the complexation reaction to take place, strong interaction between the metal ions in solution and the solid polymeric ligand must occur. It has been observed that polar solvents are most suitable for swelling of the resins. The swelling nature of the resins was found to decrease with increase in the degree of crosslinking. As the degree of crosslinking increases, the ability of the network to expand in the presence of good solvents becomes reduced and the penetration of the metal ions to the interior of the resin becomes hindered. In the presence of poor solvents, movement of the metal ions within the matrix is diffusion controlled. In crosslinked polymers, the tendency to disperse is opposed by configurational

entropy of the polymer chain held between crosslink points where they are forced to a more elongated, less probable configuration as the network expands. Though physical stability of the resin is increased with the increase in the degree of crosslinking, there should always be a balance between the required mechanical properties and the reactivity of the functional group attached to the polymer.

The physical and chemical properties of the crosslinked polymer, viz. rigidity, swelling capacity and compatibility with different solvents have a definite correlation with the variables of the macromolecular matrix. Since the crosslinked resins are insoluble, the accessibility of the functional groups is diffusion controlled and penetrant transport causes some sort of molecular relaxation, thereby concealing the functional groups deeply buried in the polymer matrix.

The metal complexation of polymer-supported dendrimers in the presence of different solvents like acetone, methanol, dioxan and DMF was studied. These resins were suspended in the solvents for swelling and then metal ion solutions were added for complexation to take place. The metal intake capacities of various resins in the presence of the above solvents were determined and furnished in tables 4. 15 to 4. 18.

Table 4.15: Effect of solvent on metal intake by PAMAM supported on PS

Solvent	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
Acetone	1.46	0.72	1.47	1.29	1.60	1.34	1.28	1.32
Methanol	1.42	0.70	1.42	1.27	1.54	1.30	1.23	1.29
Dioxan	1.40	0.63	1.36	1.26	1.52	1.26	1.19	1.25
Benzene	1.21	0.50	1.23	1.11	1.34	1.00	1.00	1.09

Table 4.16: Effect of solvent on metal intake by PAMAM supported on PMMA

Solvent	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
Acetone	5.30	3.00	5.22	5.00	5.82	3.91	3.96	3.95
Methanol	5.19	2.99	5.12	5.00	5.68	3.85	3.93	3.94
Dioxan	5.10	2.10	5.03	4.57	5.60	3.47	3.89	3.90
Benzene	4.97	1.89	4.95	4.28	5.00	3.32	3.83	3.82

Table 4.17: Effect of solvent on metal intake by PPI supported on PS

Solvent	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
Acetone	1.11	0.79	1.10	1.11	1.45	1.12	1.07	1.12
Methanol	1.10	0.76	1.00	1.10	1.37	1.08	1.00	1.10
Dioxan	1.03	0.66	0.99	1.04	1.23	0.92	0.93	1.09
Benzene	0.98	0.43	0.96	0.96	1.00	0.79	0.90	1.00

Table 4.18: Effect of solvent on metal intake by PPI supported on PMMA

Solvent	Metal intake capacity (m. equiv./g)							
	Mn(II)	Fe(III)	Co(II)	Ni(II)	Cu(II)	Pd(II)	Ag(I)	Zr(IV)
Acetone	3.80	2.00	4.02	3.90	4.31	3.20	3.17	3.20
Methanol	3.76	2.00	4.00	3.87	4.17	3.00	3.11	3.14
Dioxan	3.65	1.90	3.89	3.72	4.11	2.91	3.09	3.11
Benzene	3.10	1.62	3.67	3.52	3.97	2.00	3.00	3.01

4. 2. 4. Characterization of Polymer-Supported Metal Complexes

Different spectroscopic methods are useful in studying the structure of polymer supported metal complexes. In addition to the spectral methods like IR, UV-Vis and ESR, thermal decomposition studies are also helpful in predicting the geometry of the polymer metal complexes. In the case of IR absorption spectra, the absorption frequency corresponding to the ligand functional groups undergo a shift on complex formation. The polymer backbone as well as the chelating ligand influences the co-ordination behavior of the metal ion. The IR spectral techniques are widely used not only in the identification of ligand

functions, but also in locating the co-ordination sites in the complexes. The presence of intra-molecular hydrogen bonding to give the chelate rings can also be found out by using IR spectral technique. By studying the UV-Vis spectra and from the magnetic moment measurement, the stereochemistry of complexes can be determined. The existence of bond between the metal ion and the ligand can be established from the ESR spectral data. The character of the metal-ligand bond can be evaluated from the spectral values.

The thermal decomposition studies give idea about the thermal stability of the polymer metal complex and it also gives information about the water molecules co-ordinated to the metal ion.

4. 2. 4. a. Polymer-Supported PAMAM-Metal Complexes

In PAMAM metal complexes, it is expected that the metal ion form co-ordination bonds with the primary amino groups at the periphery of the dendrimers. The other co-ordination sites like tertiary amino groups and amide groups, present in the dendrimer have less affinity towards some transition metal ions and so they do not take part in complexation with those metal ions. The primary amino groups show characteristic bands in the FTIR spectra and on co-ordination with the metal ions these bands get shifted from their original values and this shift give an idea about complexation and structure of the complex. The primary amino groups of the dendrimer show characteristic bands at 3390 cm^{-1} and 3344 cm^{-1} due to the asymmetric and symmetric stretching. The N-H stretching band of the amide groups often present in the same region, which makes the interpretation of spectra difficult. The amide groups showed an additional peak at 1654 cm^{-1} due to the C=O stretching. The band at 1597 cm^{-1} is assigned to be the band due to the scissoring motion of the $-NH_2$ group. These three kinds of frequencies observed in the FTIR spectra of the polymer supported PAMAM dendrimers were compared with the position of the corresponding bands in the metal complexes of the supported dendrimers and the shift in their values were used to assign the structure of the complex. The UV-Vis spectra and EPR spectra of the complexes were used as additional tools

for the structure determination. Thermal analysis of the complexes showed the presence or absence of water molecules which may have taken part in complexation, which may be missed in the FTIR spectra.

4. 2. 4. a. ***1. Polymer-Supported PAMAM-Mn(II) Complex***

The complex is brown in color. During complexation the nitrogen atoms of the primary amino groups of the dendrimer form co-ordinate bonds with the manganese ion. This can be visualized from the shift in the symmetric and asymmetric stretching frequencies of the primary amino groups towards lower frequencies. The FTIR bands due to the primary amino groups get shifted from 3390 cm^{-1} and 3344 cm^{-1} to 3358 cm^{-1} and 3300 cm^{-1}respectively. This shows that the complexation was taking place with primary amino groups of the dendrimers. The shift in the bands aroused from the scissoring motion of the $-NH_2$ group shifts from 1597 cm^{-1} to 1536 cm^{-1}, which gives an additional proof for the role of primary amino groups in complexation. The carbonyl-stretching band of the amide groups remains unaltered at 1654 cm^{-1} that proves that the amide group is not involved in the complex formation. Thermal analysis of the complex showed a small weight loss of about 7% between 100-200 ^{o}C. This is due to the loss of water molecules co-ordinated to the central metal atom.

The electronic spectrum showed a broad charge transfer band at 474 nm and a ground state to first excited state transition band at 640 nm for the Mn(II) complex. The ESR parameters are $g_{\parallel}$=2.17and $g_{\perp}$=2.12 and $A_{\parallel}70x10^{-4}$ and $A_{\perp}=120x10^{-4}$. From these observations the structure of the complex can be represented as in Figure 4-7.

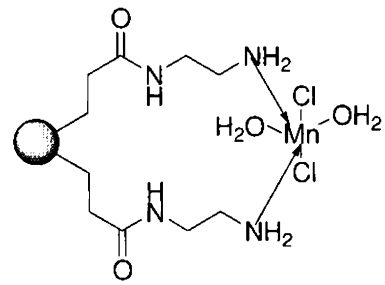


Figure 4-7. Proposed structure of polymer-supported PAMAM-Mn complex

4. 2. 4. a. 2. ***Polymer-Supported PAMAM-Fe(III) Complex***

The complex is reddish brown in color. A negative shift in the value of the stretching frequencies of primary amino groups after complexation gives the evidence that the primary amines have a considerable role in complexation. The stretching frequencies shift to a lower value by 20 cm^{-1}. The peak at 1597 cm^{-1} also showed a negative shift of 53 cm^{-1} while the carbonyl stretching band due to the amide group remains unaltered. Thermal analysis of the complex showed that the complex is stable up to 250 °C.

In the electronic spectra two bands at 399 nm and 491 nm arise and they are assumed to be due to charge transfer transition and $^6A_{1g} \rightarrow {}^4T_{1g}$ transition respectively. The ESR parameters are $g_{\parallel}$=2.11 and $g_{\perp}$=2.0 and $A_{\parallel}$=130x10^{-4} and $A_{\perp}$=160x10^{-4}. From these observations the structure of the complex can be assigned to be octahedral and can be represented as given above in the case of manganese complex.

4. 2. 4. a. 3. ***Polymer-Supported PAMAM-Co(II) Complex***

The color of the complex is dark pink. After complexation the FTIR bands were shifted negatively to 3350 and 3310 cm^{-1} respectively from their original values. The band due to the scissoring motion occupies a new position at 1540 cm^{-1} after a shift from their original value at 1597 cm^{-1}. As described above the amide groups remain unchanged after complexation. Thermal analysis of the cobalt complex showed a weight loss of about 7% between 100-200 °C. This shows that the complex contains co-ordinated water molecules. The electronic spectra of the complex showed three peaks at 576nm, 529nm and 302 nm. The former two peaks may be due to absorption characteristics of a tetrahedral geometry and the last one is due to charge transfer transition. ESR spectra of the complex gave $g_{\parallel}$=2.1 and $g_{\perp}$=2.0 and $A_{\parallel}$=80x10^{-4} and $A_{\perp}$=60x10^{-4}. From these analytical data the complex is assumed to be having an octahedral geometry.

4. 2. 4. a. 4. ***Polymer-Supported PAMAM-Ni(II) Complex***

A green colored complex was obtained. On complex formation the bands in the IR spectrum due to the stretching of primary amino groups undergo a

negative shift of 55 cm^{-1} and this shows that the primary amino groups take part in complex formation. The bending vibration of the amino groups also undergoes a negative shift of 57 cm^{-1}. As described in the above cases the amide carbonyl stretching frequency remains unaltered at 1655 cm^{-1}. The presence of water molecules in the complex was realized from the weight loss of complex observed in thermo gravimetry. The UV-Vis spectra of the complex showed two bands at 667 nm and 398 nm, which are due to due to charge transfer and d-d transition respectively. From these observations the structure of the complex can be assigned to be tetrahedral.

4. 2. 4. a. 5. ***Polymer-Supported PAMAM –Cu(II) Complex***

The complex is blue in color. The terminal amino groups of the dendrimer form co-ordination bonds with the Cu^{2+} ion. This bond formation can be observed from the shift in the stretching frequency of the primary amino group to lower wave number region. The IR spectra of the copper complex showed that the band due to the stretching of primary amino groups undergo a shift of 58 cm^{-1} and the band due to bending vibration undergoes a shift of 57 cm^{-1} towards lower wave number region. The inability of amide band to take part in complexation was visible from the unaltered position of C=O stretching band. The thermo gravimetric analysis showed that the complex was subjected to a 7% weight loss between 100-200 ^{o}C.

Electronic spectra of the complex showed two bands at 420 nm and 664 nm. The former band corresponds to charge transfer spectrum and the latter one due to the overlapping of three allowed d-d transitions. The EPR spectra gave the $g_{\parallel}=2.1$ and $g_{\perp}=2.0$ and $A_{\parallel}=8.75\times10^{-4}$ and $A_{\perp}=15\times10^{-4}$ values respectively which are corresponding to an octahedral complex. The possible structure of the complex is shown in Figure 4-8.

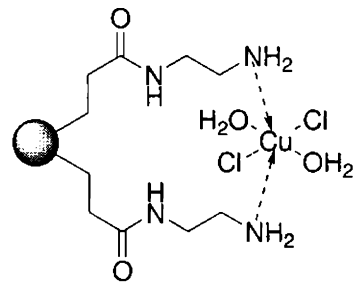


Figure 4-8. Proposed structure of polymer-supported PAMAM-Cu complex

4. 2. 4. a. 6. *Polymer-Supported PAMAM-Zr(IV) Complexes*

The complex is light yellow in color. The primary amino groups of the dendrimer undergo a shift to lower frequency region after complexation with Zr^{4+} ion. The new peaks occupy their place at 3370 cm^{-1} and at 3320 cm^{-1}. The bending band of these amino groups shifts their position from 1597 to 1550 cm^{-1}. The amide carbonyl group remains unaltered. Thermal analysis showed that the complex showed a weight loss of 3% between 100-200 cm^{-1} which is small compared to other complexes. The UV-Vis spectra of the complex showed two peaks at 424 nm and 237 nm. These bands may be due to charge transfer and d-d transitions respectively.

4. 2. 4. a. 7. *Polymer-Supported PAMAM-Ag(I) Complexes*

A brown colored complex is obtained which turn black on exposure to light and air. The primary amino groups of the dendrimer undergo a shift to lower frequency region after complexation with Ag(I) ion. The new peaks occupy their place at 3360 cm^{-1} and at 3310 cm^{-1}. The amide group did not have any role in complex formation as observed from the unaltered FTIR band. Thermal analysis showed that the complex contained water molecules co-ordiated to the complex. UV-Vis spectra of the complex showed a continuous absorption band and this may be due to the photoxidation of the silver ions which resulted in the blackening of the sample. No discrete geometry could be assigned to the complex.

4. 2. 4. a. ***8. Polymer-Supported PAMAM-Pd(II) Complexes***

The complex is brown in color. The polymer supported PAMAM-Pd complexes showed some anomaly compared to other complexes described above. In the FTIR spectra of this complex both the amide carbonyl band and primary amino group bands underwent a shift from their original values. The stretching bands due to the primary amino groups underwent a negative shift of 48 cm^{-1} and the bending band of primary amine undergo a negative shift of 43 cm^{-1}. The carbonyl stretching band of the amide underwent a shift of 57 cm^{-1} to low frequency region. This suggests that the carbonyl group plays some role in complex formation. Thermo gravimetric analysis showed that the complex do not show any considerable weight loss up to 150 °C. This shows that no water molecules take part in complexation while the amide groups of the dendrimer form co-ordination bond with the metal ions.

UV-Vis spectra of the palladium complex showed a peak at 411 nm and another one at 319 nm. The possible structure of the complex may be a square planar one as shown in Figure 4-9.

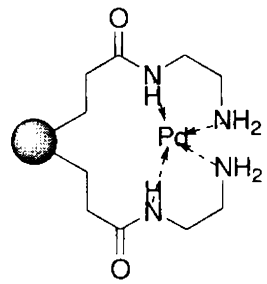


Figure 4-9. Proposed structure of polymer-supported PAMAM-Pd complex

4. 2. 4. b. Polymer-Supported PPI-Metal Complexes

Contrary to PAMAM dendrimers, PPI dendrimers contain only primary amino groups and tertiary amino groups. It is generally expected that only the primary amino group is able to form co-ordinate bonds. The tertiary amino groups generally show less tendency to take part in co-ordinate bond formation. But this condition is not always obeyed and show deviation depending on the ligand and metal. The primary amino groups show characteristic bands in the

FTIR spectra and on co-ordination with the metal ions, these bands get shifted from their original values and this shift gives an idea about complexation and structure of the complex. The primary amino groups of the dendrimer show characteristic bands at 3382 cm^{-1} and 3331 cm^{-1} due to the asymmetric and symmetric stretching. The band at 1592 cm^{-1} is assigned to be the band due to the scissoring motion of the $-NH_2$ group. These three frequencies observed in the FTIR spectra of the polymer supported PPI dendrimers were compared with the position of the corresponding bands in the metal complexes of the supported dendrimers and the shift in their values were used to assign the structure of the complex. The UV-Vis spectra and EPR spectra as well as thermo gravimetry of the complexes were used as additional tools for the structure determination.

4. 2. 4. b. ***1. Polymer-Supported PPI-Mn(II) Complex***

The color of the complex is light brown. The FTIR spectra showed that the bands due to the stretching and bending vibrations of primary amino groups of the dendrimer undergo a negative shift of 35 cm^{-1}. This shows that the primary amino groups of the dendrimer form co-ordinate bonds with the manganese ion. Thermal analysis of the complex showed a small weight loss of about 5% between 100-200 ^oC. This is due to the loss of water molecules co-ordinated to the central metal atom. The presence of co-ordinated water molecules can be identified from a broad band at around 3450cm^{-1} in the vibrational spectra.

The electronic spectrum showed a broad charge transfer band at 475 nm and a ground state to first excited state transition band at 601 nm for the Mn(II) complex The ESR parameters are $g_{\|}$=2.18 and $g_{\perp}$=2.12 and $A_{\|}=70x10^{-4}$ and $A_{\perp}120x10^{-4}$. From these observations the structure of the complex can be represented as in Figure 4-10.

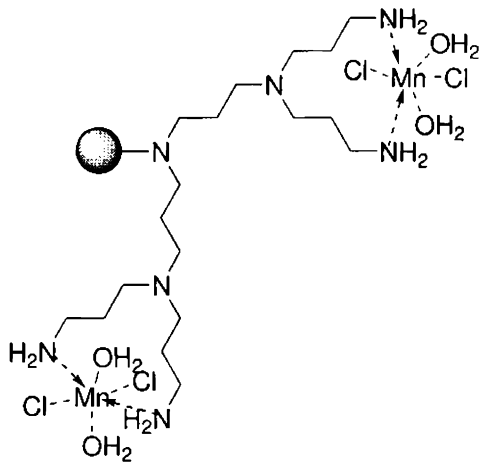


Figure 4-10. Proposed structure of polymer-supported PPI-Mn complex

4. 2. 4. b. 2. ***Polymer-Supported PPI-Fe(III) Complex***

The complex is brown in color. A negative shift in the value of the stretching frequencies of primary amino groups after complexation gives the evidence that the primary amines have a considerable role in complexation. The stretching frequencies shifts to a lower value by 22 cm^{-1}. The peak at 1597 cm^{-1} also showed a negative shift of 31 cm^{-1}. Thermal analysis of the complex showed that the complex is stable up to 250 °C. This shows that no water molecule is co-ordinated to the central metal atom.

In the electronic spectra, two bands at 390 nm and 533 nm arise and they are assumed to be due to charge transfer transition and $^6A_{1g} \rightarrow {}^4T_{1g}$ transition respectively. The ESR parameters are $g_{\parallel}$=2.1 and $g_{\perp}$=2.0 and $A_{\parallel}$=130x10^{-4} and $A_{\perp}$=160x10^{-4}. From these observations the structure of the complex can be assigned to be octahedral and can be represented as given above in the case of manganese complex.

4. 2. 4. b. 3. ***Polymer-Supported PPI-Co(II) Complex***

The complex is pink in color. After complexation the FTIR bands shifted negatively to 3330 and 3300 cm^{-1} respectively from their original values. The band due to the scissoring motion occupies a new position at 1547 cm^{-1} after a shift from their original value at 1597 cm^{-1}. Thermal analysis of the cobalt complex showed a small weight loss of between 100-200 °C. This shows that the

complex contain co-ordinated water molecules. The electronic spectra of the complex showed two bands at 565nm and 616 nm. These bands correspond to $^4A_2$ (F) → $^4T_1$ (P) and $^4A_2$ (F) →$^4T_1$ (F) transitions. ESR specta of the complex gave $g_{\|}$=2.1 and $g_{\perp}$=2.0 and $A_{\|}$=80x10^{-4} and $A_{\perp}$=60x10^{-4}. From these analytical data the complex is assumed to be having an octahedral geometry.

