METALLODENDRIMERS WITH CHELATING BIPYRIDYL LIGANDS: SYNTHESIS AND CHARACTERIZATION

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METALLODENDRIMERS WITH CHELATING BIPYRIDYL LIGANDS: SYNTHESIS AND CHARACTERIZATION

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PREFACE

Dendrimers are polymers with chemically well-defined hyper-branched three-dimensional architectures. Dendrimers are of great interest because of their unique properties that make them suitable for a number of biomedical and industrial applications. Metallodendrimers offer attractive advantages over their polymeric counterparts due to their well-defined chemical composition and precise molecular structure. Catalysis based on transition metals combine the advantages of both homogeneous and heterogeneous catalytic systems such as selectivity and recyclability.

Cyclometallated complexes have found widespread interest as species with promising properties in various applications. Herein is reported the synthesis of a series of cyclometalated platinum (II) and palladium (II) isocyanide complexes, as well as some methylisocyanide-derived palladium Chugaev-type carbene complexes. Characterization of the isocyanide complexes was achieved by ^{1}H and ^{13}C NMR and IR spectroscopies. Synthetic procedures to append cyclometallated complexes to the surface of commercially available poly (propylene imine) dendrimers (PPI) were explored but were unsuccessful due to uncontrolled reactions and cross-linking.

Subsequently we have adopted a more controlled approach in which chelating ligands are covalently attached to poly (propylene imine) dendrimers (PPI), followed by complexation with Palladium. PPI dendrimers of three successive generations have been successfully functionalized with covalently attached bipyridyl ligands on the surface of the dendrimer in a single step reaction. A novel series of metal-chelating dendrimers has

been synthesized upon complexation of chelating bipyridyl ligands with palladium. Metallodendrimers had been successfully characterized using NMR, IR and ESI mass spectrometry. It is clear that IR and NMR spectroscopy provides useful signatures for ligand attachement and complexation reactions. However, when the dendrimers become heavier, especially for dendrimers with multiple metal centers, NMR spectra become very complicated and not useful for characterization. We have also shown that ESI mass spectrometry is a very useful characterizational tool when NMR studies are not adequate.

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LIST OF ABBREVIATIONS

PPI	Poly (propylene imine) dendrimers
^{1}H NMR	Proton nuclear magnetic resonance
^{13}C NMR	13 Carbon nuclear magnetic resonance
FT-IR	Fourier transform infrared spectroscopy
CNN	6-phenyl-2, 2'-bipyridyl
NCN	1,3-di (2-pyridyl) benzene
ESI-MS	Electrospray ionization mass spectrometry
G	Generation

Chapter 1

INTRODUCTION

A Brief Historical Perspective

Dendrimers are polymers with chemically well-defined hyper-branched three-dimensional architectures. Dendrimers can be constructed in a generation-wise manner starting from a central core molecule, with each iteration leading to a higher generation material. The first example of an iterative synthetic procedure towards well-defined branched structures was reported by Vögtle, who named this procedure a "cascade synthesis”.[1] This new class of macromolecules inspired many chemists in several fields. Within a few years of this discovery, many different structural classes of dendritic macromolecules had been reported.

Tomalia’s PAMAM dendrimers were the first dendritic structures to be thoroughly investigated and have received widespread attention.[2] His group devised a stepwise synthetic route to prepare highly branched polyamidoamine dendrimers using double Michael addition of methyl acrylate to a primary amine.[3] Newkome and coworkers reported an approach for the synthesis of hydrophilic carboxylic acid terminated dendrimers with hybrid polyether and polyamide generations in the interior, referred to as Newkome’s “arborol” synthesis.[4,5] Both dendrimers are constructed divergently, implying that the synthesis is started with a multifunctional core. Repeated stepwise addition of monomers to the core leads to a new layer over the existing framework. The initial focus was on the synthesis and characterization of the dendrimers. Mulhaupt, Brabander and coworkers reported the divergent synthesis of poly (propylene imine) dendrimers following the original work of Vögtle.[1,6,7] Fréchet introduced the convergent approach, where the synthesis is started at the periphery and elaborated to the core.[8] Hawker and Fréchet synthesized a series of ester, cyano, amide or ether terminated dendrimers, out of which their aromatic polyether dendrimers are easily accessible and have been studied frequently, not only by the Fréchet group but also by other researchers.[2]

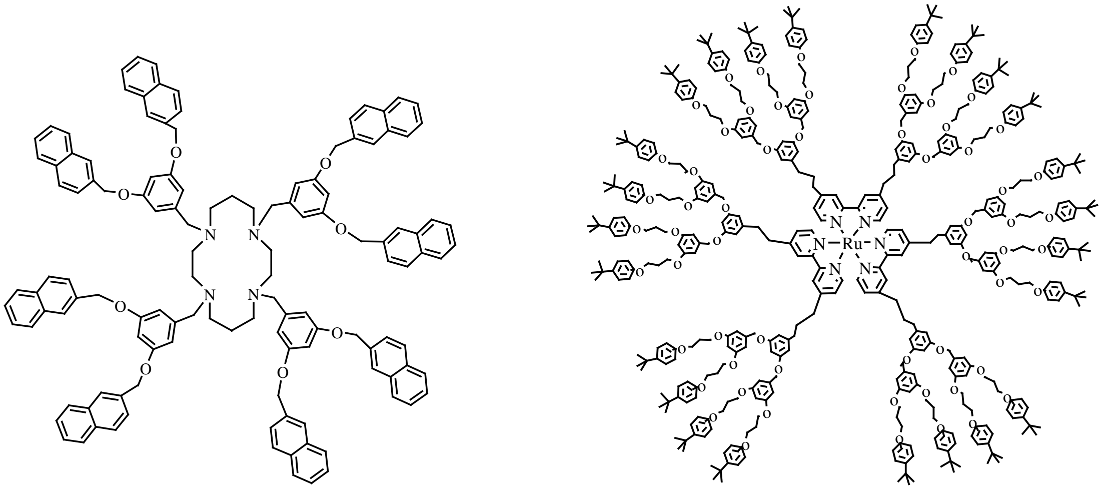


Figure 1.1 (a) Dendrimers with caclam core and (b) Dendrimer built around a $[Ru(bpy)_3]^{2+}$ type core. Adapted from reference.[9]

Miller, Neenan and coworkers reported the convergent synthesis of a series of monodisperse aromatic dendrimers consisting of phenyl rings which are symmetrically arranged.[10] These dendrimers are synthesized by a similar sequence of reactions in which the outer phenyl rings are fluorinated. Moore and co-workers synthesized the aryl-acetylene based dendrimers by a repetitive strategy involving palladium-catalyzed cross coupling reaction of a terminal acetylene with an aryl diiodide.[11,12] Additionally, many other interesting, valuable new classes of dendrimers have been developed in the last few years. Thus, a variety of dendritic scaffolds have become accessible with defined nanoscopic dimensions and discrete numbers of functional end groups. Many of the intriguing properties of dendrimers as well as their syntheses and diverse applications are discussed in excellent books and reviews that have appeared in the literature.[13,14]

Structural Features and Unique Properties

Dendrimers are highly ordered, regularly branched, globular macromolecules prepared by a stepwise iterative approach. Their structure is divided into three distinct architectural regions: (i) a core or focal moiety, (ii) layers of branched repeat units emanating from this core, and (iii) end groups on the outer layer of repeat units (Figure. 1.2). Dendrimers are differentiated from hyperbranched polymers by their structural homogeneity, in principle leading to an exact number of concentric layers of branching points, or generations.[15]

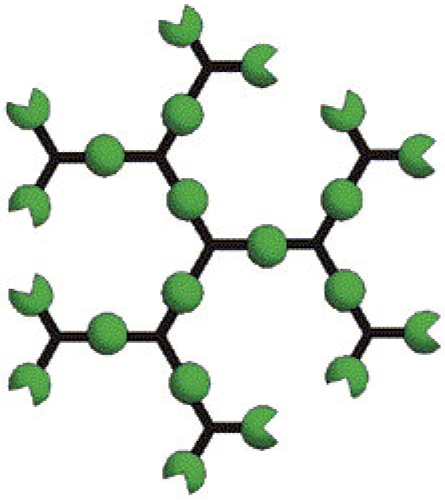


Fig 1.2 Branched architecture of a dendrimer prepared by a stepwise iterative approach. Adapted from reference.[15]

Dendrimers display unique physical properties that are significantly different from those of materials made from either linear polymers or small molecules. Dendritic molecules develop a more globular conformation as the generation size increases. The presence of large number of end groups offers possibilities of modulating the peripheral functionalities and allows the end groups to be efficiently utilized for their potential applications. The internal voids can be used to encapsulate guest molecules, and a selective binding can be achieved by controlling the degree of close packing of the dendritic shell.[16] Because of their well-defined, unique macromolecular structures, dendrimers are attractive scaffolds for a variety of biomedical and industrial applications.[15,17] For example, dendrimers have been tested in preclinical studies as contrast agents for magnetic resonance imaging (MRI), which is a diagnostic method for producing images of organs and blood vessels. Dendrimers have been used in the targeted delivery of drugs and other therapeutic agents. Drug molecules can be loaded into the interior of the dendrimers or attached to the surface groups. Dendrimers can act as carriers in gene therapy. Water-soluble dendrimers, such as PPI dendrimers, are capable of binding and solubilizing small acidic hydrophobic molecules with antifungal or antibacterial properties.[18,19]

The combination of high surface area and high solubility make dendrimers useful as nanoscale catalysts.[20] They combine the advantages of homogenous and heterogeneous catalysts, namely, the good accessibility of active sites and ease of separation from the reaction mixture.[18] There are excellent reviews that highlight major accomplishments in the field of dendrimer research to date.[13] Our research work is focused on the functionalization of PPI dendrimers with ligands, their metalation with transition metals, and their applications in catalysis. In light of the broad expansion of dendrimer research over the past years, the remainder of the discussion will focus on PPI dendrimers and metallodendrimers.

Poly (propylene imine) Dendrimers (PPI)

As mentioned, a dendritic molecule consists of three structural components: core, branch points and chain ends. A dendritic repeating unit consists of atoms from the end of one branch to the start of the next. In a PPI dendrimer, the repeating unit is a propylene imine chain, and the core is 1,4 diaminobutane, while the interior is specified as the intermediate portion between the core and the exterior. Each repeating unit is often referred to as a generation (Figure 1.3). The presence of many chain-ends is responsible for the high solubility, and high concentration of functionality of the dendrimers.[21]

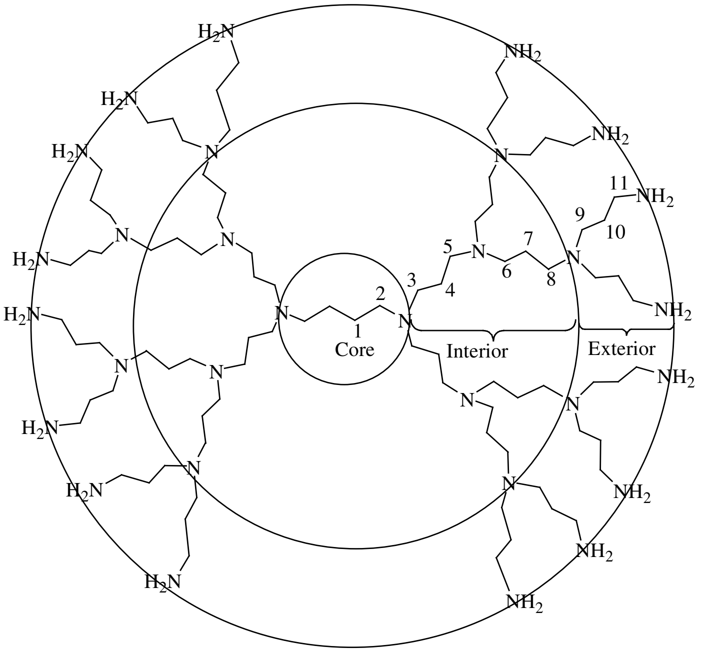


Figure 1.3 Structural components of a G3 PPI dendrimer. Adapted from reference.[18]

Mulhaupt and Brabander first reported the divergent synthesis of PPI dendrimers starting with a 1,4-diaminobutane core and successive additions of acrylonitrile followed by reduction to the amine.[6,7] PPI dendrimers can possess either nitrile or amine end chains, but primary amine-terminated PPI dendrimers have been more widely explored than their nitrile-terminated precursors due to the high thermal stability of the former.[22] The structural conformations of PPI dendrimers change with generation number. As the dendrimer becomes more crowded, the shape changes from freely rotating open chain conformations to globular or dense spherical shapes.[23] Currently, PPI dendrimers containing 4, 8, 16, 32, 64 end groups are commercially available from Aldrich Chemical Co. and DSM, The Netherlands.

Purification and Characterization of Dendrimers

Dendrimers are synthesized by divergent or convergent methods; the by-products and defect structures are often removed after the completion of each synthetic step. Low generation solid dendrimers have been successfully purified by conventional crystallizations. This technique is not useful for high molecular weight dendritic molecules due to the lack of any long-range order in the polymeric structures.[24] HPLC and gel permeation chromatography have also been used for purification of dendrimer reaction mixtures on a preparative scale.[25] Liquid chromatography has been extensively used for the purification of functionalized dendrimers, often successfully separating the desired products from the mixtures.[26]

The characterization of dendrimers is rather complex due to the size and symmetry of these macromolecules. Various NMR techniques (^{1}H, ^{13}C, ^{15}N, ^{31}P), FT-IR spectroscopy, UV spectroscopy, elemental analyses, and chromatography techniques (HPLC, SEC) are widely used, but these techniques cannot reveal small amounts of impurities especially in higher generation dendrimers. Two-dimensional NMR techniques (COSY, HMQC) make signal assignment possible with some of the poorly resolved proton spectra for lower generation dendrimers, and this technique can be used analogously with higher generation dendrimers. Fortunately, recent progress in ESI (electrospray ionization) and MALDI (matrix-assisted laser desorption ionization) mass spectrometry allows for precise analysis of dendrimers. ESI-MS has been used to identify the imperfections in both poly (propylene imine) and poly amido amine (PAMAM) dendrimers. Both these classes of dendrimers are suitable for electrospray ionization due to their polar and basic nature.[2,27] Metallodendrimers that have been studied with L-SIMS, MALDI-MS, and ESI-MS are of lower generations, and consequently, these materials contain few defect structures, even though these materials have been produced using a divergent approach.[28-30]

METALLODENDRIMERS

Classification and Applications

Metal-containing dendrimers (metallodendrimers) have attracted a great deal of attention recently because of their unique properties and useful applications. Metallodendrimers are supramolecular species that can possess novel physical, optical, electrochemical, photochemical, biological, and catalytic properties. These potential properties of dendrimers have been discussed to some degree in recent literature.[31] Organometallic dendrimers offer attractive advantages over their polymeric counterparts due to their well-defined chemical composition and precise molecular structure.[32] Catalysis based on transition metals within functionalized dendrimers is a particularly promising application. These systems can combine the advantages of both homogenous and heterogeneous catalytic systems such as selectivity and recyclability.

Metallodendrimers can be classified based on where the metal appears in the dendrimer. Incorporation of metal ions into the framework was initiated by Balzani's and Newkome's research groups in the early 1990s, either by the use of metal branching centers or by internal metal complexation or encapsulation at specific binding sites.[33,34,35] "Commonly, metals have served as *branching centers*, *building block connectors* (including core as well as monomer connections), *terminal groups*, and *structural auxiliaries*, whereby metals are introduced into a framework after dendritic construction (Figure 1.4). The latter category includes other architectures and allows for *site-specific* versus *random* inclusion".[32]

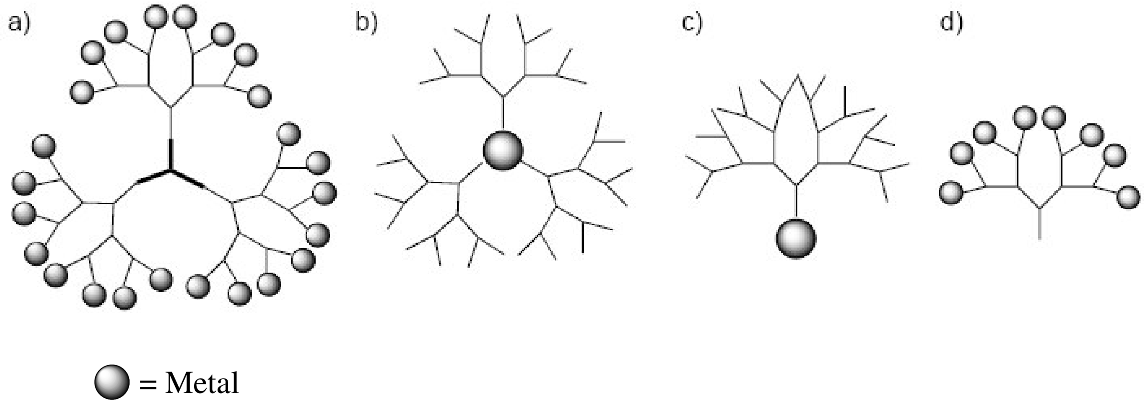


Figure 1.4 Positioning of potentially useful metals within the dendritic architectures. Adapted from reference.[36]

Metals as Branching Centers

The first synthesis of metallodendrimers possessing homo- and heterometallic branching centers (ruthenium and osmium) was reported by Balzani and cowerkers.[33,34] A decanuclear polypyridine complex (Figure 1.5) was prepared from a trigonal core, containing a metal coordinated to three 2,4-bis(2-pyridyl) pyrazine ligands.[37] Based on this synthetic strategy, Balzani's group synthesized further dendrimers possessing two or more different metals and/or ligands.[31] Each of the dendrimers is an ordered ensemble of weakly interacting units containing metals such as Ru(II) or Os(II). Campagna, Denti, Balzani and co-workers have synthesized the higher generations of this series, with dendritic structures made of Ru(II)-polypyridine complexes prepared by the complexes-as-metals and complexes-as-ligands synthetic strategies.[38]

Suzuki and co-workers reported the first synthesis of "dendritic bismuthanes" by directed tris-ortholithiation of tris [2-(diethylaminosulfonyl) phenyl] bismuthane with *tert*-butyllithium, followed by treatment with bis [2-(diethylaminosulfonyl) phenyl] bismuth iodide to give a symmetrically branched bismuthane dendrimer as the main product.[39] Bochkarev and coworkers reported the synthesis of Ge-hyperbranched macromolecules via polymerization of tris(pentafluorophenyl) germanium anions.[40] Building blocks were connected via Ge substitution in the monomers, affording the hyperbranched dendritic polymers. Molecular weights in the range from 100 000 to 170 000 amu were determined.

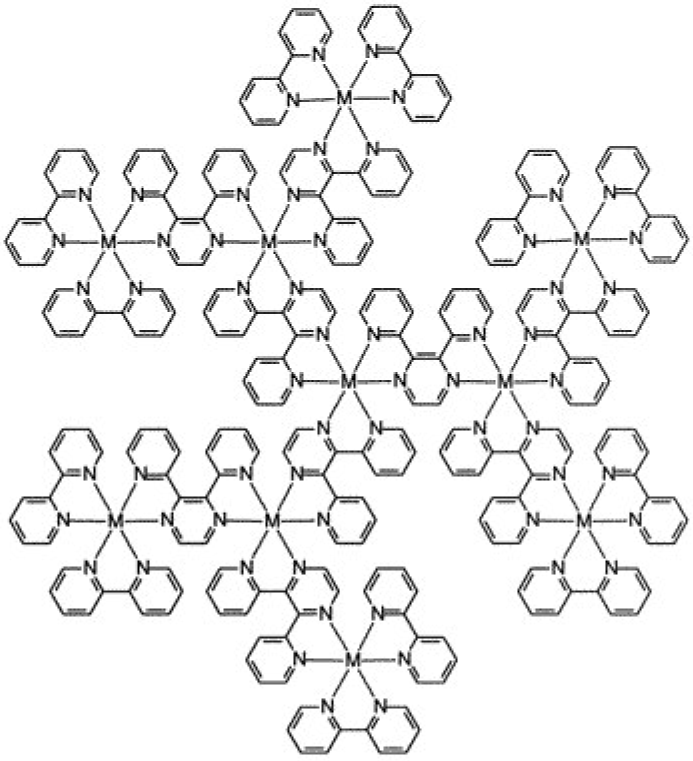


Figure 1.5 Balzani's bipyridyl-based metallodendrimers. Adapted from reference.[38]

Synthesis of the first-generation Ge-branched, alkane-based, metallodendrimers containing 12 alkene end groups (Figure 1.6) was reported by Mazerolles and co-workers.[40] Both convergent and divergent methods were applied, starting from a tetravalent core. However, the second-generation dendrimer was only obtained by a divergent approach. Purification of these metallodendrimers proved arduous using silica-based column chromatography due to the inability to remove the trace impurities formed during dendrimer construction. Further the use of IR and NMR for differentiation of generation one and generation two was not feasible.[31] Metals serving as branching centers are also well known in small, nondendritic architectures. A couple of notable examples of these have been reported based on their potential to be incorporated into the dendritic regime.[31]

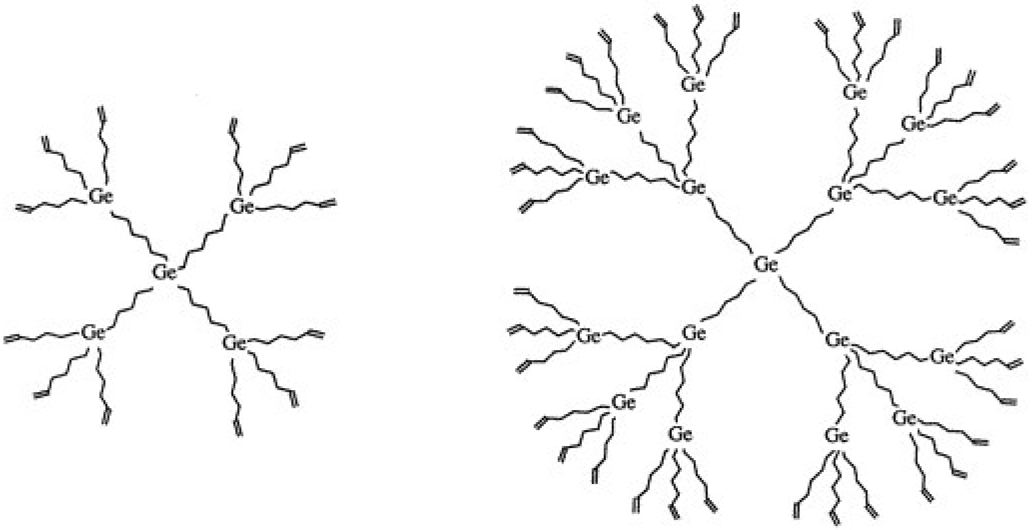


Figure 1.6. Mazerolles's Ge-branched, alkyl-based metallodendrimers. Adapted from reference.[40]

Metals as Building Block Connectors

Recently, much attention has been focused on main-group-element-based dendrimers in view of their optical properties and surface functionalization. Nanjo and Sekiguchi reported the divergent synthesis of a hybrid dendrimer with alternating Si-branching centers and Ge-branched chain connectors.[41] The structure of the first generation of the hybrid dendrimer has been established by X-ray crystallography. Newkome and coworkers first reported the preparation of dendrimers incorporating convenient ligand-metal-ligand connectivity with Ru metal centers, whereby each metal center is coordinated by two orthogonal 4'-substituted 2,2': 6', 2''-terpyridines.[42] This strategy of ruthenium connectivity has been applied to the development of metal complexes capable of connecting multiple preconstructured branched polymers.[32]

Newkome and He et al. have expanded the -<*Ru*>- single connectivity to include the incorporation of linearly connected complexes (i.e., -<*Ru*>-(*x*)-<*Ru*>-) in each arm of the metallodendrimer core.[43] Dendritic macromolecules with bis(2,2': 6', 2''-terpyridine) ruthenium (II) connectivity were synthesized. This assembly methodology, has demonstrated both the control of metal complexation sites and a degree of flexibility within the linkages.

Constable and Harverson reported a convergent strategy for the construction metallodendrimers by the reaction of coordinated nucleophiles with multifunctional electrophiles.[44] They have introduced a new type of coupling methodology for the assembly of metallodendrimers involving the reaction of coordinated 4'-hydroxy-2, 2': 6', 2''-terpyridine ligands with poly (bromomethyl) benzenes. Another convergent synthetic methodology was used to synthesize an octanuclear complex, wherein the octaruthenium species was obtained from the reaction of a nucleophilic trinuclear building block with hexakis (bromomethyl) benzene. In a later report, Constable and coworkers developed a convergent approach to synthesize metallodendrimers which have a metal as the central growth point.[45] The reaction of a nucleophile with bis(bromomethyl) benzene, which was subsequently reacted with 4,4'-dihydroxy-2,2'-bipyridine, resulted in a dinuclear complex possessing two terpyridyl Ru(II) moieties linked by an uncomplexed bipyridine ligand. Coordination to transition metals, such as Fe (II) and Co (II), afforded the desired heptanuclear metallomacromolecule (Figure 1.7).

