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Dendrimer-Transition Metal Catalyzed Oxidation and Reduction Reactions

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DENDRIMER -TRANSITION METAL CATALYZED OXIDATION AND REDUCTION REACTIONS

by

Pumza P. Zweni

B.Sc. (Honours Chemistry), University Of Natal, 1999

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IN MEMORY OF MY FATHER

Umnt' ombi akalahlwa...

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Abstract

This project was launched with the aim of developing dendrimer catalysts for oxidation and reduction reactions. Poly(amidoamine) (PAMAM) and poly(propyleneimine) (PPI) dendrimers were of interest because of their well-established synthesis.

CHAPTER 1 describes the fundamentals of dendrimers and provides a brief insight of their application in catalysis. In particular, examples of dendritic catalysts that have been previously employed as oxidation and reduction catalysts are presented.

CHAPTER 2 presents the synthesis and characterization of silica-supported PAMAM dendrimers, their phosphomethylation with Ph_2PCH_2OH, and their complexation to palladium complexes.

CHAPTER 3 reports the application of the silica-supported PAMAM – Pd complexes to the oxidation of alkenes to methyl ketones under Wacker-type conditions as well as the use of ^tBuOOH as the oxidant in these reactions.

CHAPTER 4 discusses the use of the above-mentioned complexes to catalyze the selective hydrogenation of dienes to monoolefins in the presence of H_2 under mild reaction conditions.

CHAPTER 5 presents our efforts in modifying PPI dendrimers with the salen moiety to give ligands that are coordinated to the metals Ti and V. Attempts at

using the former complexes to promote the epoxidation of alkenes and the latter complexes to catalyze the epoxidation of olefinic alcohols are discussed.

Abbreviations

acac	acetyl acetonate
ATR	Attenuated total reflectance
BET	Brunauer-Emmett-Teller
dba	dibenzylidene acetone
DCM	dichloromethane
EtOH	ethanol
FT-IR	Fourier-transform infra red spectroscopy
g	grams
GC	gas chromatography
h	hours
ICP	inductively coupled plasma spectroscopy
MeOH	methanol
mL	millileters
mmol	millimoles
MS	mass spectrometry
NMR	nuclear magnetic resonance
PAMAM	poly(amidoamine)
Ph	phenyl
PPI	poly(propyleneimine)

ppm	parts per million
psi	pounds per square inch
PV	pore volume
SA	surface area
TBHP	tertiary butyl hydroperoxide
TGA	thermal gravimetric analysis
TOF	turnover frequency
TON	turnover number

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Chapter One

INTRODUCTION

1.1 General Introduction

In light of the changing awareness and responsibility to the environment, as well as stricter environmental laws, the focus on research has shifted towards cleaner technologies. The field of catalysis is viewed as one of these technologies. Of the two classes of catalysis, heterogeneous catalysis is preferred industrially due to the fact that the separation of the reactants from the products is much easier, generates less waste, and is cheaper than homogeneous catalysis.

There have been many attempts at heterogenizing homogeneous catalysts by immobilizing them on supports such as polymers, inorganic oxides and so on. However, problems such as lower catalyst activity, leaching of the metal from the support, deactivation and decomposition of active species have been encountered. Some of these problems are a result of poor control of the location and the number of active sites.

Dendrimers*, which were discovered more than two decades ago, have opened up new realms of catalysis strategy with dendritic catalysts tending to incorporate the advantages of both homogeneous and heterogeneous catalysis.[1-3] A plethora of studies on the application of dendrimers to catalysis have been undertaken.[4-6] These studies include dendrimers functionalized with metal centers at the core, the periphery and within the dendritic structure. There are

---

* Also referred to as arborols, cascade molecules or fractal polymers.

also unique examples of dendritic catalysts that function without metal centers.[7-9]

As each generation of the dendrimer introduces an exponential growth in the number of end groups, periphery-functionalized dendrimers have a high density of functional groups from which high specificity and activity, similar to classic homogeneous catalysts can be expected. Easy catalyst separation is an important factor in any industrial process because the recovered catalyst can be reused several times. Dendrimers have a great potential in this regard. Due to their larger size relative to the reactants and the products, the separation can be done by simple techniques such as precipitation or simple filtration.

1.2 The Dendritic Structure

Dendrimers are a class of macromolecules characterized by a high degree of branching and well-defined three-dimensional structures. Unlike hyperbranched polymers that are prepared *via* single step synthesis, dendrimers are constructed through a series of iterative steps.[10] This synthetic methodology allows great control in the positioning of different functional groups within the dendrimer structure. As a result, characteristics such as shape, structure, size and solubility can be designed and fine-tuned to possess special properties ideal for a specific application.

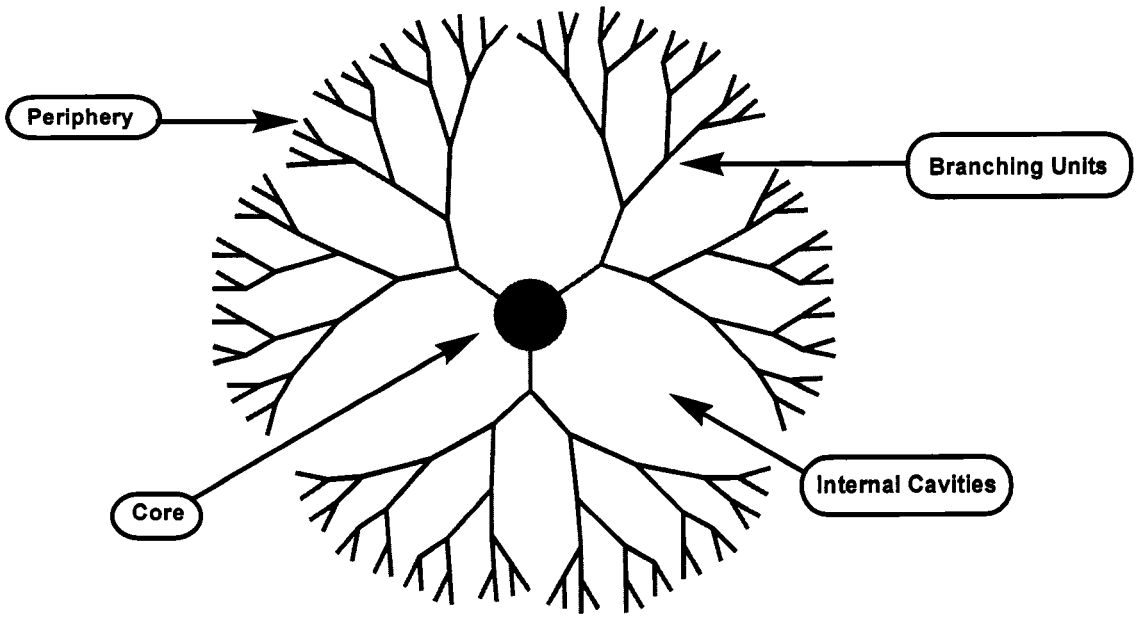


Figure 1.1 Highly Branched Globular Dendritic Structure

1.2.1 Dendrimer Core

Dendrimers can be considered as having three different regions: core, interior and periphery (Figure 1.1). The high degree-of-branching radiates from the core. Initiator cores are entities that have at least two reactive centers. Examples of initiator cores include multivalent atoms such as bismuth[11], germanium[12], ruthenium[13-19], phosphorus[20-29] and silicon[7, 30-35], as well as functionalized molecules such as diamines, triols, multifunctionalized phenyl rings, and heterocylic ligands. More complex molecules such as cubic silsesquioxanes[36, 37], iron–sulfur clusters[38, 39], and fullerenes[40, 41] have also been used. The choice of initiator cores depends on the required microenvironment as well as the desired application.

1.2.2 Dendrimer Interior

The interior layer is characterized by a repeating pattern in the structure. Each branching point within the interior represents a different generation of the dendrimer. Repeating units can either be polar or non-polar, flexible or rigid depending on the desired properties. The common repeating units that have been used in dendrimer synthesis are shown in Figure 1.2.[42] Since dendrimer growth is accompanied by an exponential increase in the number of terminal groups, most dendrimers tend to adopt a spherical shape due to the close packing of these end groups. After a certain generation number, the dendritic surface becomes so congested that further growth is slowed down. Different dendrimers will experience surface congestion at different generations depending on the multiplicity of the initiator core, the multiplicity of the branching unit as well as the length of the repeating units. For example, a dendrimer with a multiplicity of four and shorter repeating units will be expected to suffer from surface congestion at a lower generation than a dendrimer with a multiplicity of two and longer repeating units providing that the other parameters are kept constant.

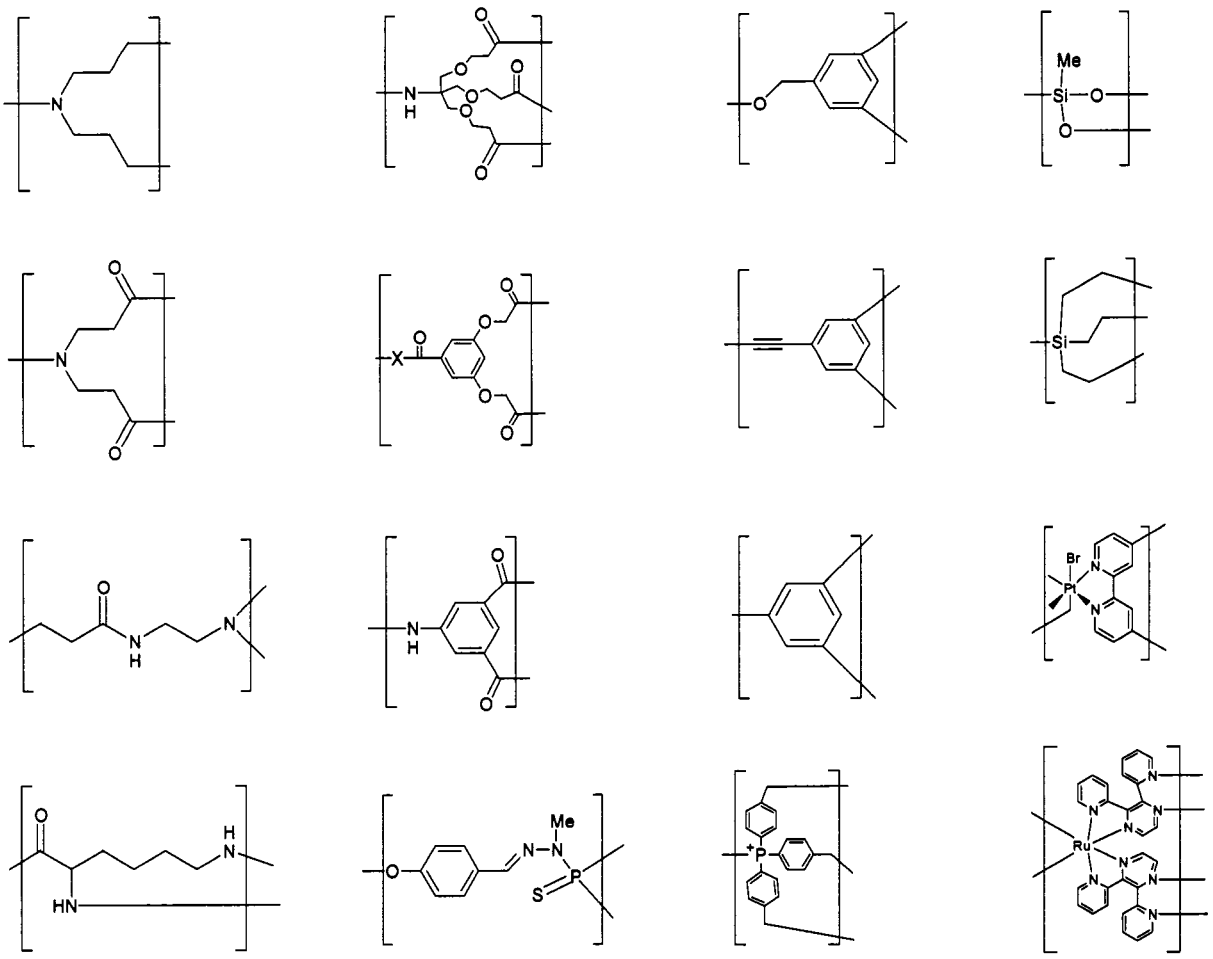


Figure 1.2 Common Dendrimer Repeat Units

1.2.3 Dendrimer Periphery

The periphery consists of a high density of functional groups. The placement of active species at the periphery of the dendrimer should allow neighbouring centers to act in a cooperative manner during catalytic reactions. Also the active species will be more easily accessible compared to the core-functionalized metal centers, hence, the periphery-functionalized metallodendrimers should suffer less from mass transport effects.

1.3 DENDRITIC CATALYSTS

There are numerous examples of dendritic catalysts with metal centers located at either at the core, periphery or within the interior structure. Several cases will be presented to illustrate each type. Placing catalytic active sites at the core can lead to catalysis that is enantioselective, size and shape selective. Two approaches have been adopted for enantioselective catalysis using core-functionalized dendrimers. In the first approach, a non-chiral metal complex is surrounded by a chiral dendritic structure. In the second approach, a chiral metal complex is surrounded by a non-chiral dendritic structure. Up to now, the second method has given better chiral induction than the former method because of interference between the chiral groups.

As mentioned earlier, periphery-functionalized metallodendrimers have high local concentrations of metal centers, which should allow neighbouring centers to act in a cooperative manner during catalytic reactions. Unfortunately, there have been limited successful reports of chiral cooperativity with periphery-functionalized dendritic catalysts.[43]

1.3.1 Catalytic Active Centers at the Core

In an effort to design molecules that would mimic enzymes, Brunner *et al.* built two classes of dendrimers with chiral backbones and named them

dendrizymes.[5, 44] The first class was synthesized with a pyridine Schiff-base core, which was surrounded by chiral repeating units (Figure 1.3). The resulting core-bound Cu (I) complexes were used to catalyze the cyclopropanation of styrene with ethyl diazoacetate (Eq 1.1). Only low ee values of up to 10 % were observed.

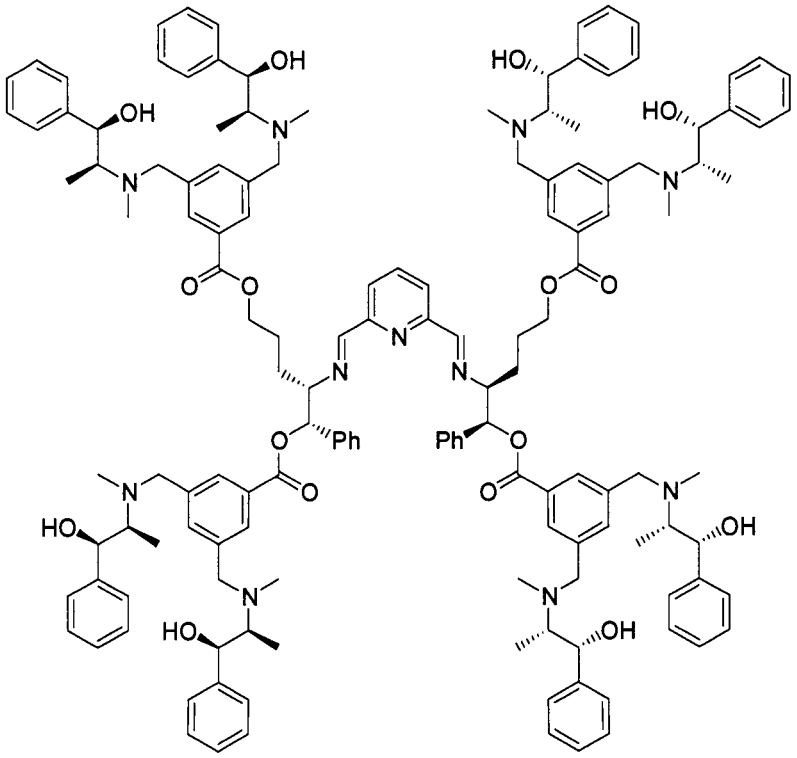
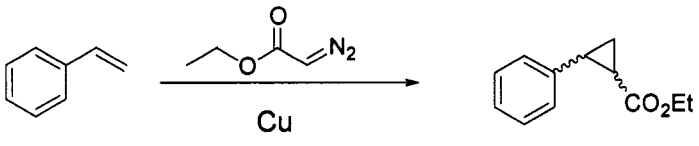


Figure 1.3 Brunner's Dendrizyme



Eq. 1.1

The second class of dendrimers was based on a diphosphine core (Figure 1.4). They have been tested in a number of reactions such as hydrogenation, hydrosilylation etc. but poor enantiselectivities were observed. Nevertheless, small changes in the dendrimer structure caused a significant difference in reactivity.

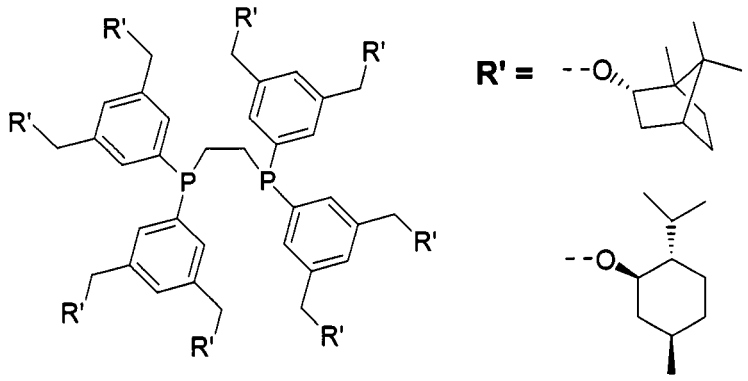


Figure 1.4 Brunner's Phosphine Dendrimer

Seebach and co-workers have employed Fréchet's poly(benzylether) dendrons attached to Ti-TADDOL (Figure 1.5) to catalyze the asymmetric reductive alkylation of benzaldehyde to diethylzinc (Eq. 1.2).[45] (TADDOL is α,α,α',α'-tetraaryl-1,3,-dioxolane-4,5-dimethanols). Enantiomeric excesses of up to 96 % were obtained. There was a decrease in catalytic activity with generations higher than three due to accessibility issues.

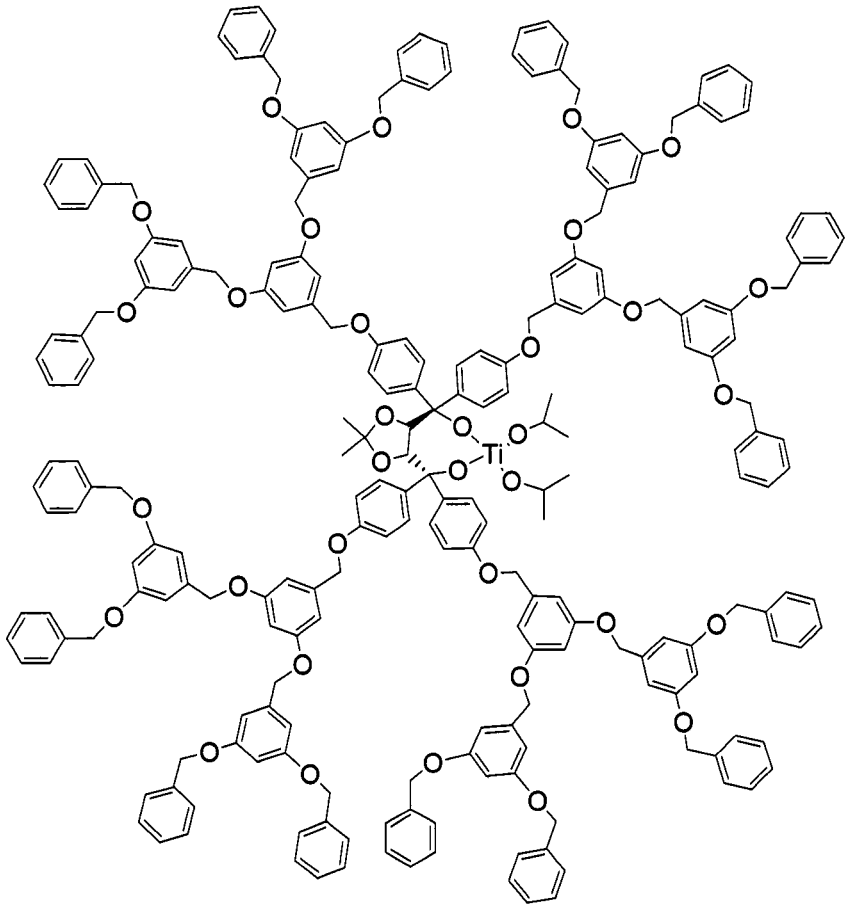
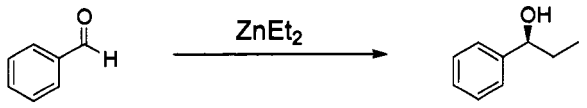


Figure 1.5 Seebach's Dendritic Ti-TADDOL catalyst



Eq. 1.2

The research group of Chow employed a Cu(II)-bisoxazoline surrounded by poly(alkyl aryl ether) dendrimers (Figure 1.6) to catalyze the Diels Alder reaction between cyclopentadiene and crotonylimide (Eq 1.3).[46, 47] They also observed a drop in activity from the third generation of the dendritic catalysts due to reduced access to the active center. Indeed, the higher generation dendrimers backfold,

because of steric constraints. This causes a hindrance around the core. Interestingly, the selectivity was slightly increased for the third generation catalyst.

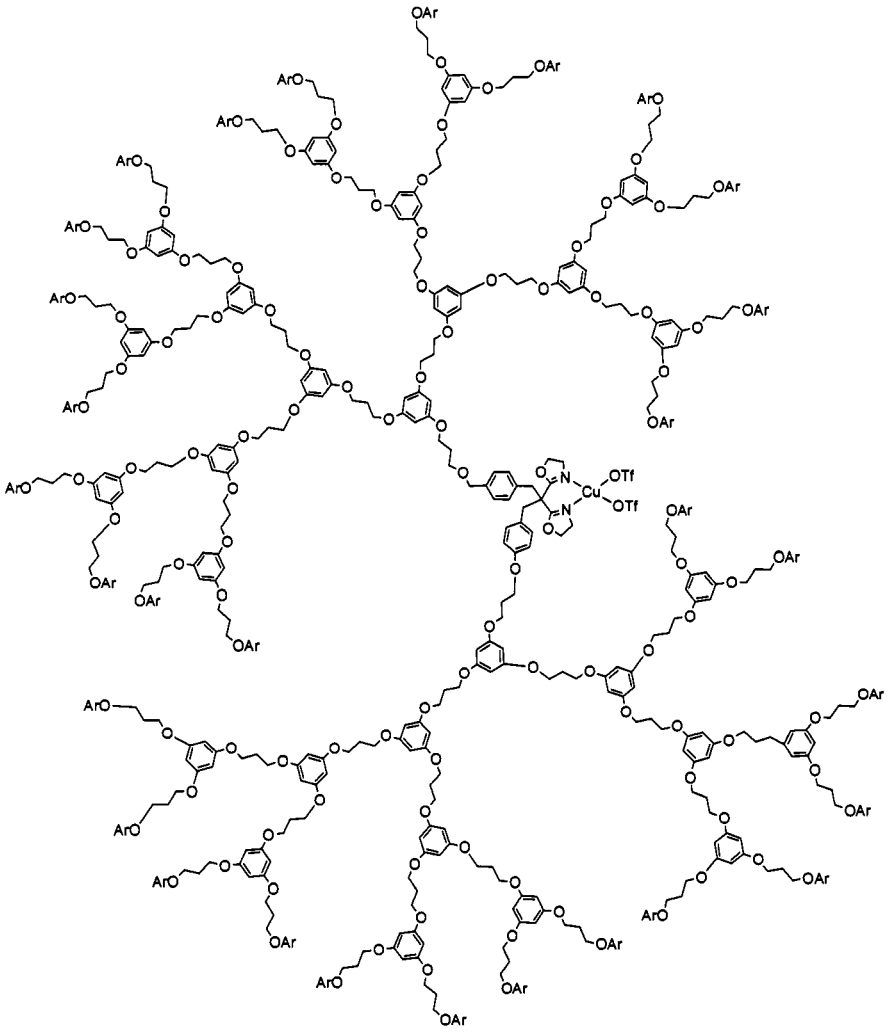
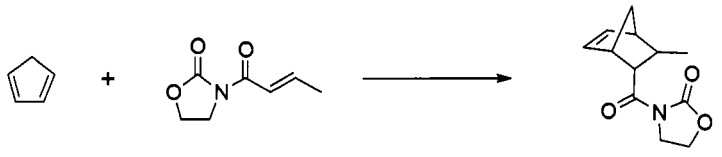
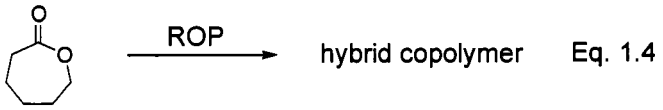


Figure 1.6 Chow's Cu (II) - Bisoxazoline Dendritic Catalyst



Eq. 1.3

One of the challenges in polymerization reactions is to prevent two growing polymer chains from reacting with each other, resulting in chain termination, which would lead to the formation of a low molecular weight (M_w) polymer. The shielding of the reactive site prevents this from happening. In dendrimer chemistry, if the reactive site is placed at the core, the bulk of the dendrimer should create a barrier around it. Fréchet *et al.* used this strategy for the anionic ring opening polymerization of ε-caprolactone (Eq 1.4).[48] Alcoholates based on poly(benzylether) dendrimers (Figure 1.7) were used as macro-initiators in this polymerization reaction. They observed that the first generation dendrimer not only gave low conversion, but also oligomers of low M_w. The fourth generation dendritic alcoholates gave higher M_w polymers with low polydispersity compared to non-dendritic alcoholates. This demonstrated that the shielding effect of the bulk of the dendrimers increased as they grew bigger.



Eq. 1.4

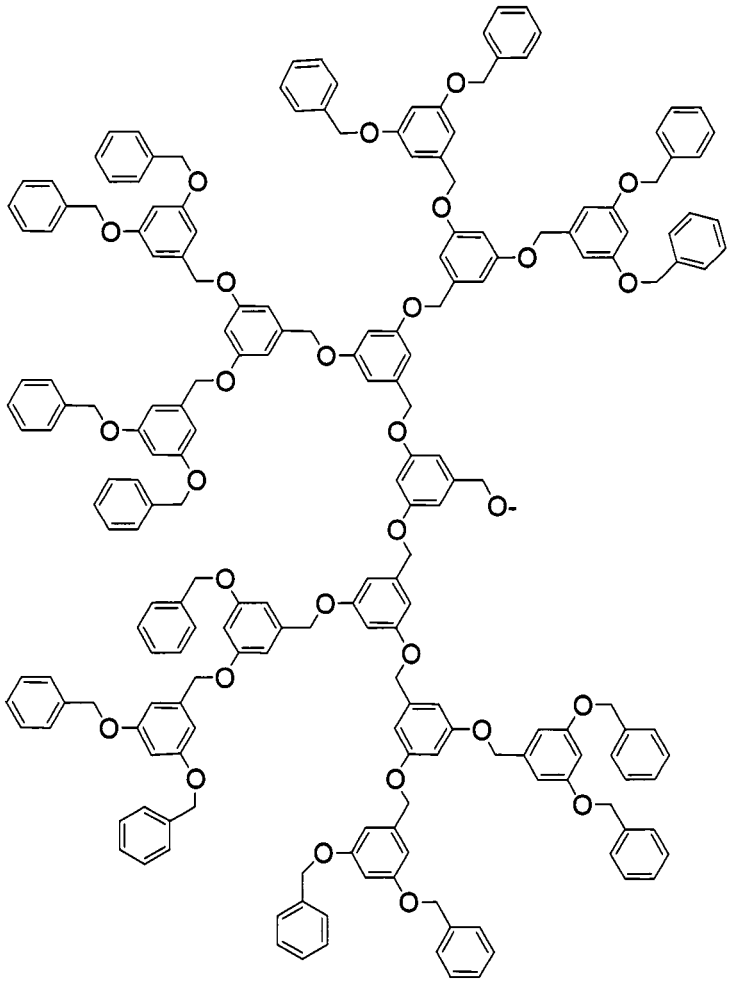


Figure 1.7 Fréchet's fourth generation alcoholate

1.3.2 Periphery Functionalized Catalysts

van Koten and van Leeuwen reported the first example of periphery-functionalized dendritic catalysts.[4] They used poly(carbosilane) dendrimers containing diamino arylnickel (II) complexes to catalyze the Kharasch addition of CCl_4 to methyl methacrylate (Eq 1.5). They placed 1,4-butanediol linkers between the carbosilane backbone and the diamino arylnickel (II) centers to prevent interactions between the metal centers (Figure 1.8). Only the 1:1 adduct was selectively produced. The catalytic activity of the zero and first generation catalysts (containing 4 and 12 nickel centers, respectively) was 20 % and 30 % lower than that of the monomeric species.

Eq. 1.5

When the diamino arylnickel (II) complexes were ligated directly to the carbosilane backbone, a pronounced negative dendritic effect* was observed for the same reaction.[49] This was attributed to the formation of mixed metal complexes due to the close interaction of $Ni^{(II)}$ and $Ni^{(III)}$ sites. By modifying the dendritic structure so that there was less steric congestion at the surface, activities were greatly improved.

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* Generally, a negative dendrimer effect is the decline in reactivity as a function of the dendrimer size.

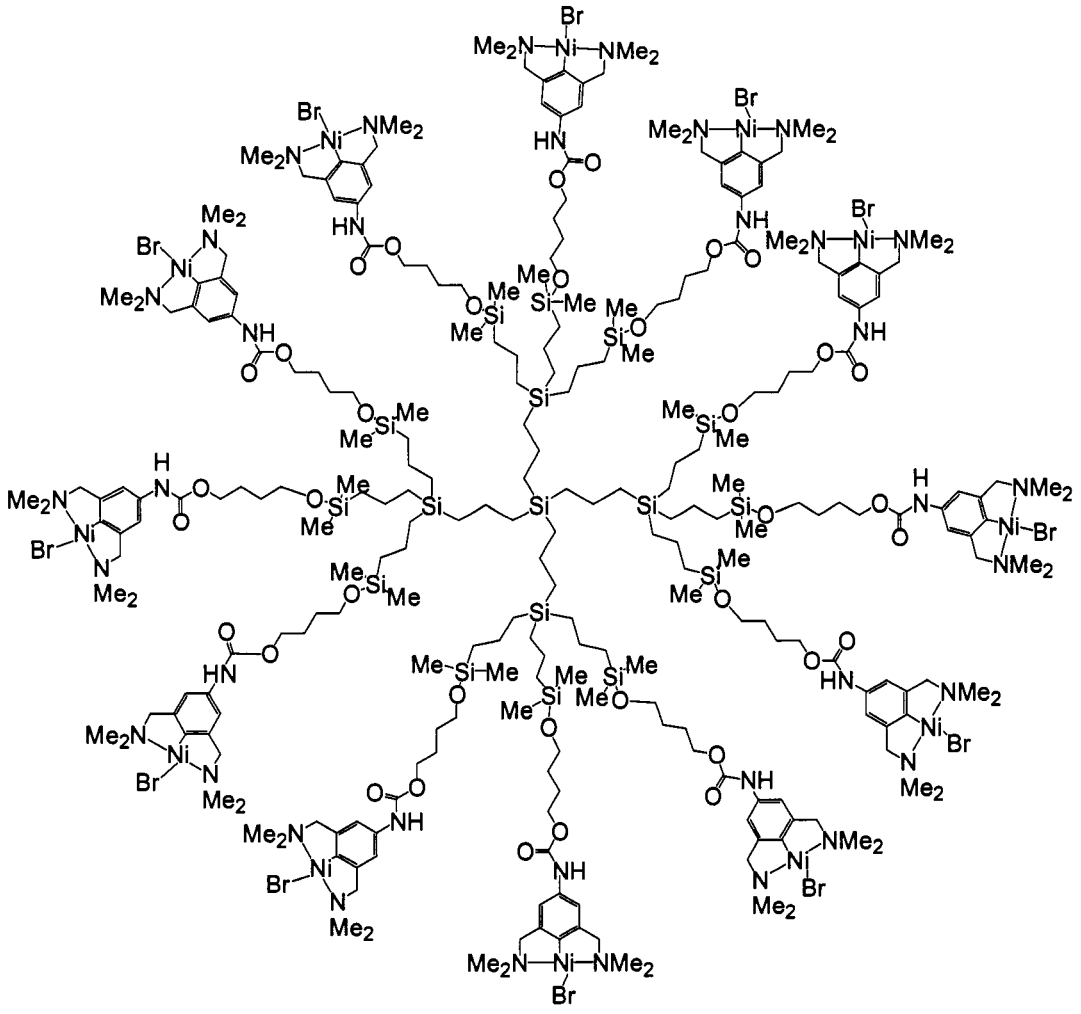


Figure 1.8 van Koten and van Leeuwen's Arylnickel (II) Dendrimer

An important contribution by Reetz and co-workers involved the introduction of diphenylphosphino groups to poly(propyleneimine) dendrimers (Figure 1.9).[50] The Pd complex displayed higher activity than the monomeric complex, $[C_3H_7\text{-}N(CH_2PPh_2)_2\text{-}Pd(CH_3)_2]$ when used as a catalyst for the Heck reaction of bromobenzene and styrene (Eq 1.6). This result was explained by the fact that the monomeric complex decomposed to metallic Pd whereas the dendritic system did not. This phenomenon was attributed to the higher thermal stability of

the dendritic complex. The latter was also tested in allylic substitution reactions (Eq 1.7) where it showed good reusability while maintaining good catalytic activity.[51] These results stimulated other research groups to investigate various dendrimer generations of similar complexes in other Pd catalyzed reactions.[52-54]

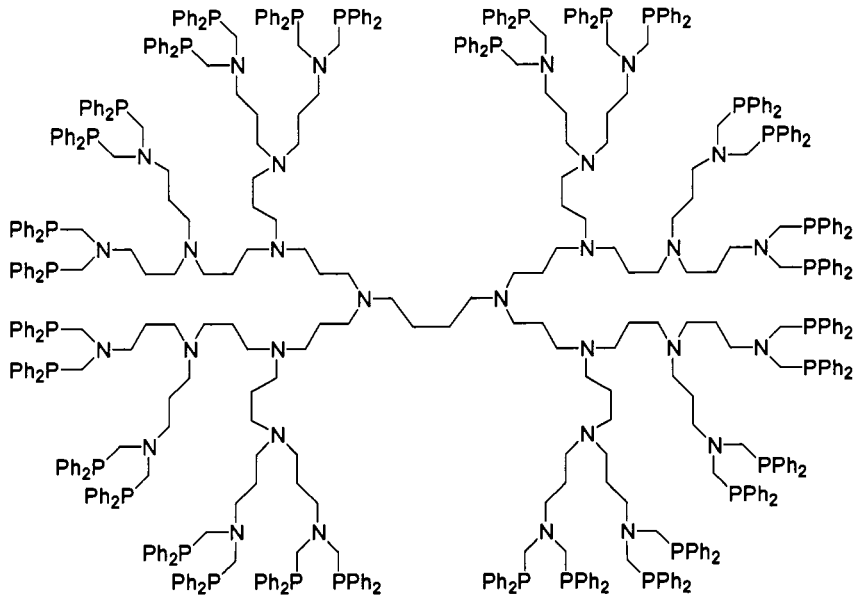
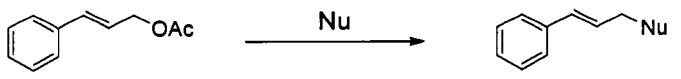


Figure 1.9 Third-Generation Polypropyleneimine Dendrimer

Eq. 1.6



Eq. 1.7

The research group of Majoral developed the synthesis of phosphine dendrimers of the type shown in Figure 1.10. [55] They synthesized up to the tenth generation dendrimers containing up to 3000 phosphorus atoms! The Pd complexes catalyzed the Stille coupling of methyl 2-iodobenzoate and 2-(tributylstannyl)thiophene (Eq 1.8) in 79 – 86 % conversion in three consecutive runs. Up to 100 % conversion was observed for the reaction of iodobenzene and tributylvinyltin (Eq 1.9). The Ru dendritic complexes were successfully applied to the Michael addition of ethyl cyanoacetate to diethyl ethylidenemalonate (Eq 1.10) and the Knoevenagel condensation of malononitrile with cyclohexanone.