4. 2. 4. b. *4. Polymer-Supported PPI-Ni(II) Complex.*

The complex is light green in color. On complex formation the bands in the IR spectrum due to the stretching of primary amino groups undergo a negative shift of 47 cm^{-1} and this shows that the primary amino groups take part in complex formation. The presence of water molecules in the complex was realized from the weight loss of complex observed in thermo gravimetry. The UV-Vis spectra of the complex showed two bands at 667 nm and 398 nm, which are due to to charge transfer and d-d transition respectively. From these observations, the structure of the complex can be assigned to be tetrahedral and can be represented as given above in the case of manganese complex.

4. 2. 4. b. *5. Polymer-Supported PPI –Cu(II) Complex*

A blue colored complex is obtained. The terminal amino groups of the dendrimer form co-ordination bonds with the Cu^{2+} ion. This bond formation can be observed from the shift in the stretching frequency of the primary amino group to lower wave number region. The IR spectra of the copper complex showed that the band due to the stretching of primary amino groups undergo a shift of 52 cm^{-1} and the band due to bending vibration undergoes a shift of 47 cm^{-1} towards lower wave number region. The thermo gravimetric analysis showed that the complex was subjected to a 7% weight loss between 100-200 ^{o}C.

Electronic spectra of the complex showed two bands at 412 nm and 653 nm. The former band corresponds to charge transfer spectrum and the latter one due to the overlapping of three allowed d-d transitions. The EPR spectra gave the $g_{\|}$=2.1 and $g_{\perp}$=1.9 and $A_{\|}$ =8.75x10^{-4} and $A_{\perp}$ =15x10^{-4} values respectively

which are corresponding to an octahedral complex. The possible structure of the complex is shown in Figure 4-11.

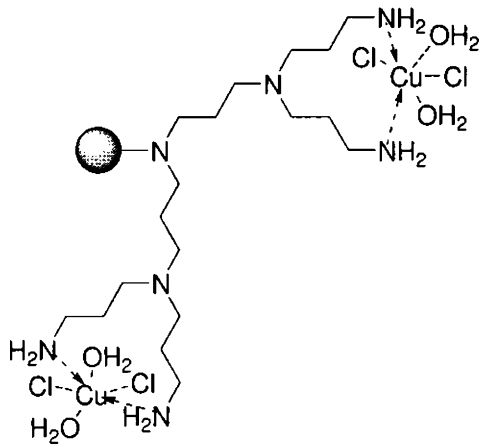


Figure 4-11. Proposed structure of polymer-supported PPI-Cu complex

4. 2. 4. b. ***6. Polymer-Supported PPI-Zr (IV) Complexes***

The complex is light yellow in color. The primary amino groups of the dendrimer undergo a shift to lower frequency region after complexation with Zr^{4+} ion. The new peaks occupy their place at 3362 cm^{-1} and at 3312 cm^{-1}. The bending band of these amino groups shift their position from 1597 to 1542 cm^{-1}. The amide carbonyl group remains unaltered. Thermal analysis showed that the complex showed a weight loss of 3% between 100-200 cm^{-1} which is small compared to other complexes. The UV-Vis spectra of the complex showed two peaks at 424 nm and 237 nm.

4. 2. 4. b. ***7. Polymer-Supported PPI-Ag (I) Complexes***

As described in the above cases, the FTIR spectra showed that the primary amino groups co-ordinate to the metal ion and it was observed from a shift in the values of the amino groups stretching frequencies from 3382 cm^{-1} and 3331 cm^{-1} to 3360 cm^{-1} and 3315 cm^{-1} . Thermal analysis showed that the complex contain water molecules co-ordiated to the complex. UV-Vis spectra of the complex showed a continuous absorption band and this may be due to the photoxidation of the silver ions which results in the blackening of the sample.

4. 2. 4. b. *8. Polymer-Supported PPI-Pd (II) Complexes*

In the FTIR spectra of this complex the primary amino group bands undergoes a shift from their original values. The stretching bands due to the primary amino groups undergo a negative shift of 40 cm^{-1} and the bending band of primary amine undergo a negative shift of 37 cm^{-1}. Thermogravimetric analysis showed that the complex showed that there was no considerable weight loss of near 100 °C which mean that no water molecules co-ordinated to the complex. UV-Vis spectra of the palladium complex showed a peak at 414 nm and another one at 315 nm A possible structure of the complex is a square planar one shown in the Figure 4-12.

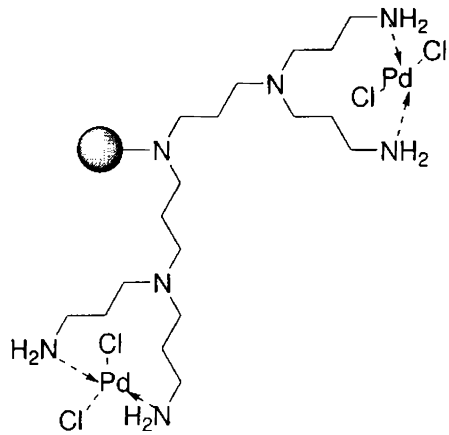


Figure 4-12 Proposed structure of polymer-supported PPI-Pd complex

4. 3. CONCLUSION

In short polymer supported complexs of Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Pd(II), Zr(IV) and Ag(I) were prepared using the polymer supported PAMAM and PPI dendriemrs as ligands. The complexes were characterized using various spectral and thermal methods. Factors influencing the complex formation were studied in detail. From there data the structure of the polymer supported complexes were predicted.

4. 4. EXPERIMENTAL

4. 4. 1. General method of preparation of the polymer-supported dendrimer metal complexes

A 50 mL round bottom flask was charged with 500 mg of the polymer carrying the respective dendrimer. A standard aqueous solution of the corresponding metal ion (20 mL, 0.02 M) was added to the flask. The reaction mixture was stirred at room temperature for a 12 h. The polymer was filtered and washed well with water. The filtrate and washings were collected together and concentrated. This concentrated solution was used for the estimation of metal ions by standard methods. The polymer-supported metal complex was washed well with methanol(20 mL x 3) dioxin (20 mL x 3) and acetone (20 mL x 3) followed by drying at 50 °C for 3 h.

To study the effect of reaction time on the metal intake by the polymer, the polymer (500 mg) was allowed to react with the metal ion solution (20 mL, 0.02 M) in water at various intervals of time. The polymer was filtered after the fixed interval and the metal intake was estimated.

The complex formation was carried out at different temperature as well as at different pH for a fixed interval of time with the polymer (500 mg) and metal ions (20 mL, 0.02 M) in water and from the amount of metal intake of the polymer the influence of these factors on complexation was generalized.

To study the effect of co-solvents on complexation, the polymer (500 m) was allowed to swell in the respective solvent (5 mL) for 1 h and then the complexation was carried out as before for 12 h. The amount of metal intake by the polymer was estimated. From this value, the best co-solvent which gave the maximum complexation was identified.

The polymer supported complexes were characterized by spectroscopic methods like FTIR, UV-Vis and EPR. TG-DTA was used for determining the thermal stability and decomposition of the polymer supported complexes.

4. 4. 2. Estimation of Iron (III)

The filtrate of the solution after complexation was concentrated and made up to a definite volume. dil H_2SO_4 (10 mL) was added to the solution during making up to prevent hydrolysis. 20 mL of this solution was pippetted out in to a beaker. NH_4OH was added to this solution till a permanent brown precipitate was formed. The precipitate was dissolved by cautious addition of dil. H_2SO_4. A slight excess of H_2SO_4 was added and the solution was heated to boiling. When the solution started boiling 1 g Zn dust was added. It was shaken gently at intervals and tested for completeness of reduction using ammonium thiocyanate solution. The solution was filtered and to the filtrate dil. H_2SO_4 and a pinch of $NaHCO_3$ were added. The filtrate containing the ferrous sulphate was titrated against a standard $KMnO_4$ solution till a permanent pale pink color appeared at the end point.

4. 4. 3. Estimation of Manganese(II)

The filtrate of the solution after complexation was concentrated and made up to a definite volume. 20 mL of this solution was pippetted out in to a conical flask and titrated directly against standard EDTA solution using eriochrome balck T as the indicator. The pH of the solution was adjusted to 10 using the NH_4OH-NH_4Cl buffer.

4. 4. 4. Estimation of Cobalt(II)

The filtrate of the solution after complexation was concentrated and made up to a definite volume.20 mL of this solution was pippetted out in to a conical flask. To this solution 20 mL standard EDTA solution was added followed by 1 mL NH_4OH-NH_4Cl buffer. The excess EDTA was back titrated against standard $ZnSO_4$ solution using eriochrome balck T as the indicator. The end point was the change in color from blue to violet.

4. 4. 5. Estimation of Nickel(II)

The filtrate of the solution after complexation was concentrated and made up to a definite volume. 20 mL of this solution was pippetted out in to a

conical flask. It was diluted to 100 mL. A small amount of freshly prepared murexide indicator was added to it followed by 10 mL 1M NH_4Cl. Concentrated NH_4OH was added dropwise till a yellow colour appears. The solution was titrated against standard EDTA solution. Towards the end point 10 mL ammonia was added to make the solution alkaline. The end point was indicated by a color change from yellow to bluish violet.

4. 4. 6. Estimation of Copper(II)

The copper ion solution obtained after complexation was made u to definite volume and 20 mL of this solution was pipetted out in to an iodine flask. Ammonium hydroxide was added dropwise till a slight precipitate was formed. It was then dissolved in minimum quantity of dilute acetic acid and one or two drops of acetic acid was added in excess. About 20 mL of 10% KI solution was added to it. The liberated iodine was titrated against standard sodium thiosulphate solution using starch as indicator. The end point was denoted by the color change from blue to white. 10 mL of NH_4CNS solution was added towards the end of titration to desorb the iodine adsorbed by the cuprous iodide.

4. 4. 7. Estimation of Palladium(II)

The Pd(II) solution obtained after complexation was mad up to definite volume. A known volume of this solution was pipetted out, diluted to 100 mL and 15mL DMG reagent was added and the solution was allowed to stand for 1 h. The precipitate was then filtered through a previously weighed sintered glass crucible after making sure that the precipitation was complete. The orange yellow precipitate was thoroughly washed, first with cold water and then with hot water, dried in an air oven at 110^{0}C and noted the weight. Drying and weighing was continued until a constant weight was obtained. The weight of palladium in the solution was calculated.

4. 4. 8. Estimation of Zirconium(IV)

The residual zirconium solution obtained after complexation was concentrated to 10 mL. About 50 mL 10% solution of diamonium hydrogen

phosphate was added and then it was diluted to 250 mL and boiled for few minutes. Finally it was digested over a water bath for 15 to 30 minutes and was cooled to about 60°C. The precipitate was washed with dilute H_2SO_4 containing diaamonium hydrogen phosphate and then with cold 5% ammonium nitrate solution until the precipitate was free from sulphate ions. Then the precipitate was dried in an air oven at 110 °C and finally ignited in a silica crucible for about 3 hour and weighed as ZrP_2O_7.

4. 4. 9. Estimation of Silver(I).

The silver ion solution obtained after complexation was made up to definite volume and 20 mL of this solution was pipetted out in to 250 mL conical flask. 5 mL 6 M nitric acid was added to followed by 1 mL iron(III) indicator solution. This solution was titrated against a standard ammonium thiocyanate solution. The end point was denoted by the appearance of a faint brown color.

REFERENCES

1. Kilway, K. V.; Deng, S.; Bowser, S.; Mudd, J.; Washington, L.; Ho, D. M. *Pure Appl. Chem.* **2006**, *78*, 855.
2. Weizman, H.; Libman, J.; Shanzer, A. *J. Am. Chem. Soc.* **1998**, *120*, 2188.
3. MacNichol, D. D. In *Inclusion Compounds 2*, Atwood, J. L., Davies, J. E. D., MacNichol, D. D. , Eds.; Academic Press: New York, **1984**.
4. Vögtle. F. *Cyclophane Chemistry: Synthesis, Structures, and Reactions*, John Wiley: Chichester, **1993**.
5. Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D. N.; Mammen, M.; Gordon, D. M. *Acc. Chem. Res.* **1995**, *28*, 37.
6. Bowden, N.; Terfort, A.; Carbeck, J.; Whitesides, G. M. *Science* **1997**, *276*, 233.
7. Terfort, A.; Bowden, N.; Whitesides. G. M. *Nature* **1997**, *386*, 162.
8. Diallo, M. S.; Christie, S.; Swaminathan, P.; Balogh, L.; Shi, X.; Um. W.; Papelis, C.; Goddard III, W. A.; Johnson, Jr. J. H. *Langmuir*, **2004**, *20*, 2640

9. Ottaviani, M. F.; Bossmann, S.; Turro, N. J.; Tomalia, D. A. *J. Am. Chem. Soc.***1994**, *116*, 661.
10. Ottaviani, M. F.; Montalti, F.; Turro, N. J.; Tomalia, D. A. *J. Phys. Chem. B*, **1997**, *101*, 158.
11. Diallo, M. S.; Balogh, L.; Shafagati, A.; Johnson Jr., J. H.; Goddard III, W. A.; Tomalia, D. A. *Environ. Sci. Technol.* **1999**, *33*, 820.
12. Floriano, P. N.; Noble IV, C. O.; Schoonmaker, J. M.; Poliakoff, E. D.; McCarley, R. L. *J. Am. Chem. Soc.* **2001**, *123*, 10545.
13. Zhou, L.; Russell, D.; H.; Zhao, M. Q.; Crooks, R. M. *Macromolecules* **2001**, *34*, 3567.
14. Ottaviani, M. F.; Valluzzi, R.; Balogh, L. *Macromolecules*, **2002**, *35*, 5105.
15. Diallo, M. S.; Christie, S.; Swaminathan, P.; Balogh, L.; Shi, X.; Um, W.; Papelis, C.; Goddard III, W. A.; Jonson Jr. J. H. *Langmuir*, **2004**, *20*, 2640.
16. Tran, M. L.; Gahan, L. R.; Gentle, I. R. *J. Phys. Chem. B*, **2004**, *108*, 20136.
17. Kulczynska, A.; Frost, T.; Margerum, L. D. *Macromolecules*, **2006**, *39*, 7372.
18. Tarazona-Vasquez, F.; Balbuena, P. B. *J. Phys. Chem. B*, **2005**, *109*, 12480.
19. Tarazona-Vasquez, F.; Balbuena, P. B. *J. Phys. Chem. B*, **2008**, 112, 4172
20. Tarazona-Vasquez, F.; Balbuena, P. B. *J. Phys. Chem. B*, **2008**, 112, 4182
21. Wan, H.; Li, S.; Konovalova, T. A.; Shuler, S. F.; Dixon, D. A.; Street, S. C. *J. Phys. Chem. C* **2008**, *112*, 1335.
22. Serroni, S.; Juris, A.; Venturi, M.; Campagna, S.; Resino, I. R.; Denti, G.; Credi, A.; Balzani, V. *J. Mater. Chem.* **1997**, 7, 1227.
23. Glazier, S.; Barron, J. A.; Houston, P. L.; Abruna, H. D. *J. Phys. Chem. B.* **2002**, *106*, 9993.
24. Barron, J. A.; Bernhard, S.; Houston, P. L.; Abruna, H. D.; Rglovsky, J. L.; Malliaras, G. G. *J. Phys. Chem. A.* **2003**, *107*, 8130.
25. Mo, Y. J.; Jiang, D. L.; Uyemura, M.; Aida, T.; Kitagawa, T. *J. Am. Chem. Soc.* **2005**, *127*, 10020.
26. Kawa, M.; Takahagi, T. *Chem. Mater.* **2004**, *16*, 2282.
27. Saudan, C.; Balzani, V.; Gorka, M.; Lee, S. K.; Maestri, M.; Vicinelli, V.; Vogtle, F. *J. Am. Chem. Soc.* **2003**, *125*, 4424.

28. Gu, T.; Whitesell, J. K.; Fox, M. A. *J. Phys. Chem. B.* **2006**, *110*, 25149.

29. Shen, L.; Shi, M.; Li, F.; Zhang, D.; Li, X.; Shi, E.; Yi, T.; Du, Y.; Huang, C. *Inorganic Chem.* **2006**, *45*, 6188.

30. Powell, C. E.; Hurst, S. K.; Morrall, J. P.; Cifuentes, M. P.; Roberts, R. L.; Samoc, M.; Humphrey, M. G. *Organometallics*, **2007**, *26*, 4456.

31. Balogh, L.; Swanson, D. R.; Tomalia, D. A.; Hagnauer, G. L.; McManus, A. T. *Nano Lett.* **2001**, *1*, 18.

32. Langereis, S.; Dirksen, A.; Hackeng, T. M.; van Genderen, M. H. P.; Meijer, E. W. *New J. Chem.* **2007**, *31*, 1152.

33. Balaji, B. S.; Obora, Y.; Ohara, D.; Koide, S.; Tsuji, Y. *Organometallics*, **2001**, *20*, 5342.

34. Enoki, O.; Imaoka, T.; Yamamoto, K. *Org. Lett.* **2003**, *5*, 2547.

35. Camerano, J. A.; Casado, M. A.; Ciriano, M. A.; Lahoz, F. J.; Oro, L. A. *Organometallics*, **2005**, *24*, 5147.

36. Naka, K.; Fujita, M.; Tanaka, K.; Chujo, Y. *Langmuir*, **2007**, *23*, 9057.

37. Onitsuka, K.; Ohara, N.; Takei, F.; Takahashi, S.; *Organometallics*, **2008**, *27*, 25.

Chapter 5

POLYMER SUPPORTED DENDRIMER METAL COMPLEXES AS HETEROGENEOUS CATALYSTS

5. 1. INTRODUCTION

Polymer supported catalysis is a well-explored area in chemistry.[1] But most of these studies are confined in the area of small molecules or metal complexes supported on polymers. Supporting well-defined and complex molecules like dendrimers on cross-linked polymers and investigating them in heterogeneous catalysis is a less known topic. There are few examples of this topic in the literature and these reports showed that heterogeneous catalysts based on dendrimers supported on insoluble materials have promising future.

The first example of the use of polymer-supported dendrimer based catalyst was reported by Arya and co-workers.[2] A PAMAM type polyamide dendrimer was synthesized on Rink amide resin using 3, 5-diaminobenzoic acid derived peptide-like monomer. The primary amino groups at the periphery of these dendrimers were decorated with diphosphine chelate ligands and their Rh complexes. The hydroformylation reaction associated with this type of catalyst design demonstrated high activity. The second- and third-generation catalysts were more active than the first generation one and could be recycled a number of times without loss of activity. Another study explored the influence of the isolation of the catalyst environment on the polystyrene-supported catalytic system in the hydroformylation reaction.[3] In a subsequent study, the polystyrene-bound lysine incorporating dendrons with four propagation sites in each monomer were converted into first- and second generation hydroformylation catalysts bearing 4 and 16 Rh complexes, respectively, on each of the dendrons. These new catalytic systems showed even higher reactivity

(enabling room-temperature hydroformylation), excellent regioselectivity and outstanding recyclability.[4] A different type of carbonylation chemistry was carried out with bisphosphine–Rh complexes immobilized on polyamide-dendronized polystyrene. The supported dendrons with 3,5- diaminobenzoic acid and lysine branching units in each generation were used to prepare the catalysts, which promoted the carbonylative ring expansion of aziridines to β-lactams. Four and sixteen catalytic unit-bearing G1 and G2 catalysts were recovered and reused three times.[5]

Portnoy and Dahan applied the phosphine-decorated polyether dendrons on polystyrene for the study of the Co-catalyzed Pauson–Khand reaction. Both 4- and 2-diphenylphosphinobenzoate bearing dendritic resins (generations 0–3) were complexed with $Co_2(CO)_8$ and the catalytic systems were tested in the intramolecular reaction of 1,6-enyne. The 4-diphenylphosphinobenzoate series of catalysts showed a remarkable increase in the yield of the Pauson–Khand product as a function of the dendron generation. This increase reflects an improvement in both the activity and selectivity of the catalytic systems.[6]

Dahan and Portnoy investigated the Heck reaction with supported dendritic catalysts. They used polystyrene-supported polyether dendritic template decorated with monodentate phosphines via an esterification reaction. For generations 1–3, as well as the analogue derived from the nondendritic Wang resin, it was possible to effectively functionalize the termini with phosphines and complex them to a Pd(0) precursor [$Pd(dba)_2$]. Two phosphine ligands were coordinated to each Pd center. The system was active for the Heck reaction of bromobenzene with various olefins under mild condition. Remarkably, a strong positive dendritic effect was observed.[7] When analogous catalysts, based on the polythioether and polyamine dendritic framework, were examined, notably lower yields were obtained.