Achar and Puddephatt created a series of convergently prepared organoplatinum dendrimer complexes by oxidative addition reactions of 1,2,4,5-tetrakis (bromomethyl)-benzene to a dimethylplatinum(II) center, giving rise to metallodendrimers containing 14 Pt centers. [31,46] Later, the same authors reported the fourth generation metallodendrimer containing 28 Pt centers, which was one of the largest reported transition-metal dendrimers.

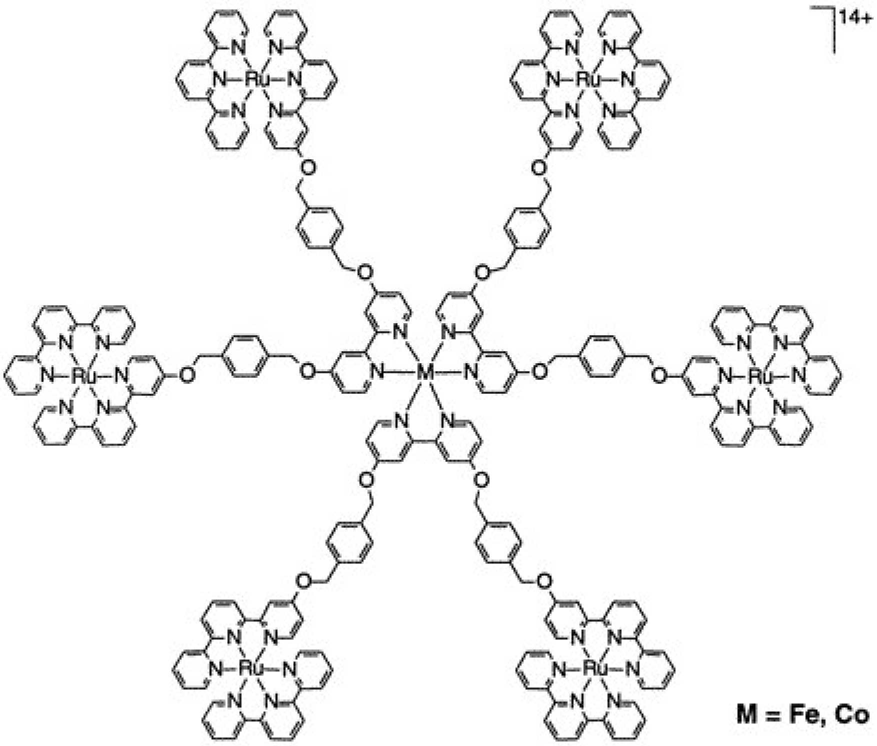


Figure 1.7 Constable's heptanuclear mixed-metal complex. Adapted from reference.[45]

Metals as Cores

There is great interest in designing dendritic catalysts, which are more active, stable and selective than their homogeneous monomeric analogues. The novel properties induced by the dendritic framework clearly depend on the location of the functional groups and metal centers within the structure. Core functionalized dendrimer systems have their ligand systems arranged such that the substrate has to penetrate the dendrimer prior to reaction. This accessibility allows reaction rates that are comparable with those of homogeneous systems. Dendrimers functionalized with transition metals in the core can potentially mimic properties of enzymes, their efficient biological counterparts. In core-functionalized dendrimers, the catalysts could especially benefit from the site isolation effect or the specific microenvironment created by the dendritic structure, and also from the local polarity effect around the catalyst created in the structure.[47] On the other hand, the solubility of the dendritic systems can be tuned by changing the end groups.

Inoue and coworkers reported a ‘caged' porphyrin-zinc complex which was the first dendritic molecule having a core photochemical functionality.[48] A novel porphyrin covalently encapsulated into a large dendritic cage was synthesized by an alkali-mediated coupling reaction of porphine [5,10,15,20-tetrakis (3', 5'- dihydroxypheny1) porphine] with dendritic bromide [3,5dialkoxybenzyl bromide] employing Fréchet's established convergent method. Metallodendrimers up to the fourth-generation were synthesized, and fluorescence quenching using the fourth-generation metallodendrimer was studied.

In mimicking biological functions of haemoproteins, one of the attractive targets is to realize the reversible dioxygen-binding activities of haemoglobin and myoglobin.

Jiang, Aida and coworkers synthesized similar metallodendrimers up to the fourth generation with Fe-containing porphyrin.[49] This dendritic iron porphyrin complex displayed reversible dioxygen-binding activity. These authors further synthesized metallodendrimers containing Zn porphyrin, which was modified with carboxylate, groups on the surface. The photoinduced electron transfer mechanism through the dendrimer architecture was studied.

Moore, Suslick, and co-workers synthesized a new class of sterically hindered Mn containing dendrimer-metalloporphyrins for use as shape-selective oxidation catalysts.[50] A series of oxidatively robust poly (phenylester) dendrimers were prepared through a convergent synthesis. Four ester-based dendritic building blocks were appended to the meta-positions of the 5,10,15,20-tetrakis(3',5'-hydroxyphenyl) porphinatomanganese (III) chloride to obtain the second and third generations of metallodendrimers (Figure 1.8).

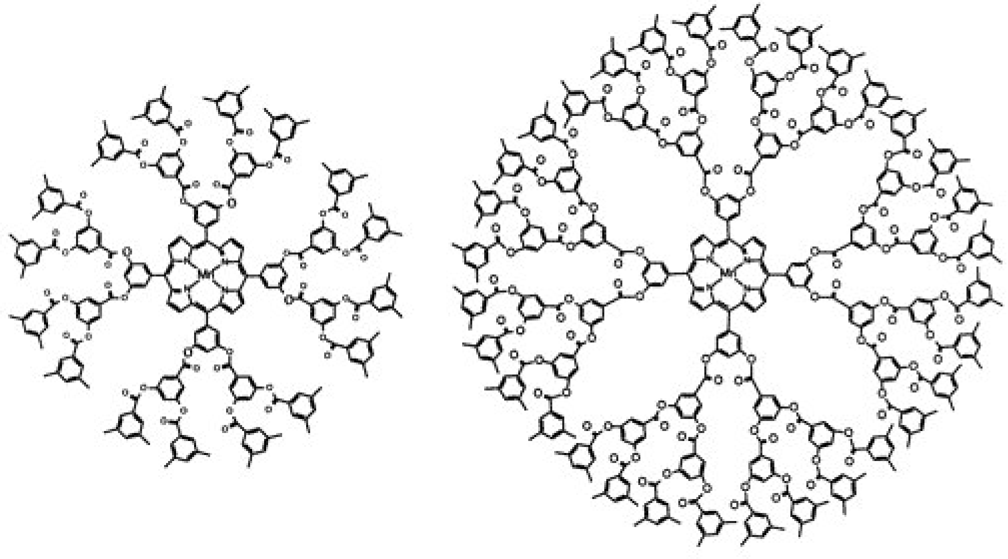


Figure 1.8 Moore and Suslick's Mn-based metallodendrimers as selective oxidation-catalysts. Adapted from reference.[50]

Both dendrimers have been examined as regioselective oxidation catalysts for both intra- and intermolecular reactions. Epoxidations of nonconjugated dienes and of 1:1 mixtures of various alkenes possessing different shapes and sizes were examined. The dendritic catalysts showed superior regioselectivity at the less hindered double bond positions when compared to the corresponding parent manganese (III) cation.

Lanthanide elements (Ln) are well known for their unique luminescence properties. Therefore self- assembly of dendritic wedges around a lanthanide core has been of particular interest. Long lifetimes and the characteristic narrow width emission make them especially useful in fibre optic application for use as signal amplifiers. Kawa and Fréchet reported lanthanide-containing metallodendrimers up to the fourth generation via the self-assembly of three polybenzyl ether dendrons by carboxylate anion coordination to a central trivalent cation (Er^{3+}, Tb^{3+}, Eu^{3+}).[51] The luminescence properties of these novel metallodendrimers, measured in both solution and in bulk, were enhanced as the size of the dendritic surroundings increased.

Vögtle, Balzani and coworkers reported the synthesis of metallodendrimers up to the third generation with a $[Ru(bpy)_3]^{2+}$ complex as a core, the largest generation possessing 54 peripheral methyl ester groups.[52] Branching was instilled using an amino triester monomer prepared via methyl acrylate addition to tris(hydroxymethy1)-aminomethane. The larger metallomacromolecule exhibited a more intense emission spectrum and a longer excited-state lifetime than the parent Ru(II) cation in aerated solutions. This was rationalized by considering the shielding effect of the dendritic scaffolding.[31]

Metal complexes with ligands consisting of bis(oxazoline) moieties are known to catalyze reactions such as cyclopropanation of olefins and the Diels-Alder reaction. Chow and Mak and coworkers reported the preparation of metallodendrimers up to the fourth generation containing bis(oxazoline)copper(II) complexes.[53] The phenolic-based dendrons are prepared by the convergent approach using a three-step iterative synthetic sequence involving alkylation followed by hydrogenolysis with a palladium catalyst. These catalysts were evaluated in the Diels-Alder reaction between cyclopentadiene and crotonyl imide.

Van Leeuwen's research group focused on the catalytic activity of a corbosilane dendrimer in an effort to control sterioselectivity of allylic alkylations.[54] A ferrocenyl diphosphine was functionalized with different generations of carbosilane dendrons, producing a series of dendrimer phosphine ligands. In situ complexation of these dendrimer phosphines with a suitable Pd^{II}-precursor followed by incubation gave the $PdCl_2$-complexed dendrimers. The Pd-dendrimers were used as catalysts in the allylic alkylation of 3-phenyl allyl acetate with diethyl 2-sodio-2-methylmalonate (Figure 1.9).

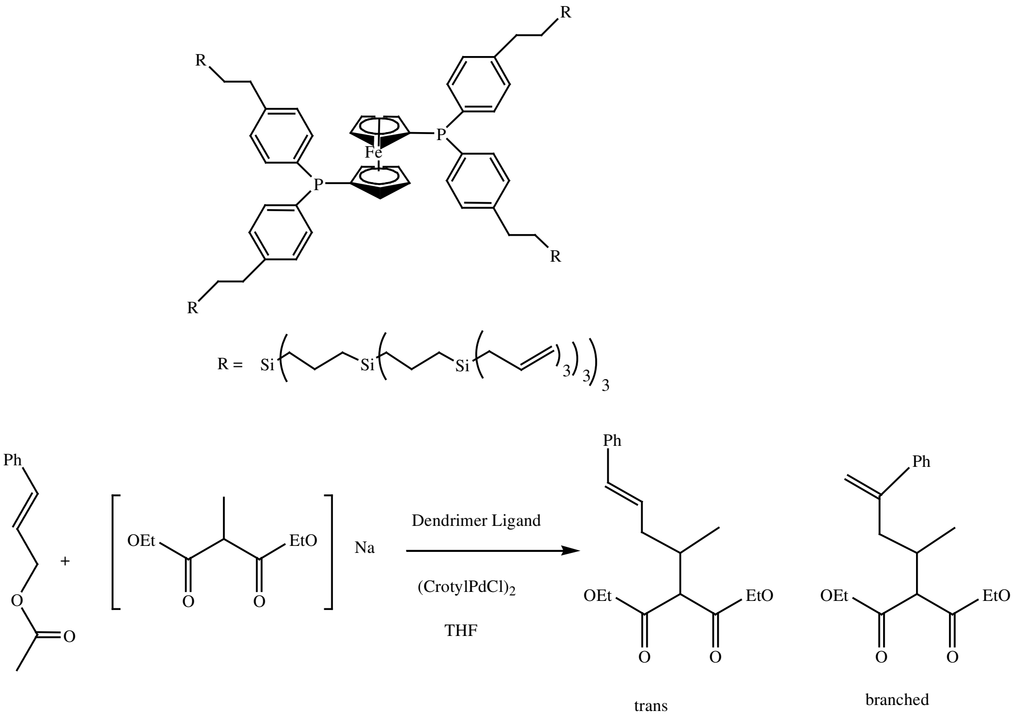


Figure 1.9 Ferrocenyl diphosphine metallodendrimer with carbosilane dendrons. Adapted from reference.[54]

Metals as Termination Groups (Surface Functionalization)

Surface functionalized dendrimers have been proposed to fill the gap between homogeneous and heterogeneous catalyst systems. Periphery-functionalized dendrimers have their ligand systems, and thus the metal complexes, at the surface of the dendrimer. The transition metals are directly available to the substrate. This accessibility allows reaction rates that are comparable with those of homogeneous systems. The periphery-functionalized systems contain multiple reaction sites and ligands, which result in extremely high local concentrations of the catalyst and ligand. This high local concentration greatly affects the catalytic performance in either a positive or a negative sense.[47]

Van Koten's group made the first catalytically active metallodendrimers up to the second generation using the first examples of dendritic carbosilane molecules.[55] The synthesis of the metallodendrimer started from carbosilane molecules containing reactive silicon chloride bonds on the surface. Twelve arylbromides were attached to the periphery via the oxidative addition of zero-valent nickel source [e.g. $Ni(PPh_3)_4$]. The resulting arylnickel species were tested as homogeneous catalysts in the atom transfer radical addition reaction (ATRA or Karsch addition reaction) of CCl_4 to methyl methacrylate. A notable advantage of these metallodendritic catalysts is their facile removal from the reaction mixture, providing a recyclable property to the "dendrocatalyst."

Van Koten reported the synthesis of carbosilane dendrimer with 12 peripheral iodoarene groups.[56] The dodecaaryliodo-terminated silicon-based dendrimer precursor was treated with palladium dibenzylideneacetone [$Pd(dba)_2$] and *N*, *N*, *N'*, *N'*-tetramethylethylenediamine (tmeda) to yield the desired metallodendrimer (Figure 1.10). This dendrimer represents the first example of palladium metals exclusively σ-bonded to the periphery of a dendritic scaffold. Dubois observed metal-metal interactions in palladium-functionalized systems.[57]

Dendrimers were constructed containing up to 15 phosphines in both the periphery and the backbone by the sequential addition of diethyl vinylphosphonate to primary phosphines followed by reduction with lithium aluminum hydride. These dendrimers were treated with $[Pd(CH_3CN)_4]\ (BF_4)_2$ to produce metalated dendrimers that catalyze the electrochemical reduction of CO_2 to CO (Figure.1.11). The rates and selectivities were compared with those of the monomeric complexes.

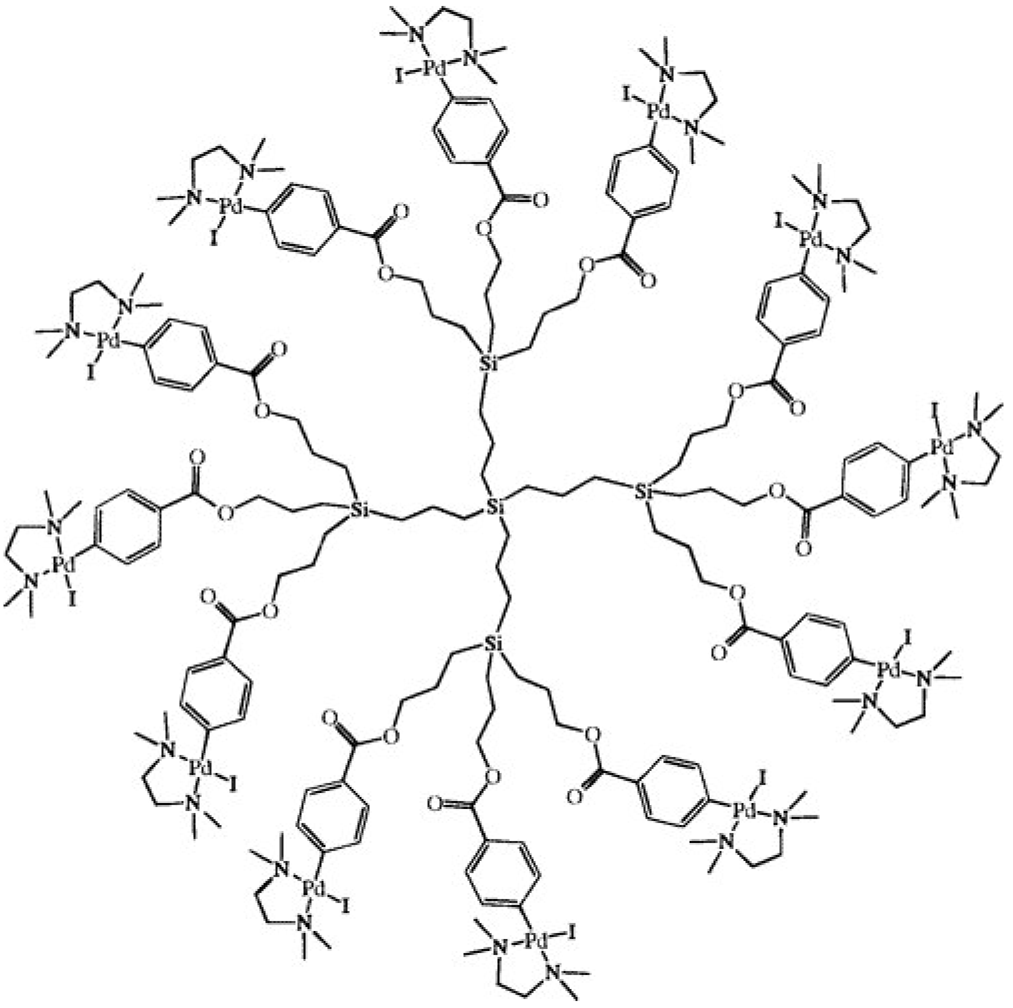


Figure 1.10 Metallodendrimer with Pd σ-Bonded to the surface. Adapted from reference.[56]

Reetz modified polypropylene imine dendrimer with chelating diphenylphosphine ligands.[58] Polyamine dendrimer was treated with Ph_2PCH_2OH to give diphenylphosphine end groups on the surface, which were then complexed with Pd, Ir, Rh, or Ni to give the corresponding dendritic complexes. The complexes were used as catalysts for hydroformylation of 1-octene. They showed a high catalytic activity compared with the monomeric complexes and could be separated by membrane separation techniques. The palladium version of Reetz's diphosphine metallodendrimers catalyzed the Heck reaction with a 4-fold increase in the turnover number compared to the monometallic complexes.[58,59]

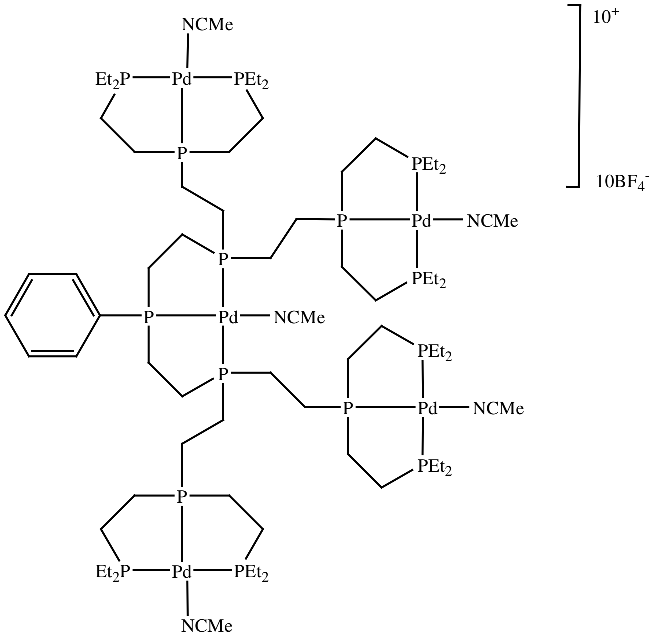


Fig. 1.11. Dubois's organophosphine dendrimers containing palladium. Adapted from reference.[57]

Reetz's diphosphine dendrimers were used by Mizugaki to synthesize the dendritic catalyst DAB-*dendr*- $[N(CH_2PPh_2)_2\ PdCl_2]_{16}$ by reaction with $[PdCl_2(PhCN)_2]$.[60] The catalysts were examined in the hydrogenation of conjugated dienes to monoenes. Excellent selectivity and higher catalytic activity were observed for the hydrogenation of cyclopentadiene to cyclopentene compared to that of the corresponding monomer and the polystyrene-bound catalyst. Generation-3 diphosphine dendrimers containing 24 Pd or Ru centers (Figure. 1.12) were used by Majoral's group to catalyze the Stille coupling reaction of methyl-2-iodobenzoate with 2-(tributylstannyl) thiophene, the Knoevenagel condensation between malononitrile and cyclohexanone leading to the corresponding unsaturated nitrile, and the Michael addition between ethyl cyanoacetate and diethylethylidene- malonate.[61] The catalysts showed a higher activity compared with that of the monomer complexes and recycling was possible without significant loss of activity.

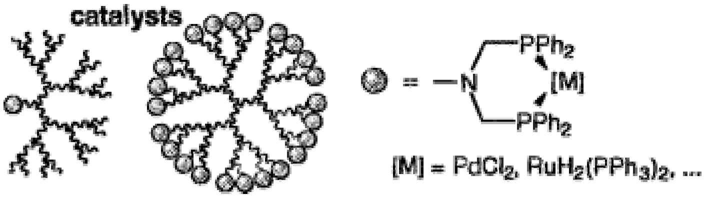


Figure 1.12 Majoral's G-3 diphosphine dendrimers containing 24 Pd or Ru atoms. Adapted from reference.[60]

Other Dendritic Architectures Containing Metals

Newkome reported the first organometallic dendrimer possessing site-specific attachment of a metal center within the structure.[62] Dendrimers containing twelve alkyne end groups were successively treated with dicobalt octacarbonyl to afford the corresponding cobalt-containing cascade that was termed a 'cobaltomicellane'. Yang synthesized the first star polysulfoxide containing dendrimers with Cu (II) ions randomly encapsulated in the framework.[63] A star polysulfoxide gives a novel binuclear bis-tripodal species by encapsulating a pair of Cu (II) ions.

Balogh and Tomalia synthesized poly(amidoamine) (PAMAM) dendrimer-templated nanocomposites.[64] A fourth generation PAMAM dendrimer was treated with copper(II) acetate, resulting in a metallodendrimer containing approximately 15-32 potential Cu(II) sites within the dendrimer. Copper(II) ions were reduced to zerovalent copper, thus providing stable metallic copper(0) dendrimer-metal nanocomposites in solution (Figure 1.13)

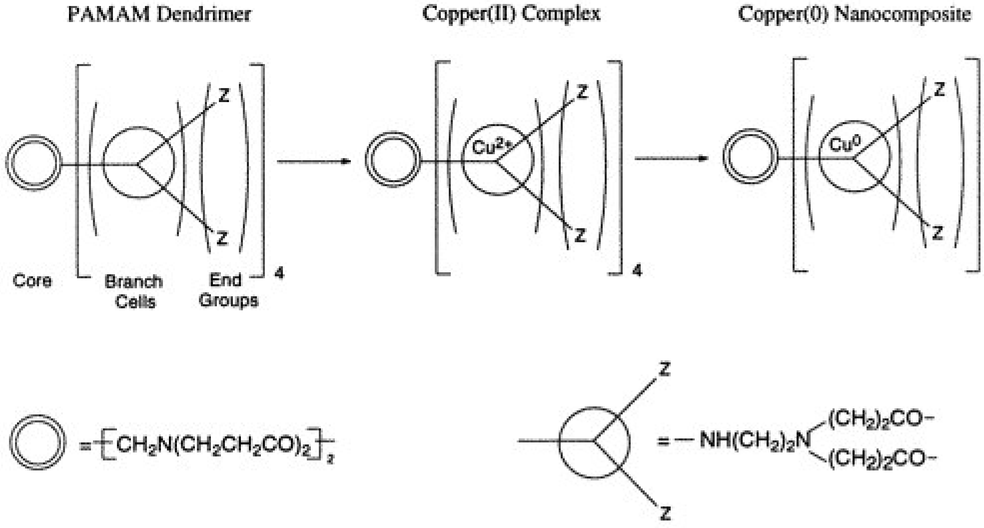


Figure 1.13. PAMAM-based Copper (II) complexes and Copper (0) nanocomposites. Adapted from reference.[64]

Crooks reported the synthesis, physical and chemical properties, and stability of Pd nanoparticles encapsulated within poly(amidoamine) (PAMAM) dendrimers.[65] Generation 4-8 amine and hydroxyl-terminated PAMAM dendrimers were treated with K_2PdCl_4, resulting in a covalent attachment of the hydrolysis product ($PdCl_3^-$) to the tertiary amines within the dendrimers. Reduction with $NaBH_4$ results in conversion of dendrimer-encapsulated $PdCl_3^-$ to nearly size monodisperse, encapsulated, zerovalent Pd nanoparticles (Figure 1.14). These materials have a number of potential applications, especially in catalysis.