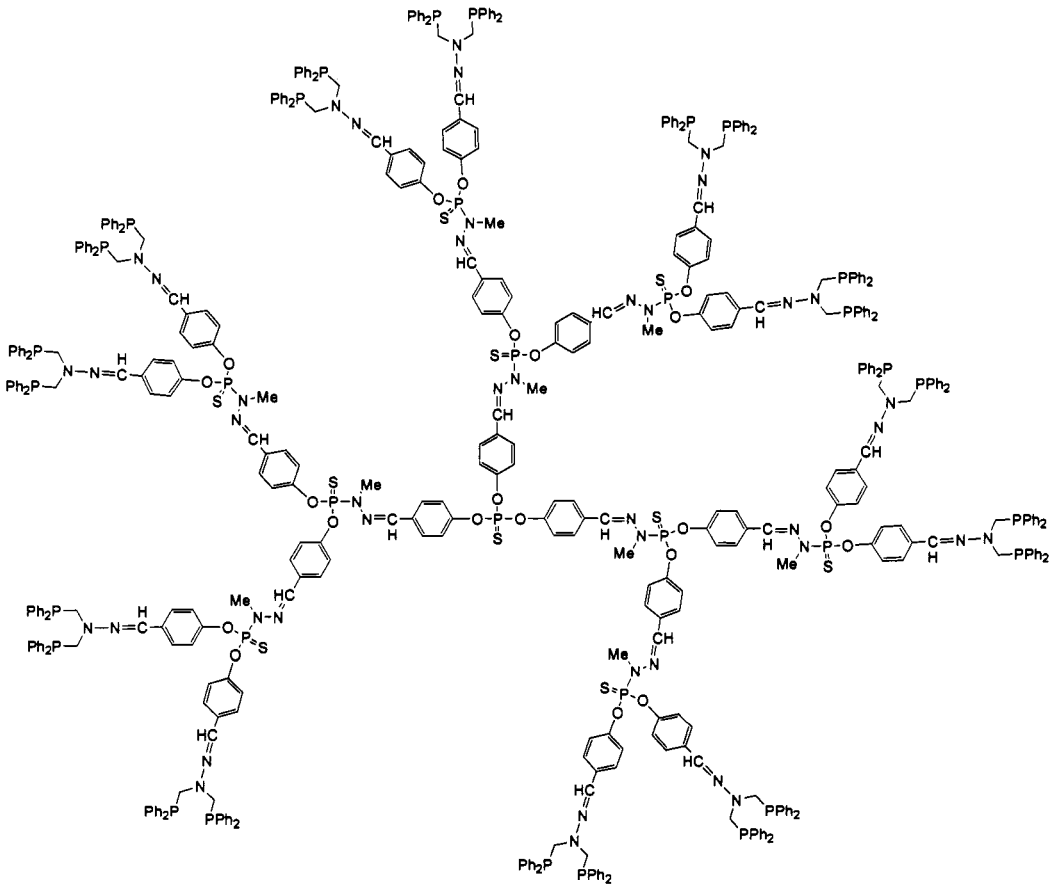
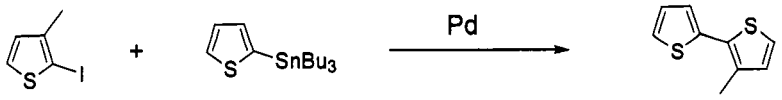
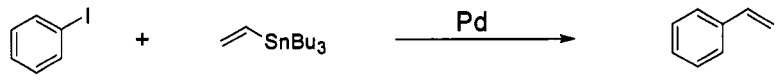


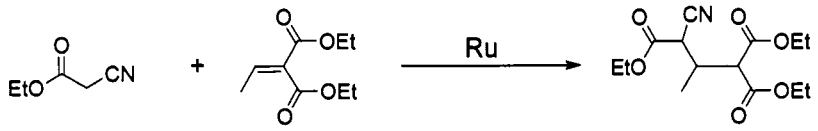
Figure 1.10 Majoral's Phosphine Dendrimers



Eq. 1.8

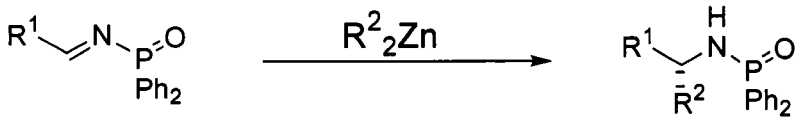


Eq. 1.9



Eq. 1.10

Soai and co-workers have studied the effect that the dendrimer backbone has on the enantioselectivity in the addition of dialkylzinc to N-(diphenylphosphinyl)imines (Eq 1.11).[56-58] In this study, flexible PAMAM, flexible poly(silane), or rigid poly(phenylethyne) dendrimers were attached to ephedrine groups (Figure 1.11). The ee values were modest with PAMAM but high with poly(silane) and poly(phenylethyne).



Eq. 1.11

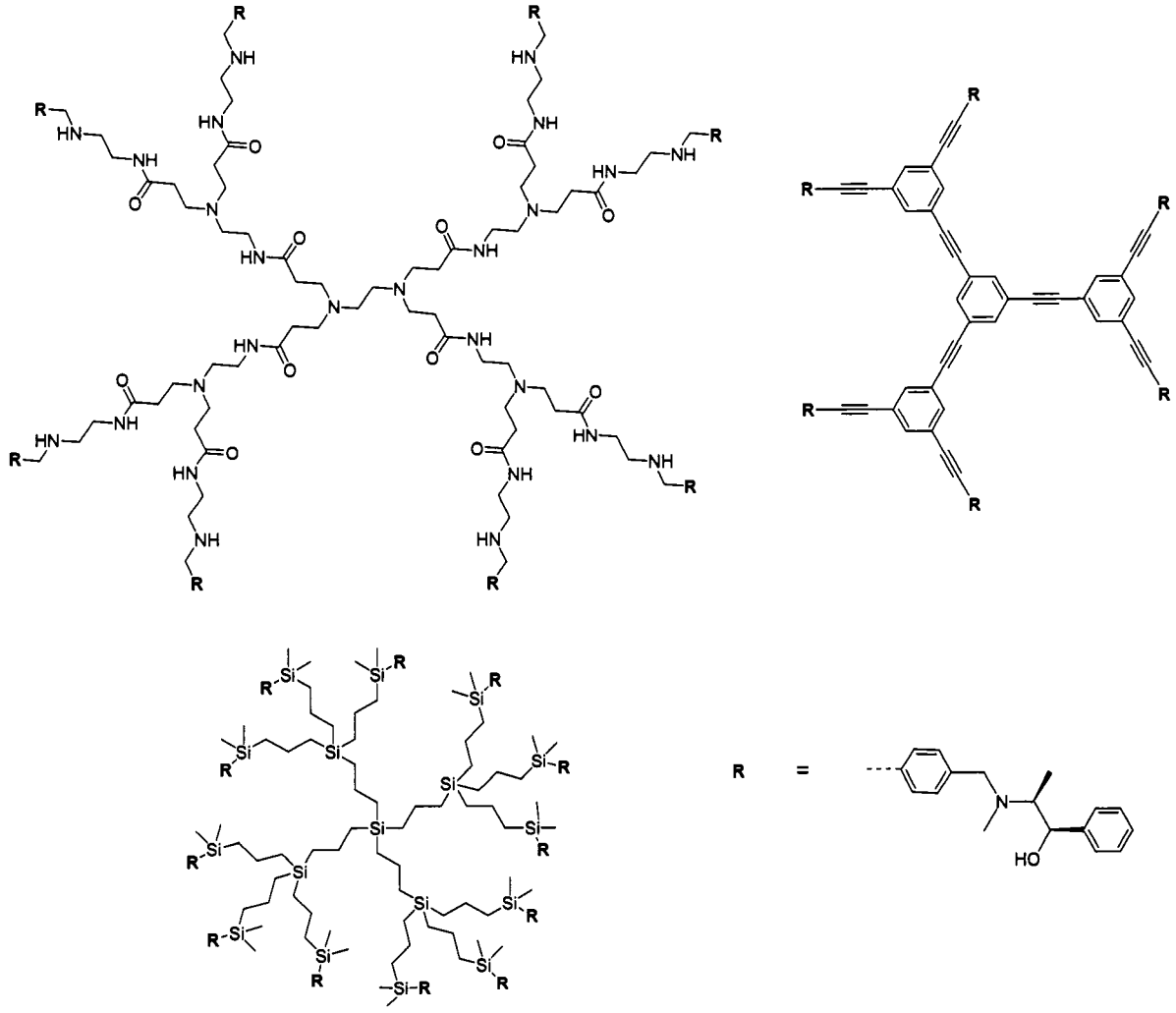


Figure 1.11 Soai's Ephedrine Functionalized Dendrimers

The rationale for the modest ee values displayed by the PAMAM dendrimer is that the flexibility of the dendrimer causes unfavourable interactions between neighbouring chiral groups, which results in a negative effect on enantiodifferentiation. No such interactions occur with the rigid poly(phenylacetylene) and flexible poly(silane) dendrimers.

1.3.3 Metal Centers within the Dendritic Structure

Dubois reported the synthesis of organophosphine dendrimers where the phosphorus was present at the core and within the dendrimer structure (Figure 1.12).[6] The Pd complexes of these organophosphines displayed rates and selectivities similar to the monomeric catalysts in the electrochemical reduction of CO_2 to CO. The authors found that there was no cooperative effect between the Pd sites within the dendritic structure, and that the catalyst was deactivated through the formation of Pd-Pd bonds. The separation of the Pd centers could eliminate this problem, thus improving the turnover number (TON) of the catalytic reaction.

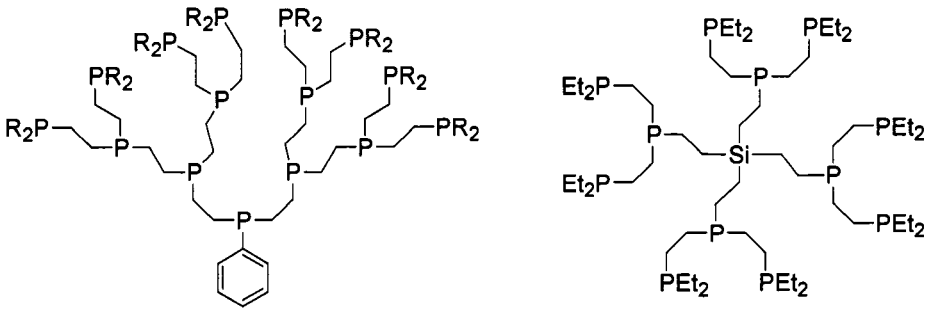


Figure 1.12 Dubois' organophosphine dendrimers

1.3.4 Supported Dendritic Catalysts

Our group has been involved with the synthesis of silica and resin supported dendrimer metal complexes (Figures 1.13 – 1.14). Rhodium complexes prepared with both types of dendrimers showed good activities for the hydroformylation of various alkenes (Eq 1.12).[59]

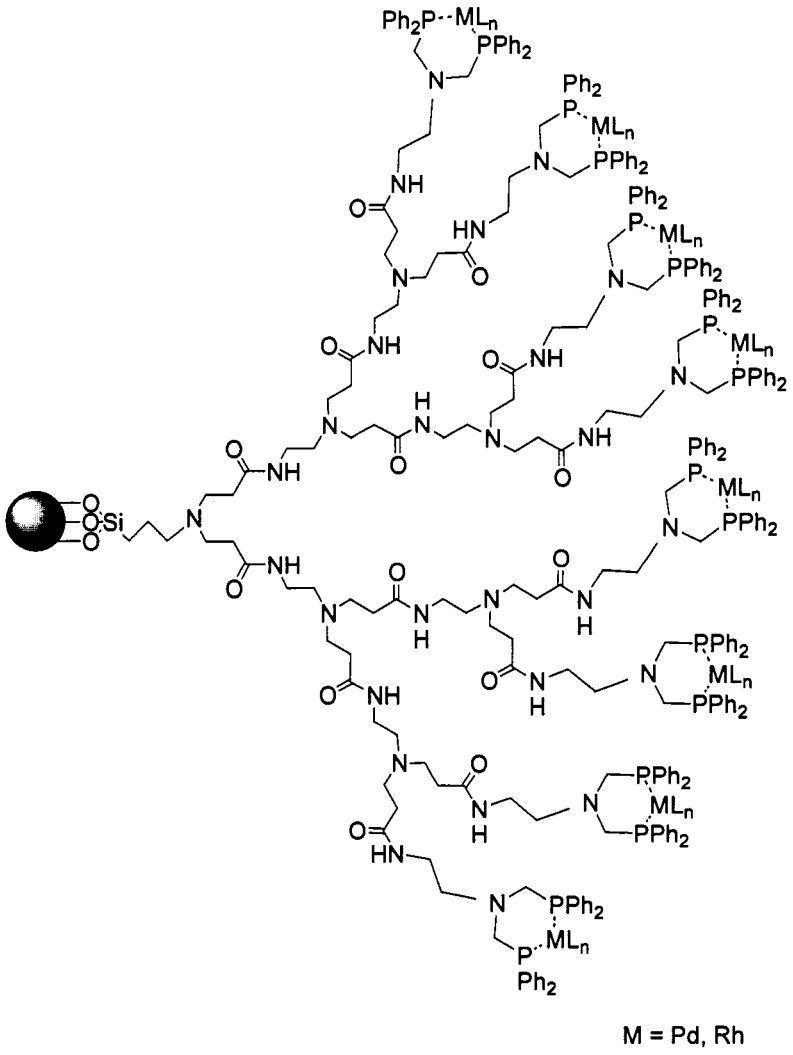


Figure 1.13 Alper's Silica Supported Polyamidoamine - TM Complexes

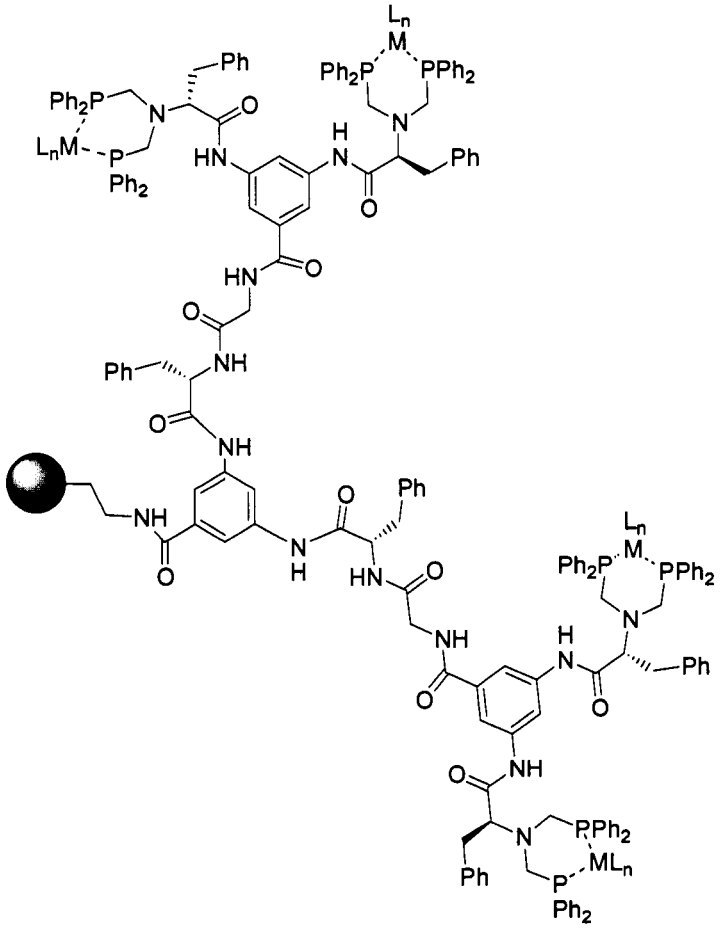
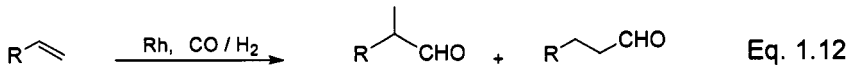


Figure 1.14 Alper's Polystyrene Supported Peptide Dendrimer - Rh Complex



Eq. 1.12

R = Ph, OAc, C_6H_{11}, etc

For the hydroformylation of styrene, regioselectivities of 25 – 30:1 (branched:linear aldehyde) were obtained using G0-G2* catalysts (Figure 1.13) at 25 °C and at 1000 psi CO/H_2. The higher generations G3-G4 gave

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* The number following the letter G refers to the generation number of the denndrimer.

regioselectivities of 8:1 (branched:linear aldehyde) at 75 °C with 1000 psi CO/H_2. The decrease in activity and selectivity was attributed to a likely steric congestion at the dendrimer surface. As a solution, dendrimers with longer spacer groups were synthesized.[60] Regioselectivities were slightly improved to 9-10:1 (branched:linear aldehyde) at 65 °C with 1000 psi CO/H_2. What was impressive was the fact that these catalysts could be recycled many times. Concerning resin-supported dendritic catalysts (Figure 1.14), excellent regioselectivities were obtained for a wide range of alkenes at 25 °C.[61] More impressive was that these catalysts could be recycled ten times while retaining high selectivities.

The Pd-complexes of silica-supported dendrimers (Figure 1.13) have been used to catalyze the Heck coupling reaction of aryl bromides[62], the carbonylation of haloarenes[63], the hydroesterification of alkenes[64] and as well as cyclocarbonylation reactions.[65]

The research group of Portnoy reported another elegant example of dendrimers immobilized on a solid support. They attached poly(benzylether) dendrons to polystyrene beads (Figure 1.15). After introducing diphenylphosphino groups to the benzyl ester terminated dendrimers, cobalt and palladium complexes were synthesized. Co-dendritic complexes provided the first example of supported dendrimer catalyzed intramolecular annulation (Eq 1.13).[66] A positive dendritic effect was observed in that the activity and selectivity increased with the growth of dendrimer.

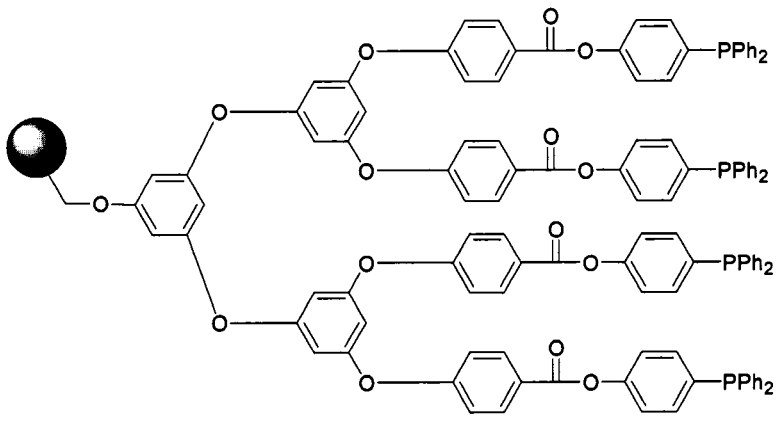
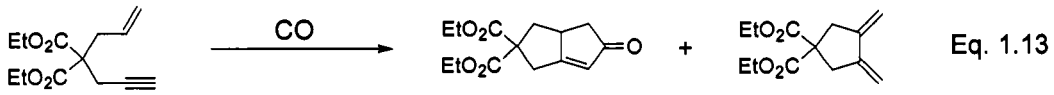


Figure 1.15 Portnoy's Third Generation Resin-Supported Dendrimer



Eq. 1.13

Eq. 1.14

R = CO_2Me, Ph, OBu

The dendritic Pd-complexes were used as catalysts for the Heck coupling reaction of bromobenzene with methyl acrylate, styrene, and butyl vinyl ether (Eq 1.14).[67] A better selectivity was observed with the dendritic catalysts than non-dendritic complexes. Once again, a positive dendritic effect was observed. In the reaction with butyl vinyl ether, the higher generation catalysts showed an augmentation in selectivity for the α-arylated product. The authors ascribe this to

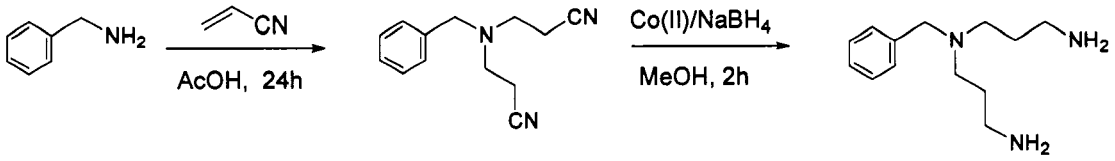
the increased polarity provided by these dendrimers. Due to the decomposition of the catalysts, the latter were not recycled.

1.4 Dendrimer Synthesis

The two main methodologies used to construct dendrimers are known as the divergent approach and the convergent approach. Both strategies involve iterative growth reactions. Other synthetic pathways have been developed in an attempt to improve these two methods. These involve double exponential and mixed growth, the use of hypercore and branched monomers, and other accelerated growth techniques.

1.4.1 The Divergent Approach

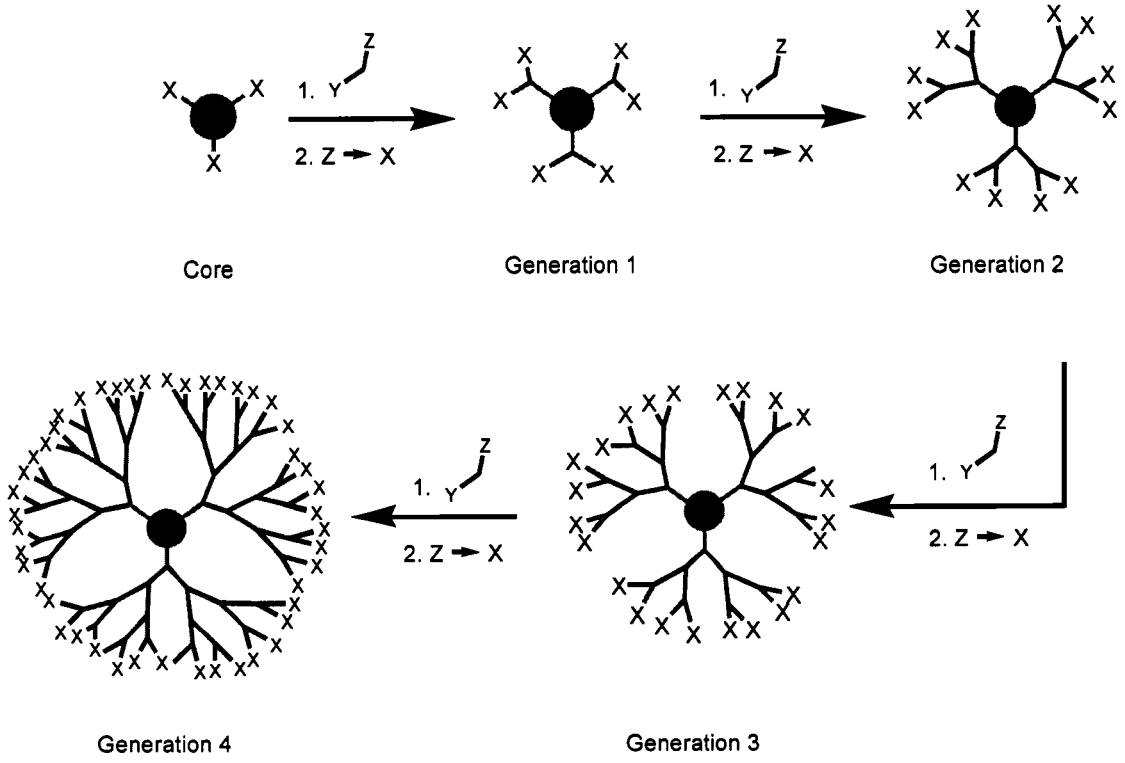
A key point in the divergent synthesis of dendrimers was established when Vögtle *et al.* reported the first successful synthesis of cascade molecules back in 1978.[1] A polyamine was constructed from benzylamine through a sequential repetition of a Michael addition on acrylonitrile followed by the reduction of the nitrile groups to primary amines (Scheme 1.1).



Scheme 1.1 Vögtle's Cascade Molecules

The divergent approach, which consists of building a dendrimer from an initiator core towards the periphery (Scheme 1.2) was further developed by the groups of Tomalia[68, 69] and Newkome.[70, 71] Each generation is accompanied by a multiplication of reactive end groups. As a result, large excesses of reagent are required to drive the reactions to completion. Large dendrimers can be assembled *via* this protocol. An example is Tomalia's 10^{th} generation PAMAM dendrimer. The problems associated with this method are purification and monodispersity. The latter is a consequence of the formation of side products rather than the desired dendrimer.

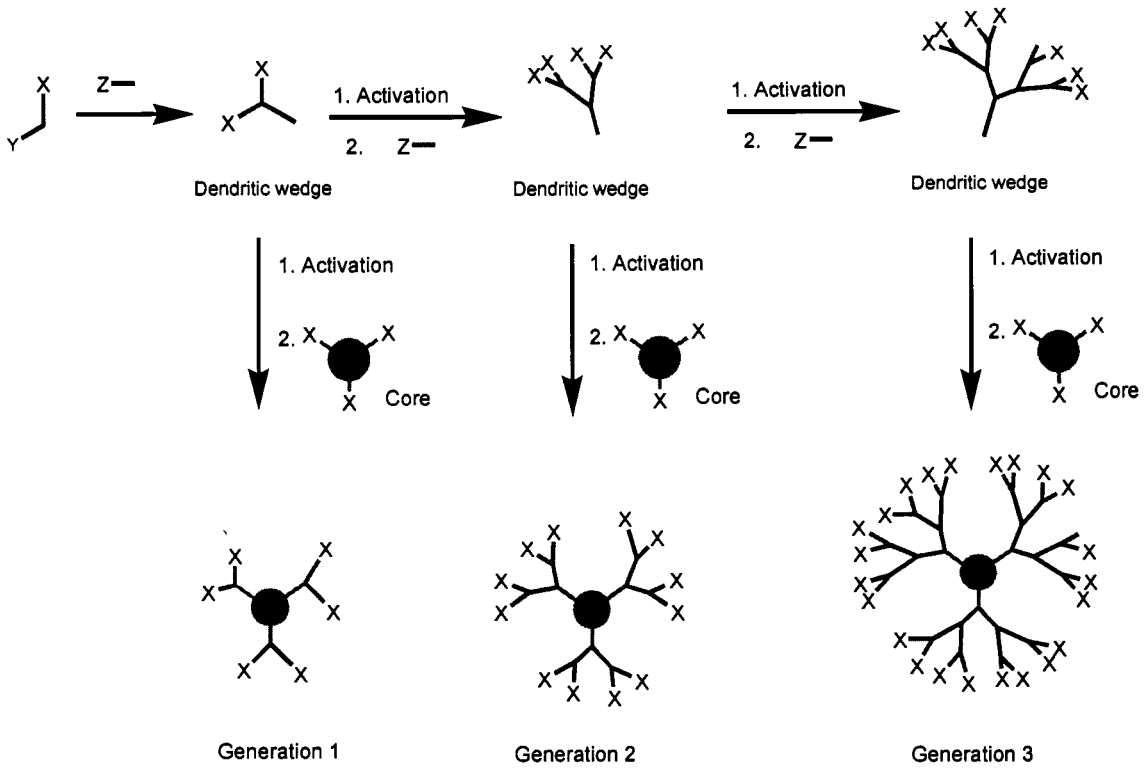
PAMAM and PPI dendrimers synthesized through the divergent approach are commercially available.



Scheme 1.2 Divergent Dendrimer Synthesis

1.4.2 The Convergent Approach

Fréchet and co-workers developed this synthetic strategy to prepare dendrimers.[72, 73] The latter are grown starting from the periphery by gradually progressing towards the core (Scheme 1.3). Dendritic wedges are built separately, and then attached *via* a single site (focal point) to give a bigger wedge. The process is repeated until the desired generation is achieved. A complete dendrimer is thus obtained by the attachment of the wedges to a core moiety.



Scheme 1.3 Convergent Dendrimer Synthesis

1.4.3 Dendrimer Characterization

The molecular weight and polydispersity of dendrimers can be determined by size exclusion chromatography and mass spectrometry. Nuclear magnetic resonance of nuclei such as ^{13}C, ^{1}H, ^{31}P, and ^{29}Si is very useful in the characterization of dendrimers. Other standard techniques such as infrared spectroscopy, viscosity and light scattering measurements have also been employed.

1.5 Catalytic Oxidation

Whether it is the conversion of alcohols to carbonyls or hydrocarbons to oxygenates, selective oxidation is an attractive method of making C-O bonds from cheap feedstocks. In the laboratory, stoichiometric amounts of oxidants such as chromates, permanganates, peracids, *etc.* are often employed. The use of such oxidants is regularly accompanied by a comparable amount of waste, which would require elaborate and expensive treatment if it were applied on a larger scale. For industrial production, environmentally benign oxidants such as air and H_2O_2 are preferred. Air is ubiquitous and H_2O_2 generates only water as a by-product. Generally, high oxidation state transition metals and their oxides are used as catalysts when air and H_2O_2 are utilized as terminal oxidants.

According to Centi, oxidation products constitute 60 % of the chemicals or intermediates derived from catalytic processes.[74] A milestone in homogeneous oxidation catalysis was the Wacker Process for the production of acetaldehyde from ethylene under aqueous acid conditions, using palladium chloride, copper chloride and air. Other important homogeneous oxidation processes are the synthesis of propylene oxide from propylene, adipic acid from cyclohexane and terephthalic acid from xylene. In heterogeneous catalysis, the turning point has been the discovery of vanadium phosphorus oxides for the selective oxidation of butane to maleic anhydride. Despite all these various catalysts, there is still a great need for better systems for selective oxidation reactions.

An elegant use of dendritic catalysts for the oxidation of various olefins was reported by Suslick *et al.* [75, 76] They prepared manganese porphyrins with different sized poly(benzylether) dendrons (Figure 1.16). The bulkier dendritic catalysts preferentially epoxidized the less sterically hindered double bonds. The bulkier dendritic complexes displayed more selectivity for the reaction of 1-alkenes than that of internal electron rich olefins, compared the non-dendritic manganese porphyrins.