Portnoy and Dahan extended the study of the afore mentioned supported dendritic phosphine-Pd complexes to the Suzuki cross-coupling reaction.[8] In this study, Wang polystyrene support was functionalized with three types of dendritic templates: poly(aryl benzyl ether), poly(aryl benzyl thioether) and

poly(aryl benzyl amine). These dendronized resins were decorated with phosphine ligands on the periphery and complexed with a Pd(0) catalytic precursor. As in the case of the Heck reaction, the system enabled the process to proceed under relatively mild conditions (at 80 °C, with NEt_3 as a base) and demonstrated a substantial positive dendritic effect. Interestingly, the Suzuki reaction was less sensitive to the nature of the dendritic backbone than the Heck reaction, as the activities of the catalysts based on polythioether and polyamine dendritic backbone were similar to that of the polyether dendron derived catalysts.

Another interesting polymer-supported dendrimer catalyst was derived by Reymond and co-workers.[9,10] A library of dendritic peptides attached to Tentagel resin were prepared and screened for their esterolytic activity. The peptide dendrons of this library were subjected to the high-throughput screening of the ability to catalyze the hydrolysis of 8-butyryloxypyrene 1,3,6-trisulfonate. This experiment revealed that the most catalytically active dendrimers in the library are those carrying the His-Ser diad in the outermost layer and hydrophobic amino acids (Ile and Val) in the innermost part of the dendritic structure. The presence of an additional histidine near the outermost layer enhanced the catalytic ability. Similar peptide dendrons from the above series prepared in a library format were screened, while still on the beads, for aldolase potential activity. Probes forming colored enaminones or releasing fluorescent fragments via enolization or retro-aldol reactions were used for the screening. Lysine- and proline-rich sequences were identified with the enaminone-forming and enolization-sensitive probes.[11]

There are few enantioselective catalysts derived from polymer-supported dendrimers. A strong positive dendritic effect on the enantioselectivity of ketone reduction was demonstrated by chiral diamines supported on dendronized polystyrene and complexed with a $Ru(BINAP)Cl_2$ precursor.[12] Dendronization of polystyrene with polyether dendrons led to a dramatic improvement in the enantioselectivity of the aldol reaction catalyzed by immobilized proline derivatives.[13] Kehat and Portnoy attached methyl ester of (2S,4R)-O-propargyl-

poly(aryl benzyl amine). These dendronized resins were decorated with phosphine ligands on the periphery and complexed with a Pd(0) catalytic precursor. As in the case of the Heck reaction, the system enabled the process to proceed under relatively mild conditions (at 80 °C, with NEt_3 as a base) and demonstrated a substantial positive dendritic effect. Interestingly, the Suzuki reaction was less sensitive to the nature of the dendritic backbone than the Heck reaction, as the activities of the catalysts based on polythioether and polyamine dendritic backbone were similar to that of the polyether dendron derived catalysts.

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N-trityl-4-hydroxyproline to the periphery benzyl azide groups of zero to third generation aryl ether dendrimers attached to polystyrene resin via the Cu catalyzed Sharpless procedure of the Huisgen azide-alkyne dipolar cycloaddition.[14] The catalyst was used in the asymmetric aldol condensation. The yield and ee showed a gradual increase from zero to third generation dendrimers. The catalyst was recycled but with lower efficiency.

In addition to these systems few dendritic catalysts supported on silica or other inorganic supports were also used for heterogeneous catalysis with promising results.[15-20]

In this chapter, application of polymer supported dendrimer metal complexes as heterogeneous catalysts is described. These complexes were screened against a number of reactions and some of the catalysts were found to be active in particular reactions. Of the reactions, which gave positive results, two were selected and studied in detail. The selected reactions were oxidation of secondary alcohols and three component Mannich reaction.

As a reaction of synthetic importance, oxidation of alcohols to aldehydes and ketones have an important role in fine chemical synthesis and pharmaceutical indutry.[21-23] A large number of reagents and catalysts are conventionally used for this oxidation.[24-28] Every year, many new catalysts are developed for this purpose.[29-38] Eventhough a large number of catalysts are used for alcohol oxidation, many of them are homogeneous catalysts. Examples of polymer supported oxidation catalysts are few in literature and many of them suffer from long reaction time and lower yield.[39-41] In this chapter, applications of polymer supported dendrimer-manganese complex as heterogeneous catalysts in oxidation of seconadry alcohols are descussed. Oxidation of various alcohols with different oxidising agents was carried out. Various factors influencing the reaction were determined. An interesting observation was that, the oxidation could be carried out in the presence of urea-hydrogen peroxide adduct (UHP). As a green oxidising agent, UHP is used widely in the transformation of a large number of functional groups in the presence of various catalysts.[42-46] The

catalysts studied here are found to be highly active compared to many previously reported systems and can be recycled at least half a dozen times.

Because of the simplicity and the availability of a large number of substrates that can undergo the reaction, Mannich reaction is a versatile reaction and used widely in the synthesis of biologically important products and natural products.[47-52] Various catalysts are used for this type of reaction ranging from strong inorganic acids or bases to transition metal complexes[51-57]. Now-a-days a special interest is aroused in three-component Mannich reaction as well as in organocatalyzed Mannich reaction because of the atom economic, environmental friendly and simple nature of the synthetic strategy.[52, 58-73] There are few examples of polymer-supported catalysts in literature used as successful catalysts in Mannich reaction.[74,75] But examples of using polymer supported dendrimer based catalysts for Mannich reaction is absent. The catalyst showed better activity in solvents like ethanol and water and this opens an environmentally friendly route to synthesise β- keto amines. Moreover the catalyst can be recycled half a dozen times without loss of activity.

5. 2. RESULTS AND DISCUSION

The polymer-supported transition metal complexes prepared as described in the previous chapter were screened as heterogeneous catalysts against various reactions. A variety of catalysts were identified which were either active in one or more reactions. The reactions and the corresponding catalysts are shown in the table 5. 1.

From these set of reactions and catalysts, two sets were selected for detailed study. They are polymer-supported Mn complex catalyzed oxidation reactions and Pd catalyzed Mannich reaction. Eventhough almost all the catalysts were found to be active in oxidation reaction, better results were given by Mn(II) complexes.

Table 5.1. Screening of catalysts against various reactions

Entry	Reaction	Metal catalyst							
		Mn	Fe	Co	Ni	Cu	Pd	Ag	Zr
1	Oxidation	√		√	√	√	√	√	
2	Epoxidation	√				√			
3	Polymerization				√				√
4	Kharash addition		√		√				
5	Diels-Alder					√	√		
6	Tetrahydroquinoline Synthesis					√	√		
7	Aldol-reaction					√	√		
8	Mannich reaction			√	√	√	√		
9	Heck reaction						√		
10	Benzazepine synthesis							√	
11	Diarylmethanol synthesis				√				

5. 2. 1. Oxidation of Alcohols

In order to study the catalytic properties of the polymer supported manganese complex, oxidation of benzoin with $K_2Cr_2O_7$ in acetone in the presence of polystyrene supported poly(amidoamine) dendrimer-manganese complex was carried out as a model reaction. Initially, the reaction was carried out in the presence of various amounts of the catalyst in acetone at room temperature. It was observed that, at very low catalyst concentration, the reaction required long time to get completed even under refluxing conditions. As the catalyst amount was increased, the reaction went to completion swiftly. When the amount of the catalyst was 5 mol % of the alcohol taken, the reaction was completed with in 3 h at room temperature (table 5.2).

Table 5. 2 Influence of the amount of catalyst on oxidation reaction

Entry	Amount of catalyst (mol%)	Time (h)	% Yield [a, b]
1	1	3	63
2	2	3	82
3	5	3	97
4	10	3	98

[a] reaction conditions: 2 mmol benzoin. 0.5 mmol $K_2Cr_2O_7$, 5 mL acetone, room temperature, PAMAM-Mn(II)-PS: [b] isolated yield of pure product

After the amount of the catalyst was optimized, the influence of solvents on the reaction was studied in the next step. The above mentioned oxidation was carried out in various solvents in the presence of 5 mol % of catalyst at room temperature. The results are summarized in table 5.3.

Table 5. 3 Solvent effect on oxidation of alcohols catalyzed by dendrimer Mn(II) complex

Entry	Solvent	Time (h)	% Yield [a, b]
1	Acetone	3	97
2	THF	3	95
3	Dioxan	3	95
4	CH_3CN	6	85
5	$CHCl_3$	6	82
6	Benzene	8	80

[a] reaction conditions: 2 mmol benzoin, 0.5 mmol $K_2Cr_2O_7$, 5 mL solvent, room temperature, PAMAM-Mn(II)-PS; [b] yield of pure product

The reaction took place easily in polar solvents like acetone, THF and dioxan. Good results were obtained in water also but the reaction was slow compared to organic solvents and it may be due to the poor solubility of the substrate in water. Solvents like acetonitrile, dichloromethane and chloroform gave poor results and this may be due to the poor solvation of the polar dendritic functionality in these solvents and this kind of solvent effect was previously observed in other reactions. Even if lower alcohols like ethanol and methanol are polar solvents and they gave good results in other reactions their use was avoided suspecting a possible competition in oxidation with the substrate alcohol.

So the reaction condition was selected in such a way that 2 mmol of alcohol was oxidized in the presence of 0.5 mmol of $K_2Cr_2O_7$ and 5 mol % of catalyst in 5 mL of acetone at room temperature. The scheme of the reaction is shown in Figure 5-1.

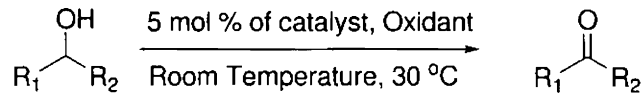


Figure 5-1. Oxidation of alcohols catalyzed by polymer supported dendrimer-Mn(II) complex.

Among the Mn(II) complexes prepared comparable activity was shown by both poly(methyl methacrylate) supported poly(amidoamine) Mn(II) complex and polystyrene supported poly(amidoamine) Mn(II) complex followed by PPI complexes. The results are summarized in table 5.4. But due to the better mechanical strength of the polystyrene support further studies were done with PAMAM-Mn(II) complex supported on polystyrene.

Table 5. 4 Influence of polymer support and dendrimer on catalytic activity of Mn(II) complexes

Entry	% Yield [a, b] with time (h) in bracket			
	PAMAM-Mn(II) on PMMA	PAMAM-Mn(II) on PS	PPI-Mn(II) on PMMA	PPI-Mn(II) on PS
1	98 (3)	97 (3)	93 (3)	85 (3)

[a] reaction conditions: 2 mmol benzoin, 0.5 mmol $K_2Cr_2O_7$ 5 mL acetone, room temperature, 5 mol% catalyst; [b] isolated yield of pure product

The generation of the dendrimer also played a role in the catalytic activity and stability of the complex. The third generation dendrimer-Mn(II) complex showed better activity compared to lower generation metal complexes in the case of both the dendrimers (table 5. 5).

All these studies showed that the third generation PAMAM-Mn(II) complex supported on polystyrene was the best catalyst due to its high activity and mechanical stability. In order to prove the efficiency of the catalyst, the oxidation of various substrates were studied using this catalyst. The results are summarized in table 5. 6.

Table 5.5 Effect of dendrimer generation on catalysis

Entry	Generation	% Yield [a,b]	
		PAMAM	PPI
1	0	30	22
2	1	51	34
3	2	86	71
4	3	97	85

[a] reaction conditions: 2 mmol benzoin, 0.5 mmol $K_2Cr_2O_7$, 5 mL acetone, room temperature, 5 mol% catalyst, catalyst is G3 PAMAM-Mn(II) on PS [b] isolated yield of pure product

It was observed that oxidation of almost all the alcohols attempted took place with in a short period of time. The size of the substrates or its electronic environment has little or no effect on the rate and yield of the reaction. But when it comes to the case of a large substrate like cholesterol, the yield and rate got diminished considerably. This may be due to the difficulty in the interaction of the large sized catalyst which is situated in the pores of the polymer with the bigger substrate and this can be considered as a molecular sieving effect. This kind of steric restriction was not present in the case of small substrates. Moreover, the poor solubility of cholesterol in solvents, which assist the dendrimer catalysts, is another reason for the poor yield.

The yield of the benzils was little low when $K_2Cr_2O_7$ was used as the oxidant. It was observed that a green colored side product was formed when potassium dichromate was used as the oxidant. This product can be isolated by column chromatography, but the primary attempts to characterize it failed, as it did not crystallize properly. This colored product was observed only when $K_2Cr_2O_7$ was used as the oxidant and the substrates were benzoin derivatives. Formation of the green color was taken as an indication of the extent of oxidation and it was at its maximum when the oxidation was complete. From these observations it was primarily attributed that the green colored material was a complex or adduct formed between the product benzil and the oxidant.

Table 5.6 Oxidation of Secondary Alcohols

Entry	Reactant	Product	% yield of the product and time for each oxidant [a, b]					
			$K_2Cr_2O_7$	Time (h)	$KMnO_4$	Time (h)	UHP	Time [c] (h)
O1	2-propanol	Acetone[d]	97	3	97	2	91	12
O2	α-phenyl ethanol	Acetophenone	97	3	98	2	92	12
O3	4-bromo α-phenyl ethanol	4-bromo acetophenone	97	3	97	2	92	12
O4	4-methoxy α-phenyl ethanol	4-methoxy acetophenone	97	4	98	2	93	12
O5	Benzhydrol	Benzophenone	97	3	99	2	93	12
O6	Benzoin	Benzil	97	3	98	3	90	15
O7	4,4′-dimethyl benzoin	4,4′-dimethyl benzil	97	4	98	3	93	15
O8	4,4′-dimethoxy benzoin	4,4′-dimethoxy benzil	94	6	97	3	87	16
O9	Furoin	Furil	95	3	97	2	93	12
O10	Cyclohexanol	Cyclohexanone[d]	98	3	99	2	97	12
O11	Cholesterol	Δ^4-cholestenone	50	24	55	20	30	24

[a] reaction conditions: 2 mmol alcohol, 0.5 mmol $K_2Cr_2O_7$ or $KmnO_4$ or 6 mmol UHP, 5 mL acetone, room temperature, 5 mol% PAMAM-Mn(II)-PS. [b] isolated yield of pure product; [c] 70^0 C, [d] no solvent, yield by GC/MS.

This kind of difficulty was not observed in the case of $KMnO_4$. The reaction went to completion with in a short period of time compared to potassium dichromate and no side product was observed. The product could be isolated easily. It was noted that there were some manganese oxide formation during the repeated cycle of catalysis. Even if it did not affect the catalyst performance, a quantitative analysis of the reaction became tedious as these oxides did not dissolve under normal conditions used in the experiment.

The problems encountered with inorganic oxidants shifted the focus to a mild oxidizing agent and the choice was urea-hydrogen peroxide adduct (UHP). UHP was freshly prepared according to a standard procedure[76] and used. The ratio of oxidant to substrate was taken as 1:6 in this case. The reaction was very slow at room temperature, but the speed of the reaction increased tremendously when the temperature was raised to 70 °C. Comparable yield was observed with UHP. After the reaction, the oxidant could be removed easily by washing with water.

The catalyst could be recycled after washing thoroughly with ethyl acetate and reused. The polymer supported PAMAM dendrimer-Mn(II) complexes are more compatible to recycling compared to PPI dendrimer-Mn(II) complex. The PAMAM complex remained catalytically active for four consecutive cycles while there was a gradual loss of activity of the PPI-Mn(II) complex. The results are presented in table 5.7. The loss of activity can be explained by the instability of the PPI dendrimer towards the reaction conditions which results in the metal leaching from the catalyst and there by a drop in activity (section 5. 2. 3)

The results showed that polymer supported dendrimer-Mn complex is a highly efficient catalyst in the oxidation of alcohols to carbonyl compounds and it outdates many previously reported polymer-supported catalysts for oxidation reaction. The catalyst is compatable and efficient with both strong inorganic oxidants and mild oxidizing agent UHP.

Table 5.7: Effect of recycling on the catalytic efficiency of Mn(II) complexes

Entry	No. of recycling steps	% Yield [a, b]	
		PAMAM	PPI
1	1	97	89
2	2	97	85
3	3	95	78
4	4	90	70
5	5	90	67
6	6	82	

[a] reaction conditions: 2 mmol benzoin, 0.5 mmol $K_2Cr_2O_7$ 5 mL acetone, room temperature, 5 mol% catalyst. [b] isolated yield of pure product

The oxidation was also performed with selected substrates using PMMA supported PAMAM-Mn(II) complex as catalyst. In this case only $K_2Cr_2O_7$ was used as the oxidant. The results are presented in table 5.8.

Table 5.8: Oxidation of Secondary Alcohols

Entry	Reactant	Product	% yield of the product and time for each oxidant [a, b]	
			$K_2Cr_2O_7$	Time (h)
1	α-phenyl ethanol	Acetophenone	98	3
2	4-bromo α-phenyl ethanol	4-bromo acetophenone	98	3
3	4-methoxy α-phenyl ethanol	4-methoxy acetophenone	97	3
4	Benzhydrol	Benzophenone	97	3
5	Benzoin	Benzil	97	3
6	4,4'-dimethyl benzoin	4,4'-dimethyl benzil	97	4
7	4,4'-dimethoxy benzoin	4,4'-dimethoxy benzil	95	5

[a] reaction conditions: 2 mmol alcohol, 0.5 mmol $K_2Cr_2O_7$, 5 mL acetone, room temperature, 5 mol% PAMAM-Mn(II)-PMMA. [b] isolated yield of pure product.

5. 2. 2. Three Component Mannich Reaction

Three-component Mannich reaction between aldehydes, amines and ketones was the second reaction studied which was catalyzed by polymer supported dendrimer metal complexes. Among the catalysts screened, palladium complex of PAMAM dendrimers gave the best results followed by Pd complex of PPI dendrimer. Initially, the reaction between benzaldehyde, aniline and cyclohexanone was studied to optimize various factors influencing the rate and yield of the reaction.

As in the previous cases, the influence of the amount of catalyst on the reaction was examined first. For this purpose, the reaction between the above-mentioned substrates in ethanol was carried out in the presence of varying amounts of the catalyst. From the isolated yield of the product, it was confirmed that only two mole percent of the catalyst was needed to drive the reaction to completion. With an amount of lower concentration of the catalyst the reaction took more time for completion (table 5.9).