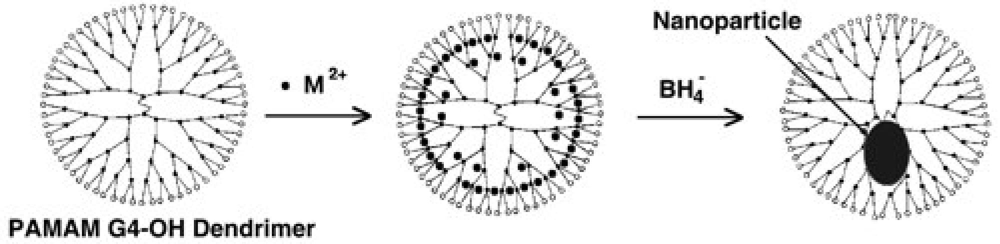


Figure 1.14. Synthesis of dendrimer-encapsulated Pd^0 nanoparticles. Adapted from reference.[65]

Composite materials consisting of noble metal (Pt^0, Pd^0) nanoparticles stabilized within dendrimer interiors are suitable for use as homogeneous hydrogenation catalysts. Dendrimer-encapsulated Pd clusters exhibited high catalytic activity for the hydrogenation of alkenes in water. The catalyst acts as both a template for the preparation of monodisperse nanoparticles and a porous stabilizer.[66] Crooks's group also reported the application of dendrimer-encapsulated Pd nanoparticles to fluorous biphasic catalysis.[67] These new catalysts show high activity and selectivity for biphasic hydrogenations of alkenes and conjugated dienes. Moreover, the catalysts can easily be recovered and used for multiple reactions by simple organic extractions.

The first example of a carbon-carbon coupling reaction catalyzed by a dendrimer-templated nanomaterial has been reported by Yeung, Crooks and coworkers.[68] Palladium nanoparticles were prepared within covalently functionalized poly(propylene imine) (PPI) dendrimers; these catalysts show a high activity in the Heck-type heterocoupling between nonactivated aryl halides and *n*-butylacrylate. The catalyst was recovered by cooling to room temperature and phase separating. Chandler reported another method for immobilizing dendrimer-encapsulated nanoparticles (DEN's) in a sol–gel silica.[69] The catalysts showed significant activities for CO oxidation catalysis but substantially less activity for toluene hydrogenation.

OBJECTIVES

The primary objective of this research is to attach well-defined palladium and platinum complexes to dendrimers. Commercially available poly(propylene imine) dendrimers have their surfaces decorated with primary amine groups. In one approach, a series of tridentate platinum and palladium isocyanide complexes were synthesized and characterized. Methods were sought to link these isocyanide complexes to the amine-terminated dendrimer by a nucleophilic reaction of the amines with the isocyanide ligands of the metal complexes.

Another goal was the ligand-functionalization of poly(propylene imine) dendrimers by a new synthetic route through the imine condensation reaction. The ligand-functionalized dendrimers were then metalated with the catalytically important transition metal palladium.

REFERENCES

(1) Buhleier, E. W.; Wehner, W.; Vögtle, F *Synthesis* **1978**, 155-158.

(2) Bosman, A. W.; Janssen, H. M.; Meijer, E. W. *Chemical Reviews (Washington, D. C.)* **1999**, *99*, 1665-1688.

(3) Tomalia, D. A.; Baker, H.; Dewald, J.; Hall, M.; Kallos, G.; Martin, S.; Roeck, J.; Ryder, J.; Smith, P. *Polymer Journal (Tokyo, Japan)* **1985**, *17*, 117-32.

(4) Newkome, George R.; Yao, Zhongqi; Baker, Gregory R.; Gupta, Vinod K. *Journal of Organic Chemistry* **1985**, *50*, 2003-4.

(5) Newkome, George R.; Lin, Xiaofeng *Macromolecules* **1991**, *24*, 1443-4.

(6) Wörner, C.; Mülhaupt, R. *Angew. Chem., Int. Ed. Engl.* **1993**, 1306-1308.

(7) De Brabander-van den Berg, E. M. M.; Meijer, E. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1308-1311.

(8) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638-7647.

(9) Ceroni, Paola; Vicinelli, Veronica; Maestri, Mauro; Balzani, Vincenzo; Lee, Sang-kyu; van Heyst, Jeroen; Gorka, Marius; Voegtle, Fritz *Journal of Organometallic Chemistry* **2004**, *689*, 4375-4383.

(10) Miller, Timothy M.; Neenan, Thomas X.; Zayas, Roberto; Bair, Harvey E. *Journal of the American Chemical Society* **1992**, *114*, 1018-25.

(11) Moore, Jeffrey S.; Xu, Zhifu *Macromolecules* **1991**, *24*, 5893-4.

(12) Xu, Z.; Moore, J. S *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 246-248.

(13) Newkome, G. R.; Moorefield, C. N.; Vögtle, F; *Dendritic Molecules: Concepts, Syntheses and Perspectives*; VCH: Weinheim, Germany, 1996.

(14) Ardoin, N.; Astruc, D. *Bull. Soc. Chim. Fr* **1995**, *132*, 875-909.

(15) Grayson, Scott M.; Frechet, Jean M. J. *Chemical Reviews (Washington, D. C.)* **2001**, *101*, 3819-3867.

(16) Yijun, Pan; Ford, W.T. Thesis Ph.D, Oklahoma State University, 1999.

(17) Klajnert, B.; Bryszewska, M. *Acta Biochimica Polonica* **2001**, *48(1)*, 199.

(18) Dian, He, Thesis, Marshall University, 2002.

(19) Twyman, L. J.; Beezer, A .E.; Esfand, R.; Hardy, M. J.; Mitchell, J. C. *Tetrahedron Lett* **1999**, *40*, 1743.

(20) Tomalia, D. A.; Dvornic, P. R. *Nature* **1994**, *372*, 617.

(21) Fréchet, J. M. J. *Science* **1994**, *263*, 1710-1715.

(22) Hummelen, Jan C.; Van Dongen, Joost L. J.; Meijer, E. W. *Chemistry A European Journal* **1997**, *3*, 1489-1493.

(23) Krieider, J.L, Thesis Ph.D, Oklahoma State University, 2000.

(24) Leon, Jeffrey W.; Kawa, Manabu; Frechet, Jean M. J. *Journal of the American Chemical Society* **1996**, *118*, 8847-8859.

(25) Hester, R. D.; Mitchell, P. H *J. Polym. Sci. Chem. Ed.* **1986**, *18*, 1727.

(26) Cohen, Seth M.; Petoud, Stephane; Raymond, Kenneth N. *Chemistry A European Journal* **2001**, *7*, 272-279.

(27) Hummelen, J. C.; van Dongen, J. L. J.; Meijer, E. W. Chem. Eur. J. 1997, 3, 1489-1493.

(28) Lau, R. L. C.; Chan, T.-W. D.; Chan, I. Y.-K.; Chow, H.-F. *Eur. Mass. Spectrom* **1995**, *1*, 371-380.

(29) Bodige, S.; Torres, A. S.; Maloney, D. J.; Tate, D. Kinsel, G. R.; Walke , A. K.; McDonnell, F. M. *J. Am. Chem. Soc.* **1997**, *119*, 10364-10369.

(30) Moucheron, C.; Kirsch-De Mesmaeker, A.; Dupont-Gervais, A.; Leize, E.; van Dorsselaer, A. *J. Am. Chem. Soc.* **1996**, *118*, 12834-12835.

(31) Newkome, George R.; He, Enfei; Moorefield, Charles N. *Chemical Reviews (Washington, D. C.)* **1999**, *99*, 1689-1746.

(32) Newkome, G. R.; Moorefield, C. N.; Vögtle, F.; Dendrimers and Dendrons ;VCH: Weinheim, Germany **2001**.

(33) Denti, G.; Serroni, S.; Campagna, S.; Ricevuto, V.; Balzani, V. *Inorg. Chim. Acta* **1991**, *182*, 127-129.

(34) Campagna, Sebastiano; Denti, Gianfranco; Serroni, Scolastica; Ciano, Mauro; Juris, Alberto; Balzani, Vincenzo *Inorganic Chemistry* **1992**, *31*, 2982-4.

(35) Newkome, G. R.; Moorefield, C. N.; Baker, G. R.; Johnson, A. L.; Behera, R. K. *Angew. Chem., Int. Ed. Engl* **1991**, *30*, 1176-1178.

(36) Oosterom, G. Eric; Reek, Joost N. H.; Kamer, Paul C. J.; Van Leeuwen, Piet W. N. M. *Angewandte Chemie, International Edition* **2001**, *40*, 1828-1849.

(37) Campagna, Sebastiano; Denti, Gianfranco; Serroni, Scolastica; Ciano, Mauro; Balzani, Vincenzo *Inorganic Chemistry* **1991**, *30*, 3728-32.

(38) Campagna, Sebastiano; Denti, Gianfranco; Serroni, Scolastica; Juris, Alberto; Venturi, Margherita; Ricevuto, Vittorio; Balzani, Vincenzo *Chemistry A European Journal* **1995**, *1*, 211-21.

(39) Suzuki, Hitomi; Kurata, Haruto; Matano, Yoshihiro *Chemical Communications (Cambridge)* **1997**, 2295-2296.

(40) Bochkarev, M. N.; Silkin, V. B.; Maiorova, L. P.; Razuvaev, G. A.; Semchikov, Yu D.; Sherstyanykh, V. I. *Metalloorganicheskaya Khimiya* **1988**, *1*, 196-200.

(41) Nanjo, Masato; Sekiguchi, Akira *Organometallics* **1998**, *17*, 492-494.

(42) Newkome, George R.; Cardullo, Francesca; Constable, Edwin C.; Moorefield, Charles N.; Thompson, Alexander M. W. Cargill *Journal of the Chemical Society, Chemical Communications* **1993**, 925-7.

(43) Newkome, George R.; He, Enfei *Journal of Materials Chemistry* **1997**, *7*, 1237-1244.

(44) Constable, Edwin C.; Harverson, Peter *Inorganica Chimica Acta* **1996**, *252*, 9-11.

(45) Constable, Edwin C.; Harverson, Peter; Oberholzer, Martin *Chemical Communications (Cambridge)* **1996**, 1821-1822.

(46) Achar, Sudhir; Vittal, Jagadese J.; Puddephatt, Richard J. *Organometallics* **1996**, *15*, 43-50.

(47) Reek, Joost N. H.; De Groot, Debby; Oosterom, G. Eric; Kamer, Paul C. J.; Van Leeuwen, Piet W. N. M. *Reviews in Molecular Biotechnology* **2002**, *90*, 159-181.

(48) Jin, Ren Hua; Aida, Takuzo; Inoue, Shohei *Journal of the Chemical Society, Chemical Communications* **1993**, 1260-2.

(49) Jiang, Dong-Lin; Aida, Takuzo *Chemical Communications (Cambridge)* **1996**, 1523-1524.

(50) Bhyrappa, P.; Young, James K.; Moore, Jeffrey S.; Suslick, Kenneth S. *Journal of the American Chemical Society* **1996**, *118*, 5708-5711.

(51) Kawa, Manabu; Frechet, Jean M. J. *Chemistry of Materials* **1998**, *10*, 286-296.

(52) Issberner, Joerg; Vogtle, Fritz; De Cola, Luisa; Balzani, Vincenzo *Chemistry--A European Journal* **1997**, *3*, 706-712.

(53) Mak, Chi Ching; Chow, Hak-Fun *Macromolecules* **1997**, *30*, 1228-1230.

(54) Eric Oosterom, G.; van Haaren, Richard J.; Reek, Joost N. H.; Kamer, Paul C. J.; van Leeuwen, Piet W. N. M. *Chemical Communications (Cambridge)* **1999**, 1119-1120.

(55) Knapen, Joan W. J.; van der Made, Alexander W.; de Wilde, Janine C.; van Leeuwen, Piet W. N. M.; Wijkens, Peter; Grove, David M.; van Koten, Gerard *Nature (London)* **1994**, *372*, 659-63.

(56) Hoare, Jason L.; Lorenz, Klaus; Hovestad, Neldes J.; Smeets, Wilberth J. J.; Spek, Anthony L.; Canty, Allan J.; Frey, Holger; van Koten, Gerard *Organometallics* **1997**, *16*, 4167-4173.

(57) Miedaner, Alex; Curtis, Calvin J.; Barkley, Robert M.; DuBois, Daniel L. *Inorganic Chemistry* **1994**, *33*, 5482-90.

(58) Reetz, Manfred T.; Lohmer, Gunther; Schwickardi, Renate *Angewandte Chemie, International Edition in English* **1997**, *36*, 1526-1529.

(59) Astruc, Didier; Chardac, Francoise *Chemical Reviews (Washington, D. C.)* **2001**, *101*, 2991-3023.

(60) Mizugaki, Tomoo; Ooe, Masahiko; Ebitani, Kohki; Kaneda, Kiyotomi *Journal of Molecular Catalysis A: Chemical* **1999**, *145*, 329-333.

(61) Maraval, Valerie; Laurent, Regis; Caminade, Anne-Marie; Majoral, Jean-Pierre *Organometallics* **2000**, *19*, 4025-4029.

(62) Newkome, George R.; Moorefield, Charles N. *Polymer Preprints (American Chemical Society, Division of Polymer Chemistry)* **1993**, *34*, 75-6.

(63) Yang, Chi; Chen, Xiao-Ming; Lu, Xiao-Quan; Zhou, Qin-Hai; Yang, Yan-Sheng *Chemical Communications (Cambridge)* **1997**, 2041-2042.

(64) Balogh, Lajos; Tomalia, Donald A. *Journal of the American Chemical Society* **1998**, *120*, 7355-7356.

(65) Scott, Robert W. J.; Ye, Heechang; Henriquez, Ronald R.; Crooks, Richard M. *Chemistry of Materials* **2003**, *15*, 3873-3878.

(66) Zhao, Mingqi; Crooks, Richard M. *Angewandte Chemie, International Edition* **1999**, *38*, 364-366.

(67) Chechik, Victor; Crooks, Richard M. *Journal of the American Chemical Society* **2000**, *122*, 1243-1244.

(68) Yeung, Lee K.; Crooks, Richard M. *Nano Letters* **2001**, *1*, 14-17.

(69) Beakley, Lindsey W.; Yost, Sarah E.; Cheng, Raymond; Chandler, Bert D. *Applied Catalysis, A: General* **2005**, *292*, 124-129.

Chapter 2

SYNTHESIS AND CHARACTERIZATION OF TRIDENTATE ISOCYANIDE COMPLEXES

Results and Discussion

Cyclometalated complexes have recently found widespread interest as species with promising properties for use in various fields.[1,2] A number of synthetic approaches to cyclometallated complexes may be envisaged. Although most of these have been investigated, the commonest method involves thermal activation of carbon-hydrogen bonds.[3] Herein is reported the synthesis of a series of cyclometalated platinum(II) and palladium(II) isocyanide complexes, as well as some methylisocyanide-derived palladium Chugaev-type carbene complexes. Characterization of the isocyanide complexes was achieved by ^{1}H and ^{13}C NMR and IR spectroscopies. The ultimate goal of the research was to link these isocyanide complexes to amine-terminated poly(propylene imine)dendrimers. Studies directed toward preparing and characterizing these metal-functionalized dendrimers are also presented.

Synthesis and characterization of isocyanide-derived palladium dicarbene complexes

Dicarbene complexes with different halide groups bound to palladium were synthesized by modification of a procedure established by Balch.[4] Carbene salt **1a** was synthesized by the addition of excess hydrazine to a stirred solution of tetrakis-(methylisocyanide) complex that was generated in situ from the reaction of $PdCl_2$ and KCl with methylisocyanide in H_2O. Complex **1a** was precipitated as an orange solid by the addition of excess $LiClO_4$, resulting in a yield of 65% (Figure 2.1).

Reaction of complex **1a** with dilute acidic solutions afforded the corresponding neutral dicarbene complexes. Dissolution of **1a** in 3M HCl followed by concentration of the solution under heating resulted in precipitation of the product (**1b**) as a white amorphous solid in a yield of 92% (Figure 2.1). Other dicarbene complexes (**1c, 1d**) were synthesized using a similar protocol by treatment with 3M HBr and 2M HI respectively. Good yields of the carbene complexes were obtained (91%, 88%).

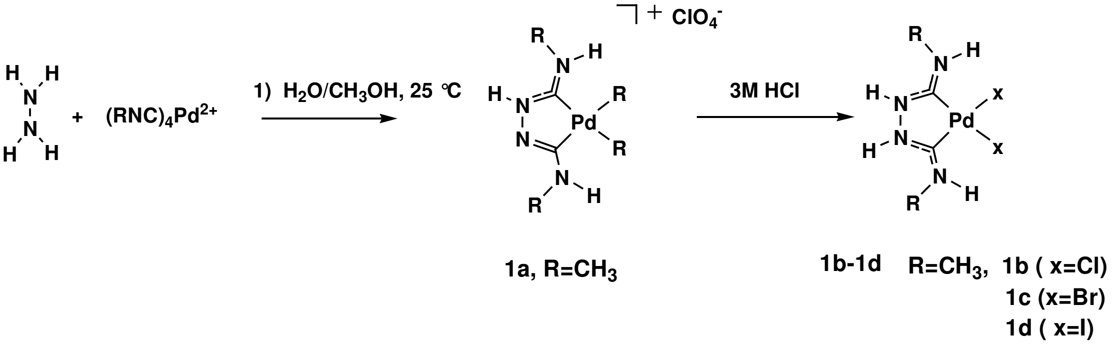


Figure 2.1 Synthesis of Chugaev-type palladium carbene complexes

The dicarbene complexes were characterized by NMR and IR spectroscopies. The ^{1}H NMR spectrum of **1a s**howed peaks at 2.65 ppm and 3.52 ppm for two different sets of methyl protons, and three peaks for NH's in a ratio of 1:1:1 at 5.56 ppm, 7.55 ppm and 10.05 ppm respectively. The ^{13}C NMR spectrum of **1a** showed two peaks at 29.7 ppm and 30.1 ppm for the methyl carbons and a characteristic peak at 132.1 ppm for the carbene carbon. Complex **2a** showed IR absorptions at 2251 and 2241 for C≡N, and 1582, 1531 for the C=N moieties.

The ^{1}H NMR spectra of neutral dicarbene complexes **1b-1d** show two peaks for NH's in a 1:1 ratio around 7.80 ppm and 10.97 ppm can be attributed to protonation of the chelating ligand of **1a** in the presence of an acid. The ^{13}C NMR spectra of complexes **1b-1d** confirm the replacement of two coordinated isocyanide ligands with halide ions (Cl^-, Br^-, I^-) by the disappearance of carbon signals corresponding to coordinated isocyanide ligands. Carbene carbon resonances were observed around 179.0 ppm for the corresponding halide complexes. The IR spectra of neutral palladium dicarbene complexes (**1b-1d**) showed absorption stretch at 1601 cm^{-1}, and 1529 cm^{-1} for C=N, and at 3362 cm^{-1}, and 3205 cm^{-1} for NH groups.

Synthesis and characterization of tridentate isocyanide complexes.

Two different types of chelating tridentate ligands **2a** [6-phenyl-2, 2'-bipyridyl (CNN)] and **2b** [1,3-di (2-pyridyl) benzene (NCN)] were synthesized by employing a modified procedure of Kauffmann's method.[5] Compound **2a** was treated with phenyllithium in ether followed by hydrolysis. Addition of $KMnO_4$ gave the crude product, which was further purified by flash chromatography to give a yield of 51%

(Figure 2.2). The tridentate ligand **2b** was synthesized using an approach developed for the preparation of pyridine-based ligands based on the Stille coupling reaction.[6] The reaction between (2-pyridyl) tri-*n*-butylstannane with 1,4-dibromobenzene in toluene in the presence of Pd $(PPh_3)_2Cl_2$ and LiCl afforded the desired product (Figure 2.2). The crude product was chromatographed to obtain **2b** as clear yellow oil in 83% yield. The tridentate ligands were characterized by ^{1}H NMR and ^{13}C NMR, and the chemical shifts were in agreement with the reported values.[6]

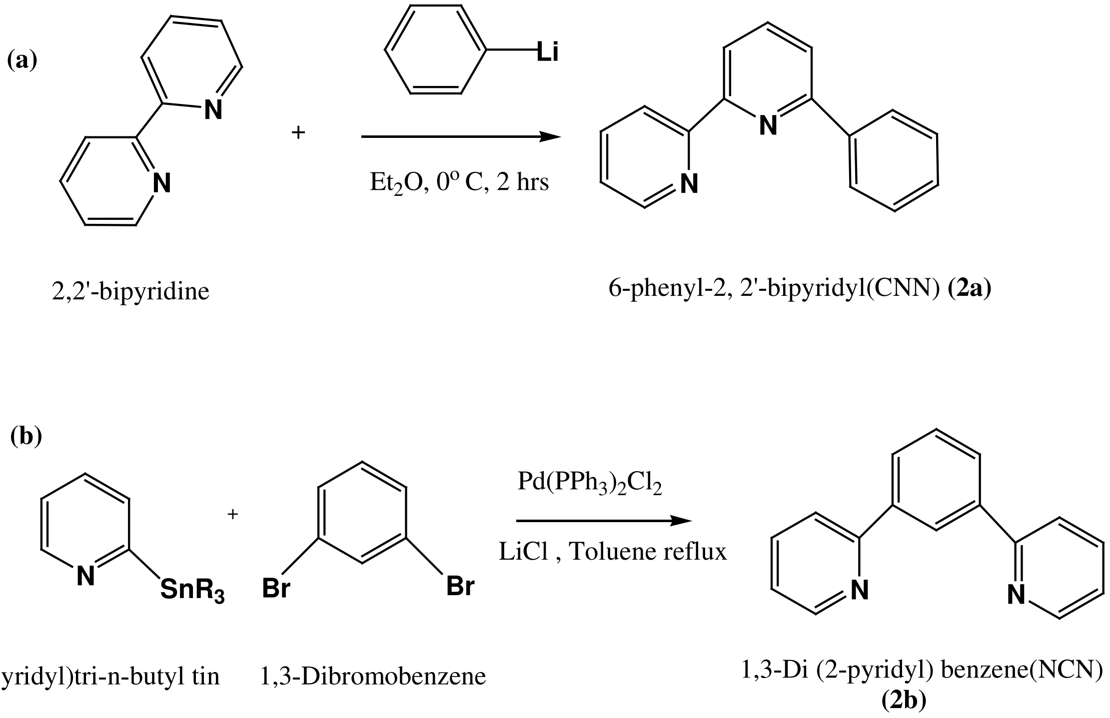


Figure 2.2 Synthesis of tridentate ligands (a) 6-phenyl-2, 2'-bipyridyl (CNN). (b) 1,3-Di (2-pyridyl) benzene (NCN)

Platinum(II) and palladium(II) tridentate complexes **3a** and **3b** were synthesized from **2a** by the procedure established by Constable and co-workers.[7] Tridentate ligand **2a** was treated with K_2PtCl_4 and K_2PdCl_4 separately at elevated temperatures in an acetonitrile-water mixture to obtain the corresponding cyclometallated neutral complexes. Treatment of **2b** with K_2PtCl_4 in HOAc under reflux conditions for 3 days afforded the cycloplatinated complex **3c** (Figure 2.3). Formation of a double palladation complex was reported when **2b** was reacted with K_2PdCl_4 in the presence of HOAc under reflux conditions, suggesting that such a complex with a single Pd-C bond is not the most stable species.[6] ^1H and ^{13}C NMR spectra of the neutral complexes were analyzed. The ^1H NMR showed the absence of hydrogen on the benzene ring due to cyclometallation. The chemical shift differences compared with the starting ligands provide a sensitive means of determining the site of metalation and the bonding mode in the corresponding ligands.

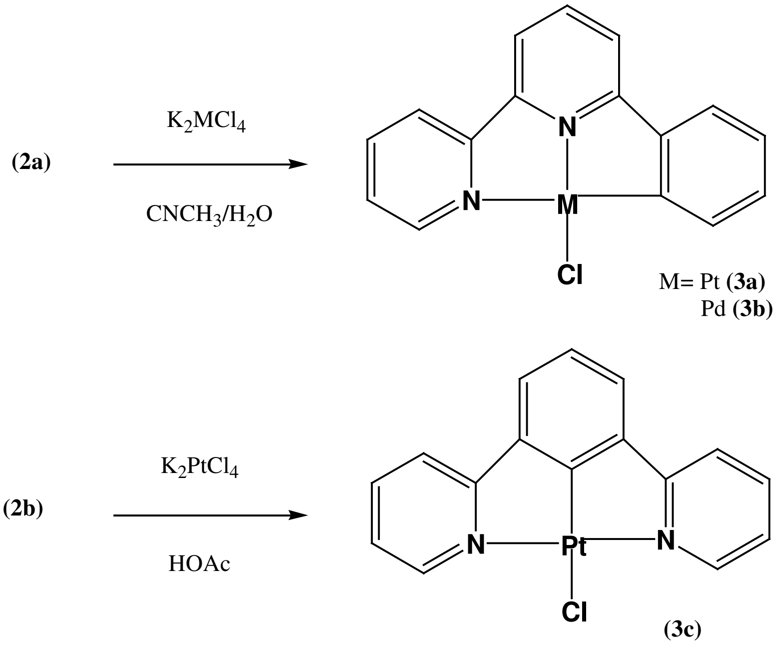


Figure 2.3 Synthesis of cyclometallated chloride complexes

Cyclometallated isocyanide complexes were synthesized by a modified procedure of Che's method.[8] The facile displacement of the chloride group from [(CNN) MCl] (M=Pt, Pd) by excess isocyanide (RNC, R= ^{t}Bu, CH_3, 2,6-$Me_2C_6H_3$) yielded the isocyanide complexes **4a-4c** and **5a-5c** as recoverable solids (Figure 2.4). Platinum isocyanide complexes (**4a-4c)** were synthesized by addition of excess isocyanide (RNC, R= ^{t}Bu, CH_3, 2,6-$Me_2C_6H_3$) to an acetonitrile solution of [(CNN) PtCl] followed by precipitation with excess $LiClO_4$ and ether. Complexes **4a-4c** gave characteristic IR absorption stretches at 2210 cm^{-1}, 2245 cm^{-1} and 2169 cm^{-1} which were at higher frequency down field compared to the $C\equiv N$ stretch of the free isocyanides (2137 cm^{-1}, 2156 cm^{-1}, 2132 cm^{-1}). The reaction between [(CNN) PdCl] and excess isocyanides (RNC, R= ^{t}Bu, CH_3, 2,6-$Me_2C_6H_3$) in CH_2Cl_2 followed by addition of $LiClO_4$/ $NaBF_4$ in acetonitrile afforded new palladium isocyanide complexes **5a-5c**. IR spectra of these complexes show characteristic absorption peaks for $C\equiv N$ at 2177 cm^{-1}, 2174 cm^{-1} and 2248 cm^{-1}.