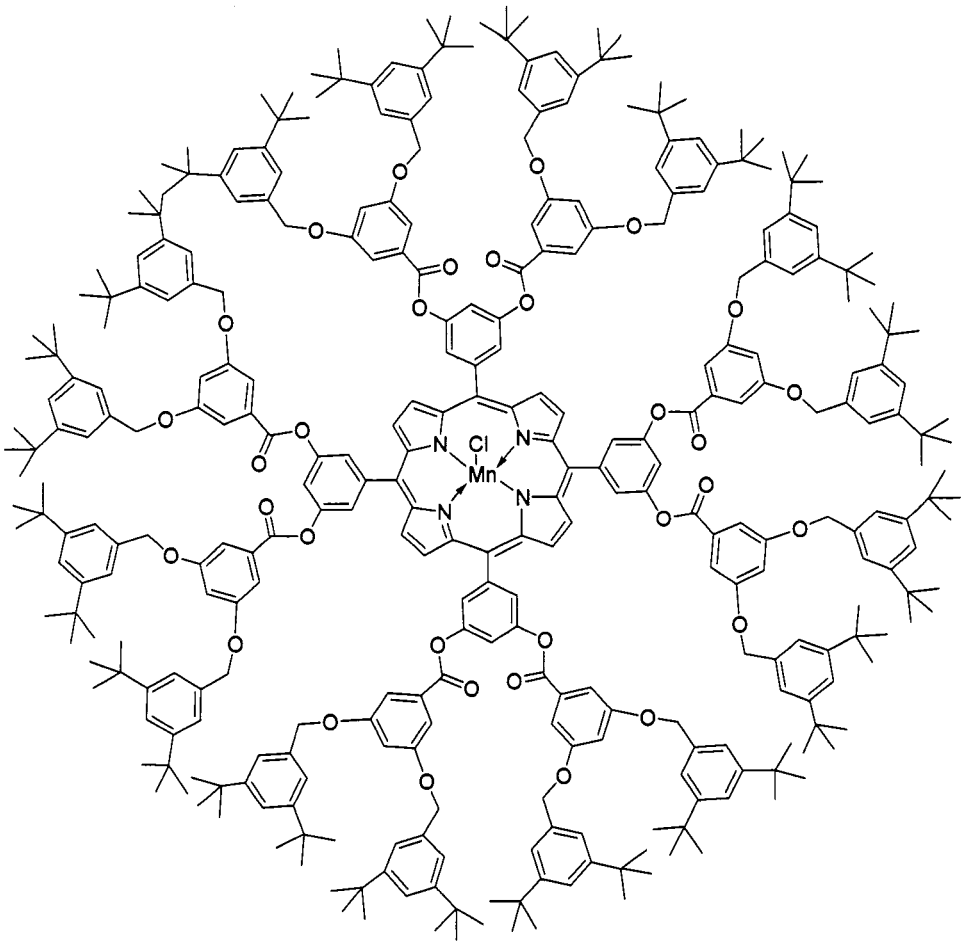


Figure 1.16 Suslick's Dendritic Manganese Porphyrin

Using alkoxy-functionalized carbosilane (Figure 1.17), Tilley and co-workers prepared dendritic Ti-complexes that were highly active and selective for the epoxidation of cyclohexene.[77]

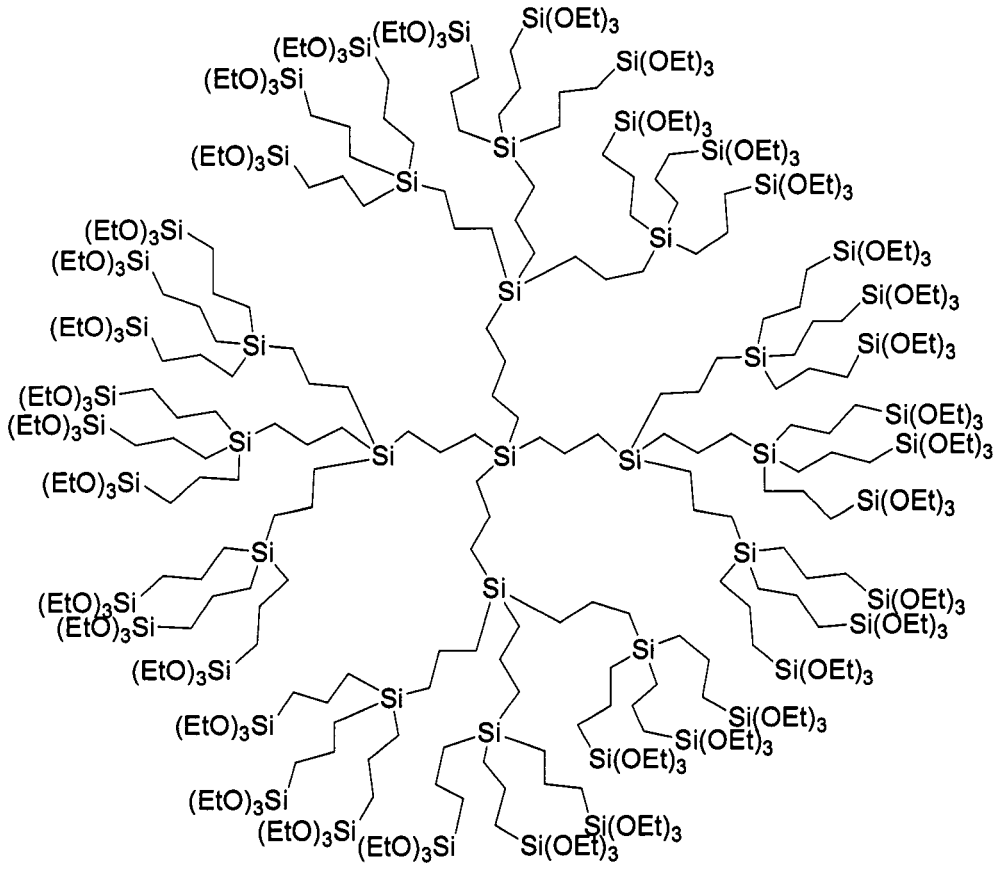


Figure 1.17 Tilley's Alkoxy Carbosilane Dendrimer

Kimura surrounded Co-phthalocyanines with Newkome's dendrimers (Figure 1.18).[78] The resulting dendritic complexes were used as catalysts for the oxidation of mercaptoethanol. The striking feature about these complexes was their stability under the reaction conditions used. Unfortunately, a negative dendritic effect was observed.

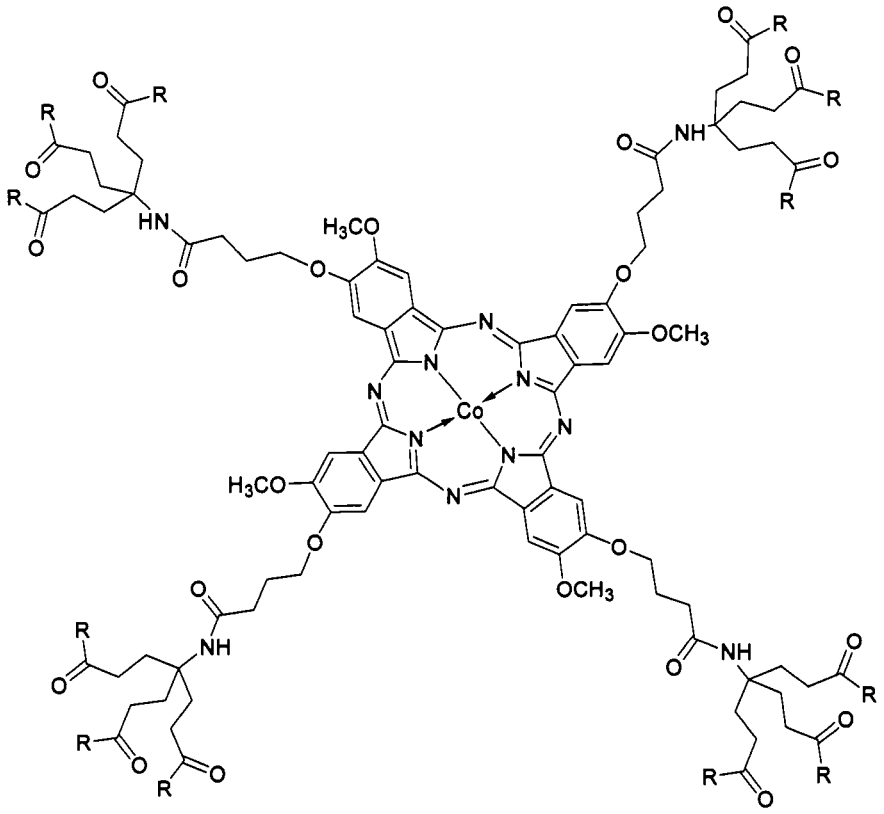


Figure 1.18 Kimura's Phthalocyanine Dendrimer

1.6 CATALYTIC HYDROGENATION

The selective hydrogenation of hydrocarbons with more than one unsaturated double bond is a simple yet important reaction. Sabatier reported the earliest example of the use of a transition metal in the presence of molecular hydrogen at the end of the 19th century. Since then, numerous examples of homogeneously and heterogeneously catalyzed hydrogenations have been described. Rhodium and ruthenium are favored for the homogeneous process while palladium has often been used for the heterogeneous reaction.

The application of transition metal-bound dendrimers to hydrogenation reactions is still at an emerging stage. Fan *et al.* published a report describing the synthesis of BINAP functionalized poly(benzylether) dendrimers and their Ru complexes (Figure 1.19).[79] For the reduction of 2-[*p*-(2-methylpropyl)phenyl]acrylic acid to ibuprofen, the dendritic Ru complexes gave higher ee's than non-dendritic Ru-BINAP. Moreover, the third generation catalyst was used in three runs without significant loss in activity.

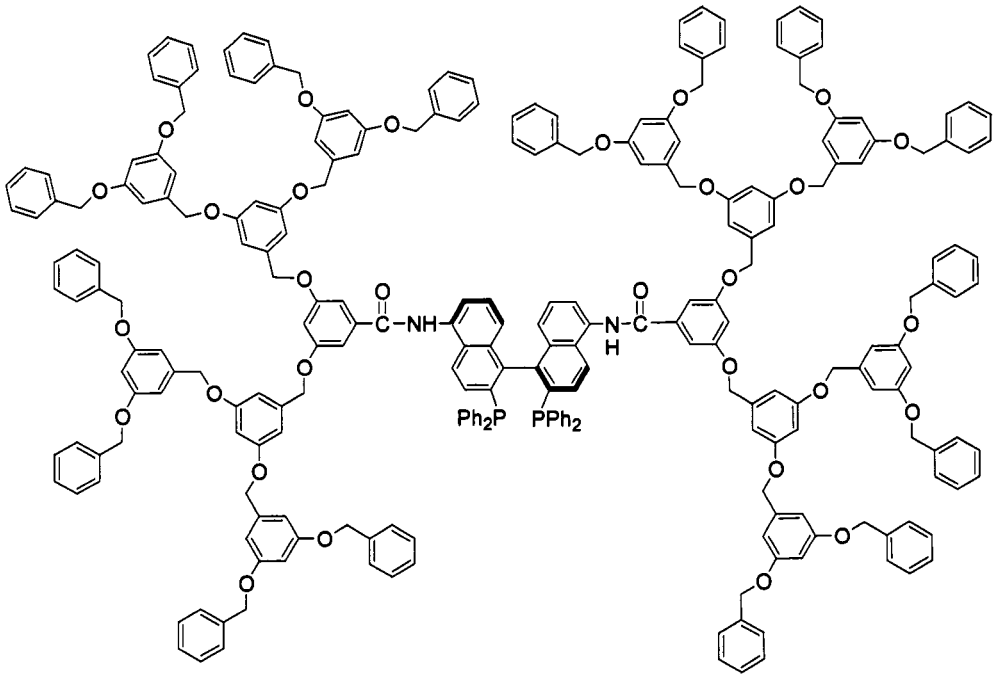


Figure 1.19 Fan's BINAP poly(benzylether) Dendrimer

Togni reported that periphery-functionalized ferrocenyl diphenylphosphine Rh complexes catalyzed the asymmetric hydrogenation of dimethyl itaconate (Figure 1.20).[80, 81] Using different core functionalities, the enantioselectivities obtained were comparable to non-dendronized Josiphos-Rh complex.

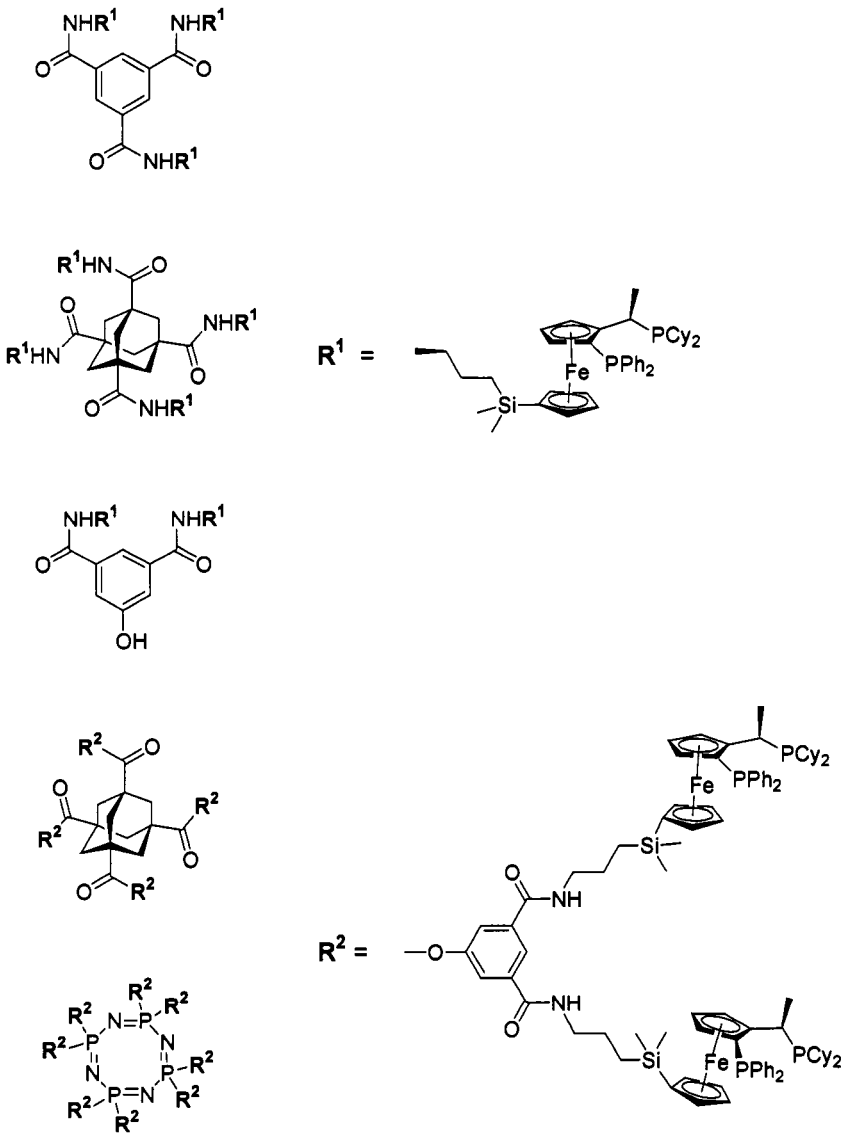


Figure 1.20. Togni's Ferrocenyl-Functionalized Dendrimers

In a different strategy, dendrimers have been utilized as templates to prepare nanoparticles with well-controlled size, stability and solubility. This approach exploits the fact that most dendrimers have well defined structures and that most dendrimer characteristics can be designed to possess the desired properties.

The groups of Crooks[82] and Kaneda[83] have independently utilized PAMAM and PPI dendrimers as templates for the synthesis of Pd nanoparticles. These nanocatalysts showed interesting substrate selectivity when used for the hydrogenation of various olefins. Crooks and co-workers have used generations G4, G6 and G8 of hydroxy terminated PAMAM. The resulting Pd nanoparticles were studied as catalysts for the hydrogenation of allyl alcohol and *N*-isopropyl acrylamide. For the latter substrate, there was a strong dependency between the hydrogenation activity and the dendrimer generation. Indeed, G6 and G8 gave TOFs that were 10 and 5 % that of G4. Allyl alcohols with substituents of different sizes on the α-position were catalyzed with the G4-Pd nanoparticles. The activity diminished with the increase in the size of the α-substituent.

Kaneda *et al.* functionalized third to fifth generation PPI dendrimers with triethoxybenzamide, prior to using them as templates for the synthesis of Pd nanoparticles. The catalytic performance of these nanocatalysts was investigated towards the hydrogenation of various olefins. The hydrogenation rates were lower than those obtained with Pd/C and they decreased in the order G3 > G4 > G5 for all substrates. The Pd nanoparticles encapsulated with G5 the dendrimer showed interesting molecular recognition properties. For example, it allowed the selective hydrogenation of certain substances. Polar substrates reacted faster than non-polar substrates when they were simultaneously present in the reaction mixture.

1.7 Research Objectives

The objective of this thesis was to prepare a general class of dendritic ligands that could be complexed to certain transition metals to give catalysts that could perform redox reactions.

Palladium was our first choice because it is a versatile transition metal. It catalyzes oxidation reactions under oxidizing conditions, and reduction reactions under reducing conditions. This thesis reports the use of silica-supported PAMAM - palladium complexes to catalyze the oxidation of alkenes to methyl ketones and the selective hydrogenation of dienes to monoolefins. The effect that the dendrimer structure had on the activity and selectivity of the above-mentioned reactions was of interest. It was also our intention to study the extent of reusability of these dendritic catalysts.

Furthermore, we synthesized titanium and vanadium complexes from salen-modified PPI dendrimers for the epoxidation of alkenes and olefinic alcohols.

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Chapter Two

SYNTHESIS OF SILICA-SUPPORTED PAMAM-PALLADIUM COMPLEXES

2.1 General Considerations

2.1.1 Instrumentation and Characterization

Solid state NMR was done on a Bruker ASX 200. Thermal gravimetric analysis (TGA) was carried out at Sasol Technology R&D, South Africa. The Pd content was analyzed by inductively coupled plasma spectroscopy (ICP) at Galbraith Laboratories, Knoxville USA.

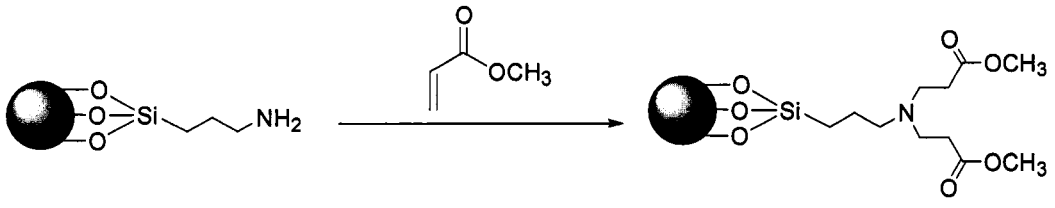
2.1.2 Reagents

Aminopropyl silica gel with a loading of 0.9 ± 0.1 mmol NH_2 / g and particle size of 35 – 70 mm was purchased from Fluka Chemical Co. 1,6-Diaminohexane and 1,12-diaminododecane were also bought from Fluka Chemical Co. Ethylenediamine was ordered from Aldrich Chemical Co. All commercial metal complexes were purchased from Strem Chemicals. Organic solvents were distilled and degassed before use. All other chemicals were used without further purification. All manipulations towards the synthesis of PAMAM – Pd complexes were carried out under inert conditions.

2.2 SYNTHESIS OF POLYAMIDOAMINE (PAMAM) DENDRIMERS

The construction of silica-supported PAMAM dendrimers was accomplished following the procedures developed by Tomalia.[1-3] The synthesis was initiated from an aminopropyl silica core through a repetition of two steps: Michael-type addition of the amino groups to methyl acrylate followed by amidation of the ester groups with a diaminoalkane. The dendrimers with methyl ester-terminal groups represent a half-generation, while those with amine terminal groups correspond to the full generation. Different amines such as ethylenediamine, 1,6-diaminohexane, and 1,12-diaminododecane were used for the amidation step. The first amine gave access to the first four generations, whereas the last two provided the first two generations.

Synthesis of Methyl Propylaminopropionate Silica 2



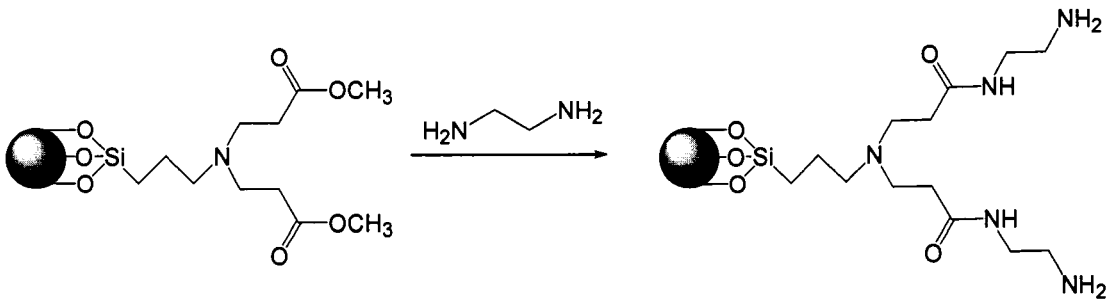
1 **2**

Scheme 2.1 Synthesis of Propylaminopropionate Silica 2

Methyl acrylate (16.4 ml, 180 mmol) was added to a suspension of aminopropylsilica **1** (20 g, 18 mmol NH_2) in dry methanol (100 ml). The mixture was stirred under N_2 at 35 °C for 3 days. After cooling, the liquid was decanted and the solid was washed with methanol (2 x 30 ml) and diethyl ether (3 x 30 ml). The residual solvent was removed *in vacuo* to give 21.7 g of product.

2.2.1 Synthesis of PAMAM Dendrimers with Ethylenediamine

Synthesis of G1: Amine-Terminated Dendrimer 3



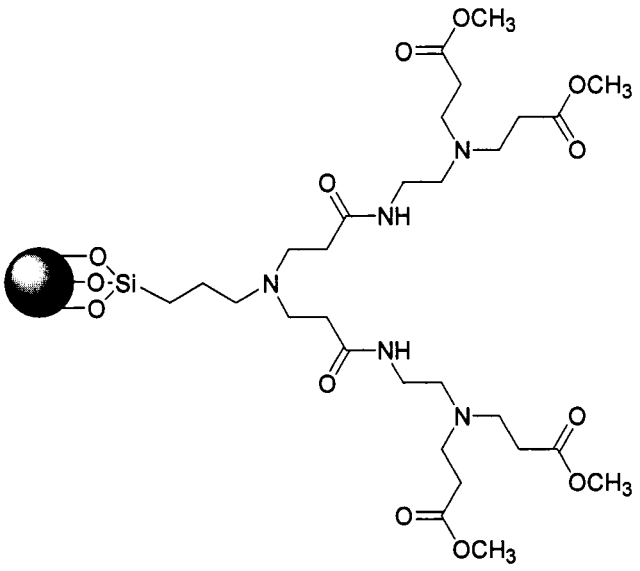
2 **3**

Scheme 2.2 Amidation of Dendrimer 2 with Ethylenediamine

Ethylenediamine (100 ml, 1.5 mol) was slowly added to a suspension of methyl propylaminoproprionate silica gel **2** (10 g) in dry methanol (100 ml). The mixture was stirred at room temperature under N_2 for 7 days. The liquid was decanted.

The mixture was then washed with methanol (30 ml) and transferred to a Soxhlet apparatus. The residual diamine was extracted with methanol over 2 days. The resulting first-generation dendrimer was washed with dichloromethane (20 ml) and then dried *in vacuo* to give 9.6 g of material.

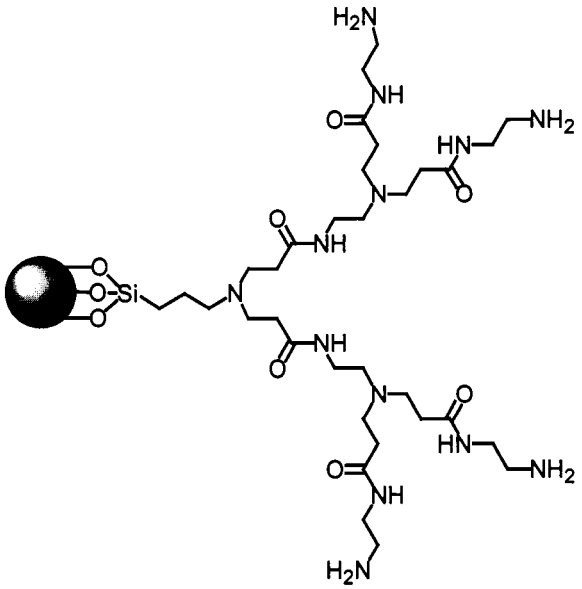
Synthesis of G1.5: Ester-Terminated Dendrimer 4



4

Methyl acrylate (45 ml, 500 mmol) was added to a suspension of 20 g of PAMAM dendrimer **3** in dry methanol (150 ml). The mixture was stirred under N_2 at 35 °C for 5 days. After cooling, the liquid was decanted. The solid was washed with methanol (30 ml), transferred to a Soxhlet apparatus, and extracted with methanol for 24 h. The solid was filtered and washed with diethyl ether (20 ml). 20 g of the dendrimer was thus obtained after drying *in vacuo*.

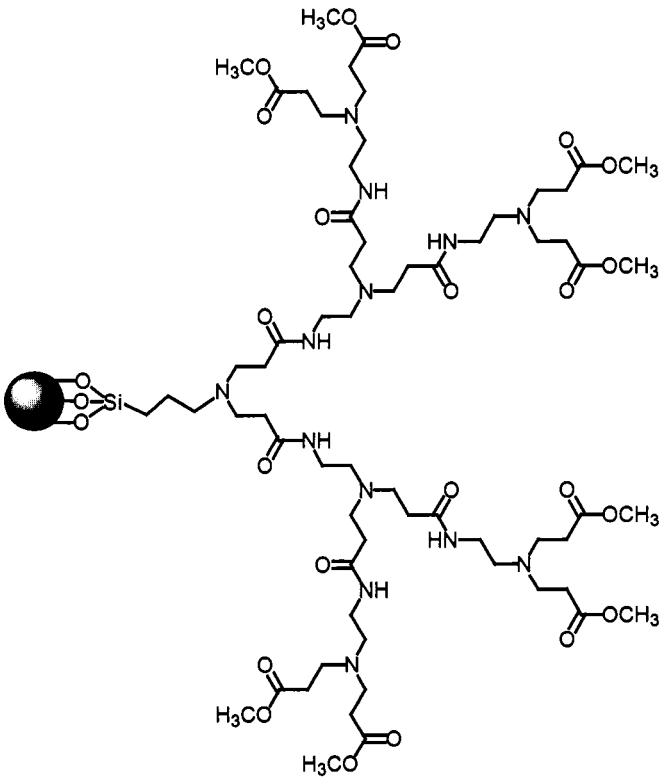
Synthesis of G2: Amine-Terminated Dendrimer 5



5

Ethylenediamine (100 ml, 1.5 mol) was slowly added to a suspension of PAMAM dendrimer **4** (5 g) in dry methanol (100 ml). The mixture was stirred at room temperature under N_2 for 7 days. The liquid was decanted. The mixture was then washed with methanol (30 ml) and transferred to a Soxhlet apparatus. The residual diamine was extracted with methanol over 3 days. The resulting second-generation dendrimer was washed with dichloromethane and then dried *in vacuo* to give 4 g of product.

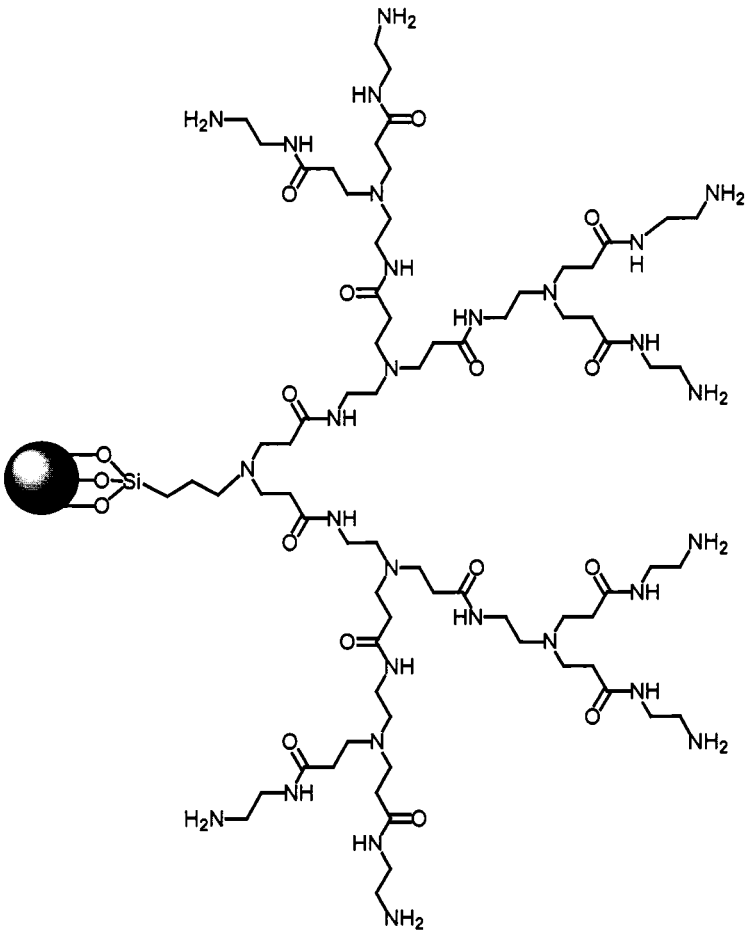
Synthesis of G2.5: Ester-Terminated Dendrimer 6



6

Methyl acrylate (60 ml, 670 mmol) was added to a suspension of 15 g of PAMAM dendrimer **5** in dry methanol (100 ml). The procedure used for the preparation of PAMAM dendrimer **4** was followed. 14.8 g of dendrimer was obtained.

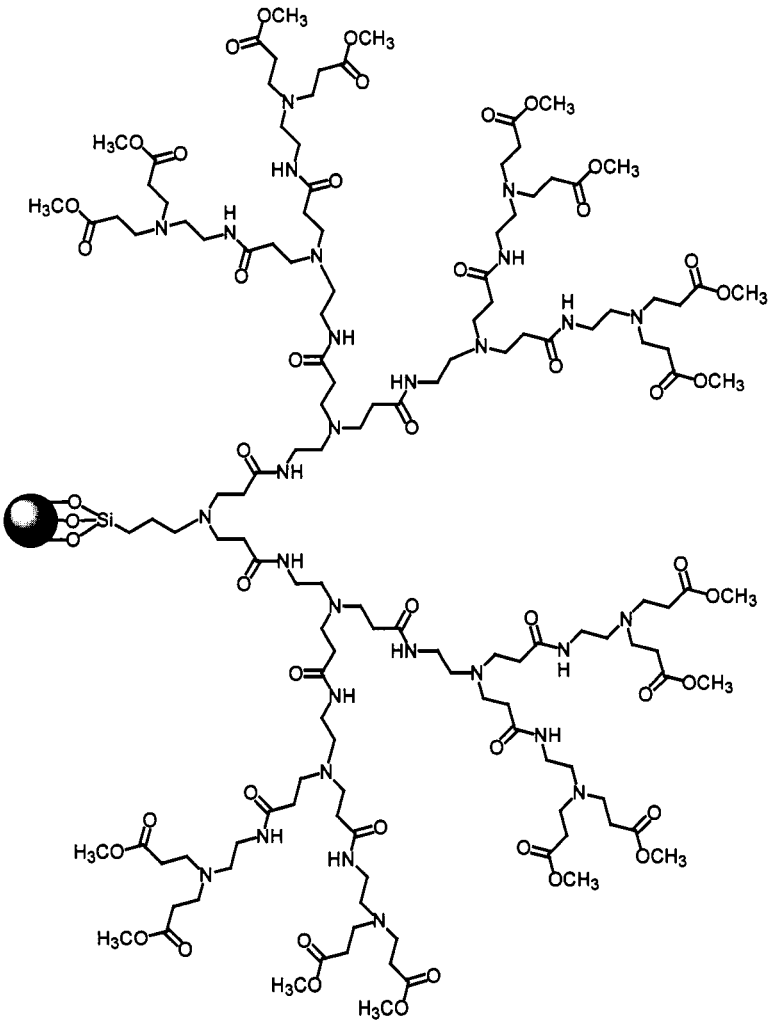
Synthesis of G3: Amine-Terminated Dendrimer 7



7

Ethylenediamine (150 ml, 2.2 mol) was slowly added to a suspension of 14.8 g of PAMAM dendrimer **6** in dry methanol (150 ml). The procedure used for the preparation of PAMAM dendrimer **5** was followed. 14 g of dendrimer was isolated.

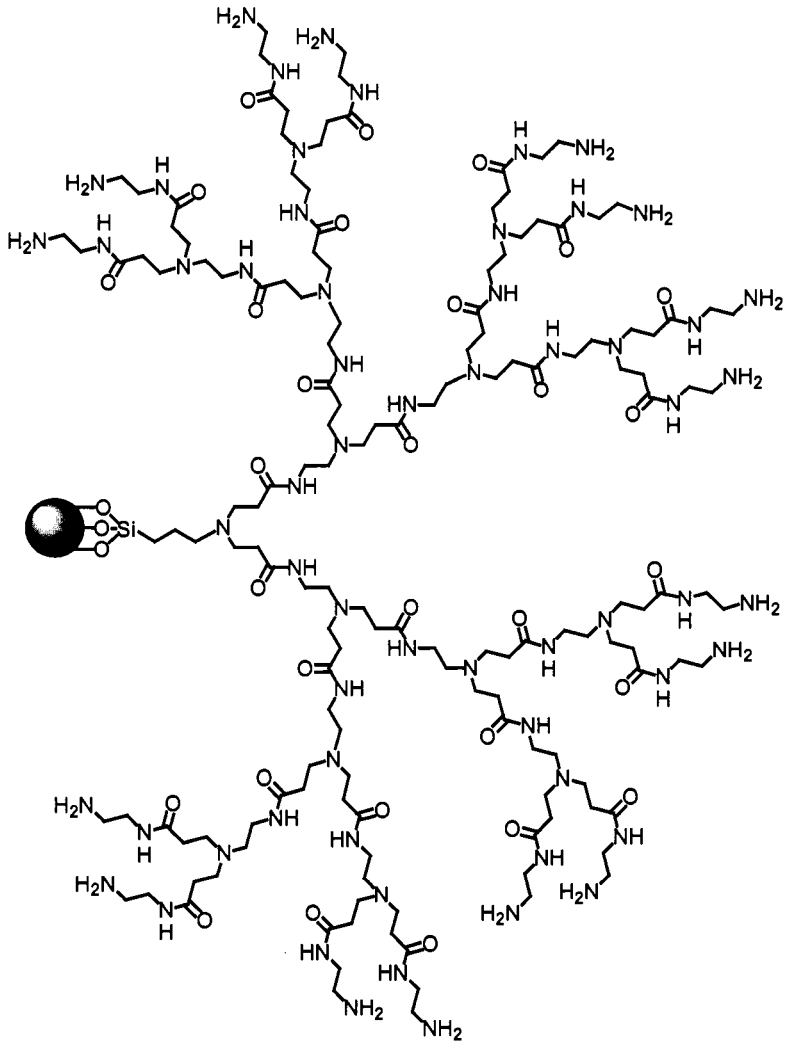
Synthesis of G3.5: Ester-Terminated Dendrimer 8



8

Methyl acrylate (60 ml, 670 mmol) was added to a suspension of 5 g of PAMAM dendrimer **7** in dry methanol (100 ml). The procedure used for the preparation of PAMAM dendrimer **4** was followed and afforded 3.9 g of solid.

Synthesis of G4: Amine-Terminated Dendrimer 9

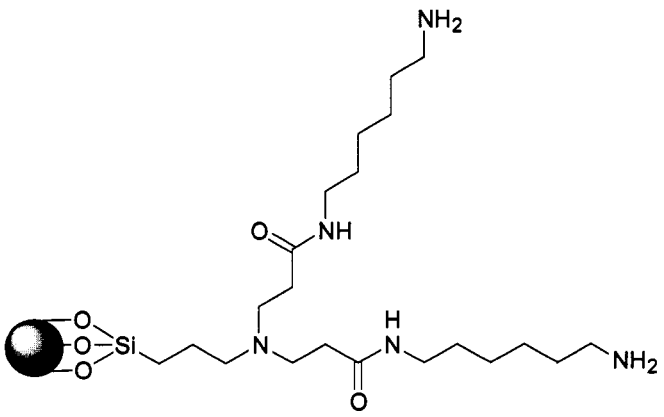


9

Ethylenediamine (100 ml, 1.5 mol) was slowly added to a suspension of 4.8 g of PAMAM dendrimer **8** in dry methanol (100 ml). The procedure used for the preparation of PAMAM dendrimer **5** was followed and gave 4 g of dendrimer.