Table 5.9: Influence of amount of catalyst on three component Mannich reaction

Entry	Amount of catalyst (mol%)	Time (h)	% Yield [a, b]
1	0.5	12	71
2	1	12	78
3	2	12	90
4	5	12	90

[a] reaction condition: 5 mmol benzaldehyde, 5 mmol cyclohexanone, 5.2 mmol aniline, catalyst is G3 PAMAM-Pd(II) on PS, 5 mL ethanol. [b] isolated yield of the product

Second factor studied was the role of solvent. In this case also, the catalyst showed the same behavior as given in the previous cases. The reaction proceeded quickly in polar solvents, while non-polar solvents gave poor results. The results are presented in the table 5. 10. The reaction proceeded well in polar solvents including water. The reason for this is that, the presence of dendrimer on polymer makes the resin as a whole more compatible to polar solvents and so

an easy interaction between the catalyst and substrates took place. The same is applicable in the case of water, but due to the poor solubility of organic substrates, make the system as a whole triphasic and so the rate of the reaction and yield was lower. In non-polar solvents, the yield and rate decreases because of the poor swelling of dendrimer based catalyst. Similar observation was obtained in the case of other catalysts described previously.

Table 5.10: Solvent Effect in Mannich Reaction

Entry	Solvent	Time	% Yield [a, b]
1	Ethanol	12	90
2	Methanol	12	90
3	Water	24	81
4	$CHCl_3$	20	80
5	Benzene	30	68

[a] reaction conditions: 5 mmol benzaldehyde, 5.2 mmol aniline, 5 mmol cyclohexanone, 5 mL solvent, 2 mol% of catalyst, catalyst is G3 PAMAM-Pd(II) on PS room temperature. [b] isolated yield of the product

Another factor which influenced the reaction was temperature and the reaction proceeded well at room temperature. So the reaction parameters were optimized and the reaction was carried out in the presence of two mole percent of the catalyst in ethanol at room temperature. Ethanol was preferred over methanol due to its low toxicity and environmental friendliness eventhough, both of them gave similar results.

The scheme of the reaction is shown in Figure 5-2.

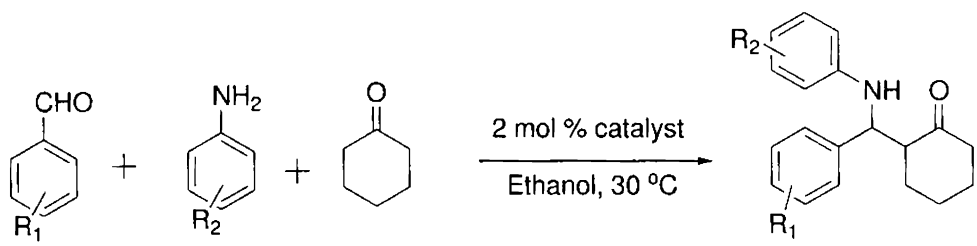


Figure 5-2. Three component Mannich reaction catalyzed by polymer supported dendrimer-Pd(II) complex

Among the Pd(II) complexes prepared better activity was shown by poly(methyl methacrylate) supported poly(amidoamine) Pd(II) complex followed by polystyrene supported poly(amidoamine) Pd(II) complex. The results are summarized in table 5. 11.

Table 5.11: Influence of polymer support and dendrimer on catalytic activity of Pd(II) complexes

Entry	% Yield [a, b] with time (h) in bracket			
	PAMAM-Pd(II) on PMMA	PAMAM-Pd(II) on PS	PPI-Pd(II) on PMMA	PPI-Pd(II) on PS
1	93 (12)	90 (12)	87(12)	82 (12)

[a] reaction condition: 5 mmol benzaldehyde, 5 mmol cyclohexanone, 5.2 mmol aniline, 2 mol% catalyst, 5 mL ethanol. [b] isolated yield of product

As mentioned in the previous reactions the generation of the dendrimer also played an important role in the catalytic activity of the Pd(II) complexes. The third generation dendrimer-Pd(II) complex showed better activity compared to lower generation metal complexes in the case of both the dendrimers (table 5. 12)

Table 5.12: Effect of dendrimer generation on catalysis

Entry	Generation	% Yield [a, b]	
		PAMAM	PPI
1	0	No reaction	No reaction
2	1	32	Negligible
3	2	81	64
4	3	90	82

[a] reaction condition: 5 mmol benzaldehyde, 5 mmol cyclohexanone, 5.2 mmol aniline, 2 mol% catalyst, 5 mL ethanol. [b] isolated yield of the product

In order to generalize the catalytic efficiency the synthesis of various β-amino ketones were carried out in the presence of G3 PAMAM-Pd(II) complex

supported on polystyrene. The polystyrene support was selected because of its mechanical stability which support the easy removal and recycling of the catalyst. The results are presented in table 5. 13

Table 5. 13: Three Component Mannich Reactions catalyzed by PAMAM-Pd(II) complex supported on polystyrene

Entry	R_1	R_2	Ketone	Time h	Yield [a, b]
M1	H	H	Cyclohexanone	12	90
M2	4-OCH_3	H	Cyclohexanone	18	81
M3	4-Cl	H	Cyclohexanone	20	85
M4	4-NO_2	H	Cyclohexanone	14	89
M5	Br	4-OCH_3	Cyclohexanone	8	92
M6	H	4-Cl	Cyclohexanone	20	90
M7	H	4-NO_2	Cyclohexanone	24	87
M8	H	2-CH_3	Cyclohexanone	20	91
M9	4-NO_2	4-OCH_3	Cyclohexanone	8	92
M10	4-Cl	4-CH_3	Cyclohexanone	12	90
M11	4-OCH_3	2-CH_3	Cyclohexanone	24	85
M12	H	H	Acetophenone	24	87
M13	H	Cl	Acetophenone	24	84
M14	3,4-OCH_3	Cl	Acetophenone	24	85
M15	4-Cl	4-Cl	Acetophenone	20	89
M16	4-OCH_3	H	Acetophenone	24	83
M17	Furfural	H	Cyclohexanone	12	90
M18	H	H	Acetone	18	90
M19	H	OCH_3	Acetone	12	90
M20	4-NO_2	4-OCH_3	Acetone	12	92

[a] reaction conditions: 5 mmol aldehyde, 5.2 mmol aniline, 5 mmol ketone, 5 mL ethanol, 2 mol% of catalyst, room temperature; [b] isolated yield of pure product

Generally, all the reactions got completed with in 12-24 h with good yield. The electron withdrawing substituents present on aniline and the electron donating substituents present on aldehydes retard the speed of the reaction and lower the yield compared to the reverse cases. The reaction was slower when

cyclohexanone was replaced by other ketones and the yields also got reduced under these conditions. Good yields were obtained for all the examples studied.

After each set of reaction, the catalyst was recycled by washing thoroughly with ethyl acetate. The catalyst was used in the next cycle of reaction (table 5.14). Polymer supported PAMAM dendrimer-Pd complex showed better efficiency compared to the PPI complex. The yield gradually decreased in the case of PPI dendrimer-Pd complex but no such effect was observed with PAMAM-Pd complex up to four cycles. This may be due to both the higher stability of the PAMAM-Pd complex towards recycling and less metal leaching from the dendrimer complex (section 5. 2. 3).

Table 5.14: Effect of recycling of catalyst

Entry	No. of recycle	% Yield [a, b]	
		PAMAM	PPI
1	1	90	87
2	2	90	85
3	3	90	80
4	4	87	73
5	5	82	70
6	6	76	

[a] reaction condition: 5 mmol benzaldehyde, 5 mmol cyclohexanone, 5.2 mmol aniline, 2 mol% polystyrene supported catalyst, 5 mL ethanol; [b] isolated yield of product

The reaction was also performed with PMMAM supported PAMAM-Pd complex and the results are presented in table 5.15. Generally better yield was obtained with PMMA supported catalysts. The effect of support on catalysis is discussed in detail in section 5. 2. 4.

Table 5.15: Three Component Mannich Reaction catalyzed by PAMAM-Pd(II) complex supported on PMMA

Entry	R_1	R_2	Ketone	Time h	Yield [a, b]
1	H	H	Cyclohexanone	12	93
2	4-OCH_3	H	Cyclohexanone	18	84
3	4-Cl	H	Cyclohexanone	20	87
4	4-NO_2	H	Cyclohexanone	14	90
5	Br	4-OCH_3	Cyclohexanone	8	90
6	H	4-Cl	Cyclohexanone	20	90
7	H	4-NO_2	Cyclohexanone	24	88
8	H	2-CH_3	Cyclohexanone	20	92

[a] reaction conditions: 5 mmol aldehyde, 5.2 mmol aniline, 5 mmol ketone, 5 mL ethanol, 2 mol% of catalyst, room temperature; [b] isolated yield of pure product

5. 2. 3 Comparison between the Two Dendrimers in Catalysis

In was observed that, PAMAM dendrimer based catalysts showed higher activity and stability in catalysis that involved transition metal complexes. This high activity of PAMAM metal complexes can be explained by comparing the structure of the PAMAM and PPI dendrimers. On comparing both the dendrimer structures, it can be concluded that the PAMAM dendrimers have longer branches compared to PPI dendrimer. Due to this, the metal ions, which are the real catalytic sites, are placed at longer distance from the support. An easy interaction between the catalyst and substrate was possible due to this in the case of PAMAM dendrimers. This made the PAMAM dendrimer complexes more effective catalysts than PPI dendrimers.

PAMAM dendrimer metal complexes showed high stability under the reaction conditions selected as observed from the low metal leaching from these catalysts. Metal complexes of PPI dendrimers gradually released the metal ions after each cycle and more than half of the metal ions got released into the solution after the fourth cycle. On the other hand, most of the metal ions remained in the polymer-supported catalyst in the case of PAMAM dendrimers

even after the sixth cycle. From the table 5.16 and 5.17 these results become clearer.

Table 5.16: Amount of Mn(II) ion remained in the catalyst after each cycle in oxidation reaction

No. of Cycles	Amount of Mn(II) ion in mmol per gram of the resin[a]	
	PPI Dendrimer	PAMAM Dendrimer
1	1.00	1.15
2	0.90	1.14
3	0.71	1.14
4	0.42	1.00
5	0.23	0.90
6	-	0.90

[a] reaction conditions: 2 mmol benzoin, 0.5 mmol $K_2Cr_2O_7$, 5 mL acetone, room temperature, catalyst is PAMAM-Mn(II) on PS or PPI-Mn(II) on PS.

Table 5.17: Amount of metal remained in the catalyst after each cycle in Mannich reaction

No. of Cycles	Amount of Pd(II) ion in mmol per gram of the resin	
	PPI Dendrimer	PAMAM Dendrimer
1	0.92	1.09
2	0.90	1.09
3	0.81	0.92
4	0.75	0.85
5	0.55	0.85
6	-	0.77

[a] reaction conditions: 5 mmol aldehyde, 5.2 mmol aniline, 5 mmol ketone, 5 mL ethanol, 2 mol% of catalyst, room temperature. catalyst is G3 PAMAM-Pd(II) on PS or G3 PPI-Pd(II) on PS

This effect is more pronounced in the case of oxidation reaction. The presence of strong oxidizing agents, which may degrade the metal complexes, may be the reason for this. Longer flexible arms of PAMAM dendrimers as well

as the presence of the amide linkage may be the reason for the stability of the PAMAM metal complexes.

5. 2. 4 Effect of Polymer Support

The role of polymer support is remarkable in solid phase organic synthesis and polymer-supported catalysis. In the case of the two supports selected for the present study, better results in catalysis were obtained with PMMA- DVB resin. The reactions always took small period of time for completion when catalysts supported on poly(methyl methacrylate) support were used. This may be due to the lower sterric hindrance offered by the support. In polystyrene support, the phenyl rings offer some sterric hindrance which prevents the interaction of catalysts and substrates to some extent. Since the PMMA resin does not contain such phenyl rings, this kind of opposition to the interaction between the catalyst and substrate are not present and so the reactions proceeded more easily. But these effects are small compared to many previously reported cases and this lower influence of support is due to the fact that the catalytic sites are kept at some distance away from the support by the dendritic backbone, which acts as a spacer. Due to the lower chain length of the PPI dendrimer compared to PAMAM which makes the PPI dendrimer complexe a less active catalyst compared to the latter. Another feature of the resin that influences catalysis is the degree of crosslinking. It is a well known fact that with increase in degree of crosslinking, the swelling of the resin get diminished, which decreases the diffusion rate and therefore lowers the reaction rate.[77] In the case of the dendrimer metal complexes also, similar results are obtained. The results are shown in table 5. 18 and 5. 19. In the case of oxidation, benzoin was subjected to oxidation in the presence of catalysts with varying crosslink density and the yield of isolated product is shown in the table. Mannich reaction between benzaldehyde, aniline and cyclohexanone was carried out in the presence of catalysts with varying degrees of crosslinking. In both cases, the amount of various catalysts were selected in such a way that the amount of metal ion remained the same for a particular reaction.

Table 5.18: Effect of support on the catalytic activity of the dendrimer-metal complex in oxidation of alcohols

Degree of Crosslinking	% Yield [a,b]	
	PS	PMMA
1%	97	98
2%	97	97
4%	92	94
6%	86	90

[a] reaction conditions: 2 mmol benzoin, 0.5 mmol $K_2Cr_2O_7$, 5 mL acetone, room temperature, 5 mol% polystyrene supported catalyst. [b] isolated yield of pure product

Table 5.19: Effect of support on the catalytic activity of the dendrimer-metal complex in oxidation of alcohols

Degree of Crosslinking	% Yield [a,b]	
	PS	PMMA
1%	90	93
2%	88	90
4%	80	83
6%	74	80

[a] reaction condition: 5 mmol benzaldehyde, 5 mmol cyclohexanone, 5.2 mmol aniline, 2 mol% polystyrene supported catalyst, 5 mL ethanol; [b] isolated yield of pure product

5. 3. CONCLUSION

The polymer supported dendrimer metal complexes prepared were screened as heterogeneous catalysts in various reactions. From these results two pairs of catalysts and reactions were selected. The polymer supported dendrimer-Mn(II) complex catalyzed oxidation reaction and the polymer supported dendrimer-Pd(II) complex catalyzed three component Mannich reaction were studied in detail. The reaction conditions were optimized to get

maximum yield. The susceptibility of the catalysts to various reaction conditions and substrates were studied. In addition the catalyst recycling was also studied.

5. 4. EXPERIMENTAL

5. 4. 1. Preparation of Urea Hydrogen Peroxide

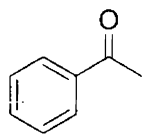
Urea-hydrogen peroxide adduct was prepared according to a standard procedure.[76] A solution of urea in 30 % hydrogen peroxide in the molar ratio 2:3 was heated for ten minutes at a temperature of 60^0 C. After cooling, it was transferred to a watch glass and allowed to evaporate slowly. The crystals formed were collected and dried. It was used as oxidant in the oxidation of alcohols.

5. 4. 2. Oxidation of Secondary Alcohols

A 10 mL round bottom flask was charged with the corresponding alcohol (2 mmol), the catalyst (5 mol% of the alcohol), and required amount of oxidant (0.5 mmol $K_2Cr_2O_7$ or $KMnO_4$ or 4 mmol of UHP). Acetone (5 mL) was added and the reaction mixture was stirred at room temperature. The progress of the reaction was monitored by TLC on silica gel coated plate, with 10:1 mixture of hexane and ethyl acetate as eluent. After the completion of reaction, the catalyst and solid oxidants were filtered off and was washed well with ethyl acetate. The filtrate and washings were collected and evaporated. Finally the pure product was isolated by column chromatography on a small silica column using hexane and ethyl acetate (10:1) as eluent. All the products were known compounds and were characterized using FTIR and ^{1}HNMR spectral analysis.

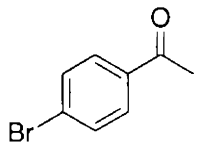
5. 4. 3. Characterization of Products

Acetophenone (Entry O2)



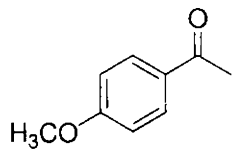
FTIR (KBr, ν_{max} (cm^{-1})) 1683; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.6 (s, 3H), 7.3-7.6 (m, 3H), 7.8-8.0 (m, 2H).

4-bromoacetophenone (Entry O3)



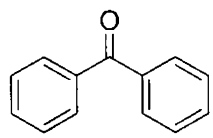
FTIR (KBr, ν_{max} (cm^{-1})) 1679; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.59 (s, 3H), 7.60-7.62 (m, 2H), 7.81-7.84 (m, 2H).

4-methoxyacetophenone (Entry O4)



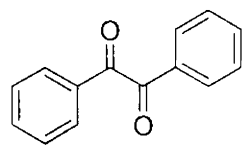
FTIR (KBr, ν_{max} (cm^{-1})) 1680; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.56 (s, 3H), 3.73 (s, 3H), 6.88-7.00 (m, 2H), 7.75-7.91(m, 2H).

Benzophenone (Entry O5)



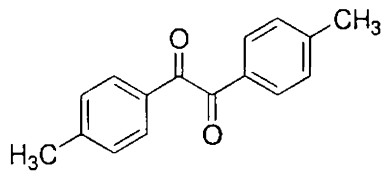
FTIR (KBr, ν_{max} (cm^{-1})) 1661; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.4-7.6 (m, 6H), 7.7-7.8 (m, 4H).

Benzil (Entry O6)



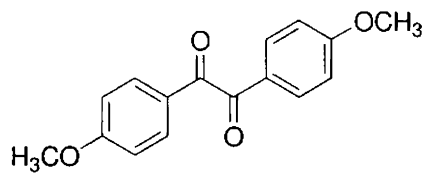
FTIR (KBr, ν_{max} (cm^{-1})) 1680; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.3-7.5 (m, 4H), 7.6-7.7 (m, 2H), 7.8-8.0 (m, 4H).

4,4'-dimethylbenzil (EntryO7)



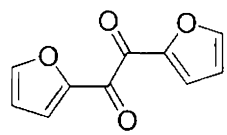
FTIR (KBr, ν_{max} (cm^{-1})) 1670; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.40 (s, 6H), 7.25-7.31 (m, 4H), 7.84-7.89 (m, 4H).

4,4'-dimethoxybenzil (Entry O8)



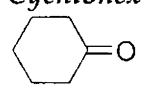
FTIR (KBr, ν_{max} (cm^{-1})) 1676; ^1H NMR ($CDCl_3$, 300 MHz): δ 3.88 (6H, OCH_3), 6.93-6.99 (m, 4H), 7.91-7.97 (m, 4H).

Furil (Entry O9)



FTIR (KBr, ν_{max} (cm^{-1})) 1671; ^1H NMR ($CDCl_3$, 300 MHz): δ 6.61 (m, 2H), 7.23 (m, 2H), 7.76(m, 2H).

Cychlohexanone (Entry O10)



FTIR (KBr, ν_{max} (cm^{-1})) 1715; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.7-1.9 (m, 6H), 2.3-2.4 (m, 4H).

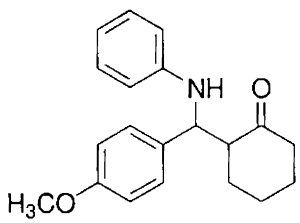
5. 4. 4. Three Component Mannich Reaction

A 10 mL round bottom flask was charged with aldehyde (5 mmol), aniline (5.2 mmol) ketone (5 mmol) and ethanol (5 mL). The reaction mixture was stirred at room temperature. The progress of the reaction was followed using thin layer chromatography on silica gel plate using hexane ethyl acetate

mixture (25:1 v/v) as eluent. After the completion of the reaction, the catalyst was filtered and washed with ethyl acetate. The filtrate and washings were combined and evaporated to remove the solvent. The final product was isolated by column chromatography on silica gel using hexane ethyl acetate mixture (20:1 v/v) as the eluent. The yield of the product was noted. The β-keto amines were characterized by FTIR and ^{1}HNMR spectroscopy.