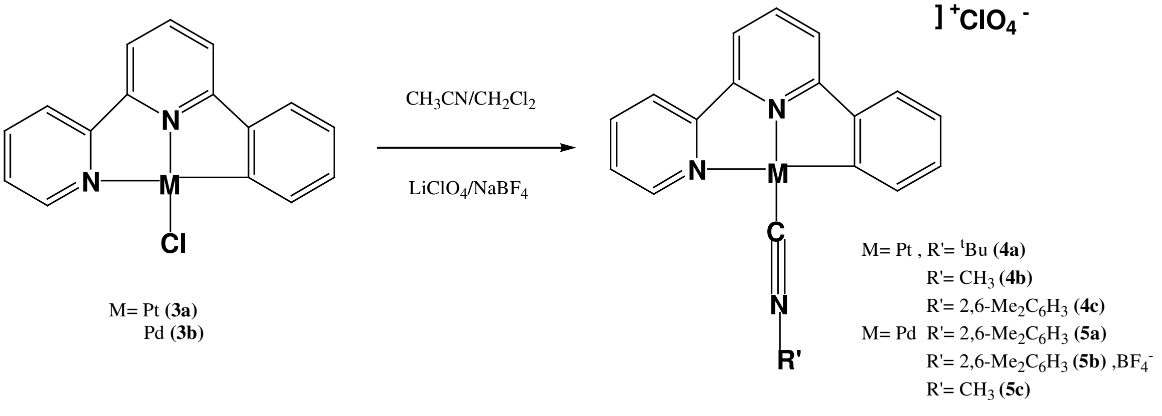


Figure 2.4. Synthesis of cyclometallated isocyanide complexes

Attempted synthetic procedures for the attachment of isocyanide complexes to PPI dendrimers

Generation of diamino-carbene derivatives by nucleophilic attack of amines at coordinated isocyanides is a common method for decades.[9] By employing this methodology using G(1-2) PPI dendrimers with four and eight surface amine functionalities, synthetic procedures to append isocyanide complexes to PPI dendrimers were explored.

Reactions of PPI dendrimers with isocyanide complexes **(4a-5c)** were carried out in dry DMF with stirring at 80°C under inert atmosphere. Spectroscopic studies indicated the presence of a carbene-metal linkage formed by the reaction of coordinated isocyanide with the amine-terminated dendrimers (Figure 2.5). For example, ^{1}H NMR spectra of the crude product of the reaction between **4c** and G1 PPI dendrimers showed a peak at 3.12 ppm, which is characteristic of methylene protons of the dendrimer upon ligation with metal complexes.[10] IR spectra showed an absorption stretch at 1656 cm^{-1} characteristic of C=N due to carbene-ligand formation. Separation of the products from unreacted starting materials and further purification could not be accomplished. Some of the reactions led to rapid, uncontrolled cross-linking and precipitation, which might be due to the presence of excess isocyanide ligands in the reaction mixtures. Several attempts to establish procedures to characterize these dendrimers complexes by MALDI-TOF mass spectrometry were not successful.

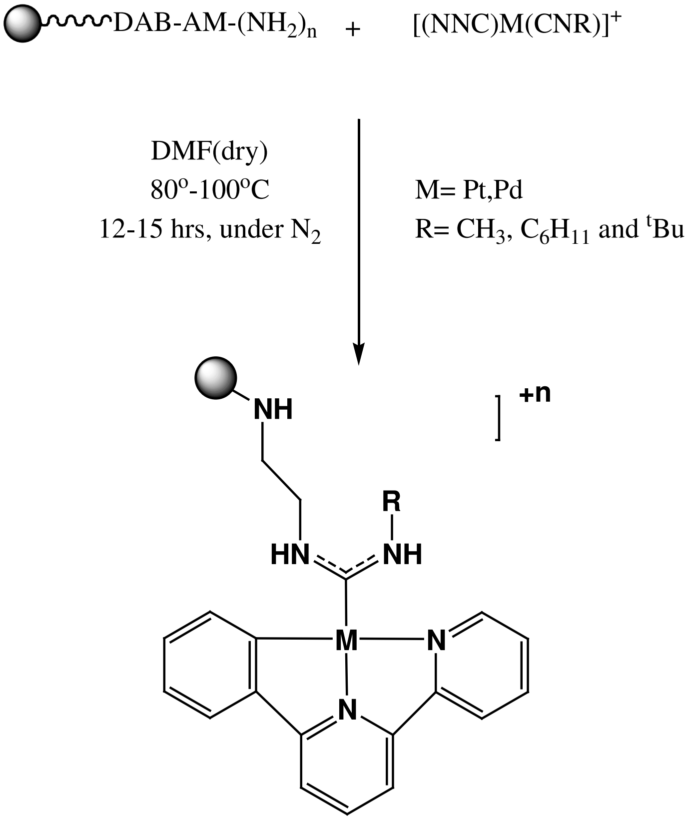


Figure 2.5. Isocyanide-based carbene ligand formation as a method for attachment of metal complexes to the PPI dendrimer.

SUMMARY AND CONCLUSIONS

A convenient route to synthesize methyl isocyanide derived palladium Chugaev-type carbene complexes has been developed. In addition, convenient synthesis of cyclometallated Pt and Pd isocyanide complexes was achieved. New platinum(II) and palladium(II) tridentate isocyanide complexes were synthesized using different isocyanides (methylisocyanide, *tert*-butylisocyanide, and 2,6-dimethylphenylisocyanide). Characterization was achieved by ^{1}H NMR, ^{13}C NMR, and IR spectroscopy. Synthetic procedures to append cyclometallated complexes to the surface of commercially available PPI dendrimers were explored but were unsuccessful due to uncontrolled reactions and cross-linking.

EXPERIMENTAL

Methylisocyanide,[11] 6-phenyl-2, 2'-bipyridyl,[5] and 1,3-di (2-pyridyl) benzene[6] were synthesized using established procedures. Isopropylisocyanide (Strem, 99%), *tert*-butylisocyanide (Strem, 98%), hydrazine hydrate (Acros), palladium chloride (Alfa, 99.9%), potassium chloride (Spectrum, crystal reagent) and lithium perchlorate (Aldrich, 95+%) were used as received (As perchlorate salts are potentially explosive, they should be handled with care). Solvents used: acetonitrile (EM Science), chloroform (Pharmco), dimethylformamide (Pharmco), methylene chloride (Pharmco), and were of reagent grade and were used as received. Phenyllithium (Acros, 2.0 M solution, 20% in dibutlyether), and diethyl ether (Acros, dried over Na and distilled).

Water was purified by an E-pure system (Barnstead). NMR solvents: $CDCl_3$ (Cambridge Isotope Laboratories, Inc, 99.8%) CD_3CN (Cambridge Isotope Laboratories, Inc, 99.8%) and DMSO-d_6 (Cambridge Isotope laboratories, Inc, 99.9%) were used as received, and in some cases they were dried over degassed 4 Å molecular sieves and stored over P_2O_5, transferred on the vacuum line into a glass bottle and stored in the glove box.

^{1}H NMR spectra were recorded on Varian 300 MHz and 400 MHz spectrometers, with chemical shifts reported in ppm and multiplicity denoted as (s = singlet, d = doublet, t = triplet, sep = septet, m = multiplet and dd = doublet of a doublet) and the coupling constants reported in Hz. ^{13}C NMR spectra were recorded on a Varian 400 MHz spectrometer (ppm). Elemental analyses were performed by Desert Analytics Laboratory, Tucson, AZ, USA. Infrared (IR) spectra were recorded as Nujol mulls on a Nicolet Protege 460 FT-IR spectrometer (using a resolution of 4 cm^{-1}).

$C_4H_9N_4Pd(CNCH_3)_2$ ClO_4 (1a)

All reactions were performed under air unless otherwise stated. Methylisocyanide (0.232 g, 5.64 mmol) was added to a stirred solution of $PdCl_2$ (0.200 g, 1.128 mmol) and KCl (0.336g, 4.512 mmol) in H_2O (20 mL) at room temperature. An excess of hydrazine hydrate (1 mL) was added to the resulting colorless solution of $[Pd(CNCH_3)_4]^{2+}$ to give a yellow solution. A saturated solution of $LiClO_4$ in H_2O was added dropwise to the yellow solution to obtain an orange colored precipitate, which was collected by suction filtration, washed with water and dried under vacuum over P_2O_5 overnight. The product was recrystallized by dissolving it in a minimum amount of hot acetonitrile and then filtered. Slow addition of diethyl ether to the filtrate gave dark yellow crystals (yield 0.465 g, 65%). Anal. Calcd. for $C_8H_{15}N_6ClO_4Pd$: C, 23.95; H, 3.77; N, 20.95. Found: C, 24.10; H, 3.91, N; 20.77 %. IR (Nujol): ν= 2251, 2241 (C≡N); 1582, 1531 (C=N); 3452, 3439, 3340 (NH) cm^{-1}. ^{1}H-NMR $(CD_3)_2SO$: 2.64 (s, 6H, CH_3 (CH_3NC)); 3.52 (s, 6H, CH_3 (CH_3NH)); 5.56 (s, 2H, NH); 7.55 (s, 1H, NH); 10.05 (s, 1H, NH). ^{13}C-NMR $(CD_3)_2SO$: 29.7 (s, overlapping, CN*C*H3); 30.1, (s, overlapping, *C*H_3NH); 132.1 (broad s, *carbene*).

$C_8H_{17}N_4Cl_2Pd$ (1b)

A 3M solution of HCl was added drop wise to compound **1a** (0.340 g, 0.848 mmol) in a round bottom flask until a colorless solution was formed. The volume of the solution was reduced by heating the reaction mixture on a hot water bath until a solid white precipitate formed, the product was collected by suction filtration, washed with diethyl ether and dried in vacuum, (yield 0.225 g, 92%). Anal. Calcd for $C_4H_{10}N_4Cl_2Pd$: C, 16.48; H, 3.46;

N, 19.22. Found: C, 16.55; H, 3.54; N, 19.07%. IR (Nujol): ν= 1601, 1529 (C=N); 3362, 3205 (NH) cm^{-1}. ^1H-NMR $(CD_3)_2SO$: 2.83 (d, 6H, $^3J_{(H-H)}$ = 5.1 Hz, CH_3); 7.80 (d, 2H, $^3J_{(H-NH)}$ =4.8 Hz NH); 10.97(s, 2H, NH). ^{13}C-NMR $(CD_3)_2SO$: 30.2 (s, *C*H_3); 179.0 (s, *carbene*).

$C_8H_{17}N_4Br_2Pd$ (1c)

A 3M solution of HBr was added dropwise to compound **1a** (0.332 g, 0.828 mmol) in a round bottom flask until a colorless solution was formed. The volume of the solution was reduced by heating the reaction mixture on a hot water bath until a solid white precipitate formed, which was collected by suction filtration, washed with diethyl ether and dried in vacuum, (yield 0.287g, 91%). Anal. Calcd for $C_8H_{17}N_4Br_2Pd$: C, 12.63; H, 2.65; N, 14.73. Found: C, 12.80; H, 2.56; N, 14.47 %. IR (Nujol): ν=1597, 1530 (C=N); 3338, 3186, 3135, 3066 (NH) cm^{-1}. ^1H-NMR $(CD_3)_2SO$: 2.83 (d, 6H, $^3J_{(H-H)}$ = 5.4 Hz, CH_3); 7.77(d, 2H, $^3J_{(H-NH)}$ = 5.1 Hz, NH); 11.08(s, 2H, NH). ^{13}C-NMR $(CD_3)_2SO$: 30.6 (s, *C*H_3); 179.0 (s, *carbene*).

$C_8H_{17}N_4I_2Pd$ (1d)

A 2M solution of HI was added dropwise to compound **1a** (0.200 g, 0.498 mmol) in a round bottom flask, and a dark brown solution was formed immediately. Upon further HI addition and reduction of volume of the solution by heating the reaction mixture on a hot water bath, a white precipitate formed, which was collected by suction filtration, washed with diethyl ether and dried in vacuum, yield 0.208g, 88%. Anal. Calcd for

$C_8H_{17}N_4Br_2Pd$: C, 10.13; H, 2.12; N, 11.81. ^{1}H-NMR $(CD_3)_2SO$: 2.84 (d, 6H, $^3J_{(H\text{-}H)}$ = 53.6 Hz, CH_3); 7.58(s, 2H, NH); 11.21(s, 2H, NH).

Synthesis of 2a [6-phenyl-2, 2'-bipyridyl (CNN)]

A solution of 3.16 g (20 mmol) of 2,2'-bipyridyl in 60 ml absolute ether was stirred at 0 °C, and 24 mmol of 0.98 M ethereal phenyllithium solution was added dropwise, producing an immediate red color. After 2 h stirring at 0° C, the product was hydrolyzed with 40 ml of H_2O. The aqueous phase was separated and extracted three times with ether, and then the combined organic extracts were dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue was dissolved in 40 ml of acetone. Small portions of a solution of $KMnO_4$ in acetone were added at room temperature with stirring until a violet color remained in the mixture. MnO_2 was filtered off, and the solvent was removed by rotary evaporation. The solid residue was purified by column chromatography (silica gel, 2:1 ether/hexane). After recrystallization from hexane, 2.36 g (51 %) of the product were obtained. ^{1}H-NMR ($CDCl_3$): 7.31 (m, *b*, 1H); 7.50 (m, *k, i*, j, 3H); 7.77 (d, *g*, 1H); 7.88 (m, *f, c,* 2H); 8.15 (dd, *l, h,* 2H,); 8.37 (d, *e*, 1H); 8.64 (d, *d*, 1H); 8.69 (dd, *a*, 1H); ^{13}C-NMR ($CDCl_3$): Aromatic (119.3, 120.3, 121.3, 123.7, 126.9, 128.7, 129.0, 136.9, 138.0, 139.3, 148.9, 155.6, 156.2, 156.4).

Synthesis of 2b [1,3-Di (2-pyridyl) benzene (NCN)]

A mixture of 1,3-dibromopyridine (1.07 g, 4.52 mmol), (2-pyridyl) tri-*n*-butylstannane (13.6 mmol), Pd $(PPh_3)_2Cl_2$ (254 mg, 0.36 mmol), and LiCl (1.92 g, 45.2 mmol) in toluene was heated under reflux conditions for 3 days. After cooling to 23°C, a saturated

KF solution (15 mL) was added, and the mixture was stirred for 30 min. The solid residue formed was filtered off; CH_2Cl_2 (200 mL) and a 5% $NaHCO_3$ solution (150 mL) were added to the filtrate. The organic phase was separated and dried ($MgSO_4$), and the solvent was evaporated. The crude product was chromatographed (silica gel; hexanes-Et_2O, 4:1 then neat Et_2O) to give a light yellow oil 2.78 g (76 %): ^1H NMR ($CDCl_3$) δ 7.23 (dm, 2H); 7.58 (t, 1H); 7.74 (tm, 2H); 7.81 (br d, 2H); 8.06 (dd, 2H); 8.65 (t, 1H); 8.71 (dm, 2H). ^{13}C NMR ($CDCl_3$) δ 120.4 (CH), 122.0 (CH), 125.2 (CH), 127.1 (CH), 128.9 (CH), 136.5 (CH), 139.5 (C), 149.3 (CH), 156.8 (C).

Synthesis of PtL(Cl) 3a [L=6-phenyl-2, 2'-bipyridyl]

A mixture of K_2PtCl_4 (0.250 g, 0.602 mmol) and 6-phenyl-2, 2'-bipyridyl (0.148 g, 0.638 mmol) was dissolved in 1:1 MeCN- H_2O (20 ml-20 ml). The reaction mixture was refluxed for 18 h to give a deep red solution, which was then evaporated to dryness. The product was extracted with dichloromethane, and the volume was reduced to 5 mL. Addition of diethyl ether yielded an orange solid, which was purified by slow evaporation of the acetonitrile. Yield: (0.209 g, 76%). ^1H NMR (DMSO-d_6): δ 7.06-7.09 (m, 1H), 7.22-7.30 (m, 2H), 7.45 (d, 1H), 7.53 (d, 1H), 7.62 (m, 1H), 7.71-7.81 (m, 2H), 7.88 (m, 1H), 8.02 (m, 1H), 9.07 (m, 1H).

Synthesis of PdL(Cl) 3b [L=6-phenyl-2, 2'-bipyridyl]

To a stirred solution of $PdCl_2$ (0.230 g, 1.297 mmol) and KCl (0.194g, 2.594 mmol) in H_2O (20 mL) was added 6-phenyl-2, 2'-bipyridyl (0.300 g, 1.297 mmol) dissolved in MeCN to make a 1:1 mixture of MeCN- H_2O. The mixture was refluxed for 18 h to give a yellow suspension, which was then evaporated to dryness. The product was extracted with dichloromethane, and the volume was reduced to 5 mL. Addition of diethyl ether yielded a yellow solid, which was recrystallized by vapor diffusion of diethyl ether into an acetonitrile solution of the complex to afford a yellow crystalline solid. Yield: (0.132 g, 79%). ^{1}H NMR (DMSO-d_6): δ 7.09 (dm, 2H), 7.51-7.54 (m, 1H), 7.63-7.67 (m, 1H), 7.77-7.81 (m, 1H), 8.04 (dd, 1H), 8.15-8.30 (m, 3H), 8.52 (d, 1H), 8.65 (dm, 1H). ^{13}C NMR (DMSO-d_6): δ119.7, 119.8, 123.1, 124.5, 124.7, 127.4, 129.6, 136.1, 140.1, 140.4, 148.0, 149.0, 153.5, 154.0, 155.1, and 163.6.

Synthesis of PtL(Cl) 3c [L=1,3-Di (2-pyridyl) benzene]

A mixture of 1,3-di (2-pyridyl) benzene (45 mg, 0.194 mmol), K_2PtCl_4 (80 mg, 0.193 mmol), and HOAc (18.75 mL) was heated at 110-115° C (reflux). The progress of the reaction was monitored by taking small, aliquots and treating them with H_2O. The appearance of a red color indicated the presence of unreacted K_2PtCl_4. After 3 days the starting Pt salt was completely consumed and the mixture was allowed to cool to room temperature. The resulting bright yellow complex was filtered off and washed with MeOH, H_2O, EtOH, and Et_2O. The filtrate was evaporated to dryness and suspended in EtOH (15 mL), giving rise to an additional precipitate, which was filtered off and washed with EtOH and Et_2O. Combined yield: 0.349 (75%). ^{1}H NMR (DMSO-d_6) δ 7.27 (t, 1H); 7.52-7.57 (m, 2H); 7.76 (d, 2H); 8.10-8.22 (m, 4H); 9.11 (dd, 2H). ^{13}C NMR (DMSO-d_6) δ 120.6, 123.3, 124.3, 125.1, 140.6, 140.6, 151.4, 161.2, 166.7.

Synthesis of 4a [(CNN)Pt(C≡N^{t}Bu)] ClO$_4$

To an orange suspension of [(CNN) PtCl] (0.150 g, 0.325 mmol) in acetonitrile (25 mL) at room temperature was added excess *tert*-butylisocyanide, ^{t}BuN≡C (0.540g, 6.50 mmol). Upon stirring, the color of the mixture changed to cloudy orange-red, then clear pale yellow after 30 min. Addition of excess LiClO$_4$ in acetonitrile followed by diethyl ether yielded a yellow precipitate, which was collected and dried. Recrystallization by slow diffusion of diethyl ether into an acetonitrile solution of the crude product afforded yellow crystals: yield (0.138 g, 84 %). ^{1}H NMR (DMSO-d$_6$): 1.71 (s, 9H, ^{t}Bu), 7.20 (m, 3H), 7.70 (m, 1H), 7.87 (m, 2H), 8.10 (d, 1H), 8.26 (m, 1H), 8.43 (t, 1H), 8.56 (d, 1H), 8.77 (d, 1H). ^{13}C-NMR (CD$_3$CN): 30.2 (C*Me$_3$*), 61.5 (*C*Me$_3$), 121.0, 121.4, 125.6, 127.0, 127.2, 130.3, 133.3, 138.1, 138.3, 142.6, 144.0, 148.0, 153.8, 156.2, 157.8, and 165.9. IR (Nujol): ν = 2210 (C≡N), 1601 (C=N) cm^{-1}

Synthesis of 4b [(CNN) Pt(C≡NCH3)]$^+$ ClO4$^-$

To an orange suspension of [(CNN) PtCl] (0.125 g, 0.270 mmol) in acetonitrile (20 mL) at room temperature was added excess methylisocyanide, CH$_3$N≡C (0.222g, 5.416 mmol). Upon stirring, the color of the mixture changed to cloudy orange-red, then clear pale yellow after 30 min. Addition of excess LiClO$_4$ in acetonitrile followed by diethyl ether yielded a yellow precipitate, which was collected and dried. Recrystallization by slow diffusion of diethyl ether into an acetonitrile solution of the crude product afforded yellow crystals: (yield 0.084 g, 56%). ^{1}H NMR (DMSO-d$_6$): 3.74 (s, 3H, CH$_3$), 7.01-7.09 (m, 3H), 7.54 (d, 1H), 7.80 (t, 1H), 7.93 (m, 1H), 8.11 (d, 2H), 8.34-8.38 (m, 2H), 8.76 (d, 1H). IR (Nujol): ν = 2245 (C≡N), 1601 (C=N) cm^{-1}

Synthesis of 4c [(CNN) PtC≡NAr']$^+$ ClO$_4^-$ (Ar'=2,6-Me$_2$C$_6$H$_3$)

To an orange suspension of [(CNN)PtCl] (0.10 g, 0.22 mmol) in acetonitrile (20 mL) was added 2,6-dimethylphenyl (Ar') isocyanide (0.03 g, 0.23 mmol). The mixture was stirred for 10 min to yield a purple precipitate and yellow solution. After addition of excess $LiClO_4$ in acetonitrile followed by diethyl ether, the resultant purple solid was collected and dried. Recrystallization by slow diffusion of diethyl ether into an acetonitrile solution afforded a purple crystalline solid: yield 0.102 g, 71%. ^{1}H NMR (DMSO-d$_6$): 2.56 (s, 6H, CH_3), 7.20 (m, 2H), 7.33 (d, 2H), 7.40-7.49 (m, 2H), 7.59 (m, 1H), 7.77 (m, 1H), 7.88 (d, 1H), 7.97 (d, 1H), 8.12 (t, 1H), 8.29 (m, 2H), 8.84 (d, 1H). IR (Nujol): ν = 2169 (C≡N), 1603 (C=N) cm^{-1}.