2.2.2 Synthesis of PAMAM Dendrimers with Diaminohexane

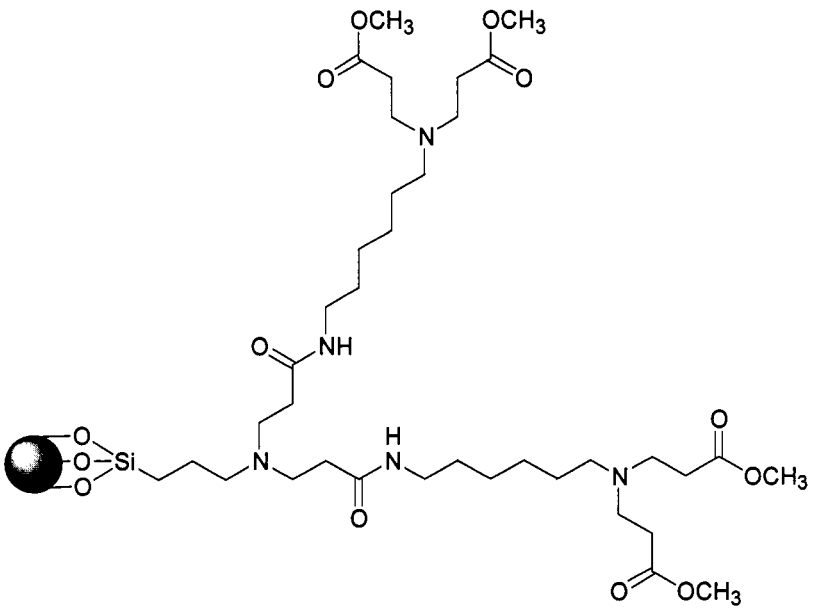
Synthesis of G1: Amine-Terminated Dendrimer 10



10

1,6-Diaminohexane (22.9 g, 197 mmol) in dry methanol (100 ml) was slowly added to a suspension of 10 g of methyl propylaminopropionate **2** in dry methanol (50 ml). The mixture was stirred at room temperature under N_2 for 7 days. The liquid was decanted. The mixture was then washed with methanol (30 ml) and transferred to a Soxhlet apparatus. The residual diamine was extracted with methanol over 3 days. The resulting first-generation dendrimer was washed with diethyl ether and then dried *in vacuo* to afford 9.4 g of product.

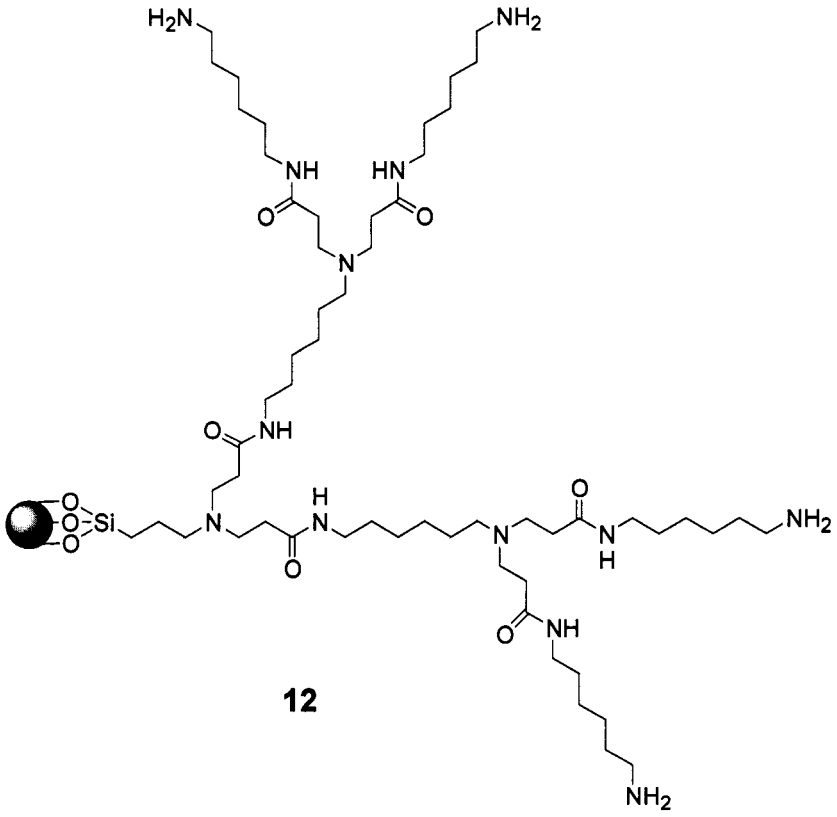
Synthesis of G1.5: Ester-Terminated Dendrimer 11



11

Methyl acrylate (12.4 ml, 138 mmol) was added to a suspension of 5 g of PAMAM dendrimer **10** in dry methanol (100 ml). The procedure used for the preparation of PAMAM dendrimer **4** was followed, with the exception that the temperature was raised to 45 °C and afforded 4.58 g of dendrimer.

Synthesis of G2: Amine-Terminated Dendrimer 12

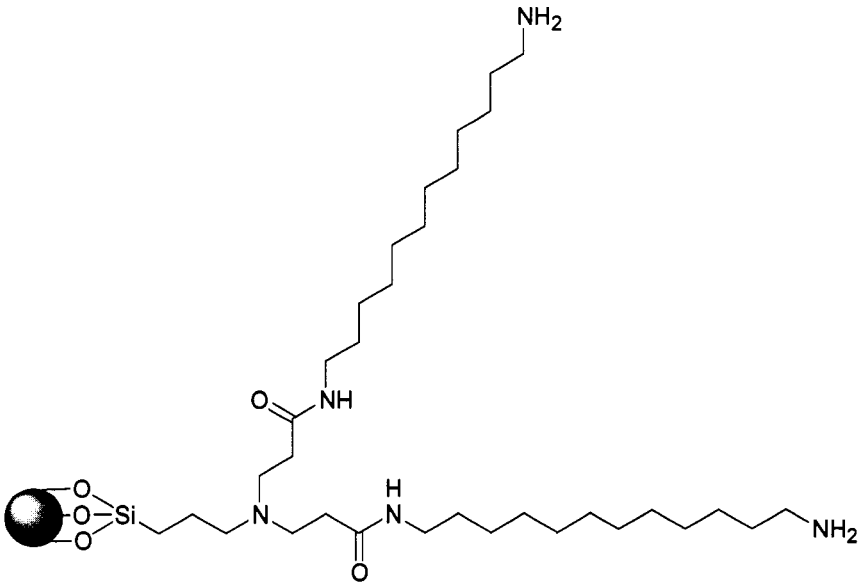


12

1,6-Diaminohexane (12.42 g, 107 mmol) in dry methanol (50 ml) was slowly added to a suspension of 4 g of PAMAM dendrimer **11** in dry methanol (100 ml). The mixture was stirred at room temperature under N_2 for 7 days. The liquid was decanted. The mixture was then washed with methanol (30 ml) and transferred to a Soxhlet apparatus. The residual diamine was extracted with methanol over 5 days. The resulting first-generation dendrimer was washed with diethyl ether and then dried *in vacuo* to give 3.78 g of product.

2.2.3 Synthesis of PAMAM Dendrimers with Diaminododecane

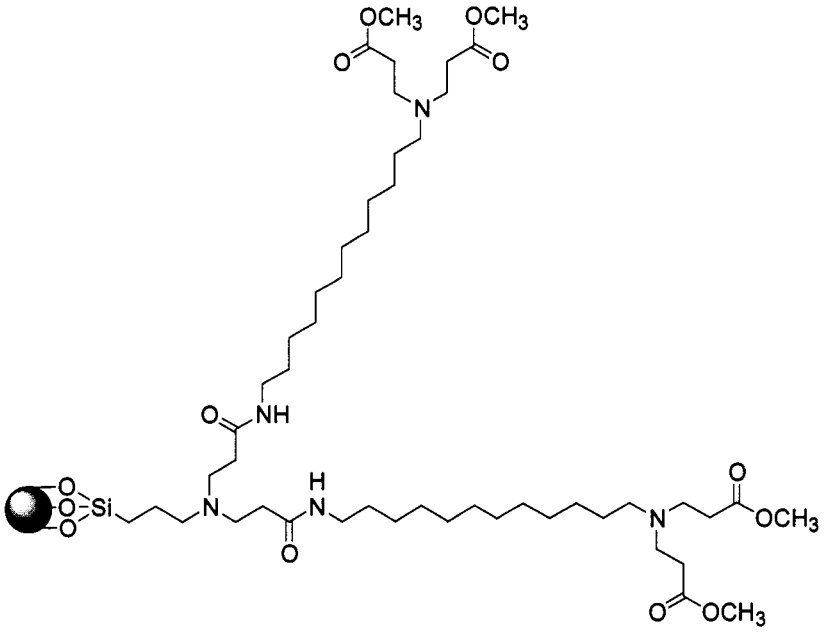
Synthesis of G1: Amine-Terminated Dendrimer 13



13

1,12-Diaminododecane (3 g, 15 mmol) in dry methanol (50 ml) was slowly added to 2 g of methyl propylaminoproprionate silica gel **2** in dry methanol (50 ml). The mixture was stirred at room temperature under nitrogen for 7 days. The liquid was decanted. The mixture was then washed with methanol (30 ml) and transferred to a Soxhlet apparatus. The residual diamine was extracted with methanol over 3 days. The resulting first-generation dendrimer was washed with diethyl ether and then dried *in vacuo* to give 2 g of product.

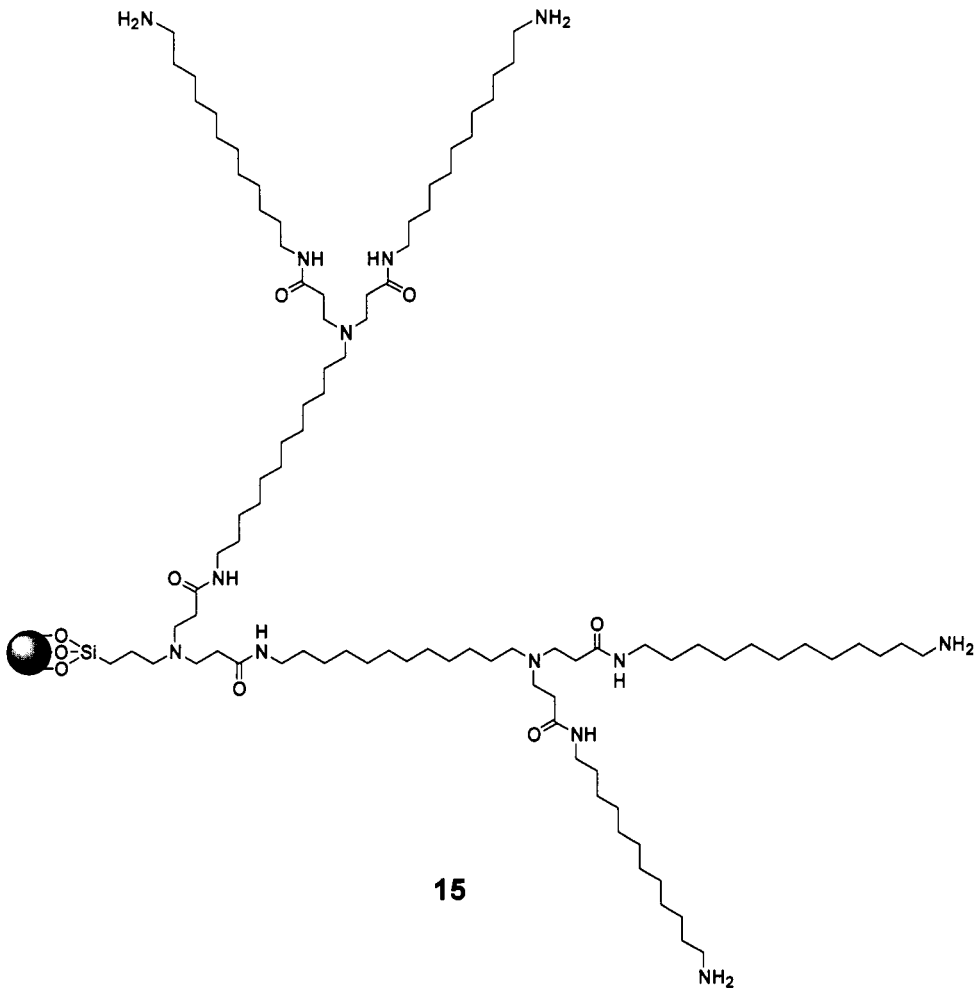
Synthesis of G1.5: Ester-Terminated Dendrimer 14



14

Methyl acrylate (4.4 ml, 49 mmol) was added to a suspension of 2 g of PAMAM dendrimer **13** in dry methanol (100 ml). The procedure used for the preparation of PAMAM dendrimer **4** was followed, except that the temperature was raised to 45 °C, and gave 1.74 g of dendrimer.

Synthesis of G2: Amine-Terminated Dendrimer 15



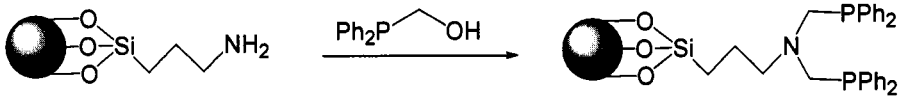
15

1,12-Diaminododecane (7.32 g, 36.5 mmol) in dry methanol (50 ml) was slowly added to a suspension of 1.5 g of PAMAM dendrimer **14** in dry methanol (100 ml). The mixture was stirred at room temperature under nitrogen for 7 days. The liquid was decanted. The mixture was then washed with methanol (30 ml) and

transferred to a Soxhlet apparatus. The residual diamine was extracted with methanol over 5 days. The resulting first-generation dendrimer was washed with diethyl ether and then dried *in vacuo* to afford 1.45 g of product.

2.3 PHOSPHOMETHYLATION OF AMINE-TERMINATED DENDRIMERS

Preparation of Compound 16

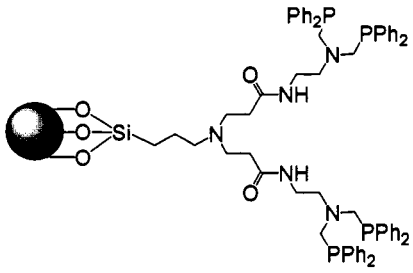


1 **16**

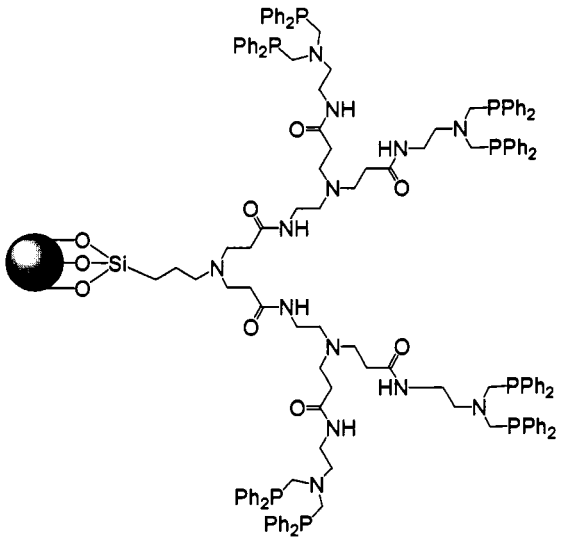
Scheme 2.3 Phosphomethylation of Aminopropylsilica

Diphenylphosphinomethanol[4, 5] was generated *in situ* by stirring diphenylphosphine (10 g, 53.7 mmol) and paraformaldehyde (1.20 g, 40 mmol) at 120 °C for 90 minutes. The pale yellow solution was then cooled to room temperature. Aminopropyl silica gel **1** (2.95 g, 2.65 mmol), dry methanol (10 ml) and anhydrous toluene (25 ml) were added to the reaction flask. The mixture was stirred at 120 °C under N_2 for 2 days. The liquid was decanted after cooling to room temperature. The product was washed with degassed dry methanol (3 x 10 ml) and anhydrous diethyl ether (2 x 10 ml) using a cannula. The residual solvent

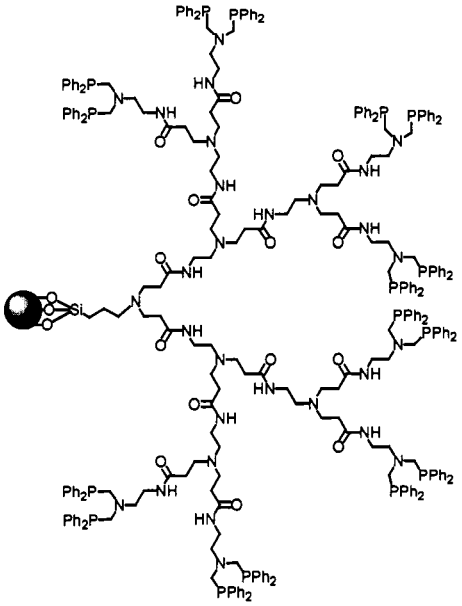
was removed *in vacuo* to afford 2.87 g of a pale yellow solid. ^{31}P CPMAS (200 MHz): -28 ppm.



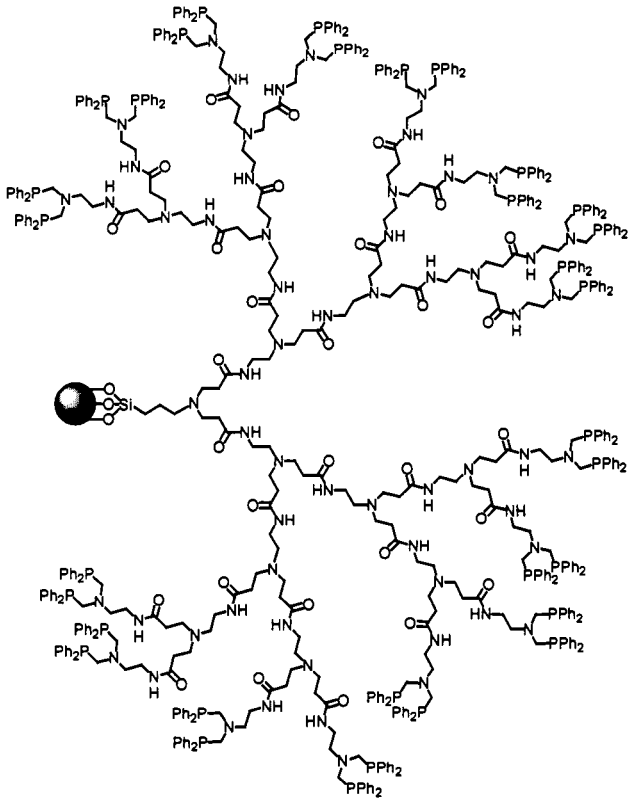
17



18



19



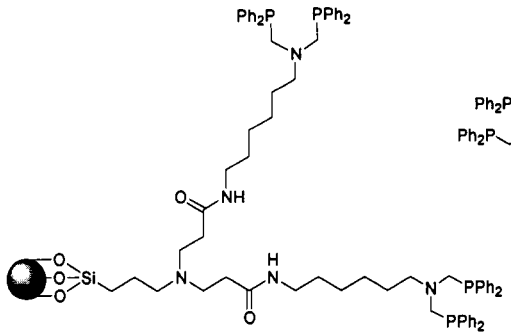
20

Preparation of Dendrimers 17 – 24

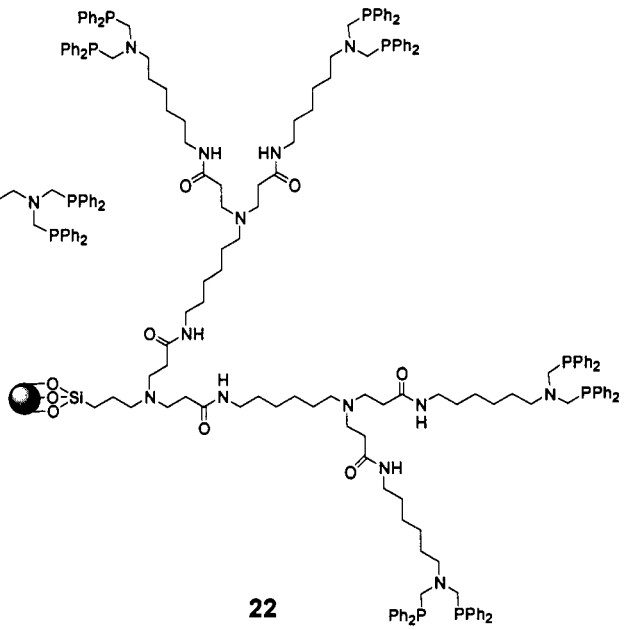
The procedure described for the synthesis of the diphenylphosphino dendrimer **16** was followed, except that the amount of amine-terminated dendrimer and the reaction time were changed. The parameters used were:

1st Generation Dendrimers	2 g	3 days
2nd Generation Dendrimers	1 g	5 days
3rd & 4th Generation Dendrimers	0.5 g	7 days

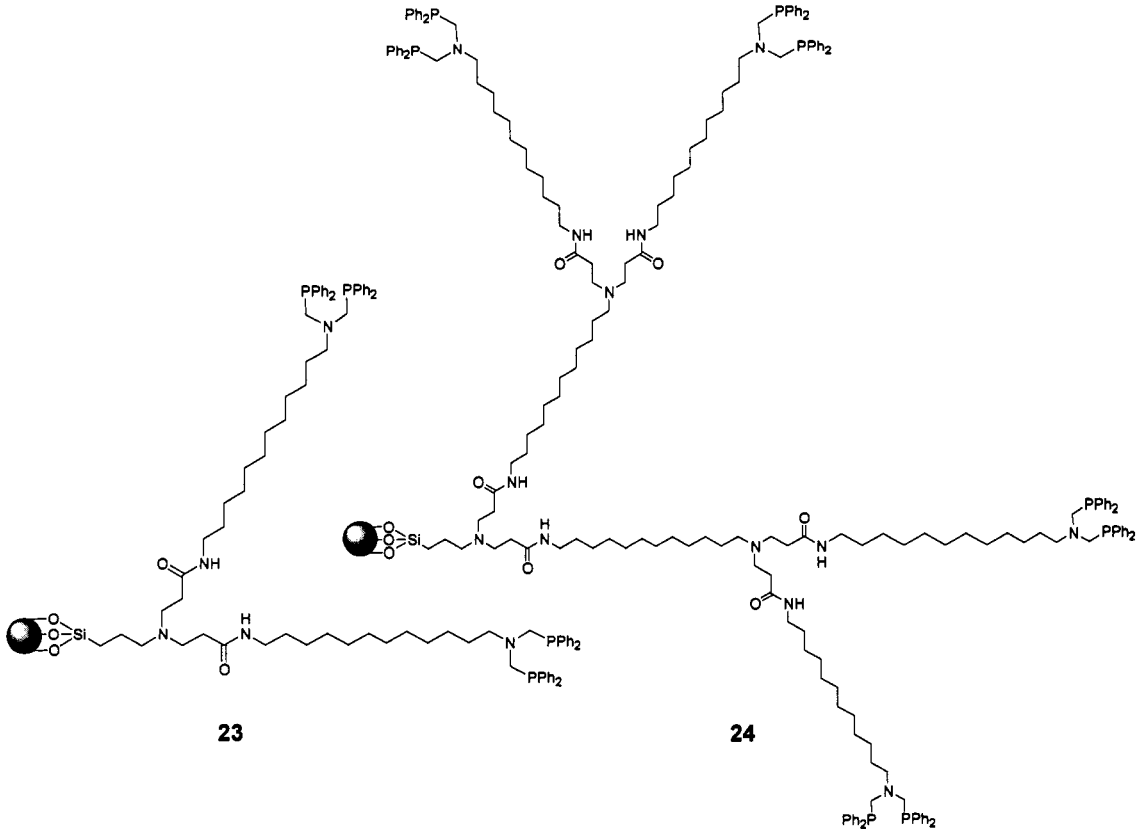
^{31}P CPMAS (200 MHz): -25 to -29 ppm



21



22



23 24

2.4 CHARACTERIZATION OF DENDRIMER LIGANDS

2.4.1 Titration

The extent of dendrimer growth for the C2 series was assessed by performing a back titration with NaOH to determine the amine content as reported by Tsubokawa and co-workers.[6] The amine content obtained for the first generation is similar to the theoretical value (Table 2.1, entry 2). The second-generation dendrimer gave a comparable amine content, while the third generation

dendrimer displayed relatively low amine content (Table 2.1, entries 3 - 4). This is an indication of a slow-down in dendrimer growth probably due to steric congestion.

Table 2.1 Determination of the amine content by titration for the C2*

Entry	Generation	Theoretical (mmol NH_2 / g)	Actual (mmol NH_2 / g)
1	0	0.9	0.8
2	1	1.5	1.4
3	2	2.2	1.8
4	3	3.5	1.4

C2* means that ethylenediamine was used for the amidation step of the dendrimer growth.

2.4.2 Thermal Gravimetric Analysis (TGA)

Sample preparation involved purging the sample with compressed air. For the initial temperature program, the sample was heated from ambient temperature to 110 °C at a rate of 5 °C/min. The temperature was held at 110 °C for 3 min. For the second temperature program, heating from 110 to 900 °C was done at 20 °C/min. The sample was held at 900 °C for 10 min and then purged with oxygen at a flow rate of 10 ml/min.

TGA results showed complete growth for the construction of the first generation dendrimer with an ethylenediamine backbone (Table 2.2, entry 1). In line with the results observed in the titration studies, the amount of grafted material decreased at higher generations (Table 2.2, entries 2 – 4). By comparing the first generation dendrimers with different spacer lengths, a decrease in the amount of grafted dendrimer was observed with the longer chains (Table 2.2, entries 1, 5 and 6). It can be deduced that the amidation step is less efficient with the longer chain diamine. This could be due to the fact that the diamines with long chains are less soluble and less reactive than the ones with short chains.

Table 2.2 BET measurements and TGA results

Entry	Dendrimer	SA (m^2 / g)	PV (cm^3 / g)	% grafted
1	G1-C2, **3**	229	0.514	92
2	G2-C2, **5**	133	0.310	72
3	G3-C2, **7**	53	0.146	58
4	G4-C2, **9**	36	0.086	52
5	G1-C6, **10**	238	0.534	61
6	G1-C12, **13**	245	0.550	56

The initial amine content of aminopropyl silica used was 0.9 mmol/g. SA= Surface area. PV = pore volume.

The Brunauer-Emmett-Teller (BET) method was used to determine the surface area and pore volume of amine-terminated dendrimers. By comparing the

dendrimers containing the same spacer, we observed a decrease in surface area with the increase in generation number (Table 2.2, entries 1-4). There was a slight variation in the surface area of dendrimers of the same generation, but with different spacer lengths (Table 2.2, entries 1, 5 and 6). G1-C12 has the highest surface area while G1-C2 has the lowest, which shows that the different spacer lengths exhibit different surface properties. The pore volume also changed in an analogous manner.

2.4.3 Solid State ^{31}P NMR

The phosphine content was determined by solid state ^{31}P NMR using methyltriphenylphosphonium bromide as the internal standard (Table 2.3).[7] The phosphomethylation step does not go to completion. At most, about 50 % of the amines were phosphomethylated by this method. What was interesting was that the phosphine content increased with the increase in the spacer length of the dendrimer i.e. C2 < C6 < C12.

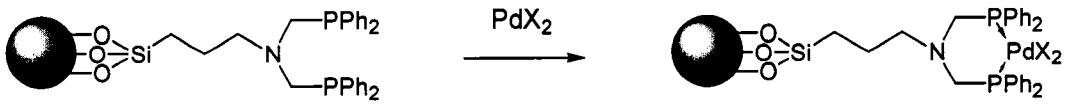
Table 2.3 Phosphine content determined by ^{31}P NMR

Entry	Dendrimer	Compound	(mmol PPh_2 / g)
1	G0-C2-PPh_2	**16**	0.45
2	G1-C2-PPh_2	**17**	0.57
3	G2-C2-PPh_2	**18**	0.42
4	G3-C2-PPh_2	**19**	0.11
5	G1-C6-PPh_2	**20**	0.68
6	G1-C12-PPh_2	**24**	0.79

C# refers to the chain length of diamine used for the amidation step of the dendrimer growth.

2.5 Preparation of PAMAM – Palladium Complexes

A general procedure was developed for the complexation of the different generations of diphenylphosphino dendrimers **16.** It is described in detail for the synthesis of the complex **25** from the dendrimer **16**.



X =	Cl	**25**
	OAc	**26**
	PPh_3	**27**
X_2 =	dba	**28**

Scheme 2.4 Complexation Step

Synthesis of Complex 25

$PdCl_2(PhCN)_2$ (256 mg, 667 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **16** (1.0 g) in dry toluene (10 ml) *via* cannula. The resulting mixture was stirred at room temperature under N_2 for 18 hrs. The solvent was decanted and the solid product was washed with DMF (3 x 10 ml) followed by diethyl ether (3 x 5 ml). After drying, a brown powder was obtained (897 mg).

Synthesis of Complex 26

$Pd(OAc)_2$ (15.4 mg, 69 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **16** (1.0 g) in dry toluene (10 ml). A pale green solid was obtained (938 mg).

Synthesis of Complex 27

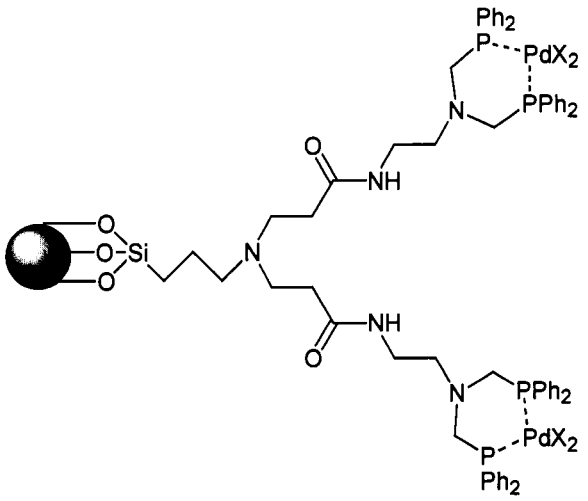
$Pd(PPh_3)_4$ (50 mg, 43 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **16** (470 mg) in dry toluene (10 ml). A brown solid was obtained (410 mg).

Synthesis of Complex 28

$Pd_2(dba)_3{\cdot}CHCl_3$ (60.0 mg, 116 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **16** (1.0 g) in dry toluene (10 ml). An orange solid was obtained (927 mg).

Synthesis of Complex 29

$PdCl_2(PhCN)_2$ (364 mg, 949 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **17** (1.0 g) in dry toluene (10 ml). A brown solid was obtained (1.1 g).



X =	Cl	**29**
	OAc	**30**
X_2 =	dba	**31**

Synthesis of Complex 30

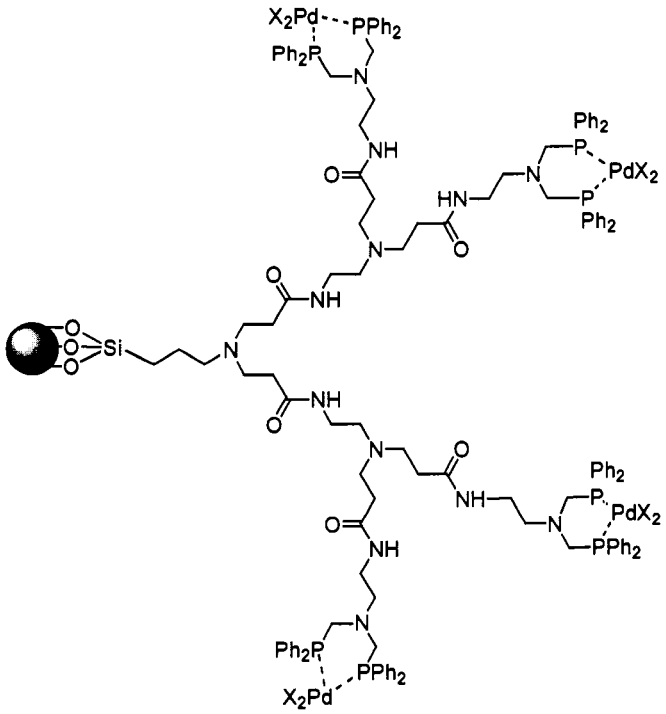
$Pd(OAc)_2$ (217 mg, 967 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **17** (1.0 g) in dry toluene (10 ml). A greenish-brown solid was obtained (673 mg).

Synthesis of Complex 31

$Pd_2(dba)_3 \cdot CHCl_3$ (74.1 mg, 143 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **17** (550 mg) in dry toluene (10 ml). A pale yellow solid was obtained (421 mg).

Synthesis of Complex 32

$PdCl_2(PhCN)_2$ (313 mg, 816 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **18** (686 mg) in dry toluene (10 ml). A brown solid was obtained (690 mg).



X = Cl **32**

OAc **33**

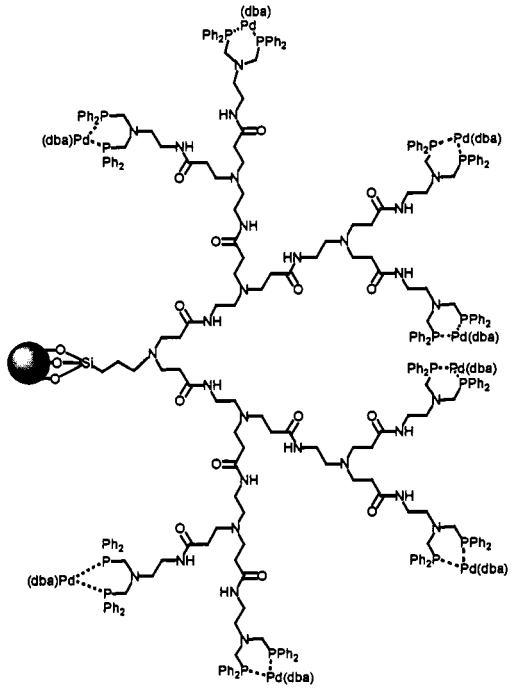
X_2 = dba **34**

Synthesis of Complex 33

$Pd(OAc)_2$ (65.9 mg, 294 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **18** (254 mg) in dry toluene (10 ml). A greyish brown solid was obtained (243 mg).