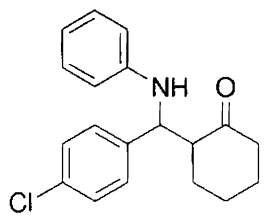
5. 4. 5. Characterization of Products

2-[1'-(N-phenylamino)-1'-(4-methoxyphenyl)]methylcyclohexanone (Entry M2)



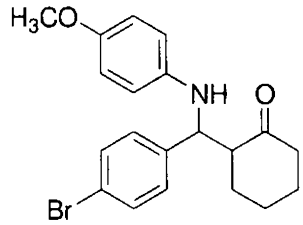
FTIR (KBr, ν_{max} (cm^{-1})): cm^{-1} 3364, 2935, 1706, 1604, 1512; ^{1}H NMR (300MHz, $CDCl_3$): δ 1.61-1.88 (6H, m), 2.31-2.43 (2H, m), 2.71-2.72 (1H, m),3.65 (s, 3H), 4.5 (1H, br), 4.54 (0.68H, d, *J* = 7.3 Hz), 4.73(0.32H, d, *J* = 4.2 Hz), 6.47-6.52 (2H, m), 6.62-6.67 (2H, m), 7.19-7.36 (5H, m).

2-[1'-(N-phenylamino)-1'-(4-chlorophenyl)]methylcyclohexanone (Entry M3)



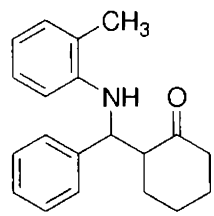
FTIR (KBr, ν_{max} (cm^{-1})) 3390, 3119, 1712, 1142, 1090; ^{1}HNMR ($CDCl_3$, 400 MHz): δ 1.70-1.57 (m, 3H). 1.90-1.86 (m, 3H), 2.31-2.30 (m, 1H), 2.41-2.37 (m, 1H), 2.73-2.71 (m, 1H), 4.59 (d, *J* =6.4 Hz, 1H), 4.68 (w, 1H), 6.50-6.48 (m, 2H), 6.63 (m, 1H), 7.07-7.03 (m, 2H), 7.25-7.23 (m, 2H), 7.31-7.27 (m, 2H).

2-[1′-(N-p-Methoxyphenylamino)-1′-(4-bromophenyl)]methylcyclohexanone (Entry M5)



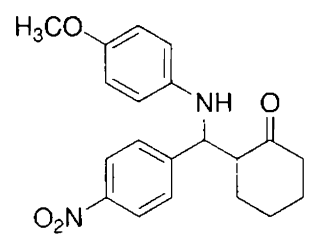
FTIR (KBr, ν_{max} (cm^{-1})) 3360, 1701, 1529, 1482, 1270, 1080, 791; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.59–1.73 (m, 6 H), 1.82–1.93 (6 H), 2.29–2.38 (m, 4H), 2.66–2.76 (m, 2 H), 3.67 (s, 3H; OMe), 3.68 (s, 3H; OMe), 4.49 (d, *J* =6.8 Hz, 1H), 4.64 (d, *J* =4.42 Hz, 1H), 6.45 (d, *J* = 5.0 Hz, 2H), 6.48 (d, *J* =5.0 Hz, 2 H), 6.65 (d, *J* =3.5 Hz, 2 H), 6.67 (d, *J* = 3.5 Hz, 2H), 7.22 (d, *J* =5.9 Hz, 2 H), 7.24 (d, *J* =5.9 Hz, 2 H), 7.39 (d, *J* = 3.4 Hz, 2 H), 7.41 ppm (d, *J* =3.4 Hz, 2H).

2-[1′-(N-o-Methylphenylamino)-1′-(phenyl)]methylcyclohexanone (Entry M8)



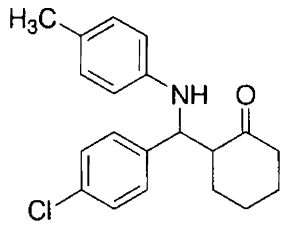
FTIR (KBr, ν_{max} (cm^{-1})) 3379, 1701, 1523, 1493, 1289; ^1H NMR (300 MHz; $CDCl_3$): δ 1.70-1.79(m, 3H, cyclohexyl), 1.83-1.94(m, 3H, cyclohexyl), 2.27(m, 2H, cyclohexyl), 2.35(s, 3H, CH_3), 2.79-2.88(m, 1H, cyclohexyl), 4.0(br, s, 1H, NH), 4.1 (q, 2H, CH_2), 6.39(d, *J* =8.0Hz, 1H, phenyl), 6.6-6.7(m, 1H, phenyl), 6.9-7.1(m, 2H, phenyl), 7.2-7.4(m, 5H, phenyl).

2-[1′-(N-p-Methoxyphenylamino)-1′-(4-nitrophenyl)]methylcyclohexanone (Entry M9)



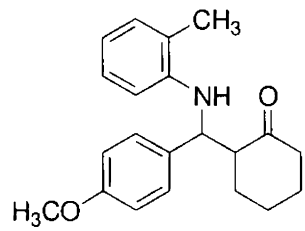
FTIR (KBr, ν_{max} (cm^{-1})) 3352, 2940, 1707, 1600, 1520, 1400, 1189, ^1H NMR ($CDCl_3$, 400 MHz): δ 1.59–2.14 (m, 4H), 2.04 (m, 2H), 2.38 (m, 2 H), 2.83 (m, 1H), 3.67 (s, 3H; OMe), 4.38 (br s,1H), 4.79 (d, *J* =4.0 Hz, 1 H), 6.45 (d, *J* =8.8 Hz, 2 H), 6.66 (d, *J* =8.8 Hz, 2 H), 7.54 (d, *J* =8.7 Hz, 2H), 8.12 ppm (d, *J* =8.7 Hz, 2H).

2-[1'-(N-p-Methylphenylamino)-1'-(4-chlorophenyl)]methylcyclohexanone (Entry M10)



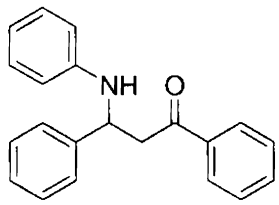
FTIR (KBr, ν_{max} (cm^{-1})) 3379, 1701, 1523, 1493, 1289, 813; ^1H NMR (300 MHz; $CDCl_3$): δ 7.42 (d, 2H, *J* = 8.27 Hz), 7.28–7.31 (m, 2H), 7.09–7.12 (m, 1H), 6.9 (d, 2H, *J* = 8.17 Hz), 6.78 (d, 2H, *J* = 7.6 Hz), 4.6 (d, 0.03H, *J* = 5.5 Hz), 4.5 (d, 0.97H, *J* = 8.22 Hz), 2.36–2.5 (m, 2H), 2.3 (s, 1H), 2.22 (s, 3H), 1.66–1.83 (m, 6H).

2-[1'-(N-o-Methylphenylamino)-1'-(4-methoxyphenyl)]methylcyclohexanone (Entry M11)



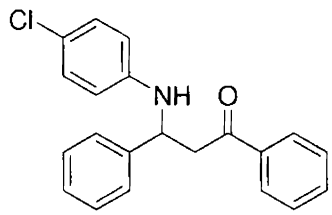
FTIR (KBr, ν_{max} (cm^{-1})) 3386, 1671, 1597, 1508, 1289, 1095, 1015, 810, 684; ^1H NMR (300 MHz, $CDCl_3$): δ 1.7-2.0(m, 6H, cyclohexyl), 2.2 (m, 2H, cyclohexyl), 2.35(s, 3 H, CH_3), 2.8(q, 1H, cyclohexyl), 3.9(s, 3H, OCH_3), 4.1(br, s, 1H, NH), 4.6(q, 2H, CH_2), 6.7(d, *J* =4.0, 1H, phenyl), 6.9(m, 1H, phenyl), 7-7.2(m, 4H, phenyl), 7.4-7.6(m, 3H, phenyl).

3-[1′-(N-phenylamino)-1′-phenyl]1-phenyl-2-propanone (Entry M12)



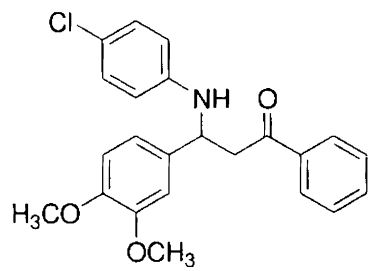
FTIR (KBr, ν_{max} (cm^{-1})) 3340, 2934, 1675, 1515, 1492, 1290, 1013; ^1H NMR (300 MHz, $CDCl_3$): δ 2.03-2.62 (m, 2H, CH_2), 4.15 (br, s, 1H, NH), 4.75-4.90 (m, 1H, CH), 6.34-6.45 (m, 2 H, phenyl), 7.20–7.25 (m, 2 H, phenyl), 7.25–7.37 (m, 4 H, phenyl), 7.39–7.48 (m, 3 H, phenyl), 7.50–7.58 (m, 2 H, phenyl), 7.87–7.96 (m, 2 H, phenyl).

3-[1′-(N-p-Chlorophenylamino)-1′-phenyl]1-phenyl-2-propanone (Entry M13)



FTIR (KBr, ν_{max} (cm^{-1})) 3373, 2924, 1666, 1507, 1489, 1286, 1003, 820, 703; ^1H NMR (300 MHz, $CDCl_3$): δ 3.25–3.49 (m, 2 H), 4.55 (br s, 1 H), 4.80–4.94 (m, 1 H), 6.34–6.45 (m, 2 H), 6.90–6.99 (m, 2 H), 7.11–7.29 (m, 4 H), 7.30–7.42 (m, 3 H), 7.43–7.54 (m, 1 H), 7.78–7.87 (m, 2 H).

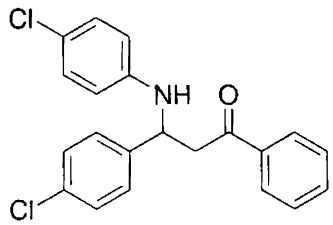
3-[1′-(N-p-Chlorophenylamino)-1′-(3, 4-dimethoxyphenyl)]1-phenyl-2-propanone (M14)



FTIR (KBr, ν_{max} (cm^{-1})) 3413, 2929, 1684, 1599, 1496, 1280, 1221, 1092, 1045, 817; ^1H NMR (300 MHz, $CDCl_3$): δ 3.03–3.21 (m, 1 H), 3.45– 3.65 (m, 4 H), 3.83 (s, 3 H), 4.66 (br, s, 1 H), 4.98–5.20 (m, 1 H), 6.27–6.42 (m, 2 H), 6.64 (dd, J = 3.3, 8.8 Hz, 1

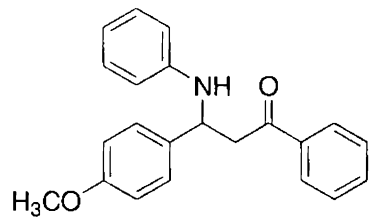
H), 6.76 (d, J = 8.8 Hz, 1 H), 6.83–6.97 (m, 3 H), 7.30–7.53 (m, 3 H), 7.85–7.96 (m, 2 H).

3-[1'-(N-p-Chlorophenylamino)-1'-(4-chlorophenyl)]1-phenyl-2-propanone (Entry M15)



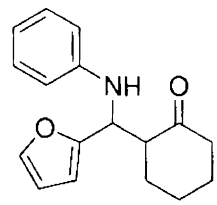
FTIR (KBr, ν_{max} (cm^{-1})) 3386, 1671, 1597, 1508, 1289, 1095, 1015, 810, 684; ^1H NMR (300 MHz, $CDCl_3$): δ 3.19–3.48 (m, 2 H), 4.55 (br s, 1 H), 4.84 (t, J = 6.5, 12.5 Hz, 1 H), 6.26–6.44 (m, 2 H), 6.82–7.04 (m, 2 H), 7.14–7.31 (m, 4 H), 7.32–7.41 (m, 2 H), 7.44–7.54 (m, 1 H), 7.73–7.90 (m, 2 H).

3-[1'-(N-phenylamino)-1'-(4-methoxyphenyl)]1-phenyl-2-propanone (Entry M16)



FTIR (KBr, ν_{max} (cm^{-1})) 3380, 1680, 1601, 1532, 1293, 1099, 1015; ^1H NMR (300 MHz, $CDCl_3$): δ 3.5(q, 2H, CH_2), 4.0(b, 1H, NH), 4.2(t, 2H, CH_2), 6.65(m, 1H, phenyl), 6.91-7.01(m, 3H, phenyl), 7.11-7.22(m, 3H, phenyl), 7.3-7.6(m, 4H, phenyl), 7-8-7.9(m, 2H, phenyl).

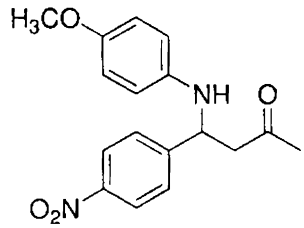
2-[1'-(N-p-Methoxyphenylamino)-1'-(2-furyl)]methylcyclohexanone (Enrty M17)



FTIR (KBr, ν_{max} (cm^{-1})): cm^{-1} 3362, 2938, 1673, 1597, 1500; ^1H NMR (300 MHz, $CDCl_3$): δ 1.60-2.40 (8H, m), 2.89-2.99 (1H, m), 4.5 (1H, br), 4.81 (0.67H, d, J = 5.3

Hz), 4.87 (0.33H, d, J = 4.7 Hz), 6.17-6.26 (2H, m), 6.61-6.71 (3H, m), 7.10-7.29 (3H, m).

2-[1'-(N-p-Methoxyphenylamino)-1'-(4-nitrophenyl)]butanone (Entry M20)



FTIR (KBr, ν_{max} (cm^{-1})) 3352, 2971, 2810, 1717, 1595, 1521, 1416, 1178; ^{1}HNMR (300Mz, $CDCl_3$): δ 2.14 (s, 3H), 2.92 (d, J = 7.5Hz, 2H), 3.68 (s, 3H), 4.86 (t, J = 7.5 Hz), 6.45 (m, 2H), 6.68, (m, 2H), 7.54 (m, 2H), 8.14 (m, 2H).

5. 4. 6. Recycling of the Catalysts

After the completion of the reaction the catalyst was filtered off and washed well with ethyl acetate followed by acetone. It was dried at room temperature under vacuum. The dried catalyst was reused in the subsequent cycles.

REFERENCES

1. *Polymeric Materials in Organic Synthesis and Catalysis*; Buchmeiser, M. R., Ed.; Wiley-VCH: Weinheim, **2003**.
2. Arya, P.; Rao, N. R.; Singkhonrat, J.; Alper, H.; Bourque, S.C.; Manzer, L. E. *J. Org. Chem.* **2000**, *65*, 1881.
3. Alper, H.; Arya, P.; Bourque, S. C.; Jefferson, G. R.; Manzer, L. E. *J. Am. Chem. Soc.***2001**, *123*, 2889.
4. Lu, S. M.; Alper, H. *J. Am.Chem. Soc.* **2003**, *125*, 13126.
5. Lu, S. M.; Alper, H. *J. Org. Chem.* **2004**, *69*, 3558.
6. Dahan, A.; Portnoy, M. *Chem. Commun.* **2002**, 2700.
7. Dahan, A.; Portnoy, M. *Org. Lett.* **2003**, *5*, 1197.
8. Dahan, A.; Portnoy, M. *J. Am. Chem. Soc.* **2007**, *129*, 5860.

9. Clouet, A.; Darbre, T.; Reymond, J. L. *Angew. Chem. Int. Ed. Eng.* **2004**, *43*, 4612.
10. Clouet, A.; Darbre, T.; Reymond, J. L. *Biopolymers*, **2006**, *84*, 114.
11. Kofoed, J.; Darbre, T.; Reymond, J. L. *Org. Biomol. Chem.* **2006**, *4*, 3268.
12. Itsuno, S.; Tsuj, A.; Takahashi, M. *Proc. 11th Int. Conf. Polym. Org. Chem., Prague*, **2004**.
13. Kehat, T.; Portnoy, M. *Proc. Int. Symp. Organocatal. Org. Synth., Glasgow*, **2006**.
14. Kehat, T.; Portnoy, M. *Chem. Commun.* **2007**, 2823.
15. Borque, S. C.; Maltais, F.; Xiao, W. J.; Tardif, O.; Alper, H.; Arya, P.; Manzer, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 3035.
16. Borque, S. C.; Alper, H.; Manzer, L. E.; Arya, P.; *J. Am. Chem. Soc.* **2000**, *122*, 956.
17. Reynhardt, J. P. K.; Alper, H. *J. Org. Chem.* **2003**, *68*, 8353.
18. Lu, S. M.; Alper, H. *J. Org. Chem.* **2004**, *69*, 3558.
19. Dahan, A.; Portnoy, M. *J. Polym. Sci. A: Polym. Chem.* **2005**, *43*, 235.
20. Kehat, T.; Goren, K.; Portnoy, M. *New. J. Chem.* **2007**, *31*, 1218.
21. Sheldon, R. A. In *Catalytic Oxidations in the Manufacture of Fine Chemicals, New Development in Selective Oxidation;* Centi, G., Trifiro, F., Eds.; Elsevier Science Publishers: B. V. Amsterdam
22. Pines, S. H. *Org. Process Res. Dev.* **2004**, *8*, 708.
23. Caron, S.; Dugger, R. W.; Ruggeri, S. G.; Ragan, J. A.; Brown Ripin, D. H. *Chem. Rev.* **2006**, *106*, 2943.
24. Tojo, G.; Fernandez, M. *Oxidation of Alcohols to Aldehydes and Ketones*, Springer Science: New York, **2006**.
25. Ley, S. V.; Madin, A. In *Comprehensive Organic Synthesis*; Trost B. M., Fleming, I., Eds.; Pergamon Press: Oxford, **1991**, Vol.7, pp 251.
26. Lee, T. V. In *Comprehensive Organic Synthesis;* Trost B. M., Fleming, I., Eds.; Pergamon Press: Oxford, **1991**, Vol.7, pp 291.
27. Sheldon, R. A.: Kochi, J. K. *Metal Catalyzed Oxidation of Organic Compounds*, Academic Press: New York, **1981**.

28. Mallat, T.; Baiker, A. *Chem. Rev.* **2004**, *104*, 3037.

29. Stoltz, B. M. *Chem. Lett.* **2004**, *33*, 362.

30. Gilhespy, M.; Lok, M.; Baucherel, X.; *Chem. Commun.* **2005**, 1085.

31. Ji, H. B; Wang, T. T.; Zhang, M. Y.; Chen, Q. L.; Gao, X. N. *React. Kinet. Catal. Lett.* **2007**, *90*, 251.

32. Sarmah, P.; Chakrabarty, R.; Phukan, P.; Das, B. K. *J. Mol. Catal. A: Chem.*, **2007**, *268*, 36.

33. Liu, C; Han, J.; Wang, J. *Synlett*, **2007**, 643.

34. Fujita, K. J.; Tanino, N.; Yamaguchi, R. *Org. Lett.* **2007**, *9*, 109.

35. Zhang, J.; Gandelman, M.; Shimon, L. J. W.; Milstein, D. *J. Chem. Soc. Dalton Trans.*, **2007**, *1*, 107.

36. Deshpande, S. S.; Jayaram, R. V. *Catal. Commun.* **2008**, *9*, 186.

37. Dapurkar, S. E.; Kawanami, H.; Suzuki, T. M.; Yokoyama, T.; Ikushima, Y. *Chem. Lett.* **2008**, *37*, 150.

38. Punniyamurthy, T.; Rout, L. *Coordination Chem. Rev.* **2008**, *252*, 134.

39. Valodkar, V. B.; Tembe, G. L.; Ravindranathan, M.; Ram, R. N.; Rama, H. S. *J. Mol. Catal, A. Chem.* **2004**, *208*, 21.