Synthesis of 5a [(CNN) PdC≡NAr']$^+$ ClO$_4^-$(Ar'=2,6-Me$_2$C$_6$H$_3$)

To a yellow suspension of [(CNN) PdCl] (0.150 g, 0.402 mmol) in dichloromethane (20 mL) was added 2,6-dimethylphenyl (Ar') isocyanide (0.055 g, 0.420 mmol), and the reaction mixture was stirred for 20 min. After addition of excess $LiClO_4$ in acetonitrile followed by diethyl ether, the resultant yellow solid was collected and dried. Recrystallization by slow diffusion of diethyl ether into an acetonitrile solution afforded a pale yellow solid: yield 0.155 g, 68%. ^{1}H NMR (DMSO-d6): 2.56 (s, 6H, CH_3), 7.17-7.24 (m, 2H), 7.40 (t, 3H), 7.43 (m, 2H), 7.46 (m, 1H), 7.80 (m, 2H), 8.28-8.35 (m, 3H), 8.60 (d, 1H), 8.83 (d, 1H). ^{13}C NMR: 18.5, 120.6, 120.6, 124.0, 126.4, 128.4, 130.8, 131.4, 135.7, 138.1, 141.3, 142.5, 148.3, 152.2, 152.5, 153.7, 153.4, and 162.9. IR (Nujol): ν = 2177 (C≡N), 1638 (C=N) cm^{-1}

Synthesis of 5b [(CNN) PdC≡NAr']$^+$ BF_4^- (Ar'=2,6-$Me_2C_6H_3$)

To a yellow suspension of [(CNN) PdCl] (0.120 g, 0.336 mmol) in dichloromethane (20 mL) was added 2,6-dimethylphenyl (Ar') isocyanide (0.046 g, 0.351 mmol), and the reaction mixture was stirred for 20 min. After addition of excess $NaBF_4$ in acetonitrile followed by diethyl ether, the resultant yellow solid was collected and dried. Recrystallization by slow diffusion of diethyl ether into an acetonitrile solution afforded a pale yellow solid: yield 0.119 g, 63%. ^{1}H NMR (DMSO-d6): 2.56 (s, 6H, CH_3), 7.17-7.24 (m, 2H), 7.40 (t, 3H), 7.43 (m, 2H), 7.46 (m, 1H), 7.80 (m, 2H), 8.28-8.35 (m, 3H), 8.60 (d, 1H), 8.83 (d, 1H). IR (Nujol): ν = 2174 (C≡N), 1638 (C=N) cm^{-1}

Synthesis of 5c [(CNN) Pd(C≡NCH_3)]$^+$$ClO_4^-$

To a yellow suspension of [(CNN) PdCl] (0.150 g, 0.402 mmol) in dichloromethane (20 mL) was added 2,6-dimethylphenyl (Ar') isocyanide (0.165 g, 4.023 mmol), and the reaction mixture was stirred for 10 min. After addition of excess $LiClO_4$ in acetonitrile followed by diethyl ether, the resultant yellow solid was collected and dried. Recrystallization by slow diffusion of diethyl ether into an acetonitrile solution afforded a pale yellow solid: yield 0.112 g, 74%. ^{1}H NMR (DMSO-d6): 3.76 (s, 3H, CH_3), 7.11 (m, 1H), 7.16-7.22 (m, 2H), 7.70 (dd, 1H), 7.77 (m, 1H), 8.00 (t, 1H), 8.20 (d, 2H), 8.33 (td, 1H), 8.49 (d, 1H), 8.66 (dd, 1H). IR (Nujol): ν = 2248 (C≡N), 1638 (C=N) cm^{-1}

REFERENCES

(1) Newkome, George R.; Puckett, Wallace E.; Gupta, Vinod K.; Kiefer, Garry E. *Chemical Reviews (Washington, DC, United States)* **1986**, *86*, 451-89.

(2) Rabe, P.; Guerchais, J. E.; Sala Pala, J.; El Khalifa, M.; Saillard, J. Y.; Toupet, L. *Polyhedron* **1993**, *12*, 1215-25.

(3) Jolliet, Philippe; Gianini, Michel; von Zelewsky, Alex; Bernardinelli, Gerald; Stoeckli-Evans, Helen *Inorganic Chemistry* **1996**, *35*, 4883-4888.

(4) Balch, Alan L.; Parks, John E. *Journal of the American Chemical Society* **1974**, *96*, 4114-21.

(5) Kauffmann, T.; Konig, J.; Woltermann, A. *Chem. Ber* **1976**, *109*, 3864-3868.

(6) Cardenas, Diego J.; Echavarren, Antonio M.; Ramirez de Arellano, M. Carmen *Organometallics* **1999**, *18*, 3337-3341.

(7) Constable, Edwin C.; Henney, Ronald P.G.; Leese, Troy A. *J. Chem. Soc. Dalton Trans* **1990**, 443-449.

(8) Lai, Siu-Wai; Chan, Michael Chi-Wang; Cheung, Kung-Kai; Che, Chi-Ming *Organometallics* **1999**, *18*, 3327-3336.

(9) Badley, E. M.; Chatt, Joseph; Richards, Raymond Leslie; Sim, G. A. *Journal of the Chemical Society [Section] D: Chemical Communications* **1969**, 1322-3.

(10) Smith, Gregory; Chen, Rui; Mapolie, Selwyn *Journal of Organometallic Chemistry* **2003**, *673*, 111-115.

(11) Schuster, R.E.; Scott, J.E.; Casanova, J. *Organic Synthesis* **2003**, *CV 5*, 772.

Chapter 3

POLY (PROPYLENE IMINE) FUNCTIONALIZED METALLODENDRIMERS: SYNTHESIS AND CHARACTERIZATION

Results and Discussion

Numerous examples of research based on surface functionalization of dendrimers have been reported in the literature.[1-2] In addition, metallodendrimers derived from poly(propylene imine) dendrimers (PPI) have been investigated as catalysts in the recent years.[3-4] The goal of this work was the functionalization of commercially available poly(propylene imine)dendrimers with catalytically important metal complexes. We herein report the synthesis and characterization of PPI dendrimers with chelating bipyridyl ligands obtained through imine condensation reactions. These dendritic ligands were then metalated with labile palladium precursors to obtain the desired metallodendrimers. The characterization of metallodendrimers was achieved by ^{1}H NMR, ^{13}C NMR, FT-IR, and electron spray mass spectrometry (ESI-MS) analyses.

Functionalization of PPI dendrimers

The functionalization of the PPI dendrimers was sought through an imine (C=N) condensation reaction. Schiff bases, also known as *N*-substituted imines, are generally obtained as condensation products of reactions between primary amines and carbonyl compounds (Figure 3.1).

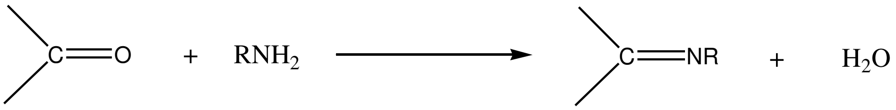


Figure 3.1 Imine formation through simple condensation reaction

The reaction is reversible and often reaches equilibrium noticeably short of completion. When the reaction is carried out with an amine that has an electronegative atom containing at least one pair of unshared electrons adjacent to the attacking nitrogen atom, such as hydroxylamine, semicarbazide or hydrazine, the equilibrium is essentially complete and the condensation product may be readily isolated.[5] The formation of imines is usually acid catalyzed. This reaction in organic solvents can be catalyzed by titanium(IV) chloride, zinc chloride, aluminum chloride or *p*-toluene sulfonic acid.

Attempts to functionalize PPI dendrimers with bipyridyl groups through condensation reactions in the presence of catalytic amounts of hydrochloric acid and *p*-toluenesulfonic acid were not fully successful. Spectroscopic studies revealed the presence of the desired condensation product. The use of strong acids might have caused side reactions, and separation of the products from the unreacted starting materials was very difficult. Attempts to remove the unreacted acid and its byproducts were also not successful, so we switched to a more simple and convenient method of functionalization. The reactions were carried out in the presence of molecular sieves, which are believed to serve as catalysts as well as dehydrating agents in organic condensation reactions (reported for small molecules).[6]

Synthesis of Dendritic Ligands

The synthesis of dendrimer bound ligands was accomplished in a single step through a simple Shiff-base condensation reaction of ketone with primary amines. Exact stoichiometric amounts of di-2-pyridylketone was added to the primary amine end groups of DAB-dendr-$(NH_2)_4$ (**1a**) in toluene in the presence of molecular sieves (Scheme 3.2). The reaction mixture was monitored by IR analysis of small aliquots of the solution and was typically allowed to react under reflux for 3 days. The G1 bipyridyl-pendant dendritic ligand (**1b**), containing four bipyridyl groups on the surface of the dendrimer was obtained as clear yellow oil in a yield of 71%. Due to difficulties in purification of products from unreacted starting materials, none of the reagents were used in excess. Ketones are less reactive than aldehydes in condensation reactions; hence, the need for longer reaction times can be attributed to the presence of more hindered ketones in the reactants.

A number of purification methods were investigated, including flash chromatography using silica gel and alumina (activated and deactivated). None of these techniques proved to be useful. Most traces of unreacted starting ketone and parent dendrimer were removed by copious washing with water, but as the product is also water-soluble, this resulted in loss of some product during the work-up. Ultimately, the crude product was further purified by size-exclusion chromatography using a Sephadex LH-20 column with methanol as the solvent.

Treatment of G2 DAB-dendr-$(NH_2)_8$ (**2a**) with eight equivalents of di-2-pyridyl ketone under similar conditions with a refluxing time of 3 ½ days afforded the dendritic ligand (**2b**) in a yield of 56% (Figure 3.2). G3 dendritic ligand (**3b**) was synthesized from G3 DAB-dendr-$(NH_2)_{16}$ (**3a**) under similar reaction conditions with a longer reaction times of five days. The product was obtained as yellow oil in 31% yield.

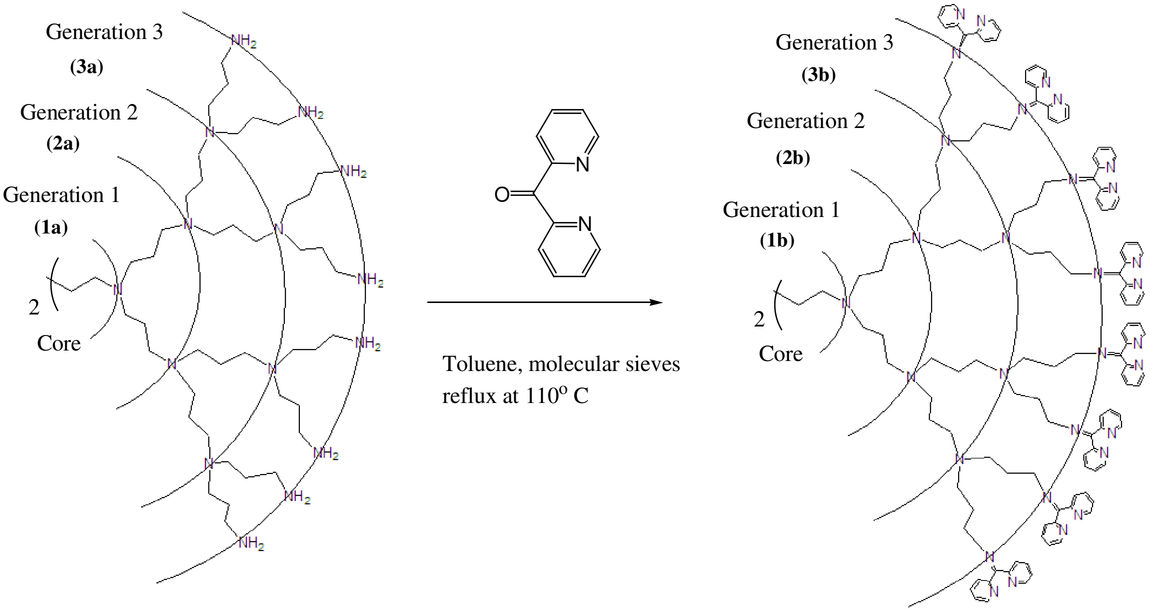
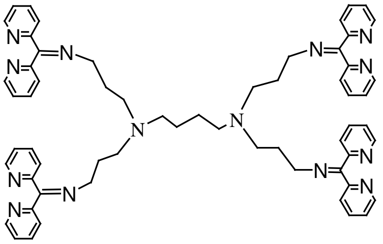


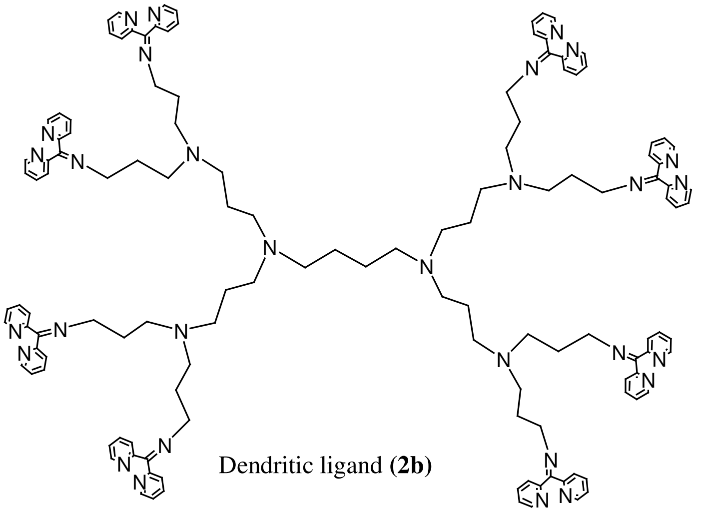
Figure 3.2. Synthesis of G (1-3) bipyridyl-terminated PPI dendrimers.

The G2 and G3 dendritic ligands contained eight and sixteen bipyridyl groups respectively, attached to the surface of the dendrimers (Figure 3.3). As the number of terminal sites increases with generation size, the reaction times were also increased to facilitate complete functionalization of the dendrimer end groups.

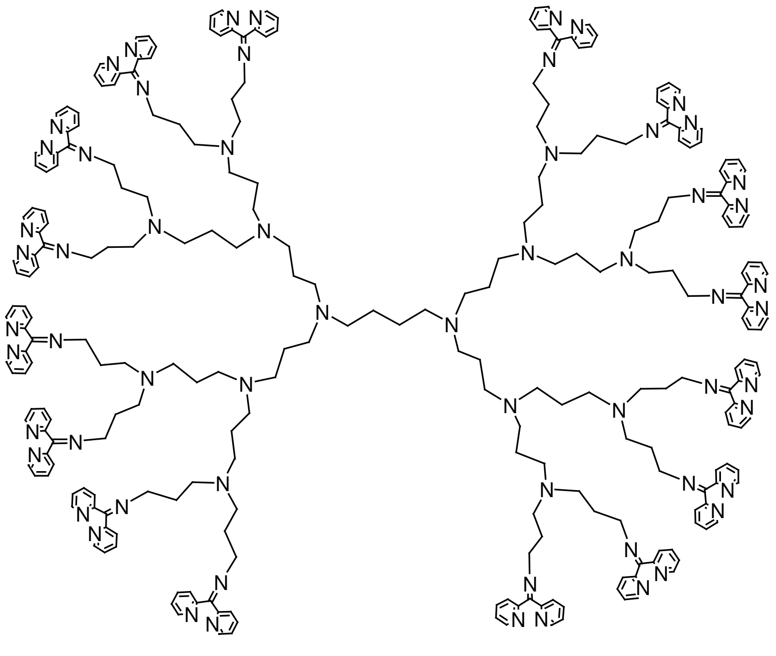
All of the dendritic ligands obtained were thick yellow oils, these samples turned thicker and darker over a period of time when stored at room temperature. In order to prevent them from decomposing, these samples were stored at -30^{0} C under inert atmosphere.



Dendritic ligand **(1b)**



Dendritic ligand (**2b**)



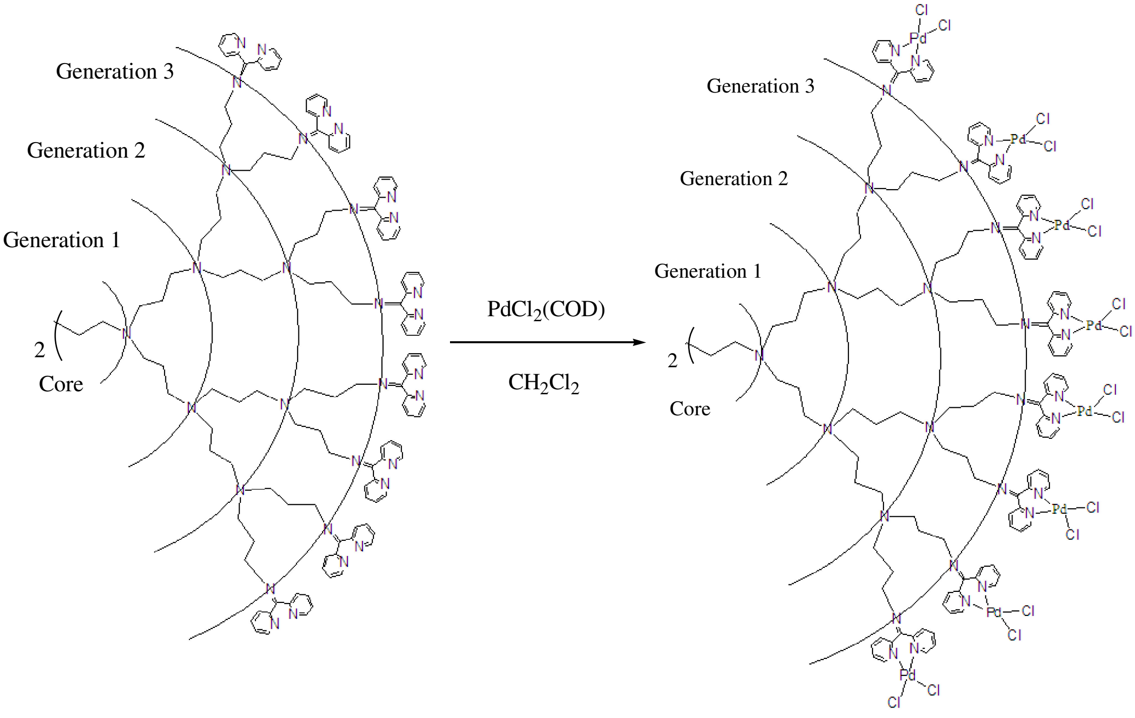
Dendritic ligand **(3b)**

Figure 3.3 Structures of (a) G2 dendritic ligand and (b) G3 dendritic ligand.

Elemental analyses were obtained for some dendrimers, but the presence of water and some other solvents likely contained within the dendrimer cavities led to significant errors in the analyses.[7]

Synthesis of Metallodendrimers

Metallodendrimers were synthesized by a one step complexation reaction of the dendritic ligands with labile palladium precursors. The surface-bound G1 Pd(II) metallodendrimer was obtained by treating the G1 dendritic ligand **(1b)** with $PdCl_2$(COD)[COD=1,5-cyclooctadiene] in dry CH_2Cl_2 with stirring at room temperature for two days (Figure 3.4). The product precipitated out immediately giving rise to a yellow solid in 89% yield.

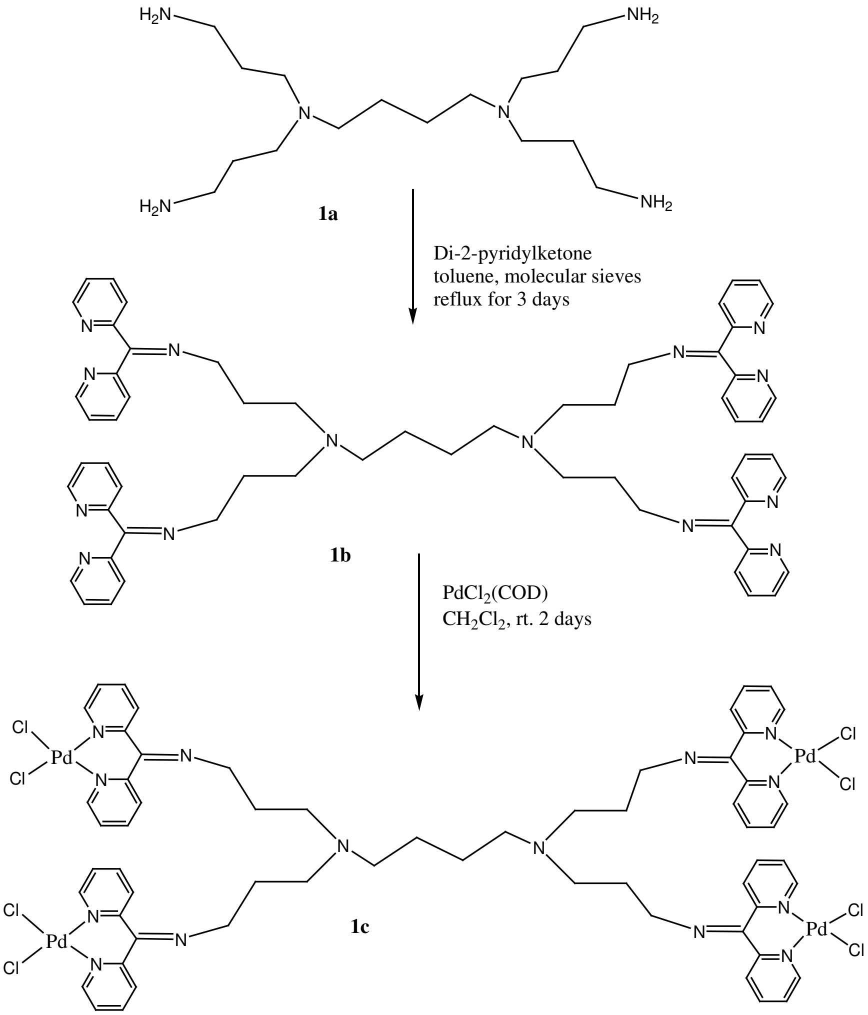


Generation (1-3) Dendritic Ligands (**1b-3b**)

Generation (1-3) Metallodendrimers (**1c-3c**)

Figure 3.4 Synthesis of G (1-3) metallodendrimers.

The metal precursor was added in a small excess to ensure complete complexation of the coordination sites. The unreacted starting materials were washed well with excess dichloromethane to remove soluble monomeric palladium complexes from insoluble dendrimer complexes. The G1 metallodendrimer **(1c)** contains four palladium centers bound to the periphery (Figure 3.5). The second and third generation metallodendrimers were synthesized using a similar protocol (Figure 3.6)



1a

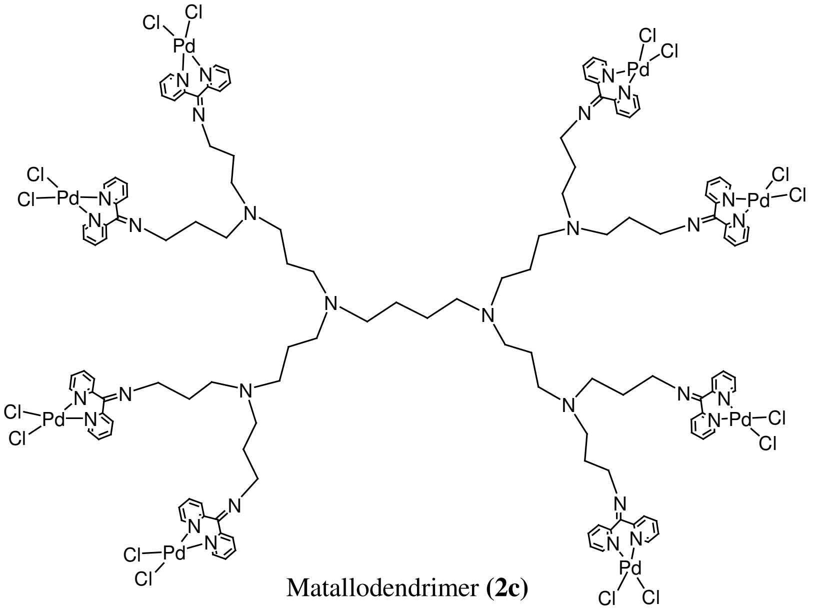
Di-2-pyridylketone
toluene, molecular sieves
reflux for 3 days

1b

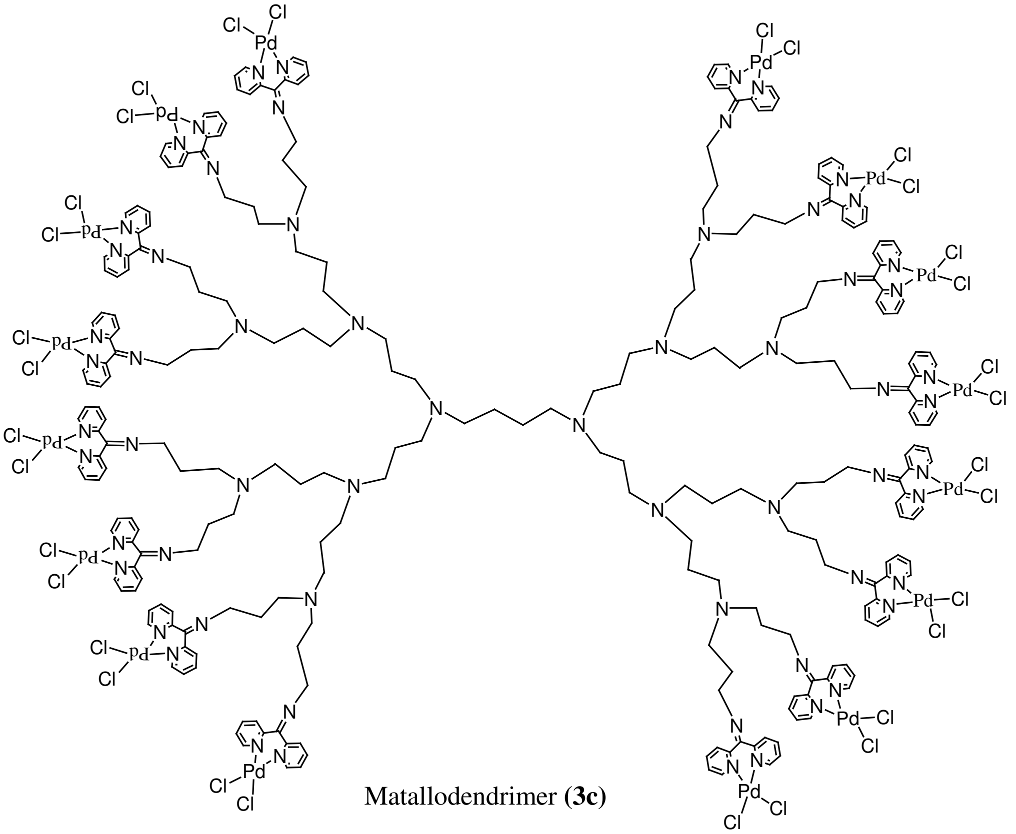
$PdCl_2(COD)$
CH_2Cl_2, rt. 2 days

1c

Figure 3.5 Schematic synthesis of G1 metallodendrimer.