Synthesis of Complex 34

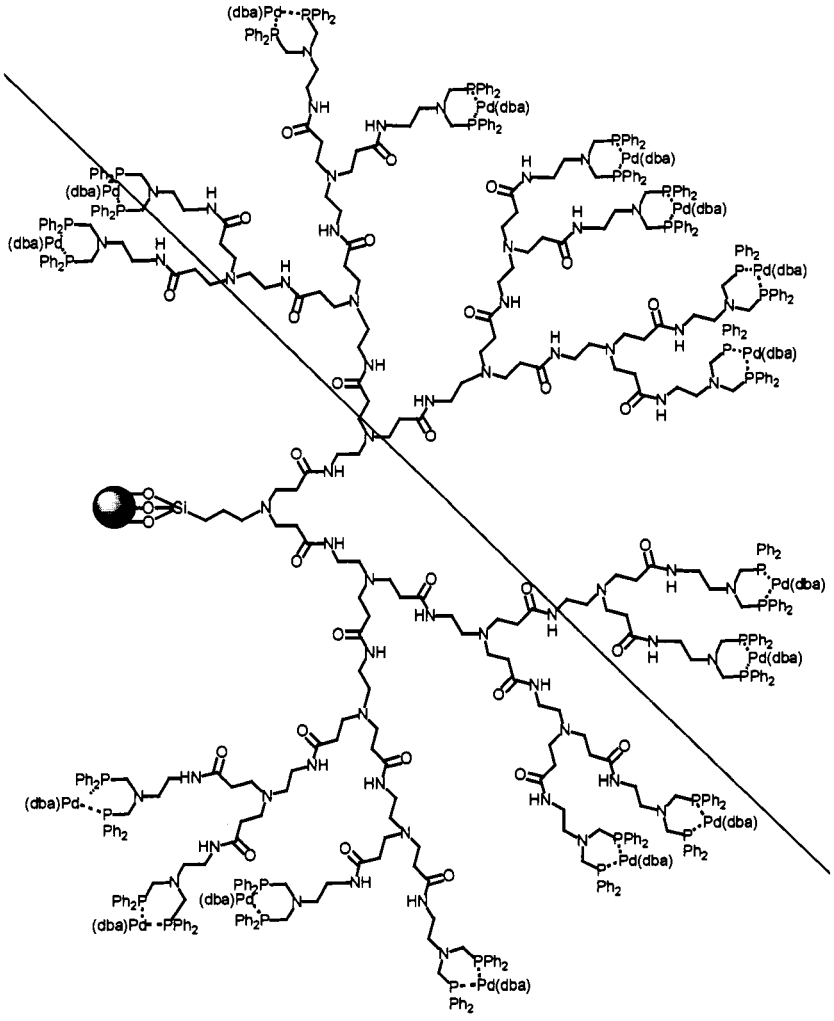
$Pd_2(dba)_3 \cdot CHCl_3$ (54.0 mg, 104 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **18** (800 mg) in dry toluene (10 ml). An orange powder was obtained (742 mg).



35

Synthesis of Complex 35

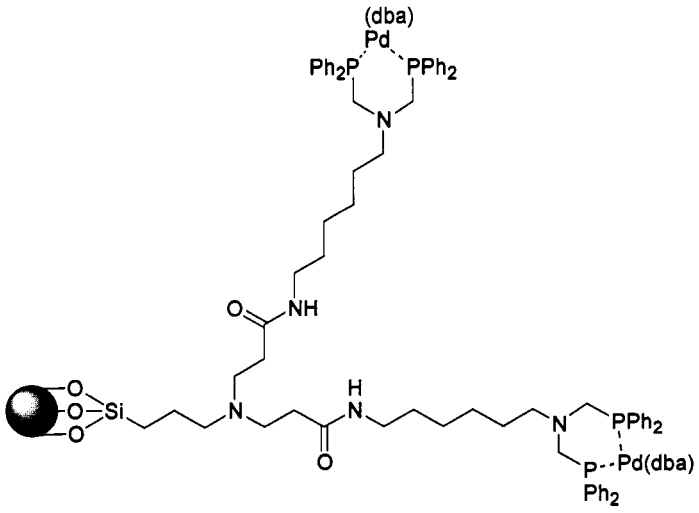
$Pd_2(dba)_3 \cdot CHCl_3$ (58.0 mg, 112 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **19** (500 mg) in dry toluene (10 ml). An orange powder was obtained (420 mg).



36

Synthesis of Complex 36

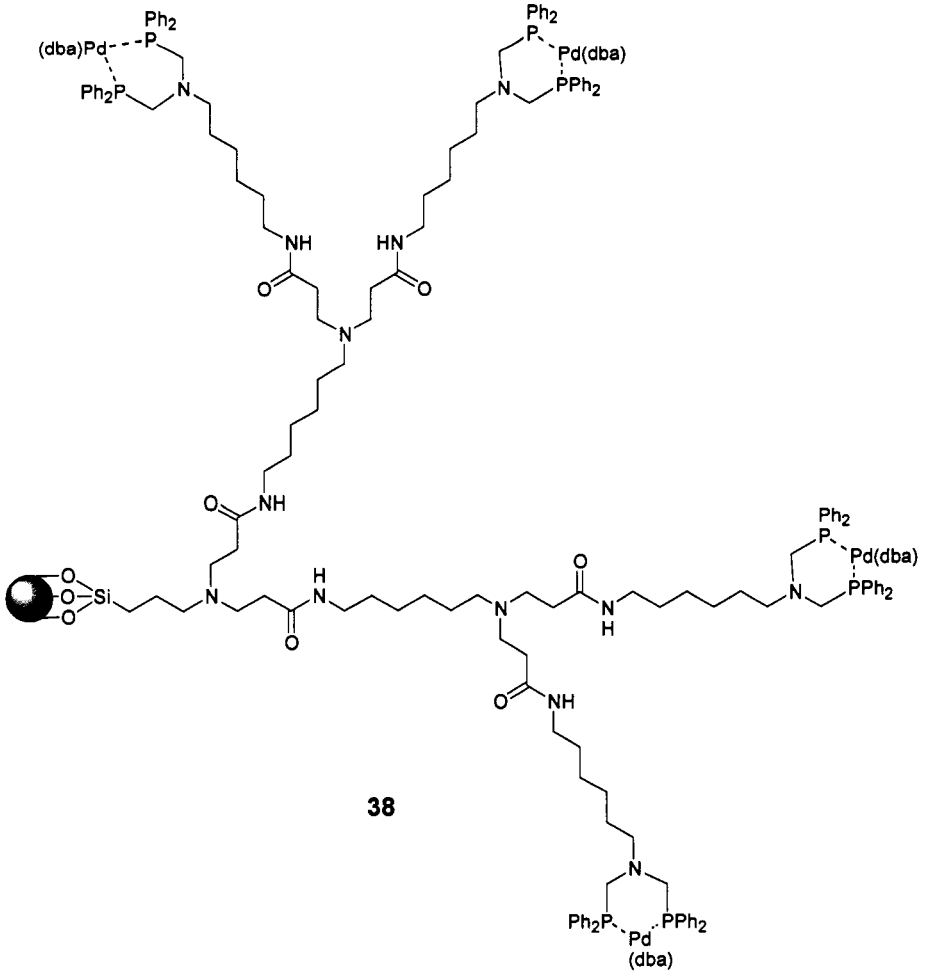
$Pd_2(dba)_3{\cdot}CHCl_3$ (25.6 mg, 112 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **20** (200 mg) in dry toluene (10 ml). An orange powder was obtained (160 mg).



37

Synthesis of Complex 37

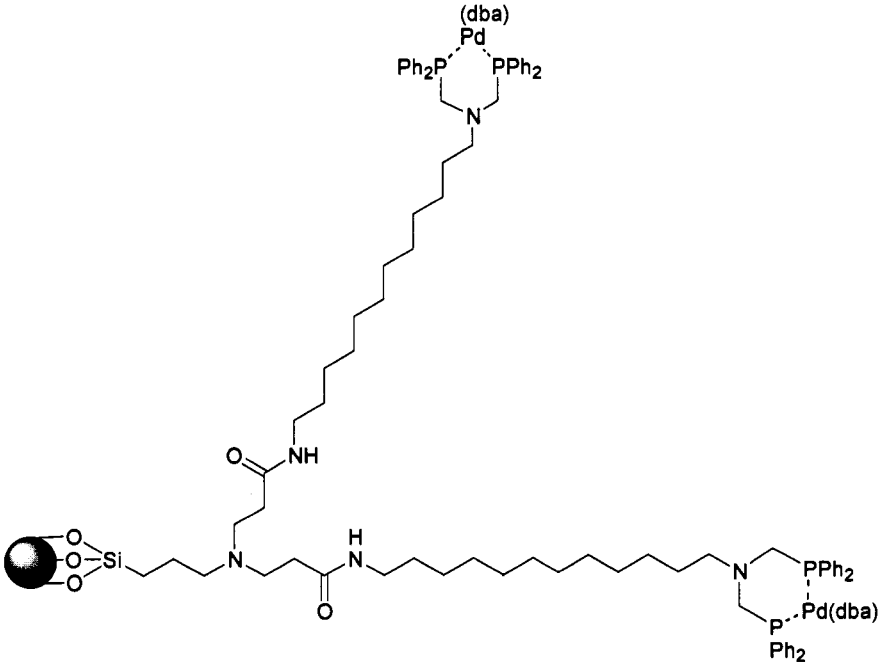
$Pd_2(dba)_3{\cdot}CHCl_3$ (59 mg, 114 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **21** (1.0 g) in dry toluene (10 ml). An orange powder was obtained (850 mg).



38

Synthesis of Complex 38

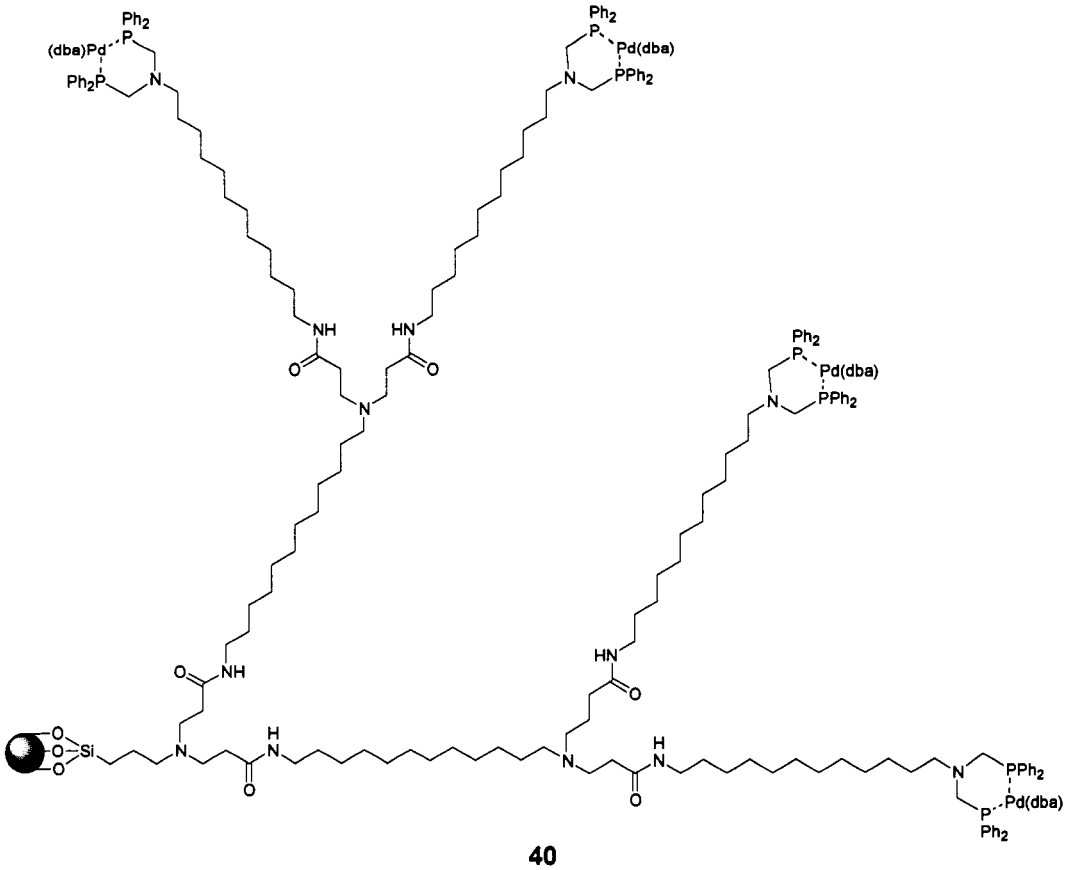
$Pd_2(dba)_3{\cdot}CHCl_3$ (102 mg, 197 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **22** (1.0 g) in dry toluene (10 ml). A reddish-brown powder was obtained (880 mg).



39

Synthesis of Complex 39

$Pd_2(dba)_3{\cdot}CHCl_3$ (60 mg, 116 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **23** (1.0 g) in dry toluene (10 ml). A reddish-brown powder was obtained (790 mg).



40

Synthesis of Complex 40

$Pd_2(dba)_3{\cdot}CHCl_3$ (100 mg, 193 μmol Pd) was dissolved in dry toluene (15 ml) in a Schlenk flask. This solution was added in small aliquots to a stirred suspension of the diphenylphosphino dendrimer **24** (1.0 g) in dry toluene (10 ml). A reddish-brown powder was obtained (1.01 g).

2.6 ICP Analysis

The Pd content was analyzed by ICP and the results are presented in Table 2.4. The determined metal loadings for these complexes were less than the expected values. The amount of Pd decreased with the increase in generation number. The growth defects caused by incomplete reactions were responsible for this phenomenon. The slight improvement in the Pd loading of the longer chain dendrimers is attributed to the higher phosphine content of these dendrimers **(Section 2.4.3).**

Table 2.4 Determination of Pd content by ICP

Entry	Generation	Complex	Pd (%)
1	0	**28**	0.86
2	G1-C2	**31**	1.13
3	G2-C2	**34**	0.80
4	G3-C2	**35**	0.59
5	G1-C6	**37**	1.52
6	G1-C12	**39**	1.72

Complexes prepared with the chloroform adduct of $Pd_2(dba)_3$.

2.7 REFERENCES

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Chapter Four

SELECTIVE HYDROGENATION OF DIENES TO MONOOLEFINS

4.1 INTRODUCTION

The catalytic selective hydrogenation of multiple unsaturated hydrocarbons can be used for synthetic and non-synthetic purposes. An example of its use is the production of flavour components, hexen-1-ol and methyl *trans*-2-hexenoate, from their parent diene compounds.[1]

For non-synthetic purposes, selective hydrogenation is used to remove dienes and other polyunsaturated hydrocarbons from alkene feedstocks. van Leeuwen showed that the presence of impurities such as alkynes, dienes and enones in alkene feedstocks can bring about deactivation in certain catalytic reactions.[2, 3] In general, the insertion of dienes to metal complexes is faster than the insertion of alkenes. Dienes tend to deactivate the catalyst by forming π-allyl species that are often inactive as catalysts. For example, in rhodium catalyzed hydroformylation, the presence of alkynes in the reaction medium can result in irreversible deactivation, while dienes simply slow down the reaction, and enones cause temporary inactivity. The removal of these impurities from alkene feedstocks is crucial for extending the catalyst lifetime. Moreover, as the alkene is often hydrogenated as well, the challenge is to find a catalytic system that can remove these minute impurities without affecting the alkene feedstocks.

The few examples of homogeneously catalyzed selective hydrogenation of dienes include the work of Dupont and co-workers. They used $Pd(acac)_2$ dissolved in the ionic liquid 1-*n*-butyl-3-methylimidazolium tetrafluoroborate ($BMIM.BF_4$).[4] Simple and functionalized dienes were transformed to their corresponding monoenes at 50 °C and 5 – 20 atm in selectivities ranging from 93 to 100 %.

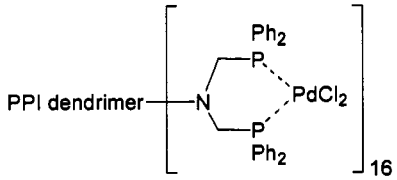


Figure 4.1 PPI- Pd Complex

Kaneda and co-workers demonstrated that the dendrimer-bound palladium complex of phosphonated poly(propyleneimine) (Figure 4.1) can selectively hydrogenate conjugated cyclic dienes to monoenes.[5] The dendrimer complex gave better results than the monomeric catalyst $[PhN(CH_2PPh_2)_2PdCl_2]$. The proposed reaction mechanism involves a Pd-H species. The equation of the reaction rate indicated that the presence of bases should speed up the reaction. The superior results obtained with the dendrimer complex were attributed to the fact that the large number of basic amino groups accelerated the reaction.

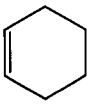
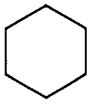
The need for more selective hydrogenation catalysts coupled with the successful application of supported Pd catalysts in hydrogenation reactions prompted us to investigate the catalytic performance of our silica supported palladium based dendrimers (**25, 31, 37 – 40**) for the selective hydrogenation of dienes to monoenes. We wanted to determine if these catalysts would display a positive or negative dendritic effect in activity and selectivity. It was our hope to transform the dienes to monoenes without any deleterious effect on the monoenes formed during the reaction. We were also interested in recycling these complexes.

4.2 Results and Discussion

Our goal was to carry out the hydrogenation reactions under mild conditions. For the optimization of the reaction conditions 1,3-cyclohexadiene and complex **25** were used as the model reaction. Since the solvent usually has an effect on the selectivity of hydrogenation reactions, we started our investigation by testing different solvents (Table 4.1). Three alcohols were screened, methanol, ethanol and isopropanol. The highest selectivity was observed using methanol, and the lowest was observed with isopropanol. Activity was highest for isopropanol and lowest for methanol. Reasonable selectivity and good activity was obtained in dichloromethane, while in acetonitrile and ethyl acetate, lower activities and selectivities were found. Since selectivity took priority over activity, methanol was used for subsequent reactions. Parameters such as temperature, pressure and

catalyst loading were also examined. A decrease in temperature and pressure led to a lower activity, but there was no effect in monoene selectivity. Increasing the substrate to catalyst ratio by a factor of ten resulted in a maximum conversion of 20 % even after prolonged reaction times.

Table 4.1 Effect of solvent on the hydrogenation of 1,3-cyclohexadiene

Entry	Solvent	Time (mins)	Conv (%)	(%) 	
1	Methanol	30	20	>99	-
2		150	>99	76	24
3	Ethanol	30	57	75	25
4		60	>99	68	32
5	Isopropanol	30	83	68	32
6		35	>99	62	38
7	Dichloromethane	30	38	80	20
8		70	>99	73	27

Reaction conditions: 0.5 ml Substrate, 50 mg Complex **25**, 5 ml MeOH, pressurized glass autoclave to 14 psi H_2, 25 °C.

After establishing the optimum conditions, we proceeded to examine the catalytic performance of the various dendrimer complexes **31, 37 – 40**. Cyclohexene was the major product for the hydrogenation of the 1,3-cyclohexadiene. Cyclohexane

and benzene were minor products using some of these complexes. 1,3-Cyclohexadiene is known to disproportionate to cyclohexene and benzene in the presence of Pd particles. Therefore, the presence of benzene in the product mixture may be an indication of traces of Pd particles within the catalyst matrix.

The G0 complex, **25** showed the highest activity with 76 % selectivity to cyclohexene (Table 4.2, entry 1). The second generation - C12 catalyst, **40,** gave complete conversion after 5 hours (Table 4.2, entry 11), while the other catalysts required 20 hours (Table 4.2, entries 3, 5, 7 and 9). Cyclohexene was the only product for all of the catalysts at conversions below 30%. At higher conversions, alkene formation began to compete with the diene for the active site. Complexes **37** and **38** of the C6 series gave similar activity, but the former afforded better selectivity. For the C12 series, the first generation catalyst is less active than the second generation. The question as to what is responsible for this difference in activity and selectivity is not easy to answer. Nevertheless, from a reaction perspective, one can achieve excellent results.

Table 4.2 Hydrogenation of cyclohexadiene

Entry	Catalyst	Time (hrs)	Conv (%)	(%)		
						
1	G0, **25**	1.75	>99	76	24	-
2	G1-C2, **31**	0.5	21	>99	-	-
3		20	>99	88	10	2
4	G1-C6, **37**	0.5	11	>99	-	0
5		20	72	97	1.5	1.5
6	G1-C12, **39**	0.5	15	>99	-	-
7		20	20	>99	-	-
8	G2-C6, **38**	0.5	N.R	-	-	-
9		20	>99	73	11	6
10	G2-C12, **40**	0.5	24	>99	-	-
11		5	>99	80	14	6

Reaction conditions: 0.5 ml Substrate, 50 mg catalyst, 5 ml MeOH, pressurized to 14 psi H_2, 25 °C.

The hydrogenation of ethyl sorbate catalyzed by $[(^tBu_2PH)PdP^tBu_2]_2$ pre-activated with O_2 gave 70 % methyl 2-hexenoate and 30 % methyl hexanoate.[6] The dendrimer complex **39** was ineffective in catalyzing the hydrogenation of ethyl sorbate. All the other dendrimer – Pd complex catalysts displayed comparable selectivity, i.e. there was no significant sensitivity to catalyst structure for this substrate (Table 4.3).

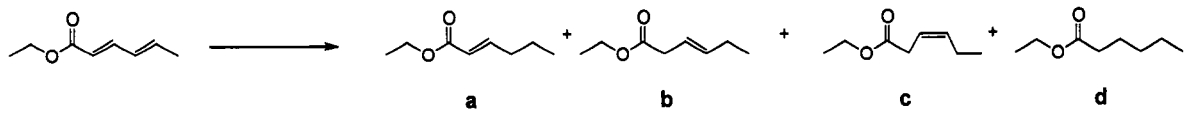


Table 4.3 Hydrogenation of ethyl sorbate

				Distribution (%)			
Entry	**Catalyst**	**Time (min)**	**Conv (%)**	**a**	**b**	**c**	**d**
1	G0, **25**	60	>99	86	4	3	7
2	G1-C2, **31**	150	>99	82	10	7	1
3	G1-C6, **37**	90	>99	77	15	5	3
4	G1-C12, **39**	420	N.R	-	-	-	-
5	G2-C6, **38**	90	>99	81	11	5	3
6	G2-C12, **40**	90	>99	80	10	7	3

Reaction conditions: 760 mg Substrate, 50 mg Catalyst, 5 ml Methanol. Pressurized to glass autoclave to 14 psi H_2, 25 °C.

Since complex **40** showed better activity than the other complexes for the hydrogenation of cyclohexadiene, it was chosen for an experiment where the recycle properties of the catalyst were tested for the hydrogenation of ethyl sorbate. When compared to the G0 catalyst **25**, the G2 complex **40** retained activity and selectivity up to eight runs while **25** began to show a decrease after three runs (Tables 4.4 and 4.5). Complex **40** was therefore shown to be an excellent catalyst for the hydrogenation of ethyl sorbate, with good selectivity for the γ,δ-double bond.

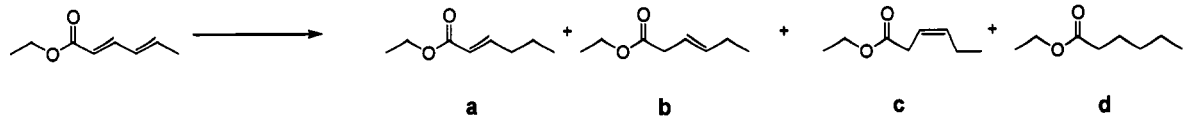


Table 4.4 Recycling of Complex **25** (G0)

G0	Run 1	60 min	86	4	3	7
	Run 2	90 min	79	11	7	3
	Run 3	90 min	75	14	8	3
	Run 4	105 min	77	11	7	5
	Run 5	160 min	63	17	10	10

Reaction conditions: 760 mg Substrate, 50 mg Catalyst, 5 ml Methanol. Pressurized to galss autoclave to 14 psi H_2, 25 °C.

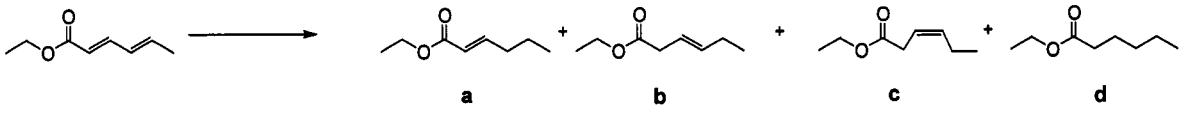


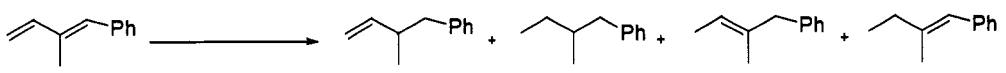
Table 4.5 Recycling of Compex **40** (G2-C12)

G2-C12	Run 1	90 min	80	10	7	3
	Run 2	90 min	81	10	7	1
	Run 3	90 min	79	10	7	4
	Run 4	90 min	81	9	5	5
	Run 5	90 min	82	9	4	5
	Run 6	90 min	81	10	7	2
	Run 7	90 min	75	11	6	8
	Run 8	90 min	73	16	9	2

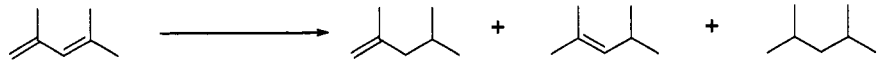
Reaction conditions: 760 mg Substrate, 50 mg Catalyst, 5 ml Methanol. Pressurized to glass autoclave to 14 psi H_2, 25 °C.

For the partial reduction of acyclic dienes, the catalytic activity decreased with the augmentation of the generation number (Table 4.6). The least substituted double bond was selectively reduced during the hydrogenation e.g. 2-methyl-1-phenyl-1,3-butadiene afforded 2-methyl-1-phenyl-1-butene in 52 – 67 % selectivity using complexes **25**, **37**, and **38**. 2,4-Dimethyl-1,3-pentadiene gave almost equal amounts of the two monoene isomers, 2,4-dimethyl-1-pentene and 2,4-dimethyl-2-pentene. For the partial hydrogenation of 3-methyl-1,3-hexadiene, the least substituted double bond was reduced in preference to the more substituted double bond. Up to 81 % selectivity was obtained with complex **37**.

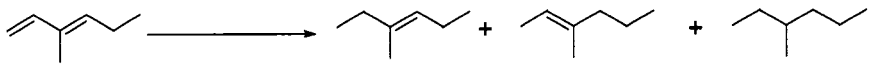
Table 4.6 Hydrogenation of acyclic dienes



25	4 h	>99 %	3	26	19	52
37	6 h	>99 %	3	33	17(1)	46
38	9 h	88 %	10	10	13	67



25	1.5 h	39 %	59 %	2 %
37	1.5 h	48 %	52 %	
38	4 h	43 %	57 %	

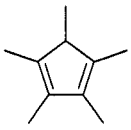
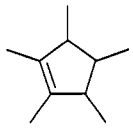
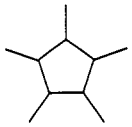


25	1.5 h	68 % (1.3)	21 %	11 %
37	3 h	81 % (1.2)	6 %	13 %
38	9 h	69 % (1.2)	7 %	24 %

Standard reaction conditions: 5.5 mmol Substrate, 50 mg Catalyst, 5 ml Methanol. Pressurized glass autoclave to 14 psi H_2, 25 °C. Number in parenthesis refers to trans to cis ratio

Table 4.7 shows the results for the hydrogenation of cyclic dienes using the complex **25**. 1-Methyl-1,4-cyclohexadiene and 1,2,3,4,5-pentamethyl-1,3-pentadiene were transformed to their corresponding monoenes in selectivities of 83 % and 78 % respectively. Non-conjugated 1,4-cyclohexadiene was converted to cyclohexene in 68 % selectivity.

Table 4.7 Hydrogenation of cyclic dienes

	90min	92%			
			83 %	13 %	4 %
	40min	>99%			
			78 %		22 %
	135min	>99%			
			68 %		32 %
	90min	43%			
			95 %		5 %
	135min	>99%	92 %		8 %
	90min	92%			
			>99 %		-
	120min	>99%	98 %		2 %

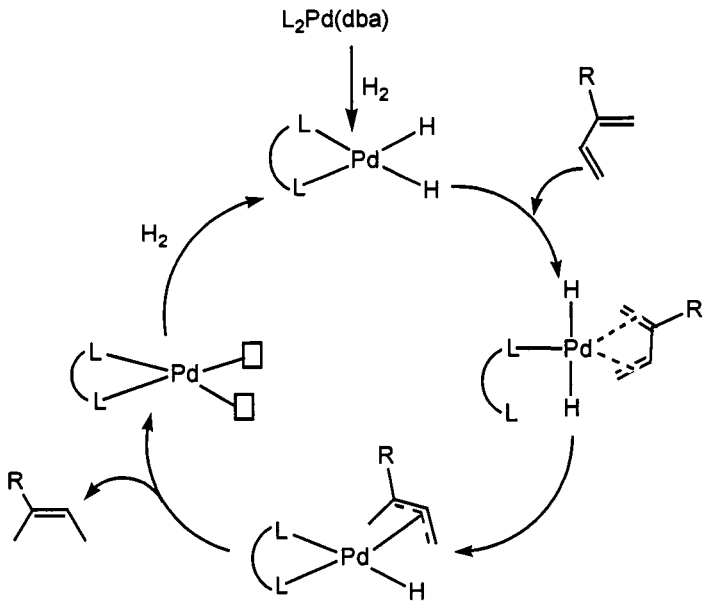
Standard reaction conditions: 0.5 ml Substrate, 50 mg Complex **25**, 5 ml Methanol. Pressurized glass autoclave to 14 psi H_2, 25 °C.

1,3-Cycloheptadiene has been selectively reduced to cycloheptene using SmI_2 / H_2O / amine mixtures in THF in >99 % yield.[7] At least 2.5 equivalents of SmI_2 were required with the reaction operating through a radical mechanism. When complex **25** was used, 92 % of cycloheptene along with 8 % of cycloheptane was

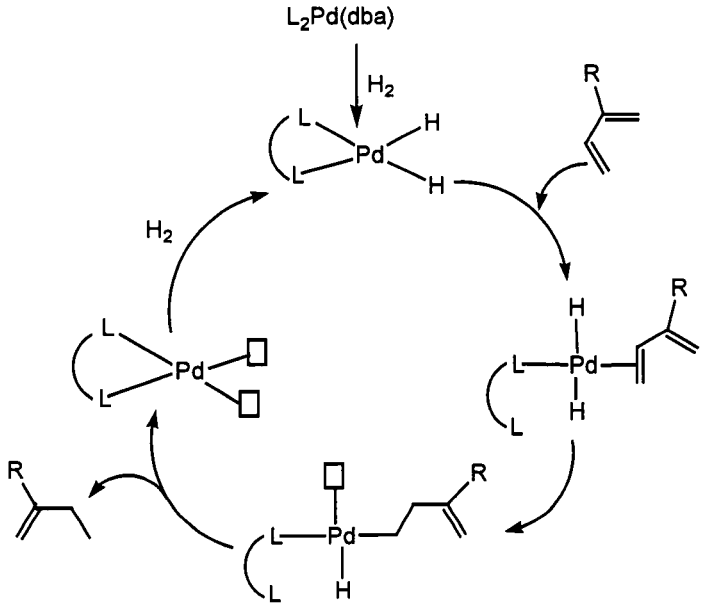
obtained. 1,3-Cyclooctadiene was reduced with 98 % selectivity towards the monoolefin, which is comparable to the result obtained using $[(^tBu_2PH)PdP^tBu_2]_2$ pre-activated with O_2.[6] The cyclic conjugated dienes showed an increase in selectivity in the order $C_6 < C_7 < C_8$ with the complex **25**.

4.3 Proposed Mechanism

Two mechanisms are proposed for this reaction. Both involve the initial generation of a Pd-H species from the reaction of the dendrimer complex with H_2 through oxidative addition. In the first mechanism (Scheme 4.1), the diene coordinates to the metal complex in a η^4- fashion. After the transfer of hydrogen, a Pd-allyl species is formed. It is at this stage that different alkene isomers can be formed because the allyl-Pd species can lead to double bond isomerization. The elimination of the monoene is accompanied by the formation of Pd (0), which upon reaction with H_2 regenerates the active Pd-H species. In the second mechanism, the diene coordinates to the metal complex in an η^2- mode. Here the steric bulk of the diene is a major factor in determining which double bond should coordinate to the metal center. Generally, the less substituted or least bulky unsaturation will preferentially bind to the metal. After monoene expulsion, the Pd-H species can be regenerated.



Scheme 4.1 Proposed Mechanism 1



Scheme 4.2 Proposed Mechanism 2

4.4 CONCLUSIONS

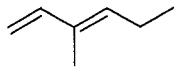
The results described herein show that silica supported PAMAM-palladium complexes can catalyze the hydrogenation of conjugated dienes to olefins in good to excellent selectivity. The higher generation catalysts also display good recycle properties; they could be reused up to eight times without loss in selectivity. This method is superior than the one reported by Dupont as it employs milder reaction conditions.

4.5 EXPERIMENTAL SECTION

4.5.1 Synthesis of Diene Compounds

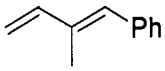
Non-commercially available conjugated dienes were synthesized through a Wittig reaction. n-Butyllitihium as a base gave low conversions, which resulted in poor yields upon isolation due to the volatile nature of the dienes. Gosselin reported a procedure that allowed distilling off of the dienes thereby, affording good yields.[8] This method made use of potassium tertiary butoxide as the base.

4.5.2 Synthesis of 3-Methyl-1,3-hexadiene



Methyltriphenylphosphonium bromide (36.0 g, 0.10 mol) was added to a stirred suspension of potassium tertiary-butoxide (11.33 g, 0.10 mol) in ether (100 ml) under a N_2 atmosphere. The yellow mixture was refluxed for 3 h after which about 30 ml of diethyl ether was distilled off. The slurry was cooled to room temperature and then to –5°C. 2-Methyl-2-pentenal (8.927 g, 0.09 mol) was added dropwise and the mixture allowed to warm up to room temperature, followed by stirring for a further 1 h. Pentane (50 ml) followed by water (25 ml) was added. The mixture was filtered through Celite and the cake washed with pentane (50 ml). The aqueous layer was extracted with pentane (3 x 20 ml). The organic layers were combined and washed with water (3 x 50 ml) and dried with $MgSO_4$. The organic solvents were distilled off. The residue was then distilled under reduced pressure to afford a colourless liquid in 65 % yield.

4.5.3 Synthesis of 2-Methyl-1-phenyl-1,3-butadiene



The above method was followed using methyltriphenylphosphonium bromide (17.97 g, 50 mmol), potassium tertiary-butoxide (5.64 g, 50 mmol), and 2-methylcinnamaldehyde (7.309 g, 50 mmol) affording a yield of 50 %.