40. Kang, Q.; Luo, J.; Bai, Y.; Yang, Z.; Lei, Z. *J. Organomet. Chem.* **2005**, *690*, 6309.

41. Nair, V. A.; Suni, M. M.; Sreekumar, K. *J. Polym. Res.* **2003**, *10*, 267.

42. Heaney, H. *Aldrichimica Acta*, **1993**, *26*, 35.

43. Varma, R. S.; Naicker, K. P. *Org. Lett.* **1999**, *1*, 189.

44. Stankovic, S.; Espenson, J. H. *J. Org. Chem.* **2000**, *65*, 5528.

45. Heaney, H.; Newbold, A. J. *Tetrahedron Lett.* **2001**, *42*, 6607.

46. Taliansky, S. *Synlett*, **2005**, *12*, 1962.

47. Blike, F. E. *Org. React.* **1942**, *1*, 303.

48. Hart, D. J.; Ha, D. C. *Chem. Rev.* **1989**, *89*, 1447.

49. Martin, S. F. *Acc. Chem. Res.* **2002**, *35*, 895.

50. Kleinman, E. F.; In *Comprehensive Organic Synthesis*; Trost B. M., Fleming, I., Eds.; Pergamon Press: Oxford, **1991**, Vol. 2, pp. 893.

51. Kobayashi, S.; Haruro, I. *Chem. Rev.* **1999**, *99*, 1069.

52. Cordova, A.; Rios, R. In *Amino Group Chemistry: From Synthesis to the Life Sciences*; Ricci, A., Ed.; Wiley-VCH: Weinheim, **2008**, pp. 185.

53. Arend, M.; Westermann, B.; Risch,N. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1044.

54. Denmark, S. E.; Nicaise, O. J. C. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A.,Yamamoto, H., Eds.; Springer: Heidelberg. **1999**; Vol. 2; pp 923.

55. Cordova, A. *Acc. Chem. Res.* **2004**, *37*, 102.

56. Blatt, A. H.; Gross,N. *J. Org. Chem.* **1964**, *29*, 3306.

57. Yi, L.; Zou, J.; Lei, H.; Lin, X.;Zhang, M. *Org. Prep. Proced. Int.* **1991**, *23*, 673.

58. List, B. *J. Am. Chem. Soc.* **2000**, *122*, 9336.

59. Notz, W.; Tanaka, F.; Watanabe, S.; Chowdari, N. S.; Turner, J. M.; Thayumanavan, R.; Barbas III, C. F. *J. Org. Chem.* **2003**, *68*, 9624.

60. Ibrahem, I.; Zoi, W.; Engqvist, M.; Xu, Y.; Cordova, A. *Chem. Eur. J.*, **2005**, *11*, 23, 7024.

61. Guo,Q, X.; Liu, H.; Guo, C.; Luo, S. W.; Yi Gu, Zhu Gong, L. *J. Am. Chem. Soc.* **2007**, *129*, 3790.

62. Ollevier, T.; Nadeau, E. *Org. Biomol. Chem.* **2007**, *5*, 3126.

63. Bigdeli, M. A.; Nemati, F.; Mahdavinia, G. H. *Tetrahedron Lett.* **2007**, *48*, 6801.

64. Liu, B.; Xu, D.; Dong, J.; Yang, H.; Zhao, D.; Luo, S.; Xu, Z. *Synth. Commun.* **2007**, *37*, 3003.

65. Dong, F.; Jun, L.; Xin-Li, Z.; Zu-Liang, L. *Catal. Lett.* **2007**, *116*, 76.

66. Li, Z.; Ma, X.; Liu, J.; Feng, X.; Tian, G.; Zhu, A. *J. Mol. Catal. A. Chem.* **2007**, *272*, 132.

67. Yamaoka, Y.; Miyabe, H.; Yasui, Y.; Takemoto, Y. *Synthesis*, **2007**, 2571.

68. Rueping, M.; Sugiono, E.; Schoepke, F. R. *Synlett*, **2007**, 1441.

69. Cheng, L.; Wu, X.; Lu, Y. *Org. Biomol. Chem.* **2007**, *5*, 1018.

70. Wu, H.; Shen, Y.; Fan, L. Y.; Wan, Y.; Zhang, P.; Chen, C. F.; Wang, W. X. *Tetrahedron*, **2007**, *63*, 2404.

71. Dziedzic, P. Ibrahem, I.; Cordova, A. *Tetrahedron Lett.*, **2008**, *49*, 803.

72. Hayashi, Y.; Urushima, T.; Aratake, S.; Okano, T.; Obi, K. *Org. Lett.*, **2008**, *10*, 21.

73. Khan, A. T.; Pravin, T.; Choudhary, L. H. *Eur. J. Org. Chem.*, **2008**, *2008*, 834.

74. Groth, T.; Grotli, M.; Meldal, M. *J. Comb. Chem.* **2001**, *3*, 461.

75. Rana, S.; White, P.; Bradley, M. *J. Comb. Chem.* **2001**, 3, 9.

76. Lu, C. S.; Hughes, E. W.; Giguere, P. A. *J. Am. Chem. Soc.* **1941**, *63*, 1507.

77. Akelah, A.; Sherrington, D. C.; *Chem. Rev.* **1981**, *81*, 557.

Chapter 6

POLYMER SUPPORTED DENDRIMER ENCAPSULATED METAL NANOPARTICLES: SYNTHESIS AND CATALYSIS

6. 1. INTRODUCTION

The current decade has witnessed the rise of nanotechnology and carrying out nanotechnology from laboratories to industry to some extent. The coming years are considered as the golden age of nanotechnology that will change the current world in a dramatic way in all fields from computers to medicine.[1] Catalysis is not an exception, catalysis is the primary area that has used nanotechnology for many years and the classic examples are the transition metal colloids used for catalysis.[2] Recent developments in instrumentation methods help us to visualize and manipulate the nanoparticles and this helps to develop novel catalysts from nanoparticles.

There are two approaches in the application of nanoparticles in catalysis. In the first, nanoparticles themselves are used as catalysts. Nanoparticles show high catalytic activity compared to bulk materials of the same composition because of two reasons. As the bulk material is reduced to particles of nanodimension, the surface area get increased appreciably and as the size get smaller and smaller the percentage of atoms present on the surface of the particle get increased. It was estimated that for a 2 nm particle, more than 90% atoms reside on the surface. Since the basics of catalysis is interaction between the reactants and the surface atoms of the catalysts, the catalytic efficiency increases with more number of surface atoms, ie, with smaller particle size of the catalyst. Another factor which governs the catalytic activity of nanoparticles is the vacant sites present on surface atoms. When an atom is situated in the interior of a bulk material, all of its coordination sites are occupied. On the other hand, for the atoms situated on the surface, there are few vacant coordination sites for interaction with the approaching reactant species. If the atom is on an edge of a

particle, there are more vacant coordination sites and the number increases again if it is on the corner. So the atoms staying at the corner of a nanoparticle is more catalytically active than a particle on the edge which in turn is more active than the particle on the surface. These facts help us to tune the catalytic activity of nanoparticles by controlling its size and shape.[3-6]

In a second approach, nanoparticles have no role in catalysis; but they merely act as carriers of catalysts.[7,8] Nanoparticles stabilized with suitable ligands are able to carry a catalyst, most probably a transition metal complex, attached to the ligand. The ligands may have two different functional centers in which one has special affinity towards the nanoparticles. These groups get attached to the nanoparticle while the rest of the ligand gets complexed with the transition metal ion that acts as the catalyst. Generally, this kind of approach is used in the case of gold nanoparticles, which have special affinity towards thiol groups. Another method of using nanoparticles as carriers in catalysis is preparation of magnetic nanoparticle core polymer shell system. The polymer shell is functionalized with suitable functional groups followed by attachment of ligands. These ligands are complexed with transition metals and used in catalysis. The advantage of these magnetic systems is their easier separation by the application of an external magnetic field. But generally, these approaches are not used widely because of the difficulty and high cost in synthesizing nanoparticles that have no particular role in catalysis.

As described above, in the first approach, the nanoparticles directly take part in catalysis. So it becomes necessary to prepare small sized and monodisperse nanoparticle, which show good stability and activity with ease of separation. One common technique used for this is generating the nanoparticles on supports such as alumina, silica or carbon by impregnating these substrates with solutions of the corresponding metal salts followed by reduction of the salt into zero valent nanoparticle by an appropriate method. Even though these nanoparticles are robust and remain unaltered even after many reaction cycles, they are usually non homogeneous and show a wide distribution of particle size. Many particles are of very big size so that they may be little or not at all active in

catalysis. Moreover, only a portion of these nanoparticles gets exposed to the reactants. Due to these reasons, only a portion of these metal particles contribute to catalysis. So it becomes necessary to synthesize nanoparticles with narrow range of particle size distribution that can be easily accessible to the substrates and easily separated from the reaction mixture. Many techniques are used for this purpose. In one approach, metal nanoparticles stabilized with organic ligands are used as catalysts in which the ligands worked as gates that control the rate of catalysis and product selectivity. Under strictly controlled condition the particle size distribution of nanoparticles can be restricted to a narrow distribution and attain excellent and selective catalysis.[9-11] In the second method, nanoparticles are synthesized in a polymer matrix by reduction of metal complexes or metal salts. These nanoparticles trapped in the polymer matrix usually show a narrow distribution of particle size and good catalytic activity.[12-14]

Dendrimers are considered as organic nanoparticles and are expected to be the quantized building blocks for nanoscale synthetic organic chemistry.[15] They are used extensively in nanochemistry because of their particular shape, nanodimensional size and very narrow size and molecular weight distribution, which are generally not attained, by polymers or inorganic nanomaterials.[16] Dendrimers have internal voids and small molecules or clusters of suitable size can fit into these voids.[17-19] Crook and Tomalia demonstrated that metal nanoparticles could be synthesized in the internal voids of dendrimers.[20,21] Dendrimers are particularly attractive hosts for catalytically active metal nanoparticles for the following five reasons: (1) bearing fairly uniform composition and structure, the dendrimer templates themselves yield well-defined nanoparticle replica; (2) the nanoparticles are stabilized by encapsulation within the dendrimer, and therefore they do not agglomerate during catalytic reactions; (3) the nanoparticles are retained within the dendrimer primarily by steric effects and therefore a substantial fraction of their surface is unpassivated and available to participate in catalytic reactions; (4) the dendrimer branches can be used as selective gates to control the access of small molecules (substrates) to the encapsulated (catalytic) nanoparticles; (5) the dendrimer periphery can be tailored

to control solubility of the hybrid nanocomposite and used as a handle to facilitate linking to surfaces and other polymers.[22] The synthesis of Dendrimer Encapsulated Nanoparticles (DEN) includes two simple steps. Initially, dendrimers of suitable generation with appropriate surface functional groups are allowed to complex with metal ions. The reduction of these dendrimer metal complexes, with a suitable reducing agent gives small nanoparticles of suitable dimensions that get trapped into the internal voids of dendrimers. Controlling the ratio of metal ions and dendrimer functional groups can regulate the size of these nanoparticles.[23] Moreover, the monomettalic, bimettalic, alloy type and core-shell nanoparticles can be synthesized by controlling various reaction parameters.[22,24-28]. Figure 6-1 represents the general method of preparation of DEN. The red spots represent the corresponding metal ion and the dark mass represents the nanoparticle.

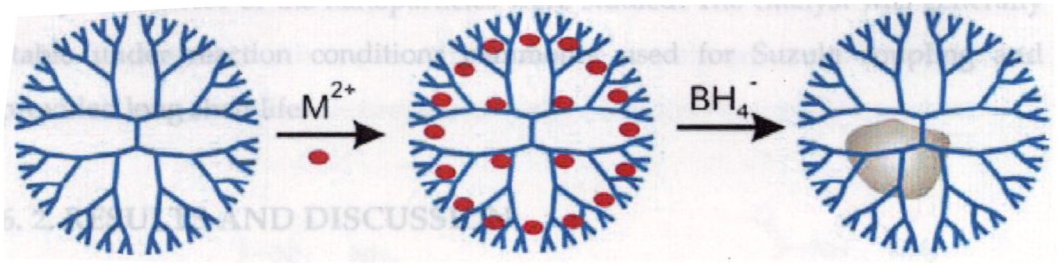


Figure 6-1. General method of preparation of DEN

These dendrimer-metal nanoparticle conjugates are used in catalysis. Admirable results are obtained in catalysis. Crooks et al. showed that dendrimer encapsulated nanoparticles can act as size and shape selective catalysts. Using dendrimers of various generations with suitable surface groups as the templates, DEN catalysts with predetermined size and shape selectivity can be prepared.[22,27,28]

There are some preliminary reports in which dendrimers are attached to carbon nanotubes followed by metal complexation and reduction of the metal to nanoparticles that remains attached to the carbon nanotube.[29]

In this chapter, the synthesis of metal nanoparticles encapsulated in polymer supported dendrimers is described. These nanoparticles were characterized by various methods. Various factors affecting the particle size and shape distribution, agglomeration of small particles to nanoclustures etc. were studied. These nanoparticles were used as heterogeneous catalysts for Suzuki coupling between aryl halides and aryl boronic acids. As a carbon- carbon bond forming reaction Suzuki coupling plays an important role in the synthesis of pharmaceuticals, natural products and advanced materials.[30,31] A large number of catalysts are reported for Suzuki coupling and many of them are highly efficient and tolerate different reaction conditions.[32-37] Polymer supported catalysts also are used in Suzuki coupling.[38-41] Fan and co-workers recently showed that palladium nanoparticles, stabilized with dendrimers containing a phosphine core in which the phosphine group was attached to the nanoparticles, were efficient catalysts for Suzuki coupling.[42] Various factors affecting the catalytic behavior of the nanoparticles were studied. The catalyst was generally stable under reaction conditions commonly used for Suzuki coupling and provided long shelf life.

6. 2. RESULTS AND DISCUSSION

6. 2. 1. Preparation of Polymer Supported Dendrimer-Metal Nanoparticle Conjugates

Polymer supported dendrimer metal complexes prepared according to the method described in the previous chapters were reduced under specific conditions to the corresponding zero valent metal nanoparticle -dendrimer conjugates attached to the insoluble polymer supports. The nanoparticles of Co, Ni, Cu, Pd and Ag were prepared by this method. Various reducing agents in different solvents were used to determine the appropriate condition for the preparation of nanoparticles of narrow size distribution. Among various reducing agents tried, better results were given by the mild reducing agent, hydrazine hydrate. $NaBH_4$ also gave good results but, generally boron hydride

reduction was associated with the problem of formation of some metal borides instead of complete reduction of metal ions. When $LiAlH_4$ was used, formation of some complex side product was observed, which required prolonged washing with NaOH solution for their complete removal. This resulted in the degradation of the dendrimer, agglomeration of nanoparticles and made the process tedious. On the other hand, when hydrazine hydrate was used in methanol, the reduction was very fast and after the reaction removal of the excess reducing agent was very easy and it included simple washing with methanol and drying in vacuum. This prevented the exposure of the nanoparticles to strong reagents. All the metals attempted gave stable nanoparticles except cobalt. The cobalt nanoparticles were oxidized soon after their exposure to atmosphere and this resulted in agglomerated particles of large size. On exposure to air, the colour of the nanoparticles changed from dark brown to pink and this is a clear indication of the instability of the nanoparticles. In the case of other metals, this kind of colour changes occurred after a long time and in certain cases after one or two years. The reaction scheme for the synthesis of polymer supported PAMAM dendrimer-Pd nanoparticle conjugates is shown in the Figure 6-2.

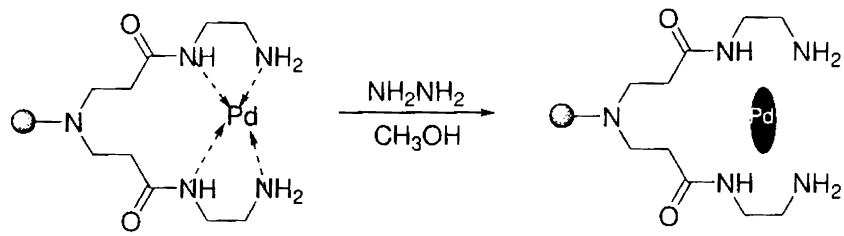


Figure 6-2. Synthesis of polymer supported dendrimer metal nanoparticle conjugates

The dendrimer nanoparticle conjugates were characterized initially by UV- Vis spectroscopy. Before reduction, the metal complexes showed characteristic d-d transition bands and metal-ligand charge transfer bands of the corresponding metal ions. After reduction, these bands disappeared or shifted due to a change in the oxidation state of the metal ions. This is due to the

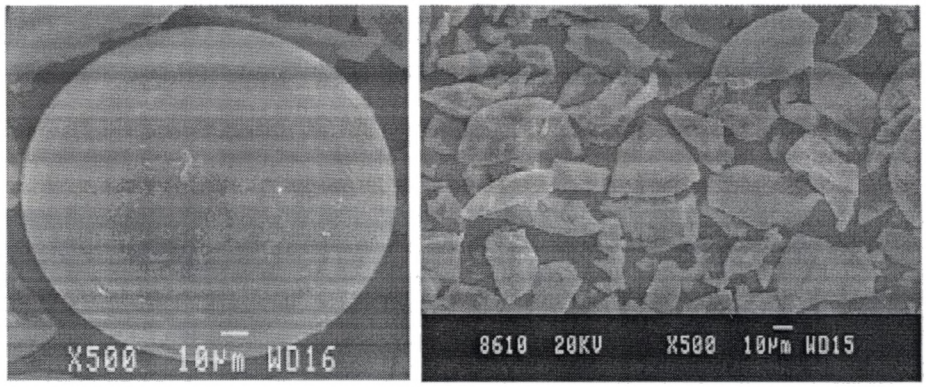
reduction of metal to zero oxidation state and due to the loss of co-ordination nature of the bond between metal and dendrimer. Uv- Vis spectral analysis showed that the peak corresponding to the metal to ligand charge transfer transition disappeared and a continuous absorption band in the visible region appeared in the case of palladium. This result agrees with previous reports describing the UV-Vis spectra of palladium nanoparticles.[43,44] The continuous absorption band in the visible region is due to the well-defined metal domain size of the nanoparticle. Silver nanoparticle showed a characteristic peak at 420 nm but the peak was broad, which meant that the particle size and shape were not uniform.[44,45] In the case of Cu, a characteristic peak appeared at 588 nm but the spectrum was broad in this case also.[46]

FTIR spectrum of the metal complexes before and after reduction showed that the bands at 3463 cm^{-1} and at 1604 cm^{-1} of the complex were shifted to 3380 cm^{-1} and 1643 cm^{-1}. This means that the complex was decomposed and the amino groups got released from complex formation. So the vibrational frequency of the amino groups shifted to a position near to their original values (3394 cm^{-1} and 1660 cm^{-1}). But still there is a small shift from the original value and this may be due to some interaction between the metal nanoparticles and the primary amino groups.

Thermal analysis showed practically no variation in the decomposition process compared to the metal complex and this may be due to the lower concentration of the metal dendrimer system compared to the polystyrene backbone.