Matallodendrimer (**2c**)



Matallodendrimer (**3c**)

Figure 3.6 G2 and G3 metallodendrimers with $PdCl_2$ moieties on the surface.

Products were obtained in high yields ranging from 86% for G2 to 81% for G3 metallodendrimers respectively. These metallodendrimers contained eight and sixteen Pd(II) metal centers on the surface. The dendrimer complexes were insoluble in the common range of solvents such as methanol, ethanol, dichloromethane, acetone, acetonitrile and benzene, but were soluble in polar aprotic solvents such as DMF and DMSO. Due to their low solubilities in common solvents, no further attempts were made to purify these metallodendrimers. Attempts to obtain elemental analysis with exact compositions were not successful. Many authors have noted that dendrimers show discrepancies between the calculated and observed analyses due to trace impurities and the tendency toward solvent inclusion. [8,9,10]

NMR and IR Spectroscopic Studies

The structural identities of dendritic ligands and metallodendrimers were confirmed by ^{1}H, ^{13}C NMR and IR spectroscopy. The conversion of ketone groups (C=O) to imines (C=N) was monitored using IR spectroscopy to observe the disappearance of C=O stretching at 1684 cm^{-1} and the appearance of a new characteristic stretching at 1633 cm^{-1} for imine formation. ^{1}H NMR spectra of G (1-3) dendritic ligands **(1b-3b)** show signals of the dendritic framework and the key signals arising from methylene protons adjacent to the imine nitrogen. These methylene proton resonances appear at δ 3.24 ppm, 3.22 ppm and 3.20 ppm for dendritic ligands (**1b-3b)** respectively.

The completion of the condensation reaction was indicated by the total absence of the NH_2 signals of the starting polyamine dendrimer at 1.3 ppm in ^{1}H NMR. This can be further confirmed by the absence of a peak around 194 ppm in ^{13}C NMR spectra due to the carbonyl carbon (C=O), and the absence of characteristic NH stretching around 3300-3400 cm^{-1} in the IR spectra. The incorporation of bipyridyl moieties at the surface of the dendrimer resulted in a further upfield shift of protons in the aromatic region.

The signals showed very little deviation in chemical shift for corresponding protons with increase in generation size. The lower generation dendrimer gave relatively simple and easily assignable ^{1}H NMR spectra; higher generation dendrimers exhibited increased signal broadening with the corresponding increase in generation. The NMR spectra of the dendrimers became more complicated with size. The aryl regions exhibited greater complexity due to the large size of the dendrimer core, and overlap of some signals was observed especially for the third generation dendrimer.[7]

Complexation of bipyridyl groups on the dendritic ligands with $PdCl_2$ lead to the expected changes in the proton resonances compared to the unmetalated dendritic ligands. The ^{1}H NMR spectra are more complicated with intense broadening of the signals. Significant down field shifts for aryl and aromatic protons was observed, and the methylene protons adjacent to the imine nitrogen showed a significant shift from 3.24 ppm to 3.45 ppm for the G1 metallodendrimer **(1c)**.[11]

^{13}C NMR spectra showed expected similarities in each of the three generations of dendrimer ligands **(1b-3b)**. No significant changes were observed with respect to the aliphatic carbons of the dendrimers. The carbon atom adjacent to the imine nitrogen showed a significant shift from 40.14 ppm for parent dendrimer to 51.01 ppm for dendrimer ligands. For G1 dendritic ligand **(1a)**, an upfield shift was seen for carbons within the dendrimer branches ($NCH_2\mathit{C}H_2CH_2N$) from 30.93 ppm to 28.08 ppm. Some extra signals were observed for higher generation ligands **(2a, 3a)** due to the increase in the number of methylene carbons within the branches as the generation size increases. Eight different signals were observed for aromatic carbons that appear further down field compared to the four carbon signals from the starting ketone. This can be attributed to the unsymmetrical imine structure formed upon connectivity with the dendrimer. The imine carbon (C=N) resonance appeared around 169 ppm for all of the dendritic ligands. IR spectra of G (1-3) metallodendrimers showed a characteristic stretch at 1581cm^{-1} for the imine (C=N) due to complexation, and no characteristic C=N absorption was observed at 1633 cm^{-1} for the uncomplexed dendrimer ligand.

Attempts to obtain interpretable ^{13}C NMR spectra for metallodendrimer **(1c)**, and ^{1}H NMR or ^{13}C NMR for G2 and G3 metallodendrimers **(2c, 3c)** were not successful. Although NMR spectral analyses have been obtained for the lower generation metallodendrimer [^{1}H NMR; 2.02-3.20 (broad, core), 70.20-9.18 (broad, bipyridyl)], the presence of multiple metal centers resulted in high molecular weights, thereby making the spectra very complicated and uninterpretable. However, given the inherent statistical errors in the dendrimers, which increase with generation size, some errors in the reactivity are inevitable during the surface functionalization and complexation reactions.[7]

Mass Spectroscopic Studies

Matrix-assisted laser desorption ionization mass spectrometry (MALDI-TOF)[12], fast atom bombardment mass spectrometry (FAB)[13]and more recently electron spray ionization mass spectrometry (ESI) [14,15,16] have become extremely powerful tools for studying supramolecular and macromolecular structures. The most significant advantages offered by ESI-MS are its high sensitivity and soft ionization with the generation of multiply charged ions allowing not only for structural information to be obtained but also for broad molecular weight ranges to be measured.[17]

The structures of dendritic ligands and their metalated analogues were fully established by positive ion ESI-MS. By definition, monoisotopic mass is calculated based on the lightest isotope of each element, which in most cases is the most intense peak in the cluster. All of the monoisotopic mass calculations for dendritic ligands are based on the lightest isotope as mentioned above. The G1 dendritic ligand **(1b)** showed clear peaks attributable to the molecular ion associated with a proton $[M+H]^+$ and a sodium ion $[M+Na]^+$ at *m/z* 981.6 and *m/z* 1003.7 respectively. Other fragments included peaks at *m/z* 760.5 $[M+H- (C_{14}H_{11}N_3)]^+$, and *m/z* 466.2 $[M+H- (C_{32}H_{33}N_7)]^+$ due to successive loss of fragments ($C_{14}H_{11}N_3$, $C_{32}H_{33}N_7$). High resolution (HR) ESI-MS shows a peak at *m/z* 981.5510 corresponding to the molecular ion associated with one proton $[M+H]^+$ (Figure 3.7).

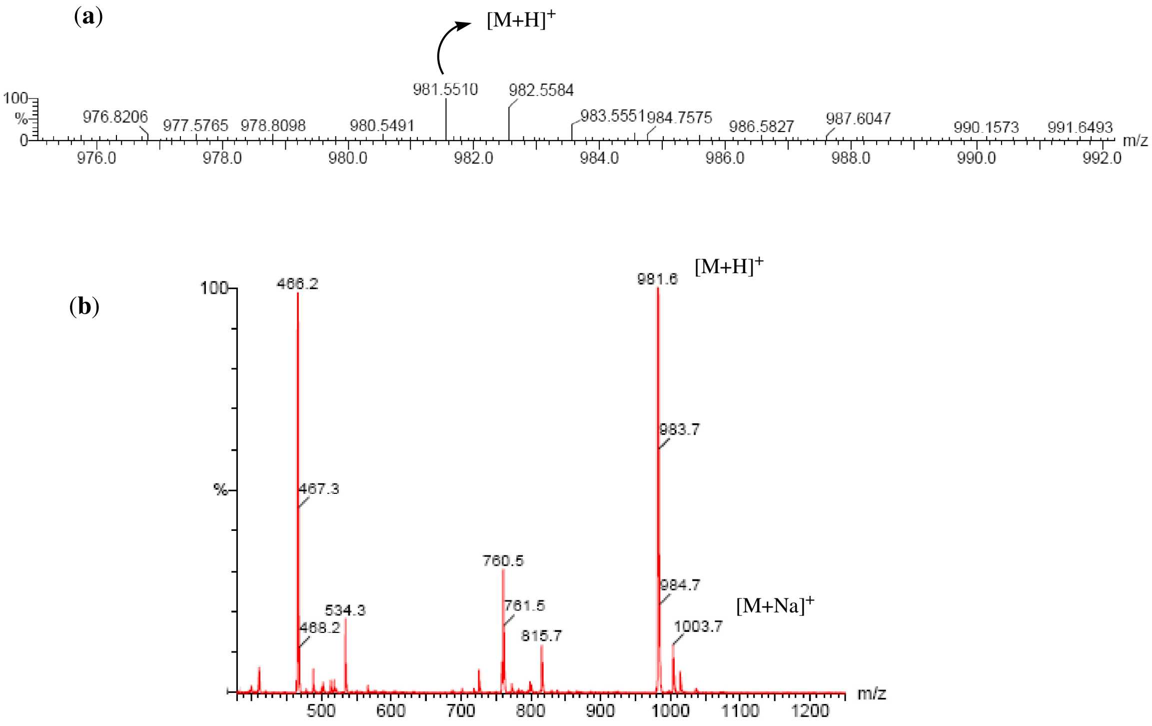


Figure 3.7 (a) HR ESI-MS of G1dendritic ligand showing $[M+H]^+$, (b) Fragmentation spectrum for G1dendritic ligand

The G2 and G3 dendritic ligands did not show fragmentation similar to the G1 ligand. The G2 ligand **(2b)** ionizes as singly and doubly charged species; peaks in ESI-MS were obtained at *m/z* 2102.2253 [$(M+H)^+$, calcd *m/z* 2102.2268] and *m/z* 1062.6421 [$(M+Na+H)^+$, calcd *m/z* 1062.6083] respectively. Other major fragments includes peaks at *m/z* 1880.1614 $[M+H-(C_{14}H_{13}N_3)]^+$ and *m/z* 1600.0490 $[M+H-(C_{31}H_{32}N_7)]^+$ for singly charged species. Peak at *m/z* 940.1245 can be attributed to $[M+2H-(C_{14}H_{13}N_3)]^{2+}$ which is doubly charged. Figure 3.8 shows the HR ESI-MS for the G2 ligand with a significant peak at *m/z* 2102.2241 [$(M+H)^+$, calcd *m/z* 2102.2268) for the protonated molecular ion.

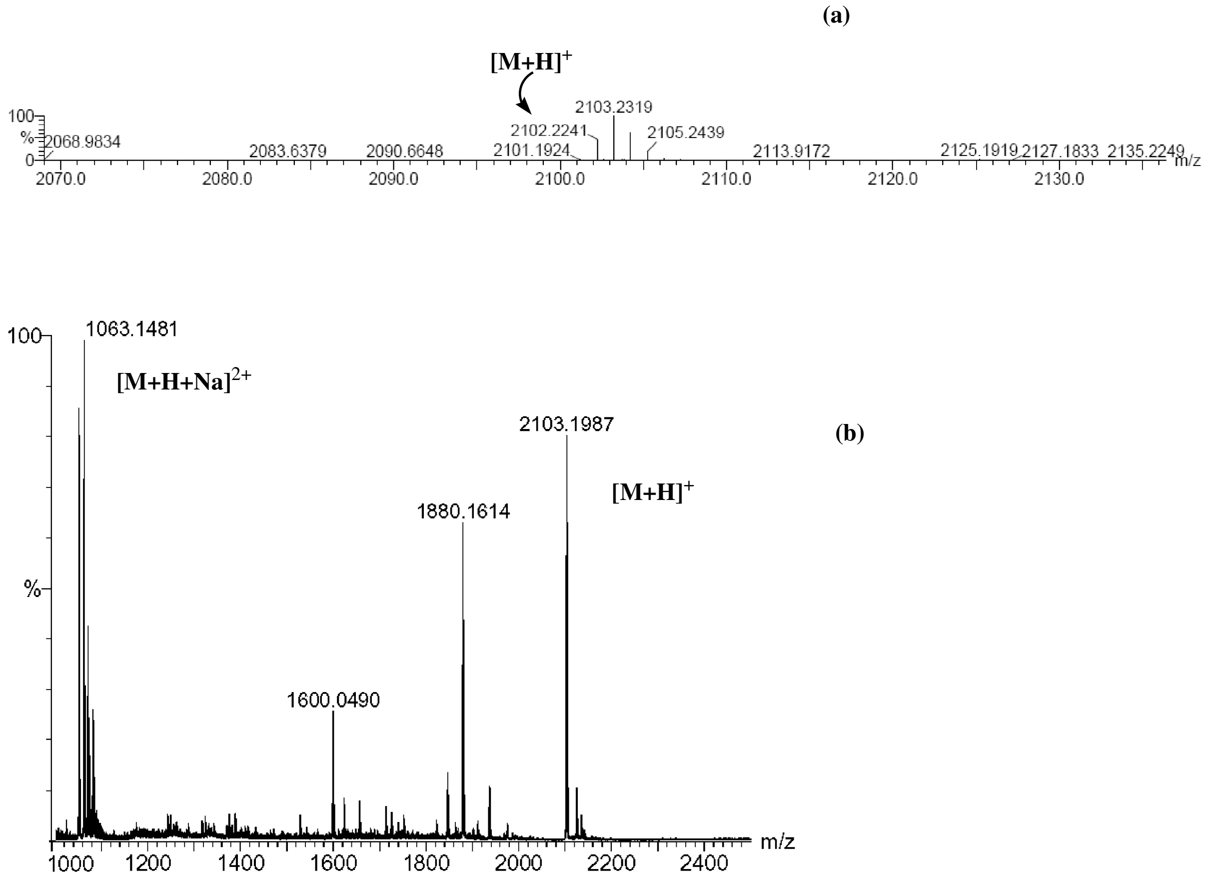


Figure 3.8 HR ESI-MS of G2 dendritic ligand showing (a) the molecular ion peak and (b) major fragments including doubly charged species.

The G3 dendritic ligand showed a different ionization pattern compared to the lower generation dendrimer ligands. The high molecular weight of the ligand does not allow direct observation of the molecular ion peak by ESI-MS.[18] HR ESI-MS for the G3 ligand shows a peak at *m/z* 2172.3013 [(M+H+H)$^{2+,}$ calcd *m/z* 2172.2925] characteristic of a doubly charged ion associated with two protons. Other fragmentation includes the base peak at *m/z* 1448.85[(M+H+H+H)$^{3+}$, calcd *m/z* 1448.5309] corresponding to a triply charged ion associated with three protons (Figure 3.9).

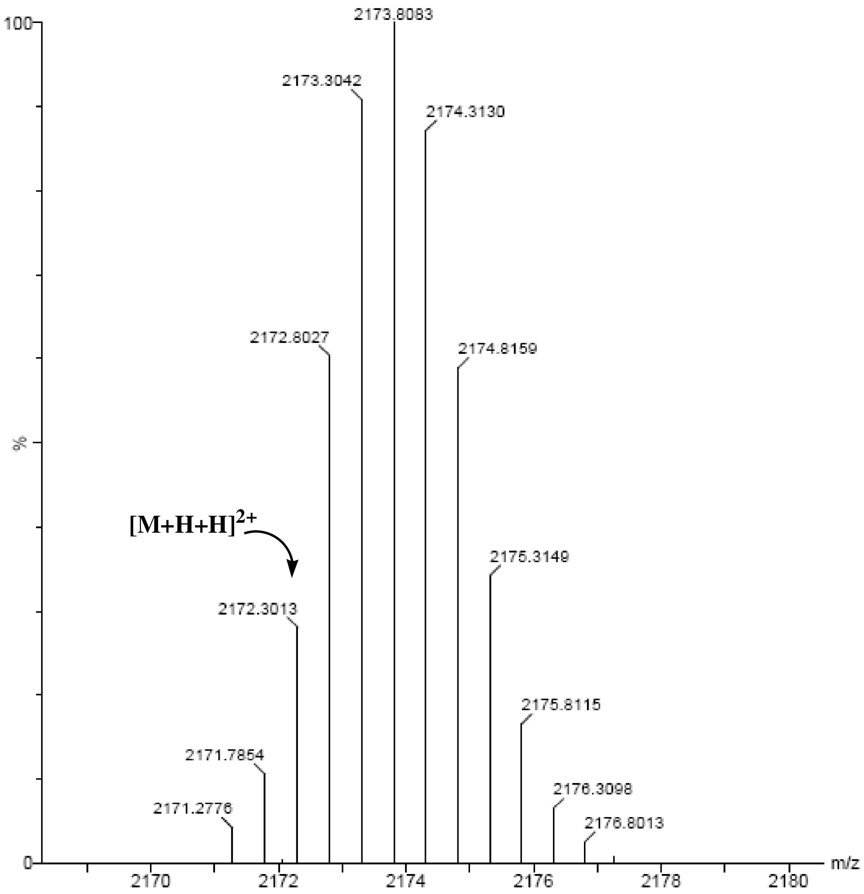


Figure 3.9 HR ESI-MS of G3 dendritic ligand showing doubly charged molecular ion [M+H+H]$^+$

MALDI-TOF has become a widely used technique in the recent years and has also been applied to dendritic systems. [12] Several attempts were made to characterize the dendritic ligands using MALDI-TOF mass spectrometry; in no case did this method provided useful results.

For the metallodendrimers **1c-3c**, reliable molecular weight determinations were obtained by ESI mass spectroscopy, especially for the lower generations. In this section all the monoisotopic mass calculations were calculated using lightest isotopes of each element except for palladium. The lightest isotope of palladium (^{102}Pd) is relatively low abundance, and can be hard to see in the isotopic cluster; hence the monoisotopic mass of (^{106}Pd) is used for practical purposes.

Figure 3.10 shows the positive ESI-MS obtained for G1 metallodendrimer, the peak around *m/z* 1688.9494 [(M)$^+$, calcd 1683.9084] corresponds to the molecular ion peak, and the peak for loss of a chloride appears at *m/z* 1648.9760 [M-Cl]$^+$. A doubly charged ionic peak was observed at *m/z* 806.9803 [(M-2Cl)/2, calcd *m/z* 806.9853] due to loss of two chloride ions. High resolution ESI-MS shows a peak at *m/z* 1648.9398 [(M-Cl)$^+$, calcd *m/z* 1648.9396], which is characteristic of the base peak resulting from loss of one chloride ion from the molecule.

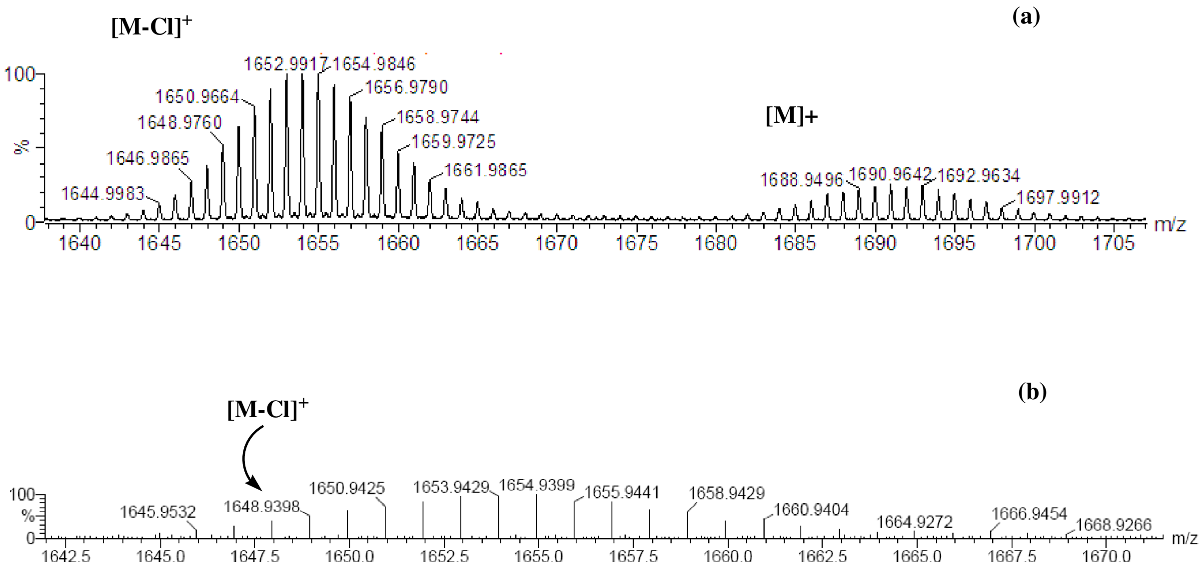


Figure 3.10 ESI-MS of G1 metallodendrimer showing [M]$^+$ and [M-Cl]$^+$.

The G2 metallodendrimer showed a similar ionization pattern compared to its G1 analogue, and the molecule exhibits +2, +3, +4 and +5 charge states. Due to an increase in the number of metal centers leading to high molecular weight, ESI-MS does not allow direct observation of the molecular ion peak. Positive ion ESI-MS for G2 metallodendrimer showed peaks at *m/z* 1719.0053 $[(M\text{-}2Cl)/2]^{2+}$, *m/z* 1134.3403 $[(M\text{-}3Cl)/3]^{3+}$, *m/z* 842.5020 $[(M\text{-}4Cl)/4]^{4+}$, and *m/z* 666.6060 $[(M\text{-}5Cl)/5]^{4+}$ for +2, +3, +4 and +5 charge states respectively (Figure 3.11). High resolution ESI-MS shows a peak at *m/z* 1719.0052 $[(M\text{-}2Cl)/2]^{2+}$ corresponding to a molecular ion resulting from the loss of two chloride ions, and this is observed to be within 2 ppm of the theoretical molecular mass.

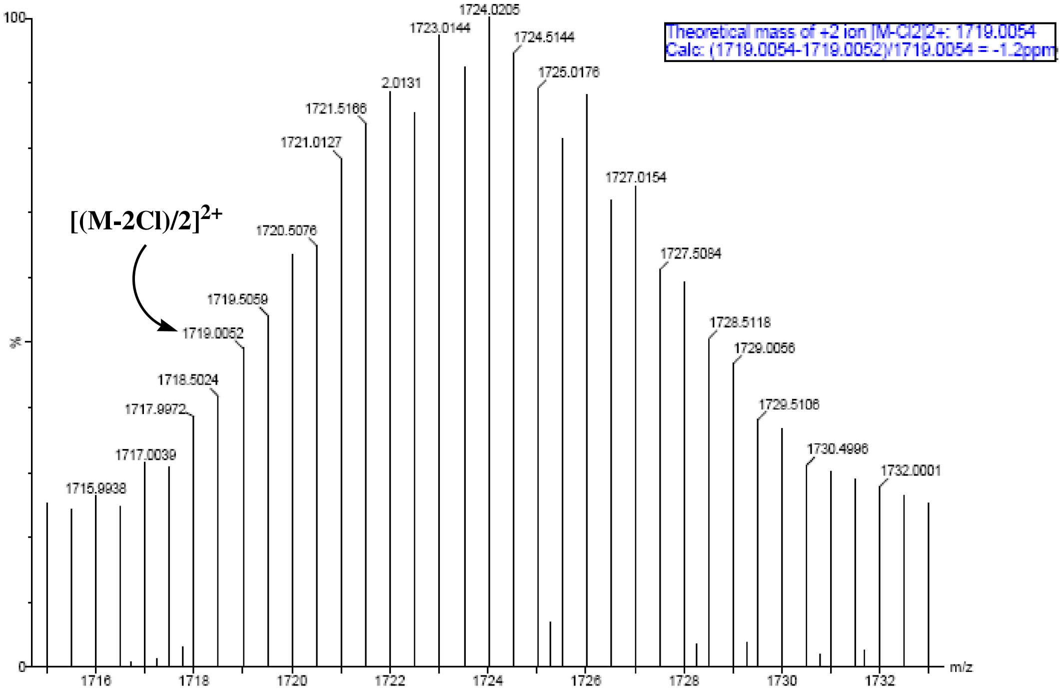


Figure 3.11 HR ESI-MS of G2 metallodendrimer **(2c)** showing doubly charged molecular ion $[(M\text{-}2Cl)/2]^{2+}$

SUMMARY AND CONCLUSIONS

Poly (propylene imine) dendrimers of three successive generations have been successfully functionalized with covalently attached bipyridyl ligands on the surface of the dendrimer in a single step reaction. Characterization has been successful achieved by ^{1}H NMR, ^{13}C NMR, and IR spectroscopies as well as mass determinations by ESI mass spectrometry. A novel series of metal-chelating dendrimers has been synthesized upon complexation of chelating bipyridyl ligands with palladium. Metallodendrimers have also been successfully characterized using NMR, IR and ESI mass spectrometry. It is clear that IR and NMR spectroscopy provides useful signatures for ligand attachment and complexation reactions. However, when the dendrimers become heavier, especially for dendrimers with multiple metal centers, NMR spectra become very complicated and not useful for characterization. We have also shown that ESI mass spectrometry is a very useful characterizational tool when NMR studies are not adequate.