4.5.4 General Procedure for the Selective Hydrogenation of Dienes

Diene (5.5 mmol) in methanol (5 ml) was added to 50 mg of the dendritic catalyst in a glass autoclave. The reaction mixture was purged three times with H_2 before pressurizing to 14 psig. The autoclave was stirred at 25 °C for the amount of time specified in the results and discussion. The liquid phase was passed through a pad of silica and then analyzed. Catalyst recycle was done after the catalyst was washed with methanol and ether.

4.6 REFERENCES

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[2] P. van Leeuwen, *App. Catal. A,* **2001**, *212*, 61.

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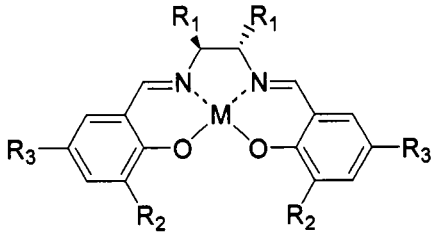
Chapter Five

EPOXIDATION OF ALKENES AND OLEFINIC ALCOHOLS

5.1 INTRODUCTION

The importance of epoxides was expressed by Seebach when he said "if carbonyl compounds have been said to be 'virtually the backbone of organic synthesis', the epoxides correspond to at least 'one of the main muscles'." [1] Epoxides can be synthesized by conventional methods such as the epoxidation of double bonds with peroxyacids and the displacement of halohydrins under basic conditions. With the advent of metal catalyzed reactions, great strides have been achieved in epoxidation reactions. Titanium, vanadium, chromium, manganese, molybdenum, and tungsten have been successfully used to catalyze the epoxidation of alkenes.

Salen ligands are attractive because they can coordinate a number of transition metals (Figure 5.1). Metallosalen complexes of Ti and V have been studied as catalysts for the reaction of Me_3SiCN with carbonyl compounds.[2-4] Cr- and Mn-salen complexes have been successfully used for the epoxidation of double bonds [5-8] while Ru-salen complexes have been investigated for the oxidation of primary alcohols[9] and sulfimidation reactions.[10-12]



M = Ti, VO, Cr, Mn

Figure 5.1. Metallosalen Complex

In dendrimer literature, the work of Jacobsen, Seebach and Kawi constitute the few examples of metallosalen complex catalyzed reactions. Jacobsen coupled PAMAM dendrimers having 4, 8, and 16 amino groups with pentafluorophenyl ester derivatives of Co-salen complexes (Figure 5.2).[13] This coupling was achieved through an amide bond. When used for the hydrolytic kinetic resolution of terminal epoxides, these dendrimeric catalysts displayed enhanced reactivity in comparison to non-dendronized catalysts.

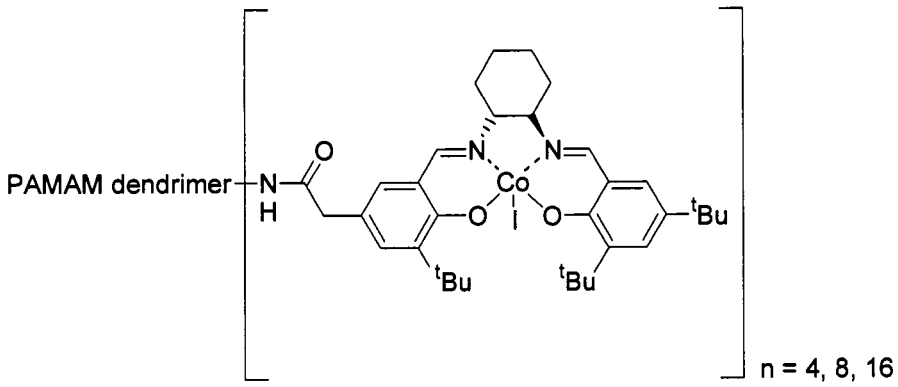


Figure 5.2 Jacobsen's Co-PAMAM Complexes

In addition to this, a positive dendrimer effect was observed, the reaction rates increased with the dendrimer generation number. This positive dendrimer effect was ascribed to cooperative effects of the neighbouring Co-units as a result of "restricted conformations imposed by the dendrimer structure".

Seebach *et al.* immobilized Mn and Cr-salen complexes on polystyrene bound poly(benzylether) dendrimers (Figure 5.3).[14] The Mn complexes were used to catalyze the enantioselective epoxidations of alkenes, while the Cr complexes were used to promote the formation of dihydropyranone from the Danishefsky diene and aldehydes. For the former reaction, the catalyst could be recycled up to ten times. In both cases, the selectivities obtained were comparable to those displayed by homogeneous catalysts.

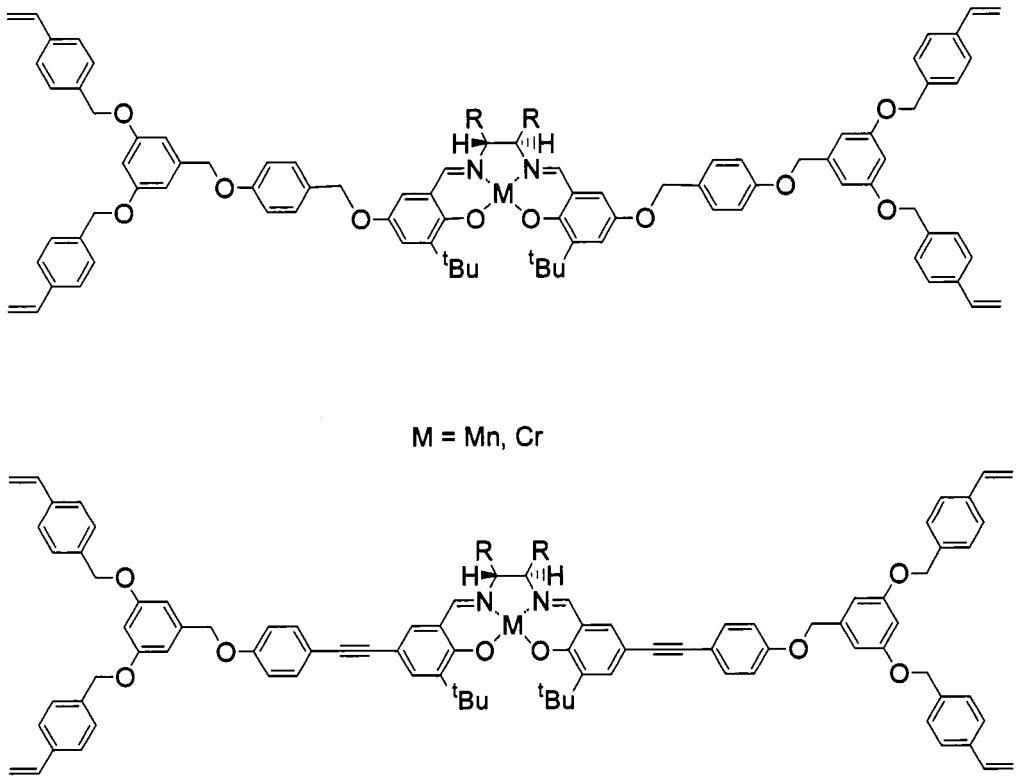


Figure 5.3 Seebach's Polystyrene bound Mn and Cr Complexes

Recently, Kawi and co-workers reported an example of periphery-functionalized Mn-salen complexes fixed on silica supported PAMAM dendrimers[15] (Figure 5.4) They used G0 – G4 complexes for the epoxidation of styrenes and obtained yields ranging from 20 % to 71 %. The yields increased with the higher generation dendrimers. The G4-catalyst could be recycled four times without any significant loss in activity. The authors reasoned that the enhanced separation of the silica matrix from the metal centers, provided by the higher generation dendrimers, enables better access to the active sites, thus leading to a better activity.

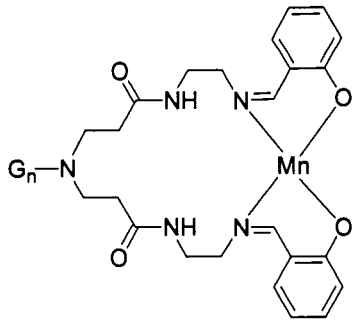


Figure 5.4 Kawi's Mn(salen) complex

The above results inspired us to investigate dendritic metallosalen complexes derived from poly(propyleneimine) (PPI) dendrimers for olefin and olefinic alcohol epoxidation. The initial goal was to establish the reactivity of Ti and V dendritic salen complexes in non-asymmetric epoxidation of alkenes and allylic alcohols. Our ultimate goal though, was to develop chiral versions of these complexes in order to perform asymmetric oxidations.

PPI dendrimers were chosen because of their commercial availability and their success with catalysts for other metal catalyzed reactions. This is the first example of salen modified poly(propyleneimine) dendrimers synthesized from dendrimers with 4, 8, 32 and 64 amino groups.

5.2 SYNTHESIS OF SALEN-FUNCTIONALIZED DENDRIMER LIGANDS

The amino groups of the first, second, fourth and fifth generation of poly(propyleneimine) dendrimers (Figure 5.5) were reacted with 2-hydroxyl benzaldehyde to give salen-functionalized ligands with 4, 8, 32 and 64 imine groups respectively (Figure 5.6). In refluxing ethanol, the condensation readily occurred to give clean product in good yield.

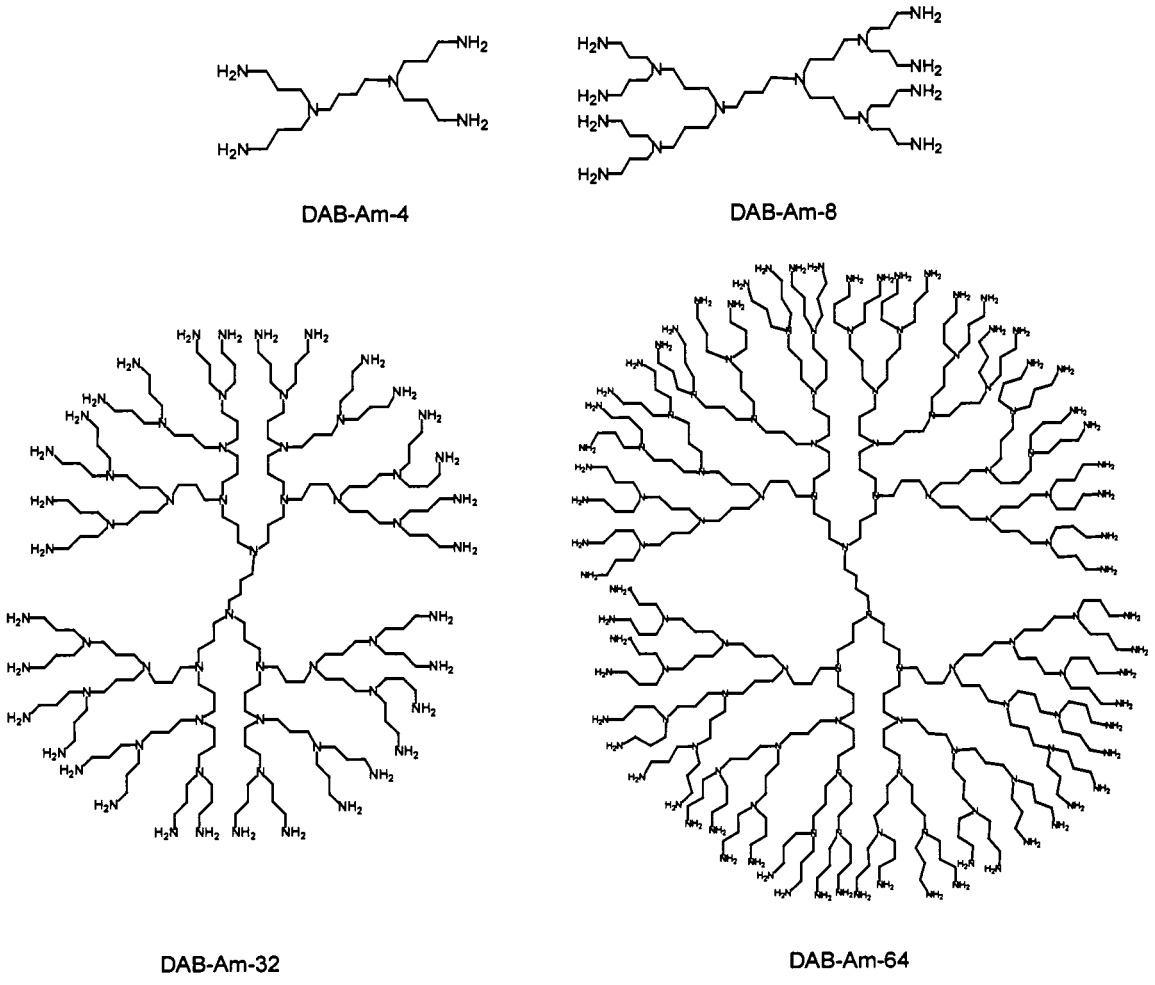
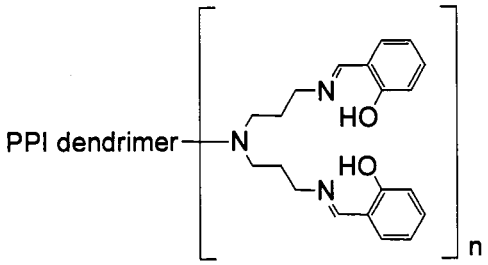


Figure 5.5 Poly(propyleneimine) Dendrimers

The dendrimer ligand **41** was isolated as a yellow solid and the ligands **42 – 44** were isolated as orange oils. The NMR spectra of these products were consistent with the proposed structures. The molecular weight obtained for **41** was 733.4 (ESI), which is also in agreement with the theoretical value. No valuable ESI data was obtained for the higher generation dendrimer ligands.

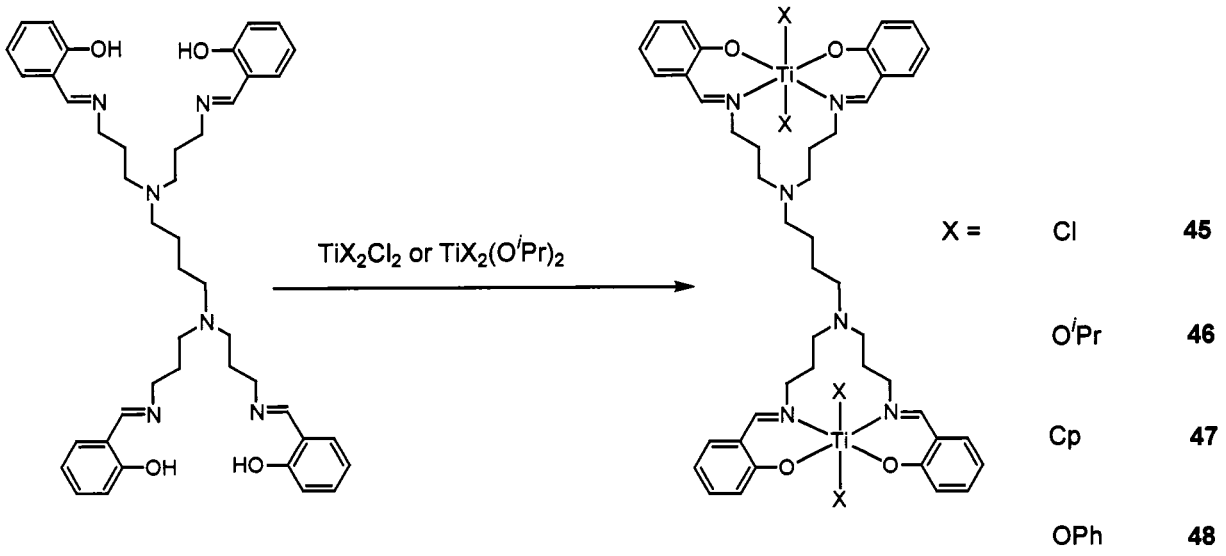


n =	2	**41**
	4	**42**
	16	**43**
	32	**44**

Figure 5.6 Salen-Functionalized PPI Dendrimers

5.3 SYNTHESIS OF PPI - BASED TI- SALEN COMPLEXES

The titanium complexes **45 – 47** were synthesized by the reaction of DAB-Am-$[H_2(salen)]_2$ with $TiCl_4$, $Ti(O^iPr)_4$, and Cp_2TiCl_2 respectively (Scheme 5.1). The complex **48** was obtained by first generating $Ti(OPh)_2(O^iPr)_2$ *in situ* from the reaction of $Ti(O^iPr)_4$ with phenol, followed by treatment with DAB-Am-$[H_2(salen)]_2$.

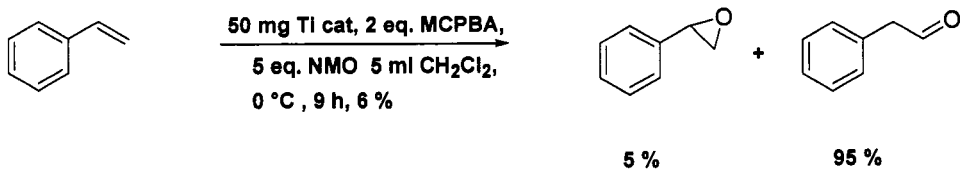


Scheme 5.1 Synthesis of DAB- $[TiX_2(salen)]_2$

5.3.1 Attempted Epoxidation of Styrene

When the complex **45** was used for the epoxidation of styrene using H_2O_2, ^tBuOOH, and PhIO, no product was detected. In the presence of NMO and MCPBA at 0 °C, 6 % conversion was observed with the major product being the

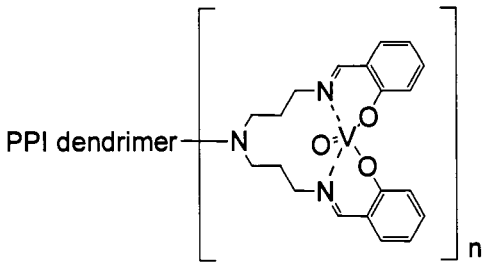
aldehyde (Scheme 5.2). There was no reaction at –78 °C and no reaction occurred with the complexes **45**, **47** and **48**.



Scheme 5.2 Epoxidation of Styrene

5.4 Synthesis of PPI - Based VO^{2+}- salen complexes

The complexation of the dendrimers **41** – **44** to $VOSO_4$ in a mixture of MeOH and THF in the presence of NaOAc gave the complexes **49** – **52** as green solids (Figure 5.7). The molecular weight obtained for the complex **49** was 863.2, which was once again consistent with the proposed structure. The solid state ^{51}V MAS NMR gave signals between –579 to –589 ppm for all these complexes. Also, the different FTIR spectra recorded for each catalytic system were comparable.



n =	2	**49**
	4	**50**
	16	**51**
	32	**52**

Figure 5.7 PPI - Based VO^{2+} Salen Complexes

5.4.1 Epoxidation of Olefinic Alcohols

The first step was to determine optimum reaction conditions. Geraniol and complex **49** were chosen for this task. The results from these experiments are presented in Table 5.1. Using aqueous tertiary butyl hydroperoxide under neat conditions, 43 % of geraniol was converted to the epoxide with 4 mol % catalyst, at 25 °C. When the amount of catalyst was decreased by a factor of four, the conversion decreased to 32 %. Increasing the temperature to 90 °C, reduced the reaction time to 1 hr compared to the 24 hrs it required at 25 °C. At this temperature the amount of catalyst could be lowered to less than 1 mol %, while

maintaining a good conversion. Using 0.55 mol % of catalyst gave 91 % conversion after 5.5 hrs.

A solvent was used for the reaction since workup was not smooth under neat conditions. By using 1 mol % catalyst in $CHCl_3$ at 90 °C, geraniol gave the epoxide in 97 % yield after 2 hrs. At 40 °C, 86 % conversion was obtained after 4 hrs. We also observed better conversions in less time when aqueous tertiary butyl hydroperoxide was replaced with tertiary butyl hydroperoxide in decane. Subsequent reactions were conducted in $CHCl_3$ at 40 °C, using tertiary butyl hydroperoxide in decane.

Table 5.1 Optimization results for the epoxidation of geraniol

Complex	Oxidant	Solvent	Mol %	Time (h)	Temp (°C)	Conv. (%)
49	TBHP	Neat	4	24	25	43
	"	"	1	24	25	32
	"	"	4	1	90	>99
	"	"	0.55	5.5	90	91
49	TBHP	$CHCl_3$	1	2	90	97
	"	"	1	4	40	86
	TBHP*	"	1	2	40	94

Reaction conditions: 5.8 mmol Substrate, 1.1 eq. TBHP (70 % aq. *tert*-butyl hydroperoxide). 2 ml $CHCl_3$. *TBHP = 5.5M *tert*-butyl hydroperoxide in decane.

The effect of the dendrimer generation on catalytic activity was investigated by using complexes **49** – **52**, which had 2, 4, 16, and 32 VO^{2+} centers per dendrimer respectively. 25 mg of catalyst was used irrespective of the dendrimer generation number. The first and second generation complexes **49** and **50** gave turnover numbers (TONs) of 93 and 102 respectively for a duration of 2 h. The fourth and fifth generation complexes **51** and **52** gave a higher value of 113 under similar conditions. When the substrate to catalyst ratio was increased by a factor of four, the TON increased to 450 using complex **51**.

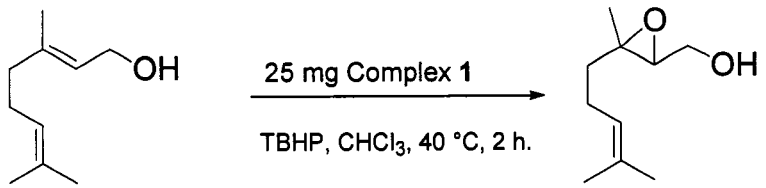


Table 5.2 Dendrimer effect in the epoxidation of geraniol

Catalyst	Conv. (%)	TON
49	94	93
50	94	102
51	>99	113
52	>99	113
51[a]	>99	450

Reaction conditions: 25 mg catalyst, 5.8 mmol substrate, 1.1 eq. *tert*-butyl hydroperoxide in decane, 2 ml $CHCl_3$, 40 °C, 2 h. [a]23 mmol substrate.

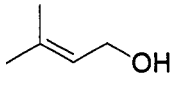
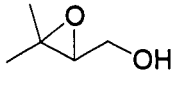
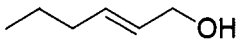
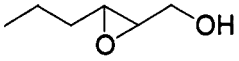
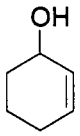
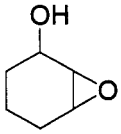
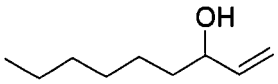
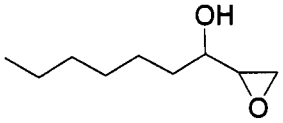
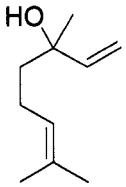
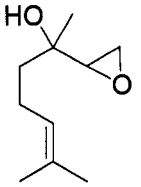
Even though there is an increase in the number of metal centers per mole of dendrimer, theoretical calculations reveal that there is a small variation in the weight of metal complex per gram of dendrimer with an increase in dendrimer generation. This means that the positive effect in reactivity with the higher generation complexes is a result of cooperativity between the metal centers.

The epoxidation of geraniol has been a subject of a number of studies. Sharpless reported 93 % yield of the epoxide using ~1.4 mol % of $VO(acac)_2$ in refluxing benzene after 4 h.[16] Using 3.6 mol % of microencapsulated $VO(acac)_2$ in hexane at room temperature, the same yield was reported after 2.5 h.[17] In 103

bar of liquid CO_2, 3.5 mol % of $VO(O^iPr)_3$ gave 98 % yield after 24 h.[18] With regards to the metal to substrate ratio, our results with the lower generation complexes **49** and **50** are comparable to those reported by Sharpless while the results with complex **51** are much better.

Other allylic alcohols were also transformed to the corresponding epoxides using complex **49** (Table 5.3). 3-Methyl-but-2-en-1-ol was completely converted after 2hrs, and 56 % of the epoxide was isolated. Hex-2-en-1-ol was completely converted after 24 hrs and the resulting epoxide was isolated in 67 % yield.

Table 5.3 Oxidation of different allylic alcohols

Substrate	Isolated Yield (%)	Product
	56*	
	67	
	20	
	26	
	22	

Reaction conditions: 25 mg Complex **49**, 5.8 mmol substrate, 1.1 eq. *tert*-butyl hydroperoxide in decane, 2 ml $CHCl_3$, 40 °C, 24 h. *Reaction time 2h.

The cyclic compound, cyclohex-2-en-1-ol gave 20 % of the epoxide while non-1-en-3-ol and linalool gave 26 and 22 % respectively. These three allylic alcohols, which have the hydroxyl group in the secondary and tertiary positions have been successfully transformed to their corresponding epoxides using VO(acac)/TBHP. It can be deduced that the dendritic vanadyl complexes promote the epoxidation of allylic alcohols with primary hydroxyl groups faster than allylic alcohols with

secondary and tertiary hydroxyl groups. Also methyl substituted double bonds react faster than unsubstituted double bonds because 3-methyl-but-2-en-1-ol and geraniol required a reaction time of 2 h while hex-2-en-1-ol took 24 h.

The homoallylic alcohol, hex-3-en-1-ol was also epoxidized to complete conversion with up to 78 % isolated yield.

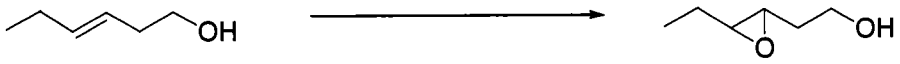


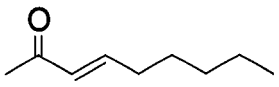
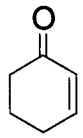
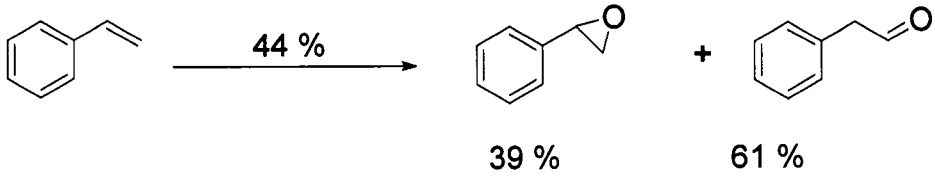
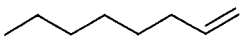
Table 5.4 Epoxidation of hex-3-en-1ol using different generations of catalysts

Catalyst	Isolated Yield (%)
$[VO(Salen)]_2$	75
$[VO(Salen)]_4$	71
$[VO(Salen)]_{16}$	78
$[VO(Salen)]_{32}$	78

Reaction conditions: 25 mg catalyst, 5. 8 mmol substrate, 1.1 eq. *tert*-butyl hydroperoxide in decane, 2ml $CHCl_3$, 40 °C, 24 h.

The results obtained for the epoxidation of other olefinic substrates are presented in Table 5.5. The epoxidation of α,β-unsaturated ketones was unsuccessful. Non-3-en-2-one gave only 9 % of the epoxide while cyclohexanone did not react at all. Styrene was converted to the epoxide and the aldehyde in 39 and 61 % yields respectively, with a total yield of 44 %.

Table 5.5 Epoxidation of Other Substrates

Substrate	GC Yield (%)
	9 %
	No Reaction
	39 % (epoxide) + 61 % (aldehyde)
	No Reaction

Reaction conditions: 25 mg Complex **49**, 5. 8 mmol substrate, 1.1 eq. *tert*-butyl hydroperoxide in decane, 2ml $CHCl_3$, 40 °C, 24 h.

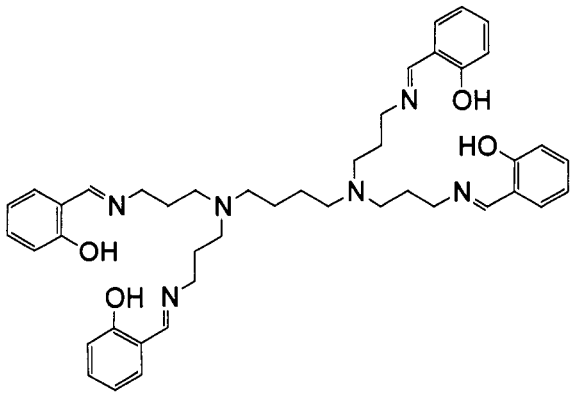
During the reaction, the catalyst is transformed to the active peroxo species. This species is completely soluble under the reaction conditions. Attempts to isolate the catalyst by precipitation techniques were unsuccessful. Unfortunately, this prohibited us from performing recycle experiments.

5.5 Conclusions

Salen modified poly(propyleneimine) – oxovanadyl complexes show a positive dendrimer effect for the epoxidation of olefinic alcohols. These catalysts gave better yields when the alcohol is in the primary position than when a secondary or tertiary alcohol is used. Even though we could not carry out recycle reactions due to the lack of catalyst recovery, the small amount of catalyst that is required as a result of the positive dendrimer effect more than compensates for this aspect.

5.6 Experimental Section

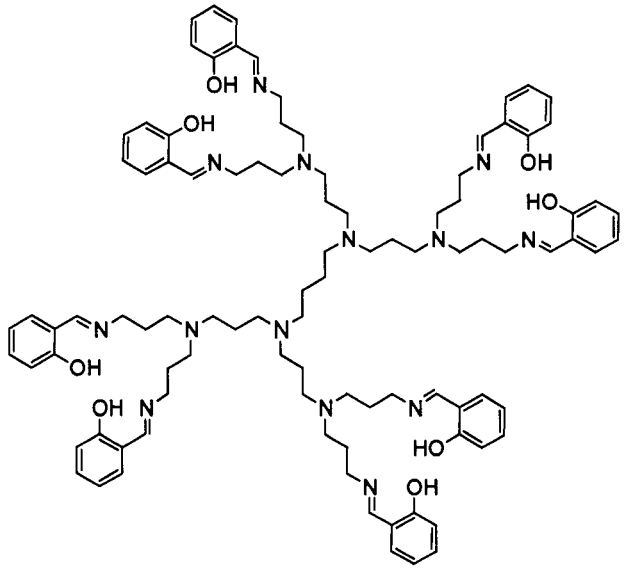
Synthesis of DAB-Am-[H_2(salen)]$_2$ 41



41

DAB-Am-4 (5.0 g, 15.8 mmol) was dissolved in ethanol (50 m) in a 250 ml two-neck round-bottom flask fitted with a condenser and a dropping funnel. Salicylaldehyde (7.72 g, 63 mmol) was dissolved in ethanol (50 ml) and transferred to the dropping funnel. The aldehyde was slowly added to the amine with continuous stirring. The resulting mixture was refluxed under N_2 for 18 h. The solvent was reduced to 30 ml, and a 5:1 mixture of hexanes-ethyl acetate was added to precipitate the product. After filtration, a yellow powder (10.54 g, 89 %) was obtained. ESI + (H^+), 733.4.

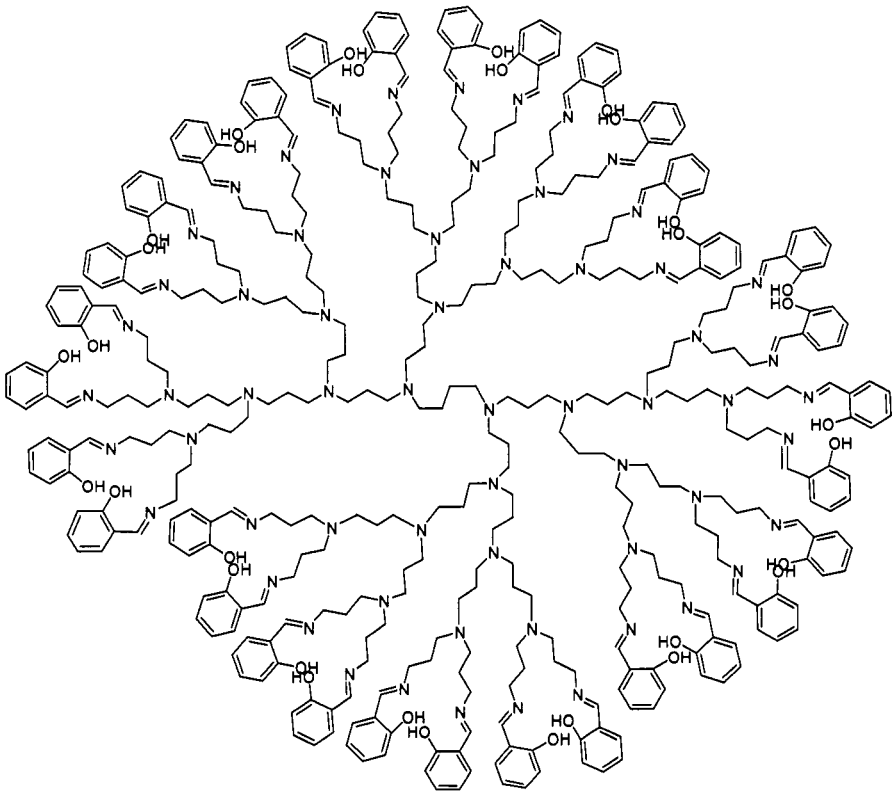
Synthesis of DAB-Am-[H_2(salen)]$_4$ 42



42

DAB-Am-8 (1.0 g, 1.29 mmol) was dissolved in ethanol (30 ml) in a 100 ml two-neck round-bottom flask fitted with a condenser and a dropping funnel. Salicylaldehyde (1.264 g, 10.36 mmol) was dissolved in ethanol (20 ml) and transferred to the dropping funnel. The aldehyde was slowly added to the amine with continuous stirring. The resulting mixture was refluxed under N_2 for 18 h. After removing solvent, the product was obtained as an orange oil (1.34 g).

Synthesis of DAB-Am-[H_2(salen)]$_{16}$ 43



43

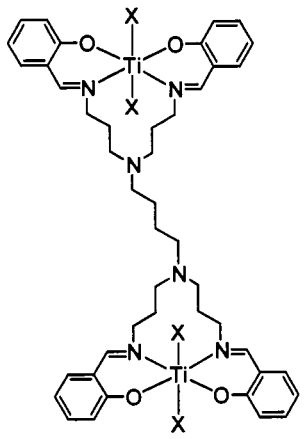
DAB-Am-32 (2.64 g, 0.75 mmol) was dissolved in ethanol (100 ml) in a 250 ml two-neck round-bottom flask fitted with a condenser and a dropping funnel. Salicylaldehyde (2.94 g, 24 mmol) was dissolved in ethanol (50 ml) and transferred to the dropping funnel. The aldehyde was slowly added to the amine with continuous stirring. The resulting mixture was refluxed under N_2 for 18 h. After removing the solvent, the product was obtained as an orange oil (4 g).