The polymer-supported dendrimer-metal nanoparticle conjugates were characterized by microscopic methods. Scanning Electron Microscopy (SEM) was used for the primary observations, which gave a clear idea about the stability of the polymer system under the reaction condition. SEM image in Figure 6-3 a showed a polystyrene bead carrying the PAMAM dendrimer- Pd conjugate. From the figure it is observed that the polystyrene beads did not undergo degradation even after all these reaction steps, which included a multi step synthesis, metal complexation and reduction. So the preparation of these

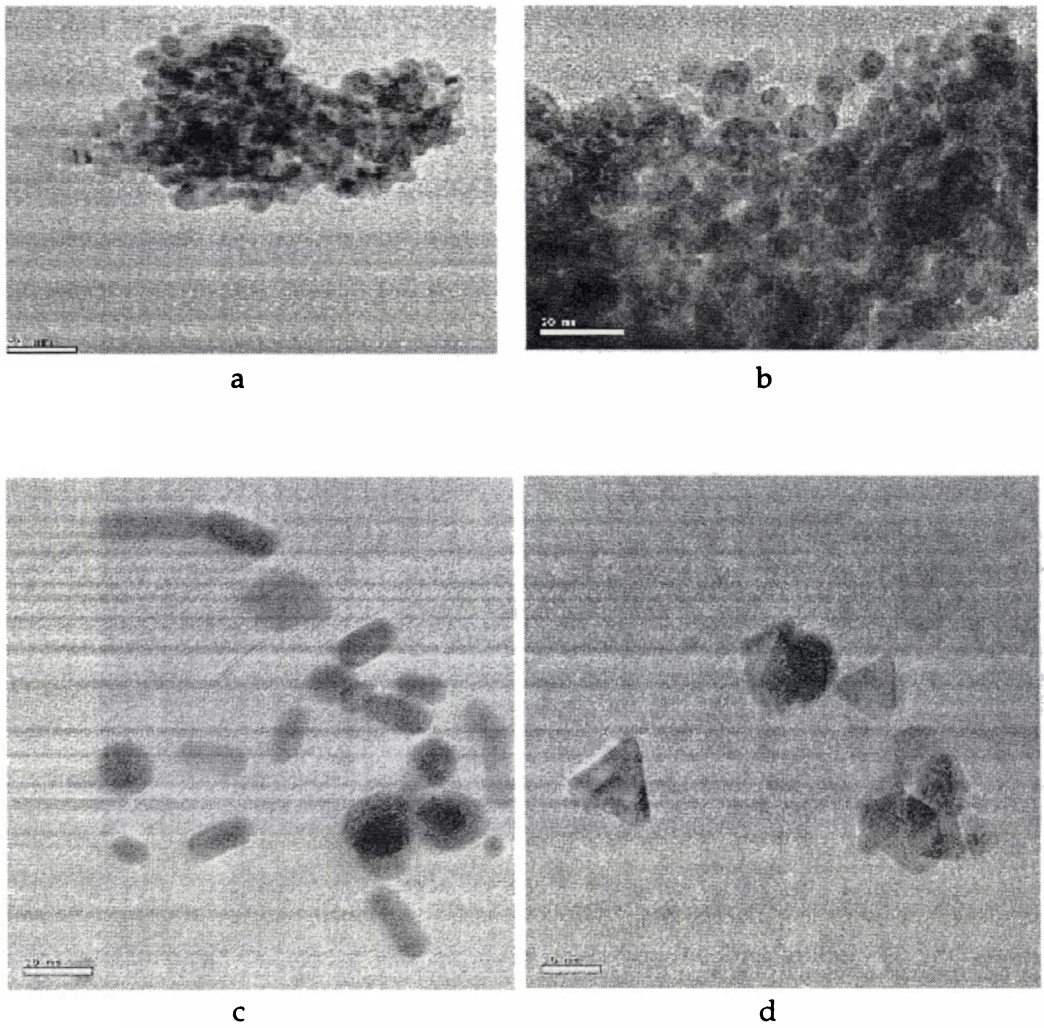
kinds of nanoparticles on polystyrene gives new opportunities in catalysis and nanomaterials. Conversely, the poly (methyl methacrylate) supports showed considerable degradation after this synthesis as described in the previous chapters and it is shown in Figure 6-3 b.



a b

Figure 6-3. SEM images of polystyrene (a) and poly(methyl methacrylate) (b) beads after the synthesis of polymer supported dendrimer metal conjugates.

This decomposition of poly (methyl methacrylate) beads impose a problem in catalyst removal as it was observed that some fine polymer particles were observed in the final reaction mixture even after the catalyst was removed by filtration. Even though these catalyst particles did not interfere with the final purification of the product by column chromatography, it resulted in the gradual loss of the catalyst. This difficulty can be circumvent to a considerable extent by using filtration setup of very fine pore size. HRTEM analysis of the polymer beads clearly showed the presence of metal nanoparticles. Figure 6-4 shows TEM images of palladium nanoparticles encapsulated in a polystyrene supported PAMAM dendrimer of three different generations.



a b

c d

Figure 6-4. Palladium nanoparticles encapsulated in polystyrene supported PAMAM dendrimers. a. first generation, b. second generation, c and d third generation

It was observed that, when lower generation dendrimers were used as templates for nanoparticle synthesis, the nanoparticles formed were of very small size (5-10 nm) but they were placed very close to each other and at a first glance, it would be thought of as big particles. Moreover, the shapes of the nanoparticles are spherical or polyhedral ones with no general trend. But when third generation dendrimer was used as the template, well-separated nanoparticles were observed. The particle size was high when third generation dendrimer was used and most nanoparticles were of 20 nm size. This may be

because, in first and second generation dendrimer nanosized cavities are not well formed due to their smaller size and fewer numbers of branches. So these dendrimers could not separate the nanoparticles from aggregation. When the dendrimer become third generation, it can separately hold the nanoparticles and there by preventing them from aggregation.

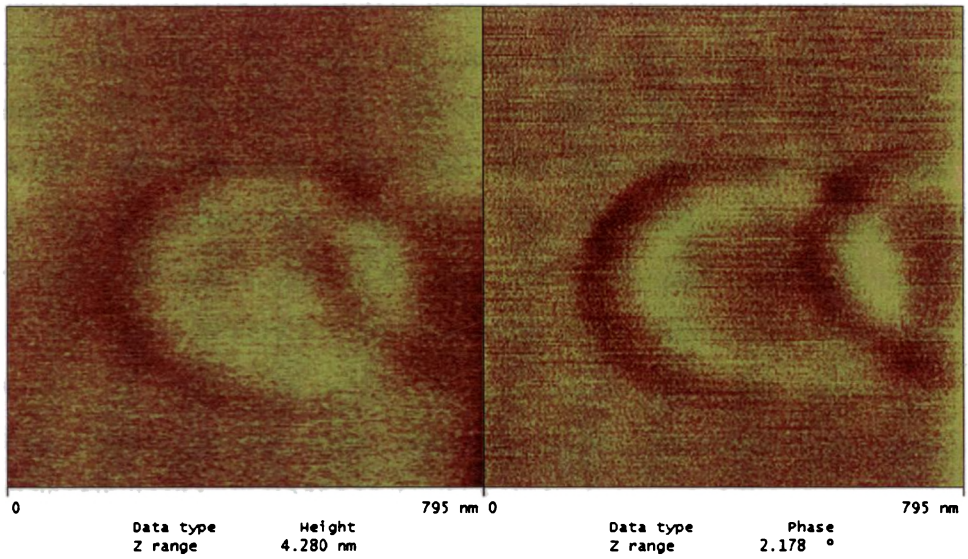


Figure 6-5. AFM image of polystyrene supported G3 PAMAM dendrimer-Pd nanoparticle conjugate

This effect is reflected in catalysis also. The reason for this is that, more number of metal ions gets coordinated to the third generation dendrimers and on reduction, all these metal ions together form larger nanoparticles. In addition to this, the metal nanoparticles were of different shapes. This may be due to the inhomogeneous environment presented due to the initial complexation of metals with dendrimer and the polymer matrix. The metal ions get complexed not only with surface primary amino groups alone, both with surface primary amino groups and internal amide groups as well as the surface primary amino groups of two neighboring dendrimers. When these metal ions get reduced, the nanoparticles obtained show variation in size and shape. Moreover the different environmental effects arise due to the morphology of the resin also have

considerable effect on controlling the size and shape of the nanoparticles. The resin contain large number of pores of various sizes and shapes and these pores control the diffusion of the metal ions during complexation and reducing agent during reduction. This regulation of reagents results in nanoparticles of various size and shapes. This was contradictory to the results observed when higher generation dendrimers in solution were used for the synthesis of dendrimer encapsulated nanoparticles. The ratio of metal ions and the amino groups of the dendrimer used in the initial complex formation step also had a decisive role in controlling the size of nanoparticle. When the ratio is 1:1, the nanoparticles formed are of smaller size and they did not show agglomeration. If the ratio is higher, i.e. higher concentration of metal ion, the nanoparticles formed are of large size. When the ratio is smaller, the nanoparticles formed are of very small size but it will result in very low metal loading in the catalyst, which means larger amount of catalyst by weight is required to drive the reaction to completion. Similar results were observed in the preparation of gold nanoparticle stabilized with PAMAM dendrimers by Esumi et al.[23]

When PMMA supported PAMAM dendrimers were used for the preparation of nanoparticles similar results were obtained except in the stability of the system as described in previous chapters.

6. 2. 2. Suzuki Coupling Catalyzed by Polymer Supported Dendrimer-Pd Nanoparticles

Polymer supported dendrimer nanoparticle conjugates as prepared above were used as heterogeneous catalyst. The selected catalyst was polystyrene supported PAMAM dendrimer encapsulated palladium nanoparticles and the reaction of choice was Suzuki coupling. This selection is based on the fact that palladium in its zeroth oxidation state is highly active catalyst in many reactions like hydrogenation, Suzuki coupling and Heck coupling while other metals used in this study are not good catalysts in their zeroth oxidation state except for hydrogenation. Suzuki coupling between aryl boronic acids and aryl halides was studied in detail and various factors

influencing the yield and rate of the reaction and the catalyst stability was studied.

Generally Pd nanoparticles are efficient catalysts in many reactions.[47] In order to learn the merits and demerits of encapsulating the nanoparticles in a polymer-supported dendrimer on their catalytic activity we used the systems as heterogeneous catalysts in Suzuki coupling between aryl boronic acids and aryl halides. The scheme of the reaction is shown in Figure 6-6.

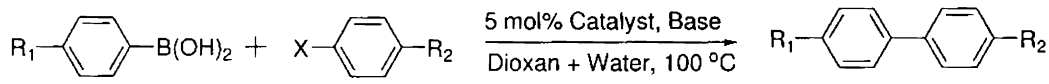


Figure 6-6. Suzuki coupling catalyzed by polymer-supported dendrimer-Pd nanoparticle conjugates

The model reaction between benzene boronic acid and 4- nitro iodobenzene was studied in dioxan in the presence of Na_2CO_3 as the base. Initially the influence of the concentration of the catalyst on the reaction was studied (table 6.1).

Table 6.1: Influence of the concentration of the catalyst on Suzuki coupling

Entry	Mol% of catalyst	% Yield [a, b]
1	1	30
2	2	52
3	3	72
4	4	84
5	5	90

[a] Reaction condition; 1 mmol 4-nitro iodobenzene, 1.2 mmol benzene boronic acid, 3 mmol Na_2CO_3, 5 mL dioxan, 100 °C. [b] isolated yield

The amount of the catalyst varied starting initially from 1 mol%. With this lower catalyst loading, the reaction was very slow and gave poor yield. The speed of the reaction as well as yield increased with increase in the amount of

the catalyst and when the amount of catalyst reached 5 mol%, the reaction proceeded at a good pace with good yield. The reaction now proceeded at a comparable speed to that of unsupported dendrimer encapsulated nanoparticles[48,49], but was slower than many homogeneous catalysts containing Pd nanoparticles[50]. This may be due to the difficulty for the substrates to access the catalytic sites, which are embedded in the dendrimer. The steric hindrance offered by the polymer support may be another reason which retards the interaction between the catalyst and the substrates.

The reaction proceeded well in polar solvents like ethanol, acetone, dioxan and THF, but slowly in nonpolar solvents like benzene and toluene (table 6.2).

Table 6.2: Influence of solvent on Suzuki coupling

ENtry	Solvent	% Yield [a, b]
1	Toluene	62
2	Ethanol	85
3	Acetone	85
4	Dioxan	90
5	THF	87
6	Dioxan + water (4:1)	95
7	THF+ water (4:1)	91

[a] Reaction condition; 1 mmol 4-nitro iodobenzene, 1.2 mmol benzene boronic acid, 3 mmol Na_2CO_3, 5 mL solvent, 100 °C. [b] isolated yield

The good performance of the catalyst in polar solvents may be due to the increased solvation of the dendrimer in these solvents while the dendritic architecture gets collapsed in nonpolar solvents that prevents smooth interaction between the substrates and catalysts.[51] Moreover, the yield increased when the reaction was carried out in the presence of water. This may be due to the enhanced solubility of the base in the presence of water.

Since the PAMAM dendrimer backbone of the catalyst contains amide groups, it was assumed that the base employed in the catalytic process may

influence the stability of the catalyst. When a weak base like Na_2CO_3 or triethyl amine was used it took longer duration for the completion of the reaction but the catalyst was stable even after three cycles and practically no metal leaching was observed. On the other hand, when a strong base like NaOH was used, it was observed that, a white colored mass was formed with in the reaction vessel after each cycle and some palladium metal was observed in it. This may be due to the decomposition of the dendritic platform under the strongly basic conditions employed. The catalyst lost its activity completely after three cycles under this circumstance. When the reaction was carried out in the presence of the white mass obtained from the decomposition of the catalyst, formation of biphenyl was observed and this is an additional proof that the catalytically active metal nanoparticles were getting detached from the polymer and the catalyst is not stable under strongly basic conditions. In addition, the water layer turned yellowish brown during the time of water-organic extraction of the product when NaOH was used in the reaction and this may be due to Pd^{2+} ions arising from the decomposed catalyst. To reduce the catalyst's contact with strong base microwave heating was employed in the place of conventional heating. The reaction was completed with in 10-15 minutes under this condition and no catalyst decomposition was observed even if NaOH was employed as the base. This was due to the faster kinetics of the catalytic process, so that the catalyst was not in contact with the base for a longer time. Such observations were reported previously in which polymer bound ester groups got hydrolyzed under conventional heating but not under microwave irradiation in Suzuki coupling conditions.[52]

Generally, aryl iodides and bromides gave good to excellent yields while chlorides gave poor yield even after prolonged reaction under refluxing conditions. The results are summarized in table 6.3. The electronic factors of substrates had no considerable effect on the reaction, but steric effect had considerable influence. As seen in the table 6. 3 the yield was decreased when substrates carrying bulkier substituents like tertiary butyl groups were used.

This is due to the limited access of bulkier substrates to the catalysts due to the steric hindrance offered by dendrimer support and polymer backbone.

Table 6.3: Suzuki coupling between aryl boronic acids and aryl halides catalyzed by polymer-supported dendrimer-Pd nanoparticle conjugates

Entry	R_1	R_2	X	Base	Time (h)	%Yield[a,b]
B1	H	NO_2	I	Na_2CO_3	24	95
B2	H	NO_2	I	NaOH	12	96
B3	H	NO_2	I	Et_3N	24	89
B4	H	NO_2	I	KOH	12	95
B5	H	H	I	Na_2CO_3	10	92
B6	H	H	Cl	Na_2CO_3	48	40
B7	H	H	Br	Na_2CO_3	30	85
B8	CH_3	NO_2	I	Na_2CO_3	12	90
B9	H	CH_3	I	Na_2CO_3	12	92
B10	CH_3	CH_3	I	Na_2CO_3	24	91
B11	H	$-C(CH_3)_2$	I	Na_2CO_3	24	72
B12	CH_3	CH_3	I	Na_2CO_3	24	70
B13	H	$-COCH_3$	Br	Na_2CO_3	24	89
B14	CH_3	$-COCH_3$	Br	Na_2CO_3	24	85
B15	H	NH_2	Br	Na_2CO_3	24	65

[a] reaction condition; 1 mmol aryl halide, 1.2 mmol aryl boronic acid, 3 mmol base, 5 mol% catalyst, 4 ml dioxan,1 ml water at 100 °C. [b] % isolated yield.

The catalyst was recycled by washing it with water, methanol and ethyl acetate followed by drying at room temperature under vacuum. The catalyst was used four times with out considerable loss of activity but the activity gradually decreased on further recycling (table 6.4).

The shelf life of the nanoparticles trapped in the polymer matrix is good. The system remains stable with no loss of catalytic activity for two years with out any special precaution to protect them from air and moisture. After two years the color of the catalyst gradually turns brownish from black. There is gradual loss of catalytic behavior also. It may be due to oxidation of Pd nanoparticles. But the catalytic activity can be retained by treatment with a reducing agent like hydrazine hydrate.

Table 6.4: Influence of recycling on the catalytic activity

Entry	No. of recycling steps	% Yield [a, b]
1	1	95
2	2	91
3	3	90
4	4	87
5	5	78

[a] reaction condition; 1 mmol 4-nitro iodobenzene, 1.2 mmol benzene boronic acid, 3 mmol Na_2CO_3, 5 mol% catalyst, 4 mL dioxan,1 mL water at 100 °C. [b]- isolated yield.

6. 3. CONCLUSION

In short polymer supported PAMAM dendrimer-Pd nanoparticle conjugates were prepared and characterized. Various factors influencing the size and shape of the nanoparticles were studied. The nanoparticles were used as heterogeneous catalysts in Suzuki coupling between aromatic halides and benzene boronic acids. The reaction conditions were optimized to get maximum yield.

6. 4. EXPERIMENTAL

6. 4. 1. General Method of Preparation of the Polymer Supported Dendrimer-Metal Nanoparticle Conjugates

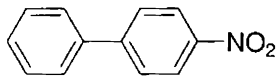
The polymer-supported metal complex prepared as described in chapter 4 (1 g) was suspended in methanol (10 mL) taken in a round bottom flask and hydrazine hydrate (1 mL, 20 mmol) was added to it with stirring. The reaction mixture was stirred at room temperature for 2 h to ensure complete reduction. It was filtered under vacuum and washed well with methanol (20mL x 5). Dried under vacuum for 24 h to obtain the nanoparticle conjugates.

6. 4. 2. General procedure for Suzuki Coupling

A 10 mL r.b flask was charged with the aryl halide (1 mmol), aryl boronic acid (1.2 mmol), and Na_2CO_3 (317 mg, 3 mmol). The catalyst (100 mg) was added to it followed by dioxan (4 mL) and water (1 mL) was added. The reaction mixture was stirred at 100 °C. The progress of the reaction was followed by TLC on silica gel coated plates using hexane, ethyl acetate mixture (10:1). After the reaction gets completed the reaction mixture was filtered and the catalyst was washed several times with small portions of ethyl acetate. The combined washings were then washed with water in a separating funnel, the organic layer was isolated and dried with 4A molecular sieves. The pure product was isolated by column chromatography on a small silica column using hexane and ethyl acetate (10:1) as eluents. The products were characterized using ^{1}HNMR spectroscopy.

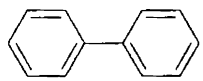
6. 4. 3. Characterization data of some representative compounds

4- Nitro Biphenyl (Entry B1)



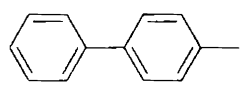
^{1}HNMR (300 MHz; $CDCl_3$): δ 7.44 (m, 1H), 7.49 (m, 2H), 7.62 (m, 2H), 7.73 (d, J = 8.80 Hz, 2H), 8.29 (d, J = 8.80 Hz, 2H).