EXPERIMENTAL

All experiments were carried out under an atmosphere of nitrogen unless otherwise stated. Palladium chloride (Alfa Aesar, 99.9%), di-2-pyridylketone (Acros, 98%), the dendritic polyamines DAB-dendr- $(NH_2)_n$ (n=4,8,16,64) were purchased from Aldrich. Bio beads [Sephadex LH-20 Amersham] were used as column packing for size exclusion chromatographic purification. Solvents were distilled from the appropriate drying agents using standard purification procedures immediately prior to use. Methylene chloride (Pharmco, purified and dried over P_2O_5), toluene (Pharmco, purified and dried over Na), methanol (Pharmco) was used as received. $(COD)PdCl_2$[19] was synthesized through established procedures. Molecular sieves (4 A, beads, 8-12 mesh) were dried prior to use. Water was purified by an E-pure system (Barnstead). NMR solvents: CD_3CN (Cambridge Isotope Laboratories, Inc, 99.8%) and DMSO-d_6 (Cambridge Isotope laboratories, Inc, 99.9%) were used as received.

^1H NMR spectra were recorded on Varian 300 MHz and 400 MHz spectrometers, with chemical shifts given in ppm. ^{13}C NMR spectra were recorded on a Varian 400 MHz spectrometer, with chemical shift in ppm. Elemental analyses were performed by Desert Analytics Laboratory, Tucson, AZ, USA. Infrared (IR) spectra were recorded as Nujol mulls and neat oils in some cases using a Nicolet Protege 460 FT-IR spectrometer (recorded using a resolution of 4 cm^{-1}). ESI-MS was carried using a Micromass Q-tof mass spectrometer; the samples were dissolved in methanol and then introduced into the spectrometer via static nanospray infusion. The instrument was calibrated using a solution of sodium formate in methanol; the sodium formate cluster masses are also used as “internal lock masses”.

Synthesis of G1 Bipyridyl dendritic ligand (lb)

To a 50 ml two neck round bottom flask was added di-2-pyridylketone (0.547 g, 2.97 mmol), and a solution of DAB-dendr-$(NH_2)_4$ **1a** (0.235 g, 0.74 mmol) dissolved in 30 ml of dry toluene. The round bottom flask was connected to a Dean-Stark apparatus fitted with a condenser and a septum for nitrogen inlet and outlet. Dry molecular sieves (~ 2g) were charged into the flask and the reaction mixture was stirred under reflux for 3 days. The reaction was monitored by IR spectra of small aliquots of the solution from the reaction flask to ensure the reaction was close to completion. The reaction mixture was cooled and filtered, and solvent was removed. The residual oil was extracted with hot methanol, and the solvent was removed under vacuum. The remaining oil obtained from the extract was dissolved in CH_2Cl_2 (25 ml) and washed copiously with water.[11] The organic layer was collected, dried over anhydrous $MgSO_4$ and filtered, and then solvent was removed and the crude product was further purified by size exclusion chromatography using a Sephadex-LH 20 column with CH_3OH as the solvent. The product was obtained as a sticky yellow oil **lb** (0.516 g, 71%). ^{1}H-NMR [$(CD_3)_2SO$, 300 MHz]; δ 1.15 (br s, $NCH_2CH_2CH_2CH_2N$, 4H), 1.60 (br t, $NCH_2CH_2CH_2N$, 8H), 2.17 (br s, $NCH_2CH_2CH_2CH_2N$, 4H), 2.32 (br t, $NCH_2CH_2CH_2N{=}C$, 8H), 3.24 (br t, $NCH_2CH_2CH_2N{=}C$, 8H), 7.27 (dd, bipy, 4H), 7.35 (m, bipy, 8H), 7.80 (m, bipy, 8H), 8.10 (dd, bipy, 4H), 8.40 (dd, bipy, 4H), 8.58 (dd, bipy, 4H). ^{13}C NMR [$(CD_3)_2SO$, 300 MHz]; δ 24.5 ($NCH_2CH_2CH_2CH_2N$), 28.1 ($NCH_2CH_2CH_2N$), 51.1 ($NCH_2CH_2CH_2N{=}C$), 51.1 ($NCH_2CH_2CH_2N{=}C$), 53.3 ($NCH_2CH_2CH_2CH_2N$), 121.0, 122.8, 123.4, 124.2, 135.8, 136.4, 148.1, 148.9, 154.9, 156.4,and 165.9 (N=C, imine). IR (neat oil, NaCl plates): ν=1634, 1584, 1566 (C=N). HR ESI-MS *m/z* 981.6 $[M+H]^+$, 1003.7 $[M+Na]^+$.

Anal.Calcd for $C_{60}N_{14}H_{64}$: C, 73.44; H, 6.57; N, 19.98. Found: C, 71.46; H, 6.80; N, 19.09.

Synthesis of G1 metallodendrimer (1c)

To a schlenk tube was added $PdCl_2(COD)$ (0.174 g, 0.610 mmol) dissolved in dry CH_2Cl_2 (10 ml). A solution of G1 dendritic ligand **1b** (0.133 g, 0.135 mmol) dissolved separately in dry CH_2Cl_2 (5 ml) was transferred to the Schlenk tube. After a few minutes, a yellow solid precipitated out from the solution. The mixture was stirred at room temperature under nitrogen for 2 days. The solid was filtered, washed with CH_2Cl_2, and dried under vacuum, yielding an amorphous yellow solid **1c** (0.203 g, 89%). ^1H NMR [$(CD_3)_2SO$, 300 MHz]; δ 1.96 (br s, $NCH_2CH_2CH_2CH_2N$, 4H), 2.65 (br t, $NCH_2CH_2CH_2N$, 8H), 2.89 (br s, $NCH_2CH_2CH_2CH_2N$, $NCH_2CH_2CH_2N{=}C$, 12H), 3.45 (br s, $NCH_2CH_2CH_2N{=}C$, 8H), Aromatic 7.21 (br d, bipy, 4H), 7.72 (br s, bipy, 4H), 7.90 (br s, bipy, 8H), 8.20 (br d, bipy, 8H), 8.87 (br d, bipy, 4H), 9.10 (br d, bipy, 4H). ^{13}C NMR [$(CD_3)_2SO$, 300 MHz]; 124.6, 126.0, 129.0, 137.9, 141.2, 150.4, 156.6. IR (neat oil, NaCl plates): $\nu=1581\ cm^{-1}$ (C=N). HR ESI-MS *m/z* 1683.9 $[M]^+$, 1648.9 $[M\text{-}Cl]^+$, 806.9 [(M-2Cl)/2] Anal. Calcd for $C_{60}N_{14}H_{64}Pd_4Cl_8$: C, 42.76; H, 3.83; N, 11.64. Found: C, 37.22; H, 3.77; N, 9.87.

Synthesis of G2 Bipyridyl dendritic ligand (2b)

To a 50 ml two neck round bottom flask was added di-2-pyridylketone (0.396 g, 2.15 mmol), and a solution of DAB-dendr-$(NH_2)_4$ **2a** (0.208 g, 0.269 mmol) dissolved in 30 ml of dry toluene. The round bottom flask was connected to a Dean-Stark apparatus fitted with a condenser and a septum for nitrogen inlet and outlet. Dry molecular sieves (~ 2g) were charged into the flask and the reaction mixture was stirred under reflux for 3 days and 12 hrs. The reaction was monitored by IR spectra of small aliquots of the solution from the reaction flask to ensure the reaction was close to completion. The reaction mixture was cooled and filtered, and solvent was removed. The residual oil was extracted with hot methanol, and the solvent was removed under vacuum. The remaining oil obtained from the extract was dissolved in CH_2Cl_2 (25 ml) and washed copiously with water. The organic layer was collected, dried over anhydrous $MgSO_4$ and filtered, and then solvent was removed. The crude product was further purified by size exclusion chromatography using a Sephadex-LH 20 column with CH_3OH as the solvent. The product was obtained as a sticky yellow oil **2b** (0.316 g, 56%). ^{1}H NMR [$(CD_3)_2SO$, 300 MHz]; δ 1.15-1.26 (br s, $NCH_2CH_2CH_2CH_2N$, $NCH_2CH_2CH_2N$, 12H), 1.59 (br d, $NCH_2CH_2CH_2N{=}C$, 16H), 2.07-2.29 (br s, $NCH_2CH_2CH_2CH_2N$, $NCH_2CH_2CH_2N$, $NCH_2CH_2CH_2N{=}C$ 36H), 3.22 (br s, $NCH_2CH_2CH_2N{=}C$, 16H), 7.20 (d, bipy, 8H), 7.31 (m, bipy, 16H), 7.78 (m, bipy, 16H), 8.10 (d, bipy, 8H), 8.38 (m, bipy, 8H), 8.56 (m, bipy, 8H). ^{13}C NMR [$(CD_3)_2SO$, 400 MHz]; δ 24.3 ($NCH_2CH_2CH_2N$), 24.5 ($NCH_2CH_2CH_2CH_2N$), 28.1 ($NCH_2CH_2CH_2N{=}C$), 51.0 ($NCH_2CH_2CH_2N{=}C$), 51.3 ($NCH_2CH_2CH_2N{=}C$), 51.5 ($NCH_2CH_2CH_2N$), 51.6 ($NCH_2CH_2CH_2N$), 54.9 ($NCH_2CH_2CH_2CH_2N$), 121.1, 122.9, 123.4, 124.3, 135.8, 136.5, 148.2, 149.1, 155.1, 156.5, and 166.1 (N=C, imine). IR (neat oil, NaCl plates): ν=1634, 1584, 1566 (C=N). HR ESI-MS *m/z* 2102.2 $[M+H]^+$, 1063.1 $[M+H+Na]^{2+}$.

Synthesis of G2 metallodendrimer (2c)

To a Schlenk tube was added $PdCl_2(COD)$ (0.163 g, 0.570 mmol) dissolved in dry CH_2Cl_2 (15 ml). A solution of G2 dendritic ligand **2b** (0.142 g, 0.067 mmol) dissolved separately in dry CH_2Cl_2 (5 ml) was transferred to the Schlenk tube. After a few minutes, a yellow solid precipitated out from the solution. The mixture was stirred at room temperature under nitrogen for 2 days. The solid was filtered, washed with CH_2Cl_2, and dried under vacuum, yielding an amorphous yellow solid **2c** (0.202 g, 86%). ^{1}H NMR [$(CD_3)_2SO$, 400 MHz]; 2.02-3.20 (broad signals, core), 70.20-9.18 (broad, bipyridyl), ^{13}C NMR [$(CD_3)_2SO$, 400 MHz]; 124.7, 126.2, 129.2, 138.1, 141.4, 148.2, 150.6, . IR (neat oil, NaCl plates): ν = 1581 cm^{-1} (C=N). + ve ESI-MS *m/z* 1683.9 [M], 1719.1 [(M-2Cl)/2], 1134.3 [(M-3Cl)/3], 842.0 [(M-4Cl)/4], 666.6 [(M-5Cl)/5].

Synthesis of G3 Bipyridyl dendritic ligand (3b)

To a 50 ml two neck round bottom flask was added di-2-pyridylketone (0.346 g, 1.88 mmol), and a solution of DAB-dendr-$(NH_2)_4$ **3a** (0.198 g, 0.117 mmol) dissolved in 30 ml of dry toluene. The round bottom flask was connected to a Dean-Stark apparatus fitted with a condenser and a septum equipped with nitrogen inlet and outlet. Dry molecular sieves were charged into the flask and the reaction mixture was stirred under reflux for 5 days. The reaction was monitored by IR spectra of small aliquots of the solution from the reaction flask to ensure the reaction was close to completion. The reaction mixture was cooled and filtered, and solvent was removed. The residual oil was extracted with hot methanol, and the solvent was removed under vacuum. The remaining oil obtained from the extract was dissolved in CH_2Cl_2 (25 ml) and washed copiously with water. The organic layer was collected, dried over anhydrous $MgSO_4$ and filtered, and then solvent was removed. The crude product was further purified by size exclusion chromatography using a Sephadex-LH 20 column with CH_3OH as the solvent. Product was obtained as a sticky yellow oil **3c**(0.162 g, 32%). ^{1}H NMR [$(CD_3)_2SO$, 300 MHz]; δ 1.25 (br s, $\mathrm{NCH_2C}H_2\mathrm{C}H_2\mathrm{CH_2N}$, $\mathrm{NCH_2C}H_2\mathrm{CH_2N}$, $\mathrm{NCH_2C}H_2\mathrm{CH_2N}$, 28H), 1.58 (br s, $\mathrm{NCH_2C}H_2\mathrm{CH_2N{=}C}$, 32H), 2.11-2.27 (br s, $\mathrm{NC}H_2\mathrm{CH_2CH_2C}H_2\mathrm{N}$, $\mathrm{NC}H_2\mathrm{CH_2C}H_2\mathrm{N}$, $\mathrm{NC}H_2\mathrm{CH_2CH_2N{=}C}$, 80H), 3.20 (br s, $\mathrm{NCH_2CH_2C}H_2\mathrm{N{=}C}$, 16H), 7.16 (d, bipy, 16H), 7.28 (br s, bipy, 32H), 7.73 (br s, bipy, 32H), 8.08 (br d, bipy, 16H), 8.35 (br s, bipy, 16H), 8.53 (br s, bipy, 16H). ^{13}C NMR [$(CD_3)_2SO$, 300 MHz]; δ 24.3 ($\mathrm{NCH_2}C\mathrm{H_2CH_2N}$, $\mathrm{NCH_2}C\mathrm{H_2}C\mathrm{H_2CH_2N}$), 28.1 ($\mathrm{NCH_2}C\mathrm{H_2CH_2N{=}C}$), 51.0 ($\mathrm{NCH_2CH_2}C\mathrm{H_2N{=}C}$), 51.3 ($\mathrm{N}C\mathrm{H_2CH_2CH_2N{=}C}$), 51.6 ($\mathrm{NCH_2CH_2}C\mathrm{H_2N}$), $\mathrm{N}C\mathrm{H_2CH_2CH_2N}$), 54.9 ($\mathrm{N}C\mathrm{H_2CH_2CH_2}C\mathrm{H_2N}$), 121.0, 122.8, 123.3, 124.2, 135.7, 136.3, 148.1, 149.9, 154.9, 156.4, 165.9 (N=C, imine). IR (neat oil, NaCl plates): ν=1634, 1584, 1566 (C=N). ESI-MS *m/z*. 2172.3 $[M+H+H]^{2+}$, 1448.5 $[M+H+H+H]^{3+}$.

Synthesis of G3 metallodendrimer (3c)

To a Schlenk tube was added $PdCl_2(COD)$ (0.133 g, 0.468 mmol) dissolved in dry CH_2Cl_2 (15 ml). A solution of dendritic ligand **3b** (0.121 g, 0.0278 mmol) dissolved separately in dry CH_2Cl_2 (5 ml) was transferred to the Schlenk tube. After a few minutes a yellow solid precipitated out from the solution. The mixture was stirred at room temperature under nitrogen for 2 days. The solid was filtered, washed with CH_2Cl_2, and dried under vacuum, yielding an amorphous yellow solid **3c** (0.160 g, 81%). ^{1}H NMR

[$(CD_3)_2SO$, 400 MHz]; 2.02-3.20 (broad signals, core), 70.20-9.18 (broad, bipyridyl), IR (neat oil, NaCl plates): $\nu = 1582$ cm^{-1} (C=N)

REFERENCES

(1) Reek, Joost N. H.; De Groot, Debby; Oosterom, G. Eric; Kamer, Paul C. J.; Van Leeuwen, Piet W. N. M. *Reviews in Molecular Biotechnology* **2002**, *90*, 159-181.

(2) Kawa, Manabu; Frechet, Jean M. J. *Chemistry of Materials* **1998**, *10*, 286-296.

(3) Reetz, Manfred T.; Lohmer, Gunther; Schwickardi, Renate *Angewandte Chemie, International Edition in English* **1997**, *36*, 1526-1529.

(4) Maraval, Valerie; Laurent, Regis; Caminade, Anne-Marie; Majoral, Jean-Pierre *Organometallics* **2000**, *19*, 4025-4029.

(5) Patia, S. *The Chemistry of the Amino Group*; Interscience Publishers, 1968, 350-351.

(6) Westheimer, F. H.; Taguchi, Kazuo *Journal of Organic Chemistry* **1971**, *36*, 1570-2.

(7) Storrier, Gregory D.; Takada, Kazutake; Abruna, Hector D. *Langmuir* **1999**, *15*, 872-884.

(8) Issberner, Joerg; Vogtle, Fritz; De Cola, Luisa; Balzani, Vincenzo *Chemistry--A European Journal* **1997**, *3*, 706-712.

(9) Archut, Andreas; Vogtle, Fritz; De Cola, Luisa; Azzellini, Gianluca Camillo; Balzani, Vincenzo; Ramanujam, P. S.; Berg, Rolf H. *Chemistry--A European Journal* **1998**, *4*, 699-706.

(10) Lange, Peter; Schier, Annette; Schmidbaur, Hubert *Inorganic Chemistry* **1996**, *35*, 637-42.

(11) Smith, Gregory; Chen, Rui; Mapolie, Selwyn *Journal of Organometallic Chemistry* **2003**, *673*, 111-115.

(12) Kawaguchi, Tohru; Walker, Kathleen L.; Wilkins, Charles L.; Moore, Jeffrey S. *Journal of the American Chemical Society* **1995**, *117*, 2159-65.

(13) Lau, R.L.C.; Chan, T.W.D.; Chow, H.F. *Eur. Mass. Spectrom* **1995**, *1*, 371-380.

(14) Stoeckigt, Detlef; Lohmer, Gunther; Belder, Detlev *Rapid Communications in Mass Spectrometry* **1996**, *10*, 521-6.

(15) Moucheron, C.; Kirsch-De Mesmaeker, A.; Dupont-Gervais, A.; Leize, E.; Van Dorsselaer, A. *Journal of the American Chemical Society* **1996**, *118*, 12834-12835.

(16) Kallos, G. J.; Tomalia, D. A.; Hedstrand, D. M.; Lewis, S.; Zhou, J. *Rapid Communications in Mass Spectrometry* **1991**, *5*, 383-6.

(17) Weener, Jan-Willem; van Dongen, Joost L. J.; Meijer, E. W. *Journal of the American Chemical Society* **1999**, *121*, 10346-10355.

(18) Cohen, Seth M.; Petoud, Stephane; Raymond, Kenneth N. *Chemistry--A European Journal* **2001**, *7*, 272-279.

(19) Cotton, F. A. *Inorganic Synthesis*; Mc Graw-Hill, 1972; Vol. 13.