Synthesis of DAB-Am-[H_2(salen)]$_{32}$ 44

DAB-Am-64 (1.60 g, 0.22 mmol) was dissolved in ethanol (100 m) in a 250 ml two-neck round-bottom flask fitted with a condenser and a dropping funnel. Salicylaldehyde (1.74 g, 14.3 mmol) was dissolved in ethanol (50 ml) and transferred to the dropping funnel. The aldehyde was slowly added to the amine with continuous stirring. The resulting mixture was refluxed under N_2 for 48 h. After removing solvent, the product was obtained as an orange oil (2.73 g).

5.6.1 Procedure for the Synthesis of PPI - Based Ti- salen Complexes

Synthesis of Complex 45



X = Cl **45**

O^iPr **46**

Cp **47**

OPh **48**

Dendrimer **41** (250 mg, 0.34 mmol) and Et_3N (1 ml) were dissolved in CH_2Cl_2 (5 ml). In a separate Schlenk flask, $TiCl_4$ (150 mg, 0.79 mmol) was dissolved in THF (15 ml) (Caution: *exothermic reaction*). The metal was added portion-wise to the ligand mixture causing an immediate precipitation. The reaction mixture was

refluxed for 1 h following which the solvent was reduced to ~5 ml and diethyl ether (10 ml) added. The mixture was filtered, washed with diethyl ether, and dried to give 379 mg of a red solid.

Synthesis of Complex 46

Dendrimer **41** (200 mg, 0.27 mmol) was dissolved in CH_2Cl_2 (10 ml). In a separate Schlenk flask, $Ti(O^iPr)_4$ (153 mg, 0.54 mmol) was dissolved in THF (10 ml). The metal was slowly added to the ligand mixture causing an instant precipitation. The reaction mixture was refluxed for 18 h. After cooling to room temperature, the mixture was filtered and washed with 1:1 pentane/CH_2Cl_2 (2 x 10 ml) and dried to give 190 mg of a yellow solid.

Synthesis of Complex 47

Dendrimer **41** (250 mg, 0.34 mmol) and Et_3N (1 ml) were dissolved in THF (10 ml). In a separate Schlenk flask, Cp_2TiCl_2 (171 mg, 0.69 mmol) was dissolved in THF (20 ml). The metal was added portion-wise to the ligand mixture. Precipitation occurred immediately upon heating. The reaction mixture was refluxed for 18 h. The solvent was reduced to ~5 ml and CH_2Cl_2 (20 ml) was added. The mixture was filtered, washed with diethyl ether, and dried to give 370 mg of an orange-yellow solid.

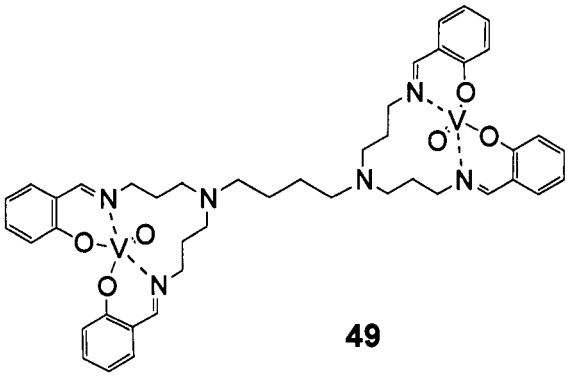
Synthesis of Complex 48

To a solution of $Ti(O^iPr)_4$ (119 mg, 0.42 mmol) in THF (10 ml) PhOH (75 mg, 0.8 mmol) was added in CH_2Cl_2 (10 ml). This solution was stirred at 25 °C for 30 minutes and then slowly added to a solution of dendrimer **41** (154 mg, 0.21 mmol) in CH_2Cl_2 (10 ml). The whole mixture was stirred for a further 3 hrs. After filtration, 251 mg of a yellow solid was obtained.

5.6.2 Procedure for the Synthesis of PPI - Based VO^{2+} Complexes

The complexation of VO^{2+} to salen modified PPI dendrimers was affected by treating the dendritic ligands with $VOSO_4$ in the presence of sodium acetate as base. The same procedure was followed for the synthesis of the different catalyst generations, however, the equivalents of $VOSO_4$ and base used were scaled according to the theoretical number of salen moieties per dendrimer. Complexes **49 – 52** were synthesized from dendritic ligands **41 – 44** respectively.

Procedure for the Synthesis of Complex 49



49

DAB-Am-$[H_2(salen)]_2$ (0.5 mmol) was dissolved in THF (10 ml) followed by the addition of sodium acetate (1.0 equiv). In a separate Schlenk flask, $VOSO_4$ (1.0 equiv) was dissolved in methanol (50 ml). The ligand mixture was slowly added to the methanol solution. Immediately a brown precipitate was formed. The reaction mixture was refluxed for 18 h. After cooling to room temperature, the

mixture was filtered under vacuum. The solid was washed with water (3 x 10 ml), methanol (3 x 10 ml) and ether (10 ml) and dried *in vacuo*. A green powder was obtained in quantitative yield.

5.6.3 General Procedure for the Epoxidation of Olefinic Alcohols

Substrate (5.8 mmol) was added to a green suspension of DAB-Am-$[VO(salen)]_x$ (25 mg) in $CHCl_3$ (2 ml). Tertiary butylhydroperoxide (6.6 mmol) was then added resulting in the formation of an orange solution. This solution was stirred at 40 °C while the reaction was monitored by TLC. The reaction mixture was then washed with sodium bisulfite prior to the isolation of product by silica column chromatography using a 1:1 ratio of ethyl acetate and hexanes as the eluent solution.

5.7 REFERENCES

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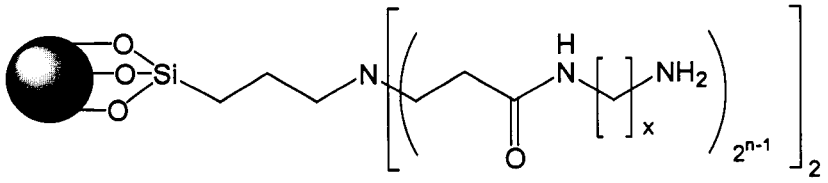
6.1 DATA FOR CHAPTER 2



		Formula	Net Formula	MW	NH_2	Theoretical Mass	Actual Mass	% Grafted
x	n				mmol / g	mg / 100 g		
2	1	$C_3H_6N + 2(C_5H_9N_2O) + 2H_2$	$C_{13}H_{28}N_5O_2$	286.4	1.49	213.368	196.8	92
2	2	$C_3H_6N + 2(C_5H_9N_2O) + 4(C_5H_9N_2O) + 4H_2$	$C_{33}H_{68}N_{13}O_6$	743	2.23	414.2169	298.7	72
2	3	$C_3H_6N + 2(C_5H_9N_2O) + 4(C_5H_9N_2O) + 8(C_5H_9N_2O) + 8H_2$	$C_{73}H_{148}N_{29}O_{14}$	1656	2.95	610.709	353.4	57
2	4	$C_3H_6N + 2(C_5H_9N_2O) + 4(C_5H_9N_2O) + 8(C_5H_9N_2O) + 16(C_5H_9N_2O) + 16H_2$	$C_{153}H_{308}N_5O_{30}$	3483	3.53	768.3288	403	53
6	1	$C_3H_6N + 2(C_9H_{17}N_2O) + 2H_2$	$C_{21}H_{44}N_5O_2$	398.6	1.38	275.0409	167.1	61
12	1	$C_3H_6N + 2(C_{15}H_{29}N_2O) + 2H_2$	$C_{33}H_{68}N_5O_2$	566.9	1.24	351.478	195.6	56

n refers to the generation number of the dendrimer.

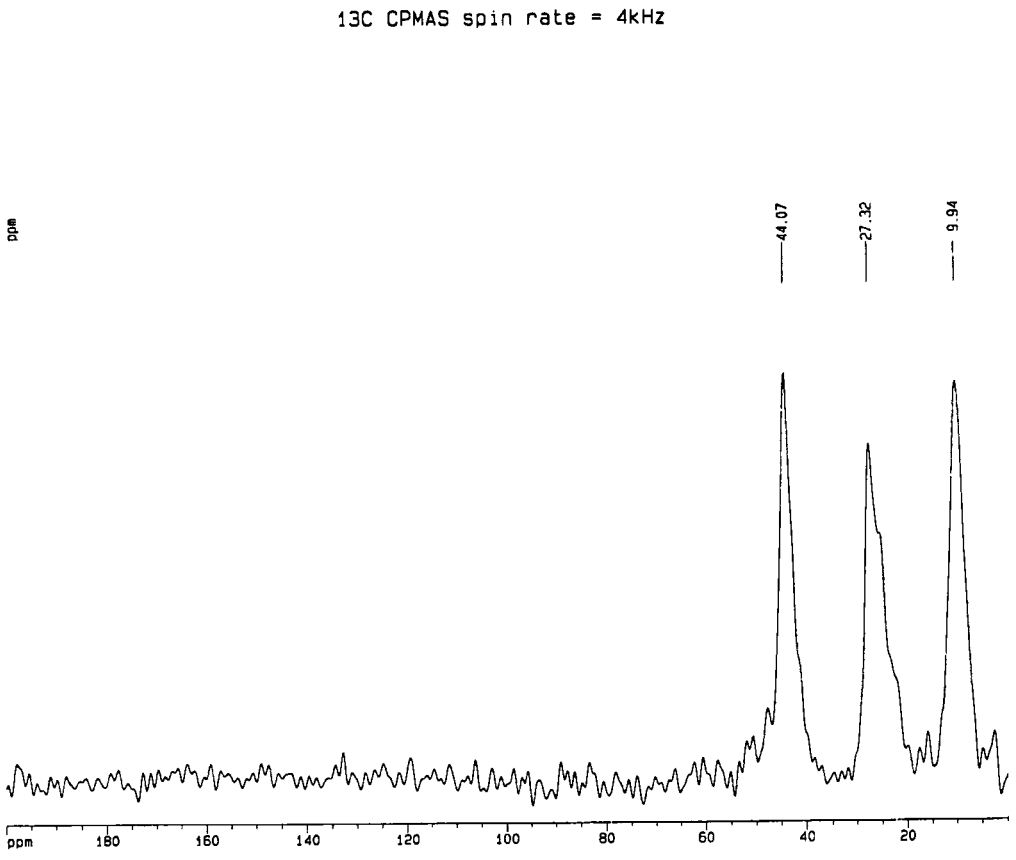
The formula refers to the organic content built on the surface of silica. It assumes that the Michael addition and the amidation steps occur with complete conversion and with absolute selectivity. It is a model of a perfect dendrimer structure. The theoretical mass of organic material is calculated by using the following equation:

$$\frac{\text{Theoretical Loading}}{\text{(no. of terminal groups) x MW}} \times 100$$

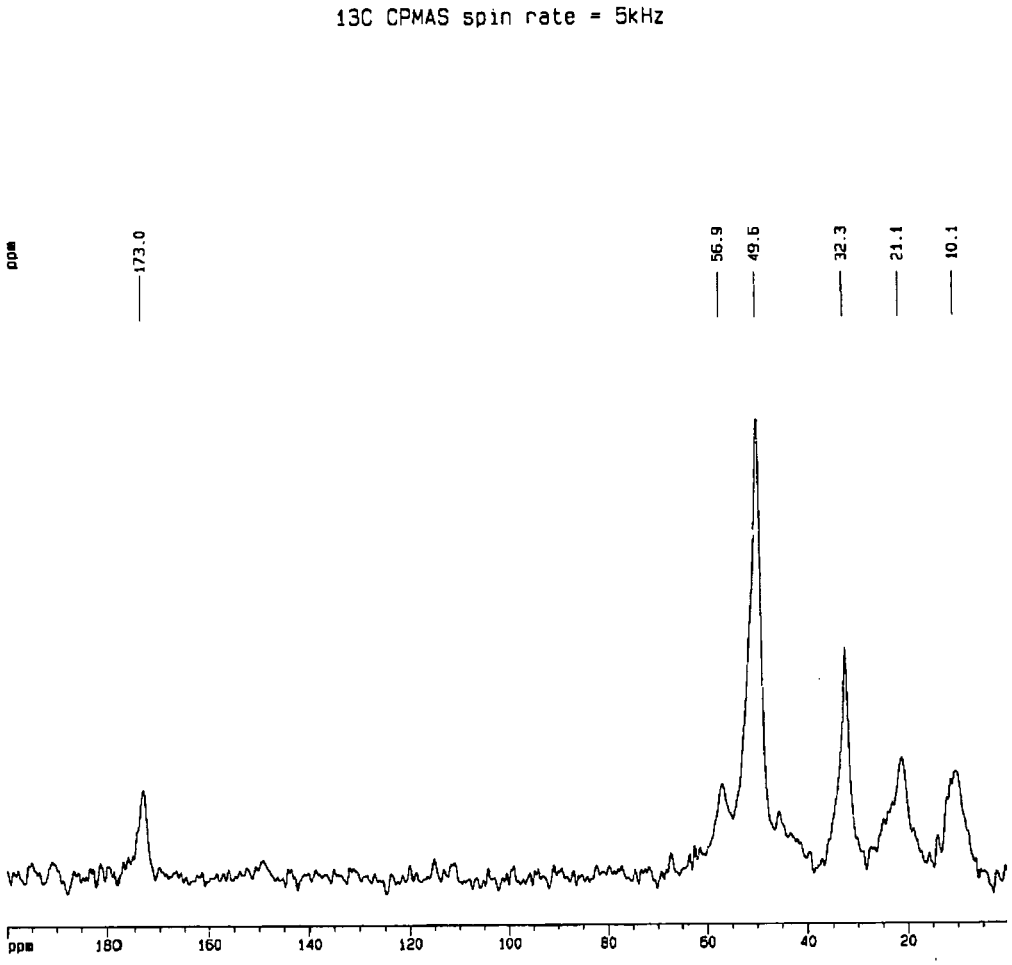
The % grafted is calculated using the equation shown below.

$$\% \text{ Grafted} = \frac{\text{Actual Mass (mass loss as determined by TGA)}}{\text{Theoretical mass}} \times 100$$

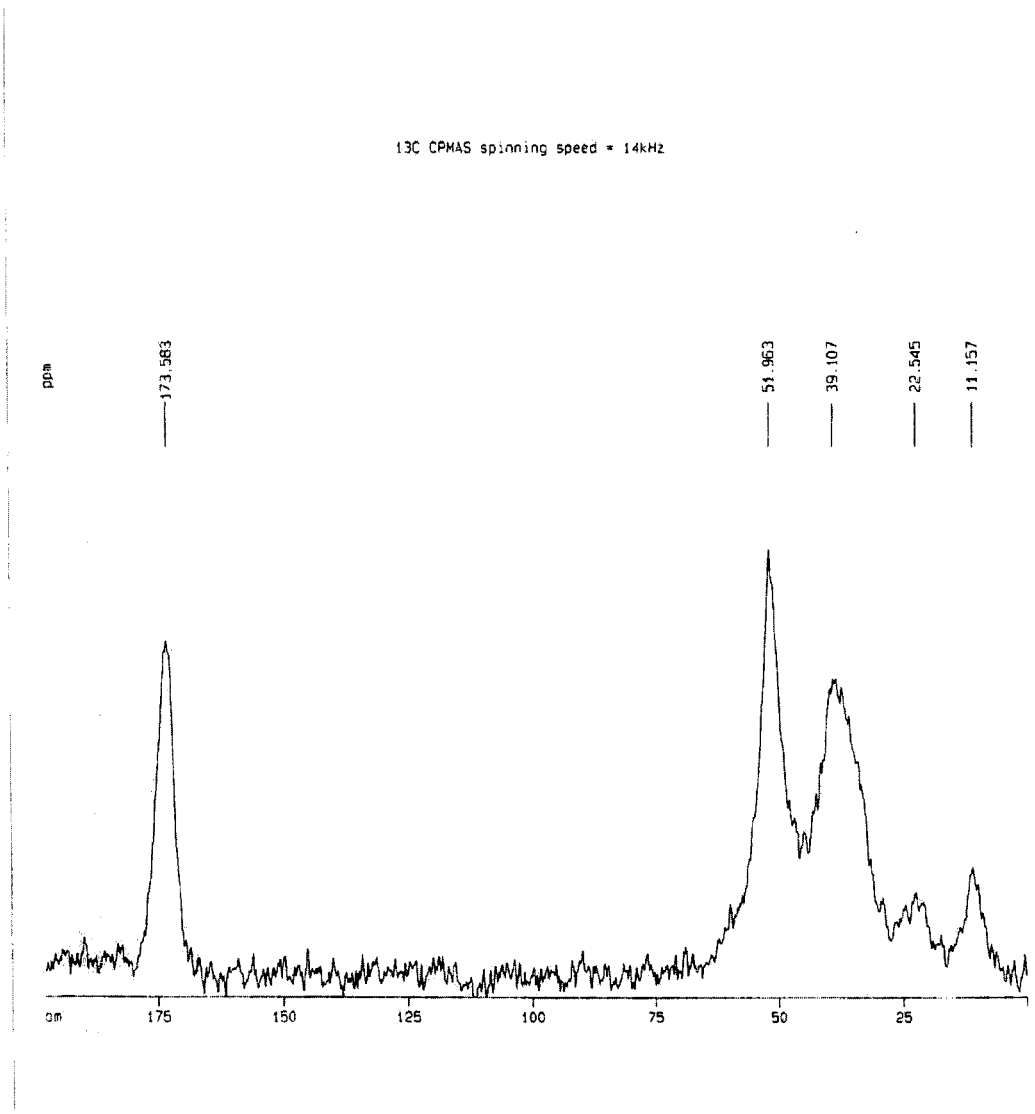
^{13}C CPMAS of Aminopropyl Silica **1**



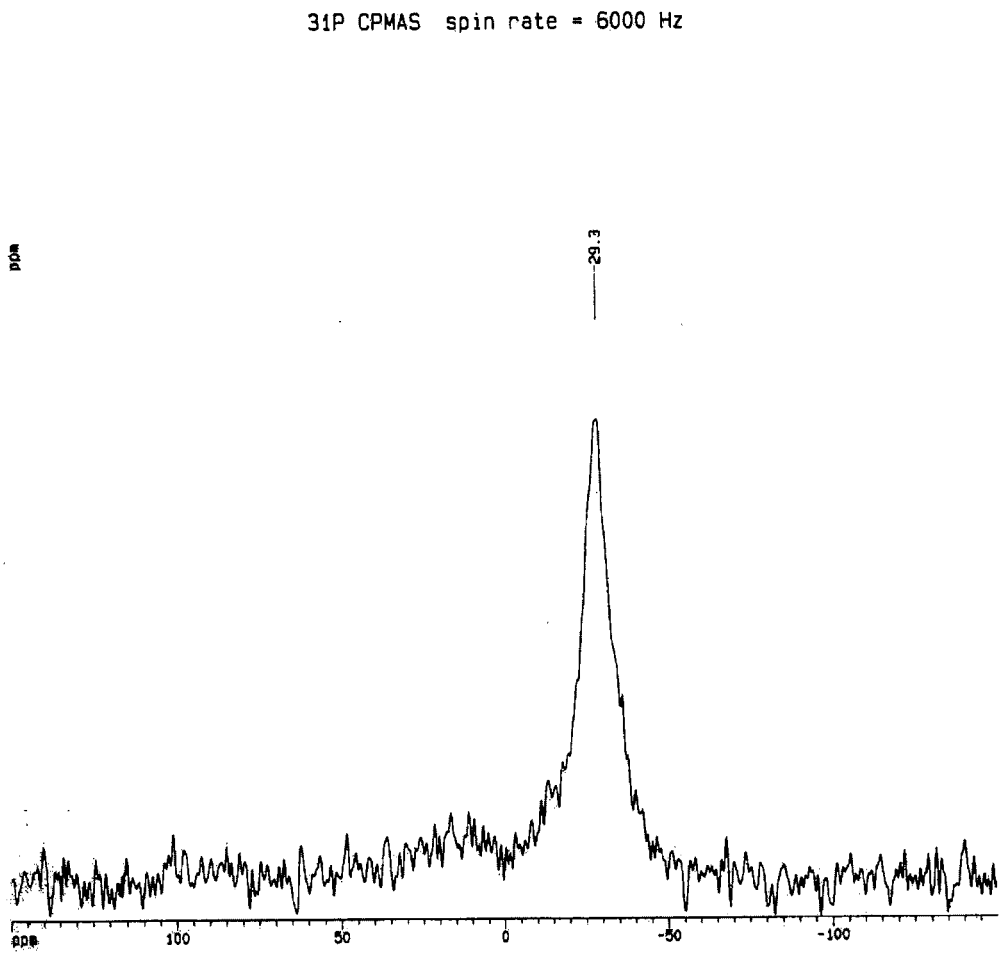
^{13}C CPMAS of Methyl Propylaminopropionate **2**



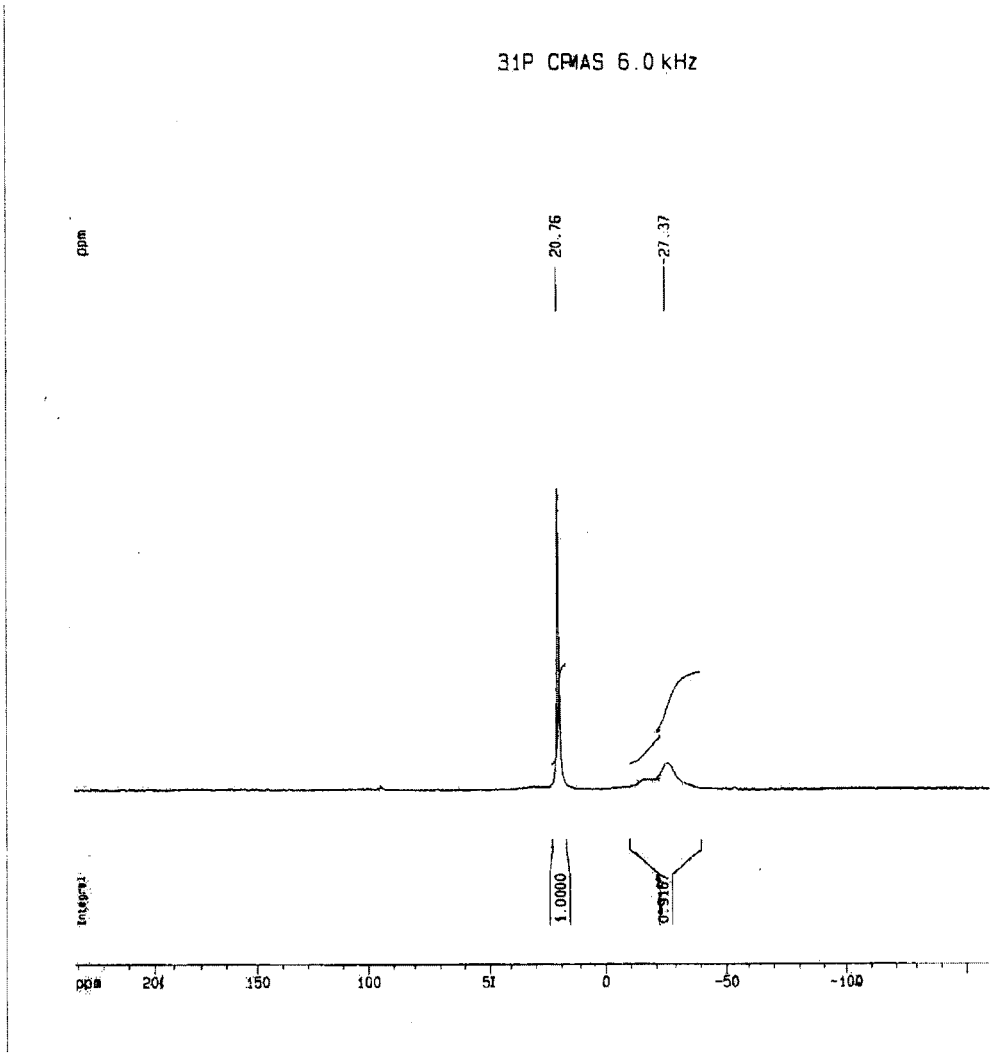
^{13}C CPMAS of Amine-Terminated Dendrimer



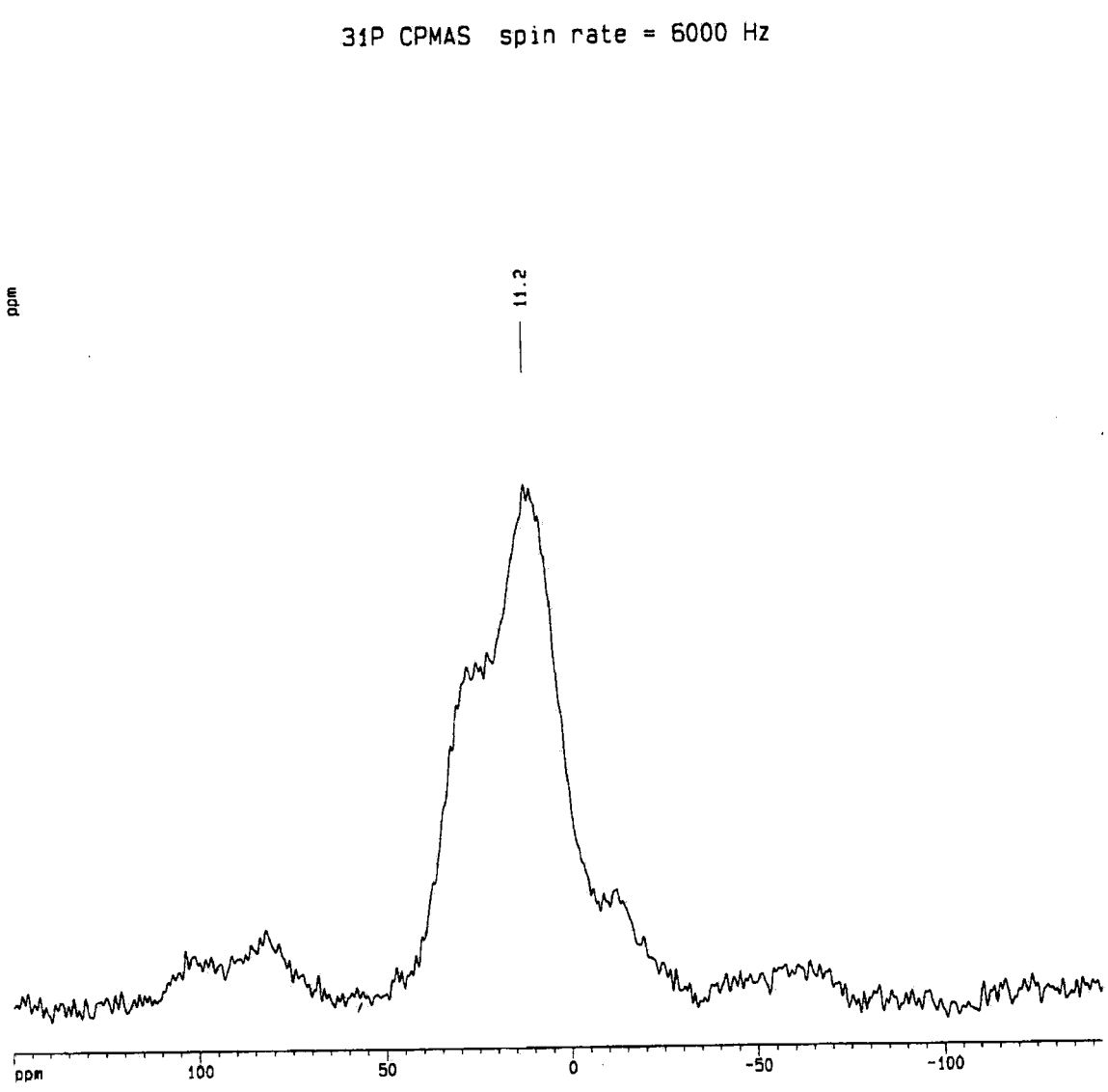
Typical ^{13}P CPMAS of Phosphine-Functionalized Dendrimer



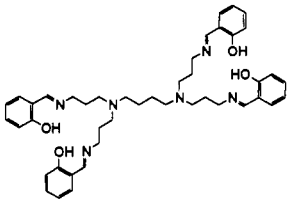
^{13}P CPMAS of a Phosphine-Functionalized Dendrimer with Internal Standard



Typical ^{13}P CPMAS of a PAMAM-Pd Complex

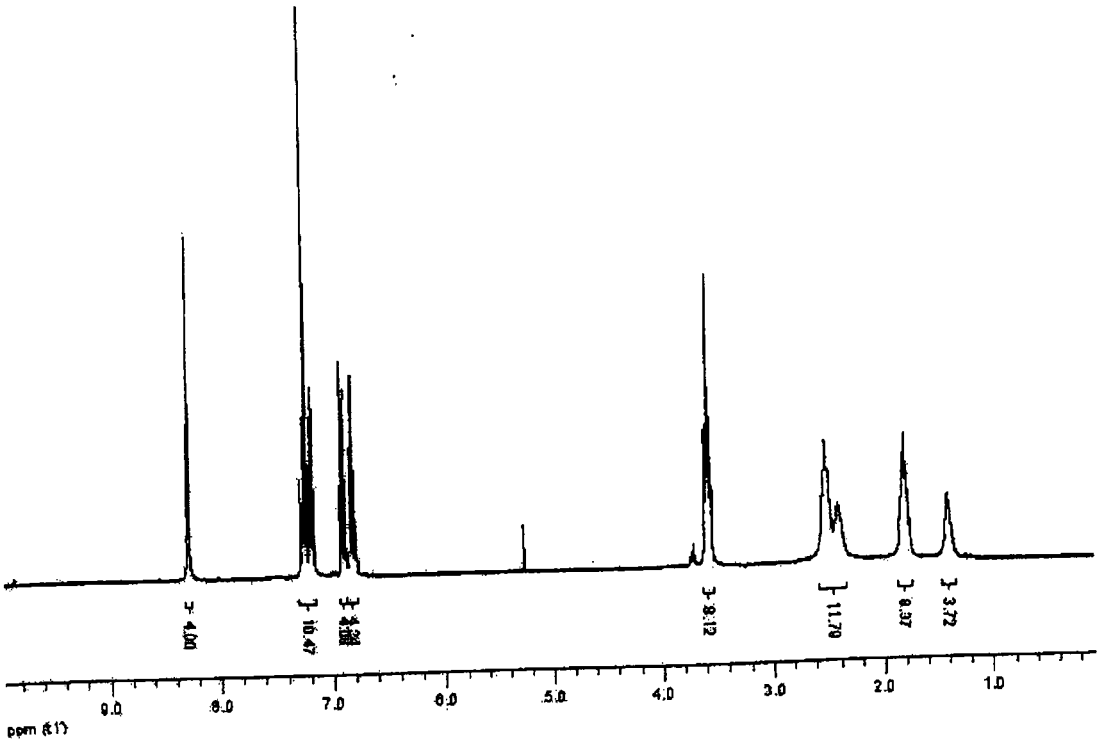


DATA FOR CHAPTER 5

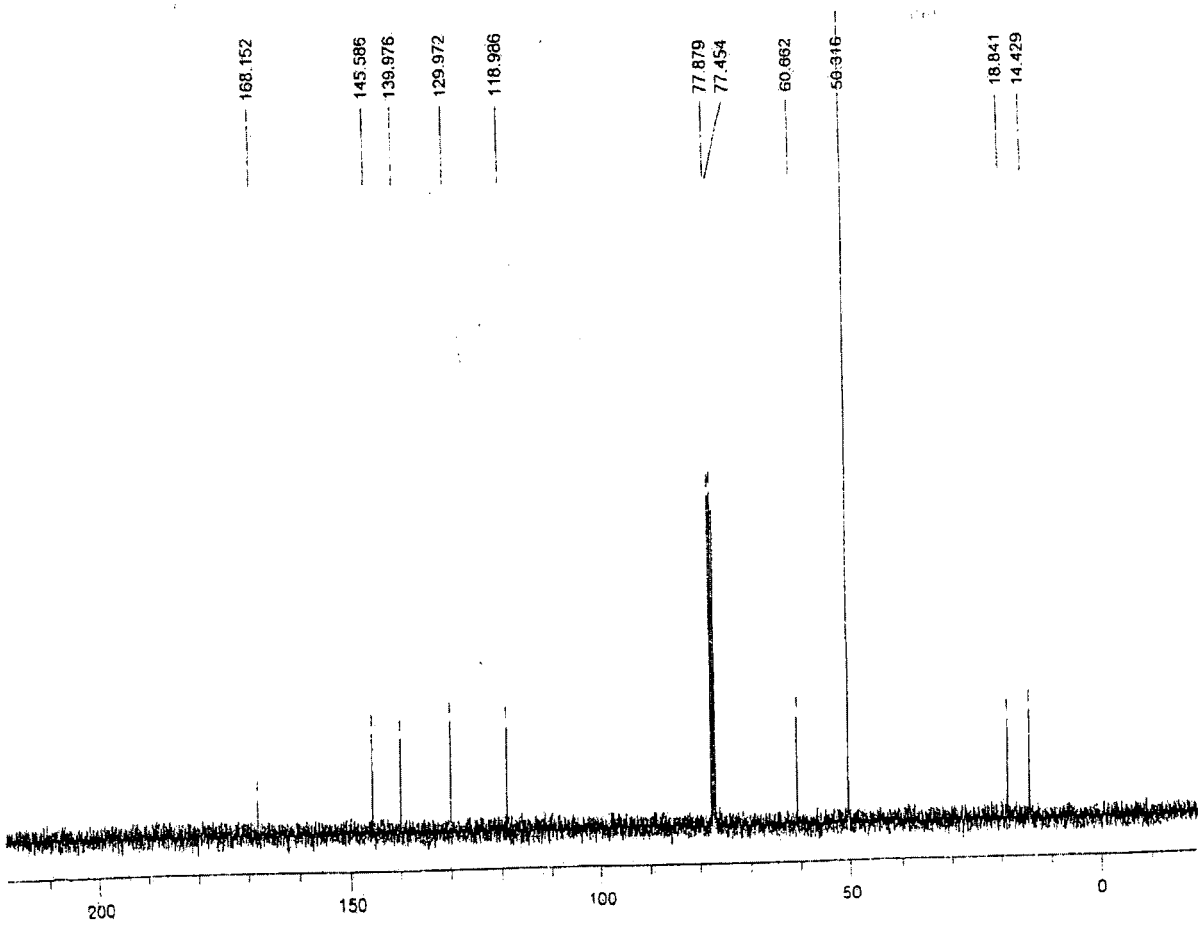


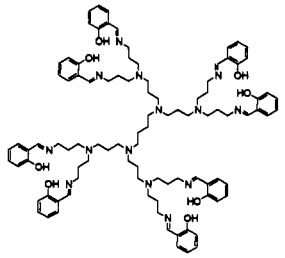
41

^{1}H NMR



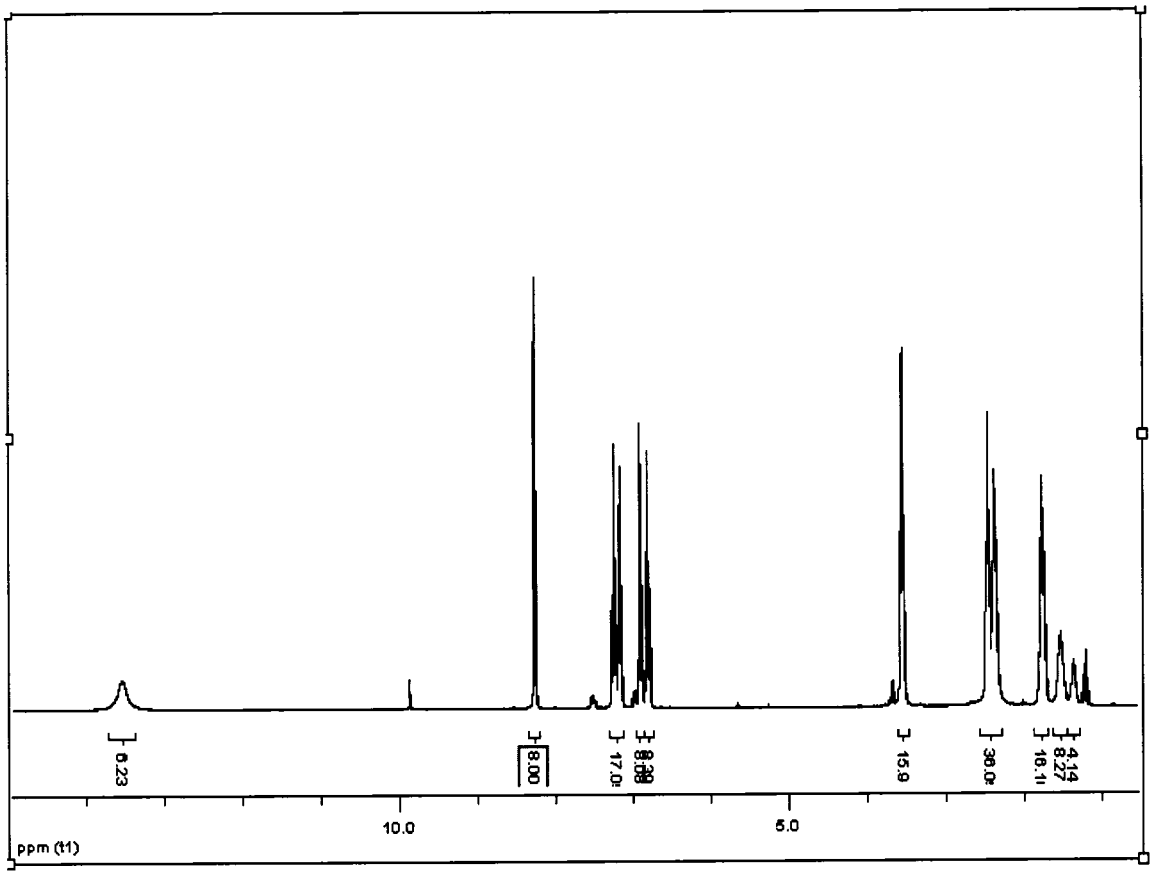
^{13}C NMR of **41**


168.152
145.586
139.976
129.972
118.986
77.879
77.454
60.662
50.316
18.841
14.429
200
150
100
50
0