Biphenyl (Entry B5)



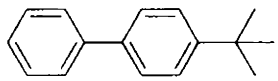
^{1}HNMR (300 MHz; $CDCl_3$): δ 7.29-7.34 (m, 2H), 7.39-7.44 (m, 4H), 7.56-7.59 (m, 4H);

4- Methyl biphenyl (Entry B9)



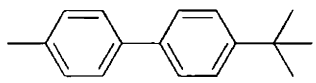
^{1}HNMR (300 MHz; $CDCl_3$): δ 2.34(s, 3H), 7.19(d, *J* = 7.3 Hz, 2H), 7.21- 7.29 (m, 1H), 7.36 (t, *J* = 6.24 Hz, 2H), 7.42 (d, *J* = 8.14, 2H), 7.51- 7.54 (m, 2H).

4- Tertiary butyl biphenyl (Entry B11)



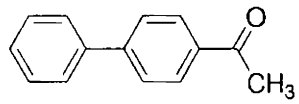
^{1}HNMR (300 MHz; $CDCl_3$): δ 1.41 (s, 9H), 7.32-7.67 (m, 9H).

4-Methyl-4-t-butylbiphenyl (Entry B12)



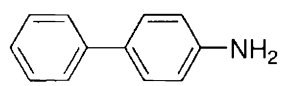
^{1}HNMR (300 MHz; $CDCl_3$): δ 1.34(s, 9H), 2.37 (s, 3H), 7.13-7.48 (m, 8H)

4- Acetyl biphenyl (Entry B13)



^{1}HNMR (300 MHz: $CDCl_3$): δ 2.64(s, 3H), 7.42-7.50(m, 3H), 7.62- 7.70 (m, 4H), 8.04 (d, *J* = 6.60 Hz, 2H).

4-Amino Biphenyl (Entry B15)



^{1}HNMR (300 MHz; $CDCl_3$): δ 3.7 (broad, 2H), 6.54 (d, *J* = 8.56, 2H), 7.23-7.3 (m, 5H), 7.48 (m, 2H).

6. 4. 4 Recycling of the Catalyst

The catalyst after the reaction was filtered and washed well with methanol (20 mL x 5) and dried under vacuum for 24 h at room temperature.

REFERENCES

1. Smalley, R. *Congressional Hearings, Summer*, **1999.**
2. Roucoux, A.; Schulz, J.; Patin, H.; *Chem. Rev.* **2002**, *102*, 3757.
3. Klabunde, K. J. In *Nanoscale Materials in Chemistry*; Klabunde, K. J., Ed.; Wiley Interscience, New York, 2001.
4. Schmid, G. In *Nanoscale Materials in Chemistry*; Klabunde, K. J., Ed.; Wiley Interscience, New York, 2001.
5. Hvolbaek, B.; Janssens, T. V. W.; Clausen, B. S.; Falsig, H.; Christensen, C. H.; Norskov, J. K. *Nano Today*, **2007**, *2*, 14 and references there in.
6. Klabunde, K. J.; Mulukutla, R. S. In *Nanoscale Materials in Chemistry*; Klabunde, K. J., Ed.; Wiley Interscience, New York, 2001.
7. Fan, J.; Gao, Y. *J. Exp. Nanoscience*, **2006**,*1*, 457.
8. Zheng, Y.; Stevens, P. D.; Gao, Y. *J. Org. Chem.* **2006**, *71*, 537.
9. Oila, M. J.; Koskinen, A. M. P. *Arkivoc*, **2006**, 76.
10. Schmid, G.; Maihack, V.; Lantermann, F.; St. Peschel. *J. Chem. Soc. Dalton Trans.* **1996**, 589.
11. Schmid, G.; Emde, S.; Maihack, V.; Meyer-Zaika, W.; St. Peschel. *J. Mol. Catal. A.* **1996**, *107*, 95.
12. Bronstein, L. M.; Sidorov, S. N.; Valetsky, P. M. *Russ. Chem. Rev.*, **2004**, *73*, 5, 501.
13. Tabuani, D.; Monticelli, O.; Chincarini, A.; Bianchini, C.; Vizza, F.; Moneti, S.; Russo, S. *Macromolecules*, **2003**, *36*, 4294.
14. Li, Y.; Hong, X. M.; Collard, D. M.; El-Sayed, M. A. *Org. Lett.* **2000**, *2*, 2385.
15. Tomalia, D. A. *Aldrichimica Acta*, **2004**, *37*, 39.
16. Majoral, J. P. *New. J. Chem.* **2007**, *31*, 1039.
17. van Hest, J. C. M.; Delnoye, D. A. P.; Baars, M. W. P. L.; van Genderen, M. H. P.; Meijer, E. W. *Science* **1995**, *268*, 1592.
18. Johan, F. G. A.; Janson, J.; Meijer, E. W.; de Brabander-van den Berg, E. M. M. *J. Am.Chem. Soc.* **1995**, *117*, 4417.

19. Johan, F. G. A.; Janson, J.; de Brabander-van den Berg, E. M. M.; Meijer, E. W. *Science* **1995**, *266*, 1266.
20. Balogh, L.; Tomalia, D. A. *J. Am. Chem. Soc.* **1998**, *120*, 7355.
21. Zhao, M.; Sun, L.; Crooks, R. M. *J. Am. Chem. Soc.* **1998**, *120*, 4877.
22. Niu, Y.; Crooks, R. M., *C. R. Chimie*, **2003**, *6*, 1049.
23. Esumi, K.; Suzuki, A.; Aihara, N.; Usui, K.; Torigoe, K. *Langmuir*, **1998**, *14*, 3157.
24. Scott, R. W. J.; Datye, A. K.; Crooks, R. M. *J. Am. Chem. Soc.* **2003**, 125, 3708.
25. Scott, R. W. J.; Wilson, O. M.; Sang-Keun Oh; Kenik, E. A.; Crooks, R. M. *J. Am. Chem. Soc.* **2004**, 126, 15583.
26. Wilson, O. M.; Scott, R. W. J.; Garcia-Martinez, J. C.; Crooks, R. M. *J. Am. Chem. Soc.* **2005**, 127, 1015.
27. Crooks, R. M.; Zhao, M.; Sun, L.; Chechik, V.; Yeung, L. K. *Acc.Chem. Res.* **2001**, *34*, 181.
28. Scott, R. W. J.; Wilson, O.M.; Crooks, R. M. *J. Phy. Chem. B*, **2005**, *109*, 692.
29. Lu, X.; Imae, T. *J. Phys. Chem. C*, **2007**, *111*, 2416.
30. Suzuki, A. In *Metal Catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley VCH, Weinheim, 1998.
31. Suzuki, A. *Chem. Commun.* **2005**, 4759.
32. Bellina, F; Carpita, A.; Rossi, R. *Synthesis*, **2005**, *15*, 2419,
33. Kingston; J. V.; Verkade, J. G. *J. Org. Chem.*, **2007**, *72*, 2816.
34. Cui, X.; Qin, T.; Wang, J. R.; Liu, L.; Guo Q. X. *Synthesis*, **2007**, 3, 393.
35. Lee, D. H.; Jung, J. Y.; Lee, I. M.; Jin, M. J. *Eur. J. Org. Chem.* **2008**, *2008*, 356.
36. Xu, C.; Gong, J. F.; Guo, T.; Zhang, Y. H.; Wu, Y. J. *J. Mol. Catal. A.; Chem.* **2008**, *279*, 69.
37. Qiu, H.; Sarkar, S. M.; Lee, D. H.; Jin, M. J. *Green Chem.* **2008**, *10*, 37.
38. Kim, J. H. Kim, J. W. Shokouhimehr, M.; Lee, Y.S. *J. Org. Chem.* **2005**, 70, 6714.

39. Hershberger, J. C.; Zhang, L.; Lu, G.; Malinakova, H. C. *J. Org. Chem.* **2006,** 71, 231.

40. Inada, K.; Miyaura, N.; *Tetrahedron*, **2000**, *56*, 8661.

41. Lee, D. H.; Kim, J. H.; Jun, B. H.; Kang, H.; Park, J.; Lee, Y. S. *Org. Lett.* **2008**, *10*, 1609.

42. Wu, L.; Li, B. L.; Huang, Y. Y.; Zhou, H. F.; He, Y. M.; Fan, Q. H. *Org. Lett.* **2006**, *8*, 3605.

43. Li, Y.; Hong, X. M.; Collard, D. M.; El-Sayed, M. A. *Org. Lett.* **2000**, *2*, 2385.

44. Panigrahi, S.; Kundu, S.; Ghosh, S. K.; Nath, S.; Pal, T. *J. Nanoparticle Res.* **2004**, *6*, 411.

45. Balogh, L.; Swanson, D. R.; Tomalia, D. A.; Hagnauer, G. L.; McManus, A. T. *Nano Lett.* **2001**, *1*, 18.

46. Wu, C.; Mosher, B. P.; Zeng, T. *J. Nanoparticle Res.* **2006**, *8*, 965.

47. Moreno-Manas, M.; Pleixats, R. *Acc. Chem. Res.* **2003**, *36*, 638

48. Pittelkow, M.; Moth-Poulsen, K.; Boas, U.; Christensen, J. B. *Langmuir*, **2003**, *19*, 7682.

49. Wu, L.; Li, B. L.; Huang, Y. Y.; Zhou, H. F.; He, Y. M.; Fan, Q. H. *Org. Lett.* **2006**, *8*, 3605.

50. Strimbu, L.; Liu, J.; Kaifer, A. E. *Langmuir*, **2003**, *19*, 483.

51. Tarazona-Vasquez, F.; Balbuena, P. B. *J. Phys. Chem. A.* **2007**, *111*, 932.

52. Blettner, C. G.; Konig, W. A.; Stenzel, W.; Schotten, T. *J. Org. Chem.* **1999**, *64*, 3885.

SUMMARY AND CONCLUSION

Over the past three decades, dendrimers have emerged as a novel class of macromolecules with applications in a wide range of natural sciences. They are macromolecules possessing a highly regular molecular topology based on an iterative growth sequence of branching units. Starting from a small "core" molecule, this may lead to large globular structures that possess a high degree of molecular uniformity. The iterative branching not only leads to an efficient and symmetrical growth pattern but potentially to a rapid multiplication of functional groups, making these molecules attractive platforms for chemical functionality. Since the first application of dendrimers in catalysis in the mid 1990s this field has advanced rapidly. As a consequence, catalytically active dendrimers have emerged as a class of molecular catalysts, which have substantially enriched the field of homogeneous and to some extent heterogeneous catalysis.

The present thesis has described the development of some heterogeneous catalysts based on polymer supported dendrimers. Attachment of dendrimers to crosslinked polymer produced new catalysts with combined benefits of both dendrimers and heterogeneous catalysts. These were used as heterogeneous catalysts in selected reactions. All possible attempts were taken to avoid halogenated and aromatic solvents and toxic reagents. In short the present work has dealt with development of environmental friendly catalysts based on dendrimers.

The thesis is divided in to six chapters. An overview of solid phase organic synthesis, polymer supported catalysts and dendrimers was given in first chapter.

In **chapter 2**, the solid phase synthesis of poly(propylene imine) (PPI) and poly(amidoamine) (PAMAM) dendrimers was discussed. Solid phase synthesis

of the dendrimers were carried out on aminomethyl polystyrene, 3-nitro 4-aminomethyl polystyrene (DVB crosslinked) and aminated poly(methyl methacrylate) (DVB crosslinked) resins. The synthesis of dendrimers began from the primary amino pendant groups on the polymer supports. The primary amino group functioned both as the core of the dendrimer and the linker that connected the support and the dendrimer. The dendrimers were synthesized up to third generation by adopting the divergent approach used in their solution phase synthesis with suitable modification so that they could be successfully transformed to the solid phase. Poly(propylene imine) dendrimers were synthesized by an acetic acid catalyzed double Michael addition of acrylonitrile to the amino groups of the supports followed by reduction of the nitrile groups to amino groups using $LiAlH_4$ in THF. Poly(amidoamine) dendrimers were synthesized by double Michael addition of methyl acrylate to the amino groups of polymer supports in methanol followed by transamination using large excess of ethylene diamine. The progress of the solid phase synthesis was followed by FTIR spectroscopy, qualitative ninhydrin test, quantitative estimation of amino groups and solid state CP-MAS ^{13}C NMR spectroscopy. After the synthesis, the dendrimers were detached from the polymer supports and analyzed using NMR spectroscopy and MALDI-TOF MS. The effect of degree of crosslinking of the supports on the synthesis was studied. A comparison between the two supports was also presented.

Chapter 3 has dealt with the application of polymer supported dendrimers as heterogeneous organocatalysts. Since the supported dendrimers described in this thesis are highly basic and the first, second and third generation dendrimers carry two, four and eight primary amino groups on the periphery respectively, the supported dendrimers performed well as efficient organocatalysts. After screening the catalytic activity these dendrimers in various reactions, Knoevenagel reaction and ring opening of epoxides, for which the catalysts showed better activity, were selected for further study.

Knoevenagel condensation between various carbonyl compounds and active methylene compounds were carried out in the presence of the supported

dendrimers. Various factors affecting the catalysis like amount of catalysts, solvent, temperature and electronic and steric nature of the substrates were studied in detail. The dendrimer catalysts showed excellent activity. Only 0.5 mole percent of catalyst was required to obtain excellent yield with in a short interval of time. About thirty styrene derivatives were prepared and all the reactions proceeded to completion with in a short period of time. The most important aspect of the catalysis by supported dendrimers was that high yields were obtained in polar protic solvents like ethanol and water. All the products were obtained in excellent yield, purity and 100% selectivity. Since no side reactions were observed and the reaction proceeded to complete conversion, no additional purification of the products was required. All products were characterized by ^{1}HMR and FTIR spectroscopic methods. The catalysts were recycled ten times with no loss of activity. The effect of generation of the dendrimer and the nature of the support on catalysis was also studied. It was found that, third generation dendrimers were better catalysts and better results were obtained when lightly crosslinked supports were used. Comparisons between the two dendrimers as well as the two supports were made.

Ring opening of epoxides with anilines was efficiently catalyzed by supported-dendrimers. Various 2-amino alcohols were synthesized from different epoxides and anilines in the presence of catalytic amounts of the supported-dendrimers. The influence of reaction conditions and nature of substrates were studied in detail. The reaction proceeded effectively in polar solvents at 50 °C. Only 2 mol% of the third generation dendrimer was required for completion of the reaction. Sixteen 2-amino alcohols were synthesized, isolated and characterized. Dendrimers of different generations were studied and found that the catalytic activity increases with increase in generation. Comparison between the two dendrimers showed that the PAMAM dendrimers were more efficient catalysts. The influence of the support on the catalytic activity was studied and found that the polystyrene supported catalysts were more active.

Chapter 4 has described the synthesis of polymer supported dendrimer metal complexes. The polymer supported dendrimers were used as ligands for the preparation of polymer-supported dendrimer-metal complexes by ligand exchange method in aqueous medium. The metal complexes of Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Pd(II), Ag(I) and Zr(IV) were prepared. The influence of various factors like reaction time, temperature and pH of the reaction medium, presence of a co-solvent and the degree of crosslinking of the polymer support were studied. The role of the support's properties and generation of dendrimer in complex formation were studied. From these experiments, suitable reaction conditions were optimized. Generally, complex formation was effective at room temperature, at natural pH of the reaction mixture in the presence of acetone as co-solvent with in a period of 12 h. It was observed that, PAMAM dendrimers were more efficient in complex formation compared to the PPI dendrimer of the same generation. The complexes prepared in this manner were characterized by various analytical techniques like FTIR, UV-Vis, TG-DTA, EPR and Solid state NMR. From these analytical data structures of the complexes were predicted.

In **chapter 5** applications of polymer supported dendrimer metal complexes as heterogeneous catalysts was described. After screening the polymer supported dendrimer metal complexes as heterogeneous catalysts against a number of reactions two reactions were identified for detailed study.

Polymer-supported dendrimer-Mn(II) complexes were found to be highly efficient catalysts in the oxidation of secondary alcohols to ketones under mild conditions. Compared to many previously reported polymer supported catalysts, the present complex showed high activity. The influence of the catalyst concentration, solvent and temperature on the catalytic activity was studied. Only 5 mol % of the catalyst was required to drive the reaction to completion. As described in the case of earlier catalysts, the catalytic activity was maximum in polar solvents. Oxidation of various alcohols was carried out in the presence of different oxidants like $K_2Cr_2O_7$, $KMnO_4$ and urea-hydrogen peroxide adduct (UHP). The problems observed during the application of strong oxidizing agents could be effectively overcome when the mild oxidizing agent UHP was used. In

many cases, the ketones were isolated in excellent yields. It was observed that PAMAM-Mn(II) complex showed better activity and stability compared to PPI-Mn(II) complexes. Comparable activity was shown by both polystyrene and poly(methyl methacrylate) supported catalysts. The catalyst was recycled up to four times with out considerable loss of activity. The ketones formed were isolated and characterized by various spectral methods.

Polymer-supported dendrimer-Pd(II) complexes were used as heterogeneous catalysts in the three component Mannich reaction between aldehydes, ketones and anilines to give β-amino ketones. Various factors influencing the reaction were studied and the condition for the maximum yield was optimized. The reaction proceeded well in ethanol in the presence of 2 mol% of the catalyst. A number of β-amino ketones were synthesized and isolated with excellent yields. The products were characterized using FTIR and ^{1}HNMR spectroscopies. The catalyst after washing with ethyl acetate was recycled six times without considerable loss of activity. In the case of Pd(II) complex also, better activity was shown by the PAMAM complex. Comparison of the catalyst supported on the two supports showed that the poly(methyl methacrylate) supported catalysts were more active.

The **sixth chapter** of this thesis has dealt with synthesis and characterization of polymer supported dendrimer encapsulated metal nanoparticles and their use in heterogeneous catalysis. Polymer supported PAMAM dendrimer nanoparticle conjugates of Pd, Cu, Ag, Ni and Co were prepared by chemical reduction of the corresponding supported dendrimer-metal complexes using hydrazine-hydrate in methanol.

The supported dendrimer-metal nanoparticle conjugates were characterized by UV-Vis spectroscopy, TG/DTA, SEM, AFM and TEM. The Pd, Cu, Ag and Ni nanoparticles were stable and showed long shelf life. It was observed that the nanoparticles prepared using first and second generation dendrimers were agglomerated while the nanoparticles prepared using the third generation dendrimers were well separated and of uniform size.

The Pd-nanoparticle conjugate prepared was used as catalyst in Suzuki coupling between aryl boronic acid and aryl halides. By varying the reaction conditions, the most suitable condition required to get better yield was arrived at. The efficiency of the catalyst was proved by preparing various biphenyls. Better results were given by the third generation dendrimer-nanoparticle conjugates as the nanoparticles were of smaller size and well-separated; they offered more surface area for heterogeneous catalysis. The catalyst was recycled four times without loss of activity. On further recycling a gradual loss of metal ions was observed and this may be due to the decomposition of the dendrimer backbone during the course of the reaction.

In general, the thesis has described the synthesis, characterization and environmental friendly catalysis by different polymer-supported dendrimers, their metal complexes and nanoparticle conjugates. The possibilities of recycling of the catalysts were explored along with chances to avoid the use of aromatic and halogenated solvents. The thesis opens new possibilities of development of environmental friendly and efficient catalysts based on supported dendrimers. In short the thesis has contributed to organic synthesis, heterogeneous catalysis and green chemistry.