APPENDIX

Figure 3.8 ^{1}H NMR spectra of DAB-AM-(NH)$_4$ in DMSO-D$_6$

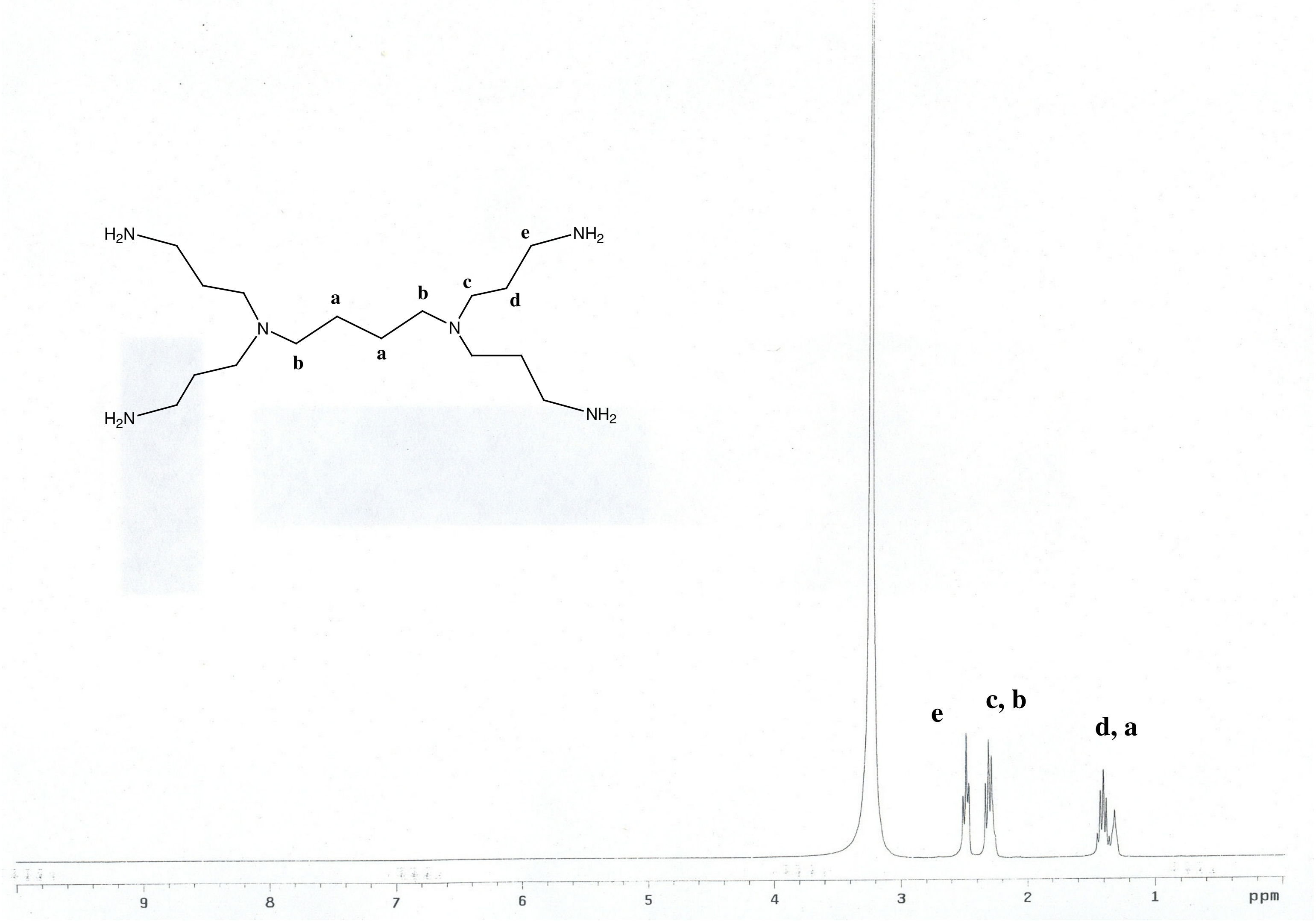


Figure 3.9 ^{13}C NMR spectra of DAB-AM-$(NH)_4$ in DMSO-D_6

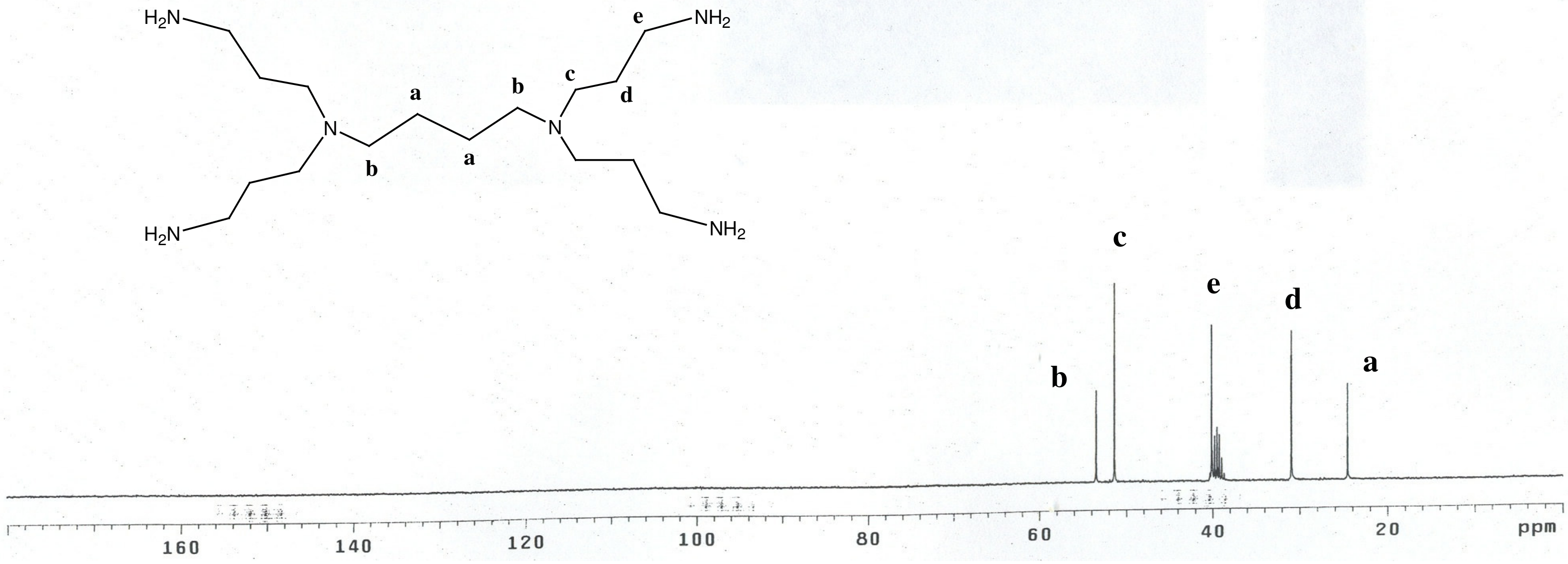


Figure 3.10 ^{1}H NMR spectra of dendritic ligand **(1b)**in DMSO-D$_6$

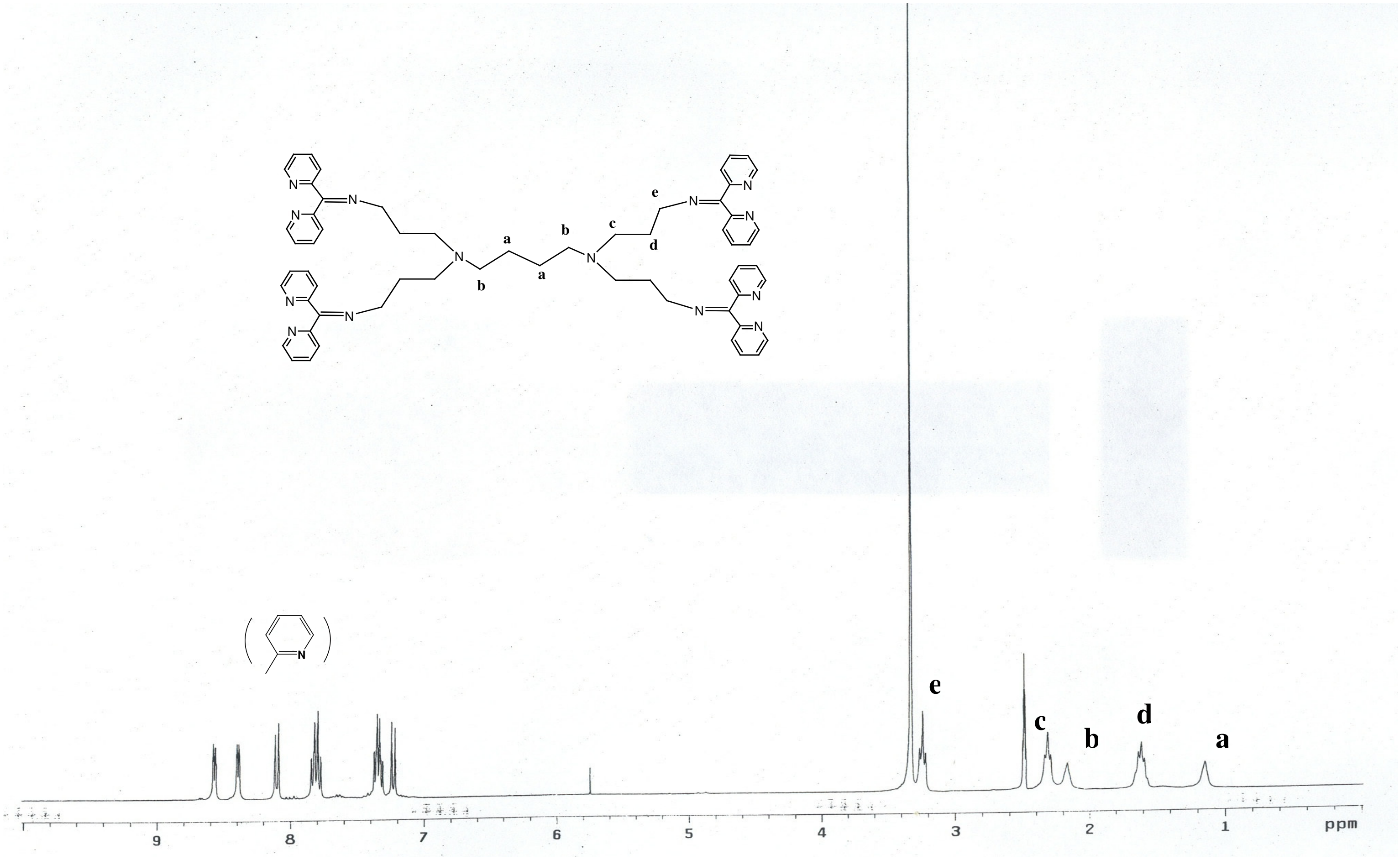


Figure 3.11 ^{13}C NMR spectra of dendritic ligand **(1b)**in DMSO-D$_6$

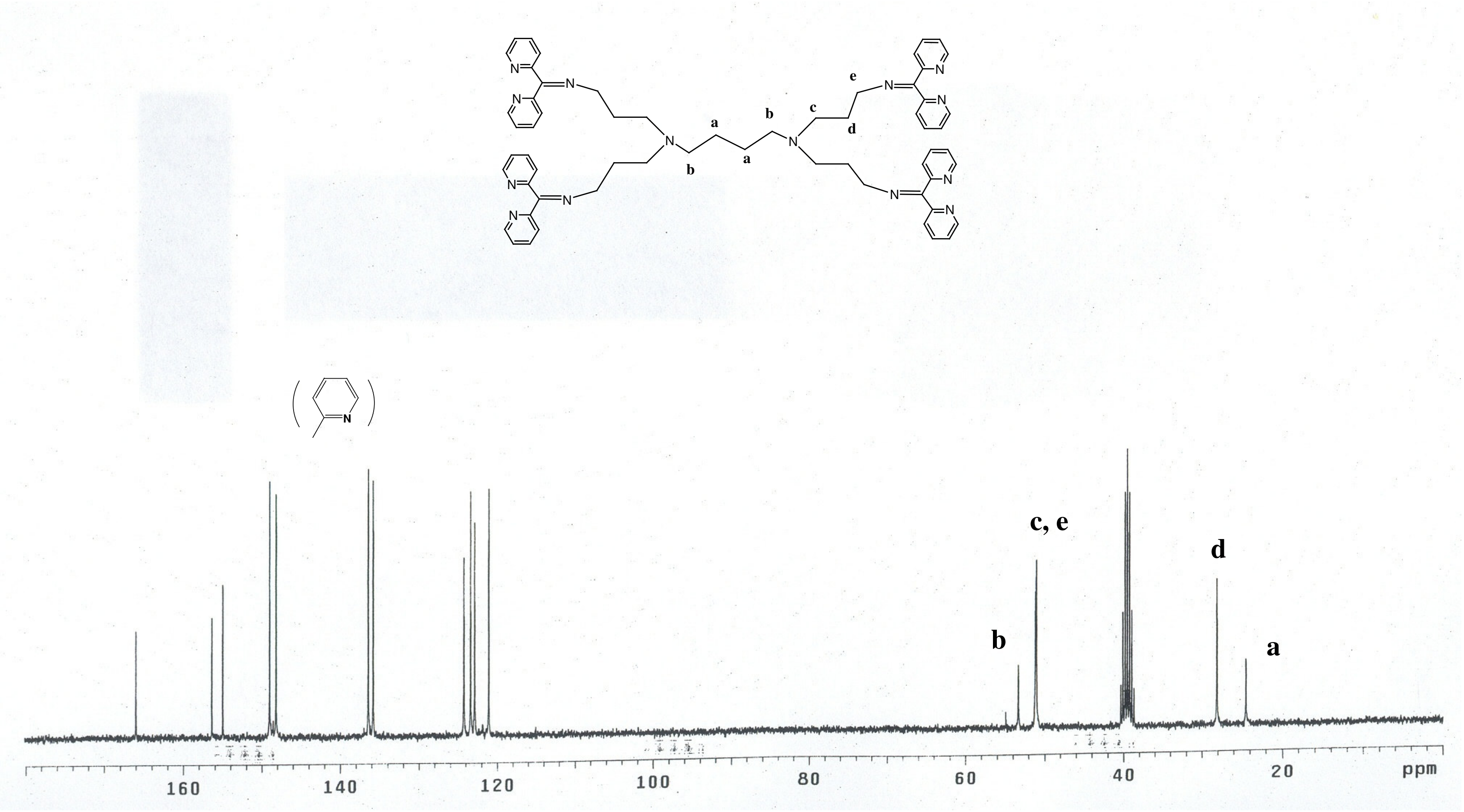


Figure 3.12 ^{1}H NMR spectra of metallodendrimer **(1c)** in DMSO-D$_6$

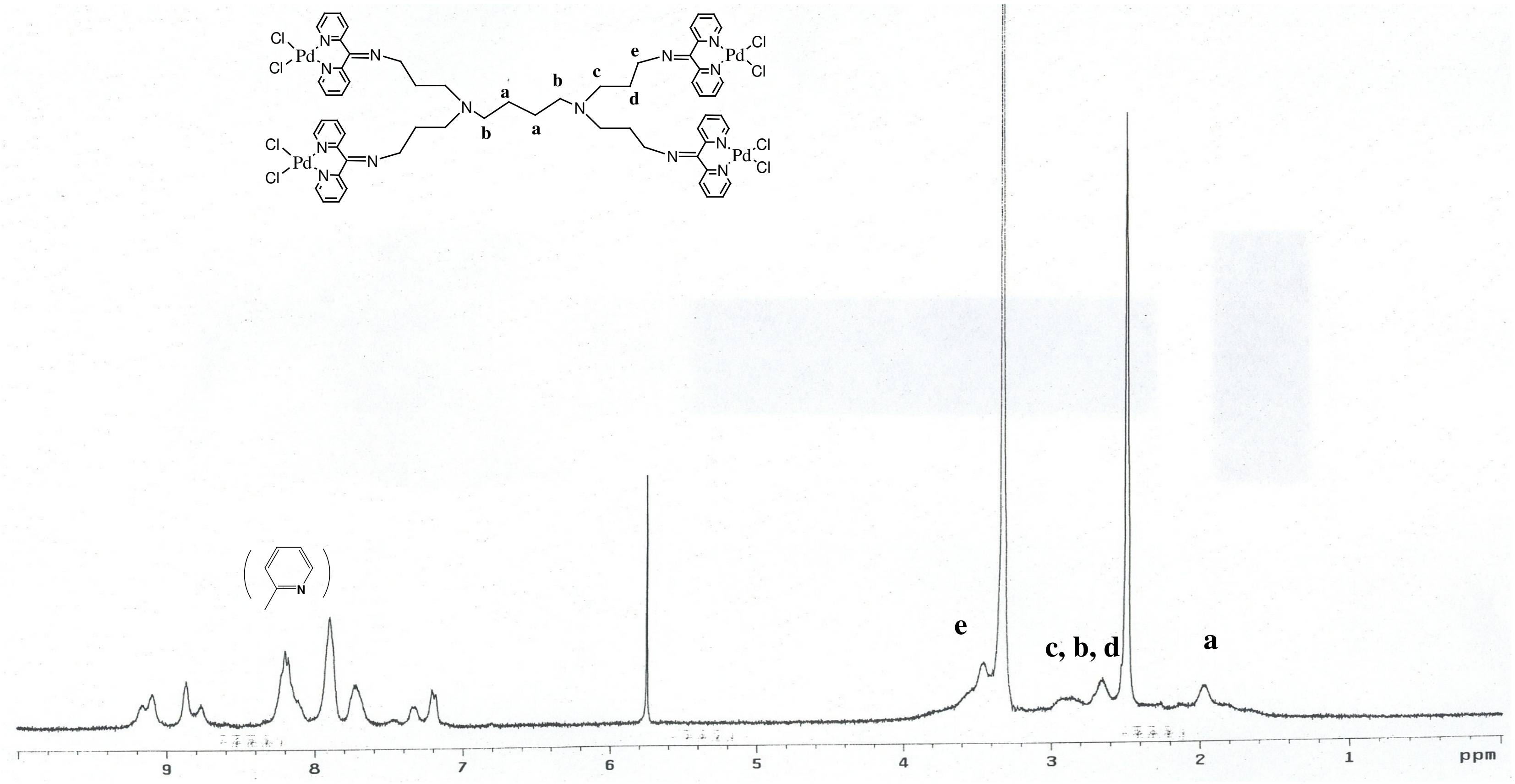


Figure 3.13 ^{1}H NMR spectra of dendritic ligand **(2b)** in DMSO-D_6

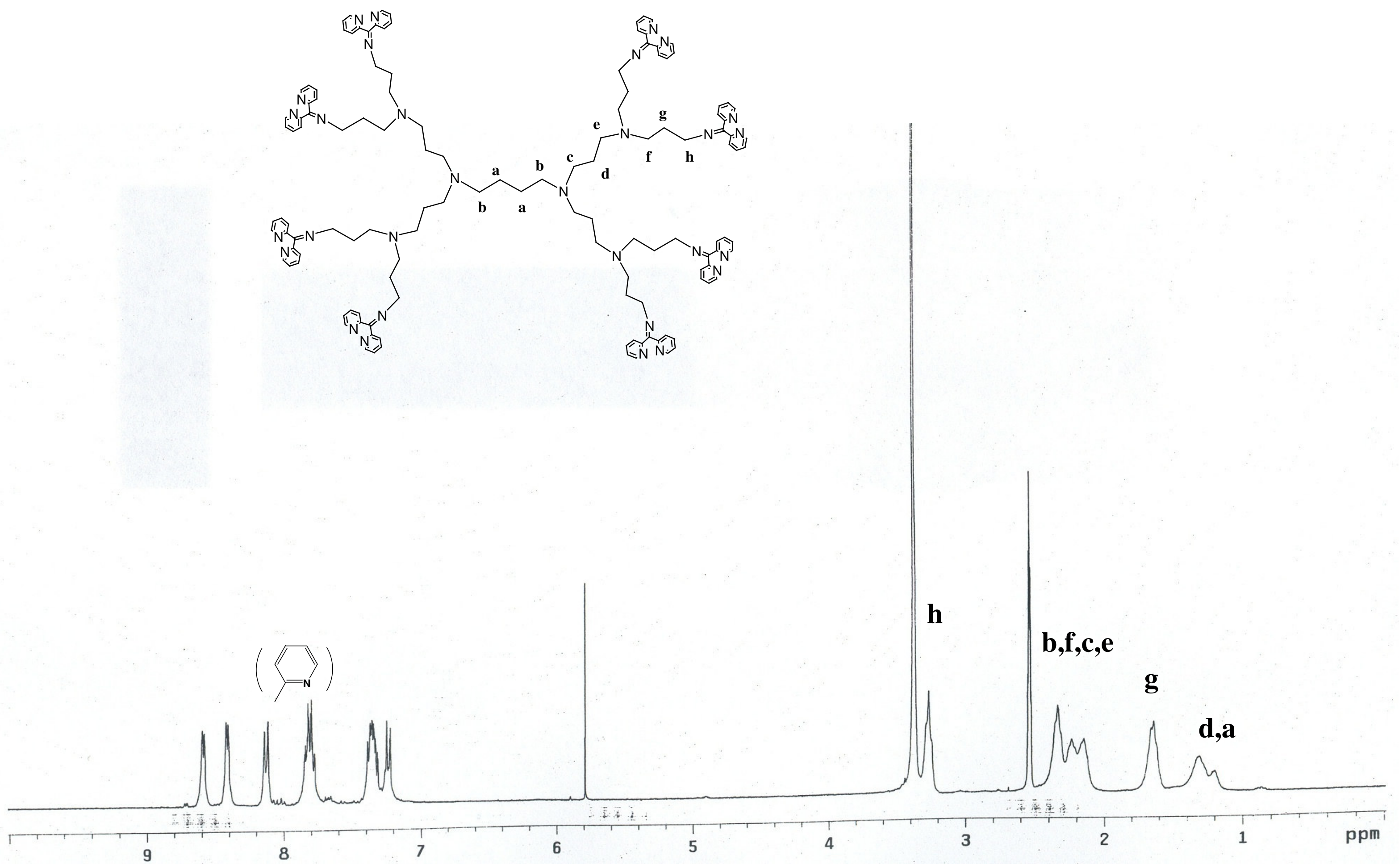


Figure 3.14 ^{13}C NMR spectra of dendritic ligand **(2b)**in DMSO-D$_6$

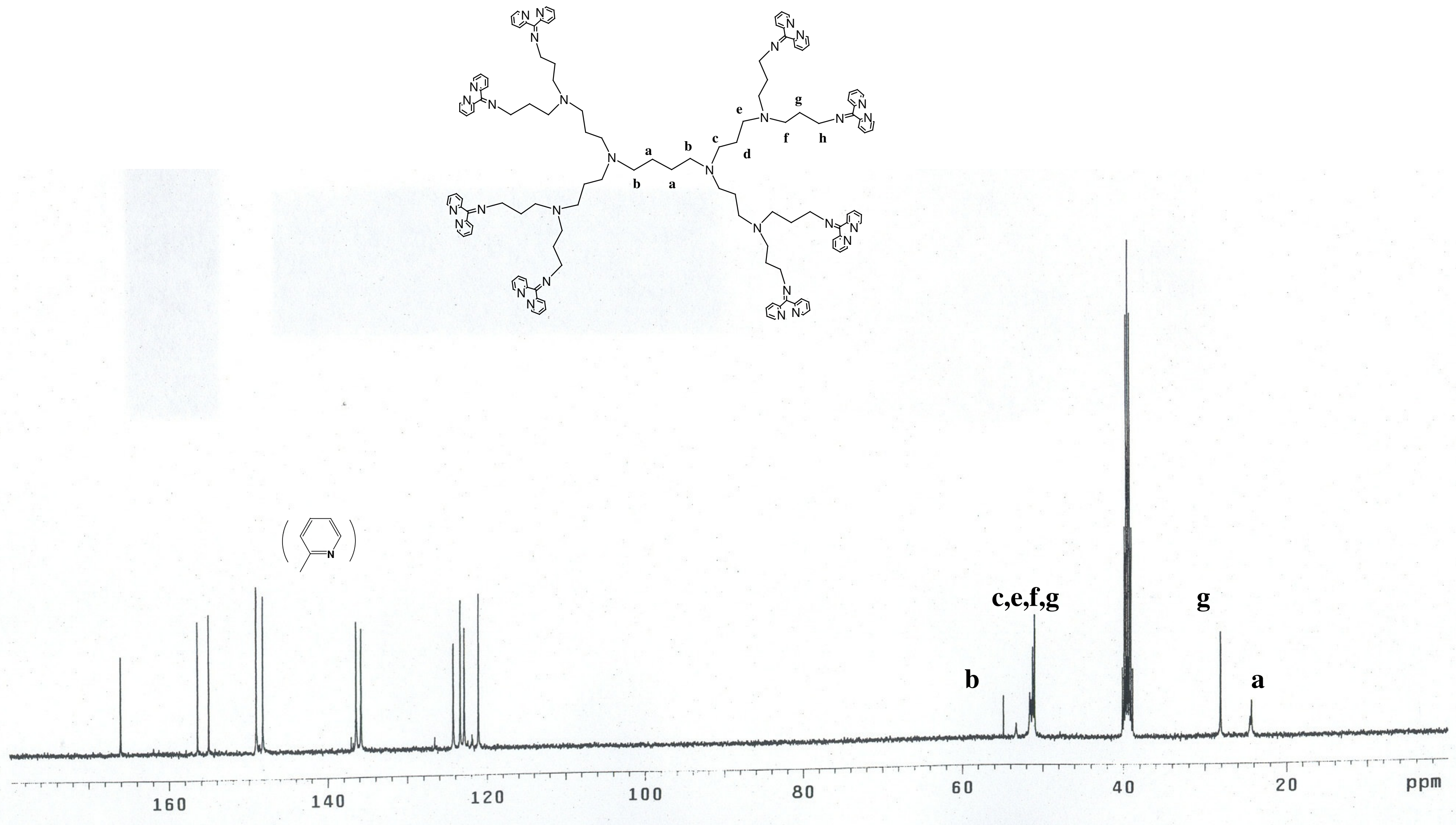
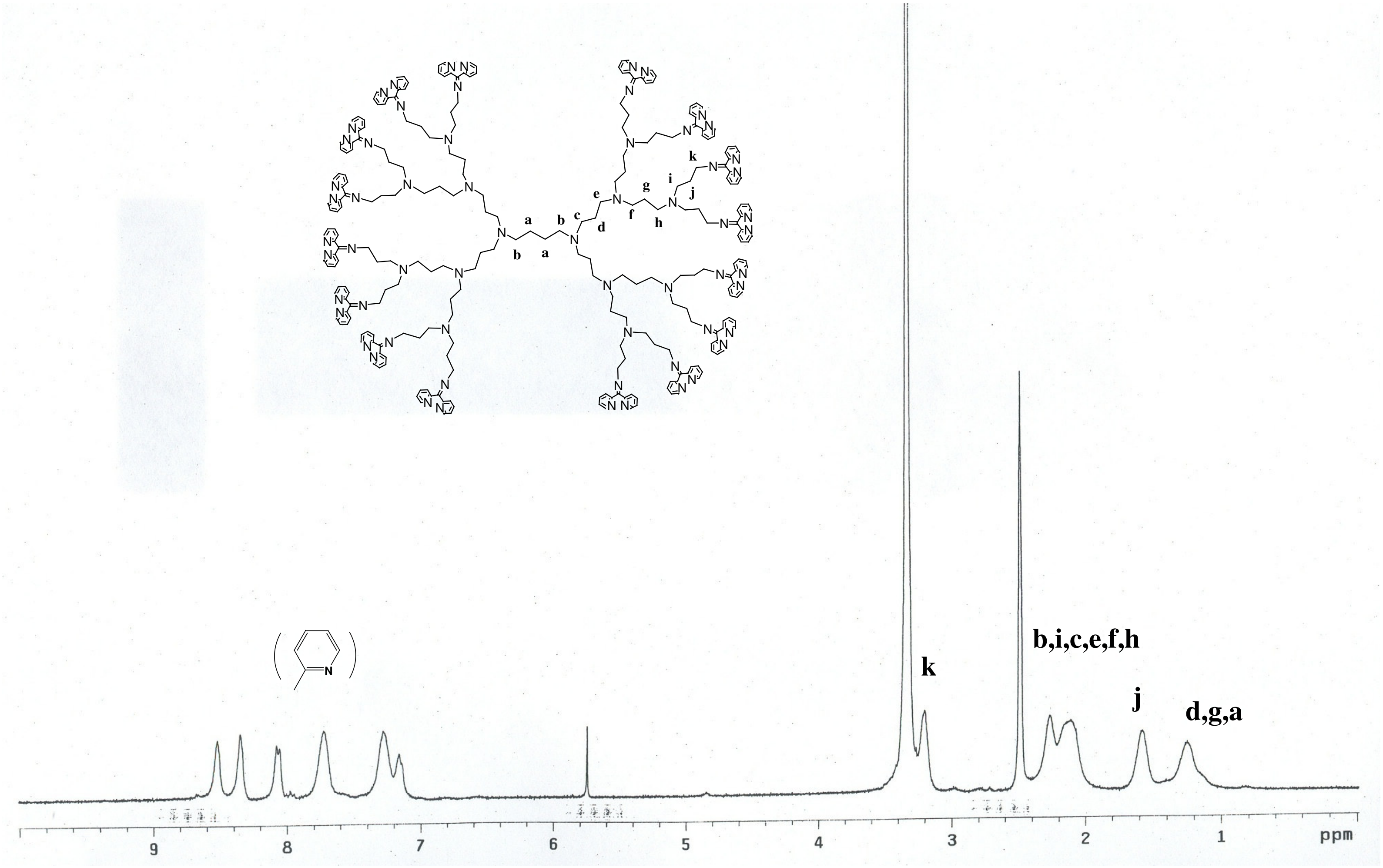


Figure 3.15 ^{1}H NMR spectra of dendritic ligand **(3b)** in DMSO-D$_6$



VITA

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Title of Study: METALLODENDRIMERS WITH CHELATING BIPYRIDYL LIGANDS: SYNTHESIS AND CHARACTERIZATION

Pages in Study: 86 Candidate for the Degree of Master of Science

Major Field: Chemistry

Abstract: Dendrimers are polymers with chemically well-defined hyper-branched three-dimensional architectures. Metallodendrimers offer attractive advantages over their polymeric counterparts due to their unique properties, which make them suitable for a number of biomedical and industrial applications. Catalysis based on transition metals combine the advantages of both homogeneous and heterogeneous catalytic systems such as selectivity and recyclability. Herein we report a more controlled approach for a covalent attachment of chelating ligands to poly (propylene imine) dendrimer (PPI), followed by complexation with Palladium. PPI dendrimers of three successive generations have been successfully functionalized with covalently attached bipyridyl ligands on the surface of the dendrimer in a single step reaction. A novel series of metal-chelating dendrimers has been synthesized upon complexation of chelating bipyridyl ligands with palladium. Metallodendrimers have also been successfully characterized using NMR, IR and ESI mass spectrometry. It is clear that IR and NMR spectroscopy provides useful signatures for ligand attachment and complexation reactions. However, when the dendrimers become heavier, especially for dendrimers with multiple metal centers, NMR spectra become very complicated and not useful for characterization. We have also shown that ESI mass spectrometry is a very useful characterizational tool when NMR studies are not adequate.

ADVISER'S APPROVAL: Legrande M. Slaughter