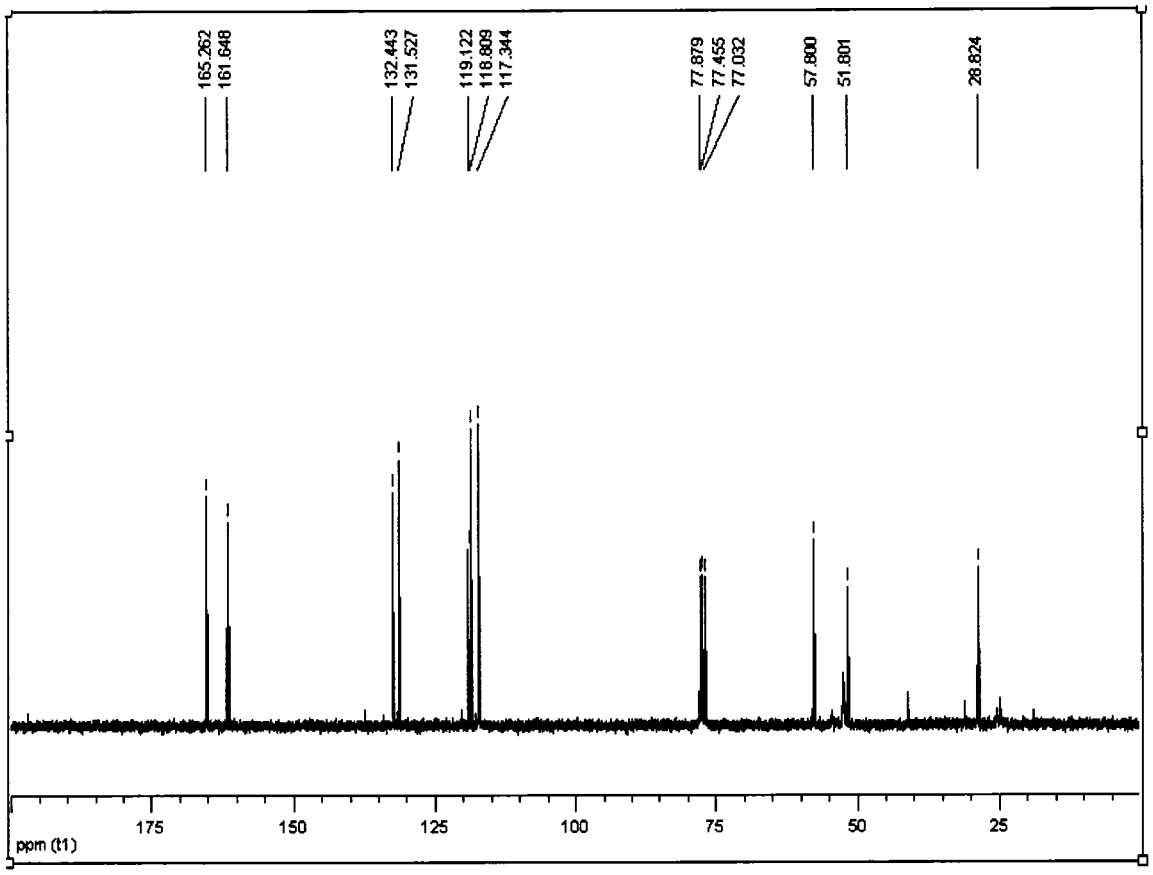


42

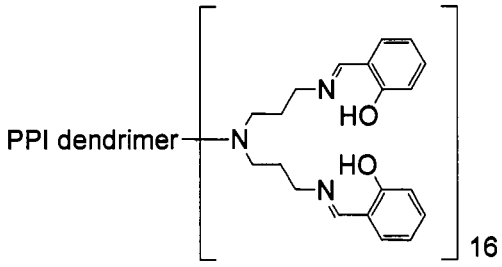
^{1}H NMR



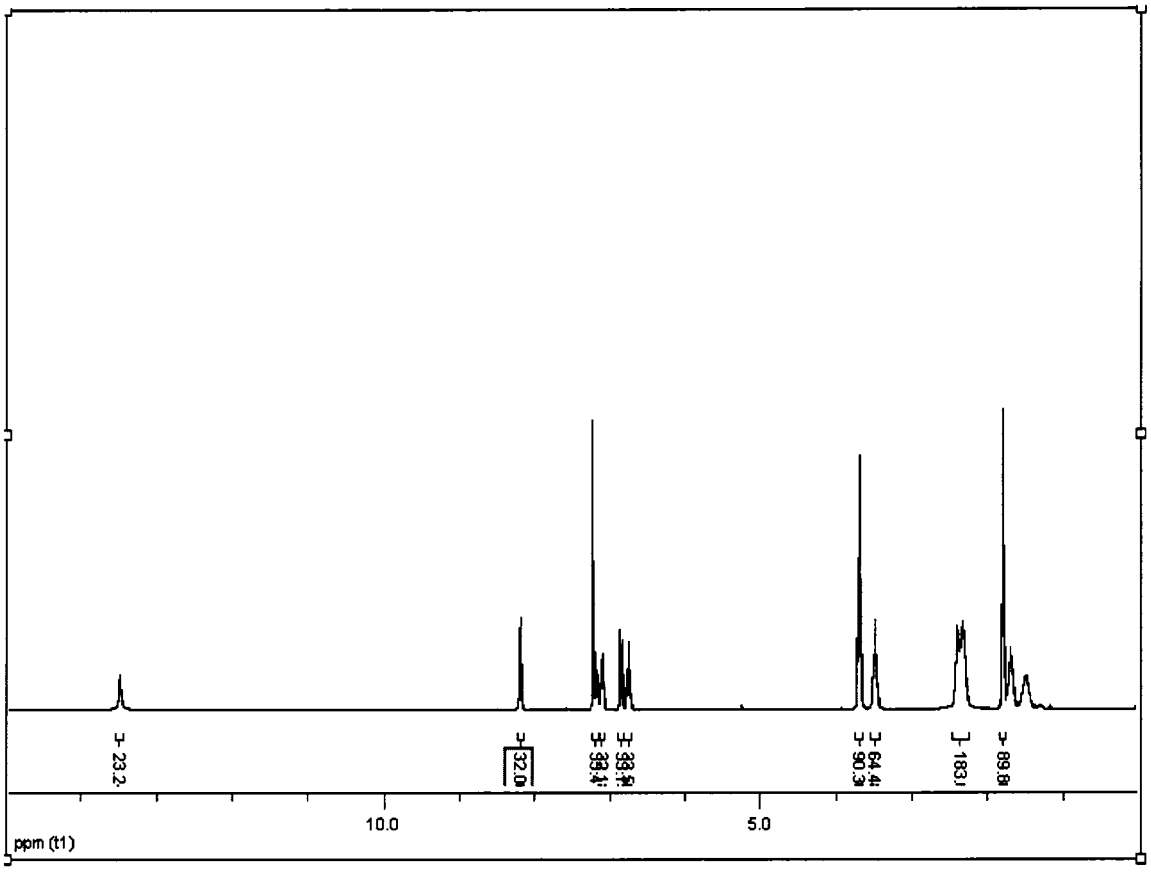
^{13}C NMR of **42**


165.262
161.648
132.443
131.527
119.122
118.809
117.344
77.879
77.455
77.032
57.800
51.801
28.824
175
150
125
100
75
50
25
ppm (t1)

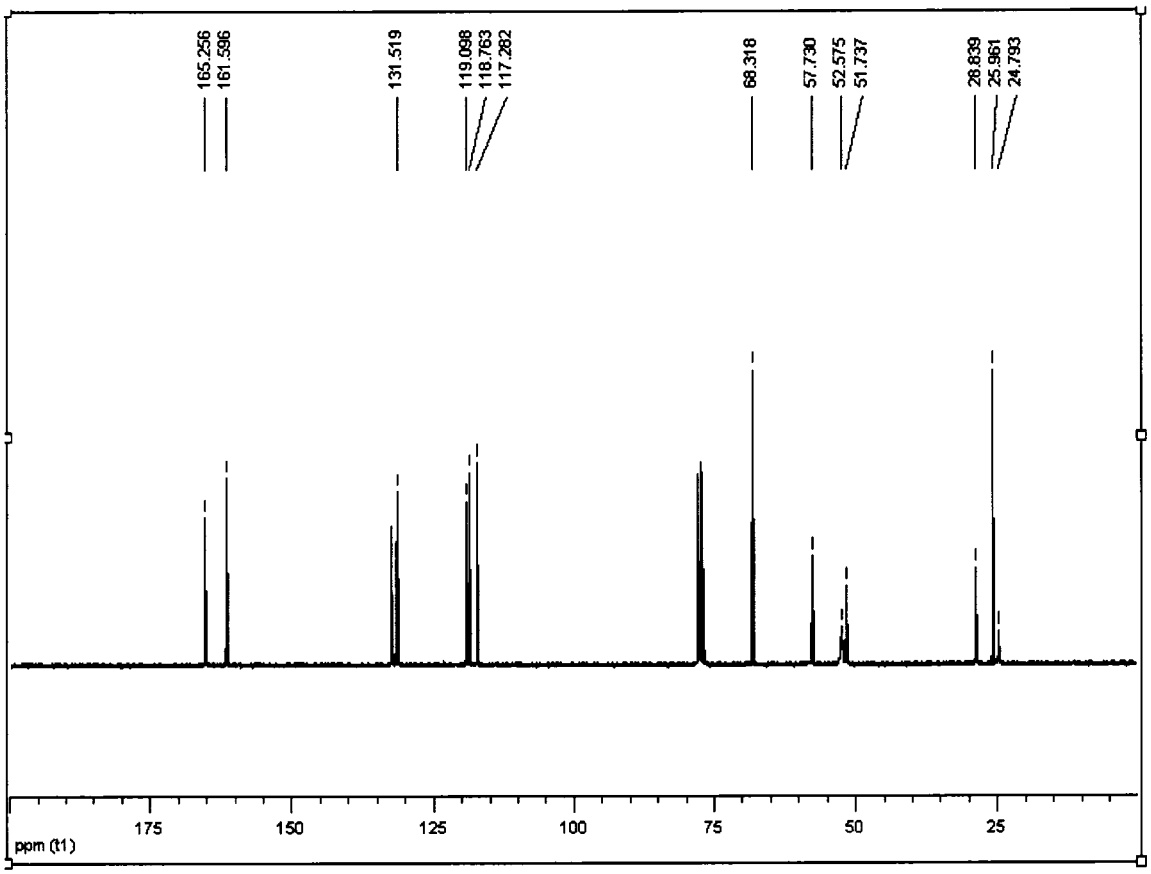
Compound 43



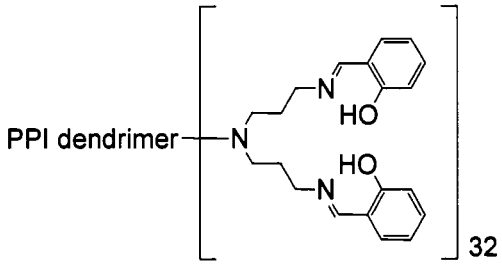
^{1}H NMR



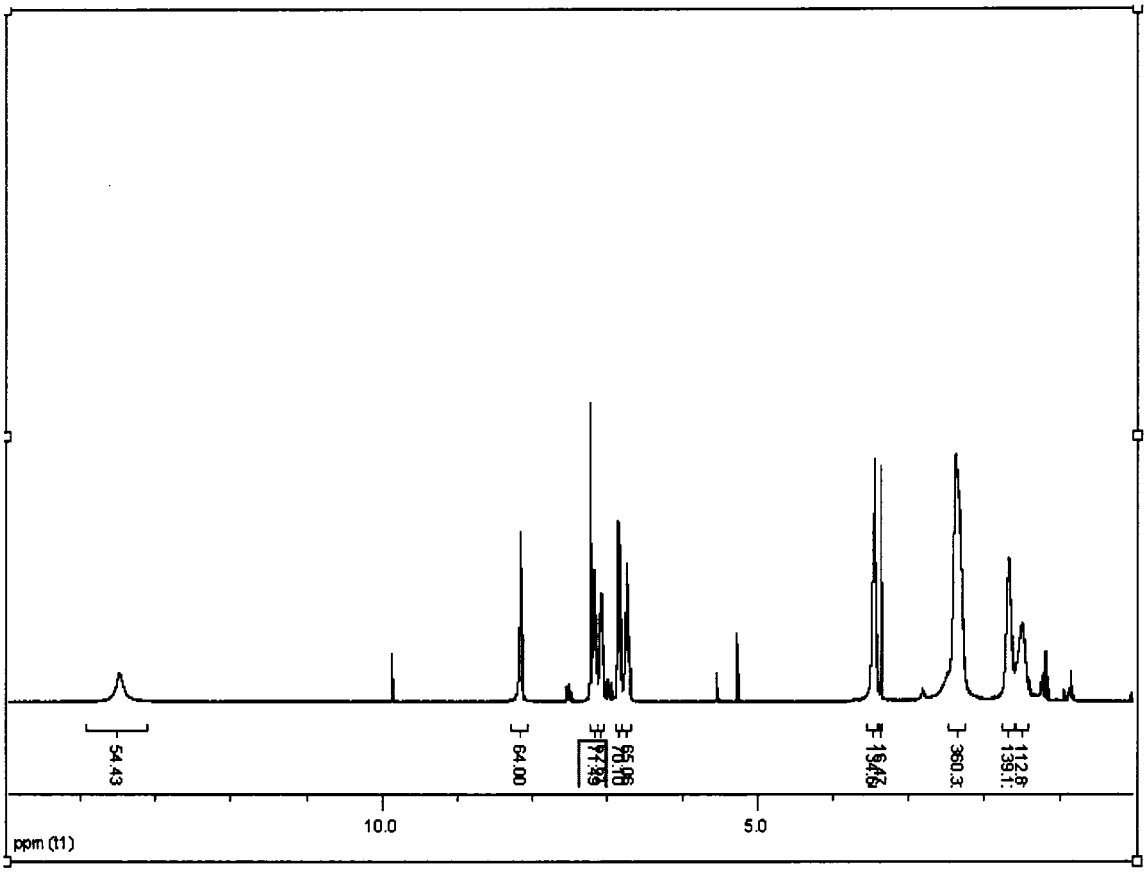
^{13}C NMR of **43**


165.256
161.596
131.519
119.098
118.763
117.282
68.318
57.730
52.575
51.737
28.839
25.961
24.793
175
150
125
100
75
50
25
ppm (t1)

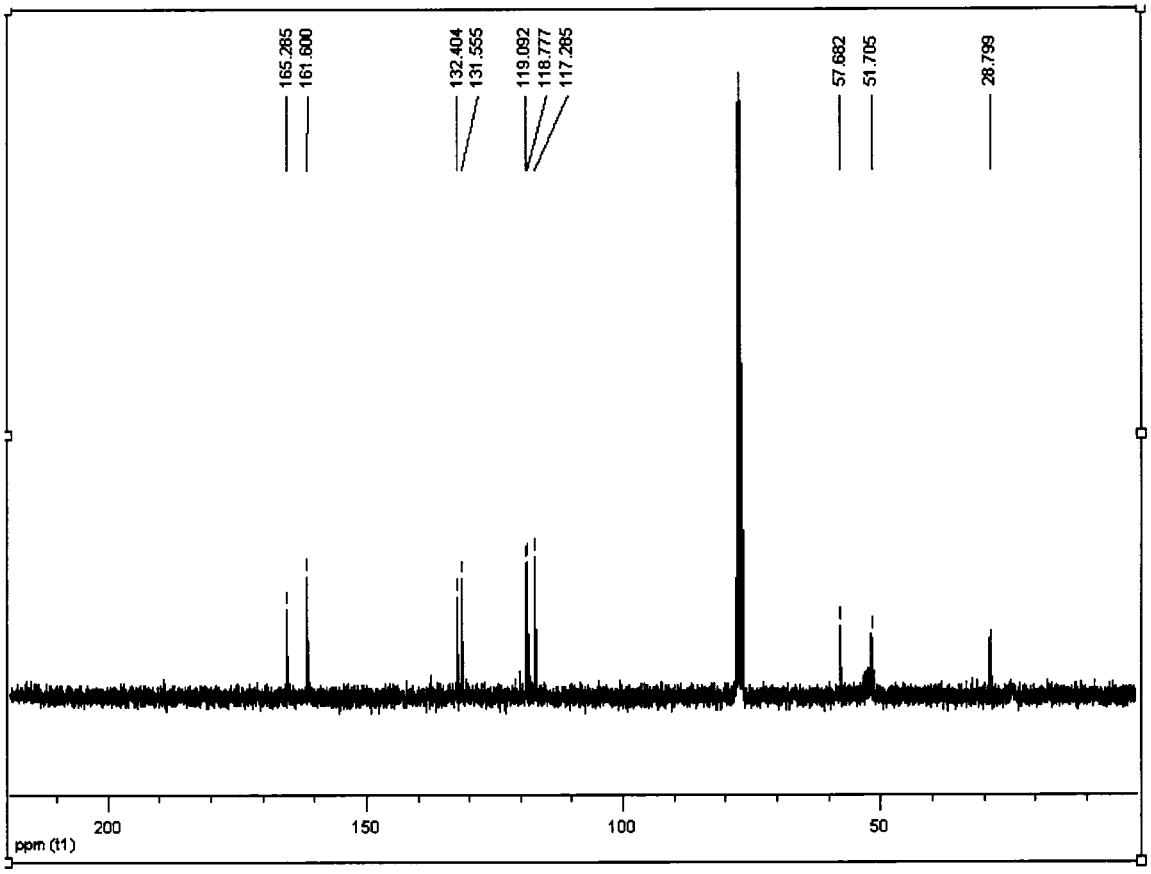
Compound 44



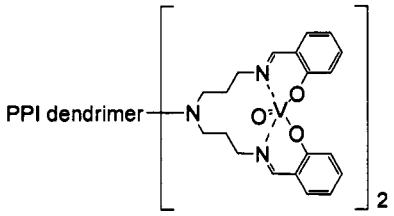
^{1}H NMR

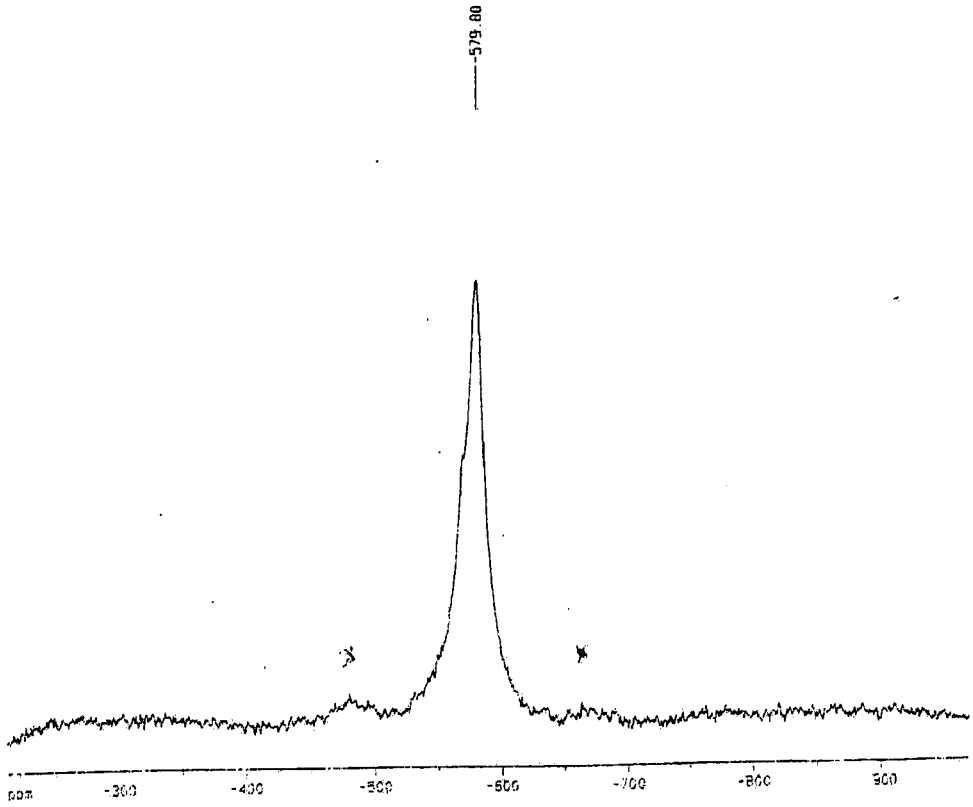


^{13}C NMR of **44**

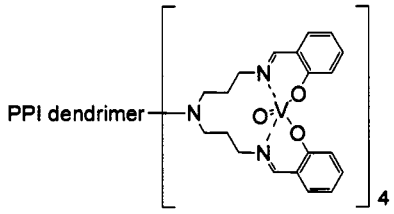

165.285
161.800
132.404
131.555
119.092
118.777
117.285
57.682
51.705
28.799
200
150
100
50
ppm (t1)

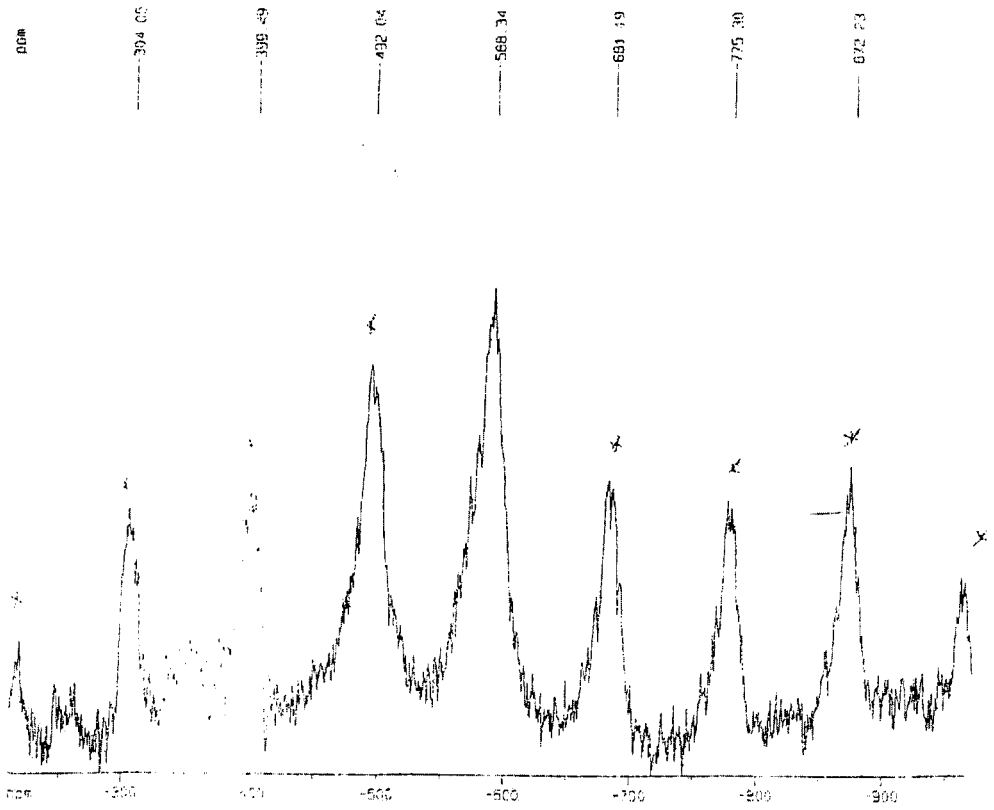
^{51}V NMR



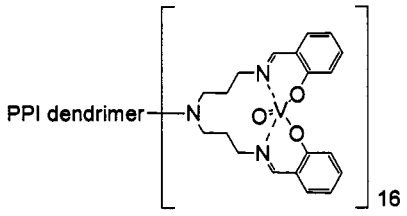


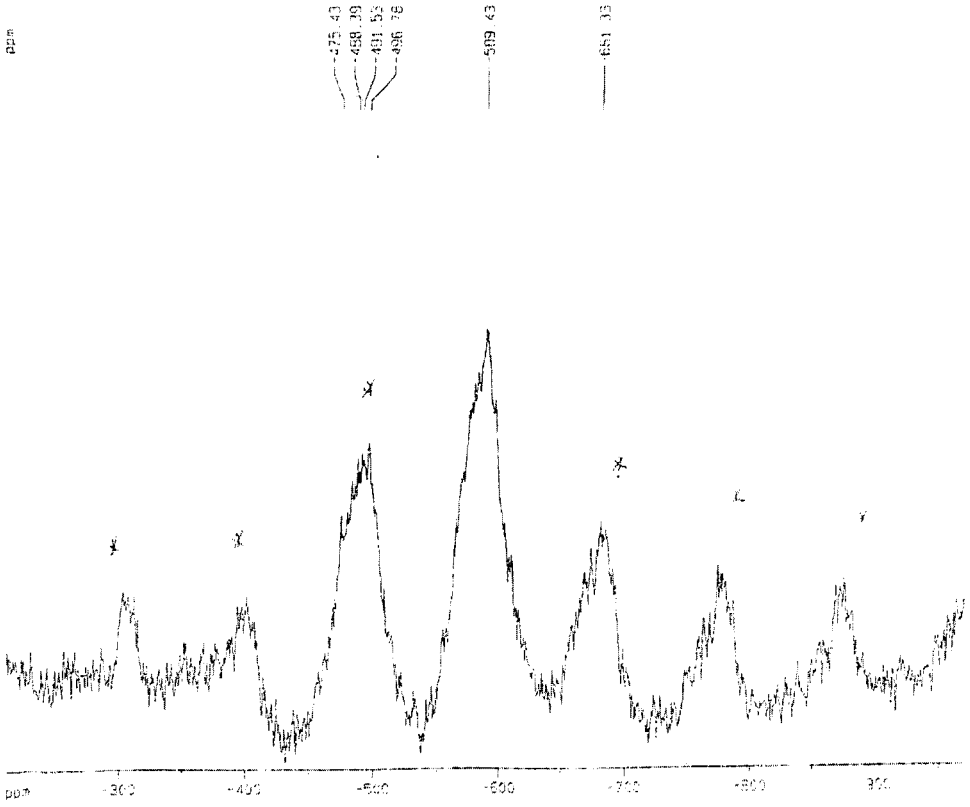
^{51}V NMR


PPI dendrimer
N
O
V
O
N
O
N
4

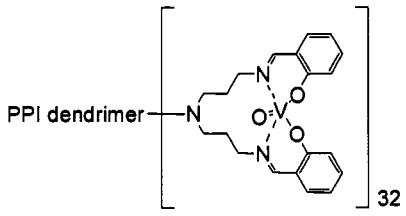

ppm
394.05
399.49
432.04
568.34
681.19
775.30
872.23
-300
-500
-600
-700
-800
-900

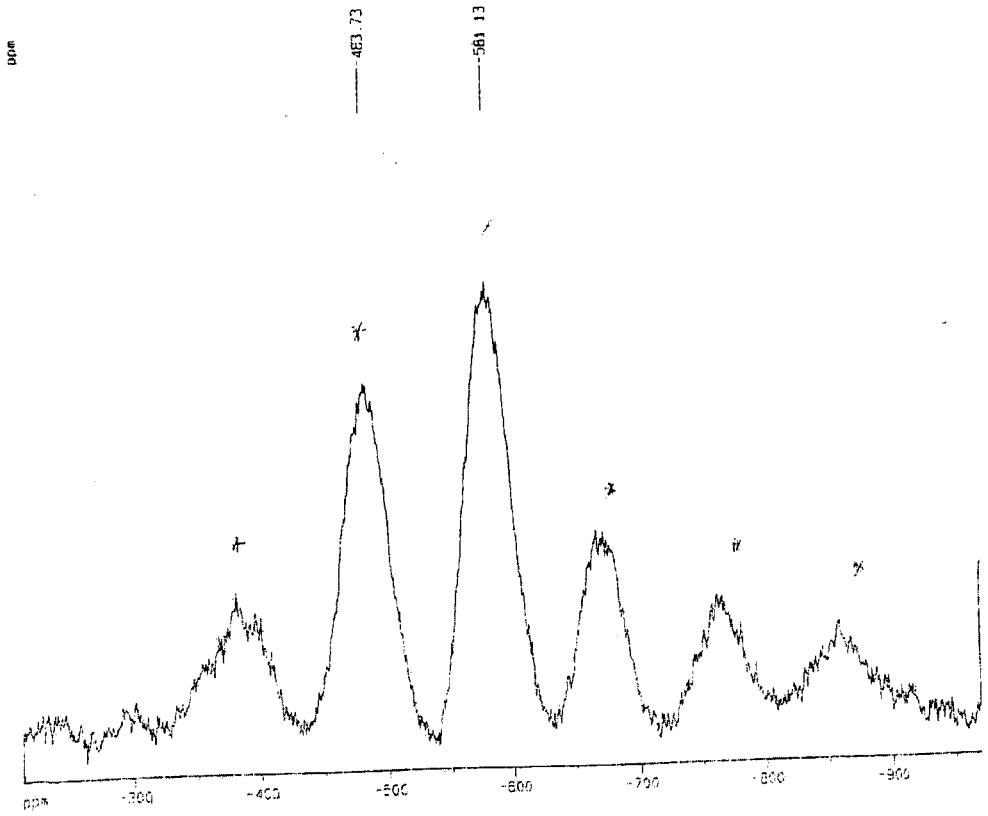
^{51}V NMR


PPI dendrimer
N
N
O
V
O
O
N
16


ppm
-475.43
-458.39
-431.55
-406.78
-589.43
-651.35
ppm
-300
-400
-500
-600
-700
-800
900

^{51}V NMR


PPI dendrimer
N
O
V
O
N
O
N
32


ppm
-463.73
-561.13
-300
-400
-500
-600
-700
-800
-900

Claims to Original Research

1. The syntheses of Pd complexes of the first and second generation of silica-supported PAMAM with 1,6-diaminohexane and 1,12-diaminododecane as amidating agents were carried out.
2. The oxidation of terminal alkenes to methyl ketones was promoted by a variety of silica supported PAMAM – Pd complexes.
3. The selective hydrogenation of dienes to monoolefins was udertaken using silica supported PAMAM – Pd complexes.
4. Novel dendritic vanadium salen complexes based on PPI dendrimers were synthesized and employed as catalysts for the epoxidation of olefinic alcohols.

Publications and Presentations

1. Pumza Zweni, Howard Alper, Dendrimer – Palladium Complex Catalyzed Oxidation of Terminal Olefins to Methyl Ketones, *Advanced Synthesis and Catalysis*, ***2004,*** 346,849 - 854
2. Pumza Zweni, Howard Alper, Selective Hydrogenation of Dienes to Monoolefins, *submitted.*
3. Pumza Zweni, Howard Alper, Epoxidation of Olefinic Alcohols Catalyzed by Vanadyl Salen-Functionalized Poly(propyleneimine) Dendrimers, *in preparation.*

- 224th American Chemical Society Meeting, August 18 - 22nd 2002, Boston, MA.
- 21st International Conference on Organometallic Chemistry, July 25 - 30th 2005, Vancouver, BC.